
# South to South

# HIV related lung disease

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# Learning objectives

## At the end of the session you will

- Understand the impact of lung disease on HIV morbidity and mortality
- Be able to diagnose and treat the most common acute and chronic lung diseases associated with HIV/AIDS

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# HIV related lung disease

General Observations

- 60% of children have chronic changes on CXR  by 2 years.
- HIV related lung diseases have increased the number of children admitted to hospital with acute lung disease by 20-40%
- More likely to develop complications and require admission for longer periods of time
- Chest diseases may require more sophisticated diagnostic techniques.

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# General Observations cont.

- Pulmonary manifestations are the most common initial manifestations
- Primary cause of death in 50% of HIV infected children
- Common pulmonary disorders are bacterial pneumonias, PCP, and LIP.

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# HIV related lung disease

- The spectrum of lung disease influenced by
  - Immunological status
  - Other co-morbid disease ie reflux
  - Use of anti-retroviral drugs
  - PCP prophylaxis

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# Acute Respiratory Disease in HIV infected children

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# Acute Respiratory Disease in HIV infected children

- Bacterial pneumonia
- *Pneumocystis jiroveci* pneumonia (PCP)
- Mycobacterium *Avium* Complex (MAC)
- Viral pneumonia
- CMV
- Fungal infections

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# Community Acquired Pneumonia

## Background and Presentation:

- Most frequently identified pathogen:
  - *S. Pneumoniae*
    - 40 x ↑ risk of developing invasive pneumococcal disease
- May have ↑ risk of
  - gram negative infections
  - complicated viral pneumonias

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# Community Acquired Pneumonia

Clinical presentation:

- similar to uninfected children
- Fever
- Cough
- Tachypnoea
- Hypoxia
- Chest retraction

Investigations:

- CXR
- Acute phase reactants (CRP)
- White cell count
- Blood culture if hospitalized
- Sputum culture

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# Community Acquired Pneumonia

**Out-Patient Treatment**

- Manage according to IMCI guidelines
  - Amoxycillin (30-80 mg/kg/day tds)

- Standard dose Amoxycillin (30-40mg/kg/day) + Co-amoxiclav (30-40mg/kg/day) if suspects
  - penicillin resistant organisms
  - beta-lactamase-producing Haemophylus influenzae
  - Staphylococcus aureus

- Erythromycin if penicillin allergic

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# Community Acquired Pneumonia

**In-Patient Treatment**

- No CNS involvement
  - Penicillin + gentamicin ± cloxacilin
- CNS involvement
  - 3rd Generation Cephalosporin +/- Vancomycin (if suspecting resistant S *pneumoniae*)
  - Discontinue vancomycin once penicillin resistant organism has been excluded
- Do **NOT** discontinue co-trimoxazole prophylaxis when treating intercurrent bacterial infections with other antibiotics

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# Pneumocystis jiroveci pneumonia (PCP)

- AIDS defining illness
- Occurs most commonly in children < 1 year
- High mortality
- Prevention (CTX prophylaxis) effective
- Early and appropriate treatment improves prognosis significantly

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# Pneumocystis Jiroveci cont.

- Signs and symptoms:
  - Onset- gradual: days-weeks
  - Febrile
  - Cough
  - HALLMARK:  tachypnea with hypoxia
  - Lung auscultation may be normal

- Investigations:
  - Oxygen saturations- usually < 90% in room air
  - CXR-  diffuse bilateral alveolar or interstitial infiltrate (patient may be hypoxic with normal CXR)

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# Management of PCP

- Begin treating for PCP immediately on suspicion (in addition to usual treatment of pneumonia), even if HIV status of child has not been established yet
- Treatment:
  - Oxygen
  - Co-trimoxazole (20 mg/kg/day of trimethoprim component) 6 hourly for 5 days, changing to oral for 3 weeks if adequate response
  - Consider adding Clindamycin 30-40mg/kg for severe disease
  - Prednisone 1-2 mg/kg daily for 2 weeks- r/o TB first
  - Morphine if severe distress and no ICU available
- Secondary PCP prophylaxis after discharge

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# Chronic Respiratory Disease in HIV infected children

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# Chronic Respiratory Disease in HIV infected children

- Lymphoid Interstitial Pneumonia
- Bronchiectasis
- Aspiration Associated Lung Disease

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# Etiology of HIV-associated Chronic Lung Disease

- Jeena P M et al. looked at causes of Persistent Lung Disease (PLD) and Chronic Lung Disease (CLD) in HIV infected and uninfected children in South Africa

- Chronic lung disease was defined as the presence of clinical and radiological features of lung disease for > 3 months
- 138/194 (71%) of the children with PLD/CLD had HIV
- Amongst HIV infected children with confirmed diagnosis
  - LIP 46%
  - TB 17%
  - Bronchiectasis 17%
  - Other interstial pneumonitis 14%

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# Why is it so difficult to establish a cause of CLD?

- Imaging findings
  - often non-specific
  - have to be interpreted in association with clinical findings & CD4 count
- Isolation of the organism
  - sputum analysis, nasopharyngeal aspirate , BAL or lung biopsy
- Treatment
  - empirical basis before a definitive diagnosis is made

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# Added difficulty with establishing a cause of CLD in HIV-infected children

- High incidence of Tuberculosis
- Many children already have structural lung damage
- Late diagnosis of HIV
- No PCP prevention
- In the absence of HAART
  - Multiple organisms/ conditions

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# What are the consequences of chronic lung disease?

- Permanent destruction of lung
- Raised pulmonary pressures with secondary right heart failure
- Recurrent admissions
- Death from respiratory failure

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# LIP

- Lymphoid Interstitial Pneumonia

Or

- Lymphocytic Interstitial Pneumonitis

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# Case definition

- ‘The presence of a diffuse, often symmetrical, reticulonodular or nodular pattern, occasionally with the presence of hilar or mediastinal adenopathy for at least 2 months without identifiable pathogen or antibiotic response, can be used as a clinical case definition.’

- The nodules are approximately 2-3 mm and are most easily recognized at the bases and the peripheral lung zones

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# Lymphoid Interstitial Pneumonia not exclusively in HIV seropositive patients

**Table 1—*Diseases Associated With LIP***

| Diseases |
|---|
| Autoimmune (39%)* |
| Sjögren syndrome[48] |
| Systemic lupus erythematosus[28–37] |
| Rheumatoid arthritis[24] |
| Juvenile rheumatoid arthritis[38] |
| Hashimoto thyroiditis[24,26] |
| Myasthenia gravis[39] |
| Hemolytic anemia[26] |
| Pernicious anemia[60] |
| Autoerythrocyte sensitization syndrome[61] |
| Chronic active hepatitis[63] |
| Celiac sprue[64] |
| Primary biliary cirrhosis[62] |
| Systemic immunodeficiency states (14%)† |
| HIV/AIDS[103] with and without DILS |
| Common variable immunodeficiency†[46,47] |
| Agammaglobulinemia†[40] |
| Miscellaneous |
| Complication of allogeneic bone marrow transplantation[48,49] |
| Pulmonary alveolar microlithiasis[50] |
| Infections including Legionella pneumonia,[51] tuberculosis, Mycoplasma, Chlamydia |
| Diphenylhydantoin use[52] |
| Pulmonary alveolar proteinosis[53] |
| Idiopathic |

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# Lymphoid Interstitial Pneumonia

- LIP represents 25 - 40% of pulmonary disease in children (3% in adults)

- Three types:
  1. lymphocytic interstitial Pneumonia (LIP)
  2. pulmonary lymphoid hyperplasia (PLH)
  3. polyclonal polymorphic B-cell lymphoproliferative disorders.

- In African children BRONCHIECTASIS is a common consequence

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# Natural History

- Not fully understood

- Clinical course variable
  - remain stable or
  - progress slowly to respiratory failure
  - spontaneous remission has been known to occur

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# Spectrum of disease

- Depends on child's immune status and viral load
- Is a CD8 response to the HIV virus.
- Radiographic findings continues to evolve as the lifespan of patients with HIV and LIP increase with HAART
- Improvement and or resolution with ART
- Conflict in the literature ? poor or good prognostic sign

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# WHO Clinical Stage

- 2005 WHO stage 3
- No presumptive clinical diagnosis

- Definitive Diagnosis
  - CXR:
    - bilateral reticulonodular interstitial pulmonary infiltrates > 2 months
    - no response to antibiotic treatment
    - no other pathogen found.
  - Oxygen saturation persistently <90%
  - Characteristic histology

- May present with cor pulmonale with ↑ exercise induced fatigue

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# Clinical Presentation

- Onset insidious

On examination:

- Pulmonary findings
  - Cough and tachypnea
  - Chest deformities
  - Auscultatory findings rare
- Extra-pulmonary findings
  - Digital clubbing in advanced cases
  - Generalized lymphadenopathy
  - Hepatosplenomegaly
  - Parotid enlargement
- May present with symptoms or signs associated with intercurrent viral or bacterial respiratory illness

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# Extra-pulmonary findings

Parotid swelling

Finger clubbing

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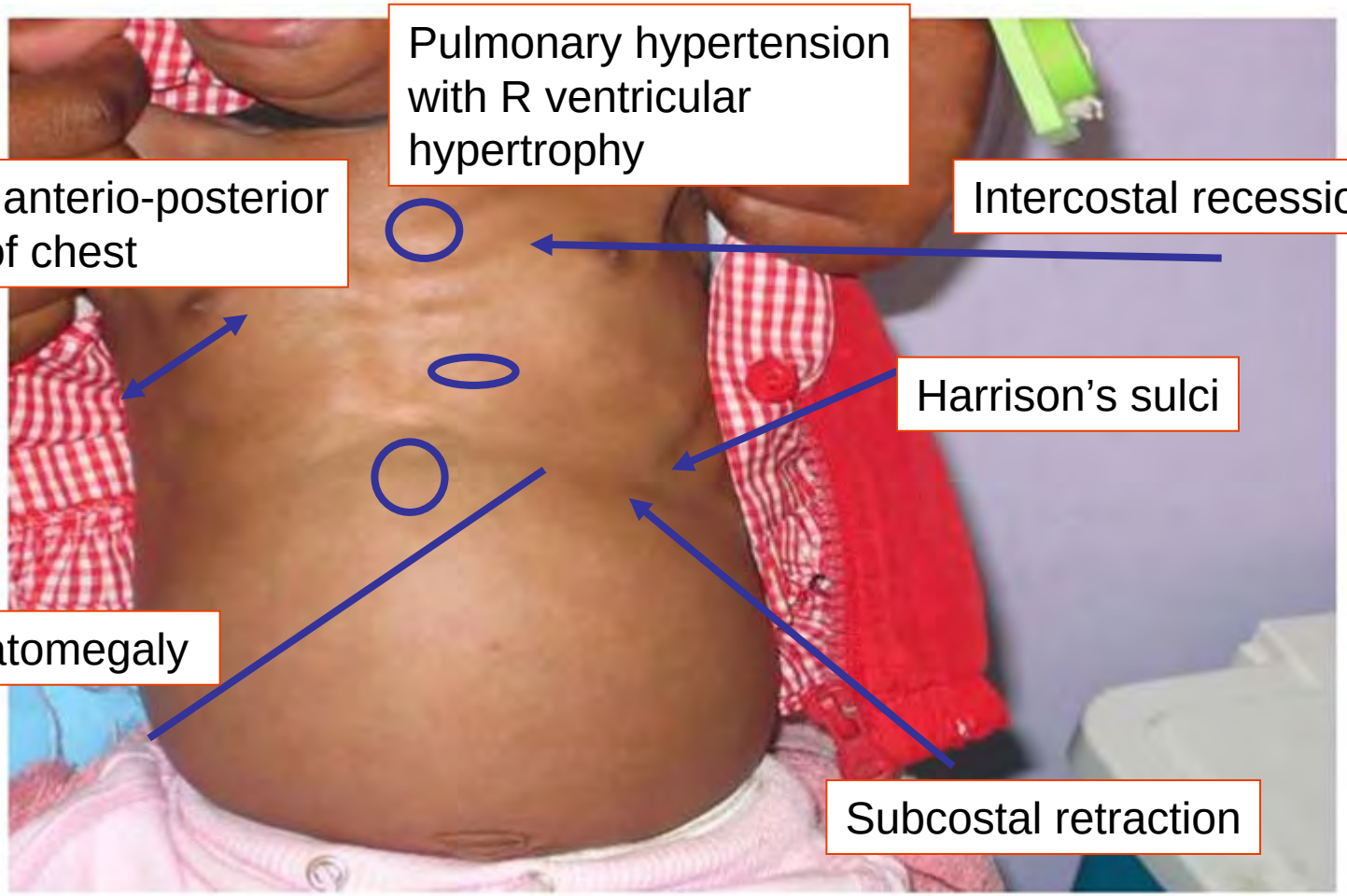
# Features suggestive of chronic respiratory illness

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# Diagnosis

- Definitive diagnosis requires open lung biopsy

- However, in patients with HIV diagnosis may be made if
  - dyspnoea with hypoxia
  - classic radiographic findings of micronodular infiltrates

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# Chest X-ray

1. LIP CXR has reticular or finely reticulonodular interstitial opacities with nodules  3 mm

2. Coarse reticulonodular interstitial opacities with nodules between 3 mm and 5 mm

3. 1 or 2 plus at least one area of patchy alveolar opacity

4. Focal alveolar consolidation  resembling pneumonia

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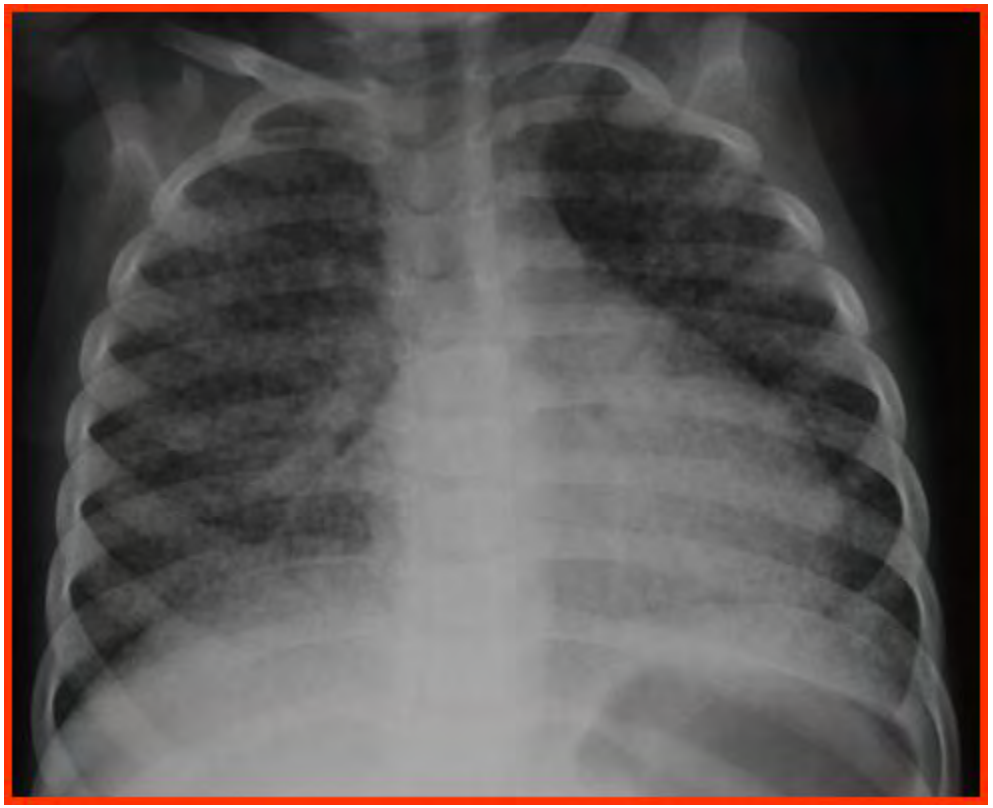
# Chest x-ray

- The radiographic findings of LIP includes a diffuse, symmetrical, reticulonodular, or nodular pattern with or without hilar or mediastinal adenopathy .



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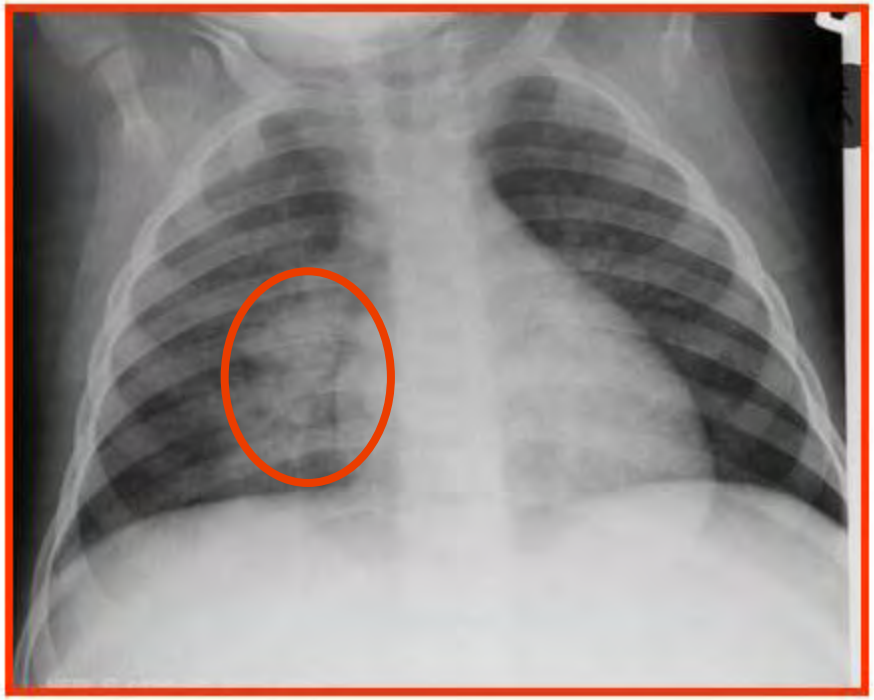
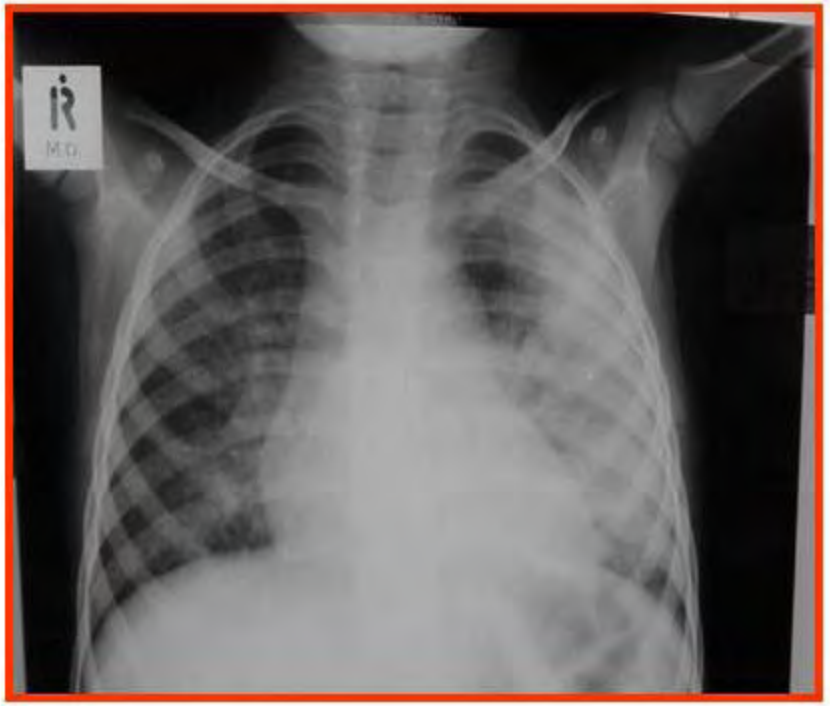
# Other CXR findings

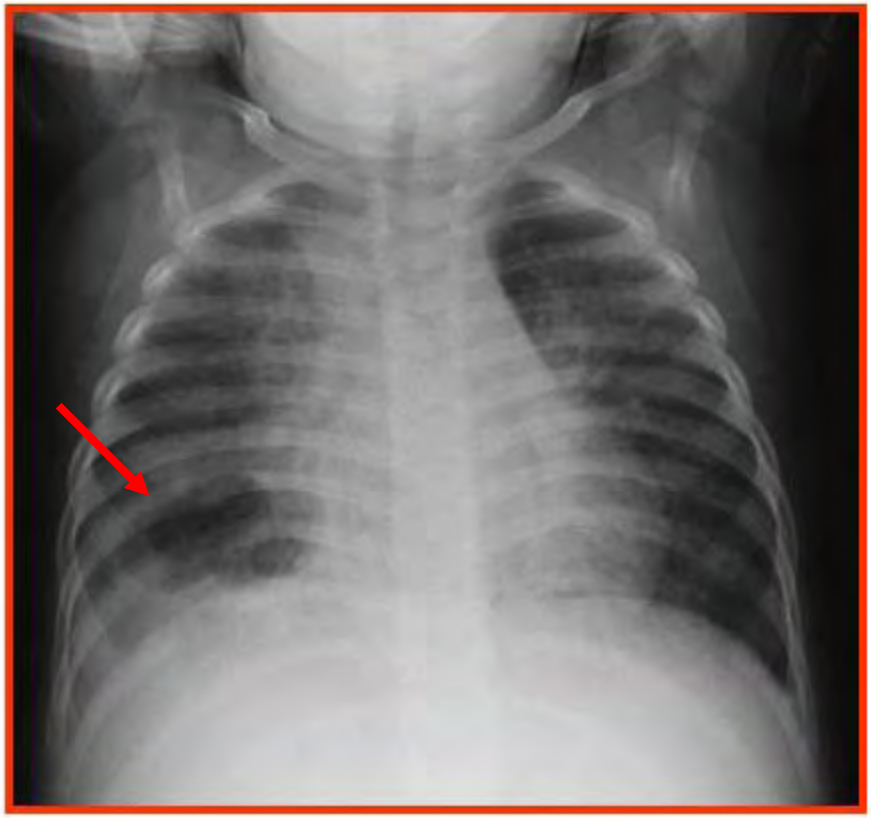


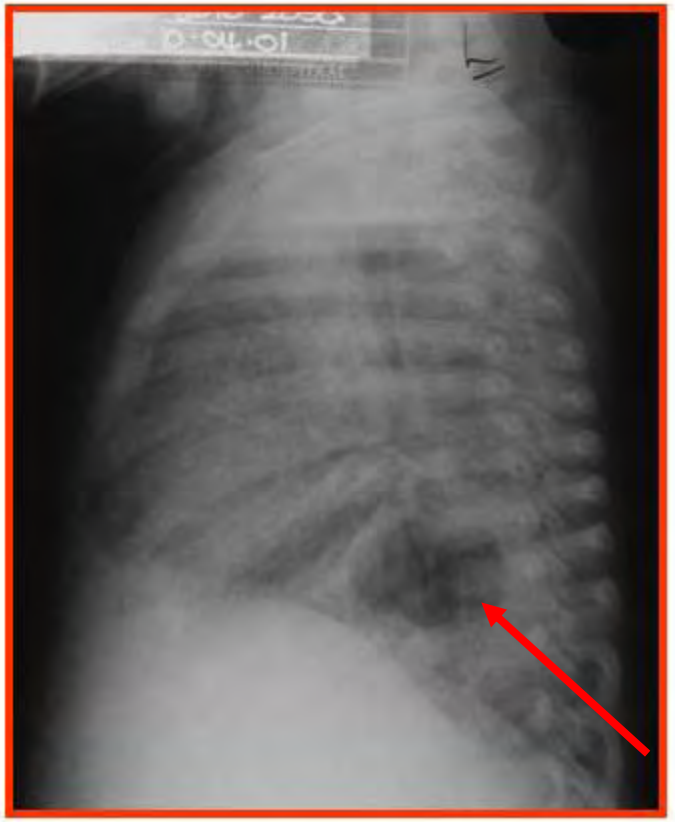
Lymph glands enlarge in LIP
Degree of enlargement: poorly described
May be difficult to distinguish from TB



Consolidation may be found

# LIP with Cystic changes





LIP with RLL cyst

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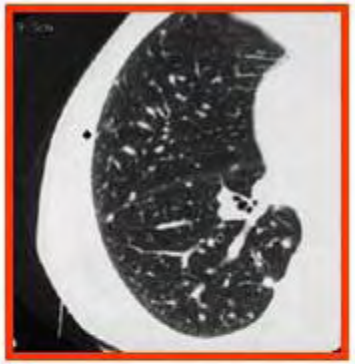
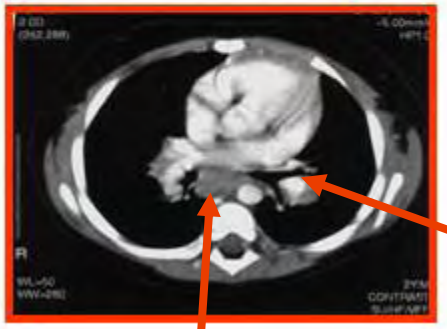
# CT scan findings

Subpleural micronodules

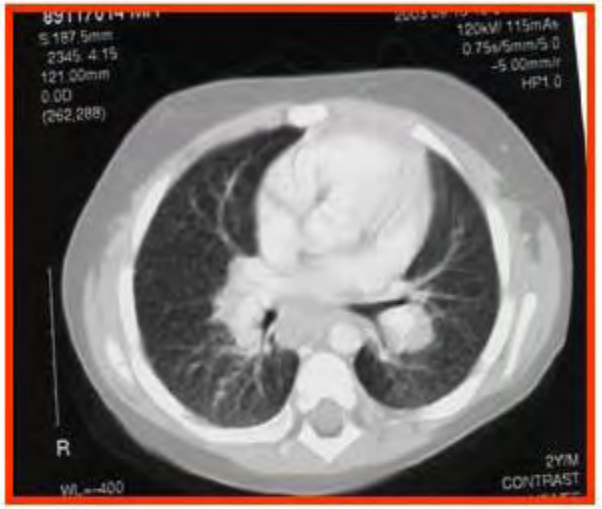




Hilar lymphnodes

Subcarinal lymphnodes

Reticulonodular pattern

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# Complications of LIP

- Recurrent lower respiratory infections
- Bronchiectasis
- Cystic lung disease
- Cor pulmonale

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# Treatment

- Supportive therapy
  - ↓ exposure to cigarette smoke / inhaled irritants
  - nutritional support
  - oxygen for hypoxemia
  - bronchodilators for reversible airway obstruction
  - antibiotics for inter-current infection
- HAART
  - symptomatic HIV disease - stage 3.
- Corticosteroid therapy
  - only indicated if respiratory failure
  - exclude TB before starting
  - ensure CTX prophylaxis

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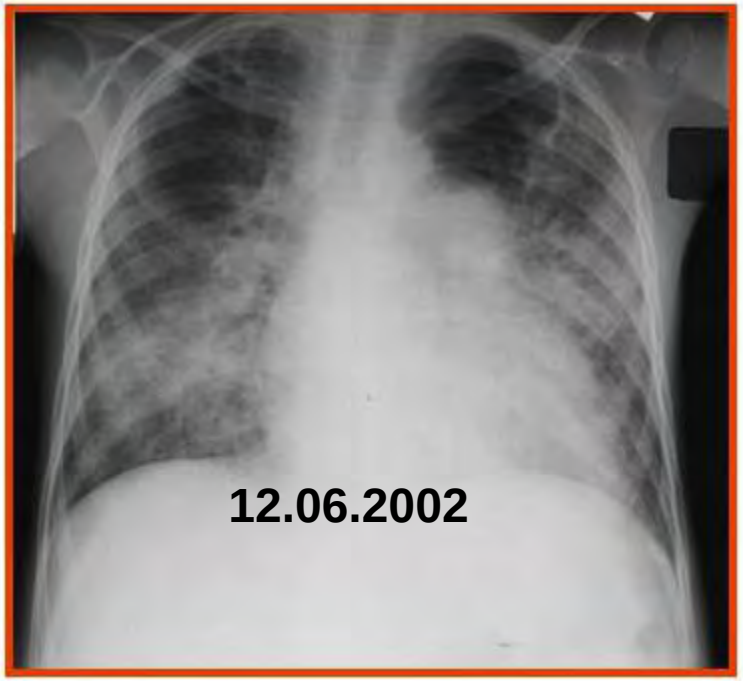
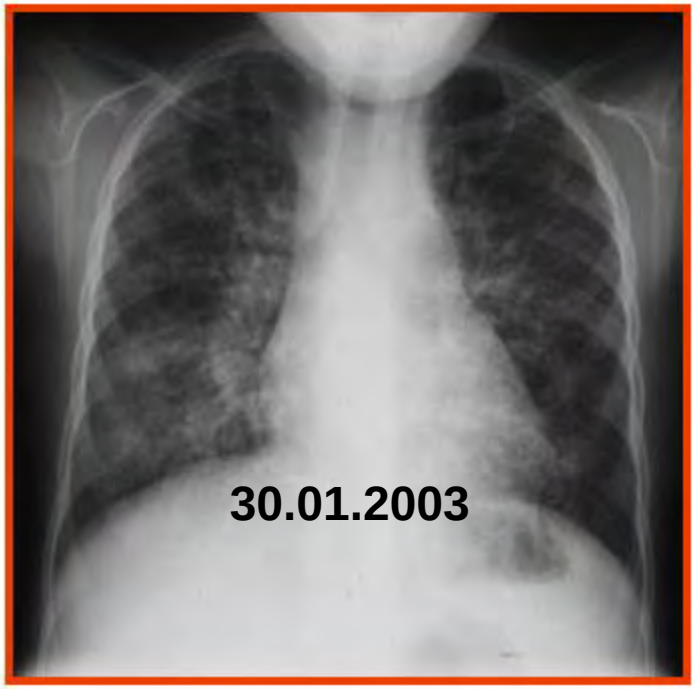
# Radiographic changes in response to HAART

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# TB LIP co-disease

- Diagnostic Dilemma as both are
  - common in sub-Saharan African children
  - presents with chronic symptoms,
  - hepato-splenomegaly
  - CXR findings similar:
    - reticulo-nodular picture
    - enlarged glands
    - can cause cavities

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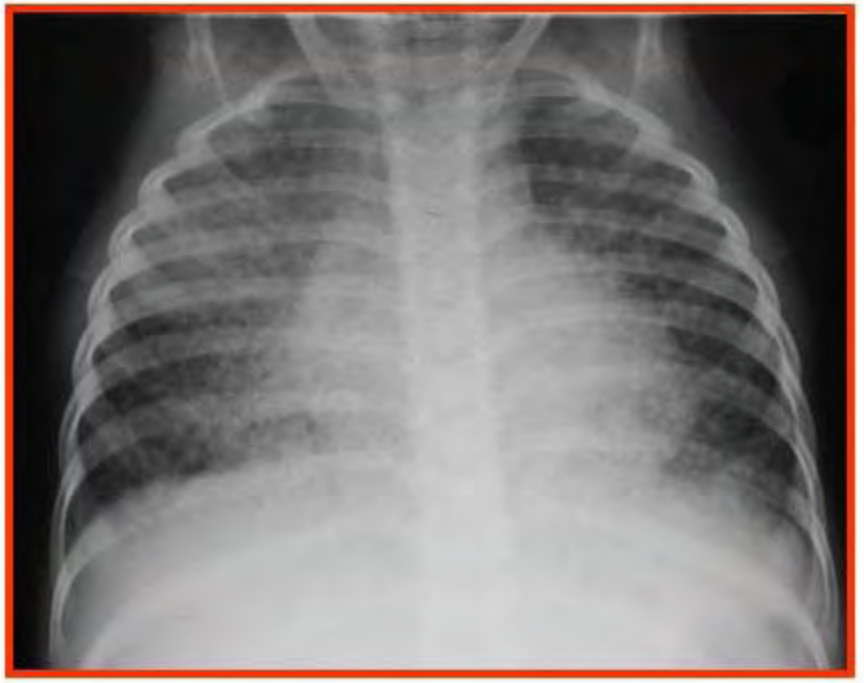
# LIP with Miliary TB

- Miliary TB more likely if
  - < 1 year of age
  - CNS involvement
  - CXR:  widespread fine ( < 2 mm ) nodules ( millet size)



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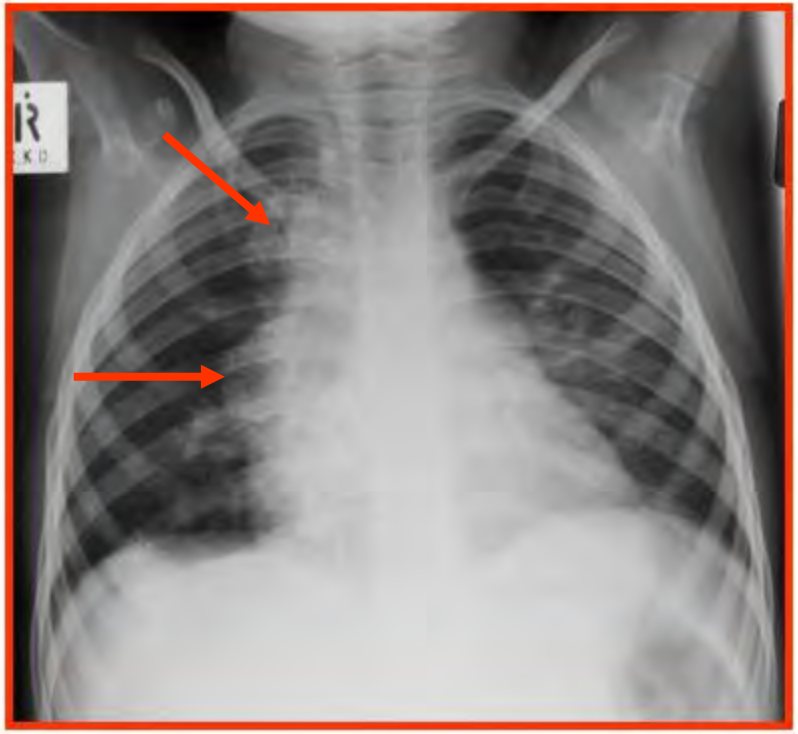
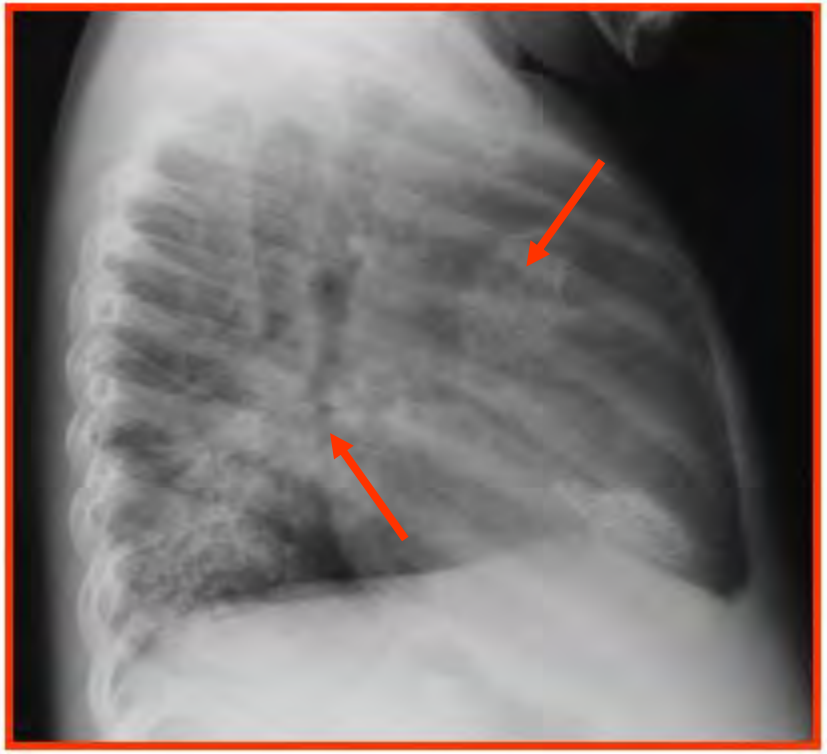
# LIP with TB





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# Long term outcome of LIP

- Largely unknown
- Conflicting evidence in literature
- Resolution of findings of LIP poor prognostic indicator if not on HAART
  - associated with reduction in CD4 count
- Resolution irrespective of patients clinical status

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# Summary

- LIP very common
- High morbidity
- Clinical Stage III disease
- WHO recommends HAART based on CD4 count
- BUT if severely symptomatic should get HAART irrespective of CD4 count
- All children with clinical features suggestive of LIP should have a CXR
- Diagnosis based on clinical features and CXR

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# Bronchiectasis

- Represents a common end stage of a number of nonspecific and unrelated antecedent events:
  - inflammatory destruction of bronchial and peri-bronchial tissue
  - irreversible dilatation of bronchial tree
  - permanent dilatation of sub-segmental airways
  - chronic daily cough

# Bronchiectasis and HIV

- Both T and B cell dysfunction + impaired local defence mechanisms
  - impaired muco-cilliary clearance
  - recurrent pulmonary infections
- Incidence 16%
- Most common causes of bronchiectasis
  - LIP
  - unresolved or recurrent pneumonia
  - TB

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# WHO Clinical Stage

- 2005 WHO Clinical Stage 3 Condition
- Clinical Diagnosis
  - history of productive cough (copious amounts of purulent sputum)
  - with or without clubbing
  - halitosis
  - crepitations and/or wheezes on auscultation
  - anorexia and FTT non-specific
- Definitive Diagnosis
  - CT scanning the gold standard
  - CXR

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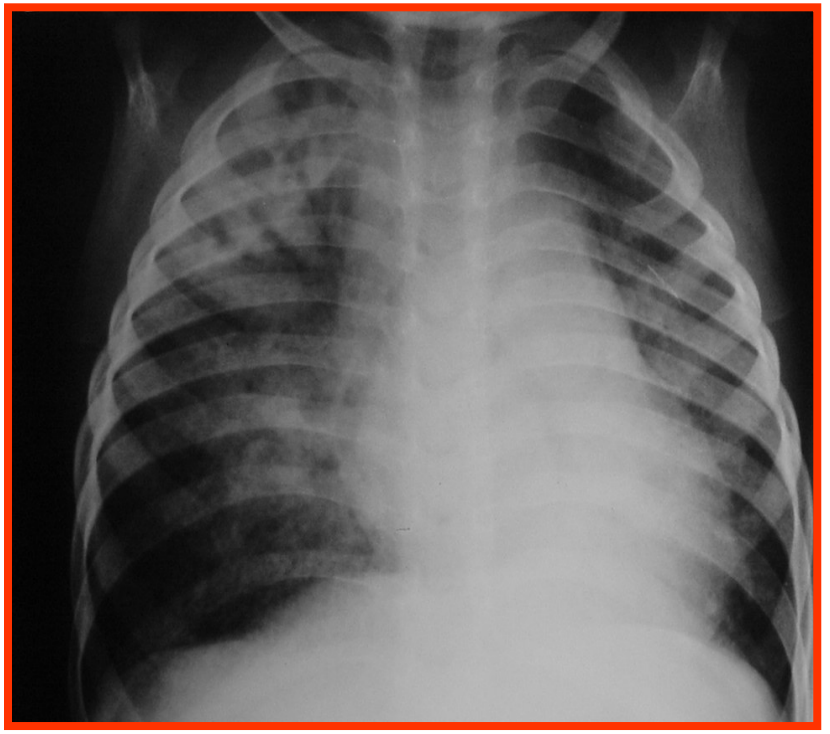
# CXR findings

- Honeycomb appearance (small cysts)
- and/or persistent areas of opacification
- and/or widespread lung destruction (fibrosis, volume loss)



Cystic spaces

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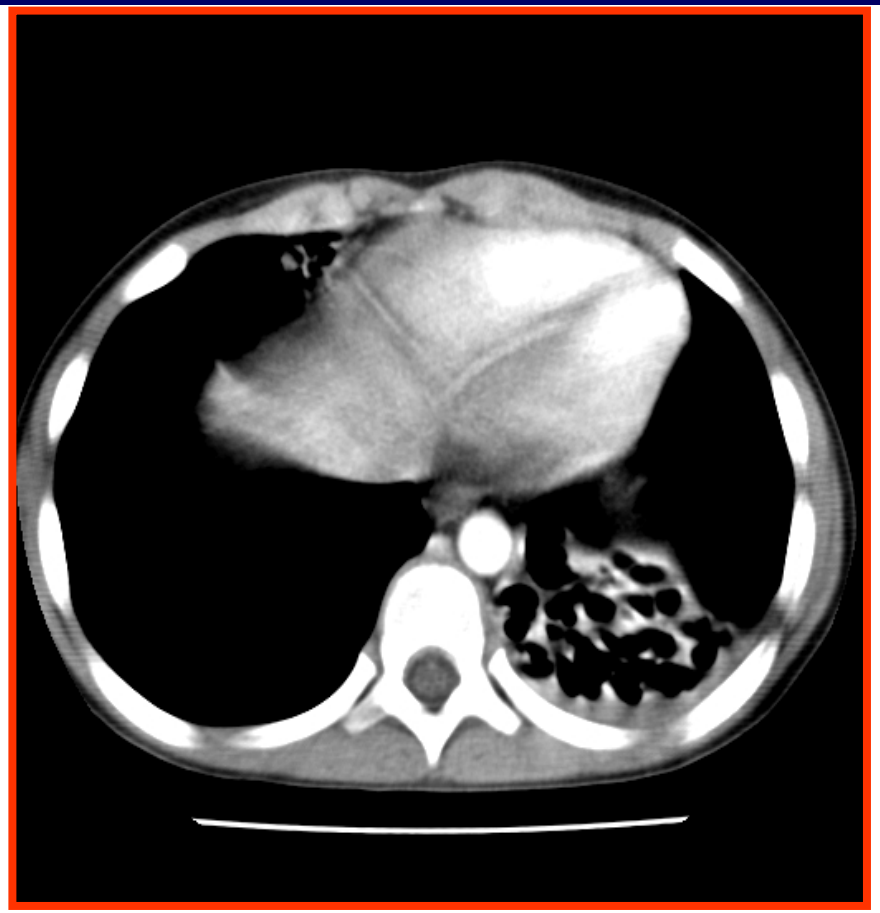
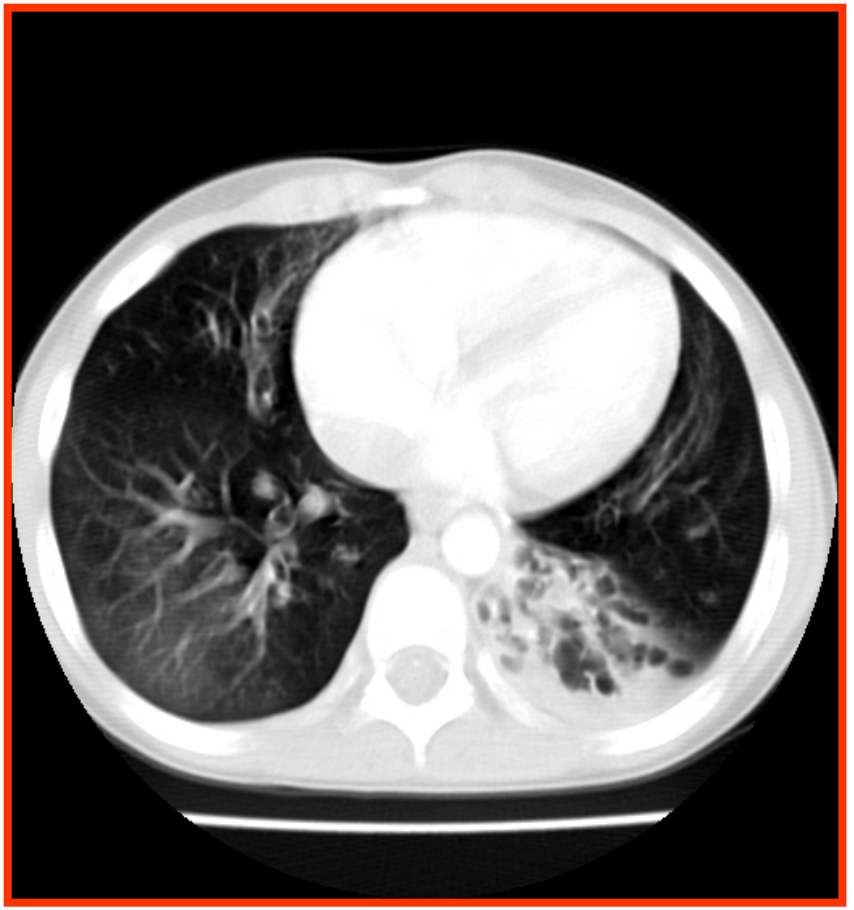
# CT-scan findings





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# Treatment

- Supportive
  - Hydration and mucous clearance
  - Postural drainage
- Systemic Antibiotic Therapy
  - During acute exacerbations
  - Treat for 2-3 weeks

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# Summary

- Suspect bronchiectasis in child with persistent night time coughing if other treatment modalities have failed
- Clubbing may not be present
- Indication for HAART
- Patients need:
  1. Chest physiotherapy and postural drainage
  2. Antibiotics for inter-current infections

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# Aspiration associated lung disease

- Common in HIV infected children
- GERD and naso-pharyngeal reflux may cause
  - Oesophagitis
  - FTT
  - Lung disease – Chronic with acute exacerbations
  - Strictures

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# Diagnosis

History

- regurgitation
- coughing spells
- milk via nose during feeds
- hoarse voice
- occasionally stridor

Clinical features

- oesophagitis
- Poor weight gain
- look for
  - lung disease
  - neurological disease

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# Investigations

- CXR
  - Recurrent, persistent or migrating lung infiltrates
- Barium swallow
  - Anatomical abnormalities
- Video Fluoroscopy
  - Suck and swallow in-coordination
- Endoscopy
  - Erosive esophagitis and complications
- Radionucleotide scintigraphy
  - GER, aspiration slow gastric emptying
- pH Studies

# Treatment

## Problematic

- Feeding adaptation
- Medical management – PPI
- Surgical – Nissan +/- PEG, Managing complications

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# Summary

- Careful history for reflux particularly important in infants

- If naso-pharyngeal in-coordination
  - look for CNS abnormality
  - consider HAART

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# South to South