AMERICAN ASSOCIATION OF FELINE PRACTITIONERS

2020 Virtual CONFERENCE

Feline Head & Neck: Diseases, Disorders, & More

October 3 & 4 and 24 & 25, 2020

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President's Welcome 2020

Welcome to our 2020 Annual *Virtual* Conference!

I can honestly say that when I became President of the AAFP, I never imagined that I would be giving a virtual welcome. Yet here we are together apart. I hope we will have some moments where we might feel the togetherness that comes with the annual in-person AAFP gathering. I hope everyone is still able to block off time for focused CE with nothing else acting as a distraction from the full experience. You can count on this virtual program and experience being the best of the best, just as you would expect every year at the Annual AAFP Conference.

I am very excited about our conference theme this year, *Feline Head & Neck: Diseases, Disorders, & More.* When we first started discussing this topic, there were a lot of questions and it seemed a bit perplexing. What does one focus on? It's not just a dental theme. It's not just about eyes, or ears, or neurology. There is so much to consider about that part of a cat's anatomy…from the physical to the behavioral, from disease to mental well-being…the cat's head and neck has it all, right down to their facial expressions from adoring love to frisky fun to pure vicious thoughts. And how remarkable that we can also use those facial expressions to assess and grade pain in our furry feline friends!

On that note, there really isn't a better way to kick off our conference than in a live session with Dr. Paulo Steagall discussing the *Feline Grimace Scale for Acute Pain Assessment.* From the moment the Grimace scales were published, I knew we had to ask Dr. Steagall to share this exciting research with us. Following our live keynote presentation, lectures by world class speakers include live and on-demand sessions, covering a wide range of topics from dermatoses to feline herpesvirus to oral neoplasia and beyond. Our Partner Symposia will offer additional topics on CKD staging and management, feline pain, osteoarthritis management, weight loss, nasogastric feeding tubes, infectious diseases, hypertension, obesity, fecal testing, and hydration. Additionally, our Partner Symposium day will include content on multimodal plans for long-term pain, identifying and diagnosing osteoarthritis, vaccinations, and nutritional management of chronic enteropathies.

I am so grateful to the sponsors who have made all of these lectures and virtual offerings possible with their generosity and support, which include Boehringer Ingelheim, Royal Canin, Zoetis Petcare, Merck, IDEXX, Hill's, Ceva, Purina, Dechra, Elanco, VetStem Biopharma, Antech Diagnostics, Mars Petcare and Trudell Animal Health. I would also like to take a moment to thank our conference partners: American Board of Veterinary Practitioners (ABVP), International Veterinary Academy of Pain Management (IVAPM), National Association of Veterinary Technicians in America (NAVTA), and the Winn Feline Foundation (Winn). We are all working to improve the lives of cats, and I must say, we make a great team!

The AAFP has truly hit this one out of the park. Treat our virtual conference in much the same way you would our in-person conference - at a new venue that you have never been to before. Start your day off right with a virtual Yoga Class! Check out the agenda, choose your favorite sessions to attend, wander around to the e-posters, attend abstract presentations, visit and chat with exhibitors in the virtual exhibit hall, attend Ask the Expert sessions, and even take part in a scavenger hunt. We are also offering an exciting new feature called Video Chat Discussion Forums, which are limited to 15 people, allowing participation in a live discussion with an expert speaker on some very exciting topics. This conference platform is deep, and it is going to be fun! I also look forward to 'seeing' everyone at the Happy Hours.

As you know, the conference will be spread out over two weekends, to allow attendees more flexibility in what lectures they attend and for how long. And if you want to watch something again, you will have access to all of the lectures until December 31, 2020.

I can't wait to see how this all looks in real-time and I can't wait to see some friendly faces again! I look forward to 'seeing' you all there!

With Kindest regards,
Kelly A. St. Denis, MSc, DVM, DABVP (Feline)
2020 AAFP President

INDEX

American Association of Feline Practitioners
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American Association of FELINE PRACTITIONERS®

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Feline Head & Neck: Diseases, Disorders, & More

2020 Virtual CONFERENCE
October 3 & 4 and 24 & 25, 2020

ALL TIMES ARE EASTERN TIME ZONE

October 2 - 12:00 pm **Attendee Access to Event and On-demand CE**

Day 1 — October 3, 2020

Live Exhibits open from 12:00 - 5:00 pm

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Yoga 101		
11:00 - 11:20 am	President's Address	Dr. Kelly St. Denis	
11:20 - 12:20 pm	Feline Grimace Scale for Acute Pain Assessment	Dr. Paulo Steagall	ZOETIS PETCARE, IVAPM
12:20 - 1:20 pm	Painful Conditions of the Head	Dr. Paulo Steagall	ZOETIS PETCARE, IVAPM
	Chronic Seizure Management for Cats	Dr. Heidi Barnes Heller	
	Technician/Nurse: Respiratory Emergencies: Triaging the Feline Patient	Ms. Alison Gottlieb	NAVTA
1:20 - 2:00 pm	Exhibit Hall Break		
2:00 - 3:00 pm	***Partner Symposia***		
	The Three "A's" of Acute Pain Management: Anticipate, Assess, & Alleviate	Dr. Sheilah Robertson	Elanco
	It's a New World: Introducing the 2020 AAFP Retrovirus Testing & Management Guidelines	Dr. Susan Little	IDEXX
	Placement & Maintenance of Nasogastric Feeding Tubes in Cats	Dr. Lisa Powell	ROYAL CANIN
	The Future is Now: 21st Century Fecal Testing Technology in Your Practice	Dr. Cory D. Penn	ZOETIS PETCARE
3:00 - 4:00 pm	Feline Oral Squamous Cell Carcinoma: Recent Advances	Dr. Michael Nolan	WINN FELINE FOUNDATION
	Neurologic Examination for Busy Practitioners	Dr. Heidi Barnes Heller	
	Technician/Nurse: Special Considerations on Feline Ears	Dr. Alison Diesel	ZOETIS PETCARE
4:00 - 4:30 pm	Exhibit Hall Break		
4:30 - 5:00 pm	Ask the Experts	Drs. Heidi Barnes Heller & Paulo Steagall	
5:00 - 6:00 pm	Virtual Happy Hour		ZOETIS PETCARE

Feline Head & Neck: Diseases, Disorders, & More

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Day 2 — October 4, 2020 — *Live Exhibits open from 11:00 am - 4:30 pm*

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
9:30 - 10:00 am	Meditation Exercises		
10:00 - 11:00 am	Finding our Path to Honor Ourselves as We Live the Veterinary Oath	Dr. Kimberly Pope-Robinson	ROYAL CANIN
11:00 - 12:00 pm	Allergic Dermatitis	Dr. Alison Diesel	ZOETIS PETCARE
	Feline Herpesvirus 101: Why, What, & How?	Dr. Jessica Meekins	
	Technician/Nurse: Feline Pain: Detecting, Identifying Options, & Advocating for your Patients	Ms. Alison Gottlieb	NAVTA
12:00 - 1:00 pm	Kitten-caboodle: A Selection of Various Feline Dermatoses	Dr. Alison Diesel	ZOETIS PETCARE
	Feline Herpesvirus: Review of Treatment Strategies	Dr. Jessica Meekins	
	Technician/Nurse: Is the Kitty Crazy? Feline Hyperthyroidism	Dr. Kathy Engler	Dechra
1:00 - 1:45 pm	Exhibit Hall Break		
1:15 - 1:35 pm	AAFP Membership Meeting		
1:45 - 2:45 pm	***Partner Symposia***		
	CKD: Prediction of Future Diagnosis, Early Diagnosis, Staging, & Management Strategies	Dr. Dennis Chew	ANTECH
	Unintentional Weight Loss: Feline Dwindles	Dr. Grant Gugisberg	Dechra
	Look What the Cat Dragged In: Emerging Infections & Infestations Facing Felines Today	Dr. Susan E. Little	MERCK Animal Health
	Pouncing on Pain: Managing Feline Osteoarthritis Cases	Dr. Elizabeth Colleran	ZOETIS PETCARE
2:45 - 3:45 pm	Otitis in the Cat: Keys to Diagnosis & Therapy	Dr. Alison Diesel	ZOETIS PETCARE
	Otic Polyp: Etiology, Presentations, & Treatments	Dr. Bryden Stanley	Hills
	Technician/Nurse: Ophthalmic Drugs & When to Use Them	Dr. Jessica Meekins	
3:45 - 4:15 pm	Exhibit Hall Break		
4:15 - 4:45 pm	Ask the Experts	Drs. Alison Diesel & Jessica Meekins	

Feline Head & Neck: Diseases, Disorders, & More

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Day 3 — October 24, 2020

Live Exhibits open from 11:00 am- 5:00 pm

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Slow Flow Yoga		
11:00 - 12:00 pm	Video Chat Discussion Forums ***Pre-registration Required***		
12:00 - 1:00 pm	Update on Treatment Strategies for Feline Chronic Gingivostomatitis	Dr. Christopher Snyder	
	Nutrition for the Hospitalized Patient	Dr. Christopher Byers	ROYAL CANIN
	Technician/Nurse: Cat Naps During a COHAT: The Complete Plan for the Feline Dental Patient	Ms. Mary Berg	NAVTA
1:00 - 1:45 pm	Exhibit Hall Break		
1:45 - 2:45 pm	Mastering Feline Dental Radiograph Interpretation	Dr. Christopher Snyder	
	Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 1	Dr. Phillip Padrid	TRUDELL ANIMAL HEALTH
	Technician/Nurse: Tips & Tricks for Great Dental Radiographs	Ms. Mary Berg	NAVTA
2:45 - 3:45 pm	***Partner Symposia***		
	Feline Hypertension: Diagnosis, Treatment, & Management	Dr. Clarke Atkins	Boehringer Ingelheim
	One Size Won't Fit All: Tailoring Weight Management Plans For Cats	Dr. Julie Churchill	MARS Petcare
	Hydration Fixation: Beyond the Water Bowl	Dr. Jason Gagne	PURINA PRO PLAN VETERINARY DIETS
3:45 - 4:15 pm	Exhibit Hall Break		
4:15 - 5:15 pm	Gastroesophageal Reflux: An Under-Recognized Source of Pain	Dr. Christopher Byers	ROYAL CANIN
	Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 2	Dr. Phillip Padrid	TRUDELL ANIMAL HEALTH
	Technician/Nurse: Pain Management & Anesthesia Concerns in Feline Dental Patients	Ms. Mary Berg	NAVTA
5:15 - 6:15 pm	Virtual Happy Hour		Boehringer Ingelheim

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Partner Symposium

Day 4 | **October 25, 2020** | *Live Exhibits open from 11:00 am- 4:00 pm*

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Yoga Building Bone Density & Balance		
11:00 - 12:00 pm	Raising Awareness of Osteoarthritis: Identify & Diagnose Affected Cats	Dr. Sheilah Robertson	Ceva
12:00 - 1:00 pm	Nutritional Management of Chronic Enteropathies: A Review of the Recent Research in Cats	Dr. Becky Mullis	Hills
1:00 - 1:30 pm	Exhibit Hall Break		
1:30 - 2:30 pm	Ask the Experts: Q&A	Drs. Debra Horwitz & Sheri Ross	Hills
2:30 - 3:30 pm	Putting Vaccines into Perspective	Dr. Christopher Lee	MERCK Animal Health
3:30 - 4:00 pm	Exhibit Hall Break		
4:00 - 5:00 pm	Creating a Multimodal Plan to Combat Long-term Pain: Why Physical & Mental Health Must be Considered	Dr. Sheilah Robertson	Ceva

All content on demand through December 31, 2020

Note: Content is subject to change.

On Demand

CATEGORY	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
Head and Neck			
Dentistry	Maximizing Regional Anesthetic & Pain Management for Dentistry & Oral Surgery Patients	Dr. Christopher Snyder	
Dentistry	Tips & Tricks for Successful Extractions & Achieving Predictable Healing	Dr. Christopher Snyder	
Dentistry	Navigating Those Dental Complications That Make You Go…Hmmm!?	Dr. Christopher Snyder	
Dermatology	Pesky Parasites & Infections Regionalized to the Head & Neck Area	Dr. Alison Diesel	ZOETIS PETCARE
Emergency/Critical Care	Management of Traumatic Brain Injury	Dr. Christopher Byers	ROYAL CANIN
Neurology	Acute Seizure Management for Cats	Dr. Heidi Barnes Heller	
Neurology	Novel Seizure Therapeutics for Cats	Dr. Heidi Barnes Heller	
Neurology	Feline Hyperesthesia, Cognitive Dysfunction, & Other Mystery Diseases	Dr. Heidi Barnes Heller	
Oncology	Measuring Feline Orofacial Cancer Pain	Dr. Michael Nolan	WINN FELINE FOUNDATION
Oncology	Nasal Tumors & Neuro-Oncology in Cats	Dr. Michael Nolan	WINN FELINE FOUNDATION
Ophthalmology	Unique Feline Corneal Diseases	Dr. Jessica Meekins	
Ophthalmology	Uveitis: Ocular Manifestations of Systemic Disease	Dr. Jessica Meekins	
Pain Management	Chronic Pain: Is It All in the Head?	Dr. Beatriz Monteiro	ZOETIS PETCARE, IVAPM
Surgery	Face & Head Reconstructive Techniques in Cats	Dr. Bryden Stanley	Hills
Technician	Cat's Don't Read Textbooks: Commonly Found Oral Pathology of Felines	Ms. Mary Berg	NAVTA
	Feline Head Trauma	Ms. Alison Gottlieb	NAVTA
	Feline Respiratory Patients: A Delicate Balance	Ms. Alison Gottlieb	NAVTA
Practice Mgmt.	Cyberbullying & the Veterinary Profession	Dr. Phillip Padrid	TRUDELL ANIMAL HEALTH
	Every Practice's Struggle: How to Attract, Retain, & Motivate Your Veterinary Talent	Dr. Taylor Tillery	MERCK Animal Health

Continued on next page

On Demand

CATEGORY	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
Partner Symposia	ABVP: Is It For Me?	Dr. Amy Hinc	
	A Transformational Nutritional Approach to Managing Cat Allergen Fel d1	Dr. Ebenezer Satyaraj	
	Hill's At Home	Various Experts	
	Regenerative Medicine & the Feline Patient	Dr. Robert Harman	
	Understanding Feline Hypertension	Dr. Clarke Atkins	
	Update on Diabetes Mellitus in Cats	Dr. Deborah Greco	
	What is it? Differentiating Medical from Behavioral	Dr. Valarie Tynes	
Oral Abstracts	How Does OA in Cats Affect Their Quality of Life	Dr. Andrea Wright	
	Identification of Risk Factors for Feline Anesthetic Mortality	Dr. JoAnne Morrison	
	The Novel UNESP-Botucatu Cat Pain Scale (UCAPS)	Dr. Paulo Steagall	
	Thyroid Troubles: Diagnosis and Management of Hypothyroidism	Ms. Stefanie DeMonaco	
	What's In Your Patient's Head: Cone Beam Computed Tomography	Dr. Katherine Knutson	
Miscellaneous			
AAFP Seminar	Creating Individualized Feline Vaccine Protocols: Key Points from the 2020 AAHA/AAFP Feline Vaccination Guidelines	Dr.'s Philip Kass & Amy Stone	
AAFP Seminar	NEW AAFP Cat Friendly Certificate Program	Dr. Kelly St. Denis	

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[1]Wernimont, S.M., et al. Food with Specialized Dietary Fiber Sources Improves Clinical Outcomes in Adult Cats with Constipation or Diarrhea (in a 2 Month Study). *FASEB J.* 2020;34(1). Some cats may require multimodal management. [2]Fritsch, D.A., et al. Food with Novel Fiber Blend Improves Clinical Outcomes and Changes Gastrointestinal Microbiome Metabolism in Dogs (in a 2 Month Study). *J Vet Intern Med.* 2019;33(5):2513.

Clarke Atkins, DVM, DACVIM

Sponsor Boehringer Ingelheim

North Carolina State University, Cary, North Carolina

Clarke Atkins, the Jane Lewis Seaks Distinguished Professor of Companion Animal Medicine (Emeritus) at North Carolina State University and Norden Outstanding Teacher Award recipient, is board-certified by the ACVIM (Medicine & Cardiology). He has served on four ACVIM or international Consensus Committees on systemic hypertension, canine mitral valve disease (2009, 2017), and cardiorenal syndrome, as well as receiving the Honorary Member Award from the American Heartworm Society in 2019. His research involves canine and feline heartworm disease and treatment of cardiovascular disease in dogs, cats, and horses. He has over 150 publications and has provided well over 1000 hours of continuing education in the U.S. and many countries around the world. Dr. Atkins continues to be active speaking and carrying out clinically-oriented research in retirement.

Heidi Barnes Heller, DVM, DACVIM (Neurology)

Barnes Veterinary Specialty Services, LLC, Madison, Wisconsin

Dr. Barnes obtained her veterinary degree from Michigan State University in 2000, followed by a rotating internship at the University of Illinois and a residency in neurology/neurosurgery at the University of Florida. Dr. Barnes is board certified from the American College of Veterinary Internal Medicine. She was the staff neurologist outside of Chicago Illinois until December 2010, after which point she joined the University of Wisconsin-Madison School of Veterinary Medicine in neurology and neurosurgery. In 2019, Dr. Barnes founded Barnes Veterinary Specialty Services; a mobile neurology and neurosurgery business serving Wisconsin and Northern Illinois with tele-neurology services worldwide.

Mary Berg, BS, RVT, LATG, VTS (Dentistry)

Partner NAVTA

Beyond the Crown Veterinary Education, Lawrence, Kansas

Mary is a Charter member of the Academy of Veterinary Dental Technicians and received her Veterinary Technician Specialty in Dentistry in June 2006. Mary currently serves at the Treasurer of the AVDT. Mary worked in research for over 29 years, specializing in products aimed at improving oral health of companion animals and continues to work with companies to evaluate the efficacy of their products. In addition to her research background, she was the practice manager and dental specialist at a general practice for 7 years, teaches veterinary technology, and is currently the president of Beyond the Crown Veterinary Education, a veterinary dental consulting service. Mary is actively involved in NAVTA, AVDT, and KVTA. She also served on committees for the AVMA and AAVSB. She has authored or co-authored over 80 articles including publications, textbook chapters, along with her own textbook. Mary was named the 2020 NAVTA Veterinary Technician of the Year. When not involved in veterinary medicine, Mary lives on a small farm near Lawrence, Kansas with her husband, Doug, a terrier mix, Gypsy, two opinionated cats named, Ricochet and Ladybug, and a 29-year-old horse.

Christopher Byers, DVM, DACVECC, DACVIM (SAIM), CVJ

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CriticalCareDVM.com, Omaha, Nebraska

Dr. Christopher G. Byers is a practicing board-certified veterinary emergency and critical care, and small animal internal medicine specialist based in Omaha, Nebraska. He received his BS degree in Animal Sciences from Colorado State University and his DVM from Cornell University's College of Veterinary Medicine. Dr. Byers' professional passions are mentoring and coaching veterinary students and colleagues in the areas of emergency and critical care, internal medicine, and communication skills. To that effect, he's been privileged to travel around the globe, partnering with veterinary professionals dedicated to advancing animal health. Dr. Byers publishes a weekly blog called CriticalCareDVM. The goals of this passion project are to educate pet parents and promote the triad of care between pet owner, primary care doctor, and board-certified veterinary specialist.

Dennis Chew, DVM, DACVIM

Sponsor ANTECH DIAGNOSTICS FOR IMAGING

The Ohio State Univeristy College of Veterinary Medicine, Columbus, Ohio

Dr. Chew is a 1972 graduate of the College of Veterinary Medicine at Michigan State University. He did a one-year internship at South Weymouth Veterinary Associates and a two-year residency in internal medicine and nephrology at the Animal Medical Center in New York City. He became a Diplomate of the American College of Veterinary Internal Medicine in 1977. Dr. Chew was an attending veterinarian at The Ohio State University College of Veterinary Medicine Teaching Hospital for 36 years and is now Professor Emeritus. Most of his work in clinics, research, and publications involves urology/nephrology in small animals. He has special interest in disorders of calcium metabolism, chronic kidney disease and vitamin D metabolite dynamics, idiopathic/interstitial cystitis of cats, and diagnostic urinary endoscopy. He has been the author of over 100 peer-reviewed publications and 2 editions of the Manual of Nephrology and Urology in Small Animals.

Julie Churchill, DVM, PhD, DACVN

Sponsor MARS Petcare

University of Minnesota College of Veterinary Medicine, Arden Hills, Minnesota

Dr. Churchill is a Diplomate of the American College of Veterinary Nutrition and member of the American Academy of Veterinary Nutrition. Dr. Churchill developed a small animal clinical nutrition service that was financially self-sustaining within 5 years. She is currently Professor, and director of the Nutrition Service and the Associate Medical Director for Specialty, Primary and Urgent Care Services at the University of Minnesota. Dr. Churchill is passionate about all aspects of small animal clinical nutrition including the role of nutrition in maintaining wellness and preventive care, obesity prevention and treatment, the nutrition needs of geriatric patients, nutritional management of kidney diseases, and critical care nutrition. She is also interested in teaching and improving client communication to successfully integrate nutrition into the care of every patient. She served on the task force to develop the AAHA guidelines for weight management. She serves as president of the Pet Nutrition Alliance (PNA) and on the educational tools committee of PNA working to develop a" Go-to" website for credible nutritional information for veterinary practice teams and consumers. Dr. Churchill also serves on the Board of the Association for Pet Obesity Prevention and is advocating for a global pet obesity initiative.

Elizabeth Colleran, DVM, MS, DABVP (Feline)

Sponsor ZOETIS PETCARE

Chico Hospital for Cats, Chico, California

Dr. Colleran is an author, keynote and veterinary conference speaker, consultant and feline specialist board certified by the American Board of Veterinary Practitioners. She has successfully created and managed two feline medicine veterinary practices. Her practice in Portland, Oregon was the first feline-only practice in Portland and her current practice; the Chico Hospital for Cat is celebrating its 22nd birthday this year. Dr. Colleran chairs the Cat Friendly Practice for the American Association of Feline Practitioners (AAFP). She has served on the AAFP board for several years including as President in 2011 and Treasurer from 2007-2009. She serves her profession as a volunteer for other veterinary organizations. Dr. Colleran is a published author and frequent contributor to several peer-reviewed publications. She has been a media spokesperson on a number of feline topics for communications campaigns and has proudly mentored many aspiring feline practitioners. Her next book for veterinarians, "The Senior Cat: Medicine and Management in the Golden Years" (working title) will be published in 2021. She loves teaching and believes it is one important way to improve health care and quality of life for felines.

Alison Diesel, DVM, DACVD

Sponsor ZOETIS PETCARE

College of Veterinary Medicine and Biomedical Sciences, Texas A&M University

Dr. Alison Diesel is a Clinical Associate Professor in dermatology at Texas A&M University. She graduated from Kansas State University College of Veterinary Medicine in 2005, then completed a rotating internship in small animal medicine and surgery at the Veterinary Referral and Emergency Center in Norwalk, Connecticut. She worked as an emergency clinician for one year prior to beginning a three-year residency in dermatology at the University of Wisconsin-Madison School of Veterinary Medicine; she became board certified (ACVD) in 2010. She joined the faculty at A&M in the fall of 2010 where she helps guide veterinary students in the management of skin disease in companion animals. Her main research interests lie in feline dermatoses, expanding knowledge of the cutaneous microbiome in companion animals, and exploring radiation therapy as an alternative treatment option for dermatological conditions.

Kathy Engler, DVM, DABVP (Canine/Feline)

Sponsor Dechra

Dechra Veterinary Products, Leavenworth, Kansas

Dr. Kathy Engler received her veterinary degree from the University of Missouri College of Veterinary Medicine in 1991. Following graduation she worked as a small animal clinician in a progressive general practice in Federal Way, WA for 5 years before joining Banfield in 1996. Dr. Engler became a Diplomate of the American Board of Veterinary Practitioners (ABVP) in 2001 and recertified in 2011. During her 18 year career with Banfield, she was a practicing clinician and Chief of Staff in the greater Seattle area; Medical Advisor consulting with doctors across the country on on-going cases and reviewing adverse case outcomes, as well as building medical education for the practice; served on the Medical Standards Board; held the position of Sr. Director of Veterinary Career Development building veterinary on-boarding and development programs; and supported the OR/SW WA market of 14 – 26 hospitals as the Medical Director for 6 years. Dr. Engler joined Dechra in September 2014 as a field based Professional Services Veterinarian. Dr. Engler enjoys biking, downhill skiing, and volunteers as a sled dog race vet for the Kuskokwim 300 out of Bethel, Alaska.

Jason Gagne DVM, DACVN

Sponsor PURINA PRO PLAN VETERINARY DIETS

Nestle Purina, St. Louis, Missouri

Dr. Jason Gagné is a Board Certified Veterinary Nutritionist® and is Purina's Director of Veterinary Technical Communications, where he leads scientific innovation and product development for the Purina® Pro Plan® Veterinary Diets Brand. Jason works closely with innovation and renovation of dietary formulations, developing clinical trials, and Sales and Marketing. Prior to, and throughout his residency at Cornell, he served as an Associate Veterinarian in a small animal practice in Syracuse, New York. Jason has authored several publications in veterinary journals and textbooks, given scientific presentations at the regional and national level, and taught a series of courses at Cornell.

Alison Gottlieb, BS, CVT, VTS (ECC)

Partner NAVTA

CROWN Veterinary Specialist, Feasterville, Pennsylvania

Alison graduated from Towson State University with a bachelor's degree in Animal Behavior. She earned certification in emergency and critical care in 2000. Alison has served on the board of AVECCT as a member at large and on the application committee. Alison is the Co-founder/Owner of Four Paws Consulting LLC, an education based veterinary consultant. She is an active member of AAFP and ISFM. Over the years Alison has published many feline articles, frequently on pain; as well as authored a chapter on pain in the ICU. Alison has lectured extensively with Australia and New Zealand being amongst her favorites. Currently Ali is the Education Coordinator at CROWN in New Jersey and resides in Bucks County, Pennsylvania. Her favorite topics/areas are anything feline, osteoarthritis, analgesia, and low stress handling. In the clinic you can usually find giving the patients cat nip and feeding cats. She spends most of her free time outside with her pit bull and her cats.

Deborah Greco DVM, PhD, DACVIM (SAIM)

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Nestle Purina PetCare, Palm Springs, California

Dr. Deborah Greco is a senior research scientist with Nestlé Purina PetCare. Her responsibilities include technical communications in the areas of small animal internal medicine, endocrinology, and nutritional science to veterinary, breeder, and public audiences throughout the world. She was a professor of small animal internal medicine at Colorado State University and an internal medicine specialist at the Animal Medical Center in New York City before joining Nestlé Purina PetCare. Dr. Greco received her DVM degree from the University of California, Davis and then completed an internship in small animal medicine and surgery at Louisiana State University. After finishing an internal medicine residency and earning a PhD degree in Physiology and Pharmacology at Texas A&M University, she became a diplomate of the American College of Veterinary Internal Medicine (SAIM). Dr. Greco received the Pfizer award for research excellence at Colorado State University and was the recipient of the American Association of Feline Practitioners research Award for her work on feline diabetes mellitus. She is a past board member of the Western Veterinary Conference.

Grant Gugisberg, DVM

Sponsor Dechra

Parkview Cat Clinic, Inver Grove Heights, Minnesota

Dr. Gugisberg has owned Parkview Cat Clinic in Inver Grove Heights, MN since 2007, having worked there as a veterinarian since 1997. He received his BS (1989) and DVM (1991) degrees from the University of Minnesota, College of Veterinary Medicine. He has lectured on feline health and wellness issues for American Humane, Petfinder Foundation, and the Minnesota State Veterinary Medical Association. Additionally, he developed a RACE approved Feline Pancreatitis course for IDEXX that was delivered regionally as well as nationally via interactive webinar. As a long time feline only practitioner, he is versed in all aspects of feline health and wellness issues.

Robert Harman, DVM, MPVM

Sponsor VetStem BIOPHARMA

VetStem Biopharma, Poway, California

Dr. Harman founded and is the CEO of Vet-Stem, the first US-based commercial veterinary stem cell company. For 15 years prior to that, he was the CEO of HTI-Bio-Services, a preclinical research company for veterinary and human pharmaceutical development. He has authored more than 500 contract study reports for human and animal health companies throughout the world and for submission to the FDA and USDA in support of the development of new human and animal health products. In his current position, he is the CEO and principal clinical development director of the programs at Vet-Stem to bring stem cell therapy to veterinary medicine. He has been a frequent speaker at stem cell conferences in North America, Central America, Europe and the Middle East. He has authored peer-reviewed publications and book chapters on stem cell therapy in veterinary medicine.

Debra Horwitz, DVM, DACVB

Sponsor Hills

Veterinary Behavior Consultations, St. Louis, MO

Dr. Debra Horwitz received her DVM from Michigan State University College of Veterinary Medicine and is a diplomate of the American College of Veterinary Behaviorists. She is a frequent lecturer in both North America and abroad on behavioral medicine. Her newest book, *Blackwell's Five-Minute Veterinary Consult Clinical Companion: Canine and Feline Behavior 2nd edition* was published in 2018. Her other books include the *BSAVA Manual of Canine and Feline Behavioural Medicine* and lead editor of *Decoding your Dog* and a co-editor for *Decoding your Cat* due out in 2020. She is a past president of the American College of Veterinary Behaviorists NAVC 2012 and NAVC 2014 Small Animal Speaker of the Year.

Christopher Lee, DVM, MPH, DACVPM

Sponsor MERCK Animal Health

Merck Animal Health, Riverside, California

Dr. Christopher A. Lee is a preventive medicine specialist who hails from sunny California, where he earned his Bachelor of Science and Doctor of Veterinary Medicine from the University of California, Davis. His focus dwells on the interlacing disciplines of infectious and parasitic diseases, toxicology, immunology, scientific study design, and epidemiology. He also previously owned a veterinary practice. This diversity establishes a foundation from which Dr. Lee constructs practical wisdom for the everyday practitioner. In his current role as Sr. Professional Services Veterinarian with Merck Animal Health, Dr. Lee provides educational and technical support for veterinary hospitals and staff in the Southern California Region on various medical topics, as well as Merck Animal Health products. Ultimately, he works to promote the veterinary profession by sitting on the NAVLE Item Writing Committee, volunteering as an ACVPM mentor, conducting various veterinary lectures nationwide, and producing free educational podcasts.

Susan E. Little, DVM, PhD, DACVM (Parasitology)

Sponsor MERCK Animal Health

Oklahoma State University, Stillwater, Oklahoma

Dr. Susan Little is Regents Professor and the Krull-Ewing Chair in Veterinary Parasitology at the Center for Veterinary Health Sciences, Oklahoma State University where she is active in veterinary parasitology teaching and oversees a research program that focuses on zoonotic parasites, ticks, and tick-borne diseases. She is Past-President of the American Association of Veterinary Parasitologists and the Companion Animal Parasite Council and currently serves as co-Director of the National Center for Veterinary Parasitology. Dr. Little is an outstanding teacher and has received two excellence in teaching awards from the national Student American Veterinary Medical Association. In 2017, she received the Distinguished Veterinary Parasitologist Award from the American Association of Veterinary Parasitologists.

Susan Little, DVM, DABVP (Feline)

Sponsor IDEXX

Bytown Cat Hospital, Ottawa, Ontario

Dr. Susan Little received her BSc from Dalhousie University (Nova Scotia, Canada) and her DVM from the Ontario Veterinary College, University of Guelph. She has been in feline practice since 1990 and achieved board certification in Feline Practice in 1997. She is part owner of two feline specialty practices in Ottawa, Canada. She is a past president of the American Association of Feline Practitioners and the Winn Feline Foundation. She is a peer reviewer for veterinary journals as well as the author of many journal articles. Dr. Little is the recipient of the Canadian Veterinary Medical Association Small Animal Practitioner Award (2010), the NAVC Small Animal Speaker of the Year Award (2013), and the International Society of Feline Medicine/Hill's Pet Nutrition Award for outstanding contributions to feline medicine (2013). She is the editor and co-author of two textbooks: *The Cat – Clinical Medicine and Management* and *August's Consultations in Feline Internal Medicine, Volume 7.*

Jessica Meekins, DVM, MS, DACVO

Kansas State University, Manhattan, Kansas

Dr. Jessica Meekins is an Associate Professor of Ophthalmology at Kansas State University. She received her undergraduate degree in biology before attending veterinary school at The Ohio State University, graduating in 2008. She then completed a one-year rotating internship at a private specialty hospital in Albuquerque, New Mexico before being accepted into the ophthalmology residency training program at Purdue University. She became a board-certified diplomate of the American College of Veterinary Ophthalmologists in 2012, and she has been on faculty at K-State for almost 8 years. Dr. Meekins' clinical and research interests include management of viral surface ocular diseases in cats.

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Beatriz Monteiro, DVM, PhD

Sponsor ZOETIS PETCARE Partner IVAPM

University of Montreal, Quebec, Canada

Dr. Beatriz Monteiro is a graduate from Sao Paulo State University (Unesp - Botucatu), Brazil. Following graduation, she completed two internships at the University of Guelph, Canada and proceeded with a PhD program at the University of Montreal. She currently works as a research assistant at the University of Montreal, while also enrolled in a Diploma program on International Animal Welfare Ethics and Law at the University of Edinburgh, and in an alternate route residency program of the American College of Animal Welfare. With over 40 publications in scientific journals, her research focuses on the assessment and treatment of pain in dogs and cats. She has also collaborated as an author in several book chapters and has acted as an invited speaker in some of the most important veterinary meetings. Dr. Monteiro is a member of the Board of Directors of the World Small Animal Veterinary Association - Global Pain Council (WSAVA - GPC), the International Veterinary Academy of Pain Management (IVAPM), as well as on the editorial board for the Journal of Feline Medicine and Surgery (JFMS) and JFMS Open Reports.

Becky Mullis, DVM, DACVN

Sponsor Hill's

Hill's Pet Nutrition, Lawrence, Kansas

Dr. Mullis received her DVM from the University of Tennessee in 2010. She then completed a small animal internship at the Regional Institute for Veterinary Emergencies and Referrals in Chattanooga, TN. After working as an emergency veterinarian for 2 years, she returned to the University of Tennessee where she completed a residency in clinical nutrition. She became a diplomate in the American College of Veterinary Nutrition in 2016. She is currently the Associate Manager of Scientific Insights at Hill's Pet Nutrition and adjunct faculty at Kansas State University, College of Veterinary Medicine. Dr. Mullis' areas of interest include dietary management of GI disease and weight management.

Michael Nolan, DVM, PhD, DACVR-RO

Partner WINN FELINE FOUNDATION

NC State College of Veterinary Medicine, Raleigh, North Carolina

Dr. Mike Nolan is an Associate Professor at North Carolina State University. He is principal investigator for several clinical trials aimed at developing novel cancer therapies. His laboratory focuses on reducing risk of severe cancer treatment-associated toxicity. Dr. Nolan also oversees the division of radiation oncology, including a world-class program in stereotactic radiosurgery.

Phil Padrid, DVM

Sponsor TRUDELL ANIMAL HEALTH

VCA/Mars Animal Health, Corrales, New Mexico

Dr. Padrid completed a Residency in Small Animal Internal Medicine at UC Davis in 1988 and a fellowship in pulmonary and critical care medicine at the medical school at UC Davis in 1990. From 1990-2000, Dr. Padrid was an Associate Professor of Pulmonary and Critical Care Medicine at the University of Chicago Pritzker School of Medicine. He is the author of greater than 70 peer reviewed manuscripts and book chapters in the fields of human and veterinary pulmonary medicine, and is acknowledged to be the first person in our profession to actively promote and research the use of inhaled medications to treat veterinary patients with respiratory disease.

Cory Penn, DVM

Sponsor ZOETIS PETCARE

Zoetis, Parsippany, New Jersey

Dr. Cory Penn received his DVM from the University of Missouri College of Veterinary Medicine in following receiving his Bachelor of Science from Eastern Illinois University. Before joining Abaxis and Zoetis, Dr. Penn worked was a small animal veterinarian and medical director in central Illinois. Dr. Penn is currently a veterinary medical lead for diagnostic instruments with Zoetis Global Diagnostics. Dr. Penn currently resides in west central Illinois with his wife Emily, three daughters, Harper, Reese, and Charlotte; and Labrador retriever, Chloe. In his free time, Dr. Penn enjoys spending time with his family and being outdoors.

Kimberly Pope-Robinson, DVM, CCFP

Sponsor ROYAL CANIN

1 Life Connected, Ellicott, Maryland

Dr. Pope has been in veterinary medicine for over 20 years, practicing in both the large and small animal sectors. In addition, she supported the position of a multi-unit manager for a large corporate practice and spent time in the pharmaceutical sector working with specialists and universities. Her career has provided her a unique understanding of the stresses involved with maintaining a career in the veterinary industry, and she now dedicates her time to providing wellbeing support for the profession through her company 1 Life Connected. She provides this support through 1 on 1 coaching, customized team events, author of "The Unspoken Life" and supplemental coloring book, and as a dynamic international speaker. Dr. Pope lives in Maryland where she enjoys spending time outside exploring and remodeling their 40+ year old home with her husband Jeff. They share their home with multiple furry and feathered friends including Dempsey (French Bulldog) and Graciebird (tuxedo DSH) often showcased in the 1 Life Connected movement social media. In addition, she is active as an athlete and has completed 10 Tough Mudders and prior to COVID 19 was working towards running a 1/2 marathon in every state.

Lisa Powell, DVM, DACVECC

BluePearl Veterinary Partners, Minnesota

Sponsor ROYAL CANIN

Lisa Powell graduated veterinary school from Texas A&M in 1995, completed a small animal rotating internship at the AMC in NYC in 1996, then went on to a residency in small animal emergency and critical care at Tufts University, finishing in 1999. She became board certified in Small Animal Emergency and Critical Care in 2000. After residency, Dr. Powell joined the faculty at the University of Minnesota where she worked as a clinical professor for 15 years. She developed the Emergency and Critical Care Residency at the University of MN, which continues to be a strong program. She is an author of more than 30 veterinary publications, and authored a book entitled *Small Animal Emergency and Critical Care: Case Studies in Client Communication, Morbidity and Mortality.* She is currently an associate emergency and critical care clinician at BluePearl Veterinary Partners in Minnesota and is a national and international speaker on all things Emergency and Critical Care! Her clinical interests include cardiopulmonary disease, severe trauma, and fluid therapy.

Sheilah Robertson, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL)

Lap of Love Veterinary Hospice, Gainesville, Florida

Sponsors Ceva Elanco

Dr. Sheilah Robertson graduated from the University of Glasgow in Scotland. After time in private practice and a surgery internship she undertook specialized training in anesthesia and pain management and completed her PhD at the University of Bristol. She is board certified in anesthesia and animal welfare by the respective American and European Colleges and holds a certificate in small animal acupuncture. In 2014, she received her graduate certificate in Shelter Medicine from the University of Florida. In 2019, she became certified as a Traditional Chinese Veterinary Medicine Palliative and End-of-Life practitioner by the Chi Institute of Chinese Medicine. She has published widely on the recognition and alleviation of pain in cats. She is a member of the AAFP Welfare Committee and was a member of the Feline Nursing Guidelines Committee. She co-chaired the AAFP Feline Anesthesia Guidelines Taskforce and was a co-author of the 2015 AAFP/AAHA Pain Management Guidelines for cats and dogs. Currently she is the senior medical director of Lap of Love Veterinary Hospice, a large network of veterinarians dedicated to end-of-life care and in-home euthanasia throughout the USA. Dr Robertson is also a courtesy Professor at the University of Florida.

Ilona Rodan, DVM, DABVP (Feline)

Cat Behavior Solutions, LLC, Madison, Wisconsin

Sponsor Ceva

Dr. Ilona Rodan is ABVP certified in feline practice since 1995. Her passion is feline behavior and how to handle cats in veterinary practices to enhance feline welfare and human safety. She is the owner and director of Cat Behavior Consultations, LLC and the former medical director and owner of the Cat Care Clinic in Madison, Wisconsin from 1987-2015. Dr. Rodan is an active volunteer of the American Association of Feline Practitioners, a Past-President, and the 2019 chair of the AAFP Cat Friendly Practice program. She has also co-chaired several guidelines and welfare position statements, including the Feline-Friendly Handling, Feline Environmental Needs, and Pain Management guidelines. She presents nationally and internationally on feline medicine and behavior, and leads workshops on feline-friendly handling. In 2005, she was awarded the AVMA Animal Welfare Award for her leadership and contributions to advancing feline medicine and behavior. Dr. Rodan has written journal articles and book chapters, and is a co-editor and co-author of the veterinary textbook, *Feline Behavioral Health and Welfare,* published in 2015.

Sheri Ross, BSc, DVM, PhD, DACVIM

University of California Veterinary Medical Center, San Diego, CA

Sponsor Hill's

After graduating from the Atlantic Veterinary College, Dr. Ross completed a Small Animal Internship at the University of Minnesota. She remained at the University of Minnesota to complete an Internal Medicine Residency combined with a PhD in Nephrology/Urology. After serving as an Assistant Clinical Professor for two years she moved to the University of California Veterinary Medical Center in San Diego to complete a Fellowship in Renal Medicine/Hemodialysis. She is currently the coordinator of the Nephrology/Urology and Extracorporeal therapy service at the UCVMC-SD. Dr. Ross has received awards for both teaching and research, has several refereed scientific publications and has been invited to speak at national and international meetings. Her specific research interests include; early diagnosis and management kidney disease, non-surgical urolith management, and novel applications of apheresis and hemodialysis.

Ebenezer Satyaraj, PhD

Nestle Purina Research, Wildwood, Missouri

Sponsor Purina Pro Plan Veterinary Diets

Dr. Satyaraj earned his PhD in Immunology from the National Institute of Immunology, New Delhi, India and completed a Fellowship in Molecular Immunology at the University of Chicago, Illinois. He subsequently accepted an Instructor's position at the Department of Medicine, Northwestern University Medical School, Chicago, IL, where he taught Immunology and conducted research in the area of autoimmunity. In 2001 he joined Molecular Staging Inc. New Haven, Connecticut, a biotech company started with technology from Yale, working in the area of cytokines and disease biomarkers, where he led research collaborations with universities and industry resulting in two seminal publications: predictive biomarkers for cerebral palsy and biomarkers for inflammatory bowel diseases. Dr. Satyaraj joined Nestle Purina in 2003, as part of the Nestlé Research Center in St Louis, MO, establishing a nutritional immunology research program, published in the field and helping launch several products globally. He implemented models for evaluating nutritional impact on the immune system and pioneered the development of the first multiplex assay panels capable of measuring canine and feline cytokines. He currently serves as Director of Molecular Nutrition at Nestlé Research Center in St Louis, MO.

Christopher Snyder, DVM, DAVDC

University of Wisconsin-Madison, School of Veterinary Medicine, Middleton, Wisconsin

Dr. Christopher Snyder is a Diplomat of the American Veterinary Dental College and Clinical Associate Professor and Residency Director of the Dentistry and Oral Surgery Service at the University of Wisconsin-Madison School of Veterinary Medicine. He has been recognized as a Founding Fellow, AVDC Oral and Maxillofacial Surgery. After graduating from The Ohio State University College of Veterinary Medicine, he completed residency training at the University of Wisconsin-Madison. Dr. Snyder has authored journal articles, textbook chapters, and has lectured nationally and internationally. He prides himself on the dental education he provides to students at the University of Wisconsin and the residents he has successfully mentored in the specialty. Dr. Snyder's academic interests include: maxillofacial trauma and reconstruction, oral surgery, creating innovating techniques in veterinary dental education, and improving techniques for regional anesthesia.

Bryden Stanley, BVMS, MVetSc, MANZCVS, MRCVS, DACVS

Sponsor Hills

Michigan State University, College of Veterinary Medicine, Okemos, Michigan

Dr. Bryden J. Stanley is Emeritus Professor of Surgery at Michigan State University's College of Veterinary Medicine. She graduated in 1982 from Murdoch University, Australia. Following a short stint in private practice, she completed an internship at Murdoch and a surgical registrarship at the University of Sydney. From 1987 to 1990, Bryden completed an ACVS surgery residency and master's degree at the University of Saskatchewan, Canada. Dr. Stanley's first faculty appointment was at the University of Edinburgh in Scotland, but she has been at Michigan State University since 1999, where she was Head of Surgery before retirement. Stanley's clinical interests are in all aspects of soft tissue surgery, particularly upper respiratory, wound management, and cutaneous reconstructive techniques. Stanley undertakes clinical research in upper respiratory diseases and wound healing. She publishes frequently, has received many teaching awards, and lectures widely at a national and international level.

Paulo Steagall, MV, MSc, PhD, DACVAA

Sponsor ZOETIS PETCARE Partner IVAPM

University of Montreal, Quebec, Canada

Dr. Paulo Steagall is an Associate professor of Veterinary Anesthesiology and Pain Management at the University of Montreal, Canada. He earned his DVM and completed a residency at Sao Paulo State University, Brazil, then earned his MS and PhD (Anesthesiology) with an emphasis on feline analgesia at the same institution. He is currently the head of a research laboratory dedicated to improving pain management in companion animals with a strong benefit to feline welfare. His laboratory has published the Feline Grimace Scale, a tool that uses changes in facial expressions to assess acute pain in cats in collaboration with researchers at the University of Montreal. His team investigates the use of novel pain assessment tools, analgesic therapies, and techniques with immediate clinical application. He is a member of the World Small Animal Veterinary Association (WSAVA) Global Pain Council, the WSAVA Dental Guidelines Committee and the chair of the WSAVA Therapeutic Guidelines group. Dr. Steagall has published more than 100 articles and several book chapters on pain management particularly in cats. He is the author of the book *Feline Anesthesia and Pain Management*. Dr. Steagall is an animal lover who enjoys good food, music, and a great conversation.

Taylor Tillery, DVM

Sponsor MERCK Animal Health

Merck, Frisco, Texas

Dr. Tillery is a Sr. Professional Services Veterinarian at Merck, where he provides technical information to veterinary health care tearms. He has extensive knowledge of small animal medicine and has aided in CVT, Veterinary Assistant training programs and is currently the Coordinator for Merck's Vet Student Ambassador Program. In addition to his DVM he is a VHMA expert trainer and is a graduate of the Veterinary Management Institute and posesses a strong passion for Wellness Care, Preventative Medicine, Veterinary Communication, Leadership, Technology and Telehealth. He is a 2018, 2019 Merck Circle of Excellence Award Winner and involved Member with AVMA, TVMA and AAFP and AAHA. When not busy with Merck matters, he enjoys seeing clients and patients, cycling, snow skiing and travel, or hanging with his Fiance and their new French Bulldog "Beaujelais" while having a nice glass of wine on a patio.

Valarie Tynes DVM, ACVB, ACAW

Sponsor Ceva

Ceva Animal Health, Sweetwater, Texas

Dr. Valarie Tynes is a native Texan and received her DVM from Texas A&M University. She worked in private practice for 14 years before returning to academia to pursue a residency in clinical animal behavior at the University of California at Davis in 2000. She has been a diplomate of the American College of Veterinary Behaviorists since 2003 and is also Board Certified in Animal Welfare. Her special interests are the behavior and welfare of pet pigs, exotic pets and zoo animals. She has been actively involved in the Fear Free initiative since its inception and serves on the Fear Free Speakers Bureau. She is a frequent speaker at veterinary meetings around the world and author of numerous articles and textbook chapters. She joined Ceva Animal Health in October of 2014 as a veterinary services specialist but continues to provide consulting services to zoos.

SATURDAY, OCTOBER 3, 2020 – DAY 1

11:20 – 12:20 pm

C ***Feline Grimace Scale for Acute Pain Assessment,*** *Dr. Paulo Steagall*
The Feline Grimace Scale (FGS) is a novel tool for acute pain assessment based on changes in facial expressions. The audience will learn about the development and validation of the FGS in a dynamic and interactive means. The speaker will share some unique "behind the scenes" stories. Participants will have the chance to test their knowledge using image assessment during the lecture.

12:20 – 1:20 pm

A **Painful Conditions of the Head,** *Dr. Paulo Steagall*
The most important painful conditions of the head will be reviewed using an evidence-based approach. The issue of oral pain after multiple dental extractions in cats will be discussed with the presentation of cutting-edge clinical research from the speaker's laboratory. Video-based learning will be used to demonstrate unique oral pain-induced behaviors.

B **Chronic Seizure Management for Cats,** *Dr. Heidi Barnes Heller*
Cats, like other animals, can be negatively impacted by a number of emotional states including anxiety, fear, and frustration. The presence of these stressors can have a number of important impacts on our ability to diagnose disease states (through altered physiology), and can contribute to the development and manifestations of various disease states, too. Although there is no simple 'test' to diagnose stress in cats, it is important to be aware of its importance, and what can be done to minimize its impact.

T **Respiratory Emergencies: Triaging the Feline Patient,** *Ms. Alison Gottlieb*
These cases are a true exercise in remaining calm and balancing stress levels with treatment. There is a fine line between gathering information and increasing stress. We will discuss stabilization, diagnostics, and potential treatment for our respiratory cat friends. A strong emphasis on low stress handling, potential pharmacologic intervention, and doing no harm will be addressed.

2:00 – 3:00 pm

P **The Three "A's" of Acute Pain Management: Anticipate, Assess, & Alleviate,** *Dr. Sheilah Robertson*
The intensity of a surgical procedure should be ***anticipated*** and preventive measures used to minimize peripheral and central sensitization. Preventive analgesia means providing treatment for as long as there is nociceptive input from the surgical site; this obviously differs between an elective kitten neuter and a fracture repair. One of the predictors of persistent post-surgical pain in humans is the intensity of pain in the first few postoperative days so this means that we must ***assess*** our patients using validated pain scoring tools. Multimodal and integrative approaches should be used to ***alleviate*** and prevent pain. This may include a non-steroidal anti-inflammatory agent to decrease inflammation, cold therapy to alter transduction, a long acting local anesthetic to disrupt transmission from the peripheral to central nervous system, and ketamine to minimize central plasticity. Anxiety exacerbates pain therefore feline friendly nursing and handling play a key role in acute pain management. This session will give a brief overview of each "A" and how to incorporate them into your practice.

P **It's a New World: Introducing the 2020 AAFP Retrovirus Testing & Management Guidelines,** *Dr. Susan Little*
In 2020, the AAFP published new guidelines for FeLV and FIV testing and management. New information on the outcomes of infection with both viruses and new diagnostic tools have changed our view of these infections. The ability to stage FeLV infections is a major advance in feline medicine. This presentation will describe a two-tier approach to retrovirus testing, current information on the health and longevity of infected cats, and changes occurring in the shelter world.

P **Placement & Maintenance of Nasogastric Feeding Tubes in Cats,** *Dr. Lisa Powell*
The goals of this session are to describe how to place nasogastric (NG) tubes in cats, discuss the benefits of NG tubes for temporary nutritional support, potential complications, and disease states where NG tubes are advantageous. The amount, type, and delivery method of food through the NG tube will be presented. Placement of an NG tube can be a way to support ill cats through a variety of disease states, decreasing illness time, hospitalization, and are usually well-tolerated.

P **The Future is Now: 21st Century Fecal Testing Technology in Your Practice,** *Dr. Cory D. Penn*
The presentation will look at the importance of fecal exams to detect intestinal parasites and how advances in recognition technology will improve detection and diagnostic testing for our patients. The learning objectives for the presentation are to understand current advances in recognition technology, understand common parasites that can be detected on fecal examination with this technology, and to understand the importance of fecal examination to diagnostic testing.

3:00 – 4:00 pm

A **Feline Oral Squamous Cell Carcinoma: Recent Advances,** *Dr. Michael Nolan*
Oral squamous cell carcinoma (SCC) is a devastating disease in cats; even with intensive combinations of surgery, chemotherapy, and radiotherapy, survival infrequently exceeds a few months. A great deal of research effort is devoted to development of new and hopefully more effective therapies for feline oral SCC. These efforts arise from both a clinical need in cats and a significant need to develop better treatment strategies for humans with a similar condition. In this lecture, attendees will learn about our experience developing a new low-cost ethanol ablation strategy for cats with oral cancer. We will also review recent scientific advances that hold promise for simultaneously improving the care of both cats and humans with oral SCC.

B **Neurologic Examination for Busy Practitioners,** *Dr. Heidi Barnes Heller*
This session will focus on honing your skills for the feline neurologic examination. We will focus on techniques and tricks for facing the feline neurologic examination.

T **Special Considerations on Feline Ears,** *Dr. Alison Diesel*
Managing ear disease in cats requires a bit of finesse and special considerations which differ from treating dogs. This session will highlight key elements of working with the feline patient with ear disease. Diagnostic tests, disease state, and elements of treatment in both the acute and chronic setting will be discussed.

4:30 – 5:00 pm

C ***Ask the Experts,*** *Drs. Heidi Barnes Heller & Paulo Steagall*
Join us for a live session, moderated by Dr. Kelly St. Denis, where attendees can ask questions for Dr. Heller Barnes and Dr. Steagall.

SUNDAY, OCTOBER 4, 2020 – DAY 2

10:00 – 11:00 am

C ***Finding our Path to Honor Ourselves as We Live the Veterinary Oath,*** *Dr. Kimberly Pope-Robinson*
We each come into this profession following and honoring the veterinary oath in our unique way. Practicing and supporting the human animal bond in various aspects of veterinary medicine. Along the way we often lose ourselves from the challenges and struggles of the space that is veterinary medicine. In this process many lose their drive to stay within the profession. The goal to career sustainability is to provide a space that allows each individual to find their unique path to honor themselves while they honor the veterinary oath. To not be told what to do, more to follow a framework to find longevity within the veterinary industry. When we uniquely honor the veterinary oath and while committing to ourselves, we excel as veterinary professionals and find our longevity within the profession. With this lecture, attendees will come away with an understanding on how to begin to find the path to honor themselves. Thereby allowing each individual to start the journey to live once again connected to the passion they hold close to their heart and then in doing so find their sustainability within the veterinary industry.

11:00 – 12:00 pm

A **Allergic Dermatitis,** *Dr. Alison Diesel*
Is it a flea allergy? Food allergy? Feline atopic syndrome? All of the above? Once we figure out which etiology of allergic skin disease we're working with, how do we determine the most appropriate therapeutic intervention with the limited options available for feline patients? This session will focus on key points of diagnosing and managing the difficult feline patient with head and neck manifestations of allergy.

B **Herpesvirus 101: Why, What, & How?,** *Dr. Jessica Meekins*
This presentation will provide a detailed review of the pathophysiology and clinical ocular manifestations of feline herpesvirus-1, from primary infection to reactivation of latent virus and recrudescent disease. We will discuss how the epithelial tropism of the virus results in the typical ocular clinical signs of conjunctivitis and corneal ulcers, in addition to reviewing the less common immune-mediated keratitis that can develop in chronically affected carrier cats.

T **Feline Pain: Detecting, Identifying Options, & Advocating for your Patients,** *Ms. Alison Gottlieb*
We will discuss pain detection, treatment options, and multi-modal therapy. Pain score options and how to use them will be discussed in addition to the best way to advocate for your patients. Ethical considerations and roadblocks to analgesia will also be discussed.

12:00 – 1:00 pm

A **Kitten-caboodle: A Selection of Various Feline Dermatoses,** *Dr. Alison Diesel*
While parasites, infections, and allergy are top etiologies for skin disease affecting the head and neck in cats, other differentials may need to be investigated. This case-oriented session will discuss selected conditions which the feline practitioner should be aware.

B **Feline Herpesvirus: Review of Treatment Strategies,** *Dr. Jessica Meekins*
This presentation will highlight best practices for targeted therapy in cats with viral surface ocular disease. We will discuss the approach to clinical decision making and when to select specific antiviral drugs. The current literature will be reviewed to present evidence-based reasoning for the selection of drugs, routes of administration, and dosages.

T **Is the Kitty Crazy? Feline Hypothyroidism,** *Dr. Kathy Engler*
This session will cover history, pathophysiology and presentation of feline hyperthyroidism. Additionally, diagnosis, treatment and patient monitoring will be addressed. Client communication will be touched on briefly, as well as resources available from Dechra to support client communication and patient management.

1:45 – 2:45 pm

P **CKD: Prediction of Future Diagnosis, Early Diagnosis, Staging, & Management Strategies,** *Dr. Denis Chew*
This session will feature how the power of artificial intelligence and machine learning allow the clinician to use the tool called RenalTech™ to predict a future diagnosis of CKD using commonly collected laboratory data parameters. This prediction is accurate up to 2 years into the future as to which cats will and which cats will not have a diagnosis of CKD during that time. An early diagnosis of CKD can occur long before a cat exhibits obvious clinical signs, but this requires astute observation and integration of findings from blood chemistry and complete urinalysis. We will review how the current level or trend for increase in BUN, serum creatinine, SDMA, and urinary protein as well as decreases in USG can be used to establish an earlier diagnosis of CKD. We will compare and contrast SDMA and serum creatinine so that they can both be used to optimize the diagnosis of CKD and then for assignment of an IRIS CKD stage. Treatment will emphasize new findings on the role of dietary phosphate in the development and progression of CKD in cats.

P **Unintentional Weight Loss: Feline Dwindles,** *Dr. Grant Gugisberg*
Senior cats are similar to geriatric humans. Unintentional weight loss in people is referred to as 'the Dwindles;' felines go through similar metabolic processes. In up to 25% of human cases a cause is never discovered, despite extensive, advanced testing. In feline patients many underlying issues may result in even higher numbers. In this lecture we'll review common geriatric diseases that cause weight loss such as pancreatitis, renal disease, hyperthyroidism, osteoarthritis, and idiopathic weight loss. Finally, we will explore management of unintentional weight loss associated with these conditions.

P **Look What the Cat Dragged In: Emerging Infections & Infestations Facing Felines Today,** *Dr. Susan E. Little*
Despite many advances in feline medicine, cats face ever increasing health challenges, many of which come in the form of infections and infestations. From common intestinal parasites to the increase in tick and mosquito vectors and the pathogens they transmit, cats – even those kept primarily or entirely indoors – are beset by risks at every turn. This presentation will update veterinarians on common and emerging infectious, parasitic, and vector-borne disease threats faced by cats and describe strategies to mitigate the danger in practice, protecting cats and their owners.

P **Pouncing on Pain: Managing Feline Osteoarthritis Cases,** *Dr. Elizabeth Colleran*
Discussions about osteoarthritis (OA) in cats are becoming more frequent and more serious as data has emerged about the incidence of OA and the profound impact it can have on Quality of Life (QOL) if left untreated. There are multiple categories of intervention that, when used in combination, can improve comfort, locomotion, and QOL. The plan for chronic pain management of OA should include several categories to achieve pain control and should be implemented as early as a diagnosis is made. The plan must take into consideration the capability of the caregiver, the personality of the cat, and the impact the plan might have on the relationship between caregiver and beloved feline. Because cats are more difficult to assess given the subtlety of emotional expression and the differences in the manifestation of pain between cats, dogs, and people, regular assessment of the efficacy of pain management and of the impact on the relationship must play an integral role in implementing a OA pain management plan. In the future, there will be new strategies for managing OA pain, for now, we will discuss the options available and a brief look at future possibilities.

SUNDAY, OCTOBER 4, 2020 – DAY 2 continued

2:45 – 3:45 pm

A **Otitis in the Cat: Keys to Diagnosis & Therapy,** *Dr. Alison Diesel*
Ear infections are generally secondary to an underlying disease process in dogs and cats. There are however distinct species differences that need to be taken into consideration when treating infection and working through differential diagnoses for otitis in the feline patient. This session will highlight a strategic plan to move past "treat for mites" when confronted with ear disease in cats.

B **Otic Polyp: Etiology, Presentations, & Treatments,** *Dr. Bryden Stanley*
Both the external ear and the middle ear in cats are anatomically quite different from the dog, so it is worth knowing the separate anatomical features. The etiology of otic polyps in cats is still elusive, but the behavior is quite consistent, typically with either a pharyngeal or an otic presentation, occasionally with both types of signs. Polyps can be bilateral, so appropriate imaging is essential. Treatment options include traction and medical management or ventral bulla osteotomy, with the latter technique having a lower recurrence rate.

T **Ophthalmic Drugs & When to Use Them,** *Dr. Jessica Meekins*
This presentation will review the most commonly prescribed topical ophthalmic drug preparations and indications for use. We will discuss the benefits and drawbacks of medical therapy for a variety of ocular conditions in cats. Antibiotic, antiviral, and anti-inflammatory drugs will be the focus of this session.

4:15 – 4:45 pm

C ***Ask the Experts,*** *Drs. Alison Diesel & Jessica Meekins*
Join us for a live session, moderated by Dr. Kelly St. Denis, where attendees can ask questions for Dr. Diesel and Dr. Meekins.

SATURDAY, OCTOBER 24, 2020 – DAY 3

12:00 – 1:00 pm

A **Update on Treatment Strategies for Feline Chronic Gingivostomatitis,** *Dr. Christopher Snyder*
This session will discuss complications that occur during extractions - both how to manage them and tips to prevent them. A variety of clinical situations will be discussed. With the prevalence of tooth resorption in feline patients, treatment decision making and actually identifying resorbing root structure is a challenge. Strategies for addressing root tips displaced in the nasal cavity or mandibular canal will be covered as well as considerations for treatment options for fractured teeth and what to do if iatrogenic mandibular fracture takes place during extraction.

B **Nutrition for the Hospitalized Patient,** *Dr. Christopher Byers*
Cats often require temporary hospitalization to help manage various health conditions. Adequate nutritional support during hospitalization is essential to prevent them from developing a negative energy balance. Attendees will review a proactive approach to providing appropriate nutritional support to hospitalized patients, including the use of temporary supplemental feeding tubes.

T **Cat Naps During a COHAT: The Complete Plan for the Feline Dental Patient,** *Ms. Mary Berg*
Performing a Complete Oral Health Assessment and Treatment (COHAT) entails much more than removing plaque and calculus from the teeth. Thorough dental cleaning consists of educating the client, an oral examination, charting disease process, pathology and anomalies, radiographs, both supra, and subgingival plaque and calculus removal, hand scaling, polishing, irrigation, and home care instructions.

1:45 – 2:45 pm

A **Mastering Feline Dental Radiograph Interpretation,** *Dr. Christopher Snyder*
The availability of intraoral radiography in general practice has resulted in practitioner's improved ability to diagnose and assess lesions of teeth and supporting bone in dentistry patients. This session will focus on reviewing normal structures, assessing both lesions that are subtle and obvious, and an emphasis will be placed on how these radiographs are going to affect prognosis or guide treatment decision making. Tips for radiographic positioning and a review of the types of acquisition hardware will be included.

B **Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 1,** *Dr. Phillip Padrid*
Chronic nasal disease in cats is a very commonly seen condition in small animal practice. The causes of sneezing, nasal discharge, and noisy breathing can include allergy, chronic viral infection, nasal foreign body, dental disease, nasal neoplasia, and lymphocytic plasmacytic rhinitis. The practitioner will learn how to distinguish the various causes of chronic nasal symptoms in cats and also learn the most up to date treatment strategies for this clinical presentation. Note: bacterial infection is NEVER the *primary* cause of these chronic signs!!

T **Tips & Tricks for Great Dental Radiographs,** *Ms. Mary Berg*
Dental radiographs are an essential part of the oral exam. The crown is just the tip of the iceberg. Approximately 42% of dental pathology is found below the gumline. Radiographs will help diagnose pathology that is not visible from the surface, confirm suspect pathology as well as help demonstrate the pathology to the client. Dental radiographs can improve the standard of care in your practice and increase your clinic's revenue. Learn methods to make taking dental radiographs a dream!

SATURDAY, OCTOBER 24, 2020 – DAY 3 continued

2:45 – 3:45 pm

(P) **Feline Hypertension: Diagnosis, Treatment, & Management,** *Dr. Clarke Atkins*
Hypertension is the most important cardiovascular disease of the aged cat. The emphasis of this presentation is the recognition, appropriate management, and prevention of target organ damage in the hypertensive cat. The use of amlodipine and telmisartan in the current days' management of systemic hypertension will be emphasized.

(P) **Feline Obesity & Behavioral Aspects,** *Dr. Julie Churchill*
Despite the knowledge that unhealthy weight gain contributes to comorbid conditions, reduced mobility, comfort, quality of life and lifespan, the prevalence of overweight cats continues to rise in the US feline pet population. The complex nature of this problem can challenge the success of treatment plans. Taking an individualized approach to weight management by partnering with cat owners and engaging and empowering the whole team are keys to successful preventive actions as well as successful weight loss and maintenance. Individualized nutritional plans will not only improve the health of the patient but also the relationship and satisfaction of clients. After participating in this session, attendees will be able to discuss the prevalence of overweight obesity in cats, be able to use communication tips to help the veterinary healthcare team build better relationships to engage and empower cat owners to part in their cat's care, and develop an individualized nutritional treatment plan to optimize the health and quality of life of overweight cats.

(P) **Hydration Fixation: Beyond the Water Bowl,** *Dr. Jason Gagne*
Water is the most essential nutrient. However, there is no consensus on optimal water intake or on the impact of adequate hydration on feline health. This presentation will review water intake, loss, and relevant physiologic idiosyncrasies of cats. We will discuss multiple strategies for increasing water intake including a novel nutrient enriched water supplement that has been shown to lead to increased fluid intake, increased urine volume, and decreased urine specific gravity.

4:15 – 5:15 pm

(A) **Gastroesophageal Reflux: An Under-Recognized Source of Pain,** *Dr. Christopher Byers*
Gastroesophageal reflux disease or GERD is relatively common in feline patients. Unfortunately, it's also under-recognized and as such, contributes to disease morbidity. Attendees will learn to recognize and proactively treat GERD.

(B) **Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 2,** *Dr. Phillip Padrid*
See Part 1 Abstract on previous page

(T) **Pain Management & Anesthesia Concerns in Feline Dental Patients,** *Ms. Mary Berg*
Pain management is more than the popular terminology. Articles first published in1928 discussed how to perform "dental anesthesia" in animals. It is an essential part of veterinary dentistry. Many of the procedures performed on animals are painful, and it is our duty as veterinary technicians to ensure that our patients are as comfortable as possible. Before performing many dental procedures or oral surgery, the delivery of local nerve blocks is an effective way to create preemptive analgesia. Local nerve blocks should be incorporated into a multimodal plan for pain control.

SUNDAY, OCTOBER 25, 2020 – DAY 4

11:00 – 12:00 pm

(S) **Raising Awareness of Osteoarthritis: Identify & Diagnose Affected Cats,** *Dr. Sheilah Robertson*
A large percentage of cats have long term pain related to osteoarthritis (OA). Our understanding of this disease has increased greatly over the last decade, yet many cats remain undiagnosed and untreated. One important way to find these cats so we can help them is by raising owner awareness of changes in behavior that may be a result of pain and not as many owners believe "just old age." This can be achieved by using owner focused questionnaires, asking open ended questions specific to each cat about their ability to perform activities that depend on mobility, and asking owners to take short video clips of their cat in the home environment. These steps, which can be performed prior to an in-clinic visit, may result in a high degree of suspicion that OA is present and provide you with a foundation for your physical examination. Additional information is gleaned from an orthopedic examination and radiographs. A treatment trial, with assessment before and after, can be used to confirm or refute a case where there is uncertainty of the diagnosis.

12:00 – 1:00 pm

(S) **Nutritional Management of Chronic Enteropathies: A Review of the Recent Research in Cats,** *Dr. Becky Mullis*
Therapeutic nutrition is a key component in the management of gastrointestinal disease. This lecture will cover the use of fiber in the management of both diarrhea and constipation and how to target the microbiome through prebiotics,probiotics and postbiotics. You will learn about the recent studies evaluating the impact of nutrition on stool quality in cats and then use this knowledge to work through the decision making process of choosing a food for a cat with chronic diarrhea.

SUNDAY, OCTOBER 25, 2020 – DAY 4 continued

1:30 – 2:30 pm Ⓢ **Ask the Experts: Q&A,** *Drs. Debra Horwitz & Sheri Ross*
Join us for this live session where you will be able to ask questions of two expert speakers, or seek guidance on a case that has you stumped. Debra Horwitz, DVM, DACVB will focus on feline behavior questions and Sheri Ross, BSc, DVM, PhD, DACVIM on internal medicine questions relating to the kidneys, urinary tract, plasma exchange, and novel applications of apheresis and hemodialysis. Dr. Jolle Kirpensteijn will moderating this interactive Q&A session.

2:30 – 3:30 pm Ⓢ **Putting Vaccines into Perspective,** *Dr. Christopher Lee*
While risk assessment represents an everyday activity for veterinarians, it does not for human physicians. This presentation explores this difference. Additionally, review basic viral characteristics as they pertain to feline core vaccines.

4:00 – 5:00 pm Ⓢ **Creating a Multimodal Plan to Combat Long-term Pain: Why Physical & Mental Health Must Be Considered,** *Dr. Sheilah Robertson*
We now know that both physical and mental health are important for overall quality of life (QoL) in cats. Many aspects of physical health can be quantified and are measurable (e.g. body condition score, complete blood chemistry profiles, etc.). However, pain, suffering, and QoL are unique to each individual and are internal states or emotions. "Objectifying the subjective" is a challenge. Assessment of a cat's mental status is performed by the clinician or owner (a proxy) so it is an "observer related outcome." The available tools and questionnaires will be discussed and most importantly we will discuss if we are asking the right questions.

Session Abstracts
ON DEMAND

Head & Neck

Dentistry

Maximizing Regional Anesthetic & Pain Management for Dentistry & Oral Surgery Patients, *Dr. Christopher Snyder*
The prevalence of periodontal disease has been reported to be as high as 80% for cats over 2 years of age. Treatment of these lesions are frequently associated with surgical discomfort. The use of multimodal approaches such as local anesthetics to address oral pain provide the benefits of decreasing reliance on a greater depth of general anesthetics and affords a smoother recovery and transition to oral pain medications. Following this lecture, attendees will be able to describe various conditions, medications and anatomic landmarks associated with administration of regional blocks for dental patients.

Tips & Tricks for Successful Extractions & Achieving Predictable Healing, *Dr. Christopher Snyder*
This session will start by discussing cost effective methods to improve the oral surgery environment to optimize successful dental treatment. We will move into discussing optimal tissue handling, and flap creation strategies for both tooth extraction or oronasal fistula closure. Following flap creation, steps/instruments and techniques for optimally exposing tooth roots, sectioning and elevation will be reviewed.

Navigating Those Dental Complications That Make You Go…Hmmm!?, *Dr. Christopher Snyder*
This session will discuss complications that occur during extractions - both how to manage them and tips to prevent them. A variety of clinical situations will be discussed. With the prevalence of tooth resorption in feline patients, treatment decision making and actually identifying resorbing root structure is a challenge. Strategies for addressing root tips displaced in the nasal cavity or mandibular canal will be covered as well as considerations for treatment options for fractured teeth and what to do if iatrogenic mandibular fracture takes place during extraction.

Dermatology

Pesky Parasites & Infections Regionalized to the Head & Neck Area, *Dr. Alison Diesel*
Otodectes? Sure…but what about other parasites that can affect the head and neck in cats? Dermatophytosis? Absolutely…but what other infectious agents should be considered in this body region? This session will discuss various parasitic and infectious agents that can manifest with skin disease of the head and neck in cats.

Emergency/ Critical Care

Management of Traumatic Brain Injury, *Dr. Christopher Byers*
Traumatic brain injury is a common presenting concern in veterinary hospitals, especially emergency rooms. Astute veterinarians regardless of practice type need to be prepared to proactively manage these patients. Attendees will learn a practical approach to management of traumatic brain injury patients in an effort to maximize the likelihood of a positive outcome.

Neurology

Acute Seizure Management for Cats, *Dr. Heidi Barnes Heller*
How do the drugs commonly used to control seizures work in cats? What has been published about feline seizure management and how can we use this data to shape our choices?

Novel Seizure Therapeutics for Cats, *Dr. Heidi Barnes Heller*
Research has repeatedly shown that cats can be challenging to medicate! My research at the University of Wisconsin was focused on identifying transdermal, extended release or novel oral anticonvulsant choices for cats. We will discuss these findings and how to apply the novel therapeutics.

Feline Hyperesthesia, Cognitive Dysfunction, & Other Mystery Diseases, *Dr. Heidi Barnes Heller*
This session will focus on some of these less common feline diseases. We will discuss diagnostic testing and available therapeutic choices for cats with these complicated diseases.

Oncology

Measuring Feline Orofacial Cancer Pain, *Dr. Michael Nolan*
Pain is a common clinical concern in cats with oral squamous cell carcinoma (SCC). Severe pain is most frequently suspected in cases with bone-invasive tumors. Our new research demonstrates that cats with oral SCC display measurable discomfort even in the absence of malignant osteolysis; these changes can be quantified using client questionnaires, clinician scoring tools, and quantitative sensory testing. An intriguing finding is that cats with oral cancer display altered somatosensory processing at sites distant from their tumor, thus providing evidence for widespread sensitization. These results are expected to enhance both the translational value of feline oral SCC in comparative oncology research, and the clinical management of discomfort caused by oral SCC lesions.

Nasal Tumors & Neuro-Oncology in Cats, *Dr. Michael Nolan*
This lecture will provide an overview of feline nasal and brain tumor management, from the perspective of a radiation oncologist. During the first half of the lecture, new data will be presented regarding treatment approaches, prognostic factors, and survival statistics for cats with nasal carcinoma. We will also discuss the pros and cons of various radiotherapeutic approaches (e.g., stereotactic radiotherapy versus conventional palliative and definitive-intent protocols) for both lymphomatous and non-lymphomatous sinonasal neoplasms in cats. During the second half, we will discuss current practice patterns and approaches in feline neuro-oncology.

Opthalmology

Unique Feline Corneal Diseases, *Dr. Jessica Meekins*
This presentation will highlight diseases that uniquely affect the feline cornea. We will discuss the pathophysiology, clinical presentation, diagnostic and treatment approach for specific feline corneal diseases, including corneal sequestrum, eosinophilic-proliferative keratitis/ conjunctivitis, and acute bullous keratopathy.

Uveitis: Ocular Manifestations of Systemic Disease, *Dr. Jessica Meekins*
This presentation will review select infectious diseases that result in ocular clinical signs in feline patients. After an overview of the clinically relevant anatomy and physiology of the uveal tract, we will focus on recognizing clinical signs of uveitis before discussing specific ocular lesions resulting from various infectious (fungal, viral, protozoal) and other systemic causes of uveitis.

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Session Abstracts
ON DEMAND

Head & Neck continued

Pain Management

Chronic Pain: Is It All in the Head?, *Dr. Beatriz Monteiro*
Chronic pain is generally a result of inflammatory, neuropathic, and functional components. It involves input from the periphery, but it is in the central nervous system that pain processing takes place. There, numerous mechanisms including positive and negative emotions modulate pain perception. This lecture will present an overview of pain pathophysiology while making the connection with feline clinical practice and common chronic painful conditions.

Surgery

Face & Head Reconstructive Techniques in Cats, *Dr. Bryden Stanley*
Owners look at the cat's faces more than any other area, and so the possibility of cosmetic change or even loss of symmetry needs to addressed with the owner before any reconstructive effort is undertaken in this area. That notwithstanding, the ultimate goals for quality of life are pain-free and functional, rather than cosmesis. Although the face and head are not that amenable to grafts or tension-relieving techniques, there are a number of fairly robust flaps that can be used to cover defects in the muzzle, head, and mandibular regions.

Technician

Cats Don't Read Textbooks: Commonly Found Oral Pathology of Felines, *Ms. Mary Berg*
It is important to realize that cats have not read textbooks when it comes to dental problems. This presentation will discuss the commonly and maybe not so commonly found oral pathology of felines. It is important to be able to identify oral pathology and anomalies as well as how to record the pathology on dental charts.

Feline Head Trauma, *Ms. Alison Gottlieb*
It happens, be prepared. Felines live in a dangerous world and deserve the best care possible. Knowing what to expect and initial assessment is crucial. This session will focus on being prepared, emergent care and monitoring these felines; the fine art of collecting data while considering; stress levels, owners, finances, and supplies will be discussed. Using the equipment and therapies available with the addition of knowledge is the key to optimal care.

Feline Respiratory Patients: A Delicate Balance, *Ms. Alison Gottlieb*
The feline respiratory patient can be incredibly stressful for everyone involved: the cat, team, and owner. Being prepared, thorough history and pure observation are ideal to approach these very delicate cases. A review of common afflictions and treatments associating with the system are discussed.

Practice Management

Cyberbullying & the Veterinary Profession, *Dr. Phillip Padrid*
The effect and influence of social media commentary on the veterinary profession is profound and is likely to increase. The effect of negative social media commentary can especially harm a practice and the physical and emotional wellbeing of our colleagues working within that practice. The goals of this seminar are to 1. identify the specific effects of social media in our profession, 2. provide insight into the reasons why clients are motivated to post positive and negative comments, 3.to increase the opportunity to encourage positive social media comments, and 4. to give members of our profession the behavioral tools to minimize the incidence and effect of of negative posts toward our hospitals and ourselves.

Every Practice's Struggle: How to Attract, Retain, & Motivate Your Veterinary Talent, *Dr. Taylor Tillery*
The ARM research is a study funded by Merck Animal Health to address one of the biggest issues in the veterinary healthcare industry. "ARM" stands for Attract, Retain, and Motivate as they relate to staffing. After asking veterinary practices around the US, a common priority surfaced; the need to retain valued veterinarians and office staff. The results of our study describe the current state of veterinary talent management in the US market, identifies key areas of interest and quantifies the value of several employee retention improvement strategies. Additional areas of discussion include the most effective ideas for improvement, expectation for compensation and benefits, private vs. corporate practice comparisons, job satisfaction analysis, and data available by role, job type, and gender. The learning objectives are how to evaluate the current state of talent management in the US market as they relate to the veterinary community and how to quantify the value of several employee retention improvement strategies.

Session Abstracts
ON DEMAND

Partner Symposia

ABVP: Is It For Me?, *Dr. Amy Hinc*
In this seminar the attendee will come to understand what Board Certification in Feline Practice by the American Board of Veterinary Practitioners means. The attendee will be walked through the application process, including credentialing and the writing of case reports.

A Tranformational Nutritional Approach to Managing Cat Allergen Fel d1, *Dr. Ebenezer Satyaraj*
Allergies to cats are the most common animal–origin allergy, and affect about 1 in 5 adults worldwide. Allergen avoidance is recommended as the most effective solution; it however involves limiting interaction with the cat or in some cases relinquishing the cat. There is a clear need for innovative approaches to manage cat allergens. While cats produce several allergens, more than 96% of people with sensitivities to cats respond to the primary cat allergen, Fel d1, a protein secreted in the saliva and sebaceous secretions of the cat. We will discuss the scientific basis of a novel nutritional approach to simply, safely, and effectively neutralize Fel d, the most potent feline allergen, utilizing an anti-Fel d1 IgY antibodies (derived from chicken egg) added to the cats' diet. A brief overview of the cat allergy problem and current approaches to manage cat allergens will be reviewed and efficacy of a feline diet with an egg product ingredient containing anti–Fel d 1 IgY antibodies in reducing active Fel d1 levels in cat saliva and hair will be discussed.

Hill's at Home, *Various Experts*
Hill's @ Home CE provides access to numerous feline CE sessions both live and on-demand. Get all your questions answered by internationally renowned experts at hillsathomece.com.

Regenerative Medicine & the Feline Patient, *Dr. Robert Harman*
Regenerative Medicine and the Feline Patient is a course designed to cover the basics about Stem Cell Therapy in veterinary medicine and how it can be applied to feline medicine. The objectives of this course are to discuss the potential mechanisms of action, efficacy, and safety. Guidelines on how to use stem cell therapy for the treatment of Arthritis, Chronic Renal Disease, IBD, and Gingivostomatitis as well as case studies and outcome data will be presented.

Understanding Feline Hypertension, *Dr. Clarke Atkins*
Diagnosing hypertension is an art, particularly in cats. We will discuss normal and abnormal blood pressures, obtaining accurate blood pressures measurements, the difference in impact of systolic and diastolic hypertension on target organs, and how to decide what is real and what it's not. Updates to the diagnosis and management of systemic hypertension in cats from the 2017 ACVIM Consensus Statement on Hypertension will be provided.

Update on Diabetes Mellitus in Cats, *Dr. Deborah Greco*
Pathogenesis of type 2 diabetes mellitus in the cat with particular emphasis on the circumstances that lead to the development of diabetes in the cat will be discussed. Discussion of the role of carbohydrates and protein in feeding cats, description of the clinical appearance of type 2 diabetes mellitus and discussion of early diagnosis and treatment including discussion of the different insulin types, choosing the appropriate insulin for a particular patient and problem-shooting insulin administration problems. There will also be a focused view of monitoring diabetic cats including urine glucose monitoring, clinical signs, and blood glucose curves. Lastly, emphasis on the new developments in monitoring diabetics such as glycosylated serum proteins (fructosamine), HbA1C and continuous glucose monitoring will be discussed.

What is it? Differentiating Medical from Behavioral, *Dr. Valarie Tynes*
The first sign of a medical condition is often a change in behavior and when behavioral conditions lead to chronic stress a medical problem is often the result. In this presentation, attendees will learn some key signs to look for when differentiating medical conditions from behavioral conditions as well as some tips for recognizing a few of the common "imposters"; those medical conditions that frequently "pose" as behavioral conditions. Most importantly, attendees should leave this presentation with a better understanding of the complex interaction between physical and behavioral health.

Oral Abstracts

How Does OA in Cats Affect Their Quality of Life, *Dr. Andrea Wright*
To understand how degenerative joint disease (DJD) in cats affects their quality of life, a conceptual framework for the assessment of health-related quality of life (HRQoL) in cats with degenerative joint disease was developed from published studies. HRQoL is considered a multi-dimensional concept, including both physical factors such as pain and physical activity, and non-physical factors which include the feelings felt by the animal, such as emotional wellbeing. The assessment of HRQoL is increasingly important in companion animals. Assessment of HRQoL can be generic or disease specific. However, the majority of HRQoL research has focused on dogs, with HRQoL studies on cats reported less frequently. Of these, there is a paucity of HRQoL research that focusses on cats with DJD. Therefore, in order to evaluate how DJD impacts HRQoL, there is a need for further research on the domains that contribute to HRQoL in cats and ultimately facilitate effective assessment of treatment interventions and their outcomes for cats with this condition.

Oral Abstracts continued

Identification of Risk Factors for Feline Anesthetic Mortality, *Dr. JoAnne Morrison*
Cats have roughly two times the risk of death from general anesthesia compared to dogs. Risk factors for anesthetic mortality that have been previously elucidated (e.g., increased ASA status, procedural complexity) do not account entirely for the increased risk seen in feline patients. The objective of this study was to determine if novel risk factors for anesthetic mortality could be identified in a population of feline patients that underwent elective anesthesia procedures. The hypothesis, briefly stated, was that cats experienced increased anesthesia mortality as a result of underlying inflammatory / immune mediated conditions which disproportionately impact the cardiopulmonary system, resulting in fatal outcomes when cats undergo general anesthesia.

The Novel UNESP-Botucatu Cat Pain Scale (UCAPS), *Dr. Paulo Steagall*
Pain assessment is a fundamental part of feline practice. This study assessed content validity, inter and intra-rater reliability of the novel short form UNESPBotucatu cat pain scale (UCAPS) in eight languages.

Thyroid Troubles: Diagnosis & Management of Hypothyroidism, *Ms. Stefanie DeMonaco*
This oral presentation will discuss the pearls of practice regarding diagnosis and management of iatrogenic hypothyroidism in cats in general practice. Over the past decade, the identification and treatment of iatrogenic hypothyroidism has become a significant part of managing hyperthyroid cats. Up to 70% of cats can become hypothyroid after treatment with radioactive iodine, with an approximate average of 10% in most studies. Hypothyroidism is associated with shortened survival and the development of azotemia in cats after treatment with radioactive iodine highlighting the importance of proper identification and care.

What's in Your Patient's Head: Cone Beam Computed Tomography, *Dr. Katherine Knutson*
Cone Beam Computed Tomography (CBCT) is a relatively recent diagnostic modality for veterinary medicine. It has been co-opted from human medicine, particularly dentistry, where it is extensively utilized in the diagnosis of pediatric oral pathologies. It is now being used in the diagnosis of skull pathologies and associated structures in feline medicine.

Miscellaneous

Creating Individualized Feline Vaccine Protocols: Key Points from the 2020 AAHA/AAFP Feline Vaccination Guidelines, *Dr.'s Philip Kass & Amy Stone*
To help you create individualized feline vaccination protocols based on risk-assessment, our learning facilitators will provide clarity on factors that increase or decrease infectious disease exposure risk, unpack the recommendations for vaccination schedules for pet and shelter cats, support decision-making for vaccination (or not) against FeLV in adult cats with emphasis on the frequency and type of vaccination depending on risk for infection, and summarize the current literature on the incidence and causality of FISS.

NEW AAFP Cat Friendly Certificate Program, *Dr. Kelly St. Denis*
The Cat Friendly Certificate Program provides you with feline-specific education to further your knowledge, skills, and best in-clinic practices. The AAFP is proud to be a trusted leader in feline care, and has developed this program for all individual veterinary team members in order to increase the standards of care provided to cats. Obtaining a certificate within this program will allow you to further enhance, deepen, and strengthen your feline expertise and demonstrate your personal commitment in caring for cats.

EVERY CAT, EVERY DAY BENEFITS
FROM WINN-FUNDED RESEARCH

In 1968, the Cat Fanciers' Association (CFA) created what would soon become Winn Feline Foundation, establishing a source of funding for medical studies to improve cat health and welfare. A 501(c)(3) non-profit charitable organization, the New Jersey-based foundation was named in honor of CFA's longtime attorney and advisor, Robert H. Winn. CFA continues to actively support the Foundation and remains dedicated to Winn's original vision — to promote the health and welfare of all cats by developing or participating in projects for their betterment, including the funding of research and education.

To date, Winn has funded over $7 million in health research for cats at more than 30 partner institutions worldwide. Our work is only made possible with the support of dedicated donors.

Just as Winn has grown, so has feline medicine. Cats are no longer viewed as small dogs; they are now a major veterinary specialty. Today, cat owners expect and receive state-of-the-art medical care. They assume their cats will benefit from similar technological advances made in human medicine — and with increasing frequency, they do.

Winn's commitment to feline health research and education has played a significant role in these achievements and will continue to do so in the years ahead.

Gifts that Keep on Giving

How Giving Helps Research supported by Winn Feline Foundation helps veterinarians improve the quality of feline health care and prevent life-threatening diseases. With the help of our expert review panel, grants are awarded twice yearly to fund groundbreaking studies. Your gifts are designed to return the love to the cats that have enriched our lives. How? By making strides in medical care and disease prevention today and through the years to come.

When you contribute to Winn Feline Foundation, you can choose where to allocate your gift:

- General health studies
- Specific research areas
- Specific breed-related health studies
- Endowment Fund
- Remembering your special love for cats in your estate plans
- Thanking your veterinarian through the Veterinary Honor Roll or a licensed technician at the Technician Honor Roll
- Remembering a beloved pet with a virtual memorial
- Making a tax-deductible donation in memory of a client's cat (Veterinarians only)
- Become a Cat Health Champion with a recurring gift
- Donating in honor or memory of a special person or cat
- Double your donation with an eligible Matching Gift by your employer.

Contact us for more information at INFO@WINNFELINEFOUNDATION.ORG or visit our website to make a difference in feline health.

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Feline Head & Neck: Diseases, Disorders, & More

2020 Virtual CONFERENCE
October 3 & 4 and 24 & 25, 2020

ALL TIMES ARE EASTERN TIME ZONE

October 2 - 12:00 pm **Attendee Access to Event and On-demand CE**

Day 1 — October 3, 2020

Live Exhibits open from 12:00 - 5:00 pm

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Yoga 101		
11:00 - 11:20 am	President's Address	Dr. Kelly St. Denis	
11:20 - 12:20 pm	Feline Grimace Scale for Acute Pain Assessment	Dr. Paulo Steagall	ZOETIS PETCARE, IVAPM
12:20 - 1:20 pm	Painful Conditions of the Head	Dr. Paulo Steagall	ZOETIS PETCARE, IVAPM
	Chronic Seizure Management for Cats	Dr. Heidi Barnes Heller	
	Technician/Nurse: Respiratory Emergencies: Triaging the Feline Patient	Ms. Alison Gottlieb	AAVTA
1:20 - 2:00 pm	Exhibit Hall Break		
2:00 - 3:00 pm	***Partner Symposia***		
	The Three "A's" of Acute Pain Management: Anticipate, Assess, & Alleviate	Dr. Sheilah Robertson	Elanco
	It's a New World: Introducing the 2020 AAFP Retrovirus Testing & Management Guidelines	Dr. Susan Little	IDEXX
	Placement & Maintenance of Nasogastric Feeding Tubes in Cats	Dr. Lisa Powell	ROYAL CANIN
	The Future is Now: 21st Century Fecal Testing Technology in Your Practice	Dr. Cory D. Penn	ZOETIS PETCARE
3:00 - 4:00 pm	Feline Oral Squamous Cell Carcinoma: Recent Advances	Dr. Michael Nolan	WINN FELINE FOUNDATION
	Neurologic Examination for Busy Practitioners	Dr. Heidi Barnes Heller	
	Technician/Nurse: Special Considerations on Feline Ears	Dr. Alison Diesel	ZOETIS PETCARE
4:00 - 4:30 pm	Exhibit Hall Break		
4:30 - 5:00 pm	Ask the Experts	Drs. Heidi Barnes Heller & Paulo Steagall	
5:00 - 6:00 pm	Virtual Happy Hour		ZOETIS PETCARE

Feline Grimace Scale for Acute Pain Assessment

Paulo Steagall, MV, MSc, PhD, DACVAA

Introduction

Pain assessment is fundamental for appropriate analgesic treatment. It should be part of every physical examination in addition to temperature, pulse, respiration (TPR) and nutritional assessment. The knowledge on feline acute pain assessment has improved over the years with the development and validation of different pain scoring systems.[1,2] Additionally, some studies have reported some factors and limitations of using these tools in clinical practice.[3-5]

Indeed, two review articles have been recently published with updates and clinical advances in the subject.[6,7] It presents a stepwise approach to feline pain assessment and recognition and discusses the advantages and disadvantages in practice.

The Feline Grimace Scale

Facial expressions of pain have been identified and validated in numerous species through the development of "grimace scales". Changes in ear and muzzle position have been identified in painful versus non-painful cats,[8] and evaluation of these features have been incorporated into the Glasgow rCMPS-F.[2] However, other facial features are also important in painful states.

This lecture will introduce for the results of the development and validation of the Feline Grimace Scale (FGS), a novel facial-expression-based pain scoring system to recognize and guide the treatment of pain in this species.[9] The audience will go through the process of construction and creation of the FGS, and then will have a chance to score some images through a dynamic interaction with the speaker.

Briefly, a prospective, observational, case-control study involving client-owned painful and non-painful cats presented to the intensive care unit of the Université de Montréal was performed. Cats were video-recorded in their cages after a physical examination and pain assessment using the rCMPS-F. Facial expressions were studied via screenshots obtained from video files. Five different action units were different between painful and pain-free cats. They included ear position, orbital tightening, muzzle tension, whiskers position and lowering of the head.[9] Then, images were scored by four raters independently, twice, and 30-days apart. For each action unit, a score from 0-2 was given. The study found that FGS scores were higher in painful versus pain-free cats. The correlation between the Glasgow composite pain scale and the FGS was very strong. The FGS showed good inter- and excellent intra-rater reliability in general.[9] Additionally, the FGS has excellent internal consistency (i.e. the action units are all important for the final score). It also showed good response to analgesic treatment (scores after analgesia were lower than before). Finally, the tool has a cut-off score of 0.39 out of 1.0. The FGS is a valid tool for acute pain assessment in cats.

A couple of new studies have also been published using the FGS. The clinical applicability of the FGS in real-time when compared with image assessment and the influence of sedation (acepromazine-buprenorphine) and surgery have been investigated. In cats undergoing ovariohysterectomy using a multimodal analgesia protocol, real-time assessment slightly overestimated image scoring with minimal clinical impact. Sedation did not influence FGS scores, however only one protocol was tested in this regard. The study demonstrated again the responsiveness of the FGS after analgesic administration.[10]

Furthermore, the FGS demonstrated good inter-rater reliability in cats undergoing multiple dental extractions and could be used for pain assessment in dentistry. The study also demonstrated that scores were not affect by the caregiver's presence.[11]

The audience is invited to visit www.felinegrimacescale.com for more information about the instrument, download the tool and factsheet, watch videos and much more!

References

1. Brondani JT, Mama KR, Luna SP, et al. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. *BMC Vet Res* 9:143, 2013.
2. Reid J, Scott EM, Calvo G. Definitive Glasgow acute pain scale for cats: validation and intervention level. Vet Rec 180:449, 2017.
3. Benito J, Monteiro B, Beauchamp G, et al. Evaluation of interobserver agreement for postoperative pain and sedation assessment in cats. *J Am Vet Med Assoc* 251:544, 2017.

4. Steagall, PV, Benito J, Monteiro BP, et al. Analgesic effects of gabapentin and buprenorphine in cats undergoing ovariohysterectomy using two pain-scoring systems: a randomized clinical trial. *J Feline Med Surg* 20:741, 2018.
5. Doodnaught G, Benito J, Monteiro B, et al. Agreement between undergraduate, graduate veterinary students and anesthesiologists on pain assessment in cats and dogs: a preliminary study. *Can Vet J* 58:805, 2017.
6. Steagall P, Monteiro B. Acute pain in cats: Recent advances in clinical assessment. *J Feline Med Surg* 21:25, 2019.
7. Monteiro B, Steagall P. Chronic pain in cats: Recent advances in clinical assessment. *J Feline Med Surg* 21:601, 2019.
8. Holden E, Calvo G, Collins M. Evaluation of facial expression in acute pain in cats. *J Small Anim Pract* 55:615, 2013.
9. Evangelista M, Watanabe R, Leung V, et al. Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. *Sci Rep* 9, 19128, 2019.
10. Evangelista MC, Benito J, Monteiro BP, et al. Clinical applicability of the Feline Grimace Scale: real-time versus image scoring and the influence of sedation and surgery. *PeerJ* 8:e8967, 2020.
11. Watanabe R, Doodnaught GM, Evangelista MC et al. Inter-rater reliability of the Feline Grimace Scale in cats undergoing dental extractions. *Front. Vet. Sci.* 7:302, 2020.

NOTES:

Painful Conditions of the Head

Paulo Steagall, MV, MSc, PhD, DACVAA

Introduction

The pain experience is a combination of sensory and emotional components. Pain causes fear, stress and anxiety, negatively impacting quality of life. It also delays recovery and induces behavioral changes that affect the owner-companion animal bond.[1]

Ocular, ear and dental painful conditions and procedures are part of the daily routine in feline practice. Despite their importance, little is known about pain-induced behavior changes of orofacial pain and how they impact feline health and welfare. The duration of and requirements for analgesic therapy are unknown and often based on human studies and anecdotal reports. These conditions are commonly neglected and underdiagnosed because the lack of education on the subject but also because validated pain assessment tools have not been developed for these conditions. Analgesic therapies and techniques have been poorly studied, particularly in cats, for painful conditions of the head.

Dental Pain

Dental and oral diseases are by far some of the most common conditions seen in feline practice. They can produce significant pain, as well as localized and potentially systemic infection.[2] Indeed, severe pain and inflammation might further impact nutrition and feeding behavior. Treatment of periodontal disease often involves general anesthesia and dental extractions.[3]

The literature specific to dental pain is quite limited in veterinary medicine. Nevertheless, recent studies from our laboratory have shed some light into the subject in cats. In a study involving cats with minimal or severe periodontal disease, several parameters were evaluated including pain scores, analgesic requirements and food intake before and after dental treatment. Cats were evaluated under general anesthesia and treatment was performed according to what was clinically recommended; they were evaluated for up to 6 days. Pain scores were significantly increased in cats with severe disease when compared with baseline and with cats with minimal disease. Prevalence of rescue analgesia was significantly higher in severe (91.7%) than minimal disease (0%). Pain scores and frequency of rescue analgesia were significantly correlated with the number of tooth extractions, gingival and calculus index. Finally, food intake was significantly lower in cats with severe dental disease.[4] We have highlighted with this publication the need for long-term analgesia after dental extractions in cats with severe oral disease. We also strongly recommend the provision of soft food for at least a week after dental extractions.

Furthermore, when the behaviors of cats with minimal and severe dental disease were compared using video-analysis before and after treatment, cats with severe disease showed specific behaviors when compared with those with minimal disease. They spent significantly less time sitting and paying attention to surroundings, and significantly more time laying down, at the back of the cage or curling the tail.[5] A video demonstrating these behaviors is freely available with the publication.

Pain assessment is a fundamental part of feline practice that leads to appropriate therapeutic decisions with significant impact in feline welfare. Our laboratory has recently shown that the Feline Grimace Scale is a reliable instrument for acute pain assessment in cats undergoing multiple dental extractions (www.felinegrimacescale.com).[6,7] The prevalence of chronic pain in cats due to periodontal disease is unknown, but it is believed to be quite prevalent if one considers the frequency at which these are diagnosed in practice. It can involve periodontal disease, but also tumors affecting the oral cavity, for example.

The treatment of dental pain is multimodal and involves pharmacological and non-pharmacological techniques.[8] In the pharmacological treatment of acute pain, local anesthetic techniques, non-steroidal anti-inflammatory drugs and opioids should always be considered. Local anesthetic techniques can be applied in cats undergoing dental extractions using species-specific anatomical landmarks. In the pharmacological treatment of chronic pain, non-steroidal anti-inflammatory drugs as well as centrally acting analgesics such as gabapentin, amitriptyline and tramadol might be considered. The advent of feline-specific anti-nerve growth factor may contribute to feline pain management in patients with dental pain once further research supports its use.

Other Conditions of the Head

Ocular and ear painful conditions and procedures have been poorly investigated. These structures are highly innervated, and it is not surprising that they can produce significant pain, inflammation and discomfort. The specific

underlying condition should be treated; however, treatment itself can be painful (e.g. enucleation, total ear canal ablation) and analgesics are commonly required. Validated pain assessment tools have not been developed for these types of conditions. For example, it is not clear how ear position and orbital tightening could be affected by ocular and ear painful conditions, for example. In general, it is well accepted that opioids and NSAID therapy are used in the perioperative period for pain relief. Local anesthetic techniques such as the peribulbar or retrobulbar block should be used before enucleation since they provide analgesia and prevent the oculo-cardiac reflex during surgery. Ice therapy can be used to reduce inflammation and edema postoperatively.[9] Adjuvant analgesics can be administered when required, especially when contraindications exist for NSAID therapy (i.e. corticosteroid administration).

This lecture will present recent knowledge on painful conditions of the head and will ultimately impact feline pain management in clinical practice with better hospital experiences and better outcomes.

References

1. Mathews K, Krone P, Lascelles D, et al. Guidelines for recognition, assessment and treatment of pain: WSAVA Global Pain Council members and co-authors of this document. *J Small Anim Pract* 2014;55(6):E10-68.
2. Niemiec B, Gawor J, Nemec A, et al. World Small Animal Veterinary Association Global Dental Guidelines. *J Small Anim Pract* (in press).
3. Bellows J, Berg ML, Dennis S, et al. 2019 AAHA Dental Care Guidelines for Dogs and Cats. *J Am Anim Hosp Assoc* 55:49, 2019.
4. Watanabe R, Doodnaught G, Proulx C, et al. A multidisciplinary study of pain in cats undergoing dental extractions: A prospective, blinded, clinical trial. *PLoS One* 14:e0213195, 2019.
5. Watanabe R, Frank D, Steagall PV. Pain behaviors before and after treatment of oral disease in cats using video assessment: a prospective, blinded, randomized clinical trial. *BMC Vet Res* 16:100, 2020.
6. Evangelista MC, Watanabe R, Leung VSY, et al. Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. *Sci Rep* 9:19128, 2019.
7. Watanabe R, Doodnaught GM, Evangelista MC, et al. Inter-rater reliability of the Feline Grimace Scale in cats undergoing dental extractions. *Front Vet Sci* 7:302, 2020.
8. Watanabe R, Marcoux J, Evangelista MC, et al. The analgesic effects of buprenorphine (Vetergesic or Simbadol) in cats undergoing dental extractions: A randomized, blinded, clinical trial. *PLoS One* 15:e0230079, 2020.
9. Wright B, Kronen PW, Lascelles D, et al. Ice therapy: cool, current and complicated. *J Small Anim Pract* 61:267-271, 2020.

NOTES:

Feline Oral Squamous Cell Carcinoma: Recent Advances

Michael Nolan, DVM, PhD, DACVR-RO

Oral squamous cell carcinoma (SCC) represents a disease for which therapeutic responses and prognosis are generally regarded as poor.

Feline oral SCC can affect the mandible, maxilla, tongue (sublingual), pharynx or tonsils. The clinical appearance tends to vary with anatomic site. For example, maxillary SCC is usually a bone-invasive and ulcerative lesion; mandibular SCC is more often proliferative and firm; lingual and sublingual SCC can have a varied appearance, with either proliferation, or ulceration and necrosis, and often with extensive infiltration beyond what is palpable (as evidenced by CT and metabolic imaging).[1-3]

At the time of diagnosis, regional lymph metastasis is observed in approximately one-third of cases; pulmonary metastasis is observed in just 10% of cases.[4] Despite a relatively high incidence of metastasis, control of the primary tumor is what drives prognosis for most cats.

Mandibular SCC

A 1992 report in JAVMA described the use of hemimandibulectomy, combined with gastrostomy tube placement and adjunctive radiotherapy in seven cats; the 1-year survival rate was 57%, and the median survival time was 14 months. Local tumor recurrence was the cause of death for 6 of the 7 cats.[5]

In a subsequent study, Northrup and colleagues reported on 42 cats undergoing mandibulectomy alone; 22 of those cats had SCC, and the median disease-free interval was 340 days. These authors found that cats survival was longest in cats with rostral tumors (911 days), and shortest when >50% of the mandible had to be resected. There was a high rate of acute complications, and aggressive supportive care including placement of a feeding tube appeared essential to success. Of the six cats undergoing resection of >50% of their mandibles 3 never regained the ability to eat.[6]

Most recently, Boston et al (2018) reported on 8 cats undergoing radical mandibulectomy, in which 75-90% of the mandible was removed, and a feeding tube was placed. Seven of the 8 cats had SCC; the mean survival time was 712 days, and at least half of the cats survived >1 year. Six of the 8 cats achieved independent food intake after surgery.[7]

Together, these results indicate that for some cats with mandibular SCC, prolonged survival may be achievable with aggressive resections +/- adjunctive radiotherapy (to the primary tumor site plus regional lymph nodes). Some of these cats will be able to eat post-operatively, but many will become dependent upon feeding tubes. And all will become heavily dependent upon meticulous care from their owners in order to maintain adequate hygiene. Agreeing to move forward with radical treatments such as those described here must be made with acknowledgement and careful consideration of the cats' quality of life, and ethical dilemmas associated with this decision-making process.

SCC of Other Oral Sites

There are anecdotal reports of radical surgeries in cats resulting in long-term survival after diagnosis for SCC. For example, a Japanese group has described (unpublished) bilateral mandibulectomy combined with glossectomy and pharyngectomy for SCC of the feline tongue, with survival times in isolated cases that exceed 18 months. And indeed, more radical maxillectomies and cervical nodal dissections are becoming increasingly common in veterinary surgical oncology. Nonetheless, because extensive oral surgery is often less well tolerated in cats than in other species, and perhaps more importantly because locoregional recurrence is common even after extensive resections, surgery is often opted against for all but small rostral mandibular SCC lesions.

There are no data describing measurable tumor responses in cats treated with non-steroidal anti-inflammatory drugs (NSAIDs) alone for oral SCC. This likely reflects the fact that overexpression of cyclooxygenase-2 is uncommon in this disease.[8] Thus, the use of NSAIDs is best reserved for alleviation of tumor-associated discomfort in cats who can tolerate such therapy.

Injectable chemotherapy is largely regarded as ineffective. Use of a liposome-encapsulated platinum drug in 18 cats with oral SCC resulted in no measurable responses.[9] A single case with short-lived response to carboplatin has been reported.[10]

More recently, there has been growing enthusiasm for use of toceranib phosphate in cats with oral SCC; in one recent retrospective study, the overall biological response rate was 56%, with a median survival time of 123 days (vs. 43 days in an untreated control group). Unsurprisingly, cats with stable disease (or measurable tumor volume reduction) experienced the longest progression-free and overall survival times; interestingly, treatment with NSAIDs was also associated with significantly improved survival in this patient population. Treatment was generally very well-tolerated.[11] The generally favorable toxicity profile of toceranib phosphate in cats was recapitulated in another recent study, which reported adverse events in 17% of cats treated with a median dose of 2.75 mg/kg PO, 3 times weekly; in only one of 35 cats was severe (grade IV) toxicity reported.[12]

Conventional hypofractionated palliative-intent radiotherapy often results in measurable tumor volume reduction, however long-term survival is uncommon; the median survival time is typically between 3 and 5 months.[13] Radiosensitizers (e.g., mitoxantrone, gemcitabine, carboplatin, intratumoral etanidazole – which is a hypoxic cell sensitizer) have been used with limited success. Likewise, use of severe hypofractionation (e.g., stereotactic radiosurgery) also appears to be of limited use in this disease.[14] Accelerated hypofractionated protocols can be associated with more acute oral mucositis and pharyngitis, but does tend to provide slightly longer periods of local tumor control (~5-6 months on average) – particularly for early stage disease (small tumors; when treated with 48 Gy in 10 daily fractions, cats with T1 tumors had a median progression-free survival time of 590 days).[15-17] And intriguing combination which has not been reported on in the published literature is the combination of a dose-intense irradiation protocol such as this, plus toceranib phosphate.

Prevention

Because feline oral SCC has such a poor prognosis, it is important to consider measures which might aid in reducing risk. Reported risk factors include use of flea collars (relative risk, RR: 5.3, p = 0.002), a diet consisting primarily of canned food (RR: 3.6; p = 0.014), and high intake of canned tuna (RR: 4.7; p = 0.004); the same study also reported a non-significant increase in risk with exposure to household environmental tobacco smoke (RR ~2; p = 0.11).[18] A subsequent study by the same research group provides additional support for a causal relationship between tobacco smoke exposure and development of feline oral SCC.[19]

Novel Therapies

Cats with oral SCC would benefit from a low-cost treatment that would provide effective palliation, and which could be administered in the primary care veterinarian's office.

Enhanced ethanol ablation (EEA) is ultra-low-cost, accessible, portable and capable of treating large lesions. Ethanol ablation induces necrosis through protein denaturation and cytoplasmic dehydration via intratumoral ethanol injection.[20] It was originally used in the treatment of hepatocellular carcinoma with 5-year survival rates comparable to surgical resection.[21] It is a well-established standard treatment option for small (<5cm), unresectable liver tumors, and has low complication rates.[22] While the liver is the most common application, ethanol ablation has successfully been used in the treatment of cardiomyopathies,[23] parathyroid[24] and pancreatic tumors[25] and metastatic lymph nodes[26,27] demonstrating that this technique could have broad clinical impact. But traditional ethanol ablation does not work well for large, superficial and/or unencapsulated tumors. To enhance the traditional ethanol ablation technique, we propose the addition of ethyl cellulose, a nontoxic viscous additive. Ethyl cellulose is ethanol-soluble, but water-insoluble. When mixed with ethanol it increases the viscosity of the solution (which alone has been shown to increase efficacy of intratumoral injections).[28] When an ethyl cellulose-ethanol solution contacts the aqueous environment it forms an ethanol-based gel. A recent publication demonstrates proof-of-concept of this EEA technique for tumor ablation in superficial chemically induced oral tumors in the hamster cheek pouch.[29] Thus, EEA is poised to have a large impact in resource-limited settings as it costs <$1 per treatment, requires no specialized equipment and can effectively treat lesions up to 5 cm.[30-33]

Upon this background, we set out to assess the safety, feasibility and biological activity of EEA for cats with sublingual SCC. With funding from the Winn Feline Foundation, a proof-of-concept clinical trial was performed in 2019. Based on our experience in 6 cats, we now feel confident in concluding that EEA is not a viable treatment option for sublingual SCC in cats; while the treatment effectively reduces tumor volume, the simultaneous loss of lingual function is poorly tolerated. However, we are greatly encouraged that EEA has demonstrable anti-tumor efficacy in the setting of feline oral SCC. Furthermore, we firmly believe that it is worth investigating the feasibility of using EEA to treat non-lingual sites for oral SCC in cats. We are actively seeking funding to allow testing of a modified EEA protocol for bone-invasive (e.g., maxillary and mandibular) SCC in cats.

Recent laboratory-based studies have identified therapeutic targets that might also ultimately yield useful treatments for feline oral SCC; these include: STAT3,[34] Bmi-1,[14] and NQO1,[35] among others.

References

1. Bilgic O, Duda L, Sánchez MD, Lewis JR. Feline Oral Squamous Cell Carcinoma: Clinical Manifestations and Literature Review. *Journal of Veterinary Dentistry.* 2015;32(1):30-40.
2. Gendler A, Lewis JR, Reetz JA, Schwarz T. Computed tomographic features of oral squamous cell carcinoma in cats: 18 cases (2002-2008). *J Am Vet Med Assoc.* 2010;236(3):319-325.
3. Yoshikawa H, Randall EK, Kraft SL, Larue SM. Comparison between 2-(18) F-fluoro-2-deoxy-d-glucose positron emission tomography and contrast-enhanced computed tomography for measuring gross tumor volume in cats with oral squamous cell carcinoma. *Vet Radiol Ultrasound.* 2013;54(3):307-313.
4. Soltero-Rivera MM, Krick EL, Reiter AM, Brown DC, Lewis JR. Prevalence of regional and distant metastasis in cats with advanced oral squamous cell carcinoma: 49 cases (2005-2011). *J Feline Med Surg.* 2014;16(2):164-169.
5. Hutson CA, Willauer CC, Walder EJ, Stone JL, Klein MK. Treatment of mandibular squamous cell carcinoma in cats by use of mandibulectomy and radiotherapy: seven cases (1987-1989). *J Am Vet Med Assoc.* 1992;201(5):777-781.
6. Northrup NC, Selting KA, Rassnick KM, et al. Outcomes of cats with oral tumors treated with mandibulectomy: 42 cases. *J Am Anim Hosp Assoc.* 2006;42(5):350-360.
7. Boston SE, van Stee LL, Bacon NJ, et al. Outcomes of eight cats with oral neoplasia treated with radical mandibulectomy. *Vet Surg.* 2020;49(1):222-232.
8. DiBernardi L, Doré M, Davis JA, et al. Study of feline oral squamous cell carcinoma: potential target for cyclooxygenase inhibitor treatment. *Prostaglandins Leukot Essent Fatty Acids.* 2007;76(4):245-250.
9. Fox LE, Rosenthal RC, King RR, et al. Use of cis-bis-neodecanoato-trans-R,R-1,2-diaminocyclohexane platinum (II), a liposomal cisplatin analogue, in cats with oral squamous cell carcinoma. *Am J Vet Res.* 2000;61(7):791-795.
10. Kisseberth WC, Vail DM, Yaissle J, et al. Phase I clinical evaluation of carboplatin in tumor-bearing cats: a Veterinary Cooperative Oncology Group study. *J Vet Intern Med.* 2008;22(1):83-88.
11. Wiles V, Hohenhaus A, Lamb K, Zaidi B, Camps-Palau M, Leibman N. Retrospective evaluation of toceranib phosphate (Palladia) in cats with oral squamous cell carcinoma. *J Feline Med Surg.* 2017;19(2):185-193.
12. Olmsted GA, Farrelly J, Post GS, Smith J. Tolerability of toceranib phosphate (Palladia) when used in conjunction with other therapies in 35 cats with feline oral squamous cell carcinoma: 2009-2013. *J Feline Med Surg.* 2017;19(6):568-575.
13. Sabhlok A, Ayl R. Palliative radiation therapy outcomes for cats with oral squamous cell carcinoma (1999-2005). *Vet Radiol Ultrasound.* 2014;55(5):565-570.
14. Yoshikawa H, Maranon DG, Battaglia CLR, et al. Predicting clinical outcome in feline oral squamous cell carcinoma: tumour initiating cells, telomeres and telomerase. *Vet Comp Oncol.* 2016;14(4):371-383.
15. Poirier VJ, Kaser-Hotz B, Vail DM, Straw RC. Efficacy and toxicity of an accelerated hypofractionated radiation therapy protocol in cats with oral squamous cell carcinoma. *Vet Radiol Ultrasound.* 2013;54(1):81-88.
16. Fidel JL, Sellon RK, Houston RK, Wheeler BA. A nine-day accelerated radiation protocol for feline squamous cell carcinoma. *Vet Radiol Ultrasound.* 2007;48(5):482-485.
17. Fidel J, Lyons J, Tripp C, Houston R, Wheeler B, Ruiz A. Treatment of oral squamous cell carcinoma with accelerated radiation therapy and concomitant carboplatin in cats. *J Vet Intern Med.* 2011;25(3):504-510.
18. Bertone ER, Snyder LA, Moore AS. Environmental and lifestyle risk factors for oral squamous cell carcinoma in domestic cats. *J Vet Intern Med.* 2003;17(4):557-562.
19. Snyder LA, Bertone ER, Jakowski RM, Dooner MS, Jennings-Ritchie J, Moore AS. p53 expression and environmental tobacco smoke exposure in feline oral squamous cell carcinoma. *Vet Pathol.* 2004;41(3):209-214.
20. Shiina S, Tagawa K, Unuma T, et al. Percutaneous ethanol injection therapy for hepatocellular carcinoma. A histopathologic study. *Cancer.* 1991;68(7):1524-1530.
21. Ryu M, Shimamura Y, Kinoshita T, et al. Therapeutic results of resection, transcatheter arterial embolization and percutaneous transhepatic ethanol injection in 3225 patients with hepatocellular carcinoma: a retrospective multicenter study. *Jpn J Clin Oncol.* 1997;27(4):251-257.
22. Adult Primary Liver Cancer Treatment (PDQ(R)): Patient Version. In: *PDQ Cancer Information Summaries.* Bethesda (MD)2002.
23. Sorajja P, Valeti U, Nishimura RA, et al. Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *Circulation.* 2008;118(2):131-139.
24. Solbiati L, Giangrande A, De Pra L, Bellotti E, Cantu P, Ravetto C. Percutaneous ethanol injection of parathyroid tumors under US guidance: treatment for secondary hyperparathyroidism. *Radiology.* 1985;155(3):607-610.
25. Jurgensen C, Schuppan D, Neser F, Ernstberger J, Junghans U, Stolzel U. EUS-guided alcohol ablation of an insulinoma. *Gastrointest Endosc.* 2006;63(7):1059-1062.

26. Artifon EL, Lucon AM, Sakai P, et al. EUS-guided alcohol ablation of left adrenal metastasis from non-small-cell lung carcinoma. *Gastrointest Endosc.* 2007;66(6):1201-1205.
27. DeWitt J, Mohamadnejad M. EUS-guided alcohol ablation of metastatic pelvic lymph nodes after endoscopic resection of polypoid rectal cancer: the need for long-term surveillance. *Gastrointest Endosc.* 2011;74(2):446-447.
28. Wang Y, Liu S, Li CY, Yuan F. A novel method for viral gene delivery in solid tumors. *Cancer Res.* 2005;65(17):7541-7545.
29. Morhard R, Nief C, Barrero Castedo C, et al. Development of enhanced ethanol ablation as an alternative to surgery in treatment of superficial solid tumors. *Sci Rep.* 2017;7(1):8750.
30. Kuang M, Lu MD, Xie XY, et al. Ethanol ablation of hepatocellular carcinoma Up to 5.0 cm by using a multipronged injection needle with high-dose strategy. *Radiology.* 2009;253(2):552-561.
31. Ebara M, Okabe S, Kita K, et al. Percutaneous ethanol injection for small hepatocellular carcinoma: therapeutic efficacy based on 20-year observation. *J Hepatol.* 2005;43(3):458-464.
32. Huang GT, Lee PH, Tsang YM, et al. Percutaneous ethanol injection versus surgical resection for the treatment of small hepatocellular carcinoma: a prospective study. *Ann Surg.* 2005;242(1):36-42.
33. Heilo A, Sigstad E, Fagerlid KH, et al. Efficacy of ultrasound-guided percutaneous ethanol injection treatment in patients with a limited number of metastatic cervical lymph nodes from papillary thyroid carcinoma. *J Clin Endocrinol Metab.* 2011;96(9):2750-2755.
34. Brown ME, Bear MD, Rosol TJ, Premanandan C, Kisseberth WC, London CA. Characterization of STAT3 expression, signaling and inhibition in feline oral squamous cell carcinoma. *BMC Vet Res.* 2015;11:206.
35. Lundberg AP, Francis JM, Pajak M, et al. Pharmacokinetics and derivation of an anticancer dosing regimen for the novel anti-cancer agent isobutyl-deoxynyboquinone (IB-DNQ), a NQO1 bioactivatable molecule, in the domestic felid species. *Invest New Drugs.* 2017;35(2):134-144.

NOTES:

Chronic Seizure Management for Cats

Heidi Barnes Heller, DVM, DACVIM (Neurology)

Introduction

Seizures occurring in cats have the same lesion localization as with dogs (prosencephalon). Seizure classification for cats is similar to dogs and is taken from either the International Veterinary Epilepsy Task Force recommendations, (IVETF), or the International League Against Epilepsy (ILAE: human classification system). See Table 1

TABLE 1: Classification schemes used for feline epilepsy

ILAE (2011) classification	IVETF classification	Definition
Genetic epilepsy	Idiopathic epilepsy	An intracranial disorder that has a confirmed genetic predisposition in the breed or animal
Unknown epilepsy	Idiopathic epilepsy	No known genetic predisposition, but no identifiable cause on diagnostic testing (MRI, CSF, laboratory)
Structural epilepsy	Structural epilepsy	An identifiable cause on diagnostic testing. E.g., brain tumor, or encephalitis.
Metabolic seizures	Reactive seizures	NOT epilepsy but is a seizure disorder. E.g. hypoglycemia.

Differential Diagnosis

The differential list is driven by the history, and neurologic examination. Idiopathic epilepsy (IE), or epilepsy of unknown origin, occurs in approximately 30- 60% of cats.[1–6] The diagnosis of IE is achieved through complete metabolic screening, acquisition of a normal brain MRI and cerebrospinal fluid (CSF) analysis. A clinical diagnosis of IE is made by ruling out all other causes of seizures. Age at diagnosis of IE varies widely in cats, therefore cats with seizure onset greater than 6 years of age should not automatically be given a poor prognosis.[1] Having said that, cats diagnosed with IE are typically younger than cats diagnosed with structural epilepsy.[1–4] Idiopathic epilepsy accounted for approximately 26% of the cats diagnosed with seizures less than 1 year of age in our recent study.[7] Structural epilepsy is the most common etiologic classification in cats of all ages and may be caused by neoplastic, inflammatory, infectious, traumatic, vascular or degenerative causes. [1,3,4,7,8] The diagnosis of SE requires the identification of an intracranial disease in an area of the brain likely cause seizures, and really needs diagnostic imaging (MRI) and spinal fluid analysis to achieve this diagnosis.

Treatment Options

Choosing the best AED should be based on the seizure phenotype, the cat's health status and owner considerations (frequency of administration, cost, and liquid vs tablet formulation).Seizure control is defined in the literature as a "greater than 50% reduction in seizures". Phenobarbital (per os) is often the drug of choice for feline seizures, regardless of the underlying cause. In a recent study, we noted that most cats attained seizure control if the phenobarbital serum concentration was between 15-40 ug/ml. Further, serum biochemistry analysis was normal in over 90% of the cats and side effects are typically rare or well tolerated. [9] *Cats do not have the same elevation in liver values as dogs, making this medication easier to tolerate long-term*.

The IVETF published guidelines for initiation of therapy for dogs, which could be extrapolated to cats. Among other parameters, the IVETF recommends starting anti-epileptic drugs (AED) when any dog has 2 or more seizures in 6 months and/or any 1 seizure lasting longer than 5 minutes.[10] A secondary reason to consider starting therapy is the presence of especially severe (e.g. aggression) or long-lasting (e.g. longer than 24 hours) clinical signs during the postictal phase. I also encourage initiation of AED if the cat is at reasonable risk of additional seizures, even if the aforementioned frequency recommendations were not met. An example of this may include a cat with a brain tumor in the parietal lobe, or a young cat with severe hydrocephalus. Other authors have advocated for more aggressive initiation of treatment and suggested AED treatment should be initiated if 2 or more seizures occur in 6 weeks.[2] Regardless, a delay in AED initiation may result in a longer time to seizure control, or seizure freedom. [11]

Phenobarbital
Phenobarbital is the most commonly used AED in cats. [9,11–13] Rare side effects and no adverse biochemical or hematological events have been reported following use in cats. [14] Side effects may include sedation, ataxia, weakness, especially during the first two weeks of treatment. Standard dosing for cats is 2-5 mg/kg *per os* q12h (reported ranges 1.8 – 10 mg/kg/day.) [2,9,11,14,15] The therapeutic interval has not been established in cats, however the dog reference interval of 15-45 mcg/mL may be used or a more narrow therapeutic window between 23- 30 mcg/mL has been recommended. [2,9,13,15] In one study, seizure control was achieved in 93% of cats with a serum phenobarbital concentration between 15 and 45 mcg/ml, regardless of underlying etiology.[9] Alternative administration routes including transdermal will be discussed in a different talk.

Levetiracetam
Levetiracetam is an AED that has a novel mechanism of action compared to other common AED. [16,17] The therapeutic interval for levetiracetam is unknown and has been extrapolated from humans for use in dogs and cats (5-45 mcg/ml).[16,18,19] Reported side effects in cats receiving levetiracetam include: mild transient hypersalivation, inappetence, and mild lethargy.[16,17] There are currently two formulations available: 1) standard release levetiracetam (SRL) and 2) extended release levetiracetam (XRL). Following pharmacokinetic analysis a dosage of 20 mg/kg *per os* q8h was recommended for cats.[16] Extended release levetiracetam is currently available in 500 mg and 750 mg size tablets. Administration of 500 mg once daily has been evaluated for safety in cats however clinical trials evaluating efficacy are lacking. Crushing, splitting or chewing the tablets is not recommended therefore its usefulness in cats has been limited. Use of XRL in cats allows decreased frequency of oral administration therefore improving the quality of life for the cat and client. Tolerance of levetiracetam has been suggested in dogs, however this has yet to be documented in cats. The lack of documentation should not exclude the possibility of long-term tolerance (termed 'honeymoon effect' by some authors); rigorous seizure frequency monitoring should be maintained if a cat receives long-term levetiracetam.

Other medications which can be used, but for which there is limited feline data, include diazepam and levetiracetam. See table 2 below for details on dosing. Bromide is not recommended for cats due to an irreversible eosinophilic bronchopneumonia.

Table 2: Common anticonvulsant drugs and doses for cats

Drug	Dose (PO)	Monitoring	Possible clinical side effects	Use
Phenobarbital	3-5 mg/kg BID	Serum levels 15-45 ug/mL	Sedation, ataxia, PP, PD	Generalized or focal seizures
Diazepam	0.5-1.0 mg/kg TID-BID	Not performed	Hepatic failure, sedation, PP, PD	Refractory generalized seizures
Levetiracetam	20 mg/kg TID	Available	Lethargy, anorexia	Adjunct to phenobarbital

References

1. Barnes HL, Chrisman CL, Mariani CL, Sims M, Alleman AR. Clinical signs, underlying cause, and outcome in cats with seizures: 17 cases (1997-2002). *J Am Vet Med Assoc*. 2004;225(11):1723-1726.
2. Pakozdy a., Halasz P, Klang A. Epilepsy in cats: Theory and practice. *J Vet Intern Med*. 2014;28(2):255-263.
3. Pakozdy A, Leschnik M, Sarchahi AA, Tichy AG, Thalhammer JG. Clinical comparison of primary versus secondary epilepsy in 125 cats. *J Feline Med Surg*. 2010;12(12):910-916. doi:10.1016/j.jfms.2010.07.001
4. Schriefl S, Steinberg TA, Matiasek K, Ossig A, Fenske N, Fischer A. Etiologic classification of seizures, signalment, clinical signs, and outcome in cats with seizure disorders: 91 cases (2000–2004). *J Am Vet Med Assoc*. 2004;233:1591-1597.
5. Wahle AM, Brühschwein A, Matiasek K, et al. Clinical characterization of epilepsy of unknown cause in cats. *J Vet Intern Med*. 2014;28(1):182-188.
6. Schwartz-Porsche D, Kaiser E. Feline Epilepsy. *Probl Vet Med*. 1989;1(4):628-649.
7. Qahwash M, Barnes Heller HL. Seizure etiologic classification and long-term outcome for cats with juvenile-onset seizures. *J Am Vet Med Assoc*. 2018;253(6):763-767.
8. Parent JM, Quesnel a D. Seizures in cats. *Vet Clin North Am Small Anim Pract*. 1996;26:811-825.
9. Finnerty KE, Barnes Heller HL, Mercier MN, Giovanella CJ, Lau VW, Rylander H. Evaluation of therapeutic phenobarbital concentrations and application of a classification system for seizures in cats: 30 cases (2004-2013). *J Am Vet Med Assoc*. 2014;244(2):195-199.
10. Bhatti SFM, De Risio L, Muñana K, et al. International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe. *BMC Vet Res*. 2015;11(1):176.

11. Pakozdy a., Sarchahi a. a., Leschnik M, Tichy a. G, Halasz P, Thalhammer JG. Treatment and long-term follow-up of cats with suspected primary epilepsy. *J Feline Med Surg*. 2012;15(4):267-273.
12. Smith Bailey K, Dewey CW. The seizuring cat. Diagnostic work-up and therapy. *J Feline Med Surg*. 2009;11(5):385-394.
13. Thomas WB. Idiopathic Epilepsy in Dogs and Cats. *Vet Clin North Am Small Anim Pract*. 2010;40(1):161-179.
14. Cochrane SM, Black WD, Parent JM, Allen DG, Lumsden JH. Pharmacokinetics of phenobarbital in the cat following intravenous and oral administration. *Can J Vet Res*. 1990;54(1):132-138.
15. Platt SR. Feline seizure control. *J Am Anim Hosp Assoc*. 2001;37(6):515-517.
16. Carnes MB, Axlund TW, Boothe DM. Pharmacokinetics of levetiracetam after oral and intravenous administration of a single dose to clinically normal cats. *Am J Vet Res*. 2011;72(9):7-12.
17. Bailey KS, Dewey CW, Boothe DM, Barone G, Kortz GD. Levetiracetam as an adjunct to phenobarbital treatment in cats with suspected idiopathic epilepsy. *J Am Vet Med Assoc*. 2008;232(6):867-872.
18. Beasley MJ, Boothe DM. Disposition of extended release levetiracetam in normal healthy dogs after single oral dosing. *J Vet Intern Med*. 2015;29:1348-1353.
19. Peters RK, Schubert T, Clemmons R, Vickroy T. Levetiracetam rectal administration in healthy dogs. *J Vet Intern Med*. 2014;28(2):504-509.

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Neurologic Examination for Busy Practitioners

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Introduction

The neurologic system is divided into CNS (Central nervous system) and PNS (peripheral nervous system). We will start with the CNS. The CNS is divided by the foramen magnum into the brain and spinal cord. To facilitate easy discussion, we will define commonly used terms. Specifically, the terms *brain, forebrain* and *hindbrain* should be understood. *Brain* refers to all neurologic tissue within the cranial vault. *Forebrain* refers to the Prosencephalon and *hindbrain* refers to the metencephalon and myelencephalon. Often, we clump parts of the CNS together in conversation to denote sections of the nervous system that commonly present with similar signs. You should also be familiar with the terms *prosencephalon* (inclusive of cerebrum, thalamus and thalamic components) and *brainstem* (inclusive of midbrain, pons and medulla oblongata). The divisions, and associated vocabulary, are as follows:

Latin name	English name	Associated cranial nerve(s)
Telencephalon	Cerebrum	CN I: Olfactory
Diencephalon	Thalmencephalon (Thalamus, metathalamus, epithalamus) Hypothalamus Subthalamus	CN II: Optic
Mesencephalon	Midbrain	CN III: Oculomotor CN IV: Trochlear
Metencephalon	Pons Cerebellum	CN V: Trigeminal
Myelencephalon	Medulla oblongata	CN VI: Abducent CN VII: Facial CN VIII: Vestibulocochlear CN IX: Glossopharyngeal CN X: Vagus CN XI: (Spinal) accessory CN XII: Hypoglossal

Cranial Nerves

There are 12 paired cranial nerves, each associated with a specific part of the CNS. All are associated with the brainstem except the sense of smell, which is in fact a collection of nerves (olfactory bulb) and projections attached to the rostral portion of the cerebrum. We will discuss assessment of cranial nerves using the neurologic examination. Localization to the peripheral portion of the nerve, or the brainstem part of the nerve, is the focus of intracranial neuroanatomic lesion localization. We will discuss this in detail below, after reviewing the pertinent anatomy.

Cranial nerve	Function	Neurologic examination
CN I: Olfactory	Smell	Watch the dog sniff, ask about eating habits. * Difficult to objectively evaluate
CN II: Optic	Sight	Menace, PLR, Cotton ball test, tracking
CN III: Oculomotor	Somatic: eye movement Innervates all extraocular muscles except lateral rectus and dorsal oblique Autonomic: Parasympathetic function to the pupil	Physiologic nystagmus (medial movement), Strabismus (if present this indicates an abnormalities of CN) PLR
CN IV: Trochlear	Eye position	Strabismus

Track B

CN V: Trigeminal **Ophthalmic** **Maxillary** **Mandibular**	Sensory to the face, cornea Close the jaw (muscles of mastication)	Sensory: Corneal reflex, blink reflex, sensory assessment of the nares and lips Motor: ability to CLOSE the jaw
CN VI: Abducent	Somatic eye movement	Physiologic nystagmus (lateral movement), Strabismus
CN VII: Facial	Somatic: muscles of facial expression Autonomic: parasympathetic innervation to the lacrimal gland, 3rd eyelid gland, palatine and nasal glands, taste rostral tongue	Menace, blink reflex, lip and ear twitch
CN VIII: vestibulocochlear	Sensory: balance and hearing Innervates: vestibulospinal tracts, MLF (eye movement), reticular formation, cerebrum and cerebellum	Physiologic nystagmus, pathologic nystagmus, positional strabismus, head position (tilt), ataxia, hearing test (BAER)
CN IX: Glossopharyngeal	Sensory to pharynx Motor to pharynx Autonomic: parasympathetic function – taste from the caudal tongue	Gag reflex
CN X: Vagus	Motor to pharynx Parasympathetic: taste to pharynx, larynx, heart rate, GI motility, other	Gag reflex
CN XI: Spinal accessory	Motor: trapezius, sternocephalicus, brachiocephalicus	Palpation of associated muscles
CN XII: Hypoglossal	Motor: tongue	Move tongue left and right, visually assess for symmetry and movement.

Cerebellum

If higher areas initiate movement, the cerebellum's main job is to coordinate movement. By using sensory tracts from the spinal cord, the cerebellum can receive information on the position and movement of the body in space and help smoothly transition from one event to the next. The cerebellum is made up of a central region, called the vermus, and two peripheral regions, called hemispheres. Evaluation of the cerebellum is largely based on gait assessment and evidence of vestibular dysfunction. Animals with cerebellar disease will have normal mentation, normal cranial nerves (other than possible vestibular disease but this isn't specifically cranial nerve related because the cerebellum has vestibular influence as well) and normal strength. Occasionally postural deficits will be noted with cerebellar disease. Most notably, animals with cerebellar disease have an intention tremor and hypermetria due to their lack of ability to smoothly transition from one voluntary movement to the next. Importantly, these animals will be *normal* at complete rest. Vestibular signs can also be associated with cerebellar disease and can be differentiated from brainstem or peripheral vestibular disease due to the concurrent presence of hypermetria, intention tremors and truncal sway. Paradoxical vestibular disease occurs when the head tilt is directed opposite the lesion. This occurs with damage in the caudal cerebellar peduncle or cerebellum. Paradoxical vestibular disease is a localization not a differential diagnosis! Animals with paradoxical vestibular disease will have hypermetria (+/- paw replacement deficits) on the side opposite the head tilt. When localizing, one should localize the lesion in the cerebellum based on the hypermetria. For example, a right sided hypermetria should indicate a right cerebellar lesion localization, regardless of the direction of head tilt.

Postural Reactions

Postural reactions are used to evaluate the sensory system from the limbs; however an intact motor system is

required for proper replacement of the foot as well. Visualize a pelvic limb paw placed in dorsal positioning (a.k.a. upside down). The sensory receptors in the foot will relay the mispositioning information up the peripheral nerve (in this example, the sciatic nerve) to the spinal cord and then, without synapsing, all the way up the spinal cord to the brainstem. For a conscious reaction, the tract will cross in the midbrain and end in the opposite cerebral cortex. At which point, the descending motor tracts will be activated to replace the foot in the proper position. All parts of this pathway must be functional for the foot to be returned to the right position. Disruption of this pathway at the peripheral nerve, spinal cord, brainstem or prosencephalon can result in paw replacement deficits. Conscious proprioception (a.k.a CPs) was the term previously used when referring the ascending sensory input from the toes to the cerebrum. As it turns out this evaluates more than just the conscious proprioceptive tracts therefore the term has been replaced by the much less easy to say, "Paw replacement test". However, this term more accurately reflects that we are not just testing conscious proprioception. In addition to the paw replacement test, proprioception can also be evaluated by hopping, tactile placing, visual placing, wheel barrowing and hemi hopping.

Motor and Gait Assessment
Gait analysis evaluates both the sensory and motor component of movement. There are three options for gait abnormalities: ataxia, paresis or lameness. Of course, animals may have a one or more of these during gait assessment. There are three recognized forms of ataxia: proprioceptive, vestibular and cerebellar. Animals with ataxia have a neurologic disease, because ataxia is considered to be evidence of poor sensory function. Paresis, results from an inability to generate a gait or the inability to support weight and is a sign of dysfunction of the motor system. Paresis may be noted with neurologic, orthopedic or myopathic diseases. Therefore, an animal with ataxia should have a neuroanatomic lesion localization when you have completed the examination, animals with purely paresis may have neurologic, orthopedic or myopathic lesion localization when the examination is completed.

As you recall there are upper motor neurons (UMN) and lower motor neurons (LMN) which govern movement in the limbs. The UMN cell bodies are intracranial, and the LMN cell bodies are in the spinal cord. Weakness of UMN manifests as decreased strength and/or movement but with intact reflexes. Weakness of LMN results in decreased strength and/or movement with reduced reflexes. Common definitions used to describe motor function are in the table below.

Term	Definition
Para-	Pelvic legs
Tetra-	All four legs
Hemi-	One half (left or right)
-plegia	Unable to move legs AT ALL
-paresis	Weak but able to move legs, on own, with or without support
Ataxia	Wobbly – i.e. failure of muscle coordination
Reflex	Non-voluntary motor reaction to sensory stimulus

Reflexes
Reflexes assessed during the examination evaluate specific lower motor neuron groups. We commonly evaluate the triceps, biceps, extensor carpi radialis and withdrawal reflex in the thoracic limb, and femoral, cranial tibialis, gastrocnemius and withdrawal reflexes in the pelvic limbs. Some neurologists will also perform the sciatic nerve reflex in the sciatic notch. A reduction or loss of a reflex indicates a problem in the stretch receptor or sensory nerve, cell body at the level of the spinal cord, motor nerve, neuromuscular junction or muscle. The cell bodies for the LMN associated with the limb reflexes are located in spinal cord segments C6-T2 and L4-S2. I do not rely heavily on hyperreflexia in clinical practice as it can vary by Practitioner and simply indicates a lesion rostral to the evaluated reflex arc. This is of limited use and therefore I focus on identifying normal or reduced reflexes in clinical patients.

Lesion Localization: Prosencephalon
After completing the neurologic examination, one will need to localize the lesion in order to produce a list of differential diagnoses. The following can be abnormal with a lesion in the Prosencephalon: seizures, change in mentation, behavior change, loss of learned response (i.e. house training), circling TOWARDS the lesion, aimless pacing or wandering, head pressing, postural reaction deficits CONTRALATERAL to the lesion, visual deficits CONTRALATERAL to the lesion with normal PLR, head or trunk twisted IPSILATERAL to the lesion and hemi-inattention or neglect of the CONTRALATERAL side.

Lesion Localization: Brainstem
When presented with a patient with a cranial nerve deficit in CN III-XII one must determine if the lesion is located in

the brainstem (i.e. centrally) or in the peripheral nerve itself (i.e. peripherally). Take the following steps to do so:

1. Identify the cranial nerve affected (i.e. facial nerve = CN 7)
2. Identify the segment of brainstem associated with the nucleus of this cranial nerve (i.e. medulla)
3. Are any **long tract deficits** (postural reaction deficits, UMN dysfunction) or **mentation changes** (obtunded, stupor, coma) present?
4. If yes, the lesion is in the brainstem segment associated with the cranial nerve (i.e. medulla)
5. If no, the lesion is in the peripheral nerve or receptor (if sensory) of the affected nerve

Lesion localization: Vestibular system: Localization of vestibular disease proves especially challenging for many students therefore this tablet has been created specifically for localization of vestibular disease. Other than the cerebellar signs, the brainstem lesion localization signs (motor tract dysfunction, ataxia, and mentation changes) can be applied to all cranial nerves III-XII. Deficits of CN I and II are unique and localized differently. (See below)

	Peripheral (CN 8)	Medulla oblongata	Cerebellum
Head tilt	+ (ipsilateral)	+ (ipsilateral)	+ (contralateral)
Nystagmus	+	+	+
Ataxia	+	+	+
Postural reaction deficits	-	+ (ipsilateral)	Possible (ipsilateral)
Paresis	-	+ (ipsilateral)	-
Decreased mentation	-	+	-
Hypermetria	-	-	+ (ipsilateral)
Intention tremors	-	-	+
Other cranial nerves	+/- (CN 7 sometimes)	+/-	-

Lesion localization: Visual system: Evaluation of the visual system from a neurologist perspective is limited to the use of menace testing, pupillary light reflex (PLR) testing and visual tracking. The menace response is a learned response therefore animals less than 3 months of age may not have appropriate menace response, and this should not be considered abnormal. Menace response is best considered if you can draw out the pathway. Cranial nerve II functionally crosses at the optic chiasm in dogs and cats. If a menacing hand gesture is made in front of the animal's face, the visual stimuli are transmitted down CN II, crossing at the chiasm, and perceived by the opposite cerebrum. To blink, a large and very complicated reflex pathway is activated which ultimately ends with synapse on the nucleus of CN VII at the level of the medulla oblongata. At this point, the animal will blink its eye. Dysfunction of CN II, opposite cerebrum, and ipsilateral CN VII can cause a menace response deficit. Therefore, PLR testing is employed to evaluate CN II from a different perspective. For PLR, light is shone into the eye and transmitted down the same CN II, however prior to entering the prosencephalon it splits from menace fibers and dives into the midbrain to synapse on the parasympathetic nucleus of cranial nerve III (PSNCN III). Parasympathetic fibers then piggyback along CN III back to the globe to constrict the pupil. Damage to CN II, midbrain or CN III can result in PLR deficits.

Lesion Localization: Spinal Cord

The spinal cord segments are divided based on the location of the LMN cell body responsible for the limb reflexes, called intumescences. If you recall, these are located at C6-T2 and L4-S2. The other spinal cord sections are C1-C5 and T3-L3 which are in essence the 'left over' non-reflex oriented sections of the spinal cord. I recommend memorizing the intumescences. At times it may be difficult to localize a patient to a peripheral neuropathy or spinal cord lesion causing lower motor neuron signs. As a rule, spinal cord compression results in initial worsening of the sensory tracts (ataxia, postural deficits), secondly the motor tracts (paresis) and finally deep pain. *If an animal is markedly weak yet has intact postural reactions it is less likely to be a spinal cord lesion and more likely to be a lesion in the peripheral nerve, neuromuscular junction or muscle.* The following table lists the abnormalities found on neurologic examination, for a patient with a myelopathy at the specified location.

Spinal cord segment	Reflexes	Gait	Postural reactions
C1-C5	Normal all limbs	Tetraparesis/plegia Ataxia all limbs	Affected all limbs
C6-T2	Reduced/absent thoracic Normal pelvic	Tetraparesis/plegia Ataxia pelvic limbs, variable thoracic limbs	Affected pelvic limbs, variable thoracic limbs
T3-L3	Normal all limbs	Paraparesis/plegia	Affected pelvic limbs

		Ataxia pelvic limbs	only
L4-S2	Normal thoracic Reduced/absent pelvic	Paraparesis/plegia Rarely ataxia of the pelvic limbs	Variable pelvic limbs

References:

1. Guyton AC, Hall JE. Textbook of medical physiology 10th ed. WB Saunders Co. Philadelphia, 2000.
2. deLahunta A, Glass E. Veterinary Neuroanatomy and Clinical Neurology 3rd ed. Saunders Elsevier. St. Louis. 2009.
3. King AS. Physiologic and Clinical Anatomy of Domestic mammals. Vol 1: Central Nervous System. Blackwell Science Oxford, 1987.
4. Taylor AR, Kerwin SC. Clinical evaluation of the feline neurologic patient. Veterinary Clinics of North America: small animal practice. 2018:48(1)1-10.
5. Rylander H. The neurologic examination in companion animals. Today's Veterinary Practice 2013(January/February): 18-22.

Lesion Localization Practice Cases

Give a single lesion localization for each of the following cases. Only the abnormalities are listed; if not listed, it's not abnormal!

1. Dog with a head tilt to the right, falling and circling right, absent paw replacement right pelvic and thoracic limbs, horizontal nystagmus (fast phase left) and mild right hemiparesis.
2. Circling to the left, right pelvic limb paw replacement deficit
3. Inability to close the right eyelid; obtunded with paw replacement deficit right pelvic limb
4. Seizures with a left pelvic limb paw replacement deficit.
5. Coma, midrange fixed pupils (unresponsive to light), tetraplegia, absent postural reactions all limbs.
6. Tetraplegia, absent conscious proprioception of all four limbs.
7. Blind, no PLR bilaterally, no menace bilaterally.
8. Inability to close the jaw (dog's inability).
9. Tetraparesis with no spinal reflexes in the front limbs and hyperactive reflexes in the pelvic limbs, absent postural reactions of all four limbs.
10. Non-ambulatory tetraparesis with reduced femoral reflexes, reduced withdrawal in all limbs, reduced (but present) postural reactions in all four limbs.
11. Medial deviation of the left eyeball

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Respiratory Emergencies: Triaging the Feline Patient

Alison Gottlieb, BS, CVT, VTS(ECC)

Triage often begins before the patient enters the building, and when they do come in; reception is the first place they stop. This is incredibly important to consider when preparing a clinic for emergencies. Educating the front desk staff is the first step in readiness and should be done on a regular basis. Educating the front desk team to briefly observe cats in carriers upon arrival is incredibly helpful. Knowing cats should never be panting or lateral in carriers can save lives. Always err on the side of caution, telling an owner to bring the pet in, or calling for a triage when it arrives. The clinics triage system varies in each clinic; this depends on the needs of the clinic and the availability of personnel. For an average size general practice, a senior nurse will usually be made aware of a potential emergency and summoned when it arrives. Often the general practice does not consider themselves the primary caretaker for serious emergencies; "we refer them out" is a common response. This could not be further from the truth. Often the most important lifesaving interventions as well as making the diagnosis are performed at the referring hospital.

Being prepared as a team and having supplies ready will save lives. From basics like towels sprayed with pheromones, stethoscope, a quiet spot and patience. The phrase "prepare for the worst and hope for the best" is the moral of the story. Have several options for delivering oxygen available, supplies for IV catheter and blood sampling (with the understanding this may not happen) potential sedation, if available an u/s machine for a quick thoracic scan. Keep in mind IV fluids are often not on the top of the list of potential treatments for most respiratory cases (with the exception of trauma). Prepare for intubation as well as CPR. Crash cart should be available and up to date. This includes ET tubes, laryngoscope tie and syringe to inflate the cuff. I also recommend having a mouth gag available, some of the worst injuries come from these situations. Have drugs available and calculate potential doses for an estimated weight. Having an alternative airway plan is imperative as well. Often cats with head trauma, upper airway disease and potential anaphylaxis are not easily intubated orally. Having red rubber catheters, IV catheters, plastic tops of ET tubes or transtracheal tubes available will save a ton of time as well.

Oxygen therapy is rarely harmful, unless the method of providing oxygen increases stress. Once it is determined that oxygen supplementation is needed there are several ways to deliver it without additional stress. One important part of supplying oxygen is to avoid using the anesthetic machine. Residual gas is always being emitted from the hoses. An easier/quicker and safer way to deliver oxygen is directly from the source to the patient. This consists of a flowmeter attached to the oxygen source (either tank or via central supply) with a simple plastic tube which then delivers 100% oxygen to your patient. The end of the tube can be attached to anything, from a mask to an ambu bag. The easiest way to provide oxygen is via mask with the rubber gasket removed. If an oxygen cage is available that is a wonderful, stress free way to supplement as well. If not a simple cat carrier or incubator can be used. The author does not recommend using an e-collar covered in plastic because a buildup of CO2 can occur, even with ventilation holes as well as undue stress.

Measuring oxygenation can be done in several ways; the quickest and easiest is mucous membrane color and respiratory rate and effort. A pulse oximeter is available to many technicians for evaluating the percentage of circulating oxygen. Pulse oximeters may not read because of hypothermia/poor perfusion. Arterial blood gasses are very stressful for the patient and difficult to obtain. This leaves radiographs, auscultation, and observing MM color, RR & RE frequently. Keep in mind the cat must be stable before any radiographs are obtained; restraint causes stress. One way to assess oxygenation in a cat is to supply them with oxygen in a stress-free environment and observe their respiratory pattern. Two very important aspects to providing cats with oxygen; do not stress and allow for carbon dioxide to escape. Usually cyanosis will not be observed until the SPO_2 is well below 80%; at this point mechanical ventilation needs to be considered.

A more accurate measurement can be obtained from an arterial blood sample; using a blood gas analyzer. The value to look at is the PaO2; it represents a measurement of the partial pressure exerted by oxygen in arterial blood. This is a reflection the body's ability to pick up oxygen from the lungs. A low PaO2 represents hypoxemia and can initiate hyperventilation. The SaO2 (pulse ox) measures the percentage of hemoglobin actually carrying oxygen; this is why 95-100% is normal. These two values are crucial to adjust oxygen concentration during mechanical ventilation.

The respiratory pattern and rate should be noted, as well as panting. Any panting in a cat is not normal. Airway can be affected by many things therefore it is especially important to assess where the respiratory problem originates before continuing. Watching the cats breathing pattern can be done while the cat is in its carrier getting supplemental oxygen or while in an oxygen cage. This is one of the least stressful and most informative tools we

have. Establishing the origin of the respiratory issue (upper or lower) is imperative for treatment. One example is the upper airway cat. The physical barrier to the lungs makes oxygen less helpful and sedation with possible intubation (either oral or transtracheal) a better plan. These cats are often quite panicked with a long inhale and quick exhale. Further treatment is dependent on the cause of the obstruction. Cats with short inhale and exhale and an increased rate may potentially have effusion, either thoracic or abdominal. Large amounts of effusion (large tumor burden /severe organomegaly) in the abdomen will inhibit the diaphragm from moving while inhaling and cause increased respiratory effort.

The feline pleural effusion patient is unfortunately a common emergency, the result of chronic disease as well as trauma. Most of the time thoracentesis is the best treatment and makes a profound difference in respiration. Having the supplies available and together in a plastic bag is an enormous time saver. This feline thoracentesis kit should contain; a three way stop cock, butterfly catheters, various syringes, empty tubes for collecting samples and optional extension sets. These cats may need sedation, however removing the effusion is imperative. Flow-by oxygen should be available if it does not cause additional stress. Thoracic auscultation should be performed (and TFAST if avail. And tolerated) to confirm effusion as well as history. Muffled lung sounds are a good indicator effusion is present, other lung sounds may indicate primary parenchymal disease which is not treated with thoracentesis. Thoracic radiographs should NEVER be obtained on a stressed respiratory patient. If the cat has muffled lung sounds, a history of effusion, cardiac disease, neoplasia, trauma, etc. and increased respiratory rate thoracentesis should be performed. The additional stress of handling these very delicate cats in x-ray is enough to cause respiratory arrest. These pre thoracentesis films (if obtained) are often non diagnostic, making them even less valuable. Once the effusion has been removed and the cat has had some sort of sedation diagnostic radiographs can be obtained.

Cats with primary lung disease (lower airway, respiratory tissue) often respond best to supplemental oxygen therapy. Decreased gas exchange at the tissue level is often the primary cause of distress. Upon presentation the feline is generally dyspneic, stressed and occasionally cyanotic. Keep in mind panting (open mouth breathing) is never normal in the cat. As with any dyspneic cat additional stress often leads quickly to respiratory arrest. Coughing has been proven to be the most common clinical sign of feline asthma. Other hallmarks specific to asthma include a history of wheezing, dyspnea, tachypnea, and loud or abnormal breathing.
Upon auscultation asthmatic cats can have pulmonary wheezes and usually lack the presence of obvious cardiac disease. Pulmonary crackles can potentially be heard in both severe asthma and heart failure. IV catheterization and minimum data base and radiographs should be acquired once the cat is stable. Once acquired may show a diffuse bronchial pattern, patchy alveolar pattern and diffuse interstitial pattern.

Immediate treatment consists of supplying rapid acting glucocorticoids and bronchodilators delivered parenterally or via inhalation. The steroid immediately reduces inflammation and bronchodilators will relax the smooth muscle of the bronchi; so that the patient's airway will open up. Long term options have improved significantly over the past few years; however the components tend to be the same combination of steroid and bronchodilators. Oral Prednisone is no longer the only option, we now have the ability to provide steroid via inhaled metered doses. The benefits of this are that the systemic side effects from Prednisone are far fewer when delivered directly to the sight of action; the same is true for bronchodilators. Both can be delivered long term at home.

Keep in mind when dealing with these cats, a little stress makes a big difference!

NOTES:

Special Considerations on Feline Ears

Alison Diesel, DVM, DACVD

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The Three "As" of Acute Pain Management: Anticipate, Assess, & Alleviate

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Introduction

In their Global Year Against Acute Pain in 2010, the International Association for the Study of Pain (IASP) introduced the motto "Anticipate, Assess, Alleviate". This emphasizes three key approaches to acute pain management. They also emphasized that management of acute pain is not a specialist's job and is a condition that medical professionals encounter on a regular basis every day. It is important to prevent or alleviate acute pain to decrease the distress it causes but also to enhance nursing care, enhance sleep and rest, decrease the stress response, catabolism and poor wound healing. Finally, poorly managed acute pain is a major predictor for developing long-term pain following surgery or trauma.

Clinically, there are two phases associated with surgery; the first is the sensory input arising directly from the surgery itself and the second is from the resultant, more prolonged inflammatory response. Acute pain begins with thermal, chemical or mechanical stimulation of the peripheral nervous system which is amplified by inflammation (transduction). Signaling from peripheral sites (transmission) causes central sensitization or plasticity which can occur very quickly as a result of changes in N-methyl-D-aspartate (NMDA) receptors in the dorsal horn of the spinal cord.

Preventive Analgesia

The term pre-emptive has been used to emphasize that administration of analgesics prior to surgery is beneficial. However, for many surgical treatments, one treatment is not sufficient therefore the term "preventive analgesia" is preferred to describe analgesic treatment before, during and after surgery. It is now understood that an *effective* and *appropriate* level of analgesia must be maintained throughout the duration of the inflammatory response. If analgesic therapy is withdrawn too early, "re-initiation" of pain is possible.[1] To prevent prolonged or persistent post-operative pain, analgesic therapy should be started prior to surgery (or a soon as possible after trauma), maintained during surgery, be robust in the immediate post-operative period and not withdrawn until the inflammatory response has subsided. Duration of treatment will depend on the degree of surgical trauma and resultant inflammation. The exact duration of the inflammatory response after different types of surgical procedures is not well documented but is obviously longer after orthopedic surgery than after a simple elective ovariohysterectomy performed through a small incision.

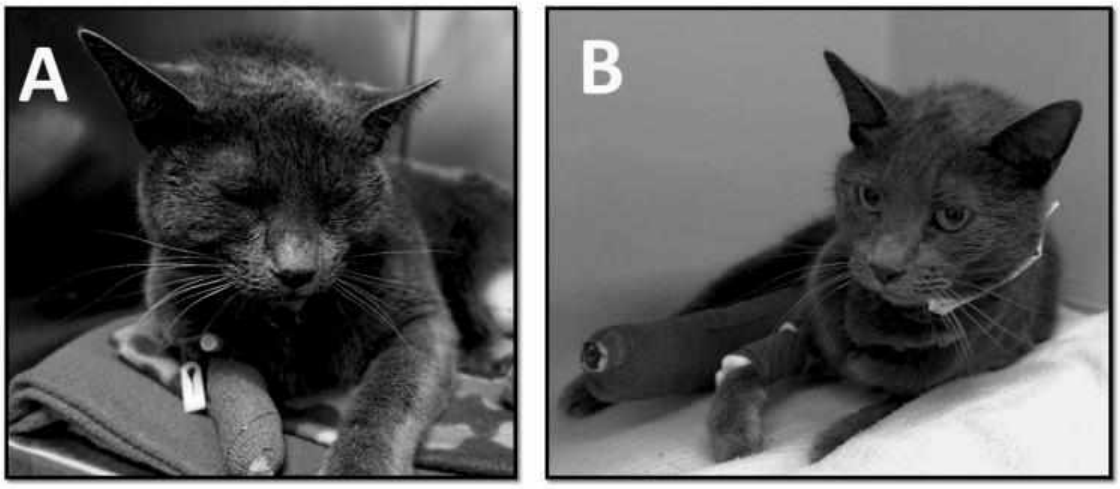
Assessment of Acute Feline Pain

It is now accepted that quantitative measurement of behavior is the most reliable method for assessing pain in animals. Validated tools are available. Brondani and colleagues developed a multidimensional composite scale based on observing cats that underwent ovariohysterectomy.[2, 3] A shorter more clinically applicable version of this tool is being developed and will be validated in cats with a wide variety of acute pain, including medical causes and will be available in multiple languages. The original Glasgow Composite Measures Pain Scale-Feline has been updated to include facial expressions of pain.[4-6] This tool was developed using cats undergoing different types of surgery or with medically related pain. It can be downloaded at: www.newmetrica.com/acute-pain-measurement/
The 7 major assessment domains in cats with acute pain are:

1. Vocalization
2. Posture
3. Attention to the wound
4. Interaction with people
5. Response to palpation of the wound or painful area
6. Facial expressions
7. Overall demeanor

Grimace Scales

The facial expressions of pain in cats include changes in ear position and tension in the muzzle.[6] A validated Feline Grimace Scale is now available and show excellent inter-rater reliability.[7, 8, 9] There is a dedicated website (www.felinegrimacescale.com) where you can download the training manual and read about how the scale was developed and soon there will be a section where you can practice your own skills at interpretation.
Since "a picture is worth a thousand words" the images below show the facial expressions of a painful cat (A) and after rescue analgesia (B). Lowered ears, "squinty eyes", tension in his muzzle, caudally retracted whiskers and a slightly lowered head all suggest this cat is experiencing pain.



Alleviation
The major classes of analgesics employed for acute pain management are:

1. Opioids
2. Non-steroidal anti-inflammatory drugs (NSAIDs)
3. Local anesthetics
4. Alpha$_2$–adrenergic agonists
5. NMDA antagonists

Opioids
Opioids have traditionally been the "backbone" of acute pain management protocols and are more effective when given before surgery (preventive strategy). An additional benefit of opioids is their anesthetic sparing effect which is not seen with NSAIDs. Opioids lower the amount of induction and maintenance agents required which often results in less cardiorespiratory depression. In cats, it is common to see euphoria, with purring, rolling, rubbing and kneading. Opioids cause marked mydriasis in cats making them unable to focus clearly, so they should be approached slowly, while being spoken to, so they are not startled, and they should be protected from bright light. Some opioids cause nausea, vomiting and salivation in cats; this is more common after morphine and hydromorphone but is rare after buprenorphine, fentanyl, methadone or butorphanol.

Methadone is unique within this class of analgesics because in addition to having mu-opioid effects it also acts at the NMDA receptor which is important in the process of central sensitization. Unlike European countries there is no veterinary formulation of methadone in the United States and the human formulation (used off label) is expensive.

Hydromorphone is widely used but is frequently associated with post-operative hyperthermia.[10, 11] Other opioids are implicated in feline post-operative hyperthermia and in many cases this is self-limiting.[12]

Buprenorphine is popular in feline pain management. Transmucosal absorption through oral mucous membranes (OTM) has been demonstrated in cats which can be utilized in the home setting.[13] A sustained release preparation of buprenorphine for subcutaneous administration has been evaluated in cats undergoing ovariohysterectomy. A single sustained release dose of 120µg/kg was as effective as 20µg/kg buprenorphine by the OTM route given every 12 hours until 60 hours after surgery. The sustained release formulation is not FDA approved for cats and there are reports of injection site reactions in cats. Simbadol™; Buprenorphine Injection for cats (1.8 mg/ml), is the first FDA approved buprenorphine for use in cats and is approved for 3 days of treatment. This product is intended for subcutaneous administration and may provide analgesia for up to 24 hours which simplifies treatment.

Epidural injection of morphine is a technique well worth considering for hind-limb surgery or trauma and abdominal surgery. Prior to surgery this is often combined with a local anesthetic to decrease sensory input to the central nervous system and few adverse events are repoted[14]. Preservative free morphine may be effective for up to 18-20 hours with few side-effects.

Non-steroidal Anti-Inflammatory Drugs (NSAIDs)
NSAIDs are excellent analgesics for acute pain, can provide up to 24 hours of analgesia after a single dose, and are not subject to the legal regulations of opioids. In the United States the only approved NSAIDs for perioperative use in cats are meloxicam and robenacoxib. Meloxicam is approved only for one single injection and repeated use is "off label". Robenacoxib is approved by the FDA for use in cats 4 months and older for the control of post-operative pain

associated with inflammation related to orthopedic surgery, ovariohysterectomy, and castration, and can be given for a maximum of three days. It is available in a tablet and injectable formulation. At clinical doses COX-1 inhibition is minimal and short lasting. Robenacoxib has a unique pharmacokinetic profile, with a short half-life but long residence time in target (inflamed) tissues. NSAIDs should not be used in patients that are hypovolemic or hypotensive and never concurrently with corticosteroids.

Local Anesthetics
Local anesthetics can provide complete analgesia with minimal side effects and can be used for many different surgical procedures including castration and ovariohysterectomy.[15] A wound or "soaker" catheter can be placed into a surgical site to provide a method for maintaining continuous analgesia. After fibrosarcoma removal in cats the use of a wound infusion catheter significantly reduced the time the cat was hospitalized [16]. Another method for delivery of local anesthesia is a lidocaine patch. When applied to shaved skin, high concentrations of lidocaine are detected at the site of application with minimal systemic absorption. A long acting liposomal suspension of bupivacaine is now FDA approved in cats for
regional (nerve blocks) post-operative pain control (Nocita® https://nocita.aratana.com/cats/).The duration of action is 72 hours.

Alpha$_2$-adrenergic Agonists
It is important to know that the dose of an alpha$_2$-adrenoceptor agonists (medetomidine and dexmedetomidine) required to provide sedation is lower than that needed for analgesia; for example in cats dose dependent sedation was seen with doses of dexmedetomidine between 2 and 40 µg/kg (intramuscular) but analgesia was only associated with the highest dose.[17] Sedation may mislead the observer to think that the animal is comfortable; however interactive assessment (palpation of the wound) will usually reveal the difference between pain and sedation. For this reason, this group of drugs are not "first line" analgesics.

NMDA Antagonists
Ketamine acts at the NMDA receptor and there is great interest in using ketamine to provide analgesia and to prevent central sensitization and "wind up". Ketamine also has anti-proinflammatory actions, which may provide additional benefits.

Gabapentin
There is little information on the use of gabapentin for acute pain in cats but there are encouraging case reports suggesting it should be investigated further. [18] Its sedating and calming effects are beneficial to enhance nursing care and decrease stress.[19]

Multimodal Analgesia
Nociception and pain involve many steps and pathways so it seems unlikely that one analgesic agent could completely prevent or alleviate pain. Multimodal analgesia describes the combined use of drugs that have different modes of action, work at different receptors and at different places in the "pain pathway" with the assumption this will provide superior analgesia or allow lower doses of each drug to be used thereby lessening any adverse side effects. A commonly used combination is an opioid plus a NSAID but more and more, clinicians are appreciating the advantage of using a local anesthetic every time they can .

Preventing and relieving pain is not all about drug therapy. Small incisions and careful tissue handling produce less inflammation and therefore less pain. Good nursing care (warm, dry, comfortable bedding) and low stress handling can have a positive effect on a patient's recovery. Icing incisions post-operatively is an underutilized "low tech" technique to add to the multimodal approach.[20]

ANTICIPATE any situation which will cause acute pain – do not overlook seemingly small but additive events; for example, placing a catheter, taking a "small" biopsy or passing a urinary catheter. Plan for the procedure before, during and afterwards; the latter includes in the hospital and when the cat goes home.

ASSESS the patient regularly; "one size does not fit all" and therefore your plan may not be enough for an individual patient. The sooner pain is recognized and treated, the less harm it can do.

ALLEVIATE this is the ultimate goal and is achievable in our feline patients if we educate ourselves and use the drugs and tools available to us.

References

1. Kissin I, Lee SS and Bradley EL, Jr. Effect of prolonged nerve block on inflammatory hyperalgesia in rats: prevention of late hyperalgesia. *Anesthesiology*. 1998; 88: 224-32.
2. Brondani JT, Luna SP and Padovani CR. Refinement and initial validation of a multidimensional composite scale for use in assessing acute postoperative pain in cats. *Am J Vet Res*. 2011; 72: 174-83.
3. Brondani JT, Mama KR, Luna SP, et al. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. *BMC Vet Res*. 2013; 9: 143.
4. Calvo G, Holden E, Reid J, et al. Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats. *J Small Anim Pract*. 2014; 55: 622-9.
5. Reid J, Scott EM, Calvo G and Nolan AM. Definitive Glasgow acute pain scale for cats: validation and intervention level. *Vet Rec*. 2017; 180: 449-53.
6. Holden E, Calvo G, Collins M, et al. Evaluation of facial expression in acute pain in cats. *J Small Anim Pract*. 2014; 55: 615-21.
7. Watanabe R, Doodnaught GM, Evangelista MC, Monteiro BP, Ruel HLM and Steagall PV. Inter-Rater Reliability of the Feline Grimace Scale in Cats Undergoing Dental Extractions. *Frontiers in Veterinary Science*. 2020: 302.
8. Evangelista MC, Watanabe R, Leung VSY, et al. Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. *Sci Rep*. 2019; 9: 19128.
9. Evangelista MC, Benito J, Monteiro BP, et al. Clinical applicability of the Feline Grimace Scale: real-time versus image scoring and the influence of sedation and surgery. *PeerJ*. 2020; 8: e8967.
10. Niedfeldt RL and Robertson SA. Postanesthetic hyperthermia in cats: a retrospective comparison between hydromorphone and buprenorphine. *Vet Anaesth Analg*. 2006; 33: 381-9.
11. Posner LP, Gleed RD, Erb HN and Ludders JW. Post-anesthetic hyperthermia in cats. *Vet Anaesth Analg*. 2007; 34: 40-7.
12. Posner LP, Pavuk AA, Rokshar JL, Carter JE and Levine JF. Effects of opioids and anesthetic drugs on body temperature in cats. *Vet Anaesth Analg*. 2010; 37: 35-43.
13. Robertson SA, Lascelles BD, Taylor PM and Sear JW. PK-PD modeling of buprenorphine in cats: intravenous and oral transmucosal administration. *J Vet Pharmacol Ther*. 2005; 28: 453-60.
14. Troncy E, Junot S, Keroack S, et al. Results of preemptive epidural administration of morphine with or without bupivacaine in dogs and cats undergoing surgery: 265 cases (1997-1999). *J Am Vet Med Assoc*. 2002; 221: 666-72.
15. Benito J, Monteiro B, Lavoie AM, Beauchamp G, Lascelles BDX and Steagall PV. Analgesic efficacy of intraperitoneal administration of bupivacaine in cats. *J Feline Med Surg*. 2016; 18: 906-12.
16. Davis KM, Hardie EM, Lascelles BD and Hansen B. Feline fibrosarcoma: perioperative management. *Compend Contin Educ Vet*. 2007; 29: 712-4, 6-20, 22-9 passim.
17. Slingsby LS and Taylor PM. Thermal antinociception after dexmedetomidine administration in cats: a dose-finding study. *J Vet Pharmacol Ther*. 2008; 31: 135-42.
18. Steagall PV and Monteiro-Steagall BP. Multimodal analgesia for perioperative pain in three cats. *J Feline Med Surg*. 2013.
19. van Haaften KA, Forsythe LRE, Stelow EA and Bain MJ. Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. *J Am Vet Med Assoc*. 2017; 251: 1175-81.
20. Wright B, Kronen PW, Lascelles D, et al. Ice therapy: cool, current and complicated. *J Small Anim Pract*. 2020; 61: 267-71.

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SPECIAL ARTICLE

Partner Symposia

2020 AAFP Feline Retrovirus Testing and Management Guidelines

Clinical importance: Feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infections are found in cats worldwide. Both infections are associated with a variety of clinical signs and can impact quality of life and longevity.

Scope: This document is an update of the 2008 American Association of Feline Practitioners' feline retrovirus management guidelines and represents current knowledge on pathogenesis, diagnosis, prevention and treatment of retrovirus infections in cats.

Testing and interpretation: Although vaccines are available for FeLV in many countries and for FIV in some countries, identification of infected cats remains an important factor for preventing new infections. The retrovirus status of every cat at risk of infection should be known. Cats should be tested as soon as possible after they are acquired, following exposure to an infected cat or a cat of unknown infection status, prior to vaccination against FeLV or FIV, and whenever clinical illness occurs. It might not be possible to determine a cat's infection status based on testing at a single point in time; repeat testing using different methods could be required. Although FeLV and FIV infections can be associated with clinical disease, some infected cats, especially those infected with FIV, can live for many years with good quality of life.

Management of infected cats: There is a paucity of data evaluating treatments for infected cats, especially antiretroviral and immunomodulatory drugs. Management of infected cats is focused on effective preventive healthcare strategies, and prompt identification and treatment of illness, as well as limiting the spread of infection.

Keywords: Feline leukemia virus; feline immunodeficiency virus; FeLV; FIV; polymerase chain reaction; PCR; diagnostics; veterinary sciences

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Introduction

Feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) are among the most common causes of infectious disease of cats and are found worldwide. A large observational study evaluated FeLV and FIV test results over a 9-year period from 2008 to 2016.[1] The data were collected from a referral laboratory database containing results from cats tested in the field using point-of-care (POC) tests. Almost 3 million test results from 68 countries grouped into seven global regions were analyzed (Table 1).

A 2006 survey of over 18,000 cats in the USA and Canada reported 2.3% of cats positive for FeLV antigen and 2.5% of cats positive for FIV antibody.[2] In 2009, a survey of over 11,000 cats in Canada reported prevalences of 3.4% for FeLV antigen and 4.3% for FIV antibody.[3] Another large study, in 2010, evaluated test results of over 62,000 cats from veterinary clinics and shelters in the USA and Canada for FeLV antigen and FIV antibody.[4] In that study, prevalence for FeLV antigen and FIV antibody was 3.1% and 3.6%, respectively. A prospective study in Europe that tested cats visiting a veterinary facility for FeLV RNA in saliva as a measure of antigenemia from September 2016 to March 2017 found an overall prevalence of 2.3%.[5] The highest prevalence was in Southern Europe (5.5%) and the lowest in Northern Europe (0.7%).

These studies show that although guidelines for prevention of infection have been available for decades, there remains a need to improve adherence to testing and vaccination recommendations.

The International Society of Feline Medicine (ISFM) is pleased to endorse these practice guidelines from the AAFP.

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Table 1 Prevalence of FeLV antigen and FIV antibody by region in samples submitted to a referral laboratory (2008–2016)

Region (number of cats tested)	FeLV antigen prevalence (%)	FIV antibody prevalence (%)
North America (2.5 million)	4	5
Caribbean (6882)	9	13
Latin America (9984)	13	7
Northern Europe (95,800)	7	7
Southern Europe (206,157)	12	12
Middle East/Africa (4787)	14	14
Asia-Pacific (81,201)	6	13

From Buch J, Beall M, O'Connor T, et al[1]
FeLV = feline leukemia virus; FIV= feline immunodeficiency virus

Pathogenesis and outcomes of infection

Feline leukemia virus infection

Transmission of feline leukemia virus

FeLV is transmitted through close contact among cats. Commonly, it is spread vertically and horizontally from infected queens to their kittens and horizontally among cats that live together or that fight. There is an age-related increase in resistance to FeLV infection; kittens have the highest risk of becoming progressively infected.[6] However, some studies have demonstrated efficient natural and experimental infection in adult cats.[7]

Outcomes of FeLV infection have been redefined and are now classified as abortive infection, regressive infection and progressive infection.

Pathogenesis of feline leukemia virus

Progressively infected cats shed infectious virus in body fluids, including saliva, nasal secretions, milk, urine and feces.[6,8] Cats typically acquire FeLV via the oronasal route but can also become infected through bite wounds. After virus exposure via the oronasal route, FeLV can be found first in the local lymphoid tissues; it then spreads via monocytes and lymphocytes (primary viremia; see 'Glossary of terms on page 24) into the periphery. During this primary viremia, the virus can infect the bone marrow.[9] After bone marrow infection, a secondary viremia can occur, with FeLV-containing leukocytes and platelets appearing in the blood, resulting in virus being detectable by immunofluorescent antibody (IFA) test.

Outcomes following exposure to feline leukemia virus

Based on molecular methods, the possible outcomes of infection following FeLV exposure have been redefined.[10–12] Outcomes of FeLV infection are now classified as abortive infection (comparable to the former 'regressor cats'), regressive infection (comparable to

the former 'latent infection', with or without previous 'transient viremia') and progressive infection (comparable to the former 'persistent viremia'). The likelihood of each outcome depends on the infection pressure and the cat's immune status, and has been described in experimental infections using specific pathogen-free cats.

In the past, exposure to FeLV has been described as resulting in abortive infection in 20–30% of cats, regressive infection in 30–40% of cats and progressive infection in 30–40% of cats.[13] However, large field studies testing simultaneously for p27 antigen, proviral DNA, viral RNA and virus-neutralizing antibodies have identified a higher proportion of cats that have presumed abortive infections based on a pattern of negative antigen and PCR tests in the presence of neutralizing antibodies. In a study of 495 owned pet cats in Germany, 4% were classified as having abortive infection, 2% as progressive and 1% as regressive.[14] In a study of 440 owned pet cats in Australia, 11% were classified as having presumptively abortive infection, 2% as presumptively regressive and 0.5% as presumptively progressive.[15] This suggests that abortive infection may be the most common outcome following exposure under typical conditions. In contrast, in two populations of cats in Australia (one group of 38 cats and one group of 51 cats) in which FeLV-infected and uninfected cats were co-mingled without separating healthy from clinically ill cats, 9% were classified as having abortive infection, 25% as regressive and 21% as progressive, suggesting that resistance to infection may be compromised by intense infectious pressure, comorbidities and a stressful environment.[15]

Viral RNA is usually detectable in plasma by real-time reverse-transcriptase polymerase chain reaction (qRT-PCR) testing within 1 week of FeLV exposure, followed by proviral DNA detection by PCR within 2 weeks of exposure and finally by FeLV antigen detection, which usually occurs by 30 days but can be longer in some cats.[16] It is not only cats with progressive infection that undergo the early phases, but also some cats with regressive infection. These regressively infected cats have similar proviral and plasma viral RNA loads in their peripheral blood at the beginning of their infection; however, in contrast to cats with progressive infection, their viral load will decrease to undetectable levels over time.[12,17]

✣ **Progressive infection** In cats with progressive infection, FeLV infection is not contained during the early stage, and extensive virus replication occurs first in the local lymphoid tissues, then in the bone marrow, and subsequently in mucosal and glandular epithelial tissues.[9] Mucosal and glandular infection is associated with excretion of infectious virus, mainly in saliva but also in other secretions. Progressive infection is characterized by insufficient FeLV-specific immunity and usually neutralizing antibodies are not detectable. Cats with progressive infection have a shorter survival time than cats with regressive FeLV infection and typically succumb to FeLV-associated diseases within several years after infection.[11,18,19]

Although guidelines for prevention of infection have been available for decades, there remains a need to improve adherence to testing and vaccination recommendations.

✣ **Regressive infection** Regressive infection is accompanied by an immune response that contains, but does not eliminate, virus replication. Viral shedding does not occur after the first antigenemic phase is over.[8,20–23] However, FeLV proviral DNA can be detected in the blood by some PCR assays.[10,17,24]

FeLV is integrated into the cat's genome and is unlikely to be completely cleared over time.[25] Regressively infected cats do not shed infectious virus. However, it has been demonstrated that proviral DNA is infectious via blood transfusion and can lead to viremia and FeLV-associated disease in susceptible recipient cats.[26] Cats with regressive infection demonstrate continuously high titers of virus-neutralizing antibodies[17] and are at low risk of developing FeLV-associated diseases.[27,28] However, reactivation can occur in cats with regressive infection, particularly if they are immunosuppressed, so they become viremic and develop FeLV-associated disease. The risk of reactivation of viremia decreases with time (duration after the cat has cleared viremia) but it has been shown that the integrated provirus retains its replication capacity, so reactivation can still occur many years after the initial exposure to FeLV.[29] In some cats, regressive infection itself might be associated with clinical disease, such as lymphoma[28,30] or bone marrow suppression.[27]

✣ **Abortive infection** Abortive infection has been observed following experimental FeLV inoculation and is characterized by negative test results for culturable virus, antigen, viral RNA and proviral DNA.[10,31] The only indication of FeLV infection is the presence of antibodies. Although not common after experimental infection, abortive infection seems to be more common in the field, as cats with natural infections can show evidence of FeLV antibodies in the absence of detectable viral RNA, proviral DNA or antigen, and without having received FeLV vaccines.[7,14,15,32]

Feline immunodeficiency virus infection

Transmission of feline immunodeficiency virus

The major mode of FIV transmission is through bite wounds that introduce saliva containing virus and FIV-infected white blood cells. Transmission of FIV from infected queens to their kittens has been demonstrated experimentally,[33,34] but appears to be uncommon in naturally infected cats.[35,36] Transmission is also uncommon among cats living together in a household without fighting; however, a certain degree of risk remains. In one household of 26 cats that were not observed to fight, FIV infection was originally diagnosed in nine cats, but spread to six other cats during a 10-year observation period.[37] This household also included cats coinfected with FeLV, which might have predisposed some cats to FIV infection. However, in a sanctuary in which eight FIV-infected cats were housed with 130 uninfected cats, no transmission was documented over several years.[38] Sexual transmission, the most common mode of transmission of human immunodeficiency virus (HIV), appears to be unusual for FIV, even though the semen of infected cats frequently contains infectious virus and biting can occur during mating.[39]

The most important measure for the control of FeLV and FIV is the identification and segregation of infected cats.

Pathogenesis of feline immunodeficiency virus

After experimental inoculation, acute FIV infection can be associated with transient fever, lymphadenopathy and lymphopenia, but this has not been reported in natural infection, perhaps because the early signs might not be noticed by cat owners. During this acute stage, FIV is detected in high concentrations in the blood by culture and PCR. Within the first few weeks of infection, both CD4+ (helper) and CD8+ (cytotoxic-suppressor) T lymphocyte concentrations decline.[40,41] The initial phase is followed by an immune response characterized by the production of FIV antibodies, suppression of circulating virus leading to a decreasing viral load, and an increase in CD8+ T lymphocytes to higher than pre-infection levels. This results in an inversion of the CD4:CD8 ratio that can persist for the rest of the cat's life. Over time, both CD4+ and CD8+ lymphocyte numbers continue to gradually decline.[42,43]

Following the primary phase, cats enter a long asymptomatic stage that can last for many years (Figure 1). During this stage, progressive dysfunction of the immune system can occur. Thus, FIV-infected cats are predisposed to chronic and recurrent infections. Neoplasia is about five times more common than in uninfected cats.[44] Although chronic inflammatory conditions and secondary infections are more common in cats with low CD4+ T lymphocyte counts, some cats with very low CD4+ counts remain healthy. Cell-mediated immunity is more profoundly affected than humoral immunity. Hyperglobulinemia, characteristic of non-specific stimulation of humoral immunity, can also occur in cats with FIV infection.[45] Survival time for FIV-infected cats is highly variable among individuals, but can be similar to that of non-FIV-infected cats.[37,45–48]

Diagnosis of retrovirus infections

The most important measure for the control of FeLV and FIV is the identification and segregation of infected cats. Thus, the American Association of Feline Practitioners (AAFP) recommends screening all cats for infection at the time they are first acquired, prior to initial vaccination against FeLV or FIV, following potential exposure to infected cats, or if clinical signs of illness are displayed.

POC tests based on ELISA or rapid immunomigration (RIM) methodologies are commonly used in veterinary practice to detect FeLV antigen and FIV antibodies in whole blood, serum or plasma. In addition, POC tests for the detection of FeLV antibodies[32] and in-house PCR tests detecting FeLV and FIV provirus[49,50] are available in some countries, but only limited data evaluating these tests are available. Referral laboratories also offer various tests for FeLV and FIV detection.

Since a positive screening test result has potentially important clinical consequences, additional testing is recommended, especially in low-risk cats (eg, apparently healthy cats, indoor-only cats) where the likelihood of a false-positive result is greater than in higher risk cats (eg, sick, outdoor access). False-positive results might, among other things, arise from improperly conducted tests or test failure. Negative test results are generally reliable when highly sensitive POC tests are used, especially in apparently healthy cats with a low-risk lifestyle. The exception would be when the cat is in the early phase of infection before FeLV antigenemia (<30 days) or FIV antibodies (<60 days) have developed. In addition, false-negative test results can arise because changes in FIV isolates may occur over time; for example, through movement of cats geographically or between countries. Indeed, a study in Europe demonstrated an increasing number of cats testing negative for FIV antibody with POC tests but positive on Western blot between 1998 and 2019 compared with cats tested in earlier years, suggesting a reduction in the diagnostic efficiency of FIV POC tests in geographic areas where cats may be infected with imported isolates.[51]

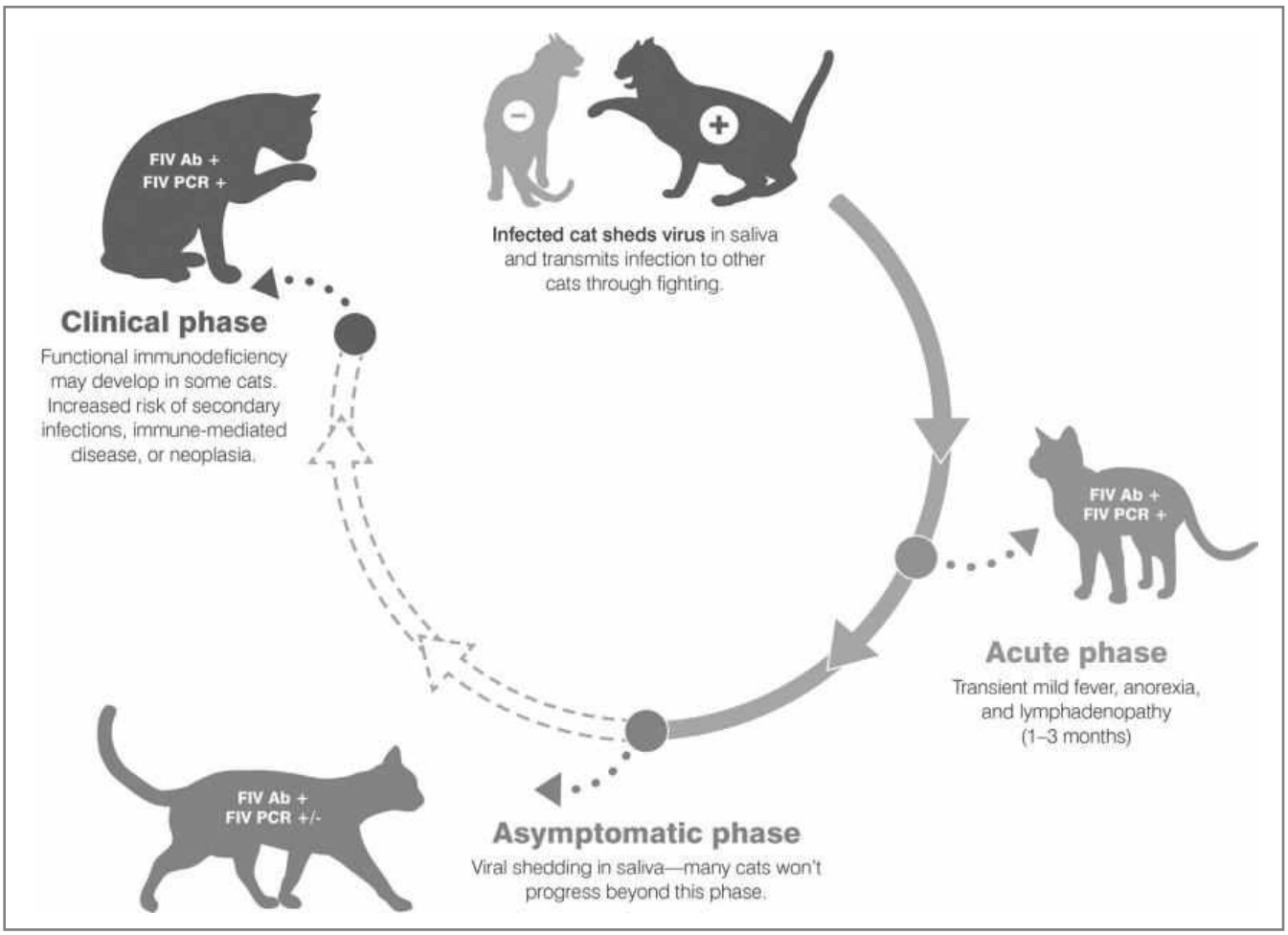

Figure 1 Outcomes of infection with feline immunodeficiency virus (FIV). Ab = antibody; PCR = polymerase chain reaction. *Courtesy of IDEXX.*

Cats are tested under various circumstances and for different reasons, so a single testing protocol is difficult to recommend for all cats. See Figure 2 for a testing protocol that can be adapted to different situations. A diagnostic tool developed in Europe for testing cats for FeLV is also available (abcdcatsvets.org). Note there are differences in test types and test performance in different countries.

Several comparison studies of FeLV and FIV tests have been performed over the years.[52–54] However, these studies are difficult to compare due to differences in study design, especially concerning the reference standards used. In addition, tests with similar names can differ among countries or might have undergone design changes over time. It is difficult to select an appropriate gold standard for FeLV diagnostic test comparison studies – there is no gold standard for antigen detection and PCR is of limited value (without concurrent results from antigen testing) since it detects not only progressively but also regressively infected cats (provirus carriers).

Feline leukemia virus infection

Diagnosis of FeLV infection is usually based on the detection of soluble FeLV p27 antigen using POC tests. Testing can be performed on serum, plasma or whole blood. FeLV antigen tests should not be performed on tears or saliva, as reported sensitivities are low.[8,55,56] In one study, use of saliva was only able to detect 54% of infected cats.[56] Testing is not confounded by maternally acquired immunity or FeLV vaccination. Most cats will test positive within 30 days of exposure, although development of antigenemia can take longer in some cats. Since the consequences of a positive screening test for FeLV are significant for the cat's future, additional testing is recommended, especially in low-risk and asymptomatic cats.[17,52,57] Immediate retesting in the event of questionable or positive FeLV p27 antigen POC test results can be performed at a referral laboratory using either a microwell plate ELISA for p27 antigen or PCR detecting FeLV provirus. Alternatively, a POC p27 antigen test of a different brand can be used.

Susceptibility to FeLV infection is highest in young cats, but the cumulative lifetime risk of exposure results in a slighter higher prevalence of infection in older cats.

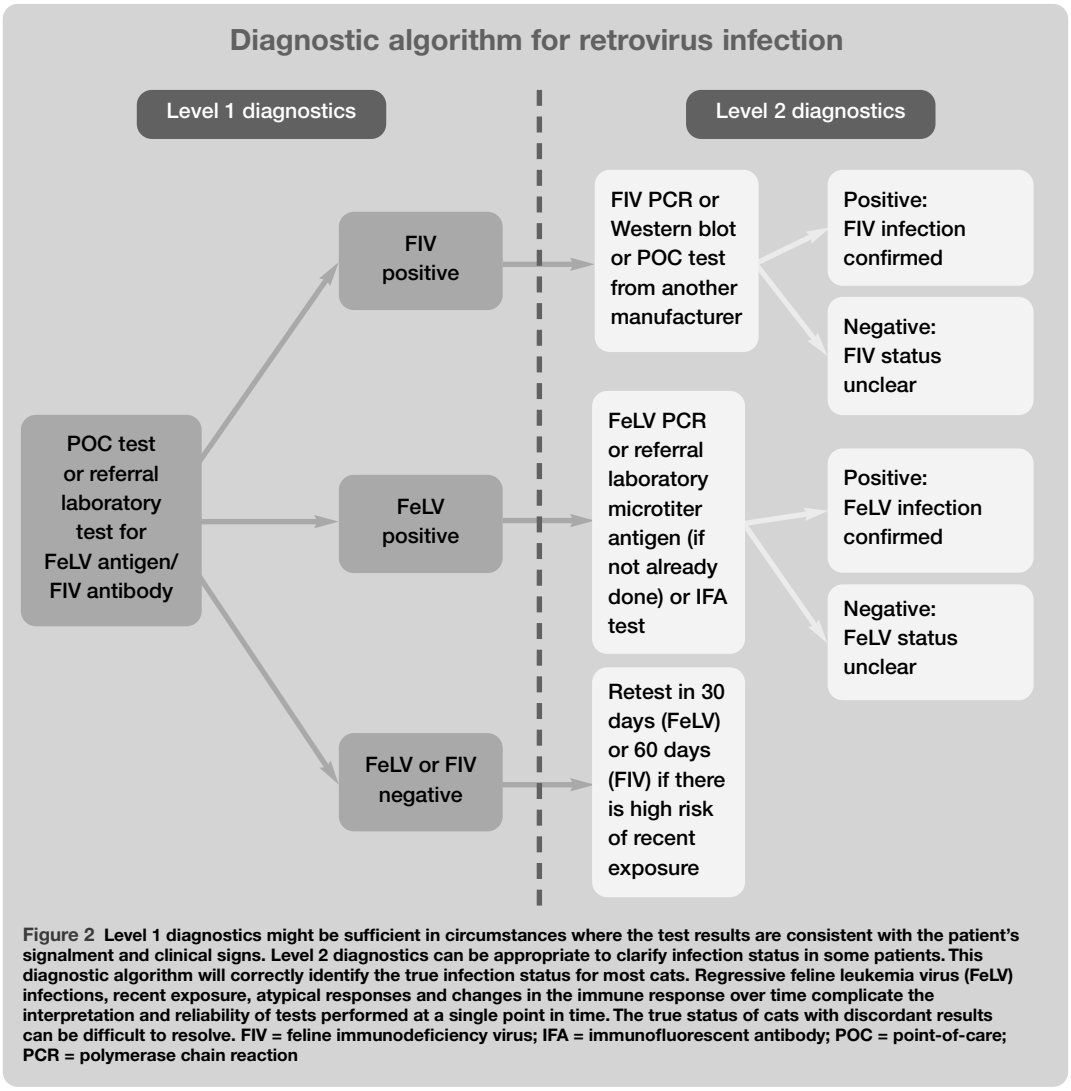

Figure 2 **Level 1 diagnostics might be sufficient in circumstances where the test results are consistent with the patient's signalment and clinical signs. Level 2 diagnostics can be appropriate to clarify infection status in some patients. This diagnostic algorithm will correctly identify the true infection status for most cats. Regressive feline leukemia virus (FeLV) infections, recent exposure, atypical responses and changes in the immune response over time complicate the interpretation and reliability of tests performed at a single point in time. The true status of cats with discordant results can be difficult to resolve. FIV = feline immunodeficiency virus; IFA = immunofluorescent antibody; POC = point-of-care; PCR = polymerase chain reaction**

Cats are tested under various circumstances and for different reasons, so a single testing protocol is difficult to recommend for all cats.

In one study, four different FeLV POC tests were compared using 146 FeLV-positive and 154 FeLV-negative serum or plasma samples. The results of two commercial ELISAs were used as the gold standard for the determination of true FeLV infection status. Sensitivity and specificity were 100% and 100% for IDEXX SNAP FIV/FeLV Combo, 89.0% and 95.5% for Witness FeLV-FIV, 91.8% and 95.5% for Anigen Rapid FIV Ab/FeLV Ag, and 85.6% and 85.7% for VetScan Feline FeLV/FIV Rapid test kits, respectively.[58] However, other studies investigating different cat populations and using different gold standards to determine infection status have revealed different results.[56,59]

Progressively infected cats can be identified using POC tests that detect soluble free FeLV p27 antigen in the blood, indicative of antigenemia; in general, antigenemia is equivalent to viremia, although exceptions have been reported.[60] Only viremic (antigen-positive) cats shed virus under natural circumstances and are infectious for other cats. This includes cats with progressive infection and cats with regressive infection in the early phase of transient viremia or after reactivation of infection.

Regressive infections are characterized by low levels of antigen and proviral DNA. At times, concentrations of one or the other can drop below the level of detection of some tests, leading to discordant results that may change over time.[61] Quantitative PCR assays for proviral DNA are becoming commercially available in more countries and they provide additional information to classify a cat's status.[15,61] Cats that initially test positive by both p27 antigen and PCR can transition to a regressive infection pattern, usually within 16 weeks of infection.

Although saliva is less sensitive than blood or serum for POC tests, it can be used for RT-PCR to detect FeLV RNA and, thus, FeLV shedding.[8,56] Detection of viral RNA in saliva is a reliable parameter of antigenemia and shedding.[62] According to a European study, detection of viral RNA in saliva swabs can be useful if blood collection is not feasible in large

groups of cats. Saliva swabs from several cats can be pooled for analysis (ideally from a maximum of 10 cats). However, if a pooled sample is positive for FeLV, individual testing must be performed to determine each cat's status.[63] In an experimental setting, RT-PCR performed on saliva and blood can detect infection as early as 1–3 weeks post-exposure.[8,16]

IFA tests for blood or bone marrow smears are available from some commercial laboratories for the diagnosis of FeLV infection. These tests detect secondary viremia once bone marrow infection is established. Before bone marrow infection is established, cats will test negative using IFA. Most cats with regressive infections and those that resist bone marrow infection will also test negative. The subjective nature of IFA interpretation and differences in performance among laboratories can lead to both false-positive and false-negative results. False-negative results may also be observed in cats with leukopenia and regressive infections.

Discordant results between antigen tests and other techniques such as PCR and IFA can occur as these tests detect the cat's stage of infection at a single point in time (Figure 3). Repeat testing over time might be needed to clarify the status of some cats. Cats with discordant test results should be considered potential sources of infection for other cats until their status is clarified.

Detection of antibodies is generally indicative of FIV infection.

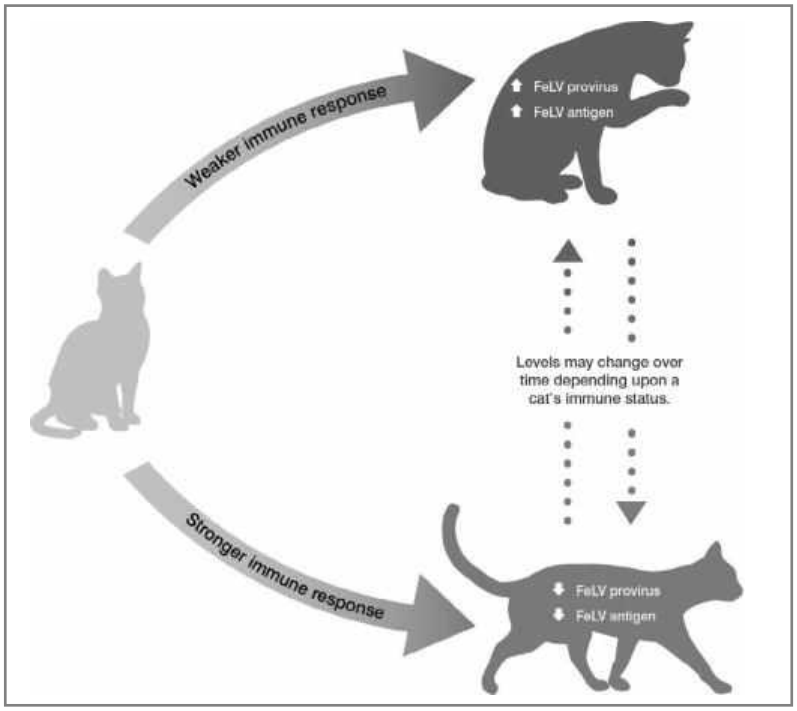

Figure 3 Feline leukemia provirus and antigen test results may vary depending on the cat's immune status at the time of testing. High levels of provirus and antigen are most commonly associated with progressive infection, while low levels of provirus and antigen are most commonly associated with regressive infection. FeLV = feline leukemia virus. *Courtesy of IDEXX. Copyright © 2019, IDEXX Laboratories. All rights reserved. Used with permission*

Feline immunodeficiency virus infection

FIV infection is most commonly diagnosed through detection of FIV-specific antibodies using POC tests performed on whole blood, serum or plasma. Infected cats usually develop high concentrations of FIV-specific antibodies, and FIV produces a persistent infection from which cats do not recover. Thus, detection of antibodies is generally indicative of FIV infection. In veterinary practice, antibodies are usually identified using either ELISAs or RIM assays, which detect antibodies to various viral antigens. Different antibodies are detected by the available POC test kits. Most cats produce antibodies within 60 days of infection.

Most currently available POC tests for FIV have been shown to be highly sensitive and specific based on various comparison studies, despite differences in study design and reference standards.[52–54] In a study comparing four different FIV POC tests in the USA using 94 FIV-positive and 97 FIV-negative serum or plasma samples, and comparing the results with virus isolation as the gold standard, sensitivity and specificity were 97.9% and 99.0% for IDEXX SNAP FIV/FeLV Combo, 94.7% and 100% for Witness FeLV-FIV, 96.8% and 99.0% for Anigen Rapid FIV Ab/FeLV Ag, and 91.5% and 99.0% for VetScan Feline FeLV/FIV Rapid test kits, respectively.[58] No significant differences in performance among the four tests were reported.

Several referral laboratory tests are available for additional testing after a positive POC test for FIV antibodies. However, establishing the true FIV infection status of cats can sometimes be difficult, even with extensive additional testing. Western blotting traditionally has been used as a gold standard diagnostic test for detection of FIV antibodies. While it did not perform as well as some POC tests in one North American study,[64] in a European study it was able to detect some cats that were antibody negative with POC tests.[51]

Detection of FIV proviral DNA or viral RNA (or both) by PCR is commonly used as an additional test by commercial laboratories in North America. However, some infected cats are not detected by PCR, which is likely due to viral sequence variation or low virus loads.[51,65–68] The primers used to amplify gene segments should be designed to bind to highly conserved regions such as the *gag* gene of FIV, since it has been shown that *env* recombinants occur commonly in naturally infected cats.[69] In addition, the accuracy of PCR results varies among different laboratories;[70] therefore, assays that have been independently validated should be used. In an independent study of 239 FIV-unvaccinated cats in Australia, the sensitivity and specificity of the FIV RealPCR

test (IDEXX Laboratories) were 92% and 99%, respectively.[66] It is reasonable to further assess cats with a positive FIV POC test result by performing additional testing (Figure 2), especially in low-risk cats. However, some high-risk cats with positive FIV POC test results, such as free-roaming, aggressive male cats, may not require additional testing.

During the early phase of FIV infection, cats can test antibody negative. Therefore, when the results of antibody testing are negative, but recent infection cannot be ruled out, testing should be repeated no earlier than 60 days after the last potential exposure. Although most cats develop antibodies within 60 days of exposure to infection, antibody development can be delayed in some cats. Throughout the asymptomatic phase of infection, FIV-specific antibodies are readily detected in the blood of most cats. However, some cats entering the terminal phase of infection might test antibody negative because of high viral loads sequestering antibodies in antigen-antibody complexes. In addition, false-negative results are possible with any test. If a cat at high risk of FIV infection with typical clinical signs is antibody negative on a POC test, follow-up testing should be performed with another method, such as PCR or Western blot.

Although POC antibody tests are convenient and highly reliable in most situations, such tests should be interpreted carefully in kittens that test positive. Antibodies are passively transferred to kittens that nurse on naturally infected or vaccinated queens. This can lead to a positive POC antibody test result up to the age of 6 months if the queen was infected. In a study of 55 kittens born to FIV-vaccinated, uninfected queens, all kittens tested positive for FIV antibodies shortly after birth and for the first several weeks of life.[71] By 12 weeks of age, all kittens tested FIV antibody negative. Under natural circumstances, if a chronically FIV-infected queen is otherwise healthy, kittens born to that queen rarely acquire FIV infection in utero or postnatally. Consequently, most kittens that test antibody positive initially will test negative when maternal antibodies have waned. Therefore, FIV antibody-positive kittens can be retested immediately with a reliable PCR assay to clarify their status. Kittens persistently testing FIV antibody positive after 6 months of age are likely to be truly infected.

The use of the FIV vaccine (Fel-O-Vax FIV; Boehringer Ingelheim) in Canada, the USA, Australia, New Zealand and Japan has complicated the diagnosis of FIV infections based on antibody detection, since vaccinated cats produce antibodies that cannot be distinguished from antibodies induced by natural infection by some commercially available tests. Antibodies can usually be detected within a few weeks of vaccination and it has been shown that they can persist for more than 7 years in some cats.[66] Fel-O-Vax FIV was discontinued in Canada and the USA in 2015 but previously vaccinated cats testing FIV-antibody positive due to vaccination will remain in the cat population for some years to come. Also cats may travel from locations where the vaccine is still in use to Canada, the USA and other countries where the vaccine is not available.

When results of FIV antibody testing are negative, but recent infection cannot be ruled out, testing should be repeated no earlier than 60 days after the last potential exposure.

Comparison of three commercially available POC antibody tests was performed in a population of 119 FIV-vaccinated and 239 FIV-unvaccinated Australian cats.[66] FIV infection status was determined by considering the results of all antibody tests together with results from PCR testing; virus isolation was used for rare discrepant cases. Two POC tests, Witness FeLV-FIV (sensitivity 100%, specificity 98%) and Anigen Rapid FIV Ab/FeLV Ag (sensitivity 100%, specificity 100%), demonstrated excellent sensitivity and specificity, and were shown to determine the true FIV infection status of cats irrespective of FIV vaccination history, if the primary vaccination had been administered at least 6 months previously. The IDEXX SNAP FIV/FeLV Combo test, however, detected antibodies induced by previous vaccination as well as those induced by FIV infection. In a follow-up study, the same research group evaluated the use of saliva (rather than blood) to diagnose FIV infection using the three POC tests and one PCR test.[72] Sensitivities were 44% (IDEXX SNAP FIV/FeLV Combo), 92% (Witness FeLV-FIV), 96% (Anigen Rapid FIV Ab/FeLV Ag) and 72% (RealPCR), whereas the specificity for all tests was similar at 98–100%. The researchers concluded that two POC test kits (Witness and Anigen) could accurately identify FIV infection using saliva, regardless of FIV vaccination history. Testing saliva could be useful in areas where FIV vaccination is available and when venipuncture without skilled restraint or sedation is not possible, such as in situations where large numbers of cats must be screened for FIV infection quickly and easily.

A study conducted in the USA also evaluated whether some POC tests could be used to differentiate between antibodies induced following FIV vaccination vs infection.[73] The study compared four tests: IDEXX SNAP FIV/FeLV Combo, Witness FeLV-FIV, Anigen Rapid FIV Ab/FeLV Ag and VetScan Feline FeLV/FIV Rapid test kits. In this study, 104 uninfected specific pathogen-free cats were vaccinated three times and plasma samples were collected 2–14 months after vaccination.

Maximizing prevention of retrovirus infection can be accomplished through a partnership between veterinarians and pet owners.

Cats were confirmed to be FIV-free by virus culture. The IDEXX SNAP FIV/FeLV Combo and the VetScan Feline FeLV/FIV Rapid tests had positive results in 102/104 and 88/104 uninfected vaccinated cats, respectively. The Witness FeLV-FIV and the Anigen Rapid FIV Ab/FeLV Ag tests correctly identified nearly all vaccinated cats as uninfected. Specificity in FIV-vaccinated cats was 98.1% for Witness FeLV-FIV, 98.1% for Anigen Rapid FIV Ab/FeLV Ag, 21.2% for VetScan Feline FeLV/FIV Rapid and 1.9% for IDEXX SNAP FIV/FeLV Combo tests.

To determine the duration of interference of diagnostic tests by FIV vaccination, a longitudinal study of vaccinated cats was conducted.[74] Kittens received a primary vaccination series according to the manufacturer's recommendations and were periodically tested over 6 months using the IDEXX SNAP FIV/FeLV Combo, Anigen Rapid FIV Ab/FeLV Ag, Witness FeLV-FIV and VetScan Feline FeLV/FIV Rapid test kits. Some cats tested positive using all tests 4 weeks after the first vaccination. Subsequently, 100% of the cats remained positive with the IDEXX SNAP FIV/FeLV Combo and 83% remained positive with the VetScan Feline FeLV/FIV Rapid test for the duration of the study, while cats tested with the Anigen Rapid FIV Ab/FeLV Ag and Witness FeLV-FIV tests became negative by 6 months after the third vaccination for FIV. It was concluded that the Anigen Rapid FIV Ab/FeLV Ag and the Witness FeLV-FIV tests could be used for the diagnosis of FIV infection in vaccinated cats, providing that primary vaccination occurred more than 6 months previously.

Prevention of retrovirus infections

Maximizing prevention of retrovirus infection can be accomplished through a partnership between veterinarians and pet owners. Implementing testing and vaccination protocols, staff and owner education, owner vaccination reminder programs and environmental management can help contain the spread of these infections.

Traditionally, FeLV infection has primarily been viewed as a concern for cats that are 'friendly' or 'social' with other cats because close, intimate contact among cats facilitates salivary transmission. This type of contact occurs among cats through nursing, mutual grooming, and sharing of food, water and litter boxes. However, infection can also occur from inter-cat aggression and studies have shown cats exhibiting aggressive behavior to have an increased risk of FeLV infection.[45,75] Less common sources of FeLV infection include contact with other body fluids (eg, tears, plasma, urine, feces), transplacental transmission, use of contaminated surgical and dental instruments, and blood transfusion.[13,26,76] While susceptibility to infection is highest when cats are young, the cumulative lifetime risk of exposure results in a slighter higher prevalence of infection in older cats.[2]

On the other hand, most natural FIV infections likely result from inter-cat aggression between 'unfriendly' cats because the major mode of transmission is through bite wounds.[45,77,78] Transmission rarely occurs from queen to kittens in a natural environment.[38,79]

Risk factors for feline leukemia virus and feline immunodeficiency virus infections

Prevention strategies start with recognition of risk factors associated with FeLV and FIV infections. Avoidance or minimization of risk factors that are amenable to control (eg, lifestyle, vaccination) should be assessed for each cat (Figures 4 and 5). Patient characteris-

Figure 4 Outdoor lifestyle is a risk factor for retrovirus infection; not all infected cats will appear ill. *Courtesy of Janet Wolf*

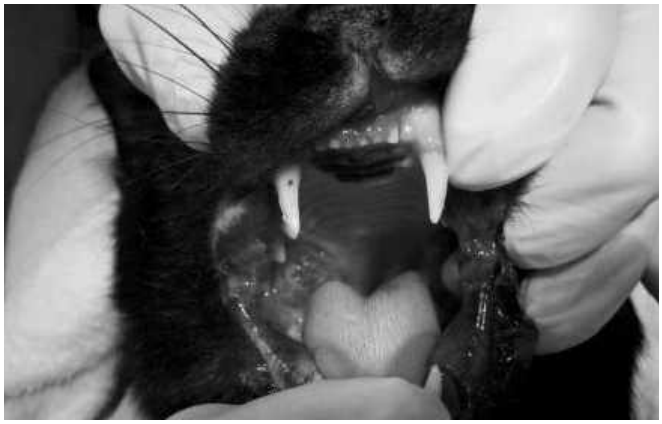

Figure 5 Inflammatory oral disease, such as gingivostomatitis, is associated with an increased risk of retrovirus infection. *Courtesy of Susan Little*

Table 2 Patient characteristics associated with increased prevalence of retrovirus infection[4,45,47,75,78,80,81]

Risk factor	FeLV	FIV
Increasing age	xx	xxx
Male sex	xx	xxx
Sexually intact status	xx	xxx
Outdoor access	xxx	xxx
Close contact with infected cats	xxx	xx
Inter-cat aggression	xx	xxx
Illness (especially oral disease, abscess, respiratory tract disease)	xxx	xxx
Kitten born to an infected queen	xxx	x

'xxx' indicates a stronger risk association than 'xx' or 'x'
FeLV = feline leukemia virus, FIV = feline immunodeficiency virus

tics associated with increased prevalence of retrovirus infection are listed in Table 2.

Vaccination

Feline leukemia virus vaccination

While testing and identification of FeLV-infected cats is necessary for preventing FeLV infection, vaccination is also an important preventive tool. Combined use of testing and vaccination programs is likely the reason for the decrease in FeLV prevalence in Europe and North America in the initial decades after the virus was discovered.[4,5,14,45,82,83] However, recent studies indicate that the prevalence of FeLV has plateaued in some countries, so increased efforts are necessary to further decrease the prevalence.[4,64,84] In one study, a history of vaccination against FeLV was associated with a reduced risk of FeLV infection in cats treated for abscesses and bite wounds.[75] Unvaccinated cats with bite wounds were 7.5 times more likely to be infected with FeLV than vaccinated cats, suggesting that FeLV vaccination provides protection.

Several vaccines for FeLV are available, including adjuvanted inactivated whole virus vaccines, recombinant subunit vaccines and a genetically engineered subunit recombinant canarypox vector vaccine. Commercially available vaccines appear to provide protection against progressive infection and FeLV-associated diseases.[11,85,86] Nevertheless, it remains difficult to assess vaccine efficacy for several reasons. Most of the published efficacy trials have been small studies conducted in research cats and have been performed or supported by the vaccine manufacturers.[86–93] Other factors that hamper interpretation of vaccine efficacy studies include lack of standard challenge and testing protocols, as well as the difficulty of infecting control groups of adult cats without inducing immune suppression.

Vaccination against FeLV does not diminish the importance of testing to identify and isolate cats that are progressively infected.

Although FeLV vaccines have been shown to protect some cats against progressive infection, vaccination will not always prevent proviral DNA integration after FeLV exposure. One study using inactivated vaccines found that, after challenge, vaccinated cats had no detectable viral antigen, viral RNA, proviral DNA or infectious virus.[94] Other studies showed that several current vaccines failed to consistently prevent proviral DNA integration following FeLV exposure.[11,16] Therefore, it cannot be concluded that FeLV vaccination protects against all outcomes of FeLV infection. Nevertheless, several current vaccines are still of great clinical importance because they appear to be efficacious at preventing progressive infection and, thus, curtailing FeLV-associated diseases.[12,86] Several early studies indicated that duration of immunity to FeLV persists for at least 12 months following vaccination[95–97] and, in one study, most cats resisted infection when challenged 2 years after vaccination.[98]

Vaccination against FeLV does not diminish the importance of testing to identify and isolate cats that are progressively infected. Vaccinated and unvaccinated cats that are progressively infected could be sources of infection for other cats. Vaccination against FeLV does not interfere with testing, as the available POC tests detect viral antigen. Therefore, the FeLV infection status of all cats, including vaccinated cats, should be determined. Administering FeLV vaccines to infected cats is of no therapeutic value and every unnecessary vaccination carries the risk of potential adverse reactions.[99] If a vaccinated cat's status is unknown and the cat is later determined to have a progressive FeLV infection, vaccine efficacy would be questioned, and vaccine failure suspected. Cats should be tested for FeLV infection before initial vaccination.

The 2013 AAFP vaccination guidelines recommended FeLV vaccination for all kittens up to and including 1 year of age, and for at-risk adult cats.[100] Vaccination of all kittens is highly recommended (at least in areas with high prevalence of infection) because a kitten's lifestyle and risk of exposure to FeLV frequently changes after acquisition. In addition, kittens are more susceptible to progressive infection, FeLV-associated disease and death if exposed to FeLV compared with adult cats.

When FeLV vaccination is determined to be appropriate, a two-dose primary series is recommended, with the first dose administered as early as 8 weeks of age followed by a second dose administered 3–4 weeks later. A single booster vaccination should be administered 1 year following completion of the initial series. Vaccination can be discontinued thereafter if there is no further risk based on

It cannot be concluded that FeLV vaccination protects against all outcomes of FeLV infection. Nevertheless, several current vaccines are still of great clinical importance because they appear to be efficacious at preventing progressive infection and, thus, curtailing FeLV-associated diseases.

lifestyle, environment and overall health status. The 2013 AAFP vaccination guidelines recommend revaccination every 2 years for cats at low risk of infection and annually for cats at higher risk, based on lifestyle, environment and overall health status. Since those vaccination guidelines were issued, FeLV vaccines with extended duration of immunity have become available. Where vaccines with a 3-year duration of immunity are available, their use can be considered. The 2013 AAFP Feline Vaccination Advisory Panel recommends administering subcutaneous FeLV vaccines in the left hindlimb distal to the stifle joint. The AAFP-recommended FeLV vaccination protocol is outlined in the box below.

Feline immunodeficiency virus vaccination

Multiple studies have shown that cats infected with FIV have low levels of morbidity and mortality with appropriate husbandry and disease management.[45] At the time of writing, only one FIV vaccine is commercially available (Fel-O-Vax FIV; Boehringer Ingelheim) and it is not available in Canada or the USA. Nevertheless, all veterinarians should be aware of this vaccine, because previously vaccinated cats are still present in Canada and the USA, and cats can relocate from other countries where the vaccine is available, such as Australia, New Zealand and Japan.

Fel-O-Vax FIV is a whole-virus, dual subtype (clades A and D), inactivated vaccine combined with an adjuvant, and is licensed for the vaccination of healthy cats 8 weeks of age or older. Variability in vaccine efficacy has been noted. One Australian study (the only field study published to date) found the vaccine had a protective rate of 56%.[101] A study using an FIV isolate in the UK found the vaccine failed to protect experimentally challenged cats.[102] A study of client-owned FIV-vaccinated cats in Australia found a lack of broadly neutralizing antibodies, suggesting cats might not be protected against some virulent recombinant strains in that country.[103]

FIV vaccination is classified as 'non-core' according to the 2013 AAFP Feline Vaccination Advisory Panel[100] and is recommended for cats at high risk of exposure, such as cats with outdoor access or those living with FIV-infected cats. The 2013 AAFP vaccination guidelines recommend owners be informed of the difficulties in interpreting some FIV test results in vaccinated cats and the low protective rate of the vaccine. In addition, the AAFP recommends that all cats, including FIV-vaccinated cats, should carry both visual and permanent identification, such as a microchip and collar (see AAFP's 2019 'Microchip Identification of Cats' position statement; catvets.com/guidelines/position-statements/microchip-identification-cats-position-statement).

AAFP Feline Vaccination Advisory Panel recommendations for feline leukemia virus vaccination[100]

Initial vaccination protocol for kittens and unvaccinated adult cats

- Administer FeLV vaccine series to all cats at risk of infection and all kittens up to and including 1 year of age
- Test all cats for retrovirus infection (regardless of age) before vaccination
- Give first vaccination as early as 8 weeks old
- Administer two vaccines, 3–4 weeks apart
- Administer FeLV booster vaccination 1 year after initial vaccine series

Revaccination protocol for cats 2 years of age and older

- **Do not revaccinate** cats with no risk of exposure, such as:
  - Cats living in a single-cat household with no exposure to other cats
  - Cats living in a household with other cats known to be FeLV negative
  - Cats with outdoor access to an enclosure only or no outdoor access
  - Cats with no exposure to either FeLV-infected cats or cats of unknown FeLV status
- **Revaccinate annually** cats with high risk of exposure, such as:
  - Cats with outdoor access
  - Cats living with known FeLV-infected cats
  - Cats in contact with cats of unknown FeLV status
- **Revaccinate every 2 years** cats with low risk of exposure, such as:
  - Cats with no history of inter-cat aggression (eg, previous cat fight bites)
  - Cats with limited outdoor access and low possibility of exposure to cats of unknown FeLV status

If the decision is made to vaccinate a cat at risk of infection (in a country where the vaccine is available), the cat should be tested for FIV immediately prior to vaccination. An initial series of three doses is administered subcutaneously 2–3 weeks apart. Annual revaccination is recommended if the risk of infection persists.

Limiting transmission in the veterinary practice

It is important that veterinarians familiarize themselves with guidelines, such as these, for management of retrovirus-infected cats, as these cats likely will survive for many years after diagnosis, especially FIV-infected cats.[47,48]

Retroviruses are unstable outside their host animals and are inactivated within a very short time on dry surfaces; therefore, they are considered to have little or no environmental persistence. Detergents and common hospital disinfectants quickly inactivate both FeLV and FIV, and there is little risk for transmission among cats by indirect exposure when simple precautions and routine cleaning procedures are followed.[104,105] Hospitalized cats should not be allowed to have direct contact with one another. Isolation of hospitalized retrovirus-infected cats in an infectious disease ward is not required; they can be kept in the general hospital wards. Furthermore, since retrovirus-infected cats are potentially immunosuppressed, they should not be placed in isolation wards with animals carrying contagious diseases, such as upper respiratory virus infection or panleukopenia, nor with dogs infected with feline-shared pathogens, such as canine parvovirus and *Bordetella bronchiseptica*.

Although casual transmission of the viruses via the environment is unlikely, both viruses are transmitted very efficiently via contaminated body fluids, especially blood. It is therefore imperative to institute and maintain appropriate clinical hygiene practices. Dental and surgical instruments, endotracheal tubes and other items potentially contaminated with body fluids should be thoroughly cleaned and sterilized between uses.[106,107] Reused suture has been shown to be a source of FIV transmission.[106] Intravenous fluid lines and bags, as well as food, can become contaminated with body fluids (especially blood or saliva) and should not be shared among patients. Hypodermic needles should not be reused and oral dosing equipment such as syringes should not be shared among animals. Animal caretakers and other hospital staff members should wash their hands after handling animals and cleaning cages.

Both FeLV and FIV can be transmitted in blood transfusions. Therefore, all blood donors should be confirmed free of infection. Cats used for blood or tissue donation should be screened and confirmed to be negative for FeLV antigen and FeLV provirus by PCR as well as for FIV antibodies.[26,108,109] PCR testing of donors with negative FeLV antigen tests is necessary because cats with regressive infections are capable of transmitting infection via blood transfusion.[26]

Hospitalized retrovirus-infected cats can be kept in the general hospital wards, but should not be allowed to have direct contact with other hospitalized cats.

Cats used for blood or tissue donation should be screened and confirmed to be negative for FeLV antigen and FeLV provirus by PCR, as well as for FIV antibodies.

Limiting transmission in the home

Ideally, retrovirus-infected cats should be confined indoors to prevent infection of other cats and to protect them against other infectious diseases. If a retrovirus-infected cat is identified in a household, the best method of preventing spread to other cats in the household is to prevent direct contact and interaction between the infected cat and its housemates, typically by isolation of infected cats from uninfected cats. Segregation of retrovirus-infected cats within a home can be difficult for owners to achieve and adherence to recommendations might be low. It is reasonable to counsel owners who are unwilling or unable to segregate infected cats on best practices to reduce the risk of disease transmission; for example, by meeting the environmental needs of all cats in the home to reduce conflict and stress, and by neutering all cats.[48,110]

Uninfected cats that reside in a household with FeLV-infected cats should be vaccinated against FeLV, even if the infected cats are isolated, because isolation and hygiene protocols might break down. Onset of protective immunity to FeLV typically takes 2–3 weeks after primary vaccination. Therefore, when a cat is vaccinated against FeLV for the first time, owners should be instructed to protect the cat from exposure to FeLV until at least 3 weeks after the final booster vaccination.[100] Owners should be informed that no FeLV vaccine is perfect and vaccination might not protect all cats against FeLV infection, especially in a high infection pressure situation. An infected queen can transmit FeLV to her kittens in utero or via infected milk.[76,111–113] Therefore, infected queens should not be used for breeding and should be spayed if their condition is sufficiently stable to permit them to undergo surgery, thus eliminating the risk of vertical transmission and reducing stress from estrous cycles.

Generally, cats in households with stable social structures where housemates do not fight are at negligible risk of acquiring FIV infection.[38] One study did report a high rate of transmission within a household without observed fighting but this household also included cats coinfected with FeLV.[37] Vaccination of uninfected housemates might be considered in countries where an FIV vaccine is available. Owners should be informed that cats that cannot live peacefully with a housemate are more likely to fight and thus uninfected cats might be at higher risk of acquiring FIV infection. No new cats should be introduced into such households as this might lead to fighting, even among cats that did not interact aggressively before.

Experimentally, it has been shown that FIV can be vertically transmitted from infected queens to their kittens.[34,114–116] Although this appears to be rare in nature,[38,78] FIV-infected queens should not be used for breeding and should be spayed if their condition is sufficiently stable to permit them to undergo surgery, thus eliminating the risk of vertical transmission and reducing stress from estrous cycles.

Considerations for multi-cat environments

Breeding catteries

The prevalence of retrovirus infections in the controlled environments of catteries appears to be low, particularly since the advent of test and removal programs for FeLV that began in the 1970s. However, certain circumstances in catteries facilitate transmission of infectious diseases, including retrovirus infections, such as group living, mingling of kittens with older cats, close contact of cats during mating, the introduction of new cats and the practice of sending cats to other catteries for breeding. Therefore, ongoing vigilance is required to prevent introduction of FeLV or FIV into catteries.

Only healthy cats should be used for breeding and the retrovirus status of all cats in the cattery (whether breeding or non-breeding) should be known. When testing is performed in the cattery for the first time, all cats should be tested for both FeLV and FIV with a POC test. Cats with negative results should be retested for both FeLV and FIV no sooner than 60 days later to detect false-negative results due to recent infection. Infected cats should be removed from the cattery. All newly acquired kittens and cats should be placed in isolation and tested for FeLV and FIV on arrival. Ideally, they should remain isolated until a second negative test for both viruses is obtained 60 days later, particularly if they originate from a cattery with unknown retrovirus status.

There is little risk of retrovirus transmission among cats by indirect exposure when simple precautions and routine cleaning procedures are followed.

Queens sent to another facility for breeding should be tested before leaving the home cattery and should only be exposed to other cats that have tested negative for FeLV antigen and FIV antibody. Upon return to the home cattery, the queen should be kept in isolation and retested for FeLV and FIV in 60 days.

Cat shows are not significant sources of retrovirus infection because cats on exhibition are housed separately and the viruses are susceptible to commonly used disinfectants. In addition, environmental contamination of surfaces is not a risk due to the fragile nature of retroviruses. Therefore, cats that have left the cattery solely to attend a cat show do not need to be retested for FeLV or FIV or isolated unless direct contact with another cat of unknown retrovirus status has occurred.

In catteries that follow testing guidelines and maintain retrovirus-negative status, vaccination against FeLV or FIV is not necessary if no cats have access to the outdoors or to cats with unknown retrovirus status. Time and resources should be focused on maintaining a retrovirus-negative cattery through testing. Some catteries do not maintain breeding toms and rely totally on breeding services from other catteries. In such circumstances, vaccination of queens against FeLV is recommended in addition to testing of queens that leave the cattery for breeding.

Cats in shelters

The sheltering industry, especially in North America, is in a state of flux as rising community demands to save healthy and treatable animals challenge traditional animal control paradigms that relied on euthanasia as a population control tool. However, the number of cats admitted to shelters, especially during kitten season, continues to outstrip the capacity of many shelters to provide optimal care and to ensure that each cat has an ideal outcome tailored to its unique circumstances. These increased expectations require shelter managers to continuously re-evaluate their protocols and resource allocations to achieve the best overall results for cats both inside and outside shelters.

Shelter management guidelines from the Association of Shelter Veterinarians (ASV) state that protection of the health and welfare of cats in shelters requires vaccination against acute life-threatening infections, parasite treatment, treatment of illness or injury, adequate nutrition, species-appropriate housing, enrichment and behavioral care.[117] Protocols regarding additional care, such as retrovirus management, should be devised based on the best allocation of available resources to sup-

port the shelter's goals, and should be updated based on the most current evidence-based medicine. These decisions must consider the financial and personnel investment associated with testing for infections that generally have a low prevalence, the predictive value of single point-in-time testing, the practicality of additional testing, the outcomes for cats testing positive and the consequences of releasing cats that might have retroviral infections.

Long-term institutionalization creates several physical and emotional threats, especially for cats. Shelter operations and animal welfare are generally best served by investing resources in supporting alternatives to shelter admission altogether or quickly transitioning shelter cats to a permanent home or return to the community.[118] This transition should include a smooth transfer of care and medical history from the shelter to a primary care veterinarian in the community, who will work with the adopter to complete any necessary preventive healthcare procedures and establish ongoing care.

The ASV recommends that cats eligible for adoption or relocation be screened for FeLV and FIV (sheltervet.org/assets/docs/position-statements/felvfivtesting.pdf). This screening is provided pre-adoption in some shelters. However, in many situations, limited shelter resources do not permit routine testing of all cats prior to adoption. In such cases, if cats are housed individually, shelters might prioritize testing higher-risk cats such as sick cats, cats with bite wounds and cats from high-risk situations such as hoarding cases. However, if cats are not tested for retrovirus infection in the shelter, a recommendation for post-adoption testing should be clearly explained to the adopter and documented in the cat's file. Arrangements should be made by the adopter to have the new cat examined and tested by a veterinarian as soon as possible. The new cat should be kept separate from other cats until the test result is known. Although most sheltered cats are free of infection, post-adoption testing is likely to result in some new pet owners confronting difficult decisions about what to do with a newly adopted cat that is subsequently diagnosed with a retroviral infection. If one cat in a litter or group is later reported to be infected, the adopters of other cats with exposure to the infected cat should be notified so that in-contact cats can be monitored and tested.

Although the prevalence of FeLV and FIV in shelter cats in North America mirrors the low rates found in pet cats, thousands of infected cats are likely to pass through shelters each year.[4] Therefore, all cats entering shelters should be considered potentially infected, regardless of the environment from which they originated. Group-housing of untested cats should be strictly avoided. Retroviruses are efficiently transmitted by contaminated body fluids, particularly blood and saliva.[26,106] For this reason, surgical and dentistry instruments, needles, endotracheal tubes and other potentially contaminated equipment should be thoroughly disinfected before use on the next patient, even cats from the same litter.[107]

All cats entering shelters should be considered potentially retrovirus infected, regardless of the environment from which they originated.

Both FeLV and FIV infection differ from other infectious diseases of importance in shelters, such as feline panleukopenia virus, feline calicivirus, feline herpesvirus and feline coronavirus, because retroviruses are easily inactivated with routine disinfection and are not spread by aerosol or indirect contact. Because of the low risk of transmission if cats are housed separately (Figure 6), testing for FeLV and FIV is optional for individually housed cats, and vaccination against FeLV or FIV is not recommended. However, in facilities in which cats are group-housed, FeLV and FIV testing is essential before cats enter the group. Cats entering foster homes should be tested if resident cats are present. For cats that are group-housed for extended periods of time or that live in sanctuaries, FeLV and FIV testing and FeLV vaccination are recommended. Long-term group housing increases the chance of exposure to infected cats inadvertently admitted with negative intake screening tests due to recent infection or regressive infection. Vaccination against FIV is not recommended in shelters because transmission of FIV among co-housed cats that do not fight appears to be uncommon,[38] the level of vaccine-induced immunity is variable,[101] and vaccine-induced positive antibody test results can complicate future determination of the true FIV infection status of vaccinated cats.

Figure 6 Cats of unknown retrovirus status should be housed individually in shelters

Table 3 Feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) testing and vaccination recommendations for healthy cats in animal shelters and free-roaming populations in North America

	FeLV/FIV testing	FeLV vaccination	FIV vaccination
Individually housed cats	Optional	Not recommended	Not recommended
Short-term group-housed cats	Recommended	Not recommended	Not recommended
Foster cats	Recommended	Optional	Not recommended
Long-term group housing and sanctuaries	Recommended	Recommended	Not recommended
Trap–neuter–return cats	Not recommended	Not recommended	Not recommended

The recommendations for FeLV and FIV testing and vaccination for shelters are summarized in Table 3.

Costs of testing can be minimized by enrolling in vendor shelter discount programs or using reference laboratories for multiple samples submitted at a time. However, some tests and laboratories are more accurate than others, so cost should not be the only consideration when selecting tests for use in shelters.[58] The presence of infection can vary within individual litters, community cat colonies and households. Therefore, it is not appropriate to conserve costs by testing one cat as a proxy for others. Practices such as testing a queen and not her kittens, or testing only a few members of a litter, colony or household, are both unreliable and a poor use of resources. Shelter medical records should individually identify each cat and accurately reflect the actual testing procedures and test brand utilized. In addition, test procedures must be performed as indicated by the manufacturer to maintain accuracy. Pooling multiple blood samples for use in a single POC test will reduce test sensitivity and should not be performed.

Although screening tests can be used in shelters, confirmation of infection poses a greater challenge because many shelters have rapid turnover of large numbers of cats and limited resources. Increased costs, delays and difficulty in interpreting discordant results are reasons why many shelters in North America do not pursue additional testing for positive POC results or avoid testing altogether. A simplified 'one and done' testing protocol with a reliable screening test will identify most infected cats (Figure 2, level 1 diagnostics). Exceptions include cats recently exposed to infection, kittens tested as unweaned neonates, and kittens with colostral antibodies against FIV. Anticoagulated whole blood is the most convenient sample for testing cats in shelters. Secondary tests such as PCR (Figure 2, level 2 diagnostics) are valuable when they corroborate screening test results, but do not always clarify the status of cats when results are discordant.

These Guidelines broadly recommend testing all cats for retroviral infection, but an exception exists for free-roaming stray and feral community cats in trap–neuter–return (TNR) programs.

Although these Guidelines broadly recommend testing all cats for retroviral infection, an exception exists for free-roaming stray and feral community cats in trap–neuter–return (TNR) programs. An overarching objective of TNR is to sterilize and vaccinate a sufficient proportion of free-roaming cats in order to reduce the population. The success of TNR programs hinges on deploying adequate financial and personnel resources to sterilize cats faster than they can reproduce. In studies in North America, the prevalence of FeLV infection is similar in outdoor owned pet cats and unowned community cats.[4] In some countries, the prevalence of FIV has been reported as higher in feral cats compared with owned cats.[4] Sterilization reduces the two most important modes of transmission: transmission from queen to kitten for FeLV and fighting among males for both FeLV and FIV.[75,119,120] Because population control of community cats requires a commitment to sterilizing the largest number of cats possible, it is recommended that resources in TNR programs be focused on maximizing the number of cats sterilized and that retroviral testing not be incorporated as a routine practice.[121]

The presence of infection can vary within individual litters, community cat colonies and households. It is not appropriate to conserve costs by testing one cat as a proxy for others.

Like the AAFP, the ASV does not recommend euthanasia of cats solely based on retrovirus infection (sheltervet.org/assets/docs/position-statements/managementofcatswhotestpositive.pdf). In response to goals to save all healthy and treatable cats, a growing number of shelters have expanded their adoption programs to include cats with FeLV and FIV infections. These cats should be held in single-cat housing or group accommodations that segregate them from uninfected cats pending adoption. There are no medical

reasons to exclude retrovirus-infected cats from public adoption rooms in shelters, off-site adoption events, or satellite adoption centers such as those at pet stores if they are housed separately and properly documented. Similarly, legislation in the USA aimed at excluding retrovirus-infected cats from shelter adoption and interstate transport programs is not supported by current medical evidence.

Some shelters have developed specific marketing and education programs to ensure that these cats do not linger unnecessarily in shelter confinement and receive the post-adoption care they require, and to minimize the risk of spreading the infection to other cats in their new homes. One report demonstrated lack of transmission between FIV-infected and uninfected co-mingled cats in a shelter, suggesting that FIV-infected cats could cohabit with compatible FIV-negative cats with little risk under some circumstances.[38] Recent studies investigating the risk of FeLV transmission in the home have not been reported, but transmission of FeLV within a home appears to be more common. This suggests that FeLV-infected cats should be adopted into homes only with other FeLV-infected cats or as single cats. Cats with FIV have been shown to survive longer in normal home environments than in a high-density cat sanctuary.[48] Since stress can exacerbate the clinical course of both FeLV and FIV infection, adoption into a home-like setting is likely to result in better long-term outcomes.

Management of retrovirus-infected cats

Longevity

Cats infected with FIV have been shown to have variable lifespans, with some infected cats living as long as uninfected cats. Long-term monitoring of a 26-cat household with endemic FeLV and FIV infections revealed that all progressively FeLV-infected cats died within 5 years of diagnosis, but FIV infection did not affect survival over the same period.[37]

A large study compared the survival of more than 1000 FIV-infected cats with more than 8000 age- and sex-matched uninfected control cats.[122] The median age of cats in the study was 5 years. Of cats not euthanized near the time of diagnosis, the median survival time after the first test was 4.9 years for FIV-positive cats and 6.0 years for negative controls. The study also compared more than 800 FeLV-infected cats with 7000 matched controls. The median age of cats in the study was 2 years. Of cats not euthanized near the time of diagnosis, the median survival time after diagnosis was 2.4 years for progressively infected FeLV cats and 6.3 years for negative controls. A high rate of euthanasia in the first year after diagnosis in the case of both retroviruses was likely due to disease conditions that prompted the veterinary visit and subsequent diagnosis of FeLV or FIV, or to euthanasia of healthy retrovirus-infected cats for the purposes of infection control.

Studies demonstrate that retrovirus-infected cats, especially FIV-infected cats, may experience normal longevity with appropriate husbandry and disease management.

As part of a large study of FIV and FeLV prevalence in owned cats in Germany, a subset of 100 cats (19 FIV positive, 18 FeLV positive, 63 uninfected) was evaluated for survival times.[45] There was no significant difference in the mean survival time of FIV-infected cats (785 days) compared with uninfected cats (620 days). However, the mean survival time of progressively infected FeLV cats (312 days) was significantly shorter compared with uninfected cats (732 days).

A retrospective case-control study used Kaplan–Meier curves to compare survival times of 76 FIV-infected and 444 uninfected owned cats in Australia.[46] Survival of FIV-infected cats was not significantly different from that of uninfected cats. Another retrospective study evaluated survival times in 58 FIV-infected cats compared with 58 age- and sex-matched uninfected cats.[47] The median survival time of FIV-infected cats after diagnosis (3.9 years) was not significantly different from that of uninfected cats (5.9 years). In an assessment of lifetime medical records for shelter cats classified as FIV infected (n = 63), progressively FeLV infected (n = 22), coinfected (n = 4) or uninfected (n = 11), longevity was similar in FIV-infected cats compared with non-infected cats.[123] Cats with progressive FeLV infection and cats coinfected with FeLV and FIV had significantly shorter lifespans as well as a higher incidence of lymphoma.

These studies demonstrate that retrovirus-infected cats, especially FIV-infected cats, may experience normal longevity with appropriate husbandry and disease management. Diagnosis of a retrovirus infection should not be the sole criterion for euthanasia. Owners should be educated in detail about options for care of infected cats. Furthermore, owners should be made aware of the potential for false-positive test results and the clinician should offer additional testing whenever possible and feasible. Provision of an accurate prognosis and careful monitoring of each cat will assist owners in the care of the retrovirus-infected cat.

Retrovirus-infected cats are subject to the same diseases that befall cats free of those infections. A disease diagnosed in a retrovirus-infected cat might or might not be related to the retrovirus infection.[120] However, knowledge of current FIV and FeLV status in such cats is important because the presence of a retrovirus infection impacts long-term management.

Housing and environment

There are benefits to housing retrovirus-infected cats indoors and allowing access to the outdoors only within secure enclosures. Benefits include reduced exposure to other infectious diseases, reduced risk of trauma and injury, and limited ability to transmit retrovirus infection to other cats. Good nutrition and husbandry, and an enriched lifestyle if confined indoors, are essential to maintain good health.[48]

Each case must be evaluated individually as some outdoor-living cats will not readily adapt to an indoor-only lifestyle. The stress of an enforced lifestyle change might have detrimental medical and behavioral effects. In some circumstances, it might be less stressful to allow retrovirus-infected cats access to the outdoors, preferably within a secure enclosure such as a 'catio'. Cats that do not exhibit high-risk behaviours (eg, breeding, reproduction, fighting) pose little risk of disease transmission to other cats.

With proper care and environmental management, FIV-infected cats can live for many years. In a 22-month study, FIV-infected cats living in homes alone or with one other cat were compared with FIV-infected cats living in a population-dense multi-cat sanctuary.[48] The latter group of cats were more likely to display clinical signs related to their disease, with 51% of these cats dying during the study period. Lymphoma was the most common cause of mortality in these cases. The FIV-infected cats living in low-population households did not display clinical signs during the study period and only one death, owing to hypertrophic cardiomyopathy (presumably unrelated), was observed. The conclusion from this study was that management and housing conditions impact the development of clinical signs, disease progression and survival time in FIV-infected cats.

Housing conditions also appear to affect outcomes for FeLV-infected cats. In a study of cats in two rescue sanctuaries that group-housed FeLV-infected cats with uninfected cats without separating clinically ill cats from healthy cats, the prevalence of FeLV was more than 20-fold higher than in the general pet cat population.[15] Not only were cats more likely to be infected in the sanctuaries, but they were also more likely to develop the progressive form of infection, leading to poorer long-term outcomes.

The apparent benefit of low-density housing can be attributed to reduced levels of environmental stress, infectious pressure and coinfections. Careful management of resources in multi-cat households might assist in reducing these stressors, leading to better clinical outcomes. Where possible, retrovirus-infected cats should be housed in low-density environments where stressors are reduced, resources are ample, and caregivers can observe patient health status carefully. Environmental needs of indoor cats have been detailed elsewhere.[110]

Where possible, retrovirus-infected cats should be housed in low-density environments where stressors are reduced, resources are ample and caregivers can observe patient health status carefully.

Healthcare

Preventive healthcare

Cats infected with FeLV or FIV should receive preventive healthcare checkups at least every 6 months for prompt detection of changes in their health status. Veterinarians should obtain a detailed history to help identify changes requiring more intensive investigation and should perform a thorough physical examination at each visit. Special attention should be paid to the oral cavity because dental and oral diseases are more common in retrovirus-infected cats.[48,123,124] Lymph nodes should be evaluated for changes in size and shape. All cats should undergo a thorough examination of the anterior and posterior segments of the eye.[125] The skin should be examined closely for evidence of external parasite infestations, fungal disease and neoplastic changes.

Retrovirus-infected cats should be prescribed appropriate prophylaxis for internal and external parasites. In areas where heartworm is prevalent, cats should be on monthly chemoprophylaxis. Use of routine, consistent parasite control according to the Companion Animal Parasite Council recommendations (capcvet.org) will reduce the risk of secondary infection and disease in these potentially immunosuppressed cats.

Nutritional support is key to maintaining good health in these patients. A nutritionally balanced and complete feline diet appropriate to the cat's life stage should be fed. Raw meat and raw dairy products should be avoided because the risk of food-borne bacterial and parasitic diseases is likely greater in these potentially immunosuppressed cats. Periodic nutritional assessments should evaluate food intake, body condition score (BCS), muscle condition score (MCS) and quality of nutrition to improve health and alert the clinician to early problems. Unexpected downward trends in body weight or reductions in BCS or MCS should prompt the clinician to investigate further. In any cat, changes in body weight can precede other signs of clinical disease by months or even years.[126,127]

A complete blood count should be performed annually for FIV-infected cats and at least every 6 months for FeLV-infected cats because of the greater frequency of virus-related hematologic disorders in FeLV-infected cats. A serum biochemical analysis and complete urinalysis (urine specific gravity, urine chemistries and sediment examination) should be performed annually for FeLV- and FIV-infected cats. Urine samples should be collected by cystocentesis so that bacterial

Vaccination should not be avoided in cats with retroviral infection because they can develop more severe clinical disease related to panleukopenia virus and upper respiratory tract infections after natural exposure compared with uninfected cats.

cultures can be performed if indicated. Fecal examinations should be performed as needed.

Vaccine selection and immunization intervals for healthy cats with FeLV or FIV infection should be based on individual risk assessments using the AAFP vaccination guidelines developed for cats in general.[100] Vaccination should not be avoided in cats with retroviral infection because they can develop more severe clinical disease related to panleukopenia virus and upper respiratory tract infections after natural exposure compared with uninfected cats.[128–131] Vaccination for rabies should follow local regulations. There is little evidence to suggest modified-live virus vaccines are a risk in retrovirus-infected cats and the response of asymptomatic retrovirus-infected cats can be similar to uninfected cats.[132]

Sexually intact male and female cats should be neutered to reduce stress associated with estrus and mating behaviors. Neutered animals are also less likely to roam away from home and interact aggressively with other cats.

Surgical management and perioperative care

In otherwise healthy, retrovirus-infected cats, surgical procedures should be used as required to maintain health and manage disease. Retrovirus-infected cats should receive the same quality of anesthetic, analgesic, surgical and perioperative care as given to all feline patients. Preoperative evaluation, including laboratory testing, should follow the same standard of care as for uninfected cats.

As for all cats, the use of perioperative antibiotics should be reserved for those individuals with clear evidence of immunosuppression and/or those undergoing surgeries where the risk of bacterial contamination is moderate to high.[133] Multimodal analgesia plans should be used in all cats when indicated, especially if they have concurrent painful conditions such as gingivostomatitis.

Management of clinical illness

Treatment of secondary diseases

Medical care of the clinically ill retrovirus-infected cat should be based on a complete review of the patient's clinical status, the owner's goals, and available therapeutics and their relative safety or toxicity. The patient should first be evaluated to determine whether the illness is unrelated to the retrovirus infection, secondary to immunosuppression from retrovirus infection or a direct cause of the retrovirus infection (see box below). Patients experiencing illness unrelated to retrovirus infection should be managed according to standard protocols for the specific health condition(s). More vigilant and frequent monitoring of retrovirus-infected patients might be indicated depending on their health condition.

Retroviruses can contribute to any illness either as a direct effect of the viral infection or a secondary effect through mechanisms such as immunosuppression. A detailed review of the clinical aspects of retrovirus infections in cats has been published and should be consulted.[7] Careful assessment of each patient will assist the clinician in determining the etiology of the problem and the type of care required.

Cats infected with FeLV or FIV are at increased risk of developing neoplasia (primarily lymphoma), bone marrow suppression, neurologic disease and infections secondary to immunosuppression. An increased risk of inflammatory oral disease has also been associated with retroviral infection in cats.[48,123,124] Retrovirus-infected patients with severe gingivostomatitis are

Establishing the cause of clinical signs in retrovirus-infected cats

Unrelated to retrovirus infection

These include diseases and illnesses common to cats regardless of retrovirus status. Examples include lower urinary tract disease, hyperthyroidism, diabetes mellitus, chronic kidney disease, etc.

Secondary to retrovirus infection

These include conditions that retrovirus-infected cats are predisposed to due to retrovirus-related immunosuppression. Examples include infectious diseases and neoplasia, as well as chronic gingivostomatitis.

Directly related to retrovirus infection

These include diseases that are caused directly by the retrovirus:

- FeLV: neoplasia (primarily lymphoma), bone marrow suppression (anemia, thrombocytopenia, leukopenia, pancytopenia), neurologic disease.
- FIV: immunosuppression, neurologic disease.

Recommended reading

- Beatty JA. **Feline immunodeficiency virus infection.** In: Ettinger SJ, Feldman EC and Cote E (eds). Textbook of veterinary internal medicine. 8th ed. St Louis, MO: Elsevier Saunders, 2017, pp 2422–2441.
- European Advisory Board on Cat Diseases Guidelines: abcdcatsvets.org/guidelines-infections.
- Hartmann K and Levy JK. **Feline leukemia virus infection.** In: Ettinger SJ, Feldman EC and Cote E (eds). Textbook of veterinary internal medicine. 8th ed. St Louis, MO: Elsevier Saunders, 2017, pp 2442–2455.
- Sykes JE. **Feline immunodeficiency virus infection.** In: Sykes JE (ed). Canine and feline infectious diseases. St Louis, MO: Elsevier Saunders, 2014, pp 209–223.
- Sykes JE and Hartmann K. **Feline leukemia virus infection.** In: Sykes JE (ed). Canine and feline infectious diseases. St Louis, MO: Elsevier Saunders, 2014, pp 224–238.
- Wilkes RP and Hartmann K. **Update on antiviral therapies.** In: Little SE (ed). August's consultations in feline internal medicine. Vol 7. St Louis, MO: Elsevier, 2015, pp 84–96.

most likely to benefit long term from full mouth extraction, with complete extraction of all tooth roots, rather than medical management. Anemia in cats infected with FeLV can be due to various causes including the direct effect of the virus on bone marrow (non-regenerative anemia), secondary infections (eg, infections with *Mycoplasma* species) and other mechanisms. An attempt should always be made to identify and treat underlying causes, especially for regenerative anemia. For a full discussion of the diagnosis and management of health conditions in retrovirus-infected cats, the reader is referred to the resources listed in the box above.

While disease status in human patients with HIV infection is assessed with various markers such as the CD4:CD8 ratio, these markers have not proven reliable in cats with natural retroviral infections. Weight loss can be indirectly related to retrovirus infection,[48] but it is also associated with many other diseases. Quality of life parameters can include the use of scoring systems, such as a modified Karnofsky score, which allows for assessment by both clinician and owner to detect diminishing quality of life.[134]

Targeted therapeutics

Highly active combination antiretroviral therapies ('drug cocktails') are the mainstay of treatment in HIV-infected patients and result in longer survival times and improved quality of life. Unfortunately, few large long-term controlled studies in naturally infected cats have shown long-lasting benefits of using antiviral drugs. Drugs available to treat retrovirus-infected cats are limited and tend to show lower efficacy in feline patients compared with human patients. Many of these drugs require impractical long-term use, are costly and often come with mild to severe toxic side effects that limit their utility.

Zidovudine (azidothymidine; AZT) is a nucleoside analog and one of the few antiviral compounds used in both FeLV and FIV infections. The drug can reduce viral load and improve immunologic and clinical status, particularly in cats with neurologic signs or stomatitis.[135] In cases where clinical illness is thought to be attributable to retroviral infection, AZT can be given at 5–10 mg/kg PO q12h. The higher dose should be used carefully in FeLV-infected cats because adverse effects, particularly non-regenerative anemia, can develop.[136]

Drugs available to treat retrovirus-infected cats are limited and tend to show lower efficacy in feline patients compared with human patients.

Interferons (human and feline) are often used in retrovirus-infected cats as antivirals and immunomodulators in the hope that viral load can be reduced and recovery from associated clinical syndromes can be facilitated. Unfortunately, well designed clinical trials of these drugs in retrovirus-infected cats are lacking or have failed to confirm therapeutic benefits. Feline interferon omega (Virbagen Omega; Virbac Animal Health) is available in some countries. A study using parenteral feline interferon omega showed a higher survival rate after 9 months in interferon-treated FeLV-infected cats when compared with a placebo-treated FeLV-infected control group.[137] Other studies provided some evidence of clinical improvement in FIV- or FeLV-infected cats,[138,139] but those beneficial effects might not have been attributed to treatment of the retrovirus infection but rather to treatment of secondary infections. No controlled studies using oral feline interferon omega in FIV- or FeLV-infected cats have been published to date. For more information on antiretroviral chemotherapy for retrovirus-infected cats, the reader is referred to published reviews.[135]

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Glossary of terms

Feline leukemia virus (FeLV) antigenemia	Presence of soluble viral capsid protein p27 in blood; in most cats considered equivalent to viremia
Feline leukemia virus infection	✣ Abortive infection: the immune response effectively eliminates the virus ✣ Progressive infection: the immune response fails to control the virus, so these cats are potentially infectious and at risk of developing FeLV-associated disease ✣ Regressive infection: the immune response suppresses (but does not eliminate) the virus, so these cats are less likely to transmit infection or develop FeLV-associated disease
Immunofluorescent antibody (IFA) test	Cytologic technique used to identify p27 FeLV antigen in the cytoplasm of infected cells in a blood smear. A positive result indicates bone marrow infection and, thus, is usually associated with progressive infection, although some IFA-positive cats can overcome viremia and become regressively infected
Polymerase chain reaction (PCR) and reverse transcriptase PCR (RT-PCR)	Molecular biology techniques used to amplify and detect viral genetic material (proviral DNA or viral RNA, respectively) by matching primers and probes (short genetic fragments) that are complementary to target regions in viral sequences integrated into the cat's genome or the pathogen, respectively. These techniques detect very small amounts of viral genetic material and can be very sensitive and specific
Proviral DNA	Viral DNA that is integrated into the DNA of the host cell; when the retrovirus infects a cell, it uses its own reverse transcriptase enzyme to produce a DNA version (proviral DNA) of its RNA genome; the proviral DNA is incorporated into the host cell's genome where it becomes a provirus
Real-time PCR and real-time RT-PCR	Molecular techniques that permit quantification of FeLV or FIV provirus (DNA) or viral RNA, respectively
Retrovirus	A family of viruses with an RNA genome that is converted to DNA by the enzyme reverse transcriptase and then integrated into the host cell genome; FeLV is a member of the Gammaretrovirus genus, and FIV is a member of the Lentivirus genus
Viremia	Presence of infectious virus in the blood, usually associated with the presence of soluble viral capsid protein p27 in blood

SUMMARY POINTS

- Retrovirus infections remain common and important diseases of cats worldwide.
- Ongoing research into viral pathogenesis and improvements in diagnostic testing continue to refine our state of knowledge about these viruses.
- Veterinary practitioners are advised to take advantage of current peer-reviewed published reviews and recommendations for testing and management of cats in different populations.
- Additional resources for interested veterinary professionals are found in the box on page 23.

Ethical approval

This work did not involve the use of animals and therefore ethical approval was not required.

Informed consent

This work did not involve the use of animals and therefore informed consent was not required. For any animals individually identifiable within this publication, informed consent for their use in the publication (either verbal or written) was obtained from the people involved.

References

1 Buch J, Beall M, O'Connor T, et al. **Worldwide clinic-based serologic survey of FIV antibody and FeLV antigen in cats.** ACVIM Forum, National Harbor, MD, 8–10 June 2017.

2 Levy J K, Scott HM, Lachtara JL, et al. **Seroprevalence of feline leukemia virus and feline immunodeficiency virus infection among cats in North America and risk factors for seropositivity.** *J Am Vet Med Assoc* 2006; 228: 371–376.

3 Little S, Sears W, Lachtara J, et al. **Seroprevalence of feline leukemia virus and feline immunodeficiency virus infection among cats in Canada.** *Can Vet J* 2009; 50: 644–648.

4 Burling AN, Levy JK, Scott HM, et al. **Seroprevalences of feline leukemia virus and feline immunodeficiency virus infection in cats in the United States and Canada and risk factors for seropositivity.** *J Am Vet Med Assoc* 2017; 251: 187–194.

5 Studer N, Lutz H, Saegerman C, et al. **Pan-European study on the prevalence of the feline leukaemia virus infection – reported by the European Advisory Board on Cat Diseases (ABCD Europe).** *Viruses* 2019; 11. DOI: 10.3390/v11110993.

6 Hartmann K and Levy JK. **Feline leukemia virus infection.** In: Ettinger SJ, Feldman EC and Cote E (eds). Textbook of veterinary internal medicine. 8th ed. St Louis, MO: Elsevier Saunders, 2017, pp 2442–2455.

7 Hartmann K. **Clinical aspects of feline immunodeficiency and feline leukemia virus infection.** *Vet Immunol Immunopathol* 2012; 143: 190–201.

8 Cattori V, Tandon R, Riond B, et al. **The kinetics of feline leukaemia virus shedding in experimentally infected cats are associated with infection outcome.** *Vet Microbiol* 2009; 133: 292–296.

9 Rojko JL, Hoover EA, Mathes LE, et al. **Pathogenesis of experimental feline leukemia virus infection.** *J Natl Cancer Inst* 1979; 63: 759–768.

10 Torres AN, Mathiason CK and Hoover EA. **Re-examination of feline leukemia virus:host relationships using real-time PCR.** *Virology* 2005; 332: 272–283.

11 Hofmann-Lehmann R, Cattori V, Tandon R, et al. **Vaccination against the feline leukaemia virus: outcome and response categories and long-term follow-up.** *Vaccine* 2007; 25: 5531–5539.

12 Hofmann-Lehmann R, Cattori V, Tandon R, et al. **How molecular methods change our views of FeLV infection and vaccination.** *Vet Immunol Immunopathol* 2008; 123: 119–123.

13 Lutz H, Addie D, Belak S, et al. **Feline leukaemia: ABCD guidelines on prevention and management.** *J Feline Med Surg* 2009; 11: 565–574.

14 Englert T, Lutz H, Sauter-Louis C, et al. **Survey of the feline leukemia virus infection status of cats in Southern Germany.** *J Feline Med Surg* 2012; 14: 392–398.

15 Westman M, Norris J, Malik R, et al. **The diagnosis of feline leukaemia virus (FeLV) infection in owned and group-housed rescue cats in Australia.** *Viruses* 2019; 11: 503. DOI: 10.3390/v11060503.

16 Hofmann-Lehmann R, Tandon R, Boretti FS, et al. **Reassessment of feline leukaemia virus (FeLV) vaccines with novel sensitive molecular assays.** *Vaccine* 2006; 24: 1087–1094.

17 Hofmann-Lehmann R, Huder JB, Gruber S, et al. **Feline leukaemia provirus load during the course of experimental infection and in naturally infected cats.** *J Gen Virol* 2001; 82: 1589–1596.

18 McClelland AJ, Hardy WD and Zuckerman EE. **Prognosis of healthy feline leukemia virus infected cats.** In: Hardy WD, Essex M and McClelland AJ (eds). Development in cancer research. Amsterdam: Elsevier Scientific Publishing, 1980, pp 121–126.

19 Helfer-Hungerbuehler AK, Widmer S, Kessler Y, et al. **Long-term follow up of feline leukemia virus infection and characterization of viral RNA loads using molecular methods in tissues of cats with different infection outcomes.** *Virus Res* 2015; 197: 137–150.

20 Pedersen NC, Theilen G, Keane MA, et al. **Studies of naturally transmitted feline leukemia virus infection.** *Am J Vet Res* 1977; 38: 1523–1531.

21 Lutz H, Pedersen NC and Theilen GH. **Course of feline leukemia virus infection and its detection by enzyme linked immunosorbent assay and monoclonal antibodies.** *Am J Vet Res* 1983; 44: 2054–2059.

22 Flynn JN, Hanlon L and Jarrett O. **Feline leukaemia virus: protective immunity is mediated by virus-specific cytotoxic T lymphocytes.** *Immunology* 2000; 101: 120–125.

23 Flynn JN, Dunham SP, Watson V, et al. **Longitudinal analysis of feline leukemia virus-specific cytotoxic T lymphocytes: correlation with recovery from infection.** *J Virol* 2002; 76: 2306–2315.

24 Pepin AC, Tandon R, Cattori V, et al. **Cellular segregation of feline leukemia provirus and viral RNA in leukocyte subsets of long-term experimentally infected cats.** *Virus Res* 2007; 127: 9–16.

25 Cattori V, Tandon R, Pepin A, et al. **Rapid detection of feline leukemia virus provirus integration into feline genomic DNA.** *Mol Cell Probes* 2006; 20: 172–181.

26 Nesina S, Helfer-Hungerbuehler AK, Riond B, et al. **Retroviral DNA – the silent winner: blood transfusion containing latent feline leukemia provirus causes infection and disease in naïve recipient cats.** *Retrovirology* 2015; 12. DOI: 10.1186/s12977-015-0231-z.

27 Stützer B, Müller F, Majzoub M, et al. **Role of latent feline leukemia virus infection in nonregenerative cytopenias of cats.** *J Vet Intern Med* 2010; 24: 192–197.

28 Stützer B, Simon K, Lutz H, et al. **Incidence of persistent viraemia and latent feline leukaemia virus infection in cats with lymphoma.** *J Feline Med Surg* 2011; 13: 81–87.

29 Helfer-Hungerbuehler AK, Cattori V, Boretti FS, et al. **Dominance of highly divergent feline leukemia virus A progeny variants in a cat with recurrent viremia and fatal lymphoma.** *Retrovirology* 2010; 7. DOI: 10.1186/1742-4690-7-14.

30 McLuckie A, Barrs V, Lindsay S, et al. **Molecular diagnosis of *Felis catus* gammaherpesvirus 1 (FcaGHV1) infection in cats of known retrovirus status with and without lymphoma.** *Viruses* 2018; 10. DOI: 10.3390/v10030128.

31 Major A, Cattori, V, Boenzli E, et al. **Exposure of cats to low doses of FeLV: seroconversion as the sole parameter of infection.** *Vet Res* 2010; 41. DOI: 10.1051/vetres/2009065.

32 Boenzli E, Hadorn M, Hartnack S, et al. **Detection of antibodies to the feline leukemia virus (FeLV) transmembrane protein p15E: an alternative approach for serological FeLV diagnosis based on antibodies to p15E.** *J Clin Microbiol* 2014; 52: 2046–2052.

33 O'Neil LL, Burkhard MJ, Diehl LJ, et al. **Vertical transmission of feline immunodeficiency virus.** *Semin Vet Med Surg (Small Anim)* 1995; 10: 266–278.

34 Allison RW and Hoover EA. **Covert vertical transmission of feline immunodeficiency virus.** *AIDS Res Human Retrovir* 2003; 19; 421–434.

35 Ueland K and Nesse LL. **No evidence of vertical transmission of naturally acquired feline immunodeficiency virus infection.** *Vet Immunol Immunopathol* 1992; 33; 301–308.

36 Pu R, Okada S, Little ER, et al. **Protection of neonatal kittens against feline immunodeficiency virus infection with passive maternal antiviral antibodies.** *AIDS* 1995; 9: 235–242.

37 Addie DD, Dennis JM, Toth S, et al. **Long-term impact on a closed household of pet cats of natural infection with feline coronavirus, feline leukaemia virus and feline immunodeficiency virus.** *Vet Rec* 2000; 146: 419–424.

38 Litster AL. **Transmission of feline immunodeficiency virus**

(FIV) among cohabiting cats in two cat rescue shelters. *Vet J* 2014; 201: 184–188.

39 Jordan HL, Howard J, Barr MC, et al. **Feline immunodeficiency virus is shed in semen from experimentally and naturally infected cats.** *AIDS Res Human Retrovir* 1998; 14: 1087–1092.

40 Egberink H and Horzinek MC. **Animal immunodeficiency viruses.** *Vet Microbiol* 1992; 33: 311–331.

41 Yamamoto JK, Pu R, Sato E, et al. **Feline immunodeficiency virus pathogenesis and development of a dual-subtype feline-immunodeficiency-virus vaccine.** *AIDS* 2007; 21; 547–563.

42 Hoffmann-Fezer G, Thum I, Herbold M, et al. **Decline in CD4+ cell numbers in cats with naturally acquired feline immunodeficiency virus infection.** *J Virol* 1992; 66: 1484–1488.

43 Hoffmann-Fezer G, Mortelbauer W, Hartmann K, et al. **Comparison of T-cell subpopulations in cats naturally infected with feline leukaemia virus or feline immunodeficiency virus.** *Res Vet Sci* 1996; 61: 222–226.

44 Hartmann K. **Role of retroviruses in feline lymphoma.** *Eur J Comp Anim Pract* 2015; 25: 4–15.

45 Gleich SE, Krieger S and Hartmann K. **Prevalence of feline immunodeficiency virus and feline leukaemia virus among client-owned cats and risk factors for infection in Germany.** *J Feline Med Surg* 2009; 11: 985–992.

46 Liem BP, Dhand NK, Pepper AE, et al. **Clinical findings and survival in cats naturally infected with feline immunodeficiency virus.** *J Vet Intern Med* 2013; 27: 798–805.

47 Ravi M, Wobeser GA, Taylor SM, et al. **Naturally acquired feline immunodeficiency virus (FIV) infection in cats from western Canada: prevalence, disease associations, and survival analysis.** *Can Vet J* 2010; 51: 271–276.

48 Bęczkowski PM, Litster A, Lin TL, et al. **Contrasting clinical outcomes in two cohorts of cats naturally infected with feline immunodeficiency virus (FIV).** *Vet Microbiol* 2015; 176: 50–60.

49 Wilkes RP, Anis E, Dunbar D, et al. **Rapid and sensitive insulated isothermal PCR for point-of-need feline leukaemia virus detection.** *J Feline Med Surg* 2018; 20: 362–369.

50 Wilkes RP, Kania SA, Tsai YL, et al. **Rapid and sensitive detection of feline immunodeficiency virus using an insulated isothermal PCR-based assay with a point-of-need PCR detection platform.** *J Vet Diagn Invest* 2015; 27: 510–515.

51 Frankenfeld J, Meili T, Meli ML, et al. **Decreased sensitivity of the serological detection of feline immunodeficiency virus infection potentially due to imported genetic variants.** *Viruses* 2019, 11. DOI: 10.3390/v11080697.

52 Hartmann K, Griessmayr P, Schulz B, et al. **Quality of different in-clinic test systems for feline immunodeficiency virus and feline leukaemia virus infection.** *J Feline Med Surg* 2007; 9: 439–445.

53 Pinches MD, Diesel G, Helps CR, et al. **An update on FIV and FeLV test performance using a Bayesian statistical approach.** *Vet Clin Pathol* 2007; 36: 141–147.

54 Sand C, Englert T, Egberink H, et al. **Evaluation of a new in-clinic test system to detect feline immunodeficiency virus and feline leukemia virus infection.** *Vet Clin Pathol* 2010; 39: 210–214.

55 Hawkins EC. **Saliva and tear tests for feline leukemia virus.** *J Am Vet Med Assoc* 1991; 199: 1382–1385.

56 Westman ME, Malik R, Hall E, et al. **Comparison of three feline leukaemia virus (FeLV) point-of-care antigen test kits using blood and saliva.** *Comp Immunol Microbiol Infect Dis* 2017; 50: 88–96.

57 Tandon R, Cattori V, Gomes-Keller MA, et al. **Quantitation of feline leukaemia virus viral and proviral loads by TaqMan real-time polymerase chain reaction.** *J Virol Methods* 2005; 130: 124–132.

58 Levy JK, Crawford PC and Tucker SJ. **Performance of 4 point-of-care screening tests for feline leukemia virus and feline immunodeficiency virus.** *J Vet Intern Med* 2017; 31: 521–526.

59 Krecic MR, Velineni S, Meeus, P, et al. **Diagnostic performances of two rapid tests for detection of feline leukemia virus antigen in sera of experimentally feline leukemia virus-infected cats.** *JFMS Open Rep* 2018; 4. DOI: 10.1177/2055116917748117.

60 Jarrett O, Golder MC and Stewart MF. **Detection of transient and persistent feline leukaemia virus infections.** *Vet Rec* 1982; 110: 225–228.

61 Beall MJ, Buch J, Cahill RJ, et al. **Evaluation of a quantitative enzyme-linked immunosorbent assay for feline leukemia virus p27 antigen and comparison to proviral DNA loads by real-time polymerase chain reaction.** *Comp Immunol Microbiol Infect Dis* 2019; 67. DOI: 10.1016/j.cimid.2019.101348.

62 Gomes-Keller MA, Tandon R, Gonczi E, et al. **Shedding of feline leukemia virus RNA in saliva is a consistent feature in viraemic cats.** *Vet Microbiol* 2006; 112: 11–21.

63 Gomes-Keller MA, Gonczi E, Tandon R, et al. **Detection of feline leukemia virus RNA in saliva from naturally infected cats and correlation of PCR results with those of current diagnostic methods.** *J Clin Microbiol* 2006; 44: 916–922.

64 Levy JK, Crawford PC and Slater MR. **Effect of vaccination against feline immunodeficiency virus on results of serologic testing in cats.** *J Am Vet Med Assoc* 2004; 25: 1558–1561.

65 Ammersbach M, Little S and Bienzle D. **Preliminary evaluation of a quantitative polymerase chain reaction assay for diagnosis of feline immunodeficiency virus infection.** *J Feline Med Surg* 2013; 15: 725–729.

66 Westman ME, Malik R, Hall E, et al. **Determining the feline immunodeficiency virus (FIV) status of FIV-vaccinated cats using point-of-care antibody kits.** *Comp Immunol Microbiol Infect Dis* 2015; 42: 43–52.

67 Nichols J, Weng HY, Litster A, et al. **Commercially available enzyme-linked immunosorbent assay and polymerase chain reaction tests for detection of feline immunodeficiency virus infection.** *J Vet Intern Med* 2017; 31: 55–59.

68 Klein D, Leutenegger CM, Bahula C, et al. **Influence of preassay and sequence variations on viral load determination by a multiplex real-time reverse transcriptase-polymerase chain reaction for feline immunodeficiency virus.** *J AIDS* 2001; 26: 8–20.

69 Bęczkowski PM, Hughes J, Biek R, et al. **Feline immunodeficiency (FIV) *env* recombinants are common in natural infections.** *Retrovirology* 2014; 11. DOI: 10.1186/s12977-014-0080-1.

70 Crawford PC, Slater MR and Levy JK. **Accuracy of polymerase chain reaction assays for diagnosis of feline immunodeficiency virus infection in cats.** *J Am Vet Med Assoc* 2005; 226: 1503–1507.

71 MacDonald K, Levy JK, Tucker SJ, et al. **Effects of passive transfer of immunity on results of diagnostic tests for antibodies against feline immunodeficiency virus in kittens born to vaccinated queens.** *J Am Vet Med Assoc* 2004; 225: 1554–1557.

72 Westman ME, Malik R, Hall E, et al. **Diagnosing feline immunodeficiency virus (FIV) infection in FIV-vaccinated and FIV-unvaccinated cats using saliva.** *Comp Immunol Microbiol Infect Dis* 2016; 46: 66–72.

73 Crawford C. **Does a DIVA test exist for differentiating FIV infection from FIV vaccination?** *J Vet Intern Med* 2016; 30: 1475–1476.

74 Westman ME, Malik R, Hall E, et al. **Duration of antibody response following vaccination against feline immunodeficiency virus.** *J Feline Med Surg* 2017; 19: 1055–1064.

75 Goldkamp CE, Levy JK, Edinboro CH, et al. **Seroprevalences of feline leukemia virus and feline immunodeficiency virus in cats with abscesses or bite wounds and rate of veterinarian compliance with current guidelines for retrovirus testing.** *J Am Vet Med Assoc* 2008; 232: 1152–1158.

76 Pacitti AM, Jarrett O and Hay D. **Transmission of feline leukaemia virus in the milk of a non-viraemic cat.** *Vet Rec* 1986; 118: 381–384.

77 Yamamoto J, Hansen H, Ho E, et al. **Epidemiologic and clinical aspects of feline immunodeficiency virus infection in cats from the continental United States and Canada and possible mode of transmission.** *J Am Vet Med Assoc* 1989; 194: 213–220.

78 Chhetri BK, Berke O, Pearl DL, et al. **Comparison of risk factors for seropositivity to feline immunodeficiency virus and feline leukemia virus among cats: a case-case study.** *BMC Vet Res* 2015; 11. DOI: 10.1186/s12917-015-0339-3.

79 de Oliveira Medeiros S, Martins AN, Dias CG, et al. **Natural transmission of feline immunodeficiency virus from infected queen to kitten.** *Virol J* 2012; 9: 99–105.

80 De Almeida NR, Danelli MGM, da Silva LHP, et al. **Prevalence of feline leukemia virus infection in domestic cats in Rio de Janeiro.** *J Feline Med Surg* 2012; 14: 583–586.

81 Ramírez H, Autran M, García MM, et al. **Genotyping of feline leukemia virus in Mexican housecats.** *Arch Virol* 2016; 161: 1039–1045.

82 Hosie MJ, Robertson C and Jarrett O. **Prevalence of feline leukaemia virus and antibodies to feline immunodeficiency virus in cats in the United Kingdom.** *Vet Rec* 1989; 125: 293–297.

83 Little S, Bienzle D, Carioto L, et al. **Feline leukemia virus and feline immunodeficiency virus in Canada: recommendations for testing and management.** *Can Vet J* 2011; 52: 849–855.

84 Hofmann-Lehmann R, Gönczi E, Riond B, et al. **Feline leukemia virus infection: importance and current situation in Switzerland.** *Schweiz Arch Tierheilkd* 2018; 160: 95–105.

85 Grosenbaugh DA, Leard T, Pardo MC, et al. **Comparison of the safety and efficacy of a recombinant feline leukemia virus (FeLV) vaccine delivered transdermally and an inactivated FeLV vaccine delivered subcutaneously.** *Vet Ther* 2004; 5: 258–262.

86 Grosenbaugh DA, Frances-Duvert V, Abedi S, et al. **Efficacy of a nonadjuvanted recombinant FeLV vaccine and two inactivated FeLV vaccines when subject to consistent virulent FeLV challenge conditions.** *Biologicals* 2017; 49: 76–80.

87 Sparkes AH. **Feline leukaemia virus: a review of immunity and vaccination.** *J Small Anim Pract* 1997; 38: 187–194.

88 Sparkes AH. **Feline leukaemia virus and vaccination.** *J Feline Med Surg* 2003; 5: 97–100.

89 Stuke K, King V, Southwick K, et al. **Efficacy of an inactivated FeLV vaccine compared to a recombinant FeLV vaccine in minimum age cats following virulent FeLV challenge.** *Vaccine* 2014; 32: 2599–2603.

90 Hofmann-Lehmann R, Levy LS and Willett BJ. **Comparing the efficacy of FeLV vaccines: Comment on: Stuke, K. et al. Efficacy of an inactivated FeLV vaccine compared to a recombinant FeLV vaccine in minimum age cats following virulent FeLV challenge** [letter]**.** *Vaccine* 2015; 33: 2737–2738.

91 Patel M, Carritt K, Lane J, et al. **Comparative efficacy of feline leukemia virus (FeLV) inactivated whole-virus vaccine and canarypox virus-vectored vaccine during virulent FeLV challenge and immunosuppression.** *Clin Vaccine Immunol* 2015; 22: 798–805.

92 Patel M, Carritt K, Lane J, et al. **Reply to immunosuppression in a comparative study of feline leukemia virus vaccines** [letter]**.** *Clin Vaccine Immunol* 2015; 22: 1296–1297.

93 Poulet H, Thibault JC and Masias A. **Immunosuppression in a comparative study of feline leukemia virus vaccines** [letter]**.** *Clin Vaccine Immunol* 2015; 22: 1294–1295.

94 Torres AN, O'Halloran KP, Larson LJ, et al. **Feline leukemia virus immunity induced by whole inactivated virus vaccination.** *Vet Immunol Immunopathol* 2010; 134: 122–131.

95 Hofmann-Lehmann R, Holznagel E, Aubert A, et al. **Recombinant FeLV vaccine: long-term protection and effect on course and outcome of FIV infection.** *Vet Immunol Immunopathol* 1995; 46: 127–137.

96 Hoover EA, Mullins JI, Chu HJ, et al. **Efficacy of an inactivated feline leukemia virus vaccine.** *AIDS Res Hum Retroviruses* 1996; 12: 379–383.

97 Harbour DA, Gunn-Moore DA, Gruffydd-Jones TJ, et al. **Protection against oronasal challenge with virulent feline leukaemia virus lasts for at least 12 months following a primary course of immunisation with Leukocell 2 vaccine.** *Vaccine* 2002; 20: 2866–2872.

98 Jirjis F, Davis T, Lane J, et al. **Protection against feline leukemia virus challenge for at least 2 years after vaccination with an inactivated feline leukemia virus vaccine.** *Vet Ther* 2010; 11: E1–E6.

99 Helfer-Hungerbuehler AK, Spiri AM, Riond B, et al. **No benefit of therapeutic vaccination in clinically healthy cats persistently infected with feline leukemia virus.** *Vaccine* 2015; 33: 1578–1585.

100 Scherk MA, Ford RB, Gaskell RM, et al. **AAFP Feline Vaccination Advisory Panel report.** *J Feline Med Surg* 2013; 15: 785–808.

101 Westman ME, Malik R, Hall E, et al. **The protective rate of the feline immunodeficiency virus vaccine: an Australian field study.** *Vaccine* 2016; 34: 4752–4758.

102 Dunham SP, Bruce J, MacKay S, et al. **Limited efficacy of an inactivated feline immunodeficiency virus vaccine.** *Vet Rec* 2006; 158: 561–562.

103 Bęczkowski PM, Harris M, Techakriengkrai N, et al. **Neutralising antibody response in domestic cats immunised with a commercial feline immunodeficiency virus (FIV) vaccine.** *Vaccine* 2015; 33: 977–984.

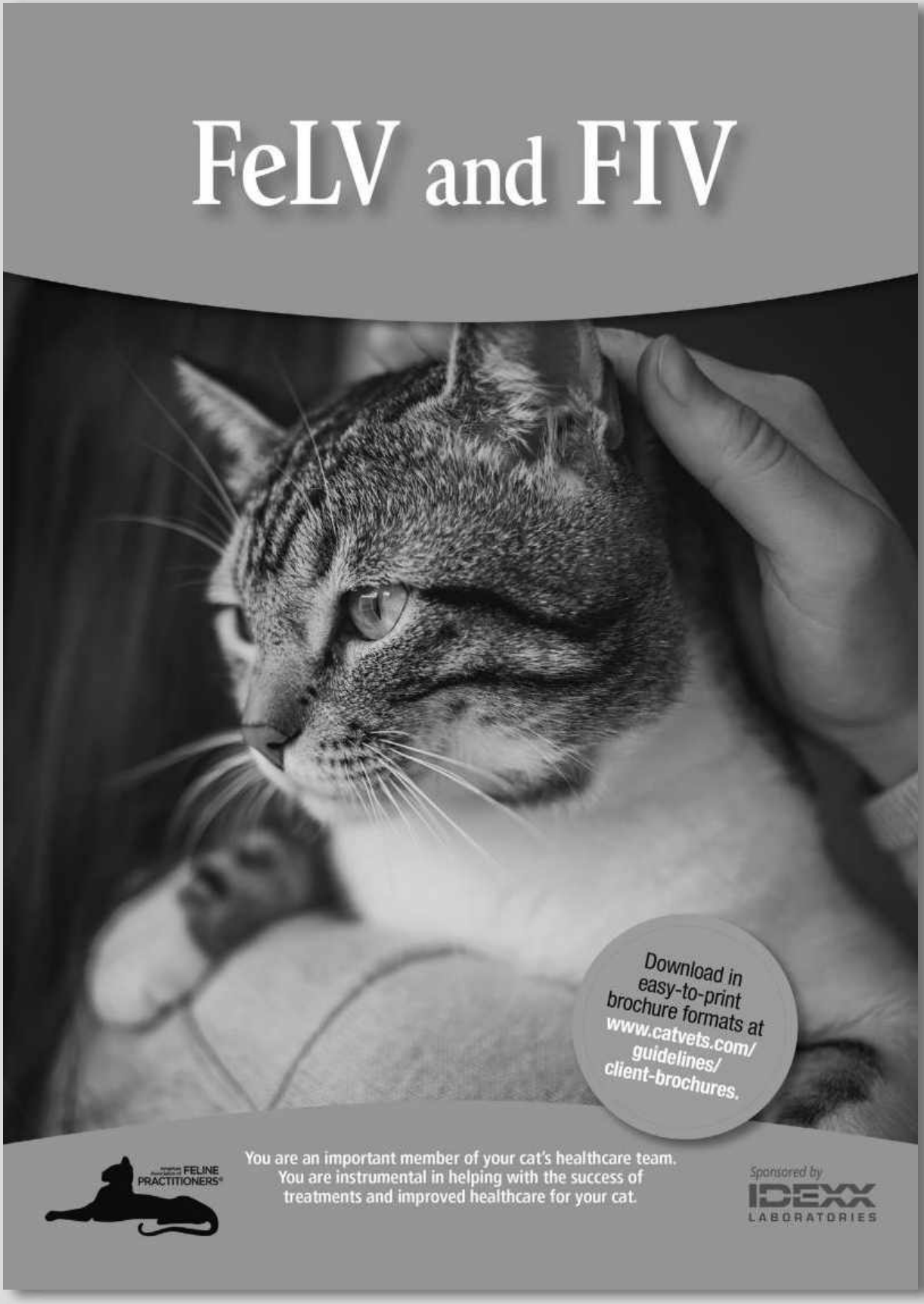
104 Kramer A, Schwebke I and Kampf G. **How long do nosocomial pathogens persist on inanimate surfaces? A systematic review.** *BMC Infect Dis* 2006; 6. DOI: 10.1186/1471-2334-6-130.

105 Terpstra FG, van den Blink AE, Bos LM, et al. **Resistance of surface-dried virus to common disinfection procedures.** *J Hosp Infect* 2007; 66: 332–338.

106 Druce JD, Robinson WF, Locarnini SA, et al. **Transmission of**

human and feline immunodeficiency viruses via reused suture material. *J Med Virol* 1997; 53: 13–18.
107 Griffin B, Bushby PA, McCobb E, et al. **The Association of Shelter Veterinarians' 2016 Veterinary Medical Care Guidelines for Spay-Neuter Programs.** *J Am Vet Med Assoc* 2016; 249: 165–188.
108 Marenzoni ML, Lauzi S, Miglio A, et al. **Comparison of three blood transfusion guidelines applied to 31 feline donors to minimise the risk of transfusion-transmissible infections.** *J Feline Med Surg* 2018; 20: 663–673.
109 Wardrop KJ, Birkenheuer A, Blais MC, et al. **Update on canine and feline blood donor screening for blood-borne pathogens.** *J Vet Intern Med* 2016; 30: 15–35.
110 Ellis SL, Rodan I, Carney HC, et al. **AAFP and ISFM feline environmental needs guidelines.** *J Feline Med Surg* 2013; 15: 219–230.
111 Hardy WD, Hess PW, MacEwen EG, et al. **Biology of feline leukemia virus in the natural environment.** *Cancer Res* 1976; 36: 582–588.
112 Levy JK. **FeLV and non-neoplastic FeLV-related disease.** In: Ettinger SJ and Feldman EC (eds). Textbook of veterinary internal medicine. 5th ed. Philadelphia: WB Saunders, 2000, pp 424–432.
113 Mims CA. **Vertical transmission of viruses.** *Microbiol Rev* 1981; 43: 267–286.
114 Boudreaux CE, Lockett NN, Chemerys DN, et al. **Maternal hematological and virological characteristics during early feline immunodeficiency virus (FIV) infection of cats as predictors of fetal infection and reproductive outcome at early gestation.** *Vet Immunol Immunopathol* 2009; 131: 290–297.
115 O'Neil LL, Burkhard MJ, Diehl LJ, et al. **Vertical transmission of feline immunodeficiency virus.** *AIDS Res Hum Retroviruses* 1995; 11: 171–182.
116 Weaver CC, Burgess SC, Nelson PD, et al. **Placental immunopathology and pregnancy failure in the FIV-infected cat.** *Placenta* 2005; 26: 138–147.
117 Newbury S, Blin K, Bushby PA, et al. **Guidelines for standards of care in animal shelters.** Association of Shelter Veterinarians. https://www.sheltervet.org/assets/docs/shelter-standards-oct2011-wforward.pdf (2010, accessed December 11, 2018).
118 Möstl K, Egberink H, Addie D, et al. **Prevention of infectious diseases in cat shelters: ABCD guidelines.** *J Feline Med Surg* 2013; 15: 546–554.
119 Levy JK. **Feline immunodeficiency virus update.** In: Bonagura J (ed). Current veterinary therapy XIII. Philadelphia: WB Saunders, 2000, pp 284–291.
120 Levy JK and Crawford PC. **Feline leukemia virus.** In: Ettinger SJ and Feldman ED (eds). Textbook of veterinary internal medicine. 6th ed. Philadelphia: WB Saunders, 2005, pp 653–659.
121 Wallace JL and Levy JK. **Population characteristics of feral cats admitted to seven trap–neuter–return programs in the United States.** *J Feline Med Surg* 2006; 8: 279–284.
122 Levy JK, Lorentzen L, Shields J, et al. **Long-term outcome of cats with natural FeLV and FIV infection.** 8th International Feline Retrovirus Research Symposium; 2006 Oct 8–13, Washington, DC.
123 McCallum H, Dunham S and Tarlinton R. **Lifetime outcomes of feline immunodeficiency virus infection** [abstract]**.** 4th International Society for Companion Animal Infectious Diseases; 2016 Oct 16–19, Bristol, UK.
124 Kornya MR, Little SE, Scherk MA, et al. **Association between oral health status and retrovirus test results in cats.** *J Am Vet Med Assoc* 2014; 245: 916–922.
125 Willis AM. **Feline leukemia virus and feline immunodeficiency virus.** *Vet Clin North Am Small Anim Pract* 2000; 30: 971–986.
126 Cupp C, Perez-Camargo G, Patil A, et al. **Long-term food consumption and body weight changes in a controlled population of geriatric cats** [abstract]**.** *Comp Contin Educ Pract Vet* 2004; 26: 60.
127 Freeman LM, Lachaud MP, Matthews S, et al. **Evaluation of weight loss over time in cats with chronic kidney disease.** *J Vet Intern Med* 2016; 30: 1661–1666.
128 Dawson S, Smyth NR, Bennett M, et al. **Effect of primary-stage feline immunodeficiency virus infection on subsequent feline calicivirus vaccination and challenge in cats.** *AIDS* 1991; 5: 747–750.
129 Lutz H, Castelli I, Ehrensperger F, et al. **Panleukopenia-like syndrome of FeLV caused by co-infection with FeLV and feline panleukopenia virus.** *Vet Immunol Immunopathol* 1995; 46: 21–33.
130 Reubel GH, George JW, Barlough JE, et al. **Interaction of acute feline herpesvirus-1 and chronic feline immunodeficiency virus infections in experimentally infected specific pathogen free cats.** *Vet Immunol Immunopathol* 1992; 35: 95–119.
131 Reubel GH, Dean GA, George JW, et al. **Effects of incidental infections and immune activation on disease progression in experimentally feline immunodeficiency virus-infected cats.** *J Acquir Immune Defic Syndr* 1994; 7: 1003–1015.
132 Bergmann M, Schwertler S, Reese S, et al. **Antibody response to feline panleukopenia virus vaccination in healthy adult cats.** *J Feline Med Surg* 2018; 20: 1087–1093.
133 Weese JS, Giguere S, Guardabassi L, et al. **ACVIM consensus statement on therapeutic antimicrobial use in animals and antimicrobial resistance.** *J Vet Intern Med* 2015; 29: 487–498.
134 Taffin ERI, Paepe D, Campos M, et al. **Evaluation of a modified Karnofsky score to assess physical and psychological wellbeing of cats in a hospital setting.** *J Feline Med Surg* 2016; 18: 913–920.
135 Hartmann K. **Efficacy of antiviral chemotherapy for retrovirus-infected cats: what does the current literature tell us?** *J Feline Med Surg* 2015; 17: 925–939.
136 Hartmann K. **FeLV treatment strategies and prognosis.** *Comp Cont Educ Pract* 2005; 27 Suppl: 14–26.
137 De Mari K, Maynard L, Sanquer A, et al. **Therapeutic effects of recombinant feline interferon-omega on feline leukemia virus (FeLV)-infected and FeLV/feline immunodeficiency virus (FIV)-coinfected symptomatic cats.** *J Vet Intern Med* 2004; 18: 477–482.
138 Gil S, Leal RO, Duate A, et al. **Relevance of feline interferon omega for clinical improvement and reduction of concurrent viral excretion in retrovirus infected cats from a rescue shelter.** *Res Vet Sci* 2013; 94: 753–763.
139 Gil S, Leal RO, McGahie D, et al. **Oral Recombinant Feline Interferon-Omega as an alternative immune modulation therapy in FIV positive cats: clinical and laboratory evaluation.** *Res Vet Sci* 2014; 96: 79–85.

Appendix: Client brochure



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Feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) can cause many types of illness as well as death in infected cats. These viruses do not infect humans or other animals.

FELINE IMMUNODEFICIENCY VIRUS

Feline immunodeficiency virus is more commonly found in male cats that are not neutered and in cats that fight with other cats. It is found less often in kittens and neutered adult cats. The virus is spread through the saliva and is usually passed to other cats by bite wounds. In North America, about 3 to 5% of tested cats are found to be infected with FIV. In Latin America, up to 25% of tested cats are found to be infected.

FELINE LEUKEMIA VIRUS

Feline leukemia virus infection is more commonly spread among cats that live together. The virus can also be spread from mother to kittens, and among cats that fight. It is mainly spread through saliva when cats groom each other, and when food and water bowls are shared. In North America, about 4% of tested cats are found to be infected with FeLV. In Latin America, up to 42% of tested cats are found to be infected.

SIGNS OF INFECTION

A cat newly infected with FIV may show mild illness, with fever or a drop in appetite. These changes do not last more than a day or two before the cat is back to normal. After the early days of infection, the cat may not be sick for months or years. These cats can still infect other cats. Later in life, the cat's infection may become active again, and the cat will show signs of sickness. When the virus is active, it can weaken the immune system, leaving the cat at risk for different infections. The virus can also cause cancers in infected cats. As it can take many years for the virus to become active again, many cats infected with FIV can live long and healthy lives.

When first exposed to FeLV, a cat might not show any signs of illness. Some cats that are exposed to FeLV can clear the virus completely from their body. Other cats are able to control the infection, preventing illness. In some cats, the infection will become active in their body and they will develop problems such as low red blood cells (anemia) or cancer. These problems can be severe and even fatal.

DIAGNOSIS

Your cat can be tested for FIV or FeLV infection. There are many times in your cat's life when your veterinarian will recommend testing. Any time your cat is sick, your cat should be tested for FIV and FeLV infection. If your cat goes outdoors, or fights with other cats, your veterinarian may recommend regular testing. If your cat is new to the family or you adopt another cat, testing is advised before introducing the new cat to other cats in the household.

If your cat tests positive for FIV or FeLV, further tests may be reommended by your veterinarian. Even if your cat's first test result is negative, your veterinarian may still advise repeat testing in the future.

PREVENTION

There are no vaccines available in the United States or Canada that can protect cats from FIV infection. FIV vaccines are only available in a few countries in the world.

Several vaccines to protect cats from FeLV infection are available. Vaccination is recommended for all kittens, again one year later, and regularly for cats that have access outdoors. Adult indoor-only cats living alone or with uninfected cats may not need to be vaccinated after the first 2 years. Your veterinarian will help assess your cat's vaccination needs.

MANAGEMENT OF INFECTED CATS

There are no treatments for either virus that will get rid of the infection. Infected cats should visit their veterinarian for regular check-ups as this will help the cat live as long as possible with good health. Your veterinarian will advise on blood testing, vaccinations, and parasite prevention. High-quality commercial diets are recommended; raw food diets may cause serious infections.

Infected pet cats should live indoors so they don't infect other cats. Other cats in the same household should be tested for FeLV and FIV. In some cases, cats that live together may need to be separated to avoid the spread of infection. Your veterinarian will help you determine what the best plan is for you and your cat(s).

Stress may play a role in triggering the virus to become active again. If there are other cats in the home, or a shortage of food bowls, water bowls, and litter boxes, it may cause stress because most cats do not like to share. Keeping litter boxes, and food and water bowls clean is also important. More information about what your cat needs to feel safe and secure indoors can be found at *www.catfriendly.com/healthyenvironment*.

Your veterinarian is your partner in caring for your infected cat. With regular healthcare checkups and a low-stress life, cats infected with FIV or FeLV may live happy and healthy lives for many years.

For more information on FIV and FeLV, visit catfriendly.com/FeLV and catfriendly.com/FIV

The client brochure may be downloaded from catvets.com/client-brochures and is also available as supplementary material at jfms.com.
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Placement & Maintenance of Nasogastric Feeding Tubes in Cats

Lisa Powell, DVM, DACVECC

Introduction

Nasogastric (NG) tubes can be an integral part of the management and treatment of cats that are ill with a variety of different diseases that result in decreased nutritional intake. The lack of adequate caloric intake prolongs illness and can result in treatment failure. NG tubes are minimally invasive, usually well-tolerated, and easy to place. The purpose of this session is to discuss the benefits of NG tube feedings, demonstrate placement procedure, and review guidelines for the amount and type of food to administer. Potential complications will be discussed. Finally, a case will be reviewed to illustrate how an NG tube can be utilized in clinical practice.

Clinical Indications

Nutritional support is indicated in cats in a variety of different situations. Situations and disease states where temporary nutritional support may be indicated include:

- Anorexia or hyporexia for longer than 4-5 days
- Pancreatitis
- Diabetic ketoacidosis
- Gastrointestinal disease (inflammatory bowel disease, dietary indiscretion, post-operative GI surgery)
- Heart failure (provide nutrition and hydration while avoiding IV fluid therapy)
- Cholangiohepatitis
- Renal failure
- Oral or facial trauma/disease
- Gastric aspiration for GI ileus
- Pediatric nutritional support

Although NG tubes are usually maintained in hospitalized patients, cats can be discharged home with the NG tube in place for continued nutritional support at home. With specific instructions and guidelines, NG tubes can remain in place for 1-2 weeks. If anorexia persists beyond this period of time, more permanent feeding tube options should be considered, such as an esophagostomy or gastrostomy tube.

Procedure for Placement of a Nasogastric Tube

There are a variety of different types of tubes that can be used for placement. Red rubber catheters, size 5Fr (or 3.5Fr in pediatrics), are often used; however, there are commercially available specific feeding tubes that can be used as well. Mila International provides a specific nasogastric tube that has centimeter markings, is radio-opaque, and has a stylet for ease of placement. In addition, connecting tubing is provided for attachment to a syringe and syringe pump or to a fluid bag containing the liquid diet. The tube has a purple end attachment, which then attaches to the purple-colored tubing line. One benefit of these colored attachments is to provide visual assurance that the food is being delivered into the proper tube, and not inadvertently into an intravenous line (See photo below).

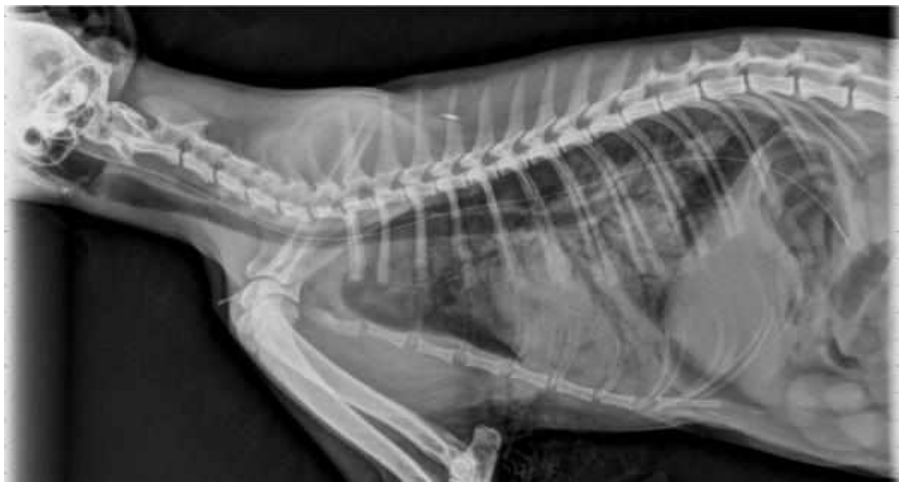
Additional supplies are listed below:

- Sedation if necessary (0.2 mg/kg butorphanol + 0.2 mg/kg midazolam IV works well)
- Proparacaine drops to place in nares as a local anesthetic

- 3-0 skin suture or skin stapler (suture is preferred)
- Lateral neck and chest radiograph for verification of proper placement

Procedure for placement of an NG tube in a cat:

1. Provide sedation if necessary. A second person is needed for restraint.
2. Measure the approximate distance to the stomach by running the tube alongside the patient from the entrance of the nares to the last rib (estimated location of the stomach).
3. Place 3-4 drops of proparacaine into both nares.
4. Hold the head up at a 45 degree angle. Pass the tube into the nares, staying as dorsal as possible while in the nasal cavity, then angling downward as the tube passes into the pharyngeal area, esophagus, and stomach.
5. There may be some difficulty passing the tube through the nasal cavity due to differences in anatomy of the nasal turbinates. If there is difficulty, take the tube out and make another attempt, moving the tube at a different angle. If unsuccessful, try the other nares.
6. Once the tube has been passed to the pre-determined cm marking, pull out the stylet and check the tube for negative pressure by attaching a 12 cc syringe to the end of the tube. If continuous air is aspirated, there is a chance the tube is inadvertently in the trachea/lung. However, there may be air aspirated from the stomach. In that case, negative pressure should eventually be achieved.
7. If negative pressure is noted, or gastric contents aspirated, suture (or staple) the tube to the lateral edge of the nares with a finger-trap suture pattern.
8. Perform a lateral neck and chest x-ray, including the stomach in the view. If the tube is in the proper location, it will be seen travelling dorsally to the larynx and into the stomach. If the tube enters the gastric fundus, proper placement has been achieved (See photo below). Ideally, the x-ray should be reviewed by a boarded radiologist to confirm proper placement in the stomach.



Food Administration Through an NG Tube

Because of the small diameter of NG tubes, only water and a liquid diet can be delivered through the tube. Commercial veterinary liquid diets, such as Vivonex (elemental diet), Royal Canin Recovery, Royal Canin Gastrointestinal Lowfat, and Royal Canin Feline Renal formula, are often used for food administration through NG tubes. The food can be delivered as an intermittent bolus (usually every 4-6 hours), or as a continuous rate infusion. When calculating nutritional needs of ill patients, the equation for resting energy requirements (RER) should be used. Previously, it was recommended to multiply the RER by an illness factor, ranging from 1.2-1.5 depending on the severity of disease. This was extrapolated from human medicine; it is not recommended in the treatment of veterinary patients. There is a danger of overfeeding when using the illness factor, and indirect calorimetry studies have shown that many ill veterinary patients do not require more than the calculated RER. Overfeeding can result in hyperglycemia, hypertriglyceridemia, azotemia, hepatic dysfunction, and can alter immune function. Hyperglycemia can result in serum hyperosmolality, osmotic diuresis, and tissue dehydration. The equation used to calculate RER in patients between 2 kg and 45 kg is:

$$(30 \times \text{body weight in kg}) + 70 = \text{kcal/day}$$

RER for patients less than 2 kg or greater than 45 kg should be calculated using the equation:

$$70\ (\text{body weight in kg})^{0.75}$$

When calculating the amount of calories to administer, it is recommended to start with 1/3 of the RER on day one, increase to 2/3 of RER on day two if feeding is tolerated, and increase to full RER on day 3. This method increases the chance of food tolerance in previously anorexic patients with concurrent illness. Gastrointestinal modulating medications, such as maropitant, metoclopramide, oral erythromycin, H-2 blockers, and ondansetron should be considered in addition to feedings. Intermittent suctioning of gastric residuals (every 4-6 hours) also increases feeding tolerance and helps reduce nausea.

Cats that are being treated for heart failure can also benefit from water administration through an NG tube, with nutritional options as well. Since IV fluid therapy is contraindicated in cats with heart failure, those that are not eating and drinking can have hydration maintained and nutrition delivered through an NG tube. RER is calculated, and the liquid diet is diluted 1:1 with tap water. As RER is increased, care must be taken to assure that the amount of water does not exceed "maintenance" daily rates. However, since furosemide is also being administered, water intake may need to be increased to maintain hydration in these patients.

Potential Complications Associated with Nasogastric Tube Placement and Use

Nasogastric tubes may be associated with complications to the patient. The most severe complication involves inadvertent placement of the tube into the trachea and bronchi, with food then being delivered into the lungs. The best way to avoid this complication is to assure proper placement with a required lateral neck and chest x-ray, ideally reviewed by a boarded veterinary radiologist. Less severe complications include tube dislodgement, epistaxis, and clogging of the tube. An E-collar should be kept on at all times to help decrease the chance of inadvertent dislodgement of the tube by the patient.

Nasogastric vs. Nasoesophageal Tubes

There has been a debate about whether an NE tube provides superior nutrition delivery vs. an NG tube. The thought is that an NG tube, because it traverses the cardiac sphincter, may cause more gastroesophageal reflux as the sphincter would be partially open. A study in the Journal of Veterinary Emergency and Critical Care (Yu et al) compared patients treated with an NG vs. an NE tube, and no difference was found when evaluating tube complications. NG tubes provide the opportunity to aspirate gastric residual fluid, which in this author's opinion, makes it a better option vs. NE tubes.

Conclusion

NG tubes can be an integral part of therapy in ill cats requiring nutritional support. Ease of placement and tolerance of NG tubes help to improve successful outcome in cats with significant disease causing decreased caloric intake. Once NG tube use increases in a hospital, it becomes part of the normal therapeutic plan for these ill cats, decreasing hospitalization time and morbidity.

References

1. Crowe DT. Use of a nasogastric tube for gastric and esophageal decompression in the dog and cat. JAVMA, 1986, May 15;188(10):1178-82.
2. Abood SK et al. Enteral feeding of dogs and cats: 51 cases (1989-1991). JAVMA, 1992, August 15;201(4):619-622.
3. Yu et al. Comparison of complication rates in dogs with nasoesophageal versus nasogastric feeding tubes. JVECC 2013;23(3):300-304

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Feline Head & Neck: Diseases, Disorders, & More

American Association of FELINE PRACTITIONERS®

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October 3 & 4 and 24 & 25, 2020

ALL TIMES ARE EASTERN TIME ZONE

Day 2 — October 4, 2020

Live Exhibits open from 11:00 am - 4:30 pm

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
9:30 - 10:00 am	Meditation Exercises		
10:00 - 11:00 am	Finding our Path to Honor Ourselves as We Live the Veterinary Oath	Dr. Kimberly Pope-Robinson	ROYAL CANIN
11:00 - 12:00 pm	Allergic Dermatitis	Dr. Alison Diesel	ZOETIS PETCARE
	Feline Herpesvirus 101: Why, What, & How?	Dr. Jessica Meekins	
	Technician/Nurse: Feline Pain: Detecting, Identifying Options, & Advocating for your Patients	Ms. Alison Gottlieb	NAVTA
12:00 - 1:00 pm	Kitten-caboodle: A Selection of Various Feline Dermatoses	Dr. Alison Diesel	ZOETIS PETCARE
	Feline Herpesvirus: Review of Treatment Strategies	Dr. Jessica Meekins	
	Technician/Nurse: Is the Kitty Crazy? Feline Hyperthyroidism	Dr. Kathy Engler	Dechra
1:00 - 1:45 pm	Exhibit Hall Break		
1:15 - 1:35 pm	AAFP Membership Meeting		
1:45 - 2:45 pm	***Partner Symposia***		
	CKD: Prediction of Future Diagnosis, Early Diagnosis, Staging, & Management Strategies	Dr. Dennis Chew	ANTECH DIAGNOSTICS and IMAGING
	Unintentional Weight Loss: Feline Dwindles	Dr. Grant Gugisberg	Dechra
	Look What the Cat Dragged In: Emerging Infections & Infestations Facing Felines Today	Dr. Susan E. Little	MERCK Animal Health
	Pouncing on Pain: Managing Feline Osteoarthritis Cases	Dr. Elizabeth Colleran	ZOETIS PETCARE
2:45 - 3:45 pm	Otitis in the Cat: Keys to Diagnosis & Therapy	Dr. Alison Diesel	ZOETIS PETCARE
	Otic Polyp: Etiology, Presentations, & Treatments	Dr. Bryden Stanley	Hills
	Technician/Nurse: Ophthalmic Drugs & When to Use Them	Dr. Jessica Meekins	
3:45 - 4:15 pm	Exhibit Hall Break		
4:15 - 4:45 pm	Ask the Experts	Drs. Alison Diesel & Jessica Meekins	

Finding our Path to Honor Ourselves as We Live the Veterinary Oath

Kimberly Pope-Robinson, DVM, CCFP

The objective of this lecture is to share the high-level view of the 1 Life Connected Movement. It takes the audience through the emotional journey, providing clarity of the struggle many face in the veterinary industry in finding career contentment. Leading the audience into the concepts of creating the path for self-forgiveness, and begin the acknowledgment of the emotional barriers that present for each of us. Therefore helping to provide the bridge to each individual in developing their own personal journey to career resiliency. Helping to move from the culture of Name, Blame, Judge to the approach of Recognize, Embrace, Connect.

The overarching concept in this shift is that we stand on our fear of failure line, above our shame ocean. In this space there are sinkers that work to pull us into that ocean. Taking the time to recognize our sinkers is the first step in understanding what pulls us into that that space of the ocean of shame, where we have the feeling of being unworthy of acceptance and belonging. As we swim in this ocean we have our cynical serpent that swims with us. As we feed the serpent with name, blame, judge, we sink deeper. You know that place, it is where we lose our faith in humanity and everyone is an A**hole and we hate the world.

In the end we cannot stop the sinkers in fact we need our sinkers as they are connected to our passion and driving much of our conviction. Recognizing this fact allows us to begin to find our unique path to sustainability. This shows up in filling our 4 well-being balloons, our mental, emotional, physical and spiritual balloons. Only we know how to fill them. Recognize, Embrace, Connect is the framework that provides the pathway to give each of us permission to find our unique path to hold both our sinkers and balloons close to us.

It is not just about putting on the positive glasses and only seeing the world in positivity. That is not a reality, as there are true risks in this industry that must be recognized. The 1 Life Connected Movement has been developed to provide the bridge to move from Name, Blame, Judge and towards Recognize, Embrace Connect. It is not about ignoring or trying to “fix” the sinkers, it is what we do with them when we recognize they start to pull us into the ocean of shame. Do we feed the cynical serpent, or do we instead move to embrace the emotions and then follow the path to connection in electing to fill our balloons.

Our wellbeing as individuals and in the profession depends on us learning to make this shift. There are 4 principles which help us to stay on this path. They include- (1) being mindful of our response, (2) creating our environment, (3) embracing our emotions, and (40 finding self-forgiveness. These will be explored in detail during this lecture.

Come be a part of the shift, Be 1 Life Connected.

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Allergic Dermatitis
Alison Diesel, DVM, DACVD

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Kitten-caboodle: A Selection of Various Feline Dermatoses
Alison Diesel, DVM, DACVD

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Otitis in the Cat: Keys to Diagnosis & Therapy
Alison Diesel, DVM, DACVD

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Feline Herpesvirus 101: Why, What, & How?

Jessica Meekins, DVM, MS, DACVO

Introduction

Feline herpesvirus-1 (FHV-1) is the most common cause of surface ocular disease in domestic cats. It is a double stranded, enveloped DNA virus that is highly contagious but easily killed in the environment.[1-3] Neuronal latency occurs after primary infection, where the virus enters a dormant state in the body and remains there for the life of the host. Periodic viral reactivation over the host's lifetime is responsible for recurrent episodes of clinical disease.

Clinical Presentation

Signalment and History

FHV-1 is ubiquitous in domestic cat populations, both mixed breed and purebred. Young kittens and juvenile cats commonly develop primary infection; naïve individuals are exposed to the highly contagious virus while in close proximity (e.g., shelters, catteries) to infected cats shedding virus.[4] Primary infection often results in both ocular and upper respiratory clinical signs, as affected cats present with signs consistent with a 'cold'. Recrudescent disease is generally characterized by ocular clinical signs, and signs are frequently either asymmetrical in severity or unilateral. Stress is a major risk factor for reactivation of latent FHV-1.[4-6]

The Ophthalmic Examination

Most veterinary practices are equipped with the basic tools for ophthalmic examination. These include a direct ophthalmoscope, a Finoff transilluminator or penlight, and fluorescein stain strips. Digital tonometers to measure intraocular pressure are also becoming more readily available in general practice. The author does not routinely measure tear production in cats, as results can vary widely amongst normal individuals and keratoconjunctivitis sicca is not a commonly recognized clinical syndrome in the species. Fluorescein staining is an important diagnostic step during initial evaluation of cats with suspected viral surface ocular disease. Rose Bengal is another diagnostic stain sometimes used in cats with surface ocular disease; unlike fluorescein, a hydrophilic stain that is imbibed by exposed corneal stroma (i.e., identifying when a corneal ulcer is present), Rose Bengal adsorbs to and is absorbed by devitalized or compromised epithelium.

The two main clinical manifestations of FHV-1 relate to the mechanisms of viral pathogenicity. FHV-1 most commonly results in ***cytolytic infection***[7] due to the epitheliotrophic nature of the virus. Corneal epithelial cells are targeted and killed as virus particles are made, leading to corneal ulceration. Likewise, the conjunctival epithelium experiences damage due to viral replication, resulting in clinical signs of conjunctivitis and serohemorrhagic ocular discharge. If the full thickness of the epithelial layer is lost, this will result in fluorescein stain uptake on the cornea, whereas partial thickness loss or damage of the corneal and conjunctival epithelium will result in Rose Bengal stain retention.

The less common ***immune-mediated stromal keratitis***[7] occurs as a reaction to viral antigens within the corneal tissue. In cats, this is not typical of primary viral infection, but rather takes time and is clinically associated with recrudescent disease in carrier cats. Previous studies have established a link between steroid use and the development of stromal keratitis, drawing the conclusion that stromal keratitis is most likely to occur after the local immune response to the virus is suppressed.[8] Stromal keratitis is characterized by corneal inflammation (blood vessel ingrowth and edema) in the absence of ulcers.

Etiology

FHV-1 is epitheliotrophic, meaning that it preferentially invades epithelial tissues of the cornea, conjunctiva, and upper respiratory tract.[9] The virus enters host epithelial cells and uses them to make new virus particles, then these epithelial cells subsequently die, rupturing to release newly formed virus. FHV-1 is highly contagious, and is most easily spread in densely populated areas such as shelters and catteries. It is shed in respiratory and ocular secretions of infected cats.[4] Cat-to-cat contact, aerosol spray due to sneezing, and less commonly, fomites such as bowls, bedding, toys, and people caring for the cats, are the primary ways the virus is spread.

Primary Infection

When considering primary infection, kittens are at the greatest risk when maternal antibodies are waning, and other young naïve cats are at risk when exposed to infected cats that are actively shedding virus. Primary infection often results in systemic illness, with upper respiratory signs, fever, and a decreased appetite as the prevailing clinical signs. Most cats recover from primary infection and become lifelong carriers of the virus.

Carrier State
The carrier state poses a unique clinical management challenge. Greater than 80% of domestic cats are estimated to be latently infected with FHV-1, serving as subclinical carriers.[6] The trigeminal ganglia have traditionally been recognized as the main site of neuronal latency,[10] but more recent research has demonstrated the presence of viral DNA in ocular tissues of normal cats.[11] Some reports additionally estimate that approximately 45% of carrier cats will experience periodic episodes of viral reactivation in their lifetimes, making recrudescent disease a clinically important problem.[6]

Concurrent Conditions
Several clinically impactful ocular sequelae may occur after FHV-1 infection. Symblepharon, which is the formation of adhesions in areas where epithelial damage and ulceration develop, may form between the cornea and conjunctiva or between different areas of the conjunctiva. Depending on the extent of involvement, corneal-conjunctival symblepharon can be particularly problematic as it may lead to vision impairment or even blindness. Conjunctiva to conjunctiva symblepharon is generally less significant, though if extensive it can cause issues with mobility of the eyelids or third eyelid due to formation of restrictive bands of scar tissue. Symblepharon may also lead to occlusion of the lacrimal puncta and chronic epiphora; this can be confirmed by a negative Jones test (failure of passage of fluorescein dye down the nasolacrimal system to the ipsilateral nostril after application to the eye).

Tear film deficiencies may also arise as a sequela of herpetic surface ocular disease.[12] A qualitative mucin layer deficiency is most common, and occurs due to chronic conjunctival inflammation and destruction of the mucin producing goblet cells. Keratoconjunctivitis sicca is also a recognized clinical sequela of FHV-1 infection, though due to the variability in tear measurement (Schirmer tear test, or STT) values in normal cats, results of objective tear assessment may be difficult to interpret.

In severe cases, usually with primary infections, progressive corneal disease and globe perforation are possible. The majority of herpetic corneal ulcers remain superficial, since the virus targets the epithelium. However, secondary bacterial infection of a viral ulcer may occur, and when this happens the typical clinical worsening with depth and malacia should be expected as a result of enzymatic destruction of the corneal stroma by inflammatory cells. Another more severe sequela that occurs in neonatal kittens is ophthalmia neonatorum, in which infection is trapped behind the fused eyelids prior to normal physiologic opening at approximately two weeks old.[13] Kittens experiencing ophthalmia neonatorum may be particularly severely affected with corneal disease, with a greater risk of corneal rupture.

Historically, there has been much speculation regarding whether unique feline corneal diseases such as sequestrums and eosinophilic-proliferative keratitis/conjunctivitis may be caused by FHV-1. To the author's knowledge, a definitive link or association between FHV-1 and these unique feline corneal diseases has not been established.

Differential Diagnosis
There are three other etiologic considerations for infectious feline conjunctivitis: *Chlamydia felis*, feline calicivirus, and *Mycoplasma* sp. Chlamydial conjunctivitis typically occurs unilaterally in young cats less than 5 years old, while calicivirus infection should be accompanied by non-ocular clinical signs such as oral ulceration. *Mycoplasma* sp. may be a component of the normal feline conjunctival flora, and overgrowth is usually part of a co-infection with a virus or *C. felis*. In general, signalment, history, clinical signs, and response to treatment are the guidelines that lead to the most accurate diagnosis. In the majority of cases, FHV-1 will be the underlying cause of surface ocular disease.

Chlamydia felis
Chlamydia felis is an obligate intracellular bacterium and it may be seen in cytologic preparations as a basophilic intracytoplasmic inclusion roughly 25% the size of the epithelial cell nucleus. Clinical signs occur in young cats less than 5 years old, and are primarily unilateral conjunctivitis and chemosis with no corneal ulcers. Non-ocular signs of chlamydial infection, specifically referable to the GI tract and respiratory system, may be present.

Chlamydial infections are generally very responsive to tetracycline antibiotic therapy. Ocular disease is managed with a topical tetracycline (Terramycin®), though sometimes chronic refractory cases require oral tetracycline administration. If oral therapy is required, care should be taken to educate clients on the risk of esophageal stricture with oral doxycycline administration.[14] To avoid this problem, the author recommends administering an oral fluid bolus after tablets are given or using a liquid formulation compounded into a suspension.

Feline Calicivirus
Calicivirus is a non-enveloped, single-stranded RNA virus that survives well in the environment outside a host. Ocular clinical signs associated with calicivirus infection are usually mild conjunctivitis, but not corneal ulcers; ocular

signs are not always present. The virus is a respiratory tract pathogen, and may cause oral ulceration as well as polyarthritis as major non-ocular clinical signs. When calicivirus is suspected, the cat should undergo a thorough complete oral and physical examination to screen for the presence of oral or lingual ulcerations, or joint disease, which may be associated with calicivirus infection.

Some cats are chronically infected with calicivirus and periodically shed the virus. Recovery, when it occurs, is spontaneous. It is important to note that traditional antiviral therapy is ineffective against calicivirus since it is an RNA virus. Treatment is targeted at supportive care during the natural course of disease.

Mycoplasma sp.
Mycoplasma are the smallest free-living organisms, classified as prokaryotes. They lack a cell wall, and are considered somewhere between a bacterium and a virus. They have been isolated from both sick and healthy cats, and their role as a pathogen in infectious conjunctivitis remains unclear. Mycoplasmal overgrowth most likely occurs as part of a co-infection with FHV-1 or *C. felis*, or less commonly, calicivirus. Mycoplasmal overgrowth typically resolves during the course of treatment for the other more pathogenic causes of feline conjunctivitis.

Conjunctival cytology or PCR of a conjunctival swab is diagnostic for mycoplasmal infection. For cytology, multiple intracytoplasmic basophilic tiny dots are seen clustered within epithelial cells. PCR is sensitive for the detection of mycoplasmal DNA, however since *Mycoplasma* sp. have been identified in healthy cats, their role as disease-causing agents must be interpreted carefully on a case by case basis.

Treatment of mycoplasmal conjunctivitis is the same as for chlamydial conjunctivitis, and consists of topical tetracycline antibiotics. The oral route may be used for refractory cases, and a 10 mg/kg/day dose divided into q12 h intervals is recommended. Due to the aforementioned risk of esophageal stricture with tablet or capsule formulations of oral doxycycline, an oral fluid bolus 'post pill' or a liquid formulation is preferred for oral dosing.

Diagnostic Examination
In the majority of cases, the diagnosis of FHV-1 is made presumptively based on history, clinical signs, and response to therapy. However, there are a number of diagnostic tests that may be performed in an effort to confirm the diagnosis. There are challenges, benefits, and drawbacks to consider when deciding on whether to pursue diagnostic testing for FHV-1. The major diagnostic challenge is definitively confirming FHV-1 as the causative agent of surface ocular disease in chronically affected carrier cats for which virus replication and shedding varies substantially. Since FHV-1 is so prevalent in the domestic cat population, the odds of the virus causing surface ocular disease in a particular cat are very strong.

Virus isolation may be performed, but requires special considerations in the collection and transport of samples since live virus is required for sample analysis.[15] Serum antibody titers are another diagnostic option, however antibody production indicates natural exposure or vaccination, but not always active disease. Molecular diagnostics, specifically PCR, have become the most sensitive test to detect viral DNA in a sample. But, PCR will amplify genetic material from virus fragments and not necessarily viable, actively replicating virus.[16] Since some ophthalmologically normal cats have been demonstrated to harbor viral DNA on the ocular surface, the significance if a positive PCR result may be difficult to interpret.

These tests are not only sometimes challenging to interpret, but can also be associated with significant cost; because results may not add to the overall clinical picture, in the author's opinion it is often more appropriate to focus the client's financial resources toward treatment costs.

Conjunctival cytology is a quick, easy, inexpensive test that can be performed in the clinic during an outpatient visit. It can support the diagnosis of viral conjunctivitis, but it is not specifically diagnostic since viral inclusions occur intranuclearly and cannot be detected by standard light microscopy. Intracytoplasmic inclusions that are typical of chlamydial or mycoplasmal infections, however, may be identified and lend support to a possible bacterial cause for conjunctivitis. In acute cases of viral surface ocular disease, a predominantly neutrophilic inflammation is present.[15] In more chronic cases with milder clinical manifestations, a mononuclear inflammation composed of lymphocytes and plasma cells is present.

References

1. Eleraky NZ, Potgieter LN, Kennedy MA. Virucidal efficacy of four new disinfectants. *J Am Anim Hosp Assoc* 2002;38:231-234.
2. Scott FW. Virucidal disinfectants and feline viruses. *Am J Vet Res* 1980;41:410-414.
3. Povey RC, Johnson RH. Observations on the epidemiology and control of viral respiratory disease in cats. *J Small Anim Pract* 1970;11:485-494.

4. Gaskell RM, Povey RC. Transmission of feline viral rhinotracheitis. *Vet Rec* 1982;111:359-362.
5. Pedersen NC, Sato R, Foley JE, et al. Common virus infections in cats, before and after being placed in shelters, with emphasis on feline enteric coronavirus. *J Feline Med Surg* 2004;6:83-88.
6. Gaskell RM, Povey RC. Experimental induction of feline viral rhinotracheitis virus re-excretion in FVR-recovered cats. *Vet Rec* 1977;100:128-133.
7. Nasisse MP. Feline herpesvirus ocular disease. *Vet Clin North Am Small Anim Pract* 1990;20:667-680.
8. Nasisse MP, Guy JS, Davidson MG, et al. Experimental ocular herpesvirus infection in the cat. Sites of virus replication, clinical features and effects of corticosteroid administration. *Invest Ophthalmol Vis Sci* 1989;30:1758-1768.
9. Gaskell RM, Povey RC. Feline viral rhinotracheitis: sites of virus replication and persistence in acutely and persistently infected cats. *Res Vet Sci* 1979;27:167-174.
10. Gaskell RM, Dennis PE, Goddard LE, et al. Isolation of felid herpesvirus I from the trigeminal ganglia of latently infected cats. *J Gen Virol* 1985;66 (Pt 2):391-394.
11. Townsend WM, Jacobi S, Tai SH, et al. Ocular and neural distribution of feline herpesvirus-1 during active and latent experimental infection in cats. *BMC Vet Res* 2013;9:185.
12. Lim CC, Reilly CM, Thomasy SM, et al. Effects of feline herpesvirus type 1 on tear film break-up time, Schirmer tear test results, and conjunctival goblet cell density in experimentally infected cats. *Am J Vet Res* 2009;70:394-403.
13. Andrew SE. Ocular manifestations of feline herpesvirus. *J Feline Med Surg* 2001;3:9-16.
14. German AJ, Cannon MJ, Dye C, et al. Oesophageal strictures in cats associated with doxycycline therapy. *J Feline Med Surg* 2005;7:33-41.
15. Nasisse MP, Weigler BJ. The diagnosis of ocular feline herpesvirus infection. *Veterinary & Comparative Ophthalmology* 1997;7:44-51.
16. Lutz H, Leutenegger C, Hofmann-Lehmann R. The role of polymerase chain reaction and its newer developments in feline medicine. *J Feline Med Surg* 1999;1:89-100.

NOTES:

Feline Herpesvirus: Review of Treatment Strategies

Jessica Meekins, DVM, MS, DACVO

Introduction
Treatment of FHV-1 consists of targeted antiviral therapy and various other components, depending on the individual case. Because stress can exacerbate herpetic flare-ups, the ease of administering a specific treatment must be considered. It may be counterproductive to prescribe certain therapies if a client must go to extreme measures to 'force' the treatment. We do not have a single perfect treatment or a cure for FHV-1, so treatment strategies must take into consideration the individual cat/owner relationship and what will accomplish the most with the least stress for cat and owner.

When to Treat?
In general, the author uses three guidelines to determine when antiviral intervention is warranted: 1) if conjunctivitis is moderate to severe, 2) if a corneal ulcer is present, or 3) if there is significant blepharospasm. Because conjunctivitis and corneal ulcers result in ocular pain, a varying degree of blepharospasm often accompanies the other sign(s).

In very mild cases of herpetic surface ocular disease, in which no corneal ulcers are present and conjunctivitis is mild, disease is generally self-limiting in an immunocompetent cat and the best option may be not to treat. A cat with a competent immune system should be able to combat the virus without treatment if disease is mild. In cases of primary infection, concurrent systemic illness is common. Fever, respiratory signs, and decreased appetite are the prevailing non-ocular clinical signs, and supportive care is necessary in these cats. As previously discussed, the majority of cats experiencing primary infection are young. Systemic antibiotics to prevent or treat secondary bacterial infections are often necessary in these cases, along with supporting hydration and stimulating the appetite.

How to Treat?
After deciding whether antiviral therapy may be beneficial, the route of administration should be decided. If clinical signs are confined to the eye, the author starts with topical therapy alone. If respiratory signs are present in addition to ocular signs, systemic therapy is indicated. However, both topical and oral routes of administration may be used simultaneously; in some cats with ocular clinical signs refractory to topical therapy, oral therapy can be used alone or in combination with topical therapy.

The duration of treatment is possibly the most important factor to consider. Due to the virostatic nature of the available antiviral drugs, virus replication is decreased but virus is not actively killed. Thus, treatment should be continued at least one week beyond clinical resolution to decrease the risk of flare-up if treatment is discontinued too abruptly.

Topical Antiviral Therapy
No topical antiviral drugs are approved for use in cats in the United States. The two topical antivirals used regularly by the author are cidofovir 0.5% and idoxuridine 0.1%, and both of these drugs must be compounded. There are benefits and drawbacks to each. Cidofovir has been shown to lessen the duration of clinical signs and virus shedding in experimentally infected cats with twice daily treatment frequency.[1] However, it is quite expensive when compared to idoxuridine, which is often half the cost (or less) of cidofovir. Idoxuridine must be given more frequently, at minimum 4-6 times per day, so the trade-off is cost for treatment frequency when comparing these drugs. Trifluridine, with the brand name Viroptic®, is a commercially available human product used to treat herpes simplex keratoconjunctivitis, however anecdotally it is very topically irritating and poorly tolerated when administered to cats.[2]

In general, the author has experienced very few side effects of topically administered cidofovir and idoxuridine. Specifically, cats infrequently develop an intolerance to cidofovir that manifests as an ulcerative blepharitis, which resolves slowly after discontinuation of treatment.

Systemic Antiviral Therapy
There is a commercially available famciclovir product called Famvir®, made by Novartis, which is currently the only appropriate oral antiviral option for cats. Based on recent research, a dose range has been optimized for oral administration.[3,4] A 40 mg/kg dose given twice daily is the author's standard practice. This is based on information that showed similar peak plasma concentrations in a lower dose group despite another study with improved clinical outcome in a higher dose group.[5] Though some of the literature supports three times daily dosing, from a practical standpoint twice daily administration is more feasible for most cat owners and anecdotally is associated with improved clinical outcome. Prior to the publication of new research investigating the pharmacokinetics of famciclovir

after oral administration, many clinicians would attribute therapeutic effect to doses as low as 62.5 mg per cat once to twice per day. In the author's practice, most adult cats receive approximately 250 mg orally every 12 hours, however dosages should be adjusted in cats with kidney disease since the drug undergoes renal metabolism. It is very important never to prescribe valacyclovir to cats, as it causes fatal renal tubular necrosis, hepatic atrophy, and severe bone marrow suppression.[6]

The Role of Lysine

Lysine is an amino acid supplement that works by antagonizing arginine, which is essential to viral replication.[7] The adult cat dosage is 1000 mg daily, generally divided into two 500 mg doses. There are many lysine options on the veterinary market. Lysine is not a targeted antiviral treatment, but it may prove beneficial as a nutraceutical and 'immune booster' in many cats. The major caveat is that the administration of lysine must be stress-free, which is why several highly palatable treat formulations now exist.

Other Therapies

If a corneal ulcer is present, a prophylactic topical antibiotic is necessary to prevent secondary bacterial infection. In some cases, when there is an obvious border of loose epithelium at the edges of the ulcer, topical anesthesia and a cotton swab debridement is indicated to physically remove some of the viral load from the cornea. A grid keratotomy or other advanced debridement should generally not be performed due to the risk of corneal sequestrum formation in cats.[8] In herpetic corneal ulcers, epithelium is loose due to the virus invading and destroying epithelial cells, so gentle and minimally invasive physical removal of the devitalized epithelium (e.g., cotton swab debridement) along with antiviral therapy is the most appropriate treatment plan in an effort to achieve ulcer healing.

Occasionally, the degree of ocular surface inflammation associated with viral replication is profound. Some cats will benefit from topical non-steroidal anti-inflammatory treatment if antiviral therapy alone does not result in improvement in clinical signs. Topical NSAIDs should be used judiciously and usually should be avoided when corneal ulcers are present. Topical and subconjunctival steroids should never be used, due to their exacerbation of FHV-1 clinical disease.[9]

References

1. Fontenelle JR, Powell CC, Veir JK, et al. Effect of topical ophthalmic application of cidofovir on experimentally induced primary ocular feline herpesvirus-1 infection in cats. *American Journal of Veterinary Research* 2008;69:289-293.
2. Andrew SE. Ocular manifestations of feline herpesvirus. *J Feline Med Surg* 2001;3:9-16.
3. Thomasy SM, Covert JC, Stanley SD, et al. Pharmacokinetics of famciclovir and penciclovir in tears following oral administration of famciclovir to cats: a pilot study. *Veterinary Ophthalmology* 2012;15:299-306.
4. Sebbag L, Thomasy SM, Woodward AP, et al. Pharmacokinetic modeling of penciclovir and BRL42359 in the plasma and tears of healthy cats to optimize dosage recommendations for oral administration of famciclovir. *Am J Vet Res* 2016;77:833-845.
5. Thomasy SM, Shull O, Outerbridge CA, et al. Oral administration of famciclovir for treatment of spontaneous ocular, respiratory, or dermatologic disease attributed to feline herpesvirus type 1: 59 cases (2006-2013). *J Am Vet Med Assoc* 2016;249:526-538.
6. Nasisse MP, Dorman DC, Jamison KC, et al. Effects of valacyclovir in cats infected with feline herpesvirus 1. *Am J Vet Res* 1997;58:1141-1144.
7. Stiles J, Townsend WM, Rogers QR, et al. Effect of oral administration of L-lysine on conjunctivitis caused by feline herpesvirus in cats. *Am J Vet Res* 2002;63:99-103.
8. La Croix NC, van der Woerdt A, Olivero DK. Nonhealing corneal ulcers in cats: 29 cases (1991-1999). *Journal of the American Veterinary Medical Association* 2001;218:733-735.
9. Nasisse MP, Guy JS, Davidson MG, et al. Experimental ocular herpesvirus infection in the cat. Sites of virus replication, clinical features and effects of corticosteroid administration. *Invest Ophthalmol Vis Sci* 1989;30:1758-1768.

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Otic Polyp: Etiology, Presentations, & Treatments

Bryden Stanley, BVMS, MVetSc, MANZCVS, MRCVS, DACVS

The middle ear consists of the tympanic membrane, tympanic cavity (enclosed by the osseus bulla), auditory canal (eustachian tube) and three auditory ossicles (malleus, incus, stapes). Otoscopic examination of a normal ear reveals a portion of the small, dorsal pars flaccida, the tough, glistening pars tensa, and the outline of the attachment of the malleus. Most of the tympanic cavity is air filled. It is lined with squamous and ciliated columnar epithelium. The osseus bulla extends ventrally and can be readily palpable in most dogs, either externally or per os (under anesthesia, lateral and caudal to the epiglottis). Several nerves, including the facial and sympathetic nerves, traverse the dorsal portion of the tympanic cavity. The auditory tube is very short in the dog and cat (~8mm). The tympanic cavity of the cat has an almost complete osseus septum separating it into dorsolateral and ventromedial compartments.

Aural neoplasia is relatively uncommon in the dog, but accounts for about 27% of all feline skin tumors. Cats more often malignant (up to 50%) than dogs. Tumors can originate from skin, adnexal structures (eg, glands) or connective tissue. Most common in dogs: histiocytoma of the pinna, ceruminous gland adenoma or adenocarcinoma, squamous cell carcinoma (SCC), and malignant melanoma. In cats, inflammatory polyps, SCC (late metastasis), and ceruminous gland adenoma or adenocarcinoma. No breed or sex predilection has been established for feline or canine aural neoplasia, although white cats are at higher risk for developing squamous cell carcinoma. Older animals usually, except for histiocytoma.

The exact etiology of otic polyps (also known as nasopharyngeal polyps, otopharyngeal polyps, inflammatory polyps of the middle ear) in cats is unknown, but because of the often young age of presentation, a congenital predisposition has been suspected. Histology shows chronic inflammatory fibrous changes, and it has been postulated that early viral infections (e.g., calicivirus) may play a role in their development. Shar-Peis may also be predisposed to otic polyps.

These masses are benign growths arising from the mucosa of the tympanic cavity (mostly), with frequent pedunculated extension into the nasopharynx and/or the external ear canal. They can occur unilaterally or bilaterally. Clinical signs vary, depending on the anatomic location of the masses. Signs of external and/or middle ear disease, respiratory stertor, dyspnea and dysphagia. Usually younger cats present (median of 1 to 2 years), but older cats too. Should be considered in ANY cat presented with signs of upper respiratory or ear disease.

Diagnosis is obtained via careful oral examination (under general anesthesia, retracting the soft palate rostrally), as well as bilateral otoscopic examination. CT of head is routinely performed and preferred imaging modality if available. If not available, open mouth radiographic views of the bulla. It is important to check out all three locations - nasopharynx, middle ear, external ear.

Treatment

Polyps can be removed from the nasopharynx or external ear canal by traction alone. Recurrence is common in those removed under traction alone and a VBO is generally recommended as the gold standard. Post-operative management of those removed under traction alone is:

- 0.5mg dexamethasone po Q12 for 2 weeks, then taper
- Marbofloxacin 3-5 mg/kg po Q24 for one month
- Synotic® for one month

Performing a ventral bulla osteotomy will ensure that all polyp is removed. Dexamethazone SP (IV 0.5 mg/kg, single dose) is administered pre-operatively. Nasopharyngeal polyps can first be removed by rostral reflection of the soft palate, followed by traction and cutting of the polyp pedicle.

The cat is then positioned into dorsal recumbency. The tympanic bulla in the cat is divided by a bony septum into dorsolateral and ventromedial compartments, both of which must be carefully entered for exploration and removal of polyps and mucoid discharge. Lavage and really, really gentle and meticulous curettage with a neurological curette is performed. A 5 Fr red rubber catheter should be inserted from the middle ear and passed through the external ear to a non-sterile assistant. Following easy passage of the catheter, the area is lavaged liberally and closed routinely, with a small Penrose drain (optional). Otic examination before recovery is essential to ensure complete removal of all polypoid material.

A concurrent bacterial otitis is common so culture and sensitivity at time of surgery and a 10-14 day course of appropriate antibiotics are recommended.

Transient post-operative Horner's syndrome in the cat is very common, and sometimes vestibular signs (head tilt, nystagmus, ataxia). Don't plan on sending these guys home the next day.

Edema can result from pharyngeal surgery, so pre-operative corticosteroids and close post-operative monitoring for respiratory distress. Be prepared for re-anesthesia and temporary tracheostomy tube placement. These little kitties have small airways, and it doesn't take much swelling for them to obstruct.

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Feline Pain: Detecting, Identifying Options, & Advocating for your Patients

Alison Gottlieb, BS, CVT, VTS(ECC)

As patients, cats are often not willing participants. This must be taken into consideration when caring for them and often requires creativity and compromise. One of the greatest challenges in treating feline pain is *recognizing* their pain. Overcoming this obstacle is crucial to providing the best patient care. Understanding painful conditions and signals will empower nurses to better advocate for their feline patients.

We have come a long way and there have been several important catalysts to this change. The most distinct of these include Federal legislation for research, strong position statements from prestigious corporations and organizations (including the American Animal Hospital Association and the Association of American Feline Practitioners), and patient advocates - including veterinary technicians and pet owners.

There are a range of pain states and classifications; however, each needs to be addressed swiftly. These pain states can be chronic, acute, acute that becomes chronic, acute on chronic, and the incredibly profound yet overlooked emotional pain. Acute pain is severe, short in duration and alleviated once the body has healed. Acute pain can originate from medical, surgical or trauma-related incidents and provide more obvious, visual or measurable cues. These pain cues provide increased opportunities for analgesia or other interventions that are vital for optimal patient care. Chronic feline pain is the ultimate challenge, significantly more problematic to identify than the acute version.

Types of Pain

Pain is often described by its physiological origin and can be either somatic or visceral. Somatic pain is easy to localize and represents pain originating from skin, muscle, joints and deep tissue. Visceral pain results from inflammation, distension, or stretching of the internal organs. This pain is not well localized and is often described as aching, cramping, deep pain, or pressure. This type of pain can result in referred pain or pain that is perceived to originate from a location other than the initial noxious stimulus. Both somatic and visceral pain are classified as nociceptive pain and is a normal response to painful stimuli. Neuropathic pain results from injury to nerves in either the central nervous system or the peripheral body. It can be described as burning, tingling, shooting, stabbing, or shocking. Damaged nerve fibers send incorrect signals to the brain. Neuropathic pain can be more difficult to treat than nociceptive. These types of nociceptive pain are physiologic pain, meaning that they serve a protective function for the body. They keep us away from danger and ensure that we rest once injured. If physiologic pain is allowed to continue, maladaptive or chronic pain rapidly ensues. Maladaptive pain is pain that serves no biological function. This leads to chronic pain or pain that persists despite recovery and healing from the initial noxious stimulus.

Pain Recognition

Recognizing and assessing pain in cats is not an exact science and many components contribute and several are subjective. Veterinary medicine has the virtually impossible task of determining pain in non-verbal patients as patients cannot tell us where it hurts so we have to attempt to evaluate pain in other ways. Considering the degree of injury or illness as well as behavioral and physiologic changes is a valid place to start however, assessment should not end there. When assessing pain, it is imperative to also evaluate the response to analgesia and consider additional measures when indicated. Analgesia in the veterinary emergency room often relies on blind faith, assuming pain is involved weather demonstrated by the patient or not. In his paper, Professor Davis remarks: "*One of the psychological curiosities of therapeutic decision-making is the withholding of analgesic drugs, because the clinician is not absolutely certain that the animal is experiencing pain. Yet the same individual will administer antibiotics without documenting the presence of a bacterial infection*."(Davis 1983)

Behavioral Changes

Behavioral changes are not always present or clear in animals; severe debilitation, injury, neurologic damage and bandages may interfere with clearly observing pain behaviors. Even though the majority of our patients are domesticated (perhaps with the exclusion of feral cats) they are not far removed from their wild instincts. They are conditioned (if physically able) to conceal signs of pain to protect themselves as prey which may skew recognition.

The most accurate way to assess pain is not to assess it at all, but to assume it exists. Anthropomorphism is the concept of applying human characteristics to animals and for the most part is a desirable ideology. For several reasons, this philosophy is not only applicable but imperative in the area of feline analgesia. The assumption should

be made that any injury, disease, or procedure that causes discomfort to a human would have a similar effect on an animal. Dogs, cats, and humans all have similar anatomy and physiology of their nervous systems (why human analgesics are first tested on animals), therefore, is it reasonable to conclude that pain is experienced comparably between said species. Anticipating the degree of pain expected between different injuries, disease, and procedures (e.g. mild, moderate, or severe pain) assumes pain will be present regardless of whether or not the patient clearly displays outward signs of pain. For example, in the emergency room mild pain may commonly include; intravenous catheter placement, small lacerations, cystitis, abscesses, otitis, and many other conditions. Moderate pain may be caused by urethral obstructions, cystotomy, mild pancreatitis or enucleation. Severe pain might include ear canal ablation, amputation, fracture/repair, declaw, peritonitis, necrotizing pancreatitis, thoracotomy, thrombosis, mastectomy, thermal injury, and cancer pain. In general; the greater the inflammation the greater the pain. It is important to realize however that every patient in an individual and specific procedures and conditions may cause increased pain than would be expected (i.e. hyperalgesia) in some individuals. The establishment of chronic pain make may this especially common.

Stress in the ICU

Stress is common in the intensive care unit and comes in three forms: environmental, physiological and emotional. Environmental stress includes factors such as heat, cold, or noise stress. The beeping of machines, dogs barking, nurses talking, bright lights at night, overhead pages, and radio noises can occur nearly constantly in many veterinary emergency rooms and critical care units. Cats unfortunately are often exposed to dogs for the first time as well and can easily become frighten. Physiological stresses include pain or other noxious stimuli as a result of an injury or due to patient treatment (e.g. venipuncture, bandage placement, wound lavage, intravenous or urinary catheterization, etc). In the veterinary critical care unit, we see emotional stress created when pets are separated from their owners and home. Often cats have never been away from their owner or out of their house. Other animals have an adverse to being caged or crated or picked up. For all animals they are now in an unfamiliar environmental with new smells and sounds which in itself creates stress.

Physiologic Consequences of Pain and Stress

Not only are there ethical and moral reasons for treating pain and stress in our patients, there are physiologic reasons for analgesia as well. Prolonged stress can negatively affect every aspect of physiology; including cardiovascular health, immune function, GI motility, and hemostasis. Similarly, pain creates undesirable physiological effects, which have been shown to increase mortality in critical patients. Conversely providing appropriate analgesia leads to better outcomes. A study demonstrated infants undergoing open heart surgery had fewer complications and post-operative deaths when deep anesthesia with post-operative opioids were employed. Pain and stress are intertwined, pain causes stress and stress can amplify pain. Pain can activate the hypothalamic-pituitary-axis leading to numerous physiologic consequences including activation of the sympathetic nervous system resulting in vasoconstriction, increased afterload, increases heart rate, increased blood pressure, and dilated pupils. Endocrine response produces an increase in cortisol and other hormones as well as a decrease in insulin secretion resulting in weakened immune function, hyperglycemia, and insulin resistance.
Nursing considerations for the emergency & critical care patient

Especially when staffing is short and the work load high, it is easy for all of us to forget the basics of good nursing care which have a significant influence on overall patient comfort and well-being. The successful veterinary technician is first and foremost an excellent observer. Prescribed medications and therapeutic interventions (e.g. cold compressing a surgical site) are performed on time and to completion. Scheduling bolus opioid administration immediately prior to moving a patient can be of benefit. Staff communication and appropriate record keeping are also important to achieve appropriate nursing care. The veterinary technician must always act as the cat's advocate, regularly assessing patient comfort, and bringing inadequate patient comfort concerns to the attention of the attending veterinarian promptly. Recording therapies carefully including the time performed, achieved level of effectiveness, and patient mentation assures consistent patient care.

Patients should be checked constantly for cleanliness. This cannot be overstated. Any cleanliness concerns should be addressed immediately. Hospitalized cats that are not NPO must have easy access to clean water and fresh food at all times. Small quantities of fresh food should be offered regularly. The diet that is provide should be given with consideration to the pet's normal diet. For example, some cats prefer dry food and will not eat wet cat food when its provided in hospital. Bedding should be deep and soft and changed regularly. One important feline consideration is scent marking. Cats will mark their bedding and changing it may create additional stress of having to mark new bedding. Consider keeping clean bedding with cats.

Veterinary intensive care units are often busy and noisy. This can lead to increased patient anxiety and sleep deprivation and may have an impact on patient morbidity and mortality. Silencing monitors, avoiding excessive conversation or room traffic, turning down or off bright overhead lights, moving noisy patients away from the other

patients, are just some techniques to ensure cats are able to rest in a lower stress environment. Hospital temperature should also be considered and kept within comfortable ranges.

Regular inspection of intravenous and urinary catheters, tubes, and bandages is also very important. These interventions must be kept clean, dry, and comfortable at all times. If they do not meet this expectation they should be fixed, replaced, or removed. Is there catheter induced pheblitis? Is the nasogastric tube poorly secured and rubbing the patient's eye? Is the urinary catheter poorly secured and causing tension on the patient's external genitalia? The astute veterinary technician is always searching for ways to make their patient more comfortable.

Cats should be provided with clean litter pans which are then changed frequently. Using plastic pans or empty boxes that more closely resemble their pan at home helps with familiarity. Often flat trays we provide are not "pan like". In addition using clay litter when applicable will also help with familiarity. Many do not use pellet type litter at home which may increase stress. Cats that are anemic or have incisions/open wounds do however require pellet litters. It is ideal to maintain a canine free area for feline patients. Keep in mind many cats have not had exposure to dogs in their everyday setting which can greatly add to patient stress. Occasionally changing the size or location of a cage will aid in relieving anxiety, either smaller or larger and perhaps away from vocal animals when able. Cats often find comfort in hiding and should be provided with a hiding box or towel covering part of the cage. Often times offering a bit of cat nip can relax a feline patient. Tools such as a Thundershirt™ and pheromone diffusers and sprays may be beneficial and are inexpensive to employ. Gentle and calm interaction, including soothing voices, petting, attention, and social interaction also go a great way to reducing stress in hospitalized patients. These tender love and care (TLC) basics are just as, if not more important, than anything else we do as veterinary nurses.

Opioids are the most widely used and effective drugs for the treatment of acute pain. Interesting they are poorly effective in the treatment of established chronic pain. Opioids work by mimicking the actions of endogenous opioids peptides (e.g. endorphins, enkephalins, dynorphins) at mu, kappa, or delta receptors located throughout the central nervous system and periphery (e.g. eyes, synovial and pleural membranes, etc.). In the veterinary emergency and critical care setting, the most frequently used mu agonist opioids include fentanyl, remifentanil, oxymorphone, hydromorphone, and methadone. These drugs are efficacious in treating mild to severe pain. The partial mu agonist opioid buprenorphine and the mu antagonist/kappa agonist drugs butorphanol and nalbuphine are also utilized frequently for less intense more mild pain. All of the drugs described can be administered via intermittent bolus administration or as a constant rate infusion. Opioids that have very short duration of effect, including remifentanil, fentanyl, and butorphanol, almost always require constant infusion to be of clinical benefit.

Select Locoregional Analgesic Techniques

The term locoregional is used to define any analgesic technique that is restricted to a localized region as contrasted by a technique that is administered to the whole body. Sodium channel blockers such as lidocaine, bupivacaine, and ropivicaine are local anesthetics agents that easily lend themselves to locoregional analgesic techniques but are likely far underutilized in the veterinary emergency and critical care setting. These drugs are inexpensive, versatile and easy to use, safe, and incredibly effective when employed as part of multimodal analgesia. In human pain management and anesthesiology, locoregional analgesic techniques undergo widespread use. In some settings administration of a locoregional analgesic technique alone or in conjunction with an opioid or other drugs can prevent the need for heavy sedation or general anesthesia.

Proper technique and dosing of local anesthesia is imperative to ensure effective analgesia and patient safety. Although numbers vary between sources, in general 5mg/kg of lidocaine and 2mg/kg bupivacaine should not be exceeded in cats. This "do not exceed" dose is well below true toxic doses but should always be calculated to ensure no more than this dose is used and toxicity is well avoided. Aspiration prior to drug administration is essential before injection to ensure accidental perivascular injection does not occur.

Anxiolytics & Sedation

As part of improving patient comfort in the emergency and critical care setting, providing patients with tranquilization, anxiolytics, or sedation may be necessary. This may be to avoid patient injury to a surgery site, allow for patient rest and sleep, to reduce stress to other hospitalized patients, or to reduce overall individual patient stress. Some of the more commonly used pharmacological agents are discussed below.

Gabapentin should be considered for every feline patient! For pre-visit as well as in hospital anxiety and stress. This is not exclusively for sedation but anti-anxiety as well. NO CAT LEAVES MY HOUSE WITHOUT IT! Even compliant cats have stress associated with veterinary medicine of all kinds. Employing gabapentin will help reduce anxiety as well as treat pain and it is widely available and inexpensive. Originally developed as an antiepileptic drug, it was eventually found to have a significant effect on many forms of pain in humans. Gabapentin interrupts the calcium channels (which pain travels) which alleviates the severity and presence of several types of pain. Gabapentin can be

found as a liquid elixir or can be compounded into tablets of various doses. Some liquid formulations add xylitol for flavor, avoid these formulations and opt for liquids that employ alternative flavoring. Typically, the powder contained in 100mg capsules is palatable and can be administered in small amounts of food. One study found that with the introduction of gabapentin, the affected cat displayed a decrease in pain-associated behaviors including aggression, avoiding human interaction, and loss of appetite. Gabapentin is very effective as a pharmacologic element of multimodal analgesia in patients with chronic pain. It is safe to combine with other therapies and geriatric or compromised patients. The recommended dose for cats starts at 5 to 10 mg/kg PO q8–12h and may be increased to 50 mg/kg PO q8gh. Patients should be reevaluated every 5-7 days and increased as needed.

Benzodiazepines such as midazolam and diazepam are reversible tranquilizers that possess anti-anxiety effect. They provide these effects predominantly through GABA-A receptors agonism. These drugs also result in amnesia and have anti-convulsant and weak muscle relaxant effect. Benzodiazepines have minimal effect on cardiopulmonary function which may make them attractive for use in emergency and critical care patients. They are often combined with opioids for procedural sedation, as premedication before anesthesia, and to provide neuroleptanalgesic induction in critical patients. It is very important to understand however that the expected effects of benzodiazepines in people may differ greatly from their effect in cats. This class of drug works well in the extremely young, extremely old, or extremely sick cat. In patients that do not fit this profile, benzodiazepines commonly result in extrapyramidal effects including excitement, increased locomotion, restless, vocalization, and dysphoria. For this reason, benzodiazepines are often a first choice class of drugs to provide anti-anxiety effect and tranquilization in hospitalized patients.

The alpha 2 agonist dexmedetomidine possessed analgesic, muscle relaxant, sedative, and anxiolytic properties. The drug is gaining wide popularity in human intensive care units for these purposes. One of many reasons for this is that dexmedetomidine itself causes limited respiratory depression and is less likely to result in endotracheal intubation than other classes of drugs such as benzodiazepines. This is not always the case, however, when dexmedetomdine is used in conjunction with other drugs such as opioids. Dexmedetomidine is reversible with atipamazole. Low doses of dexmedetomidine via constant rate infusion can be potential useful agents to provide sedation and anti-anxiety effect for select patients in the veterinary critical care unit.

Trazodone is an oral serotonin antagonist-reuptake inhibitor that veterinary medicine has discovered when used alone or in conjunction with other medications can aid in treating anxiety based behavioral disorders in dogs and recently cats. Trazodone was first developed as an antidepressant, anxiolytic, and anti-compulsive agent for humans, however significant drowsiness was reported with trazodone administration. One recent veterinary study showed cats tolerated trazadone with no adverse effects at oral doses of 50, 75 and 100mg with the greatest sedative effect at 50mg. Patients generally appear more calm and comfortable but not particularly sedate. Trazadone should not be given concurrently with other drugs that increase serotonin or its reuptake (e.g. tramadol, fluoxetine, amitriptyline, etc) as serotonin syndrome may occur.

Veterinary technicians are patients' advocates, which means serving as client educationalists and persistent reminders. Feline pain can be so elusive and well disguised that it's often overlooked. Educating clients on detecting pain in their cats is a collaborative effort that begins with client education about behaviors associated with pain and the need to be on the lookout for pain cues at home. I assume we are all often asked by lay people how we do this job. I am frequently asked how do you do see cats sick and potentially dying all day. My response is drugs! …….for the cats. I can sleep at night and return tomorrow knowing I advocated for drugs. Analgesics, TLC and anti-anxiolytics are the best I can do. As a tech I do not control the decision making or treatment plans; much like the cat. We can however make their stay as comfortable, low stress and pain free as possible.

References

1. Anand, K.J.S.,and P.R.Hickey. (1992). Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. New England Journal of Medicine 326: 1-9
2. Davis, L. E .1983. Species differences in drug disposition as factors in alleviation of pain. Animal Pain: Perception and Alleviation. New York: Springer.
3. Rollins, B.E., 1998. The Unheeded Cry. Iowa State University Press, Ames, Iowa. P195-200.
4. Orlando,J.M., Case,B.C., Thomson, A.E., Griffith, E., Sherman, B.L.. 2016; Use of oral trazodone for sedation in cats: a pilot study .Journal of Feline Medicine and Surgery 18(6): pp. 476-482.

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Is the Kitty Crazy? Feline Hyperthyroidism

Kathy Engler, DVM, DABVP (Canine/Feline)

Introduction

Feline hyperthyroidism (FHT) is the most common endocrine disease affecting older cats. Prevalence has been reported as 10% in cats older than 10 years of age[1] and is expected to rise. FHT is described as a "new" disease given it was first reported in 1979. It was understood to not simply be an underdiagnosed disease because thyroid adenomas were reported at a very low incidence prior to 1979.[1,6-7]

Pathophysiology

Located within the neck, the thyroid gland is divided into right and left lobes. These glands produce the hormones thyroxine (T4) and triiodothyronine (T3). The major secretory product of thyroid gland is T4 which is 99% protein bound. It is considered the pre-hormone of T3 which is the active form in circulation.

Thyroid hormones affect all body systems and are essential for regulation of body heat, normal muscle growth, skeletal maturation, and mental development. Thyroid hormones, in physiologic quantities, are anabolic. In conjunction with growth hormone and insulin, protein synthesis is stimulated and nitrogen excretion is reduced. However, in excess (hyperthyroidism), they can be catabolic, with increased gluconeogenesis, protein breakdown, and nitrogen wasting.

FHT has been defined as a multi-systemic disorder arising from excess production of the active thyroid hormones T3 and/or T4 from an abnormally functioning thyroid gland.[1, 2] Benign adenomas cause 98% of cases of FHT but 2% of thyroid tumors are malignant.[50] Most patients (70-75%) with FHT have bilateral disease, whereas 20-25% are unilateral adenomas.

The cause of tumor growth is unknown. It is thought to be a combination of factors including genetics, contaminants in the environment, and certain compounds found in commercial diets. The genetics of hyperthyroidism are not straightforward as tumor growth is not a single point mutation. However, several studies have found that Siamese and Burmese breeds are less likely to develop hyperthyroidism than other breeds.[8] Tumor growth due to environmental exposure is contributed to bisphenol exposure from canned cat food, iodine in cat food, and polybrominated diphenyl ethers (PBDE's) that are concentrated in cat litter, carpets, and clothes to name a few. Once ingested, PBDE's act as endocrine disrupting signals and stimulate tumor growth. Felines are likely at higher risk due to grooming behaviors. Prevalence, in part, is expected to rise because there is no indication that use of PBDE's will be discontinued, and remnants can remain in environment 7-8 years after initial exposure.

Clinical Signs

Because thyroid hormones affect all body systems, clinical signs are generalized, and typically chronic in nature. The classic presentation of a hyperthyroid cat is one who is over 8 years of age, active with a good appetite and has some weight loss.[2]

Clinical signs can be placed into four categories: cardiorespiratory, gastrointestinal, urogenital and central nervous system. Often times there is comorbidity.

- Cardiorespiratory signs include cardiac murmurs, arrhythmias and tachypnea.
- Gastrointestinal signs include weight loss in the face of increased appetite, vomiting, and diarrhea.
- Urogenital signs include polyuria and polydipsia.
- Central nervous signs include: increased vocalization, increased activity, agitation and decreased grooming.

Other disease processes which mimic the clinical presentation of FHT are diabetes mellitus type 2, gastrointestinal malabsorption or digestion, neoplasia specifically gastrointestinal lymphosarcoma, chronic kidney disease and parasitism.

Physical Exam

Classically, weight loss and muscle loss (the epaxial muscles especially), is notable. The cat may appear unkempt.

Palpably enlarged thyroid glands are suggestive, but not necessarily indicative, of clinical hyperthyroidism.[20] Heart murmurs and arrhythmias are often auscultated in FHT. Abnormal size, shape or consistency of the kidneys or intestinal tract may suggest comorbidities.

The identification of hypertension in cats with FHT is critical for their health. Because systemic blood pressure can be difficult to assess in a cat out of its normal environment, performing a complete fundic exam may determine whether hypertensive retinopathy is present. Additionally some cats can develop hypertension after re-establishment of euthyroidism.[21]

Diagnosis
The definition of FHT is a cat with one or more clinical signs and a persistently elevated T4, or free T4 by equilibrium dialysis (free T4 by ed). Baseline labwork including chemistry, complete blood count, urinalysis and T4 value is recommended for any geriatric cat. Imaging such as radiographs, abdominal ultrasound and echocardiogram are important to rule out other diseases with clinical signs similar to hyperthyroidism. In the rare FHT cases that are not straightforward, less commonly used diagnostics such as a thyroid stimulating hormone test in combination with a T4 value, T3 suppression test, and nuclear scintigraphy may be indicated.

The 2016 AAFP guidelines have outlined a simplified approach that encompasses a range of six distinct case presentations from overt FHT to no clinical evidence of the disease.

Treatment
After establishing a diagnosis of FHT, the clinician and client have multiple treatment options: medical treatment, radioactive iodine, surgical thyroidectomy, and dietary via Hill's® y/d™.

Choosing which therapy often depends on the cat's age, comorbidities, treatment cost, and the clinician's recommendation, and expertise. The goal of therapy is to restore euthyroidism, avoid hypothyroidism, and minimize side effects of treatment. In general, treat all cats diagnosed with FHT, any comorbidities and monitor closely.
The clinician should be aware that iatrogenic hypothyroidism (IH) as a result of treatment is more common than realized, estimates of prevalence are 20-48%.[25] IH in cats has been linked to reduced survival time, justifying recommendations to monitor cats receiving treatment closely. Two common comorbidities of FHT are chronic kidney disease, and cardiac disease. In both cases, it is important to determine degree of pathology prior to treatment.

Medical Treatment
Anti-thyroid drugs can be used long term as a sole treatment, or short term, to stabilize the patient before surgery, anesthesia, or if radioiodine therapy is not immediately available.[35-37]

Felimazole® Coated Tablets (methimazole)
Dosing guidance:

- Starting dose 2.5 mg orally every 12 hours
- Adjust dose based on T4 levels and clinical response
- Adjust dose in 2.5 mg increments per day (not per dose)
- Do not exceed 20 mg in 24 hours or 10 mg per dose.

The goal of therapy is to have the total T4 levels measure in the lower half of the reference range, which is typically 1-4 micrograms/dL. After the cat becomes euthyroid with q12h dosing, giving the total daily dose q24h may maintain euthyroidism and increase owner compliance.[39,40]
Relatively mild clinical side effects may occur within 4-6 weeks of starting therapy. Common side effects include loss of appetite, vomiting, and lethargy. They tend to be transient and may resolve even with continued administration of the drug.
More severe side effects can occur, including changes in the liver, skin, and blood parameters. Pet owners should be advised to monitor their cats closely for any signs of illness once treatment has been started. If a cat becomes ill while on Felimazole® Coated Tablets (methimazole), the owner should stop treatment and contact his or her veterinarian immediately. Contraindications include do not use in pregnant or lactating animals, as well as in animals with blood cell or bleeding pathologies.

Transdermal Methimazole
In cases where patients do not comply with oral treatment, methimazole has been compounded into a transdermal gel. When using transdermal therapy, the following should be considered:

- The recommended starting dose is higher than oral therapy.[40]
- Some studies have found transdermal gel is associated with less gastrointestinal side effects than oral treatment.[42, 43]
- Human exposure is a possibility. In addition to direct risk of environment contamination, there is also an in vitro study that found penetration of the gel from the inner pinna to the external pinna.[43]

- Transdermal methimazole has not undergone any safety and efficacy trials and is not approved by the FDA; practitioners should make prudent choices in compounding this product.

Advantages of Prescribing Felimazole Coated Tablets® vs Human Generics and/or Compounded Transdermals

- Felimazole® Coated Tablets (methimazole) is the only FDA approved form of methimazole for the treatment of hyperthyroidism in cats.
- Available in both 2.5 mg and 5.0 mg tablets for accurate dosing.
- Tablets are small and sugar coated, making oral administration easier.
- Coated tablets minimize risk of human contact with active ingredient (see package insert).
- Client brochures and technical materials for veterinarians.
- Product support available through the Veterinary Technical Services Team.

Radioactive Iodine

Treatment with radioactive iodine is potentially curative and is considered the treatment of choice for FHT. The distinct advantages are:

- The potential to eliminate benign thyroid tumors or hyperplastic thyroid tissue with a single treatment.
- Treatment of functional extrathyroidal tissue, which may occur in 10–20% of cases.[44, 45]
- No general anesthesia and minimal side effects.
- Successful treatment has been achieved in approximately 95% of cases.

The risk of definitive therapy is that the patient may become permanently hypothyroid and require supplementation. Such a sequelae is very unlikely.[35] Isolation post treatment is a drawback to some owners; local and state laws dictate length of isolation.

Surgical Thyroidectomy

Surgical thyroidectomy is associated with a high rate of both short- and long-term success, with most studies showing >90% of cats achieving euthyroidism postoperatively. Relapse rates are fairly low, approaching 5% within 3 years.[47] It may be the treatment of choice in a patient difficult to medicate. Thyroidectomy provides a potential cure and isolation post treatment isn't required. Furthermore it may be the only potentially curative option in geographical areas that do not provide I-131 treatment. The major complication following surgery is hypocalcemia (low blood calcium), which occurs when both parathyroid glands are inadvertently removed or injured during the surgical procedure.

Dietary

A restricted-iodine diet (Hill's Prescription diet y/d Feline; Hill's Pet Nutrition) containing 0.2 ppm (mg/kg) iodine on a dry matter basis is currently available for the management of FHT. With good client compliance, 75% of cats have significantly reduced T4 and improvement of clinical signs within 28 days of starting the diet.48, 49 Drawbacks of dietary therapy include: the patient must eat, and only eat, y/d™ for life (even suspension for compounded medications can contain iodine); palatability can be a concern in 12% of cases48 and of cost is not insignificant at approximately $1100/year.

Monitoring

Monitoring is necessary to asses control of the disease, avoid iatrogenic hypothyroidism, and assess comorbid disorders. Hematology biochemistry and T4 should be evaluated after 3 weeks, and then at 6 weeks of treatment. Thereafter, bloodwork should be monitored every 3 months and the dose adjusted as necessary. Cats receiving doses greater than 10 mg per day should be monitored more frequently. Other labwork may be needed if there is presence of other disease. Monitoring blood pressure and possibly retinal anatomy may be necessary as well.

Concurrent Treatment of FHT and CKD

FHT can cause increased glomerular filtration rate and decreased muscle mass, both of which can mask underlying kidney disease. Staging of CKD should be done according to IRIS guidelines, which includes measurement of blood pressure and urine protein quantification.[28] Whether non-azotemic, or azotemic at the time of diagnosis, treat per IRIS guidelines and avoid iatrogenic hypothyroidism.[32] Post treatment azotemia occurs in 20-33% of cats regardless of treatment modality, and no reliable predictors have been identified.

Some practitioners believe that intentionally keeping patients slightly hyperthyroid in order to increase renal perfusion

and therefore minimizing azotemia is advantageous. Such an approach actually is deleterious and causes worsened renal damage.[32]

Concurrent Treatment of FHT and Cardiac Disease

If evidence of cardiac disease is present at the time of FHT diagnosis, the recommendation is to achieve euthyroidism and then reevaluate. Thyrotoxic cardiac changes and systemic hypertension may resolve with hyperthyroidism treatment.[33] N-terminal probrain natriuretic peptide (NT-proBNP) levels will rise in both cases of FHT and hypertrophic cardiomyopathy however the levels are expected to normalize in the case of FHT. If proBNP levels are still elevated three months after achieving euthyroidism, the patient should be evaluated for hypertrophic cardiomyopathy.[34]

Prognosis

Overall success of management of FHT is 83–99%, depending on the patient's clinical status and treatment modality. Radioiodine and surgery are potentially permanent cures for both adenomas and carcinomas. Methimazole and dietary therapy will control clinical disease in milder cases, and in cats with significant comorbidities. Median survival for treated hyperthyroid cats without concurrent chronic kidney disease is approximately 5.3 years.[6]

Summary

FHT is now the most common endocrine disease in middle-aged and older cats. The cause is unknown; it is suspected to be a combination of genetic and environmental factors. Total thyroid hormone (T4) should be routinely checked as part of baseline labwork. Screen, stage, and treat comorbidities as indicated. Diagnosis of FHT is usually straightforward and includes a persistently elevated T4 and/or free T4 by ed along with corresponding clinical signs. Treatment modalities available are: medical treatment Felimazole® Coated Tablets (methimazole), the only FDA approved drug to treat FHT); radioactive iodine; surgical thyroidectomy and dietary therapy. Success rate of all treatments is generally good at 83-99%. Regular monitoring of a hyperthyroid cat is important not only to assess therapeutic efficacy but also to detect iatrogenic hypothyroidism and confirm comorbidities that become evident with resolution of the hyperthyroid state. Morbidity and mortality in the well-managed hyperthyroid cat are more strongly influenced by the presence and severity of the comorbid disease than by FHT itself.

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References

1. Mooney CT. Hyperthyroidism. In Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*. St. Louis: Elsevier, 2010, pp 1761-1779
2. AAFP 2016 Feline Hyperthyroidism Guidelines
3. Milner RJ, Channell Cd, Levy JK, et al. Survival times for cats with hyperthyroidism treated with iodine 131, methimazole, or both: 167 cases (1996–2003). *J Am Vet Med Assoc* 2006; 228: 559–563.
4. Hibbert A, Gruffydd-Jones T, Barrett EL, et al. Feline thyroid carcinoma: diagnosis and response to high-dose radioactive iodine treatment. *J Feline Med Surg* 2009; 11: 116–124.
5. Evidence to contradict mutational disease: Hammer KB, Holt DE and Ward CR. Altered suppression of G proteins in thyroid gland adenomas obtained from hyperthyroid cats. *Am J Vet Res* 2000; 61: 874-879
6. Carcinomas: Turrel JM, Feldman EC, Nelson RW, et al. Thyroid carcinoma causing hyperthyroidism in cats: 14 cases (1981-1986). *J Am Vet Med* Assoc 1988; 193: 359-364
7. Scarlett JM, Moise NS and Rayl J. Feline hyperthyroidism: a descriptive and case control study. *Prev Vet Med* 1988; 7: 295–310.
8. Kass PH, Peterson ME, Levy J, et al. Evaluation of environmental, nutritional, and host factors in cats with hyperthyroidism. *J Vet Intern Med* 1999; 13: 323–329.
9. Wakeling J, Everard A, Brodbelt d, et al. Risk factors for feline hyperthyroidism in the UK. *J Small Anim Pract* 2009; 50: 406–414.
10. Edinboro C, Scott-Moncrieff J, Janovitz E, et al. Epidemiologic study of relationships between consumption of commercial canned food and risk of hyperthyroidism in cats. *J Am Vet Med Assoc* 2004; 224: 879–886.
11. Kang JH and Kondo F. Determination of bisphenol A in canned pet foods. *Res Vet Sci* 2002; 73: 177–182.
12. Dye JA, Venier M, Zhu L, et al. Elevated PBDE levels in pet cats: sentinels for humans? *Environ Sci Technol* 2007; 15: 6350–6356.
13. Guo W, Park JS, Wang Y, et al. High polybrominated diphenyl ether levels in California house cats: house dust a primary source? *Environ Toxicol Chem* 2012; 31: 301–306.
14. Mensching dA, Slater J, Scott JW, et al. The feline thyroid gland: a model for endocrine disruption by polybrominated diphenyl ethers (PBDEs)? *J Toxicol Environ Health A* 2012; 75: 201–212.
15. Norrgran J, Jones B, Lindquist NG, et al. Decabromobiphenyl, polybrominated diphenyl ethers, and

brominated phenolic compounds in serum of cats diagnosed with the endocrine disease feline hyperthyroidism. *Arch Environ Contam Toxicol* 2012; 63: 161–168.
16. Court MH and Freeman LM. Identification and concentration of soy isoflavones in commercial cat foods. *Am J Vet Res* 2002; 63: 181–185.
17. Wedekind KJ, Blumer ME, Huntington CE, et al. The feline iodine requirement is lower than the 2006 NRC recommended allowance. *J Anim Physiol Anim Nutr (Berl)* 2010; 94: 527– 539.
18. Edinboro CH, Scott-Moncrieff JC and Glickman LT. Feline hyperthyroidism: potential relationship with iodine supplement requirements of commercial cat foods. *J Feline Med Surg* 2010; 12: 672–679.
19. Edinboro CH, Pearce EN, Pino S, et al. Iodine concentration in commercial cat foods from three regions of the USA, 2008–2009. *J Feline Med Surg* 2013; 15; 717–724.
20. Norsworthy Gd, Adams VJ, McElhaney MR, et al. Relationship between semi-quantitative thyroid palpation and total thyroxine concentration in cats with and without hyperthyroidism. *J Feline Med Surg* 2002; 4: 139–143.
21. Morrow Ld, Adams VJ and Syme HM. Hypertension in hyperthyroid cats: prevalence, incidence, and predictors of its development. J Vet Intern Med 2009; 23: 699
22. Peterson M, Melian C, Nichols R. Measurement of Serum Concentrations of Free Thyroxine, Total Thyroxine, and Total Triiodothyronine in Cats with Hyperthyroidism and Cats with Nonthyroidal Disease. J Am Vet Med Assoc 2001;218:529-536.
23. Peterson ME, Guterl JN, Nichols R, et al. Evaluation of Serum Thyroid-Stimulating Hormone Concentration as a Diagnostic Test for Hyperthyroidism in Cats. *J Vet Intern Med* 2015;29:1327-1334.
24. C. Aldridge, E.N. Behrend, L.G. Martin, K. Refsal, R.J. Kemppainen, H.P. Lee, and K. Chciuk. Evaluation of Thyroid-Stimulating Hormone, Total Thyroxine, and Free Thyroxine Concentrations in Hyperthyroid Cats Receiving Methimazole Treatment. *J Vet Intern Med* 2015;29:862–868.
25. Williams T, Elliott J and Syme H. Association of iatrogenic hypothyroidism with azotemia and reduced survival time in cats treated for hyperthyroidism. *J Vet Intern Med* 2010; 24: 1086–1092
26. Peterson ME. Diagnosis and Management of Iatrogenic Hypothyroidism In: Little SE, ed. August's Consulations in Feline Internal Medicine. St. Louis, MO: Elsevier, 2015;260-269.
27. Peterson ME, Nichols R, Rishniw M. Serum thyroxine and thyroid-stimulating hormone concentration in hyperthyroid cats that develop azotaemia after radioiodine treatment. *Journal of Small Animal Practice*; 2017; 58:519-530.
28. IRIS CKd Guidelines. Substaging by arterial blood pressure. http://www.iris-kidney.com/guidelines/ (2013, accessed November 2, 2015)
29. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA. © 2016 IDEXX Laboratories, Inc
30. M E Peterson, F V Varela, M Rishniw, D J Polzin. Evaluation of Serum Symmetric Dimethylarginine Concentration as a Marker for Masked Chronic Kidney Disease in Cats With Hyperthyroidism. *J Vet Intern Med.* January 2018;32(1):295-304.
31. diBartola S and Brown S. The kidney and hypertension. In: Bongura J (ed). Kirk's current veterinary therapy XIII. Philadephia: WB Saunders, 1999, p 137. 51
32. diBartola S, Rutgers H, Zack P, et al. Clinicopathologic findings associated with chronic renal disease in cats: 74 cases (1973–1984). *J Am Vet Med Assoc* 1987; 190: 1196–1202
33. Weichselbaum RC, Feeney dA and Jessen CR. Relationship between selected echocardiographic variables before and after radioiodine treatment in 91 hyperthyroid cats. *Vet Radiol Ultrasound* 2005; 46: 506–513.
34. Sangster JK, Panciera dL, Abbott JA, et al. Cardiac biomarkers in hyperthyroid cats. J Vet Intern Med 2014; 28: 465–472.
35. Scott-Moncrief JC. Feline hyperthyroidism. In: Feldman EC, Nelson RW, Reusch CE, et al (eds). Canine and feline endocrinology and reproduction. 4th ed. St Louis, Mo: Elsevier, 2015: 136–195.
36. Mooney CT. Feline hyperthyroidism: diagnostics and therapeutics. Vet Clin North Am Small Anim Pract 2001; 31: 963–983
37. Trepanier LA. Pharmacologic management of feline hyperthyroidism. *Vet Clin North Am Small Anim Pract* 2007; 37: 775–788
38. Baral RM and Peterson ME: Hyperthyroidism. In: Little SE (ed). The cat: clinical medicine and management. St Louis, Mo: Elsevier Saunders, 2012, pp 571–583.
39. Trepanier LA, Hoffman SB, Kroll M, et al. Efficacy and safety of once versus twice daily administration of methimazole in cats with hyperthyroidism. *J Am Vet Med Assoc* 2003; 222: 954–958.
40. Trepanier LA, Peterson ME and Aucoin dP. Pharmacokinetics of intravenous and oral methimazole following single- and multipledose administration in normal cats. *J Vet Pharmacol Ther* 1991; 14: 367–373
41. Felimazole® Product Insert, Dechra Veterinary Products
42. Sartor LL, Trepanier LA, Kroll MM, et al. Efficacy and safety of transdermal methimazole in the treatment

of cats with hyperthyroidism. *J Vet Intern Med* 2004; 18:651-655
43. Kate E Hill1, J Paul Chambers1, Boyd R Jones1, Charlotte F Bolwell1, Dani Aberdein1 and Paul C Mills2. Trans-pinnal movement of methimazole: an in vitro study showing that methimazole can cross from the inner to outer pinna of cats. *Journal of Feline Medicine and Surgery* 2015: 1-7
44. Peterson ME and Broome MR. Thyroid scintigraphic findings in 917 cats with hyperthyroidism. *J Vet Intern Med* 2012; 26: 754
45. Mooney CT and Peterson ME. Feline hyperthyroidism. In: Mooney CT and Peterson ME (eds). BSAVA manual of canine and feline endocrinology. 4th ed. Quedgeley, Gloucester, UK: BSAVA, 2012, pp 199–203
46. Peterson ME, Becker DV. Radioiodine treatment of 524 cats with hyperthyroidism. *JAVMA* 1995; 207: 1422-1428
47. Naan EC, Kirpensteijn J, Kooistra HS, et al. Results of thyroidectomy in 101 cats with hyperthyroidism. *Vet Surg* 2006; 35: 287–293
48. van der Kooij M, Becvárová I, Meyer HP, et al. Effects of an iodinerestricted food on client- owned cats with hyperthyroidism. *J Feline Med Surg* 2014; 16: 491–498
49. Hui TY, Bruyette dS, Moore GE, et al. Effect of feeding an iodine restricted diet in cats with spontaneous hyperthyroidism. *J Vet Intern Med* 2015; 29: 1063–1068
50. Carcinomas: Turrel JM, Feldman EC, Nelson RW, et al. Thyroid carcinoma causing hyperthyroidism in cats: 14 cases (1981-1986). J Am Vet Med Assoc 1988; 193: 359-364

NOTES:

Ophthalmic Drugs & When to Use Them

Jessica Meekins, DVM, MS, DACVO

Introduction

There is a wide variety of ophthalmic medications available for use in veterinary medicine, with many 'human' drugs used in an off label manner in our patients. Since it can be impractical to keep a full complement of ophthalmic medications in stock in a general practice setting, it is common to prescribe certain medications to be filled at outside human pharmacies. Clients can become easily overwhelmed when contemplating the need to apply medications to their cat's eyes, so the veterinary nurse serves a crucial role in client education. Two key elements to ensuring compliance and increasing the likelihood of a good treatment outcome include: 1) emphasizing the reason for prescribed medications, and 2) demonstrating their use.

Antimicrobials

Antibiotics

The two most common indications for use of topical antibiotics in cats with surface ocular disease are: 1) prophylaxis to prevent secondary bacterial infection of herpetic corneal ulcers, and 2) for the treatment of bacterial (chlamydial) conjunctivitis. The normal feline surface ocular flora consists predominantly of gram positive bacteria (Staphylococcus, Streptococcus, Corynebacterium), so there are several topical antibiotic options to prevent bacterial infection of a viral ulcer. The author commonly prescribes **tobramycin** or **neo/poly/gram** if solution formulations are desired, and **erythromycin** or **gentamicin** for ointment formulation options, based on the client's ability to successfully apply the medication directly to the eye.

If chlamydial conjunctivitis is suspected or confirmed with cytology or PCR, **Terramycin®** (oxytetracycline hydrochloride and polymixin B) is the author's preferred topical antibiotic, as chlamydial organisms tend to be highly susceptible to tetracycline antibiotics.[1] Occasionally, mycoplasmal overgrowth is implicated as a cause of infectious conjunctivitis in cats, however *Mycoplasma* sp. are considered normal flora of the feline ocular surface, and overgrowth tends to develop during co-infection with a viral or chlamydial primary cause. At any rate, even if mycoplasmal overgrowth is suspected, the organism is highly susceptible to broad spectrum topical ophthalmic antibiotics that would be selected to treat primary bacterial (chlamydial) conjunctivitis.

Fluoroquinolones (**ciprofloxacin**, **ofloxacin**, **moxifloxacin**) and **chloramphenicol** (not commercially available in the United States) are the only topical antibiotics that penetrate intact epithelium. If a cat has a deeper corneal (stromal abscess, in which a pocket of infection is trapped below fluorescein negative intact corneal epithelium) or intraocular infection, these are the only antibiotic selections that will appropriately penetrate to the target area within the cornea or inside the eye.

Antivirals

It is important to remember that the majority of conjunctivitis cases in cats are viral, not bacterial, in etiology. If feline herpesvirus-1 (FHV-1) is suspected, antibiotic therapy is only necessary if a corneal ulcer is present (in order to prevent secondary bacterial infection). Antiviral therapy is key to hasten the resolution of FHV-1 surface ocular disease. However, because stress can exacerbate herpetic flare-ups, the ease of administering a specific treatment must be considered. It may be counterproductive to prescribe certain therapies if a client must go to extreme measures to 'force' the treatment. Treatment must take into consideration the individual cat/owner relationship and what will accomplish the most with as little stress as possible for all involved (cat and owner!).

After deciding whether antiviral therapy may be beneficial, the route of administration should be decided. If clinical signs are confined to the eye, the author starts with topical therapy alone. If respiratory signs are present in addition to ocular signs, systemic therapy is indicated. However, both topical and oral routes of administration may be used simultaneously; in some cats with ocular clinical signs refractory to topical therapy, oral therapy can be used alone or in combination with topical therapy.

No topical antiviral drugs are approved for use in cats in the United States. The two topical antivirals used regularly by the author are **cidofovir 0.5%** and **idoxuridine 0.1%**, and both of these drugs must be compounded. There are benefits and drawbacks to each. Cidofovir has been shown to lessen the duration of clinical signs and virus shedding in experimentally infected cats with twice daily treatment frequency.[2] However, it is quite expensive when compared to idoxuridine, which is often half the cost (or less) of cidofovir. Idoxuridine must be given more frequently, at minimum 4-6 times per day, so the trade-off is cost for treatment frequency when comparing these drugs.

Trifluridine, with the brand name **Viroptic®**, is a commercially available human product used to treat herpes simplex keratoconjunctivitis,[3] however anecdotally it is very topically irritating and poorly tolerated when administered to cats.

In general, the author has experienced very few side effects of topically administered cidofovir and idoxuridine. Specifically, cats infrequently develop an intolerance to cidofovir that manifests as an ulcerative blepharitis, which resolves slowly after discontinuation of treatment.

There is a commercially available **famciclovir** product called **Famvir®**, made by Novartis, which is currently the only appropriate oral antiviral option for cats. Based on recent research, a dose range has been optimized for oral administration.[4,5] A 40 mg/kg dose given twice daily is the author's standard practice. This is based on information that showed similar peak plasma concentrations in a lower dose group despite another study with improved clinical outcome in a higher dose group.[6] Though the literature supports three times daily dosing, from a practical standpoint twice daily administration is more feasible for most cat owners and anecdotally is associated with improved clinical outcome. Prior to the publication of new research investigating the pharmacokinetics of famciclovir after oral administration, many clinicians would attribute therapeutic effect to doses as low as 62.5 mg per cat once to twice per day. In the author's practice, most adult cats receive approximately 250 mg by mouth every 12 hours, however dosages should be adjusted in cats with kidney disease since the drug undergoes renal metabolism. It is very important never to prescribe valacyclovir to cats, as it causes fatal renal tubular necrosis, hepatic atrophy, and severe bone marrow suppression.[7]

Lysine is an amino acid supplement that works by antagonizing arginine, which is essential to viral replication.[8] The adult cat dosage is 1000 mg daily, generally divided into two 500 mg doses. There are many lysine options on the veterinary market. Lysine is not a targeted antiviral treatment, but it may prove beneficial as a nutraceutical and 'immune booster' in many cats. The major caveat is that the administration of lysine must be stress-free, which is why several highly palatable treat formulations now exist.

The duration of treatment is possibly the most important factor to consider. Due to the virostatic nature of the available antiviral drugs, virus replication is decreased but virus is not actively killed. Thus, treatment should be continued at least one week beyond clinical resolution to decrease the risk of flare-up if treatment is discontinued too abruptly.

Anti-inflammatories

Corticosteroids[9,10]

Topical steroids have few and very distinct clinical applications for treatment of surface ocular disease in cats. Given that any administered steroid, either topical or systemic, may reactivate latent FHV-1, the benefits and drawbacks of the most appropriate course of therapy must be considered. The only surface ocular disease for which topical steroid therapy is routinely used is eosinophilic-proliferative keratitis/conjunctivitis (EPKC), a surface ocular inflammatory disease unique to cats that involves infiltration of the ocular tissues by eosinophils and mast cells. EPKC lesions are generally very responsive to local steroid therapy. **Prednisolone acetate** or **dexamethasone** (alone or in a combination product that contains antibiotics, **neo/poly/dexamethasone**) are commonly used, and **hydrocortisone** is avoided because it is not as potent and it poorly penetrates the corneal tissue.

Even though it may be appropriate based on the underlying diagnosis, the risk of herpetic reactivation must be considered in any cat receiving topical steroid therapy. If a patient is at high risk for a herpetic flare-up, the author considers prescribing concurrent antiviral therapy in an effort to decrease that risk. Careful questioning of the client is necessary to determine if there may be a history of previous recurrent viral surface ocular disease, and if so, antivirals can be prescribed topically or systemically to be administered during topical steroid treatment.

Alternatively, topical compounded **megestrol acetate 0.5%** was recently investigated as another option specifically to treat EPKC with good success.[11] Megestrol acetate has weak glucocorticoid activity, and thus may be less likely to trigger herpetic reactivation when compared to topical steroids. This alternative therapy may be considered in cats at high risk for reactivation of latent herpesvirus.

Non-steroidal anti-inflammatories (NSAIDs)[12]

Occasionally, cats suffer from significant viral surface ocular inflammation that is not sufficiently controlled with targeted antiviral therapy. In these circumstances, there may be some benefit to treating affected cats with topical NSAID therapy (**flurbiprofen 0.03%**, **diclofenac 0.1%**, **ketorolac 0.5%**) in an effort to alleviate the pain associated with local inflammation. A recent investigation by the author found no effect of commonly prescribed topical NSAIDs on corneal sensitivity in normal cats (publication in press), calling into question the therapeutic utility of these drugs in alleviating corneal pain. However, to the author's knowledge, no controlled studies have been conducted on the use of topical NSAIDs to treat corneal pain in cats with active surface ocular inflammation.

Intraocular (uveitis) vs. surface ocular disease
Cats suffer from intraocular in addition to surface ocular disease. If the presenting complaint is uveitis with no evidence of surface ocular disease, a topical steroid or NSAID should be selected for symptomatic treatment of intraocular inflammation. The risk of herpetic reactivation must still be considered in a cat treated with topical steroids with a history of viral surface ocular disease; if the concern is significant, either concurrent antiviral therapy or the use of topical NSAIDs in lieu of steroids should help to mitigate the risk of viral reactivation at the ocular surface while treating intraocular disease.

Other immunomodulatory drugs
While cats do not typically experience the surface ocular immune-mediated diseases we commonly encounter in other species, steroid-sparing immunomodulatory drugs like **cyclosporine** and **tacrolimus** may have use in the management of certain feline surface ocular diseases.[13] Cyclosporine is available in a commercial veterinary product (**Optimmune®**) or it can be compounded into higher concentrations. There is not a commercially available tacrolimus product, so all formulations must be compounded.

Cats uncommonly develop keratoconjunctivitis sicca (KCS, or dry eye disease), which is the surface ocular disease most frequently managed with these drugs in small animal practice. Cats do occasionally develop qualitative tear film deficiencies, generally affecting the mucin layer of the tear film due to damage of the conjunctival goblet cells after chronic viral conjunctivitis.[14,15] Cyclosporine has been shown to increase the number of mucin-producing conjunctival goblet cells in humans,[16] therefore it may have a clinical application in cats with qualitative tear film deficiency. These steroid-sparing topical drugs have also been used to manage the unique feline surface ocular condition EPKC,[13] particularly in cats at high risk for reactivation of viral keratoconjunctivitis. To the author's knowledge, there are no publications implicating cyclosporine or tacrolimus on the reactivation of latent FHV-1.

Ocular hypotensive medications
Cats develop glaucoma most often as a complication of chronic uveitis,[17] though there have been scattered reports of primary (hereditary) glaucoma.[18] Carbonic anhydrase inhibitors (CAIs) such as **dorzolamide**[19-21] and beta-blockers such as **timolol**[21,22] are the most effective and well-tolerated ocular hypotensive medication available for use in cats. Due to the limited systemic absorption of topically applied medications, there is generally little concern about systemic side effects with these drugs. Historically, prior to the development of topical CAIs, orally administered CAIs were poorly tolerated in cats and resulted in significant side effects. These concerns have effectively been eliminated with the use of topical CAIs.

Other
There is a wide array of tear substitute lubricant products, both veterinary and human, that can be purchased over the counter online or at any retail store that sells eye care products. When recommended, it is important to emphasize that a gel formulation (rather than a liquid solution) be purchased in order to increase the contact time and tissue coating effects of the product. The author most commonly recommends a lubricating gel for brachycephalic cats in an effort to promote surface ocular health and diminish the local effects of 'breed standard' periocular conformation on chronic surface ocular irritation.

References

1. Andrew SE. Ocular manifestations of feline herpesvirus. *J Feline Med Surg* 2001;3:9-16.
2. Fontenelle JR, Powell CC, Veir JK, et al. Effect of topical ophthalmic application of cidofovir on experimentally induced primary ocular feline herpesvirus-1 infection in cats. *American Journal of Veterinary Research* 2008;69:289-293.
3. Nasisse MP, Guy JS, Davidson MG, et al. In vitro susceptibility of feline herpesvirus-1 to vidarabine, idoxuridine, trifluridine, acyclovir, or bromovinyldeoxyuridine. *Am J Vet Res* 1989;50:158-160.
4. Thomasy SM, Covert JC, Stanley SD, et al. Pharmacokinetics of famciclovir and penciclovir in tears following oral administration of famciclovir to cats: a pilot study. *Veterinary Ophthalmology* 2012;15:299-306.
5. Sebbag L, Thomasy SM, Woodward AP, et al. Pharmacokinetic modeling of penciclovir and BRL42359 in the plasma and tears of healthy cats to optimize dosage recommendations for oral administration of famciclovir. *Am J Vet Res* 2016;77:833-845.
6. Thomasy SM, Shull O, Outerbridge CA, et al. Oral administration of famciclovir for treatment of spontaneous ocular, respiratory, or dermatologic disease attributed to feline herpesvirus type 1: 59 cases (2006-2013). *J Am Vet Med Assoc* 2016;249:526-538.
7. Nasisse MP, Dorman DC, Jamison KC, et al. Effects of valacyclovir in cats infected with feline herpesvirus 1. *Am J Vet Res* 1997;58:1141-1144.
8. Stiles J, Townsend WM, Rogers QR, et al. Effect of oral administration of L-lysine on conjunctivitis

caused by feline herpesvirus in cats. *Am J Vet Res* 2002;63:99-103.
9. Wilkie DA. Control of ocular inflammation. *Vet Clin North Am Small Anim Pract* 1990;20:693-713.
10. Holmberg BJ, Maggs DJ. The use of corticosteroids to treat ocular inflammation. *Vet Clin North Am Small Anim Pract* 2004;34:693-705.
11. Stiles J, Coster M. Use of an ophthalmic formulation of megestrol acetate for the treatment of eosinophilic keratitis in cats. *Vet Ophthalmol* 2016;19 Suppl 1:86-90.
12. Giuliano EA. Nonsteroidal anti-inflammatory drugs in veterinary ophthalmology. *Vet Clin North Am Small Anim Pract* 2004;34:707-723.
13. Spiess AK, Sapienza JS, Mayordomo A. Treatment of proliferative feline eosinophilic keratitis with topical 1.5% cyclosporine: 35 cases. *Vet Ophthalmol* 2009;12:132-137.
14. Lim CC, Cullen CL. Schirmer tear test values and tear film break-up times in cats with conjunctivitis. *Vet Ophthalmol* 2005;8:305-310.
15. Lim CC, Reilly CM, Thomasy SM, et al. Effects of feline herpesvirus type 1 on tear film break-up time, Schirmer tear test results, and conjunctival goblet cell density in experimentally infected cats. *Am J Vet Res* 2009;70:394-403.
16. Kunert KS, Tisdale AS, Gipson IK. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporine. *Arch Ophthalmol* 2002;120:330-337.
17. Wilcock BP, Peiffer RL, Jr., Davidson MG. The causes of glaucoma in cats. *Vet Pathol* 1990;27:35-40.
18. Hampson EC, Smith RI, Bernays ME. Primary glaucoma in Burmese cats. *Aust Vet J* 2002;80:672-680.
19. Rankin AJ, Crumley WR, Allbaugh RA. Effects of ocular administration of ophthalmic 2% dorzolamide hydrochloride solution on aqueous humor flow rate and intraocular pressure in clinically normal cats. *Am J Vet Res* 2012;73:1074-1078.
20. Rainbow ME, Dziezyc J. Effects of twice daily application of 2% dorzolamide on intraocular pressure in normal cats. *Vet Ophthalmol* 2003;6:147-150.
21. Dietrich UM, Chandler MJ, Cooper T, et al. Effects of topical 2% dorzolamide hydrochloride alone and in combination with 0.5% timolol maleate on intraocular pressure in normal feline eyes. *Vet Ophthalmol* 2007;10 Suppl 1:95-100.
22. Wilkie DA, Latimer CA. Effects of topical administration of timolol maleate on intraocular pressure and pupil size in dogs. *Am J Vet Res* 1991;52:432-435.

NOTES:

CKD: Prediction of Future Diagnosis, Early Diagnosis, Staging, & Management Strategies

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Chronic kidney disease (CKD) is characterized by the development of intrarenal lesions that are irreversible and variably progressive.[1,2] These lesions are clinically associated with decreased GFR, loss of renal excretory ability, decreased ability to conserve electrolytes and proteins, reduced ability to maximally concentrate urine, and decreased ability to synthesize calcitriol and erythropoietin depending on how advanced the disease has become. The definition of "chronic" requires documentation of an ongoing intrarenal process from 1 to 3 months.

The frequency for the diagnosis of CKD is more common in cats compared to dogs, especially in geriatric cats. Azotemic CKD was diagnosed in 8 to 31% of geriatric cats in several studies.[3-6] The prevalence for a highly likely diagnosis of CKD for cats in primary care practices was 17%, and increased to 42% when a probable diagnosis of CKD was considered.[7] When CKD included IRIS stage 1 and stage 2 cats, the prevalence of CKD in random source control cats of various ages was detected in 50% and in 68.8% of cats that also had a diagnosis of degenerative joint disease.[5] In one study, CKD was the leading cause for mortality in cats ≥ 5 years of age and the number two cause of death in cats of all ages examined at primary care practices.[8]

The initial clinical diagnosis of CKD is made on some combination of findings from owner reported clinical signs, physical examination (especially large or small kidneys, irregular kidneys, hard kidneys), systemic blood pressure, renal imaging, urinalysis, urine biochemistry (UPC), and serum biochemistry (BUN, creatinine, phosphorus, SDMA). A specific diagnosis for the underlying CKD is often not possible and many are diagnosed with "idiopathic" chronic interstitial nephritis. Tubulo-interstitial nephritis of unknown origin is the most common cause of azotemic CKD in the cat, as in the dog. Glomerulonephritis as the cause for CKD is less common in cats than in dogs. Cats have several renal diseases that deserve additional consideration, including breed-related predilection for renal amyloidosis (Abyssinian, Oriental Short Hair) and polycystic kidney disease (Persian, Himalayan). Cats also have greater frequency of CKD associated with renal LSA than dogs. Peri-nephric pseudocyst can be associated with CKD in cats and should be considered as a differential diagnosis for apparent renal enlargement in addition to renal LSA and hydronephrosis.

Prediction of a CKD Diagnosis

An increased risk for the diagnosis of CKD was shown for cats that had thin body condition, a diagnosis of periodontal disease or cystitis, had undergone anesthesia, or were noted to have dehydration in the preceding year. Neutered male cats were at increased risk compared to spayed females for CKD in the same study.[9] Periodontal disease was associated with increased risk for a future diagnosis of CKD, with the greatest risk for cats with stage 3 or 4 periodontal disease. Anesthesia or a diagnosis of cystitis within the past year were also risk factors for a diagnosis of CKD to emerge.[10]

An early study using multivariable analysis showed that serum creatinine in combination with renal proteinuria (UPC or UAC) predicted the onset of azotemic CKD in client-owned cats within one year. However, the sensitivity and specificity for this prediction was not sufficiently high for routine use in clinical practice. USG was lower at the start of the study for cats that developed azotemia within one year compared to those that did not do so. At 12 months, USG decreased in both groups, but more so in cats that developed azotemia. USG was significant in the univariable but not the multivariable analysis.[11]

Concentrations of the phosphatonin FGF-23 (fibroblast growth factor-23) predicted which healthy geriatric cats would develop azotemia within 12 months in one study. Cats with the lowest FGF-23 concentrations did not develop azotemia during this time, whereas cats with intermediate or high levels of FGF-23 emerged with either a serum creatinine of 1.6 to 2.0 mg/dL or > 2.0 mg/dL respectively.[12] FGF-23 is not yet available as a biochemical test that can be ordered from commercial veterinary laboratories.

The power of artificial intelligence and machine learning was harnessed to develop a proprietary renal diagnostic index (RenalTech™; Antech Diagnostics and Imaging) that was launched in late 2019. This index generates a prediction whether CKD in cats will develop over the next two years. Large data sets from many primary care practices using the same analyzers and electronic medical record system were used to develop and then test the predictive model in cats. BUN, serum creatinine, USG, and age engage the algorithm over different time points for analysis from within the laboratory data system. These 4 parameters were determined to be the most useful and accurate parameters to predict a future diagnosis of CKD from an initial 35 that were evaluated. This index performed well for accuracy (hybrid of sensitivity and specificity), sensitivity (ability to identify those with a future diagnosis of CKD), and specificity (ability to identify those that will not achieve a diagnosis of CKD) in a recent report. This diagnostic index identified 63% of

cats that developed a diagnosis of CKD 1 year before the diagnosis and 44% of cats 2 years before the diagnosis. The ability to identify cats that did not develop CKD over the next 2 years remained over 99%.[7]

This renal diagnostic index has been further developed to add dipstick values for urine protein and pH as well as the total white blood cell count in blood to the cascade of algorithms depending on results of the initial 4 parameters. The addition of these 3 parameters can improve accuracy for the prediction of a future CKD diagnosis at times; the algorithm makes the decision to use only the initial 4 parameters or to add the other 3 as needed. The algorithm can work to analyze data from a single time point, but performance of the prediction improves when multiple time points for data evaluation are used for analysis. The prediction also works better when all the data points are available for evaluation. Accuracy of the prediction is better when USG is entered into the calculations, but a USG can be imputed if there is no USG available for a particular visit. Laboratory data fed into the algorithm should be generated from the same analyzers (all reference lab or all in-house analyzers, not a mixture of results from different analyzers) in order to improve the prediction accuracy. A score is generated between 0 and 100 with low scores predicting cats that are not likely to develop CKD within 2 years and high scores predicting cats that are likely to develop CKD within 2 years. Most cats fall into the category of either not likely or highly likely to develop CKD within the next 2 years. This algorithm is able to identify subtle changes and trends in data that may not be obvious to the primary attending veterinarian. The generated score is not reported on the lab sheet. Instead the status is reported as Positive, Negative, or Inconclusive. Most cats with an Inconclusive status will be reported as either Negative or Positive at the next visit when additional data points are entered into the algorithm. The RenalTech status that is generated and reported in the lab results is intended to provide a reminder to the attending veterinarian about the likelihood of a CKD diagnosis to emerge over the next two years. This likelihood could then inform decisions to provide more detailed client education, recommendations for other diagnostics (UPC, blood pressure) and implementation of treatment (diet, drugs), if any is indicated. An advantage for the use of this renal index is that routinely measured parameters in the medical record are available for analysis and scoring by the algorithm. In order for the first RenalTech status to be reported by Antech, enough data, including USG, must be in the laboratory system to compare data over at least two visits. An updated RenalTech status will be reported as more data enters the laboratory system and algorithm computations are performed during subsequent visits. Ongoing studies are needed to determine if this renal index can predict the emergence of CKD by IRIS stage and how this index compares with prediction of a future diagnosis of CKD based on various combinations of UPC, USG, SDMA, and FGF-23.

Earlier Diagnosis of CKD: BUN, Creatinine, SDMA as Surrogates of GFR

Measurement of serum creatinine concentration is the most commonly used surrogate to estimate GFR in the clinics, as it is not technically feasible or practical to measure GFR directly. Serum creatinine is generally preferred over BUN for evaluation of renal function since creatinine has fewer non-renal variables. Symmetric dimethylarginine (SDMA) is a molecule that is also a surrogate for the evaluation of GFR in the cat[13] that has some advantages over measurement of serum creatinine. SDMA results from methylation of arginine that occurs in all nucleated cells. SDMA is excreted exclusively into urine and consequently increases in blood when GFR decreases. SDMA is not influenced by lean muscle mass whereas serum creatinine is related to lean muscle mass. Since creatinine arises from muscles, animals with decreased muscle mass will have lower serum creatinine concentrations than would otherwise develop. During progression of CKD, loss of lean muscle mass can parallel loss of renal function which results in little change in serum creatinine concentration. This phenomenon reduces the ability for serum creatinine to detect ongoing CKD progression early. It is important to remember that any surrogate for GFR will be influenced by pre-renal, primary renal, and post renal factors. It is also important to remember that the finding of normal serum creatinine, BUN, and/or SDMA concentrations does NOT exclude the presence of primary renal disease. In a patient with primary renal disease, a serum creatinine concentration above the reference range (> 2.0 mg/dL) is often interpreted to be associated with a loss of > 75% of renal mass and GFR. When a lower value for the upper limit of serum creatinine such as 1.4, 1.5, or 1.6 mg/dL is used, an increased serum creatinine concentration is associated with a loss of about 50% renal mass and GFR. It appears that on average, SDMA increases at a time when about 40% of renal mass and GFR has been lost, though SDMA can increase in CKD patients when there is as little as 25% loss of renal mass and GFR at times.[14,15]

Concentrations of SDMA have been shown to increase above the reference range before serum creatinine increased in multiple studies of dogs and cats eventually diagnosed with azotemic CKD.[14,16-18]SDMA increased many months before serum creatinine when relatively high values for the upper limit of creatinine reference (above 2.0 mg/dL) ranges were used to diagnose the onset of CKD. When lower creatinine values were used for the upper limit as the comparator, SDMA still increased before creatinine but by a shorter time. Initial studies were reported in dogs and cats living in colonies at a pet food company and in a colony of dogs with hereditary nephritis. Recent reports in client owned dogs and cats show that SDMA is a more sensitive diagnostic indicator for the development of azotemic CKD than is serum creatinine. LC/MS has been used as the gold standard to measure SDMA in most studies in dogs and cats. In clinical practice, an automated method using a proprietary immunoassay is available for measurement of SDMA through IDEXX and an ELISA method to measure SDMA has recently become available through Antech. The upper reference range for adult cats is nearly identical for both labs, with < 14 ug/dL by IDEXX and < 15 ug/dL by Antech. A high correlation between SDMA values generated by IDEXX and Antech was shown in a recent white

paper.[19] SDMA was increased much more frequently than serum creatinine in cats when measured on the same sample (diagnostic discordance) in one white paper[20], but it is not yet clear how many of these patients will progress to azotemic CKD.

Staging of CKD – International Renal Interest Society (IRIS) Updates

Staging of CKD is a process that occurs AFTER CKD has been diagnosed. This staging system does not indicate the underlying cause for the CKD, which requires other diagnostic workup to determine a specific cause. A staging system based on the level of serum creatinine concentration was developed by IRIS (International Renal Interest Society) for use cats that are hydrated and stable (See Table). A stable creatinine is defined by documentation of < 20% variability in serum creatinine when measured again on at least 2 occasions 2 weeks apart[21] by the same lab. Sub-staging is then based on the degree of proteinuria as measured by UPC and also the magnitude of blood pressure risk. Staging and sub-staging using this system is designed to identify and mitigate potentially reversible risk factors such as renal proteinuria and systemic hypertension. Normal and stage 1 CKD cats have serum creatinine concentrations < 1.6 mg/dl (< 140 µmol/L) and SDMA < 18 ug/dL. Normal cats have a UPC < 0.2, UPC 0.2-0.4 is considered to be borderline increased, and overt proteinuria exists when the UPC is > 0.4 in cats. Details of this staging system can be found online at http://www.iris-kidney.com.

SDMA was recently added to the IRIS staging system to further characterize CKD in patients in which serum creatinine concentration underestimates the level of decreased excretory renal function at times. Most often, serum creatinine and SDMA will match up for the assignment of the same IRIS CKD stage, but at times there will be discordance between them. At times of discordance, the higher stage should be assigned based on the higher value between SDMA and serum creatinine, allowing a more appropriate CKD stage assignment. Most often this discordance will occur with a higher SDMA compared to serum creatinine due to loss of lean muscle mass in CKD patients; lower serum creatinine is documented since muscle is the source of serum creatinine.

IRIS CKS Stage 1 is the most difficult to assign with certainty. Since these patients are non-azotemic (based on serum creatinine), some other index of renal disease must be present. This could include some combination of sub-maximally concentrated urine without identification of a non-renal cause, abnormal renal palpation or renal imaging, renal proteinuria, trend of serum creatinine to increase within the reference range, cylindruria and decreased or decreasing GFR (iohexol clearances). The finding of an SDMA that is consistently 14 to < 18 ug/dL provides one potential entry point into IRIS Stage 1 CKD.[22] CKD Stages 2-4 are easily assigned, based on the magnitude of increased serum creatinine and SDMA in a stable hydrated patient. Sub-staging is then based on the magnitude of UPC and systemic blood pressure.[22]

Table. IRIS CKD Cats Staging Guidelines (Updated 2019) (www.iris-kidney-com)

Stage		Cat	Units	Comments
	Creatinine SDMA	< 1.6 < 140 < 18	mg/dL umol/L ug/dL	Other abnormalities are found that support primary kidney disease (USG, renal imaging, UPC, others) SDMA persistently > 14 ug/dL may be used to diagnose CKD
2	Creatinine SDMA	1.6 – 2.8 140 – 250 18 – 25	mg/dL umol/L ug/dL	Clinical signs minimal or absent
3	Creatinine SDMA	2.9 – 5.0 251– 440 26 – 38	mg/dL umol/L ug/dL	Early and Late-Stage 3 based on severity of clinical signs
4	Creatinine SDMA	> 5.0 > 440 > 38	mg/dL umol/L ug/dL	Increasing risk for systemic signs and uremic crisis

Progression of CKD

Progression of CKD refers to ongoing loss of functional renal mass and accumulation of primary chronic renal lesions (tubulo-interstitial nephritis, fibrosis, and nephron drop-out) associated with decreasing GFR.[1,2] When enough loss of nephron mass occurs, increases in BUN, creatinine, SDMA, and phosphorus will be detected in serum biochemistry. Progressive loss of excretory renal function and ability to concentrate urine will occur if the cause of the initial renal injury is not detected and stopped early, as can occur with various types of immune-complex glomerulonephritis, familial glomerular disease, and renal amyloidosis. The "inexorable progression" of CKD occurs after a substantial amount of renal mass has already occurred. This type of progression can continue even when the original cause of the renal injury has been stopped. Based on experimental data, this type of self-progressive destruction of the kidney likely occurs in cats when there is loss of at least 75% of the original renal mass. Glomerular hyperfiltration and glomerular hypertension are considered to be important players that exist in the surviving single nephrons in advanced CKD that contribute to this type of progression. Systemic hypertension, PTH, CKD- BMD (bone mineral disease associated with phosphorus, FGF-23, Klotho, ionized calcium) and oxidative stress are also likely to contribute to progression.

CKD is variably progressive in cats with azotemia, though some cats appear stable for long periods of time (physical exam and laboratory parameters). The rate of progression must be determined for each individual cat over time. An increase in serum creatinine of ≥ 25% over baseline during the next 12 months was observed in 47% of cats with newly diagnosed azotemic CKD (serum creatinine > 2.0 and UG < 1.035) in one study. Many cats of this study had slowly progressive or nonprogressive CKD when assessed by IRIS stage. Thirty-three percent of cats initially diagnosed in IRIS stage 2 did not advance to a higher stage during the year of this study. Very few cats initially diagnosed in IRIS stage 2 advanced to IRIS stage 4 by the end of the study whereas 62% of the cats initially diagnosed in IRIS stage 2 advanced to IRIS stage 3 within 12 months.[23] About 31% of apparently healthy geriatric cats developed azotemia within 12 months of an earlier study.[11] It is not known how many cats initially diagnosed with IRIS stage1 CKD will progress to IRIS stage 2 or higher.

Risk Factors for Progression of CKD

Serum creatinine at the time of CKD diagnosis predicted survival in cats with CKD in most studies[24-27] but not in one.[28] Phosphorus retention in the body is a well-known risk factor for progression of CKD in cats based on accumulation of renal lesions, loss of excretory function, and decreased survival time.[12,24,29-34] In one study, an increase of serum phosphorus of 1 mg/dL increased the risk of progression by 43% within one year.[23] Serum phosphorus was the only variable predictive of survival of CKD cats in another study; the risk for death increased by 11.8% for each increase in serum phosphorus of 1 mg/dL.[24] Cats with serum phosphorus < 4.7 mg/dL at the time of CKD diagnosis lived longer than CKD cats with higher values.[26] CKD cats that maintained a serum phosphorus < 4.5 mg/dL lived considerably longer than cats with higher values in one study.[35] Phosphorus retention within the body occurs during CKD even when serum phosphorus is still within the reference range, as suggested by increased concentrations of PTH and FGF-23.[27,29,36]

Sometimes the calcium x phosphorus product (CPP) reveals abnormalities when neither the calcium nor phosphorus alone do so; this concept is less well studied in cats than in dogs. In one study of CKD cats, a higher CPP was associated with progression.[37] CPP was related to magnitude of increased serum creatinine cats with CKD and was higher in cats with gastric mineralization.[38]

CPP has been positively associated with FGF-23 concentrations.[12] Increased FGF-23 at diagnosis was an independent predictor of survival time and progression of CKD within the next 12 months, along with plasma creatinine, UPC, and age. The highest levels of FGF-23 were associated with a 4 times increased risk of death. It is unknown if FGF-23 is solely a marker of CKD or if it can also directly create renal injury.[27]

Indoxyl sulfate (IS) is a uremic toxin that can serve as a biomarker to predict CKD progression. Levels of IS were significantly higher in cats that had progression of their CKD, both in IRIS stage 2 and 3. Progression was defined as an increase in IRIS renal stage or an increase in serum creatinine of ≥ 0.5 mg/dL within a 3-month period.[37] In another study of cats diagnosed with CKD and serum creatinine ≥ 1.6 mg/dL, higher levels of both IS and FGF-23 were associated with renal progression. Progression was defined as an increase of serum creatinine ≥ 0.5 mg/dL over baseline within 3 months. The combination of FGF-23 and IS predicted progression of CKD in these cats more precisely when used together rather than separately. Both IS and FGF-23 concentrations were highly correlated with phosphorus, indicating an intimate association of phosphate metabolism and CKD progression in this study.[39]

Proteinuria and Systemic Hypertension

Proteinuria as measured by UPC at the time of CKD diagnosis in cats predicted survival time and progression.[23,26,27,40] A high UPC predicted progression of all CKD cats in one study[23] and was found to be an independent risk factor for shorter survival times in another study.[26] A UPC of > 0.4 at the time of CKD diagnosis in cats was associated with the shortest survival time, intermediate survival was found for those with a UPC of 0.2 to 0.4 and the longest survival times were found in cats with a UPC < 0.2.[41] A UPC ≤ 0.2 had the longest survival and UPC > 1.0 the least survival in CKD

cats of another study.[26] Small differences in UPC appear to have a large impact on the projected survival time in CKD cats.

Blood pressure was infrequently measured (1.3% of all cats examined and in 4.4% of cats ≥ 9 years of age) in one general practice primary care study. Blood pressure most commonly was measured in cats with clinical signs of illness, followed by cats under anesthesia, monitoring of pre-existing disease, monitoring of pre-existing hypertension, and very uncommonly during geriatric health visits. When blood pressure was measured, 19.5% (282 of 1445) were documented to have hypertension, and CKD was the most common co-morbidity (46.1%) at the time of hypertension diagnosis. Idiopathic hypertension accounted for 30.5% of hypertensive cats but many cats did not have extensive investigation for an underlying cause. Cats with CKD or diabetes mellitus and hypertension had increased risk for death in this study. Hypertensive cats that were screened for the development of hypertension lived longer than cats that had their hypertension discovered related to onset of clinical signs. Most cats with hypertension in this study had ≥ 180 mm Hg systolic blood pressure which provides severe risk for target organ damage. This study suggested that tighter control of blood pressure during treatment in hypertensive cats resulted in less morbidity from target organ damage.[42]

Up to 65% of cats with CKD evaluated at referral hospitals have systemic hypertension.[43,44] The prevalence of systolic hypertension was considerably lower at 19.4% when evaluated in cats in primary care practice.[45] The documentation of systemic hypertension was not associated with the magnitude of azotemia in two studies.[43,45] Plasma potassium concentrations were significantly lower in CKD cats that were documented to have hypertension in one study, but the magnitude of difference between that in the normotensive and the hypertensive group was small.[45] The prevalence of hypokalemia in azotemic cats is common and was about 30% in one report.[46] Systemic hypertension potentially increases progression of CKD as high systemic pressures are transmitted to the glomerulus which then increase the degree of glomerular hypertension in remnant nephrons. The increased glomerular pressure as well as an increase in transglomerular passage of plasma proteins can result in glomerulosclerosis and tubulo-interstitial inflammation which further reduces functional nephron mass.[21]

In cats with CKD, 105 of 265 (40%) were hypertensive at initial evaluation. Twenty-seven of the160 (16.8%) initially non-hypertensive CKD cats and 9 of the 133 (6.8%) healthy cats ≥ 9 years of age developed hypertension ≥ 3 months after the first visit. Systolic blood pressure increased with age in all cats and serum creatinine was an independent predictor for the development of new onset hypertension. Results from this study provide support for the recommendation to regularly monitor blood pressure in elderly cats, especially those with CKD.[47]

Studies of clinical cats with CKD have failed to show that systemic hypertension decreases survival, likely due to effective antihypertensive treatment that readily returns systemic blood pressure to normal. No studies include non-treated client-owned hypertensive cats as a control group, as withholding this treatment is unethical. Clinically relevant reduction in the magnitude of systemic hypertension is readily achieved with amlodipine in most CKD cats at 0.125 mg/kg to 0.25 mg/kg once daily by mouth.[48-51] Survival did not decrease in CKD cats that were hypertensive at the time of diagnosis following treatment that lowered systemic blood pressure. Systolic blood pressure along with creatinine was associated with the magnitude of proteinuria.[41] In another study of 141 client-owned cats with systolic hypertension treated with amlodipine, survival was only related to UPC and not the degree of blood pressure control achieved. The degree of proteinuria before and after treatment, was strongly associated with survival. The degree of proteinuria was greatest in cats in the upper quartile of blood pressure and lowest in cats in the lower quartile of blood pressure. Treatment with amlodipine resulted in a significant decrease in UPC in these CKD cats, an effect that was greater in cats with higher UPC before treatment. Amlodipine dosed at 0.625 mg/cat once daily provided effective control of blood pressure in 50% of hypertensive cats; the other 50% required a dose escalation to 1.25 mg/cat per day in the same study.[48] It seems paradoxical that proteinuria predicted survival of CKD cats and that blood pressure was related to the degree of proteinuria, yet blood pressure was not related to survival in two studies.[41,48]

Treatment of CKD with Renal Diets and Intestinal Phosphate Binders

Commercially available renal diets are lower in protein, calcium, phosphorus, and sodium content, and higher in potassium, alkali precursor (usually citrate), omega-3, and energy content, compared to diets designed for healthy cats. It is important to consider intake of nutrients on an energy density basis (mg or G per 100 or 1000 kcal) in order to compare diets. It is well established that diets formulated to treat renal disease confer benefits to CKD cats in IRIS stages 2 to 4. Benefits include both increased survival time and fewer episodes of a uremic crisis that would require hospitalization for treatment.[31,52,53] Since many nutrients are altered in these diets, it is not possible to identify an individual nutrient change that confers benefits. However, it appears that phosphorus restriction may be the single most important nutrient alteration.

There is some controversy regarding the use of renal diets for cats in IRIS CKD stages 2 to 4.[54,55] Protein restriction in renal diets can reduce lean body mass and quality of life due to protein:calorie malnutrition, especially in the earlier stages of CKD. The goal is to provide minimal protein restriction while maximizing the degree of phosphorus

restriction. More severe restriction of dietary protein intake is generally indicated during advanced phases of CKD in which generation of uremic solutes and toxins might be lessened with lower protein intake. Adequate consumption of calories is always important, otherwise dietary proteins will be consumed as an energy source along with generation of more waste products that can accumulate in the circulation.

Phosphorus Control

Phosphorus content varies widely in commercially available foods. Renal diets are specifically formulated to reduce phosphorus content to limit total body phosphorus accumulation during CKD. Commercial foods can have phosphorus contents approaching 500 mg/100 kcal, whereas the average phosphorus content in feline renal diets is about 100 mg/100 kcal, slightly below the AAFCO minimum of 125 mg/100 kcal.[56] Normal histologic renal structure was better preserved in cats with CKD fed phosphorus-restricted diets compared to those fed higher levels of phosphorus.[30] Extended survival for CKD cats fed a renal diet was largely attributed to the degree of phosphorus and PTH control in one study.[31]

Targeted serum phosphorus control is recommended. IRIS (2019) recommends the chronic maintenance of serum phosphorus < 4.6 mg/dL and > 2.7 mg/dL in cats with CKD stages 2 to 4. The value for phosphorus-restricted diets has not been determined for IRIS stage 1. Alternatively, maintaining serum phosphorus in the lower half of the reference range is recommended to minimize adverse effects during CKD. It is more difficult to achieve targeted levels of serum phosphorus in cats that are eating more, eating a higher content phosphorus diet, eating diets that are high in inorganic phosphorus content, and cats that have poor renal excretory function associated with advanced CKD (higher IRIS stage). Serum phosphorus control requires a combination of feeding a phosphorus-restricted renal diet and the administration of intestinal phosphate-binding agents.

Intestinal phosphate binding compounds are based on salts of aluminum, calcium, lanthanum, iron, or sevelamer. Most doses of phosphate binders are 30 to 60 mg/kg/day divided into food, but higher doses may be needed to achieve the desired targeted level of serum phosphorus. The goal is for the binder in the food to bind with phosphate and be eliminated in the feces before being absorbed into the circulation. Binders that are not absorbed into the circulation are more desired so as to lessen potential toxicity. Lanthanum carbonate has been studied extensively in cats for safety and efficacy, and has been found to be an excellent phosphate binder with minimal to no recognized toxicity in cats.[32] Epakatin® (Vetoquinol) provides a combination of calcium carbonate and chitosan designed for phosphate binding; it is likely that calcium carbonate provides most of the binding. This product has demonstrated efficacy in decreasing serum phosphorus in cats with early clinical CKD that were eating regular maintenance diets.[57] Lower serum phosphorus and PTH resulted when this phosphate binder was added to a maintenance diet for cats with experimental CKD equivalent to IRIS stage 1 and 2.[58]

The first step in serum phosphorus control is to feed a phosphorus-restricted renal diet. If the targeted level of serum phosphate is not achieved with this diet, a different diet with a lower content of phosphate can be fed or add an intestinal phosphate binder to the renal diet. Phosphate binders can be added to regular maintenance foods when CKD cats will not eat a renal diet, though this makes it more difficult to achieve the targeted serum phosphate level. Phosphate binders should be mixed into or adhere to the food; this is easier with wet foods. A concern is that binders added to food will inhibit food intake in cats, especially in cats that are azotemic and not feeling well.

In early stages of CKD, dietary phosphorus restriction alone can achieve the desired serum phosphorus concentration, but this is unlikely as CKD advances. Adding phosphate binders to maintenance diets of cats in early CKD can also be successful, but this is also unlikely to be effective in more advanced states of CKD. Doses of phosphate binders are sequentially increased as needed after evaluation of fasting serum phosphorus measured in about 4 weeks. Rarely, hypophosphatemia can occur; if this occurs the phosphate binder should be stopped and restarted at a lower dose. It is not always possible to achieve the targeted level of serum phosphorus despite the feeding of a renal diet and high doses of phosphate binders. Toxicity is a concern with administration of high doses of phosphate binders. Aluminum toxicity has not been specifically studied in cats with CKD, but it is of increasing concern in dogs with CKD.[59,60] Measurement of serum calcium should be sequentially evaluated in cats receiving calcium-containing phosphate binders to ensure that hypercalcemia does not develop. Lanthanum salts appear to be the most effective and safe phosphate binders for CKD cats, but this product is very expensive.[32] Iron salts for use in cats with CKD have been developed but not yet marketed.[61] Combination of different classes of intestinal phosphate binders may allow better phosphate control without increasing the chances for toxicity. In the future, the effectiveness of total body phosphate control will likely involve measurement of vitamin D metabolites, FGF-23, Klotho, and indoxyl sulfate in addition to the more commonly measured serum phosphorus and PTH.

We don't often think of adverse effects from eating a renal diet that is phosphate restricted in cats with CKD. It is difficult to decrease serum phosphorus too much during the feeding of reduced phosphate renal diets in cats with CKD if the initial phosphorus concentration exceeds the upper reference range. An early study showed that 2 of 15 CKD cats developed hypercalcemia along with low serum phosphorus and undetectable PTH during the feeding of a

phosphate restricted renal diet. The low circulating PTH and phosphorus returned to higher levels and the high calcium decreased to normal levels when the renal diet was stopped and a diet higher in phosphate content was fed.[36] The feeding of a renal diet is more apt to result in hypophosphatemia when the initial serum phosphorus is near the lower limit for the reference range. Consequently, laboratory monitoring should be conducted more closely in these CKD cats to determine if the continued feeding of a renal diet is safe or not. Nineteen cats with CKD were fed different phosphorus levels in their renal diets over a period of 45 months in a recent observational study. CKD cats of this study were considered to have early disease as 10 were in stage 1 and 9 were in stage 2. Nearly 90% of early CKD cats developed hypercalcemia (15/17 ionized hypercalcemia; 5/7 total hypercalcemia) while consuming a low-calcium low-phosphorus renal diet (Ca:P ratio of 1.8) providing phosphorus content at 0.96 g/1000kcal for the first 17 months of this study. The hypercalcemia resolved in most CKD cats when the phosphorus content in the renal diet fed was increased to 1.35 to 1.60 g/1000 kcal in a diet that was considered to be moderate-calcium and moderate-phosphorus (Ca:P ratio of 1.3 to 1.6).[62] An increased Ca:P ratio can lead to increased calcium bioavailability for intestinal absorption that could contribute to development of hypercalcemia.[36,62] Phosphate restricted renal foods generally have a higher Ca:P ratio than grocery store foods. Ionized hypercalcemia is observed in some cats at the time of CKD diagnosis[63,64], a finding that might be triggered at times by the feeding of a renal diet.[64] It appears that dietary phosphate restriction is not appropriate for all cats with CKD.[65]

Adverse Effects of Diets on Healthy Cats

There is renewed interest in dietary phosphorus content and effects on renal function in healthy cats.[66-69] Cats eventually diagnosed with CKD consumed significantly more protein and phosphate prior to a diagnosis of CKD compared to cats that did not develop CKD. This suggests a link between chronic consumption of high phosphate content diets as a possible cause of CKD in cats.[68]

Adverse effects on renal function occurred when high-phosphorus food (>5X maintenance requirements) was fed to normal cats for 29 days. Endogenous creatinine clearance decreased in cats fed the high phosphorus diet, indicating decreased excretory renal function. Glucosuria and microalbuminuria were only observed in cats consuming high-protein diets; they also showed considerably more phosphate excretion into urine.[67] Two levels of dietary phosphate (1.2 vs 4.8 g/1000 kcal) were studied in normal cats but was stopped prematurely after 4 weeks. Cats consuming high phosphorus showed a dramatic decrease in GFR and changes in renal ultrasonography. A study feeding lower dietary phosphorus (1.3 vs. 3.6 g/1000 kcal) for 28 weeks showed no changes in GFR, but altered renal echogenicity and nephrolithiasis was observed in 36% of cats consuming the higher phosphorus diet. A Ca:P ratio close to 1.0 resulted in less structural changes observed on ultrasonography. It was concluded that in cats, the no observed adverse effect level (NOEL) for dietary phosphorus is < 3.6 g/1000 kcal.[68]

Dietary phosphorus bioavailability is highly influenced by whether phosphorus is organic or inorganic. Organic sources of dietary phosphorus are generally less available. In cats, postprandial serum phosphorus concentrations increased to a much greater extent when inorganic dietary sources of phosphorus were utilized.[66,70] Higher phosphate urinary excretion is associated with higher renal tubular fluid phosphorus concentration which is potentially toxic to renal tubules (phosphatopathy) and may promote renal mineralization.[71-73]

Diets for CKD IRIS Stage 1

There is no evidence that diets or drugs can prevent the advancement of IRIS stage 1 cats to stages 2 to 4. IRIS stage 1 is the most difficult to assign with certainty in cats with serum creatinine < 1.6 mg/dL. Some cats with IRIS stage 1 either do not progress to higher stages, or progress very slowly. In these cats, IRIS stage 1 may indicate previous kidney damage and nephron mass loss that was minor and not currently progressive.

Healthy geriatric cats were fed a reduced protein and phosphate content food that was supplemented with some combination of fish oil, L-carnitine, and medium chained triglycerides. No changes attributed to diet were found for GFR, BUN, creatinine or SDMA over the six months of this study. Some cats likely had IRIS stage 1 CKD based on increased SDMA in combination with a reference range creatinine concentration.[17]

Client-owned cats ≥ 9 years old with serum creatinine within the reference range were fed a test food or owner-choice foods for 6 months. The test food was increased in content of fish oil, antioxidants, botanicals, amino acid supplements, and highly bioavailable protein. Cats consuming the test food decreased serum creatinine and BUN slightly while there was no change in cats consuming owner-choice foods. SDMA increased and USG decreased slightly in cats consuming owner-choice food, and did not change in cats fed the test food. UPC did not change in either group. It was suggested that geriatric cats with IRIS stage 1 (reference range creatinine and increased SDMA) eating the test diet had greater stability of renal function compared to cats eating owner-choice foods. A limitation of this study was that GFR was not measured as the gold standard for excretory renal function and renal mass.[74] Longer studies are needed to determine if any of these cats had progressive chronic kidney disease severe enough to escalate to IRIS stage 2.

Two commercial renal diets (Diet A Royal Canin Renal Support Feline Dry; Diet B Hills Prscription Diet k/d Feline with chicken, dry) were fed to cats with CKD IRIS stage 1 and 2 for 6 months. Cats consuming diet A had significant loss of body weight and lean body mass, whereas cats fed diet B had a significant increase in body weight and no change in lean body mass. More calories were consumed by cats eating diet B than diet A. Serum creatinine increased in both groups, but a greater increase was observed in cats consuming diet A. Biomarkers of kidney function were more stable for cats eating diet B[75] but these changes were small.

The interested reader is referred elsewhere for recommendations regarding the management of hypertension[33,49,76-78], renal proteinuria reduction and RAAS inactivation[79-81], and management of CKD- MBD (CKD- mineral bone disease) including the use of calcitriol.[29]

References

1. McLeland SM, Cianciolo RE, Duncan CG, et al. A comparison of biochemical and histopathologic staging in cats with chronic kidney disease. *Vet Pathol* 2015;52:524-534.
2. Lawson J, Elliott J, Wheeler-Jones C, et al. Renal fibrosis in feline chronic kidney disease: known mediators and mechanisms of injury. *Vet J* 2015;203:18-26.
3. O'Neill DG, Church DB, McGreevy PD, et al. Prevalence of disorders recorded in cats attending primary-care veterinary practices in England. *Vet J* 2014;202:286-291.
4. Lulich JP, O'Brien TD, Osborne CA, et al. Feline renal failure: questions, answers, questions. *Compendium on Continuing Education for the Practicing Veterinarian* 1992;14:127...152.
5. Marino CL, Lascelles BD, Vaden SL, et al. Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies. *J Feline Med Surg* 2014;16:465-472.
6. Lund EM, Armstrong PJ, Kirk CA, et al. Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. *J Am Vet Med Assoc* 1999;214:1336-1341.
7. Bradley R, Tagkopoulous I, Kim M, et al. An algorithm based on routien clinical blood and urine results predicts chronic kidney disease in cats two years before diagnosis. *JVIM* 2019 Under Review
8. O'Neill DG, Church DB, McGreevy PD, et al. Longevity and mortality of cats attending primary care veterinary practices in England. *J Feline Med Surg* 2015;17:125-133.
9. Greene JP, Lefebvre SL, Wang M, et al. Risk factors associated with the development of chronic kidney disease in cats evaluated at primary care veterinary hospitals. *J Am Vet Med Assoc* 2014;244:320-327.
10. Trevejo RT, Lefebvre SL, Yang M, et al. Survival analysis to evaluate associations between periodontal disease and the risk of development of chronic azotemic kidney disease in cats evaluated at primary care veterinary hospitals. *J Am Vet Med Assoc* 2018;252:710-720.
11. Jepson RE, Brodbelt D, Vallance C, et al. Evaluation of predictors of the development of azotemia in cats. *J Vet Intern Med* 2009;23:806-813.
12. Finch NC, Geddes RF, Syme HM, et al. Fibroblast growth factor 23 (FGF-23) concentrations in cats with early nonazotemic chronic kidney disease (CKD) and in healthy geriatric cats. *J Vet Intern Med* 2013;27:227-233.
13. Braff J, Obare E, Yerramilli M, et al. Relationship between serum symmetric dimethylarginine concentration and glomerular filtration rate in cats. *J Vet Intern Med* 2014;28:1699-1701.
14. Nabity MB, Lees GE, Boggess MM, et al. Symmetric Dimethylarginine Assay Validation, Stability, and Evaluation as a Marker for the Early Detection of Chronic Kidney Disease in Dogs. *J Vet Intern Med* 2015;29:1036-1044.
15. Nabity MB, Lees GE, Cianciolo R, et al. Urinary biomarkers of renal disease in dogs with X-linked hereditary nephropathy. *J Vet Intern Med* 2012;26:282-293.
16. Relford R, Robertson J, Clements C. Symmetric Dimethylarginine: Improving the Diagnosis and Staging of Chronic Kidney Disease in Small Animals. *Vet Clin North Am Small Anim Pract* 2016;46:941-960.
17. Hall JA, Yerramilli M, Obare E, et al. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. *Vet J* 2014;202:588-596.
18. Hall JA, Yerramilli M, Obare E, et al. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med* 2014;28:1676-1683.
19. Ogeer J, Aucoin D, Andrews J. Antech SDMA ELISA Performs Well in Comparison Study with IDEXX SDMA and Liquid Chromatography Mass Spectrometry (LCMS) AM-200-01-01 08-20. *Antech Diagnostics, Inc*, 2020;1-3.
20. IDEXX. SDMA impacts how veterinarians diagnose and manage kidney disease in dogs and cats. https://www.idexx.com/files/sdma-data-white-paper.pdf: IDEXX, 2016.
21. Grauer GF. Feline friendly article: feline chronic kidney disease. *Today's Veterinary Practice* 2015;5:36-41.
22. IRIS. IRIS Straging of CKD (Modified 2019) http://iris-kidneycom/ 2019; http://iris-kidney.com/pdf/staging-of-ckd.pdf#page=6.

23. Chakrabarti S, Syme HM, Elliott J. Clinicopathological Variables Predicting Progression of Azotemia in Cats with Chronic Kidney Disease. *J Vet Intern Med* 2012;26:275-281.
24. Boyd LM, Langston C, Thompson K, et al. Survival in cats with naturally occurring chronic kidney disease (2000-2002). *J Vet Intern Med* 2008;22:1111-1117.
25. Kuwahara Y, Ohba Y, Kitoh K, et al. Association of laboratory data and death within one month in cats with chronic renal failure. *J Small Anim Pract* 2006;47:446-450.
26. King JN, Tasker S, Gunn-Moore DA, et al. Prognostic factors in cats with chronic kidney disease. *J Vet Intern Med* 2007;21:906-916.
27. Geddes RF, Elliott J, Syme HM. Relationship between Plasma Fibroblast Growth Factor-23 Concentration and Survival Time in Cats with Chronic Kidney Disease. *J Vet Intern Med* 2015;29:1494-1501.
28. Elliott J, Barber PJ. Feline chronic renal failure: clinical findings in 80 cases diagnosed between 1992 and 1995. *J Small Anim Pract* 1998;39:78-85.
29. Foster JD. Update on Mineral and Bone Disorders in Chronic Kidney Disease. *Vet Clin North Am Small Anim Pract* 2016;46:1131-1149.
30. Ross LA, Finco DR, Crowell WA. Effect of dietary phosphorus restriction on the kidneys of cats with reduced renal mass. *Am J Vet Res* 1982;43:1023-1026.
31. Elliott J, Rawlings JM, Markwell PJ, et al. Survival of cats with naturally occurring chronic renal failure: effect of dietary management. *J Small Anim Pract* 2000;41:235-242.
32. Kidder AC, Chew D. Treatment options for hyperphosphatemia in feline CKD: what's out there? *J Feline Med Surg* 2009;11:913-924.
33. Acierno MJ, Brown S, Coleman AE, et al. ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med* 2018;32:1803-1822.
34. de Brito Galvao JF, Nagode LA, Schenck PA, et al. Calcitriol, calcidiol, parathyroid hormone, and fibroblast growth factor-23 interactions in chronic kidney disease. *Journal of veterinary emergency and critical care* 2013;23:134-162.
35. Geddes RF, Finch NC, Syme HM, et al. The role of phosphorus in the pathophysiology of chronic kidney disease. *Journal of veterinary emergency and critical care* 2013;23:122-133.
36. Barber PJ, Rawlings JM, Markwell PJ, et al. Effect of dietary phosphate restriction on renal secondary hyperparathyroidism in the cat. *J Small Anim Pract* 1999;40:62-70.
37. Chen CN, Chou CC, Tsai PSJ, et al. Plasma indoxyl sulfate concentration predicts progression of chronic kidney disease in dogs and cats. *Vet J* 2018;232:33-39.
38. McLeland SM, Lunn KF, Duncan CG, et al. Relationship among serum creatinine, serum gastrin, calcium-phosphorus product, and uremic gastropathy in cats with chronic kidney disease. *Journal of Veterinary Internal Medicine* 2014;28:827-837.
39. Liao YL, Chou CC, Lee YJ. The association of indoxyl sulfate with fibroblast growth factor-23 in cats with chronic kidney disease. *J Vet Intern Med* 2019.
40. Elliott J, Syme HM. Proteinuria in chronic kidney disease in cats--prognostic marker or therapeutic target? *J Vet Intern Med* 2006;20:1052-1053.
41. Syme HM, Markwell PJ, Pfeiffer D, et al. Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. *J Vet Intern Med* 2006;20:528-535.
42. Conroy M, Chang YM, Brodbelt D, et al. Survival after diagnosis of hypertension in cats attending primary care practice in the United Kingdom. *J Vet Intern Med* 2018.
43. Kobayashi DL, Peterson ME, Graves TK, et al. Hypertension in cats with chronic renal failure or hyperthyroidism. *J Vet Intern Med* 1990;4:58-62.
44. Stiles J, Polzin DJ, Bistne SI. The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism. *J Am Anim Hosp Assoc* 1994;30:564–572.
45. Syme HM, Barber PJ, Markwell PJ, et al. Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation. *J Am Vet Med Assoc* 2002;220:1799-1804.
46. DiBartola SP, Rutgers HC, Zack PM, et al. Clinicopathologic findings associated with chronic renal disease in cats: 74 cases (1973-1984). *J Am Vet Med Assoc* 1987;190:1196-1202.
47. Bijsmans ES, Jepson RE, Chang YM, et al. Changes in systolic blood pressure over time in healthy cats and cats with chronic kidney disease. *J Vet Intern Med* 2015;29:855-861.
48. Jepson RE, Elliott J, Brodbelt D, et al. Effect of control of systolic blood pressure on survival in cats with systemic hypertension. *J Vet Intern Med* 2007;21:402-409.
49. Huhtinen M, Derre G, Renoldi HJ, et al. Randomized placebo-controlled clinical trial of a chewable formulation of amlodipine for the treatment of hypertension in client-owned cats. *J Vet Intern Med* 2015;29:786-793.
50. Stepien RL. Feline systemic hypertension: Diagnosis and management. *J Feline Med Surg* 2011;13:35-43.
51. Elliott J, Barber PJ, Syme HM, et al. Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases. *J Small Anim Pract* 2001;42:122-129.
52. Plantinga EA, Everts H, Kastelein AM, et al. Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets. *Vet Rec* 2005;157:185-187.

53. Ross SJ, Osborne CA, Kirk CA, et al. Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. *Journal of the American Veterinary Medical Association* 2006;229:949-957.
54. Scherk MA, Laflamme DP. Controversies in Veterinary Nephrology: Renal Diets Are Indicated for Cats with International Renal Interest Society Chronic Kidney Disease Stages 2 to 4: The Con View. *Vet Clin North Am Small Anim Pract* 2016;46:1067-1094.
55. Larsen JA. Controversies in Veterinary Nephrology: Differing Viewpoints: Role of Dietary Protein in the Management of Feline Chronic Kidney Disease. *Vet Clin North Am Small Anim Pract* 2016;46:1095-1098.
56. Chew DJ, Parker VJ. Decreasing Total Body Phosphorus Burden in Chronic Kidney Disease. 2015 Ohio State & IAMS Symposium Proceedings: Small Animal Renal & Urinary Health 2015;40-44.
57. Wagner E, Schwendenwein I, Zentek J. Effects of a dietary chitosan and calcium supplement on Ca and P metabolism in cats. *Berliner und Munchener tierarztliche Wochenschrift* 2004;117:310-315.
58. Brown SA, Rickertsen M, Sheldon S. Effects of an intestinal phosphorus binder on serum phosphorus and parathyroid hormone concentration in cats with reduced renal function. *International Journal of Applied Research in Veterinary Medicine* 2008;6:155-160.
59. Segev G, Naylor S, Cowgill LD. Hematological and Neurological Side Effects Associated with the Use of Aluminum Based Phosphate Binders in Dogs with Chronic Kidney Disease. *Israel Journal of Veterinary Medicine* 2016;71:31-38.
60. Segev G, Bandt C, Francey T, et al. Aluminum toxicity following administration of aluminum-based phosphate binders in 2 dogs with renal failure. *J Vet Intern Med* 2008;22:1432-1435.
61. King JN, Delport PC, Luus HG, et al. Efficacy and acceptability of the new oral phosphate binder Lenziaren in healthy cats fed a renal diet. *J Vet Pharmacol Ther* 2015;38:278-289.
62. Schauf-Bailon S, Bijsmans E, Atwal J, et al. Cats with early stage CKD may benefit from moderate restriction in dietary phosphorus. Virtual ACVIM Forum 2020.
63. Schenck PA, Chew DJ. Prediction of serum ionized calcium concentration by serum total calcium measurement in cats. *Can J Vet Res* 2010;74:209-213.
64. van den Broek DH, Chang YM, Elliott J, et al. Chronic Kidney Disease in Cats and the Risk of Total Hypercalcemia. *J Vet Intern Med* 2017;31:465-475.
65. Elliott J. Phosphate and Bone Mineral Disturbances in Early Stage Feline Chronic Kidney Disease. Virtual ACVIM Forum 2020.
66. Coltherd JC, Staunton R, Colyer A, et al. Not all forms of dietary phosphorus are equal: an evaluation of postprandial phosphorus concentrations in the plasma of the cat. *Br J Nutr* 2019;121:270-284.
67. Dobenecker B, Webel A, Reese S, et al. Effect of a high phosphorus diet on indicators of renal health in cats. *J Feline Med Surg* 2018;20:339-343.
68. Boswald LF, Kienzle E, Dobenecker B. Observation about phosphorus and protein supply in cats and dogs prior to the diagnosis of chronic kidney disease. *J Anim Physiol Anim Nutr (Berl)* 2018;102 Suppl 1:31-36.
69. Alexander J, Stockman J, Atwal J, et al. Effects of the long-term feeding of diets enriched with inorganic phosphorus on the adult feline kidney and phosphorus metabolism. *Br J Nutr* 2018:1-21.
70. Finco DR, Barsanti JA, Brown SA. Influence of dietary source of phosphorus on fecal and urinary excretion of phosphorus and other minerals by male cats. *Am J Vet Res* 1989;50:263-266.
71. Kuro-o M. The FGF23 and Klotho system beyond mineral metabolism. *Clin Exp Nephrol* 2017;21:64-69.
72. Kuro-o M, Moe OW. FGF23-alphaKlotho as a paradigm for a kidney-bone network. *Bone* 2016.
73. Kuro-o M. Klotho, phosphate and FGF-23 in ageing and disturbed mineral metabolism. *Nat Rev Nephrol* 2013;9:650-660.
74. Hall JA, MacLeay J, Yerramilli M, et al. Positive Impact of Nutritional Interventions on Serum Symmetric Dimethylarginine and Creatinine Concentrations in Client-Owned Geriatric Cats. *PLoS One* 2016;11:e0153654.
75. Hall JA, Fritsch DA, Jewell DE, et al. Cats with IRIS stage 1 and 2 chronic kidney disease maintain body weight and lean muscle mass when fed food having increased caloric density, and enhanced concentrations of carnitine and essential amino acids. *Vet Rec* 2018.
76. Taylor SS, Sparkes AH, Briscoe K, et al. ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats. *J Feline Med Surg* 2017;19:288-303.
77. Coleman AE, Brown SA, Traas AM, et al. Safety and efficacy of orally administered telmisartan for the treatment of systemic hypertension in cats: Results of a double-blind, placebo-controlled, randomized clinical trial. *J Vet Intern Med* 2019;33:478-488.
78. Glaus TM, Elliott J, Herberich E, et al. Efficacy of long-term oral telmisartan treatment in cats with hypertension: Results of a prospective European clinical trial. *J Vet Intern Med* 2019;33:413-422.
79. Pressler B. A practical guide to antiproteinuric drugs in dogs. *Veterinary Medicine* 2013;108:392-397.
80. Lees GE, Brown SA, Elliott J, et al. Assessment and management of proteinuria in dogs and cats: 2004 ACVIM Forum Consensus Statement (small animal). *J Vet Intern Med* 2005;19:377-385.
81. Vaden SL, Elliott J. Management of Proteinuria in Dogs and Cats with Chronic Kidney Disease. *Vet Clin North Am Small Anim Pract* 2016;46:1115-1130.

Unintentional Weight Loss: Feline Dwindles

Grant Gugisberg, DVM

Background
Dwindles in humans is defined as weight loss of 4%–5% or more of body weight within 1 year, or 10% or more over 5–10 years or longer. It is associated with increased mortality or morbidity or both.[1,2] Additional terms applied to this syndrome include *Human Dwindles, Anorexia-Cachexia Syndrome, and Unintentional Weight Loss of Seniors.* Teng et al showed lifespan decreased when cats had a BCS less than 5 out of 9.[3]

Specific recommended testing in humans includes complete blood count, basic metabolic panel, liver function tests, thyroid function tests, C-reactive protein levels, erythrocyte sedimentation rate, glucose measurement, lactate dehydrogenase and urinalysis.[4] Additional testing includes chest radiography, fecal occult blood testing, and abdominal ultrasonography. Even with a comprehensive workup a readily identifiable cause is not found in 16% to 28% of cases.[4]

Feline Unintentional Weight Loss
Weight loss assessment starts with a great history. Specific items to pay particular attention to include subtle changes in eating patterns, water consumption, box changes and mobility issues. Mobility issues are not just limping. They can be more subtle. Changes in sleeping spots, bunny hopping, or even sitting or lying down to eat are also common.

As part of the physical the practice must make sure to obtain accurate weight measurements on a feline specific or baby scale. Scales should be assessed periodically to ensure ongoing accuracy. Weight, body condition score (BCS), and muscle condition score (MCS) should be noted at each visit.

A complete physical exam should be performed that includes a complete oral exam --scary but essential! Specific attention to the area under the tongue and fauces is important. Performing a fundic exam and measuring blood pressure (recommend using Parks Medical Doppler) is also recommended. Thyroids are palpated in all cats – you will be surprised how many cats have non-functional palpable thyroid tissue. Not all thyroid enlargements are associated with hyperthyroidism. Palpate the abdomen with special attention to the intestines, colon, and pancreatic region. A great practice tip to develop competency - especially for vets early in their career - is to palpate all anesthetized patients.

The Laboratory Can Be Your Friend
Cats are often referred to as “the great pretenders” – they hide disease from both owners and veterinarians. Sometimes the lab can provide answers. A chemistry panel, complete blood
count (CBC), and total T4 are a minimal workup. Additionally, I believe a Spec fPL (Idexx) and urinalysis, by cystocentesis, should be performed. The lab is a revenue source that cannot be replaced by the internet.

From there, additional testing for me starts with an ultrasound. The ultrasound is a great non-invasive, point of care option. It’s great for looking at inflammation within the abdomen! The more you do, the more your competency will improve. Radiographs may occasionally be helpful to identify issues within the chest such as a tumor or to assess the severity of osteoarthritis. Remember the majority of cats have radiographic evidence of osteoarthritis, so pain assessment is critical. Finally CT/MRI and abdominal exploratory may be the best option for owners willing to consider radiation or chemotherapy.

Human Dwindles Versus Feline Dwindles
A readily identifiable cause is not found in 16% to 28% of human cases.[4] In feline patients a number of issues suggest the incidence is even higher. These issues include our patient’s inability to define their symptoms, client’s inability to define the symptoms their pet is experiencing, limited fund availability for patient tests, and limited diagnostic access. Finally, many clients write off their cat’s weight loss as a sign that they are “just old.”

Common Weight Loss Conditions
We’ve covered the essentials of the examination and lab work. Through this workup we will identify many common causes of weight loss. These include dental disease, upper respiratory infections, hyperthyroidism, renal disease,

diabetes mellitus, GI diseases (chronic pancreatitis, IBD, "Triaditis", "Inflammatory Cat"), cancer, and osteoarthritis. Don't forget environmental stressors such as a move, addition of another cat or dog, or diet transition.
In a necropsy study performed at UC Davis, chronic pancreatitis was found in 67% of cats.[5] In a similar human study, the incidence was 0%.[6] This is a high priority area to explore in feline health. An elevated Spec fPL along with mild monocytosis is a common laboratory finding in feline pancreatitis patients. I consider it a marker of the bigger category of "Inflammatory Cat" syndrome.

Finally there is the diagnosis of "open". But that is ok. The MDs cannot sort it out in all people, and we cannot sort it out in all cats. You are not a failure as a veterinarian if you don't know. What matters is that you do a good exam, do appropriate lab work, and communicate efficiently.

Remember – most of the time we will identify feline weight loss and be more concerned about it than the owner. Thus, it is our job as veterinary professionals to work hard to convince owners of the urgency of this issue. We need to sort out underlying diseases as well as to continually question potential environmental stressors.

Therapy for Unintentional Weight Loss
Is it art or science? Panda, S.C. concluded a paper by saying that the art and science of medicine are complementary.[7] For successful practice, a doctor has to be an artist armed with basic scientific knowledge in medicine.
Dr. Grant's tidbits on feline unintentional weight loss:

-Poor intake – owners may not recognize under consumption
-Cats may be eating more "gravy-based foods"
-Eating center decline - Remind the appetite center
-Nausea is not always manifested by vomiting!
-Cat's love to be inflammatory!
-Maybe there is a disease process we have not identified but its cause may benefit from treatment.
-Where's the inflammation? Where's the cancer?

In humans there is well documented declines in the eating center associated with the aging of the brain. As an example of this, target markets for ice cream are focused on two age groups, 6-12 years old and people over 75![8] Based on my experience, it is likely that this eating center decline also occurs in senior and geriatric cats. Mirtazapine is a drug available to us to address this issue, due to an orexigenic effect resulting from stimulation of nuclei within the hypothalamus.[9] It is used in both human and feline medicine for weight gain.

Food
Canned food is lower in calories than dry food, yet owners think it is "so rich." The gravy product formulations are even lower in calorie than dried food. With myriad dietary choices, I suggest making a list of the tastiest foods in your experience. Discuss daily caloric needs with your cat owners. As people age, numerous changes occur in the intestinal tract - decreased secretion of hydrochloric acid and pepsin, reduced absorption of several substances (e.g. sugar, calcium, iron), digestion and motility remain relatively unchanged, amylase remains constant whereas other enzymes (lipase, trypsin) decrease dramatically, and with advancing age a progressive reduction in liver volume and liver blood flow may occur.[10] We can assume that as cats age some if not all of these changes also occur. We know cats more than 10 years of age have a reduced ability to digest protein, which is reduced up to 25% when they reach their teens.[11,12] Combine this with a metabolism that is stable to increase with age, unlike people and dogs, and we begin to see why this is an unfortunate setup for unintentional weight loss in our aging feline patients.[11,12]
Aggressive nutritional management such as feeding tubes may be required to support some of our patients. 55% of cats have been losing weight for over 21 days prior to presentation![13] Remember once the BCS is less than 5/9 survivability is decreased.[3]

Nausea Management
Cats do not have to be vomiting to be nauseous. Instead nauseous cats may be excited for food, but then walk away or take a few bites before walking away. Antacids such as H2 receptor agonists (ex. famotidine, Pepcid by Johnson and Johnson) or proton pump inhibitors (i.e. omeprazole, Prilosec by AstraZeneca), work well in my experience. Recognize that famotidine may only work effectively as an acid blocker for 7-10 days. Antiemetics may work via 5-HT serotonin receptor antagonism (i.e. ondansetron, Zofran by GlaxoSmithKline) or NK-1 antagonism (i.e. Cerenia, maropitant licensed by Zoetis), both effective ways to manage nausea. Mirtazapine is another drug that antagonizes 5-HT serotonin receptors.[9]

Vitamin Supplementation
Cobalamin supplementation may be beneficial, especially with suspected digestive issues. In one uncontrolled study, investigators found that cases with severe hypocobalaminemia may benefit from supplementation.[14]

Steroids
Cats love to have inflammation. When using steroids remember cats lack enzymes to convert prednisone to prednisolone. You must use prednisolone in cats. Other options include dexamethasone, triamcinolone or methylprednisolone. Transdermal steroids are not absorbed.

Pain Management
Two main areas to consider pain as a contributing factor to feline weight loss are osteoarthritis and gastrointestinal disease. A therapeutic trial to assess pain may be beneficial. Gabapentin and buprenorphine are both excellent options. NSAIDS are approved in cats currently only as a single dose for surgery in the US.

Environmental Stress Management
Numerous options are available to help the stressed cat. Play is critical and has been shown to decrease symptoms associated with lower urinary tract disease. Food puzzle toys with tasty treats may help encourage both play and eating. Calming pheromones diffusers such as Feliway (Ceva Animal Health, LLC) or pheromone collars. Additionally, calming nutraceuticals or pharmacologic intervention may be warranted in severe cases.

Weight Gain Therapy
Managing feline unintentional weight loss goes beyond managing clinical signs like inappetence, nausea, and vomiting. While controlling these signs is the first step in managing feline weight loss, we also need to aim for weight gain and improved body and muscle condition. These are significant markers of treatment response when managing feline unintentional weight loss. Many owners aren't fully aware or able to communicate their cat's clinical status. Assessing weight, body condition (via BCS), and muscle condition (via MCS) allows us to objectively measure our patient's body composition and response to treatment. Are we on the right track or do we need to adjust course or alter the level of nutritional support?

A relatively new addition to our toolkit is an FDA approved transdermal mirtazapine labeled for the management of feline weight loss (Mirataz, Dechra Veterinary Products, LLC). Former use of human labelled oral mirtazapine tablets presented a real challenge to our cat owners and posed a risk of toxicity due to inadvertent overdosage.[15] Originally labeled for depression in humans, mirtazapine has an established history in veterinary medicine, including the management of feline weight loss.[9,16,17,18,19,20]

Obtaining FDA approval in 2018, Mirataz features proprietary Accusorb technology that provides reliable transdermal absorption of mirtazapine. Mirtazapine has a multimodal mechanism of action, antagonizing α2-adrenergic, serotonin, and histamine receptors in the central nervous system. This leads to an increase in serotonin & norepinephrine in the synaptic cleft. Inhibition of 5-HT2 serotonin receptors may account for mirtazapine's orexigenic effect. As a transdermal, this is a reliable formulation that is convenient for our clients to apply.

The label for Mirataz is broad and does not specify disease. A 1.5 inch ribbon of ointment, equivalent to approximately 2 mg of mirtazapine, is applied to the inside of the pinna once daily. The client owned cats that participated in the clinical study had a range of clinical illnesses (including kidney & liver disease) and gained 3.9 % of their body weight after just 14 days of use.[17] The most common side effects to monitor for with Mirataz are application site irritation, behavior change (vocalization & hyperactivity), and vomiting.

In addition to improved client compliance with a transdermal, Mirataz has the inherent advantage of having undergone safety and efficacy testing during the FDA approval process. Mirataz also exhibits valuable pharmacokinetic characteristics that equate to reduced exposure and reduced risk of adverse effects compared to human mirtazapine tablets. These pharmacokinetic parameters are beneficial drug characteristics for all our feline patients, but are particularly valuable for our patients with liver or kidney disease, where drug metabolism, elimination, or clearance may be reduced. While Mirataz's pharmacokinetic characteristics result in more consistent serum levels, there is a precaution on the label for cats with liver and kidney disease. Clinically Mirataz administered topically, according to label, to cats with suspected kidney disease has been shown to be safe, with no difference in incidence of overall adverse events or behavioral adverse events (vocalization and hyperactivity) compared to placebo cats.[21]

Summary
Unintentional weight loss is a common disorder in cats. Owners need help recognizing this issue. Each cat needs a tailored diagnostic and treatment plan to help owners that are bonded with their feline friend and offer these patients the best chance of success. Management may require multi-modal therapy. Depending on the cause of the weight loss, therapy may be short term or in many cases there will be a need for chronic therapy.

References
1. Egbert AM. Nutr Rev. 1996; 54 (1 Pt 2): S25-30.

2. Alibhai SM, Greenwood C, Payette H. CMAJ. 2005;172 (6): 773–780.
3. Teng KT et al. J Fel Med Surg. 2018; 20 (12): 1110-1118.
4. Gaddey HL. Am Fam Physician. 2014; 89(9): 718-722.
5. De Cock HE et al. Vet Pathol. 2007; 44(1): 39-49.
6. Stamm, BH : . Hum Pathol 15: 677–683, 1984
7. Panda SC. Mens Sana Monogr. 2006; 4(1):127–138.
8. Canadian International Markets Bureau AMERICAN EATING TRENDS REPORT; 2012
9. Agnew W, et al. J Feline Med Surg. 2014; 16(9): 749-756.
10. Br J Clin Pharmacol. 2004 Jan; 57(1): 6–14.
11. Laflamme DP. Vet Clin North Am Small Anim Pract. 2005;35(3); 713-742.
12. Sparkes AH. Top Companion Anim Med. 2011; 26: 37-42.
13. Data of File. REF 0272. Kindred Biosciences, Inc.
14. Ruaux CG, Steiner JM, Williams DA. J Vet Int Med. 2005; 19(2): 155-160.
15. Ferguson LE., et al. J Feline Med Surg. 2016;18(11):868-874.
16. Quimby, JM et al, J Vet Pharmacol Ther. 2010; 34, 388-396.
17. Quimby JM, et al. Vet J. 2013;197(3): 651-655.
18. Poole M et al. J Vet Pharmacol Ther. 2019;42(2):179-188.
19. Quimby JM, et al. J Vet Intern Med. 2011;25(5):985-989.
20. Quimby JM, et al. J Feline Med Surg. 2020;22(4):376-383.
21. Mason BL, et al. J Vet Int Med. 2019; 128-129.

NOTES:

Look What the Cat Dragged In: Emerging infections & Infestations Facing Felines Today

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Introduction

Despite incredible advances in feline medicine, cats face ever increasing health challenges, many of which come in the form of infections and infestations. From common intestinal parasites to the increase in tick and mosquito vectors and the pathogens they transmit, cats – even those kept primarily or entirely indoors – are beset by risks at every turn. The recent description of feline susceptibility to SARS-CoV-2, the virus responsible for the COVID-19 pandemic, is of great concern to many cat owners and has brought renewed attention to the myriad infections cats face. While our understanding of feline SARS-CoV-2 is continuing to evolve, we know that many already established infections and infestations pose serious risks to feline health. This presentation updates veterinarians on established and emerging infectious, parasitic, and vector-borne disease threats faced by cats and describes practical strategies to mitigate the dangers, protecting cats and their owners.

Intestinal Parasites

Feline infection with intestinal parasites is surprisingly ubiquitous. Shelter surveys document *T. cati* infections in 20% to more than 40% of cats.[1] *Toxocara cati* is also the helminth most frequently identified on fecal flotation of pet cats. Samples tested in 2020 revealed a state-wide prevalence in cats receiving veterinary care as high as 7%, making roundworms two- or three-times more common in pet cats than pet dogs in the same region.[2] Feline roundworm infections are most prevalent in the midwestern and northeastern US, regions of the country where cats may be less likely to be maintained on broad spectrum parasite control with efficacy against intestinal parasites.[2] Roundworm infection can occur following ingestion of larvated eggs or paratenic hosts; association of feline roundworm infection with the presence of *Taenia taeniaeformis* tapeworms suggests ingestion of prey species is the most common route.[1] Kittens with roundworms may develop ill thrift and a pot-bellied appearance. Cats remain susceptible to *T. cati* infection throughout life. In adult cats, the nematodes often migrate from the intestine to the stomach and cause vomiting, resulting in large, often still-motile worms discovered by the owner in vomit.[3] Feline hookworms (*Ancylostoma tubaeforme*, *A. braziliense*) are less often identified and, although diagnosed in cats across the US, more prevalent in the Gulf Coast states.[2] While less pathogenic than hookworms in dogs, feline hookworms can cause blood loss and anemia.[3] Feline infections with roundworms and hookworms also create a zoonotic concern. Current estimates suggest that 5% of people in the US have antibodies indicating past or current infection with *Toxocara* spp.[4]

Cats are also frequently infected with intestinal protozoa, including *Giardia*, *Cystoisospora* spp., and *Tritrichomonas blagburni*. While these feline parasites present no (*Cystoisospora* spp., *T. blagburni*) or very low (*Giardia*) zoonotic risk, feline protozoal infection can still lead to clinical disease, causing at-times severe or chronic diarrheal illness. *Giardia* infection is common in cats, with 3.9% of cats testing positive in the US in 2020.[2] Infection with *Giardia* occurs following ingestion of cysts from fecal-contaminated water, food, or fomites. Cysts are immediately infective when shed and thus are readily ingested by cats, resulting in re-infection through self-grooming. The feline assemblage of *Giardia* (F) is only reported from cats and not been described in humans (A&B), although human assemblages of *Giardia* have been rarely reported from cats.[5] Coccidia (*Cystoisospora* spp.) infect kittens and cats upon ingestion of sporulated oocysts from a contaminated environment or ingestion of cystozoites in the tissue of a paratenic (transport) host. Most feline coccidia infections are asymptomatic, although in young kittens, severe disease leading to diarrhea, dehydration, weight loss, and death can result.[6] Although less routinely identified than *Giardia* or coccidia, trichomoniasis caused by *T. blagburni* (= *T. foetus*) is often seen in cats, especially in multi-cat households. Transmission of *T. blagburni* occurs through ingestion of trophozoites during co-grooming or through shared litterboxes. Many infected cats, especially adults, do not show clinical signs. When clinical signs are present, intermittent, extremely malodorous, mucoid diarrhea is most commonly described; feces often contain fresh blood, and fecal incontinence and flatulence may be reported by the owner.[7]

Ticks, Fleas, and Mosquitoes

Cats are at high risk of infestation with and blood feeding by fleas, ticks, and mosquitoes. Cat fleas (*Ctenocephalides felis*) are the most important ectoparasite of cats worldwide. Already distributed globally, *C. felis* populations are expected to increase in intensity as warming temperatures allow more generations to develop in a given year.[8] Clinic and field surveys report identifying flea infestations on approximately 20% of pet cats and 70-90% of feral cats. Experimental infestations show that ~one-fourth of fleas feed within 5 minutes of reaching a host and almost all feed in less than an hour. In addition to causing blood loss, anemia, and pruritus, fleas serve as vectors of other agents that infect cats and may themselves produce a zoonotic risk, including *Bartonella* spp., *Rickettsia* spp.,

haemoplasma, and *Dipylidium caninum*.[8] As many as 50% of fleas collected from cats in veterinary clinic surveys harbor one or more pathogens. Spillover of *C. felis* from untreated domestic cats can also threaten wildlife health.[9]

Ticks are also commonly reported from cats in North America. Tick infestations are routinely identified on feral cats, and clinic surveys document that infestations are found on cats and dogs in approximately the same proportion as respective clinic visits.[10,11] *Ixodes scapularis*, *Dermacentor variabilis*, and *Amblyomma americanum* constitute the majority of infestations seen, with both immature and adult deer ticks and lone star ticks frequently reported from cats.[11,12] These ticks carry pathogens that can lead to disease in cats, including anaplasmosis (*Anaplasma phagocytophilum*), cytauxuzoonosis (*Cytauxzoon felis*), ehrlichiosis (*Ehrlichia* spp.), and Lyme disease (*Borrelia burgdorferi*). The recently established *Haemaphysalis longicornis* (longhorned tick) is also reported from cats in the eastern US, while cats in the western US are commonly infested with *I. pacificus*, *Dermacentor* spp., and *Otobius megnini* (spinose ear tick). [11,12] Although ticks are most often identified on cats that spend at least some time outside, tick infestations are also reported from cats described by their owners to have an entirely (100%) indoor lifestyle.[11] Tick infestations on indoor-only cats, similar to flea infestations on this population, likely occur following introduction of ticks to the home on the owners' clothing or from other pets (e.g. dogs) allowed outside. Similarly, mosquito species that are frequently found in and around homes (e.g. *Aedes albopictus*) feed on cats with the same propensity as dogs, contributing to a risk of feline heartworm infection.[13]

Diagnostic Tests

A thorough feline wellness examination should always include testing for internal parasites, external examination for ectoparasites, and consideration of blood testing for heartworm, other vector-borne infections, and viral pathogens.

Fecal examination Fecal flotation by centrifugation is uniformly recommended to provide the greatest sensitivity of detection of eggs, cysts, and oocysts of feline nematodes and protozoa; combining centrifugal flotation with antigen tests for nematodes and, when diarrhea is present, for *Giardia*, further enhances detection of parasite infections.[2] Adequate fecal samples can be difficult to obtain in cats with diarrhea; recovery and identification of *T. blagburni* trophozoites may require per rectum sample collection using saline flush or deep fecal loop.[7] A history of intestinal parasite diagnosis has been shown to be associated with reported current use of preventive in pet owners.[14] Due to issues of compliance and the relatively limited spectrum of some control products, intestinal parasites are often identified in pet cats maintained on preventives. Accordingly, and due to the zoonotic risk posed by some feline intestinal parasites, even cats prescribed a preventive should be tested annually by fecal examination.[2]

Ectoparasite examination. A careful, thorough external examination using a flea comb and systematically examining the skin both dorsally and ventrally often reveals evidence of fleas, flea-allergy dermatitis, or ticks. On infested cats, a majority of adult fleas are found on the head or neck compared to the ventrum, and fleas are rarely found on the legs and tail.[8] Similarly, a majority of *I. scapularis* ticks on cats are found attached to the head and neck, whereas *D. variabilis* ticks are most often attached on the dorsal head and back. In contrast, both adult and immature *A. americanum* ticks – which are common parasites of cats in the eastern US – are most often found ventrally, in the axillary and inguinal region or attached on the tail or perianal region.[11] Although feline grooming is not adequate to entirely eliminate flea or tick infestations, a significant number of ectoparasites are removed by the cats. When mite infestation is suspected in a pruritic cat, fecal flotation should be performed as ingested mites are often more readily found in feces than recovered by skin scrape. Flea populations on infested cats are reduced by ~one-third after 3 days, primarily due to removal through grooming, and flea allergic cats groom more assiduously and remove more fleas than non-allergic cats. Fleas fed on allergic cats also produce fewer eggs.[8] Evidence of lesions of flea allergy dermatitis or flea infestation (e.g., frass), or direct recovery of fleas or ticks during the course of a physical examination reveals a health threat to the cat and can motivate many clients to use ectoparasite control products to protect the cat from future infestations.

Testing for vector-borne infections. At present, routine, annual screening of cats for vector-borne infections is not widely practiced. However, cats benefit from testing for antibodies to or antigen of *Dirofilaria immitis* to assess baseline infection status when heartworm preventive is first instituted in adult cats, or at the first annual appointment if preventive use is started in young kittens.[2] When cats present with evidence of clinical disease and heartworm infection is suspected (e.g. respiratory disease, chronic vomiting), both antibody and antigen tests should be performed. Detection of *D. immitis* antigen in cats is enhanced when samples are treated first to disrupt immune complexes.[15] Cats can also be tested for antibodies to common tick-borne infections (*A. phagocytophilum*, *B. burgdorferi*, *Ehrlichia* spp.) using widely available patient-side assays; although not optimized for feline samples, these assays are useful for identifying antibodies that confirm past or current infections in cats. In regions where *B. burgdorferi* and *A. phagocytophilum* are commonly transmitted, such as the Northeast, upper Midwest, mid-Atlantic, and West Coast states, identification of these tick-borne infections in cats through routine screening may allow earlier treatment, limiting the severe clinical disease sequelae that have been reported in some feline patients.[16] A positive tick-borne disease antibody test also alerts the owner that tick control is needed in their cat. In cats that present with

a febrile illness and a flea- or tick-borne infection is suspected, panel testing with a combination of serology and PCR assays for the most likely pathogens is recommended. Early in infection the PCR assay is more likely to be diagnostic, while with established, disseminated infections, serology may prove more fruitful. Unfortunately, patient side antibody tests for *Cytauxzoon felis* are not yet commercially available. When the severe disease associated with cytauxzoonosis is suspected, stained blood smears should be examined for piroplasms and whole blood submitted for PCR assay.[17]

Treatment and Prevention Strategies

Successful management of intestinal parasites, ectoparasites, and vector-borne diseases in cats requires (1) shared awareness by owners and veterinarians about the infection risk and how common these agents are in pet cats, and (2) clear understanding of the strengths and limitations of diagnostic tests, treatments, and prevention strategies. Cats allowed outdoors will almost inevitably become infected and infested with parasites, but parasites and parasitic diseases are also diagnosed in cats who are described by their owners as indoor-only. Although many owners remain unaware, predatory behavior is common in pet cats and directly linked to elevated infection risk for *Toxocara cati*, *Taenia taeniaeformis*, *Cystoisospora* spp., and many other parasite infections. Cats allowed to explore outside are also likely to acquire fleas and ticks deposited by untreated pets or peridomestic wildlife in the same environment, and are at elevated risk of infection with vector-borne disease agents. However, indoor-only cats are not protected from infection risk by virtue of their lifestyle alone. Mosquitoes that transmit heartworm readily enter houses and apartments, and fleas and ticks can be brought in on owners' clothing or the fur of untreated dogs that share the home. In addition, intestinal parasites may be introduced via arthropods (crickets, roaches), especially on a screen porch or terrace, or in soil adhered to shoes.

Treatment for parasites and vector-borne infections. Broad spectrum parasite control selection should take into consideration the zoonotic risk posed by *Toxocara cati*, the most common intestinal nematode in pet cats, and *Ancylostoma tubaeforme*. Several treatments are available to address active infections when diagnosed, including pyrantel, emodepside, and macrocyclic lactones (epirinomectin, moxidectin, and selamectin.) Macrocyclic lactones also protect cats from heartworm infection and are approved to be administered routinely to eliminate any newly acquired intestinal nematode infections before they become patent. Feline tapeworms (*Taenia* spp., *Dipylidium caninum*) are treated with praziquantel or epsiprantel; recent data indicate that *D. caninum* in cats is distinct from the species infecting dogs.[18] Label-approved treatments are not available for feline intestinal protozoa in the US. However, fenbendazole, with or without metronidazole, can be used to manage clinical giardiasis in cats, and coccidiosis caused by *Cystoispora* spp. responds to ponazuril treatment. *Tritrichomonas blagburni* is more difficult to treat, but off-label use of ronidazole is recommended. Cats being treated with rondiazole must be closely monitored for neurologic signs and treatment discontinued should ataxia, lethargy, or other adverse effects be observed.[2,7]

Infestations with fleas and ticks are readily treated with safe, effective, persistent compounds that not only eliminate existing infestations but, depending on the compound used, can prevent re-infestation for several weeks or months. Available systemic feline flea and tick control products include fluralaner and sarolaner; topical residual products such as flumethrin / imidacloprid collars and fipronil are also available. Longer-acting products are particularly useful in cats because they reduce the frequency of treatment needed, protecting the human-cat bond, and in the case of fluralaner, have been shown to eliminate environmental flea infestations with a single administration.[19] Tick control is also critically important in cats, including indoor-only cats at risk from ticks introduced to the home by people or other pets; many cat owners remain unaware of the severe feline health risk ticks pose.[11] Although treatments are available for most flea- and tick-borne infections, prognosis is guarded, and fatalities can occur even when aggressive treatment is instituted at initial presentation.[17]

Preventing feline parasites and vector-borne infections. As parasite and vector populations increase across the US and the threat of these infections grows, consistent parasite control for pet cats, including those kept primarily or entirely indoors, remains critically important. A recent comparison study from Canada shows that cats are more frequently infected with intestinal parasites than dogs.[20] For safety reasons, permethrin-based repellents cannot be used in cats, and yet cats also remain at risk of blood feeding by mosquitoes and ticks. Products that combine a macrocyclic lactone with efficacy against intestinal nematodes and heartworm with an isoxazoline effective against both fleas and ticks provide the widest available spectrum of protection and keep cats safe from a broad swath of infections.

Administering parasite control products routinely and consistently (year-round) to pet cats – as recommended by the Companion Animal Parasite Council[2] – insures that existing parasites will be treated and that new infections and infestations will be controlled, limiting pathology and reducing pathogens that create feline health and zoonotic risks. Feline heartworm infections are more frequently identified in cats with outdoor access and those with other health problems (e.g. abscesses, bite wounds, respiratory disease), but mosquitoes readily come indoors and heartworm can be identified in any cat.[21] Although they protect cats from potentially fatal heartworm infection and treat and

control feline roundworms and hookworms, only approximately 10–15% of pet cats receiving veterinary care are prescribed a preventive.[21] Similarly, ticks are most commonly identified in younger male cats with outdoor access, although a recent national survey documented tick infestations in indoor-only cats and cats as old as 19 years.[11] Selecting broad spectrum feline parasite control strategies that protect cats from heartworm, intestinal parasites, fleas, and ticks comprehensively addresses concerns about these infections, protecting both the health of the cat and the relationship between the cat and its owner.

References

1. Little S, Adolph C, Downie K, et al: High prevalence of covert infection with gastrointestinal helminths in cats. *JAAHA* 51:359, 2015.
2. Companion Animal Parasite Council, capcvet.org. Parasite Prevalence Maps; Guidelines. 2020.
3. Bowman DD: Helminths. In Bowman DD, editor: *Georgis' Parasitology for Veterinarians*, 10th Edition. Elsevier, 2014, p122–240.
4. Berrett AN, Erickson LD, Gale SD, et al: *Toxocara* seroprevalence and associated risk factors in the United States. *AJTMH* 97:1846, 2017.
5. Scorza V: Giardiasis. *Clinician's Brief*. February:71, 2013.
6. Bowman DD: Protista. In Bowman DD, editor: *Georgis' Parasitology for Veterinarians*, 10th Edition. Elsevier, 2014, p87–121.
7. Gruffydd-Jones T, Addie D, Belák S, et al: Tritrichomoniasis in Cats: ABCD guidelines on prevention and management. *J Fel Med Surg* 15:647, 2013.
8. Rust MK: The biology and ecology of cat fleas and advancements in their pest management: a review. *Insects* 8:118, 2017.
9. Clark NJ, Seddon JM, Šlapeta J, Wells K: Parasite spread at the domestic animal - wildlife interface: anthropogenic habitat use, phylogeny and body mass drive risk of cat and dog flea (*Ctenocephalides* spp.) infestation in wild mammals. *Parasit Vectors* 11:8, 2018.
10. Thomas JE, Staubus L, Goolsby JL, Reichard MV: Ectoparasites of free-roaming domestic cats in the central United States. *Vet Parasitol* 228:17, 2016.
11. Little SE, Barrett AW, Nagamori Y, et al: Ticks from cats in the United States: Patterns of infestation and infection with pathogens. *Vet Parasitol* 257:15, 2018.
12. Saleh MN, Sundstrom KD, Duncan KT, et al: Show us your ticks: a survey of ticks infesting dogs and cats across the USA. *Parasit Vectors* 12:595, 2019.
13. McCall JW, Genchi C, Kramer LH, et al: Heartworm disease in animals and humans. *Adv Parasitol* 66:193, 2008.
14. Stafford K, Kollasch TM, Duncan KT, et al: Detection of gastrointestinal parasitism at recreational canine sites in the USA: the DOGPARCS study. *Parasit Vectors* 13:275, 2020.
15. Little SE, Raymond MR, Thomas JE, et al: Heat treatment prior to testing allows detection of antigen of *Dirofilaria immitis* in feline serum. *Parasit Vectors*. 7:1, 2014.
16. Hoyt K, Chandrashekar R, Beall M, et al: Evidence for clinical anaplasmosis and borreliosis in cats in Maine. *Top Companion Anim Med* 33:40, 2018.
17. Nagamori Y, Reichard MV: Feline tick-borne diseases. *Today's Vet Pract* 3:69, 2015.
18. Labuschagne M, Beugnet F, Rehbein S, et al: Analysis of Dipylidium caninum tapeworms from dogs and cats, or their respective fleas - Part 1. Molecular characterization of Dipylidium caninum: genetic analysis supporting two distinct species adapted to dogs and cats. *Parasite* 25:30, 2018.
19. Ranjan S, Young D, Sun F: A single topical fluralaner application to cats and to dogs controls fleas for 12 weeks in a simulated home environment. *Parasit Vectors* 11:385, 2018.
20. Morandi B, Greenwood SJ, Conboy GA, et al: Endoparasites in dogs and cats diagnosed at the Veterinary Teaching Hospital (VTH) of the University of Prince Edward Island between 2000 and 2017. A large-scale retrospective study. *Prev Vet Med* 175:104878, 2020.
21. Levy JK, Burling AN, Crandall MM, et al: Seroprevalence of heartworm infection, risk factors for seropositivity, and frequency of prescribing heartworm preventives for cats in the United States and Canada. *J Am Vet Med Assoc* 250:873, 2017.

NOTES:

Pouncing on Pain: Managing Feline Osteoarthritis Cases

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All types of injury can cause pain. Pain is a deeply individual experience as it is not simply the neural experience of pain but the perception of pain within the context of life experience "it's not just what you feel but how it makes you feel". The sensory component is nociception, the stimulation of peripheral neural receptors, by a noxious stimulus either deliberately, as in surgical trauma, or accidental. The inflammatory component is the immune response to injury and is the activation of a cascade of mediators. Pain changes the organism. Change occurs over time and results in pathologic pain or maladaptive pain sensations. That is pain beyond the ordinary or expected response. There are multiple ways in which this manifests. Hyperalgesia is an exaggerated response to a painful stimulus. Allodynia is a painful experience of a stimulus that would not ordinarily be experienced as pain. Pain can also spread beyond where it would ordinarily be experienced or last longer than would be expected. Under some circumstances, genomic or phenotypic changes can occur resulting in neuropathic pain wherein pain is considered a disease of the central nervous system. Understanding the mechanisms of pain is essential for its successful management and prevention. It is also essential for creating an urgency about controlling pain. Well-managed pain does not necessarily result in the maladaptive pain, particularly when controlled early in its inception.

Osteoarthritis (OA) is a very common disease in the older cat. Prevalence figures for radiographic disease vary widely and range to as high as 91% depending upon the group studied. Radiographic evidence is not necessarily required for a diagnosis of OA as well. Osteoarthritis can be defined as a degenerative disorder of the synovial joints characterized by the deterioration of the articular cartilage and by the formation of new bone at the joint surfaces and margins. Most cats show bilateral and symmetrical disease in multiple joints, most commonly elbow, stifle and hips. Radiographically visible DJD is very common in domesticated cats, even in young animals and is strongly associated with age.

Joint pain secondary to OA is one of the most prevalent chronic pain in cats. It is comprised primarily of inflammatory pain and likely involves components of neuropathic pain. The factors contributing to OA-related pain include:

- pathologic changes in the osteoarthritic joint
- neuroplastic changes to the nervous system
- general factors including obesity, genetics, environment, comorbidities and others

Thus, the pain profile of the feline patients may differ widely, making it more important to recognize the behavior alterations of the individual cat. OA will have different clinical presentations with widely divergent experience of pain.

In addition, the cat is far more difficult to evaluate for chronic pain because of their evolution as solitary hunters. They need a smaller repertoire of inter- and intra-species social communication compared with the dog. Cats are often described as "aloof" and "independent" which could stem from the lack of obvious facial expressions and visually expressive characteristics of the dog.

Their need to express themselves is diminished by their independence. Cat communication has been largely overlooked as it lacks the drama and intensity of dogs. Cats in the wild live alone and must compete with each other for food and other resources. Cats are deliberately inscrutable. Letting on that a good meal is nearby or that a safe resting place has been discovered will not result in a good outcome for that cat. Conversely, letting on that one is injured, sick or exhausted may lead to becoming another's prey. The subtlety of signaling has led to a misunderstanding of the health care and quality of life care cats require.

In addition, changes in mobility are less evident in cats than dogs due to their small body size and normal behavioral repertoire, particularly their tendency to withdraw, sleep or hide. Pain scores rely on the detection of these behavioral changes to assess pain and its effect on the ability to perform desired activities and to enjoy historically pleasurable experiences.

There then becomes the experience of the cat in the veterinary setting. Separation anxiety is recognized in dogs when their owners are away. For the territorial cat, separation anxiety occurs when they are taken from their place of safety. The sensations of pain induce behavioral change that may look similar to the experience of a cat experiencing stress.

Defensive aggression, withdrawing or inhibiting behavior, changes in maintenance behaviors such as grooming or eliminating can be indicative of either. The cat is usually not willing to walk for a gait evaluation in the exam room and

may avoid contact with a stranger that could indicate either fear or pain. The place for evaluation of OA pain then becomes the home. Validated pain assessment tools give the caregiver the ability to assess change in behavior and daily routine.

There are currently 2 owner-based partially validated clinical instruments for use in cats with OA.

1. The Feline Musculoskeletal Pain Index (FMPI) involves caregiver assessment of the severity and impact on QOL of chronic pain in their cat. FMPI has been used in several investigations. The most recent version consists of 17 items pertaining to mobility, ability to perform daily activities and interaction with other pets and people. Each item is scored in a range from "normal" to "not at all" with respect to the cat's ability or willingness to perform the activity. The FMPI differentiates pain-free from painful cats with OA and helps with assessing response to treatment. However, it is not clear if it can discriminate severity of pain at this time. www.painfreecats.org
2. Client Specific Outcomes Measure (CSOM). The CSOM is an instrument that was originally developed for dogs and then applied to cats. The test has been used in some studies for its validation. It is based upon owner assessment of the impact of chronic pain on a cat's ability to perform specific activities that are particular to the individual cat. There are no set items to be scored. Instead, the owner, with the help of veterinarian or technician, will choose three activities that are observed at home. The CSOM can be time-consuming to implement because of its customized construction, requiring clear understanding by caregivers.

The author employs FMPI along with an animation developed to teach caregivers (and veterinarians/staff) to distinguish between the typical behaviors of cats when they are employed normally or by a cat in pain. https://www.chicocats.com/blog Before COVID-19, we would have looped this on screen savers in exam rooms and in the reception closed television. We now send it to any caregiver with an older cat who can view online videos. Educating caregivers require easy, short video experiences. By teaching them the difference in common behaviors between OA pain and normal behavior we can then ask them to submit video of their cat in a normal home circumstance for assessment.

The transition to video assessment is not always simple. The caregiver must be instructed on content, length, distance from subject and method of submission. A 30 minute close up of a cat moving in the house is not an efficient use of anyone's time. The distance from the cat should be 3 – 4 feet to give the cat room to move and to capture the motion of the whole body. After the caregiver has viewed the animation at least twice, they are asked to capture one or 2 of the actions in them in 2 minutes or less. The first few attempts can be quite discouraging. A staff member can help by viewing a submission and coaching the caregiver to create a more useful segment.

Once an understanding of the signs of pain in cats has been conveyed and the importance of its control understood by caregivers. A plan for treatment of OA pain that balances the goals of the caregiver can be created. These goals go beyond the successful management of pain and include the preservation of the loving relationship between cat and caregiver. The home range for the cat is a place of predictability and safety so that change is tolerable. When actions are taken by the caregiver that cause stress or fear in the cat, the relationship can be grievously harmed by the event. Many issues of compliance with medical recommendations come down to the erosion of relationship. When the cat who slept routinely with the owner, now hides under the bed when approached by the caregiver, the emotions for both parties are harmed. The caregiver feels sad or guilty and the cat feels fear or anxiety.

Thus, the plan must be one that considers the ability and commitment of the caregiver, cost of care, the availability of resources. The owner will be more likely to embrace the suggestions in a multimodal pain management plan if they feel really involved in its formulation, if the goals and objectives are important to them, and if they don't feel pressurized, tested or judged. How the owner approaches the task will differ from one individual to another. Nurturing the trusting relationship between caregiver and veterinarian will simplify planning.

Repeated use of FMPI over time will help the caregiver remain committed to the process as improvement in mood, mobility and overall QOL improve. This interrogation can also assist in modifying a plan, with the caregiver, to improve QOL as new modalities arise or therapies are attempted and discarded as impossible. The decision to discontinue a therapy will occur particularly if the relationship between caregiver and cat is harmed.

The initial plan will vary, adjusted to the patient and the caregiver's evalulation of response over time. The major components of the plan are the following:

Weight Loss

Many cats with chronic pain of OA are overweight or obese. The cycle continues as pain decreases activity. Excess weight increases the load on abnormal joints, creating more pain. In addition, white adipose tissue (WAT) secretes

adipokines which are potent inflammatory mediators which increase the overall inflammation of the entire cat, including already inflamed joints. Weight loss in cats can be challenging because healthy weight loss is slow and may not be readily apparent to reinforce the effort. A combination of increased low impact exercise and calorie restriction can be very helpful.

Pharmaceutical Therapies for OA Pain
Administering medication to cats can be challenging for owners, yet adequate therapy relies on good owner compliance. Along with NSAIDs, many cats will be receiving other medications and the 'administration burden' may be daunting for owners, leading to inconsistent dosing. To help long-term use, a drug should ideally be highly palatable and taken voluntarily by the cat — for example, in food or as a treat — and veterinary pharmaceutical companies undertake much research into this.

Currently, in the USA there are no NSAIDs registered for long-term use in cats. Meloxicam is registered in Europe for the alleviation of pain and inflammation in acute and chronic musculoskeletal disorders, but in the USA it is only registered as a single injectable dose for postoperative pain and inflammation in cats. Positive effects of meloxicam on signs of OA in cats have been reported in open-label studies, and two masked, placebo-controlled studies. Published studies suggest meloxicam liquid is highly palatable in cats.

Robenacoxib is an NSAID that has been recently introduced into canine and feline medicine. Presently, robenacoxib tablets are registered in the USA for cats for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration at an oral dosage of 1.0–2.4 mg/kg q24h, for up to 3 days. Because of the need for long term management of pain in older cats and the common comorbidity of CKD, a recent study examined the use of rebenacoxib over a 30 day period in older cats including a subset of cats with CKD.

In all 193 cats and the subgroup of 40 animals with concurrent CKD, there were no differences between groups in frequencies of reported adverse events, body weight change or results of serum or urine chemistry or hematology variables.

Robenacoxib was well tolerated when administered daily for 1 month in cats with osteoarthritis, including cats with evidence of concurrent CKD. There was no clinical indication of damage to the gastrointestinal tract, kidney or liver.

Additionally, owners must be consistent and remember to administer the drug. Based on the long duration of action of many NSAIDs in cats, this should be at a set time on treatment days. Creative reminder systems may help ensure cats receive medication on the correct day(s), at the correct time(s) and at the correct dose. Giving medication along with a daily food ration (which should also be done for safety) can provide a built-in reminder system for owners and encourage owner involvement in the monitoring process.

ISFM and AAFP Consensus Guidelines: Long-Term Use of NSAIDs in Cats includes the following guidelines for their use in chronic OA pain:
Panel recommendations
Dosing frequency

- To avoid potential side effects, owners should be encouraged to work on titrating to the 'lowest effective dose' that works for their cat, with the understanding that this may change over time. This dose may often be less than the labelled dose.[13,14,21]
- In overweight or obese cats, it is prudent to calculate initial doses for NSAIDs according to their lean or ideal bodyweight.
- When attempting to reduce the overall dose of an NSAID, it would seem prudent to reduce the label dose but maintain the label frequency, where possible.
- The panel recognizes that intermittent therapy, for example 2–3 times weekly rather than daily, is better than no therapy at all, and anecdotally appears efficacious in some cats. However, there may be a risk of significant periods of time when no effective therapy, or suboptimal therapy, is being achieved.
- Intermittent drug withdrawal, a reduced frequency of dosing, or a reduction of the dose may all help owners to assess drug efficacy.
- The panel sees little rationale for pulse therapy with NSAIDs unless the underlying disease process varies sufficiently in severity that it does not require consistent analgesic/anti-inflammatory therapy.

Other drugs that are commonly used for pain management include gabapentin, amantadine, amitriptyline and opioids. Presently the use of gabapentin in a recent investigation was the drug most commonly prescribed for chronic pain in cats. The dose should be titrated to most effective dose. However, in humans a slow increase in dose adjustment helps to prevent dizziness and fatigue. This method could be used to both prevent side effects and observe the lowest effective dose. Dosing is generally started at 50-100 mg at night and increased every 5-7 days to

effect. There are no studies of efficacy for amantadine or amantadine. Because of potential side effects with long term use, buprenorphine should be reserved for short term use of breakthrough pain.

Environmental Enrichment/Modification
Environmental enrichment remains an important component of pain management strategies. A stimulating environment or being engaged in activities distracts humans from their pain and the same could be said for cats.

Planning for environmental enrichment as a component of pain management also must consider the whole cat. In the presence of cognitive dysfunction, for example, any change to the environment may have a negative effect. This is because these cats often become very stressed and cope poorly with change; whether that change is in the environment, their daily routine, their diet or the members of the household with which they live. While it can be tempting for people to add a younger cat to the family, the impact on an older cat, particularly one with chronic pain could be devastating both for the cat and the caregiver. Stress can precipitate behavior problems.

Planned accommodation should take place quite slowly and in the company of a favored person. Addition of synthetic feline facial pheromone diffusers may be beneficial. Understanding an individual cat's preferred activities and locations should be part of the equation. Cats in pain may not groom well and the addition of that activity performed by preferred human with a desirable type of grooming device could improve comfort.
Warm resting places that are easily accessible are helpful. Steps should be short and require no jumping up or down. Cat trees or window perches that encourage outdoor observation should have the first step up be quite close to the ground.

Heated bedding can provide joint comfort and is available in a wide variety of forms. Consideration should be given to safety and those not required to be plugged in to function are preferred.

Neutraceuticals and Supplements
Polysulfated Glycosaminoglycan (Adequan®) injections have both chondroprotective and chondrostimulation properties and, though long-term studies are lacking, many practitioners believe it is helpful at the same dose and interval as dogs. In the author's practice Adequan is given subcutaneously by the owner at home, after learning to administer the injection in the practice. After the induction period injections are given in an interval indicated by the cat's comfort, usually 9-14 days. This delivery method is easier on both cat and caregiver than administering unpalatable oral medication.

There are multiple mobility diets for cats that contain omega-3 fatty acids, green-lipped mussel and glucosamine/chondroitin. Research has shown that these diets improve mobility; however they may be inappropriately high in calories for an obese patient. In addition, recent research suggests that older cats, the population most likely to be diagnosed with OA, need additional protein as they age. Care should be taken to insure protein adequacy.

Supplements that contain omega-3 fatty acids are common. Care should be taken to find one that is palatable or easy to deliver. There is evidence that cats on diets supplemented with O-3 are more active. Because empirical evidence is lacking and the positive data is observational, the risk of forcing a supplement that is not palatable is not recommended. Other supplements like green-lipped mussel and curcumin have not been studied in cats. The problem of palatability may limit their use.

Cannabinoids are derived from the hemp plant, which contains multiple biochemicals with beneficial properties: they are anti-oxidants as well as immunomodulators (which makes them anti-inflammatory), plus they also decrease the perception of pain. There are obviously numerous legal and regulatory issues surrounding what products can be recommended for animals. At this time, only whole hemp-based products (with low enough THC levels to be legal) are sanctioned for animal use. Lack of research has been problematic as well. Cannabidiol, for example, is a potent liver enzyme inducer, which makes it capable of reducing the activity of many other medications. Since arthritis management commonly involves many products, it is important to be cautious where drug interactions are possible.

Acupuncture
Acupuncture is a safe method of pain relief and should be integrated into a multimodal pain management plan wherever possible. It is minimally invasive and can be used with other modalities. The NIH has stated that "acupuncture provides pain relief and improves function for people with arthritis and serves as an effective complement to standard care". The author's experience is that cats tolerate acupuncture well and even some seem to enjoy it. Caregivers report that it helps.

Therapeutic Laser
LASER is an acronym for Light Amplification by Stimulated Emission of Radiation. Other terms include low-level light therapy (LLLT), "cold laser," and more recently photobiomodulation (PBM) therapy. The benefit increases over time with more sessions. Most cats seem to enjoy the warmth of the laser light which is targeted on tissue to engage the mitochondria causing increased circulation, reduce pai, reduced inflammation and enhanced tissue healiong.

PEMF
Pulsed electromagnetic field (PEMF) therapy is a non-invasive, nonthermal treatment that involves pulsing electromagnetic fields in tissue to promote healing (Strauch et al., 2009). PEMF devices have been approved by the U.S. Food and Drug Administration (FDA) to treat nonunion
fractures and cleared to treat post-operative pain and edema, osteoarthritis, and plantar fasciitis. The Assisi targeted PEMF device consists of a single loop antenna and battery-powered
pulse generator. The targeted PEMF waveform was designed to reduce inflammation in soft tissue. Characteristics of the waveform, such as the long burst width and the high frequency 27.12 MHz carrier wave, result in very efficient delivery of electric field to tissue, and, therein, beneficial clinical effects with small doses of treatment.

The benefits of this therapy include reduced patient handling on the part of the caregiver, painless reduction in OA inflammation, safety, and efficacy. The therapy is delivered in 15 minutes sessions which can be repeated multiple times a day. The delivery options include a loop that can be placed under bedding, carriers, and bedding that contain the technology. The body of evidence for its use in cats is growing.

Physical Therapy
Controlled exercise, passive range of motion (ROM) and massage are all physical rehabilitation techniques that can be incorporated into a pain management plan. While these activities have not been evaluated in cats, they are beneficial in dogs and children with chronic pain. It is reasonable to assume they may be helpful and add to the enrichment by providing pleasurable interaction with caregivers and alleviate some types of discomfort.

References

1. Enomoto, M., Lascelles, B. D. X., & Gruen, M. E. (2020). Development of a checklist for the detection of degenerative joint disease-associated pain in cats. Journal of Feline Medicine and Surgery. https://doi.org/10.1177/1098612X20907424
2. Gaynor J. S. , Hagberg S., et al. (2018) Veterinary applications of pulsed electromagnetic field therapy in *Research in Veterinary* Science, 1-18.
3. Sparkes, A. H., Heiene, R., Lascelles, B. D. X., Malik, R., Real, L., Robertson, S., … Taylor, P. (2010). ISFM and AAFP Consensus Guidelines: Long-Term use of NSAIDs in Cats. Journal of Feline Medicine and Surgery, 12(7), 521–538. https://doi.org/10.1016/j.jfms.2010.05.004
4. King, J. N., King, S., et al. (2016). Clinical safety of robenacoxib in feline osteoarthritis: results of a randomized, blinded, placebo-controlled clinical trial. Journal of Feline Medicine and Surgery, 18(8), 632–642. https://doi.org/10.1177/1098612X15590870
5. Klinck, M. P., Monteiro, B. P., et al. (2018). Refinement of the Montreal Instrument for Cat Arthritis Testing, for Use by Veterinarians: detection of naturally occurring osteoarthritis in laboratory cats. Journal of Feline Medicine and Surgery, 20(8), 728–740.
6. Enomoto, M., Mantyh, P.W., et al. (2018) Anti-nerve growth factor monoclonal antibodies for the control of pain in dogs and cats. Vet Record open access.

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Feline Head & Neck: Diseases, Disorders, & More

2020 Virtual CONFERENCE
October 3 & 4 and 24 & 25, 2020

ALL TIMES ARE EASTERN TIME ZONE

Day 3 — October 24, 2020

Live Exhibits open from 11:00 am- 5:00 pm

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Slow Flow Yoga		
11:00 - 12:00 pm	Video Chat Discussion Forums ***Pre-registration Required***		
12:00 - 1:00 pm	Update on Treatment Strategies for Feline Chronic Gingivostomatitis	Dr. Christopher Snyder	
	Nutrition for the Hospitalized Patient	Dr. Christopher Byers	ROYAL CANIN
	Technician/Nurse: Cat Naps During a COHAT: The Complete Plan for the Feline Dental Patient	Ms. Mary Berg	NAVTA
1:00 - 1:45 pm	Exhibit Hall Break		
1:45 - 2:45 pm	Mastering Feline Dental Radiograph Interpretation	Dr. Christopher Snyder	
	Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 1	Dr. Phillip Padrid	TRUDELL ANIMAL HEALTH
	Technician/Nurse: Tips & Tricks for Great Dental Radiographs	Ms. Mary Berg	NAVTA
2:45 - 3:45 pm	***Partner Symposia***		
	Feline Hypertension: Diagnosis, Treatment, & Management	Dr. Clarke Atkins	Boehringer Ingelheim
	One Size Won't Fit All: Tailoring Weight Management Plans For Cats	Dr. Julie Churchill	MARS Petcare
	Hydration Fixation: Beyond the Water Bowl	Dr. Jason Gagne	PURINA PRO PLAN VETERINARY DIETS
3:45 - 4:15 pm	Exhibit Hall Break		
4:15 - 5:15 pm	Gastroesophageal Reflux: An Under-Recognized Source of Pain	Dr. Christopher Byers	ROYAL CANIN
	Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 2	Dr. Phillip Padrid	TRUDELL ANIMAL HEALTH
	Technician/Nurse: Pain Management & Anesthesia Concerns in Feline Dental Patients	Ms. Mary Berg	NAVTA
5:15 - 6:15 pm	Virtual Happy Hour		Boehringer Ingelheim

Update on Treatment Strategies for Feline Chronic Gingivostomatitis

Christopher Snyder, DVM, DAVDC

Introduction

There are many instances in veterinary practice where cats cannot be treated the same as small dogs. Veterinary dentistry is no different. While the prevalence of periodontal disease in cats is similar to the widespread prevalence seen in dogs, other conditions show up much more frequently in cats such as tooth resorption and generalized stomatitis. The prevalence of tooth resorption and stomatitis in cats remains greater than any other species and remains problematic and frustrating to treat. Fortunately, many cats with stomatitis tend to be successfully managed in private practice. Those that demonstrate failure to respond to treatment may require creative intervention.

Early stages of feline chronic gingivostomatitis is typically confined to just the gingiva. As inflammation spreads and involves other tissues, diagnosis becomes more conclusive. During the early stages where inflammation is limited to the gingiva, periodontal disease (as common in cats as it can be in dogs- up to 80% over the age of 3 years) and tooth resorption should be ruled out. While periodontal disease in felines is a disease condition of attachment loss of by constituents of the periodontium, the practitioner must be cautious about deciding how aggressively to treat periodontal disease. Efforts to rehabilitate locations affected by periodontal disease may undermine the ultimate treatment recommendation of extraction for management of stomatitis patients. To further complicate matters, teeth affected by Type 2 tooth resorption (replacement resorption of the root and loss of the periodontal ligament space) should not undergo crown amputation since retention of root remnants may continue to contribute a trigger or nidus for stomatitis.

Stomatitis

Feline stomatitis is currently referred to as feline chronic gingivostomatitis (FCGS). In previous naming iterations of the condition, it had most recently been called *lymphoplasmacytic gingivostomatitis (LPGS)*. The condition involves inflammation and widespread involvement of structures in the mouth including: gingiva, mucosa, and may extend to include the tongue and palatoglossal arches. Etiologies of this condition are poorly understood and seem to impact three different demographics of cats. The earliest manifestation of the condition occurs in kittens at the time of vaccines. It is unknown if this is related to vaccine administration or the eruption of deciduous teeth. The second phase of life associated with stomatitis is at the time of the eruption of permanent teeth. The last phase of commonly associated with stomatitis is in adulthood. Breed predispositions may include Maine Coons and Siamese breeds (in Europe) while other studies demonstrate no breed predilection. Calici virus has been proposed to be associated with stomatitis development with 70-90% of cats testing positive compared with 20% of the general population. It is believed that the virus may damage host cell membranes easing the penetration of antigenic stimuli. Many cats demonstrate increased globulins on blood work suggesting an immune response, possibly due to a hypersensitivity to oral flora. Proposed triggers for hypersensitivity have also included constituents of the periodontal ligament structure or the tooth itself (as evidenced by refractory symptoms persisting only until tooth roots remnants are removed.) Working up these patients should include a biopsy of effected tissues, a thorough cleaning and meticulous homecare. This combination offers the best chance for medical management for patients affected by this condition. Testing for FeLV and FIV may be recommended since an aberrant immune system related to concurrent disease may negatively impact the prognosis for achieving a well-controlled state long term in these patients. Cases non-responsive to medical management improve with dental extractions (as high as 87% demonstrate some degree of improvement). Cats living in multi-cat environments may be more commonly affected early in life which may be possibly associated with increased stressors and the transmission of unknown viruses or microorganism triggers. In affected cats, bacterial culture and sensitivity has not been touted as providing fundamental indication guiding successful treatment. Aside from a normal population of oral flora, one study has reported a high proportion of cats positive with a pure culture of *Pasturella multocida*. Any antibiotic use prior to surgery (to improve the health of tissues) should provide adequate coverage for the *Pasturella* species such as amoxicillin-clavulanic acid or doxycycline.

Mast cells have been established to be present in the gingiva of cats affected with periodontitis, FCGS and tooth resorption by Arzi, Murphy et al. The presence of mast cells in all three disease conditions despite the associated degree of inflammation suggests the mast cells may be reactive to an antigenic or non-antigenic stimulus. Involvement of the cell type is can be associated with the release of cytoplasmic pro-inflammatory mediators which contributing to the presenting pathology. A variety of genetic or infectious causes have been suggested. These mast cells play an integral role not only in host immune response to triggers, but also an important mediator of inflammation and tissue repair. Because of the nonspecific involvement of mast cells in FCGS, investigative treatment approaches remain focused on identifying a cause or trigger for the condition.

Biopsy is commonly performed to aid in ruling out the presence of neoplasms (squamous cell carcinoma or lymphoma) which could be at risk for developing due to malignant transformation of chronically inflamed tissues. The author has seen two cases of non-healing extraction sites which had been biopsied prior to completing full mouth extractions. Feeling comfortable about the absence of malignancy makes the idea of full mouth extractions a more palatable treatment to the client and reasonable for the patient. Distribution of inflammatory cells in the histopathology report may also suggest whether the patient is suffering from an advanced case of severe periodontal disease (inflammatory cells +/- bacteria found in superficial cell layers) versus an FCGS case where inflammatory cells are expected to be found deeply infiltrating tissues.

During initial treatment and work-up of FCGS cases, routine preanesthetic blood work should be performed to rule out concurrent metabolic disease conditions that may impact anesthetic risk (renal disease, hepatic disease) or impact post-surgical healing (diabetes). Once anesthetized, patients should receive a thorough dental cleaning and oral examination. Dental radiography should be performed evaluating for any reasons indicating extraction (tooth resorption, endodontic disease, retained root fragments). Cats demonstrating signs of stomatitis have been shown by Farcus et al., to be more greatly affected by horizontal bone loss, suffer external inflammatory resorption and have more retained roots. Teeth affected by tooth resorption should undergo complete extraction regardless of the presence of periodontal ligament seen radiographically (*Types 2* and *3*) since elements of the tooth structure or periodontal ligament may contribute as trigger for the hypersensitivity. Diligent home care aimed at plaque control with tooth brushing, oral rinses (chlorhexidine), topical gels (bovine lactoferrin), systemic antibiotics and recommendations for dental diets may aid in the management of symptoms. Doxycycline would be an appropriate for antibiotic of choice, started at the therapeutic dosage of 5mg/kg q12hrs and potentially reduced to a sub-antimicrobial dose of 2mg/kg q12hrs. Aside from being the appropriate spectrum of microflora, doxycycline demonstrates properties of being actively concentrated in secreted in gingival crevicular fluid as well as functioning as an anti-collagenase. Patients not responding to the first attempts at medical management require dental extractions of either partial mouth, or full-mouth extractions. Patients demonstrating a hypersensitivity to normal oral flora may demonstrate limited improvement on broad-spectrum antibiotics however the opportunistic infection may be better managed.

Other medical therapies mentioned in the literature have included other immunomodulatory drugs and chemotherapeutics. In a study by Hennet, feline recombinant interferon omega was shown to be an effective treatment in refractory cases of stomatitis following extraction in which cats were Calici virus positive. Omega interferon has been successful in symptom management when delivered *per os* and is believed to incite a cytokine cascade resulting in immunomodulatory effects in the mucosal tissues. Variations on the administration of Omega interferon have been reported to include submucosal injections and oral gavage. One dosing regimen involves diluting a 10mu vial in 100mL bag of sterile saline and ten fractions of 10mL are created and frozen. One 10mL vial is dispensed at a time where 1mL is administered daily on alternating sides of the mouth. This results in treatment for 100 days. Submucosal (intralesional) administration of omega interferon has subsequently been suggested to be not as effective and more costly. Recent information suggests that autogenous stem cell therapy may offer hope for cats refractory to other treatments for FCGS. In a study by Arzi, 5 of 7 cats demonstrated improvement in oral inflammation following autogenous adipose-derived stem cells that were administered intravenously. Obstacles remain as to the use of this technique in clinical practice, however novel experimental approaches frequently result in the commercialization of the therapy.

More frequently, selective or full mouth extractions are necessary to remove the nidus for inflammation. In general, the more generalized and severe the inflammation, the less likely it is that selective removal of teeth will provide complete resolution of clinical signs. Complete removal of teeth, in this situation, may offer a 60% chance for complete return to a normal mouth without inflammation if there is no evidence of inflammation into surrounding tissues (lateral aspects of the tongue, lip folds, or mucocutaneous junctions.) Because of the extreme invasiveness of full mouth extractions, these cases should be initially managed with a combination of dental cleanings, selective extractions and home care. Because the nidus for the hypersensitivity is never completely removed in these animals, some patients continue to relapse with severe clinical signs. Full mouth extractions both minimize the tooth surface for plaque accumulation as well as remove the physical tooth structure and periodontal ligament structure, which may serve as the overt cause of the hypersensitivity. It does seem well established that the more generalized and severe the disease, the less of chance the mouth will respond completely to full mouth extractions however room for improvement usually results.

In a study by Hung et al., bovine lactoferrin was shown to augment and extend improvements in clinical symptoms, lesion symptoms, quality of life and body weight scores in cats with stomatitis. Lactoferrin is protein rich with approximately 700 amino acids and a strong iron binding affinity. The proven antimicrobial, anti-inflammatory and anti-carcinogenic properties are attributed with reducing interferon-y and IL-2. Applied topically as a spray twice

daily, cats showed a significant long-term improvement of lesions and quality of life scores as compared to the piroxicam-only group. After 4 weeks of either the combination or the just piroxicam, all cats were placed on the combination of lactoferrin and piroxicam. Following the completion of the 12-week study, cats were maintained on twice-daily lactoferrin indefinitely with more than 50% of those cats continuing to demonstrate improvement of clinical signs and improved quality of life. Overall, piroxicam was shown to significantly improve symptom scores acutely, and the addition of lactoferrin augmented improvement of symptoms, lesions, quality of life and patient body weight. Lactoferrin's impact on symptomology is likely associated with "strong antimicrobial effects" and function as an immune modulator and anti-inflammatory agent inhibiting proliferation of peripherally circulating monocytes and down regulation of cytokines.

Carbon dioxide (CO_2) laser treatment has been suggested as a treatment for refractory cases of stomatitis following full mouth extractions. Laser ablation of affected tissue results in reorganization and scar tissue formation, which is believed to be associated with less discomfort. Ablation of the proliferative and friable tissue found in the palatoglossal arches is also believed to remove a source of tissue riddled with deeply seeded bacteria which contribute as a trigger for the immune response.

Use of diets or supplements high in omega-3 fatty acids have been proposed to aid in the modulation of inflammation associated with stomatitis. Anecdotal reports have suggested that omega-3 fatty acids may affect platelet function and result in additional hemorrhage at the time of extractions. One study looking at omega-3: omega-6 ratios showed decreased pro-inflammatory cytokines in serum however there was no noticeable improvement in the health of the oral tissues during the four-week period of the study.

Extended medical management should only include immunosuppressive doses of steroids if absolutely necessary. Oral dosing of prednisolone suspensions offers the best opportunity to titrate the dose and minimize side effects. Stomatitis patients frequently show a favorable improvement in clinical signs and manifestations from oral administration of doxycycline. Doxycycline should be administered as a suspension and can begin at 5mg/kg twice daily. Aside from bactericidal/bacteriostatic properties of this antibiotic, it also demonstrates anti-collagenase properties, blocks matrix metalloproteinase (MMPs) and has been shone to concentrate in the crevicular fluid. Some cats may benefit from this medication lifelong with the goal that the titrated maintenance dose is sub antimicrobial.

As an adjunct, and ideally a replacement for steroid therapy, cyclosporine has shown promise both anecdotally and in the literature for management of refractory cases. To date the best responses to treatment have been centered on removing the likely inflammatory trigger (oral bacteria or tooth itself) or modulating the immune system. In one study by Lommer, refractory cases having received partial-mouth or full-mouth extractions were placed on cyclosporine at 2.5 mg/kg q12hrs or placebo. Six weeks following initiation of treatment, >50% improvement was noted in cats with stomatitis receiving the treatment. Further analysis suggests that achieving a serum cyclosporine level >300ng/mL showed an improvement in stomatitis symptoms in 72% of patients. Despite being more expensive, use of cyclosporine for the management of refractory cases offers symptomatic management without steroids' side effects.

Summary

All indications, both from histologic and response to treatment perspectives point to FCGS occurring as a result of an antigenic trigger. While the true etiology of the condition remains elusive, new information is constantly being unearthed. Without a silver bullet treatment for the condition, current recommendations still hold true to the stepwise process of: ruling out comorbid disease states, dental cleaning, biopsy the mouth to rule out neoplasia, and first attempting home care and non-invasive medical management (doxycycline therapy, topical medicaments) before resorting to extractions. If, following extractions there is failure for improvement in patient comfort and tissue health, a variety of other treatment modalities can be pursued including laser ablation, cyclosporine and steroid therapy.

References/Suggested Reading

1. Special Issue Feline Dentistry Part 2. Journal of Feline Medicine and Surgery 2015;17(1)
2. Farcas N, Lommer MJ, Kass PH et al. Dental radiographic findings in cats with chronic gingivostomatitis (2002-2012). J Am Vet Med Assoc 2014;244:339-345
3. Hennet P. Chronic gingivostomatitis in cats: long term follow-up of 30 cases treated by dental extractions. J Vet Dent 1997;14:15-21.
4. Hung YP, Yang YP, Wang HS et al. Bovine lactoferrin and piroxicam as an adjunct treatment for lymphocytic gingivitis stomatitis in cats. Vet J 2014;202:76-82
5. Lommer MJ. Efficacy of cyclosporine for chronic, refractory stomatitis in cats: a randomized, placebo-controlled, double blinded clinical study. J Vet Dent 2013;30(1):8-17
6. Arzi B, Mills-Ko E, Verstraete FJM, et al. Therapeutic Efficacy of Fresh, Autologous Mesenchymal Stem Cells for Severe Refractory Gingivostomatitis in Cats. Stem Cells Translational Medicine, 2016;5(1), 75–86

7. Winer JN, Arzi B, Verstraete FJM. Therapeutic Management of Feline Chronic Gingivostomatitis: A Systematic Review of the Literature. Frontiers in Veterinary Science, 2016;3(Suppl 1), 54.
8. Anderson JG, Peralta S, Kol A, Kass PH, Murphy B. Clinical and histopathologic characterization of canine chronic ulcerative stomatitis. Vet Path. 2017;54(3):511-519.
9. Gracis M, Reiter AM, Ordeix L. Management of selected non-periodontal inflammatory, infectious and reactive conditions. BSAVA Manual of Canine and Feline Dentistry and Oral Surgery, 4th ed. Reiter AM, Gracis M, eds. BSAVA 2018
10. Lee DB, Verstraete FJM, Arzi B. An update on feline chronic gingivostomatitis. Vet Clin Sm Anim 2020: 1-10
11. Peralta S, Carney PC. Feline chronic gingivostomatitis is more prevalent in shared households and its risk correlates with the number of cohabiting cats. *J Fel Med Surg*, 2019;21(12):1165–1171

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Mastering Feline Dental Radiograph Interpretation

Christopher Snyder, DVM, DAVDC

An accurate appreciation for normal radiographic anatomic variation is key to not getting confused when interpreting oral radiographs. In many situations when radiographic peculiarities arise, it is always a safe approach to begin evaluation by comparing the contralateral side. From normal developmental of teeth, to skeletal anatomy, identifying when findings are normal and unusual versus pathologic can be challenging.

Normal Anatomy
Enamel and dentin are comprised of a greater percentage of minerals than bone, so they appear more radiodense. The periodontal ligament is primarily comprised of collagen so it should show as a distinct radiolucent line. The periodontal ligament should be thin, well demarcated, and of consistent width throughout the outline of the tooth. The pulp chamber is located in the center of the tooth root and should be of uniform diameter throughout. Whenever a radiographic abnormality is suspected, radiographic comparison is recommended of the contralateral or comparable tooth. Remember that as the tooth matures, the pulp chamber narrows as secondary dentin is produced. If a widened pulp chamber is identified compared to neighboring or contralateral teeth, chronicity of the lesion is demonstrated. The younger the patient (the wider the pulp chamber) the more profound the difference will be in the amount of secondary dentin laid down in six months. Mature patients can have very little change in pulp chamber diameter from year to year.

Root Development
Normal tooth development includes the eruption of tooth structure with a matured enamel covering. Beneath the enamel is a tooth root predominately comprised of pulp tissue. The pulp is a combination of vascular, connective and nervous tissue. The outer surface of the pulp tissue contacting dentin is lined with odontoblasts. The odontoblasts responsibility is to continue the deposition of dentin throughout the maturation process of the tooth. The deposition of dentin is accelerated in younger patients with appreciable radiographic differences being obvious enough to discern as quickly as every 6 months for the first few years of the patient's life. As dentin is deposited the pulp cavity narrows. Whenever a discrepancy between comparable contralateral or occlusal teeth is noted, teeth with widened pulp chambers should be carefully scrutinized as to their vitality. Radiographically confirmed non-vital teeth are a source of pain and prone to infection. Extraction or endodontic therapy should be elected.

Foramina
The robust blood supply of the oral cavity is made possible by the abundance of neurovascular structures entering and exiting the flat bones of the skull. Sometimes these foramina can be misinterpreted as pathologic changes. Common foramina misinterpreted for pathology include: the incisive foramen, the infraorbital canal, mental foramina and palatine fissures. An easy test to determine the relationship between the radiolucency and neighboring tooth structure is to first compare the contralateral side and if pathology is still expected, consider taking multiple radiographic angles of the tooth in question. Because of the 2-dimensional superimposition of 3-dimensional structures, by changing the angle of radiographic exposure, anatomic structures not associated with the tooth should be noted to move relative to the tooth structure. When periapical pathology is real, no matter how the angle of exposure changes, the relationship between the root structure and the pathology will remain the same.

Retained Deciduous Teeth
The relationship between successional teeth and their deciduous precursors is such that permanent tooth buds arise from the migration of germinal tissue responsible for forming the deciduous tooth. This means that disruption in this process can result in the normal development of a deciduous tooth without the permanent counterpart. Comparatively, if a deciduous tooth never develops, but should be present, then the permanent counterpart will not be present. Occasionally it can be noted that the deciduous tooth is present without the permanent counterpart. Frequently these teeth look smaller than the neighboring permanent teeth. Radiographically, retained deciduous teeth will have a more developed pulp chamber (they have been developing longer than the newly erupted permanent teeth) will be less radiodense (nature didn't intend these teeth to last the entire life of the patient) and may have smaller roots. The presence of unexfoliated deciduous teeth in itself is not a problem. The risk/benefit of maintaining the tooth for its functionality typically outweighs the risk of this less robust tooth fracturing. In situations where the tooth is less functional, and clients elect for a predictable outcome, extraction can be performed.

Root Dilaceration and Accessory Roots
Both root dilaceration and accessory tooth roots create complications during extraction. Root dilaceration refers to the presence of curved roots. This is most commonly noted in mandibular roots of small breed dogs and is rarely

appreciated in cats. It has been repeatedly reported that the genetic control of the size of the bones of the mandible does not simultaneously govern the size tooth development in dogs. As breeds have been selectively bred for traits such as body size, this has resulted in the flat bones of the skull developing into such sizes that are too small relative to the size of developing teeth. The roots' attempt to develop in this undersized bone creates curving or hooking of tooth roots in effort to stay anchored in bone. Dilaceration of the root itself doesn't warrant intervention however it should be a strong consideration in how to approach and plan surgical extractions when these teeth do warrant extraction. Fracturing roots off, or worse yet, fracturing the mandible are the major areas of concern when treating these teeth which is more a concern for canine teeth in cats.

Accessory roots are also a developmental abnormality that require serious consideration when planning extractions. Whenever teeth develop additional roots, more than normal, decisions about where/how to section the tooth and how much alveolar bone should be removed needs to be evaluated. The presence of accessory roots in itself is not a reason for intervention and is most commonly appreciated in cats located at the maxillary third premolar location.

Root Resorption and Ankylosis

Presence of a periodontal ligament reassures the practitioner that a soft tissue separation exists between the tooth an alveolar bone which will serve as some "wiggle room" for placement and action of the dental elevator. The main cause for root resorption is some source of inflammation. Instances where resorption has occurred, but a periodontal ligament remains visible may demonstrate the tooth is weakened and may fracture during elevation. Instances of root resorption with ankylosis (bony fusion between cementum and alveolar bone) should prepare the veterinarian for a more complicated extraction that will likely take longer. I always encourage veterinarians to feel comfortable estimating a higher cost for clients when extractions are expected to be difficult. It has been shown that in cats with evidence of feline chronic gingivostomatitis there was increased prevalence of horizontal bone loss, external inflammatory root resorption and retained root fragments.

Types of Feline Tooth Resorption

Tooth resorption is a process commonly seen in all cats- from feral, to large wild cats to domesticated cats. Radiographic evaluation of the affected teeth is necessary to guide appropriate treatment recommendations. Since the process is a mixed destructive and productive condition, loss or involvement of the tooth crown may or may not be indicative of the extent of root involvement. Type I tooth resorption is defined as a tooth undergoing resorption whereas the root structure and periodontal ligament are clearly defined. Teeth undergoing Type I resorption are treated with extraction since leaving remaining root structure behind to undergo replacement resorption is believed to be require inflammatory mediators which could contribute to discomfort. Type II resorption is defined as a tooth undergoing resorption whereas the periodontal ligament is no longer visible, indicative of replacement resorption taking place converting root structure to bone-like material. Crown amputation of these teeth are considered an appropriate treatment option as long as other radiographic signs of tooth non-vitality do not exist. Roots having already undergone resorption are believed to have undergone replacement resorption and the act of trying to extract these difficult teeth is felt to be more invasive and painful than helpful. Type III resorption is defined as a multi-rooted tooth with different roots undergoing different types of tooth resorption. In a two rooted tooth undergoing Type III resorption, one root will show evidence of the periodontal ligament being present while the other root demonstrates lack of radiographic evidence of periodontal ligament presence and therefore undergoing Type II replacement resorption. The root with the periodontal ligament present should be extracted while the root undergone replacement resorption should be crown amputated.

Pulp Chamber Abnormalities

Occasionally radiographic evaluation of a tooth may demonstrate various abnormalities of the pulp chamber. Pulp chambers can be noted to be too large (indicative of tooth non-vitality and arrested dentin production), too small (pulp canal obliteration and accelerated dentin production may occur as a result of chronic inflammation or pulpitis) or contain mineralized material. Pulp stones are sometimes incidental findings in a pulp chamber. While pulp stones have very little clinical significance, unless root canal therapy was to be attempted around these mineralizations, these radiodensities are also believed to be the result of pulpal inflammation and those teeth should be monitored with serial radiographs.Internal root resorption can sometimes also be found on radiographic evaluation. Odontoclastic differentiation within the pulp chamber can result dentin resorption within the pulp cavity. These lesions should be differentiated from external root resorption by comparing multiple oblique angles of the same tooth. If the resorbing area does not move from the central location within the canal system, internal resorption is confirmed. External root resorption will result in the resorbing area being cast to the edge of the tooth root on oblique views.

Positioning for Feline Radiographs

Maxillary fourth premolar teeth are particularly challenging to image in cats due to superimposition of the zygomatic arch. This superimposition can be overcome by using the *Extraoral Technique* of laying the sensor on the table,

against the maxilla and outside the cat's mouth. By exposing the film through the cat's mouth propped open, an image is created that removes the zygomatic arch and more clearly depicts the cheek teeth. *Reminder*: using this technique creates "backwards images" (right side looks like the left.) This occurs because the convention of labial mounting is based on the sensor being in the mouth and radiation originating from extraoral. Remember to relabel these images so people don't get confused!

Prevalence of Cone Beam Computed Tomography (CBCT)

The advent and popularity of CBCT has sparked fierce debate over whether CBCT can effectively replace digital dental radiography. One CBCT study compared conventional intraoral radiography for the identification and evaluation of normal anatomic structures in cats and showed that CBCT was better suited for identification for most anatomic landmarks than radiography. In another study by the same authors, when comparing CBCT to intraoral radiographs to evaluate for 14 categories of pathology, CBCT was found to be more sensitive than radiography when the combination of three digital reconstructive/reformatting techniques were used. Inherent limitations to the replacement of intraoral radiography by CBCT includes: capital equipment costs, operator-specific understanding of software and interpretation as well as limitations for interoperative use of CBCT imaging during procedures.

Post-Procedural Radiographs

There are many circumstances where dental radiographs following extraction are helpful and provide the practitioner with reassurance that the job is complete. Post extraction radiographs are recommended in the 2019 AAHA Dental Guidelines in all cases. Gaining confidence is gross appearance of root structures after extraction and being able to compare them to pre/post operative films helps to build confidence. Post extraction radiographs may also be beneficial for sharing with clients at discharge to help justify procedural cost and objectify the pathology and the treatment. Printed dental radiographs provide the client with tangible information that can sometimes soothe concerns over client-perceived feelings that "unneeded procedures" were performed (you know, those clients who say their animal's mouth isn't painful but your exam and radiographs show otherwise!)

Occasionally you may have patients who have received advanced dental procedures (root canal, vital pulp therapy/pulp capping.) Dental radiographs should always be taken of these teeth out of convenience whenever the cat is anesthetized to monitor success of the advanced dental treatment. Comparing immediate post treatment radiographs to present day films are usually necessary to comment on the success of the procedure. Be sure to share these films with whoever performed the original procedure and ask to be shown how to evaluate success.

References

1. Atlas of Dental Radiography in Dogs and Cats. Authors: Gregg DuPont and Linda DeBowes 2008
2. Veterinary Dentistry: Principles and Practice. Robert Wiggs and Heidi Lobprise. 1997
3. To see an objective, independent evaluation of multiple image sensors and associated images, visit www.vetdentalrad.com. A free CD with sample images can be requested which may help determine which system is right for your practice.
4. Farcas N, Lommer MJ, Kass PH, Verstraete FJ. Dental radiographic findings in cats with chronic gingivostomatitis (2002–2012). Journal of the American Veterinary Medical Association. 2014;244(3):339-45.
5. Peralta S, Verstraete FJ, Kass PH. Radiographic evaluation of the types of tooth resorption in dogs. American journal of veterinary research. 2010;71(7):784-93.
6. Lemmons M. Clinical feline dental radiography. The Veterinary clinics of North America. Small animal practice. 2013;43(3):533-54.
7. Harvey CE, Orsini P, McLahan C, Schuster C. Mapping of the radiographic central point of feline dental resorptive lesions. Journal of veterinary dentistry. 2004;21(1):15-21.
8. Heney CM, Arzi B, Kass PH, Hatcher DC, Verstraete FJ. The Diagnostic Yield of Dental Radiography and Cone-Beam Computed Tomography for the Identification of Dentoalveolar Lesions in Cats. Frontiers in veterinary science. 2019;6.
9. Heney CM, Arzi B, Kass PH, Hatcher DC, Verstraete FJ. Diagnostic yield of dental radiography and cone-beam computed tomography for the identification of anatomic structures in cats. Frontiers in veterinary science. 2019;6.

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Gastroesophageal Reflux: An Under-Recognized Source of Pain

Christopher Byers, DVM, DACVECC, DACVIM (SAIM), CVJ

Background Information
At its simplest, the esophagus is hollow distensible tube approximately 20 cm in length. The wall has four layers (from exterior to interior): adventitia, muscularis layer, submucosa, and mucosa. The majority of the feline esophagus is composed of striated muscle, but the caudal third contains smooth muscle. The esophagus is innervated by both somatic and autonomic branches of the vagus nerve. The former control the cranial portion of the feline esophagus (including the upper esophageal sphincter) while the latter controls the caudal portion of the feline esophagus (including the lower esophageal sphincter).

The process of swallowing is a multistep process. When a bolus of food enters the caudal pharynx, afferent fibers send sensory transmissions to the brain. Subsequently, breathing is temporarily inhibited, and primary peristalsis is stimulated. Secondary peristalsis is triggered by esophageal distension by the food bolus. As the food bolus travels caudally in the esophagus, transmission of sensory information elicits relaxation of the lower esophageal sphincter to allow food to pass appropriately from the esophagus to the stomach.

Gastroesophageal reflux (GER) is defined as one of the following:
1. Decrease in esophageal pH <4 for more than 30 seconds
2. Increase in esophageal pH >7.5 for more than 30 seconds
3. Change in esophageal impedance for more than 30 seconds

Reflux Protection
The upper esophageal sphincter (UES) and lower esophageal sphincter (LES) are normal anatomical barriers that protect the esophageal mucosa. The UES is formed by the cricopharyngeal and thyropharyngeus muscles, and the LES is ~1.4 cm long at the level of diaphragm. Normal LES tone in adult cats is 58 +/- 17 mmHg (Reynold *et al*, 1984), and kittens have lower pressures (Hillemeier *et al*, 1985).

The esophageal mucosa is composed of stratified squamous epithelia and mucous glands. The former has a high rate of turnover. Saliva is alkaline, and thus may counteract acidic reflux. Esophageal contents are typically readily propelled into the stomach via peristalsis. A mucosal fold/shelf on the gastric side of LES has a functional valve-like effect.

Anesthesia
Anesthesia induction induces relaxation of the LES, thus increasing the risk of gastroesophageal reflux. Morphine is associated with a dose-dependent increase in the risk of gastroesophageal reflux during the subsequent anesthetic. Propofol administration to feline patients is associated with a higher incidence of gastroesophageal reflux compared to thiopental administration There is apparently no difference in reflux rate among halothane, isoflurane, or sevoflurane. In some species, administration of intravenous atropine has been seen to be associated with the onset of gastroesophageal reflux. A previous study determined the effects of intramuscular meperidine/promethazine/chlorpromazine (MPC), oral midazolam, and oral chloral hydrate on esophageal sphincter function in 25 cats (Croffie *et al*, 1999). They measured UES and LES pressures initially without sedation and then following sedation with each sedative. All three sedatives significantly decreased both UES and LES pressures compared to the control.

Assessment
Gastroesophageal reflux is traditionally clinically silent. For example, anesthesia-related reflux events go unnoticed unless a large volume of gastric content is refluxed, manifesting as refluxate dripping from the mouth and/or nose and pooling underneath the head. Therefore, diagnosing GER can be challenging and requires capsules that transmit esophageal pH, pH probes, and/or impedance probes.

Esophageal pH monitoring is typically performed with esophageal or trans-nasal catheters/probes. The catheter-free Bravo™ Calibration-Free Reflux Testing System (Medtronic) is a catheter-free system used frequently in humans and has been executed in both cats and dogs. This system uses a small capsule (Bravo™ Reflux Capsule) attached to the wall of the esophagus that transmits data to a receiver (Bravo™ Reflux Recorder) worn by a patient. Data are then downloaded for analysis. The main disadvantage of the Bravo™ Calibration-Free Reflux Testing System is it only measures esophageal pH; no impedance data is recorded.

Impedance techniques are based on measurements of the electrical impedance between closely arranged electrodes mounted on a thin intraluminal probe. Impedance is inversely proportional to the electrical conductivity of the luminal contents and the cross-sectional area between the two electrodes. Air has low conductivity and causes an increase in impedance, whereas swallowed or refluxed material has a high conductivity and causes a decrease in impedance. Changes in impedance allow the detection of fluid in the esophagus irrespective of the pH of that fluid.

Determining the cause of a patient's reflux is further challenging. A thorough patient evaluation has three major steps, particularly:

1. History review, including recent drug administration and sedation/anesthesia events
2. Physical examination
3. Diagnostic testing

Diagnostic tests that may be appropriate for patients with suspected or confirmed gastroesophageal reflux are:

- Thoracic radiography – to screen for aspiration pneumonia/pneumonitis, mediastinal masses, megaesophagus
- Videofluoroscopy – to screen for swallowing disorders and hiatal hernia
- Esophagoscopy – to evaluate for erosions/ulcers, hemorrhage, LES dilation, strictures, masses
- AChR antibody – to screen for myasthenia gravis
- Esophageal manometry & pH/impedance testing
- Gastrin concentration
- Electrodiagnostics & muscle/nerve biopsies – to help screen for myopathies and neuropathies
- Lead level
- Antinuclear antibody level – to screen for systemic lupus erythematosus
- Thyroid profile – to screen for hypothyroidism (rare in cats)
- ACTH stimulation test – to screen for hypoadrenocorticism (rare in cats)

Treatment

Pharmacological interventions for GER include:

- Antacids
- Prokinetics
- Medications enhance LES tone
- Medications to prevent LES relaxation
- Cytoprotection

Previous studies (e.g.: Garcia *et al*, 2017; Sutalo *et al*, 2015) showed omeprazole (1.1-1.3 mg/kg q12 hr) was superior to other antacids for increasing gastric and esophageal pH. Cisapride (2.5 mg PO q12 hr; 15-30 minutes prior to feeding) may stimulate the smooth muscle in the caudal third of the feline esophagus (Washabau *et al*, 1997), and is considered superior to metoclopramide. When using metoclopramide, high doses (0.5 mg/kg q6-8 hr PO, SC, IM) and constant rate infusions (0.1 mg/kg/hr IV CRI) are recommended. Erythromycin (0.5-1.0 mg/kg PO q8 hr) may be effective as it mimics the effect of both motilin and 5-hydroxytryptophan type 3 ($5HT_3$), enhances gastric emptying, and stimulates migrating motility complexes and antegrade peristalsis. This medication also increases lower esophageal pressure. Ranitidine (2.5 mg/kg IV slowly q12 hr; 3.5 mg/kg PO q12 hr) may stimulate gastrointestinal mobility by inhibiting acetylcholinesterase activity at muscarinic receptors and increase LES tone. Sucralfate (100-250 mg PO q6-8 hr) may have some cytoprotective effects via stimulation of prostaglandin E_2 and I_2; it may also bind to intact mucosa to form a protective layer. Adequate multimodal analgesia and nutritional support should be provided.

While medical treatments aim to decrease refluxate acidity, they do little to prevent reflux of gastric contents. Anti-reflux surgery in humans is performed both laparoscopically and endoscopically to improve esophageal barrier pressure through a process called fundoplication. Endoscopic interventions currently available in humans are:

- Intraluminal valvuloplasty / transoral incisionless fundoplication (TIF) – Medigus Ultrasonic Surgical Endostapler (MUSE™)
- Radiofrequency therapy – Stretta®
- Injection of foreign material – polymethyl-methyacrylate (Plexiglas™), hydrogel (Gatekeeper®), ethylene vinyl alcohol copolymer (Enteryx®)

While these interventions are routinely employed for people with gastroesophageal reflux disease (GERD), studies have not yet been performed in cats. With proper investigation, these minimally invasive procedures may prove to be helpful in our feline patients.

References
Available upon request

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Nutrition for the Hospitalized Patient

Christopher G. Byers, DVM, DACVECC, DACVIM (SAIM), CVJ

Normal Intestinal Barrier

The intestinal barrier is composed of a monolayer of epithelial cells and displays a number of specialized protective adaptions, including tight junctions, secretions that coat the apical epithelial surface, commensal gastrointestinal bacteria, and a local immune system (gut-associated lymphoid tissue / GALT). The intestinal epithelium is considered the first line of defense for the intestinal barrier. Tight junctions seal the paracellular spaces. Secretions prevent direct access by microorganisms to the intestinal mucosa. Specifically, goblet cells secrete mucus at the epithelial surface, and Paneth cells secrete microbicidal alpha-defensins, lysozyme and cathelicidins upon exposure to bacterial antigens. Normal gastrointestinal microbiota helps the patient digest cellulose, salvage energy, and synthesize vitamin K. Anaerobes, the most abundant bacteria in the gastrointestinal tract (GIT), compete with potential pathogens for nutrients and mucosal attachment sites. The GALT is the largest lymphoid system in the body, composed of three compartments: intra-epithelial lymphocytes, lamina propria (containing solitary lymphoid follicles and Peyer's patches) and mesenteric lymph nodes. The majority of lymphocytes within Peyer's patches are B-cells that can form immunoglobin A (IgA) that is apically secreted to decreased adherence of pathogens.

Sequelae of Malnutrition

Malnutrition is defined as any nutritional disorder resulting in inadequate or unbalanced nutrients. Undernutrition and overnutrition are the two forms of malnutrition, although malnutrition and undernutrition are often used interchangeably. One must recognize the difference between simple (uncomplicated) starvation and stressed (hypermetabolic) starvation. Simple starvation occurs in healthy animals that have experienced an acute disruption of caloric intake. In affected patients, glycogen stores serve as the primary source of energy; these stores are rapidly depleted, and a metabolic shift to the preferential use of stored adipose occurs. During stressed starvation, a pro-inflammatory milieu induces a catabolic state, and energy predominantly comes from accelerated proteolysis; adipose is preserved in the face of lean muscle tissue loss. Cardiac arrest, pulmonary failure and immunosuppression occur when more than 25% of amino acids come from skeletal muscle and organ tissue.

Table #1: Major Differences Between Simple & Stressed Starvation

	Simple Starvation	Stressed Starvation
Energy Expenditure	Decreased	Increased
Fuel Source	Glucose / Fat	Protein
Gluconeogenesis	1+	3+
Protein synthesis	Decreased	Markedly Decreased
Catabolism	Not occurring	3+
Amino acid oxidation	+/-	3+
Ureagenesis	+/-	2+
Ketosis	+/-	+
Responsiveness	3+	1+
Rate of malnutrition	1+	3+

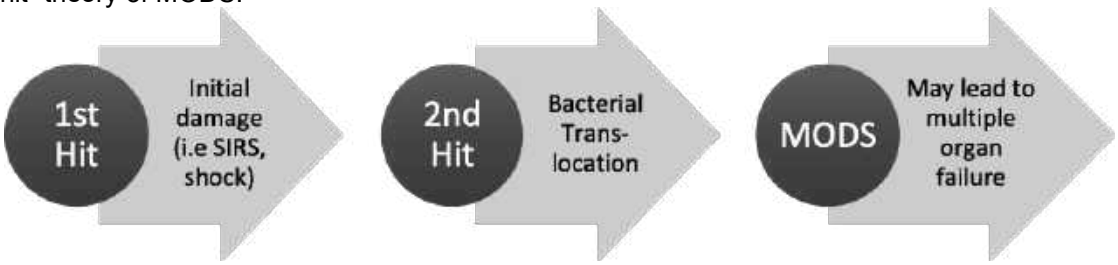
Adapted from Zoran DL, ACVIM Forum 2003.

Inadequate enteral nutrition induces enterocyte atrophy and cholestasis with subsequent down regulation of gastrointestinal and pancreatic enzymes, as well as reduced small intestinal absorption in as little as 48 hours. Major complications of malnutrition may be categorized as decreased tissue synthesis and repair, decreased immunocompetence, and altered intermediary drug metabolism.

Multi-Organ Dysfunction Syndrome

A patient's primary condition (i.e. trauma, shock, SIRS) can readily induce splanchnic hypoperfusion; this hypoperfusion is often called the "first hit" of the "two-hit" theory of multi-organ dysfunction syndrome (MODS). Tissue oxygen delivery (DO_2) is reduced by hypoperfusion, resulting in decreased production of adenosine triphosphate (ATP). Tissue ischemia induces the formation of oxygen free radicals and pro-inflammatory cytokines that contribute to hemodynamic derangements and tissue injury. Bacterial endotoxin, infections, enzymes and environmental factors readily cause GIT mucosal immune dysregulation. Specifically, neutrophils and macrophages are activated as part of the "first hit." The pro-inflammatory cytokines tumor necrosis factor (TNF-alpha) and interleukin-6 (IL-6) induce the production of IL-1-beta that subsequently binds to IL-1 receptors located near the tight junction complexes within the GIT. This binding activates a potent inflammatory cascade propagated by nuclear factor kappa-beta (NF-KB) that facilitates the synthesis of myosin L-chain (MLC) kinase to degrade the cytoskeletal network and tight junction

proteins. These changes are exacerbated by inadequate nutritional intake that leads to enterocyte atrophy caused by a lack of luminal nutrients, GALT dysfunction and altered permeability of the GIT. Subsequently bacteria and/or bacterial toxins translocate to induce systemic inflammation and organ dysfunction, thus serving as the “second hit” of the “two hit” theory of MODS.



Common manifestations of MODS in dogs and cats include:

- Gastrointestinal – paralytic ileus, ulceration
- Cardiopulmonary – dysrhythmias, hypoxemia, hypoventilation
- Coagulation – prolonged partial thromboblastin time, prolonged prothrombin time, thrombocytopenia, thrombocytopathia
- Hepatic, Renal – hyperbilirubinemia, elevated aminotransferases, azotemia, proteinuria
- Vascular – vasodilation, hypotension

Implementing Nutritional Support

As a profession, we do not consistently provide adequate nutrition for hospitalized patients, particularly the critically ill. Thus, this population commonly becomes deficient in both protein and calories, further increasing their risk for developing systemic inflammatory response syndrome (SIRS) and MODS. In contrast Michel et al showed patients with temporary supplemental feeding tubes placed during hospitalization tended to receive their feeding prescription. A patient should not be allowed to enter a negative energy balance unless the owner imposes restrictions that prevent the recommended nutritional support.

Patients should be thoroughly evaluated prior to initiating nutritional therapy. Several risk factors that may indicate a predisposition to malnutrition are more than 5 days of hyporexia/anorexia, serious underlying disease, and marked protein losses. Body condition scores (BCSs) are clinically useful for nutritionally evaluating patients, as they are not influenced by fluid shifts that effect body weight. Commonly accepted indicators of malnutrition include poor hair quality, muscle wasting, unintentional weight loss (>10%), diminished wound healing, hypoalbuminemia, lymphopenia, and secondary coagulopathy.

Enteral Support

Feeding should be provided as soon as possible to every patient for whom feeding is not contraindicated. There are few reasons nutritional intervention should be withheld, including dehydration, hypotension, hypothermia, electrolyte imbalances, glucose abnormalities, acid-base derangements, inability to protect airway, and a need for sedation/anesthesia. Any derangement should be corrected expeditiously, and then nutritional support should be initiated immediately. Patients unable to protect their airway should not be fed orally but should be supported via a temporary supplemental feeding tube and/or parenteral nutrition. Recognizing most critically ill animals have been hyporexic or anorexic prior to hospitalization and small intestinal villous atrophy may occur within 24 hours, this patient population should be fed as soon as they are hemodynamically stable to help counter the catabolic stress of illness/disease. If a patient requires sedation or anesthesia for a diagnostic test and/or therapeutic procedure, one should consider concurrently placing a temporary supplemental feeding tube. There is mounting evidence early enteral nutrition (EN) in patients with major illnesses is well tolerated and positively affects patient outcome. Klaus et al demonstrated early EN was well tolerated in feline patients with severe pancreatitis. Klaus et al documented similar results in cats with suspected acute pancreatitis.

The site of feeding within the GIT is dependent on a variety of patient factors, and whenever possible, one should adhere to the adage, “if the gut works, use it!” However, patients with a completely dysfunctional GIT may benefit from parenteral (partial vs. total) nutrition (sole therapy vs. concurrently with EN). Of course, per os support is ideal, but many critically ill patients are not able or are unwilling to ingest adequate calories voluntarily. Thus, temporary supplemental feeding tubes should be strongly advocated for patients with a functional or partially functional GIT. For those with a functional upper GIT who will likely require nutritional support for less than 3-5 days, one should consider placing a nasogastric (NG) or esophagostomy (E) tube. If enteral support will be needed for more than 3-5 days, one should consider placing a gastrostomy (G) tube or percutaneous endoscopic gastrostomy (PEG) tube. For patients with a dysfunctional upper GIT, a jejunostomy (J) tube is most appropriate. Feeding tubes are typically very

well tolerated and may truly be life-saving interventions. Patients with temporary feeding tubes require frequent monitoring for a few but potentially serious complications, including:

- Mechanical – obstruction, inadvertent removal
- Gastrointestinal – vomiting, diarrhea, regurgitation, abdominal discomfort secondary to cramping, aspiration pneumonitis
- Metabolic – refeeding syndrome, CHF, hyperglycemia

A patient's daily resting energy requirement (RER) may be calculated using the following equation: kcal/day = 70 x (body weight in kilograms)$^{0.75}$. Frequent patient reassessment is required, as energy requirements may be as high as 2RER in the critically ill. Common nutritional goals in critically cats include:

- Protein / nitrogen: 6-8 g/100 kcal/day (normal); 4 g/100 kcal/day (hepatic encephalopathy)
- Carbohydrate: 5-8 g/100 kcal/day
- Fat: 2-3 g/kg/day

Microenteral nutrition (MEN) is defined as the delivery of small volumes of water, electrolytes and easily absorbed nutrients directly to the GIT to maintain mucosal integrity. It is commonly used in critically ill patients who are not able to tolerate full enteral nutrition and is initially recommended for all patients with GIT dysfunction. Goals of MEN include maintenance of gastrointestinal mucosal blood flow to reduce incidence of GIT ulceration, prevent down regulation of gastrointestinal and pancreatic enzymes, reduce cholestasis, and to help preserve GALT. Microenteral feeding is commonly achieved via constant rate infusion (CRI) through temporary supplemental feedings. Isotonic crystalloid solutions are readily available and can easily be formulated to contain 5-20% dextrose. Pre-made electrolyte solutions are also commercially available alternatives. The initial infusion rate is 0.25-0.5 mL/kg/hr and should be gradually increased to 1-2 mL/kg/hr over a 24-hour period for tolerating therapy.

Once MEN infusion rates reach 1-2 mL/kg/hr, one should attempt to transition a patient to a gruel or liquid diet. Gruel and liquid diets may also be administered via CRI, but bolus feedings may also be viable. Campbell JA *et al* demonstrated no difference in tolerability or ability to reach nutritional targets between the two administration methods. Elemental (monomeric) diets are mixtures of amino acids, peptides (di- and tri-) and monosaccharide sugars, but to the author's knowledge there are no currently available monomeric diets specifically developed for use in dogs and cats. Polymeric diets contain polypeptides, proteins and polysaccharides that are digested in the GIT prior to absorption. Infusion rates should be increased 25-30% every 8-12 hours until 100% RER is being delivered, ideally within 48-72 hours of initiating nutritional support. The canine stomach may expand to hold 80-90 mL/kg; the feline stomach may hold 60 mL/kg, but diseased cats often have lower gastric distensibility (20 mL/kg). Enteral fluid volume must be accounted for when determining intravenous fluid requirements for a patient.

Parenteral Support

For patients with a completely dysfunctional GIT, parenteral nutrition (PN), a mixture of amino acids, glucose and lipids, should be used either alone or ideally in conjunction with enteral nutrition to provide energy requirements. Parenteral nutrition is not without complications and has a reputation of causing more harm than good. Devising a PN formulation that optimizes recovery and minimizes complications is currently challenging. Chan et al showed patients receiving enteral nutrition and partial PN survived more than those receiving only partial PN. In contrast Queau *et al* documented most complications accompanying PN did not affect survival. Some believe many of the misconceptions and complications may be due to over-estimation of caloric needs rather than the form of nutritional support. When calculating the number of calories required for a patient, some aim to meet all caloric requirements with lipids and dextrose; they then provide additional amino acids as required by the patient but do not take into account the calories this component provides (~4 kilocalories per gram once metabolized). The belief is an animal not provided with their entire energy requirements in the form of dextrose and lipids will use the provided amino acids for energy rather than protein synthesis. However, there is little evidence to support this hypothesis. Overall there is evidence to show provision of more calories than the estimated RER is associated with the development of hyperglycemia and possibly decreased survival.

The time at which PN should be implemented is currently controversial. Optimal timing of implementing parenteral nutrition (PN) is very controversial at the moment. Casaer *et al* demonstrated enteral support followed by PN within 48 hours of ICU admission was associated with high morbidity and mortality compared to enteral support followed by delayed PN. We do not yet know if such data should be extrapolated to veterinary patients.

References

1. Baldwin K, Bartges J, Buffington T, *et al*. AAHA nutritional assessment guidelines for dogs and cats. J Am Anim Hosp Assoc 2010;46(4):285-96.
2. Brunetto MA, Gomes, MO, Andre MR, *et al*. Effects of nutritional support on hospital outcome in dogs and cats. J Vet Emerg Crit Care 2010;20(2):224-31.

3. Campbell JA, Jutkowitz LA, Santoro KA, *et al*. Continuous versus intermittent delivery of nutrition via nasoenteric feeding tubes in hospitalized canine and feline patients: 91 patients (2002-2007). J Vet Emerg Crit Care 2010;20(2):232-6.
4. Klaus JA, Rudloff E, Kirby R. Nasogastric tube feeding in cats with suspected acute pancreatitis: 55 cases (2001-2006). J Vet Emerg Crit Care 2009;19(4):337-46.
5. Mansfield CS, James FE, Steiner JM, *et al*. A pilot study to assess tolerability of early enteral nutrition via esophagostomy tube feeding in dogs with severe acute pancreatitis. J Vet Intern Med 2011;25(3):419.25.

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Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 1
Phil Padrid, DVM

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Diagnosis & Treatment of Chronic Nasal Disease in Cats: Part 2
Phil Padrid, DVM

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Cat Naps During COHAT: The Complete Plan for the Feline Dental Patient

Mary Berg, BS, RVT, LATG, VTS (Dentistry)

Performing a Complete Oral Health Assessment and Treatment (COHAT) entails much more than removing plaque and calculus from the teeth. Thorough dental cleaning consists of educating the client, an oral examination, charting disease process, pathology and anomalies, radiographs, both supra, and subgingival plaque and calculus removal, hand scaling, polishing, irrigation, and home care instructions.

The 12 Steps:

1. General health examination – including blood work, bite evaluation
2. Oral examination of each tooth under anesthesia
3. Calculus and plaque removal from crowns of teeth
4. Sub-gingival scaling, root planing, and curettage
5. Tooth polishing
6. Irrigation
7. Fluoride Application (controversial)
8. Irrigation
9. Post cleaning examination and x-rays
10. Dental Charting
11. Home care instructions
12. Follow-up appointment – evaluate healing and effectiveness of home care

Education

There are many ways in which to educate the client on the importance of dental health. It is essential to explain the disease progression from the formation of dental plaque to dental calculus or tartar and then gingivitis and to the destruction of the periodontal tissues, including the loss of the bone supporting the tooth and tooth loss.

A picture is worth a thousand words. Visual aids such as posters in the treatment rooms showing the progression of oral disease and the impact on the internal organs can be used to gain the client's interest. Pictures of healthy mouths versus diseased mouths are another useful tool. The use of plastic models that have a healthy side and a diseased side is a hands-on way to show disease. These are all helpful in the educational element of dental procedures.

Preventive Antibiotic Therapy

Questions are often asked about the use of preventive antibiotic therapy in patients who present for a dental cleaning. The main objective of preventive antibiotic therapy is to prevent treatment-induced bacteremia. Bacteremia will typically clear in approximately 20 minutes. The use of preventive antibiotics should only be necessary for patients that are not able to cope with this treatment induced bacteremia. Geriatric or debilitated animals, patients with a pre-existing heart or system disease or immunocompromised patients should receive preventive antibiotic therapy.

Preventive antibiotic therapy will also aid in controlling wound infections. Animals with gross infections (marked swelling, pus formation, fever, lymphadenopathy, and elevated WBC count), or chronic stomatitis may also benefit from receiving antibiotics before treatment. Clinical judgment should be used in the diagnosis of the infection and the use of antibiotic therapy.

The choice of antibiotic and protocol for delivery is controversial. The antibiotic chosen must be active against Gram-positive and Gram-negative aerobes and anaerobes. Just as important as the choice of antibiotic is the timing of delivery. The generally accepted protocol should have antibiotics administered within two hours of the surgery and not continued for more than four hours after the procedure. Also, antibiotics must be delivered at a dose high enough to reach a tissue level of four times higher than the MIC of the causative organisms.

In addition to preventive antibiotic therapy, antiseptics have a role in veterinary dental procedures. Antiseptics help to reduce the number of bacteria in the oral cavity before and during procedures. Chlorhexidine gluconate is the antiseptic of choice for use in animals. A rinse of the oral cavity with an antiseptic before procedures result in a cleaner environment to work in and can reduce bacteremia induced by dental procedures. It will also reduce the number of bacteria that are aerosolized by dental equipment, such as ultrasonic scalers, and benefit the persons

involved in the procedure. Bacteria may still be present in the operatory for up to 12 hours post-treatment. Remember to always protect yourself by wearing eye protection, masks, and gloves.

Oral Examination

An oral examination on a conscious patient is essential but often limited to a visual inspection and digital palpation. This examination includes palpation of the facial bones, zygomatic arch, temporomandibular joint, salivary glands, and lymph nodes. Dental occlusion should also be evaluated by gently retracting the lips to look at the soft tissue, the bite, and the buccal aspects of the teeth.

Once the animal is anesthetized, a thorough oral examination can be completed. All the structures of the oral cavity must be evaluated to include the oropharynx, lips, and cheeks, mucous membranes, hard palate, the floor of the mouth and tongue as well as the teeth. The periodontium (gingiva, periodontal ligament, cementum, and alveolar bone) of each tooth needs to be evaluated. In animals with large amounts of calculus on the teeth, it may be necessary to remove these deposits to access the periodontium accurately. The use of a calculus removal forceps is a recommended method to remove supragingival calculus. Use care when using this instrument to ensure that the gingiva and tooth crown are not damaged.

When evaluating the periodontium, a periodontal probe, a dental explorer, and a dental mirror are used. The following indices should be assessed for each tooth; gingivitis, periodontal probe depth, gingival recession, furcation involvement, mobility, and periodontal attachment levels. Details of these indexes will be covered in other presentations.

Charting and Recording

The information gathered during the oral examination and subsequent treatment need to be recorded. Because periodontal disease is a progressive disease, charting is an essential aid for follow-up visits. A basic dental record consists of written notes, diagnostics, radiographs, and a dental chart. There are numerous types of dental charts available. A dental chart will have a diagram of the oral cavity on which notations can be made, along with either fill in or check off formats to provide a convenient recording. Color coding the different indices will make reading the chart easier. A simplified version of the chart can be made and given to the client, indicating problem areas, treatment, and home care instructions.

Charting should be done in the initial stages of the dental procedure. A final charting completed as a last step in the procedure involves a review of the previously performed diagnostic and periodontal charting. This final charting should include any additional treatment performed.

Dental Radiographs

The most beneficial diagnostic tool in veterinary dentistry is the dental x-ray machine. Even teeth that appear to be healthy may have conditions that are not clinically visible. Studies have shown that almost 42% of pathology in animals' mouth is found by radiography

It is vital to take full survey radiographs of periodontal patients before every professional periodontal treatment.

Supragingival Plaque and Calculus Removal

As stated earlier, gross calculus can be removed by using a calculus removal forceps. Ultrasonic or sonic scalers are useful to remove the remainder of the supragingival calculus deposits. There are three types of ultrasonic scalers available, magnetostrictive stacked, magnetostrictive with Ferrite rod, and piezo, all of which work similarly. The ultrasonic scalers vibrate in the range of 18,000 to 45,000 cycles per second. When appropriately used, the vibration breaks up or pulverizes the calculus on the tooth surface. These instruments can damage the teeth by mechanical etching and thermal injuries if not used properly. Supragingival scaling uses a steady, generous supply of water to aid in the prevention of overheating the tooth along with a high power setting. When using the smaller, periodontal tip designed for subgingival scaling, less water is needed, and the power settings should be decreased.

The instrument should be grasped lightly in a modified pen grasp. The handpiece is balanced on the index or middle finger. The instrument, not the hand, must be allowed to do the work, the hand is merely a guide. The handpiece should be used with a light touch with minimal pressure, keeping the tip moving on the tooth. Stopping in any one area can cause damage.

The side of the broad tip (beavertail) should be used for cleaning and held parallel to the long axis of the tooth. Never hold the tip at a 90˚ angle to the tooth surface as this can damage the tooth and provides less of a cleaning surface, thus being less effective. The ultrasonic scalers can create a tremendous amount of heat. It is important to

only spend a short time (~ 10 seconds or less) on each tooth. If you need more time to remove calculus from a tooth, scale the remaining teeth, and return to the tooth after it has had time to cool off.

In addition to the ultrasonic scalers, sonic and rotary scalers are available. The sonic scaler requires the use of compressed air to operate. It produces less heat, thereby reducing the chance of thermal damage. The sonic scalers are an excellent choice for the removal of supra-gingival calculus; however, their inability to effectively scale sub-gingivally is due to the lack of desirable range of motion. The use of the rotary scaler is controversial. This instrument demands careful use by an experienced and skilled operator. Extreme etching can occur as the six-sided burr rotates at 300,000 rpm. If contact is made with the enamel, a traumatic injury will occur.

Subgingival Calculus Removal
A curette or a specific ultrasonic scaler tip should be used to remove subgingival calculus. Several companies make scaler tips that are specifically designed for this procedure. The removal of this subgingival calculus is vital to the success of the treatment. If not removed, bacteria will continue to destroy the periodontium and further bone loss and eventual tooth loss.

Hand Instrument Technique
Hand scaling of the root to remove subgingival calculus deposits can be done if a perio tip is not available. A curette is used for this procedure and has a sharp side and a rounded side. The sharp side is placed toward the tooth surface and the round side toward the gingival tissue. The curette should adapt to the curvature of the tooth surface. If it does not, the opposite end should be used. The curette is inserted into the pocket with the face, or sharp side, facing the root surface. The instrument is moved over the calculus and positioned so that the cutting surface is under the calculus. A rocking pull stroke is used to remove the calculus from the root surface. This procedure is repeated until all calculus is removed.

Check for Missed Plaque or Calculus
An explorer can be used to check the tooth surface for the remaining calculus. The crown can be inspected for any missed plaque by the application of a disclosing solution or for missed calculus by air drying, which will make the calculus appear chalky white. Disclosing solutions should be applied then gently rinsed with water to observe any remaining plaque or calculus. This technique must be used with care as it may cause staining of the hair around the patient's mouth. It is, however, more reliable than the air-drying technique. A black-light is another option that may be used to detect missed plaque and calculus

Polishing
Polishing with a prophy cup and paste applied with an electrical or air-powered polisher is an important step. This step will remove any missed plaque and smooth out the minute scratches on the tooth surface. When etching occurs, it gives the plaque bacteria more surface area to attach to the tooth. The prophy cup on a low-speed handpiece moves at approximately 3,000 to 8,000 rpm. Disposable prophy cups are available and are inexpensive. The advantage is they don't need to be cleaned after each use.

An inexpensive prophy paste can be made by mixing flour pumice with glycerin. There are many commercially available prophy pastes on the market that are more convenient to use. These prophy pastes range in grit and hardness from fine to extra course.

Irrigation
Irrigation of the mouth following calculus removal and polishing is vital. All pieces of calculus and prophy paste must be removed from the mouth to avoid aspiration upon recovery. The mouth can be irrigated with the air-water syringe or with a spray bottle filled with water or chlorhexidine gluconate. The gingival sulcus should be flushed to remove debris and help oxygenate the intrasucular tissues. Saline, stannous fluoride, or diluted chlorhexidine gluconate (0.12%) can be used. The advantage of chlorhexidine is its ability to adhere to oral tissues and release its agents slowly.
There is some controversy as to whether fluoride is necessary for veterinary dental health.

Home Care Instructions
A client who understands the importance of oral care and is willing to perform the home care to ensure that their pet's mouth heals and remains healthy will be happier. Education will help to develop a strong relationship between client and clinic. Explaining to the client why home care is essential, and demonstrating how to administer the care is critical to gaining compliance.

Handouts can be individualized for the patient is another way of showing the client the importance of dental health. This handout should include a simplified dental chart for making notations, such as probe depth, furcation formation,

or tooth loss. The prescribed treatment plan should be included on this handout so the client can then take it home with them as a reminder of the treatment necessary for their pets.

Conclusion

Complete dental cleanings for a periodontal patient involves many steps. Each step is vital to the success of the procedure. The success of the procedure is not determined when the animal recovers and leaves the hospital. Ensuring compliance of home care instructions and follow up examinations are critical to the overall success.

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Tips & Tricks for Great Dental Radiographs

Mary Berg, BS, RVT, LATG, VTS (Dentistry)

Here are some quick tips for great x-rays every time:

1. You need a diagnostic x-ray – not a perfect x-ray. A diagnostic x-ray includes visualization of 2-3 mm of bone around the apex of the root and the level of the alveolar bone. The crown does not need to be on the x-ray.
2. The entire tooth does not need to be on one view. If both roots are visible but on two separate x-rays, it's okay!
3. Get all the teeth in as few views as possible. This saves time and gives a quick survey of the oral cavity. If more detail is needed, additional views should be obtained.
4. Every patient, every time! Not only will this help you become faster at taking x-rays, but it is also better medicine. Remember, the patients can't tell us where it hurts.
5. Proper positioning of the animal is critical! Sternal recumbency for the maxillary views and dorsal recumbency for the mandibular views. Ensure that the dental arcade is parallel to the table, and the mouth is straight, not tilted in either direction.
6. The sensor (film) should have the teeth on the very edge of the sensor with the remainder of the sensor inside the mouth, and the sensor should be flat or parallel to the table for maxillary views.
7. High and through the eye on the maxilla!
8. The sensor should be placed flat or parallel to the table view for the mandibular teeth.
9. Don't fight the tongue for mandibular views!
10. If the x-ray doesn't show what you want to see, determine if the sensor has moved first before changing your tube head.
11. Ideally, the tooth roots should be the same length in the x-ray as in the mouth. If the roots are too long to increase your angle, they are too short, decrease your angle. Think about the position of the sun and your shadow. It will help you correctly adjust your tube head.
12. ALWAYS x-ray missing teeth and pre and post extractions.
13. Practice makes perfect!!!

Dental radiographs are an essential part of the oral exam. The crown is just the tip of the iceberg. Approximately 42% of dental pathology is found subgingivally. Radiographs will help diagnose pathology that is not visible from the surface, confirm suspect pathology, as well as help, demonstrate the pathology to the client. Survey radiographs can also increase your clinic's revenue.

Ideally, a full survey set of radiographs should be taken on all patients annually. This survey series should have all the teeth in as few x-rays as possible. Radiographs are essential when the following problems are present: periodontal disease, endodontic disease, tooth resorption, draining tracts, trauma, oral masses, dental abnormalities, and pre, intra, and post-surgical evaluations.

Dental radiograph units are relatively inexpensive. You can check with dental supply companies and purchase used units very reasonably. Medical radiograph machines can be used but are inconvenient, and they don't show the detail necessary to make a definitive diagnosis. Dental radiograph units allow for accurate positioning without having to move the patient. They are compact, maneuverable, have limited settings, and less radiation scatter. The settings for kVp and milliamperage are preset, leaving exposure time as the only adjustable setting.

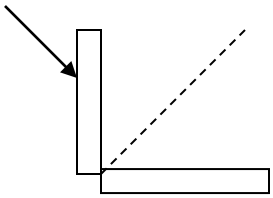
As with all radiation, it is essential to observe radiation safety guidelines. The amount of radiation should be kept to a minimum. When possible, step out of the room, if that isn't possible, stay at least 6 feet away and out of the line of the beam. Always wear your film badge. There is a full range of positioning devices available to help keep the film in place. A gauze 4X4 works very well, are disposable and inexpensive.

Proper patient and sensor positioning will make taking dental x-rays easier. For maxillary views, the patient should be placed in sternal recumbency with the maxillary arch parallel to the table. Place the patient in dorsal recumbency with the mandibular arch parallel to the table for the mandibular views. The sensor should be placed flat in the mouth flat (or parallel to the table) with the cord coming out the front of the mouth for all views.

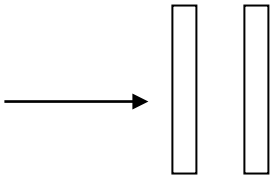
A full radiographic survey will include; anterior maxilla, anterior mandible, posterior maxilla (left & right), posterior mandible (left & right).

There are two intraoral radiograph techniques commonly utilized in veterinary dentistry. The simplest is the parallel technique and is used in the caudal mandible. The parallel technique is only used to obtain a diagnostic radiograph of the mandibular molar if both roots are no visible using the bisecting angle technique. In the parallel technique, place the sensor parallel to the mandible with the beam directed 90-degree angle to the sensor.

The other technique is the bisecting angle. The bisecting angle minimizes distortions of the teeth and is used for the anterior teeth, maxilla, and mandible, the posterior maxilla teeth. In this technique, aim the beam at the imaginary line bisecting the plane of the tooth and the plane of the film.



Bisecting Angle

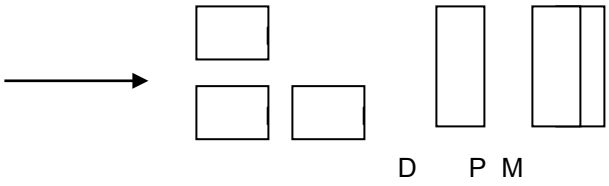


Parallel Technique

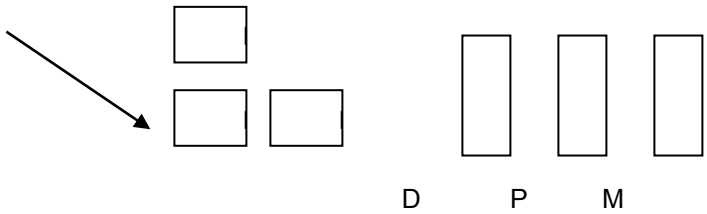
If the beam is not perpendicular to the bisecting angle, the image of the tooth will be distorted. If the angle is too low, it will cause elongation and too high it will cause foreshortening. However, since the bisecting angle technique can be challenging to understand for many individuals, a method that uses the angles on the tube head to assist in positioning is much easier to understand. This technique requires the patient to be correctly positioned as state earlier in sternal or dorsal recumbency. See the Easy Guide to Dental X-ray Positioning.

The maxillary P4 is a three rooted tooth. If you use the bisecting angle technique, the palatal root will be superimposed behind the mesiobuccal root. Using the SLOB rule will result in viewing all three roots. (Same Lingual, Opposite Buccal) The tube head is shifted slightly rostral or caudal to visualize all three roots. If the tube head is moved caudally, the palatal or lingual root will be most caudal on the radiograph. If the tube head is moved rostrally, the lingual root will be the most rostral root on the radiograph. Remember, the tube head pulls the palatal root towards itself. PP = Pulls Palatal

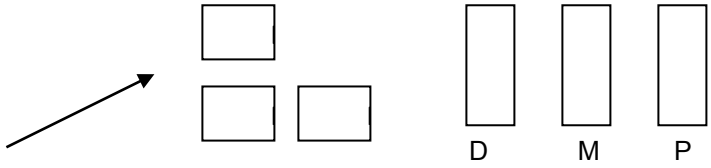
Standard bisecting angle:



SLOB Rule tubehead caudal



SLOB Rule tubehead rostral



Maxillary radiographs may result in the superimposition of the zygomatic arch over the apex of the roots. With the advancement in digital x-ray technology, it is not as crucial that the zygomatic arch avoided as the apexes of the roots can be seen through the arch.

Table 2: Examples of Angles for Dental Radiographs - Feline

Tooth	Tube Head Angle	Comments
Maxilla		
109-106 & 209-206 (Molars & Premolars)	30 -40°	Through the eye
104 & 204 (Canines)	50°	Aim at the medial canthus of the eye
203 -103 (Incisors)	45°	
Mandible		
309-307 & 408-407 (Molars & Premolars)	50-60°	Tongue can be between sensor and teeth
304-404 (Canines and Incisors)	50-60°	
304 & 404 (Canines Isolated)	50-60°	Oblique

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Pain Management & Anesthesia Concerns in Feline Dental Patients

Mary Berg, BS, RVT, LATG, VTS (Dentistry)

Pain management is more than the latest popular terminology. Articles first published in1928 discussed how to perform "dental anesthesia" in dogs. It is an integral part of veterinary dentistry. Many of the procedures performed on animals are painful, and it is our duty as veterinary technicians/nurses to ensure that our patients are as comfortable as possible. Before performing many dental procedures or oral surgery, the delivery of local nerve blocks is an effective way to create preemptive analgesia. Regional nerve blocks should be incorporated into a multimodal plan for pain control.

Definition
The International Association for the Study of Pain defines pain as an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Consequences of Pain
Pain can be pathologic if left untreated. Pain can cause an increased risk of infection, delayed wound healing, reduced food and water intake; inability to move, altered sleep patterns; and altered behavior patterns. Some or all of these consequences may prolong convalescence and may predispose the patient to an adverse outcome.

Strategies for Pain Management
Pain should be controlled at each of the sites along the pain pathway. Different modalities of treatment can be combined, or used alone, to produce the desired effect in a specific area. Local and regional anesthetics and alpha-2 agonists will block the transmission of pain. Anti-inflammatory drugs work at the site of transduction and modulate the pain response. Opioids modulate pain perception, both centrally and locally.
Preventive analgesia protocols will decrease the total volume of required analgesics. If pain control does not start until after a patient is showing discomfort, a higher level of drugs will be needed to stop this increased sensitivity to noxious stimuli in the central nervous system. This condition is also known as "wind-up." A multimodal approach to pain management before, during, and after a procedure will reduce "wind-up" and result in a more comfortable patient. Combining pain medications and sedatives in the pre-anesthetic protocol will decrease the need for a high concentration of inhalation anesthetics. Providing anti-inflammatory drugs at the beginning or end of a procedure will reduce the local pain response due to tissue manipulation. Instructing clients to follow the prescribed dosing schedule of postoperative oral medication will help to eliminate the chance of overdosing a patient.

Pre-anesthetic Drugs:
Many drugs aid in pre-anesthetic, systemic pain control. These include hydromorphone, butorphanol, morphine, and medetomidine. All of these drugs work differently in the brain. Many factors play a role in determining the correct drugs, including the patient's condition, cost, and the type of procedure: full mouth extractions are more painful than a single tooth extraction. It is not within the scope of this paper to cover each of the possible pre-anesthetic drug combinations. Every patient must be thoroughly evaluated to determine the best choice for that individual.

During the Procedure
Regional and local anesthetic blocks are used in dentistry to control pain at the site of the procedure. In the past, the drugs of choice for this procedure were lidocaine hydrochloride 2% -combined with bupivacaine 0.5%. Lidocaine provides a quick onset of action of about two minutes but has a duration of only one to two hours. Bupivacaine has a delayed onset of four to eight minutes, but has a duration of four to ten hours. Studies have shown that the combination of these drugs **decreases** the duration of the block. Bupivacaine should be used alone. The delayed onset can be negated by the appropriate timing of the injection after a thorough oral examination followed by the administration of the blocks before performing painful procedures. The patient must be monitored very closely during the administration of a regional nerve block because bupivacaine can cause cardiac depression, seizures, and respiratory distress if given at too high a dose, or if administered intravenously. The recommended total dosing for bupivacaine is 2.0mg/kg. The total volume per injection site is 0.1 to 0.15ml for cats. If more than one region of the mouth is to be blocked, caution must be taken not to exceed the maximum total dosage.

The duration of the block can be increased by the addition of an opioid, such as buprenorphine, to the bupivacaine. The addition of a 0.003mg/kg to the dose of bupivacaine is all that is needed to extend the length of the block. While no studies in cats have been published, the addition of dexmedetomidine combined with the local anesthetic agents has been shown to have a significantly prolonged action in humans and rats. Dexmedetomidine enhances the anesthetic action, via the alpha-2 A receptors. A suggested dexmedetomidine dose of 1-2 mcg/kg, added to the

anesthetic drug while monitoring the patient's heart rate, ECG, blood pressure, and SpO_2, and providing supplementary oxygen, is recommended.

Drug	Feline Dose
Bupivacaine	Up to 2 mg/kg total dose
Buprenorphine	~0.003 mg/kg combined with an anesthetic agent. Mix immediately before use.
Dexmedetomidine	1-2 mcg/kg combined with an anesthetic agent.

Alternatives to Bupivacaine
Bupivacaine is the most commonly used analgesic agents for dental nerve blocks. Bupivacaine has recently been difficult to obtain due to backorder issues. There are highly effective alternatives being used in many dental practices. Ropivacaine 0.5% is being used at the same dosages as bupivacaine with success. Individuals have reported that combining ropivacaine with buprenorphine at 0.003 mg/kg has worked well as a replacement analgesic.

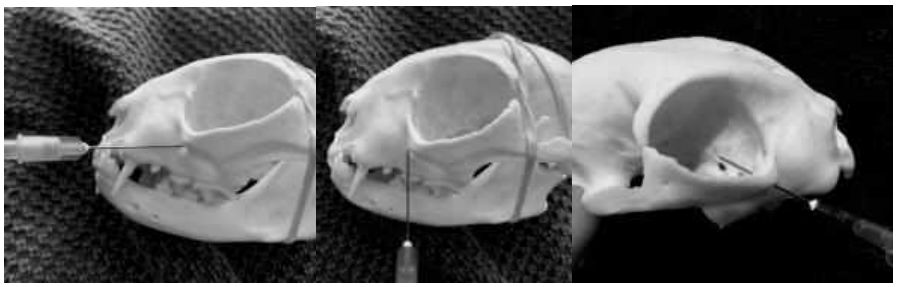
Materials
The materials needed for intraoral regional blocks are the disposable gloves, the drug of choice, a 1mL syringe, and assorted needles, depending upon the site to be blocked. Generally, a 25 or 27g X 5/8" needle is used for most blocks. The procedure is described below. It is advisable to ensure that a sharp needle is used for each block to minimize tissue damage. The needle should be replaced after the withdrawal of the drug from the vial and replacement after each injection.

Warning
Although some experts advocate the insertion of the needle deep into the foramen, the techniques described in this text will involve a less invasive technique, which will decrease the likelihood of nerve damage while performing nerve blocks. In these techniques, the analgesic is deposited at the opening of the foramen, and with gentle massage and gravity, the drug is moved into the foramen. The nerves will be surrounded by the analgesic, resulting in an effective block.

Step by Step Procedure

1. Determine the need and location for the placement of a dental nerve block based on the oral examination and dental radiographs.
2. Gather materials needed for administration. (See Materials)
3. Calculate the proper dosage and load syringe, replace the needle
4. Locate the proper landmark in the oral cavity
5. Insert needle and aspirate to ensure appropriate placement. If blood is aspirated, obtain a new needle and syringe.
6. Inject proper amount of agent into the location
7. Withdraw the needle and apply digital pressure to aid the agent into the appropriate foramen
8. Patiently wait until the block to take effect before starting the dental procedure

Maxillary Infraorbital Nerve Block
The maxillary infraorbital nerve block will affect the bone, soft tissues surrounding the canines and incisors. The infraorbital foramen is easily palpated in the maxilla, just distal to the third premolar. (Figure 1 and 2) It is imperative to keep the syringe and needle bevel towards the bone and parallel to the palate, and do not advance the needle too far into the foramen, especially in cats. (Photo 3) The infraorbital foramen is located within 4mm of the medial canthus of the eye. Caution must be used to avoid any ocular injury. Once the analgesic is administered, remove the needle, tip the nose up, and apply gentle pressure to move the drug into the foramen.



Figures 1 & 2: Needle placement for the maxillary infraorbital nerve block.
Figure 3: Advancing the need to far into the foramen may lead to ocular damage in cats.

Maxillary Nerve Block
The caudal maxillary nerve block will affect the bone, teeth, and soft tissue rostral to the first maxillary molar on the injected side. In cats, the caudal maxillary nerve block is performed at the base of the 'V' notch or divot near the soft palate juncture, palpable just medial to the caudal root tips of the maxillary fourth premolar. Aspirate and inject slowly.
The infraorbital neurovascular bundle is affected by this block. (Figure 4) By entering at an angle, as shown in the photo, there is less likelihood of advancing too far, resulting in ocular damage. (Figure 5) Advance the needle dorsally to a level just beyond the root tips of the last molar, then aspirate to ensure the needle is not in a blood vessel and slowly inject the agent. This technique is preferred over the infraorbital nerve block, for providing analgesia for the entire maxillary quadrant.

Figure 4: Infraorbital neurovascular bundle
Figure 5: Needle place for the caudal maxillary nerve block

Middle Mental Nerve Block in Cats
The middle mental foramen is very small and difficult to locate in cats, making this block hard to place. In cats, the labial frenulum landmark is used as a guide, but the foramen very small and is rarely palpable. The author rarely uses places this block due to the limitation of effectiveness due to the difficulty of placement.

Mandibular Nerve Block
The mandibular (inferior alveolar) nerve block will affect all bone, teeth, and soft tissue of the injected mandible. It can be performed either extra orally or intraorally. In the extraoral approach, an accurate placement technique can be achieved by drawing a line directly down from the lateral canthus of the eye and inserting the needle at that location. The needle is inserted at the lingual aspect of the ventral mandible and advanced dorsally to the midpoint between the ventral and dorsal borders of the mandible. The needle may be palpated from the inside of the mouth to ensure proper placement on the medial aspect of the mandible. The injection is as previously described.

The intraoral technique requires palpation of the mandibular foramen. It is located on the lingual aspect of the mandible, two-thirds of the distance from the last molar to the mandibular angular process (see diagram above). The needle is inserted intraorally, on the lingual surface of the mandible, adjacent to the foramen. Aspiration and injection are as previously described.

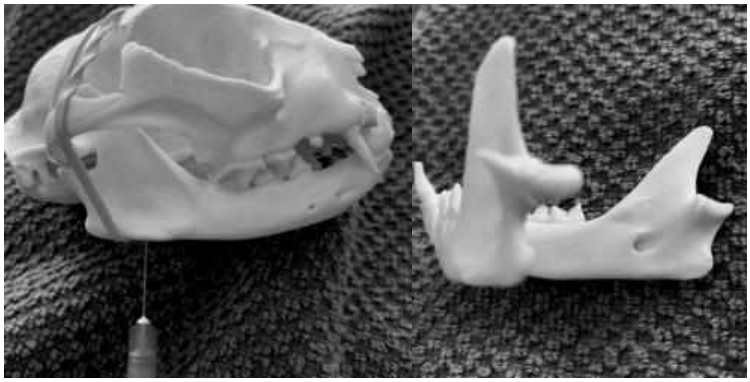


Figure 8: Proper needle placement at the entrance of the inferior alveolar foramen.
Figure 9: The inferior alveolar foramen

Care must be taken to ensure the placement of the mandibular block does not lead to the self-mutilation of the tongue during recovery. The extraoral approach limits the likelihood of accidental numbing of the tongue. To ensure a safe recovery, place the animal in sternal recumbency with the tongue in its normal position and not protruding from the mouth or out the side of the mouth. Monitoring patients receiving a mandibular block closely during recovery is critical.

Determine the Success of the Block
A dental nerve block can be considered successful when a painful oral surgery or procedure can be completed on a patient with a gas anesthetic rate of 1% or less for the entire length of the procedure, and the patient wakes without distress. They may even eat shortly following the surgery.

Postoperative Pain Control
Upon recovery from anesthesia, it is vital to keep patients comfortable and slowly encourage a return to regular eating habits as soon as they are awake and walking. The short-term use of a canned diet, or moistened dry kibble, will decrease mechanical trauma to the oral surgical site and may be easier to chew. (It is recommended that dry kibble is soaked until it is soft to avoid dietary upset due to a change from dry to canned food and to allow the patient to be maintained on its same diet.)

Many drugs are available for postoperative pain management. The most commonly used medications are non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. An excellent reference for veterinary medications and dosages is *Plumb's Veterinary Drug Handbook, 6th Edition*; Plumb, Donald, 2008 Wiley-Blackwell Publishing (www.wiley.com)

Non-steroidal anti-inflammatory drugs: NSAIDs are used to treat pain and extreme sensitivity associated with inflammation. Most NSAIDs used in veterinary medicine are Cox-2 selective. The breakdown of arachidonic acid by cyclooxygenase (Cox) enzymes, released at the site of surgery, produces prostaglandins. Further production is created by the development of cytokines and growth factors at the site. Prostaglandins are a component of the inflammatory cascade and contribute to the sensitization of neurons to noxious stimuli. Inhibition of Cox enzymes will limit prostaglandin production so that painful inflammation is reduced.

Conclusion
In conclusion, dental nerve blocks are inexpensive to perform, easy to master, and have a significant impact on patient comfort. They can be an invaluable part of a balanced anesthetic protocol when combined with other analgesic modalities. A multimodal approach to dental analgesia is desired. The duration and extent of the oral procedure will help to determine the desired drug protocol. The goal is to have a comfortable patient that eats well and heals quickly and to have happier pet owners. The benefits of placing dental nerve blocks far outweigh the risks to the patient.

NOTES:

Feline Hypertension: Diagnosis, Treatment, & Management

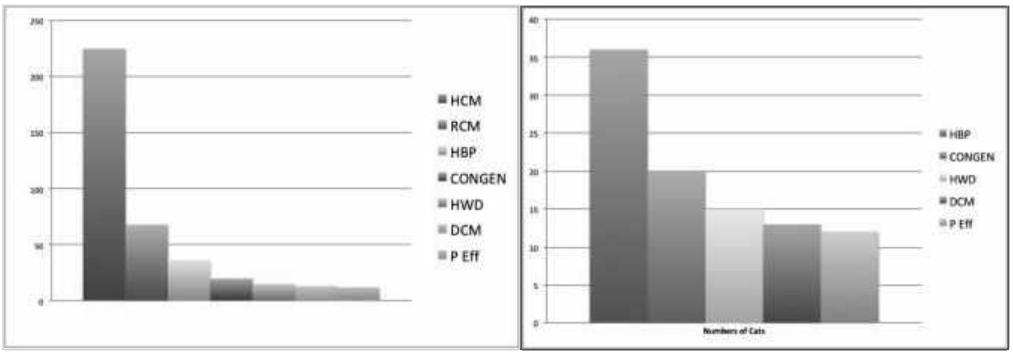
Clarke Atkins, DVM, DACVIM

Systemic hypertension (SHT, HBP, HTN), the most common cardiovascular disease of the aged cat and the most important vascular disease in cats, damages a host of target organs. Hence, its recognition and management is emerging as a critical component of small animal geriatric medicine. However, the importance of SHT in animals is generally under-estimated.

Importance of Systemic Hypertension in Cats

In an unpublished review of over 3500 feline acquisitions – cats of all ages, we found that about 1% of cats were hypertensive in the 5 year period we sampled. One can see that the prevalence of SHT and all other cardiovascular diseases lag behind the most common cardiomyopathies (HCM and RCM; Fig 1). However, when we remove these 2 types of cardiomyopathies from consideration (Fig 2), we see the relative importance of cardiovascular disease in cats other than HCM and RCM. Importantly, the average age of HCM cats is ~6.5 years and RCM ~9 years, while the mean age for HBP is 15 years. Therefore, HBP is the most common vascular disease in cats, the most common cardiovascular disease in aged cats, and it is treatable.

Figure 1 Figure 2

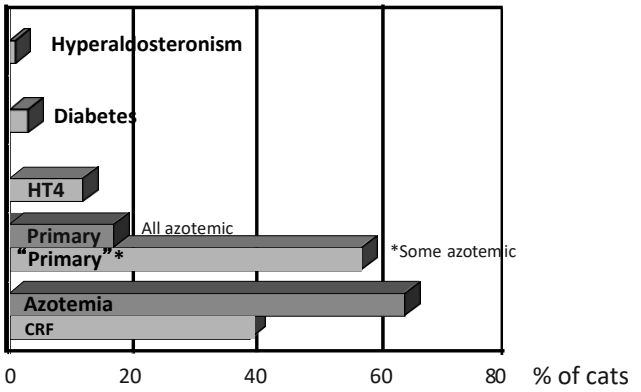


Etiology & Pathogenesis

Recently, the physiology of blood pressure (BP) control, as well as what is known of the etiology and pathogenesis of SHT in the cat been nicely reviewed.[1] Hypertension in animals has largely been thought to be secondary to other disease (e.g. renal disease and endocrinopathies), as opposed to idiopathic (primary, essential), as is the case in most human hypertensives. More recently, this has been called into question. A report of 69 hypertensive cats, seen at North Carolina State University (NCSU) for ocular disease, revealed that at least 17% (Fig 1), and possibly as many as 50%, of cats had no identifiable cause for their SHT (primary, idiopathic, or essential hypertension).[2] Elliott and associates showed that approximately 20% of hypertensive cats, diagnosed in "primary-care" practice, were idiopathic.[3] While generally accepted that primary SHT exists, the exact incidence is unclear because the cats with SHT and normal creatinine concentrations may have sub-clinical renal disease causing or contributing to SHT. It is very difficult to eliminate the contribution of chronic kidney disease (CKD).

Described and potential etiologies of secondary hypertension include chronic and acute renal disease, hyperthyroidism (HT4), hypothyroidism, hyperadrenocorticism, hyperaldosteronism, pheochromocytoma, diabetes mellitus, and obesity (Fig 3). Clearly, though often sub-clinical, chronic kidney disease (CKD) has the greatest association with SHT (Fig 3). One report suggests that approximately 29% of elderly cats with chronic renal disease were hypertensive[4], with a range from 4 studies of 19-65%.[5] However, in cats with CKD, but normotensive at diagnosis, only 17% went on to develop SHT.[6]

Figure 3. Associations of proven SHT in 99 cats (Atkins, DeFrancesco, NCSU, unpublished).[7] These associations do not, however, prove a causal relationship. Note that 19% of cats (labeled Primary) had no identifiable cause/association (including chronic renal failure or azotemia) for SHT. However, if even mildly azotemic cats were considered to have *secondary* SHT (due to mild CKD), then nearly 60% of cats would be considered "Primary". The truth probably lies between these 2 figures, but it is probably safe to assume that ≥20% of hypertensive cats are idiopathic.



The pathogenesis of hypertension is complex, not well understood, and beyond the scope of this work. However, several studies have indicated that the renin-angiotensin-aldosterone system (RAAS) is probably abnormally activated in many or, perhaps, most cats with systemic hypertension, particularly with concurrent renal disease, and certainly after therapy with loop diuretics and vasodilators.[8,9] Despite logic and their utility in hypertensive humans, monotherapy with angiotensin-converting enzyme inhibitors (ACE-I) have not been shown to adequately control hypertension in cats, and the mineralocorticoid receptor antagonist (MRA), spironolactone, has been little studied in animals with SHT. Recently, the angiotensin II (AgII) receptor (AT1) blocker (ARB), telmisartan has proven effective in hypertensive cats and in cats with proteinuria.[10,11]

Importance of RAAS-Supressive Therapy

Despite the fact that ACE-I have not proven to adequately control BP (blood pressure), as a monotherapy in cats, ***RAAS suppression is indeed crucial in most, if not all feline hypertensives***. The reasons for this are:

1. Pathological RAAS activation is present in CKD, and CKD with SHT, and probably SHT alone. RAAS should be considered to be activated in all cases.
2. RAAS suppression contributes to BP control, even when not adequate alone.
3. If SHT is adequately controlled with amlodipine, for example, RAAS activity continues to damage target organs.
4. Some antihypertensives (hydralazine, amlodipine [in dogs], and diuretics actually activate the RAAS in the process of lowering BP. Some (amlodipine in people) activate the sympathetic nervous system (SNS).
5. Because of cross-talk between the SNS and RAAS, RAAS suppression is accompanied by SNS suppression. This helps to lower BP and t (HR) and reduces target organ damage (TOD) caused by sympathetic stimulation.

The RAAS is well known to produce or contribute to TOD in SHT. Even if BP is adequately controlled, in the absence of RAAS suppression, RAAS activity persists, caused by underlying renal disease, diuretics, vasodilators, and possibly other factors, continues to wreak havoc on the myocardium; vascular walls and function; the kidneys; and probably the eye and CNS, and diabolically contributes to ongoing or worsening SHT. The focus of my presentation and this manuscript is the RAAS in feline SHT and its effect on blood pressure, and the heart, vessels, and kidney.

Aldosterone & Angiotensin II as Toxins

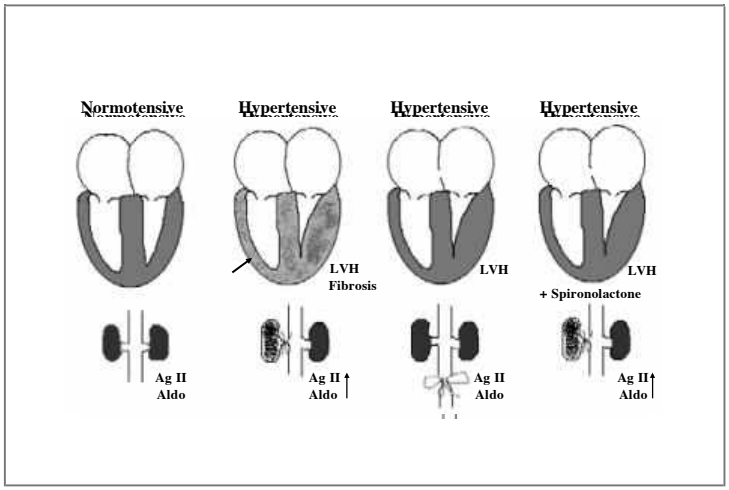
RAAS and Target Organ Damage: Heart

In an unpublished review of 99 cases of proven feline SHT, 82% showed some indication of cardiac disease by auscultation (murmur or gallop), ECG, thoracic radiography, or ECHO. Despite this, only 3% of these cats presented with heart failure. While, as shown below, RAAS activation plays a role in this process, it is not likely the sole cause, as was shown by Snyder in 2001.[12] Fourteen hypertensive cats (mean Systolic BP, 217mmHg) were treated for $\geq$ 3 months with amlodipine monotherapy. The average systolic BP fell to 142mmHg, and the percent with left ventricular hypertrophy (LVH) fell from 78-43%. This study is important because it shows us that hypertensive LVH is reversible when BP is lowered and that this result can obtained without RAAS suppression.

The heart is targeted by SHT in 2 general processes. First, the components of the RAAS, primarily angiotensin II and aldosterone and their down-stream products (e.g., free oxygen radicals), produce inflammation and cardiac remodeling, consisting of hypertrophy, myocyte death, replacement fibrosis, and primary interstitial fibrosis. Secondly the heart suffers increased loading conditions with RAAS activation: preload with Na^+ and H_2O retention

and afterload with peripheral arteriolar thickening and dysfunction. The role of the RAAS, namely aldosterone, as a "cardiac toxin" was demonstrated elegantly in work by Brilla, et al. (Fig 4).[13] In rats, using remnant kidney and aortic banding models of SHT, the investigators proved that myocardial fibrosis, accompanying pressure-induced LVH, was due to systemic factors, not increased systemic vascular resistance (SVR) alone. This was concluded because, with the remnant kidney model (RAAS activation - elevated serum angiotensin II and aldosterone concentrations) *both* ventricles experienced fibrotic change, while only the LV was concentrically hypertrophied. With aortic banding (no RAAS activation), there was again LVH, but unaccompanied by fibrosis, indicating the role of RAAS in hypertensive kidney fibrosis, while the hypertrophy was produced by increased afterload (SVR), with possible, but unproven effects of RAAS. In the remnant kidney model, ventricular fibrosis was blocked with spironolactone, meaning that aldosterone played the major role in fibrotic change.[13]

Fig 4.



Additionally, Atkins and DeFrancesco showed HR to be elevated in feline SHT (unpublished data), with 99 hypertensive cats demonstrating an average HR of 210bpm, elevated, compared to published normal values (168bpm). [7] Chronic HR elevation contributes to HBP and is damaging to the cardiovascular system. In this study, the double-product (systolic BP x HR), an indicator of cardiac work, was 2x normal. Additionally, 46% of hypertensive cats were tachycardic with HR >200bpm.

Fujii and Wakao studied HR variability in a canine model of mild, normotensive, experimental mitral regurgitation, to quantify SNS and parasympathetic nervous system tone.[14] They showed SNS hyperactivity in the dogs with mitral regurgitation and no clinical signs. Administration of benazepril blunted the SNS activity and significantly lowered HR.[15] This shows the cross-talk between RAAS and SNS, the insidious nature of abnormal neurohormonal activity, and that RAAS suppression can act as a de facto "beta blocker".

RAAS and Target Organ Damage: Kidney

That the RAAS is activated and plays a role in the pathology of renal disease and SHT is clear, and demonstrated by the following.

1. Renoprotective effects of ACE-I, particularly with glomerular disease[16,17]
2. Antihypertensive effects of ACE-I[16,17]
3. Increased serum aldosterone concentrations in normotensive cats with acute polycystic kidney disease.[18]
4. Increased serum aldosterone concentrations in feline chronic renal failure (CRF) [19,]
5. Increased serum aldosterone concentrations in CRF with SHT [20,21]

There is a substantial body of evidence in laboratory rodents, that ATII and aldosterone, likely acting in concert, are "nephrotoxic". This is based on direct (hormone infusion) and indirect (RAAS suppression) evidence. Angiotensin II-infused rats not only develop chronic hypertension and vascular remodeling, but also develop glomerular and tubulointerstitial injury. [22,23] When ATII was sub-acutely (2 weeks) infused to cause only moderate hypertension, renal changes included focal tubulointerstitial injury, cast formation, interstitial monocyte infiltrate, mild interstitial fibrosis, and phenotypic modulation with increased alpha-smooth muscle actin expression. A study using a 2-clip model to create renovascular hypertension in rats compared chronic therapy with captopril, hydralazine, and hydrochlorothiazide (HCTZ) alone and a combination of captopril plus HCTZ. Only captopril (alone or in combination

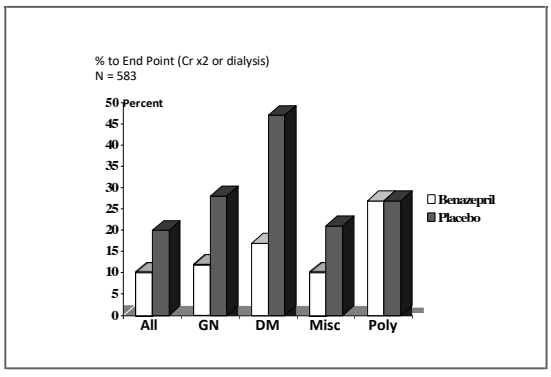
with HCTZ) benefited survival, demonstrating renal damage to be relatively pressure-independent, but RAAS-dependent.[24]

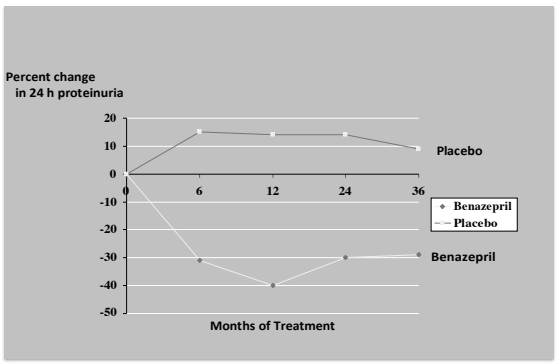
Increased aldosterone secretion, due to circulating and possibly, tissue RAAS activation, also contributes to the development and progression of renal pathologic remodeling and dysfunction. Uni-nephrectomized rats, infused continuously with aldosterone and fed a high salt diet, develop progressive proteinuria, increased generation of reactive oxygen species (ROS), and damage to glomerular podocytes.[25] In these rats, the MRB, eplerenone, was shown to prevent the increase in ROS in podocytes and to virtually eliminate the development of proteinuria and podocyte damage. In a rat remnant kidney model of glomerulosclerosis, spironolactone treatment led to reduction in glomerular injury, a benefit that was amplified by concurrent control of SHT. [26] This failure to significantly affect the proteinuria was postulated to be due to irreversible podocyte damage and/or unique pathophysiology of this rat model. In a rat model of type-2 diabetic nephropathy, the combination of an ACEI (lisinopril) and an MRB (eplerenone) led to a reduction in proteinuria, glomerulosclerosis, and renal expression of type I and IV collagen greater than that seen with ACEI monotherapy.[27] Mono- and dual-therapy with eplereonone and lisinopril each led to a significant reduction in renal expression of other pro-fibrotic and pro-inflammatory cytokines, including plasminogen activator inhibitor-1, transforming growth factor-beta, connective tissue growth factor, and fibronectin, supporting the RAAS' role in activation of these mediators. In an adriamycin nephrosis model of chronic proteinuria, spironolactone led to reduction in glomerular lesions, whereas monotherapy with lisinopril did not. Only the combination of spironolactone and lisinopril led to a reduction in proteinuria.[27]

In clinical medicine, the importance of RAAS in renal disease, with and without, SHT is clear, as well. Three human studies are particularly relevant. First 583 patients with renal disease (serum creatinine $\leq$ 3) of multiple causes, were treated with either placebo or benazepril. [28] The negative outcome of doubling of creatinine or need for dialysis was reached over twice as often in placebo-treated patients and the fall in UP:C was significantly greater in the patients treated with RAAS-suppression (Fig 5). The greatest results were seen in patients with proteinuria and there was no benefit in those with polycystic kidney disease. Similar results were obtained a decade later in a similar study in which patients had serum creatinine values up to 5. [29] These studies are particulary important because they demonstrate the safety of ACE-I in renal disease and show that virtually all renal disease, except polycystic kidney disease, benefit from RAAS suppression.

In another human study, Ligtenberg, et al. studied the effect of enalapril on SNS activity in patients with CRF. [30] They showed that patients with CRF and SHT, but not CHF, had elevated skeletal muscle SNS activity (2x controls), plasma norepinephrine concentrations, and plasma renin activity (5.5x). The BP and SNS activity were lowered with the ACE-I, while amlodipine lowered BP but *increased* SNS activity. This study demonstrates the cross-talk between SNS and RAAS and that SNS is abnormally activated in subjects with renal disease and HBP.

Figure 5. As described in text above. Cr = serum creatinine concentration, GN = glomerulonephritis, DM = diabetic nephropathy, Misc = all other diseases, Poly = polycystic kidney disease. [30]





Pertinent animal patient studies include a blinded trial, comparing placebo to enalapril, in dogs with biopsy-proven glomerulonephritis. In placebo-treated dogs, UP:C, UP:C corrected for glomerular filtration rate (GFR), and systolic BP all rose over the 6 months of the study, while these parameters fell in ACE-I treated dogs.[16]

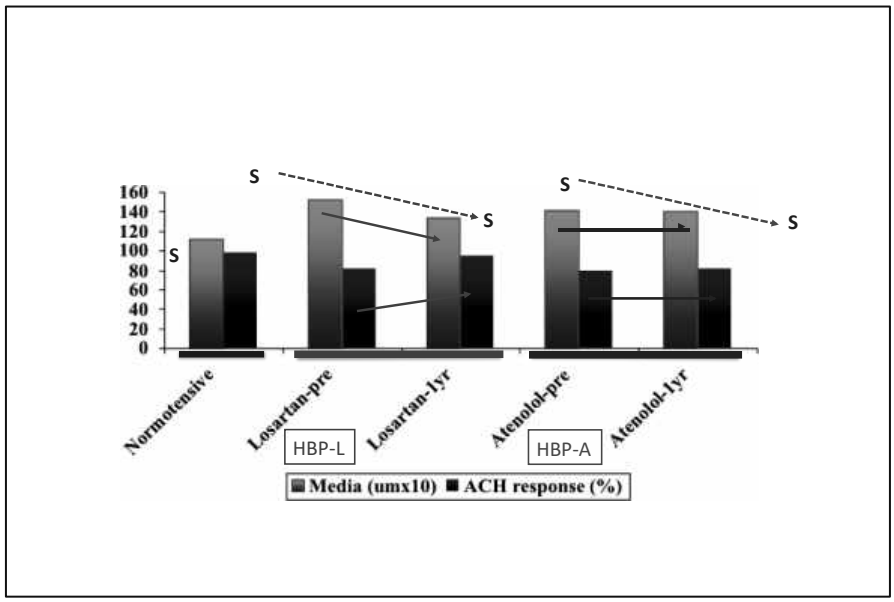
The beneficial effect of RAAS suppression has been shown in cats with renal disease, treated with benazepril, in which treated cats enjoyed a reduction in systolic and glomerular blood pressures of 11% and 16% respectively; a reduction in UP:C; slowed UP:C progression in the most severely affected cats; and weight gain. [17]

RAAS in Target Organ Damage: Vasculature

Evidence of aldosterone excess contributing to vascular dysfunction and fibrosis was demonstrated in a study in which aldosterone infusion to rats led to an increase in oxidative stress within the vascular walls and impaired vascular relaxation, associated with a decrease in endothelial derived relaxation factors.[31] Mineralocorticoid blockade with spironolactone reversed this negative effect, which has been hypothesized to be due, in part, to aldosterone-related enhancement of endothelin expression in arterioles.[32]

Additionally, in a study of hypertensive people, biopsies of resistance arterioles were obtained both prior to, and after control of hypertension for one year, with either atenolol or the ARB, losartan (Fig 6).[33] The authors showed that both medial hypertrophy and vascular dysfunction were reversed in the patients receiving losartan-induced RAAS suppression, but not those made normotensive *without* RAAS suppression (atenolol). This beneficial effect was concluded to be due both to the blockade of ATII's action at the AT_1 receptor (AT1R), and the resultant reduction in aldosterone secretion. In a similar study design, in which hypertension was controlled with either atenolol or the MRB, eplerenone, MRB therapy led to a reduction in arterial stiffness, whereas the atenolol-treated patients experienced progressive arterial stiffening, despite equal BP reduction. The MRB-treated groups also experienced reduction in the media collagen to elastin ratio and a decrease in circulating inflammatory mediators.[34]

Fig 6. As described in text above. S = systolic blood pressure, HPB-L = hypertension, receiving losartan, and HBP-A = hypertension, treated with atenolol, arrows represent the change over one year's time. [33]



Aldosterone has been hypothesized to contribute directly to endothelial dysfunction. Endothelial function was assessed in a small group of patients with NYHA class II or III heart failure, using bilateral forearm venous occlusion and plethysmography. The patients receiving spironolactone, in addition to standard diuretic/ACEI therapy, had an increased forearm blood flow in response to acetylcholine administration and a decreased vasoconstrictor response to AT I, but not ATII administration, when compared to patient controls [34]

A second hypothesized mechanism for improved blood flow is increased nitric oxide bioactivity. Aldosterone has been shown to up-regulate components of the RAAS, including ACE activity and ATII-stimulated signal transduction in vascular smooth muscle and myocardium, leading to increased local activity of RAAS in the these tissues.[35-38] Spironolactone, therefore, appears to improve endothelial dysfunction, increase nitric oxide bioavailability, and decrease vascular conversion of AT I to ATII.

RAAS in Feline Systemic Hypertension

Suppression of RAAS activity with ACEI, ARB and MRA, alone or in combination has been shown to improve BP control and reduce TOD in people with systemic hypertension. Whereas in people, SHT is usually primary (essential), in dogs and cats it is usually secondary to an underlying renal or endocrine disorder.

In cats, SHT is usually secondary to renal and/or endocrine disease (e.g. hyperthyroidism). Plasma aldosterone concentrations and the aldosterone to renin ratio in azotemic, hypertensive cats have been shown to be significantly elevated, as compared to normotensive cats.[39] In the non-azotemic, hypertensive cats in this study, plasma aldosterone concentration was also elevated, but independent of plasma renin activity, which was actually depressed in this group. In this "low-renin" group, the cats' aldosterone concentrations and aldosterone to renin ratios were not

supportive of hyperaldosteronism. In fact, their neurohormonal profile was similar to that of low-renin hypertension, which is diagnosed disproportionately in human patients of African ancestry. In humans, low-renin hypertension is most often due to either a low-renin essential hypertension or primary aldosteronism. It has been shown in people that the MRA, eplerenone, and the ARB, losartan, are equivalent in lowering BP in the high-renin patient, yet eplerenone is superior to losartan in the low-renin patient.[40] Despite this, the author is unaware of studies using MRA therapy in feline SHT.

The RAAS is activated in experimental and natural feline CKD, which is strongly associated with SHT.[41-43] Benazepril has been evaluated in cats with CKD (proteinuric and non-proteinuric), and it is well tolerated and significantly reduces proteinuria. [44] Although this study did not document a benefit of benazepril therapy on renal survival (endpoint of death or euthanasia due to renal disease or need for parenteral fluid therapy), renal survival times were inversely related to initial UP:C. Importantly, proteinuria has been shown to predict progression of azotemia[45] and is negatively associated with survival in cats with chronic renal disease[46] and systemic hypertension.[47] Recently, the ARB, telmisartan, has been compared to benazepril in cats with chronic kidney disease and proteinuria.[48] Telmisartan, over the 6-month treatment period, and led to a significant reduction in proteinuria at all time points, whereas the reduction seen in the benazepril group did not reach significance. As with dogs, combination RAAS blockade has not been evaluated in hypertensive cats. Finally, benazepril has been shown to lower BUN, serum creatinine concentration, and BP in cats with polycystic kidney disease.[49] This is in stark contradistinction to the findings in human polycystic kidney disease, in which patients so afflicted did not benefit from ACEI.[50]

Therapy – Evidence Favoring RAAS Suppression in Treating Hypertension

Therapies for feline hypertension (Table 1 - Formulary) have varied and have not often been systematically evaluated. Those therapies that have been employed and reported upon include diuretics (furosemide), angiotensin-converting enzyme inhibitors (ACE-I; captopril, enalapril, lisinopril, and benazepril), beta-blockers (propranolol and atenolol), calcium channel blockers (CCB; diltiazem and amlodipine), and the ARB, telmisartan. This discussion will be limited to RAAS suppressive therapies and amlodipine, because of its importance in treatment of feline SHT. Atenolol deserves mention for HR control in hyperthyroid and otherwise tachycardic cats.

Littman, retrospectively evaluated 24 cats with chronic renal failure (CRF) and SHT, found that the most effective antihypertensive therapy was the combination of a beta-blocker and an ACE-I and that there was a poor response to furosemide.[48] Jensen prospectively studied 12 similarly affected cats and found that the response to an ACE-I or beta-blocker alone was poor.[49] Another retrospective study of 12 hypertensive cats with CRF and unresponsive to other therapy, showed amlodipine to lower BP by $\geq$20% in 11.[50] Snyder demonstrated BP control in a randomized, blinded, placebo-controlled study of amlodipine in hypertensive cats, as well.[51] Finally, the NCSU study retrospectively found amlodipine to lower BP $\geq$20% in 30 of 32 hypertensive cats with 28 of 32 becoming normotensive.[52] Quoting the 2017 ACVIM Consensus Panel on Hypertension, *"Despite the potential role of either systemic or intra-renal RAAS axis in the genesis or maintenance of hypertension, CCB, specifically amlodipine besylate, has been the first choice for antihypertensive therapy due to established efficacy in cats with idiopathic hypertension or those with CKD. A mean decline of 28-55 mmHg is typically observed in cats within the hypertensive to severely hypertensive categories. Despite dramatic antihypertensive efficacy, longitudinal control of SBP with amlodipine besylate has not been shown to increase survival time in hypertensive cats."* [53] While the author agrees with this position, he advocates the use of RAAS suppressive therapy with or without (usually with) amlodipine in every case, except those in which treating twice daily invokes extreme hardship or is impossible. Amlodipine has been used safely and effectively in conjunction with other agents used to treat SHT. Importantly, amlodipine had not proven to improve survival in HBP, despite superior efficacy at lowering BP and reducing proteinuria, as do RAAS-suppressive agents. This may be an unfair challenge for any of these agents, at the advanced age at which the diagnosis of SHT is made.

Diltiazem, alone, with a beta-blocker, or with an ACE-I, has also lowered BP in the majority of cats so treated. The literature and clinical experience would, nevertheless, lead one to appropriately conclude that amlodipine is the single best agent for managing BP in feline SHT. This said, beta-blockers have a specific role in slowing heart rate and blocking the cardiovascular effects of T_3 in hyperthyroidism; ACE-I and ARB, in combating drug-induced or spontaneous activation of the RAAS, for preserving renal function[54,55], and for proven effects in lowering BP[56,57]; spironolactone for its aldosterone-antagonistic effects[13]; and furosemide (possibly with nitroglycerin) for use in heart failure accompanying hypertension (See Table).

A recent study in normal laboratory cats showed that the ARBs, telmisartan and irbesartan, and the ACEI, benazepril, significantly attenuated an Ang I-induced BP response, whereas losartan did not.[58] The effect of telmisartan was significantly greater than that of the other 3 drugs, 90-minutes after oral administration. Telmisartan and benazepril were also compared 24-hours after their oral administration, and telmisartan, again, led to a more significant attenuation of an Ang I-induced rise in BP.

The AgII receptor (AT1) blocker (ARB), telmisartan, has been recently approved for treating hypertension in cats in Europe. Telmisartan has been compared to benazepril in cats with chronic kidney disease and proteinuria.[48] Over the 6-month treatment period, telmisartan led to a significant reduction in proteinuria at all time points, whereas the reduction seen in the benazepril group did not reach significance. Studies in healthy, anesthetized cats demonstrated that, at 2 mg/kg, telmisartan significantly reduced the BP rise in response to Angiotensin I infusion. [59] At 3mg/kg, the anti-pressor effect was significantly better than that of benazepril. In a placebo-controlled study of telmisartan, given at 2 mg/Kg/day, provided a significant reduction in BP (20 mmHg vs 9 mmHg in placebo group) in hypertensive cats at 2 weeks and at 1 month, 55% of treated cats had a >20 mmHg fall in BP vs 28% of the placebo group. [60] The combination of amlodipine and telmisartan has been well tolerated in clinical cases.[61]

Addition of a MRA to the treatment regimen is increasingly employed in humans with resistant hypertension, already receiving an ACEI and/or ARB.[62-63] A recently completed randomized, placebo controlled human clinical trial found that spironolactone was superior to the addition of either a beta blocker or an alpha-1 blocker in patients with resistant systemic hypertension (persistent, despite triple therapy with an ACE, ARB, and CCB).[64] From this study, it appears that spironolactone is the best additional drug for such resistant SHT. Mineralocorticoid receptor antagonist "add-on therapy of SHT has not yet been evaluated in veterinary patients.

Other therapeutic considerations include: whether there is activation of the RAAS (initially or iatrogenically), the role of the SNS, renal function and the effects of hypertension on renal function, salt intake, presence of heart failure (uncommon), and the presence of reversible causes of hypertension (e.g. hyperthyroidism, diabetes mellitus, adrenal tumors). Additionally, I try to limit the number of pills to 1 (or 2) daily to reduce strain on the human-animal bond. If the goal of 1 pill per day is ever reality, it would ideally be a RAAS-suppressive drug (ACEI, ARB, or MRA) or beta-blocker.

Table 1.

Cardiovascular Formulary for the Hypertensive Cat

Drug	Trade Name*	Formulation(s) **	Dosage	Use
Amlodipine	Norvasc Amodip	1.25 mg tablets 1.25 chewable	.625 PO qd-bid	Antihypertensive
Diltiazem	Cardizem	30 mg tablets	7.5 mg PO tid	Lusitrope, Vasodilator, Negative chronotrope
Diltiazem - LA				
	Dilacor XR	180, 240 mg caps.	30 mg PO bid	*same*
	Cardizem CD	180, 240 mg caps.	45 mg PO qd	*same*
Enalapril	Enacard (Vasotec)	1, 2.5, & 5 mg tablets	.5 mg/kg PO qd	ACE-I (CHF, GN, Hypertension)
Benazepril	Lotensin (Foretkor)	5 & 10 mg tablets	.25-.5 mg/kg PO qd-bid	*Same*
Spironolactone	Aldactone Prilactone		2-3 mg/kg PO qd	Antihypertensive, CHF
Telmisartan	Semintra	Liquid 10 mg/mL	1.5 mg/kg BID x14d; 2mg/kg qd	Anithypertensive, Anti-proteinuric
Atenolol	Tenormin	25 mg tablets	6.25-12.5 mg PO qd	Negative chronotrope, Antiarrhythmic, Lusitrope, Antihypertensive
Nitroglycerin	Nitrol, Nitro-Bid	2% ointment	1/8–¼ inch topically tid for 24 hours	Venodilator (CHF)
LMW Heparin	Fragmin	2500 U/.2 ml	100 U/kg SQ qd	Anticoagulant
Aspirin		81 mg	40-80 mg q72h	Anticoagulant
Clopidogrel	Plavix	75 mg	17.5 mg daily	Anticoagulant

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One Size Won't Fit All: Tailoring Weight Management Plans for Cats

Julie Churchill, DVM, PhD, DACVN

Why Are Weight Loss Programs So Difficult?

An all too common and frustrating aspect of small animal practice is the discussion about weight loss and obesity. This discussion can be sensitive, and recommendations frequently go unheeded. Before this lack of success in helping pets achieve and maintain healthy weight leads causes the veterinary healthcare team to ignore this disease, consider it an opportunity to try another way to help these patients. Pet obesity continues to be the most common nutritional disorder of pets identified in veterinary practice and a major health concern worldwide.[1] With an estimate of as much as 59% or more cats being overweight or obese, this represents a tremendous opportunity for veterinary professionals to impact cat health and increase practice visits.

Definition & Diagnosis

The most common and clinically practical method of diagnosing obesity is a body condition scoring (BCS) system. It is important to remember that BCS only assesses body fat, while muscle condition scoring should be used to quantify lean body mass (i.e., an obese pet, which is a BCS 8-9/9, could also have severe muscle wasting). Each BCS is generally defined as a 10-15% increase or decrease from ideal body weight. The Global Pet Obesity Initiative(GPOI), which has garnered the support of 23 professional veterinary organizations (including AAFP), urges the adoption of a universal 9-point BCS scale to promote the veterinary teams ability to more consistently and accurately assess the cat's body condition, and clearly communicate with colleagues and clients. The GPOI also calls for a uniform definition of obesity (30% above ideal body weight) and recognition of obesity as a disease. The 2014 American Animal Hospital Association Weight Management Guidelines for dogs and cats recommend that body weight, body condition scoring, and muscle condition scoring be documented in the record at every visit. Early diagnosis of unhealthy weight gain can promote earlier intervention and successful management.

Prevention

Obesity in all species is more easily prevented than treated, and veterinarians play an important role in educating clients before the pet becomes obese. As a reminder, the veterinary healthcare team should provide a nutritional assessment for every cat at every visit. This process can quickly identify nutritional risk factors and determine if a more in-depth evaluation should be done to fully assess and make nutritional recommendations. An assessment of all patient's nutritional status is now considered a fifth vital assessment. Every nutritional assessment and recommendation should include 3 components: the patient, the diet and feeding management factors. An accurate diet history is invaluable when assessing of the nutritional health of the patient and will be vital to formulating an individualized diet plan. A discussion of body weight, body condition, and feeding amounts is an important part of the initial puppy and kitten visits. This should be reinforced and diet recommendations modified at the time of spay/neuter when energy requirements are known to decrease by up to 30%.

Increase Success of Weight Loss Programs

When unhealthy weight gain does occur, a weight loss plan is in order. In our practice, there are three essential elements of a successful weight loss program. If care is taken to assure each of these components is present, it greatly contributes to successful weight loss as well as client and veterinarian satisfaction.

1. **Establish owner commitment**: Assess the client's readiness for change. If they are ready to act, proceed with your nutritional plan. If not, employ ways to move them from thinking (contemplation) to doing (action).
2. **Customize the weight loss plan**: Partner with clients to make an individualized plan that works for the client and meets the nutritional needs of the cat. A careful and complete diet history (food and treat types, amounts, schedule etc), reveals important information about how the family relates to the cat through food and often provides insight about potential challenges the client will face. The diet history also reveals information about the pet's nutritional status which is often imbalanced from additional treats and human foods added to commercial products. Because of individual variation in energy needs of cats, the diet history can provide information about current caloric intake which can then serve as an accurate starting point for the food dose calculation (start at 75-80% of current intake).
3. **Reassess:** Initially biweekly follow-up will help support clients, assure a healthy rate of loss (0.5-1.5% body weight per week) and provide early detection of potential relapses

Tools to Increase Owner Commitment Communication is Key

Believe in Value

Most veterinary professionals acknowledge that pets are healthier when at their ideal body weight, but this may not translate to believing the value of recommendations and costs of a weight loss program. A team approach to pet

weight loss should be centered around a shared belief that nutrition is “best medicine.” If the veterinary professionals are skeptical of the value provided by a weight loss plan, clients will feel the same way. Determine the costs of care or reduction in quality of life for common comorbid conditions which develop subsequent of weight gain (management of diabetes mellitus, osteoarthritis). Thus, the ‘value’ of achieving healthy weight and reducing risks of comorbid conditions can be communicated to clients. Providing personalized veterinary nutritional counseling for all staff members is an excellent way to teach nutrition in a relatable, non-threatening and meaningful manner, and demonstrate convincing results. This will empower staff members to share personal experiences with the clinic’s recommended diets, weight loss products, feeding management ideas, exercises, and other proposals with clients. All team members should be trained and involved in the discussion and justification of fees.

Assess Readiness for Change

One of the most difficult tasks is to be the first one to inform an unaware client their pet is overweight. Before instituting a weight loss program, begin by assessing the client’s ability to change. Prochaska’s “readiness for change” model[5] can help veterinary professionals better understand the change process, successfully partner with pet owners, and customize recommendations that best suit each client’s needs. In this way, the veterinary staff can use the “right” approach for the “right” client at the “right” time. Implementing a weight loss plan when the client is ready to act on this advice will improve success and more efficiently use the veterinary team’s time and resources. The best predictors of adherence to a weight loss program are the veterinary professional's interviewing skills and qualities of the veterinary-client interaction. In order to improve adherence, it is essential to establish an atmosphere of trust and demonstrate concern for both the patient and the client's well-being. It is also important to understand how behavior change takes place

Psychologists have developed several models that help guide our understanding of how humans make changes in behavior to improve health. The “stages of change” model, also known as the transtheoretical model (TTM), developed by James Prochaska and colleagues, can be used to assess the client’s readiness to change their behavior. Using this model can help the veterinary professional better understand the change process and provide useful strategies to customize their recommendations to the client. TTM helps us better partner with our client and patient to provide an individualized plan to best suit their needs. Implementing a weight loss plan *when* the client is ready to act on this advice will improve the success and be a more efficient use of time.

Step 1: Identify the Stage of Change.

The 5 stages of change and characteristic attributes of clients:

1. **Precontemplation**—the person has no intention of taking action in the next 6 months. These clients might commonly be referred to as resistant, unmotivated or unaware, but clearly, they are not ready to change. In reality, it is often our intervention programs that have not been ready for them.
2. **Contemplation**—the person is aware of pros and cons of changing and *intends* to change in next 6 months. They may be stuck “thinking about it”, intending to change “soon”.
3. **Preparation**— the person plans to take action in the next month. Clients may have recognized the problem and sought advice already from books or online or by talking to a pet store employee, trainer or veterinary professional. Recruit these people for action-oriented programs.
4. **Action**—the person has taken action that is significant enough to result in a reduction of risks for disease. For example, the client may have reduced treats or selected a different pet food. However, the change would not be considered a significant action unless it reduced calories by at least 10% ***and*** provided complete and balanced nutrition. Veterinary professionals can help refine the plan to achieve healthy weight loss.
5. **Maintenance**—the individual continues action to prevent relapse.

Step 2: Understand the Change Process.

By understanding the stages of change the health professional can adapt their communication to meet the stage of the client. If a client is in one of the early stages, it isn’t the time to try and implement a weight loss plan for this pet. It’s equally important that we don’t ignore this patient’s obesity. Don’t give up. These patients warrant a monitoring plan. It may take time and several visits to establish rapport and build the trust necessary to move the client along to the next stage, hopefully closer to being ready to “take action” and implement a weight loss program for their pet and ultimately take steps to improve their health.

Step 3: Select a Stage-appropriate Intervention.

The failure of many weight loss programs are often because of a mismatch between the type of intervention and the client's readiness to change. Many traditional programs are action-oriented while the majority of clients are not in the action stage. See the table for examples of communication tools to identify the client’s stage of change and how to communicate best to match the client’s readiness.

When a partnership is formed with the client you create an environment that supports change. By understanding the stages of change the veterinarian can help move the client from *thinking* to *doing*. Selecting the right intervention at the right time for the right client can tremendously improve the clinical outcome. Successfully managing obesity can change a frustrating problem to a rewarding one. The pet achieves greater health, an improved quality of life and pet owners become loyal clients because they have been active partners in the healthcare plan.

Engage the Team
Ideally, every member of the health care team has a role in weight loss programs. Veterinary teams need a clear, logical, and methodical approach to consistently and effectively counsel clients on a pet's diet, lifestyle, and quality of life. The nutritional counseling workflow should be based on a team's nutritional competency and dietary philosophy, individualized communication styles of team members and clientele, and infrastructure constraints such as number of staff, exam rooms, length of appointments, and equipment. Having specific staff as the contact point ensures consistent support and bonds the client to the practice.

The veterinary care team should use open ended, non-judgmental questions when collecting the diet history and the client's perception of the pet's weight. This is often an opportunity to educate clients about what a healthy cat looks (and feesl) like and to correct misperceptions to encourage acceptance that weight loss impacts the pet's health positively. When pet owners remain hesitant, offer concerns and educate about increased health risks associated with unhealthy weight gain. Empathy is a powerful communication tool. Acknowledge that food is an important part of the human animal bond that unhealthy weight gain is a common problem in pets, and weight loss does have challenges. Make clients an integral part of the team. Partner with clients in the development of the weight loss program and assure them that the team shares the struggles and the successes. Ask clients to weigh in on their feeding preferences and routines in order to take their perspectives into account. Ask them to commit to a 6-month plan to allow time for realistic gradual weight loss and life style changes.

Tools for Developing the Treatment Plan
Detailed mechanics of a weight loss plan are detailed in the 2014 AAHA weight management guidelines, however the brief overview includes these steps:
1. Assess the body condition score (BCS) and determine the patients ideal body weight (BW)
2. Calculate the estimated daily energy requirement for weight loss.
   $(0.8\text{-}1 \times [\text{Ideal } BW_{kg}]^{0.75}) = \text{kcal/day}$
3. Select a diet with high protein and reduced caloric density. Cats protein > 110 gms/1000 kcal. Decide which therapeutic products to stock in the practice, so clients can leave with food they need. Consider creative ways to change feeding management (food puzzles) and increase activity and hunting behavior.
4. Provide the client with a specific recommendations including a) specific food product(s) including treats b) amount to feed c) frequency of feeding and d) a monitoring and follow up plan. Provide instructions in writing and document in the medical records.
5. Recheck patients regularly monitoring rate of loss and weight loss adjustments. Schedule the recheck visits before the client leaves the clinic.
6. Incorporate activity plans and environmental enrichment ideas.

Tips & Tools for Successful Reassessment
As the weight loss plan is developed, the client should be enlisted as a partner and informed that regular follow up will help avoid pitfalls frustrations and failures. Set a shared goal to improve the cat's health with a healthy rate of loss (.05-1% BW/week). During the monthly follow-up visits, reinforce weight loss goals and highlight the successes. Photographs and videos can demonstrate changes in body condition and improvements in patient mobility. Provide the opportunity to discuss challenges and adjust the plan in response to problems the client or cat is encountering.

Continue the Care
Routine monitoring is still required after weight-loss goals are reached. Rebound weight gain is common and repeating a weight loss plan is even more challenging the second time. Discuss the shift from weight loss to weight maintenance with the client ahead of time and emphasize the goal of preserving health benefits achieved from successful weight loss. Formerly obese patients will likely need long term dietary modification to prevent weight gain. Teach owners to assess BCS and reinforce this at every visit. Provide an honest assessment of BCS to owners at each visit.

Get Creative
Combining great communication and the medical components will ensure successful implementation of weight loss programs in practice. Frequent follow up will build client loyalty and allow better oversight to assure healthy progress for the patient and satisfaction for the client and the whole veterinary practice team. Creative programs may be worth considering

- Package plan- fee structure to include multiple visits and/or therapeutic foods
- Social media promoting success stories
- Support groups led by staff to teach BCS assessment, and discuss tips and tools

Summary

Excess weight gain in cats is prevalent and associated with other comorbidities. The veterinary health care tream can play a valuable role in the cat's health and longevity. By implementing a complete nutritional assessment at every patient visit, the veterinary team has the opportunity to help proactively prevent unhealthy weight gain and establish the veterinary care team as an expert in their cat's nutrition. Every member of the veterinary healthcare team can play a vital role in communicating, engaging and supporting the cat owner in implementing weight management plans. Utilizing the readiness for change model can improve the timing and success of the treatment plan. Consistent messaging from the team will provide good service and great care to the client and the cat. Cat's are unique, and no single approach or weight management plan will meet the needs of all cats or their families. An individualized plan including specific feeding recommendations and monitoring will increase the chance of success.

References

1. Baldwin K, Bartges J, Buffington T, et al. AAHA nutritional assessment guidelines for dogs and cats. *J Am Anim Hosp Assoc* 2010; 46(4): 285-96.
2. WSAVA Nutritional Assessment Guidelines. *Journal of Feline Medicine & Surgery* 2011; 13(7): 516-25.
3. World Small Animal Veterinary Association Global Nutrition Toolkit: https://www.wsava.org/WSAVA/media/Documents/Guidelines/WSAVA-Global-Nutrition-Toolkit-(English).pdf, accessed August 2020.
4. Fahey GC, Barry KA, Swanson KS. Age-related changes in nutrient utilization by companion animals. Annu Rev Nutr. 28:425-445, 2008.
5. Deng P, Iwazaki E, Suchy SA, et al. Effects of feeding frequency and dietary water content on voluntary physical activity in healthy adult cats. *J Anim Sci* 2014; 92: 1271–1277.
6. Scarlett JM, donoghue S, Saidla J, et al. Overweight cats: prevalence and risk factors. *Int J Obes Relat Metab Disord* 1994; 18 Suppl 1: S22–S28.
7. https://petobesityprevention.org/2018, accessed July 5, 2019.
8. Brooks D, Churchill J, Fein K, et al. AAHA Weight Management Guidelines for Dogs and Cats. JAAHA 50:1-10, 2014.
9. Richardson A, Birchenall-Sparks MC Age-related changes in protein synthesis.. Rev Biol Res Aging 1:255–73,1983.
10. Laflamme D. Nutrition for aging cats and dogs and the importance of body condition. Vet Clin North Am Small Anim Pract 35:713–42, 2005.
11. Nutrient requirements of dogs and cats. National Research Council. The National Academies Press. Washington DC, 119, 2006.
12. Hewson-Hughes, Hewson-Hughs, Miller et al. Geometric analysis of macronutrient selection in the adult domestic cat. Felis catus. J Exp Biol 2011: 214, 1039-1051.
13. Zoran DL, Buffington CA. Effects of nutrition choices and lifestyle changes on the well-being of cats, a carnivore that has moved indoors. JAVMA, 2011:239: 596-606.
14. Laflamme DP, Hannah SS. Discrepancy between use of lean body mass or nitrogen balance to determine protein requirements for adult cats. J Fel Med Surg 2013:15;691-697.

Pet Obesity and General Pet Nutrition Resources

1. BSAVA. Obesity. 2019 https://bit.ly/2Pb9oRa.(accessed August 2020).
2. Association for Pet Obesity Prevention. The global pet obesity initiative position statement.2019. https://petobesityprevention.org/about/#GPOI (accessed August 2002).
3. Banfield Pet Hospital NAVC Veterinary Emerging Topics [VET] report 2020, https://www.banfield.com/exchange/latest-thinking/vet-report/overview (accessed August 2020)
4. Baldwin K, Bartges J, Buffington T, et al. AAHA nutritional assessment guidelines for dogs and cats. *J Am Anim Hosp Assoc* 2010; **46**(4): 285-96.
5. Churchill J. Increase the success of weight loss programs by creating an environment for change. Compend Contin Educ Vet 2010;32(12):E1.
6. 2014 AAHA Weight Management Guidelines for Dogs and Cats: https://www.aaha.org/aaha-guidelines/weight-management-configuration/abstract/ Association for Pet Obesity Prevention Website: www.petobesityprevention.org
7. World Small Animal Veterinary Association Global Nutrition Toolkit: https://www.wsava.org/WSAVA/media/Documents/Guidelines/WSAVA-Global-Nutrition-Toolkit-(English).pdf, accessed August 2020. Note that this site has resources for pet owners and for veterinarians on pet nutrition topics.

8. Tufts Clinical Nutrition Service Petfoodology Website: www.petfoodology.org
University website created by board-certified veterinary nutritionists with frequently updated blogs on pet nutrition.

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Hydration Fixation: Beyond the Water Bowl

Jason Gagne, DVM, DACVM

Water is considered the most essential nutrient supporting countless metabolic functions. While estimates for feline daily water requirements exist,[1] there is no clear definition of optimal hydration for the healthy cat or for cats with various medical conditions. The typical recommendation is to provide fresh water at all times. No consensus exists regarding optimal water intake in cats or the overall impact of adequate hydration in health.

Total body water (TBW) of adult cats in lean body condition is about 60% of body weight.[2,3] Approximately two thirds of total body water resides in the intracellular fluid compartment and one third is extracellular fluid (interstitial fluid and plasma).[4] Water moves between these fluid compartments in dynamic equilibrium. The regulation of water balance is controlled by various neurohormonal mechanisms including the renin-angiotensin-aldosterone system and antidiuretic hormone (vasopressin) which respond to increases in plasma osmolality or decreases in blood volume. Water is lost from the body via urine (obligatory and free water loss), feces, and insensible losses including evaporation during respiration. The quantity and nutrient composition (i.e. protein and mineral cations and anions) of the food consumed by an individual contribute to the renal solute load that dictates obligatory urinary water loss. The amount of urinary free water loss (water unaccompanied by solute) is controlled by stimulation or inhibition of antidiuretic hormone in response to serum osmolality.[4] In health, the cat maintains homeostatic water balance (net zero gain or loss) such that daily water loss is offset by the daily water intake.

Water intake is achieved from a combination of voluntary drinking ("free water"), water consumed as a component of food ("combined water") and water produced endogenously during the oxidation of macronutrients ("metabolic water"). Metabolic water contributes ~5-10% of the daily water requirement. The amount of water produced by the oxidation of protein (approximately 41 ml per 100 gm), fat (~107 ml per 100 gm), and carbohydrate (~60 ml per 100 gm) translates into 10-16 ml of water from the metabolism of each 100 kcal of metabolizable energy.[1] Voluntary water intake is driven physiologically by thirst that is mediated directly by the hypothalamus, specifically specialized cells in the organum vasculosum of the lamina terminalis that respond to shifts in the osmolality of the extracellular fluid. However compared to dogs, cats appear to have a less effective and complete response to dehydration suggesting the cat may have a lower thirst drive.[5,6]

Daily water intake requirements have been reported using three different methods. The first method considers water intake relative to body weight. For example, an adult cat needs approximately 50 ml of water per kg body weight per day.[7] The second method considers water intake relative to dry matter intake of food. A general guideline using this method suggests healthy adult non-reproducing dogs and cats at a comfortable environmental temperature require 2 to 3 ml of water per gram of dry matter food consumed.[1] The third method considers water intake relative to caloric intake with a requirement of 0.1-0.2 ml water per kilojoule consumed.[8] This method provides a convenient means of estimating a healthy pet's water needs while accounting for differences in both diet composition and activity level. Daily water requirement parallels daily energy requirement. Each of these methodologies results in a milliliter per day water requirement that falls within the range of resting to maintenance energy requirement expressed as kilocalories per day.

The moisture content of the diet influences the amount of water consumed by drinking (free water ingestion). Cats consuming canned foods, which typically contain 70-75% moisture, ingest a large portion of their daily water intake from their food ("combined water"), thus they drink very little or not at all. In contrast, cats consuming dry kibble foods, which typically contain <10% moisture, ingest less water from the food but voluntarily drink a greater volume of free water compared to cats consuming canned cat food.[9,10] Pet owners will often observe their cat drinking more water when consuming a dry diet. They may express concern that the cat drinks less water when consuming a canned pet food. However, studies demonstrate that cats fed lower moisture foods consume less total water (free + combined water intake) compared to cats consuming higher moisture foods.[10,11] The daily water:calorie ratio for cats eating a dry food has been observed to be 0.6-0.7[9,12,13] compared to 0.9[14] for cats consuming wet food. The higher water: calorie ratio for cats consuming wet food compared to dry supports the hypothesis that the amount of water a cat voluntarily consumes when eating a dry food does not compensate for the water provided in wet cat foods. For this reason, feeding foods with a higher moisture content is often recommend for cats with a history of certain medical conditions such urolithiasis. However, it would be remiss to assume only moisture content of a food impacts water balance. The quantity of food and the nutrient composition of the food including protein and mineral cations and anions contribute to the potential renal solute load that drives obligatory urinary water loss. Therefore, when evaluating research studies looking at the effect of diet on hydration, urine volume or urine dilution, one must

consider not only the moisture content of the diet but also the nutrient composition of the diet(s) and amount consumed.

There is no consensus regarding “optimal” hydration for healthy cats nor for cats with health conditions that might lead to increased water loss (e.g. chronic kidney disease) or conditions that might benefit from increased urine volume or dilution (e.g. urolithiasis). If one assumes cats eating a dry food with ad libitum access to water maintain euhydration, then cats consuming a high moisture wet food might be experiencing a relative diuresis.[1] Alternatively, if one assumes cats consuming wet food maintains euhydration, perhaps cats consuming dry food could be in a state of relative hypohydration.[15] In human medicine the concept of the “hydration process” defined as total body water turnover (i.e. the volume of water added to and removed from the total body water pool each day) has been proposed.[16] There is evidence that humans in a chronic low hydration process (low daily water intake with low urine volume output) may have detrimental health consequences particularly with regard to constipation, urolithiasis[17] and chronic kidney disease.[18] Whether this applies to the feline population is unknown. However, several studies suggest inadequately hydrated cats may be predisposed to illnesses including chronic kidney disease, obesity, urolithiasis, constipation, and diabetes mellitus.[19-23] It may be prudent to develop strategies to increase voluntary water intake in addition to the current recommendation to feed high moisture foods to cats with specific medical conditions such as urolithiasis.[24]

Veterinarians often recommend water fountains, various types of water bowls, positioning bowls in multiple locations, or adding flavoring agents to increase water intake. However, there is very little data to support or refute the efficacy of these interventions and there may be individual preference requiring trial and error with each patient. One clinical trial using a crossover design compared water intake and urine concentration in a small number of healthy cats offered water from a bowl versus water fountain. In this small population of cats, use of a drinking fountain did not result in a substantial increase in water consumption nor dilution of urine based on urine osmolality and urine specific gravity.[25] Another randomized crossover design study quantified water intake in healthy laboratory cats offered still, circulating or free-falling water. In this study, the bowl type had no appreciable effect on water intake. The authors recommend alternative methods to increase water intake beyond providing unique water bowls to augment water intake.[26]

A nutrient-enriched water product containing organic osmolytes derived from whey protein isolate and glycerin offers a strategy for improving hydration indices in cats. These nutrients are categorically considered osmolytes. Osmolytes are molecules that cells use to regulate water movement across the plasma membrane driven by osmotic pressure gradients within each cell.[26] The entry of water into cells leads to cell swelling, and conversely, loss of cellular water upon dehydration leads to cell shrinkage.[27] While cells utilize electrolytes for regulating cell volume, cells also utilize organic osmolytes for osmoregulation as a means of circumventing excessive cytosolic inorganic ion concentrations that would interfere with cellular ion gradients and proper cell function.[28] Consequently, ingestion of water enriched with organic osmolytes such as amino acids derived from whey protein isolate and glycerin will aid in both the absorption of water by the cells in the gut and peripheral tissue, as well as encourage retention of water by the body by promoting movement of water from the vascular space into the cells and supporting healthy hydration.

In one study[13] eighteen healthy adult cats were fed the same dry extruded diet formulated to meet adult feline maintenance. All cats were offered tap water (TW) ad libitum for a one-week baseline period (days -7 to -1). Cats were then randomized into two groups. The control group continued to receive TW ad libitum as the sole water source for the duration of the study. The second group of nine cats were initially offered the nutrient enriched water (NW) ad libitum as their only water source from Day 0 through Day 10. Then from Day 11 until completion of the study (Day 56) the test group was offered the option of either NW or TW ad libitum in separate bowls to determine water preferences. Positioning of the bowls was alternated daily. TW and NW intake was recorded daily throughout the duration of the study using an automated monitoring system. Blood and urine samples were collected at predetermined times for analysis. Baseline TW and caloric intake were similar between groups. During week one of the treatment phase, liquid intake did not increase significantly for the TW group whereas the NW group had a mean free liquid consumption increase of approximately 60% compared to baseline [mean +/-SE 93+/- 9 g/day at baseline and 148 +/-26 g/day (P=0.01)] when NW was the sole water source. In addition, the amount of liquid consumed during week 1 was significantly (P=0.03) greater for this group than for the TW group. During the remainder of the study when the NW group had access to either NW or TW, the NW group continued to have significantly greater mean weekly liquid intake compared to baseline ranging from approximately 40% to 118% whereas the TW group had minimal variation in liquid intake compared to baseline over the 8-week treatment phase. During the water preference phase, overall mean +/- SD percentage of total daily water ingested as NW was 96.6 +/- 3%. Therefore, the increase in total free liquid drinking in the NW group during the course of the study was a direct result of the cats preferentially selecting the NW over the TW.

Urine indices including urine volume and urine specific gravity were also evaluated in this study.[13] Urine samples were collected via cystocentesis on days -1, 8, 15, 30, and 56. In addition individual 48-hour urine sample collection was obtained from each cat on days 28 through 30 or 31 through 33 to measure total urine output volume. Mean urine output was significantly (*P*=0.010) higher in the NW group (15.2 ml/kg/day) compared to the TW group (10.3 ml/kg/day). The NW group had a 33% lower mean USG (1.040 +/- 0.002 g/mL) versus the TW group (1.054 +/- 0.001 g/mL) (*P*=<0.001). Mean glomerular filtration rate did not differ between groups and maintenance of serum BUN, creatinine and phosphorus within reference range support the conclusion that the NW group maintained healthy kidney function. This study had a small sample size and individual response was variable with regard to consumption of the NW (3 cats increased liquid intake by <25%, 3 cats increased intake by 25-75%, and 3 cats increased intake by >75%). However, these findings suggest that a water supplement may serve as an alternative or complementary method to increase water ingestion in cats.[13]

To gain more insight regarding optimal formulation and dose of the nutrient-enriched water product, a study was undertaken to investigate water intake and urine measures in healthy cats provided free-choice access to the whey protein and glycerin nutrient-enriched water with (NWP) or without (NW) added poultry flavoring at incrementally increasing doses over a 10-17 day period.[27] Thirty-six cats participated in this trial. All cats consumed the same dry kibble fed to maintain stable body weight. Control cats (n=4) received food and ad libitum tap water (TW) throughout the study. Cats in the NW and NWP groups (n= 16/group) received the food and TW for the first week (baseline) and then were assigned to receive a third bowl with either NW or NWP at 1x the baseline TW consumption baseline (17 days), then 1.5x (10 days) and then 2x (10 days). This study concluded that increasing the volumes of NW or NWP resulted in increased free liquid consumption and was associated with greater urine output and dilution as measured by urine specific gravity.

Another study evaluated two similar nutrient-enriched water supplements that differed only in the gum content.[28] In this study 36 healthy cats were fed the same therapeutic urinary dry cat food (Purina® ProPlan® Veterinary Diets UR Urinary® St/Ox®). The control group (n=12) received food and ad libitum tap water. The two treatment groups (n=12 in both groups) received food, ad libitum tap water and one of two nutrient-enriched water products offered at a dose of 36 ml/kg BW twice daily in a third bowl. During the treatment period both groups receiving a nutrient-enriched water product had an significant increase (P <0.001) in total liquid intake (40.5 and 38.8 mL/kg BW/d) compared to the control cats (25.7 mL/kg BW/d), and a significant increase (*P* <0.0001) in urine volume (23.1 and 21.1 mL/kg BW/d) compared to the control cats (11.7 mL/kg BW/d). In addition, urine specific gravity was significantly (*P* <0.0001) decreased in cats consuming either of the nutrient-enriched water products compared to the control group. To date these studies have looked at healthy adult cats. Future studies focusing on cats with conditions that may benefit from increased water intake and/or increased urine output are warranted.

The use of a nutrient-enriched water supplement as part of a preoperative fluid protocol for a brief anesthetic event has recently been reported.[29] This study measured hydration parameters in 53 young (4.1 years +/- 1.6 years) healthy domestic shorthair cats undergoing a brief dental cleaning as a model for a short anesthetic procedure (mean length of anesthesia < 20 minutes). Group NW (n=14) was offered 50 ml of a nutrient-enriched water supplement 2-3 hours prior to anesthesia with no intravenous fluid administration. Group F (n=20) was offered 50 ml of tap water 2-3 hours prior to anesthesia and received 10 ml/kg BW/hr of Lactated Ringer's during anesthesia. Group no-F (n=20) was offered 50 ml of tap water 2-3 hours prior to anesthesia with no intravenous fluids during anesthesia. Serum chemistry, serum osmolality, total body water (TBW) measured by quantitative magnetic resonance[3] were obtained at baseline (2-3 hours prior to anesthesia), immediately prior to anesthesia, and immediately after anesthesia. Cats offered the NW ingested more liquid compared to cats offered tap water [42.1+/-13.4 g versus 2.9 +/- 1.9 g]. There was no difference in percentage TBW at baseline between groups. Immediately prior to anesthesia, the NW group had a %TBW increase of 0.9% (+/-0.3% SE; *P*<0.001) from baseline and the NW group's %TBW was statistically higher than the %TBW for both groups offered tap water. The tap water groups (Group F and Group no-F) had a numerical but non-significant decrease in %TBW immediately prior to anesthesia when compared to baseline. This suggests the cats ingesting the nutrient-enriched water supplement 2-3 hours prior to anesthesia began the procedure in a more hydrated state compared to those offered tap water. After the dental cleaning the %TBW for the NW group returned to baseline, the group receiving IV fluids during the procedure remained stable but the group receiving no IV fluids had a significant decrease of 0.9% (+/- 0.2%SE *P*<0.001) compared to baseline. This data suggests pre-anesthesia liquid therapy with a nutrient-enriched water supplement can prevent natural loss of TBW that occurs when no IV fluids are provided during a short anesthetic procedure. Cats in the NW group appeared equally hydrated as assessed by TBW using QMR compared to cats administered IV fluids or better hydrated than cats receiving no IV fluids following completion of a brief anesthetic procedure. The clinical applications for the use of a nutrient-enriched water supplement as part of a pre-anesthetic protocol to support comprehensive perioperative fluid therapy or as a possible alternative to intravenous fluid therapy in specific brief procedures when fluid therapy is at the discretion of the attending veterinarian warrants further investigation.

In summary, water is often an overlooked nutrient. However, it is well recognized that hydration is critical to feline health. As we learn more about optimal hydration and optimal fluid turnover through future research, we can begin to apply these principles to healthy cats and cats with conditions that may benefit from increased fluid intake, better total body hydration, and/or increased urine volume.

References

1. Water. *Nutrient Requirements of Dogs and Cats National Research Council*. Washington D.C.: The National Academies Press, 2006;246-251.
2. Stanton CA, Hamar DW, Johnson DE, et al. Bioelectrical impedance and zoometry for body composition analysis in domestic cats. *American journal of veterinary research* 1992;53:251-257.
3. Zanghi BM, Cupp CJ, Pan Y, et al. Noninvasive measurements of body composition and body water via quantitative magnetic resonance, deuterium water, and dual-energy x-ray absorptiometry in cats. *American journal of veterinary research* 2013;74:721-732.
4. Wellman ML, DiBartola SP, Kohn CW. Applied physiology of body fluids in dogs and cats In: DiBartola SP, ed. *Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice*. 4th ed. St. Louis, MO: Elsevier, 2012;2-25.
5. Anderson RS. Water balance in the dog and cat. *Journal of Small Animal Practice* 1982;23:588-598.
6. Adolph EF. Tolerance to heat and dehydration in several species of mammals. *Am J Physiol* 1947;151:564-575.
7. Schaer M. General principles of fluid therapy in small animal medicine. *The Veterinary clinics of North America Small animal practice* 1989;19:203-213.
8. Cave N. Dry matter, wet matter, does it matter? *Purina Companion Animal Nutrition Summit*. San Jose, Costa Rica, 2019;33-37.
9. Seefeldt SL, Chapman TE. Body water content and turnover in cats fed dry and canned rations. *American journal of veterinary research* 1979;40:183-185.
10. Buckley CM, Hawthorne A, Colyer A, et al. Effect of dietary water intake on urinary output, specific gravity and relative supersaturation for calcium oxalate and struvite in the cat. *The British journal of nutrition* 2011;106 Suppl 1:S128-130.
11. Xu H, Greco D, Zanghi B, et al. The effect of feeding inversely proportional amounts of dry versus canned food on water consumption, hydration, body composition, and urinary parameters in cats (abstr). 39th World Small Anim Vet Assoc Cong 2014;852.
12. Finco DR, Adams DD, Crowell WA, et al. Food and water intake and urine composition in cats: influence of continuous versus periodic feeding. *American journal of veterinary research* 1986;47:1638-1642.
13. Zanghi BM, Gerheart L, Gardner CL. Effects of a nutrient-enriched water on water intake and indices of hydration in healthy domestic cats fed a dry kibble diet. *American journal of veterinary research* 2018;79:733-744.
14. Jackson O, Tovey J. Water balance studies in domestic cats. *Feline Pract* 1977;7:30-33.
15. Zanghi BM. Water needs and hydration for cats and dogs. *Purina Companion Animal Nutrition Summit*. Vancover, Canada, 2017;15-23.
16. Perrier ET, Armstrong LE, Daudon M, et al. From state to process: defining hydration. *Obesity facts* 2014;7 Suppl 2:6-12.
17. Manz F, Wentz A. The importance of good hydration for the prevention of chronic diseases. *Nutr Rev* 2005;63:S2-5.
18. Strippoli GF, Craig JC, Rochtchina E, et al. Fluid and nutrient intake and risk of chronic kidney disease. *Nephrology (Carlton, Vic)* 2011;16:326-334.
19. Greene JP, Lefebvre SL, Wang M, et al. Risk factors associated with the development of chronic kidney disease in cats evaluated at primary care veterinary hospitals. *J Am Vet Med Assoc* 2014;244:320-327.
20. Rowe E, Browne W, Casey R, et al. Risk factors identified for owner-reported feline obesity at around one year of. *Preventive veterinary medicine* 2015;121:273-281.
21. Lekcharoensuk C, Osborne CA, Lulich JP, et al. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2001;219:1228-1237.
22. Foley P. Constipation, tenesmus, dyschezia, and fecal incontinence In: Ettinger S, Feldman E,Cote E, eds. *Textbook of Veterinary Internal Medicine*. 8th ed. St. Louis, MO: Elsevier, 2017;171-174.
23. Ohlund M, Egenvall A, Fall T, et al. Environmental Risk Factors for Diabetes Mellitus in Cats. *Journal of veterinary internal medicine / American College of Veterinary Internal Medicine* 2017;31:29-35.
24. Lulich JP, Berent AC, Adams LG, et al. ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats. *Journal of veterinary internal medicine / American College of Veterinary Internal Medicine* 2016.
25. Grant DC. Effect of water source on intake and urine concentration in healthy cats. *Journal of feline medicine and surgery* 2010;12:431-434.

26. Robbins MT, Cline MG, Bartges JW, et al. Quantified water intake in laboratory cats from still, free-falling and circulating water bowls, and its effects on selected urinary parameters. *Journal of feline medicine and surgery* 2019;21:682-690.
27. Zanghi BM, Wils-Plotz E, DeGeer S, et al. Effects of a nutrient-enriched water with and without poultry flavoring on water intake, urine specific gravity, and urine output in healthy domestic cats fed a dry kibble diet. *American journal of veterinary research* 2018;79:1150-1159.
28. Wils-Plotz E, DeGeer S, Zanghi B. Nutrient-enriched water supplements nutritionally support hydration in the domestic cat (abstr). American College of Veterinary Medical Forum 2019.
29. Zanghi B, McGivney C, Eirmann L, et al. Hydration measures in cats during brief anesthesia: Intravenous fluids verus pre-procedure water supplement ingestion (abstr). American College of Veterinary Medical Forum 2019.

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Feline Head & Neck: Diseases, Disorders, & More

2020 Virtual CONFERENCE
October 3 & 4 and 24 & 25, 2020

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Partner Symposium

Day 4 — **October 25, 2020** — *Live Exhibits open from 11:00 am- 4:00 pm*

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
10:00 - 10:30 am	Yoga Building Bone Density & Balance		
11:00 - 12:00 pm	Raising Awareness of Osteoarthritis: Identify & Diagnose Affected Cats	Dr. Sheilah Robertson	Ceva
12:00 - 1:00 pm	Nutritional Management of Chronic Enteropathies: A Review of the Recent Research in Cats	Dr. Becky Mullis	Hills
1:00 - 1:30 pm	Exhibit Hall Break		
1:30 - 2:30 pm	Ask the Experts: Q&A	Drs. Debra Horwitz & Sheri Ross	Hills
2:30 - 3:30 pm	Putting Vaccines into Perspective	Dr. Christopher Lee	MERCK Animal Health
3:30 - 4:00 pm	Exhibit Hall Break		
4:00 - 5:00 pm	Creating a Multimodal Plan to Combat Long-term Pain: Why Physical & Mental Health Must be Considered	Dr. Sheilah Robertson	Ceva

All content on demand through December 31, 2020

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Raising Awareness of Osteoarthritis: Identify & Diagnose Affected Cats

Sheilah Robertson, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL)

Introduction

Chronic pain can be defined as "pain without apparent biological value". Pain is always unpleasant and can only be perceived in a conscious state and it is an emotion, something that is difficult to objectively measure. Pain has a sensory and an affective component, meaning "how it feels" and "how it makes the cat feel". In humans, chronic pain has been defined in different ways. One approach is to link it to time; for example, "any pain that lasts more than 3-6 months", but is this set timeline relevant in cats? Pain that "persists beyond the normal tissue healing time" is another definition. This latter definition indicates that a clear demarcation between acute and chronic pain does not always exist and that they may exist in a continuum.[1] A person or an animal may have "chronic pain" but no clear inciting cause can be identified. It makes sense that if we understand the underlying cause of the pain our treatment plan can be specific and targeted; as an analogy, we don't treat all infections with the same antibiotic and in some cases, antibiotics are not even appropriate. Based on the concept of treating the underlying cause, Woolf proposed that the two terms, *adaptive* and *maladaptive* be used to describe pain.[1, 2] [Figure 1]

Adaptive Pain

Adaptive pain includes nociceptive and inflammatory pain. Nociceptive pain is activated by high threshold noxious stimuli such as heat and is an "early warning" or protective mechanism; it may or may not result in tissue damage but is essential for survival. Tissue damage (e.g. a surgical incision) results in inflammatory pain with local tissue becoming more sensitive to stimuli. Inflammatory pain is considered adaptive because it serves a purpose by helping the animal protect itself against further injury. It is typically easy to identify the cause of adaptive pain and normally it is reversible or self-limiting if treated appropriately.

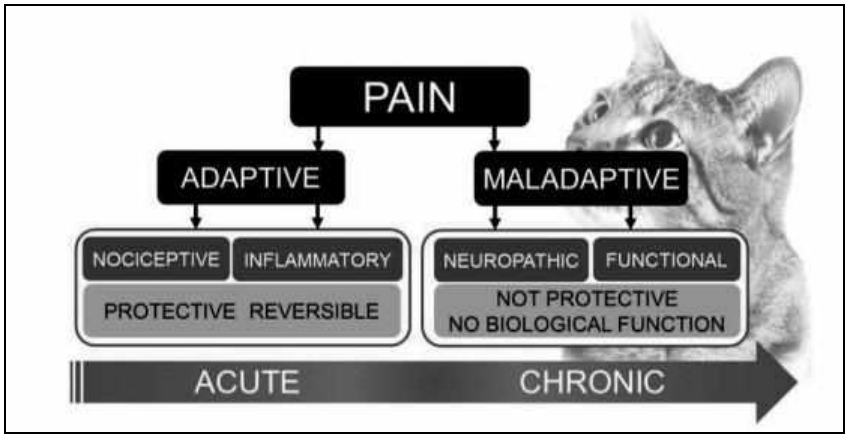
Maladaptive Pain

Maladaptive pain is not protective, it has no biological value, but is the cause of great suffering in humans and animals and should be considered a disease in itself. It results from changes in pain processing systems and can be separated into two types:

1. *Neuropathic pain*; this is a result of neural tissue damage, central or peripheral.
2. *Functional pain*; no neural damage or inflammation can be detected, but the driving force for pain is a malfunction or dysfunction in the nociceptive system.

In maladaptive pain there is amplification and facilitation of what can be thought of as "pain traffic" and increased sensitivity to stimuli. Pain can be spontaneous due to generation of nociceptive input from the central nervous system itself. Other things that contribute to maladaptive pain are an imbalance between inhibitory and excitatory nociceptive input, altered descending inhibition and decreased activation of endogenous analgesic systems (e.g. the endogenous opioid system) and spontaneous ectopic discharge from injured nerves. The separation between adaptive and maladaptive pain is not always clear cut and several painful long-term conditions in cats have an inflammatory component.

Figure 1. Pain terminology



Another term that is important to the concept of maladaptive pain is *central plasticity* (also called central sensitization) which is initiated through cellular wind-up. *Wind-up* is defined as a neuron's increased response and output following identical, repeated stimuli. The term central plasticity refers to an autonomous global response that continues after the stimulus stops, or which is sustained by low level nociceptor input in the periphery.[3] Because some processing systems are down-regulated the term central plasticity is more descriptive than central sensitization. The result of these changes is hyperalgesia (increased pain from a stimulus that normally provokes pain) or allodynia (pain resulting from a stimulus that would not normally provoke pain), and expansion of the receptive field of neurons. For an excellent review of maladaptive pain see the article by Adrian *et al*.[4]

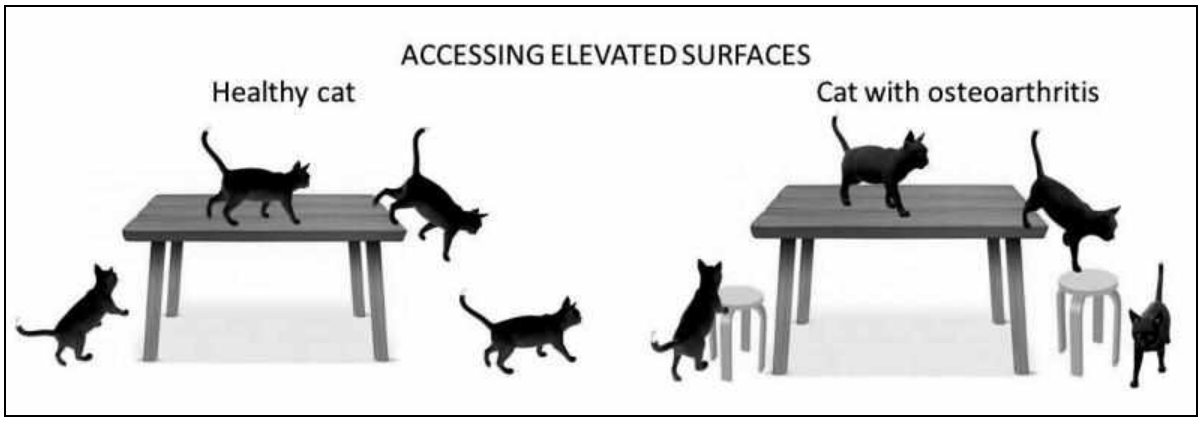
Examples of Maladaptive Pain

An obvious example of neuropathic pain is a nerve sheath tumor. Surgery causes nerve damage and if "something goes wrong" and healing is abnormal, or acute pain management is inadequate this may lead to persistent postsurgical or postoperative pain which is a long-term and maladaptive condition; this is seen in some cats after onychectomy or other amputations. An example of functional pain in humans is fibromyalgia. Although the term is new to veterinary medicine cats with orofacial pain syndrome may have functional pain. In many long-term painful conditions in cats, there is a complex combination and overlap of adaptive (inflammatory) and maladaptive (neuropathic and functional) pain. It is likely that with each disease and even in each individual, different neurobiological processes will be at play and vary over time, making treatment challenging and the response to analgesics unpredictable.

The list of conditions with a pain component known to affect the wellbeing of cats over long periods is extensive and includes, but is not limited to, neoplasia, treatment related pain (radiation therapy), osteoarthritis, dental and oral disease, inflammatory bowel disease, persistent post-surgical pain and non-healing wounds. As many as 90% of cats have radiographic changes suggestive of osteoarthritis and many of these (approximately 45-50%) have pain and mobility impairment, yet it is estimated that less than 10% of cats are actually treated. We are missing a lot of cats than can be helped.

Owner Education and Assessment Tools

One important way to find these cats so we can help them is by raising owner awareness of changes in behavior that may be a result of pain and not as many owners believe "just old age". Campaigns aimed at owners may help raise awareness – an example is to show owners the differences between normal and affected cats when performing specific maneuvers; one example is shown below.



Owner evaluations are important in the assessment of long-term pain because owners know their cat best and spend the most time with them and can assess behaviors that cannot be observed during a clinic visit (e.g. using a litter box, interaction with other people and pets in the household). In addition, there is a possibility that when in stressful environment (a hospital) stress induced analgesia may occur. How evaluation tools that include both the owner and veterinarian should be constructed optimally for cats is not fully understood.

There is, however, a growing understanding of behaviors that may be related to musculoskeletal disease in cats, but one assessment tool may not be applicable to all cats due to different lifestyles (e.g. indoor versus outdoor). There are no fully validated pain scales for cats with osteoarthritis but the following three are useful:

1. The Feline Musculoskeletal Pain Index (FMPI).[5] The latest version of this tool is available at: https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/
2. The Client Specific Outcomes Measure (CSOM).[6]

3. The Montreal Instrument for Cat Arthritis Testing (MI-CAT).[7]

The FMPI and CSOM are questionnaire based and completed by the owner. The MI-CAT is designed for veterinarians and includes assessment of movement and posture and has been tested using mechanical threshold testing (von Frey), activity monitors (accelerometers). It is undergoing further refinement and validation as a screening tool and as a method of detecting treatment effects.

General categories for assessment include:

- General mobility (quality of movement - ease of movement, stiffness)
- Performing activities (playing, jumping up and jumping down, using a litterbox)
- Eating, drinking
- Grooming
- Social activities involving people and other pets
- Changes in temperament

Because of the difficulty of performing a complete orthopedic examination and observing a cat's normal activity in a consulting room, it is extremely helpful to ask owners to capture video clips of their cats in their own home environment for preliminary assessment. Radiographs will often be part of a complete work up, but there is often little correlation between clinical findings (pain in a joint) and radiographic findings, and vice-versa.

Objective measures of movement can be captured using activity monitors (accelerometers) attached to cat's collars or harnesses; these "Feline Fitbits" are sensitive to changes in acceleration and can identify cats with osteoarthritis from normal cats and the impact of treatment.[8]

Quantitative Sensory Testing (QST)

Ideally, we need to test the somatosensory system to determine the degree of malfunction present and to direct our treatment plan. QST measures the frequency or intensity of different stimuli required to elicit a response by the patient. The stimuli used include mechanical, heat, cold and vibration, and are widely used in humans. When central plasticity has occurred changes in sensation to these stimuli can be measured. QST is in its infancy in veterinary medicine, however by using mechanical sub-threshold repetitive stimuli, Guillot and colleagues could discriminate cats with osteoarthritis from non-affected cats.[9]

Quality of Life Scores

Pain may only be one component of what is affecting a cat's quality of life (QoL). A large percentage of cats with osteoarthritis also have chronic kidney disease.[10] In addition to assessing the impact of pain on the cat's life an overall QoL assessment is warranted. A QoL tool for cats with osteoarthritis has been developed, and interestingly, 60% of "things" that owners thought contributed to their cat's QoL were non-active items.[11] Because older cats often have several comorbidities, an overall health related QoL (HRQoL) may be more valuable. The CHEW questionnaire is one approach but still requires testing as a screening tool.[12] An on-line tool which assesses the emotional and physical impacts of disease is available from Newmetrica (HRQL Instrument for cats: https://www.newmetrica.com/).

Clinical Application of Assessment

Re-evaluation over time will help determine the impact of pain and the efficacy of treatment. Many long-term pain conditions wax and wane, and the drivers of pain may also change over time. It is helpful to have owners keep a diary of their cat's activity and behaviors, so they can look back and see how things have changed. Additionally, photographs and videos can be dated and cataloged.

Assessing Stress and Anxiety

In humans the "pain-anxiety-depression" connection is particularly evident in chronic pain syndromes.[A] Because of this, cognitive behavioral therapy, relaxation techniques and so-called "double duty" medications such as antidepressants are part of the overall treatment plan. A behavioral questionnaire and / or examination should also be part of the work-up in cats with chronic pain.

Cognitive Function Testing

In humans, cognitive dysfunction (CD) or decline is reported to be accelerated in patients with maladaptive pain. CD is recognized in cats, usually senior or geriatric cats that are also likely to have a maladaptive pain condition such as OA, therefore cognitive function testing is something we should consider in this population. This is an interesting area of future research as we still have a lot of dots to connect.

References

1. Woolf CJ. What is this thing called pain? *J Clin Invest*. 2010; 120: 3742-4.
2. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med*. 2004; 140: 441-51.
3. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain*. 2011; 152: S2-15.
4. Adrian D, Papich M, Baynes R, Murrell J and Lascelles BDX. Chronic maladaptive pain in cats: A review of current and future drug treatment options. *Vet J*. 2017; 230: 52-61.
5. Gruen ME, Griffith EH, Thomson AE, Simpson W and Lascelles BD. Criterion Validation Testing of Clinical Metrology Instruments for Measuring Degenerative Joint Disease Associated Mobility Impairment in Cats. *PLoS One*. 2015; 10: e0131839.
6. Lascelles BD, Hansen BD, Roe S, et al. Evaluation of client-specific outcome measures and activity monitoring to measure pain relief in cats with osteoarthritis. *J Vet Intern Med*. 2007; 21: 410-6.
7. Klinck MP, Monteiro BP, Lussier B, et al. Refinement of the Montreal Instrument for Cat Arthritis Testing, for Use by Veterinarians: detection of naturally occurring osteoarthritis in laboratory cats. *J Feline Med Surg*. 2017: 1098612X17730172.
8. Guillot M, Moreau M, d'Anjou MA, Martel-Pelletier J, Pelletier JP and Troncy E. Evaluation of osteoarthritis in cats: novel information from a pilot study. *Vet Surg*. 2012; 41: 328-35.
9. Guillot M, Taylor PM, Rialland P, et al. Evoked temporal summation in cats to highlight central sensitization related to osteoarthritis-associated chronic pain: a preliminary study. *PLoS One*. 2014; 9: e97347.
10. Marino CL, Lascelles BD, Vaden SL, Gruen ME and Marks SL. Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies. *J Feline Med Surg*. 2014; 16: 465-72.
11. Benito J, Gruen ME, Thomson A, Simpson W and Lascelles BD. Owner-assessed indices of quality of life in cats and the relationship to the presence of degenerative joint disease. *J Feline Med Surg*. 2012; 14: 863-70.
12. Freeman LM, Rodenberg C, Narayanan A, Olding J, Gooding MA and Koochaki PE. Development and initial validation of the Cat HEalth and Wellbeing (CHEW) Questionnaire: a generic health-related quality of life instrument for cats. *J Feline Med Surg*. 2016; 18: 689-701.

A. https://www.health.harvard.edu/healthbeat/the-pain-anxiety-depression-connection

Suggested Reading

Monteiro B and Lascelles D. Assessment and Recognition of Chronic (Maladaptive) Pain. In: Steagall P, Robertson S and Taylor P (eds) *Feline Anesthesia and Pain Management.* Wiley Blackwell, 2018, pp 241-256.

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Nutritional Management of Chronic Enteropathies: A Review of the Recent Research in Cats

Becky Mullis, DVM, DACVN

The gastrointestinal microbiome is a growing area of research and is important for pet health. The food a cat consumes is the source of nutrition for the GI microbial community and influences both the composition of the bacterial population and the metabolism that occurs. The bacteria in the GI tract are functionally and compositionally diverse, allowing contribution to energy homeostasis, metabolism, gut epithelial cell health, and immunologic activity. This population is not static and can change due to medications such as antibiotics, environmental factors, disease states as well as dietary influences.

When looking at the impact of food on the microbiome, we need to evaluate the degree of digestibility of the food. Those nutrients that are not digested and absorbed reach the colon and are available for microbial metabolism. Nutritional or dietary changes can result in changes in the microbiome in a relatively short period of time. Nutritional interventions that can alter the microbiome include prebiotics, probiotics and changes in the macronutrients provided by the food. Today, we will focus primarily on prebiotics.

Prebiotics are "selectively fermented ingredients that allow specific changes, both in the composition and/or activity in the GI microflora that confer benefits upon host well-being and health"[1,2]. Traditional sources of fiber in pet food include beet pulp (soluble and insoluble fibers) and cellulose (insoluble, non fermentable fiber) but many other sources such as fruit, corn, barley and oat fibers are also utilized and can be fermented by the GI microbiome. There is a limited amount of published literature on the microbiome in cats but some does exist. Researchers have found that cats with inflammatory bowel disease have an altered GI microbiota when compared to healthy cats[3]. In the case of cats with constipation, there is no clear link between constipation and GI microbiome composition, but evidence from human studies suggests a link[4,5]. Additionally, an interventional study in cats with constipation evaluated a multi-strain probiotic. After treatment, there were improvements in fecal score and mucosal histology and also significant increases in populations of Streptococcus and Lactobacillus[6].

Recently, there was an abstract published that outlined a study evaluating the impact of using a fiber enhanced food with prebiotics on cats with either constipation or diarrhea[7]. This 56 day prospective, randomized, blinded, positive controlled study was conducted with 43 client-owned cats with diarrhea or constipation. Cats were recruited from 22 veterinary clinics across the United States. The eligibility of each cat was assessed by medical, drug, and dietary histories, physical examination, and laboratory analysis of blood and urine. Cats were excluded from this study if they were under 1 year of age, had systemic disease including kidney disease (IRIS stage 3 or greater), were unwilling or unable to exclusively consume the study food, had megacolon or were otherwise unlikely to benefit from a fiber supplemented food, chronically used colonic motility drugs, or were currently receiving oral antibiotics or probiotics and were unwilling to discontinue. Enrolled cats were randomized to one of two complete and balanced dry therapeutic foods (easy to digest Control Food or Gastrointestinal Biome) for 56 days. Veterinarians performed physical examinations, evaluated clinical signs of constipation or diarrhea and rated the cat's response to the study food at days 1, 2, 3, 4, 28 and 56 using a defined scale (Negative Response, No Response, Positive Response, and Complete Response). Pet owners evaluated stool quality on a daily basis, and recorded stooling behaviors and quality of life on days 1, 14, 28 and 56. Statistical comparisons over time were analyzed compared to baseline as well as between foods over time.

At the conclusion of this study, significantly more cats fed Gastrointestinal Biome had a positive or complete response than cats fed Control Food ($p < 0.01$). Veterinarians did not report any negative assessments for cats fed Gastrointestinal Biome after Day 28. Finally, none of the cats experienced recurrence of constipation or diarrhea during the 8 week study period. These results demonstrate that a high fiber food with prebiotics can work quickly to improve diarrhea or constipation in client-owned cats, within 24 hours. Additionally, the majority of cats with diarrhea or constipation fed this food are likely to have a positive or complete response within 72 hours.

While we have more to learn about the feline microbiome, there is good evidence that nutrition should play a key role in the management of cats with gastrointestinal disease.

References:

1. Gibson, G. R., Probert, H. M., van Loo, J. A. E., Rastall, R. A., and Roberfroid, M. B. (2004). Dietary modulation of the human colonic microbiota: updating the concept of prebiotics. *Nutr. Res. Rev.* 17, 259–275.
2. Gibson, G. R., Rastall, R. A., Scott, K. P., Tuohy, K. M., Hotchkiss, A., Dubert-Ferrandon, A., et al. (2010). Dietary prebiotics: current status and new definition. *Food Sci. Technol. Bull. Func. Foods* 7, 1–19.
3. Garraway, K., Johannes, C. M., Bryan, A., et al. (2018). Relationship of the mucosal microbiota to gastrointestinal inflammation and small cell intestinal lymphoma in cats. *J. Vet. Intern. Med.* 32, 1692–1702.
4. Tigchelaar, E. F., Bonder, M. J., Jankipersadsing, S. A., Fu, J., Wijmenga, C., and Zhernakova, A. (2016). Gut microbiota composition associated with stool consistency. *Gut* 65, 540–542.
5. Vandeputte, D., Falony, G., Vieira-Silva, S., Tito, R. Y., Joossens, M., and Raes, J. (2016). Stool consistency is strongly associated with gut microbiota richness and composition, enterotypes and bacterial growth rates. *Gut* 65, 57–62.
6. Rossi, G., Cerquetella, M., and Scarpona, S. (2018). Effects of probiotic bacteria on mucosal polyamines levels in dogs with IBD and colonic polyps: a preliminary study. *Benef. Microbes* 9, 247–255.
7. Wernimont, S.M. et al. Food with Specialized Dietary Fiber Sources Improves Clinical Outcomes in Adult Cats with Constipation or Diarrhea *FASEB* J. 2020;34(1).

NOTES:

Putting Vaccines into Perspective

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Introduction
What has saved more lives (cat, human, dog, or otherwise) than vaccines? Only one modern advancement in civilization has achieved this. Risk assessment represents an integral aspect of clinical practice and the delivery of vaccinations.

Risk Assessment and Human Medicine
Hepatitis B Virus (HBV) vaccine represents an unsuccessful attempt at risk assessment. This situation explains the shift towards mass vaccination protocols. Looking back at the incidence of other vaccinate-able diseases before the availability of prevention provides perspective on vaccine protocols.

Utilizing this human medical perspective, the importance of strictly adhering to vaccine guidelines, such as the *2013 AAFP Feline Vaccination Advisory Panel Report* and *2020 AAFP Feline Retrovirus Testing and Management Guidelines*, become apparent.

While rabies is considered a core vaccine for cats in the continental United States, some pet owners are unaware of the importance of maintaining vaccination with their indoor-only cats. Using California urban data as an example, both indoor and outdoor cats need protection for this dangerous zoonotic disease.

Viral Basics
Reviewing DNA versus RNA viruses and enveloped versus non-enveloped viruses provides useful clinical information. Understanding these characteristics regarding core feline vaccines supports the need to maintain strict adherence to the *2013 AAFP Feline Vaccination Advisory Panel Report*.

References
1. New World Encyclopedia. (2016, December 23). Caduceus. Retrieved August 10, 2020, from https://www.newworldencyclopedia.org/entry/Caduceus
2. Stepchew, D. (2011, September 07). The Battle of Greek Gods: The Caduceus vs. The Rod of Asclepius. Retrieved August 10, 2020, from https://www.medelita.com/blog/the-caduceus-vs-the-rod-of-asclepius/
3. Andre, F. (2011, March 04). Vaccination greatly reduces disease, disability, death and inequity worldwide. Retrieved August 10, 2020, from https://www.who.int/bulletin/volumes/86/2/07-040089/en/
4. Cooper, H. (2016, April 04). Vaccines Save Lives. Retrieved August 10, 2020, from https://pulse.seattlechildrens.org/vaccines-save-lives/
5. Plotkin SL, Plotkin SA. A short history of vaccination. In: Plotkin SA, Orenstein WA, eds. *Vaccines*, 4th edn. Philadelphia: WB Saunders; 2004: 1-15.
6. CDC. (2017, March 16). Epidemiology and Prevention of Vaccine-Preventable Diseases. Retrieved August 1, 2018, from https://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html
7. CDC. (2010, June 25). Table 1b. Incidence per 100,000 population of acute, symptomatic hepatitis A, by state/area and year - United States, 1996-2008. Retrieved August 1, 2018, from https://www.cdc.gov/hepatitis/statistics/2008surveillance/table1b.htm
8. CDC. (1987, June 19). Recommendations of the Immunization Practices Advisory Committee Update on Hepatitis B Prevention. Retrieved August 1, 2018, from https://www.cdc.gov/mmwr/preview/mmwrhtml/00019181.htm
9. Roush, S. W. (2007, November 14). Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. Retrieved August 2, 2018, from https://jamanetwork.com/journals/jama/fullarticle/209448
10. Hinman, A. R., Orenstein, W. A., Bloch, A. B., Bart, K. J., Eddins, D. L., Amler, R. W., & Kirby, C. D. (1983, May/June). Impact of measles in the United States. Retrieved August 2, 2018, from https://www.ncbi.nlm.nih.gov/pubmed/6878996
11. CDC. (2018, February 05). Measles. Retrieved August 11, 2020, from https://www.cdc.gov/measles/about/history.html
12. U.S. Census Bureau. (2018, June 8). Population. Retrieved August 2, 2018, from https://www.google.com/publicdata/explore?ds=kf7tgg1uo9ude_&met_y=population&hl=en&dl=en
13. Lambert, N., Strebel, P., Orenstein, W., Icenogle, J., & Poland, G. A. (2015). Rubella. *Lancet (London, England)*, *385*(9984), 2297–2307. http://doi.org/10.1016/S0140-6736(14)60539-0
14. CDC. (2016, March 31). Rubella (German Measles, Three-Day Measles). Retrieved August 2, 2018, from https://www.cdc.gov/rubella/about/in-the-us.html
15. Lambert, N., Strebel, P., Orenstein, W., Icenogle, J., & Poland, G. A. (2015). Rubella. *Lancet (London, England)*, *385*(9984), 2297–2307. http://doi.org/10.1016/S0140-6736(14)60539-0
16. CDC. (2017, November 17). Stop Rubella - Make Sure Every Child Gets the Rubella Vaccine. Retrieved August 2, 2018, from https://www.cdc.gov/globalhealth/immunization/infographic/stop_rubella.htm
17. Burling AN, Levy JK, Scott HM, et al. Seroprevalences of feline leukemia virus and feline immunodeficiency virus infection in cats in the United States and Canada and risk factors for seropositivity. *J Am Vet Med Assoc*. 2017;251(2):187-194. doi:10.2460/javma.251.2.187

18. Cornell University College of Veterinary Medicine. (2018, July 23). Feline Leukemia Virus. Retrieved August 3, 2018, from https://www2.vet.cornell.edu/departments-centers-and-institutes/cornell-feline-health-center/health-information/feline-health-topics/feline-leukemia-virus
19. Little, S., Levy, J., Hartmann, K., Hofmann-Lehmann, R., Hosie, M., Olah, G., & Denis, K. S. (2020). 2020 AAFP Feline Retrovirus Testing and Management Guidelines. *Journal of Feline Medicine and Surgery, 22*(1), 5-30. doi:10.1177/1098612x19895940
20. Association of Feline Practitioners: AAFP, & IDEXX Laboratories. (2009). Feline Retroviral Management Guidelines. Feline Retroviral Management Guidelines. Retrieved August 3, 2018, from https://www.catvets.com/public/PDFs/PracticeGuidelines/RetrovirusGLS-Summary.pdf.
21. California Department of Public Health. (2020). Rabies Surveillance in California Annual Reports. Retrieved August 10, 2020, from https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/RabiesSurveillanceinCAAnnualReports.aspx
22. California Department of Public Health. (2020). Rabies Surveillance in California Annual Report 2018. *Rabies Surveillance in California Annual Report 2018*. https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/RabiesSurveillanceinCAAnnualReport2018.pdf
23. California Department of Public Health. (2020). Rabies Surveillance in California Annual Report 2017. *Rabies Surveillance in California Annual Report 2017*.
24. California Department of Public Health. (2020). Rabies Surveillance in California Annual Report 2017. *Rabies Surveillance in California Annual Report 2017*.
25. Los Angeles Times. (1994, August 18). Woman Stabs Rabid Mountain Lion to Death During Attack on Campers. Retrieved August 10, 2020, from https://www.latimes.com/archives/la-xpm-1994-08-18-mn-28630-story.html
26. California Department of Public Health. (2020). Rabies Surveillance in California Annual Reports. Retrieved August 10, 2020, from https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/RabiesSurveillanceinCAAnnualReports.aspx
27. County of Los Angeles Public Health. (2016, February 11). Rabies Map 2015. Retrieved August 10, 2020, from http://publichealth.lacounty.gov/vet/rabiesmap2015.htm
28. County of Los Angeles Public Health. (2015, February 20). Rabies Map 2014. Retrieved August 10, 2020, from http://publichealth.lacounty.gov/vet/rabiesmap2014.htm
29. County of Los Angeles Public Health. (2014, February 20). Rabies Map 2013. Retrieved August 10, 2020, from http://publichealth.lacounty.gov/vet/rabiesmap2013.htm
30. Coyne, K. P., Dawson, S., Radford, A. D., Cripps, P. J., Porter, C. J., Mccracken, C. M., & Gaskell, R. M. (2006). Long-term analysis of feline calicivirus prevalence and viral shedding patterns in naturally infected colonies of domestic cats. *Veterinary Microbiology, 118*(1-2), 12-25. doi:10.1016/j.vetmic.2006.06.026
31. Rupprecht, C., By, & Last full review/revision Aug 2018 | Content last modified Aug 2018. (2018, August). Rabies in Cats - Cat Owners. Retrieved August 11, 2020, from https://www.merckvetmanual.com/cat-owners/brain,-spinal-cord,-and-nerve-disorders-of-cats/rabies-in-cats
32. Virus Pathogen Risource (ViPR). (2020, January 31). Rhabdoviridae Taxonomy Browser. Retrieved August 11, 2020, from https://www.viprbrc.org/brc/home.spg?decorator=rhabdo
33. Rhodes A. J. (1981). Strains of rabies virus available for preparation of sylvatic rabies vaccines with special reference to vaccines prepared in cell culture. *The Canadian veterinary journal = La revue veterinaire canadienne*, *22*(8), 262–266.
34. CDC. (2016, July 13). Pneumococcal Vaccines (PCV13 and PPSV23). Retrieved August 6, 2018, from https://www.cdc.gov/vaccines/hcp/adults/downloads/fs-pneumo-hcp.pdf
35. CDC. (2015, September 08). Epidemiology and Prevention of Vaccine-Preventable Diseases. Retrieved August 6, 2018, from https://www.cdc.gov/vaccines/pubs/pinkbook/rota.html
36. Immunization Action Coalition. (2018, May). Meningococcal: Questions and Answers. Retrieved August 6, 2018, from http://www.immunize.org/catg.d/p4210.pdf
37. CDC. (2017, December 14). Influenza (Flu). Retrieved August 6, 2018, from https://www.cdc.gov/flu/protect/vaccine/quadrivalent.htm
38. CDC. (2017, December). 2018 Recommended Immunizations for Children from Birth Through 6 Years Old. Retrieved August 6, 2018, from https://www.cdc.gov/vaccines/parents/downloads/parent-ver-sch-0-6yrs.pdf
39. Shore, J. (2020, March 06). Feline Herpes Virus (FHV-1) reagents. Retrieved August 11, 2020, from https://thenativeantigencompany.com/feline-herpes-virus/
40. Sykes J. E. (2014). Feline Panleukopenia Virus Infection and Other Viral Enteritides. *Canine and Feline Infectious Diseases*, 187–194. https://doi.org/10.1016/B978-1-4377-0795-3.00019-3

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Creating a Multimodal Plan to Combat Long-term Pain: Why Physical & Mental Health Must be Considered

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Introduction

Maladaptive (chronic) pain is complex, exists in a continuum and is seldom static (i.e. there are good days and bad days). A combination of inflammatory and maladaptive (neuropathic and / or spontaneous) pain is often present. It is now recognized that in people, osteoarthritis (OA) has a component of neuropathic and functional pain which explains the clinical signs in many human and animal patients. There is also new scientific understanding of the "mind-body" connection in patients with chronic pain. Research on neural pathways suggests there is substantial overlap between how the brain processes emotional and physical pain.[1, 2] This is why chronic pain is often alleviated by prescribing antidepressant and traditional analgesic drugs.

Clear communication with the client is essential at the outset of a treatment plan. The owner must understand that comfort but not cure is the goal in many cases (e.g. osteoarthritis and some cancers); it is rare to achieve complete resolution of clinical signs of pain. It is helpful to describe maladaptive pain as a disease in itself. Treatment requires a committed and compliant owner and the financial, and emotional cost, and time investment required to care for a pet with a long-standing disease should not be under-estimated. A discussion of euthanasia as a treatment option is essential because there will come a time when it is no longer possible to adequately relieve pain. These discussions should start early and be revisited regularly. Quality of Life assessments over time are vital to allow adjustments in treatment plans, to ensure treatment is adequate and to assist in decision making about euthanasia.

Approach to Treatment

Identifying the source, type and cause of pain is not always easy and often the first approach is a "best guess" and may consist of a short course of treatment with an analgesic to gauge the response before long-term planning. This "trial and error" approach is what leads to disappointment and frustration, as the first plan does not always reap the desired results. A multimodal approach is required but the following owner and cat factors must be considered:

1. Drug burden (how many drugs and how often?)
2. Ease of administration (palatability, owner's skill)
3. The cat's tolerance to drugs and their administration
4. Access to, and the cat's tolerance to non-drug therapies

The factors listed above will dictate how well the owner can adhere to the treatment plan for their cat.

Pharmacologic Therapy

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the primary and first line drug therapy for OA in all species including humans. In cats, NSAIDs can be effective for alleviating the pain associated with OA and several studies show that after intervention, cats become more active and their ability to jump up (and down) improves.[3, 4] We have less experience and fewer choices with chronic use of NSAIDs in cats than we do in other species. For this reason and because of diverse opinions and conflicting information, the International Society of Feline Medicine (ISFM) and the American Association of Feline Practitioners (AAFP) published a set of guidelines for the Long-Term use of NSAIDs in cats.[5] Meloxicam has market authorization for long-term use in cats in some countries (not the United States). Meloxicam has efficacy in cats with OA based on different methods of evaluation.[3, 4, 6] Cats are notoriously difficult to medicate but the liquid formulation of meloxicam is palatable and well accepted by most cats; in addition, the liquid formulation facilitates accurate dosing.[7] Many older cats with OA also have chronic kidney disease (CKD), however studies show that, with caution, these cats can still benefit from NSAID administration and there are studies reporting the use of meloxicam in this population.[8, 9] In these cats, CKD was stable. Studies show that in a euvolemic state, renal perfusion is not prostaglandin (PG) dependent but in the face of hypovolemia or hypotension, vasodilatory PGs are important for maintaining perfusion. The owner and veterinarian should work together to find the lowest effective dose for each individual patient; in countries where it is authorized, the label dose is 0.05 mg/kg PO once daily but many cats do well on doses of 0.01-0.03 mg/kg.[7] Client education is essential – for example if the cat refuses to eat, vomits or has diarrhea, the veterinarian must be contacted. Robenacoxib is also palatable and has been studied in cats with OA, with and without kidney disease, over a 28-day period with no reported adverse effects.[10] Use for more than 3 days is off-label in the USA, but it has recently received authorization for the "treatment of pain and inflammation associated with chronic musculo-skeletal disorders" in cats by the European Medicines Agency. An open access review (Long-term use of non-steroidal anti- inflammatory drugs in cats with chronic kidney disease: from controversy to optimism) has recently been published by the World Small Animal Veterinary Association's Global Pain Council.[11]

Tramadol has undergone pharmacokinetic and efficacy studies in laboratory cats and client owned cats.[12, 13] Although deemed efficacious in these studies, it's lack of palatability and adverse side effects including, sedation, dysphoria, diarrhea and inappetence is a major drawback for clinical use.[13]

Gabapentin is frequently prescribed by veterinarians, yet the efficacy of gabapentin has only recently been reported in a small group of cats.[14, 15] Treatment was associated with improvement in activities that owners had identified as being impaired, but based on activity monitors overall activity levels were lower when cats were receiving gabapentin compared to placebo treatment. Sedation was the most common side effect.[15]

Non-drug Treatments

Nutritional supplements or nutraceuticals may be beneficial in animals with DJD, however there are few well controlled studies in animals and because these supplements are not classified as drugs, there is little oversight of quality control and no requirement to prove efficacy prior to marketing. However, some of the commercially available "joint diets" that contain the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), green-lipped mussel extract and glucosamine/chondroitin sulfate are beneficial.[16] In cats, the recommended dose of EPA plus DHA is 50 mg/kg/day.

Physical rehabilitation is one of the most rapidly growing areas in veterinary medicine. Treatment modalities include but are not limited to laser therapy, electrical stimulation, manual techniques including joint mobilization, passive range of motion exercises, massage, trigger point therapy and therapeutic exercise. Acupuncture is now a respected component of treatment in human pain clinics and endorses by the National Institutes of Health. Many veterinarians are pursuing formal training in this discipline and reporting beneficial results in cats with maladaptive pain. Although there is a need for well controlled clinical studies there is general agreement that many cats greatly benefit from these therapies, especially when an integrative approach is used.

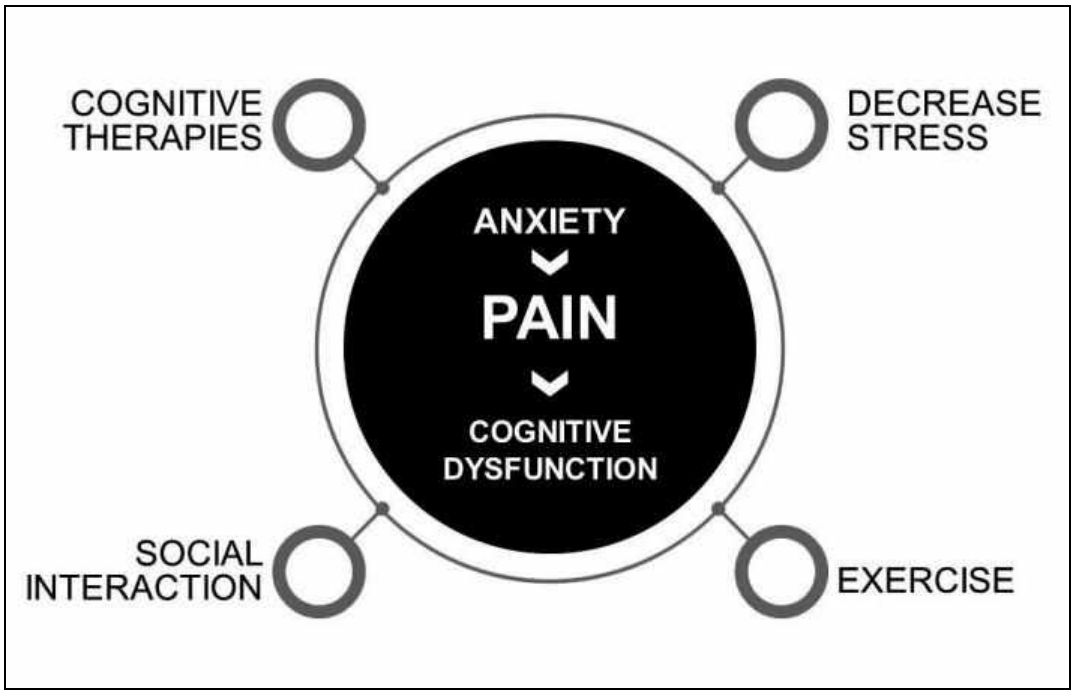
Many owners want to be part of the treatment plan for their cat and we can teach them how to perform range of motion exercises, therapeutic exercises and gentle massage; this enhances the human-feline bond and distraction techniques have a positive impact on pain. The ideal (thermoneutral) thermal environment for cats is > 85^{o}F (29^{o}C); this is especially important for cats that are inactive, thin, or sarcopenic. With age, the ability to thermoregulate also diminishes. Clearly it is not possible to provide that temperature throughout the home, but microclimates can be created; for example, a place to rest or sit can be in direct sunlight (even better if the cat can watch birds and other activities outside for enrichment), a hiding place can be in a small room free from drafts and a heating device used just in that room, or heat provided by a warming blanket under bedding or box they like to rest in. Cats with impaired mobility will need assistance with some "every day" activities. These include but are not limited to:

- Accessing elevated places – use steps, chairs and boxes to make this easier
- Eating and drinking – elevate food and water bowls
- Using a litter-box – ensure this is "easy entry" with a low access point
- Doing their "favorite thing" – this will be different for each cat
- Grooming – owners can assist with this

Alleviating Stress and Anxiety

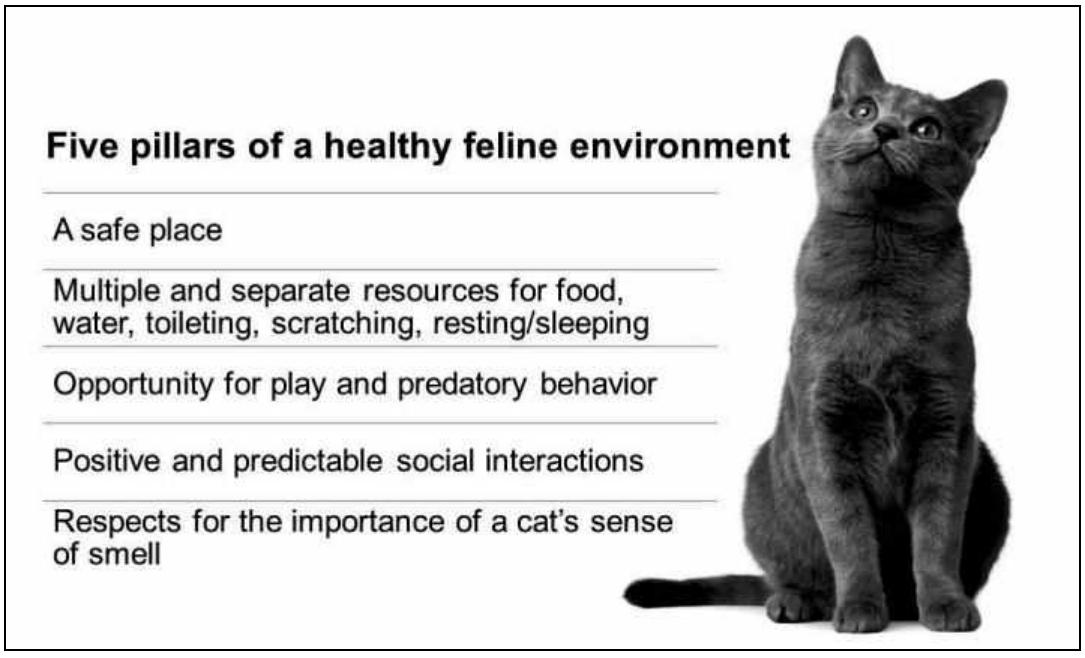
In humans addressing stress and anxiety is often part of a treatment plan for long-term pain. In cats it should be confirmed that they have appropriate environmental enrichment and that stressors are not present in the home (e.g. inter-cat aggression, owner using punishment for unwanted behaviour). Anxiety exacerbates pain, and in turn pain accelerated cognitive decline (Figure 1). Addressing the unique needs of cats is, in my opinion one of the most important parts of treating any chronic illness including pain, yet one that is often ignored. Remember that cats are territorial and often solitary animals and like to have control of their living space – for example have a safe place or an escape route.

Figure 1. The interplay of pain, stress, anxiety, and cognitive function.



The American Association of Feline Practitioners and the International Society of Feline Medicine have published guidelines on the environmental needs of cats.[17] (also see resources). They describe the Five key components of a feline environment (Figure 2).

Figure 2: The five pillars of a healthy feline environment (AAFP/ISFM).



Pheromones

Cats use olfactory and chemical information to evaluate their surroundings. They mark their territory with their face and body to establish the boundaries where they feel secure and safe. Synthetic pheromones (e.g. Feliway® Classic diffuser or spray, Feliway® MultiCat diffuser, CEVA, www.ceva.us) can be used to reduce anxiety and increase grooming. Feliscratch (CEVA, www.ceva.us) can be applied where scratching is desired and will stimulate normal scratching behavior and stretching which are beneficial for cats with osteoarthritis.

Emerging Modalities for Maladaptive Pain

Biological Therapies

There has been a huge growth in the use of monoclonal antibodies to treat numerous diseases in humans and this has spilled over into veterinary medicine. Neutralizing antibodies to nerve growth factor (NGF) provide pain relief in humans, rodent models and dogs and cats with osteoarthritis.[18] In cats, a fully felinized anti-NGF antibody (NV-02) which is administered by subcutaneous injection has undergone clinical trials.[18] Based on client specific outcome measures (CSOMs), the Feline Musculoskeletal Pain Index (FMPI) and activity measured using accelerometers, a positive effect on pain and mobility was reported within three weeks after treatment and lasted six weeks.[18]

Piprants

A new class of drugs called piprants are being widely studied and one such drug, grapiprant, is now available for the treatment of osteoarthritis associated pain in dogs. Grapiprant is a selective antagonist of the EP4 receptor, one of the four prostaglandin E_2 (PGE_2) receptor subtypes. There are likely to be fewer unwanted side-effects with this class of drug because the COX-1 and COX-2 pathways are not affected and the safety data in cats, including administration at high doses encouraging.[19] Currently it is not FDA approved for use in cats.

Maladaptive pain is a disease in itself, and the most common inciting causes in cats is osteoarthritis. Osteoarthritis is not a curable disease but there is a lot we can do to restore comfort and enjoyment of life to affected cats. Although there are effective drug therapies, these should not be used in isolation. Providing an appropriate, and often modified, environment will take your treatment success to the next level.

References

1. Kross E, Berman MG, Mischel W, Smith EE and Wager TD. Social rejection shares somatosensory representations with physical pain. *Proc Natl Acad Sci U S A*. 2011; 108: 6270-5.
2. Sturgeon JA and Zautra AJ. Social pain and physical pain: shared paths to resilience. *Pain Manag*. 2016; 6: 63-74.
3. Bennett D and Morton C. A study of owner observed behavioural and lifestyle changes in cats with musculoskeletal disease before and after analgesic therapy. *J Feline Med Surg*. 2009; 11: 997-1004.
4. Gruen ME, Griffith E, Thomson A, Simpson W and Lascelles BD. Detection of clinically relevant pain relief in cats with degenerative joint disease associated pain. *J Vet Intern Med*. 2014; 28: 346-50.
5. Sparkes AH, Heiene R, Lascelles BD, et al. ISFM and AAFP consensus guidelines: long-term use of NSAIDs in cats. *J Feline Med Surg*. 2010; 12: 521-38.
6. Gruen ME, Griffith EH, Thomson AE, Simpson W and Lascelles BD. Criterion Validation Testing of Clinical Metrology Instruments for Measuring Degenerative Joint Disease Associated Mobility Impairment in Cats. *PLoS One*. 2015; 10: e0131839.
7. Gunew MN, Menrath VH and Marshall RD. Long-term safety, efficacy and palatability of oral meloxicam at 0.01-0.03mg/kg for treatment of osteoarthritic pain in cats. *J Feline Med Surg*. 2008; 10: 235-41.
8. Gowan RA, Lingard AE, Johnston L, Stansen W, Brown SA and Malik R. Retrospective case-control study of the effects of long-term dosing with meloxicam on renal function in aged cats with degenerative joint disease. *J Feline Med Surg*. 2011; 13: 752-61.
9. Gowan RA, Baral RM, Lingard AE, et al. A retrospective analysis of the effects of meloxicam on the longevity of aged cats with and without overt chronic kidney disease. *J Feline Med Surg*. 2012.
10. King JN, King S, Budsberg SC, et al. Clinical safety of robenacoxib in feline osteoarthritis: results of a randomized, blinded, placebo-controlled clinical trial. *J Feline Med Surg*. 2015.
11. Monteiro B, Steagall PVM, Lascelles BDX, et al. Long-term use of non-steroidal anti-inflammatory drugs in cats with chronic kidney disease: from controversy to optimism. *J Small Anim Pract*. 2019; 60: 459-62.
12. Monteiro BP, Klinck MP, Moreau M, et al. Analgesic efficacy of tramadol in cats with naturally occurring osteoarthritis. *PLoS One*. 2017; 12: e0175565.
13. Guedes AGP, Meadows JM, Pypendop BH and Johnson EG. Evaluation of tramadol for treatment of osteoarthritis in geriatric cats. *J Am Vet Med Assoc*. 2018; 252: 565-71.
14. Adrian DE, Rishniw M, Scherk M and Lascelles BDX. Prescribing practices of veterinarians in the treatment of chronic musculoskeletal pain in cats. *J Feline Med Surg*. 2018: 1098612X18787910.
15. Guedes AGP, Meadows JM, Pypendop BH, Johnson EG and Zaffarano B. Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats. *J Am Vet Med Assoc*. 2018; 253: 579-85.
16. Lascelles BD, DePuy V, Thomson A, et al. Evaluation of a therapeutic diet for feline degenerative joint disease. *J Vet Intern Med*. 2010; 24: 487-95.
17. Ellis SL, Rodan I, Carney HC, et al. AAFP and ISFM feline environmental needs guidelines. *J Feline Med Surg*. 2013; 15: 219-30.

18. Gruen ME, Thomson AE, Griffith EH, Paradise H, Gearing DP and Lascelles BD. A Feline-Specific Anti-Nerve Growth Factor Antibody Improves Mobility in Cats with Degenerative Joint Disease-Associated Pain: A Pilot Proof of Concept Study. *J Vet Intern Med*. 2016; 30: 1138-48.
19. Rausch-Derra LC and Rhodes L. Safety and toxicokinetic profiles associated with daily oral administration of grapiprant, a selective antagonist of the prostaglandin E2 EP4 receptor, to cats. *Am J Vet Res*. 2016; 77: 688-92.

Resources
2013 AAFP/ISFM Environmental Needs Guidelines:
https://catvets.com/guidelines/practice-guidelines/environmental-needs-guidelines

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Feline Head & Neck: Diseases, Disorders, & More

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Dentistry	Navigating Those Dental Complications That Make You Go…Hmmm!?	Dr. Christopher Snyder	
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Ophthalmology	Uveitis: Ocular Manifestations of Systemic Disease	Dr. Jessica Meekins	
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Feline Head & Neck: Diseases, Disorders, & More

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	Update on Diabetes Mellitus in Cats	Dr. Deborah Greco	Purina Pro Plan Veterinary Diets
	What is it? Differentiating Medical from Behavioral	Dr. Valarie Tynes	Ceva
Oral Abstracts	How Does OA in Cats Affect Their Quality of Life	Dr. Andrea Wright	
	Identification of Risk Factors for Feline Anesthetic Mortality	Dr. JoAnne Morrison	
	The Novel UNESP-Botucatu Cat Pain Scale (UCAPS)	Dr. Paulo Steagall	
	Thyroid Troubles: Diagnosis and Management of Hypothyroidism	Ms. Stefanie DeMonaco	
	What's In Your Patient's Head: Cone Beam Computed Tomography	Dr. Katherine Knutson	
Miscellaneous			
AAFP Seminar	Creating Individualized Feline Vaccine Protocols: Key Points from the 2020 AAHA/AAFP Feline Vaccination Guidelines	Dr.'s Philip Kass & Amy Stone	AAHA
AAFP Seminar	NEW AAFP Cat Friendly Certificate Program	Dr. Kelly St. Denis	Cat Friendly Practice

Note: Content is subject to change.

Maximizing Regional Anesthetic & Pain Management for Dentistry and Oral Surgery Patients

Christopher Snyder, DVM, DAVDC

Introduction

Regional anesthesia and pain management are fundamentally important skills to successfully leverage for the benefit of our dentistry and oral surgery patients. Despite these patients being under general anesthesia while undergoing procedures, there are inherent benefits to practicing techniques that will allow for the reduction of inhalant anesthesia, improve recovery and improve the patient's comfort at the time of discharge. Anatomy of the face and mouth is complex. There are many locations and combination of locations where local anesthetics can be administered which will result in regional anesthesia.

Key Etiologic and Pathophysiologic Points

Regional anesthesia can offer many benefits by reducing the animal's response to painful stimuli during the procedure as well as provide postoperative analgesia. Primarily speaking, benzodiazapines, phenothiazines and general anesthetics have no primary analgesic activity. These medications alter the state of consciousness and abolish the perception of pain. Peripheral sensitization, or a reduction in the threshold necessary for stimulus transduction occurs due to the effects of tissue injury and inflammation. Inflammatory mediators including prostaglandin E2, bradykinin, neurotrophic factors (NGF) and the activation of mast cells contribute to peripheral sensitization. These inflammatory mediators lower the activation threshold and increase the amount of Na+ flowing across the channel. Once the general anesthetic medications are metabolized, the patient is vulnerable to the sensation of pain.

Local anesthetics work by inhibiting transmission through their effects on Na+ channels. By preventing depolarization and propagation of neural signals to the brain, pain can be effectively blocked. While local blocks reduce the amount of perceived pain and amount of required general anesthesia and associated unwanted side effects, the patient's comfort can be improved. Effective local blocks are not a replacement for safe, effective general anesthesia. The addition of local blocks to the anesthesia and analgesia protocol will provide the benefits of polypharmacy which can be recognized as threefold. These drugs: (1) prevent peripheral and central sensitization, (2) reduce the adverse effects associated with larger doses of medication and (3) provide better postoperative pain management to smooth out the recovery of the patient.

Studies measuring minimum alveolar concentration have shown that administration of local anesthetics reduce the amount of inhalant necessary to keep 50% of patients asleep during a given stimulus. The use of local anesthetics preventing the propagation of nerve impulses may be beneficial on its own but may be further improved through the addition of opioids or alpha2 agonists administered locally.

When given as a local anesthetic, the lidocaine family of drugs provides a variety of options with different onsets of action and different durations of action. Doses should not exceed 2mg/kg in cats and frequently effects can be appreciated at lower doses. Lidocaine is commonly used in human regional and local anesthesia because a quick onset and short duration of action is desirable. Compliance with human patients for taking oral medications is quite good and return to function (frequently the workplace) is important. In companion animal dentistry, bupivacaine is a popular medication used off label because of its longer duration of action. Depending on placement the duration of action may be 6 to 10 hours. Recent canine study information suggests that duration of action may vary by individual, but that bupivacaine may last 1-3 days in that species. Time to onset of action is longer with bupivacaine than lidocaine, some texts referring to a 20-minute period necessary before the nerve impulses are effectively blocked. Lidocaine is labeled for veterinary use while bupivacaine does not carry that label for veterinary use. The most common concentration of bupivacaine is 0.5% (5mg/mL) while lidocaine is 2% (20mg/mL). Mixing these drugs should be discouraged until substantiated research is preformed determining that the drug remains active and what the concentration of active drug is. A recent publication demonstrated that mixing lidocaine and bupivacaine worked longer than lidocaine alone in canine patients. That study's results with bupivacaine mixed with lidocaine demonstrated a shorter duration of action than a study using bupivacaine alone. This begs the question whether mixing the two drugs results in a reduction in the prolonged effect of bupivacaine alone?

Administration of local anesthetic, and availability of active forms of the local anesthetic, can be influenced by the local acidity of the tissues it is infused upon. While tissue pH may interfere with the pKa of the local anesthetic , actively inflamed tissues have not shown to negatively impact the oral absorption of sublingual buprenorphine in one study by Stathopoulou.

Key Clinical Diagnostic Points
Using the techniques covered in this presentation, it has been the experience of the author that small dosages are sufficient to achieve the desired result of local blockade. Using the techniques discussed, the entire mouth can be anesthetized through the administration of local anesthetic in only four locations.

Bupivacaine
0.1-0.15mL per site (cat or small dog)

The various blocking locations are listed below.

Infraorbital Block

Location: immediately within the infraorbital canal
What it blocks: maxillary incisors, canine tooth, PM2, +/- PM3, buccal mucosa, ipsilateral lip, ipsilateral soft tissue of that side of the face
What it won't block: palatal mucosa, PM4 (commonly extracted), may not completely anesthetize for extraction of the central incisors due to crossover innervation

Caudal Maxillary Block

Location: advance the needle parallel with the hard palate trough the infraorbital canal to approximately half the length of the most lateral surface of the zygomatic arch
What it blocks: all the maxillary teeth in that quadrant, ipsilateral lip, ipsilateral hard/soft palatal mucosa, ipsilateral soft tissues on that side of the face
What it won't block: may not completely anesthetize the central incisors
Alternative approaches: A subzygomatic approach for maxillary nerve block is described in cats however effectiveness may be associated with amount of experience

Middle Mental Block

Location: half the height of the mandible in the caudal aspect of the labial frenulum. Enter in through the mesial aspect of the labial frenulum and place the needle against periosteum half the height of the mandible and centered over the caudal aspect of the frenulum attachment
What it blocks: ipsilateral lip and rostral soft tissues, incisors? and canine tooth?
What it won't block: Questionable coverage for the ipsilateral mandibular incisors and canine tooth (probably due to diffusion into the mandibular canal)

Caudal Mandibular Block (Inferior Alveolar Block)

Location: two main approaches
1. Intraoral: half the distance between the angular process and the mucosa immediately caudal to the first molar (lingual side of the mandible)
2. Extraoral: palpate the ventral notch of the mandible (sublte in most cats), half the distance of the length of the notch, place needle perpendicular to the notch and immediately on the lingual surface, advance needle ½ cm

What it blocks: all ipsilateral mandibular teeth, rostral mandibular soft tissues
What it won't block: questionable coverage for caudal mandibular soft tissues, if applied correctly, should not risk anesthetizing the tongue
Note: *It has been shown that intraoral administration of the caudal mandibular block is more accurate than the extraoral approach in a study in dogs- this may be useful in helping to reduce the risk of inadvertent blocking of the sensory innervation to the tongue.*

Once the needle has been placed, it is important to aspirate, and re-aspirate, while rotating the needle 90° along its long axis to ensure the injection is not given intravascular. Medication should be administered with the needle being placed on periosteum for the middle mental, and caudal mandibular blocks. Even if the bevel is not directly over the nerve, by being deposited on periosteum, the local will cover more surface area and increase the chance that the nerve will be coated. Once the local has been administered, the needle should be withdrawn and digital pressure should be placed for 1 minute to provide adequate time to prevent hematoma formation.

There is reasonable expectation that the addition of opioids to a local block may improve postoperative analgesia long after the effects of the sodium channel blockade wear off. In a study performed in dogs comparing bupivacaine versus bupivacaine + buprenorphine (15mcg) it was shown that 3 of 8 dogs with the combination demonstrated analgesia 72-hours post administration while 2 of 8 dogs experienced analgesia 5 days following administration. It has been well established that *mu* receptors exist in the peripheral nervous system and are up-regulated when exposed to chronic noxious stimulation. Dentistry patients undergoing procedures for acute injuries, such as tooth

fracture, are less likely to demonstrate the benefits of opioids in their local blocks as compared to cats with stomatitis or tooth resorption. Chronic conditions may make some drugs work better or last longer.

There are several situations where long-term desensitization of a surgery site may be undesirable. Patients suffering from an oronasal fistula already have a loss of bone and a communication between the oral and nasal cavities. Repairing these defects and having the surgery site be completely numb may result in the animal becoming preoccupied with feeling the sutures on their tongue and subsequently tongue thrusting through the surgery site up into their nasal cavity. Similar potential situations exist with maxillectomy patients. It is this author's experience and recommendation that using short acting local anesthetics like lidocaine followed by aggressive post-operative pain management will result in a comfortable patient after surgery with decreased risk of tongue thrusting. Procedures involving the tongue should never receive local block administration because these patients will be at very high risk of self-trauma and risk "chewing their tongue off." Use of large volumes when performing local blocks has also been anecdotally reported in resulting in this form of self-mutilation. Sticking with the small volumes and accurate placement afford good results with decreased risk.

Whenever there is potential for the local block needle to traverse through an area of possible tumor, the local block should not be performed. Seeding tumor cells through the infraorbital canal may extremely complicate treatment options available for a maxillary tumor. Using a 25 gauge 1 inch to 27 gauge 1.5-inch needle helps reduce possible nerve injury.

Complications

Complications with local anesthetic blocks have been reported in the literature. Paraesthesia, altered sensation and motor changes are occasionally reported anecdotally from practitioners. It is unclear as to where the origin of nerve injury associated with local anesthesia comes from. While histologic nerve changes associated with local anesthetic administration are reported in veterinary patients (Correspondence: J Anthony), true clinical significance should be considered since similar blocks have been performed in humans for decades with a low incidence of true complications. Peripheral nerve paraesthesia is a rare complication reported in humans. One human dental textbook reports an occurrence of 1 case in 1 million injections. Peripheral nerve paraesthesia and subsequent self-mutilation of the veterinary patients' tongue has been only anecdotally reported. The technique for proper needle placement for local anesthetic placement is different than it is for venipuncture. After initial needle penetration, the needle should be guided into position for local administration. When these needles are guided through foramen (as in the infraorbital or caudal maxillary blocks) the needle should be advanced slowly and in most situations the needle bevel with help to displace the neurovascular bundle as the bevel is advanced. Nerves penetrated by needle placement can have variable effects- from no change to permanent sensory or motor dysfunction.

There is a school of thought that nerve injury associated with local blocks may not be directly related to physical damage by needle placement. Peripheral nerve ischemia associated with the addition of epinephrine to a local block may also be associated with nerve injury. The addition of epinephrine to long acting local blocks has therefore been recommended against for that very reason. Beyond the delayed absorption of local anesthetics by the vasoconstriction associated with epinephrine, it has been shown that this catecholamine has some alpha-2 agonist analgesic activity.

The use of small doses in regional anesthesia and aspiration immediately after needle placement can help avoid inadvertent intravascular injection. The most common complications with intravascular injections of local anesthetics include seizures and cardiac toxicity. Bupivacaine has a high affinity for cardiac sodium channels and can cause brady-dysrhythmias as well as ventricular tachycardia and ventricular fibrillation in humans.

The complications of inadvertent anesthesia of the tongue and iatrogenic globe penetration with the needle while performing the maxillary nerve block should both be effectively prevented by close attention to careful needle placement. Iatrogenic perforation of the globe by a needle during local anesthetic placement has a high mortality rate to the eye.

Conclusions

Effective local blocks are not a replacement for safe, effective general anesthesia or multimodal postoperative pain management. Use of local anesthetic agents helps to reduce the amount of inhalant general anesthesia required to keep a veterinary patient anesthetized. The unwanted, most frequently seen complications associated with general anesthesia in veterinary patients who are anesthetized for any reason are hypotension, cardiac dysrhythmias, hypercapnea and hypoxemia. Multimodal analgesia anesthesia can help reduce these unwanted side effects by reducing the amount of gas required to keep the patient anesthetized.

References

1. Beckman BW. Pathophysiology and management of surgical and chronic oral pain in dogs and cats. J Vet Dent 2006 Mar; 23(1):50-60
2. Becerra JR, Tisotti TD, Baier ME, et al. Subzygomatic and infraorbital approaches for maxillary nerve blockade in cats' cadaver. Ciência Rural. 2018;48(4).
3. Gaynor JS, et al. Complications and mortality associated with anesthesia in dogs and cats. J Am Anim Hosp Assoc 1999; 35:13-17
4. Goudie-DeAngelis EM, Snyder CJ, Raffe MR, David FH. A pilot study comparing the accuracy of two approaches to the inferior alveolar nerve block in canine cadavers. Intern J Appl Res Vet Med 2016;14(1):49-58
5. Grubb T, Lobprise H. Local and regional anaesthesia in dogs and cats: Overview of concepts and drugs (Part 1). Vet Med Sci. 2020 May 1.
6. Grubb T, Lobprise H. Local and regional anaesthesia in dogs and cats: Descriptions of specific local and regional techniques (Part 2). Vet Med Sci. 2020 May 1.
7. Lamont LA. Multimodal pain management in veterinary medicine: the physiologic basis of pharmacologic therapies. Vet Clin North Am Small Anim Pract 2008 Nov; 38(6):1173-1186
8. Snyder LBC, Snyder CJ, Hetzel S. Effects of buprenorphine added to bupivacaine infraorbital nerve blocks on isoflurane minimum alveolar concentration using a model for acute dental/oral surgical pain in dogs. J Vet Dent. 2016;33(2):90-96.
9. Snyder CJ, Snyder LBC. Effect of mepivacaine in an infraorbital nerve block on minimum alveolar concentration of isoflurane in clinically normal anesthetized dogs undergoing a modified form of dental dolorimetry. J Am Vet Med Assoc. 2013;242(2):199-204.
10. Pascoe, Peter J. "The effects of lidocaine or a lidocaine-bupivacaine mixture administered into the infraorbital canal in dogs." Am J Vet Res 2016;77(7):682-687.
11. Perry R, Moore D, Scurrell E. Globe penetration in a cat following maxillary nerve block for dental surgery. J Feline Med Surg 2015;17(1):66-72
12. Stathopoulou TR, Kouki M, Pypendop BH, et al. (2018). Evaluation of analgesic effect and absorption of buprenorphine after buccal administration in cats with oral disease. J Feline Med Surg, 2018;20(8):704–710
13. Steagall PV, Monteiro BP. Acute pain in cats: recent advances in clinical assessment. J Feline Med Surg 2019; 21:25–34.
14. Volk HA, Bayley KD, Fiani N, Billson FM. Ophthalmic complications following ocular penetration during routine dentistry in 13 cats. New Zealand veterinary journal. 2019 2;67(1):46-51.
15. Watanabe R, Doodnaught G, Proulx C, et al. A multidisciplinary study of pain in cats undergoing dental extractions: A prospective, blinded, clinical trial. PloS one. 2019;14(3).

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Tips & Tricks for Successful Extractions & Achieving Predictable Healing

Christopher Snyder, DVM, DAVDC

Visualizing the Extraction

A myriad of dental and oral conditions of exist where tooth extraction is a possible treatment option. Frequently, when practitioners or students encounter difficulty with tooth extraction the solution tends to embody the need for better visualization. The various techniques and strategies we use to tackle this issue in practice likely involve some equipment you may already have. Proper visualization of the surgery site, which can be quite small, can be improved with the use of proper illumination and magnification. Illumination of the surgery site can occur both from directionally focused surgery lights as well as surgical lights that can be worn on the head or attached to surgical loupes. Surgical loupes provide magnification worn like glasses and can be fixed (through the lens) mounted magnifiers or 3rd generation surgical loupes that permit being flipped up as well as adjusted for various inter-pupillary distances. Most commonly used magnification in practice is 2-2.5x. Third generation loupes can be ideal in multi-doctor practices where the loupes can be shared and adjusted for each operator. Active suction can also be beneficial during surgical extractions since it permits visualization into an alveolus when looking for a tooth root as well as to evacuate blood from a surgery site. Dental radiography should also not be overlooked as a mechanism with which to visualize the structures being operated on.

Intraoral Radiography as a Means to Managing Complications

Intraoral radiography has become commonplace in many practices and has become 'recommended' in hospitals accredited by the American Animal Hospital Association. In practices where dental radiography has not been prevalent, the use of models or photos accompanied by photos of pathology can be helpful at demonstrating the importance of radiographs to completely appreciate the extent of disease. The most recent generation of clear acrylic dental models include plastic teeth that are radiodense. This provides an opportunity for client education, practice radiographic positioning without worrying a patient is under general anesthesia and can serve as a reminder intraoperatively how to approach extraction.

Radiographic evaluation is especially important in 1) assessing the health of periodontal structures associate with treatment success, and 2) as an important diagnostic and treatment planning tool. For the treatment of periodontal disease, ruling out periapical pathology and endodontic health status is important to assess the long-term goal of preventing pain and infection. In situations of root resorption, identifying root fractures or establishing the presence of gross boney pathology, the aid of a dental radiograph helps the veterinarian anticipate complications such as fractured or missing roots as well as to determine if biopsy of an underlying condition is indicated.

At 6 months of age (conveniently coinciding with spay/neuter age), all permanent teeth should have erupted. Regardless of patient size, any unerupted teeth should be radiographed during the spay/neuter anesthetic episode. Occasionally, early identification of unusual lesions radiographically can afford the patient treatment before lesion progression or the onset of symptoms. In the cases of compound odontomas, small tooth-looking structures are present and early identification and treatment reduces the impact that the expansile cystic lesion create on surrounding tissues. Not only complete removal of pathology is an important benefit of radiography, but also avoidance of complications such as iatrogenic mandibular fracture due to abnormal (dilacerated or curved) root is also valuable.

Correct treatment choice and efficient extraction or crown amputation is a major justification for the use of intraoral radiography. While the cause(s) of feline tooth resorption remains an enigma, treatment options have not changed. Fractured tooth roots is a common frustration when performing tooth extraction and being able to identify *Type 2* tooth resorption (loss of the periodontal ligament structure) which opens the opportunity for crown amputation in certain situations. Without radiography, overlooking affected teeth (stage 4c where resorption is predominately affecting just the root) would result in underdiagnoses of a painful condition. In cats, radiographic confirmation of complete removal of tooth structure can be particularly reassuring, especially while treating conditions reliant on complete extraction.

Surgical Flap Creation

Creation of mucogingival flaps may be one of the most impactful methods to improve surgical exposure and enable successful extraction of teeth. Many tenants of creation of mucogingival flaps are the same as creating flaps to close oronasal fistulas. In both situations, having wide based flaps, with divergent releasing incisions, create an environment conducive to healing. Divergent vertical releasing incisions create a flap, that as it is advanced over an extraction site or over an oronasal fistula, will enable the dissipation of tension through further advancement.

Because the flap gets wider as it is advanced, situations where voids extent to the edge of an incision, these voids can be successfully closed tension free by advancing the flap further and bringing with it wider, and wider tissues. The second inherent value to divergent releasing incisions and wide based flaps is that they are more likely to preserve a robust blood supply to preserve the flap vitality. Following flap elevation and extraction, incising through periosteum lining the flap will allow for maximal advantage of mucosal stretch to ensure the site is closed tension free. Mucoperiosteal flaps should always be closed with simple interrupted sutures with the corners tacked down first. By using simple interrupted pattern, even if a single suture tears through or unties, the entire flap won't become lax as it would with a similar situation with simple continuous closure.

In situations where a repair is being designed for oronasal fistula closure, simple and straightforwad techniques should always be attempted first. As second and third lines of defense there are intricate flaps (angularis oris, split palatal-U, double hinge flaps, and island pedicle flaps) as well as complicated grafting techniques (auricular cartildge, myofascial plane grafts and synthetic or cadaveric sheets or obturators.) All closure techniques hinge on the premise that a tension-free, air-tight seal is created. Bone graft material should never be placed into an oronasal fistula site due to the impending expensive sneeze to follow in recovery. The occlusion and relationship of the mandibular canine tooth with the maxillary buccal mucosal advancement flap should be carefully evaluated to ensure the occlusal tooth does not create tension on the maxillary flap. A primary cause for maxillary canine tooth extraction site dehiscence, in my experience, is tied to occlusal pressure from the mandibular canine tooth cusp and revision surgery should be delayed for 6 weeks while tissues heal and reorganize.

Instrumentation

Appropriate instruments for extraction should be chosen and kept sharp. Holding periosteal and dental elevators in the palm of the hand and with a "short stop grip" provides the finger as a bumper and prevents inadvertent damage to neighboring tissues if the instrument slips. Accidental, iatrogenic slippage and penetration of the instrument into the brain is likely to result in a fatal outcome while penetration into the globe will also likely result in enucleation (due to septic uveitis). There are many fewer examples in the literature of iatrogenic globe penetration where the patient maintains the eye- there are many more examples of cases that inadvertently suffered globe penetration during local anesthetic administration or dental extraction.

There are likely many more than three ways to handle dental elevators than what I describe here, however being creative and approaching dental elevation from various angles can be useful tools in your armamentarium. Catious use of elevating against a neighboring healthy tooth or root as a fulcrum is the philosophy behind the "fulcrum and lever" technique. The "lever and wheel technique" also utilizes neighboring tooth crowns to provide an upward force to elevate the tooth from the alveolus by rotating the elevator along its long axis. Lastly, the "luxator and wedge (+/- rotation) technique simply applies a force between the tooth root and bone. Remember that dental elevators are typically not as sharp as luxators and the sharp luxators are usually only used as a wedge between root and bone because forces in any other directions risk fracturing the instrument. Hopefully, using your dental elevators in a variety of ways will facilitate loosening the tooth before removal- remember the: fulcrum and lever, lever-and-wheel and luxator-wedge and rotation techniques!

Delayed absorbable suture tends to be the suture of choice for closure of oral surgery sites. While the suture does take a longer than necessary time to resorb, the pro-inflammatory nature and high tissue drag of chromic gut tends to be gone too quickly in patients with delayed healing due to comorbidities. In cases of advanced periodontal disease or the friable nature of inflamed oral mucosa associated with cases of feline chronic gingivostomatitis, taking large suture bites, into healthy tissue can be advantageous. Judicious use of antibiotic therapy, especially doxycycline suspension in stomatitis cases, the handling of tissues in surgery can be made more ammenable.

Dealing with Deciduous Teeth

In itself, removal of deciduous teeth is not a complication however the close relationship between the deciduous tooth roots and permanent tooth buds makes injury to the developing permanent tooth easy to do. An overarching theme is that deciduous teeth are not designed to last an animal's entire life- if there is ever an issue with a deciduous tooth, the correct treatment is always extraction. When elevating deciduous teeth be mindful that the deciduous tooth roots rest buccal to the developing tooth bud- that being said, you should avoid placing the dental elevator, or elevating the deciduous tooth root tip toward, the lingual surface of the deciduous tooth root. I think of it this way- bodies have evolved with organ placement in locations that they are protected- permanent teeth develop closer to the middle of the body (palatal or lingual) relative to the deciduous counterparts in a sense the location is better protected. During the early stages of mineralization, damage to the developing permanent tooth can result in arrested development, enamel hypomineralization or hypocalcification. The maxillary canine teeth are the only exception to the location rule- the developing permanent tooth bud is oriented mesial (rostral) to the deciduous tooth crown. In situations where retained deciduous teeth exist, radiographs should always be taken to discern permanent from deciduous however it is a safe bet that the deciduous teeth will be buccal to the permanents with the exception

of deciduous maxillary canines sitting caudal to the developing permanent teeth. Retained or persistent deciduous teeth are not as common in cats, however whether it is removing retained or fractured deciduous teeth, care should be taken to respect the developing permanent teeth.

References

1. Perry R, Moore D, Scurrell E. Globe penetration in a cat following maxillary nerve block for dental surgery. *J Fel Med Surg*. 2015;17(1):66-72
2. Volk HA, Bayley KD, Fiani N, Billson FM. Ophthalmic complications following ocular penetration during routine dentistry in 13 cats. *New Zealand Vet J*. 2019;67(1):46-51
3. Smith MM, Smith EM, La Croix N, Mould J. Orbital penetration associated with tooth extraction. *J Vet Dent* 2003;20(1):8-17
4. Milella L, Gurney M. Dental and oral surgery. *In: BSAVA Manual of Canine and Feline Anaesthesia and Analgesia* 2016;BSAVA Library:272-282
5. Alessio TL, Krieger EM. Transient unilateral vision loss in a dog following inadvertent intravitreal injection of bupivacaine during a dental procedure. *J Amer Vet Med Assoc* 2015;246(9):990-3
6. Duke FD, Snyder CJ, Bentley E, Dubielzig RR. Ocular trauma originating from within the oral cavity: clinical relevance and histologic findings in 10 cases (2003–2013). *J Vet Dent* 2014;31(4):245-8
7. Reiter AM, Soltero-Rivera MM. Applied feline oral anatomy and tooth extraction techniques: an illustrated guide. *J Fel Med Surg* 2014;16(11):900-13
8. Moore JI, Niemiec B. Evaluation of extraction sites for evidence of retained tooth roots and periapical pathology. *J Amer Anim Hosp Assoc* 2014;50(2):77-82
9. Kirby S. Extractions in feline dentistry: part I–what to do when tooth resorption is present. *Companion Animal* 2014;19(3):148-56

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Navigating Those Dental Complications That Make You Go…Hmmm!?

Christopher Snyder, DVM, DAVDC

Have you ever been in the course of an extraction and encountered a complication that gives you pause? Something that makes you stop, think and look at your instrumentation only to leave you thinking "How will I MacGyver this one?" If you've never encountered complications when performing extractions, either you're not performing extractions early enough for the patient's benefit, or you've not been extracting enough teeth. Some complications can be more troublesome to solve then others, but identification and treatment decision making may go something like this…

Tooth Resorption and Fractured Roots

Keep in mind there are 5 *Stages* of tooth resorption and the progression of the resorptive process advances not only on an individual *cat* basis, but also on an individual *tooth* basis. It has not been well documented how painful the resorptive process is with the exception that it is clinically appreciable that Stage 3 resorption (pulp chamber exposure) is very painful. Intraoral radiography is necessary to determine which *Type* of tooth resorption exists. Radiographic evaluation for the presence of periodontal ligament (PDL) (Type 1 root resorption) necessitates the recommendation of extraction since continued root resorption is necessary for the tooth to become completely resorbed and would be impossible to accurately determine if it were painful. Typically, unless there is inflammatory root resorption where the PDL is present, but root structure may be compromised, extracting these teeth is routine. Type 2 resorption (loss of the PDL) occurs as replacement resorption takes place. For instances where teeth undergoing type 2 resorption need to be extracted, successful extraction can be more onerous. It is commonly observed that so long as there is a difference in radiodensity where resorbing root structure exists, there can be an appreciated difference in between bone and resorbing root during extraction. Following creation of a surgical flap and removal of alveolar bone, resorbing root structure can be identified by a beige color and hard tissue that does not bleed. Considering the obvious challenge of not having a PDL space to elevate within, these extractions should be expected to be performed with better surgical exposure than usual- having ample exposure with a wide surgical flap and buccal bone removal extended almost the full length of the root is frequently necessary. Resorbing tooth roots that fracture during extraction can frequently be removed with similar efforts to improve surgical exposure and visualization.

Once mucogingival flap elevation has taken place, and buccal bone removal is performed providing exposure to the lateral surface of the root, small carbide burs should be used to outline the root structure and create space where small dental elevators or root picks can be placed. The resorbing nature of these roots should create the expectation that root fragments will need to be removed in pieces and multiple radiographs necessary along the way to confirm complete removal. Resist the tendency to "bur out" the remaining resorbing root structure since certain conditions may not be resolved with managing root structures in this way. Leaving resorbing root structure behind may be particularly detrimental in instances of: 1) proof of concurrent endodontic disease (wide pulp chamber or periapical radiolucency), 2) generalized evidence of stomatitis, 3) remaining root structure with PDL present and 4) patients who may be prognostically worse off should they develop feline chronic gingivostomatitis in the future (FeLV, FIV positive patients.)

Iatrogenic Creation of an Oronasal Fistula

Oronasal fistula development is most likely to occur when performing extraction of maxillary canine teeth. Only a thin shelf of bone separates the root of canine teeth from the nasal cavity. Oronasal fistula development can spontaneously develop due to endodontic disease and subsequent periapical bone resorption and fistula formation might not be recognized until extraction is performed. Iatrogenic cause of oronasal fistula formation can best be prevented by resisting the tendency to place dental elevators or luxators along the palatal aspect of these teeth. Apical pressure, on the palatal surface can easily result in perforation through alveolar bone and exposure of the nasal cavity. Due to the curvature of the canine teeth, consider facilitating better surgical exposure with larger flaps, and more buccal bone removal with grooves or motes along the PDL space to facilitate instrument placement.

Iatrogenic Mandibular Fracture

Iatrogenic mandibular fracture during extraction is a complication that can occur in cats, especially when performing extraction of canine teeth. Fractures at the location of the canine teeth may be predisposed for a couple reasons. Firstly, the diameter of the canine tooth at this location of the mandible contributes a large amount. In dogs, it has been shown that as breed of dogs get smaller, the ratio of root to bone of canine teeth at this location increases. This ratio of tooth root to bone was also found to be greatest compared to the next largest tooth in the dog's mouth (mandibular first molar). A similar study has not been investigated in cats and while it is reasonable to expect the

root's contribution will be greater than the M1 roots, there may be less of an effect on body weight relative to increasing tooth root size. Because of the nature of larger roots, the force distribution through bone in this location creates a stress riser because of the PDL's soft tissue nature. A second reason for a propensity for fracture in this location may include the confounding nature that mandibular symphysis does not provide much structural support to bone rostral to the canine tooth. Elevation along the mesial aspect of the canine tooth and a lack of support to the rostral bone can precipitate fracture. Additionally, the curvature of the mandibular canine teeth makes it difficult to fit an elevator or luxator along the distal surface which may result in attempt to elevate along the lingual surface. The thin bone in this location may also result in fracture. As a general rule, avoid placement of elevators and luxators along the lingual or palatal aspects of canine teeth to avoid those potential complications.

Preventing Iatrogenic Mandibular Fracture or Oronasal Fistula Development

Canine teeth may be some of the most difficult to remove, not only over concern about creation of complications, but also because they just seem to require the most work. In an effort to make extraction of these teeth easier, and avoid the aforementioned complications, consider modifying your extraction approach. A large component to these teeth requiring more work to remove is due to their attachment in the alveolus, to bone. The amount of surface area of PDL that must be severed or loosened to facilitate removal is large. One tactic to improving access to these teeth includes facilitating better access to the mesial and distal surfaces for elevation. In most scenarios, crown amputation of any teeth facilitates straight-line access to remaining root structure. This can be particularly helpful at avoiding the lingual/palatal aspects of the canine teeth. Serial sectioning can also be a useful tool at avoiding iatrogenic complications. Sectioning root structure in to 2 or 3 segments results in smaller surface area for PDL to retain the root in bone. Using this technique may require removal of additional buccal bone than usual, however if it results in preventing oronasal fistula formation or mandibular fracture, then it's a win-win!

Retrieving Root Displaced Root Tips

Frequently, the loss of visualization of a displaced tooth root can be a great cause of anxiety. Concerns with root fragments displaced in the nasal cavity are centered around not being able to visualize where the root went, causing more trauma/bleeding by looking for it and being left with an oronasal fistula. The greatest concerns for displaced mandibular tooth roots are damaging the mandibular canal contents (and the subsequent brisk bleeding associated with it) or thoughts that removing too much bone will result in pathologic jaw fracture. Luckily, in both situations, displaced tooth roots into these cavernous spaces don't tend to go far. The presence of nasal turbinates helps keep root fragments locally restricted and displaced fragments in the mandibular canal are similarly restricted from going far. Whenever a root fragment goes missing, the first step should be imaging the patient to determine what direction the root has been displaced. Multiple views (lateral/dorsal/oblique) may be necessary to appropriately judge where the fragment is, and the use of overlying 25g needles at various places can help direct where further surgical exploration should take place. The most precise tactic for determining where the root fragments may have displaced to would be CT but even cone beam CT may only be a luxury to most practices. Once the location of the root fragment can be determined, careful removal of overlying bone is the best approach to removal. In situations where the fragment maybe closely associated with neurovascular structures, use of diamond burs for bone removal or piezo surgery units both reduce the potential for further trauma and bleeding. The combination of radiography, ample surgical exposure, suction, light and magnification are all conditions that can improve successful retrieval.

Treatment Decision-making with Fractured Teeth

Teeth develop and the inside of the tooth matures in a similar way to how trees lay down concentric rings. Trees grow by laying down rings of cambium, which results in the outside circumference getting larger. Teeth are similar but deposit mineralized material (dentin) in completely the opposite direction- from the periphery working toward the center. The newly erupted tooth is comprised of mostly soft tissue (pulp) internally which is comprised of arteries, veins, nerves, lymphatics and connective tissues. The large pulp chamber is lined with odontoblasts that lay down additional dentin as the tooth ages. This results in the internal pulp diameter (soft tissue) narrowing as additional dentin is laid down (hard tissue). No matter what intervention a veterinarian (or veterinary dentist) involves, a tooth will never be as strong as what nature intended. Performing a procedure designed to replace the pulpal contents with something foreign (root canal therapy) results in a tooth that is structurally weaker than a natural tooth but at least it is not a source of infection and pain.

Any time deciduous (primary) teeth are damaged, the correct treatment is always extraction. Permanent teeth on the other hand are worth preserving. If a permanent tooth in a patient less than 18 months old is fractured, vital pulp therapy should be performed to create a new barrier against oral bacteria. The goal is to use specific materials (calcium hydroxide or mineral trioxide aggregate) that will resist infection/pain while maintain the health of the odontoblasts required for additional dentin to be deposited. Performing a root canal on a tooth in a patient younger than 12 months of age in a cat may be challenging because files aren't wide enough to clean all of the canal walls simultaneously. Even if files were large enough, the remaining dentin may not be strong/ durable enough to withstand a life span's use and abuse. Consideration and client education should take place when considering

advanced endodontic procedures in cats. Existing teeth demonstrating resorption should suggest that patient may be at risk for developing future resorption of teeth currently under consideration for endodontic therapy. Teeth considered for endodontic therapy should almost never undergo advanced endodontic treatment since future extraction is likely necessary and if root canal sealers and obturants are used, they will need to be removed from the bone-like material associated with replacement resorption.

What Should I Place in the Alveolus?

A variety of options exist for products to place into extraction sites. In most situations, removal of the tooth structure, especially if it is infected, should resolve the issue and result in spontaneous healing. Under normal circumstances, expect the socket to fill with bone over the course of 2-4 months. If material is indicated to place into an alveolus, knowing the advantages and disadvantages of each materials is helpful. *Autogenous bone grafts* typically refer to harvesting cancellous bone (less frequently cortical bone chips.) This is the golds standard for encouraging new bone deposition in the extraction site. Stem cells, bone morphogenic proteins, antibacterial properties of blood clots and the recruitment of fibroblasts are all helpful to immediately place into the extraction site if expedited bone deposition is desired. The disadvantage of autografts is the additional anesthetic time required to harvest the graft as well as additional surgery site monitoring. Commercially available *allografts* commonly refer to decalcified freeze-dried a bone graft which are harvested and processed from cadavers. The decalcification process destroys most all antigenic stimuli but with that removes stem cells and bone morphogenic proteins which are both pivotal to the early recruitment and differentiation of osteoblasts. The decalcified bone matrix serves as a scaffold for osteoblastic deposition and as new bone is deposited, the process of creeping substitution results in resorption new bone deposition in the location of the decalcified graft. The advantage of allografts is they are commercially sourced while the disadvantage is they are recommended to be species specific and the cost of the graft. Synthetic bone graft materials (*alloplasts*) are commonly made up of hydroxyapatite with inorganic minerals. Similar to allografts, these materials provide scaffolding for osteoblastic bone deposition. Advantages include commercial availability, ease of sterilely sharing one dose across multiple patients and the lack of species specificity. The disadvantage is that the inorganic mineral in these materials can take many, many years to be completely resorbed. When considering various alloplasts, consider materials that are quicker to resorb- these materials frequently are predominately comprised of calcium and phosphate. Studies in rabbits have shown that regardless of blood clot to autograft, at 4 months post extraction all sockets are filled with bone. The real question is, how quickly do you really need that bone?

References

1. Reiter AM, Brady CA, Harvey CE. Local and systemic complications in a cat after poorly performed dental extractions. *J Vet Dent.* 2004;21(4):215-21.
2. Gengler B. Exodontics: Extraction of teeth in the dog and cat. *Vet Clin Sm Anim Pract*. 2013;43(3):573-85.
3. Holmstrom SE, Bellows J, Juriga S, Knutson K, Niemiec BA, Perrone J. 2013 AAHA dental care guidelines for dogs and cats. *J Amer Animal Hosp Assoc*. 2013;49(2):75-82.
4. Bellows J, Berg ML, Dennis S, Harvey R, Lobprise HB, Snyder CJ, Stone AE, Van de Wetering AG. 2019 AAHA Dental Care Guidelines for Dogs and Cats. *J Amer Animal Hosp Assoc*. 2019;55(2):49-69.
5. Oxford M. Dental extraction techniques in dogs and cats. *Companion Animal*. 2018;23(6):336-41.
6. Silva AM, Souza WM, Souza NT, Koivisto MB, Barnabé PD, Poló TD. Filling of extraction sockets with autogenous bone in cats. *Acta cirurgica brasileira*. 2012;27(1):82-7.
7. Clark DE. Endodontics of dogs and cats: an alternative to extraction. *Australian veterinary journal*. 1995;72:383-9.

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Pesky Parasites & Infections Regionalized to the Head & Neck Area
Alison Diesel, DVM, DACVD

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Management of Traumatic Brain Injury

Christopher G. Byers, DVM, DACVECC, DACVIM (SAIM), CVJ

Pathophysiology
Traumatic brain injury (TBI) is a non-degenerative, non-congenital acute insult to brain parenchyma from an external mechanical force. The results of TBI may be temporary or permanent and can include physical and behavioral changes. The cranial vault has a set volume and three major components: brain parenchyma, cerebrospinal fluid (CSF), and blood. Primary and secondary TBI can induce changes in one or more of these components, ultimately creating increased intracranial pressure (ICP). This relationship is called the Monroe-Kellie Doctrine.

Traumatic brain injury is typically categorized as primary or secondary. Primary TBI is damage to intracranial structures at the time of initial impact (i.e.: intracranial hemorrhage leading to mass compression, direct neuronal-axonal damage, contusion, concussion, cerebral lacerations caused by skull fractures). Damage may be focal or diffuse. Veterinarians have no control over primary TBI. Secondary TBI involves severe disturbances in regulation of cerebral blood flow (CBF) and energy metabolism that predisposes cerebral tissue to ongoing brain injury. This type of injury occurs minutes to hours after the original traumatic event, and as such, is also called delayed injury. Both intracranial and extracranial factors can exacerbate secondary TBI.

Intracranial Factors
Excitotoxicity and Neuronal Sensitivity - Initial impact causes massive depolarization and ion fluxes in neurons, astrocytes, and glial cells. Adenosine triphosphate (ATP) is expended to restore normal electrochemical gradients. This restorative attempt is primarily achieved by the Na^+-K^+-ATPase pump. Trauma-associated hypotension, hypoxemia, and/or local disruption of cerebral blood flow diminishes the amount of available ATP through reduction of substrate delivery.

Glutamate (GLUT) is an excitatory neurotransmitter directly and indirectly responsible for Ca^{2+} influx into cytosol from extracellular fluid (ECF) or internal stores. A rise in cytosolic Ca^{2+} causes changes in enzyme function and activation of secondary messenger systems. The normal ECF GLUT is very low (0.6 umol/L). When ECF GLUT reaches 2-5 umol/L, there is massive neuronal excitation. Normally energy-dependent uptake transporters in neurons and astrocytes efficiently clear GLUT. With TBI there is an uncontrolled release of GLUT from intracellular stores. When coupled with energy depletion, this energy-dependent uptake system fails.

Various GLUT receptors (e.g.: NDMA, AMPA, kainite) facilitate influx of Ca^{2+} and sodium. A massive influx of Ca^{2+} and Na^+ into cells causes membrane depolarization. Subsequently, there is activation of secondary voltage-gated Ca^{2+} channels to cause further influx of Ca^{2+}. The Ca^{2+} cytotoxic effects include uncoupling of oxidative phosphorylation, activation of several enzyme systems, and alterations of vascular sensitivity.

Extracranial Factors
Systemic insults may readily contribute to secondary brain injury, including hypotension, hypoxia, systemic inflammation, glucose derangements, CO_2 derangements, hyperthermia, electrolyte imbalances, and acid-base disturbances

Initial Assessment
Veterinarians should initially perform a primary survey in patients with TBI. Thorough evaluation of a patient's airway, breathing, and cardiovascular status (i.e. ABCs) is of paramount importance. The airway should be intubated if there is any concern for airway obstruction and/or abnormal ventilation. As quickly as possible and ideally before any therapies, one should obtain an appropriate minimum database:

- Packed cell volume (PCV) / Total solids (TS)
- Blood pressure (BP)
- Blood glucose (BG)
- Blood gas analysis (venous or arterial)

Many patients with TBI have experienced polytrauma. Therefore, complete blood and urine testing (e.g.: CBC | CHEM | UA) to help assess organ function is ultimately indicated.

Patients with TBI commonly present in hypovolemic shock. Volume resuscitation with isotonic crystalloids, hypertonic crystalloids, and/or synthetic colloids should target endpoints of resuscitation, including heart rate & rhythm,

respiratory rate, blood pressure, glucose, lactate, pulse pressure, and mentation. Systemic hypotension must not be tolerated, as cerebral perfusion pressure (CPP) is largely dependent upon mean arterial pressure (MAP):

CPP – MAP - ICP

Patients that do not respond to volume resuscitation may require inotropic and/or vasopressor support.

Modified Glasgow Coma Scale
The modified Glasgow coma scale (mGCS) assesses three domains: level of consciousness (LOC), brainstem reflexes, and motor responses.

Motor Activity	Score
Normal gait, normal spinal reflexes	6
Hemiparesis, tetraparesis or decerebrate activity	5
Recumbent, intermittent extensor rigidity	4
Recumbent, constant extensor rigidity	3
Recumbent, constant extensor rigidity with opisthotonus	2
Recumbent, hypotonia of muscle, depressed or absent spinal reflexes	1

Brain Stem Reflexes	
Normal pupillary light reflexes and oculocephalic reflexes	6
Slow pupillary light reflexes and normal-to-reduced oculocephalic reflexes	5
Bilateral unresponsive miosis with normal-to-reduced oculocephalic reflexes	4
Pinpoint pupils with reduced-to-absent oculocephalic reflexes	3
Unilateral, unresponsive mydriasis with reduced-to-absent oculocephalic reflexes	2
Bilateral, unresponsive mydriasis with reduced-to-absent oculocephalic reflexes	1

Level of Consciousness	
Occasional periods of alertness and responsive to environment	6
Depression or delirium, capable of responding but response may be inappropriate	5
Semi-comatose, responsive to visual stimuli	4
Semi-comatose, response to auditory stimuli	3
Semi-comatose, responsive only to repeated noxious stimuli	2
Comatose, unresponsive to repeated noxious stimuli	1

Patients are stratified into one of three categories:

- mGCS = 3-8: suggests grave prognosis
- mGCS = 9-14: suggests guarded prognosis
- mGCS = 15-18: suggests good prognosis

A recent study evaluated and validated both the modified Glasgow Coma Scale and Animal Trauma Triage score in injured cats (Lapsley *et al*, 2019). The mGCS showed fair performance overall for prediction of mortality, but the point estimate of performance improved when restricted to head trauma patients. The motor component of the mGCS showed the best predictive performance; however, the full score performed better than the motor component alone. When assessment was restricted to patients with head injury, there was no difference in performance between the ATT and mGCS scores. Anecdotal evidence suggests patients with severe TBI (mGCS score <8) can dramatically improve within 24-48 hours. A patient's mGCS can improve dramatically after successfully restoring cardiovascular stability.

The AVPU scale has fewer variables than the mGCS and consists of assessing the patient's state of consciousness by classifying their clinical status using scores from 1 to 4: the patient is alert, the patient responds to verbal stimulation, the patient responds to painful stimuli, the patient does not respond (Rabelo, 2008). This scale does not take into account motor activity or brainstem reflexes.

SCORE	STATE OF CONSCIOUSNESS
A-1	Patient is alert
V-2	Patient responds to verbal stimulation
P-3	Patient responds to painful stimulation
U-4	Patient does not respond

Diagnostic Imaging
Skull imaging may yield uniquely important information for TBI patients with progressive neurologic signs and/or those manifesting neurologic deficits that don't resolve with appropriate stabilization. Computed tomography (CT) and/or magnetic resonance imaging (MRI) are highly sensitive modalities for TBI patients; radiography rarely yields diagnostically useful information. Common CT scans abnormalities are skull fractures, hydrocephalus, parenchymal injuries, hemorrhage, and mass effect.

Monitoring
Patients with TBI are quintessentially critical patients. Adherence to Kirby's Rule of 20 can help guide therapeutic interventions. Mean arterial pressure should be maintained >80 mmHg (or systolic >100 mmHg) to prevent inappropriate decreases in CPP. Telemetry is helpful to monitor for the Cushing's reflex. Patients often develop hyperglycemia post-TBI. The degree of hyperglycemia has been correlated with the severity of TBI, but not with outcome. The benefit of tight glycemic control in TBI patients is currently controversial, since this therapy has not consistently been associated with reduced mortality and infusion has led to hypoglycemia. Studies investigating tight glycemic control in cats have not been conducted. Current recommendations are to avoid iatrogenic hyperglycemia and hypoglycemia.

Intracranial Pressure Measurement
Intracranial pressure (ICP) monitoring may be useful and should be maintained below 20 mmHg to maintain CPP >60 mmHg. Measuring ICP involves placing a pressure transducer most frequently within the skull. Such monitoring is infrequently performed in veterinary medicine. Currently, ICP measurement is recommended in human patients with severe traumatic brain injury and an abnormal CT scan.

Therapies
Hyperosmotic / Diuretic Agents
Mannitol: Mannitol 25% is a hyperosmotic agent that has improves neurologic outcome in TBI patients. Reported beneficial effects are an ability to reduce cerebral edema, increase CPP, and enhance CBF. Mannitol should always be given as a slow bolus (0.5-1.0 g/kg IV over 15 minutes), as constant rate infusions (CRIs) and periods of prolonged administration are associated with alternations in blood-brain barrier (BBB) permeability. Mannitol administration can cause rebound hypotension and can induce a profound diuresis and subsequent hypovolemia. As such, isotonic crystalloid and/or synthetic colloids should be administered to maintain euvolemia. Mannitol boluses should be infused if serum osmolality is >320 mOsm/L.

Hypertonic saline: As an alternative to mannitol, hypertonic saline 7% (3-5 mL/kg IV over 15 minutes) has similar osmotic effects due to the inability of sodium to cross the BBB. This fluid also causes rapid volume expansion, as well as positive inotropy and vasoregulatory and immunomodulatory effects. Unlike mannitol, hypertonic saline does not induce rebound hypotension. Administration is contraindicated in those with hyponatremia and hypernatremia.

Furosemide: Furosemide readily induces intravascular volume depletion and systemic hypotension. This medication should only be administered to those patients with other indications for it (i.e.: oliguric/anuric acute kidney injury, cardiogenic pulmonary edema).

Oxygen Therapy
Cerebral hypoperfusion is a main precipitator of secondary TBI. Therapy should be initiated to restore and maintain adequate cardiopulmonary function. Oxygen-carrying capacity should also be maintained. Interestingly, all global perfusion parameters may be normal and oxygen delivery (DO^2) to injured areas or regions supplied by dysregulated vascular tissue may still be inadequate. Supplemental oxygen should be provided to all TBI patients, ensuring P_aO_2 >90 mmHg and S_pO_2 >95%.

Reducing Cerebral Metabolism
Barbiturates: Barbiturates have been investigated in TBI patients due to their ability to globally decrease cerebral energy requirements. Such an effect would render neuronal tissue less sensitive to marginal blood and oxygen flow. Two human clinical trials have failed to show barbiturates prevent ICP increases and worse neurologic outcome. However, one study of refractory increased ICP showed barbiturate administration did result in improved neurologic recovery. Currently there are no prospective animal studies.

Hypothermia: The main proposed mechanism of action for temperature control therapy is reduction of cerebral metabolic rate. Other possible benefits include reducing post-traumatic release of excitatory neurotransmitters and attenuation of BBB permeability. While several small trials and laboratory studies have yielded positive results for those TBI patients treated with hypothermia, meta-analysis failed to document hypothermia was a beneficial therapy.

Decreasing Cerebral Blood Volume
Head Elevation: Elevating a patient's head 15-30 degrees increases cerebral venous drainage and subsequently reduces cerebral blood volume; care must be taken to avoid occlusion of the jugular veins.

Hyperventilation / Hypoventilation: Hyperventilation may yield a low P_aCO_2 to induce vasoconstriction that may inappropriately reduce CBF and CPP. Conversely, hypoventilation results in a rise in P_aCO_2 that causes vasodilation and potentially deleterious increases in CBF, ICP and CPP. Hyper- and hypoventilation should be avoided, and P_aCO_2 should be maintained between 35-40 mmHg. Short-term hyperventilation to achieve P_aCO_2 between 25-35 mmHg may be helpful in patients with severe, acute intracranial hypertension.

Decompressive Craniectomy
A decompressive craniectomy is defined as removal of part of the skull to increase the volume of the cranial vault. Currently, human recommendations call for decompressive craniectomies within twelve hours for patients with intracranial hypertension that doesn't respond to aggressive medical management. The RESCUEicp study in human TBI patients compared decompressive craniectomy to standard medical care. Results at six months showed decompressive craniectomy in patients with TBI and refractory intracranial hypertension resulted in lower mortality (26.9% in surgical group vs. 48.9% in medical group) and higher rates of vegetative state (8.5% in surgery group vs. 2.1% in medical group). Other meaningful statistics were lower severe disability (dependent on others for care; 21.9% in surgery group vs.14.4% in medical group) and upper severe disability (independent at home; 15.4% in surgery group vs. 8.0% in medical group). Moderate disability and good recovery were similar between both groups. To date, there are no meaningful veterinary data on the use of decompressive craniectomy in TBI patients.

Analgesia
Patients with TBI benefit from adequate pain control. The ideal analgesic should be short acting, have a rapid onset of action, and be completely reversible. Pure-mu opioids (i.e.: fentanyl, morphine, hydromorphone, methadone) are preferred. Adequate monitoring must be employed due to the potential for these medications to induce cardiopulmonary depression and hypotension.

Inflammatory Neuroprotection
Neurodegenerative inflammation and edema seen after TBI is linked to the dysfunction of the blood-brain barrier (BBB) that occurs after the insult. The protective effects of the BBB are contingent on the presence of uninterrupted, selective endothelial cells which moderate the entrance of blood-borne particles. The health of these endothelial cells is intimately connected to the health of supportive astrocytes. Head trauma allows exogenous proteins and peripheral immune cells to enter the brain parenchyma to activate microglia. This causes an immune response that persists for as long as the BBB is compromised. Microglial activation is initially a protective response, but the activation can become excessive and self-perpetuating over time. Invading peripheral cells release pro-inflammatory mediators that exacerbate the inflammatory process and increase the permeability of the BBB. This elevated permeability to large molecules and cells shifts the osmotic pressure within the brain, causing edema and an increase in intracranial pressure.

Inflammation has generally been assumed to be neurodegenerative in nature. However, we are learning inflammation during acute stages of TBI may be necessary to clear damage and set the stage for remodeling efforts. Immunity promotes regeneration in peripheral tissues and appears to initially have a similar role in the central nervous system. Microglial danger-associated molecular pattern (DAMP) receptors detect extracellular ATP. As a result of this ligand-receptor interaction, microglia change shape to help clear debris and support the BBB; capillary leakage is also attenuated. Inhibition of these microglial actions has been associated with increased capillary leakage and brain parenchymal neural cell death.

Minocycline has both neuroprotective and anti-inflammatory properties. This tetracycline derivative can cross the BBB and has been shown to minimize the release of pro-inflammatory cytokines (e.g.: IL-1β, IL-6, matrix metallopeptidase 9) by inhibiting the over-activation proliferation of microglia. Some animal models have documented significant reduction in both inflammation and tissue damage while others have failed to document beneficial effects.

Melatonin from the pineal gland readily passes through cell membranes due to its lipophilic properties. Through inhibition of microglia, this hormone has anti-inflammatory effects, particularly reducing pro-inflammatory cytokine secretion (e.g.: IL-1β, TNF-α). Like minocycline, the clinical effects of melatonin administration in those with TBI are variable.

Statin drugs have been shown to be both neuroprotective and anti-inflammatory in murine models of subarachnoid hemorrhage. This class of drug inhibits various signaling pathways (e.g.: Toll-like receptor 4; some G-proteins; nuclear factor $\kappa\beta$) that ultimately leads to reduced microglial activation. Statins also inhibit epidermal growth factor

(EDGF) receptors, thus contributing to decreased astrocyte activation. The reduced activation of both microglia and astrocytes, there is a subsequent reduction of pro-inflammatory cytokines. Statin administration in TBI patients (both human and animal models) has been associated with increased neuronal survival, growth, reduced functional impairment, and minor improvements in amnesia and disorientation.

Corticosteroids are traditionally considered to have potent anti-inflammatory effects. For this reason, many logically believe this class of medication is beneficial in patients with TBI. Multiple studies have investigated their effects on this type of injury. In 2004, a definitive study of more than 10,000 adults with head injury was published. These patients had a Glasgow Coma Scale ≤14 and were started on a 48-hour infusion of methylprednisolone or placebo that within eight hours of injury. After six months, the risk of death was higher in the corticosteroid group compared to the placebo group (25.7% vs. 22.3%). To date, there is no veterinary evidence corticosteroids are indicated or beneficial in TBI patients. There are many potential adverse effects, including gastrointestinal ulceration, hyperglycemia, poor wound healing, and/or infections.

Anticonvulsant Therapy
Generalized seizures are common in people following TBI. These events are classified as immediate (within 24 hours of injury), early (within 24 hours to 7 days of injury), and late (more than 7 days after injury). In humans, anticonvulsant treatment may be used to reduce the occurrence of immediate and early seizures in high-risk patients; Prophylactic anticonvulsant therapy has no effect on the incidence of late seizure activity. Prevention of immediate and early seizures has no statistically significant impact on long-term outcome or the development of late seizures.

References
Available upon request

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Acute Seizure Management for Cats

Heidi Barnes Heller, DVM, DACVIM (Neurology)

Introduction

Seizures are a common reason cats present to a veterinarian. The neuroanatomic lesion localization for any animal with seizures is the prosencephalon, or forebrain. Seizures are caused by hypersynchronous neuronal activity; too much excitation or too little inhibition of neuronal activity. [1] There are three phases to any seizure: 1) Pre-ictal phase, 2) Ictus and 3) Post ictal phase. During the pre-ictal phase cats may exhibit specific behavior such as hiding or seeking behavior, nausea, vomiting or aggression. The pre ictal phase may last for seconds or hours. The ictus, or what most of us recognize as "the seizure" typically involves both somatic and autonomic systems. Seizures may be described as focal, complex focal or generalized. Neuronal "resetting" occurs during the post ictal phase. Common clinical signs during the post ictal phase may include hiding, blindness, or ataxia.

Acute Seizure Management

Benzodiazepine

Diazepam

Diazepam has been the main anticonvulsant treatment for veterinary patients.[5–8] It is generally regarded as safe for cats and can be administered intravenous, per rectum and intranasal. However, no published data is available evaluating rectal or intranasal administration in cats!! Oral administration is not recommended for cats due to a link with acute hepatic failure however oral administration is not ideal for acute seizure management due to the risk of injury to the owner, the long time to peak diazepam concentrations and diminished anticonvulsant activity. [9]

Intravenous administration of diazepam is the most common route of diazepam administration in emergency seizure treatment.[7,10–12] The standard dosage is 0.5 mg/kg intravenous, to effect.

Intranasal diazepam administration has gained more favor recently in veterinary medicine due to its relative ease of administration, and avoidance of the first pass effect of metabolism however be aware that no published data is available in cats. Two approaches have been described for use in dogs and this is translated to use in cats in my practice: 1) nasal drop technique: this requires the administrator to drop a commercially available parenteral solution into the nares over a 30 second period and 2) a nasal atomizer technique: this utilizes a atomizer specifically designed for attachment to a leurlock syringe for rapid administration of the same commercially available parenteral solution into the nares.[13] The atomizer is preferred for dogs and my recommendation for cats for at home cluster care. Client awareness on the lack of controlled studies is critical when prescribing this home care. Care should be exercised when administering intranasal products to avoid inadvertent bite wounds due to the proximity to the mouth.

Midazolam

Midazolam is a water-soluble benzodiazepine drug with a higher binding affinity compared to diazepam however bioavailability is between 50-70% depending on the administration route. Standard doses are 0.2 mg/kg for all administration routes.[5,14,15] Recently, attention has been focused on intranasal routes of administration for which midazolam has become especially favored. [5,8,15] Gel formulations increase bioavailability, and result in shorter time to maximal concentration (12 minutes vs 18 minutes for the solution) because of increased viscosity. Based on clinical evidence, intranasal midazolam is currently my recommended treatment for at-home seizure control. Rectal midazolam is not recommended.

Levetiracetam

Levetiracetam has received a lot of attention since it was first documented for use in veterinary medicine in 2004.[16] It is considered a relatively safe drug for feline use by Charalambous et al in a systematic review in 2018.[17] Mild clinical effects including GI upset or sedation have been noted.[18] Interestingly when levetiracetam is administered with diazepam in human epileptic trials, seizure control is improved compared to either drug in isolation.[20] This may account for the improved seizure control noted in the canine studies rather than a reflection of the efficacy of levetiracetam alone for acute seizure management. It remains to be seen if levetiracetam alone or in combination with diazepam is a more effective anticonvulsant for cats.

Levetiracetam has also been evaluated for rectal and intramuscular administration in dogs however studies in cats are limiting. At this time, I do not recommend using rectal or intramuscular levetiracetam in cats with acute seizures.

Propofol

Propofol is a common anesthetic drug that has shown to have both proconvulsive and anticonvulsive properties.[26] The anticonvulsive properties are thought to be secondary to GABA activation by propofol.[26] Subanesthetic dosages

of 1.0-3.5 mg/kg for bolus treatment or 0.1-0.25 mg/kg/minute for constant rate infusion have been described.[27] Propofol can cause respiratory suppression therefore bolus dosing should be titrated to the lowest effective dose while attentive respiratory monitoring is performed. Intubation may be required if apnea is encountered during treatment. Propofol withdrawal may result in distal limb twitching which may be difficult to distinguish from seizure activity. Finally, extended exposure to propofol in cats may result in Heinz body anemia therefore a CBC analysis is recommended every 24 hours during constant rate infusion use of propofol.

Summary

There is an overall lack of feline specific data available for acute seizure management in cats. Although more data is available for canine seizure control, both species are often treated based on human clinical trial data or simply because we understand the drugs to be safe rather than documenting efficacy.

References

1. Fisher RS, Van Emde Boas W, Blume W, et al. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia*. 2005;46(4):470-472.
2. Pakozdy A, Gruber A, Kneissl S, Leschnik M, Halasz P, Thalhammer JG. Complex partial cluster seizures in cats with orofacial involvement. *J Feline Med Surg*. 2011;13:687-693.
3. Koepp MJ, Caciagli L, Pressler RM, Lehnertz K, Beniczky S. Reflex seizures, traits, and epilepsies: From physiology to pathology. *Lancet Neurol*. 2016;15(1):92-105.
4. Lowrie M, Bessant C, Harvey RJ, Sparkes A, Garosi L. Audiogenic reflex seizures in cats. *J Feline Med Surg*. 2015;18(4):328-336.
5. Eagleson JS, Platt SR, Elder Strong DL, et al. Bioavailability of a novel midazolam gel after intranasal administration in dogs. *Am J Vet Res*. 2012;73(4):539-545.
6. Boothe DM. Anticonvulsant Therapy in Animals. *Vet Clin NA Small Anim Pract*. 1998;28(2):411-448.
7. Patterson ENE. Status Epilepticus and Cluster Seizures. *Vet Clin North Am Small Anim Pract*. 2014;44(6):1103-1112.
8. Charalambous M, Bhatti SFM, Van Ham L, et al. Intranasal Midazolam versus Rectal Diazepam for the Management of Canine Status Epilepticus: A Multicenter Randomized Parallel-Group Clinical Trial. *J Vet Intern Med*. 2017;31(4):1149-1158.
9. Center SA, TH E, Rowland P, et al. Fulminant hepatic failure associated with oral administratino of diazepam in 11 cats. *J Vet Med Assoc*. 1996;209(3):618-625.
10. Platt SR. Feline seizure control. *J Am Anim Hosp Assoc*. 2001;37(6):515-517.
11. Boothe DM. Anticonvulsant therapy in small animals. *Vet Clin North Am Anim Pract*. 1998;28(2):411-448.
12. Brigo F, Nardone R, Tezzon F, Trinka E. Nonintravenous midazolam versus intravenous or rectal diazepam for the treatment of early status epilepticus : A systematic review with meta-analysis. *Epilepsy Behav*. 2015;49:325-336.
13. Musulin SE, Mariani CL, Papich MG. Diazepam pharmacokinetics after nasal drop and atomized nasal administration in dogs. *J Vet Pharmacol Ther*. 2011;34(1):17-24.
14. Schwartz M, Munana K, Nettifee-osborne J, Messenger KM, Papich MG. The pharmacokinetics of midazolam after intravenous , intramuscular , and rectal administration in healthy dogs. *J Vet Pharmacol Ther*. 2012;36:471-477.
15. Charalambous M, Volk HA, Tipold A, et al. Comparison of intranasal versus intravenous midazolam for management of status epilepticus in dogs: A multi-center randomized parallel group clinical study. *J Vet Intern Med*. 2019.
16. Steinberg M, Faissler D. Levetiracetam Therapy for Long-Term Idiopathic Epileptic Dogs. *J Vet Intern Med*. 2004;18(3):410.
17. Charalambous M, Pakozdy A, Bhatti SFM, Volk HA. Systematic review of antiepileptic drugs' safety and effectiveness in feline epilepsy. *BMC Vet Res*. 2018;14(1).
18. Charalambous M, Shivapour SK, Brodbelt DC, Volk HA. Antiepileptic drugs' tolerability and safety – a systematic review and meta-analysis of adverse effects in dogs. *BMC Vet Res*. 2016;12(1):79.
19. Hardy BT, Patterson EE, Cloyd JM, Hardy RM, Leppik IE. Double-Masked, Placebo-Controlled Study of Intravenous Levetiracetam for the Treatment of Status Epilepticus and Acute Repetitive Seizures in Dogs. *J Vet Intern Med*. 2012;26(2):334-340.
20. Modur PN, Milteer WE, Zhang S. Sequential intrarectal diazepam and intravenous levetiracetam in treating acute repetitive and prolonged seizures. *Epilepsia*. 2010;51(6):1078-1082.
21. Patterson EE, Goel V, Cloyd JC, et al. Intramuscular, intravenous and oral levetiracetam in dogs: Safety and pharmacokinetics. *J Vet Pharmacol Ther*. 2008;31(3):253-258.
22. Peters RK, Schubert T, Clemmons R, Vickroy T. Levetiracetam rectal administration in healthy dogs. *J Vet Intern Med*. 2014;28(2):504-509.
23. Cagnotti G, Odore R, Bertone I, et al. Open-label clinical trial of rectally administered levetiracetam as

supplemental treatment in dogs with cluster seizures. *J Vet Intern Med*. 2019;33(4):1714-1718.
24. Cagnotti G, Odore R, Gardini G, et al. Pharmacokinetics of rectal levetiracetam as add-on treatment in dogs affected by cluster seizures or status epilepticus. *BMC Vet Res*. 2018;14(1):10-15.
25. De Risio L, S P. *Canine and Feline Epilepsy*. Boston: CABI; 2014.
26. Steffen F, Grasmueck S. Propofol for of refractory seizures in dogs and a cat with intracranial disorders. *J Small Anim Pract*. 2000;41(November):496-499.
27. Heldmann E, Holt DE, Brockman DJ, Brown DC, Perkowski SZ. Use of propofol to manage seizure activity after surgical treatment of portosystemic shunts. *J Small Anim Pract*. 1999;40(12):590-594.

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Novel Seizure Therapeutics for Cats

Heidi Barnes Heller, DVM, DACVIM (Neurology)

Introduction

Seizures occur secondary to hypersynchronous neuronal activity that results from an imbalance of excitatory and inhibitory neurons. [1] When anti-epileptic drugs (AED) are recommended for long-term seizure clients are faced with a tough decision. Oral phenobarbital formulations such as liquid or tablet, require the medication to be placed into a cat's mouth or food for consumption. When administered as prescribed, seizure control can be achieved in 93% of cats with serum concentrations between 15-40 µg/ml.[2,3] Naturally, oral administration is difficult for some cat owners due to potential fractious cat behavior. Inconsistent anti-convulsant drug administration may result in breakthrough seizures and emergency room visits, thus risking a negative impact on the human-animal bond. [4] What do you do?

Transdermal Medication

Phenobarbital was initially evaluated by my research team in healthy cats in two formulations: 1) Lipoderm Activemax® and 2) PLO gel. We were able to demonstrate that the phenobarbital was detectable after 14 days dosing (at steady-state), and in fact serum phenobarbital concentrations were between 15-45 ug/ml in most cats.[5] Lipoderm Activemax® was easier for clients to use so it was selected as the carrier for a subsequent prospective fixed-order crossover clinical trial evaluating transdermal and oral phenobarbital use in epileptic cats. For the prospective cross-over fixed order clinical trial, transdermal phenobarbital was dosed at 9 mg/kg q12h and oral phenobarbital was dosed between 2-3 mg/kg PO q12h. Although most owners reported transdermal application as the preferred route, transdermal phenobarbital resulted in more breakthrough seizures and more adverse clinical side effects than oral administration in one study. [6] Furthermore, more dosage adjustments were required during transdermal administration. These findings were unexpected and were unfavorable for long-term phenobarbital administration using a transdermal product however clients continue to request this product. Therefore, when prescribing I recommend monitoring serum phenobarbital concentrations 14 days after starting the medication and any dose adjustment, and close monitoring of the seizure calendar along with proactive dose adjustment to stay within the therapeutic serum concentration of 15-45 ug/ml.[5]

Although transdermal application of phenobarbital was well received by clients, we began investigating the use of levetiracetam as an alternative transdermal anticonvulsant medication. Using the lipoderm carrier molecule used previously in the transdermal phenobarbital studies we applied transdermal levetiracetam at a dosage of 60 mg/kg q8h to 8 healthy cats. Following 7 days of administration (steady-state is supposedly achieved in 3 days), we evaluated serum levetiracetam concentrations at peak and estimated trough. Serum levetiracetam concentrations were above the minimum human therapeutic range at all time points and side effects were minimal.[7] Transdermal levetiracetam has not yet been evaluated in an epileptic cat population therefore clinical efficacy remains unknown. Use of transdermal levetiracetam should be limited to cats resistant to other currently available treatment options until further clinical trials can be performed.

Extended-release Levetiracetam

Although transdermal products were well liked by the client and well tolerated by the cat, we began to explore other choices for long-term seizure management. Extended-release formulations are designed to allow for less frequent dosing intervals compared to intermediate release forumulations.[8] Currently extended-release tablets are available in 500 and 750 mg sizes ONLY and these tablets cannot be crushed, split, chewed or otherwise disrupted or their extended-release properties may be lost. Intermediate release levetiracetam (IRL) dose recommendations are 20 mg/kg per os q8hr for cats, and canine extended release levetiracetam (XRL) doses are 30 mg/kg per os q12h. For a standard 5 kg size cat, the extended-release product was well outside of the dosing recommendation. However, the clinical and biochemical adverse effect profile was low, and toxicity level was high, therefore we elected to evaluate the use of extended-release levetiracetam in cats 5 kg or greater. We performed single-dose pharmacokinetic analysis in healthy cats with body weight ≥ 5 kg and recommended 500 mg XRL once daily based on this data.[9] Due to the high dosage (approximately 100 mg/kg) we were concerned about side effects following long-term administration, therefore we subsequently administered this dosage to 9 healthy cats once daily over 10 days to assess for side effects. Minimal side effects were noted, and mean serum concentrations remained above the minimum human therapeutic range. *This study supported the use of once daily XRL in epileptic cats; however, it has not been evaluated further in the epileptic cat population.* Therefore, caution should be exercised if practitioners elect to prescribe this medication for an epileptic cat. Seizure monitoring is our best monitoring tool because we do not have a feline (or canine) therapeutic range for levetiracetam. The only reference range available is a human reference range, which has not been verified for used in veterinary patients. Clinical efficacy is unknown based on these studies.

Novel Oral Phenobarbital Product

After evaluating the extended-release products, we elected to return to phenobarbital and next try to develop a modified oral phenobarbital product that utilized the ease of transdermal phenobarbital but had the stability of oral pharmacokinetics. First, we performed a taste-test to determine the "best" flavor enhancer. Second, the added flavor was combined with a novel oral gel and phenobarbital powder to produce a produce that was designed to rub on the paw and be licked off by the affected cat. Twelve healthy cats were administered 3 mg/kg oral (topically applied) phenobarbital q12h for 14 days. On the 15th day, blood was drawn to measure serum phenobarbital concentrations. Median (range) trough, 1, 2, 4, and 6 hour serum phenobarbital were 26.0(16-35), 28.5(19-36) 29.0(19-36), 29.0(17-38), and 29.0(18-35) µg/ml, respectively. Serum phenobarbital concentrations were between 15-40 µg/ml at all time points. Seven of 12 (58%) of cats had adverse clinical effects reported which included lethargy, ataxia, vomiting, diarrhea and sedation. Owners reported 100% cat compliance for administration of the product.

Conclusion

Be aware of the limitations in knowledge when utilizing a novel anticonvulsant and ensure that this knowledge is passed along to the client. These clinical trials enrolled a small number of healthy cats (other than the prospective clinical phenobarbital clinical trial) and were administered for a limited amount of time. Chronic administration of transdermal phenobarbital identified a significant difference between serum phenobarbital concentrations and dosage which could not have been predicted based on the pilot healthy cat study. Our overall goal remains focused on the identification of novel anti-convulsant drugs that are safe, effective and easy to administer for cats and their caregivers. By providing less stressful, easier and safer medication, alternatives we hope to improve the quality and quality of life for epileptic cats and strengthen the human-animal bond, promoting health for both cats and their caregivers.

References

1. Fisher RS, Van Emde Boas W, Blume W, et al. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia*. 2005;46(4):470-472.
2. Finnerty KE, Barnes Heller HL, Mercier MN, Giovanella CJ, Lau VW, Rylander H. Evaluation of therapeutic phenobarbital concentrations and application of a classification system for seizures in cats: 30 cases (2004-2013). *J Am Vet Med Assoc*. 2014;244(2):195-199.
3. Pakozdy A, Sarchahi AA, Leschnik M, Tichy AG, Halasz P, Thalhammer JG. Treatment and long-term follow-up of cats with suspected primary epilepsy. *J Feline Med Surg*. 2013;15(4):267-273.
4. Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. *Epilepsy Behav*. 2002;3(4):338-342.
5. Delamaide Gasper J a, Barnes Heller HL, Robertson M, Trepanier L a. Therapeutic serum phenobarbital concentrations obtained using chronic transdermal administration of phenobarbital in healthy cats. *J Feline Med Surg*. 2014;17(4):359-363.
6. Barnes Heller H, Trepanier LA, Robertson M, Mei C. Prospective crossover clinical trial comparing trnasdermal versus oral phenobarbital administration in epileptic cats. *J Feline Med Surg*. 2019:1-7.
7. Smith C, Barnes Heller HL, Reif N, Van Hesteren M, Reinhart JM. Serum levetiracetam concentrations after transdermal levetiracetam administration, 3 times daily, to healthy cats. *J Vet Intern Med*. 2019;33(2):827-830.
8. Leppik IE, Hovinga C a. Extended-release antiepileptic drugs: A comparison of pharmacokinetic parameters relative to original immediate-release formulations. *Epilepsia*. 2013;54(1):28-35.
9. Barnard L, Barnes Heller H, Boothe DM. Pharmacokinetics of single oral dose extended release levetiracetam in healthy cats. *J Vet Intern Med*. 2018;32(1):348-351.

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Feline Hyperesthesia, Cognitive Dysfunction, & Other Mystery Diseases

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Feline Hyperesthesia Syndrome

Appropriately termed a 'mystery disease', feline hyperesthesia syndrome (FHS) has an unknown etiology to date. Clinical signs often include skin rippling over the dorsum, tail chasing and self-trauma, sudden jumping and running for no obvious reason and occasionally vocalization during episodes. Interestingly most cats are young (less than 1 year of age). The etiology has been proposed to be behavioral (due to the lack of identifiable organic disease), seizure disorder (due to the paroxysmal type clinical signs and directed motor activity), or a collection of multiple factors including behavioral and environmental.

Obtaining a diagnosis is complex because as of yet, we don't understand the etiology! Therefore, as a neurologist I attempt to rule out organic CNS disease. This includes MRI, spinal tap, sometimes muscle biopsies and electrodiagnostic evaluation for peripheral neuropathy/myopathy.

A recent retrospective study evaluated 7 cats with this clinical picture and did not identify any neurologic cause in these cats.[1] Treatment with gabapentin, meloxicam, antibiotics, phenobarbital, prednisolone, and topiramate were tried in multiple cats. Clinical improvement was noted in 6 of 7 cats using gabapentin alone (2 cats), gabapentin, cyclosporine, and amitriptyline (1 cat), gabapentin, prednisolone, phenobarbital (1 cat) or gabapentin, topiramate and meloxicam (1 cat).

Treatment in my practice consists of anticonvulsants to rule out/in epileptic activity, and pain management. Referral to a behaviorist, dermatologist and/or internist is often made as well because of the complex and unknown nature of this mystery disease.

Cognitive Dysfunction

Cognitive dysfunction syndrome (CDS) is a term used to describe deterioration of mental capabilities associated with age.[2] Clinical signs referable to cognitive dysfunction can also be associated with other age-related illnesses (e.g. osteoarthritis, structural intracranial disease such as neoplasia, or cardiovascular disease). See table 1 for an outline of behavior changes seen in cats with CDS.

The underlying etiology of CDS is yet unknown. Causes such as oxidative stress/damage, neurodegeneration and vascular changes are among the leading hypothesis for human and canine CDS, and therefore suspected to be similar in CDS. Deposits of extracellular B-amyloid and intracellular accumulation of microtubule-associated protein tau have been seen in human patients with cognitive dysfunction. [3,4] Similarly, B-amyloid deposits and increased tau has been detected in aged cats with cognitive decline, however it remains unclear what the significance to this finding is for cats.[3,5,6]

Lysosomal storage disorders result in neuronal degeneration and, in some cases, cognitive decline. One such lysosomal storage disorder is Niemann-Pick Type C disease (NPC) in which a dysfunction in specific genes results in lysosomal storage of cholesterol and glycosphingolipids. The link between these storage products and dementia is unknown and still under investigation. [5]

Obtaining a diagnosis of feline CDS is challenging. Currently, the diagnosis is made by ruling out structural brain and systemic causes for disease. This may include complete blood count, full biochemistry panel including thyroid screening, urinalysis, chest radiographs, blood pressure assessment, brain MRI and possibly spinal tap. Imaging changes associated with canine CDS include increased depth of the sulci, dilation of ventricles secondary to neuronal loss (called ex vacuo hydrocephalus) and a measurably small interthalamic adhesion. Similar changes could be expected for feline CDS however documentation of this is limited. A reduction in neurons and the density of synapses has been noted in aging cats. Additionally, reduction of the production of acetylcholine in the brain may result in declines in learning and memory in cats.[5]

Currently there are no proven treatments for feline CDS. Treatment options are either modified from canine health studies, or proposed without clinical trial and based on anecdotal evidence. [2] The addition of antioxidants (B vitamins, vitamin C, other) as well as fish oil were evaluated for use in cats in one study and showed promise.[7] The use of S-adenosyl-L-methionine (SAMe) has been recommended for cats based on a study that identified improved performance on cognitive testing. This study only found significant improvement in cognitive function testing in the least affected cats.[8] In addition to medical management, environmental management with ready access to food, water, litter box and areas of comfort (beds, hiding spots) is recommended. Environmental stimulation with low

impact toys, or bird feeders in which the cat can choose to ignore any activity if they do not feel inclined to engage are recommended. Finally, focused veterinary visits can be important for cat owners to feel supported through the aging process. Focused questing, or examinations specifically evaluating body weight, urine production (to assess for signs of dehydration), behavior changes and mobility can guide veterinary practitioners to assist cats, and cat owners, earlier in the course of disease and to identify concurrent morbidities that may contribute to, or be confused with, cognitive dysfunction.

Table 1: Clinical behavioral changes associated with CDS in cats. (REFR)
Increased vocalization, especially at night
Altered social interaction and relationships, either with other or another pet.
Altered sleep/wake patter
House soiling
Spatial Disorientation or confusion (i.e. forgetting the location of the litterbox)
Temporal disorientation (i.e. forgetting if they have been fed)
Altered activity (i.e. aimless wandering)
Anxiety
Learning and memory dysfunction

References:

1. Amengual Batle P, Rusbridge C, Nuttal T, Heath S, Marioni-Henry K. Feline hyperaesthesia syndrome with self-trauma to the tail: retrospective study of seven cases and proposal for an integrated multidisciplinary diagnostic approach. *J Feline Med Surg*. 2019;21(2):178-185.
2. Miele A, Sordo L, Gunn-Moore DA. Feline Aging: Promoting Physiologic and Emotional Well-Being. *Vet Clin North Am - Small Anim Pract*. 2020;50(4):719-748.
3. Gunn-Moore D, McVee J, Bradshaw JM, Pearson GR, Head E, Gunn-Moore FJ. Ageing changes in cat brains demonstrated by B-amyloid and AT8-immunoreactive phosphorylated tau deposits. *J Feline Med Surg*. 2006;8(4):234-242.
4. Fiock KL, Smith JD, Crary JF, Hefti MM. B-Amyloid and Tau Pathology in the Aging Feline Brain. *J Comp Neurol*. 2020;528(1):108-113.
5. Vite CH, Head E. Aging in the canine and feline brain. *Vet Clin North Am - Small Anim Pract*. 2014;44(6):1113-1129.
6. Youssef SA, Capucchio MT, Rofina JE, et al. Pathology of the Aging Brain in Domestic and Laboratory Animals, and Animal Models of Human Neurodegenerative Diseases. *Vet Pathol*. 2016;53(2):327-348.
7. Pan Y, Araujo JA, Burrows J, et al. Cognitive enhancement in middle-aged and old cats with dietary supplementation with a nutrient blend containing fish oil, B vitamins, antioxidants and arginine. *Br J Nutr*. 2013;110(1):40-49.
8. Araujo JA, Faubert ML, Brooks ML, Landsberg GM, Lobprise H. NOVIFIT® (NoviSAMe®) tablets improve executive function in aged dogs and cats: Implications for treatment of cognitive dysfunction syndrome. *Int J Appl Res Vet Med*. 2010;10(1):90-98.

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Measuring Feline Orofacial Cancer Pain

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Oral squamous cell carcinoma (SCC) is a common and locally aggressive cancer in cats. Its biological behavior is similar to human papilloma virus-negative head and neck SCC (i.e., HPV-negative HNSCC). The pain which accompanies head and neck SCC is similar in both species. Thus, feline oral SCC may be a useful translational model for oral cancer pain in humans. With that background, we set out to establish robust outcome measures that can be used to measure and characterize oral cancer pain in cats.

Via a prospective controlled observational clinical study, we evaluated 3 different types of pain and/or sensitivity assessment methods: client questionnaires, clinician-based pain scales, and quantitative sensory testing (QST).

The result of this work is that we have developed and tested outcome measures that will enable robust research in a naturally occurring feline model of oral cancer pain. Our methods appear to be reliable (i.e., produce repeatable results within individual cats), responsive to analgesic therapy, and they discriminate between healthy and tumor-bearing cats. Interestingly, our results also suggest that cats with tongue cancer not only develop pain in their mouth, but also seem to have regional peripheral, and widespread sensitization; this is consistent with the widespread somatosensory sensitization that is reported in human HNC patients and which can be measured in other animal models of oral cancer pain.[1]

Many of these tools and results can now also provide useful insight for clinical management of cat in the veterinary clinic.

Owner-Reported Quality of Life Questionnaire for Cats with Oral SCC
A recently published scale for evaluating QOL in dogs with cancer (CORQ) was modified to create the preliminary FORQ (preFORQ) -- **F**eline oral cancer **O**wner-**R**eported quality of life **Q**uestionnaire.[2,3] The preFORQ included a total of 24 questions grouped within four categories as described above. Pet owners were requested to score each question with regard to frequency and severity; responses were based on behaviors observed over the preceding 7 days. If a behavior had been seen, the frequency was categorized as: none, rarely (1-2 days), sometimes (3-4 days), usually (5-6 days), or always (every day). Severity was scored as: none, mild, moderate, severe, or very severe. The research team later assigned response numbers, ranging from 0 to 4 with zero reflecting a response of “none” and 4 being either “always” or “very severe”. A total score was calculated; higher scores reflected lower QOL. A 100 mm VAS item was also included at the end of the questionnaire to serve as a single measure of overall QOL; respondents were asked to mark along a line representing somewhere between the “worst imaginable quality of life” (0 mm) and “perfect quality of life” (100 mm).

To refine the instrument, each individual item in the preFORQ was analyzed by the non-parametric Mann-Whitney test to evaluate whether that item discriminated between the two groups. Any score comparison with a *P*-value > 0.2 (appropriate for the small sample size in this study) was to be removed from the questionnaire when creating the “proposed FORQ”.

Clinician Pain Scoring Instrument for Assessing Orofacial Pain in Cats with Oral SCC
The UNESP-Botucatu MCPS for cats with oral diseases was modified to generate the **F**eline **O**rofacial **P**ain **S**cale for **C**ancers, (FOPS-C).[4,5] In the category of miscellaneous behavior, the abnormal behavior of “lick and/or bites the surgical wound” was changed to “licks, has ptyalism and/or chattering (jaw shakes)”. Categories in the instrument pertained to: miscellaneous behavior; reaction to palpation around the mouth and on the head; vocalization; posture; comfort; activity; attitude; or appetite. Each category was scored on a 4-point scale, with 0 indicating normal (or no change) and 3 denoting significantly altered behavior. The clinician gave a score based on the description provided. In the evaluation of appetite, a small amount of canned commercial cat food was offered. In instances where fasting had to be performed at the time of the pain scoring (e.g., in preparation for general anesthesia), the scores were based on the amount of food the cat had consumed at its most recent meal.

Electronic von Frey
An EVF apparatus (BIO-EVF3, Bioseb, Chavillecedez, France) was used to assess mechanical sensory thresholds. A plastic pipette tip was loaded on the mounting accessory of a hand-held device that can record the applied force. The force was gradually increased manually until a positive response was elicited, with the upper cut-off limit set as 500 g. Positive responses included vocalization, head withdrawal, paw withdrawal, attempt to ‘bat’ or paw at the device, or trying to bite the device. Tests were repeated five times with an interstimulus interval of approximately 1

minute. The mean of all five trials was used for data analysis. Lower thresholds indicate greater sensitivity. Measurements were acquired at anatomic sites based on anatomy of the three branches of the trigeminal nerve, which mediates somatosensory input from most of the orofacial region. The mandible and tongue are innervated by the mandibular branches, and the maxillary cutaneous region is innervated by maxillary branches of the trigeminal nerve. Since the input from one area of the face may result in changes in sensitivity in another facial region, we selected four measurement sites: (1 and 2) just medial to the bilateral mandibulae (intermandibular space), (3) the ipsilateral maxilla, along the path of the maxillary branch, and (4) on the dorsal aspect of the right metacarpus – a site distant to the mouth, which served as the control.[6] For subjects in the healthy cat cohort, the right maxilla was always tested.

Cochet-Bonnet Aesthesiometer

The afferent impulses of corneal reflexes are mediated by the ophthalmic division of the trigeminal nerve. Corneal touch threshold (CTT) values were measured using a Luneau Cochet-Bonnet aesthesiometer (Western Ophthalmics, Lynwood, WA) with a monofilament nylon fiber of 0.12 mm diameter, as previously described.[7] Testing was performed on all enrolled cats, unless they had pre-existing corneal diseases (e.g., corneal scarring, ulcers). The cats were gently manually restrained with their head up; their body was cradled between the restrainer's chest and forearm. All measurements were made by a single veterinarian, in a quiet and well-lit room. The instrument was held perpendicular to the cornea, and the aesthesiometer filament was applied centrally, on the left cornea. Testing started with a filament length of 60 mm and the filament was shortened by 5 mm at each subsequent test (to increase resistance) until a corneal blink was elicited. A CTT was defined by the length of filament that elicited a blink reflex following 2 of 3 applications. The absence of corneal damage was confirmed via fluorescein staining at the conclusion of each testing session.

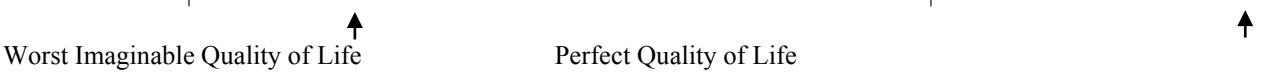
The QST tools are largely impractical for use in routine clinical practice because they require special equipment. However, the information gained from these assays is invaluable. Knowledge that cats with oral SCC experience peripheral and widespread sensitization even when they have subclinical oral pain resulting from tongue cancer should be useful with regard to informing the clinical approach to such cats – indeed, our results indicate that it would be a mistake to withhold systemically-administered analgesics from any cat with tongue cancer. And these results are expected to be broadly applicable to any form of invasive oral cancer – for example, we'd expect similar results for a cat with destructive nasal lymphoma or aural adenocarcinoma.

The client and clinician surveys are expected to provide useful clinical tools to assist in identification of pain, and assessment of overall quality of life. Additional testing is needed, to validate these tools with regard to their ability to detect and respond to pain caused by other forms of head and neck cancer, and to detect cancer treatment associated discomfort.

The refined, proposed feline oral cancer owner-reported quality of life questionnaire (proposed FORQ).

During the past 7 days, my cat:	No	If YES, ***how often*** did your cat have it?				If YES, ***how severe*** was it usually?			
		Rarely	Sometimes	Usually	Always	Mild	Moderate	Severe	Very severe
Behavior									
• Had low energy?	○	○	○	○	○	○	○	○	○
• Was reluctant to wake up?	○	○	○	○	○	○	○	○	○
• Had trouble getting comfortable?	○	○	○	○	○	○	○	○	○
• Could not maintain hygiene (i.e., grooming)?	○	○	○	○	○	○	○	○	○
• Had decreased appetite?	○	○	○	○	○	○	○	○	○
Activity									
• Did not do what he/she likes (e.g. chasing, playing, etc.)?	○	○	○	○	○	○	○	○	○
• Did not act like his/her normal self?	○	○	○	○	○	○	○	○	○
• Had decreased enjoyment of life?	○	○	○	○	○	○	○	○	○
• Did not sleep well?	○	○	○	○	○	○	○	○	○
Oral/facial discomfort									
• Had excessive drooling?	○	○	○	○	○	○	○	○	○
• Had difficulty eating his/her normal	○	○	○	○	○	○	○	○	○
• Was offered and had trouble eating	○	○	○	○	○	○	○	○	○
• Had trouble lying down his/her head?	○	○	○	○	○	○	○	○	○
• Felt discomfort or pain near the	○	○	○	○	○	○	○	○	○

For this <u>final question</u>, please mark an ***X*** along the line to show your cat's overall ***current*** quality of life.



Worst Imaginable Quality of Life Perfect Quality of Life

Clinician Feline Orofacial Pain Scale for Cancers (FOPS-C)**.**

Subscale 1: PAIN EXPRESSION (0-12)		
Miscellaneous behavior	Observe and mark the presence of the behaviors listed below **A** - The cat is laying down and quiet, but moving its tail **B** - The cat contracts and extends its thoracic limbs and/or contracts its neck muscles **C** - The cat's eyes are partially closed (eyes half closed) **D** - The cat licks, has ptyalism, and/or chattering (jaw shakes)	
	• All above behaviors are absent	0
	• Presence of one of the above behaviors	1
	• Presence of two of the above behaviors	2
	• Presence of three of the above behaviors	3
Reaction to palpation of the area around the mouth cavity	• The cat does not react when the mouth is touched or pressed	0
	• The cat does not react when the area around the mouth is touched, but does react when it is touched and pressed. It may vocalize and/or try to bite	1
	• The cat reacts when the mouth is touched and when pressed. It may vocalize and/or try to bite.	2
	• The cat reacts when the observer approaches the mouth. It may vocalize and/or try to bite. The cat does not allow palpation around mouth cavity.	3
Reaction to palpation of the head	• The cat does not react when the head is touched	0
	• The cat does not react when the head and neck are touched, but does react when it is pressed. The neck is tense	1
	• The cat reacts when the head and neck are touched and when pressed. The neck is tense	2
	• The cat reacts when the observer approaches the head. It may vocalize and/or try to bite. The cat does not allow palpation of the head and neck	3
Vocalization	• The cat is quiet, purring when stimulated, or meows interacting with the observer, but does not growl, groan, or hiss	0
	• The cat purrs spontaneously (without being stimulated or handled by the observer)	1
	• The cat growls, howls, or hisses when handled by the observer (when its body position is changed by the observer)	2
	• The cat growls, howls, hisses spontaneously (without being stimulated or handled by the observer)	3
	Subtotal	
Subscale 2: PSYCHOMOTOR CHANGE (0-12)		
Posture	• The cat is in a natural posture with relaxed muscles (it moves normally)	0
	• The cat is in a natural posture but is tense (it moves little or is reluctant to move)	1
	• The cat is sitting or in sternal recumbency with its back arched and head down; or The cat is in dorso-lateral recumbency with its pelvic limbs extended or contracted	2
	• The cat frequently alters its body position in an attempt to find a comfortable posture	3
Comfort	• The cat is comfortable, awake or asleep, and interacts when stimulated (it interacts with the observer and/or is interested in its surroundings)	0
	• The cat is quiet and slightly receptive when stimulated (it interacts little with the observer and/or is not very interested in its surroundings)	1
	• The cat is quiet and "dissociated from the environment" (even when stimulated it does not interact with the observer and/or has no interest in its surroundings) The cat may be facing the back of the cage	2
	• The cat is uncomfortable, restless (frequently changes its body position), and slightly receptive when stimulated or "dissociated from the environment" The cat may be facing the back of the cage	3
Activity	• The cat moves normally (it immediately moves when the cage is opened; outside the cage it moves spontaneously when stimulated or handled)	0
	• The cat moves more than normal (inside the cage it moves continuously from side to side)	1

	• The cat is quieter than normal (it may hesitate to leave the cage and if removed from the cage tends to return, outside the cage it moves a little after stimulation or handling)	2
	• The cat is reluctant to move (it may hesitate to leave the cage and if removed from the cage tends to return, outside the cage it does not move even when stimulated or handled)	3
Attitude	Observe and mark the presence of the mental states listed below A- **Satisfied:** The cat is alert and interested in its surroundings (explores its surroundings), friendly and interactive with the observer (plays and/or responds to stimuli) - *The cat may initially interact with the observer through games to distract it from the pain. Carefully observe to distinguish between distraction and satisfaction games* B- **Uninterested:** The cat does not interact with the observer (not interested by toys or plays a little; does not respond to calls or strokes from the observer) - *In cats, which don't like to play, evaluate interaction with the observer by its response to calls and strokes* C- **Indifferent:** The cat is not interested in its surroundings (it is not curious; it does not explore its surroundings) - *The cat can initially be afraid to explore its surroundings. The observer needs to handle the cat and encourage it to move itself (take it out of the cage and/or change its body position)* D- **Anxious:** The cat is frightened (it tries to hide or escape) or nervous (demonstrating impatience and growling, howling, or hissing when stroked and/or handled) E- **Aggressive:** The cat is aggressive (tries to bite or scratch when stroked or handled)	
	• Presence of the mental state A	0
	• Presence of one of the mental states B, C, D, or E	1
	• Presence of two of the mental states B, C, D, or E	2
	• Presence of three or all of the mental states B, C, D, or E	3
	Subtotal	
Subscale 3: PHYSIOLOGICAL VARIABLES (0-3)		
Appetite	• The cat is eating normally	0
	• The cat is eating more than normal	1
	• The cat is eating less than normal	2
	• The cat is not interested in food	3
	Subtotal	
	Total Score	

References

1. Ye Y, Bernabé DG, Salvo E, et al. Alterations in opioid inhibition cause widespread nociception but do not affect anxiety-like behavior in oral cancer mice. *Neuroscience* 2017;363:50-61.
2. Giuffrida MA, Brown DC, Ellenberg SS, et al. Development and psychometric testing of the Canine Owner-Reported Quality of Life questionnaire, an instrument designed to measure quality of life in dogs with cancer. *J Am Vet Med Assoc* 2018;252:1073-1083.
3. Giuffrida MA, Farrar JT, Brown DC. Psychometric properties of the Canine Symptom Assessment Scale, a multidimensional owner-reported questionnaire instrument for assessment of physical symptoms in dogs with solid tumors. *J Am Vet Med Assoc* 2017;251:1405-1414.
4. Stathopoulou TR, Kouki M, Pypendop BH, et al. Evaluation of analgesic effect and absorption of buprenorphine after buccal administration in cats with oral disease. *J Feline Med Surg* 2018;20:704-710.
5. Brondani JT, Mama KR, Luna SPL, et al. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. *BMC Veterinary Research* 2013;9:143.
6. Jääskeläinen SK. Clinical neurophysiology and quantitative sensory testing in the investigation of orofacial pain and sensory function. *J Orofac Pain* 2004;18:85-107.
7. Blocker T, Van Der Woerdt A. A comparison of corneal sensitivity between brachycephalic and Domestic Short-haired cats. *Vet Ophthalmol* 2001;4:127-130.

NOTES:

Nasal Tumors and Neuro-Oncology in Cats

Michael Nolan, DVM, PhD, DACVR-RO

Nasal Tumors

Sinonasal tumors can be classified as being either intranasal and/or nasopharyngeal, or affecting the nasal planum.

Tumors of the Nasal Planum

Squamous cell carcinoma (SCC) is the most common neoplasm affecting the nasal planum of cats; less commonly, cats develop mast cell tumors in this location. Feline nasal planum SCC most often presents as a crusting and/or ulcerated and bleeding lesion that progresses with time. Cats may paw or rub at their face, indicating discomfort. Important differential diagnoses include herpetic infection (including related eosinophilic granulomatous lesions), insect bites and solar damage; notably, immune-mediated disease of the feline nasal planum is uncommon. History and physical examination usually helps to prioritize the list of differential diagnoses. For example, insect bites have an acute onset of ulceration, often with minimal (if any) crusting; herpetic infections may have a waxing and waning history and often occur in younger cats. Concern for SCC should be highest in older cats (median age of onset is 12 years) with unpigmented skin (Siamese cats are underrepresented). Many cats are treated for nasal planum with a presumptive diagnosis; this is often done due to the perception that biopsy at this site is difficult and associated with heavy bleeding. However, two reasonable options exist: (1) punch biopsy; and (2) shave biopsy. Both procedures require general anesthesia. Punch biopsies can be performed using a 4-millimeter punch tool. Ideally, the biopsy should take mostly eroded/ulcerated skin, but also including a small amount of the edge where the ulcer meets normal skin; apply digital pressure until hemorrhage subsides and then close primarily using suture. My preferred technique for first-line diagnostics is a shave-biopsy. This is performed using a scalpel blade to held parallel to the nasal planum to slice off the top portion of lesional epidermis and superficial dermis. Place the sample into 10% neutral buffered formalin for histopathologic evaluation, and apply gentle digital pressure to stop bleeding; suture is usually not possible, and is rarely needed. The disadvantage of shave biopsies is that they only evaluate the most superficial tissues, but the distinct advantage is that the procedure is quick, associated with minimal and manageable bleeding, and minimizes cosmetic damage.

SCC of the feline nasal planum most often develops because of exposure to ultraviolet light (i.e., sun exposure). The lesions are referred to as “actinic”. While cutaneous facial SCC lesions in cats can metastasize, that occurs very late in the course of disease, and for most cats. Staging with regional lymph node cytology is reasonable in cats with palpable lymphadenomegaly; and certainly it would not be wrong to evaluate thoracic radiographs; however, in most cases, it would also be very reasonable to forgo these tests. Indeed, it is the tumor on the nasal planum which dictates prognosis for most cats. Most lesions will be visible before they have breached the basement membrane; this early stage of disease is referred to as “carcinoma *in situ*”. With time, the SCC lesions will become more invasive; they eventually will invade deeply into the nasal planum, and laterally into haired skin. This is an important consideration: while *in situ* disease is usually very manageable, invasive SCC lesions are difficult to manage, and poorly responsive to therapy.

Surgery: Nasal planectomy, performed by an experienced surgeon, is generally well-tolerated, and reasonably cosmetic results can often be achieved. Because less invasive measures can be used to effectively control superficial SCC of the feline nasal planum, extensive surgery is usually best reserved for deeply invasive tumors. Curettage and diathermy has also been reported, and represents a good option for superficial disease.[1]

Photodynamic Therapy: In one study of 55 cats, 96% of cats benefitted from treatment and 85% had complete responses. However, half of cats with a complete response experienced disease recurrence, at a median of 5 months.[2] Indeed, enthusiasm for PDT is limited by this short duration of response, paired with a lack of access to PDT in many locales within the US. Advent of newer photosensitizers may improve therapeutic efficacy.

Cryotherapy: With a contact applicator, 2 rapid freezes and 2 slow thaws using liquid nitrogen can be useful for superficial nasal planum SCC lesions. In the original study describing this technique, 11/15 cats had recurrence at a median of 5 months.[3] However, retreatment is possible, and outcomes may be more favorable for smaller tumors (i.e., <1cm diameter), making this a reasonable option when more effective therapies (e.g., strontium or electrochemotherapy) are not accessible.

Radiation Therapy: External beam radiation is typically reserved for palliation of invasive SCC when surgery is opted against. Plesiotherapy (single fraction of strontium-90) can be highly effective for superficial disease; nearly all cats will have a measurable response to therapy and 85-88% have complete responses; in one study, the median

progression-free survival time exceeded 4.5 years.[4,5] This type of radiation is accessible in many veterinary radiation oncology and ophthalmology centers.

Chemotherapy: Four weekly treatments with intralesional carboplatin (in a water-sesame oil emulsion) has been associated with a response rate of at least 67%, with a 1-year progression free survival rate of 55%.[6] Electrochemotherapy is an appealing option; response rates are typically >50%, and response duration often exceeds 2 years.[7-9]

Retinoids: Imiquimod 5% cream (Aldara) is a topical agent that is useful for cutaneous SCC; it is immunostimulating, and works by activating toll-like receptor 7 (TLR7).[10] It has been proposed for use in nasal planum SCC, but is generally avoided for this particular indication, due to risk of ingestion.

NSAIDs: There are no published reports of using NSAIDs for management of feline nasal planum SCC; furthermore, a low likelihood of response is implied by low immunoreactivity for cyclooxygenase-2 reactivity in most feline cutaneous SCC tumors

Intranasal, Sinonasal, and Nasopharyngeal Tumors
Initial workup for any cat with chronic nasal discharge, sneezing, epistaxis and/or stertorous breathing should include testing to evaluate for infectious causes (e.g., cytologic evaluation of nasal swabs to evaluate for cryptococcosis, cryptococcal antigen titers, retroviral testing). More advanced diagnostics should generally include imaging of the nasal cavity (radiography, or computed tomography when available), rhinoscopy, and biopsy for histopathology (+/- fungal cultures). When rhinoscopy is unavailable, blind biopsy can be performed with either a curette, or flush biopsy. Caution should be exercised with flush biopsies, particularly when integrity of the cribriform plate has not been evaluated via cross-sectional imaging. The most common intranasal malignancy of cats is lymphoma; and the second most common is adenocarcinoma.

Sinonasal Lymphoma
Most cats with nasal lymphoma are older and FeLV antigen negative. Although lymphoma is localized to the nose in most cats, dissemination to distant organs is reported in approximately 20% of cases; therefore, complete staging should include fine needle aspiration (FNA) and cytology of the mandibular (+/- medial retropharyngeal) lymph nodes, thoracic radiographs and abdominal ultrasound.

In the United States, modified CHOP protocols are typically recommended as the chemotherapy protocol of choice for feline nasal lymphoma. In Europe and Australia, it is common to omit doxorubicin, in favor of COP protocols. The median remission duration for cats treated with chemotherapy alone is 151-380 days,[11] which is generally inferior to that expected for radiotherapy alone (wherein most cats will experience remissions that last for 1.5+ years).[12] For this reason, when systemic involvement has been ruled out, the preferred first-line treatment is external beam radiotherapy; and chemotherapy as monotherapy is generally reserved for cases where radiotherapy is inaccessible, or when there is disseminated (extranasal) disease present at diagnosis.

Indeed, combinations of chemotherapy and radiation therapy are associated with the longest reported survival times.[13] What is unknown is how to optimally time these procedures. Oncologists generally fall into one of two camps: (1) those who recommend CHOP immediately following irradiation; and (2) those who recommend reserving CHOP as a rescue treatment when cats fail radiotherapy. Those in “camp 1” argue that intensive up-front treatment is the best way to procure long-term tumor control and minimize risk of either locoregional tumor progression or distant dissemination. Those in “camp 2” contend that radiotherapy alone is sufficient to achieve durable locoregional control in many cats, and early treatment with chemotherapy may make the lymphomatous cells that do eventually disseminate more drug resistant. There are insufficient data to know which approach is better.

Unsurprisingly, with or without chemotherapy, use of higher doses of radiation leads to improved probability of durable locoregional control.[13] In a recent study, 29 cats treated with a weekly hypofractionated radiation protocol (16-32 Gy total), the response rate was high (90%), but the duration of response and survival times were modest (median overall survival time of 421 days).[14] With higher dose protocols, outcomes appear to be improved; this is reflected in results of another recent study that reported on outcomes of 51 cats, the majority of whom were treated with 42 Gy in 10 daily fractions, and none of whom were treated with <30 Gy total. In that study, the median overall survival time was 922 days. Interestingly, nearly half of the cats in that study did experience disease progression at some point during the study period; 15/51 cats had systemic progression of their disease, while 10/51 had nasal or regional nodal progression. This study does suggest that outcomes could be improved upon if cats were to routine receive not just nasal irradiation, but also prophylactic (concurrent) irradiation of their regional lymph nodes; no cat receiving prophylactic nodal irradiation had progression in their lymph nodes.[15]

Non-Lymphomatous Sinonasal Tumors
A variety of different carcinomas and sarcomas have been reported in the feline nasal cavity; the most common is adenocarcinoma. Regardless of histology, tumor behavior and treatment outcomes appear broadly similar. Most solid sinonasal malignancies will remain localized to the head and neck, and most to the nose; regional metastasis to lymph nodes is reported in a minority of cases. In a report of 123 cats with sinonasal tumors, 21 had regional lymphadenopathy but non showed cytologic evidence of metastasis.[16] More recently, in a study of cats with intranasal carcinomas, metastatic carcinoma cells were identified in 6/22 cats for which lymph nodes were sampled (unpublished data, courtesy of Dr. Hiroto Yoshikawa at North Carolina State University). Distant metastasis is a late occurrence and rarely influences clinical outcome.

Treatment of choice for localized non-lymphomatous nasal tumors is external beam radiotherapy. In a 2014 study that included 36 cats with nonlymphomatous nasal tumors, weekly hypofractionated (palliative-intent) radiotherapy, the median overall survival time was 450 days. In a 2020 study reporting use of a different hypofractionated radiotherapy protocol (42 Gy in 10 daily fractions), the overall response rate was 74%; the median time to progression was 269 days, and the median overall survival time was 452 days. Interestingly, these authors reported that cats with epistaxis had longer survival than those without; perhaps epistaxis facilitated early diagnosis and treatment.[17] Based on an unpublished study by Yoshikawa et al (personal communication, 2020), the overall response rate for irradiation of cats with intranasal carcinoma was 90%, and cats treated with definitive-intent (either stereotactic or full-course) radiotherapy lived significantly longer than those undergoing palliative-intent radiation therapy (721 versus 282 days). In that study, cats with low stage tumors (i.e., unilateral tumors that did not extend beyond the nasal cavity) and those without lymph node metastasis had the best outcomes.

The utility of systemic drug therapies is unclear. There are no published data regarding the efficacy of toceranib phosphate (Palladia) for feline nasal tumors and the data in dogs is limited (currently, just about a half-dozen cases). There are anecdotal reports of clinical responsiveness in both species, thus, this could be a consideration in select cases. Similarly, there are limited data regarding injectable chemotherapy for solid malignancies of the feline nasal cavity, though extrapolating from the canine data suggests a potential benefit in cases where radiotherapy is not an option.

Neuro-Oncology
CNS Lymphoma
Central nervous system involvement is reported in approximately 12% of cases of feline lymphoma. Most of these cats will be young, and FeLV antigen positive. For cats with spinal lymphoma, neurologic deterioration is typically rapid, and there is often no sign of disease outside of the CNS. Analysis of cerebrospinal fluid yields a positive diagnosis in a minority of cases, and this likely reflects the anatomic localization of the lymphoma to sites that would not readily shed cells into the CSF. Instead, diagnosis is often presumptive, and made after identification of masses on magnetic resonance imaging. Some cats will respond to chemotherapy, but response duration and overall prognosis is generally considered poor.[18,19] For cats who are FeLV negative and have localized CNS lymphoma, radiotherapy may be beneficial.

Brain Tumors
Meningioma is the most common intracranial tumor in cats, accounting for 58% of cases (29). In most cats, the tumors will be solitary and non-invasive to adjacent neuroparenchyma. Surgical excision is well-tolerated and effective. Affected cats are prone to development of multiple meningiomas; there are no known effective prevention strategies, however, additional new tumors can be treated with surgery as they develop. Anecdotally, cats also respond favorably and tolerate stereotactic radiotherapy/radiosurgery for this disease.

Spinal Tumors
Lymphoma is the most common spinal malignancy in cats; the second most common neoplasm affecting the feline spinal column is osteosarcoma (representing about a quarter of all cases), with a much lower incidence of spinal gliomas and meningiomas in this species.[20] When possible, cytoreduction should be pursued for nonlymphomatous malignancies of the feline spine. While the median survival time was only 88 days in a series of 5 cats undergoing cytoreductive surgery for vertebral osteosarcoma,[21] outcomes could likely be improved with provision of adjunctive definitive-intent radiotherapy. In a study of 16 cats with spinal meningioma, the median survival time after surgery was 426 days.[22]

References

1. Jarrett RH, Norman EJ, Gibson IR, Jarrett P. Curettage and diathermy: a treatment for feline nasal planum actinic dysplasia and superficial squamous cell carcinoma. *J Small Anim Pract.* 2013;54(2):92-98.
2. Bexfield NH, Stell AJ, Gear RN, Dobson JM. Photodynamic therapy of superficial nasal planum squamous cell carcinomas in cats: 55 cases. *J Vet Intern Med.* 2008;22(6):1385-1389.

3. Lana SE, Ogilvie GK, Withrow SJ, Straw RC, Rogers KS. Feline cutaneous squamous cell carcinoma of the nasal planum and the pinnae: 61 cases. *J Am Anim Hosp Assoc.* 1997;33(4):329-332.
4. Hammond GM, Gordon IK, Theon AP, Kent MS. Evaluation of strontium Sr 90 for the treatment of superficial squamous cell carcinoma of the nasal planum in cats: 49 cases (1990-2006). *J Am Vet Med Assoc.* 2007;231(5):736-741.
5. Goodfellow M, Hayes A, Murphy S, Brearley M. A retrospective study of (90)Strontium plesiotherapy for feline squamous cell carcinoma of the nasal planum. *J Feline Med Surg.* 2006;8(3):169-176.
6. Théon AP, VanVechten MK, Madewell BR. Intratumoral administration of carboplatin for treatment of squamous cell carcinomas of the nasal plane in cats. *Am J Vet Res.* 1996;57(2):205-210.
7. Spugnini EP, Pizzuto M, Filipponi M, et al. Electroporation Enhances Bleomycin Efficacy in Cats with Periocular Carcinoma and Advanced Squamous Cell Carcinoma of the Head. *J Vet Intern Med.* 2015;29(5):1368-1375.
8. Tozon N, Pavlin D, Sersa G, Dolinsek T, Cemazar M. Electrochemotherapy with intravenous bleomycin injection: an observational study in superficial squamous cell carcinoma in cats. *J Feline Med Surg.* 2014;16(4):291-299.
9. Spugnini EP, Vincenzi B, Citro G, et al. Electrochemotherapy for the treatment of squamous cell carcinoma in cats: a preliminary report. *Vet J.* 2009;179(1):117-120.
10. Peters-Kennedy J, Scott DW, Miller WH, Jr. Apparent clinical resolution of pinnal actinic keratoses and squamous cell carcinoma in a cat using topical imiquimod 5% cream. *J Feline Med Surg.* 2008;10(6):593-599.
11. Vail DM, Moore AS, Ogilvie GK, Volk LM. Feline lymphoma (145 cases): proliferation indices, cluster of differentiation 3 immunoreactivity, and their association with prognosis in 90 cats. *J Vet Intern Med.* 1998;12(5):349-354.
12. Sfiligoi G, Théon AP, Kent MS. Response of nineteen cats with nasal lymphoma to radiation therapy and chemotherapy. *Vet Radiol Ultrasound.* 2007;48(4):388-393.
13. Haney SM, Beaver L, Turrel J, et al. Survival analysis of 97 cats with nasal lymphoma: a multi-institutional retrospective study (1986-2006). *J Vet Intern Med.* 2009;23(2):287-294.
14. Fujiwara-Igarashi A, Fujimori T, Oka M, et al. Evaluation of outcomes and radiation complications in 65 cats with nasal tumours treated with palliative hypofractionated radiotherapy. *Vet J.* 2014;202(3):455-461.
15. Meier VS, Beatrice L, Turek M, et al. Outcome and failure patterns of localized sinonasal lymphoma in cats treated with first-line single-modality radiation therapy: A retrospective study. *Vet Comp Oncol.* 2019;17(4):528-536.
16. Mukaratirwa S, van der Linde-Sipman JS, Gruys E. Feline nasal and paranasal sinus tumours: clinicopathological study, histomorphological description and diagnostic immunohistochemistry of 123 cases. *J Feline Med Surg.* 2001;3(4):235-245.
17. Stiborova K, Meier VS, Takada M, et al. Definitive-intent radiotherapy for sinonasal carcinoma in cats: A multicenter retrospective assessment. *Vet Comp Oncol.* 2020.
18. Spodnick GJ, Berg J, Moore FM, Cotter SM. Spinal lymphoma in cats: 21 cases (1976-1989). *J Am Vet Med Assoc.* 1992;200(3):373-376.
19. Lane SB, Kornegay JN, Duncan JR, Oliver JE, Jr. Feline spinal lymphosarcoma: a retrospective evaluation of 23 cats. *J Vet Intern Med.* 1994;8(2):99-104.
20. Marioni-Henry K, Van Winkle TJ, Smith SH, Vite CH. Tumors affecting the spinal cord of cats: 85 cases (1980–2005). *Journal of the American Veterinary Medical Association.* 2008;232(2):237-243.
21. Marioni-Henry K. Feline spinal cord diseases. *Vet Clin North Am Small Anim Pract.* 2010;40(5):1011-1028.
22. Rossmeisl JH, Jr., Lanz OI, Waldron DR, Shires PK, Zimmerman KL, Sego LH. Surgical cytoreduction for the treatment of non-lymphoid vertebral and spinal cord neoplasms in cats: retrospective evaluation of 26 cases (1990-2005). *Vet Comp Oncol.* 2006;4(1):41-50.

NOTES:

Unique Feline Corneal Diseases

Jessica Meekins, DVM, MS, DACVO

Introduction

Though viral surface ocular disease is arguably the most common and clinically relevant ophthalmic disease encountered in cats, there are several other unique surface ocular diseases with which a feline practitioner should be familiar. These include corneal sequestrum, eosinophilic-proliferative keratitis/conjunctivitis, and acute bullous keratopathy.

Corneal Sequestrum

By definition, a corneal sequestrum is a focal area of coagulation necrosis within the corneal stroma. Histopathology of keratectomy samples reveal apoptosis of keratocytes and collagen disarray.[1] The exact etiopathogenesis of corneal sequestrums is not understood, but it appears to be a corneal disease unique to cats with few exceptions. Chronic corneal ulceration or irritation are the most important risks factors associated with the development of sequestrums.

Brachycephalic breeds, including Persians and Himalayans, are predisposed.[1,2] This is probably due to breed-related periocular conformation, such as medial canthal entropion with trichiasis, macropalpebral fissure, shallow orbits with relatively large globe size, and lagophthalmos, all resulting in chronic corneal irritation. In non-brachycephalic cats, chronic viral corneal ulcers may increase risk of sequestrum formation.[3] In this population of cats, the risk of sequestrum is more likely related to chronically exposed corneal stroma rather than any direct effect of the virus inducing sequestrum formation; after all, many more cats develop herpetic ulcers than form sequestrums.

The clinical appearance of sequestrums is classic, and diagnosis can be made based on examination alone. There is a spectrum of clinical appearances for sequestrums. Variably colored (amber brown to dark black) corneal stromal discoloration develops, often in discreet plaque-like lesions. Sometimes, early sequestrums can have the appearance of indistinctly marginated faint brown 'dust' trapped below intact epithelium. Vascular response and epithelial disruption (fluorescein stain retention, indicative of corneal ulceration) are also variable in their presence. Cats with sequestrums may exhibit different degrees of ocular discomfort, from a total absence of squinting to marked blepharospasm. Brachycephalic cats have diminished corneal sensation when compared to their non-brachycephalic counterparts,[4] which in some cases serves to prevent significant sequestrum-associated discomfort but can also result in exacerbation of conditions that lead to sequestrum formation.

Surgery is often required to treat corneal sequestrums.[5-9] Spontaneous sloughing has been reported, however it is difficult to judge the depth of stromal involvement, so allowing a sequestrum to slough or attempting manual removal may result in a significant corneal defect. A keratectomy allows controlled removal of the sequestrum, and the surgeon can be prepared to perform an ancillary grafting procedure if the sequestrum involves more than 50% of the corneal thickness. Cyanoacrylate glue application and other minimally invasive techniques have also been described.[10] With new corneal imaging modalities such as high resolution ultrasound, pre-surgical planning is becoming easier. Due to the need for microsurgical training when performing surgery on the cornea, keratectomy for sequestrum removal is considered a referral procedure.

If the sequestrum occupies the anterior corneal stroma, the keratectomy site is allowed to heal as an iatrogenic corneal ulcer after surgery. However, early sequestrum recurrence has been anecdotally reported in cases in which the keratectomy site (e.g., exposed corneal stroma) is not covered in some way, so the author prefers to place a bandage contact lens and temporary tarsorrhaphy to minimize risk of recurrence as the keratectomy site is re-epithelializing. Occasionally, contact lenses will start to develop an amber-brown discoloration that is typical of early sequestrum formation.[11]

The published recurrence rate for sequestrums is 5-20%,[6,9,12] and the same eye or the fellow eye may be at risk for new sequestrum development at any time in the future. There is no widely accepted or proven method of preventing sequestrum formation. Efforts should be directed at promoting surface ocular health by using lubricants or recommending surgical correction of profound conformational abnormalities that may be contributing to surface ocular irritation. Furthermore, any cat with a history of chronic, recurrent herpetic corneal ulcers may be at risk for sequestrum formation, emphasizing the need to achieve prompt healing of viral corneal ulcers.

Eosinophilic-Proliferative Keratitis/Conjunctivitis (EPKC)
EPKC consists of proliferative lesions of the cornea and/or conjunctiva composed of eosinophils and mast cells.[13,14] As with sequestrums, the exact cause of EPKC is not well-understood. Due to the predominant cell types, speculation has focused on allergic disease. Also, because EPKC is unique in cats, some investigators have hypothesized that the condition may be a manifestation of viral surface ocular disease. Neither of these theories is proven.

Clinical signs of EPKC are variable, but in general consist of white to pink, raised, proliferative, irregular corneal lesions that tend to start at the lateral limbus. Lesions are often unilateral.[15] When the conjunctiva is involved, it is often thickened, hyperemic, irregular, and proliferative, though white plaques are not as commonly seen within the conjunctival tissue. EPKC is easily diagnosed on cytology with support of the clinical appearance of the lesion. Mast cells and eosinophils should never be present in corneal or conjunctival cytology, so identifying them confirms the diagnosis of EPKC. In a recent study, eosinophils were identified in 92% of conjunctival scrapings.[15]

EPKC lesions are generally very responsive to local steroid therapy. This is one of the only surface ocular conditions for which topical steroids is indicated in cats. Prednisolone acetate or dexamethasone are commonly used, and hydrocortisone is avoided because it is not as potent and it poorly penetrates the corneal tissue. Frequency of treatment is dictated by the severity of the lesion, but a general guideline is 3-4 times per day at the time of diagnosis with slow tapering as the lesion(s) improve and resolve.

The risk of herpetic reactivation must be considered in any cat receiving topical steroid therapy for EPKC.[16] If a patient is at high risk for a herpetic flare-up, the author considers prescribing concurrent antiviral therapy in an effort to mitigate that risk. Careful questioning of the client is necessary to determine if there may be a history of previous recurrent viral surface ocular disease, and if so, antivirals can be prescribed topically or systemically to be administered during EPKC topical steroid treatment.

Alternatively, topical compounded megestrol acetate was recently investigated as another option to treat EPKC with good success.[17] Megestrol acetate has weak glucocorticoid activity, and thus may be less likely to trigger herpetic reactivation when compared to topical steroids. Topical compounded cyclosporine has also been evaluated for use in treatment of EPKC with promising results.[18] These alternative therapies may be considered in cats at high risk for reactivation of latent herpesvirus.

Long term maintenance therapy may be necessary to control EPKC, but this is determined on a case by case basis. The author attempts to taper to the lowest possible dosing frequency to maintain remission, and the only way to truly know if a cat requires long term maintenance treatment is to challenge it by discontinuing therapy after a prolonged tapering period. If EPKC flares up during the initial taper, a cat will likely need more long term, if not lifelong, maintenance therapy.[15]

Acute Bullous Keratopathy (ABK)
ABK is defined as the rapid formation of corneal edema with large bullous lesions. Corneal melting and perforation of the markedly abnormal stromal are possible complications. The cause remains unknown, though the condition appears to predominantly affect young cats.[19] Based on a retrospective study, identified risk factors include chronic systemic immune suppression, specifically with cyclosporine and prednisolone.[19] Not surprisingly, associated conditions are those for which chronic immune suppression is common, such as inflammatory bowel disease, immune-mediated hemolytic anemia, asthma, stomatitis, and the altered immune system that accompanies FeLV infection.[19]

The most commonly recommended treatment for ABK is a third eyelid flap. While the exact mechanism by which a third eyelid flap results in resolution of lesions associated with ABK is poorly understood, one theory is that the tamponade effect achieved with the flap provides structural support.

Medical therapy, specifically hyperosmotic agents such as 5% NaCl, may be used in an attempt to draw fluid from the dramatically edematous cornea. Topical antibiotics and antivirals are also often prescribed, though no infectious etiology has been identified.[19]

To perform a third eyelid flap, the patient is anesthetized and the eye is prepared in a routine fashion. The eyelashes and periocular hair should be clipped, and a combination of dilute 1:50 betadine solution and eyewash are used in several cycles to cleanse the ocular surface. The dorsolateral eyelid is grasped with forceps, and non-absorbable suture (for example, 3-0 to 4-0 nylon or silk) is passed through the skin to emerge from the conjunctival fornix. The needle is then passed in-and-out horizontally and parallel to the leading margin of the third eyelid, attempting to engage the cartilage. Next, the needle is passed back through the conjunctival fornix and out via the skin adjacent to

the initial suture pass. Stents are often used to prevent damage to the skin by the sutures. If possible, two separate sutures are placed, then the third eyelid is pulled upward and the sutures are secured such that the third eyelid covers the corneal surface.

The Role of FHV-1 in Unique Feline Corneal Diseases

The role of FHV-1 in unique feline corneal diseases is unclear. Because FHV-1 can be so distinctly problematic from a feline ophthalmology perspective, researchers have understandably investigated the possible connection between viral surface ocular disease and these unique corneal disease manifestations. In the literature, between 18 and 55%[20,21] of cats with corneal sequestrums have been PCR positive for FHV-1 DNA. However, a low percentage of brachycephalic cats in one study were PCR positive, leading to the conclusion that other factors, such as breed-standard conformation that results in chronic surface ocular irritation, may be influencing sequestrum development.[20] This finding lends additional support to the theory that chronic irritation and ulceration, rather than FHV-1, may be the main risk factor for the development of sequestrums.

In a retrospective study of EPKC, more than 75% of affected cats were PCR positive,[20] but this finding should be interpreted with caution. Considering that many normal cats harbor viral DNA at the ocular surface, simply identifying viral DNA is not enough to definitively establish a cause and effect relationship between FHV-1 and other unique feline ocular surface diseases.

In summary, several unique feline corneal diseases exist and are easily identifiable based on clinical appearance. A definitive etiopathogenesis has not been determined for these conditions, and the role of FHV-1 in their development remains unclear.

References

1. Cullen CL, Wadowska DW, Singh A, et al. Ultrastructural findings in feline corneal sequestra. *Veterinary Ophthalmology* 2005;8:295-303.
2. Startup FG. Corneal Necrosis and Sequestration in the Cat - a Review and Record of 100 Cases. *Journal of Small Animal Practice* 1988;29:476-486.
3. Nasisse MP. Feline herpesvirus ocular disease. *Vet Clin North Am Small Anim Pract* 1990;20:667-680.
4. Blocker T, Van Der Woerdt A. A comparison of corneal sensitivity between brachycephalic and Domestic Short-haired cats. *Vet Ophthalmol* 2001;4:127-130.
5. Laguna F, Leiva M, Costa D, et al. Corneal grafting for the treatment of feline corneal sequestrum: a retrospective study of 18 eyes (13 cats). *Vet Ophthalmol* 2015;18:291-296.
6. Andrew SE, Tou S, Brooks DE. Corneoconjunctival transposition for the treatment of feline corneal sequestra: a retrospective study of 17 cases (1990-1998). *Veterinary Ophthalmology* 2001;4:107-111.
7. Barachetti L, Giudice C, Mortellaro CM. Amniotic membrane transplantation for the treatment of feline corneal sequestrum: pilot study. *Vet Ophthalmol* 2010;13:326-330.
8. Dulaurent T, Azoulay T, Goulle F, et al. Use of bovine pericardium (Tutopatch(R)) graft for surgical repair of deep melting corneal ulcers in dogs and corneal sequestra in cats. *Vet Ophthalmol* 2014;17:91-99.
9. Graham KL, White JD, Billson FM. Feline corneal sequestra: outcome of corneoconjunctival transposition in 97 cats (109 eyes). *J Feline Med Surg* 2017;19:710-716.
10. Pumphrey SA, Desai SJ, Pizzirani S. Use of cyanoacrylate adhesive in the surgical management of feline corneal sequestrum: 16 cases (2011-2018). *Vet Ophthalmol* 2019;22:859-863.
11. Featherstone HJ, Sansom J. Feline corneal sequestra: a review of 64 cases (80 eyes) from 1993 to 2000. *Vet Ophthalmol* 2004;7:213-227.
12. Morgan RV. Feline Corneal Sequestration - a Retrospective Study of 42 Cases (1987-1991). *Journal of the American Animal Hospital Association* 1994;30:24-28.
13. Paulsen ME, Lavach JD, Severin GA, et al. Feline eosinophilic keratitis: a review of 15 clinical cases. *Journal of the American Animal Hospital Association* 1987;23:63-69.
14. Morgan RV, Abrams KL, Kern TJ. Feline eosinophilic keratitis: a retrospective study of 54 cases: (1989-1994). *Veterinary & Comparative Ophthalmology* 1996;6:131-134.
15. Dean E, Meunier V. Feline eosinophilic keratoconjunctivitis: a retrospective study of 45 cases (56 eyes). *J Feline Med Surg* 2013;15:661-666.
16. Nasisse MP, Guy JS, Davidson MG, et al. Experimental ocular herpesvirus infection in the cat. Sites of virus replication, clinical features and effects of corticosteroid administration. *Invest Ophthalmol Vis Sci* 1989;30:1758-1768.
17. Stiles J, Coster M. Use of an ophthalmic formulation of megestrol acetate for the treatment of eosinophilic keratitis in cats. *Vet Ophthalmol* 2016;19 Suppl 1:86-90.

18. Spiess AK, Sapienza JS, Mayordomo A. Treatment of proliferative feline eosinophilic keratitis with topical 1.5% cyclosporine: 35 cases. *Vet Ophthalmol* 2009;12:132-137.
19. Pierce KE, Jr., Wilkie DA, Gemensky-Metzler AJ, et al. An association between systemic cyclosporine administration and development of acute bullous keratopathy in cats. *Vet Ophthalmol* 2016;19 Suppl 1:77-85.
20. Nasisse MP, Glover TL, Moore CP, et al. Detection of feline herpesvirus 1 DNA in corneas of cats with eosinophilic keratitis or corneal sequestration. *Am J Vet Res* 1998;59:856-858.
21. Stiles J, McDermott M, Bigsby D, et al. Use of nested polymerase chain reaction to identify feline herpesvirus in ocular tissue from clinically normal cats and cats with corneal sequestra or conjunctivitis. *Am J Vet Res* 1997;58:338-342.

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Uveitis: Ocular Manifestations of Systemic Disease

Jessica Meekins, DVM, MS, DACVO

Introduction

Uveitis, or intraocular inflammation, may be an ocular manifestation of systemic disease. The uveal tract is the middle or vascular tunic of the eye, and it is divided into the anterior (iris and ciliary body) and the posterior (choroid) components. The uveal tract allows for a direct connection between the eyes and the body. While certain local disease processes confined to the eye can also lead to uveitis, the clinician must always consider that a cat diagnosed with uveitis is potentially experiencing an ocular manifestation of a more widespread problem.

Clinical Presentation

Signalment and History

Uveitis can affect cats of any age or breed, however certain age groups (kitten vs. adult cat) or specific risk factors (indoor vs. outdoor) may influence the initial clinical suspicion of uveitis etiology. Because the clinical signs of uveitis can be subtle, the history may vary widely from a sudden onset change in appearance of the eye(s) to a more slowly progressive change occurring over several weeks. Vision status as perceived by the owner can be quite variable, and is dependent on the location and severity of inflammation within the eye(s). Cats are very adept at adjusting to even advanced vision loss, such that some owners are unaware of marked vision impairment until it is brought to their attention based on the results of an ophthalmic examination.

The Ophthalmic Examination

Most veterinary practices are equipped with the basic tools for ophthalmic examination. These include a direct ophthalmoscope, a Finoff transilluminator or penlight, and fluorescein stain strips. Digital tonometers to measure intraocular pressure are also becoming more readily available in general practice. Each ophthalmic examination should start with a basic neuro-ophthalmic assessment, so that the examiner can confirm vision status and generally identify clues regarding the location of inflammation within the eye. Menace response, palpebral reflex, dazzle reflex, and pupillary light reflexes are important aspects of the initial assessment.

Aqueous flare, or protein within the anterior chamber fluid, is considered the pathognomonic sign of anterior uveitis. Protein leaks into the aqueous humor as a result of inflammation of the anterior uveal blood vessels. Using the direct ophthalmoscope, the examiner aims the small slit beam of light into the eye. In a normal eye, the light strikes the cornea and the surface of the iris and lens, and the clear space in between represents the anterior chamber. In an eye with aqueous flare, that clear space is instead occupied by a diffuse, homogenous haziness. This is sometimes described as ‘headlights in fog’ and represents the Tyndall effect, whereby light is scattered by particles (i.e., protein) within a fine suspension (i.e., the aqueous humor).

Two other important signs of anterior uveitis are miosis (a small pupil) and hypotony (low intraocular pressure). The pupil constricts with uveitis due to the effects of inflammatory mediators on the iris tissue, while the intraocular pressure is low due to decreased production of aqueous humor by the ciliary body; the ciliary body epithelium experiences dysfunction in an inflammatory environment.

There are several other clinical signs of anterior uveitis, including keratic precipitates (clumps of white blood cells on the corneal endothelium) and the accumulation of other ‘materials’ in the anterior chamber (hypopyon, hyphema, fibrin). Together, these signs are the most important clues to lead the clinician to a preliminary diagnosis of anterior uveitis. While all signs are not necessarily present simultaneously, any combination of one or more signs is usually enough to make a diagnosis.

Posterior uveitis can be more difficult to recognize, depending on the degree of anterior uveitis that may be causing opacity in the front aspect of the eye and on the examiner’s experience with performing and interpreting fundic examinations. Significant manifestations of posterior uveitis include retinal detachment, retinal hemorrhage, and inflammatory infiltrates within or below the retina resulting in altered tapetal reflectivity. Depending on the severity of posterior uveitis, there may be signs of its presence during the initial neuro-ophthalmic assessment; for instance, an eye with a retinal detachment or significant posterior inflammatory infiltrates should have a diminished or absent menace response and abnormalities in the resting pupil size and pupillary light reflexes. However, neuro-ophthalmology is a complicated topic, and partial retinal detachments or focal areas affected by inflammatory infiltrates may result in no signs or very subtle signs of neuro-ophthalmic deficits.

Whenever possible, the pupils of a cat with uveitis should be dilated to screen for involvement of the posterior segment. This will allow the examiner to identify abnormalities at the periphery of the ocular fundus that may be missed during a non-dilated exam. The eye is screened for signs of retinal detachment, hemorrhage, or altered reflectivity of the tapetum. Hypo-reflectivity occurs when material (fluid, cells, organisms) leaks out of the choroidal blood vessels and collects in the subretinal space. Remember that the tapetum is located within the choroid, so any material that leaks from the choroid will settle in between the retina and the tapetum, effectively dampening the tapetal 'shine' as viewed by the examiner.

While signs of anterior uveitis are arguably easier to recognize than posterior uveitis, fundic examination is an important part of a complete ophthalmic examination. Certain etiologies of uveitis preferentially affect different areas of the uveal tract and result in somewhat classic or characteristic lesions, so it is important to fully evaluate the eyes of each cat to screen for involvement of all aspects of the uveal tract (i.e., panuveitis).

Etiology

The uveal tract is the location of the blood-ocular barrier, with the blood-aqueous barrier anteriorly and the blood-retinal barrier posteriorly. The blood-aqueous barrier is formed by the endothelium of the iris blood vessels and the non-pigmented epithelium of the ciliary body, while the blood-retinal barrier is formed by the endothelium of the retinal blood vessels and the retinal pigment epithelium.[1] This barrier effectively protects the delicate tissues of the eye from the rest of the body, separating the intraocular structures from the blood entering the eye from systemic circulation. This protective barrier fails when inflammation leads to breakdown of its various components, resulting in exposure of the eye to elements from the body.

Infectious Organisms

There are a wide variety of infectious agents that may result in uveitis as an ocular manifestation of systemic disease.[2,3] The geographic specificity of select agents should be considered when building a list of potential infectious causes of uveitis in a cat. Viral (FIV,[4] FeLV,[5] FIP[5]), bacterial (bartonellosis,[6] leptospirosis), rickettsial (Ehrlichiosis, Lyme disease, Rocky Mountain Spotted Fever), protozoal (toxoplasmosis,[7] cytauxzoonosis[8]) and fungal (histoplasmosis, blastomycosis, cryptococcosis, coccioidomycosis) are part of a list that is by no means exhaustive. In general, younger cats and those that have access to the outdoors are considered at an increased risk of infectious uveitis, though a fair number of cats housed exclusively indoors are diagnosed with systemic infections causing uveitis.

Neoplasia

Ocular neoplasia is divided into primary and metastatic. While primary intraocular tumors (i.e., diffuse iris melanoma) may cause uveitis later in the course of disease, metastasis is considered the more common manifestation of neoplastic uveitis. The most common metastatic tumor to the feline eye is lymphoma,[5] though any distant site tumor may spread to the eye.[9]

Idiopathic/Immune mediated

A large proportion of adult cats, particularly indoor-only cats, are diagnosed with idiopathic lymphocytic-plasmacytic uveitis, which is essentially a form of immune-mediated uveitis.[10] The trigger for this attack of the host immune system against the eye is not well-understood, and idiopathic uveitis must be a *diagnosis of exclusion* after eliminating any potential systemic diseases that could be manifesting in the eye.

Concurrent Conditions

Non-ocular conditions that exist concurrently with uveitis are often referable to the underlying etiology and how it affects other organ systems. The most important ocular sequela of uveitis is secondary glaucoma,[11] which can be blinding and painful. Uveitis leads to glaucoma via several mechanisms. Acutely, the material that leaks into the anterior chamber (fibrin, cells) can physically block the fluid drainage angle located at the base of the cornea and iris (i.e., iridocorneal angle). Chronically, the outflow of fluid can be obstructed at the level of the pupil (posterior synechiae) or at the angle opening (pre-iridal fibrovascular membrane [PIFM] or peripheral anterior synechiae).[12] Acutely, the changes that result in an inappropriately high pressure (remember, the pressure inside the eye should be low in an inflammatory environment) are reversible; chronically, the changes are irreversible and secondary glaucoma will be managed long term.

Pupil block occurs when posterior synechiae, or adhesions between the pupil margin and the lens, develop circumferentially for 360 degrees. This effectively prevents fluid being produced at the ciliary body from flowing through the pupil, which is necessary in order for it to be drained from the eye at the level of the iridocorneal angle. In an inflammatory environment, the iris tissue becomes 'sticky' and prone to attaching to any closely located structure(s). The pupil also typically becomes small, which increases the proximity of the iris tissue to the lens behind

it. It is then easy for the iris at the pupil margin to come into contact with surface of the lens, forming adhesions that, if extensive, block fluid flow through the pupil.

The angle opening can be affected in two distinct ways. First, the cytokines and other inflammatory mediators that circulate inside the eye in an inflammatory environment promote the formation of a fibrovascular membrane on the iris surface (i.e., PIFM). This PIFM carpets the iris surface and ultimately grows across the angle opening, establishing a barrier to normal fluid outflow. Clinically, a PIFM can be identified during ophthalmic examination by observing a fine network of blood vessels on the iris surface and/or by noting a color change to the iris. The color change is most obvious in cats with blue irides.

The second mechanism of angle opening blockage occurs when the base of the iris swells and becomes displaced anteriorly, allowing the tissue to contact the peripheral cornea at the level of the angle opening. As was described regarding the pathophysiology of posterior synechiae development, similarly the tissue at the iris base is sticky and prone to attaching to neighboring structures. In this example, the iris tissue sticks permanently to the peripheral cornea and leads to a fluid outflow obstruction.

Differential Diagnosis
The clinical signs of uveitis are distinct. No other ophthalmic disease results in aqueous flare or hypotony, and the only other disease that may cause a miotic pupil is Horner's syndrome, a condition resulting from disruption of the sympathetic innervation to the eye and associated structures. Though there may be some overlap of clinical signs caused by uveitis and Horner's syndrome, anterior chamber infiltrates (flare, hypopyon, hyphema, fibrin) should be absent and the intraocular pressure should be normal in an eye with miosis due to sympathetic denervation to the eye. This makes the differentiation between the two conditions fairly straightforward.

Diagnostic Evaluation
A detailed history and thorough physical examination should be performed in any cat diagnosed with uveitis. The history should include information on environment (indoor/outdoor), vaccination and preventative status, and any travel history. The general physical examination is aimed at identifying any non-ocular abnormalities that may help narrow the list of potential uveitis etiologies. If any abnormalities are encountered, diagnostics can be targeted at further characterizing these findings. It is prudent to start with a minimum database (CBC, serum biochemical profile, urinalysis) in order to identify any non-specific changes that may accompany certain etiologies, as well as to provide baseline information on patient status prior to implementing treatment. Thoracic and abdominal imaging may be pursued, depending on physical examination findings. Selected infectious disease screening tests may also be performed; at minimum, an FIV/FeLV combo test should be done, even if the cat was previously tested and negative. This is particularly important if the cat has outdoor access and increased risk of exposure to these highly transmissible retroviruses due to contact with other, potentially infected cats. Other testing can then be prioritized based on the clinician's index of suspicion for specific etiologies; a number of academic and private sector diagnostic laboratories offer a broad array of antigen testing, serology, and molecular diagnostics.

Management
Controlling inflammation, alleviating pain, and minimizing the development of sequelae are the goals of uveitis therapy. Specific therapy, such as antimicrobials for infectious uveitis or chemotherapy drugs for neoplastic (metastatic) uveitis, should be implemented in addition to symptomatic therapy when a specific cause is identified during diagnostic workup.

Anti-inflammatory therapy
Route of administration and type of drug are two important considerations when building the treatment plan for feline uveitis. Anterior uveitis is generally easier to treat when compared to posterior uveitis; topical ophthalmic preparations (drops, gels, ointments) are only able to penetrate to the level of the lens, so this route of treatment is ideal for anterior uveitis. Posterior uveitis, on the other hand, requires systemic therapy in order for the drug to reach its target within the back of the eye at the choroid. Options for systemic anti-inflammatory therapy are limited in cats, largely due to the decreased capacity for hepatic glucaronidation in the species.

Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are used to control inflammation in cats with uveitis.[13-15] NSAIDs commonly used by the author include flurbiprofen, diclofenac, and ketorolac. These drugs are most appropriately used in cats with an ocular comorbidity that precludes the use of topical steroids (i.e., a corneal ulcer or increased risk of reactivation of latent herpesvirus), or they can be used in combination with topical steroids for an enhanced anti-inflammatory effect in more severe or medically refractory cases of uveitis. In general, steroids are preferred for their increased potency in more rapidly and effectively controlling active uveitis. When signs of active anterior uveitis are identified on ophthalmic examination, topical steroids (NeoPolyDex, 0.1% dexamethasone, or 1% prednisolone acetate) should be prescribed unless there is a specific contraindication to their use. NeoPolyBac

with Hydrocortisone is inappropriate for treatment of anterior uveitis because hydrocortisone does not penetrate inside the eye.[13,14] The frequency of topical anti-inflammatory therapy is dictated by the severity of the inflammation, generally 2 to 4 times per day.

Because of the limited systemic absorption of topically applied medications, NSAIDs and steroids can be used together topically and topical steroids can be used even if there is concern for infectious uveitis. It is also generally safe to prescribe a topical NSAID and a systemic steroid, or a topical steroid and a systemic NSAID. Anterior uveitis should be treated with topical +/- systemic anti-inflammatory therapy, but posterior uveitis must be treated with systemic therapy in order to reach the affected tissue within the back of the eye. In the United States, systemic NSAID options are limited to meloxicam as a single parenteral or oral dose, and robenacoxib, which is labeled to be given parenterally or orally once per day for up to 3 consecutive days. In a study evaluating the ability of robenacoxib to inhibit experimentally induced anterior uveitis, there was no difference in uveitis scores for treated vs. control cats, calling into question the utility of this 'cat-friendly' NSAID in the treatment of uveitis.[16] However, it remains to be determined if robenacoxib may be beneficial in cats with naturally occurring uveitis.

The other option for systemic anti-inflammatory therapy in cats is corticosteroids. It is fairly common to prescribe an anti-inflammatory dose of oral prednisolone in cats with posterior uveitis, especially when an infectious etiology is deemed unlikely.

Mydriatic (anticholinergic) Therapy
Atropine is a useful addition to the medical therapy plan in feline uveitis.[17] Spasms of the ciliary body muscle are responsible for the pain that accompanies uveitis, and atropine alleviates pain by temporarily paralyzing that robust intraocular muscle. Atropine treatment also serves an important role in minimizing sequelae of uveitis, by dilating the pupil to decrease the risk of posterior synechiae formation and by stabilizing the blood-aqueous barrier.[17,18] In a non-inflamed eye, the effects of atropine can be quite long; depending on the species, the pupil may remain dilated for days to a week or more. While some clinicians advocate using pupil dilation as the determining factor for dosing frequency with atropine, it is important to note that the mydriatic effects have a longer duration than the cycloplegic effects. This means that consistent treatment is necessary for the duration of active uveitis signs in order to achieve all the benefits of atropine therapy. From a practical perspective, it is also important to consider that atropine has a bitter taste; some clinicians believe that ointment should be used instead of solution in cats in an effort to mitigate the hypersalivation that can accompany a dose of topical ophthalmic atropine. However, some cats are so sensitive to the bitter taste of atropine that hypersalivation occurs no matter what formulation is used.

In the author's experience, the majority of adult cats with anterior uveitis are ultimately diagnosed with idiopathic uveitis, while cats with posterior uveitis are often experiencing an ocular manifestation of systemic disease (infection, neoplasia, etc.). Any cat, regardless of age or exposure risk, may develop uveitis due to systemic disease, thus idiopathic uveitis must remain a diagnosis of exclusion after eliminating specific causes with a targeted diagnostic workup.

References

1. Raviola G. The structural basis of the blood-ocular barriers. *Exp Eye Res* 1977;25 Suppl:27-63.
2. Lappin MR. Feline infectious uveitis. *J Feline Med Surg* 2000;2:159-163.
3. Lappin MR, Marks A, Greene CE, et al. Serologic prevalence of selected infectious diseases in cats with uveitis. *J Am Vet Med Assoc* 1992;201:1005-1009.
4. English RV, Davidson MG, Nasisse MP, et al. Intraocular disease associated with feline immunodeficiency virus infection in cats. *J Am Vet Med Assoc* 1990;196:1116-1119.
5. Peiffer RL, Jr., Wilcock BP. Histopathologic study of uveitis in cats: 139 cases (1978-1988). *J Am Vet Med Assoc* 1991;198:135-138.
6. Ketring KL, Zuckerman EE, Hardy WD, Jr. Bartonella: a new etiological agent of feline ocular disease. *J Am Anim Hosp Assoc* 2004;40:6-12.
7. Davidson MG. Toxoplasmosis. *Vet Clin North Am Small Anim Pract* 2000;30:1051-1062.
8. Meekins J, Cino-Ozuna AG. Histologic identification of intraocular Cytauxzoon felis in three cats. *JFMS Open Rep* 2018;4:2055116918813242.
9. Cassotis NJ, Dubielzig RR, Gilger BC, et al. Angioinvasive pulmonary carcinoma with posterior segment metastasis in four cats. *Vet Ophthalmol* 1999;2:125-131.
10. Chavkin MJ, Lappin MR, Powell CC, et al. Seroepidemiologic and clinical observations of 93 cases of uveitis in cats. *Progress in Veterinary & Comparative Ophthalmology* 1992;2:29-36.
11. Wilcock BP, Peiffer RL, Jr., Davidson MG. The causes of glaucoma in cats. *Vet Pathol* 1990;27:35-40.
12. Peiffer RL, Jr., Wilcock BP, Yin H. The pathogenesis and significance of pre-iridal fibrovascular membrane in domestic animals. *Vet Pathol* 1990;27:41-45.

13. Wilkie DA. Control of ocular inflammation. *Vet Clin North Am Small Anim Pract* 1990;20:693-713.
14. Holmberg BJ, Maggs DJ. The use of corticosteroids to treat ocular inflammation. *Vet Clin North Am Small Anim Pract* 2004;34:693-705.
15. Giuliano EA. Nonsteroidal anti-inflammatory drugs in veterinary ophthalmology. *Vet Clin North Am Small Anim Pract* 2004;34:707-723.
16. Sharpe EK, Meekins JM, Roush JK, et al. Effect of oral administration of robenacoxib on inhibition of paracentesis-induced blood-aqueous barrier breakdown in healthy cats. *Am J Vet Res* 2018;79:443-449.
17. Klauss G, Constantinescu GM. Nonhypotensive autonomic agents in veterinary ophthalmology. *Vet Clin North Am Small Anim Pract* 2004;34:777-800.
18. Stocker FW. Experimental studies on the blood-aqueous barrier; electrophotometric measurements of fluorescein content of aqueous after intravenous injection of fluorescein, the eye being under the influence of physostigmine, pilocarpine, neostigmine or atropine. *Arch Ophthal* 1947;37:583-590.

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Chronic Pain: Is It All in the Head?

Beatriz Monteiro, DVM, PhD

Introduction

Pain is a personal, complex, and multidimensional experience involving sensory and emotional components. The intensity of pain does not correlate linearly with the severity of the pathology; rather, it involves several factors which can increase or decreased the painful experience. For example, stress response and cognitive functions of the brain including fear, memory, anxiety, and distraction can all modulate/influence the perception of pain. Equally important factors include genetics and neuro-hormonal mechanisms of stress (Roy *et al.*, 2009; Melzack and Katz, 2013; Monteiro and Steagall, 2019; Monteiro, 2020).

Although the true incidence of chronic pain in cats remains unknown, these patients can be affected by several chronic painful conditions including: osteoarthritis (OA), cancers, dental pain, persistent postoperative pain (e.g. chronic pain following onychectomy or other amputations, thoracotomy), chronic wounds, otitis, ophthalmic conditions, gastrointestinal conditions, feline idiopathic cystitis, feline hyperesthesia syndrome and/or diabetes-induced neuropathy.

Pain is now considered as the 4th vital sign, and its assessment should be incorporated into the clinical evaluation of all patients. We, animal health professionals, need to be prepared to appropriately assess and treat pain to mitigate animal suffering to the best of our abilities (Mathews *et al.*, 2014). Understanding mechanisms of pain and the influences that contribute to decreased or increased pain sensation are paramount for its appropriate assessment and treatment.

Osteoarthritis

Osteoarthritis is the most understood chronic painful condition in cats. The prevalence of radiographic signs of OA increases with age. Joints commonly affected by OA include the elbow, hips, stifle and tarsus, as well as the thoracic and lumbar vertebral column. Risk factors for OA probably include age, obesity, lifestyle, genetics and co-morbidities (Clarke *et al.*, 2005; Clarke and Bennett, 2006; Lascelles *et al.*, 2010).

Effects in Function and Quality of Life

Chronic pain negatively affects quality of life by impairing mobility and function and resulting in negative emotional states. It also negatively affects social relationships and causes changes in behavior (i.e. new behaviors that appear and old behaviors that disappear). For these reasons, feline health and welfare become compromised and the human-animal bond becomes weaker (Monteiro and Steagall, 2019; Monteiro, 2020).

Effects in the Sensory Profile

Cats with OA can present with widespread increased sensory sensitivity (i.e. they just 'hurt' more everywhere) and with features of central sensitization (i.e. pain facilitation – it is easier for a pain message to be generated and maintained in the central nervous system) (Monteiro *et al.*, 2020).

Understanding the Sensory System

Peripheral versus central input

The more we study pain, the more we learn how complex it is. The pathophysiology of pain is approached in a simplified manner to understand its clinical presentation and therapy (Meintjes, 2012):

- Peripheral nociceptors are present in the skin, muscles, joints and viscera. The activation of nociceptors results in membrane depolarization and generation of an action potential (i.e. pain message).
- Inflammation from an osteoarthritic joint or a tumor will result in the activation of these peripheral nociceptors generating a pain message. This pain message is then transmitted from the primary afferent (1st order neuron) to the dorsal horn of the spinal cord.
- In chronic pain, such as OA, cancer and dental pain, a component of inflammation is present. This chronic inflammation results in sustained nociceptive input from the periphery to the spinal cord. As a consequence, structural and functional changes occur in central nervous system affecting how pain is processed.
- Modulation of pain occurs at the dorsal horn of the spinal cord where the nociceptive message travels via 2nd order neuron to the cerebral cortex (3rd order neuron). During the modulation process, the nociceptive message may be amplified or inhibited.

- Pain modulation is influenced by several internal and external factors. For example, individuals might be genetically predisposed to have more pain facilitation and less pain inhibition. The environment (e.g. comfortable, calm, clean, predictable and safe versus noisy, thermal discomfort, stressful) can influence how pain is modulated and the coping abilities of the individual.
- Emotions can also modulate pain and it is generally accepted that negative emotions exacerbate pain whereas positive emotions decrease pain. This principle lays the foundation for the role of 'care' or 'TLC' in the management of pain.
- Perception of pain occurs when there is the conscious experience of pain.

Types of Pain

Chronic pain is also known as maladaptive pain. It is characterized by neuropathic or functional pain, such that the degree of pain does not necessarily correlate with the pathology observed or perceived by the individual. It is not associated with healing. It persists beyond the expected course of an acute disease process and it has no clear endpoint. Patients with chronic pain generally have a combination of inflammatory and neuropathic pain components.

- Inflammatory pain occurs when there is actual tissue injury or immune cell activation. These events result in the release of inflammatory mediators from cells and chemical changes in the tissues around the nociceptors which amplify the nociceptive input to the spinal cord. This occurs by facilitation or direct nociceptor activation.
- Neuropathic pain is associated to a primary lesion or dysfunction of the nervous system. This results in complexes mechanisms including sensitization of neural connective tissues, ectopic excitability, cross-excitation, gliopathy and neuro-immune interactions (Grubb, 2010).
- Examples of neuropathic pain include nerve compression, infiltration by cancers, amputations, intervertebral disk disease, nerve damage during dental extractions, osteoarthritis, among others. In humans, neuropathic chronic pain is generally considered to cause more severe and long-lasting pain, and to be less responsive to analgesics. In addition, it causes greater dysfunction and poorer indices of quality of life when compared with other types of chronic pain.
- Central sensitization is the increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input. It is expressed as pain hypersensitivity and sustained cerebral nociceptive inputs. These processes translate clinically to hyperalgesia (i.e. increased pain from a stimulus that normally provokes pain) and allodynia (i.e. pain due to a stimulus that does not normally provoke pain) (IASP Tak Force on Taxonomy, 1994).

The assessment and management of pain are best approached in a mechanism-based manner; thus, an understanding of pain mechanisms and their translation to clinical presentation is paramount. For example, non-steroidal anti-inflammatory drugs act primarily in the periphery and will work best in patients with pain coming mainly from the periphery, whereas analgesics such as gabapentin, tramadol and amitriptyline act centrally and will work best in patients with a greater degree of central sensitization. Drugs acting to reinforce the inhibitory system, such as anti-depressants are expected to benefit patients with a deficient inhibitory system.

Osteoarthritis, cancer and orofacial disease are the most commonly painful conditions seen in cats and pain in these patients can manifest very differently from patient to patient. Regardless, they are generally affected by widespread increased sensory sensitivity characterized by peripheral and central sensitization (8, 9, 10). Understanding these mechanisms and the target of analgesic drugs helps us to better assess and treat chronic pain.

Positive Emotions and Pain

As previously discussed, pain in patients with OA is generated in the joints and transmitted to the spinal cord where it can be modulated (i.e. enhanced or inhibited) before it is consciously perceived in the brain cortex. Pain perception is highly influenced by emotions and it is generally accepted that positive emotions inhibit pain (Roy *et al.*, 2009). Pain can also be affected by numerous variables including cognition, past experiences, environmental and social contexts which in turn affect emotions. For these reasons, promoting positive emotions (Boissy *et al.*, 2007; Lawrence, Vigors and Sandøe, 2019) in cats with chronic pain can contribute to both analgesic effects and improved feline welfare.

Positive emotions can be provoked for example by enrichment – The environment can be enriched by providing mental and physical stimulation to allow for expression of species-specific behaviors such as hunting, jumping, running, playing, etc. This can be achieve with the use of toys, condos, perches, elevated surfaces, scratching posts, and others (Ellis *et al.*, 2013; Heath and Wilson, 2014). The feeding can also be enriched to provide for exploratory and hunting behavior in order to make the experience of 'eating' last longer and be more interesting. It also increases satiety. Both feeding and environmental enrichment contribute to increased physical activity, weight loss and increased positive emotions which in turn contribute to reduce pain experience. Another manner of provoking positive

emotions is by promoting positive social relationships with humans and other animals (Boissy *et al.*, 2007; Lawrence, Vigors and Sandøe, 2019).

References

1. Boissy, A. *et al.* (2007) 'Assessment of positive emotions in animals to improve their welfare', *Physiology and Behavior*. Elsevier Inc., pp. 375–397. doi: 10.1016/j.physbeh.2007.02.003.
2. Clarke, S. P. *et al.* (2005) 'Prevalence of radiographic signs of degenerative joint disease in a hospital population of cats', *Veterinary Rec*, 157, pp. 793–799.
3. Clarke, S. P. and Bennett, D. (2006) 'Feline osteoarthritis: a prospective study of 28 cases', *J Small Anim Pract*, 47(August), pp. 439–445.
4. Ellis, S. L. H. *et al.* (2013) 'AAFP and ISFM Feline Environmental Needs Guidelines', *Journal of Feline Medicine and Surgery*, 15(3), pp. 219–230. doi: 10.1177/1098612X13477537.
5. Grubb, T. (2010) 'Chronic Neuropathic Pain in Veterinary Patients', *Topics in Companion Animal Medicine*. Elsevier Inc., 25(1), pp. 45–52. doi: 10.1053/j.tcam.2009.10.007.
6. Heath, S. and Wilson, C. (2014) 'Canine and feline enrichment in the home and kennel: A guide for practitioners', *Veterinary Clinics of North America - Small Animal Practice*. W.B. Saunders, pp. 427–449. doi: 10.1016/j.cvsm.2014.01.003.
7. IASP Tak Force on Taxonomy (1994) 'Part III: Pain Terms, A Current List with Definitions and Notes on Usage', in Merskey, H. and Bogduk, N. (eds) *Classification of Chronic Pain*. Second edi. Seattle: IASP Press, pp. 209–214.
8. Lascelles, B. D. X. *et al.* (2010) 'Cross-sectional study of the prevalence of radiographic degenerative joint disease in domesticated cats', *Veterinary Surgery*, 39(5), pp. 535–544. doi: 10.1111/j.1532-950X.2010.00708.x.
9. Lawrence, A. B., Vigors, B. and Sandøe, P. (2019) 'What Is so Positive about Positive Animal Welfare?—A Critical Review of the Literature', *Animals*. MDPI AG, 9(10), p. 783. doi: 10.3390/ani9100783.
10. Mathews, K. *et al.* (2014) 'Guidelines for recognition, assessment and treatment of pain: WSAVA Global Pain Council members and co-authors of this document.', *J Small Anim Pract*, 55(6), pp. E10-68.
11. Meintjes, R. A. (2012) 'An overview of the physiology of pain for the veterinarian', *Veterinary Journal*. Elsevier Ltd, 193(2), pp. 344–348. doi: 10.1016/j.tvjl.2012.03.001.
12. Melzack, R. and Katz, J. (2013) 'Pain', *WIREs Cogn Sci*, 4, pp. 1–15.
13. Monteiro, B. P. (2020) 'Feline Chronic Pain and Osteoarthritis', *Veterinary Clinics of North America - Small Animal Practice*. W.B. Saunders, pp. 769–788. doi: 10.1016/j.cvsm.2020.02.003.
14. Monteiro, B. P. *et al.* (2020) 'Quantitative sensory testing in feline osteoarthritic pain – a systematic review and meta-analysis', *Osteoarthritis and Cartilage*. W.B. Saunders Ltd, 0(0). doi: 10.1016/j.joca.2020.04.006.
15. Monteiro, B. P. and Steagall, P. V. (2019) 'Chronic pain in cats: Recent advances in clinical assessment', *Journal of Feline Medicine and Surgery*, 21(7), pp. 601–614. doi: 10.1177/1098612X19856179.
16. Roy, M. *et al.* (2009) 'Cerebral and spinal modulation of pain by emotions', *Proceedings of the National Academy of Sciences*, 106(49), pp. 20900–20905. doi: 10.1073/pnas.0904706106.

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Face & Head Reconstructive Techniques in Cats

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Anatomical Review

The mucosa of the upper lip is more generous than that of the lower lip, which becomes narrower rostrally. But the lower lip is easier to mobilize rostrally than the upper lip. The lower lip has a firm attachment to the gum between the lower canine and first premolar – the interdental ligament - it prevents the lower lip from sagging and is important to restore it when reconstructing this area.

Between the inner mucosa and the skin of the lips and cheeks are two layers of muscles – the superficial orbicularis oris and the deeper buccinator. There are many superficial facial muscles around here: the levator nasolabialis, caninus, levator labii maxillaris, platysma, zygomaticus, sphincter colli profundus-pars palpebralis and frontalis. These muscles are critical for facial expression in humans, but not as critical for dogs and cats. However, including these superficial muscles brings into a reconstructive effort will bring bulk, protection and good vascularity to the repair. The superficial temporal muscle of the head and the platysma of the neck are well developed in the dog and also useful to include in reconstructive efforts.

The blood supply to the lips, cheeks, and lesser extent head, is bountiful. The facial artery divides to supply the cheeks through the superior and inferior labial, and the angularis oris arteries. The infraorbital artery comes directly off the maxillary artery (which is the major terminating branch of the external carotid, so - high pressure!) and supplies a rich arterial network of blood to the upper lip and muzzle. The head is mostly supplied from the branches of the superficial temporal artery, which is the minor terminating branch off the external carotid. There are about six branches off the superficial temporal which cover most of the head. This wonderful arborization and collateral circulation makes it easier to develop flaps with a good chance of surviving.

The parotid salivary duct opens through the cheek on a small papilla opposite the caudal part of the upper fourth premolar tooth. The main duct of the zygomatic gland opens lateral to the caudal part of the upper first molar tooth. During tumor removal, the parotid duct can either be ligated, or preserved by relocating it through the mucosa and spatulating its end.

Types of Wounds Requiring Reconstruction

One of the most common defects requiring reconstruction is following wide tumor excision. Appropriate staging and careful planning usually enables both resection and reconstruction to occur under one anesthetic episode. Trauma, including bite wounds are also pretty common. These wounds should always be cleansed, explored, debrided and lavaged before reconstruction. Insect and spider bites and stings can also occur around the head, resulting in marked localized necrosis. Several debridement episodes maybe required before a healthy wound bed is evident. Some conformational defects can also be corrected with reconstruction, such as cheiloplasties, nasal fold excisions in brachycephalics dog. Nasal solar (actinic) dermatitis can occur with chronic UV exposure in dogs and cats with nonpigmented or depigmented nasal plana. Electrical burns, chemical burns are also seen on occasion. These are best managed with repeated débridements until full extent of necrosis is evident. Reconstruction should not occur until the wound is stable. Areas of radiation dermatitis or bone necrosis can be challenging, as the perfusion is fragile, skin less elastic, and dermal fibrosis will complicate reconstructive efforts. Bringing in a blood supply from outside the irradiated area is imperative.

Surgical Considerations for Facial Surgery

Humans look at their pets' faces more than other areas, and even if they are not as facially expressive as humans, cosmetic outcome may be of greater concern to the owner compared to other areas of the body. The primary goal for the animal, however, is restoration of pain-free function. To some extent, cosmesis and function are complementary. For example, restoring an accurate lip or lid margin is beneficial both for function and appearance. But we still need to manage the owner's expectation of the final outcome –most owners will readily accept a degree of cosmetic change if they recognize an improvement in quality of life following surgery. Due to the availability of tissues in dogs, mobilizing local tissues with tension-relieving techniques and simple flaps will enable closure of many small to moderate defects. Cats lack this redundancy and generally have a 'tighter' face - usually a more elaborate plan is required to reconstruct effectively.

Most defects in dogs and cats can be repaired with a carefully planned, single stage procedure, in contrast to human plastic surgery, where multi-staged procedures are more common. Our patients have the advantage of having a dense fur coat to mask deficits and cover scars, and facial asymmetry is less obvious in the elongated muzzle.

Skin Flaps for the Face
There are several extremely useful subdermal plexus flaps that the surgeon can utilize around head, including single pedicle advancement flaps, H-plasties, rotation flaps and lip-to-lid procedures. Local flaps are preferred to free cutaneous grafting and distant flaps, because of the difficulty immobilizing this area, securing bandages, preventing licking and other self-trauma. Single pedicle advancement flaps can be developed from either or both sides of the muzzle, utilizing the loose upper labial skin. These flaps can also be dissected on a deep plane, down to the bone if necessary, to provide more secure coverage for defects that include nasocutaneous fistulation.

Axial pattern flaps incorporate a direct cutaneous artery and vein into its base, providing better perfusion and allowing larger flaps to be developed. Useful axial pattern flaps for the face and neck include: the *omocervical* (based on the superficial cervical branch of the omocervical artery), the *superficial temporal*, and the *angularis oris*. A somewhat less dependable axial pattern flap is the *caudal auricular*. For the caudal muzzle area and between the eyes, the superficial temporal axial pattern flap will provide a padded, hirsute and quite robust coverage. This flap incorporates a consistent vascular pedicle (the cutaneous branch of the superficial temporal artery), so is quite reliable. Additionally, the frontalis muscle and fascia that can be transferred concomitantly provides support over any defect in the bone. The angularis oris or facial flap allows for a large caudodorsad-oriented flap based at the commissure of the lip to be developed and rotated into maxillofacial defects in dogs and cats. It is perfused by three arteries (the superior and inferior labial, and the angularis oris) that arborize and throw off yet another cutaneous perforator within its base. This flap is extremely robust and versatile for large facial and muzzle defects, and also for intraoral defects.

Lip Reconstructions
Restoration of lip integrity and function can be achieved by ensuring meticulous positioning of lip margins and strong anchorage to the gingival and mandibular tissues. Accurate alignment of the mucocutaneous junction should always be performed as the first step of reconstruction, usually with a figure-of-eight suture. This is also critical for the eyelid margins, as both lid notches and suture material will cause corneal trauma and interfere with normal precorneal tear film distribution. This lecture will not include eyelid reconstruction due to time limitation.

Incising wobbly lips can be tricky, so stabilizing and stretching the lip onto a firm surface (e.g., wooden tongue depressor, folded drape, or Jaeger lid plate) will facilitate clean, accurate cutting. Proposed incision lines should be drawn with a sterile marker before commencing surgery. In highly mobile area such as the lips, it is vital that apposition is secure and free of tension, in order to avoid dehiscence. Full thickness repairs should be undertaken in three or four layers: mucosa (or submucosa), deep musculature, superficial musculature and subcutaneous tissue, and skin. Fine (4-0) rapidly absorbable, monofilament suture material (4-0) in a continuous pattern (for fewer knots) is preferred.

As lip surgeries are classified as clean-contaminated procedures, prophylactic antibiotics are indicated (usually a single intravenous bolus of a broad-spectrum antibiotic at time of induction). Although self-trauma is not typical, an E-collar should be placed for the post-operative week.

Wedge and Rectangular Lip Resection
Full thickness segmental resection of the lip is indicated for debridement of complicated or infected trauma, or more commonly for tumor resections with adequate margins (usually 1cm – 2cm). A wedge resection is easiest to close (in three or four layers), as there is minimal disparity between edges. Mild disparity can be accommodated by placing tension at either end of the suture line. Significant disparity is corrected by removing a Burow's triangle from the dorsal end of the long side. A square defect can be converted to a pentagon to facilitate closure, or closed as a Y. Larger rectangular defects will require labial advancement.

Labial Advancement Flap
Labial or buccal advancement flaps are flaps based adjacent to the commissure of the mouth, and can be used to repair larger rostral maxillary or mandibular labial defects. These full thickness flaps will result in a shorter oral commissure, but are very useful for large defects. A shortened oral commissure generally does not cause a problem, and a second procedure can easily be performed to lengthen it if necessary (rarely). The cheek tissue and commissure is richly perfused and heals well. A full thickness incision parallel to the lip margin is made, extending caudad to the commissure (it can actually arc down behind the commissure a little if necessary). It is helpful to preserve about 5mm of labial mucosa coming off the gingiva to facilitate mucosal suturing. The flap is elevated and advanced rostrad into the defect, and sutured in four layers. For lower lip reconstruction, the interdental attachment must be recreated to avoid drooping of the lip.

Rotating Buccal Flaps

In addition to the labial advancements, commissure rotation and buccal rotation flaps can be performed with larger defects. These techniques actually rotate the commissure to form the upper lip. Transposition flaps can also be developed based at the commissure. Several flaps based on the angularis oris vascular pedicle and adjacent pedicles have been described to mobilize cheek tissue, which can preserve the commissure. These latter flaps are very versatile and robust and can be utilized for very large facial and muzzle defects.

Lip Avulsions

Lower labial avulsions occur from shear trauma (high rise fall [cats], car accident, chasing rabbits down a hole) and other trauma may be sustained concurrently, such as mandibular fracture, tooth disruption or extraction, diaphragmatic hernia, pelvic fracture, etc. Disruption usually occurs at the rostral gingival border, leaving little tissue with which to anchor the hanging lower lip. To ensure healing without complication, the wound must be healthy, and the lip secured firmly back to the gum. This involves thorough cleansing and debridement of the wound, converting it, if possible, to clean-contaminated status. Drainage (usually a small closed-suction device or a Penrose) should be provided as part of the wound repair. Sutures should be meticulously placed from the buccal mucosa around the incisor teeth. In the absence of incisors, transosseous sutures, placed through small holes drilled through the mandible, are required to secure the lip. An additional tension-relieving stent suture, traversing full thickness, may be indicated in more dramatic avulsions.

Reconstruction of the Nares

When reconstructing defects of the muzzle and planum, it is vital that the animal can breathe through its nasal cavity. Although cats and dogs (especially so) have no problem with open mouth breathing, the inability to sleep well at night can be quite stressful to pet and owner. If trauma or surgery has resulted in obliteration of the nares, they can be reconstructed and free mucosal grafts inserted to restore nasal mucosa. Wide holes (slightly larger than final desired diameter) are created into the nasal cavity, usually with a Steinman pin. Haemorrhage is controlled with pressure, whilst the grafts are harvested. Thin mucosal grafts are harvested from the mucosa under the tongue and sutured into an inverted tube over rolled Penrose drains. They are then inserted into the apertures and the rostral border of the inverted mucosal tube sutured to the skin. The soft, constant pressure of the latex maintains contact between the graft and recipient bed and prevents motion at this interface. The first 72 hours is critical for plasmatic imbibition, inosculation and neovascularization to occur. An E-collar should be worn for the post-operative week, and the Penrose drains removed just before this time (approximately five days).

Post-operative Care

Investment into preventing post-operative pitfalls will not only improve outcomes, but will also inspire further attempts in reconstruction.

Pain – Almost all our patients will require some form of analgesia. Fentanyl (pre-operative patch or constant rate infusion), cocktails (hydromorphone/lidocaine; morphine/ketamine/lidocaine), tramadol, butorphanol, carprofen and meloxicam are the most commonly used analgesics in our hospital.

Hydration – Dehydration will compromise flap perfusion significantly. Intravenous fluids should be maintained until the animal is eating and drinking completely normally.

Antibiotics – Antimicrobial coverage is generally given during a reconstructive surgery, but continuing coverage will depend on wound status and results of cultures and sensitivity.

Sedation – Acetyl promazine is an excellent sedative in most cases when used in combination with pain medications. Often animals are exhausted by the trauma, the hospitalization, and constant nursing care, but find it difficult to settle in the strange environment. Sedation will often enable a good sleep period as well as help prevent self-mutilation.

Drainage – Many of the reconstructions around the head and neck will heal more effectively if some form of drainage is provided. Obliteration of dead space cannot generally be achieved by bandaging in this area, so drainage is especially important. Active, closed-suction drains are preferred, and are commercially available. They can also be made from butterfly catheters and syringes or vacutainers. Drainage should be measured over each 24 hour period and continued until drainage decreases.

Protection - It is incredibly frustrating for vet and owner alike when a reconstructive effort is ruined by patient self-trauma. Elizabethan collars are almost mandatory unless a suture line extends to the neck. The collar should be large enough so that the animal cannot rub its face on the ground. Bandaging paws may also help.

Feeding– Many animals will not eat in the post-operative period, either because of hospitalization stress, pain medications, sedation, pain, or a combination of these. Ensuring an adequate nutritional plane is critical for wound healing in both cats and dogs. Cats have the added risk of hepatic lipidosis if they are anorexic for more than a couple of days. Anticipating loss of appetite and placing a gastrostomy or oesophagostomy feeding tube will often prevent a drop in albumin, and optimize outcomes in surgery.

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Cats Don't Read Textbooks: Commonly Found Oral Pathology of Felines

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Cats are not small dogs. It is equally important to realize that cats have not read textbooks when it comes to dental problems.

It is crucial to be able to identify oral pathology and anomalies. It is equally important to record the pathology on dental charts. A thorough dental examination includes both conscious and anesthetized examinations as well as charting disease processes, pathology and anomalies, and treatment plans.

Being aware of dental formulas, oral anatomy, as well as terminology, is crucial to proper charting. The head type of the animal, as well as malocclusions, needs to be noted.

Feline Dental Formulas:

Adult Cats	Kittens
2x(3/3I, 1/1C, 3/2P, 1/1M) = 30	2x(3/3i, 1/1c, 3/2p) = 26

Gingivitis Index (GI):
The gingival index (GI) is a measurement of gingival health. The assessments of gingival changes using the following criteria.

0 - normal healthy gingiva
1 - moderate inflammation, moderate redness, not bleeding on probing, edema
2 - moderate inflammation, moderate to severe redness, edema, bleeding upon probing
3 - severe inflammation, severe redness, edema, ulceration, spontaneous bleeding

Each tooth is given the most severe score.

Probe Depth (PD):
Probe depth (PD) is a measure of the depth the periodontal pockets often found in periodontal disease. The probe depth is measured at multiple sites of the tooth. A periodontal probe with millimeter markings is gently placed between the free gingiva and the tooth surface and carefully advanced until soft tissue resistance is felt. The tip of the probe should be parallel to the long axis of the tooth. The pocket depth is recorded as the distance in mm from the free gingival margin to the bottom of the pocket. The probe may be glided or walked along the tooth to measure the varying pocket depths. A gingival sulcus depth is 0.5 to 1mm in cats is normal. Measurements over these values should be recorded in the appropriate location on the dental chart.

Gingival Recession:
Gingival recession is also measured with the periodontal probe. It is the distance from the cemento-enamel junction(CEJ) to the margin of the free gingiva. At sites with gingival recession, the probe depth may be normal despite the loss of alveolar bone. Areas of gingival recession should be noted on the dental chart.

Furcation Index (FI):
The furcation index (FI) measures the loss of bone support in multi-rooted teeth. A periodontal probe is placed perpendicular to the long axis of the tooth and slid along the free marginal groove to the furcation site. The following criteria are used to assign a numerical score.

0 - no loss of bone support
1 - horizontal loss of supporting tissues not exceeding one-third of the width of the tooth
2 - horizontal loss of supporting tissues exceeding one-third of the width of the tooth but no encompassing the total width of the furcation area.
3 - horizontal loss of supporting tissue allowing for through and through exposure

A furcation index of 1-3 should be noted on the dental chart.

Mobility Index (MI):
The mobility index (MI) measures the loss of bone support by indicating the amount of movement of the tooth. The length of the periodontal probe is placed on the buccal surface of the crown of the tooth, and gentle pressure is applied to the tooth. The following criteria are used to assign a numerical score.

0 - no mobility

1 - perceptible mobility but less than 1 mm buccolingually
2 - definite mobility between 1-2 mm
3 - gross mobility exceeding 2 mm buccolingually and/or vertical mobility
A mobility index of 1-3 should be noted on the dental chart.

Periodontal Attachment Level (PAL):
In the PAL, the pocket depth is measured from the base or apex of the pocket to the cemento-enamel junction. PAL is a more accurate assessment of tissue loss in periodontitis. PAL can be directly measured, or it can be calculated as the sum of PD plus gingival recession.

Probe Depth (aka – pocket depth) is an essential part of charting. This loss of attachment is created by the progression of periodontal disease and, therefore, a vital piece of information. The normal healthy mouth has a probe depth of 1-3 mm in dogs and 1 mm or less in cats. Any probe depth greater than this should be recorded on the chart. The probe should be walked around all sides of the tooth to ensure all pockets are recorded.

Stage of Periodontal Disease:
The stages of periodontal disease can be used to help price and schedule periodontal therapies but also need to be recorded so that the progression of the disease can be determined. These stages are determined by either measuring clinical attachment level or radiographically.

- Stage 1 -Gingivitis only with attachment loss.
- Stage 2 - Less than 25% attachment loss. Grade 1 furcations present.
- Stage 3 - 25 to 50% attachment loss. Grade 2 furcations present
- Stage 4 - Over 50 % attachment loss. Grade 3 furcations present.

Oral masses need to drawn onto the chart and noted. This includes epuli and gingival hyperplasia. This is important to note these to have a record of the mass and be able to observe changes in future examinations as well as gingivectomies or the removal of excess gingival tissues.

Supernumerary Teeth:
Supernumerary or “extra” teeth are common in cats and may result in crowding and misalignment of the teeth. The mandibular fourth premolars are the most common supernumerary tooth observed in cats. Supernumerary teeth that cause crowding should be extracted with oral surgery early.

Gemination:
Gemination has been observed in both deciduous and permanent teeth. It is an attempt to merge two teeth. This results in a tooth with two completely or incompletely separated crowns, each with a single pulp chamber and a shared root canal. Etiology is unknown, but trauma could be one cause, although a genetic tendency has been observed. It can be challenging to differentiate between supernumerary and germination without dental x-rays.

Stomatitis
Gingivostomatitis is a chronic, painful condition that can be very difficult to diagnose and treat. Multiple tests are needed to rule out other problems. Make sure the animal is FeLV/FIV negative; you may want to consider Calicivirus testing. Most treatments are ineffective; to date, the best treatment is a complete dental extraction surgery, including the removal of all dentin. This treatment is usually effective in about 80% of the cases.

Juvenile Hyperplastic Gingivitis:
Juvenile hyperplastic gingivitis occurs between 6 to 8 months of age after the permanent teeth have erupted. This condition is common in Persian and Abyssinian cats, but it can happen in any breed. The gingiva is severely inflamed with overgrowth of gingiva onto the crowns of the premolars and molars. This overgrowth can result in pseudopockets. Treatment involves cleaning of the teeth every 3-6 months and a gingivectomy of hyperplastic gingival tissue.

Juvenile Onset Periodontitis:
Juvenile onset periodontitis occurs before the age of 9 months of age. Siamese, Maine Coon, and DSH cats are predisposed. A typical presentation is a malodor at the time of permanent tooth eruption. An oral examination reveals marked inflammation at the gingival margin and can extend in the attached gingiva.

Tooth Resorption:
Tooth Resorption (TR) can be challenging to classify. The five stages of TR’s that are determined by the amount of crown involved in the lesion.

- Stage 1- Lesions extend only into the cementum. This stage occurs only subgingivally. – Very difficult to detect

- Stage 2 - Lesions progress through the cementum into the dentin of the root or crown, but the pulp is not exposed. Hyperplastic gingiva may cover these defects.
- Stage 3 - Lesions progress into the pulp chamber. Bleeding on probing and spontaneous fractures of the crown may occur.
- Stage 4 - Lesions destroy a significant amount of the crown.
- Stage 5 - Lesions have significant root replacement resorption with the healing of the gingiva. There will not be any clinically apparent tooth tissue.

In addition to the stages of TR's, they can be classified based on the radiographic appearance of the periodontal ligament space:

- Type 1 - Lesions are caused by inflammation. The root appears normal, and the periodontal ligament space is still observable.
- Type 2 - The affected tooth is ankylosed to the alveolus. This type of lesion is not associated with periodontal disease
- Type 3 - The affected tooth has one root with type 1 TR and one root with Type 2 TR.

Chronic Alveolar Osteitis:
This condition is commonly associated with the maxillary canines of cats. It produces a pronounced bulging appearance of the osseous tissue at the upper canines. Suspicious tissue should be biopsied, but in most cases, this condition is the result of chronic inflammation. Periodontal pockets may be present, and the teeth should be treated appropriately. There may be sufficient inflammation and loss of attachment to warrant extraction.

Super Eruption or Canine Extrusion:
In conjunction with chronic alveolar osteitis or alone, cats can have a unique response where the maxillary canine teeth appear to extrude. The teeth appear longer than normal and have an increased amount of gingival extrusion. The extruded teeth may also cause trauma to the lower lip. If the tooth is not mobile, does not have periodontal pockets or radiographic signs of excessive bone loss, they can be saved. It may be necessary to blunt the tips of these canines to minimize lip trauma.

Discolored Teeth:
Discolored teeth should be thoroughly evaluated to determine if the discoloration is due to extrinsic or intrinsic staining. Extrinsic staining comes from accumulations on the surface. Intrinsic stains are secondary to endogenous factors that discolor the underlying dentin. Transillumination with a fiberoptic light can assist in distinguishing between vital and necrotic pulp. Radiographs of affected teeth can be very useful in identifying pathology associated with discolored teeth.

Fractured Teeth:
In cats, the pulp chamber extends to just under the crown tip compared to an adult dog, which usually has several millimeters of protective dentin under the enamel. When trauma occurs, and the pulp chamber is opened, bacteria often enter the chamber, infecting the pulp. This infection may lead to the periodontal ligament, periapical tissues, and alveolar bone.

Cats rarely show obvious signs of endodontic disease. Occasionally there may be a draining tract either ventral to the orbital rim or under the chin. Some cases of chronic rhinitis are secondary to long-standing fractured teeth. Dental x-rays can help detect pulpal or periapical pathology.

Oral Tumors and Swellings:
Swelling and growths of the oral cavity can be common. Etiologies of oral masses range from cyst, infection, and inflammation to benign and malignant tumors.

Eosinophilic ulcers most commonly affect the upper lip at the philtrum but may occur anywhere in the oral cavity. Ulcers on the upper lip usually have a carved out appearance with a yellow center. Clinically these lesions can be mistaken for neoplasia. This lesion can be caused by underlying diseases such as allergies to foods or fleas. Diagnosis requires a deep incisional biopsy. These eosinophilic ulcers can also occur on the tongue.

Squamous Cell Carcinoma occurs primarily on the gingival tissue or the tongue. Rarely it can occur on the palate, pharynx, or the tonsils. The median age for oral SCC is 11 to 13 years of age; however, affected cats as young as three months to as old as 21 years have been reported. The most common finding is facial swelling or asymmetry noted by the owner or veterinarian during the examination. Other signs can be excessive salivation, anorexia, weight loss, and malodor. A hard mass will usually be noted on the maxilla or mandible. The tumor can affect the tongue

ventrally near the frenulum, which often appears thickened or ulcerations. If the mass occurs on the gingiva, there may be increased mobility of the adjacent teeth due to the loss of bone structure.

Fibrosarcoma is the second most common tumor in the cat. Even though this is the second most common tumor is occurs very rarely. FSA usually affects cats 13 years or older; however, cats ranging in age from 1 to 21 years of age can be affected. Lesions are typically located rostrally on the gingiva. Presenting signs are similar to those of SCC.

Oral Trauma:
Maxillary and mandibular fractures can occur secondary to trauma. Temporomandibular Joint Dislocation may present as a dropped jaw. The dislocation can be either unilaterally or bilateral.

References

1. Bellows, J., Feline Dentistry: Oral Assessment, Treatment and Preventative Care, Wiley-Blackwell, 2010
2. Logan, EI, Boyce EN: Oral Health Assessment in Dogs: Parameters and Methods. *J. Vet Dent* 11(2): 58-63.
3. Harvey, CE, Emily, PP: Periodontal Disease. In Harvey, CE, Emily, PP: *Small Animal Dentistry*. St. Louis: Mosby, 1993
4. Logan, EI, Finney, O, Hefferren, JJ: Effects of a Dental Food on Plaque Accumulations and Gingival Health in Dogs. J Vet Dent 19(1), 15-18.
5. Holmstrom, SE: *Veterinary Dentistry for the Technician and Office Staff.* W.B. Saunders Company, 2000
   Gorrel, C: *Veterinary Dentistry for the General Practitioner.* Saunders, 2004
6. Lobprise, H: Clinical Companion, Five Minute Consult - Small Animal Dentistry, Blackwell, 2007.

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Feline Head Trauma

Alison Gottlieb, BS, CVT, VTS(ECC)

Feline head trauma is often associated with; high rise syndrome, vehicular trauma, predators and humans. These cats need to be treated as polytrauma when presenting at the clinic. Most of the time we do not have the luxury of knowing what kind of trauma our patients have suffered, therefore we must assess all systems simultaneously and immediately. The respiratory pattern and rate should be noted, as well as panting. Any panting in a cat is not normal. Airway can be affected by any trauma; it is very important to assess where the respiratory problem originates before continuing. Oxygen supplementation via mask should be supplied while other systems are checked; oxygen never hurts, unless the mask itself stresses the patient. For cats that are stressed oxygen should be provided via oxygen cage. Auscultation should be quickly performed (if possible) before placing in O2. Listen to lung sounds of all four quadrants, if they sound muffled (along with shallow respiration) pleural space occupancy should be considered. If the patient is stable a thoracic radiograph can be taken, however this is not usually the scenario and thoracocentesis to alleviate a potential pneumo or hemo thorax should be performed without a radiograph.

A quick assessment of the cardiovascular system includes: heart rate, MM color, CRT, pulse quality and rhythm. If temperature is attainable take it; if not (due to stress) assume the cat is hypothermic and consider heat. Shock should be assumed, pale MM, prolonged CRT, weak/thready pulses and bradycardia. Yes, bradycardia rather than tachycardia is common in a shocky cat, however tachycardia does not rule out shock.

Hemorrhage tends to be a more severe problem for cats, simply because they have less of it to lose, as well as the lack of ability to contract their spleen. This may be evident upon presentation, or because of severe hypotension may not be observed until after IV fluids have been administered. Pressure should be applied to any actively bleeding vessels.

Neurological status is extremely important when dealing with trauma and will usually dictate treatment. Level of conscious, motor activity, pain response, pupil size and reactivity all provide important information as to neurologic function. If any improvement of neurologic function is seen within 48 hours the prognosis is considerably better. Also in reverse if no improvement or worse neurologic function in 48 hours the prognosis is poor.

Traumatic brain injury is traditionally broken down into primary and secondary categories. Primary brain injury is the result of the trauma itself (bleeding bruising of tissue in the brain) while secondary brain injury comes after the original insult. This is due to inflammation, reactive neurotransmitters and changes in cell membranes. The secondary component is where we come in.

Secondary treatments are based upon optimizing cerebral perfusion pressure (CPP), which increases oxygen delivery which decreases ischemia of brain tissue due to hypoxia. CPP is based on Mean arterial pressure (MAP) – Intracranial pressure (ICP). Therefore, it is imperative the ICP is not equal to or higher than MAP, otherwise CPP drops below 0. MAP is increased to normal values through traditional fluid shock doses, using hypertonic saline can assist in this as well. If pressure continues to increase the cushings reflex may be observed. In this case the MAP increases as a response to low CPP followed by a reflexive bradycardia. This manifests as severe hypertension with bradycardia. This drives our treatment towards decreasing intracranial pressure in general. Placing cats on a board or bedding at a 30° angle will help gravity facilitate cerebral drainage. Avoiding jugular occlusion for venipuncture or catheter placement also aids in not obstructing drainage. The Glasgow coma scale (below) may help predict outcomes as well as alert to important changes. This should be evaluated every 4 to 6 hours.

Recumbent patient care in general should be employed. Well padded, turning frequently (prevention of decubital ulcers and atelectasis) eye care/lube, range of motion exercise, oral care and urinary care via a catheter. Blood pressure is monitored to alert to changes in ICP. EKG will also help alert to cushings reflex response. Body temperature needs to be watched as and often supplemented. Cats with head trauma often can not control their temperature.

Nutrition tends to be the hardest thing to address in the feline trauma patient. Head trauma or any type of oral trauma a feeding tube must be placed. Appetite stimulants, a quiet box, catnip, and sometimes sitting and talking to them when you offer food can all be helpful for getting these patients eating. Make sure pain is being adequately managed; this tends to be a frequent cause of anorexia. Force feeding is highly discouraged, this often leads to increased stress and food aversion, neither helpful when treating the feline patient. Aside from the fact that they tend

to be finicky eaters, hepatic lipidosis is a very real secondary problem to feline illness and must be addressed. If the patient is not eating after 24 hours of hospitalization a feeding tube should be considered.

Additional interventions include pharmaceuticals. Cyproheptadine (2-4 mg per cat PO; SID or BID) can be given 30 minutes before food is offered. This is an antihistamine which has a side effect of an increased appetite. Diazepam (0.05-0.4 mg/kg IV, IM or PO) works like magic when used as a feline appetite stimulant. When given IV, will cause a cat to lunge forward into a bowl of food. Onset is rapid and the effects are short term, so be prepared with several varieties of food available as soon as injection is given. Mirtazapine (remeron) is a human antidepressant which has proven to show profound increase in appetite in cats. They are usually made in 15mg tabs and cat doses were ¼ tab (3.75mg) per cat every three days. The results of this dose produced increased mania (presumably due to serotonin) and an increased appetite for 1-2 days. The recommended dose has since been amended to 1.8mg/cat EOD. This dose has resulted in less mania and more reliable and consistent appetite stimulation. Cats are also susceptible to developing food aversion. This occurs when food is left in the cage for extended periods of time with a sick anorexic cat. Think about it if you were not feeling well would you want to sit next to an old cold veggi-burger. Force feeding is not recommended for this reason as well as the threat of aspiration and undo stress.

If none of these treatments stimulate the patients appetite it is time to place a tube. What type of tube depends on the disease process and the clinician. This procedure is done to administer short-term nutritional support to a patient when they are not eating enough nutrition to meet its daily caloric needs. There are two forms of feeding tubes that can be placed which allow the patient to continue to eat and drink. The types are; nasoesophageal (NE) tube and nasogastric (NG) tube. These tubes can be kept in place from several days to weeks; however, they are contradicted in patients predisposed to aspiration, esophageal dysfunction and patients that are actively vomiting. They are also contradicted in patients that have injuries to the head and neck or surgical procedures of the nasal cavity, pharynx or esophagus. Surgery is required for all other enteral support routes. These procedures include pharyngostomy tubes, esophagostomy tubes, gastrostomy tubes and enterotomy tubes.

Esophagostomy tubes are placed when head trauma is present. They bypass the head and usually do not require the patient to wear an e-collar. The tube is inserted directly into the cranial esophagus and advanced to the end of the esophagus and capped. Sutures are then placed, and the neck is wrapped with a bandage. Gastrotomy tubes are inserted directly into the stomach and are indicated when esophageal injury or disease is present. A French Pezzar mushroom-tip catheter should be used, which keeps the tube in the stomach and helps to create a seal. These tubes can be placed two ways; via laparotomy or percutaneous placement using an endoscope. These too need to be capped, sutured, and wrapped.

Modified Glasgow Coma Scale	
	Score
Motor activity	
Normal gait, normal spinal reflexes	6
Hemiparesis, tetraparesis, or decerebrate rigidity	5
Recumbent, intermittent extensor rigidity	4
Recumbent, constant extensor rigidity	3
Recumbent, constant extensor rigidity with opisthotonus	2
Recumbent, hypotonia of muscles, depressed or absent spinal reflexes	1
Brainstem reflexes	
Normal PLR and oculocephalic reflexes	6
Slow PLR and normal to reduced oculocephalic reflexes	5
Bilateral unresponsive miosis with normal to reduced oculocephalic reflexes	4
Pinpoint pupils with reduced to absent oculocephalic reflexes	3
Unilateral, unresponsive mydriasis with reduced to absent oculocephalic reflexes	2
Bilateral, unresponsive mydriasis with reduced to absent oculocephalic reflexes	1
Level of consciousness	
Occasional periods of alertness and responsive to environment	6
Depression or delirium, capable of responding, but response may be inappropriate	5
Semicomatose, responsive to visual stimuli	4
Semicomatose, responsive to auditory stimuli	3
Semicomatose, responsive only to repeated noxious stimuli	2
Comatose, unresponsive to repeated noxious stimuli	1
MCGS Score	**Score**
3-8	**Grave**
9-14	**Guarded**
15-18	**Good**

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Feline Respiratory Patients: A Delicate Balance

Alison Gottlieb, BS, CVT, VTS(ECC)

The dyspneic feline is one of the most difficult emergencies to treat. The basis of any treatment is to quickly identify the underlying problem, treat, supply oxygen and all without increasing stress levels which will fuel dyspnea and ultimately lead to respiratory arrest. Getting a complete and detailed history from the owner is one way to gather information without stressing the patient. Other than trauma the most common feline respiratory emergencies include cardiac (or cardiac related) disease, neoplasia and asthma. Though they all present in respiratory distress the treatment is quite different. Our desire to be hands on must be kept in check. Often removing the patient from the carrier, supplying flow-by oxygen, and placing an IV catheter or obtaining radiographs or Spo2 will significantly increase stress and lead to staff members getting injured and respiratory arrest. Placing flow-by oxygen with the least amount of stress will often help and can be done while patient is still in their carrier. Simultaneous observation of respiratory pattern and obtaining history is much safer than obtaining diagnostics. Any dyspneic animal needs the same considerations; supply oxygen and reduce stress. With cats this consists of a hands-off approach, any diagnostics will cause an increase in stress and should be avoided. Oxygen can be supplied several ways; however, the focus should be kept on limiting stress. An oxygen cage with circulating temperature control is optimal. The cat can be easily observed and receive oxygen without being restrained. Other options include a cage which can be adapted with a plexiglass door with an opening for oxygen. Heat tends to build up with no escape, and they can be time consuming to adapt. Several incubator type devices are also available which do allow for some gas exchange and temperature relief. As animals ventilate carbon dioxide (CO_2) is released into the environment. If a cat is in an enclosed area the CO_2 levels will increase leading to acid-based disturbances which can further compromise respiration. Other ways of supplying oxygen tend to stress the dyspneic cat. These include using a mask (with the rubber gasket removed) or by holding a tube from 100% oxygen supply in front of the cat. If either of these cause stress to the patient discontinue immediately. Always be prepared to sedate, intubate and ventilate this patient if previous interventions do not improve patient condition.

Differentiating between origins and providing treatment can be done without radiographs. History, respiratory pattern, and auscultation should provide adequate information to proceed. If it is not sedation and/or thoracocentesis need to be considered immediately. Having a kit ready at all times is very helpful in providing this treatment in the most efficient way possible. Simply having a bag with supplies (three way stop-cock, two extension sets, butterfly or IV catheters, various syringes and tubes for samples) available in your crash cart is an easy way to facilitate this. If effusion is suspected the only way to improve respiratory compromise is thoracocentesis. Oxygen supplementation will not be significantly beneficial if lung space is compromised by effusion. Clip and prep the area ventrally between 7th and 9th cranial rib on right side. Patient respiratory rate and effort will immediately improve. Effusion should be measured and analyzed; oxygen therapy continued, and once patient is stable diagnostics may begin. Often Furosemide (Lasix 2mg/kg IV or IM) a loop diuretic, is given to decrease pre-load on the heart as well as to eliminate any pulmonary edema that may be present. Lasix alone will not get rid of large amounts of effusion and should be given along with physical removal of effusion.

Secondarily, these cats can develop acid base disturbances. A venous or arterial blood gas is an easy way to monitor the acid base status. Blood gas analysis provides information about pulmonary function and acid-base status. These results are essential for diagnosis and treatment of patients with either respiratory or metabolic abnormalities. Acid-base status can be evaluated on arterial (ABG) or venous(VBG) samples, however for oxygenation evaluation an arterial sample is the only one appropriate. Feline patients are not fond of arterial blood sampling, and stress is not our friend. Venous blood gasses will provide important information without oxygen. Four key pieces of information are provided from the ABG; Oxygen (PaO_2), carbon dioxide ($PaCO_2$), blood pH and bicarbonate (HCO_3). Being aware of normal values is an integral part of blood gas analysis.

Normal values:

pH- 7.35-7.45
- <7.35 – acidosis
- >7.45 – alkalosis

PaO_2- >90 mmHg
- 75-89mmHg – mild hypoxia
- <75mmHg – severe hypoxia

$PaCO_2$-30-40 mmHg
- <30 mmHg – alkalosis
- >40 mmHg – acidosis

HCO_3- 18-24 mEq/L

<18 mEq/L – acidosis
>24 mEq/L – alkalosis

Blood pH provides information about the patient's acid-based status. Any significant variation in the blood pH can compromise essential body functions including; electrolyte imbalance, enzyme activity, and basic cellular function. The pH remains stable by balancing acid and base. The acid is represented by carbon dioxide (PaCO2) and the base is bicarbonate (HCO3). If the HCO3 is the liable factor for the change in pH the condition is potentially metabolic and if PaCO2 is the determining factor the condition may be respiratory. This information in conjunction with the history, clinical signs and other measured parameters will help provide a course for treatment.

PaCO2 measures the partial pressure of carbon dioxide in the arterial blood, which indicates the effectiveness of ventilation. Respiratory rate determines PaCO2 and as it increases (hyperventilation) CO2 decreases (hypocapnea), as the respiratory rate decreases, CO2 increases (hypercapnea). Respiratory rate changes occur in patients with primary pulmonary disease or central nervous system (CNS) impairment. Respiratory rate changes may also occur as a response to a metabolic disorder causing an abnormal pH. Respiratory compensation occurs when the body attempts to correct an acidosis or alkalosis by altering respiration to either increase or decrease the level of CO2. For example, a decrease in the blood pH and HCO3 indicate a primary metabolic acidosis, in response the respiratory rate would increase to decrease the CO2 and therefore attempt to self-correct the imbalance.

PaO2 is a measurement of the partial pressure exerted by oxygen in arterial blood. This reflects the body's ability to pick up oxygen from the lungs. A low PaO2 represents hypoxemia and can initiate hyperventilation. The SaO2 (pulse ox) measures the percentage of hemoglobin actually carrying oxygen, this is why 95-100% is normal. These two values are crucial to adjust oxygen concentration during mechanical ventilation.

Serum bicarbonate levels provide information about the metabolic aspect of acid-base balance. HCO3 is controlled by renal retention and excretion, this can be accurately measured in either venous or arterial samples. An increase in HCO3 results in a metabolic alkalosis, while an abnormally low HCO3 results in a primary metabolic acidosis. Primary metabolic acid-base disorders are predominantly corrected by treating the underlying disease. The kidneys respond to respiratory acid-base disturbances by retaining and excreting excessive amounts of HCO3. This compensatory response is much slower than respiratory changes.

Primarily respiratory alkalosis which may be followed by a compensatory metabolic acidosis is commonly seen if respiratory rate is increased resulting in low CO2. If gas exchange is affected an arterial sample will result in a low PaO2 often with increased CO2 which demonstrates the decreased exchange. These patients need sedation and mechanical ventilation or sedation and euthanasia. Sedating and intubating must happen immediately, even if mechanical ventilation is not available at your facility.

Respiratory distress quickly progresses to respiratory arrest in cats. The addition of stress can escalate symptoms quickly. Each step should be taken slowly, and great care taken to beware of the cats response. That one last piece of tape can make all the difference.

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Cyberbullying & the Veterinary Profession
Phil Padrid, DVM

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Every Practice's Struggle: How to Attract, Retain, & Motivate Your Veterinary Talent

Taylor Tillery, DVM

Introduction
Small Business owners were asked what their top challenge was in 2019. The #1 challenge of these business owners was hiring qualified/ good staff and retaining them.[2] This much mirrors a common theme often repeated in the veterinary space around veterinary employers of all sizes; challenges with attracting, retaining and motivating veterinary talent.

Research Parameters:
A Merck Sponsored double blinded study was completed by MarketVision Research from Dec 13th -31st, 2018. The double-blinded, randomized survey analyzed responses of 250 US veterinarians of whom had been in practice at least 2 years and were not more than 2 years away from retiring. The Objective was to understand how veterinary practices can better attract, hire, train and retain high performing veterinarians in a rapidly evolving market.

Insights:
Retaining highly trained and valued associate vets is a significant and growing challenge for veterinary practices in the US. 55% of US practices have had a valued associate vet leave in the past 3 years. Compared to 10 years ago, associate vets are more likely to be looking for new opportunities. This study found one out of four veterinarians actively looking for a new position outside of their current practice. Associates are leaving for a multitude of reasons that include; better opportunities for career growth, more accommodating or flexible schedules, management challenges, or opportunities for better compensation.

Associate Retention Opportunities:
Some potential opportunities to improve upon for veterinary practices looking to boost their retention of valued associates were associated with respondents: feeling overworked, stressed, under paid and under-appreciated.

Desired vs Current Veterinary Salaries
In our Study 51% of associates veterinarians believe they should make a salary of $115 or higher, but only 24% earned this salary or greater. The Merck Animal Health Veterinarian Wellbeing Study II found that the main reasons for veterinarians not recommending their profession was due to high student debt, increased stress and low incomes.[4] The study also found that male veterinarians reported earning higher salaries than their female counterparts. This identified a potential lack of wage equality and that opportunities remain for adjustment of female salaries to be at parody of their male colleagues. For responses to be included in this study veterinarians had to be out in practice for at least 2 years. It is important to thus note that according to AVMA data 2018 grads that were companion exclusive had an average starting salary of $86,982.[1]

Veterinary Associate Joy:
A previous Merck sponsored Wellbeing Study had illustrated that only 41% of veterinarians would recommend the Veterinary Profession to a friend or stranger which is far below many other professional careers.[2] In an effort to better understand what veterinarians enjoy most about their job, the ARM survey had them to rank the BEST aspect of being a vet. The top responses included caring for animals, building relationships with pet owners, variety in their work opportunities, making pet owners happy, and a reduction in administrative work.

ARM (Attract, Retain, Motivate) Opportunities:
Focusing further on some of the key issues reported from US veterinarians from the survey allowed for the mapping of possible solutions to retain veterinary talent. The top 6 recommended staffing solutions to attract, retain or motivate that were:

1. Consider offering more flexible hours or working schedules.
2. Explore opportunities to help associate vets pay or minimize their student debt.
3. Establish clear opportunities for career progression and growth of associate vets.
4. Tie pay raises and/or bonus opportunities to practice and/or output goals.
5. Develop a formalized 360º Feedback/ Review process for all staff.
6. Support opportunities for training and professional growth.

Most associates reported that these retention methods were not being implemented by their current or past employers over the previous 3-years. In addition, those considering or recently having accepted a new position would most likely have remained with their prior employer if these recommendations had been part of the clinic culture.

Merck Animal Health remains committed to the Veterinarian and their importance in the veterinary industry. We continue to pursue a deeper understanding via science and data of some of the largest challenges of our profession and to work with industry partners and organizations to help provide solutions to ensure the future health and success of the Veterinary Profession.

References

1. Employment, Starting Salaries, and educational indebtedness of year 2018 graduates of US veterinary medical colleges; Bain, B Salois, M JAVMA Vol 254/# 9
2. https://wellsfargoworks.com/insights/press-release/small-business-optimism-declines-amid-decreased-revenues 8/10/2020
3. Volk JO, Hartmann G. How wellness plans grow veterinary practice. J Am Vet Med Assoc. 2015;247(1):40-41. doi:10.2460/javma.247.1.40
4. Volk JO, Schimmack U, Strand EB, Vasconcelos J, Siren CW. Executive summary of the Merck Animal Health Veterinarian Wellbeing Study II. J Am Vet Med Assoc. 2020;256(11):1237-1244. doi:10.2460/javma.256.11.1237

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A Transformational Nutritional Approach to Managing Cat Allergen Fel d1
Ebenezer Satyaraj, PhD

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Regenerative Medicine & the Feline Patient

Robert Harman, DVM, MPVM

Introduction

You may be familiar with Stem Cell Therapy (SCT) as something that is used widely in canine and equine patients to treat orthopedic and internal medicine diseases. In feline medicine, the most published stem cell therapies are in chronic kidney disease, gingival stomatitis, and inflammatory bowel disease. A recent review article highlights these therapies[1]. Osteoarthritis (OA) is very common in older cats, but perhaps not diagnosed or recognized nearly as often as in canines. In a survey of the incidence of OA, 90% of cats 12 years of age or older had radiographic evidence of OA[2]. In the author's registry, 13% of the clinical feline patients were treated for osteoarthritis.

VetStem Biopharma (VSB) is a veterinary cell therapy company. It has provided cell processing, storage and cell doses for therapy in 31 species of domestic and exotic animals since 2002 with total treatments of greater than 17,000. VSB has also conducted pilot and formal FDA randomized clinical studies and has over 15 peer-reviewed published studies and book chapters dedicated to cellular therapy. This retrospective is intended to review literature and the VSB clinical patient registry data on the use of stem cell therapy in domestic and exotic felines.

What is Stem Cell Therapy?

Stem cell therapy is a subset of the broad category of regenerative medicine. There are a variety of sources and types of stem cells. This article will focus only on adult stem cells and not embryonic stem cells. In the literature, you will find considerable debate about definitions, but broadly, adult stem cells are cells that respond to local environmental cues (e.g. inflammation, ischemia) and then act in one or more manners to reduce inflammation and pain, reduce degeneration, or manage/stimulate repair of tissues and organs. These stem cells are released from their storage sites and are activated by injury signals, taking their "instructions" from cells and cytokines at the injury site. This means the stem cells can provide "injury-specific" or "adaptive" response in many different tissue sites, making them unique in the realm of therapies. Most often these adult stem cells are called mesenchymal stem cells (MSCs) as initially these cells were found in bone marrow, adipose, and other mesenchymal tissues. In order to best understand how to utilize stem cell therapy, we will briefly review the following mechanisms of action:

- Cell/Tissue Regeneration
- Anti-inflammatory
- Immunomodulatory
- Pain Block

Cell/Tissue Regeneration

The MSC has been shown to impact cellular regeneration by at least three different mechanisms: (1) direct differentiation; (2) growth factor stimulation of local progenitor cells; (3) growth factor stimulation of angiogenesis. Researchers in osteoarthritis therapy have published on the impacts of stem cell therapy in the regeneration of cartilage. Serious full-thickness cartilage lesions have been healed with hyaline cartilage in rigorous rabbit models of stifle injury [3]. Similarly, it has been shown that adipose stem cells have the ability to be chondroprotective as demonstrated in the rabbit cruciate ligament injury induced OA study [4]. In a human dose-escalation study of adipose stem cell effects on cartilage regeneration, histology demonstrated significant hyaline-like cartilage regeneration and patients had improved knee function at 6 months after injection[5]. In liver fibrosis, stem cells have been shown to stimulate mitosis of the remaining normal hepatocytes but also to block and resolve fibrosis. In a recent presentation at the American Association of Zoologic Veterinarians (2019), Dr. Matt Kinney presented a case series of adipose stem cell treatments for acute on chronic liver fibrosis in Cheetahs demonstrating significant prolongation of quality of life by intravenous administration of adipose stem cells. This was based upon considerable preclinical research showing blockade of fibrosis and stimulation of hepatic regeneration[6, 7].

Blood flow is required for adequate healing of tissue damage and lack of blood leads to chronic non- healing wounds. MSCs have been shown to produce angiogenic factors such as vascular endothelial growth factor (VEGF) and insulin-like growth factor (IGF-1) that recruit endothelial lineage cell types and induce

vascularization[8]. In a canine study of oral ulcers, ASCs stimulated vasculogenesis and improved healing rates compared to controls or dexamethasone treated ulcers[9].

Anti-inflammatory Mechanisms

Inflammatory conditions such as osteoarthritis (OA), gingivostomatitis, IBD and many others dominate our clinical case load. Chronic inflammation underlies many dermatology conditions and is central to formation of scar tissue. The chronic inflammation in OA causes pain and reduction in joint function, which impairs the quality of life for the patient. MSCs have anti-inflammatory functions and capabilities that may assist in turning a degenerative joint into a regenerative joint. MSCs have been shown to respond to triggers such as interlukin-1ß (IL-1ß) and tumor necrosis factor-alpha (TNF-α) by producing anti- inflammatory compounds such as IL-1 receptor antagonist protein (IRAP), hepatocyte growth factor (HGF), and transforming growth factor-beta (TGF-β)[10, 11]. These anti-inflammatory cytokines are a powerful balance to inflammation in the joint and other locations in the body.

Immunomodulatory Mechanisms

In a practical sense, MSCs have the ability to shift a patient from a TH1 (inflammatory) phenotype to a TH2 (anti-inflammatory) phenotype with a reduction in TNF-α and interferon-gamma (INF-γ) [12]. These strong immunomodulatory capabilities are being harnessed to treat a number of veterinary immune- mediated diseases such as feline gingivostomatitis [13], dry eye [14], and inflammatory bowel disease [15]. Immune-mediated arthritis and multiple sclerosis have been effectively treated with intravenous stem cell therapy[16-18].

Pain Block Mechanisms

Pharmacological interventions in veterinary pain management have been mainly palliative. Although they temporarily relieve pain, they do not address the core underlying mechanisms causing the pain. Neurotropic factors are critical in the development and survival of neurons and they participate in the regeneration and repair of nerves [19, 20]. MSCs have been shown to produce an array of cytokines and growth factors, including many neurotropic factors[21].

In published studies regarding the use of ASCs in the treatment of OA in the canine, pain measures such as pain on joint manipulation, visual analogue scores of lameness, or gait analysis have been substantially improved [22-26]. In a recent publication of a large-scale randomized clinical trial on the effect of allogeneic (donor) ASCs in OA, pain on manipulation was also improved [27]. In a large (1,128 patients) case-control human study of adipose SVF injection for OA, 63% showed at least a 75% improvement in pain score at 12 months after injection with no serious side effects[28].

Neuropathic pain may come from physical (impingement, trauma, burn), chemical, or biologic direct damage to nerves. Intravenous stem cell therapy has been shown effective in reducing pain for extended periods of time in animal models and in the clinic [29-32]. A recent review of stem cell therapy in veterinary pain management covers this topic [33].

Sources of Stem Cells

Mesenchymal stem cells are a class of adult stem cells arising from tissues including adipose, bone marrow, and many others. MSCs can be sourced from most tissues with blood vessels, but adipose appears to be a superior source [34, 35], and it is the most commonly used source in veterinary medicine. As stated by the authors of the 2018 feline review article above, “currently, adipose-derived MSCs (mesenchymal stem cells) are most commonly used in clinical applications due to ease of attainment and their superior proliferative ability[1].”

How Are Stem Cells Used Clinically?

Typically, stem cell therapy is applied via local tissue injection at the site of injury or disease or via a vascular route. Targeted delivery to the CNS can be done via intrathecal injection. Intravenous administration is most commonly used for systemic diseases and particularly in immune-mediated diseases where access to the immune system is needed. Stem cells are applied clinically to: (1) improve quality of life (reduce pain and disability); (2) reduce progression of degeneration; and (3) repair/regenerate damaged tissues and organs. Cells used therapeutically today, unless inside of an FDA clinical trial, must be autologous (from the patient). Generally, tissue is extracted, and cells are isolated from the tissue for use in the same patient. In the case of adipose tissue, there are published reported uses of either use non-cultured stromal vascular fraction (SVF) cells or culture expanded cells. SVF cells can be used freshly or after thawing from cryobanking. The SVF contains adipose stromal cells (ASC) as well as

pericytes, endothelial cells and cells of hematopoietic lineage. It is critical to do any cell isolation according to FDA guidance or utilize a company that is FDA compliant.

Many degenerative and chronic diseases require multiple doses over the lifetime of the patient. As such, it is wise to cryobank part of the initial cells for use in the future.

Domestic and Exotic Feline Use

Overview

Based on the VSB clinical therapy patient registry and the peer-reviewed literature[1], the most prevalent stem cell therapy targets in feline medicine are generally the following:

- Chronic kidney disease
- Osteoarthritis
- Gingivostomatitis
- Inflammatory bowel disease

There are no peer-reviewed publications on stem cell use in OA in cats. However, there are over 100 canine studies including blinded, controlled studies that practitioners can use for guidance. In addition, there are a large number of human OA studies using stem cells. At VetStem Biopharma, SVF and ASC therapeutic cells have been provided to practitioners for over 30 feline cases where OA was the primary complaint. These are prospective cases and not controlled clinical trials. The mechanisms of action and pathophysiology of the OA and orthopedic soft tissue disease are quite similar between mammalian species.

For reference, VetStem has provided therapeutic stem cells (SVF, ASC) to practitioners to treat the following conditions in domestic cats (Table 1) and for use in exotic cats (Table 2):

Table 1. Feline conditions treated with adipose stem cell therapy from VetStem

Disease or Condition	#	% of
Chronic kidney disease	16	64%
Osteoarthritis	33	13%
Gingivostomatitis	30	12%
Inflammatory bowel	12	5%
Neurologic conditions	6	2%
Autoimmune conditions	5	2%
Other (liver, granuloma)	7	3%
Total	**26**	

Table 2. Exotic cat adipose stem cell collection and/or therapy from VetStem

Species	Disease	# Cases
Panther	OA – Elbow, hip	2
Leopard	OA - shoulder	1
Cougar	OA - hip	1
Lion	None – storage	1
Cheetah	Liver fibrosis	2
Total		**7**

The use of stem cells in exotic species has recently been reviewed in the new Fowler's Zoo and Wild Animal Medicine book[36].

Chronic Renal Disease

Chronic kidney disease (CKD) in the feline is a major cause of debilitation and death[37]. Recent reviews suggest that CKD may be the number one cause of morbidity and mortality in the aged cat. Therapies available include medical management, dietary control, dialysis and kidney transplant[38]. For most cat owners, dialysis and kidney transplant are beyond economic and practical reach. In the last decade, refereed journal articles have been published showing the possibility of using mesenchymal stem cells as a therapeutic option. The authors hypothesized that intravenous mesenchymal stem cell therapy could improve the clinical course of CKD[39-42]. We have compiled the data from 40 clinical cases treated by veterinarians using intravenous administration of adipose-derived stem cells for CKD.

A total of 40 cats were treated and had adequate pre and post treatment data for analysis. The average age for cats was 12.2 years and the average body condition score was 3.0/5.0. The average dose was 4.92 x 10^6 nucleated cells using a Nucleocounter™ with an average number of initial doses per case of 1.8 and the average total doses of 3.3. Clinical pathology data is reported for pre-treatment, at 180 days, and at 330 days, with averages as follows: BUN: 61.9, 52.0, 60.8, Creatinine: 3.96, 3.03, 3.78. By day 180, on average, BUN improved 16.0% and creatinine improved 23.5%.

Clinical Pathology Data		
Parameter	**BUN**	**Creatinine**
Pre-Rx	61.90	3.96
180 Days	52.00	3.03
Percent Improvement	16.0%	23.5%
330 Days Follow-up	60.80	3.78

Feline CKD Case Series	
# Cases Treated	40
Average Age (yrs)	12.2
Average Dose*	4.92 x 10(6)
Initial Doses	1.8
Total Doses	3.3
*** Total nucleated cells, Nuclecounter**	

There was a trend to significant improvement in BUN and creatinine at 180 days. Improvement in these parameters was seen through an average of 330 days in a population of significantly diseased patients in which these parameters would have been expected to deteriorate. There were no reported adverse events in these treated cats. This study was not blinded. This limitation makes outcome conclusions more difficult, however the study measures indicate that the therapy may be providing clinical benefit with low risk. Additional controlled studies are planned to further evaluate the benefit of cell therapy in CKD.

Osteoarthritis

While orthopedic conditions are prevalent in the feline patient, often owners do not recognize the signs, or are unwilling to explore treatment options more than NSAIDs or pain medication. So, you may feel uncomfortable recommending SCT as an option. But what about those patients that have renal complications or owners who would prefer a more natural approach? SCT may be a great option for those patients. To date, VetStem has veterinary clients who have treated over 30 feline patients for osteoarthritis as the primary complaint. Stem cells are a reasonable treatment modality as they are anti- inflammatory, block pain, and regenerate tissue, without the level of side effects of some drugs. VetStem processed cells have also been used to treat several Exotic felines for orthopedic conditions (see table below).

Table 3. VSB Feline patient registry cases of exotic felids with osteoarthritis

Species	Disease	Number
Panther	OA – Elbow, hip	2
Leopard	OA – shoulder	1
Cougar	OA – hip	1
Total		**4**

Feline Chronic Gingivostomatitis (FCGS)

Feline chronic gingivostomatitis (FCGS) is a severe oral inflammatory disease of cats with an estimated prevalence of 0.7%–12% of the US cat population[43-45]. Clinical signs are moderate to severe oral pain and discomfort, including inappetence, reduced grooming, weight loss, and hypersalivation[45, 46]. The most common treatment is full mouth extraction with approximately 60% of cats responding. Those cats that do not respond well to the extractions can require lifelong therapy with antibiotics, corticosteroids, and pain medication (refractory FCGS)[45]. The pathogenesis of FCGS is not well understood but is proposed to be due to the host immune system responding inappropriately to chronic oral antigenic stimulation, possibly secondary to underlying oral bacterial or viral infections[47, 48]. Arzi et al. at UC Davis have conducted and published two studies on the use of adipose-derived stem cells to treat refractory FCGS in cats with full mouth extractions. The first study evaluated autologous adipose stem cells in a two-dose regime of 20 million stem cells per dose intravenously. Five of seven cats had either complete remission or substantial clinical improvement[13]. In the second study, they used allogeneic (donor) adipose stem cells and found 4/7 cats responded with three cats as non-responders[49].

VetStem has provided stem cell processing for 30 cats with FCGS. While we do not have outcome data on all of the cases, we have collected evidence from owners and veterinarians that the cats have done well after the injections. Two injections are given intravenously two weeks apart. FCGS is a frustrating disease to manage and Stem Cell therapy may be a treatment method that could have long lasting positive effects, without negative side effects or dwindling effect after repeating treatments as corticoid steroids do.

Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD) in cats is a group of idiopathic, chronic gastrointestinal disorders characterized by mucosal inflammation[50, 51]. IBD is commonly distinguished from food-responsive and antibiotic-responsive causes of enteropathy by their response to immunosuppressive therapy as opposed to dietary or antibiotic therapy alone. While the underlying cause of IBD remains unknown, accumulating evidence suggest that intestinal inflammation results from altered interaction between gut microflora and the immune system in the mucosa of the host[52, 53]. A review of the literature regarding cell-based therapy of Crohn's Disease and Ulcerative Colitis (the two most prominent of the inflammatory bowel diseases in the human) yields a vast array of animal model and human clinical trials that support the concept of cell therapy for IBD[54-59]. T cells in the gut mucosa are considered the primary effector cells and are responsible for the production of cytokines that are responsible for inflammation[53]. Mesenchymal stem cells have shown the ability to migrate to areas of inflammation, down-regulate inflammation, modulate the immune system, stimulate neoangiogenesis, and repair damaged tissues[60]. Human Phase III pivotal studies are underway in the US and other countries with very encouraging outcomes to date. The EU has now approved an adipose stem cell therapy for use in humans with Crohn's fistulas. The therapeutic value of stem cell use for IBD is theorized from the animal model and human data available in the literature and the data regarding mechanisms of action of stem cells.

IBD Case Study

Patient Name: Lovey
Breed: Himalayan
Age: 4 years
Sex: Female Spayed

Lovey was treated with a commercially available flea prevention treatment and shortly after displayed a clinical reaction. Her clinical signs were inappetence, emesis and diarrhea. She lost weight rapidly and thus was taken to the specialty center. Patient had lost a significant amount of body weight and was dehydrated. Intravenous fluids were started. The differential list of possible causes was lymphoma, IBD and foreign body. Endoscopy was performed to rule out lymphoma and to determine if IBD was the cause of the symptoms. At this time a feeding tube was placed into the patient and adipose was collected in order to provide autologous stem cells for treatment, if appropriate. A total of 26.35 grams of adipose tissue was processed at the VetStem Biopharma laboratory yielding 5.44 million stem cells. This was only about 206,000 cells per gram which is considered low. Debilitated animals tend to have lower cells per gram. Pathology results showed no lymphoma but was positive for IBD, so treatment with stem cells was determined to be a viable option.

A single dose with a total of 3.2 million stromal vascular cells were given intravenously approximately 5 days after the endoscopy and placement of the feeding tube. Within two days of receiving the stem cells the feeding tube was removed as the patient appeared ready to eat and was attempting to remove the feeding tube herself. Appetite returned but vomiting and diarrhea did not return. Patient steadily gained her weight back. None of the symptoms recurred. No pharmacologic interventions were used. Lovey lived to be 13 years old.

Summary

Stem cell therapy for orthopedic conditions has been used for a considerable length of time with a solid safety profile in animals and humans. In the cat, CKD has predominated the discussion of cell therapy with clinical evidence for efficacy and safety in this disease. In other internal medicine diseases such as IBD, asthma and FCGS, there is early investigational evidence. In orthopedics, especially OA, there is a large volume of evidence on the efficacy and safety in intraarticular therapy in many species of mammals to support the practitioner in making an informed and evidenced-based decision on therapy of their feline patients.

The ability of the cells to reduce inflammation and regulate the immune system response indicates that it may be useful in a range of disease processes. The VSB patient registry data across 31 species indicates that stem cell therapy results are similar in different species and is it is likely that stem cell physiology is highly conserved across all mammals as a way to regenerate and improve function and quality of life. With the limited number of approved medications for the feline patient, the use of autologous cells may be one of the best and safest options.

References

1. Quimby J.M. and Borjesson D.L. (2018) Mesenchymal stem cell therapy in cats: Current knowledge and future potential**.** *J Feline Med Surg*(3). 20**,** 208-216.
2. Hardie E.M., Roe S.C. and Martin F.R. (2002) Radiographic evidence of degenerative joint disease in geriatric cats: 100 cases (1994-1997)**.** *J Am Vet Med Assoc*(5). 220**,** 628-632.
3. Dragoo J.L., Carlson G., McCormick F., Khan-Farooqi H., Zhu M., Zuk P.A., et al (2007) Healing full-thickness cartilage defects using adipose-derived stem cells**.** *Tissue Eng*(7). 13**,** 1615-1621.
4. Toghraie F.S., Chenari N., Gholipour M.A., Faghih Z., Torabinejad S., Dehghani S., et al (2011) Treatment of osteoarthritis with infrapatellar fat pad derived mesenchymal stem cells in Rabbit**.** *Knee*(2). 18**,** 71-75.
5. Jo C.H., Lee Y.G., Shin W.H., Kim H., Chai J.W., Jeong E.C., et al (2014) Intra-articular injection of mesenchymal stem cells for the treatment of osteoarthritis of the knee: a proof-of-concept clinical trial**.** *Stem Cells*(5). 32**,** 1254-1266.
6. Eom Y.W., Shim K.Y. and Baik S.K. (2015) Mesenchymal stem cell therapy for liver fibrosis**.** *Korean J Intern Med*(5). 30**,** 580-589.
7. Seki A., Sakai Y., Komura T., Nasti A., Yoshida K., Higashimoto M., et al (2013) Adipose tissue-derived stem cells as a regenerative therapy for a mouse steatohepatitis-induced cirrhosis model**.** *Hepatology*(3). 58**,** 1133-1142.
8. Chen L.T., E.E.; Wu, P.Y.G; Wu, Y. (2008) Paracrine factors of mesenchymal stem cells recruit macrophages and endothelial lineage cells and enhance wound healing**.** *PLoS One*. 3**,** e1886.
9. Alamoudi N.M., El Ashiry E.A., Farsi N.M., El Derwi D.A. and Atta H.M. (2014) Treatment of Oral Ulcers in Dogs Using Adipose Tissue-Derived Mesenchymal Stem Cells**.** *J Clin Pediatric Dent*(3). 38**,** 215-222.
10. Lyer S. and Rojas M. (2008) Anti-inflammatory effects of mesenchymal stem cells: novel concept for future therapies**.** *Expert Opin Biol Ther*. 8**,** 569-582.
11. Uccelli A., Moretta L. and Pistoia V. (2008) Mesenchymal stem cells in health and disease**.** *Nat Rev Immunol*(9). 8**,** 726-736.
12. Melief S.M., Zwaginga J.J., Fibbe W.E. and Roelofs H. (2013) Adipose tissue-derived multipotent stromal cells have a higher immunomodulatory capacity than their bone marrow-derived counterparts**.** *Stem Cells Transl Med*(6). 2**,** 455-463.
13. Arzi B., Mills-Ko E., Verstraete F.J., Kol A., Walker N.J., Badgley M.R., et al (2016) Therapeutic Efficacy of Fresh, Autologous Mesenchymal Stem Cells for Severe Refractory Gingivostomatitis in Cats**.** *Stem Cells Transl Med*(1). 5**,** 75-86.
14. Villatoro A.J., Fernandez V., Claros S., Rico-Llanos G.A., Becerra J. and Andrades J.A. (2015) Use of adipose-derived mesenchymal stem cells in keratoconjunctivitis sicca in a canine model**.** *Biomed Res Int*. 2015**,** 527926.
15. Webb T.L. and Webb C.B. (2015) Stem cell therapy in cats with chronic enteropathy: a proof-of- concept study**.** *J Feline Med Surg*(10). 17**,** 901-908.
16. Ichim T.E., Harman R.J., Min W.P., Minev B., Solano F., Rodriguez J.P., et al (2010) Autologous stromal vascular fraction cells: a tool for facilitating tolerance in rheumatic disease**.** *Cell Immunol*(1). 264**,** 7-17.
17. Riordan N.H., Ichim T.E., Min W.P., Wang H., Solano F., Lara F., et al (2009) Non-expanded adipose stromal vascular fraction cell therapy for multiple sclerosis**.** *J Transl Med*. 7**,** 29.
18. Rodriguez J.P., Murphy M.P., Hong S., Madrigal M., March K.L., Minev B., et al (2012) Autologous stromal vascular fraction therapy for rheumatoid arthritis: rationale and clinical safety**.** *Int Arch Med*. 5**,** 5.
19. Apfel S. (1999) Neurotrophic factors in peripheral neuropathies: Therapeutic implications**.** *Brain Pathol*. 9**,** 393-413.
20. Ossipov M. (2011) Growth factors and neuropathic pain**.** *Curr Pain Headache Rep*. 15**,** 185-192.
21. Chen Q., Long Y., Yuan X., Zou L., Sun J., Chen S., et al (2005) Protective effects of bone marrow stromal

cell transplantation in injured rodent brain: synthesis of neurotrophic factors. *J Neurosci Res*(5). 80, 611-619.
22. Black L., Gaynor J., Gahring D., Adams C., Aron D., Harman S., et al (2007) Effect of adipose- derived mesenchymal stem and regenerative cells on lameness in dogs with chronic osteoarthritis of the coxofemoral joints: A randomized, double-blinded, multicenter, controlled trial. *Vet Ther*(4). 8, 272-284.
23. Black L., Gaynor J., Adams C., Dhupa S., Sams A.E., Taylor R., et al (2008) Effect of intraarticular injection of autologous adipose-derived mesenchymal stem and regenerative cells on clinical signs of chronic osteoarthritis of the elbow joint in dog. *Vet Ther*(3). 9, 192-200.
24. Cuervo B., Rubio M., Sopena J., Dominguez J.M., Vilar J., Morales M., et al (2014) Hip osteoarthritis in dogs: a randomized study using mesenchymal stem cells from adipose tissue and plasma rich in growth factors. *Int J Mol Sci*(8). 15, 13437-13460.
25. Guercio A., Di Marco P., Casella S., Cannella V., Russotto L., Purpari G., et al (2012) Production of canine mesenchymal stem cells from adipose tissue and their application in dogs with chronic osteoarthritis of the humeroradial joints. *Cell Biol Int*(2). 36, 189-194.
26. Vilar J.M., Morales M., Santana A., Spinella G., Rubio M., Cuervo B., et al (2013) Controlled, blinded force platform analysis of the effect of intraarticular injection of autologous adipose- derived mesenchymal stem cells associated to PRGF-Endoret in osteoarthritic dogs. *Vet Res*. 9, 131-136.
27. Harman R., Carlson K., Gaynor J., Gustafson S., Dhupa S., Clement K., et al (2016) A Prospective, Randomized, Masked, and Placebo-Controlled Efficacy Study of Intraarticular Allogeneic Adipose Stem Cells for the Treatment of Osteoarthritis in Dogs. *Front Vet Sci*. 3, 81.
28. Michalek J., Moster R., Lukac L., Proefrock K., Petrasovic M., Rybar J., et al (2017) Stromal vascular fraction cells of adipose and connective tissue in people with osteoarthritis: A case control prospective multi-centric non-randomized study. *Glob Surg*(3). 3, 1-9.
29. Guo W., Wang H., Zou S., Gu M., Watanabe M., Wei F., et al (2011) Bone marrow stromal cells produce long-term pain relief in rat models of persistent pain. *Stem Cells*(8). 29, 1294-1303.
30. Huh Y., Ji R.R. and Chen G. (2017) Neuroinflammation, Bone Marrow Stem Cells, and Chronic Pain. *Front Immunol*. 8, 1014.
31. Klass M., Gavrikov V., Drury D., Stewart B., Hunter S., Denson D.D., et al (2007) Intravenous mononuclear marrow cells reverse neuropathic pain from experimental mononeuropathy. *Anesth Analg*(4). 104, 944-948.
32. Siniscalco D., Giordano C., Galderisi U., Luongo L., de Novellis V., Rossi F., et al (2011) Long- lasting effects of human mesenchymal stem cell systemic administration on pain-like behaviors, cellular, and biomolecular modifications in neuropathic mice. *Front Integr Neurosci*. 5, 79.
33. Gaynor J., Landry R. and Harman R.: Pain relief and stem cell therapy. In *Veterinary Practice News*, January 2018 edition. pp. 44; 2018:44.
34. Vidal M.A., Walker N.J., Napoli E. and Borjesson D.L. (2012) Evaluation of senescence in mesenchymal stem cells isolated from equine bone marrow, adipose tissue, and umbilical cord tissue. *Stem Cells Dev*(2). 21, 273-283.
35. Zhu Y., Liu T., Song K., Fan X., Ma X. and Cui Z. (2008) Adipose-derived stem cell: a better stem cell than BMSC. *Cell Biochem Funct*(6). 26, 664-675.
36. Kinney M. and Harman R.: Stem cell therapy in zoo medicine. In *Volume* 9. Edited by RE M, N L, P C. Fowler's Zoo and Wild Animal Medicine: Elsivier; 2019: 138-144
37. Boyd L.M., Langston C., Thompson K., Zivin K. and Imanishi M. (2008) Survival in cats with naturally occurring chronic kidney disease (2000-2002). *J Vet Intern Med*(5). 22, 1111-1117.
38. Roudebush P., Polzin D.J., Ross S.J., Towell T.L., Adams L.G. and Dru Forrester S. (2009) Therapies for feline chronic kidney disease. What is the evidence? *J Feline Med Surg*(3). 11, 195-210.
39. Berent A. (2014) New techniques on the horizon: interventional radiology and interventional endoscopy of the urinary tract ('endourology'). *J Feline Med Surg*(1). 16, 51-65.
40. Choi S., Park M., Kim J., Hwang S., Park S. and Lee Y. (2009) The role of mesenchymal stem cells in the functional improvement of chronic renal failure. *Stem Cells Dev*(3). 18, 521-529.
41. Donizetti-Oliveira C., Semedo P., Burgos-Silva M., Cenedeze M.A., Malheiros D.M., Reis M.A., et al (2012) Adipose tissue-derived stem cell treatment prevents renal disease progression. *Cell Transplant*(8). 21, 1727-1741.
42. Semedo P., Correa-Costa M., Antonio Cenedeze M., Maria Avancini Costa Malheiros D., Antonia dos Reis M., Shimizu M.H., et al (2009) Mesenchymal stem cells attenuate renal fibrosis through immune modulation and remodeling properties in a rat remnant kidney model. *Stem Cells*(12). 27, 3063-3073.
43. Arzi B., Murphy B., Cox D.P., Vapniarsky N., Kass P.H. and Verstraete F.J. (2010) Presence and quantification of mast cells in the gingiva of cats with tooth resorption, periodontitis and chronic stomatitis. *Arch Oral Biol*(2). 55, 148-154.
44. Harley R., Gruffydd-Jones T.J. and Day M.J. (2011) Immunohistochemical characterization of oral mucosal lesions in cats with chronic gingivostomatitis. *J Comp Pathol*(4). 144, 239-250.

45. Jennings M.W., Lewis J.R., Soltero-Rivera M.M., Brown D.C. and Reiter A.M. (2015) Effect of tooth extraction on stomatitis in cats: 95 cases (2000-2013). *J Am Vet Med Assoc*(6). 246, 654- 660.
46. Pedersen N.C. (1992) Inflammatory oral cavity diseases of the cat. *Vet Clin North Am Small Anim Pract*(6). 22, 1323-1345.
47. Lommer M.J. (2013) Efficacy of cyclosporine for chronic, refractory stomatitis in cats: A randomized, placebo-controlled, double-blinded clinical study. *J Vet Dent*(1). 30, 8-17.
48. Lommer M.J. and Verstraete F.J. (2003) Concurrent oral shedding of feline calicivirus and feline herpesvirus 1 in cats with chronic gingivostomatitis. *Oral Microbiol Immunol*(2). 18, 131-134
49. Arzi B., Clark K.C., Sundaram A., Spriet M., Verstraete F.J.M., Walker N.J., et al (2017) Therapeutic Efficacy of Fresh, Allogeneic Mesenchymal Stem Cells for Severe Refractory Feline Chronic Gingivostomatitis. *Stem Cells Transl Med*(8). 6, 1710-1722.
50. Jergens A.E. (1999) Inflammatory bowel disease. Current perspectives. *Vet Clin North Am Small Anim Pract*(2). 29, 501-521, vii.
51. Jergens A.E., Moore F.M., Haynes J.S. and Miles K.G. (1992) Idiopathic inflammatory bowel disease in dogs and cats: 84 cases (1987-1990). *J Am Vet Med Assoc*(10). 201, 1603-1608.
52. Chichlowski M. and Hale L.P. (2008) Bacterial-mucosal interactions in inflammatory bowel disease: an alliance gone bad. *Am J Physiol Gastrointest Liver Physiol*(6). 295, G1139-1149.
53. Lanzoni G., Roda G., Belluzzi A., Roda E. and Bagnara G.P. (2008) Inflammatory bowel disease: Moving toward a stem cell-based therapy. *World J Gastroenterol*(29). 14, 4616-4626.
54. de la Portilla F., Alba F., Garcia-Olmo D., Herrerias J.M., Gonzalez F.X. and Galindo A. (2013) Expanded allogeneic adipose-derived stem cells (eASCs) for the treatment of complex perianal fistula in Crohn's disease: results from a multicenter phase I/IIa clinical trial. *Int J Colorectal Dis*(3). 28, 313-323.
55. Garcia-Olmo D., Garcia-Arranz M., Garcia L.G., Cuellar E.S., Blanco I.F., Prianes L.A., et al (2003) Autologous stem cell transplantation for treatment of rectovaginal fistula in perianal Crohn's disease: a new cell-based therapy. *Int J Colorectal Dis*(5). 18, 451-454.
56. Garcia-Olmo D., Garcia-Arranz M., Herreros D., Pascual I., Peiro C. and Rodriguez-Montes J.A. (2005) A phase I clinical trial of the treatment of Crohn's fistula by adipose mesenchymal stem cell transplantation. *Dis Colon Rectum*(7). 48, 1416-1423.
57. Garcia-Olmo D., Herreros D., De-La-Quintana P., Guadalajara H., Trebol J., Georgiev-Hristov T., et al (2010) Adipose-derived stem cells in Crohn's rectovaginal fistula. *Case Rep Med*. 2010, 961758.
58. Garcia-Olmo D., Herreros D., Pascual I., Pascual J.A., Del-Valle E., Zorrilla J., et al (2009) Expanded adipose-derived stem cells for the treatment of complex perianal fistula: a phase II clinical trial. *Dis Colon Rectum*(1). 52, 79-86.
59. Garcia-Olmo D., Herreros D., Pascual M., Pascual I., De-La-Quintana P., Trebol J., et al (2009) Treatment of enterocutaneous fistula in Crohn's Disease with adipose-derived stem cells: a comparison of protocols with and without cell expansion. *Int J Colorectal Dis*(1). 24, 27-30.
60. Caplan A.I. and Dennis J.E. (2006) Mesenchymal stem cells as trophic mediators. *J Cell Biochem*(5). 98, 1076-108

NOTES:

Understanding Feline Hypertension

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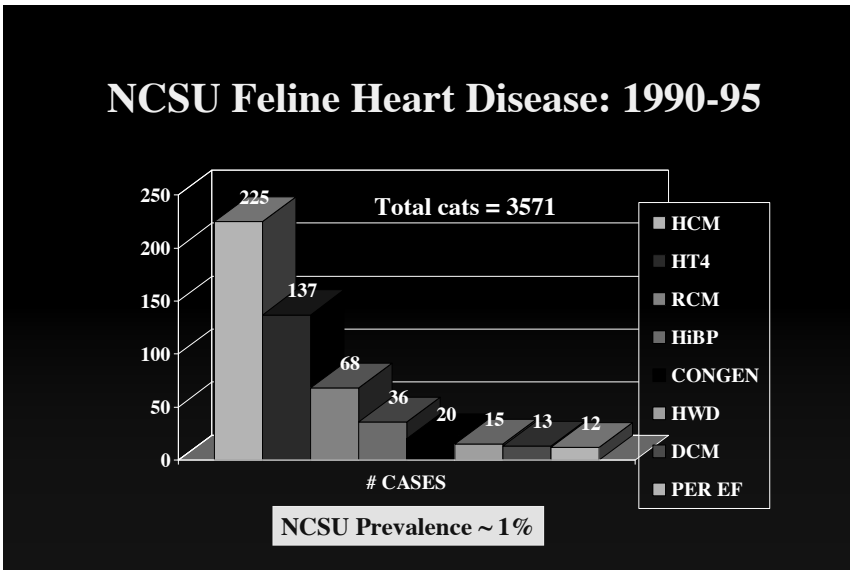
Hypertension is the most important cardiovascular disease of the aged cat and the most important vascular disease in cats (see Fig). Hence, its recognition and appropriate treatment is emerging as a critical component of small animal geriatric medicine. There are a host of target organs of hypertension. Our experience has shown that hypertensive cats have associated disease, in order of prevalence, of the eye, kidney, heart, and central nervous system.[1]



Etiology

Hypertension in animals has largely been thought to be secondary to other disease (e.g. renal disease and endocrinopathies), as opposed to idiopathic (primary, essential), as is the case in most human hypertensives. This has recently been called into question. A report of 69 hypertensive cats, seen at North Carolina State University (NCSU) for ocular disease, revealed that at least 17% (Fig 1), and possibly as many as 50%, of cats had no identifiable cause for their systemic hypertension (primary or essential hypertension).[1] Elliott and associates showed that approximately 20% of hypertensive cats, diagnosed in "primary-care" practice, were idiopathic[2].

Described and potential etiologies of secondary hypertension include chronic and acute renal disease, hyperthyroidism, hypothyroidism, hyperadrenocorticism, hyperaldosteronism, pheochromocytoma, diabetes mellitus, and obesity (Fig 1). Clearly chronic renal disease has the greatest association with hypertension and may often be causal. A recent report suggested approximately 29% of elderly cats with chronic renal disease were hypertensive.[3] with a range of 4 studies from 19-65%.[4]

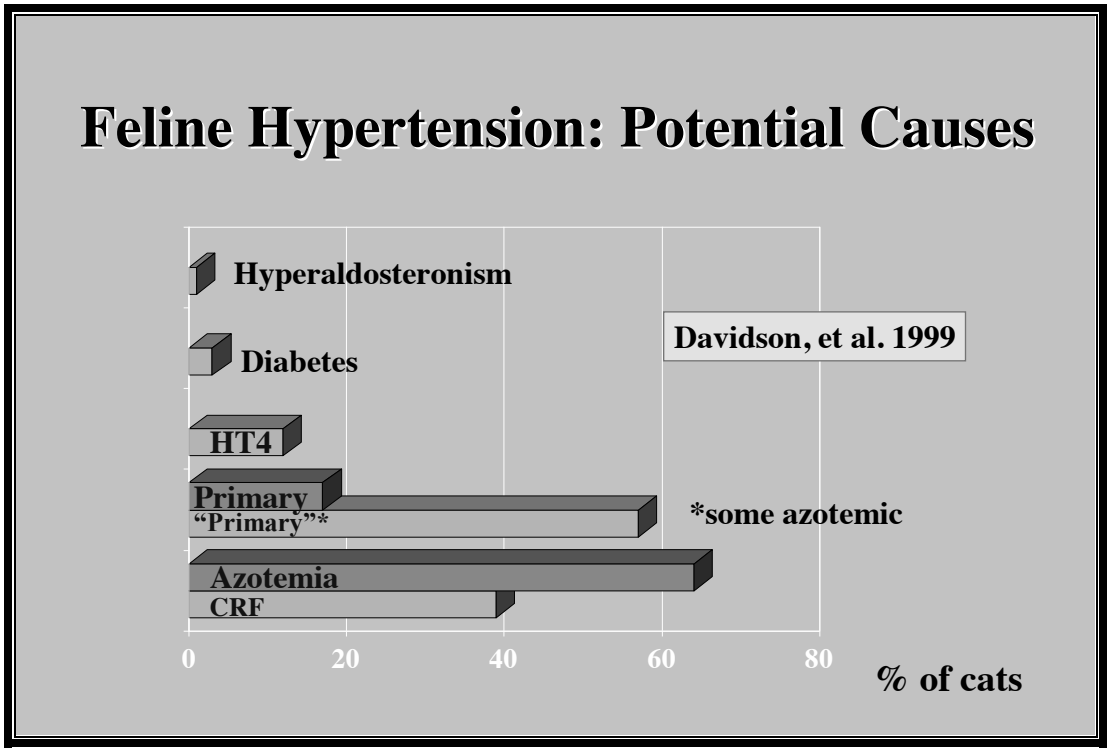


Figure. Associations of proven hypertension in 93 cats. Note that this does prove a causal relationship. Also noteworthy, 19% of cats had no identifiable cause. If mildly azotemic cats without chronic renal failure are considered to be idiopathic (ie because hypertension can beget renal disease), then the majority of hypertensive would be considered primary. The truth probably lies between these 2 figures, but it is safe to assume that 20% or more of hypertensive cats are idiopathic.

Pathogenesis

The pathogenesis of hypertension is complex, not well understood, and beyond the scope of this work. However, several studies have indicated that the renin-angiotensin-aldosterone system (RAAS) is probably abnormally activated in many or, perhaps, most cats with systemic hypertension, particularly with concurrent renal disease, and certainly after therapy with loop diuretics and vasodilators.[5,6] For more detail, see notes and presentation "Feline Hypertension: Diagnosis, Risks, and Management" associated with this AAFP program.

Diagnosis

Guidelines of 2007 & 2017 ACVIM Panel on Hypertension*

Status	SBP (mmHg)		DBP (mmHg)	Rx/Monitor□
Normal	<140#	and	<90	None
Pre-hypertensive	140-159	or	90-99	None; Q3-6 m
Stage 1 hypertension**	160-169	or	100-109	RAAS-I##; Q1-3 m
Stage 2 hypertension***	≥180	or	≥110	RAAS-I +/- Amlod

*Adapted from ACVIM Consensus Panel on Hypertension 2007 and 2017
**Kidneys at risk
***All target organs at risk
#2007 ACVIM Consensus, normal <150, pre-hypertensive 150-159
□Treatment; monitoring interval
##RAAS-I, Renin-Angiotensin-Aldosterone System-Inhibitors (ACE-I, ARB, MRA)

Diagnostic Methodology. We currently use the Doppler method, which has the distinct disadvantage of not providing diastolic or mean blood pressures in most instances. We use the tail as our first appendage for blood pressure measurement, followed by the palmar surface of the front leg and finally dorsal surface of the rear leg.

Cuff width is important and should approximate 30-40% of the circumference of the appendage used. Too small a cuff tends to overestimate and too large to underestimate true systemic blood pressure. The cuff position should approximate the level of the heart.

Current recommendations are that blood pressure be measured in a quiet area prior to examining the patient, typically in the presence of the owner and after a 5-10 minute period of acclimation. The ACVIM Panel on Hypertension suggests discarding the first measurement, then obtaining a minimum of 3, preferably 5-7, consecutive measurements with less than 20% variability in systolic blood pressure. The conditions (including animal's disposition), cuff size, site and all measurements should be recorded in the medical record. Many clinicians require that hypertension be documented on more than one occasion before accepting the diagnosis. Below are published values for feline systemic blood pressures (systolic = SBP, mean = MBP, diastolic = DBP) obtained by various means.

Arterial blood Pressure (mmHg) Values Obtained From Normal Cats.

(Adapted from 2007 & 2017 ACVIM Consensus Statement Guidelines; Partial list)

Method	# Cats	SBP	MBP	DBP
Intra-arterial (Direct)				
Brown et al, 1997	6	125 ± 11	105 ± 10	89 ± 9
Belew et al, 1999	6	126 ± 9	106 ± 10	91 ± 11
Oscillometry				
Bodey et al, 1998	104	139 ± 27	99 ± 27	77 ± 25
Mishina et al, 1998	60	115 ± 10	96 ± 12	74 ± 11
Doppler Method				
Klevans et al, 1979	4		139 ± 8	
Kobayashi et al, 1990	33		118 ± 11	
Sparkes et al, 1999	50		162 ± 19	
Payne, et al, 2017	**780**		**122 ± 12**	**normal 110-134**

Therapy

Until recently, therapies for feline hypertension have varied and have not often been systematically evaluated. Therapies that have been employed and reported upon include diuretics (furosemide and spironolactone), angiotensin-converting enzyme inhibitors (ACE-I; captopril, enalapril, lisinopril, and benazepril), beta-blockers (propranolol and atenolol), and calcium channel blockers (diltiazem and amlodipine). Littman, retrospectively evaluated 24 cats with chronic renal failure (CRF), found that the most effective antihypertensive therapy was the combination of a beta-blocker and an ACE-I and that there was a poor response to furosemide.[7] Jensen prospectively studied 12 similarly affected cats and found that the response to an ACE-I or beta-blocker alone was poor.[8] Another retrospective study of 12 hypertensive cats with CRF and unresponsive to other therapy, showed amlodipine to lower blood pressure by ≥20% in 11.[9] Snyder demonstrated blood pressure control in a randomized, blinded, placebo-controlled study of amlodipine in hypertensive cats, as well.[10] Finally, the NCSU study retrospectively found amlodipine to lower blood pressure ≥20% in 30 of 32 hypertensive cats with 28 of 32 becoming normotensive.[1] Diltiazem and beta-blockers alone or with ACE-I also lowered blood pressure in the majority of cats so treated. The literature and clinical experience would, nevertheless, lead one to appropriately conclude that amlodipine is the single best agent for the management of feline systemic hypertension. This said, beta-blockers

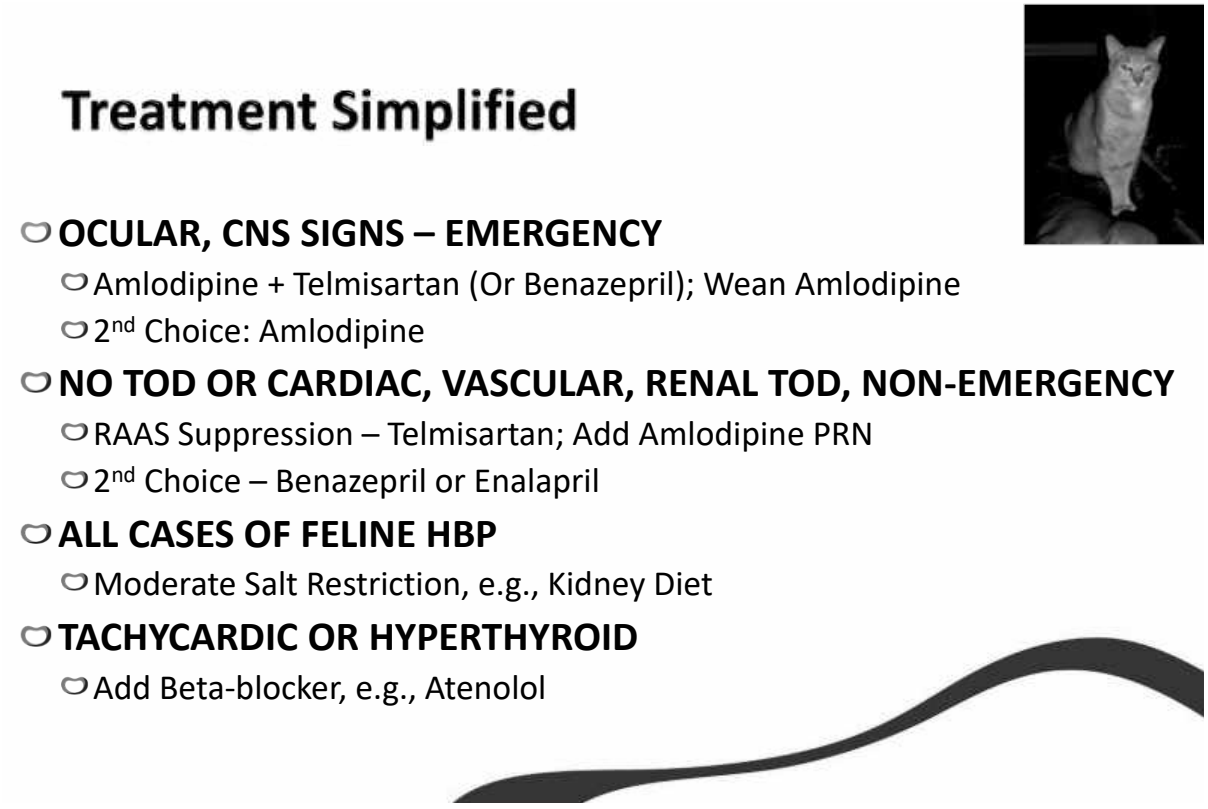
have a specific role in slowing heart rate and blocking the cardiovascular effects of T_3 in hyperthyroidism; ACE-I in combating drug-induced or spontaneous activation of the RAAS, for preserving renal function[11,12], and for proven effects in lowering blood pressure[13,14]; spironolactone for its aldosterone-antagonistic effects[15]; and furosemide (possibly with nitroglycerin) for use in heart failure accompanying hypertension.

(See Table).

Recently, several large clinical trials have shown both telmisartan and amlodipine to be effective in managing systemic hypertension in cats. As discussed in detail in the notes and presentation "Feline Hypertension: Diagnosis, Risks, and Management", RAAS suppression is imperative in treating hypertension. For this reason, RAAS-I should be included with amlodipine and telmisartan has better blood pressure lowering properties than ACE-I so far utilized in cats. Hence, telmisartan would appear to be the ideal drug for treatment of this syndrome, with amlodipine reserved for emergencies and resistant hypertension.

Other therapeutic considerations include: whether there is activation of the RAAS (initially or iatrogenically), the role of the sympathetic nervous system, renal function and the effects of hypertension on renal function, salt intake, presence of heart failure (uncommon), and the presence of reversible causes of hypertension (e.g. hyperthyroidism, diabetes mellitus, adrenal tumors). Additionally, I try to limit the number of pills to 1 (or 2) daily to reduce strain on the human-animal bond.

In deciding on a therapeutic approach, the author divides cats as follows: reversible cause - yes or no; with or without presumed RAAS activation (renal failure, heart failure, or treatment with vasodilators or loop diuretics); and by presence or absence of tachycardia (>200 bpm). The only common treatable cause of feline hypertension is hyperthyroidism, which is treated with methimazole, surgery, or ^{131}I. In these cats, because of the effects of T_3 on beta receptors, I employ a beta-blocker, such as atenolol (6.25-12.5 mg PO daily), to reverse the cardiovascular effects of hyperthyroidism prior to or until more definitive therapy is efficacious. If unsuccessful, I add enalapril at 0.5 mg/kg/day PO. In all cases, I employ a moderately salt-restricted diet (one designed for kidney patients) to lessen total body sodium without worsening renal function or severely activating the RAAS.



Cardiovascular Formulary for the Hypertensive Cat

Drug	Trade Name*	Formulation(s) **	Dosage	Use
Amlodipine	Norvasc Amodip	1.25 mg tablets 1.25 chewable	.625 PO qd-bid	Antihypertensive
Diltiazem	Cardizem	30 mg tablets	7.5 mg PO tid	Lusitrope, Vasodilator, Negative chronotrope
Diltiazem - LA				
	Dilacor XR	180, 240 mg caps.	30 mg PO bid	*same*
	Cardizem CD	180, 240 mg caps.	45 mg PO qd	*same*
Enalapril	Enacard (Vasotec)	1, 2.5, & 5 mg tablets	.5 mg/kg PO qd	ACE-I (CHF, GN, Hypertension)
Benazepril	Lotensin (Foretkor)	5 & 10 mg tablets	.25-.5 mg/kg PO qd-bid	*same*
Spironolactone	Aldactone Prilactone		2-3 mg/kg PO qd	Antihypertensive, CHF
Telmisartan	Semintra	Liquid 10 mg/mL	1.5 mg/kg BID x14d; 2mg/kg qd	Anithypertensive, Anti-proteinuric
Atenolol	Tenormin	25 mg tablets	6.25-12.5 mg PO qd	Negative chronotrope, Antiarrhythmic, Lusitrope, Antihypertensive
Nitroglycerin	Nitrol, Nitro-Bid	2% ointment	1/8–¼ inch topically tid for 24 hours	Venodilator (CHF)
LMW Heparin	Fragmin	2500 U/.2 ml	100 U/kg SQ qd	Anticoagulant
Aspirin		81 mg	40-80 mg q72h	Anticoagulant
Clopidogrel	Plavix	75 mg	17.5 mg daily	Anticoagulant

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Update on Diabetes Mellitus in Cats

Deborah Greco, DVM, PhD, DACVIM (SAIM)

Diabetes mellitus is one of the most common feline endocrine diseases, affecting one in every 200 to 300 cats, or roughly 240,000 diagnosed cases per year.[1] Despite the increasing frequency of the disease in the cat population, treatment of diabetic cats is frustrating and often associated with serious complications.

While insulin therapy and high-fiber diets have been mainstays of diabetes treatment, many diabetic cats experience complications associated with this therapy, such as hypoglycemia and progressive neuropathy.[2-7] In a recent study, 10 percent of diabetic cats had documented hypoglycemia caused by an insulin overdose.[6] Obese cats (>6 kg) were more likely to become hypoglycemic and lack autonomic warning signs of hypoglycemia. [6] Because of the difficulty in achieving adequate glycemic control with insulin therapy in cats, diabetic neuropathy is a common finding in diabetic cats. In one study, all diabetic cats suffered from subclinical forms of diabetic neuropathy as evidenced by impaired motor and sensory peripheral nerve conduction.[7] In summary, current dietary and insulin therapy is associated with increased risk of severe hypoglycemia and often results in poorly-controlled diabetes and progressive neuropathy in cats with type II diabetes.

The latest clinical and histologic evidence now suggests that type II diabetes is the most frequently occurring form of diabetes in cats and people.[2-4] Type II diabetes in cats is characterized by an impaired ability to secrete insulin following a glucose stimulus and is caused by both a defect in pancreatic beta cells and by peripheral insulin resistance.[2-4] The etiology of type II diabetes is undoubtedly multifactorial; obesity, genetics, diet, and islet of amyloidosis are involved in the development of this form of diabetes in humans and cats.[2-4] It is now recognized that the classic metabolic abnormalities found in type II diabetes—decreased insulin secretion and peripheral insulin resistance—may be consequences of abnormal amyloid production by pancreatic cells.[2-4] Despite the prevalence of type II diabetes in cats, the advanced nature of their disease (amyloid deposition, glucose toxicity) often requires that insulin therapy be instituted.[2]

Insulin is often used to treat diabetes in cats and dietary fiber has been suggested to improve diabetic control in cats.[8] In one study, 23 client-owned diabetic cats were fed canned high-insoluble fiber or low-fiber diets in a 16 week crossover design.[8] While only 13 of the 23 cats finished the study, nine of the 13 showed improvement on the high-fiber diet.[8] The insoluble fiber diet had a significant effect on mean daily caloric intake, and the mean fasting blood glucose and mean glycosylated hemoglobin concentrations.[8] However, the effects on mean fasting blood glucose and glycosylated hemoglobin could have resulted from a reduction in caloric intake alone. Furthermore, this study looked at canned high-fiber diets rather than dry high-fiber diets. The carbohydrate content of dry diets, especially those containing high-insoluble fiber, is approximately 36 to 40 percent. In contrast, the canned high-fiber diets are approximately 23 percent carbohydrate as fed. It is entirely possible that the improvement in glycemic control in these patients could have been due to a change from dry to canned cat food.

Unique Mammal

The cat is an obligate carnivore and, as such, is unique among mammals in its insulin response to dietary carbohydrates, protein, and fat. The feline liver exhibits normal hexokinase activity, but glucokinase activity is virtually absent.[9] Glucokinase converts glucose to glycogen for storage in the liver and is important in metabolizing excess post-prandial glucose. Normal cats are similar to people humans in that glucokinase levels drop precipitously with persistent hyperglycemia in people with type II diabetes. Amino acids, rather than glucose, are the signal for insulin release in cats.[10] In fact, a recent publication demonstrated more effective assessment of insulin reserve in cats using the arginine response test rather than a glucose tolerance test.[11]

Another unusual aspect of feline metabolism is the increase in hepatic gluconeogenesis seen after a meal. Normal cats maintain essential glucose requirements from gluconeogenic precursors (*e.g.,* amino acids) rather than from dietary carbohydrates. As a result, cats can maintain normal blood glucose concentrations even when deprived of food for more than 72 hours.[10] Furthermore, feeding has very little effect on blood glucose concentrations in normal cats.[2,12] In summary, the cat is uniquely adapted to a carnivorous diet and is not metabolically adapted to ingestion of excess carbohydrates.

Carbohydrates Equal Catabolism

When type II diabetes occurs in cats, the metabolic adaptations to a carnivorous diet become even more deleterious, leading to severe protein catabolism; feeding a diet rich in carbohydrates may exacerbate hyperglycemia and protein wasting in these diabetic cats. In fact, in human beings with type II diabetes, the first recommendation is to restrict

excess dietary carbohydrates such as potatoes and bread and to control obesity by caloric restriction.[13] Furthermore, people with type II diabetes have improved glycemic control and nitrogen turnover during weight loss when a low-energy, high-protein diet is combined with oral hypoglycemic therapy.[14]

A low-carbohydrate, high-protein diet, which is similar to a cat's natural diet (mice), may ameliorate some of the abnormalities associated with feline diabetes. In initial studies using a canned high-protein, low-carbohydrate diet and the starch blocker acarbose insulin injections were discontinued in 58 percent of cats, and those with continued insulin requirements were regulated on a much lower dosage (1 U b.i.d.).[15] Comparison of canned high-fiber vs. low-carbohydrate diets in 63 client-owned diabetic cats showed that those fed low-carbohydrate diets were three times more likely to discontinue insulin injections.[16]

The diet formulation is critical in that most dry cat food formulations contain excessive carbohydrates; therefore, canned cat foods and preferably high-protein formulations should be used for initial treatment of diabetic cats. Because weight reduction also decreases insulin resistance, cats should be fed no more than 30 kcal/lb of ideal body weight in two equal meals per day. Initially, caution should be used when changing from dry to canned foods, as insulin requirements may decrease dramatically, and a reduction in insulin dosage may be required. Feeding canned high-fiber or high-protein, low-carbohydrate diets can improve glycemic control. However, cats fed high-protein, low-carbohydrate diets are more likely to no longer require exogenous insulin injections.[15-17]

Insulin Treatment

In order to mimic the physiologic release of insulin, ideally insulin should be given with each meal. However, the timing of the insulin injection has recently been called in question by several veterinary endocrinologists. *Some authors argue that insulin should be injected one-two hours PRIOR to feeding to attenuate the post-prandial effect.* The obvious concern with this timing of insulin is what to do if the animal will not eat. However, many suggest that this is a more "physiologic" way to administer insulin. In dogs, this author would be concerned about injecting insulin in this manner; however, in cats since they spend most of their time in a "post-prandial" state because of hepatic gluconeogenesis, I believe this type of insulin injection timing could work. The author recommends feeding the animal and injecting the insulin at the same time. If the animal does not eat, the insulin dosage can be reduced (usually by one-half) or skipped entirely and the animal evaluated by the veterinarian to determine the cause of the anorexia.

The author recommends administration of insulin at sites along the lateral abdomen and thorax. Clipping or shaving a 2 x 2" square of haired skin on the lateral thorax or abdomen will assist the owner in accurate insulin placement. It often helps to reinforce verbal instructions with written regardless of the insulin formulation being used. Avoid the scapular area or nape of neck as insulin is poorly absorbed from these sites.

Table 1: Insulin formulations in cats: species source and type, syringe type, and typical dosing frequency.

Insulin	Conc	Syringe	Dosing	Frequency	Comments
Glargine	U-100	U-100	2 U/cat	BID	Best for remission
PZI	U-40	U-40	0.8/kg	BID-SID	SID in 50%

Monitoring Diabetes in the Cat

It appears that methods of assessing long-term glycemic control are better indicators of response to therapy with oral hypoglycemics than are spot glucose determinations or blood glucose curves. In humans, the response to treatment is measured by a decrease in hemoglobin A1C with most oral hypoglycemic agents yielding a modest decrease of about 1-2%. (Kimmel 2005) The author prefers to monitor the resolution of clinical signs of diabetes mellitus, such as polydipsia and polyuria, and serum fructosamine concentrations in cats undergoing oral hypoglycemic therapy. Serum fructosamine concentrations lower than 400-450 micromol/L are consistent with moderate to good long-term control of hyperglycemia. Body weight should increase or remain stable, appetite should remain good and polydipsia/polyuria (as blood glucose drops below the renal threshold for glucose) should resolve with effective oral hypoglycemic therapy.

Continuous glucose monitoring devices (CGMS) may be used to monitor therapy and are a good way to avoid the stress induced hyperglycemia that results from glucose curves. The author uses the Libre Freestyle CGMS.

Urine Glucose Monitoring in cats on glargine : Use Glucotest strips or nonabsorbable litter pan (Breeze by Tidy Cats) and Bayer glucose strips

Start at 2 units glargine BID, daily urine glucose monitoring

IF neg x 2 days: 1 U BID, IF neg x 2 days: 1 U SID, IF neg x 2 days: discontinue insulin

References

1. Panciera DL, Thomas CB, Eicker SW, et al. Epizootiologic patterns of diabetes mellitus in cats. *J Amer Vet Med Assoc* 1990;197:1504-1508.
2. Rand JS. Management of feline diabetes. *Aust Vet Practit* 1997;27:68-75.
3. O'Brien TD, Butler PC, Westermark P, et al. Islet amyloid polypeptide: A review of its biology and potential roles in the pathogenesis of diabetes mellitus. *Vet Pathol* 1993;30:317-332.
4. Lutz TA, Rand JS. A review of new developments in type 2 diabetes mellitus in human beings and cats. *Brit Vet J* 1993;149:527-536.
5. Crenshaw KL, Peterson ME. Pretreatment clinical and laboratory evaluation of cats with diabetes mellitus: 104 cases (1992-1994). *J Amer Vet Med Assoc* 1996;209:943-949.
6. Whitely NT, Drobatz KJ, Panciera DL. Insulin overdose in dogs and cats: 28 cases (1986-1993). *J Amer Vet Med Assoc* 1997;211:326-330.
7. Cuddon P. Diabetic neuropathy, in *Proceedings*. Amer Coll Vet Int Med. 1999;650-653.
8. Nelson RW, Scott-Moncrieff C, DeVries S, et al. Dietary insoluble fiber and glycemic control of diabetic cats (abstract). *J Vet Intern Med* 1994;8:165.
9. Ballard FJ. Glucose utilization in mammalian liver. *Comp Biochem and Physiol* 1965;14:437-443.
10. Kettlehut IC, Foss MC, Migliorini RH. Glucose homeostasis in a carnivorous animal (cat) and in rats fed a high-protein diet. *Amer J Physiol* 1978;239:R115-R121.
11. Kitamura T, Yasuda J, Hashimoto A. Acute insulin response to intravenous arginine in nonobese healthy cats. *J Vet Intern Med* 1999;13:549-556.
12. Martin GJW, Rand JS. Lack of correlation between food ingestion and blood glucose in diabetic cats, in *Proceedings*. 15th Annu Am Coll Vet Int Med 1997;670.
13. Unger RH, Foster DW. Diabetes mellitus. In: Wilson and Foster (eds). *Williams Textbook of Endocrinology*. Philadelphia, Pa: WB Saunders Co, 1998,973-1060.
14. Gougeon R, Jones JHP, Styhler K, Marliss EB, Morias JA. Effects of oral hypoglycemic agents and diet on protein metabolism in type 2 diabetes. *Diabet Care* 2000;23:1-8.
15. Mazzaferro E, Greco DS, Turner AS, et al. Treatment of feline diabetes mellitus using an alpha-glucosidase inhibitor (acarbose) and a high protein, low carbohydrate diet. *J Fel Med Surg* 2003;5:183-190.
16. Bennett N, Greco DS, Peterson ME, et al. Comparison of a low carbohydrate vs. high fiber canned diet for the treatment of diabetes mellitus in cats. *J Fel Med Surg* 2006;8:73-84.
17. Frank G, Anderson W, Pazak H, et al. Use of a high protein diet in the management of feline diabetes mellitus. *Vet Therapeut* 2001;2:238-246.
18. Engerman RL, Kern TS. Hyperglycemia and development of glomerular pathology: Diabetes compared with galactosemia. *Kidney Int* 1989;36:41-45.
19. Munana KR: Long-term complications of diabetes mellitus, Part I: Retinopathy, nephropathy, neuropathy. *Vet Clin North Am* 1995;25:715-730.
20. Kraus MS, Calvert CA, Jacobs GJ, et al. Feline diabetes mellitus: a retrospective mortality study of 55 cats (1982-1994). *JAAHA* 1997;33:107-111.
21. Bruskiewicz KA, Nelson RW, Feldman EC, et al. Diabetic ketosis and ketoacidosis in cats: 42 cases (1980-1995). *JAVMA* 1997;211:188-192.
22. Goossens MM, Nelson RW, Feldman EC, et al. Response to insulin treatment and survival in 104 cats with diabetes mellitus (1985-1995). *JVIM* 1998;12:1-6.
23. Peterson ME. Diagnosis and management of insulin resistance in dogs and cats with diabetes mellitus. *Vet Clin N Amer* 1995;25:691-713.
24. Peterson ME, Taylor RS, Greco DS, et al. Acromegaly in 14 cats. *JVIM* 1990;4: 192-201.
25. Fleeman, L. M. and Rand, J. S. Management of canine diabetes. Endocrinology, 2001;31: 855-880. Greco DS. Diabetes mellitus. In Birchard, Birchard & Sherding (eds). *Small Animal Medicine and Surgery*. 3rd ed. Elsevier, 2006;376-389.
26. Greco DS. Diagnosis of diabetes mellitus in dogs and cats. *Vet Clin North Am* 2001;31:845-53.
27. Bennett N, Papich MG, Hoenig M, Fettman MJ, Lappin MR. Evaluation of transdermal application of glipizide in a pluronic lecithin gel to healthy cats. Am J Vet Res. 2005 Apr;66(4):581-8.
28. Brunker JD, Seyfert TM, Maxwell LK, McFarlane DM Evaluation of an incretin mimetic (exanatide) as an effective adjunctive treatment for diabetes mellitus in cats. Update AAFP grants. 2011.
29. Diamant M, Van Gaal L, Stranks S, Northrup J, Cao D, Taylor K, Trautmann M..Once weekly exenatide compared with insulin glargine titrated to target in patients with type 2 diabetes (DURATION-3): an open-label randomised trial. Lancet. 2010 Jun 26;375(9733):2234-43.
30. Feldman EC, Nelson RW, Feldman MS. Intensive 50-week evaluation of glipizide administration in 50 cats with previously untreated diabetes mellitus. J Am Vet Med Assoc. 1997 Mar 15;210(6):772-7.
31. Gilor C, Graves TK, Gilor S, Ridge TK, Rick M. The GLP-1 mimetic exenatide potentiates insulin secretion in healthy cats. Domest Anim Endocrinol. 2011 Jul;41(1):42-9. Epub 2011 Apr 6.
32. Mazzaferro E, **Greco DS**, Turner AS, Fettman MJ. Treatment of feline diabetes mellitus using an alpha-

glucosidase inhibitor (acarbose) and a high protein, low carbohydrate diet. J Fel Med Surg; 2003: 5(3)183-190.
33. Moeller TM, Greco DS. Retrospective study comparing glipizide and PZI in control of diabetes mellitus in cats. Soc Comp Endo Proc 2005.

NOTES:

What is it? Differentiating Medical from Behavioral

Valarie Tynes, DVM, ACVB, DACAW

Introduction

Physical and behavioral health are often intricately interrelated. After all, the first sign of a medical problem can be a behavior change and behavior problems are often associated with anxiety and stress which can further contribute to medical problems. In some cases, even after a medical condition is treated, the behaviors that were "practiced" as a result of the condition, can continue due to the associative learning that occurred. In those cases, some behavioral therapy may be necessary in addition to medical therapy. This interplay requires that the clinician take a holistic approach to pet health and address both medical and behavioral needs of the pet if the cat is to stay healthy and remain in its home.

Clinical Presentation

Signalment and History

When cats are presented with a change in behavior, the most important aspect of the signalment that may indicate a medical condition instead of a behavioral condition is the age of the cat. If the cat is over 5-6 years of age and the behavior is truly acute in onset, then a medical condition should be first on the list of differentials.

Most behavior problems develop in adolescence. Behavior problems that develop in older animals are less common and when they do occur are usually a result of a traumatic event or some very disruptive and stressful change in the social environment. This means that after looking at the age of the cat, a social history will also need to be assessed, when it comes to cats, a brief, basic history form that the owner can complete prior to the appointment or while they await their appointment will help save a great deal of time. Things that may be needed, include: the total number of cats in the household, age of acquisition, sex, neuter status, order in which they were acquired, and then a brief description of the relationship between the cats. It may be easiest to allow the owners to describe these relationships in their own words at first but ultimately you want to know the following about each feline dyad: do they rub each other when greeting? Do they sleep together (with bodies touching, not at opposite ends of a couch) and do they groom each other? If cats do not do at least 2 of these 3 things regularly, it is unlikely that they have a good, friendly relationship. If they don't, this does not mean that conflict is guaranteed to exist in the home, but it does mean that there is a chance that conflict and therefore stress is present in the home, especially if adequate resources are not present so that the cats can avoid each other if they wish. If there is social stress present in the home that can be contributing to whatever problems are present, whether they be medical or behavioral.

Another important aspect of signalment to discuss is temperament. If you are presented with an adult animal that appears to be exhibiting new anxiety related behaviors; then finding out that, according to the owner, the cat "has always been a little bit shy or timid" makes it more likely that the cat may actually have a behavioral problem. If on the other hand, the cat has always been friendly and outgoing but suddenly at 5 or 6 years of age, is exhibiting a sudden behavior change, then a medical problem should be suspected.

The biggest challenge with all of this history taking is of course relying on the owner report and while owners invariably do know their pets well, they are not always reliable at interpreting behaviors well. One of the most difficult things to do from a diagnostic point of view may be to recognize when a behavior is truly "new" and when it is simply an escalation of an existing problem and this is why understanding temperament and body language is critical. Many owners never associate the fact that their cat has always hissed at strange cats it sees through the windows with the fact that it has now attacked its housemate, or a person in the home, and is behaving aggressively towards them.

All of the above of are general "rules of thumb" and will not replace a thorough history and examination but in our non-verbal patients it is critical to understand that just because the evidence of a physical problem cannot be found on examination, does not mean that the problem must be "behavioral" in origin. It may simply mean that you cannot find the origin of the physical problem.

Behavior of Illness and Pain

The behavior of illness in cats can be more subtle than in some animals since they appear to be very good at hiding signs of illness until they are quite sick.[1] Anorexia may often be the first sign noted. Their fastidious nature makes it easy for them to mask many signs. For example, if they have diarrhea, they may clean themselves so well that the owner may not notice the signs until the cat becomes too ill to groom themselves thoroughly. Therefore, a cat with an unkempt coat should be examined closely for signs of illness or injury that prevent it from cleaning itself. An ill cat may also be less interested in social interactions and may hide.[1]

The behavior of pain in cats can be even more subtle especially in the case of the early stages of pain due to osteoarthritis. Signs of pain in cats can simply be reduced activities, but may also include restlessness, increased irritability or aggression, hiding and avoidance, vocalization, night waking or house soiling.

The Role of Stress on Health and Behavior

It is common for us to think about the effect of disease on behavior but stress will have an effect on health as well as behavior due to its effects on the HPA axis and the noradrenergic system. While stress is supposed to be an adaptive response that triggers psychological, behavioral, endocrine and immune effects designed to help the body return to homeostasis, when the stress is chronic (or the changes to do not allow the animal to return to homeostasis) the long term effects can include reduced immune function, gastrointestinal distress, decreased growth rates, fatigue and hypertension, to name just a few. Chronic stress can even lead to structural and functional changes in the brain.[2]

Common Medical Causes of Behavior Change

Urinary Tract Disease

The association between urinary tract disease and house soiling in the cat probably creates one of the most frustrating medical/behavioral challenges you will face in practice. This is the most common situation where a medical problem can create a behavior problem and the medical problem may be cured but the behavioral problem will continue in many cases if it is not treated separately with appropriate environmental and behavioral management techniques. The most logical approach to these problems begins with recognizing that house soiling can occur as a result of several different behaviors and you must first determine which behavior is being performed before you can begin appropriate treatment. These different activities include:

- Urine marking or spraying (Urine deposition on a specific location for the purpose of leaving a message)
- Urination outside of the box (Urination solely for the purpose of emptying the bladder)
- Defecation outside of the box (Very rarely associated with marking – will be covered with GI)

Stress from a variety of different environmental situations can contribute to either form of urinary house soiling.

Feline Idiopathic Cystitis (FIC) is the most common urinary tract disease that will lead to house soiling and FIC is a diagnosis of exclusion. The cause is currently unknown but a variety of different causative factors are suspected. FIC is believed to be analogous to interstitial cystitis in humans, a painful, inflammatory condition of the bladder in which increased urothelial permeability is a primary feature. Cats with FIC appear to have altered bladder permeability as well, and several studies have documented its association with stress.[3,4,5] Cats with FIC appear to have increased sympathetic activity, [3,6] be more sensitive to environmental stress, and have a decreased ability to cope with changes in their environment. Therefore, if FIC is suspected, the treatment plan must by definition include treating the cause which may very well be social stress in the household. Regardless of the originating cause for urination outside of the box, the clinician must be aware that if the cat has been using another location for any length of time, then the cat may have developed not only a preference for another location, but possibly an aversion for the box as well. This will require treatment of the medical condition as well as the behavioral condition as many cats will not spontaneously return to their litter box just because their medical condition has been cured.

Gastrointestinal Disease

Any gastrointestinal disease that results in increased motility, diarrhea, constipation or decreased control of defecation can lead to house soiling so any defecation outside of the box should always be explored first as a medical issue. Diseases of the GI tract causing pain, discomfort and nausea may lead to altered appetite, anxiety, irritability, night waking, repetitive pacing, vocalization and avoidance. Some oral behaviors have even been associated with disease. For example, in one study, 7 out of 8 cats presented with pica had mild to moderate gastritis or enteritis and 3 improved by 50% or greater with treatment.[7] Ultimately, the clinician must keep in mind however, that stress can also have profound effects on the GI system and result in changes in GI motility, permeability, electrolyte absorption, rate of gastric emptying and can increase the colonic inflammatory response.[8]

Dermatological Disease

Hair loss, pruritis, repetitive behaviors such as tail chasing and even the vaguely defined “feline hyperesthesia” are just some of the more common clinical signs or conditions often associated with dermatological disease that are frequently mistaken for behavioral problems. In one study of cats presented to a dermatologist with a presumptive diagnosis of psychogenic alopecia, 76% of the cats were found to have evidence of medical conditions causing pruritis.[9] When in situations where they feel frustrated or conflicted, many animals will exhibit displacement grooming behavior (displacement behaviors are behaviors that are shown out of context for the situation and can usually be attributed to some type of stressor) so when overgrooming cannot be attributed to a physical problem, it may be associated with psychological stressors. However, stress has been shown to be able to worsen pruritis so this is another situation where the physical and behavioral may be very intricately related.

Cats have also been known to overgroom an area due to pain in an underlying organ or joint.

Feline hyperesthesia is a poorly understood syndrome, known by a variety of different names including rolling skin syndrome, twitchy skin syndrome, and feline neurodermatitis, to name a few. The term really should not be used as a diagnosis because no single underlying cause has been found. Cats with this problem may demonstrate short bouts of thoracolumbar skin rolling or rippling. They may appear anxious or agitated, demonstrate exaggerated tail movements, running, vocalizations, and self-directed aggression that includes licking, plucking, biting or chewing directed at the tail, lumbar, flank or anal areas. In some cases, these behaviors have been found to be a result of severe pruritis but in other cases have appeared to be a result of focal seizures, or sensory neuropathies. Systemic diseases such as toxoplasmosis and hyperthyroidism should be ruled out, as well as painful spinal or skin conditions, severe pruritus, FLUTD, anal sacculitis, or myositis as they may all contribute to the behavior. Any disease condition affecting the central nervous system or that alters the cat's reactivity to stimuli will need to be ruled out if presented with a cat showing signs similar to feline hyperesthesia.[10]

Endocrine Disease
In cats, hyperthyroidism and diabetes mellitus are the most common endocrine diseases to result in problem behavior. Behavioral signs might include increased activity, hyperphagia, polydipsia, increased irritability, house soiling, and intercat or owner directed aggression. Signs of hypertension associated with thyroid disease might include nighttime waking, vocalization, irritability, aggression and changes in activity levels. Diabetes mellitus can lead to changes in appetite and polyuria and polydipsia that may lead to house soiling.

Cognitive Dysfunction Syndrome (CDS)
Signs of CDS often do not become sever in cats until they are over 15 years of age but early screening will help clinicians to recognize the signs while early intervention is still practical and useful. Signs associated with CDS can be identified by using the DISHAA screening tool (**D**isorientation, alterations in social **I**nteractions, changes in **S**leep-wake cycles, **H**ouse soiling, altered **A**ctivity levels and increased **A**nxiety). In cats, changes in self- hygiene and appetite may also be seen. Night time waking and pacing appear to be frequently associated with CDS in cats but these behaviors can also be associated with pain so careful examinations and in some cases presumptive therapy with analgesics or anti-inflammatories should be considered.

References

1. Hart BL: Biological basis of the behavior of sick animals. *Neurosci Biobehav* Rev 12: 123-137,1988.
2. McEwen BS: The neurobiology of stress: From serendipity to clinical relevance. *Brain Res* 886: 172 -189, 2000.
3. Buffington CAT, Teng B & Somogyi GT: Norepinephrine content and adrenoceptor function in the bladder of cats with feline interstitial cystitis. J Urol 167:1876–1880, 2002.
4. Westropp JL, Kass PH & Buffington CAT: Evaluation of the effects of stress in cats with idiopathic cystitis. Am J Vet Res 67: 731–736, 2006.
5. Stella J, Croney C & Buffington CAT: Effects of stressors on the behavior and physiology of domestic cats. Appl Anim Behav Sci 143: 157–163, 2013.
6. Buffington CAT & Pacak K: Increased plasma norepinephrine concentration in cats with interstitial cystitis. J Urol 165: 2051–2054, 2001.
7. Demontigny-Bedard I, Beauchamp G, Belanger M-C et al: Gastrointestinal evaluation of cats presented with pica. Proceedings of the 2016 Veterinary Behavior Symposium, San Antonio, TX p 40-44.
8. Bhatia T & Tandon RK: Stress and the gastrointestinal tract. J Gastroenterol Hepatol 20: 332–339, 2005.
9. Waisglass SE, Landsberg GM, Yager JA, et al: Underlying medical conditions in cats with presumptive psychogenic alopecia. J Am Vet Med Assoc 228: 1705–1709, 2006.
10. Ciribassi J: Feline hyperesthesia syndrome. Comp Cont Ed Vet 31 (6): 254, 2009.

NOTES:

Feline-Friendly Handling to Enhance Feline Welfare

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Introduction

Feline-friendly handling benefits all practices that work with cats, increasing feline welfare, client loyalty, and human safety. As veterinarians and technicians, our oaths state that we will protect animal welfare, defined as protecting both the physical and psychological well-being of animals. This includes protection of an individual animal's ability to cope mentally and physically at any point in time.[1] Many cats suffer from poor welfare, unable to cope, habituate or adapt to unfamiliar situations or individuals, both in the home and veterinary practice. Understanding the species is the foundation of feline-friendly handling and improved welfare during veterinary visits. Cats are unique as the only solitary hunter that can live amicably with people.[2] As such, they have strong survival instincts and protective mechanisms when they perceive threats - not uncommon during veterinary visits. Recognizing and alleviating the cat's challenges surrounding veterinary care prevents feline fear, frustration, and pain, and the associated unwanted behavioral responses. The outcome is more relaxed cats and clients, and enhanced job satisfaction and safety for team members.

How Veterinary Visits Impact Feline Welfare – The Good and the Bad

There is no doubt that veterinary care positively impacts feline welfare, improving quality and length of life. However, the challenges to the cat that surround the visit also impair welfare. Fortunately, if we recognize and make changes, most of the negative issues can be alleviated. Recognizing what the multiple feline challenges are is essential to enable us to make changes. They often start at home and continue from waiting area to wards. Any stressor can negatively impact the cat, but multiple stressors are cumulative.[3] Two important surveys identify the challenges that impair feline welfare.[4,5]

What Welfare Experts and Veterinarians Say

A survey of animal welfare experts and veterinarians, both with and without expertise in animal welfare, were asked how veterinary visits impact canine and feline welfare. They identified 85 factors of which 70% significantly impaired patient welfare.[4] The factors included olfactory, auditory, novel environment, separation from family, inadequate analgesia, physical restraint, and the attitude of veterinary team members.[4] Fortunately, they also thought that 68% of the identified factors could be improved in an average veterinary clinic.[4]

What Owners Say

A survey of more than 1,000 cat owners suggests that cats show impaired welfare during all stages of the veterinary visit – starting at home, in the waiting room, moving to the exam room, on the exam table, and after returning home.[5] Owners also said that restraint, pain, and anxiety led to aggression directed towards veterinarians and owners.[5] Even though cat owners love their cats,[6] the 2017-18 AVMA Pet Ownership and Demographics Sourcebook indicated that only 54.3% of households with cats as the only companion animal visit the veterinarian at least annually.[7] The average number of annual veterinary visits was 0.7% and distress of the veterinary visit was noted as a major factor.[7] Owners seek a veterinarian based on their knowledge, kindness, compassion, and respectful handling of cats and will often change veterinarians if these are not provided.[6,7]

Short- and Long-term Impacts of Veterinary Care on Welfare

Cats have good long-term memory, and previous negative experiences can impact how a cat will respond in the future.[8,9] For example, a cat that is painful or fearful during a veterinary visit may respond with anxiety and aggression at future visits. Also, there is evidence that a negative veterinary experience in young puppies can impact their long-term welfare, leading to chronic fear or anxiety regardless of environment, and this is likely to occur in kittens too.[4] Some cats may do better with house calls, but most do well in practices as long as measures are taken to provide a safe space (e.g., the bottom half of the carrier), respectful handling, and familiarity of team members.[10] In fact, cats do well during second visits when the veterinarian and team members are familiar.[10]

Understanding the Cat and Why They React as They Do

How Cats Differ From Other Social Species

Although the domestic cat is a social species, there is one fundamental difference between them and other domestic animals. Whereas all other domestic animals evolved from pack animals, cats evolved from an asocial and solitary hunter, *Felis silvestris lybica*.[2] Aside from becoming a social species, the domestic cat has retained all ~~of~~ other of its' ancestor's protective behaviors. Even indoor only cats are still solitary hunters and survivors, needing to protect ~~t~~themselves at all times. The cat's strong protective mechanisms include territoriality, keen senses, and communication, all which function to prevent conflict and potential injury that could impact its survival. These survival

mechanisms are commonly observed during veterinary visits. It is critical to appreciate that the cat does not want to be aggressive – this is its last resort. Fortunately, we can support our feline patients and reduce undesirable behavioral responses by providing an environment that respects the cat's senses, safe territory, and respectful handling. Although feline communication developed to protect oneself against unfamiliar cats, we can learn to interpret vocalizations, body language and facial expressions (see **Table 1**) and how to respond to prevent escalation of responses to aggression.

How Cats Are Similar to Other Mammals
Cats are sentient beings, able to experience both positive and negative experiences, with an awareness to seek the positive and avoid the negative.[1] Promoting positive emotions and minimizing the negative (e.g., fear) enhances feline welfare.[11] Each cat needs to feel safe and to be able to find pleasure and comfort in their environment.[1]

The Individual Cat
A cat's individual ability to cope in different environments and situations is based on its genetics, its parents' sociability to humans, and their own experiences.[12,13] The most significant experiences occur during the sensitive period of development, between 2-9 weeks of age.[13] If a kitten is handled positively and frequently during this stage and by people of different genders and ages, including children, the cat will be more amenable to handling and less fearful of even unfamiliar people for life.[14] If instead a cat was never socialized to people early in life, it will be more fearful during veterinary visits.[14] If an individual has an adverse experience at any time, such as tight restraint, pain, or fear during a veterinary visit, it can lead to the cat becoming highly reactive at future visits.

Feline Stressors Trigger Negative Emotions and Behavioral Responses
The multiple challenges surrounding the veterinary visit trigger negative emotional responses that function to support survival. These negative emotions are fear/anxiety, frustration, and pain.[3] More than one negative emotional system can be triggered at the same time; for example, fear or anxiety can exacerbate pain, further impairing an individual's ability to cope.[15,16] Behavioral responses function to prevent altercations and are communicated by posturing, facial expressions, vocalizations, and behavior changes. Preventing stressors alleviates the cat's negative emotions and self-protective behavioral responses. When stressors cannot be prevented or when cats still demonstrate behaviors that indicate negative emotions, it is critical to identify the emotional motivation to prevent and treat the problem.[17,18]

Preventing Stressors, the Evidence, and How to Incorporate Into Practice
There are multiple stressors that surround the veterinary visit, starting and often ending at home. We can alleviate these stressors using an evidence-based approach. See **Table 2** for steps to alleviate feline stressors, with evidence and details presented here.

It Starts at Home: Carrier Training
Promoting positive emotions begins with training cats to the carrier at home.[19] Treats provided during training allow exploring or foraging for food which is part of a positive emotional motivation system. Two studies indicate why carrier training for cats is important to alleviate feline and owner distress, as well as increasing human safety. In the first, behavioral conditioning was used in laboratory cats to train them to voluntarily enter a carrier using treats.[20] The average training time was 7 subsequent once-a-day sessions (average 6-9 sessions), with gradual increases in time in the carrier and with the door closed for up to 2 minutes.[20] As the final step, cats were carried within the carriers from one area to another. Carrier and transport training, even in initially fearful cats, improved feline welfare and human safety.[20]

In the second study, cats were trained to a cat carrier and transport by car.[19] This training reduced signs of stress during transport, increased interest in food at the practice, and shortened the duration of the veterinary visit.[19] These studies demonstrate the importance encouraging and educating cat owners to train their cats to carriers.[19]

Promoting Positive and Preventing Negative Feline Senses
Cats perceive the world differently from humans. Recognizing that they have superior senses of smell and hearing can enhance development of a better practice environment. Although not as keen, visual and tactile senses are highly important in how we work with cats and will be addressed under handling.

Cat noses are about one thousand times more sensitive than ours, and cats also possess a vomeronasal organ to detect scent.[21] Treats or highly palatable cat food serve to promote positive emotions during carrier training and at the veterinary practice (note: only relaxed cats will take treats). Unfamiliar or unpleasant scents and should be minimized or completely avoided when possible. These include the smells of unfamiliar people, other companion animals, disinfectants with scent, perfumes, and rubbing alcohol.

Cats can hear both higher and lower frequencies, as well as the ultrasonic chatter of rodents, making their range

of hearing superior to most mammals, including people and dogs.[22,23] "Cat Music" has been found to decrease stress in awake cats,[24] while classical music reduced anesthetic doses when compared to all other music genres.[25] Loud noises such as phones, centrifuges, washers, dryers, human voices, and the sounds of other animals should be avoided when possible and minimized when not.

One Room/One Suite
As it takes 5-10 minutes for a cat to acclimate to a new location,[26] it is best to have the cat keep the cat in one room or kennel. For outpatients, take the cat directly from vehicle to exam room, minimizing the sights, sounds and smells of the busy practice. A concierge service is highly successful, with cat and owner remaining in a temperature-controlled vehicle until the exam room is ready, avoiding a waiting room with other pets. If not possible, have a feline-only waiting area, cover the carrier with a towel impregnated with synthetic feline pheromones (Classic), and place the carrier on an elevated surface.

Prepare the exam room with all that may be needed for the appointment prior to bringing the cat to the room. Have towels, a cat bed or other place to hide, treats, a small pet scale, and sample collection supplies in the room. As most practices do not have multiple otoscopes/ophthalmoscopes, blood pressure machines, etc., these can be carried in when the doctor +/- technician/assistant enter the room, preventing the commotion of frequent trips in and out of the exam room. If transport to another area of the practice is necessary, carry the cat within its closed and covered carrier, avoiding high traffic and noisy areas.

If hospitalization or boarding is needed, the cage or suite should be prepared with all the cat's needs prior to removing the cat from the exam room. If the cage needs minor cleaning, "spot clean" without chemicals and without disturbing the cat;[27] instructions can be found at https://www.sheltermedicine.com/library/resources/?r=spot-cleaning-cat-cages. These cats feels safer and are much more likely to positively interact with caregivers.

The Fewer People, the Better
With the following steps, most cats can be handled by the examiner alone. There should be no more than 2 handlers at most as the more people that attempt to handle a cat, the more fearful it will become. Sedation or rescheduling a preventive care appointment is recommended if the cat cannot be handled comfortably. When indicated, give sedation also in the exam room.

Safe Territory and Hiding Options
Hiding is an important coping strategy in an unfamiliar environment, and studies have proven hiding options reduce distress and negative emotions, enhancing human safety.[28-31] All cats need safe territory for survival, especially in a novel environment.[28] Options to hide should be provided during appointments, hospitalization, and boarding. Hiding options in hospital and boarding suites allows for more restful sleep and improved recovery.[20-30] Cats housed in cages are more likely to approach people and retreat less when provided a hiding option,[30] facilitating removal from the suite. Often, exams and pain scores can be done while the cat feels hidden.

Examination and completion of many procedures can also be performed with little or no assistance due to the cat's increased sense of security in its safe territory or hiding place. The handler's position to the side of the cat – and not in front – reduces threat and furthers the cat's sense of being hidden.

Hiding options that allow easy access for veterinary care include the bottom half of a hard-sided carrier, a soft-sided carrier with a large opening, a cardboard box with an opening on the side, a high-sided or igloo cat bed, and towels rolled into a donut-shape to surround a cat. The latter is an excellent choice for patients recovering from anesthesia to expedite needed care.

Why Restraint Doesn't Work and What Works Best
There are many articles that allude to the fact that cats are more reactive with physical restraint, increasing the likelihood of human injury.[32-38] Surveys indicate that injury rates are reduced for veterinary professionals in Cat Friendly Practices because of the cat-friendly environment and more gentle handling techniques.

Evidence was provided in 2018 and 2019, confirming that cats respond negatively to tight restraint when compared to passive handling techniques.[35] Tight restraint consisted of placing a cat in lateral recumbency, its' back against the holder and front and back legs held, a position that allows little to no movement. Passive or gentle handling allowed the cat to stand, sit, or lay down, with the ability to move head, body, and limbs. Odds of struggling was 8.2 times higher with tight vs. passive restraint, exams took longer with full restraint, and cats were more likely to escape after it. Body postures and behaviors indicated distress with tight restraint.[36] Additionally, cats showed aversion towards the environment where they had been tightly restrained, choosing to spend more time in the environment where they were passively handled.[35]

Another study indicated that gentle or passive handling was superior not only to tight restraint, but also to clipnosis and scruffing.[37] Tight restraint and clipnosis showed the most negative behavior responses.[37] Blinded observers reviewed videos and pictures of posturing, and identified that cats that were handled gently showed less signs of distress than with other handling techniques.[37]

Scruffing, shaking, forceful stretching, and restraint gloves lead to loss of sense of control, negative emotions, and undesirable behavioral responses, including increased potential for aggression.[3] International Cat Care has developed "Pledge to go 'scruff-free'", https://icatcare.org/our-campaigns/pledge-to-go-scruff-free/,advocating against scruffing cats as it exacerbates feline distress and potential for human injury. Fortunately, another study indicated that a complete physical examination was possible without any restraint in 76% of cats.[38]

Much of the physical examination can be done by the examiner alone. If the cat chooses to remain within the carrier, this is an ideal place to examine the cat if the carrier top can be removed or there is a wide opening to the carrier. Cats that like to sit on laps may prefer to be snuggled in the examiner's lap, facing the client or hidden within bedding.

Preferred Areas of Touch
Cats prefer human touch in the same regions that socially bonded cats groom one another to strengthen the social bond.[39,40] These regions are over the cat's facial glands that produce pheromones to communicate between members of the same species. These glands are the temporal glands between the ears and eyes where the fur is often thinner, the cheek glands, perioral glands around the corners of the mouth, and the submandibular gland in the area of the chin. Massaging, petting, or gently rubbing these areas while remaining to the side of the cat helps to reduce feline distress.

Appointment Flow
Ideally, bring the cat directly from the vehicle to the exam room and allow the cat the choice to remain in the carrier while obtaining the history. This is a great time to assess the emotional state of the cat from a distance and to think about the best options for handling this individual cat. The majority of cats prefer to remain within the carrier – even if not carrier trained – throughout the visit. Most of the examination can be done while the cat remains in the carrier and facing away from you, further alleviating feline distress and increasing accuracy of exam findings and diagnostic tests. For cats that choose to remain within the carrier, do whatever is possible there. In these cases, the cats will be weighed at the end of the examination. If the cat displays signs of fear (see below), cover the cat loosely with a towel when the carrier lid is removed for further hiding opportunity. Only remove the cat from the carrier once, thus reducing arousal. When all that needs to be done with the cat is completed, let the cat return to the carrier of it wishes prior to further client communication and education.

Allowing clients to remain with their cats during all out-patient procedures usually reduces stress for both cats and owners, and increases client appreciation and respect for the veterinary care provided in your practice. It is helpful for most cats to have the owner remain in the room minimally for the blood pressure if they do not want to observe diagnostics.[26]

The Order of the Examination
Start with what is least distressing for that individual cat, usually auscultation of heart and lungs. Most cats do best if orthopedic and oral examinations are performed at the end of the examination because these sites are more likely to be painful and cats are usually less familiar with owners touching them. If the cat has chosen to remain hidden within the carrier, the retinal exam can be done after auscultation and palpation. Only then should the cat be removed from the carrier and weighed. Move the scale covered with a towel close to the carrier. Place a treat on the towel and allow the cat to choose to go onto the scale by itself. If the cat stays in the carrier, zero the scale and gently pick up the cat only a few inches above the carrier and scale, and place on the scale. Diagnostics, starting with blood pressure, and treatments should follow. Most Cat Friendly Practices do not take temperatures in apparently healthy and awake patients. There is a wide variability between axillary and rectal temperatures, making axillary temperature measurements unreliable.[41]

Understanding and Working with Cats with Negative Emotions
Although these are called negative emotions, they have important functions to support the cat. Fear/anxiety function to ensure the individual's survival, frustration to ensure control in a solitary survivor, and pain to preserve physical comfort and body function.[17]

Fear/Anxiety

Fear and anxiety are part of the same emotional system, with the intent to ensure survival either by distancing or not interacting with perceived threat.[17] Fear responses negatively impact feline welfare and the ability to learn to new tasks.[19]
Mildly fearful cats respond with inhibition (previously called freezing). Although the inhibited cat often remaining motionless or less active, it is essential that fear not be exacerbated as the fear response will likely progress to avoidance (fleeing) or repulsion (aggression).[3]
Consider why the cat is fearful based on its genetics and previous experiences. If the fearfully inhibited cat is permitted to remain in a hiding place such as the bottom half of the carrier or high-sided cat bed, it will likely remain quiet and hidden throughout the exam, and is more amenable to handling.
If fear progresses to avoidance (fleeing), do not chase the cat, as it can rapidly escalate to self-protective repulsion (fight). Instead, provide a quiet, dark or soft-lit room with several readily accessible hiding options and leave the cat alone as highly aroused cats can take hours to calm down. Owner education, having the owner "drop off" the cat for several hours, and moving on to the next appointments to keep on schedule are helpful steps. If the cat is apparently healthy, another option is to reschedule the appointment, providing client education to prevent fear at future appointments.
If repulsion occurs, remember that the cat is not 'bad' or 'evil', but rather frightened and attempting to protect itself. Sedation or anesthesia with analgesia should be administered to prevent potential injury and exacerbated feline fear and anxiety at future visits.

The client should be educated to carrier training their cat and to bring familiar and favorite items to future visits if not done previously. Recommend anxiolytics for future appointments at least until the cat does not associate visits with fear. Remind owners to keep the cat within the carrier with the door closed at subsequent appointments and to let veterinary professionals remove the cat from the carrier.

Frustration
Frustration is the inability to be in control, to access safety, or receiving less or no reward than anticipated.[42] It is seen in two different situations, the first as a kitten or cat receiving less attention or reward than anticipated, such as in a caged cat pawing through a kennel door for food, play, or attention.[43] The second is inability to control and access safety, such as with tight restraint or when taking a cat out of a cage.[42] In these situations, fear and frustration often occur concurrently, and frustration intensifies and accelerates behavior responses to aggression.[17]

Reduce frustration by letting out a cat pawing at a carrier, and provide consistent and predictable attention and feedings to cats pawing or pacing in a kennel. Use only gentle and respectful handling instead of tight restraint to prevent fear and frustration. For cats housed at the practice, place hiding options in kennels, and remove cats from the kennel within the hiding option. Some cats never do well in the confinement of a kennel, but do not show frustration if placed in a small room (e.g., isolation room) with perch and hiding place. When these recommendations are followed, sedation and anesthesia are rarely indicated.

Pain
Pain is both a sensory and an emotional response, impacting not only physical function but also the emotional welfare of the patient.[44] The emotional system of pain is motivated to preserve physical comfort and body function.[17]

Degenerative joint disease (arthritis), lower urinary tract disease and periodontal disease are well-recognized painful and chronic conditions in cats. Since fear/anxiety can exacerbate pain, resolution includes both minimizing stressors and administering analgesia.[45]

As signs of pain are often subtle and chronic pain in common, handle each cat as potentially painful. Analgesia should be given to painful and potentially painful cats either at home for cats with chronic painful conditions or during appointments when pain is noted. Dermatologic conditions, including pruritis, are painful. Procedures such as holding for radiographs and anal sac expression also require analgesia. The reader is referred to the AAFP Feline Anesthesia Guidelines for more specific information on sedation and anesthesia, and the 2015 AAHA/AAFP Pain Management Guidelines for Dogs and Cats to help recognize painful conditions.[46]

Pharmacological Treatments
Pharmacotherapy can significantly lessen a cat's distress when indicated, but does not replace a cat-friendly environment and feline-friendly handling. When making decisions about pharmacotherapy, we must recognize the emotional motivation for observed behaviors. Anxiolytics should be given to fearful cats, analgesia to painful cats, and cats with frustration may need both depending on the source of frustration.

Anxiolytic Prior to Veterinary Visit – Who Needs It and What to Give
Gabapentin has been proven to be an excellent anxiolytic in cats, and more effective than other pharmacologic

agents or nutracueticals.[47,48] Studies demonstrate that the lowest cat stress scores are at 2-3 hours.[47,48] In practice, the general dose is 20mg/kg or 100mg/cat, but some cats become very sedated.[48] Gabapentin is renally excreted and it is questioned whether the dose should be decreased by 50% in cats with chronic kidney disease.[49] Gabapentin comes in 100mg capsules, and the capsule can be opened and the tasteless powder mixed into canned food. It does not work transdermally.[50] Cats that have had a negative experience previously at the veterinary practice benefit from a combination of carrier training and gabapentin at future visit(s). Additionally, cats born to feral parents, those not socialized to people during the sensitive period, or that have had a bad experience at any time in life - even if not associated with veterinary visits – are good candidates to receive gabapentin prior to veterinary visits. It should be given at home, 2-3 hours in advance of transport as it is not effective if a cat is already aroused. It can be given before outpatient appointments or admittance for procedures including anesthesia or boarding. Gabapentin can be given with other agents, including trazadone, lorazepam, and Zylkene.

Sedation

There is less need for sedation when cats are given gabapentin prior to veterinary visits and handled respectfully. Sedation is indicated if a cat cannot be respectfully and safely handled with a maximum of 2 people, if the cat is struggling, hissing, lunging or showing or protective signs. Anesthesia is also necessary for some patients; often the preference for an apparently healthy cat is to reschedule the appointment, combining an examination with a needed procedure (e.g., dental prophylaxis). In these cases, send home a prescription of gabapentin and advice on carrier training.

Benefits of sedation for examination of certain patients and for procedures include less physical restraint, decreased stress, simpler airway management, avoidance of inhalants and rapid recovery.[51] Good feline sedation options are dexmedetomidine and alfaxalone, usually in combination with other drugs such as opioids for analgesia. Alfaxalone (2mg/kg) is apparently safer in cardiac disease, and occult heart disease is not uncommon in cats. This information has not been confirmed in cats with hypertrophic cardiomyopathy, but is based on studies in healthy cats indicating no change in echocardiographic measurements with alfaxalone,[52] whereas dexmedetomidine may cause decreased heart rate, increased blood pressure, and echocardiographic changes of both atrial and ventricular size and function.[51, 53]

Butorphanol provided superior sedation and a lower incidence of vomiting than buprenorphine when given intramuscularly in combination with dexmedetomidine.[54] For more information, see the 2018 AAFP Anesthesia Guidelines.

Conclusion

Feline-friendly handling techniques prevent feline stressors, subsequently reducing the negative emotions and behaviors that team members often consider difficult.

Table 1. Recognizing the behavioral response to negative emotions helps recognize when different methods for handling and working with cats are important.

Body Postures	Facial Expressions	Inhibition of normal behaviors
Hiding Crouched Head lower than rest of body In the back of the carrier or cage Tense muscles Hypervigilant Piloerection Trembling Sweaty paws Unsheathing claws Swatting Lunging	Dilated or oblong pupils Pupils fixated on the subject Ears held back or rotated to the side Whiskers splayed out Lip licking Rapid blinking Drooling Mouth open – hissing, shrieking	Inappetence or not eating Failure to groom Failure to eliminate Lack of play behavior Failure to sleep - Hypervigilant - Feigned sleep

Table 2. Reducing feline stressors surrounding veterinary visits reduces negative emotions and associated behaviors. These steps in order include:

- It starts at home: Carrier training
- Promoting positive and preventing negative feline senses
- One room/one suite
- The fewer people, the better
- Safe territory and hiding options
- Why restraint doesn't work and what works best
- Preferred areas of touch

- Appointment flow
- Order of examination

References

1. Ryan S, Bacon H, Endenburg N, et al. WSAVA Animal Welfare Guidelines 2018, J Small Anim Pract 2019 May;60(5):E1-E46.
2. Driscoll CA, Macdonald DW, O'Brien SJ. From wild animals to domestic pets, an evolutionary view of domestication. Proc Natl Acad Sci USA 2009 Jun 16;106 Suppl 1:9971-8.
3. Panksepp J. Affective neuroscience: the foundations of human and animal emotions. New York: Oxford University Press; 1998.
4. Dawson LC, Dewey CE, Stone EA. A survey of animal welfare experts and practicing veterinarians to identify and explore key factors thought to influence canine and feline welfare in relation to veterinary care. Anim Welf 2016; 25:125–134.
5. Mariti, C., Bowen, J.E., Campa, S., Grebe, G., Sighieri, C., 2016. Guardians' perceptions of cats' welfare and behaviour regarding visiting veterinary clinics. J. Appl. Anim. Welf. Sci. 19 (4), 375–384.
6. Mars PetCare 2018
7. 2017-18 edition of the AVMA Pet Ownership and Demographics Sourcebook
8. Fiset S, Dore FY. Duration of cats' (Felis catus) working memory for disappearing objects. Anim Cogn 2006; 9:62–7.
9. Vitale Shreve KR, Udell MA. What's inside your cat's head? A review of cat (Felis sylvestris catus) cognition research past, present and future. Anim Cogn 2015;18(6):1195-206.
10. Nibblett BM, Ketzis JK, Grigg EK 2015. Comparison of stress exhibited by cats examined in a clinic versus a home setting. Appl Anim Behav Sci 173, 68-75.
11. Mellor DH. Updating Animal Welfare Thinking: Moving beyond the "Five Freedoms: towards "A Life Worth Living". Animals (Basel) 2016 Mar 14;6(3).
12. Stella J, Croney C. Coping Styles in the Domestic Cat (Felis silvestris catus) and Implications for Cat Welfare. Animals (Basel) 2019 Jun 18;9(6).
13. Karsh EB, Turner DC. The human–cat relationship. In: Turner DC, Bateson P, eds. The domestic cat: the biology of its behaviour. 1st ed. Cambridge, UK: Cambridge University Press; 1988:159–177.
14. Casey RA, Bradshaw JWS. The effects of additional socialisation for kittens in a rescue centre on their behavior and suitability as a pet. Appl Anim Behav Sci 2008; 114:196-205.
15. Hellyer P, Rodan I, Brunt J. AAHA/AAFP pain management guidelines for dogs and cats. J Feline Med Surg 2007; 9:466–480.
16. Khasar SG, Burkham J, Dina A, et al. Stress induces a switch of intracellular signaling in sensory neurons in a model of generalized pain. J Neurosci 2008; 28: 5721–5730.
17. Heath S. understanding Feline emotions... and their role in problem behaviours. J Feline Med Surg (2018) 20, 437–444.
18. Ellis SLH. Recognising and assessing feline emotions during the consultation: History, body language and behavior. J Feline Med Surg (2018) 20, 445–456.
19. Gruen ME, Thomson A, Clary G, et al. Conditioning Laboratory Cats to Handling and Transport. Lab Anim (NY). 2013 Oct; 42(10): 385–389.
20. Pratsch, L, Mohr N, Palme R, et al. Carrier training cats reduces stress on transport to a veterinary practice. Appl Anim Behav Sci 2018; 206: 64-74.
21. Bradshaw J. Normal feline behaviours... and why problem behaviours develop. J Feline Med Surg 2018 May;20(5):411-421.
22. Heffner RS, Heffner HE. Hearing range of the domestic cat. Hear Res 1985; 19(1):85-8.
23. Ramsier MA, Cunningham AJ, Moritz GL. Primate communication in the pure ultrasound. Biol Lett 2012; 8(4):508-11.
24. Hampton A, Ford A, Cox RE 3rd, et al. Effects of music on behavior and physiological stress response of domestic cats in a veterinary clinic. J Feline Med Surg. 2019 Feb 12
25. Mira F, Costa A, Mendes E. A pilot study exploring the effects of musical genres on the depth of general anesthesia assessed by haemodynamic responses. J Feline Med Surg 2016; 8:673–678.
26. Sparkes AH, Caney SM, King MC, et al. Inter- and intra-individual variation in Doppler ultrasonic indirect blood pressure measurements in healthy cats. J Vet Intern Med 1999; 13: 314–318.
27. Newbury S, Blinn MK, Bushby PK, et al. Guidelines for Standards of Care in Animal Shelters, 2010, Association of Shelter Veterinarians. Medical Health and Physical Well-Being; pp. 18–25.
28. Carlstead K, Brown JL, Strawn W. Behavioral and physiological correlates of stress in laboratory cats. Appl Anim Behav Sci 1993; 38:143–158.
29. Kry K, Casey R. The effect of hiding enrichment on stress levels and behaviour of domestic cats (Felis sylvestris catus) in a shelter setting and the implications for adoption potential. Anim Welf 2007;16(3):375– 383.
30. Vinke CM, Godijn LM, van der Leij WJR. Will a hiding box provide stress reduction for shelter cats? Appl Animal Behav Sci 2014; 160:86–93.
31. Ellis JJ, Stryhn H, Spears J. Environmental enrichment choices of shelter cats. Behav Processes 2017;141(3):291-296.
32. Fritschi L, Day L, Shiragni A, et al, Injury in Australian veterinarians, Occupational Medicine 2006;56:199–203.
33. Employee Injury Trends at Veterinary Practices, AVMA PLIT safety bulletin, Vol.15, No. 3, Summer 2007.
34. Rodan I, Sundahl E, Carney H, et al. AAFP and ISFM feline-friendly handling guidelines. J Feline Med Surg 2011;13:364–75.
35. Moody CM, Mason GJ, Dewey CE, et al. Testing two behavioural paradigms for measuring post-handling cat aversion behavior. Appl Anim Behav Sci 2019:210:73-80.
36. Moody CM, Picketts VA, Mason GJ, et al. Can you handle it? Validating negative responses to restraint in cats. Appl

Anim Behav Sci 2018;204:94-100.
37. Moody CM, Mason GJ, Dewey CE, Niel L. Getting a grip: cats respond negatively to scruffing and clips. Vet Record, Vet Rec 2020 Mar 28;186(12):385.
38. Glardon OJ, Hartnack, Horisberger. Analyse du comportement des chiens et des chats pendant l'examen physique en cabinet vétérinaire. Schweizer Archiv für Tierheilkunde (2010), 152, 69-75.
39. Ellis SLH, Thompson H, Guijarro C, et al: The influence of body region, handler familiarity and order of region handled on the domestic cat's response to being stroked. Appl Anim Behav Sci 2015; 173: 60-67.
40. Soennichsen S, Chamove AS. Responses of cats to petting by humans. Anthrozoos 2002; 15: 258–265.
41. Goic JB, Reineke EL, Drobatz KJ. Temperature measurement in dogs and cats. J Am Vet Med Assoc 2014 May 15; 244c(10): 1170-5.
42. Panksepp J, Wright JS, D€obr€ossy MD, Schlaepfer TE, Coenen VA. Affective neuroscience strategies for understanding and treating depression from preclinical models to three novel therapeutics. Clin Psychol Sci. 2014;2:472–494.
43. Gourkow N, Fraser D. The effect of housing and handling practices on the welfare, behaviour and selection of domestic cats (Felis sylvestris catus) by adopters in an animal shelter. Anim Welfare 2006; 15: 371–377.
44. Reid J, Scott M, Nolan A, Wiseman-Orr L. Pain assessment in animals. In Pract. 2013; 35:51–56.
45. Mathews K, Kronen PW, Lascelles D, et al. WSAVA Guidelines for recognition, assessment, and treatment of pain. J Small Anim Pract 2014: 55: E10-68.
46. Epstein ME, Rodan I, Griffenhagen G, et al. AAHA/AAFP pain management guidelines for dogs and cats. J Feline Med Surg 2015; 17: 251–272.
47. Pankratz KE, Ferris KK, Griffith EH, et al. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined community cats: a double-blind, placebo-controlled field trial. J Feline Med Surg, 2017.
48. van Haaften KA, Forsythe LRE, Stelow E A, et al. (2017). Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. J Am Vet Med Assoc. 251(10), 1175–1181.
49. Denenberg S, Dubé MB. Tools for managing feline problem behaviours. J Feline Med Surg, 2018:20, 1034-1045.
50. Arian D, Papich MG, Baynes R, et al. The pharmacokinetics of gabapentin in cats. J Vet Intern Med 2018 Nov;32(6):1996-2002.
51. Robertson SA, Gogolski SM, et al. AAFP Feline Anesthesia Guidelines. Feline Med Surg (2018) 20, 602–634.
52. Ribas T, Bublot I, Junot S, et al. Effects of intramuscular sedation with alfaxalone and butorphanol on echocardiographic measurements in healthy cats. J Feline Med Surg 2015; 17: 530–536.
53. Johard E, Tidholm A, Ljungvall I, et al. Effects of sedation with dexmedetomidine and buprenorphine on echocardiographic variables, blood pressure and heart rate in healthy cats. J Feline Med Surg 2018; 20: 554–562.
54. Bhalla RJ, Trimble TA, Leece EA, Vettorato E. Comparison of intramuscular butorphanol and buprenorphine combined with dexmedetomidine for sedation in cats. J Feline Med Surg 2018 Apr;20(4):325-331.

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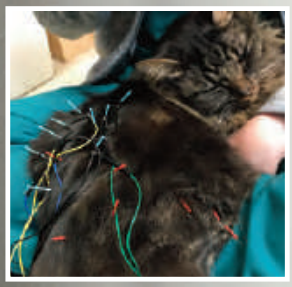

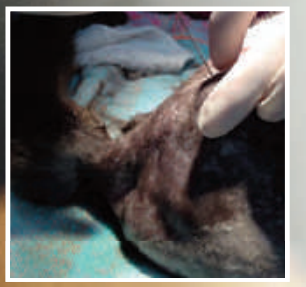

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