ALLERGIES TO CATS A ONE HEALTH PERSPECTIVE

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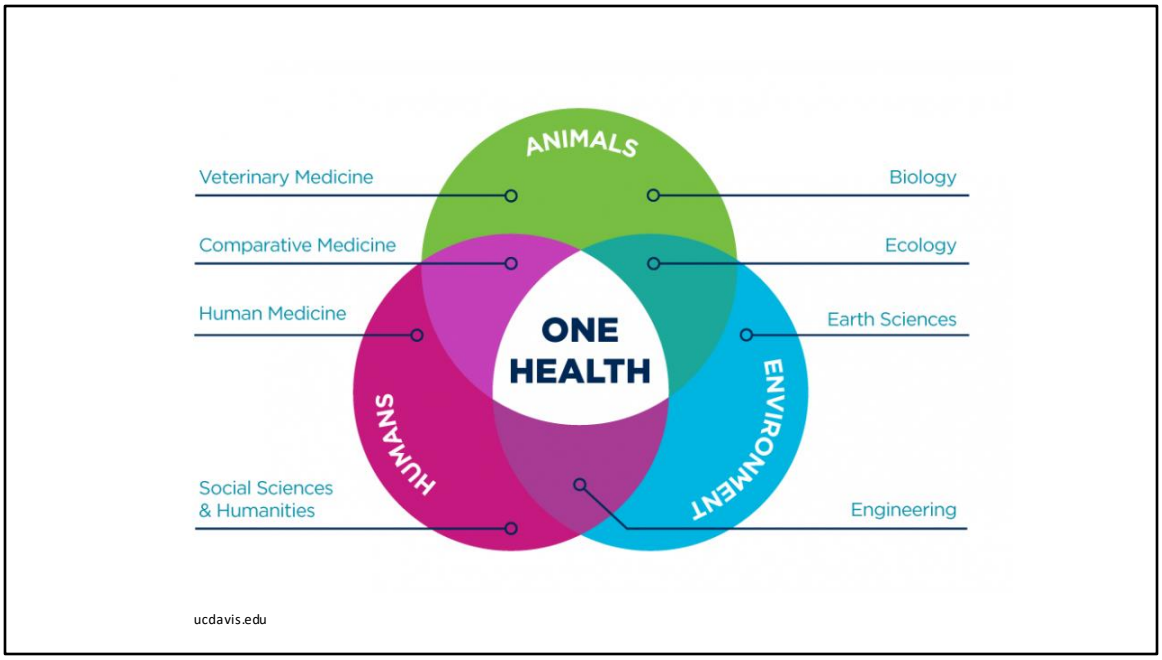
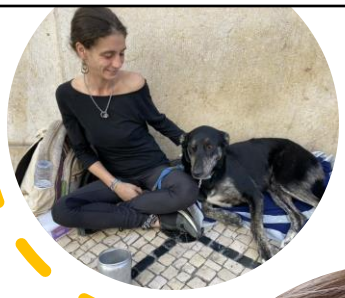


One Health exemplifies how different professions intersect and collaborate to achieve the mission of improving animal and human health.

Human-Animal Bond

- "A mutually beneficial and dynamic relationship between people and animals that is influenced by behaviors that are essential to the health and well-being of both." (AVMA 2016)
- Biophilia hypothesis: humans possess an innate tendency to seek connections with nature and other forms of life
- ~60% of US population has a household pet
- Approx. $30 billion spent on pet food, $20 billion on veterinary care in US
- Secondary (or primary) "family" members
- ~20% of US households adopted pets during the pandemic



Pet Companionship

Positives:

- Companionship
- Reduces loneliness
- Provides unconditional love
- Reduces stress and anxiety
- Teaches responsibility
- Improves physical and emotional health
- **Reduced risk of allergies and eczema in children**

Negatives:

- Maintenance
- Expense
- Property damage
- Time constraints
- Zoonoses
- Bites
- **Allergies**

FIG 1. Percentage of people living with pets (Growth from Knowledge survey of >27,000 internet users in 22 countries).[10]

Schoos A-MM, Nwaru BI, Borres MP. *J Allergy Clin Immunol.* 2021;147:1164-73.

Allergic Disease

IgE-mediated immune response (hypersensitivity reaction) to environmental allergens following sensitization →

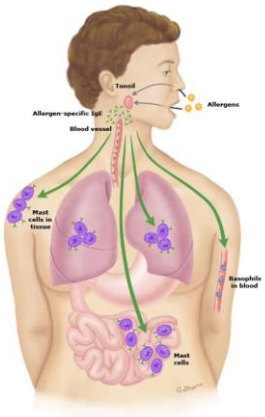
- Rhinitis/sinusitis
  - Rhinorrhea, nasal obstruction, cough, itching, fatigue, sleep disruption
- Allergic conjunctivitis
  - Bilateral itching, tearing, and/or burning of the eyes
- Eczema
  - Intensely itchy erythematous patches involving scalp, extremities, or trunk
- Asthma
- Food allergies
- Anaphylaxis

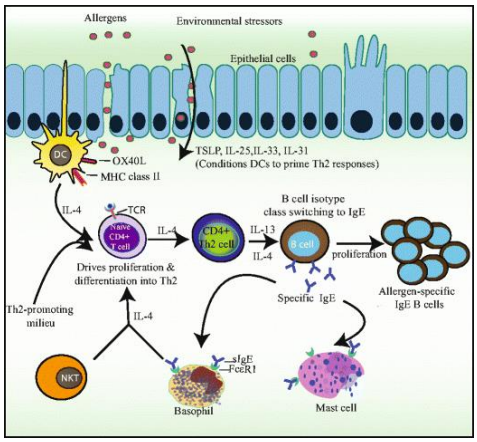
Allergic Disease

- Asthma prevalence among youth in US has tripled and food allergies have doubled since 1970s
- Genetic evolution unlikely explanation for this increase
- Possible explanations:
  - Urbanization → ↑ indoor allergen exposure
  - Increasing use of antibiotics → change in microbiome
  - Global warming → longer and more intense exposure to allergens (e.g., pollens)
  - Hygiene hypothesis – less exposure to viruses, bacteria, helminths → ↓type 1, ↑type 2 immune response → atopy and auto-immune diseases
- Possible role of epigenetic change (DNA methylation, histone modification, non-coding RNA-associated gene splicing)

Asthma prevalence has been steadily increasing worldwide and there isn't a singular explanation of why this is happening--it appears to be multifactorial.

Allergic Sensitization

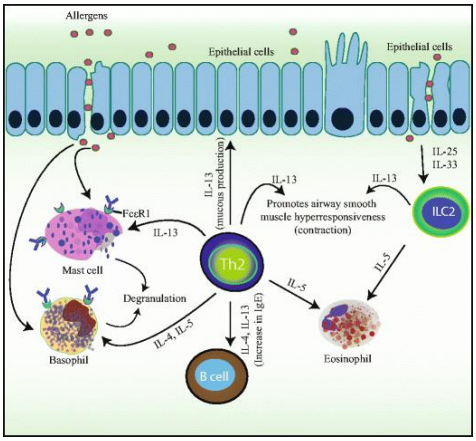




Sinder SB, et al. *Clinic Rev Allerg Immunol* 2018;55:190-204.

Mucosal dendritic cells capture allergen and transport to the lymph nodes.
Within LNs, allergen-specific T 2 helper cells proliferate and produce Interleukin-4 and IL-13 favoring B cell isotype class switching.
A memory pool of allergen-specific B and Th2 cells are generated.

Allergic Response

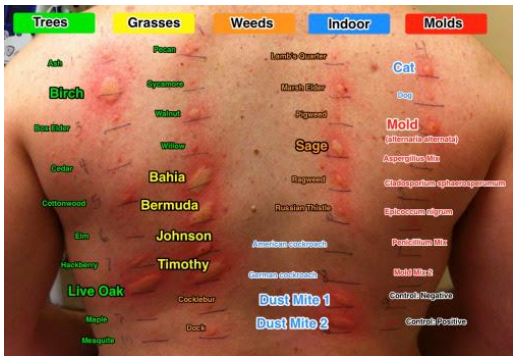


Sinder SB, et al. *Clinic Rev Allerg Immunol* 2018;55:190-204.

Previously sensitized allergens lead to IgE cross-linking on and activation of basophils and mast cells causing degranulation and release of histamine, proteases, prostaglandins, leukotrienes and cytokines. Allergen-specific Th2 cells are activated and produce IL-4, IL-5 and IL-13 which maintain allergen-specific IgE levels, eosinophilia, mucus production and recruitment of inflammatory cells.

Diagnosing Allergies

- **Skin prick tests:**
  - inexpensive, simple, and quick to perform but standardization is difficult
- **Serum-specific IgE**
  - Used when patient's symptoms and skin test results are contradictory
  - Expensive
- **Sensitization ≠ Allergic disease**
- **Allergic disease** = Allergen-specific IgE + symptoms upon exposure



Sensitization means IgE antibodies are generated in response to an environmental allergen, but that doesn't necessarily mean that someone will develop allergic symptoms.

Cat Allergens

TABLE 1 Human sensitization rates to feline-origin allergens. (Excerpted from EAACI Molecular Allergology User's Guide, 2016.)

Allergen	Biochemical name	Human sensitization rate
Fel d1	Uteroglobin	60%-100%
Fel d2	Serum albumin	14%-54%
Fel d3	Cystatin	10%
Fel d4	Lipocalin	63%
Fel d5	Immunoglobulin A	38%
Fel d6	Immunoglobulin M	unknown
Fel d7	Lipocalin	38%
Fel d8	Latherin-like protein	19%

Satyaraj E, Wedner HJ, Bousquet J. *Allergy* 2019;74 (Suppl. 107):5-17.

Fel d1 is the most important feline allergen in humans.

Fel d 1

- 35-38 kDa glycoprotein - 2 identical heterodimers
- Major allergen of domestic cats
- Biological function unknown
- Salivary and sebaceous glands are the main production sites
- Cat grooming behavior spreads Fel d 1 to skin, fur, and the environment
- Uncastrated males > castrated males > females
- Adult cats > kittens; younger cats > older cats
- Coat color and hair length do not matter
- Head > chest
- Up to 80-fold difference in salivary Fel d 1 levels among individual cats
- There are no hypoallergenic breeds (? Siberian, Siamese, Bengal, Sphynx)
- Found in 99% of US homes; also in classrooms, cars, stores, and planes
- Lightweight and sticky
- 60% of airborne Fel d 1 sticks to small respirable particles, which are inhaled

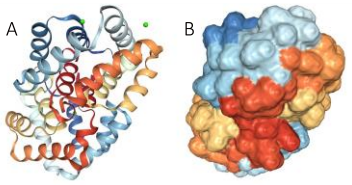


FIGURE 2 Fel d 1 crystalline (A) and three-dimensional (B) structures, showing four subunits composed of two covalently linked heterodimers containing two distinct chains. From https://www.rcsb.org/structure/2EJN, open source image [Color figure can be viewed at wileyonlinelibrary.com]
Satyaraj E, Wedner HJ, Bousquet J. *Allergy* 2019;74 (Suppl. 107):5-17.

- People become exposed to Fel d1 because it is so prevalent in the environment, and its small size makes it easy to inhale.
- Fel d1 can remain in the environment for prolonged periods.
- Major allergen of domestic cats. Anti-Fel d 1 specific IgE found in serum of 80-95% of patients allergic to cats
- The biological function of Fel d 1 is unknown.
    - ? transport of steroids, hormones, or pheromones
- While washing cats reduces Fel d 1 on skin and fur. The levels return to baseline in two days.

Cats and Allergies

- Allergic sensitization to cat allergens
  - Presence of Fel d 1-specific serum IgE antibodies
  - 10-25% of patients are sensitized to cat allergens in allergy clinic-based studies
  - 5.5x increase between 1970s and 1990s
  - 95% of cat-allergic patients produce IgE to Fel d 1
- Anti-Fel d 1-specific IgE levels correlate with severity of allergic symptoms
- Threshold for symptoms: 8 µg Fel d 1/g of dust (typical house levels: 10-1000 Fel d 1 µg/g of dust)
- ~30% of asthma attacks attributable to cat allergen exposure in sensitized subjects
- One of the main reasons why owners abandon cats to shelters
- Most cat-allergic people with asthma are sensitized to cats but do not live with cats
- Children living in a house with a cat are **less** likely to be sensitized to cat allergens
- Highest levels of cat exposure → decreased sensitization
- Living with a cat → cat-specific tolerance
  - IgG Abs to Fel d 1 increase as level of cat allergen exposure increases
  - Increased IgG_4 levels are associated with decreased symptoms
  - Similar response as immunotherapy
- Similar findings not seen with allergies to dust mites and cockroaches

- Sensitization from prior exposure to cats primes the pump in individuals who have allergic disease so when they become exposed to more cats, or to Fel d1, they develop allergic symptoms.
- Allergies is one of the main reasons people relinquish cats to shelters. However, if they want to keep their cat and their doctor says get rid of the cat because of allergies, people often change doctors.

Asthma: Overview

- Most potentially dangerous complication of cat allergies in humans
- A heterogeneous disease characterized by airway inflammation (eosinophils, neutrophils, lymphocytes) → variable airflow limitation and hyperresponsiveness on spirometry
- Defined by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough that varies over time and intensity
- Can occur at any age
- Some patients can develop persistent airway structure changes with smooth muscle hypertrophy, sub-basement membrane fibrosis and chronic mucus hypersecretion

Asthma is an increasingly common problem, with 8% of the population clinically affected. Cat allergies are a known asthma trigger, and in very reactive people can cause significant disease.

Asthma: Epidemiology

- Prevalence
  - ~240 million worldwide
  - Prevalence varies among countries:
    - ~8% in US (M>F in children, F>M in adults, Black>White)

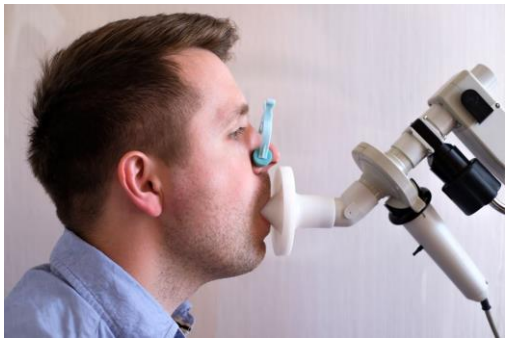
- Increasing prevalence since 1970s
  - Increased clinician and public awareness
  - Increased risk factors:
    - Obesity
    - Tobacco smoke exposure
    - Low vitamin D levels
    - Urbanization → exposure to air pollution and indoor allergens

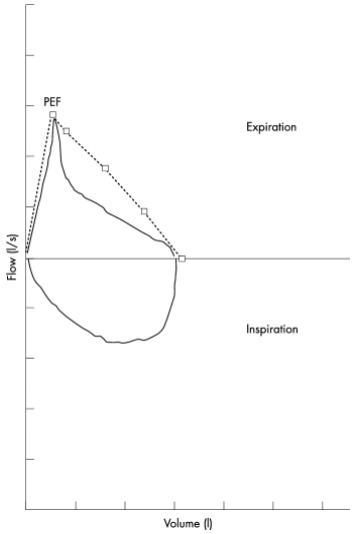
Asthma: Diagnosis

- Symptoms: Episodic wheezing, cough, shortness of breath, chest tightness
- Triggers: Exercise, cold air, **allergens**, tobacco smoke, occupational exposure, air pollution, respiratory infections, aspirin
- Personal or family history of atopy
- History of asthmatic symptoms as a child
- Spirometry: >10% improvement in airflow with administration of short-acting bronchodilator **OR** >20% decrease in airflow with administration of a bronchoconstrictor (methacholine, mannitol)
- Increased eosinophils on bronchial washings
- Fractional exhaled nitric oxide (FeNO)

Asthma: Triggers

- Allergies--including cat exposure
- Occupational exposures
- Air pollution
- Smoking
- Exercise (esp. in cold air)
- Viral, bacterial, and parasitic infections
- Stress
- Medications (Aspirin, beta-blockers)





This is an example of spirometry, used to diagnose asthma in humans. The chart shows a flow-volume loop that illustrates airflow obstruction seen in asthma.

Asthma Phenotypes

Phenotype-Specific Asthma Therapeutic Targeting

Presentation	Phenotype	Therapeutic intervention
Noneosinophilic	Paucigranulocytic/ Neutrophilic	IL-17 antagonists Macrolide antibiotics, methotrexate, phosphodiesterase IV inhibitors
Eosinophilic	Allergen exacerbated	Allergen avoidance immunotherapy anti-IgE IL-4 antagonists IL-13 antagonists IL-4/IL-13 dual antagonists
	Idiopathic eosinophilic	Corticosteroids IL-5/IL-5 receptor antagonists
	Aspirin-exacerbated respiratory disease	Leukotriene modifiers Aspirin desensitization

Abbreviation: IL, interleukin; IV, intravenous.

Borish L. Ann Allergy Asthma Immunol 2016;117:108-114.

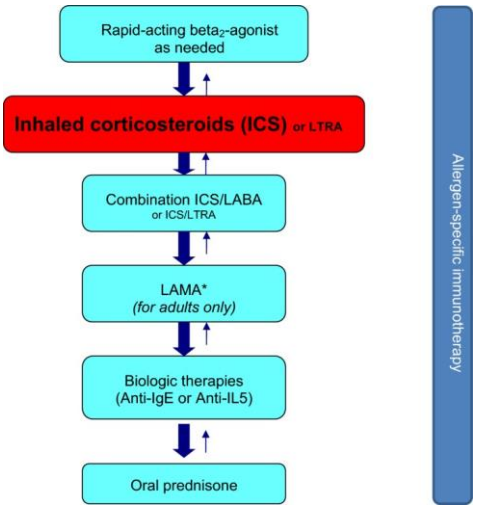
Allergic asthma is eosinophilic, but asthma can also be triggered by non-allergic inflammation, such as with air pollution, medications, or stress.

Not Everyone Who Wheezes has Asthma

- Can be mistaken for asthma:
  - Chronic obstructive pulmonary disease
  - Bronchitis
  - Heart disease
  - Vocal cord dysfunction
  - Gastroesophageal reflux
  - Subglottic stenosis and upper airway tumors
  - Factitious asthma

Factitious asthma is caused by emotional stresses that result in abnormal closure of the vocal cords.

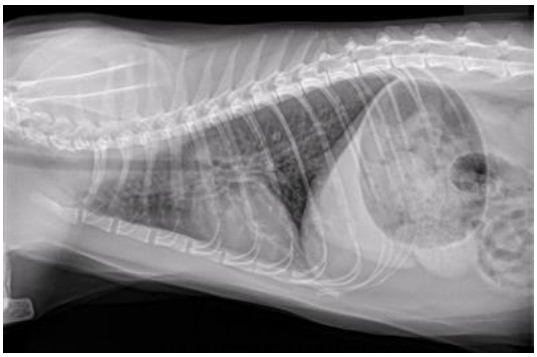
Asthma Treatment



Allergy Asthma Clin Immunol. 2018; 14(Suppl 2): 50.

Asthma treatment uses a step-wise escalation of medications based on symptom response. This ladder starts at the top and works down--treatment can also be de-escalated if asthma symptoms are stable.

Asthma: Cat vs. Human



In veterinary medicine, there are significant radiographic airway changes that are usually not present with human asthma, which implies that feline asthma may actually be better characterized as eosinophilic pneumonia. Human eosinophilic pneumonia is an allergic disease with marked radiographic abnormalities.

If you have allergies, the longer you live with your cats the better your symptoms (and life!) will be!

Stay tuned for
Allergies to Cats –
A One Health Perspective
Part 2 in the
January 2024 CFP Newsletter