

Farmer's Lung Disease

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Our Environment



Our lungs are susceptible to damage caused by inhaled toxic materials and irritants because the surface area of our lungs exposed to air is so large and body's need for oxygen so great.

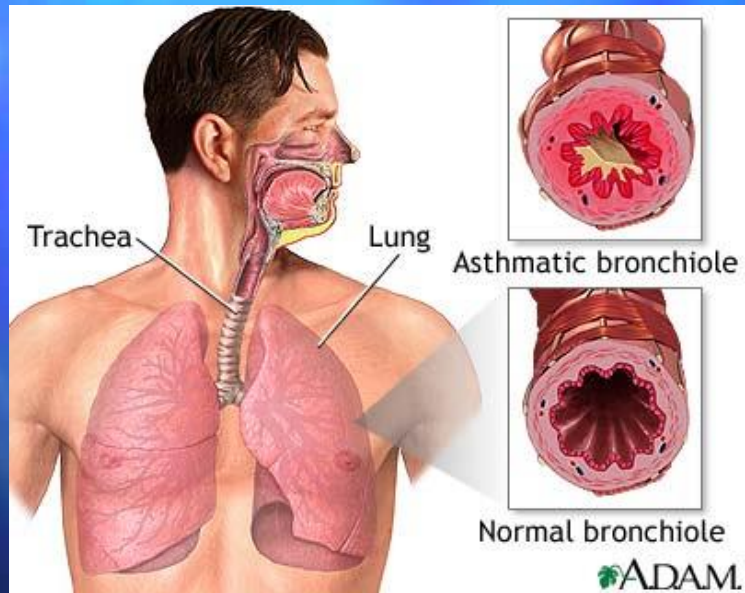
Occupational Lung Hazards

- Lung hazards come in many forms



Respiratory Diseases in Agriculture

- Occupational asthma




- Asphyxiation
- (gas/fumes in lungs)



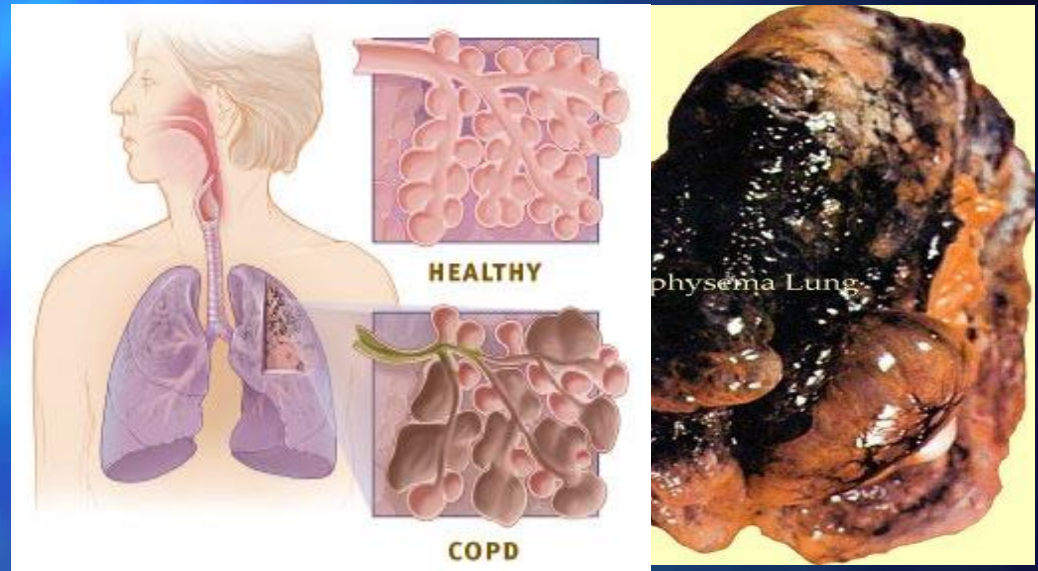
Respiratory Diseases in Agriculture

**Organic Dust Toxic Syndrome (ODTS)-
Common lung illness**

■ **Lung cancer**



■ **Chronic Obstructive Pulmonary (Lung) Disease- emphysema, bronchitis**



Farmer's Lung-allergic reaction

Hypersensitivity pneumonitis - microorganisms (1)

<u>Disease</u>	<u>Source</u>	<u>Agent</u>
Farmer's Lung	Hay, straw	Micropolyspora faeni Thermoactinomyces spp
Mushroom worker's lung	Compost	Thermoactinomyces spp
Woodworker's lung	Wood pulp	Alternaria spp
Malt worker's lung	Whiskey maltings	Aspergillus spp
Sequoiosis	Redwood	Aureobasidium pullulans
Bagassosis	Bagasse	Thermoactinomyces spp

Hypersensitivity pneumonitis - microorganisms (2)

<u>Disease</u>	<u>Source</u>	<u>Agent</u>
Sewage worker's lung	Sewage	Cephalosporium
Maple bark stripper's lung	Maple	Cryptostroma corticale
Suberosis	Cork	Penicillium frequentens
Paprika splitter's lung	Paprika	Mucor stolonifer
Detergent worker's lung	Detergents	Bacillus subtilis
Humidifier lung	Water in humidifier	Thermophilic organisms

Hypersensitivity pneumonitis – (3)

Disease

Source

Agent

Animal source

Wheat weevil lung Grain dust Sitophilus granaris

Pigeon breeder's lung Excreta Pigeons

Furrier's lung Hair Animal furs

Fish-meal worker's lung Meal Fish

Rodent handler's lung Urinary protein Rodents

Plant source

Coffee worker's lung Coffee bean Coffee

Woodworker's lung Wood dust Gonystylus bacanus

HYPERSENSITIVITY PNEUMONITIS = EXTRINSIC ALLERGIC ALVEOLITIS

- **Bird Keepers' Lung = 83.4%**
- **Farmer's Lung = 8.9%**
- **Mushroom alveolitis = 7.7%**

Muller S. Z Gesamte Inn Med
1990 Oct; 45(19): 581-4

Hypersensitivity pneumonitis: Japanese Nationwide Epidemiological Study

- **Total HP cases = 835 (653 definite, 182 probable)**
- **Occupational HP = 115 (13.8%)**
- **Farmer's lung = 68 (59% of Occup. HP)**
- **Chemical HP = 19**
- **antibody analysis and environmental challenge differences were notable; careful interview and an antigen panel match are the key to accurate diagnosis**

Yoshida et al, Occup Environ Med.
1995 Sep; 52(9): 750-4

Interstitial lung disease

- Early stage and acute is alveolitis (injury with inflammatory cell infiltration)
- Late stage characterised by fibrosis

Clinical effects due to hypoxia (respiratory failure) and cardiac failure

Chronic Interstitial Disease

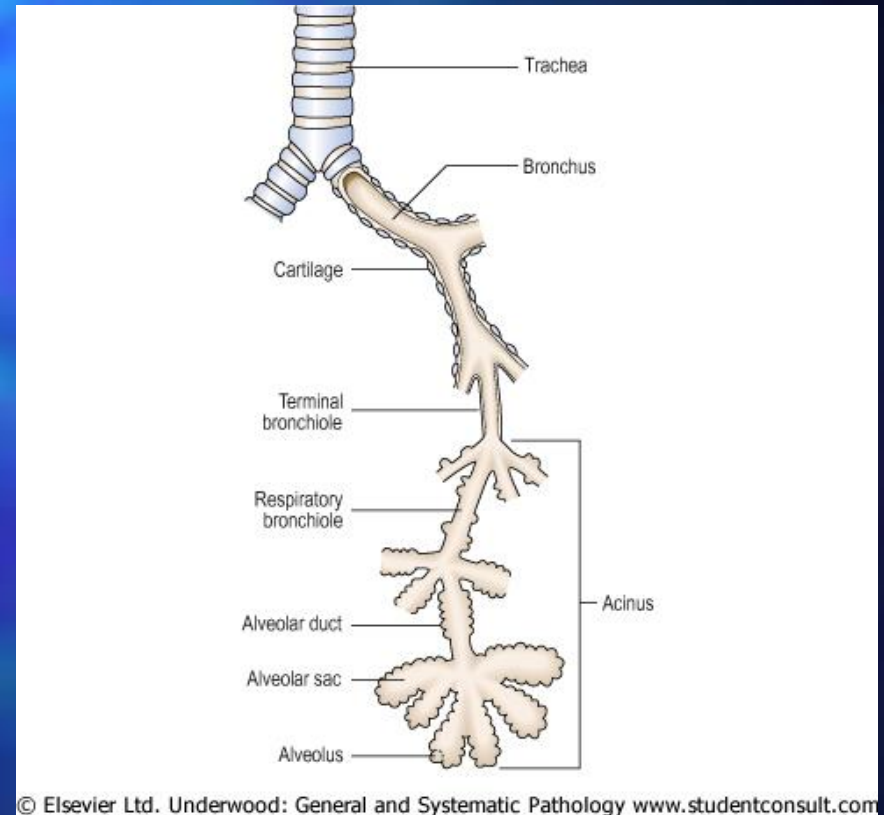
- Idiopathic pulmonary fibrosis (IPF)
- Sarcoidosis
- Extrinsic allergic alveolitis
(hypersensitivity pneumonitis)
- Pneumoconiosis
- Connective tissue diseases

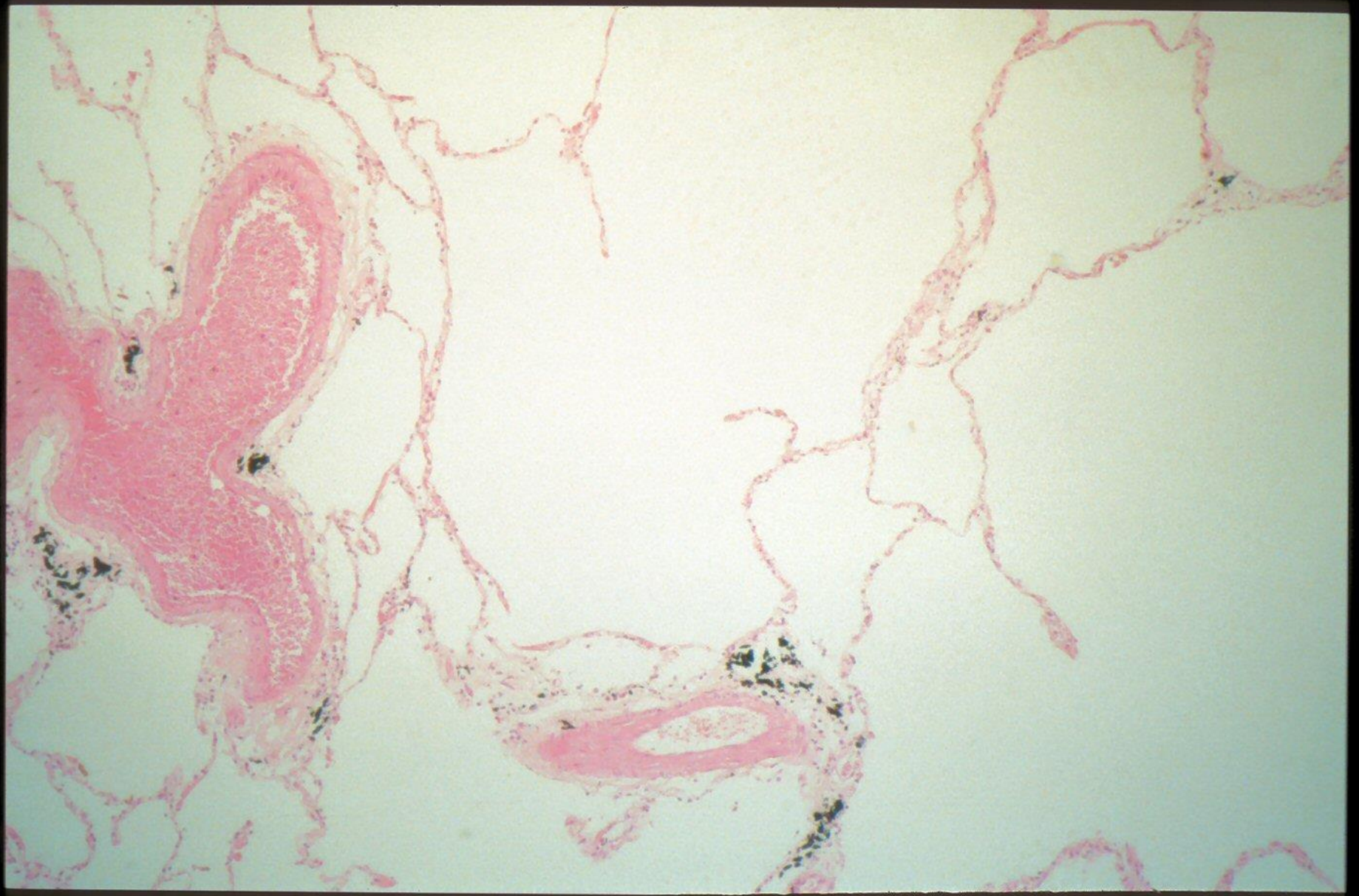
Extrinsic allergic alveolitis (hypersensitivity pneumonitis)

- **Chronic inflammatory disease**
 - Small airways
 - Interstitium
 - Occasional granulomas
- **Allergic origin**
 - Type III hypersensitivity
 - Type IV hypersensitivity

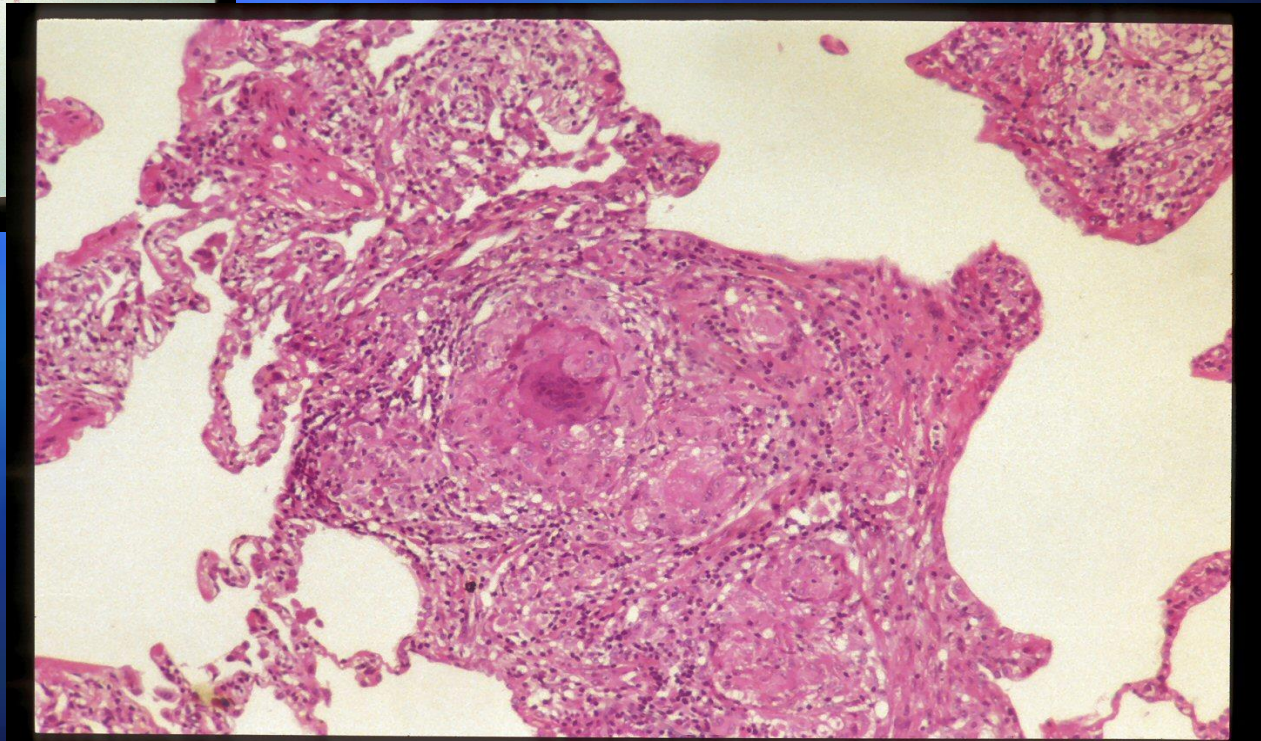
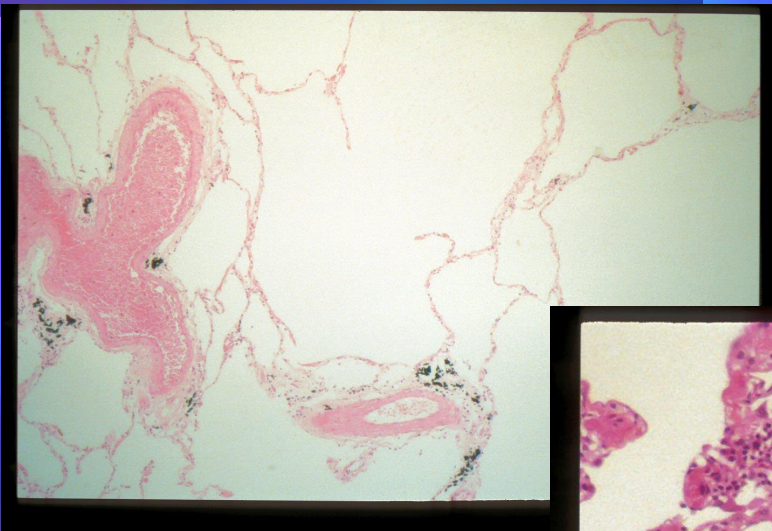
Pulmonary interstitium

- Alveolar lining cells (types 1 and 2)
- Thin elastin-rich connective component containing capillary *blood vessels*





Inflammation in hypersensitivity pneumonitis



Grain Dust-Farmer's Lungs



Etiology: Farmer's Lung

Streptomyces thermohygroscopicus (EPST) is a thermoactinomycete which has been found to be related to Farmer's Lung Disease

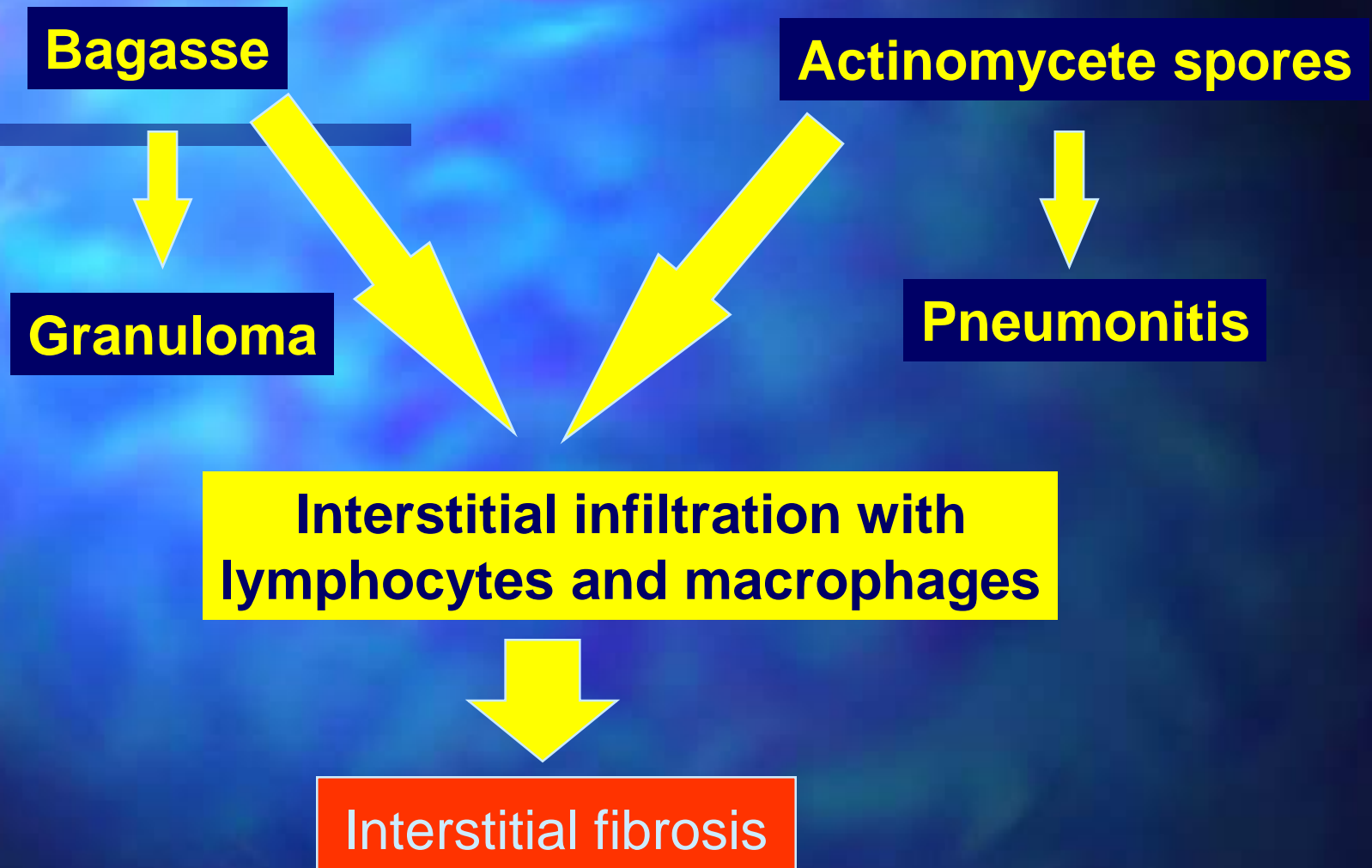
Dai HP. Chung Hua Chieh Ho Ho Hu
Hsi Tsa Chih. 1989 Oct; 12(5); 282-319

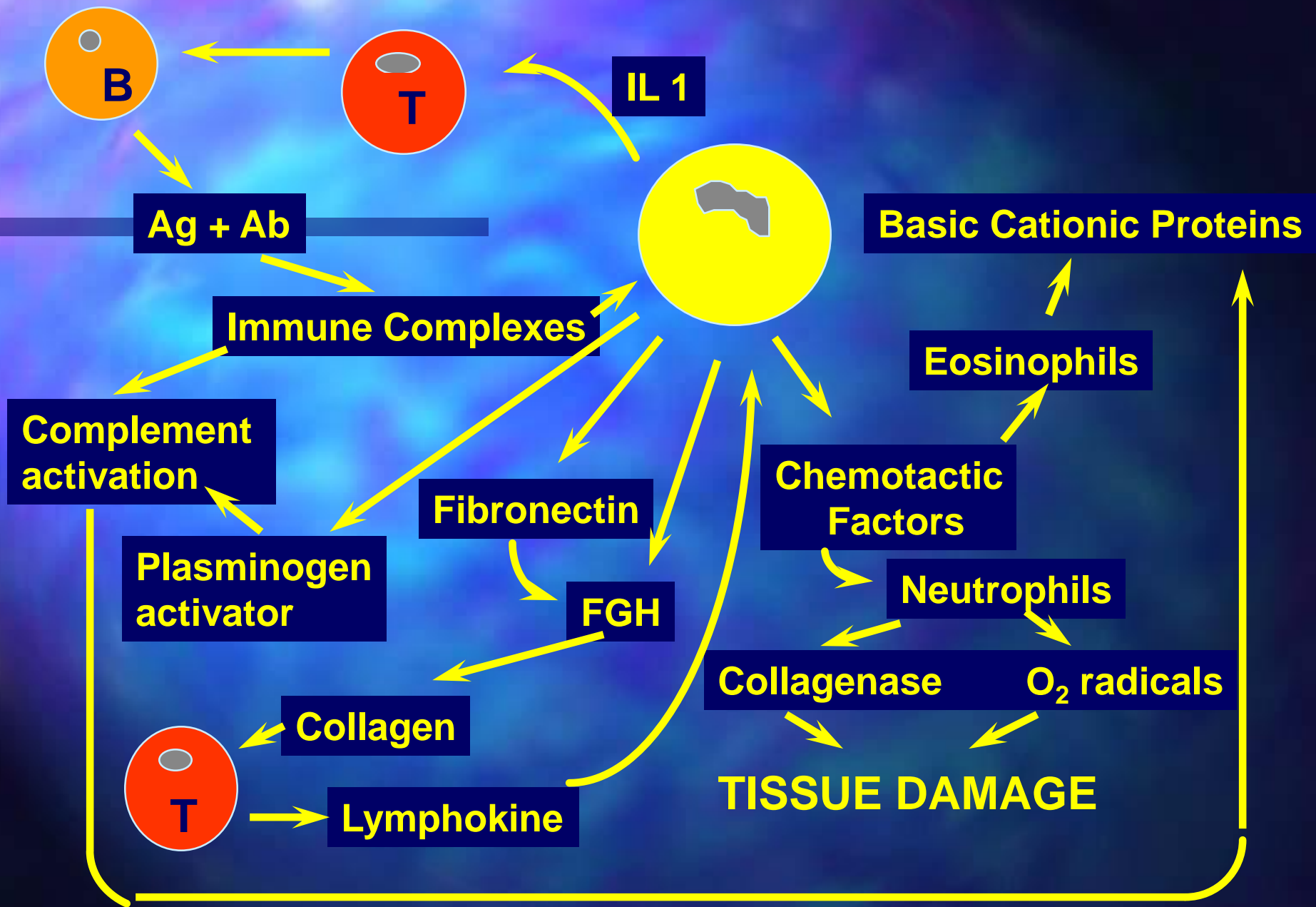
Etiology: Bagassosis

Thermoactinomyces sacchari

Boiron et al. Clin Allergy
1987 July; 17(4): 355-63

PATHOPHYSIOLOGY OF BAGASSOSIS





TYPES OF INJURY IN NON-MALIGNANT INTERSTITIAL LUNG DISEASE

- FIBROSIS
- DISTORTION
- DESTRUCTION

Interstitial Lung Disorders of Known Etiology: Forms of Injury

	Distortion	Fibrosis
Inorganic dusts	-	+
Organic dusts	+	-
Gases	-	+
Fumes	-	+
Radiation	-	+
Poisons	-	+

SYMPTOMS OF FIBROSIS

- **DYSPNEA**
- **DRY, IRRITATING, AND PERSISTENT COUGH**
- **SUBSTERNAL DISCOMFORT**
- **ANOREXIA**
- **WEIGHT LOSS**
- **ARTHRALGIA**

HIGH INDEX OF SUSPICION!!!

EAA: symptoms

- flu-like illness
- cough
- high fever, chills
- dyspnea, chest tightness
- malaise, myalgia
- 4-8 hours after exposure
- - chronic disease: dyspnea in strain, sputum production, fatigue, anorexia, weight loss

PHYSICAL SIGNS OF FIBROSIS

- TACHYPNEA
- LOWER LOBE FIBROSIS ---> FINE, END-INSPIRATORY CREPITATIONS, WHICH DISAPPEAR WITH POSITION
- FINGER CLUBBING
- CYANOSIS

Hypersensitivity pneumonitis (bagassosis) : Report of 5 cases

- **sex : all males**
- **age range : 29 - 52 y.o.**
- **work exposure : 1 in sugar mill; 4 in paper mill**
- **length of exposure : 2 days to 15 years**
- **common symptoms : cough, dyspnea, fever**
- **chest x-ray : reticulonodular (3), reticular (1), and
, miliary nodular (1)**
- **BAL : predominantly lymphocytic**
- **ABG : hypoxemia**
- **PFT : restrictive**
- **Dlco : decreased (43 - 78%)**

**Hur et al, Kao Hsiung I Hsueh Ko Hsueh Tse
Chih 1994, Oct; 10(10) 558 - 64**

Diagnosis

- Compatible clinical picture (symptoms, chest x-ray or CT, lung function changes) of HP

- Presence of precipitating antibodies

- Bronchoalveolar lavage

- Lung biopsy

Objective testing to establish work-relatedness:

- Returning to work induce similar symptoms and signs

- Specific challenge tests – more difficult to do.

Occupational hypersensitivity pneumonitis: diagnosis

Major Criteria (requires at least 2):

1. Symptoms compatible with hypersensitivity pneumonitis
2. Exposure to an antigen by history or detection of antibody in serum or bronchoalveolar lavage (BAL) fluid
3. Chest radiograph or HRCT with compatible findings
4. Lymphocytosis in lung lavage fluid if BAL is performed
5. Compatible histopathologic changes on lung biopsy, if biopsy is performed
6. Reproduction of symptoms and laboratory and lung function abnormalities after exposure to the suspect workplace

Minor Criteria:

1. Dyspnea on exertion
2. Bibasilar dry inspiratory crackles
3. Recurrent febrile episodes
4. Decreased lung diffusion capacity (DLCO)
5. Arterial hypoxemia at rest or with exercise

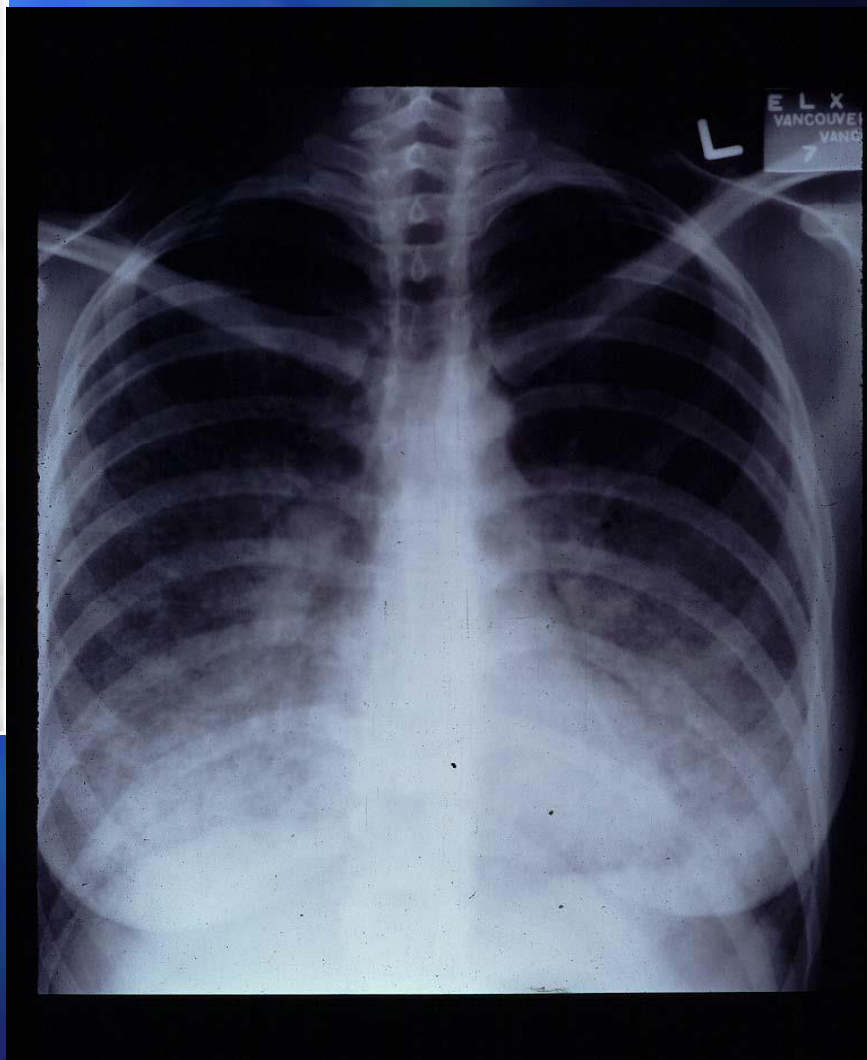
Diagnosis of Hypersensitivity pneumonitis

Chest x-ray

- Acute: Diffuse ground-glass infiltrates, nodular or striated patchy opacities. Up to 20% have normal CXR.
- Subacute: Same as acute, may have sparing of lung bases
- Chronic: Upper lobe fibrosis, reticular opacities, volume loss, honeycombing
- may be normal or show patchy or diffuse infiltrates or discrete nodular infiltrates. There may be honeycombing.



Immunol Allergy Clin N Am 31 (2011) 769–786



Mushroom Workers' Lung
(*Thermoactinomyces vulgaris*)

Diagnosis of Hypersensitivity pneumonitis

CT scan

- is diagnostic showing the details of fibrosis, honeycombing and nodules.

EAA: HRCT, acute disease



EAA: HRCT, chronic disease



Diagnosis of Hypersensitivity pneumonitis

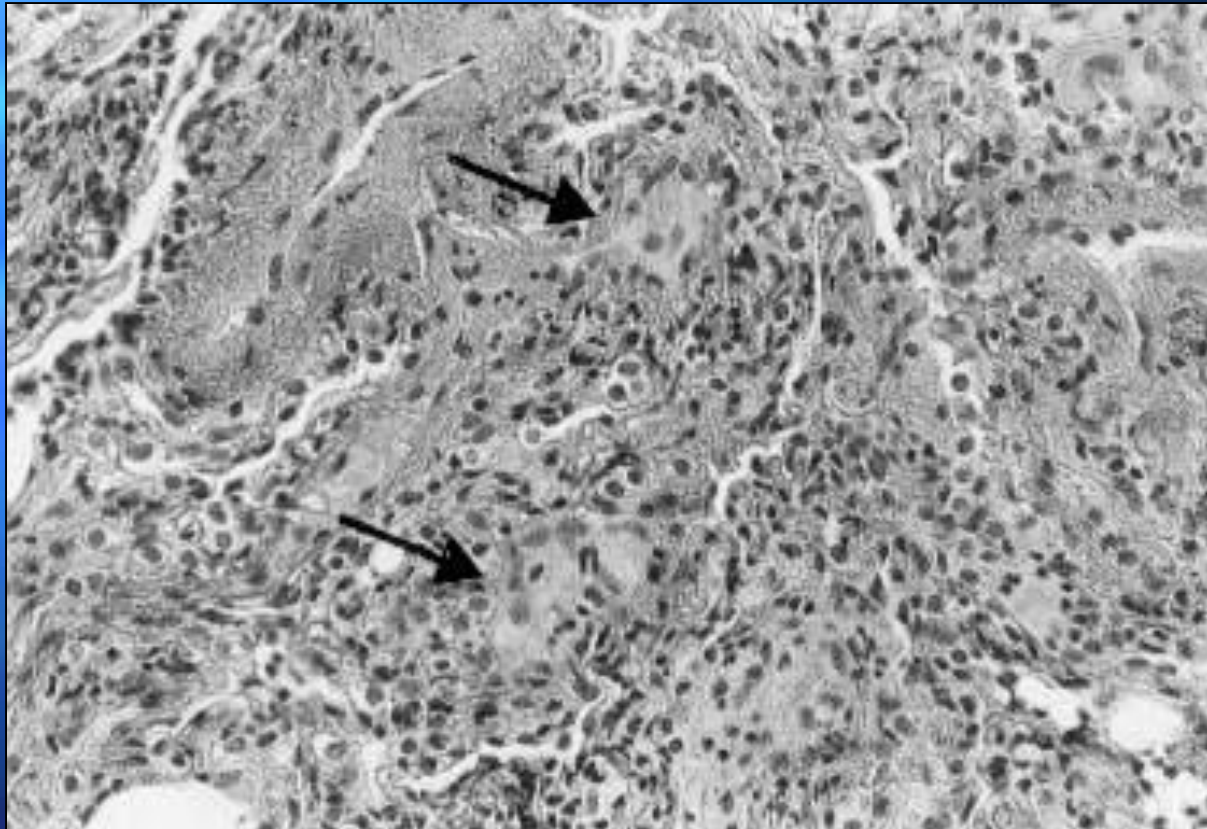
Pulmonary function test (PFT)

shows a restrictive or obstructive pattern, decreased lung volume, impaired diffusion capacity, bronchial hyper reactivity and reversibility.

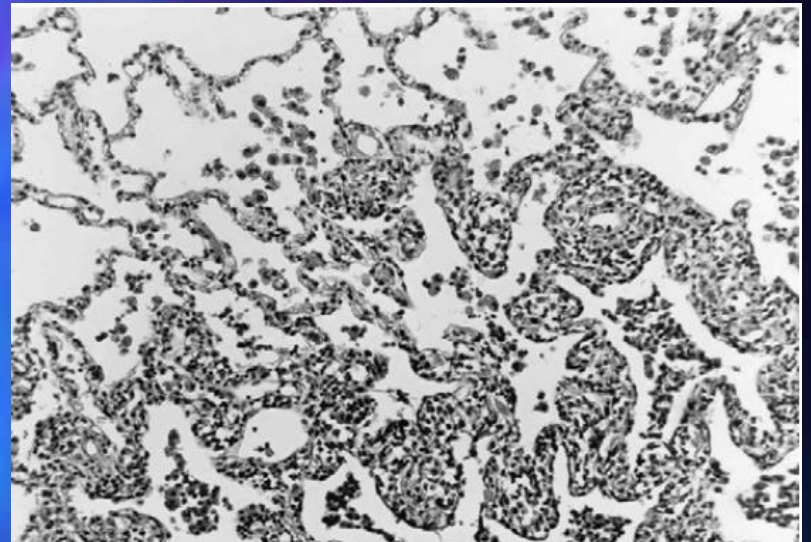
Lung biopsy through bronchoscopy may be diagnostic.

Inhalation challenge i.e. a positive response to inhaled antigen may be done for transient airflow obstruction.

Diagnostic Accuracy of Transbronchial Biopsy in Acute Farmer's Lung Disease*. Lacasse, Yves; MD, MSc; Fraser, Richard; Fournier, Marcien; Cormier, Yvon. **Chest. 112(6):1459-1465, December 1997.**



Diffuse lymphocytic infiltration and clusters of epithelioid cells (arrows) in farmer's lung (hematoxylin-eosin staining; original magnification x300).



Immunol Allergy Clin N Am 31 (2011) 769–786

■ Pathology:

Granulomatous inflammation around the alveoli and the peripheral bronchioles.

Exudate with plasma cells and lymphocytes.

Macrophages, epitheloid cells and giant cells in the granulomas in the middle of the inflammation process.

After the exposure ceases the reaction disappears in 3-4 months.

Diagnosis: ELISA vs. CIE for detection of Ab against *Thermoactinomyces sacchari*

Diagnostic Procedure	Sensitivity	Specificity
ELISA	82%	88%
CIE	60%	58%

Boiron et al, Clin Allergy 1987 July; 17(4): 355-63

Diagnosis of Hypersensitivity pneumonitis

Lab Tests

- May have increased **inflammatory markers** (erythrocyte sedimentation rate, C-reactive protein)
- Leukocytosis and increased gamma globulins typically seen
- Specific IgG antibody to offending agent can be detected and checked serially to detect response to treatment

Not always present (likely because many unknown antigens)

Low specificity (10% of people exposed to farmer's lung antigen develop antibodies; only 0.3% show symptoms)

- Rheumatoid factor often positive (unknown cause)
- Negative blood, sputum, throat cultures

Diagnosis of Hypersensitivity pneumonitis

Lab Tests

- **Bronchoalveolar lavage (BAL)**
 - Acute form with neutrophils and CD4 T lymphocytes
 - Chronic form with high number of CD8 T lymphocytes
 - BAL may help to differentiate chronic hypersensitivity pneumonitis from sarcoid, which has high CD8 T lymphocytes
- Neutrophilia, lymphopenia, increased ESR, C reactive protein, rheumatoid factor, raised serum immunoglobulins.

Table 1. Sensitivity and specificity of serological tests (electrosyneresis and double diffusion) with the four antigens

Antigen	Area under the ROC curve (SD)	Selected threshold	Sensitivity (95 % CI)	Specificity (95 % CI)	LR +*	Odds ratio (CI 95 %)
Electrosyneresis						
<i>A. corymbifera</i>	0.944 (0.045)	2 arcs	86.7 (59.5–98.0)	100 (100–100)	–	–
<i>E. amstelodami</i>	0.871 (0.067)	3 arcs	66.7 (38.4–88.1)	100 (100–100)	–	–
<i>W. sebi</i>	0.687 (0.098)	2 arcs	46.7 (21.3–73.4)	93.3 (68.0–98.9)	7.00	12.25 (1.69–88.94)
<i>S. rectivirgula</i>	0.756 (0.090)	2 arcs	46.7 (21.3–73.4)	93.3 (68.0–98.9)	7.00	5.69 (1.03–31.46)
Double diffusion						
<i>A. corymbifera</i>	0.813 (0.080)	1 arc	73.3 (44.9–92.0)	93.3 (68.0–98.9)	11.00	38.5 (5.64–262.60)
<i>E. amstelodami</i>	0.713 (0.095)	1 arc	53.3 (26.6–78.7)	86.7 (59.5–98.0)	4.00	7.43 (1.37–40.32)
<i>W. sebi</i>	0.687 (0.098)	1 arc	73.3 (44.9–92.0)	60.0 (32.3–83.6)	1.83	4.12 (0.91–18.63)
<i>S. rectivirgula</i>	0.698 (0.097)	1 arc	66.7 (38.4–88.1)	66.7 (38.4–88.1)	2.00	4 (0.9–17.72)

*LR+, Positive likelihood ratio.

Table 2. Sensitivity and specificity of serological tests (ELISA IgG and IgA) with the four antigens

Antigen	Area under the ROC curve (SD)	Selected threshold	Sensitivity (95 % CI)	Specificity (95 % CI)	LR +*	Odds ratio (CI 95 %)
ELISA IgG†						
<i>A. corymbifera</i>	0.633 (0.103)	>214†	46.7 (21.3–73.4)	86.7 (59.5–98.0)	3.50	5.69 (1.03–31.46)
<i>E. amstelodami</i>	0.620 (0.103)	>534†	46.7 (21.3–73.4)	86.7 (59.5–98.0)	3.50	3.79 (0.79–18.26)
<i>W. sebi</i>	0.758 (0.089)	>195†	60.0 (32.3–83.6)	93.3 (68.0–98.8)	9.00	21 (3.06–144.09)
<i>S. rectivirgula</i>	0.624 (0.103)	>153†	86.7 (59.5–98.0)	40.0 (16.4–67.7)	1.44	4.33 (0.76–24.70)
ELISA IgA†						
<i>A. corymbifera</i>	0.638 (0.102)	≤104†	53.3 (26.6–78.7)	80.0 (51.9–95.4)	2.67	4.57 (0.95–22.03)
<i>E. amstelodami</i>	0.644 (0.100)	≤19†	33.3 (11.9–61.6)	93.3 (68.0–98.9)	5.00	7 (0.87–56.54)
<i>W. sebi</i>	0.522 (0.107)	>256†	40.0 (16.4–67.7)	86.7 (59.5–98.0)	3.00	4.33 (0.76–24.70)
<i>S. rectivirgula</i>	0.547 (0.107)	≤44†	33.3 (11.9–61.6)	93.3 (68.0–98.9)	5.00	7 (0.87–56.54)

*LR +, Positive likelihood ratio.

†Absorbance.

Differential diagnosis of occupational hypersensitivity pneumonitis

Acute Form	Disorder	Trigger
Farming	Silo unloader's disease	Nitrogen dioxide
Organic dust toxic syndrome	Humidifier fever, animal house fever, grain fever, pulmonary mycotoxicosis	Endotoxin, mycotoxin
Inorganic dust toxic syndrome	Acute berylliosis	Beryllium dust: aerospace, nuclear, ceramics, dental
Textile dust	Byssinosis Mill fever Weaver's cough	Cotton dust and endotoxin Tannins in cotton mill dust, kapok Tamarind seed powder
Bird raising	Psittacosis	<i>Chlamydia psittaci</i> infection

Differential diagnosis of occupational hypersensitivity pneumonitis

Chronic Form

Inorganic respiratory dust syndromes	Silicosis and siderosis	Silica in mining, quarrying, drilling, foundry working, ceramics manufacturing, sandblasting
	Chronic berylliosis	Beryllium dust -aerospace, nuclear, ceramics, dental
	Asbestosis	Fibrous silicate minerals (eg, chrysotile)
	Coal worker's pneumoconiosis	Mixed dust consisting of coal, kaolin, mica
	Talcosis and calcicosis	Leather, ceramic, paper, plastics, rubber, building, paint, or cosmetic industries; limestone dust
Food industry	Flavor-worker's lung	Diacetyl butter flavor ketone in microwave popcorn
	Rice-miller's syndrome	Rice husk dust containing silica
Textile dust	Byssinosis	Cotton, hemp, flax, jute, sisal
	Nylon flock	Pulverized fibers applied to fabrics
	Ardystil syndrome	Acramin-FWN (a polyamidoamine)
Lifeguards	Lifeguard lung	Trichloramine and/or endotoxin
Office buildings	Sick building syndrome	VOC, smoke, poor ventilation, dampness

Treatment of Hypersensitivity pneumonitis

The condition should be diagnosed by occupational history, lifestyle, livelihood, *H/o* exposure to antigens .

The exposure should be checked by wearing of appropriate masks, pollen masks, personal dust respirators, air helmets, ventilated helmets with fresh air.

Avoidance of offending antigen is primary therapy.

Corticosteroids

- Prednisone: 1–2 mg/kg/day, to max of 50–60 mg p.o. daily
 - Initial course of 1–2 weeks with progressive taper
 - Low-dose therapy (20 mg p.o. daily) may be as effective as avoidance
- Maintenance dose may be continued at the lowest possible dosage if symptoms recur

EAA: prognosis

Continuing exposure, relapsing disease leads to pulmonary fibrosis, permanent loss of pulmonary function and cor pulmonale.

When Finnish cases with farmer's lung were followed for 10 years, 23% had findings of pulmonary emphysema or pulmonary fibrosis.

EAA: prevention

- reduction of dust exposure
- work hygienic improvements
- adequate respirators always during exposure
before any symptoms!
- occupational health care:
 - information
 - follow-up
 - finding symptomatic workers in time, to prevent permanent loss of pulmonary function.

Occupational Lung Health Monitoring



Questionnaires

'Fitness to wear' respirator testing



Chest x-rays



Lung function tests (spirometry)

Annual Lung Function Tests

- Grain
- Industry
- Workers



Workers in livestock confinement buildings



Dairy farmers



Workers who smoke



People with history of bronchitis, asthma or frequent lung infections

Conclusion

Farmer's lung is the most usual form of **extrinsic allergic alveolitis**. Chronic form leads to severe disability.

Reduction of the exposure to biological dust by work hygienic improvements and using adequate respirators is important. The humidifiers and other sources of exposure should be cleaned.

Early recognition of the symptoms is essential.

ODTS is a milder syndrome, symptoms can be prevented using respirator when exposed.

MARAMING SALAMAT

PO!