Disclosure

Research Grants/Contracts
Boehringer-Ingelheim
Pulmonary Fibrosis Foundation
France Foundation
NIH
Key Concepts: Hypersensitivity Pneumonitis

• A mishmash of names—
  – Extrinsics Allergic Alveolitis=Hypersensitivity Pneumonitis
  – AND specific names related to specific antigen/environment, mushroom worker’s lung, farmer’s lung etc..

• Caused by sensitization to repeated inhalation of (often organic) antigens

• A granulomatous interstitial lung disease affecting interstitium, alveoli and bronchioles
  – Acute/inflammatory and chronic/fibrotic forms
  – Is NOT asthma but certain exposures (ie. mold) may be associated with asthma and hypersensitivity pneumonitis and the diseases may coexist in the same exposed individual
### Key Concept: Asthma vs. HP: Allergic Lung Diseases

<table>
<thead>
<tr>
<th></th>
<th>Asthma</th>
<th>Hypersensitivity Pneumonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Type-1 allergic airway response characterized by Th2 cells and IgE</td>
<td>Type III allergic inflammation reaction driven by Th1 cells and IgG</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Bronchial inflammation which may become chronic and irreversible</td>
<td>Interstitial and alveolar disease and exists in chronic fibrotic forms</td>
</tr>
<tr>
<td><strong>Physical Exam</strong></td>
<td>Wheezing (episodic) Normal oxygen</td>
<td>Crackles, inspiratory squeaks Hypoxemia in severe cases Clubbing in chronic cases</td>
</tr>
<tr>
<td><strong>PFT’s</strong></td>
<td>Obstructive defect Spirometry with BD Methacholine PEFR</td>
<td>Restrictive (or obstructive) Total lung volumes Diffusion impairment</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td>Normal</td>
<td>Abnormal (centrilobular nodules, reticular markings, ground glass, fibrotic changes)</td>
</tr>
</tbody>
</table>

- Asthma and HP are both allergic diseases caused by repeated exposures
- Some exposures are associated with asthma and HP (ie. Mold, Isocyanates)
Key Concepts: Hypersensitivity Pneumonitis & Exposure

- **Exposure**
  - Clinical history is key to uncovering possible exposures
  - Clinical/radiographic/pathologic patterns may suggest HP and prompt search for antigen
  - Antigen identification improves outcomes for acute and chronic/fibrotic HP patients and current/future exposed groups
Where do Exposure-Related ILDs “Fit” in the ILD Universe...

ILD

ILD of Known Associations

Exposures
Connective Tissue Diseases
Genetic

ILD of Unknown Associations

Idiopathic Interstitial Pneumonias
Major
Idiopathic Pulmonary Fibrosis
NSIP
RB-ILD
DIP
COP
Unclassifiable

Other Pathologies (ie. LAM)

Rare
LIP
Pleuroparenchymal Disease
Interstitial Lung Disease

The Interstitium

Space lined by alveolar epithelial cells, capillary endothelial cells and supporting connective tissue.

Asthma: normal interstitium
- abnormal airway,
- normal interstitium

HP: abnormal interstitium
- nonspecific interstitial mononuclear inflammation
- loosely formed granulomatous lesions.

- ILD: To make matter confusing...
  - Not all ILD is only interstitial including....
  - HP for example involves small airway, alveolar spaces

Courtesy of Robert Homer, MD PhD
## ACOEM 2015 Guidelines: Occupational Interstitial Lung Disease Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumoconiosis</td>
<td>Non-neoplastic reaction of lung to inhaled mineral or organic dusts</td>
<td>• Asbestosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Silicosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Coal Worker’s Pneumoconioses</td>
</tr>
<tr>
<td>Hypersensitivity Pneumonitis</td>
<td>Large family of disorders of immune response to inhaled antigens including</td>
<td>• Farmer’s lung (thermophilic actinomycetes)</td>
</tr>
<tr>
<td></td>
<td>• Microbial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Animal proteins</td>
<td>• Bird fancier’s lung (avian proteins)</td>
</tr>
<tr>
<td></td>
<td>• Chemicals</td>
<td>• Due to metal working fluids</td>
</tr>
<tr>
<td>Other Granulomatous Diseases</td>
<td>Chronic immune and foreign body responses to antigens in lung</td>
<td>• Beryllium disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hard metal disease (tungsten carbide)</td>
</tr>
<tr>
<td>Diffuse Interstitial Fibrosis</td>
<td>Response to severe lung injury</td>
<td>• Diffuse alveolar damage related to nitrogen oxides</td>
</tr>
<tr>
<td>including irritant inhalation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>injury</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
‘OHP [Occupational Hypersensitivity Pneumonitis] is an immunologic lung disease with variable clinical presentation and outcome resulting from lymphocytic and frequently granulomatous inflammation of the peripheral airways, alveoli, and surrounding interstitial tissue which develops as the result of a non-IgE-mediated allergic reaction to a variety of organic or low molecular weight agents that are present in the work environment.’
## Occupational Causes of Hypersensitivity Pneumonitis: “Categorized by Job”

<table>
<thead>
<tr>
<th>Disease</th>
<th>Antigen</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer’s lung</td>
<td>Thermophilic actinomycetes <em>Aspergillus</em> <em>Micropolyspora faeni</em> <em>Saccharopolyspora rectivirgula</em></td>
<td>Moldy hay, straw</td>
</tr>
<tr>
<td>Hot tub lung</td>
<td>Mycobacterium avium complex</td>
<td>Mist from hot tubs</td>
</tr>
<tr>
<td>Humidifier lung</td>
<td>Bacteria - <em>Thermoactinomyces candidus</em>, <em>Bacillus</em> spp, Thermophilic actinomycetes</td>
<td>Mist from standing water</td>
</tr>
<tr>
<td></td>
<td><em>Fungi - Aureobasidium pullulans</em> <em>Amoebae - Naegleria gruberi</em></td>
<td></td>
</tr>
<tr>
<td>Chemical worker’s lung—iso cyanate HP</td>
<td>Isocyanates (TDI, HDI, MDI)</td>
<td>Plastics, resins, paints</td>
</tr>
<tr>
<td>Metalworking fluids</td>
<td>Nontuberculous mycobacterium</td>
<td>Mist from metal working fluids</td>
</tr>
<tr>
<td>Woodworker’s lung</td>
<td>Alternaria, <em>Penicillium</em> spp</td>
<td>Wood pulp, dust</td>
</tr>
</tbody>
</table>

Quirce et al. Allergy 2016..
# Occupational Causes of Hypersensitivity Pneumonitis: “Categorized by Exposure”

<table>
<thead>
<tr>
<th>Category</th>
<th>Agent</th>
<th>Occupational jobs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td>Thermophilic actinomycetes</td>
<td>Farmers’lung, ventilation system, mushroom</td>
</tr>
<tr>
<td></td>
<td>Nontuberculous mycobacterium</td>
<td>Spa workers, machine operators, MWF</td>
</tr>
<tr>
<td></td>
<td>Acinetobacter</td>
<td></td>
</tr>
<tr>
<td>Fungi</td>
<td>Alternaria</td>
<td>Humidifier, wood worker</td>
</tr>
<tr>
<td></td>
<td>Aspergillus spp.</td>
<td>Stucco, tobacco, malt</td>
</tr>
<tr>
<td></td>
<td>Penicillium</td>
<td>Cork, cheese, food processing</td>
</tr>
<tr>
<td></td>
<td>Mushrooms</td>
<td>Mushroom workers</td>
</tr>
<tr>
<td>Enzyme</td>
<td>Phytase</td>
<td>Animal feeding,</td>
</tr>
<tr>
<td>Animal &amp; insect</td>
<td>Avian serum and feather protein</td>
<td>Bird breeders</td>
</tr>
<tr>
<td>protein</td>
<td>Rat serum proteins</td>
<td>Laboratory workers</td>
</tr>
<tr>
<td>Plant proteins</td>
<td>Woods: ramin, pine</td>
<td>Food processors</td>
</tr>
<tr>
<td>Low molecular</td>
<td>Diisocyanates</td>
<td>Chemical/polyurethane industry</td>
</tr>
<tr>
<td>weight</td>
<td>Acid anhydrides</td>
<td>Plastic workers, aircraft industry</td>
</tr>
<tr>
<td></td>
<td>Acrylate</td>
<td>Dental technicians</td>
</tr>
<tr>
<td></td>
<td>Dimethylphthalate and styrene</td>
<td>Yacht manufacturing</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical agents: pcn</td>
<td>Pharmaceutical industry</td>
</tr>
<tr>
<td>Metals</td>
<td>Cobalt</td>
<td>Hard metal workers</td>
</tr>
<tr>
<td></td>
<td>Zinc</td>
<td>Smelters</td>
</tr>
<tr>
<td></td>
<td>Zircuronium</td>
<td>Ceramicworkers</td>
</tr>
</tbody>
</table>
Epidemiology: Conundrums in Calculating Prevalence/Incidence

- Overall incidence in general population low
  - 0.3-0.9 per 100,000 individuals

BUT.......
What is True Risk?

• What is the true HP prevalence in specific exposed cohorts?
  – 1.3%-12.9% farmers
  – 8.0-10.4% pigeon breeders
  – 5.6% metal working fluids
  – 0.9-4.7% isocyanates

• What is the impact of specific HP “outbreaks” on the assessment of “overall risk”?
  – 15% contaminated air conditioner?
  – 27% swimming pool?

Quirce et al. Allergy 2016..
### Proposed Hypersensitivity Pneumonitis Classification: Acute and Chronic

<table>
<thead>
<tr>
<th>Clinical Behavior</th>
<th>Typical HRCT Image</th>
<th>Histopathology</th>
</tr>
</thead>
</table>
| **Acute HP, symptom duration usually few weeks/months (<6 mos to ~24 weeks)** | • Mostly reversible  
• Complete resolution  
• Symptom resolve completely after antigen avoidance | • Upper- and middle lobe predominant ground glass opacities, poorly defined centrilobular nodules, mosaic attenuation, air trapping | Inflammatory (cellular) HP  
• Lymphoplasmocytic/mononuclear macrophage infiltrats  
• Airway-centric lymphocytic infiltrates/peribronchiolar  
• Poorly/loosely formed granulomas  
• Multinucleated giant cells  
• NSIP cellular like |
| **Chronic HP, symptom duration several months (>6 mos to >~24 wk)** | • Potentially reversible to some extent  
• Risk of progression | • Upper- and middle-lobes predominant fibrosis, peribronchovascular fibrosis, honeycombing, mosaic attenuation, air trapping or centrilobular nodules, relative sparing of bases | Fibrotic HP  
• UIP-like  
• NSIP fibrotic-like  
• Airway-centered fibrosis, NOS  
• Unclassifiable  
• Histopathologic signs of inflammatory HP can be present on the background of fibrosis |

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Vasakova et al. AJRCCM 2017.
CASES
Case 1

- 55-year-old healthy man who worked as a pipe fitter presented in 2004 with dry cough, progressed despite antibiotic treatment for URI, and was eventually admitted

- Physical Examination: +crackles

- What are your next steps?
Next Steps

- Full Pulmonary Function Testing and HRCT

- Chest CT Scan—ground glass abnormalities, centrilobular nodules, mosaic attenuation

- PFT:
  - FVC 63%; DLCO 45%
Pulmonary Function Testing in HP

- Reduced FVC on spirometry can suggest but cannot diagnose a restrictive defect
- Reduced TLC on lung volumes = Restrictive defect
  - Restrictive impairment but obstructive can occur (given involvement of airways)
- Diffusion impairment
- 6 minute walk test for exercise desaturation

Gupta et al AJIM 2016.
Hypersensitivity Pneumonitis: Acute

Key Points: Imaging

- Ground glass attenuation (alveolitis)
- Centrilobular nodules
- Mosaic attenuation (due to small airway disease)

In suspected HP, hypersensitivity, high resolution chest CT Scan with inspiratory and expiratory imaging pneumonitis should be performed.

CXR may be normal or reveal only subtle abnormalities.
Histopathology

- Poorly formed granulomas
- Peribronchiolar, lymphocytic infiltrate

Key Points: Tissue

- Bronchoscopy vs. VATS (Surgical Lung Biopsy)
  - Transbronchial biopsy may yield enough tissue given disease around airway
  - BAL (Bronchoalveolar lavage) reveal lymphocytosis

- Pathology not necessary in all patients in appropriate clinico-radiographic setting with identified exposure
# Taking Occupational History

<table>
<thead>
<tr>
<th>Job type and activities (each job)</th>
<th>Products company</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Job title</td>
</tr>
<tr>
<td></td>
<td>Years worked</td>
</tr>
<tr>
<td></td>
<td>Equipment description</td>
</tr>
<tr>
<td></td>
<td>Equipment material</td>
</tr>
<tr>
<td></td>
<td>Process changes</td>
</tr>
<tr>
<td></td>
<td>Temporal associations between symptoms &amp; workdays</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure estimate</th>
<th>Visible dust/mist</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visible dust in sputum (nasal drainage)</td>
</tr>
<tr>
<td></td>
<td>Hours worked</td>
</tr>
<tr>
<td></td>
<td>Engineering controls</td>
</tr>
<tr>
<td></td>
<td>Personal protective equipment (respirators)</td>
</tr>
<tr>
<td></td>
<td>Engineering controls (wet process, local exhaust ventilation, storage location)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bystander exposures</th>
<th>Any coworkers/colleagues symptomatic?</th>
</tr>
</thead>
</table>
Patient History

- Employed as pipe fitter last 3 years in an automotive company
- Symptoms started after 2 tanks of metalworking fluids cleaned
- Recent process change
- Several coworkers had symptoms

- Clinical course:
  - Discharged on steroids with taper off of 6 months
  - After 4 months CT Scan/PFTs improved

Gupta et al AJIM 2016.
### Investigation

<table>
<thead>
<tr>
<th>Plant type</th>
<th>Plant A</th>
<th>Plant B</th>
<th>Plant C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant type</td>
<td>Auto parts (braking systems)</td>
<td>Auto parts (driveline components)</td>
<td>Auto parts (convertor clutches, suspension and differentials)</td>
</tr>
<tr>
<td>Cases/No. Employees</td>
<td>8/1350</td>
<td>4/1135</td>
<td>1/340</td>
</tr>
<tr>
<td>Type MWF</td>
<td>Semi-synthetic</td>
<td>Semi-synthetic</td>
<td>Semi-synthetic</td>
</tr>
<tr>
<td>Air monitoring</td>
<td>Below PEL</td>
<td>Not obtained</td>
<td>Below PEL</td>
</tr>
<tr>
<td>MWF bio-sampling</td>
<td>Mycobacterium immunogenum</td>
<td>Mycobacteria</td>
<td>No bacteria fungi</td>
</tr>
</tbody>
</table>

**Interventions**
- Substitution of MWF
- Addition of biocide
- Medical monitoring of employees
- Sampling for bacterial and fungal contamination
- 2/7 returned to work with no recurrence

Gupta et al AJIM 2016.
• 45 yo vocational school machine shop teacher with cough, SOB, fatigue with mild improvement over summer
• Work up:
  • DLCO 57%
  • BAL: 58% lymphocytosis
  • Lung biopsy (VATS)= Hypersensitivity Pneumonitis
• Outcome: 3 mos work removal, prednisone tx led to improvement
• Investigation:
  • MWF>1 year old
  • MWF culture Pseudomonas pseudoalcaligenes
  • Replaced with fungicide/bactericide formulation
  • Maintenance schedule instituted
Hypersensitivity Pneumonitis From Metalworking Fluids

• Referred to as coolants, cutting compounds, fluids or oils, lubricants or metal working fluids that reduce heat and friction and remove small metal pieces during machining aerosolized into small droplets

• 4 types
  • Straight (60-85% mineral oil, neat—used prior to 1970)
  • Emulsion of oil and water
  • Semisynthetic (5-50% and emulsifies into water)
  • Synthetic (no mineral oil)

• Additives

• Contaminants with dust, debris, metal, hydraulic oil, bacteria & fungi
Best Practices—Metalworking Fluids

- **OSHA**: Safety and Health Best Practices Manual based on
  - OSHA Metalworking Fluids Standard Advisory Committee (1999)
  - Organization Resources Counselors (1999)

- **Exposure Limits**
  - OSHA: 5mg/m$^3$ TWA for oil mist, PNOC 15 mg/m$^3$
    - OSHA Standards Advisory Committee recommended PEL 0.4 mg/m$^3$ thoracic particulate or 0.5 mg/m$^3$ total particulate
  - NIOSH criteria document REL MWF aerosols 0.4mg/m$^3$ thoracic particulate mass correspond 0.5 mg/m$^3$ for total particulate mass
OSHA: Minimizing Bactericidal and/or Fungi Growth

- Clean system before introducing fresh metalworking fluid
- Operate system at correct concentration
  - Low concentration decreased tool life
  - High concentration dermatitis, foaming and heavy residues
- Ensure makeup water quality
  - Ca and Mg are “hard” form scale and form soaps
  - Sulfates promote sulfate reducing bacteria
  - Chlorides corrosive
- Incorporate biocides against diverse array of microorganisms (some select out certain organisms i.e. Nontuberculous mycobacterium)
- Good filtration system
- Control Tramp oil resulting from machine tool hydraulic lube systems leaking into MWF provides food for microbes and an area for reduced oxygen growth lead to anaerobic bacteria growth

https://www.osha.gov/SLTC/metalworkingfluids/exposure.html
CASE (SERIES) 2
Case Series:

Patient 1 spa maintenance worker since 2007 presented with cough, hemoptysis and dyspnea for 6 months in 2009
  – CXR: diffuse interstitial prominence
  – Sputum: Mycobacterium avium-intracellulare
  – CT Chest: diffuse scattered areas of ground glass with no cavitation
  – Prescribed rifampin, ethambutol, clarithromycin
  – Pulmonologist suspected work and reassigned to laundry with recovery

Patient 2 tub maintenance workers since 2006 presented in 2009 for cough
  – Sputum grew MAC
  – Prescribed Zpak, rifampin, ethambutol
  – No bronch due to financial constraints
  – Reassigned to laundry improved
Case Series: Mycobacterium Avium Exposure in Spa Workers

- Investigation coordinated by New Mexico Occupational Health Surveillance Program
  - Compliance authorities New Mexico Environment Department and Swimming Pool Program
  - CDC Environmental Microbiology Lab and NIOSH Division of Respiratory Disease Consulted

- Investigation including
  - Questionnaire
  - Environmental sampling

# Investigation

## Table 1: Self-reported symptoms by job exposure category

<table>
<thead>
<tr>
<th>Condition</th>
<th>Tub cleaner (N=13)</th>
<th>Tub worker (N=23)</th>
<th>Non-exposed (N=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry cough</td>
<td>1</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Cough with phlegm</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Wheeze</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Tiredness</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Chills</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Shortness-of-breath</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Weight loss</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Chest tightness</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

## Table 2: Mean number of symptoms and odds ratios by job exposure category — all employees

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>Percent (N)</th>
<th>Mean symptoms/worker</th>
<th>Odds ratio* (OR)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tub cleaner</td>
<td>22.8 (13)</td>
<td>2.31</td>
<td>9.6</td>
<td>1.5–72.7</td>
</tr>
<tr>
<td>Tub worker</td>
<td>40.4 (23)</td>
<td>1.26</td>
<td>6.5</td>
<td>1.3–42.3</td>
</tr>
<tr>
<td>Non-exposed</td>
<td>36.8 (21)</td>
<td>0.29</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

*Note: For any respiratory symptoms, by exposure category, compared with unexposed individuals.*
Site Inspection

• “Filter deck” focus
  – Tub cleaning involves cleaning each tub filter 1x week
  – Performed in poorly ventilated filter deck
  – Hose with pressure nozzle to dislodge debris creating aerosols
  – Respirators not worn
Environmental Sampling and Isolates Similar to MAC in Patient

- All water samples rapid and slow growing mycobacteria (>800 CFU/mL)

- HPLC, PCR and 16S rRNA sequencing helped identify 2 patient isolates and the 13 environmental isolates as MAC

- PFGE revealed 2 environmental isolates closely related to patient
  - **Pulsed-field gel electrophoresis (PFGE)** is a laboratory technique used by scientists to produce a DNA fingerprint for a bacterial isolate

Intervention

- Enclosure of filter deck
- Establishment of independent industrial hygienist
- PPE
- Discontinue wooden tubs
- Use a EPA registered tuberculocide to treat surfaces and not hydrogen peroxide
Nontuberculosis Mycobacterium

- **Habitats:**
  - Normal inhabitants of natural waters, drinking water and soil
  - Can be recovered from biofilms, aerosols

- **Conditions**
  - Humidity
  - Disinfection
    - Mycobacterium more resistant to chlorine than other water borne microorganisms
    - Disinfection may lead to selection of mycobacterium and in absence of competition slow growing can grow as well

- **Guidelines**
  - No specific guidelines beyond sanitation procedures
    - In general resistant to certain common treatments and should use specific tuberculocides
  - US EPA/WHO recommendations for MAC include
    - Prevention and removal of biofilms
CASE 4
Case 4

- 49 year female presented to her PCP for progressive SOB, fatigue, cough and check flushing

- **Workup**
  - CXR: bilateral interstitial changes in mid and lower lung zones
  - PFT: DLCO 52%; TLC 71%
  - Biopsy: lymphocytic and plasma cell infiltrates with small epithelioid granulomas with giant cells and early interstitial fibrosis
  - Patient: Antibody titers Aspergillus fumigatus

- **Environmental samples:**
  - Wipe samples Aspergillus fumigatus, Penicillium and Mucor

Improvements in DLCO Away from Work...
Site Investigation

• **Observations**
  – Building 50 feet from swamp
  – Condensed water from cooling system accumulated in horizontal drain pans at base of each subunit intake
  – Settled water on roof
  – Stained ceiling and carpet
  – Relatively humidity 72%
  – Reports of water leakage
  – No regular maintenance

• **Environmental Sampling**
  – 3 unpaired building samples 124-310 colony forming units including Cladosporium, penicillium and Alternaarisa but no aspergillus

Recommendations:
  – Surveillance
  – Focused on humidity control
Mold Remediation: US EPA

Table 2: Guidelines for Remediating Building Materials with Mold Growth Caused by Clean Water

<table>
<thead>
<tr>
<th>Material or Encumbrance Affected</th>
<th>Cleanup Method</th>
<th>Personal Protective Equipment</th>
<th>Containment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mold growth in materials</td>
<td>Method 1: Wet vacuum (in the case of porous materials, some mold spores/fragments will remain in the material but will not grow if the material is completely dried). Steam cleaning may be an alternative for carpets and some upholstered furniture.</td>
<td>N-95 respirator, gloves, and goggles</td>
<td>Full Containment System and use of containment area</td>
</tr>
<tr>
<td>Mold growth in materials</td>
<td>Method 2: Damp-wipe surfaces with plain water or with water and detergent solution (except wood — one wood floor cleaner, scrub as needed)</td>
<td>N-95 respirator, gloves, and goggles</td>
<td>Partial Containment System and use of containment area</td>
</tr>
<tr>
<td>Mold growth in materials</td>
<td>Method 3: High-efficiency particulate air (HEPA) vacuum after the material has been thoroughly dried. Dispose of the contents of the HEPA vacuum in well-sealed plastic bags.</td>
<td>N-95 respirator, gloves, and goggles</td>
<td>None</td>
</tr>
<tr>
<td>Mold growth in materials</td>
<td>Method 4: Discard - remove water-damaged materials and test in plastic bags while inside of containment, if present. Dispose of as normal waste. HEPA vacuum area after it is dried.</td>
<td>N-95 respirator, gloves, and goggles</td>
<td>None</td>
</tr>
</tbody>
</table>

Personal Protective Equipment (PPE)

- N-95 respirator
- Goggles/eye protection
- Gloves
- Disposable overalls
- Goggles/eye protection
- Full: Gloves
- Disposible full body clothing
- Head gear
- Foot coverings
- Negative air pressure with HEPA filter

Containment

- Limited: Use polyethylene sheeting to floor around affected area with a slit entry and covering flap
- Maintain area under negative pressure with HEPA filtered fan unit
- Block supply and return air vents within containment area
- Full: Use two layers of fire-retardant polyethylene sheeting with one airlock chamber
- Maintain area under negative pressure with HEPA filtered fan exhausted outside of building
- Block supply and return air vents within containment area
Case 5

60-year-old woman who presents with chronic insidious dyspnea on exertion and nonproductive cough

- Upper lobe predominant
- Air trapping
- Ground glass
Case: Chronic Hypersensitivity Pneumonitis—Bird Fancier’s Lung

- On further history, she took care of a property where there was a poultry farm with a chicken coop for many years

- Denies symptoms related to work
Serum Precipitins

- Serum IgG antibodies
- Standardization lacking
- Evidence of exposure may not correlate with disease
- False negative depending on antigen selected or time since exposure
- Common HP panels include:
  - *Alternaria*, *Aspergillus fumigatus*, *Aureobasidium pullularia*, *Micropolyspora faeni*, *Penicillium*, *Phoma herbarum*, *Thermactinomycetes vulgaris*, *Trichoderma viride*
Specific Inhalation Challenge Testing

- Inhalation of diluted antigen extraction in a monitored setting
- Testing include: spirometry, CBC, CXR, O2 sat
- Positive result
  - Decrease FVC>15% or DLCO 20%
  - 10-15% FVC decrease + 1 other criteria (WBC increase, O2 dec 3%, increase body temp, clinical symptoms)
  - FVC decrease<10% with 3+ above criteria
- Contraindicated with severe disease
- Currently limited to specialized centers and research purposes

Higher utility with avian and fungal exposures

Munoz et al. ERJ 2014.
Where do Exposure-Related ILDs “Fit” in the ILD Universe....

ILD

ILD of Known Associations

- Exposures (including HP, pneumoconiosis)
- Connective Tissue Diseases
- Genetic

ILD of Unknown Associations

- Idiopathic Interstitial Pneumonias
  - Major
    - Idiopathic Pulmonary Fibrosis
      - NSIP
      - RB-ILD
      - DIP
      - COP
    - Unclassifiable
  - Rare
    - LIP
    - Pleuroparenchymal Disease

Other Pathologies (ie. LAM)

Chronic HP vs. IPF
Certain radiographic and pathologic features can distinguish chronic HP from IPF
– Morell et al (2013): 20/46 IPF patients reclassified as chronic HP with many demonstrating +bronchial challenge testing, BAL lymphocytosis, positive serum precipitins

But chronic HP can present with form that is indistinguishable from IPF
– Chung et al (2017): 37% fibrotic HP radiographic UIP; 30% high confidence UIP pattern
Differentiating Chronic HP from IPF

<table>
<thead>
<tr>
<th>Imaging (CT)</th>
<th>Upper lobe predominance</th>
<th>Peripheral, predominantly basal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distribution</td>
<td>Frequent</td>
<td>Absent/Limited</td>
</tr>
<tr>
<td>Mosaic attenuation</td>
<td>Frequent</td>
<td>Absent</td>
</tr>
<tr>
<td>Nodules</td>
<td>Often</td>
<td>Absent/Limited</td>
</tr>
<tr>
<td>Interlobular septal thickening</td>
<td>Often</td>
<td>Frequent (typical for UIP pattern)</td>
</tr>
<tr>
<td>Honeycombing</td>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Bronchocentricity</td>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Discrete cysts</td>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Consolidation</td>
<td></td>
<td>Absent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bronchoalveolar lavage (BAL)</th>
<th>Lymphocytosis &gt; 25–30%</th>
<th>Lymphocytosis &lt; 20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroblast foci</td>
<td>Often</td>
<td></td>
</tr>
<tr>
<td>Granulomas/giant cells/Schaumann bodies</td>
<td>Frequent</td>
<td></td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>Honeycombing</td>
<td>Often</td>
<td></td>
</tr>
<tr>
<td>Paraseptal subpleural distribution</td>
<td>Frequent</td>
<td></td>
</tr>
<tr>
<td>Bronchocentricity</td>
<td>Frequent</td>
<td></td>
</tr>
</tbody>
</table>
Time for an International Consensus on Hypersensitivity Pneumonitis
A Call to Arms

PULMONARY PERSPECTIVE

Hypersensitivity Pneumonitis: Perspectives in Diagnosis and Management

Martina Vasakova¹, Ferran Morell², Simon Walsh³, Kevin Leslie⁴, and Ganesh Raghu⁵

¹Department of Respiratory Medicine, First Faculty of Medicine of Charles University, Thomayer Hospital Prague, Prague, Czech Republic; ²Vall d’Hebron Institut de Recerca, Servei de Pneumologia, Hospital Universitari Vall d’Hebron, Departament de Medicina, Universitat Autònoma de Barcelona, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias, Barcelona, Catalonia, Spain; ³King’s College National Health Service Hospital Foundation Trust, Denmark Hill, London, United Kingdom; ⁴Mayo Clinic, Scottsdale, Arizona; and ⁵Center for Interstitial Lung Diseases, University of Washington Medical Center, Seattle, Washington

ORCID ID: 0000-0002-0424-9941 (M.V.).
Key Points: Hypersensitivity Pneumonitis

- HP is an allergic granulomatous interstitial lung disease caused by sensitization to antigens (often organic)
  - Certain exposures associated with HP and asthma and HP contact investigations may reveal asthma like symptoms in other exposed individuals
- Acute and chronic forms exist
- Specific standards (i.e., OSHA) may be lacking or disease may occur in the presence of exposures under recommended limits
- The presence of HP should prompt investigation into the environment, particularly the presence of multiple workers, in similar facility
- Continued medical surveillance program and a written industrial hygiene plan are critical to continued prevention of disease
Acknowledgements

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