Diffuse parenchymal lung diseases

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- **Diverse group of rare inflammatory disorders that involve lung parenchyma , distal airways and alveoli**

  (diffuse infiltrative lung disease, interstitial pneumonitis)

  - impaired gas exchange (alveololar-capillary membrane damage)
  - decreased lung compliance a decreased lung volume (VC, TLC)

Classification

ILD of specific (known) cause	
Aspiration syndromes	GER, swallowing dyscoordination, anatomical disorders
Postinfectious bronchitis obliterans	
Radiation and drug impairment	
Hypersensitivity pneumonitis	Inhalation organic antigens, „hot tube lung"
Primary pulmonary processes	
Idiopathic interstitial pneumonias	IPF, NSIP, DIP, AIP, LIP, RB-ILD, COP-BOOP
Diffuse aleveolar hemorrage	With capillaritis Without capillaritis – idiopathic pulmonary hemosiderosis
Pulmonary alveolar proteinosis	
Pulmonary infiltrates with eosinophilia	
Pulmonary microlithiasis	
Pulmonary vascular disorders	
Pulmonary lymphatic disorders	
Systemic disorders eith pulmonary involvment	SLE, sytemic sclerosis, Sjogren
Disorders unique to infancy	

Disorders unique to infancy

Diffuse developmental disordres	Acinar dysplasia
	Congenital alveolar dysplasia
	Alveolar capilary dysplasia with misalingment of pulmonary veins
Growth abnormalities	Chronic neonatal lung disease
	Pulmonary hypoplasia
	Chromosomal abnormalities
	Associated with congenital heart disease
Surfactant dysfunction disorders	Surfactant protein B mutations
	Surfactant protein C mutations
	ABCA3 mutations
	NKX2,1 (TTF-1) mutations
	Histology consistent with surfactant dysfunction without recognized genetic disorder
Neuroendocrine cell hyperplasiqa	
Pulmonary interstitial glycogenosis	

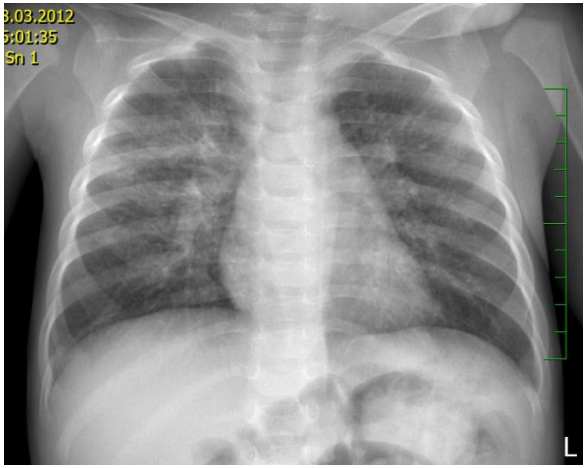
Clinical presentation

- Chronic cough
- Fatigue
- Exercise intolerance (postexertional dyspnea)
- Weight loss
- Postexertional cyanosis
- Myalgia, Arthralgia
- Later troubles at rest (dyspnea, tachypnea)
- Spontanneous pneumothorax

- (Lifethreatening) acute intersticial pneumonia

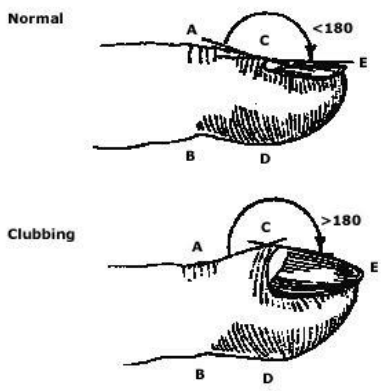
Diagnosis

1. History including enviromental influences
2. Physical examination
3. Pulmonary function tests
   - F-V curve, bodypletysmography, difusing capacity
   - Physical activity tolerance testing
4. Chest X ray
5. Laboratory tests
   - Direct detection of etiol. agent
   - Microbiology
   - Serology, PCR
   - Markers of inflammation
   - Imunology, autoantibodies, specific IgG4
6. Chest HRCT

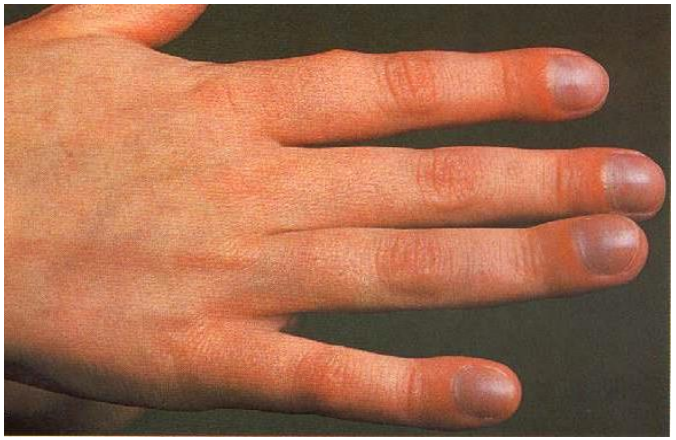


Physical examination

- Initially normal
- Basal crepitations, cracles
- Tachypnea
- Exertional ... Cyanosis at rest



- Digital clubbing (40 - 75 %)

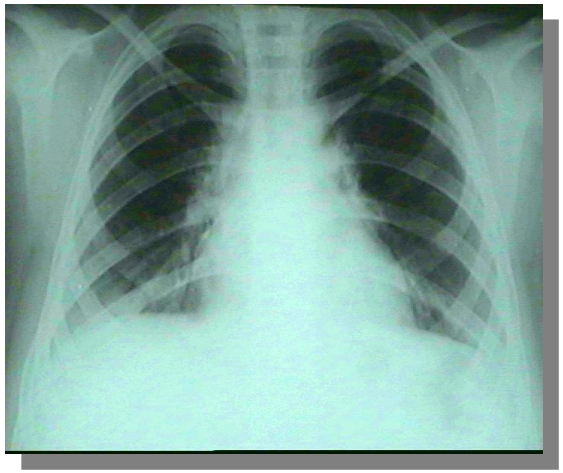


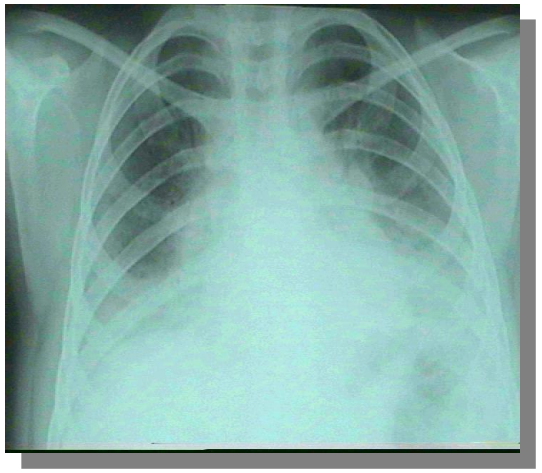
Pulmonary function tests

- **Flow-volume curve**
  Decreased volume (VC)
  Relative increased flows
  Often peripheral obstruction
  ..
- **Body plethysmography**
  decreased TLC
  decreased compliance
- **Diffusing capacity**
  decreased DLCO
- **Excercise testing**
  postexertional hyposaturation

Imaging

- X-ray
  - **normal (10-15 %), difffuse infiltrative changes, reticular or reticulonodular changes mostly in lower lobes**
  - honeycombing lung





HRCT

- Increased interstitial markings
- Irregularity and minimal thickening of visceral pleura
- Irregular vascular lineation
- Elongation and accentuation of interlobular septs
- Reticulonodular markings
- Ground glass opacities
- Diffuse infiltrates in combination wits cystic formations (2-4 mm)
- Honeycombing

Laboratory tests

- Microbiology
- Serology and PCR

  Mycoplasma, fungal inf., adenovirus, RSV, metapneumovirus, parvo B19, EBV, CMV

- Markers of inflammation, ESR
- ACE (elevated in sarcoidosis)

- Immunology – immunoglobulins, Tcell subtypes, autoantibodies, specific IgG4

Diagnostic protocol

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2. Physical examination
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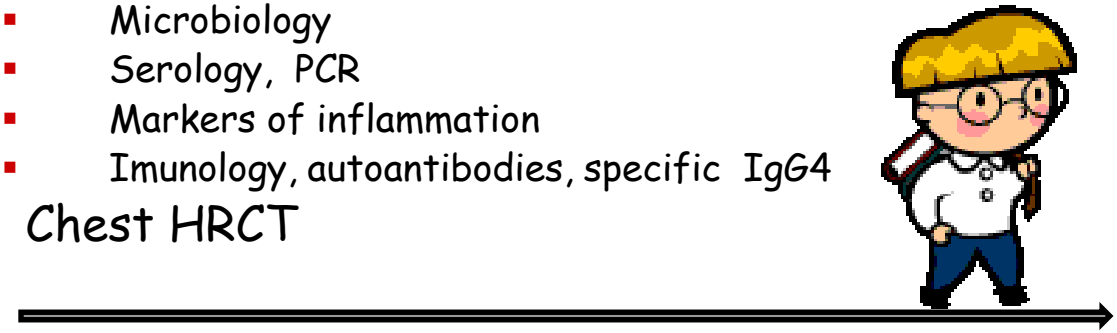
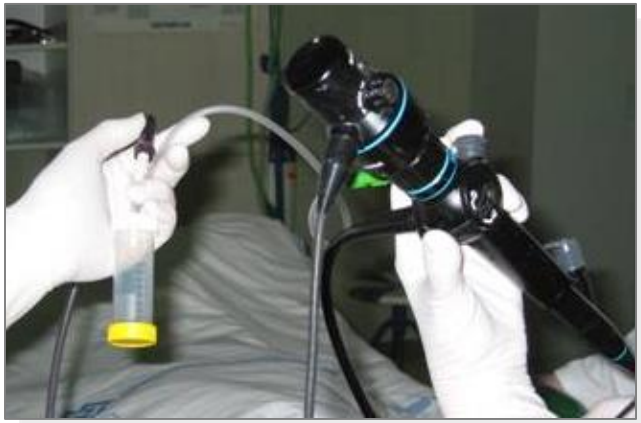


7. Bronchoscopy + bronchoalveolar lavage
8. pH probe, barium swallow ⟹ **chronic aspiration**
9. Lung biopsy

Bronchoalveolar lavage

- Differential count
- (bronchial and alveolar fractions)
  - **Normal:**
    - **AM** **> 86 %**
    - **Ly** **< 10 %**
    - **PMN** **< 3 %**
    - **Eo** **< 1 %**

- Microbiology
- PCR diagnostic
- Immunology



Lung biopsy

- Transbronchial lung biopsy
- Videoassisted lung biopsy
- Open lung biopsy

- Diagnosis confirmation, classification
- Exclusion of infection and malignancy
- Disease activity determination

Differential diagnosis

- **Infection in the immunocompromised patient**
- **Recurrent aspiration**
  - gastroesophageal reflux
  - swallowing dyscoordination
  - anatomic abnormalities of the larynx, trachea, or oesophagus
- Congestive changes related to **cardiovascular disease**
- Abnormalities of the pulmonary vasculature

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Unique forms of interstitial lung diseases of infancy

- Premature babies with early RDS ---- -chronic neonatal lung disease
- **Full-term newborn without complications**
- Tachypnea, dyspnea
- Cracles, (wheezing)
- Hypoxemia

} **without a clear underlying cause**

Laboratory tests normal, no signs of infection

Chest X-ray: diffuse infiltrates, hyperinflation

HRCT: hyperinflation, ground glass opacities

Lunf function: airtrapping

Lung biopsy

Surfactant

- Type II cells–60% of alveolar epithelial cells

- Lipoprotein
  - Phospholipids 85%
  - Specific proteins 10%
    - SP-A (5%)
    - SP-B (2%)
    - SP-C (2%)
    - SP-D (1%)
  - lipids 5%

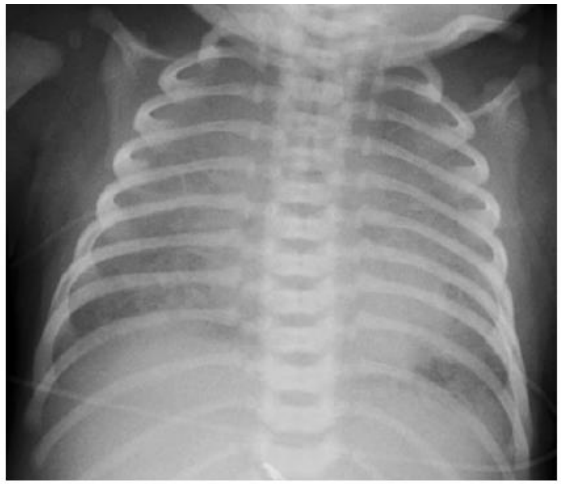
- Membrane transporter, member A3

ABCA3 – transport of phospholipids essential for surfactant function to lamellar bodies

Surfactant dysfunction disorders

SP-B deficiency

autosomal recessive



Respiratory failure within 3 months of birth unresponsive to medical therapy

Histology: pulmonary alveolar proteinosis

Surfactant dysfunction disorders

ABCA3 mutations and SP-C mutations

autosomally recessive

autosomally dominant

History of neonatal lung disease, older infants

Adult form NSIP, DIP

Persistent tachypnea of infancy / Neuroendocrine cell hyperplasia of infancy

- tachypnea, cracles, hypoxemia
- absence of an underlying disease to explain the symptoms
- Chest X-ray: hyperinflation
- HRCT: hyperinflation and areas ground glass opacities
- Lung function: air trapping

- Lung biopsy: bombesin immunohistochemistry- **hyperplasia of neuroendocrine cells in the distal airways and aggregates of neuroendocrine cells in the lobular parenchyma**

- symptoms may persist for months to years

Pulmonary interstitial glycogenosis

- tachypnea since birth X-ray: diffuse infiltrates of unknown etiology
- Biopsy: interstitial proliferation of bland, nondescript histiocytic type cells and minimal or no inflammation
- cells contained **monoparticulate glycogen**
- Infants remained tachypneic for months

Therapy

- **O_2 therapy** based on day and night time SaO_2 levels
- **Oral prednisolone** (1–2 mg/kg/day) or
- **Pulsed intravenous methylprednisolone**

- Children with significant disease are best treated with **pulsed methylprednisolone at least initially** (10–30 mg/kg/day for 3 days consecutively at monthly intervals). The minimum number of cycles recommended is three, but treatment may need to be continued for > 6 months depending on response.
- The disease may **then be controlled with oral prednisolone** preferably given as an alternate day regime. In a few cases oral prednisolone is used from the beginning simultaneously with intravenous methylprednisolone but this should only be required in those with very severe disease.

Therapy

hydroxychloroquine (6–10 mg/kg/day in two divided doses).

azathioprine (2–3 mg/kg/day),
cyclosporin (6 mg/kg/day)
cyclosphosphamide (1–1.5 mg/kg/day)
methotrexate (2.5–7.5 mg/kg/week).

Lung or heart-lung transplantation

„Take home massage“

- Do not minimize symptoms
- History, incluning enviromental
- Early lung function testing(TLC a Cst)
- Objectification of excercise toleration
- Immunology
- HRCT
- Bronchoscopy and BAL
- Lung biopsy