

INTERSTITIAL LUNG DISEASE

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Benchmarks

- ACOEM Practice Guidelines
 - ▣ Authoritative guidance, updated, evidence-based
 - ▣ Lung Disease Guidelines in progress
 - Occupational Interstitial Lung Disease
 - Airways Disorders
- ATS 2004 Revised Criteria for the Diagnosis of Non-Malignant Asbestos-Related Disease
- This presentation
 - ▣ A general approach to ILD → OILD
 - ▣ Specific ILDs, esp. pneumoconioses
 - ▣ Implications

Medical Evaluation of Occupational Lung Diseases - Modalities

Primarily diagnostic

- Chest film, CT
- Spirometry, DL_{CO}
- Blood gases
- Methacholine challenge
- Biopsy (Ca, IPF, granulomatous disease)

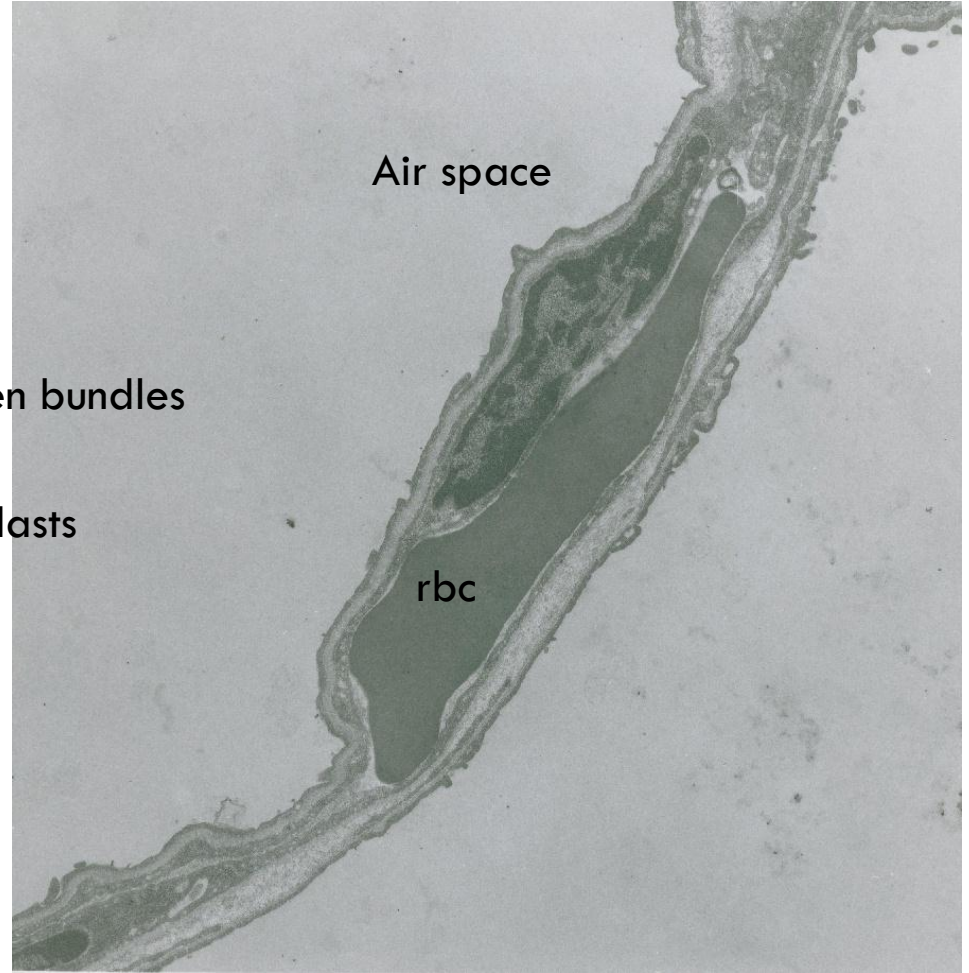
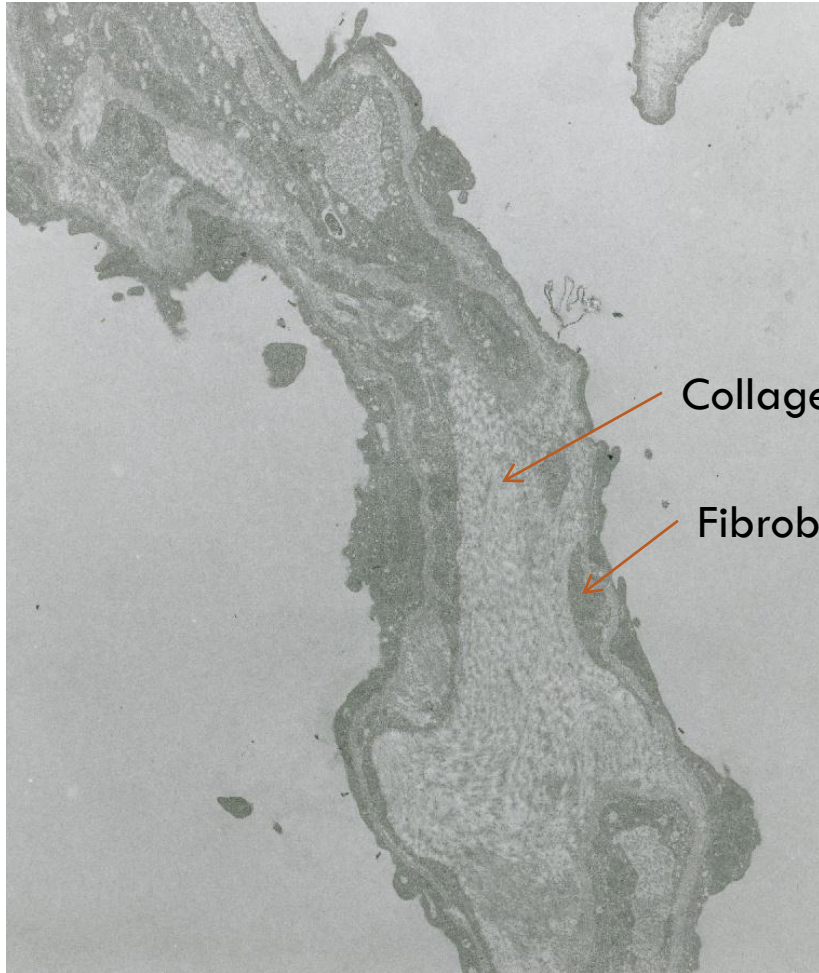
Primarily occupational

- Occupational history
- Impairment evaluation
- Provocative testing (rare)
- Serology (for HP)
- Biopsy (avoid)
- Cardiopulmonary exercise testing

What is the interstitium?

- Fabric of connective tissue that supports its many structures
- Expands and contracts with ventilation
- Surrounds the air spaces, brings blood in close proximity to air with separation but minimal impedance to diffusion
- Serves as a conduit and fluid channel for lymphatic drainage and the migration of immune cells
- Collects and sequesters a fraction of insoluble particles that deposit in the lung

Interstitialium and Alveolar Wall



What is interstitial disease?

□ Acute

- Edema, per se or a stage on the way to alveolar edema
- Infection (e.g. mycoplasma)
- Inflammation

□ Chronic

- Fibrosis, end stage of inflammation
- Often involves some degree of bronchiolitis.

Operational Classification

- Pneumoconioses
- Granulomatous disease
- Hypersensitivity pneumonitis
- Diffuse interstitial fibrosis
 - ▣ Idiopathic pulmonary fibrosis (= “usual interstitial pneumonia”)
 - ▣ Giant cell interstitial pneumonia (“GIP”)
 - ▣ Other interstitial pneumonias

How is it diagnosed?

- Usually, obvious because patient belongs to a high-risk group
 - Demographics, family history (some IPF)
 - Occupational history
 - Exceptions: sarcoid, IPF
- Chest film – most often
- Restrictive pattern on PFTs
 - Reduced FVC, preserved FEV₁, decreased RV
 - This is a late change, however.
- Biopsy – normally to be avoided!

Clinical Evaluation - History

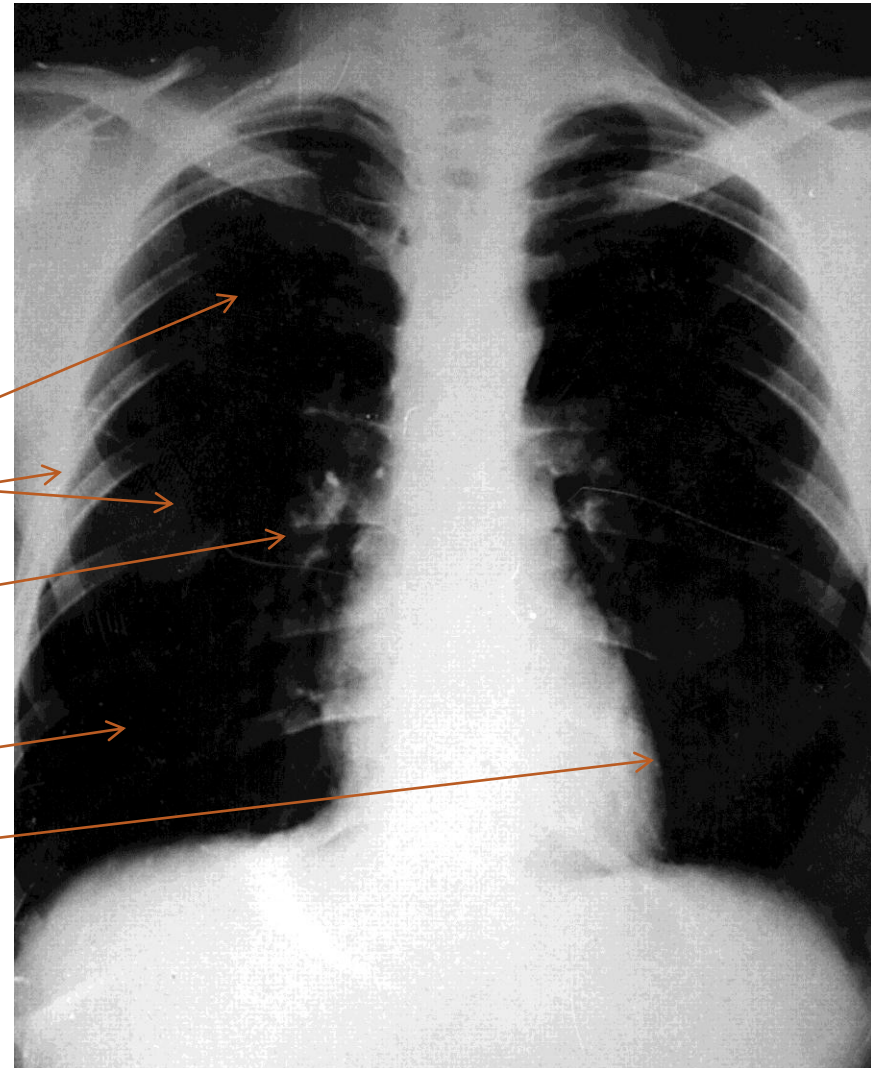
- History of present illness
 - ▣ Useful to rule out nonoccupational ILD
 - ▣ Consider drug reactions, cancer, inflammatory bowel dz, rheumatologic/autoimmune/collagen vascular dz
 - ▣ Time course may distinguish eosinophilic pneumonias, drug reactions, other diseases
 - ▣ Not very useful for OILD
- Occupational history - essential

Clinical Evaluation – Symptoms and Signs

- Nonspecific
 - SOB is disproportionate to PFTs!
 - Cough
 - Clubbing: suggests asbestosis, pigeon breeders' HP, cancer
- Chest film
- PFTs: obstructive early → restrictive late

Chest film

- Plain film and digitized images
- B reader program
- Important features:
 - ▣ Parenchyma (upper)
 - ▣ Pleura
 - ▣ Hilum
 - ▣ Parenchyma (lower)
 - ▣ Superimposition



Pulmonary Function Testing and Cardiopulmonary Evaluation

- Vital capacity
- Flow rates (e.g. FEV₁)
- Lung Volumes and Diffusing Capacity (CO)
- Bronchodilators: Pre-, Post-Shift
- Bronchoprovocation Testing
 - ▣ Methacholine Testing
 - ▣ Specific Agents
- Metabolic Treadmill
 - ▣ Oxygen Consumption
 - ▣ Anaerobic Threshold

Process leading to interstitial diseases may cause:

- Airway irritation
- Mild obstructive defect
- Acute symptoms (cough)
- Extrathoracic disease

Interstitial Lung Disease *itself* causes:

- Restrictive defect
 - Cough and SOB
 - Pulmonary hypertension
- Shunting and V/Q mismatch
 - Abnormal CO diffusing cap
 - Desaturation with exercise
 - Clubbing (uncommon)

Restrictive Patterns

Causes

- Extrathoracic
 - ▣ Obesity
 - ▣ Pregnancy
 - ▣ Chest wall deformity
 - ▣ Clothing or external device (e.g. corset, cuirass)
- Intrathoracic
 - ▣ Pneumonectomy
 - ▣ Pleural thickening
 - ▣ Interstitial Fibrosis

Indicators

- Restrictive Defects are usually identified by reduced Forced Vital Capacity (FVC) during spirometry
- However, FVC is effort dependent
- More conclusively measured by Total Lung Capacity (TLC)

Usually in medicine, diagnosis is primarily for treatment. Not here.

- Identification
 - Diagnosis
 - **Causation** →
 - Functional evaluation
 - Treatment
 - Prognosis
- sentinel event monitoring
 - causation
 - apportionment
 - causal circumstances
 - current impairment
 - future impairment
 - fitness to work

Challenges

- Occupational v. nonoccupational
- Identifying the responsible agent in a case of mixed-dust pneumoconiosis or hypersensitivity pneumonitis or when the history is unclear
- Ruling IPF in (it can't be easily ruled out)
- Differentiating between sarcoidosis and beryllium disease

Approach to Evaluation

- Evidence of structural lesion consistent with the interstitial process (e.g. asbestosis)
 - ▣ In practice, evidence of a structural lesion is usually demonstrated by chest film with or without CT
- Evidence of causation by an agent
 - ▣ Evidence of causation by a *particular* agent may be more difficult but is usually satisfied by the occupational history
- Exclusion of alternative diagnoses
 - ▣ may require additional clinical tests and even biopsy

ILD depends more on *structural* features than functional assessment.

- Anatomical changes
- Histological changes
- Malignant potential
- Mechanical

interference with function

- Markers of exposure
- Markers of effect
- Markers of outcome

It's the other way around with airways disease.

However, causes of ILD may also cause some airways dysfunction.

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How Do You Know It is a Pneumoconiosis?

- Occupational history of exposure to a *mineral or metal dust*
 - ▣ Organic dust pneumoconioses exist but are rare
 - ▣ GIP is associated with exposure to “hard metal” (esp. W content) but is rare
- Compatible clinical and laboratory findings
 - ▣ Diagnosis is primarily by chest film
- No alternative diagnosis likely
 - ▣ This does *not* mean that it is a diagnosis of *exclusion!*
 - ▣ Pneumoconiosis is a diagnosis of *context!*

Which Common Pneumoconiosis Is It?

- Occupational history
 - Silica
 - Asbestosis
 - Coal workers' pneumoconiosis
- Chest film
 - Rounded opacities and cardinal features of silicosis
 - Irregular opacities and cardinal features of asbestosis
- Pathology
 - biopsy rarely indicated
 - asbestos bodies *useful* for identifying asbestosis

Silicosis

- Silicosis
 - ▣ Simple
 - ▣ Chronic nodular silicosis
 - ▣ Accelerated silicosis
 - ▣ Acute silicosis
 - ▣ Silicotuberculosis
- Associated conditions
 - ▣ Autoimmune disorders
 - esp. systemic sclerosis
 - ▣ Nephritis
 - ▣ Lung cancer



Asbestos-Related Disorders

- Asbestosis
- Pleural plaques
- Rounded atelectasis
- Chronic obstructive airways disease
- Cancer
 - Lung cancer
 - Mesothelioma
 - Larynx, colon, other



If any occupational physician in this room cannot recognize this as advanced asbestosis, please recognize that you are in trouble!

Rounded Atelectasis



Coal Workers' Pneumoconiosis



Which “Modern” Pneumoconiosis Is It?

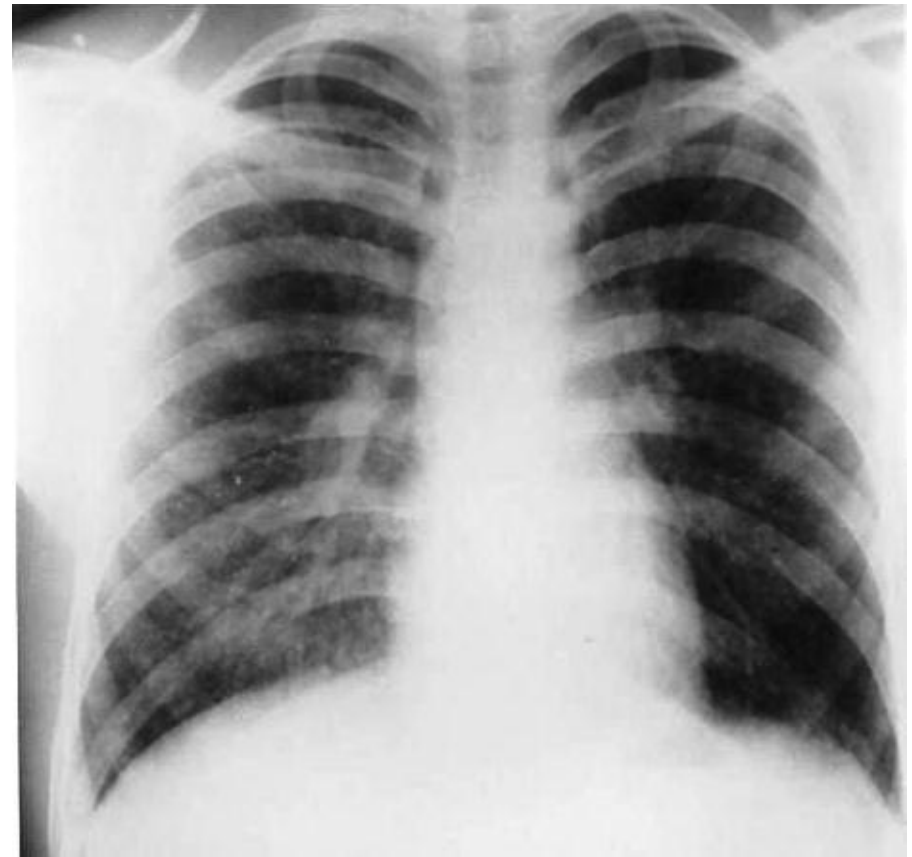
- Occupational history
 - ▣ Hard metal, tungsten-cobalt (W, Co) steel alloy
 - ▣ Beryllium (granulomatous)
 - ▣ Mixed dust
- Chest film
- Pathology may be required to identify GIP, or in evaluation of suspected sarcoidosis
- Hard metal disease may be associated with cobalt-induced bronchoreactivity

Biopsy

- May be required where there is a diagnostic dilemma:
 - ▣ IPF v. sarcoid v. asbestos, silicosis (rarely and may carry risk)
 - ▣ Diffuse ILDs
- Not acceptable just for medicolegal purposes
- Histology
 - ▣ Pattern of fibrosis may suggest IPF
 - ▣ Silicotic nodules, coal dust macules
 - ▣ Asbestosis, asbestos bodies (not fibers), silica particles
 - ▣ EDXA to identify composition of particles: may be important in mixed dust or unknown pneumoconiosis

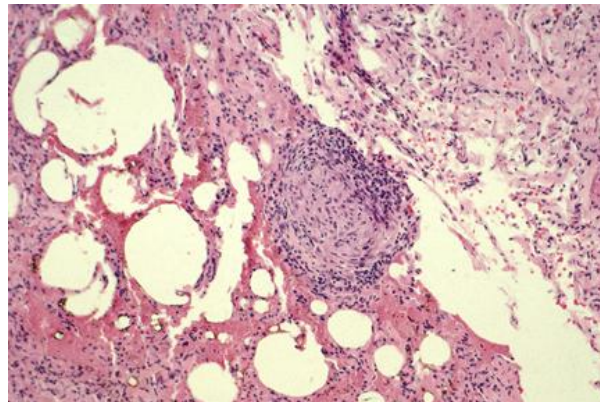
Hypersensitivity Pneumonitis

- Typical presentation of farmer's lung
- ≠ “silo-fillers’ disease”
- Infiltrate → fibrosis
- Cytokine-mediated disease
- Provoked by persistent antigen
- Often preceded by airways prodrome



Granulomatous Disease

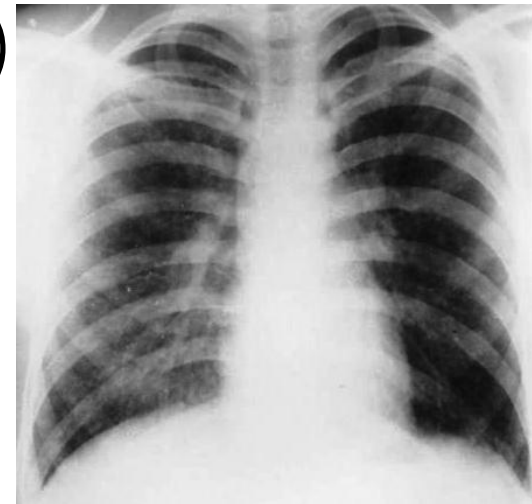
- Sarcoidosis is the big differential diagnosis
 - ▣ Eosinophilic granuloma possible but not without eos
 - ▣ Miliary TB possible but would be clinically obvious
 - ▣ Hypersensitivity pneumonitis causes lung granulomas
- Beryllium identified by occupational history
 - ▣ Zirconium can also cause isolated granulomata
- Confirmation by Be lymphocyte proliferation test (available at National Jewish Hospital)
 - ▣ Not a screening test



Which HP Could It Be?

- Occupational history of exposure to high MW, persistent antigen
 - ▣ Agricultural settings, especially in wet climates → R/O farmers' lung
 - ▣ Birds, esp. pigeons → R/O “pigeon breeders' lung”
 - ▣ HVAC or older AC system, ventilation repairs → R/O humidifier lung (diff includes *Legionella*)
 - ▣ Rehabilitation of old buildings
- Serum antibody: “HP Panel”

Farmers' lung



HP Panel

HP Panel CPT

Micropolyspora faeni IgG

Thermoactinomyces vulgaris IgG

Aspergillus fumigatus IgG 86606

Penicillium Chrysogenum/notatum IgG

Alternaria tenuis/alternata IgG

Trichoderma viride IgG

Aureobasidium pullulans IgG

Phoma betae IgG

Related Tests & Panels:

Bird Fancier's Precipitin Panel I

Bird & Mold Precipitin Panel II

Bird Fancier's Profile Panel III

Other protein antigens & haptens

The historically common hypersensitivity pneumonitides were:

- Farmer's lung
- Pigeon breeders's lung
- Humidifier lung

- Useful in presumptive, “classical” cases
- Range of specific antibody determinations limited
- Labs often offer secondary panels for less common antigen.
- These panels have been “abused” in fishing expeditions without good indications.

Which “Modern” HP Could It Be?

- Occupational history of exposure to low MW antigen
 - ▣ Isocyanate
 - ▣ Trimellitic anhydride
 - ▣ Pyrethrum powder (pesticide)
- Harder to diagnose
 - ▣ Requires high index of suspicion
 - ▣ Compatible history of exposure
 - ▣ No HP panel available or practical



TDI-induced HP

Diffuse Interstitial Disease

Occupational

- Giant cell interstitial pneumonia
 - ▣ Most often seen in grinding, toolmaking with hard metal
 - ▣ Uncommon
- Deep lung injury with honeycombing
 - ▣ Catastrophic event, so history is known
 - ▣ Bronchiolitis obliterans

Nonoccupational

- Idiopathic pulmonary fibrosis (= UIP)
 - ▣ Resembles asbestosis, pathologically distinct
 - ▣ Sporadic (older) or hereditary (younger) forms
 - ▣ Elevated cancer risk
 - ▣ Generally requires biopsy
- Many other interstitial pneumonias (nomenclature issues)
- “Other” – many but individually uncommon!

Differential Diagnosis of Diffuse ILDs

Not Rare but Uncommon

- Infection
 - ▣ AIDS
 - ▣ Mycoplasma
 - ▣ Mycobacteria
 - ▣ Legionella (humidifier lung)
 - ▣ Psittacosis (pigeon breeders' lung)
 - ▣ Cryptococcosis (bird source)
- Drug reaction
- Autoimmune, rheumatological, collagen-vascular disorders
- Post-radiation (therapeutic)
- Graft v. host

Rare

- Paraquat toxicity (suicide)
- Storage diseases
 - ▣ Gaucher's disease
 - ▣ Amyloidosis
- Tuberos sclerosis
- Infection
 - ▣ Whipple's disease
- Lymphangiitic spread of cancer (rare in this presentation)

Principles of Management

- When an OILD is suspected:
 - ▣ Diagnosis first
 - ▣ Document level of impairment, track
 - ▣ Treat according to condition
 - ▣ Protection at workplace to prevent progression
 - Pneumoconioses: removal not indicated if <OEL
 - Be disease: removal from exposure required
 - HP: removal or effective protection essential
- Otherwise, symptomatic treatment once fibrosis is established

Essential Questions

- ❑ What is the nature of the process?
- ❑ What exposure in the worker's employment history may have been responsible?
- ❑ What permanent level of impairment can be predicted?
- ❑ What can be done to control or limit the disease process?
- ❑ Are other people in the workplace likely to be affected, now or in the future?

Causation

- Specific, responsible exposure
- Work relationship
- Circumstances of exposure
- Possible interactions
- Interpretation:
 - ▣ underlying cause
 - ▣ proximate cause
 - ▣ aggravation
- Cannot/should not use epidemiological principles for the individual case:
 - ▣ Patients \neq populations
 - ▣ Hill criteria do not apply.
 - ▣ Epi inferences are post hoc, single cases are Bayesian.
 - ▣ Standard of certainty is not the same.
 - ▣ WC Acts are clear.

Social function

Specific Functions

- sentinel event monitoring
- Causation/causality
- apportionment
- causal circumstances
- current impairment
- future impairment
- fitness to work

Institutions

- Workers' compensation
 - Occupational health regulation
 - Employer responsibility
 - (Public health)
 - (Human rights)
- } ?

Social dimension: why accurate diagnosis, causality is important.

Values

- Equity
- Fairness (Justice)
- Sufficiency
- Transparency

Means

- Standardization
- Consistency
- Predictability
- Reliability
- Rapidity
- Validity