AEROALLERGENS

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Richard W. Weber, M.D. Disclosures

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COMMON BIOLOGIC AEROALLERGEN SOURCES

<table>
<thead>
<tr>
<th>Allergen Source</th>
<th>Particle Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td>Cells, fragments, metabolites</td>
</tr>
<tr>
<td>Thermophilic actinomycetes</td>
<td>Spores, metabolites</td>
</tr>
<tr>
<td>Algae</td>
<td>Cells, fragments, metabolites</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Metabolites</td>
</tr>
<tr>
<td>Fungi</td>
<td>Spores, mycelial fragments</td>
</tr>
<tr>
<td>Ferns &amp; mosses</td>
<td>Spores</td>
</tr>
<tr>
<td>Grasses, weeds, &amp; trees</td>
<td>Pollens</td>
</tr>
<tr>
<td>Arthropods</td>
<td>Feces, saliva, body parts</td>
</tr>
<tr>
<td>Birds</td>
<td>Feces, epidermal debris</td>
</tr>
<tr>
<td>Mammals</td>
<td>Dander, saliva, urine</td>
</tr>
</tbody>
</table>

(Burge HA, 1992)
Principles of Pollen Aerobiology

- Characteristics of Wind Pollinated Plants
  - Incomplete flowers (spatially separate male & female)
  - Male flowers exposed to wind
  - Petals & sepals insignificant or absent
  - Absent attractants (color, aroma, nectar)
  - Pollen grains small & dry, reduced ornamentation
Principles of Pollen Aerobiology

- Thommen’s Postulates (Thommen AA, 1930)
  - Pollen must contain excitant of hay fever
  - Pollen must be anemophilous
  - Pollen must be produced in sufficiently large amounts
  - Pollen must be buoyant to carry long distances
  - Plant must be widely & abundantly distributed

Principles of Pollen Dispersal

- Settling velocity versus wind velocity
- Settling velocity of spherical objects in size range of pollen (20-40 μm) is proportional to diameter & density: 2-6 cm/sec
- Average wind velocities 1-10 m/sec
- Capture of pollen grains @ sea:
  - Sauk – 300 miles from land
  - Erdtman 750 km from land
- Raindrop scavenging – proportional to droplet velocity & inversely to droplet size – light drizzle better than short heavy downpour
Respirable Pollen Grain Particles

- Airborne ragweed allergen on <5μm particles detected on volumetric samplers during and after season (Busse et al. JACI 1972;50:289-93; Habenicht et al. JACI 1984;74:64-7)
- Grass pollen starch granules (0.12-4.67μm) released with cycle of wetting, drying, & wind, containing Group 1 allergen (Taylor et al. JACI 2002;109:51-6)

Respirable Pollen Grain Particles

- Birch pollen cytoplasm fragments (0.03-4μm) released with cycle of wetting, drying, & wind, containing Bet v 1 allergen (Taylor et al. Clin Exp Allergy 2004;34:1591-6)
- Massive release cytoplasmic material coated with group 13 (polygalacturonase) allergens with exposure grass pollens (Phleum) to rainwater (Swoboda et al. J Immunol 2004;172:6490-6500)
- Ragweed pollen releases 0.5-4.5μm granules containing Amb a 1 & NAD(P)H oxidase (Bacsi et al JACI 2006;118:844-50)

Respirable Pollen Grain Particles

- Cytoplasmic particles 0.5-4.5μm release demonstrated in following pollens
  - Perennial ryegrass
  - Timothy grass
  - Birch
  - Short ragweed
  - Redroot pigweed
Augmentation of Pollen-induced Allergic Inflammation

- Adjuvant role of diesel exhaust particles in allergen sensitization
  - Relationship of truck traffic & pollen sensitization in schoolchildren. (Janssen et al. Environ Health Prespect 2003;111:1512-8)
- Pollens contain intrinsic NADPH oxidase, increasing reactive oxygen species (ROS) & products of oxidative stress (GSSG, 4-HNE); recruitment of PMNs, mucin production. (Boldogh et al. J Clin Invest 2005;115:2169-79)


- Methods
  - Asthma admissions in 14 regional health authorities (RHAs) in England for 2 age groups: 0-14yrs, & >15yrs
  - Thunderstorms measured daily in each RHA using density of lightning flashes (sferics)
  - Grass pollen counts available in 5 RHAs
  - Relative asthma excesses for moderate & exceptionally high sferic densities measured using log linear autoregression, pooled over RHAs with geometric means

- Results
  - Exceptional sferic densities associated with relative excess risk of ~25% in both age groups
  - Moderate sferic densities with slight excess, significant only with both groups together
  - High grass pollen counts for previous 5 days amplified the thunderstorm excess asthma risk: 16% excess asthma in children & ~50% in adults; with high sferic density, there was an estimated 45% increase in children & a near doubling in adults
Thunderstorm outflows preceding epidemics of asthma during spring and summer. Marks GB et al: Thorax 2001;56:468-71

- **Methods**
  - Case control study in 6 towns in SE Australia
  - Epidemic case days (n=48) & control days (n=191) delta observed & expected asthma visits
  - Thunderstorms & associated cold fronts and outflows (pollen concentrated in shallow band of air)
  - Hourly pollen count relation with one severe asthma epidemic

- **Results**
  - Outflows detected in 33% of epidemic days & 3% of control days, OR 15.0 (CI 6.0-37.6)
  - Association strongest in late spring and summer
  - Onset of one severe asthma epidemic coincided with arrival of thunderstorm outflow & 4-10 fold increase in grass pollen concentration
Outdoor Mold Exposure

- Prevalent on dry, windy days (especially grasslands & grain fields)
  - *Alternaria* & *Cladosporium*
- Prevalent at night and humid, rainy days
  - Ascospores
  - Basidiospores (mushrooms, puffballs, rusts, smuts)
- Counts increased with temperature, decreased with relative humidity, rainfall; rural > urban
  - *Alternaria*, *Cladosporium*, *Epicoccum*, *Torula*

MOLD SPORES: Impact on PFT, Asthma morbidity & mortality

- High basidiospore counts correlated with:
  - medication use & nocturnal awakenings in NZ
    (Epton et al. Thorax1997;52:528-34)
  - New Orleans asthma
    (Salvaggio et al. JACI 1971;48:96-114)
- *Cladosporium* +10,000/m$^3$ = PEFR -1.0L/min; *Epicoccum* +60/m$^3$ = -1.5L/min & increased AM cough OR 1.8.

- Chicago asthma deaths correlated with mold spore counts: molds >1000p/m$^3$ OR 2.16, each rise of 1000 p/m$^3$ increased risk 20%.
  (Targonski et al. JACI 1995;95:955-61)
- Fatal or near fatal asthma coincided with *Alternaria* season in Minnesota
- *Alternaria* counts correlated with mean monthly asthma medication score (r=0.599, p=0.04), PEFR (r=0.737, p=0.006), FEF_{25-75} (r=0.914, p=0.0001), & PEF variation (r=0.901, p=0.0001)
  (Kilic et al. Allergol Immunopathol 2010;38:122-8)
INDOOR ALLERGENS

• Sources
  – indoor-outdoor interchange
  – indoor sources

• Types
  – dust mite/insect emanations
  – mold exposure
  – animal proteins

Exposure to multiple indoor allergens in US homes and relationship to asthma.
Salo et al JACI 2008;121:678-84

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Seasonal variation in airway hyperresponsiveness and natural exposure to house dust mite allergens in patients with asthma. van der Heide S et al: JACI 1994;93:470-5

- **Methods**
  - 9 asthmatics with only dust mite allergy followed 1 year
- **Results**
  - Der p 1 in living room & bedroom lowest in Mar-May, highest Aug-Oct
  - histamine PC\textsubscript{20}FEV\textsubscript{1} most severe in Aug-Nov, least in Mar


- **Methods**
  - Dust samples from bed, bedroom floor, & kitchen of 20 homes (houses & apartments)
  - Temperature, absolute & relative humidity
  - Der f 1, Der p 1, Fel d 1, Bla g 1
  - June 1995-June 1996
Monthly measurements of indoor allergens and the influence of housing type in a northeastern U.S. city.
Chew et al: Allergy; 1999;54:1058-66

• Results
  – Der p 1 & Der f 1 peaked in beds & floors in autumn; fall:spring 2.2:1
  – Fel d 1 peaked in winter & spring; 2.4x higher spring:summer; homes with cats 224x higher than those without
  – Bla g 1 peaked in summer; 2.1x higher summer:winter; apartments:houses 5x higher

Dog allergen (Can f 1) and cat allergen (Fel d 1) in US homes: Results from the National Survey of Lead and Allergens in Housing.
Arbes et al JACI 2004;114:111-7

• 831 US homes: dust from bed, bedroom & living room floors, sofa analyzes for Can f 1 & Fel d 1
• Dog &/or cat in 49.1% homes
• Can f 1 in 100.0% homes (GM=4.69 μg/g) Fel d 1 in 99.9% homes (GM=4.73 μg/g)
• Dog(+) GM=69; cat (+) GM=200 Dog & cat (-) GM >1.0

Distribution, aerodynamic characteristics, and removal of the major cat allergen Fel d 1 in British homes.

• Methods
  – dust collected 50 homes with a cat & 50 homes without
  – airborne Fel d 1 measured in 50 cat homes & 75 homes without
  – Anderson sampler for particle size in 10 levels in home with 4 cats, repeated 1, 2, 4, 7, 14 days after removal from living room.
  – HEPA filter in 7 homes
Distribution, aerodynamic characteristics, and removal of the major cat allergen Fel d 1 in British homes. Custovic et al: Thorax 1998;53:33

- Results
  - Fel d 1 260x less in catless l.r. carpet
  - airborne levels found in all homes with cats (0.7-38ng/m³)
  - low levels in 22/75 without cat (b0.24-1.78ng/m³)
  - >9μm particles = 49% allergen recovered, small particles <4.7μm = 23% total

Distribution, aerodynamic characteristics, and removal of the major cat allergen Fel d 1 in British homes. Custovic et al: Thorax 1998;53:33

- Results
  - Fel d 1 levels reduced by 61.7% 2 days after removal (accounted for by removal of larger particles, >4.8μm)
  - small particles (<4.8μm) remained unchanged 1-4 days, then slowly decreased to 33% by day 14
  - HEPA filter resulted in reduction in airborne particles (p=0.008)


- Methods
  - dust collected from Wellington and Christchurch hotels, hospitals, rest homes, churches, primary schools, childcare centers, cinemas, bank offices, airplanes, and North Island ski lodges
  - building characteristics, temperature and relative humidity
  - Geometric means of Fel d 1 (μg/g dust) for floors (203), beds (64), and seats (24)

- Results
  - Detectable levels of Fel d 1 in 95% of floors, 91% beds, & 100% of seats
  - Fel d 1 higher in cinema (36.8, 20.8-65.3) & airplane seats (33.3, 28.0-39.7) than on respective floors (3.6, 2.5-5.1; 2.4, 1.8-3.0)
  - Floors in public buildings lower than domestic dwellings without cats
  - Fel d 1 levels higher in carpeted floors (p<0.001), lower in banks & hospitals (p<0.001)

Deposition of cat (Fel d 1), dog (Can f 1), and horse allergen over time in public environments - a model of dispersion.
Egmar et al: Allergy 1998;53:957

- Methods
  - 6 furniture stores in Stockholm with mattress “test rooms”
  - Animal dander [c] analysed by ELISA & CCIE
  - 17 unpacked new mattresses, 15 old, tried by customers mattresses

- Results
  - 15/17 factory-new mattresses had detectable levels of Fel d 1 & Can f 1, no horse (six mattresses were stuffed with horse hair)
  - Used mattresses higher than new (p<0.001)
  - Allergen [c] correlated with length of time mattresses tried by customers, rapidly in highly frequented stores; in 3wks reached [c] found in homes with former pets

- **Methods**
  - Tristan da Cunha eliminated cats in 1974
  - Cross-sectional survey & allergy ST
  - Dust samples 20 homes Der gp 1 & Fel d 1

- **Results**
  - Cat ST (+) 20.1% (57/284) islanders, 12.8% (6/47) born in or after 1975; 5/6 born <5yrs of cat elimination, 2 attended school off island
  - Low level Fel d 1 in 1/20 homes; all had Der p 1 or Der f 1

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National prevalence and exposure risk for mouse allergen in US households. Cohn et al JACI 2004;113:1167-71

- 831 US homes: dust from bed, bedroom, kitchen, & living room floors, sofa analyzes for Mus m 1 [c]
- Mus m 1 detected in 82% homes
- Kitchen floor >1.6 μg/g (sensitizing level) in 22% homes
- >1.6 μg/g in high-rise, mobile, older, or low-income homes

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Mouse allergens in urban elementary schools and homes of children with asthma. Sheehan et al Ann Allergy Asthma Immunol 2009;192:125-30
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Exposure to mouse allergen in U.S. homes associated with asthma symptoms.
Salo et al Environ Health Perspect 2009;117:387-91

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EFFECT OF CAT REMOVAL ON ALLERGEN CONTENT IN HOUSEHOLD-DUST SAMPLES
Wood et al: JACI 1989;83:730
• 15 homes with serial dust collections for 9-43 weeks after cat removal
• Major cat allergen Fel d 1 monitored baseline values from 7.8 - 436.7 U/gm
• Levels declined gradually by 20-24 wks
  8/15 homes had levels similar to control homes
• 2 homes after very aggressive environmental control measures had very sharp drops
  7/15 homes had persistent levels >20 wks
• Removing allergen from indoor environment may be very difficult

Measurement and characterization of cockroach allergens detected during normal domestic activity.
De Lucca et al: JACI 1999;104:672-80
• Methods
  – Air sampling 10 houses during low & no disturbance
  – Inhaled particles collected with intra-nasal samplers
  – Particle size, morphologic characteristics & relative Bla g 1 [c]
• Results
  – Bla g 1 in all homes geo mean 1.5U/g, 0.2-9.4 U/g
  – Bla g 1 in 8/10 intranasal samples
  – Bla g 1 containing particles ranged from 3-350 μm (large particles fibers or flakes), majority >10μm

Results of the National Cooperative Inner-City Asthma study (NCICAS) environmental intervention to reduce cockroach allergen exposure in inner-city homes.
• Methods
  – 265/331 families with cockroach (+) asthmatic children
  – 2 applications cockroach insecticide
  – Education on cockroach allergen removal
  – 48 homes Bla g 1 in dust kitchen, bedroom & TV/living room
Results of the National Cooperative Inner-City Asthma study (NCICAS) environmental intervention to reduce cockroach allergen exposure in inner-city homes. Gergen PJ et al: JACI 1999;103:501-6

• Results
  – @ 2 mos kitchen Bla g 1 down from 68.7U/g to 33.6U/g p<.05
  – % homes >8U/g baseline homes down @ 6 mos, 86.8% to 64.3% p<.05
  – @ 12 mos returned or exceeded baseline
  – 50% families followed cleaning instructions, with no greater effect

Fungi & Other Microorganisms Associated with Dampness in Buildings

• Aspergillus spp.
• Penicillium spp.
• Stachybotrys chartarum
• Trichoderma spp.

Mold and Asthma Symptoms?