
بسم الله الرحمن الرحيم

Hypersensitivity pneumonitis (HP)

BY

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Definition:

- **Hypersesitivity pneumonitis (HP) or Extrinsic allergic alveolitis (EAA)** refers to a group of inflammatory lung diseases caused by repeated exposure to a wide variety of different antigenic materials (usually organic, may be chemicals) leading to immunological sensitization.

- The typical clinical events are transient fever, myalgia, arthralgia, dry cough, breathlessness and hypoxaemia that occur 2 to 9 h after exposure and resolved in 12 to 72 h without specific treatment.

Pathogenesis:

- The 3 main types of antigen are:

@ Microbial agent

- Bacteria as Thermophylic Spp, Bacillus sp
- Fungi as Aspirgellus, Penicilliuum

@ Animal agent

As bird protein in pigeon dropping and excreta, chicken, duck and Budgerigar feather

@ Chemicals

As isocyanate, copper sulfate and some pesticides and some drugs

Sources of antigen

Antigenic source	Probable antigen	Disease
Plant products		
Moldy hay	Thermophilic actinomycetes	Farmer 's lung
Moldy pressed sugarcane	Thermophilic actinomycetes	Bagassosis
Contaminated wood dust	Bacillus subtilis Alternaria	Wood dust HP
Grain weevils in wheat flour	Sitophilus granarus proteins	Miller's lung

Antigenic source	Probable antigen	Disease
Animal products		
Pigeon dropping	Altered pigeon serum	Pigeon breeder lung disease
Chicken feathers	Chicken feathers, proteins	Chicken breed's lung
Domestic and wild bird product	Bird proteins	Bird fancier's lung
Urine, serum, fur	Animal protein	Animal handler's lung

Antigenic source	Probable antigen	Disease
Others		
Contaminated humidifiers, air conditioner, heating systems	Thermophilic actinomycetes, T.Candidus, T. valgaris, Penicillium spp., Amoeba, Klebsiella spp., Mycobact.avium complex.	Ventilator lung Humidifier lung
House dust, bird dropping (?)	Trichosporon cutaneum	Japanese summer house HP
Paints, resin and plastic	Chemical antigens	Isocyanate and trimetallic HP

Pathogenesis, cont.

- Both environmental and host factors play a role in development of HP
- Exposure factors as antigen concentration, duration and frequency of exposure, particle size and solubility
- Host factors also play a role as not all exposed develop the disease

Pathogenesis, cont.

* Repeated exposure leads to immunological sensitization and subsequent immune mediated lung inflammation

* **Two types of hypersensitivity reactions occur:**

1. **Type III** or immune complex-mediated hypersensitivity reaction.
2. **Type IV** or T cell-mediated hypersensitivity reaction.

Pathology:

- Centrilobular bronchiolitis
- and interstitial lymphocytic infiltration
- with or without loosely formed small granulomas interspersed in the interstitium .

- Specific findings vary with the stage of the disease at time of biopsy.


Clinical syndromes

Three Forms of presentations:

- Acute HP
- Subacute
- Chronic

Acute HP:

- Results from intermittent intense exposure
- *General symptoms:* occur 2 to 9 h fever, headache, chills, malaise and myalgia.
- *Pulmonary symptoms:* dyspnea and nonproductive cough.

Physical examination:

- Fever, tachycardia
- Cyanosis
- Bibasilar crackles in the lungs

- The symptoms and signs resolve without specific treatment in 1 to 3 days

Subacute or chronic HP

- Results from continual low level of exposure to an antigen.
- General symptoms: weight loss and anorexia.
- Pulmonary symptoms: progressive dyspnea & dry cough.
- Symptoms are usually present months to years

Physical examination of chronic HP:

- No fever but tachypnea
- Clubbing not common
- Bibasilar crackles in the lungs
- Respiratory failure
- Corpulmonale

- The sypmtom are present months to years.

Diagnosis:

1- History is *the cornerstone* for diagnosis of HP

- A temporary relationship between exposures and symptoms
- A high index of suspicious with remission of symptoms after removal from environment and recurrence of these symptoms with a return to that environment all suggest HP.

2 -The presence of serum antibody (precipitin)

indicates exposure and sensitization and is not diagnosis of the disease as not all exposed subjects develop the disease

3- Chest radiographs

- **Acute HP**
  - Normal
  - Nodular, ground glass, consolidation
  - linear shadows
- These radiodensities are diffuse and poorly defined and tend to occur in the lower lobes and spare the apices.

- **In chronic HP**

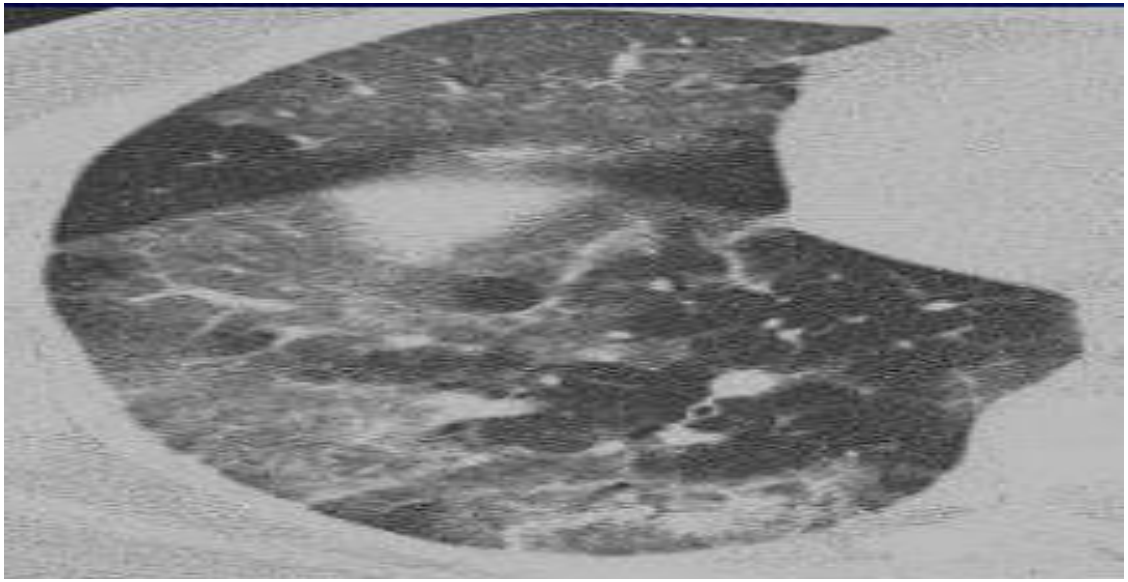
  - Diffuse linear
  - Nodular
  - Loss of volume
  - Sparing of the bases and upper lobe predominance

4- High resolution CT

- HRCT is more sensitive than X ray
- Half of patients with normal chest radiographs have characteristic findings of centrilobular ground-glass and nodular opacities on CT.

- **In acute HP**

  - **Areas of consolidation and ground-glass opacities in centrilobular and bronchovascular distribution .**



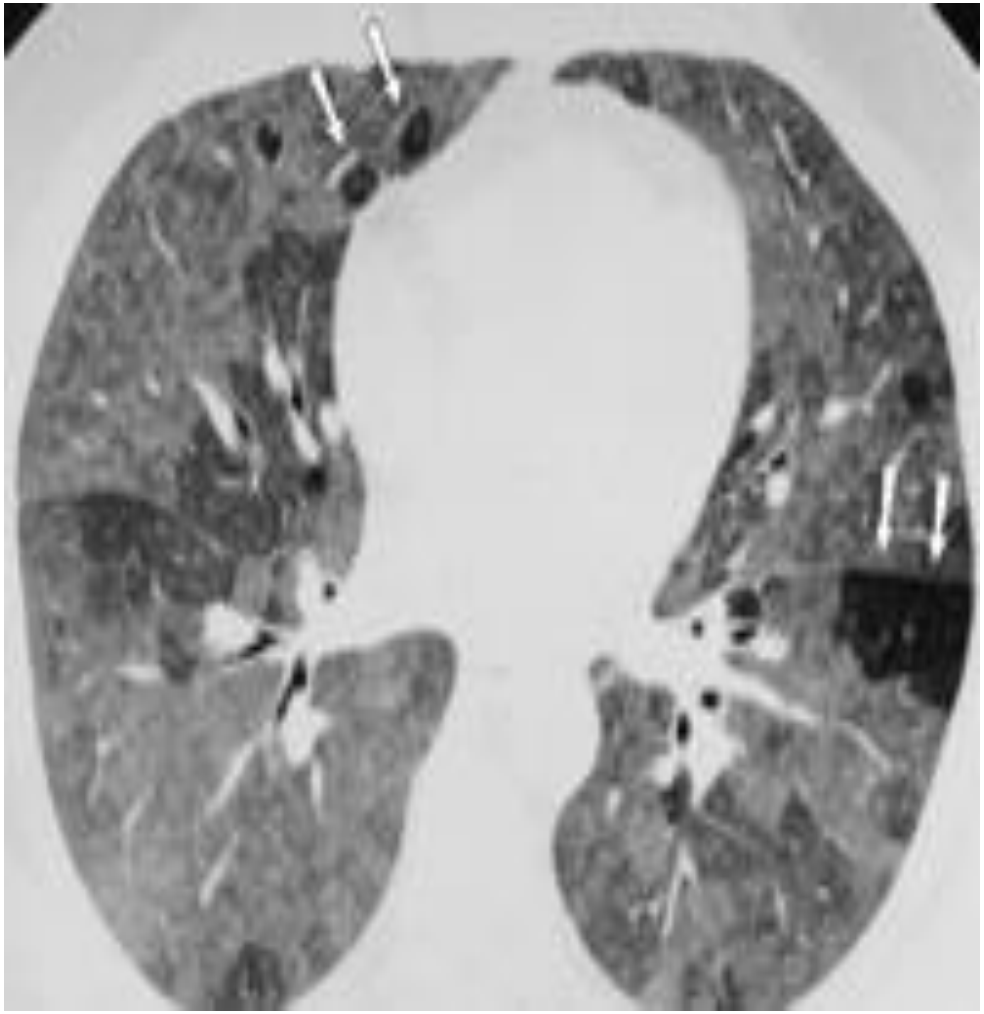
Acute HP (bird fancier's lung) ground-glass opacities.

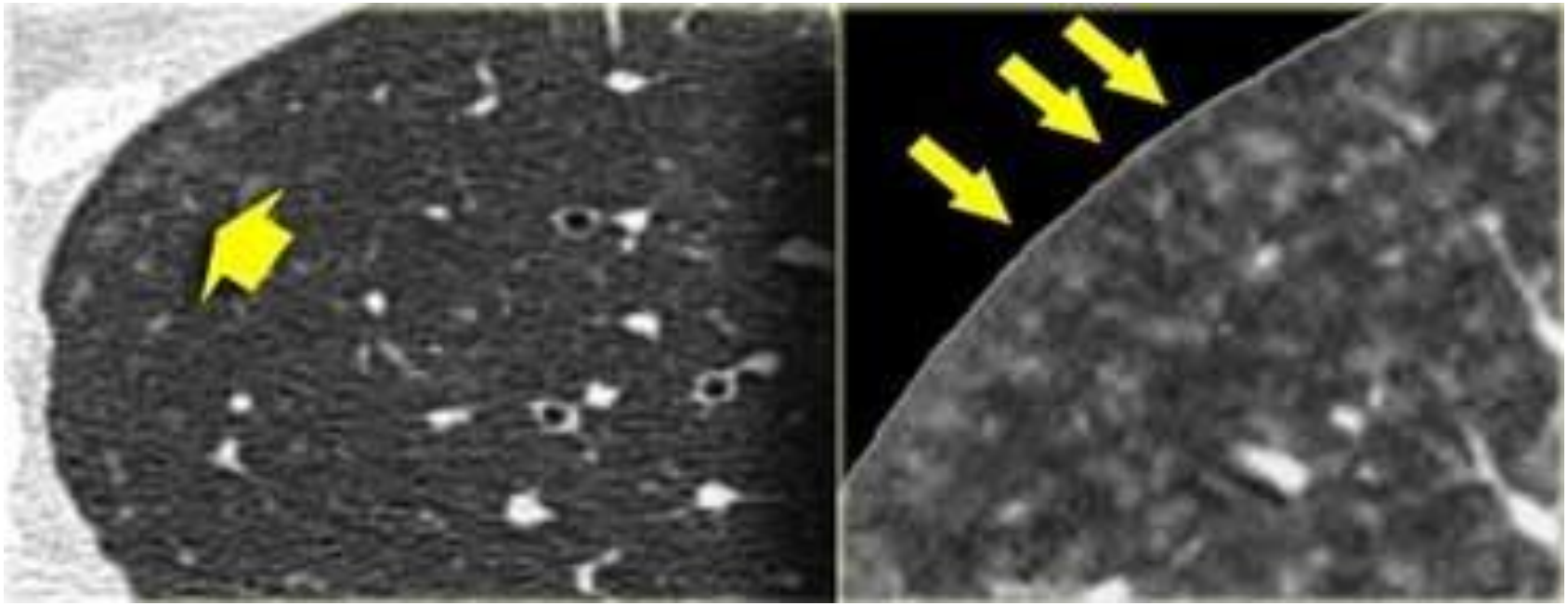
- Acute HP consolidation and ground-glass opacities in centrilobular and bronchovascular distribution.

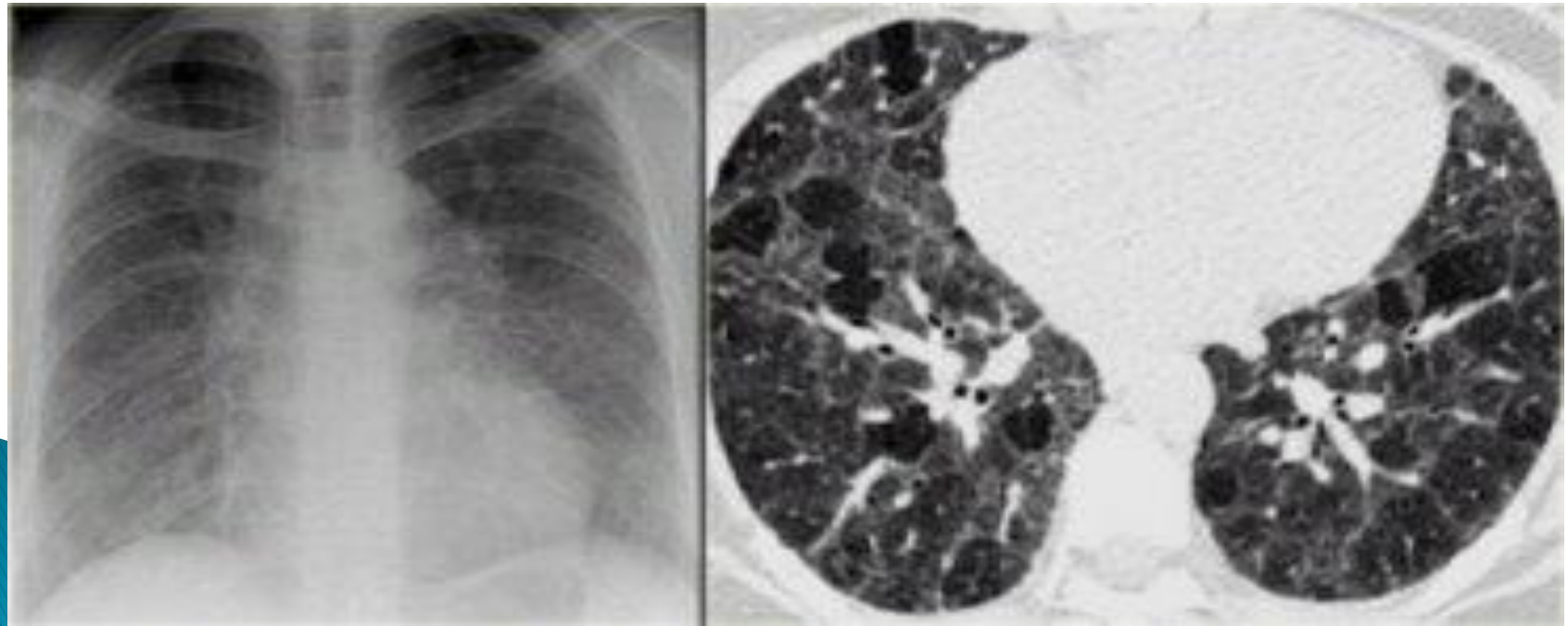
Subacute HP:

Consist of varying proportions of:

- ground-glass opacity,
- poorly defined centrilobular nodules, and
- areas of decreased attenuation (air-trapping)
- and mosaic pattern and predominantly in the lower lobes

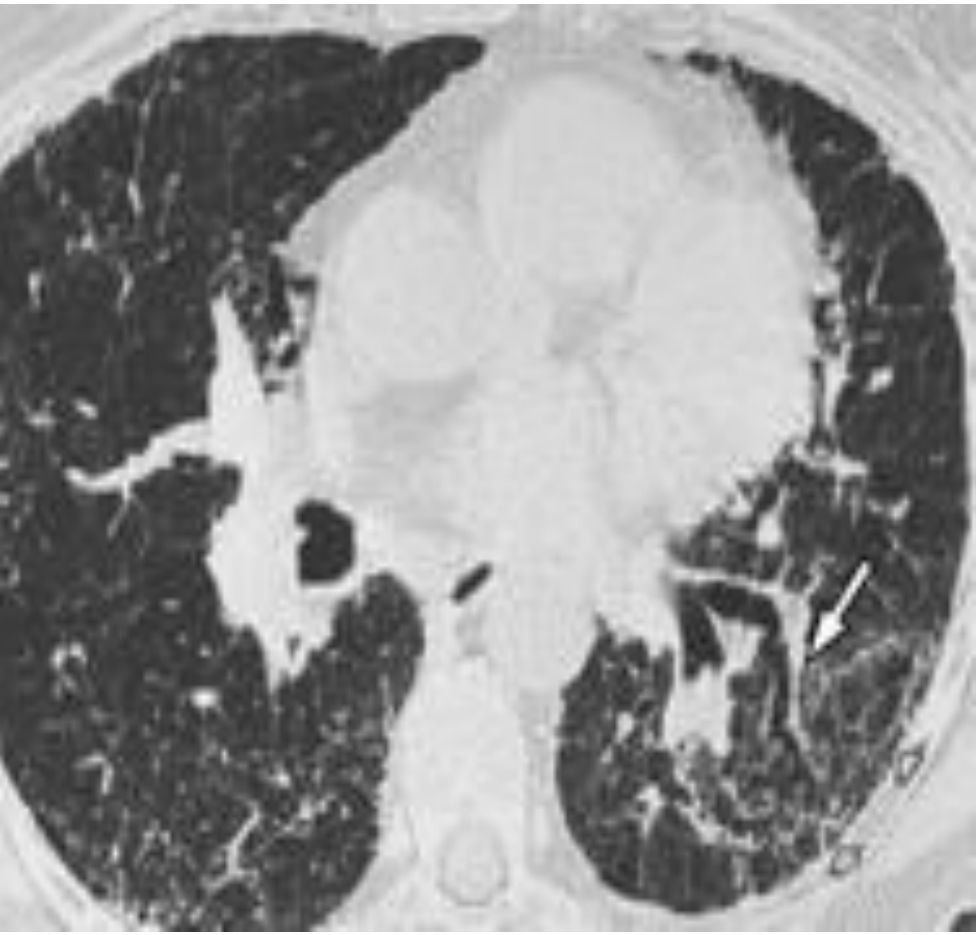


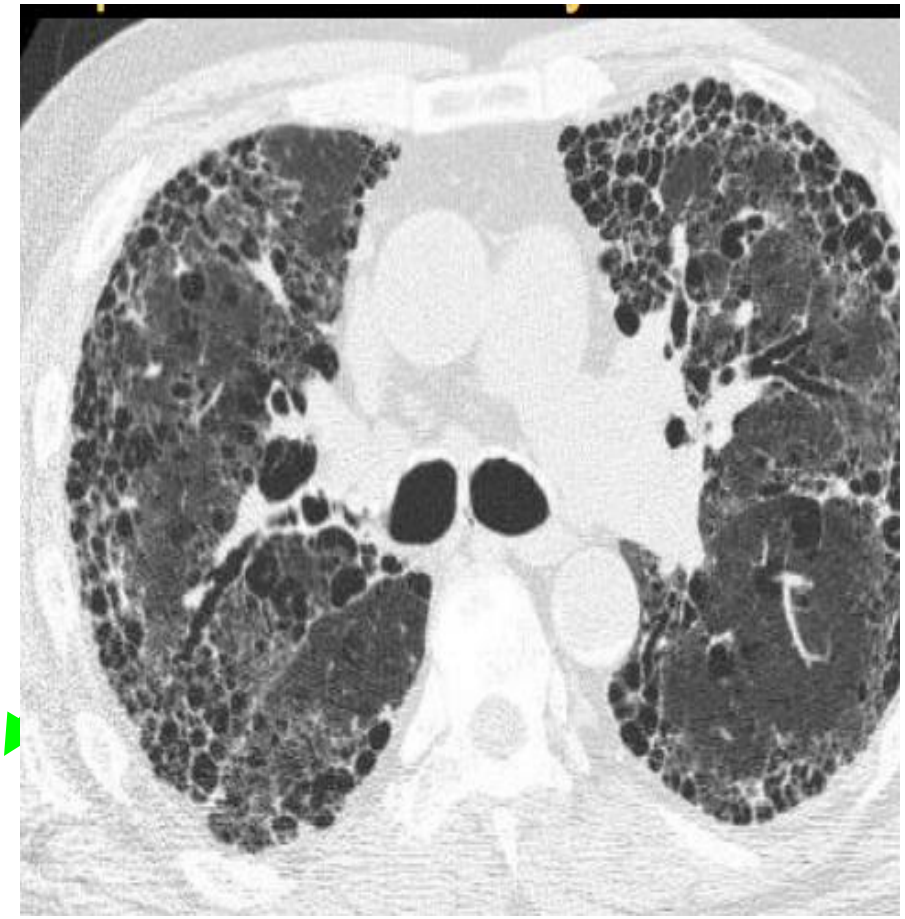




In chronic HP:

- nodules
- irregular linear opacity
- traction bronchiectasis
- architectural distortion
- honeycombing
- mid to upper lobe predominance





5- Pulmonary function tests:

- Restrictive ventilatory defec
- Arterial hypoxemia with hypocapnea
- Increased A-a oxygen gradient either at rest or after exercise is common .
- Decreased diffusing capacity for CO (DLCO)
- A mild obstructive pattern is sometimes observed .

6- Inhalation challenge:

- Performed in natural environment or in the laboratory, can be useful in the diagnosis of HP.
- A specific inhalation challenge in the laboratory can be useful for diagnosis if the agent is unknown and can delivered by a nebulizer to patient.

7- Bronchoalveolar lavage fluid:

- Acute phase: is characterized by an increased number of neutrophils and CD4+ T lymphocytes.
- Subacute/chronic phase: increased number of CD8+ T lymphocytes

BALF: CD4:CD8 ratio is less than 1.

8- Lung biopsy:

Indicated when the clinical features and environmental history leave the diagnosis unclear. Lung biopsy often reveals:

- **Centrilobular bronchiolitis**
- **interstitial lymphocytic infiltration**
- **loosely formed small granulomas in the interstitium**

Diagnostic criteria

The diagnosis requires the presence of

(1) four or more major criteria,

(2) at least 2 minor criteria, and

(3) exclusion of other lung diseases with similar clinical features.

Major criteria

1. Symptom compatible with HP.
2. Evidence of exposure to antigen (history or serum antibody or BAL antibody).
3. Radiographic findings compatible with HP
4. BAL lymphocytosis.
5. Histological findings compatible with HP (biopsy).
6. Positive “natural challenge” that produces symptoms and objective abnormalities either through controlled inhalational challenge or after re-exposure to the offending environment

Minor criteria

1. Bibasilar rales.
2. Decreased CO diffusing capacity.
3. Arterial hypoxemia.


Differential Diagnosis

- **Acute HP**

- Pulmonary edema.
- Organic dust toxic syndrome.
- Infectious pneumonia (viral origin or mycoplasmal origin).
- Acute interstitial pneumonia
- Acute eosinophilic oneumonia

- **Chronic HP**

- IPF.
- Other causes of pulmonary fibrosis .
- Granulomatous pneumonitis (sarcoidosis).

Prognosis:

- **In acute phase**

  The prognosis is excellent.

- **The subacute/chronic phase**
  - Variable clinical course but usually favorable.
  - If patients are removed from exposure before there are permanent radiologic or physiological abnormalities; the prognosis is excellent.
  - If exposure persists, 10 to 30 % of patients will progress to diffuse pulmonary fibrosis with resultant cor pulmonale and death .

Tratment:

A- Avoidance of further exposure
B- Medical therapy
C- Treatment of complications
D- Pulmonary rehabilitation

A- Avoidance of further exposure:

- Identifying the offending antigen and avoiding further exposure.
- Wearing a mask can decrease the intensity of exposure .
- Change the work.

B- Medical treatment:

- **Acute HP** is often reversible with avoidance of further exposure.
- Corticosteroids may be useful in severe acute or subacute cases . *Prednisone 40 to 60 mg/day* is given for 2 weeks followed by a gradual decrease over 1 to 2 months
- **In chronic stage:** Steroid treatment can delay further damage to the lungs and help preserve their function .
- Azathioprine and cyclophosphamide may be tried in resistant cases

C- Treatment of complications as respiratory failure and heart failure

D- Pulmonary rehabilitations in severely damaged lung


Thank you