PULMONARY COMPLICATIONS OF HIV
INTRODUCTION

INFECTIONOUS:
- Mycobacterium tuberculosis
- Mycobacterium avium-intracellulare

FUNGAL PNEUMONIA:
- Pneumocystis carinii pneumonia
- Cryptococcus neoformans
- Histoplasma capsulatum
- Aspergillus fumigatus
- Coccidioides immitis

BACTERIAL PNEUMONIA

VIRAL PNEUMONIA

NON-INFECTIONOUS:
- LIP & NSIP
INTRODUCTION:
- Tuberculosis is most common opportunistic infection in HIV infected patients in India & worldwide. Previously it was Pneumocystis carinii pneumonia.

EPIDEMIOLOGY:
- Worldwide, approx. one-third of all AIDS related deaths are associated with TB.
- Of the 5 million adults with HIV infection in south east Asia, 1.5 million are infected with TB.
TB & HIV: The Twin Epidemics

TB & HIV IN TANDEM
- World population 6 billion
- TB infection 2 billion
- HIV infection 30 million
- TB & HIV infection 15 million

1/3rd of AIDS patients worldwide have TB

2/3rds of AIDS patients in sub-Saharan Africa have TB & HIV
Impact of TB on HIV:

- TB shortens survival of patients with HIV infection
- TB accelerates progression of HIV with 6-7 fold increase in viral load.
- Risk of death in HIV infected patients with TB is twice of that in HIV infected patients without TB. The high mortality rate among patients with TB is due to progressive HIV infection rather than TB.
- TB is the cause of death for one out of every three people with AIDS worldwide.
Impact of HIV on TB:

- HIV most powerful risk factor for progression from latent TB infection to TB disease.
- HIV+ person infected with M.tb has 50% lifetime risk of developing TB as compare to 10% in HIV- person.

PATHOGENESIS:

- Due to progressive depression of CMI in patients with HIV disease, immune system cannot hold the organisms in check. Rapid multiplication occurs in multiple organs simultaneously.
- HIV infected patients with dormant TB infection will have reactivation of latent infection because of diminished CMI.
CLINICAL PRESENTATION

- TB disease occurs in HIV infected persons at all CD4 T lymphocyte counts.
- Clinical, radiographic & histopathologic presentation of HIV related TB depends on degree of immunodeciency.
- With CD4 count >350/µL HIV related TB appears like TB in HIV uninfected persons.
At CD4 count <50/µL, extrapulmonary TB (pleuritis, pericarditis, meningitis) is common. Tuberculosis pleural effusion is more common in HIV+ persons.

In presence of marked immunosuppression sputum smears may be negative for AFB even in presence of extensive radiological changes & mantoux skin test also may be negative.

HIV infected smear- pulmonary TB patients have worse prognosis than HIV+ patients with smear + pulmonary TB. Delay in diagnosis of TB is assoc. with worse outcomes.
<table>
<thead>
<tr>
<th>EARLY DISEASE</th>
<th>LATE DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(CD4&gt;350/µL)</strong></td>
<td><strong>(CD4&lt;200/µL)</strong></td>
</tr>
<tr>
<td>1. Pulmonary disease more common</td>
<td>1. Extrapulmonary disease more common</td>
</tr>
<tr>
<td>2. Upper lobe involvement</td>
<td>2. Lower lobe involvement</td>
</tr>
<tr>
<td>3. Cavitation +</td>
<td>3. Cavitation -</td>
</tr>
<tr>
<td>5. Sputum for AFB usually+</td>
<td>5. Sputum for AFB usually-</td>
</tr>
<tr>
<td>7. Tuberculin skin test +</td>
<td>7. Tuberculin skin test -</td>
</tr>
</tbody>
</table>
This patient has tuberculosis with bilateral upper lobe involvement and a thin-walled cavitating lesion at left upper lobe and extensive infiltrates in the left lung.
Chest radiograph of an HIV-infected patient with a CD4 count of < 50 cells/mm³ showing as diffuse infiltrates, focal alveolar consolidation, and intrathoracic lymphadenopathy.
30-year-old woman with HIV infection. CT scan shows focal area of consolidation in left upper lobe. Note bronchopericardial fistula (arrow).
"We cannot win the battle against AIDS if we do not also fight TB. TB is too often a death sentence for people with AIDS. It does not have to be this way."
MANAGEMENT OF HIV ASSOCIATED TB:

AIMS OF ANTI-TUBERCULOSIS TREATMENT ARE:

- To cure patient of TB
- To prevent death from active TB
- To prevent relapse
- To decrease TB transmission to others

 DOT S is strongly recommended for patients with HIV related TB. It improves outcome of disease & is cost effective.
RECENT WHO RECOMMENDATIONS:

- In HIV infected patients with drug susceptible TB, standard six month regimen 2(HRZE)+4(HR) results in prompt sterilization of sputum & low t/t failure rates, as in HIV – persons.
- Minimal duration of therapy is six months but if clinical or bacteriologic response is slow, t/t should be given for nine months, or for four months after culture becomes negative.
- In general anti TB treatment is same in HIV+ & HIV- TB patients but thiacetazone is absolutely C/I in HIV infected persons as it causes exfoliative dermatitis or Steven Johnson syndrome and can be fatal.
People with TB and HIV should complete their TB therapy prior to beginning of antiretroviral therapy unless there is high risk of HIV disease progression and death during period of TB t/t (i.e., CD4 count <200/µL or presence of disseminated TB). Thus with CD4 count >200/µL complete six months ATT first and then start ART.

With CD4 count b/w 50-200/µL give intensive phase of ATT followed by Rifampicin free continuation phase i.e. INH & Ethambutol for 9 months-1 year followed by ART.
With CD4 count <50/µL, ART is started with ATT. Here either Rifampicin free ATT is given i.e 2(HZES)+9(HZS) as Rifampicin induces cyt P-450 & decreases blood levels of ART resulting in development of resistance. Thus,

- Rifampicin + Protease inhibitor —: C/I
- Rifampicin + NNRTI —: C/I
- NRTI can be safely coadministered with ATT.

If P/I or NNRTI is to be started after giving Rifampicin then at least 2 wks should elapse after last dose of Rifampicin for reduction of enzyme inducing activity prior to start of ART.

Rifabutin is less potent cyt P-450 inducer & can be used with NNRTI. It is not available in India.
Rifampicin is given with ART with following reservations:

- First line regimen includes Zidovudine/lamivudine or stavudine/lamivudine plus either an NNRTI or Abacavir.
- If NNRTI based regimen is used Efavirenz is preferred drug as its potential to aggravate hepatotoxicity of ATT appears less than Nevirapine.
- Except for Saquinavir, P/I are not recommended during ATT with Rifampicin due to their interactions.
CHEMOPROPHYLAXIS

Acc. to ATS once active TB has been ruled out chemoprophylaxis is given for all HIV infected persons with:

- Positive tuberculin skin test (>5mm induration)
- Recent close contact with active TB patient without positive tuberculin skin test

- Preferred regimen is INH for 9 mnths.
- This is not followed in India
CLINICAL CASE

A 27-year-old counselor from a community-based AIDS agency presents and requests a TB skin test. She is HIV positive and complains of a smoker's cough with no systemic symptoms. She has no known contact with an active case of TB but she knows that, in the past, people who have used the facility have been diagnosed with TB. She has not previously been skin tested. The PPD skin test shows 7 mm of induration. A chest x-ray is normal. Because of the cough, sputum induction is carried out and the smear is negative for acid fast bacilli but the culture is positive for *M. tuberculosis*. 
This case highlights the importance of excluding the possibility of active TB before initiating treatment for latent tuberculous infection.
**Mycobacterium avium complex disease**

**ETIOLOGY:**
- M. avium is etiological agent in > 95% of patients with AIDS who develop MAC
- Mostly occurs when CD4 count < 50/µl

**CLINICAL PRESENTATION:**
- Most common presentation is disseminated disease with fever, weight loss, night sweats, diarrhoea, abdominal pain & lymphadenopathy
- **LOCALIZED SYNDROME:** Cervical or mediastinal lymphadenitis, pneumonitis, pericarditis, CNS infection
- **Chest X-ray:** B/L lower lobe infiltrate suggestive of miliary spread. Alveolar or nodular infiltrates with hilar or mediastinal LAP also occur
The chest radiograph (left) and computed tomographic images (right) show bilateral bronchiectasis and multiple nodules (arrows) suggesting associated bronchiolitis. Multiple cavities and subpleural consolidation are also evident.
**DIAGNOSIS:**

- Culture of blood, bone marrow, sputum or other body fluids
- Two consecutive sputum samples positive for MAC is highly suggestive of pulmonary infection

**TREATMENT:**

- Combination of Clarithromycin & Ethambutol is preferred
- Rifabutin can be added as third drug
FUNGAL PNEUMONIA
**Pneumocystis carinii Pneumonia**

**INTRODUCTION:**
- Pneumocystis pneumonia is often AIDS defining illness in patients infected with HIV.
- It occurs mostly with CD4 count < 200/µL.
- *Pneumocystis jiroveci* refers to distinct species that infect humans.
- PCP in HIV is a result either of reactivation of latent infection or new exposure to organism.
- Transmission occurs by airborne route.
Risk Factors For PCP IN HIV:

- CD4 count < 200/µL
- Previous episode of PCP
- Oral thrush
- Recurrent bacterial pneumonia
- Unintentional weight loss
- Higher plasma HIV RNA
EPIDEMIOLOGY:
PCP is single most common cause of pneumonia in patients with HIV infection in USA.

PATHOGENESIS:
- P. carinii is an obligate extracellular parasite that binds to and damages type I pneumocytes causing compensatory hypertrophy of type II pneumocytes. Hydrophobic surfactant protein SP-B & SP-C regulate alveolar surface tension.
- P. carinii infection reduces expression of SP-B & SP-C and alters biophysical properties of surfactant, causing hypoxemia, decreased lung compliance and microatelectasis.
CLINICAL PRESENTATION:
- Progressive exertional dyspnoea
- Nonproductive cough
- Low grade fever
- Retrosternal burning
- Pleuritic chest pain

EXAMINATION:
- Tachypnea, tachycardia, cyanosis
- Chest exam: no findings/bibasilar rales
**Lab Findings:**

- ABG shows hypoxemia from mild to mod (po2 > 70 mmHg & (A-a)DO2 < 35 mmHg) to mod to severe levels (po2 < 70 mmHg & (A-a)DO2 > 35 mmHg)
- Raised LDH levels
- Reduced DLCO

**Chest X-ray:** may be normal in early disease
- Faint bilateral interstitial infiltrate in later disease
- Classic finding of dense bilateral perihilar infiltrate is unusual in patients with AIDS.
Atypical findings:
- Focal infiltrates
- Nodular appearance
- Upper lobe cavitary disease (in patients receiving aerosolized pentamidine)
- Subpleural cyst formation
- Small pleural effusion
- Hilar lymphadenopathy

HRCT:
B/L ground glass opacification
Pneumocystis carinii Pneumonia in HIV positive Patient.
High resolution CT in HIV-positive child, demonstrating patchy mosaic ground-glass opacity highly suggestive of PCP.
**DIAGNOSIS:**

*Demonstration of trophozoite or cyst by microscopical examination in specimens of:*

- Induced sputum with hypertonic saline
- Bronchoalveolar lavage fluid
- Transbronchoscopic or surgical lung biopsy

**Stains:** Trophic forms stained with Wright Giemsa, Gram Weigert or Papanicolaou stains.

- Cysts stained with methanamine silver, crystal violet, toluidine blue, or calcoflour white.
MANAGEMENT OF PCP:

Trimethoprim-Sulphamethoxazole (TMP-SMX) is t/t of choice.

Dose:
- TMP = 15-20mg/KG/day
- SMZ = 75-100mg/KG/day

- OPD therapy of TMP-SMX is effective in patients with mild to mod disease.
- Patients with documented PCP & mod to severe disease (Po2<70mmHg & (A-a)DO2>35mmHg) should receive corticosteroid therapy.

Alternative Regimens:
- Dapsone & TMP
- Primaquine & Clindamycin
- i/v Pentamidine
**PROPHYLAXIS FOR PCP:**

*Prophylaxis for PCP in HIV infection should be given to patients with:*

- CD4 count < 200/µL
- CD4/total lymphocyte ratio < 1:5
- Oropharyngeal thrush or unexplained fever > 2wks
- Presence of another AIDS defining illness like Kaposi sarcoma, cryptococcal meningitis
- All patients with previous PCP

*Prophylactic agent of choice:* 1 DS tab of TMP/SMX per day

- This also provides prophylaxis against Toxoplasmosis & bacterial infections.
- Prophylaxis for PCP can be discontinued in patients treated with HAART who have good suppression of HIV & CD4 count > 200/µL for at least 3-6 mths.
ADVERSE REACTIONS OF TMP-SMX TREATMENT:

- Rash including Steven Johnson syndrome
- Fever
- Leukopenia
- Thrombocytopenia
- Azotemia
- Hepatitis
Clinical History: 25 year-old with AIDS - progressive SOB with clinical CXR and ABG inconclusive.

Findings: First CXR: No evidence of acute cardiopulmonary disease.

Follow-up CR: Bilateral interstitial and alveolar consolidation.
Diagnosis

*Pneumocystis Carinii Pneumonia* (PCP) or PCP with more localized bacterial pneumonia.
ACUTE SINUSITIS AND BRONCHITIS

**Etiology:**
Prevalent during all stages of HIV infection
- Severe cases occur in patients with low CD4 counts
- Maxillary sinus is most commonly involved
- H.influenzae, Strep.pneumoniae

**Clinical features:**
- Fever
- Nasal congestion,
- Headache

**Diagnosis:** CT/MRI

**Treatment:** App. ATB therapy
BACTERIAL PNEUMONIA

INTRODUCTION:

- Pulmonary disease is one of the most frequent complications of HIV disease.
- Most common manifestation of pulmonary disease in HIV is Pneumonia
- Two most common causes of pneumonia are bacterial infections and P.carinii infection

EPIDEMIOLOGY:

- Patients with HIV infection have six fold increase in pneumococcal pneumonia & 100 fold increase in pneumococcal bacteremia
ETIOLOGY:

- Most common is Strep. Pneumoniae followed by H. influenzae, Pseudomonas aeruginosa and S. aureus.

PATHOGENESIS:

- B-cell defect to produce pathogen specific Ab.
- Impaired neutrophil function & number or both
CLINICAL FEATURES:

- HIV infected patients with bacterial pneumonia present in similar way as those without HIV i.e acute illness with chills and rigors, pleuritic chest pain & purulent sputum.

EXAMINATION:

- Fever, tachypnoea, tachycardia, rales or rhonchi

*Chest X-ray:* Lobar consolidation is typical pattern

- Atypical: multilobar, nodular, reticulonodular patterns
Posteroanterior (A) and lateral (B) chest radiographs demonstrate focal consolidation in the right lower lobe, which was owing to a community-acquired bacterial pneumonia.
DIAGNOSIS:

- Chest X-ray, blood culture, TLC, Gram stain & culture of sputum sample should be done before ATB administration.
- Sputum sample for AFB staining & culture should be done in HIV infected hospitalized patients with pulmonary infiltrates.
- As PCP is common HIV related respiratory infection & may coexist with bacterial pneumonia, induced sputum examination for PCP should be done.
MANAGEMENT:

- Extended spectrum cephalosporin (eg. Cefotaxime, ceftriaxone) or floroquinolone (eg. levofloxacin, moxifloxacin) should be used.

Severe infection: Combination therapy with cephalosporin & macrolide or quinolone should be used.

PREVENTION:

- Adults with CD4 count > 200/µL should receive single dose of 23 valent polysaccharide pneumococcal vaccine.

- Annual administration of influenza vaccine prevents pneumococcal superinfection with influenza.
HISTOPLASMOSIS:

ETIOLOGY:
- Caused by dimorphic fungus *Histoplasma capsulatum*.

EPIDEMIOLOGY:
- Occurs in 2-5% patients with AIDS
- Disseminated histoplasmosis occurs with CD4 count < 150/µL.
- Localized histoplasmosis occurs with CD4 count > 300/µL.

MODE OF INFECTION:
- Inhalation of microconidia
- Reactivation of latent infection
CLINICAL FEATURES:
- Most common presentation of histoplasmosis in patients with AIDS is disseminated multiorgan disease with fever, fatigue & weight loss.
- Respiratory symptoms of cough, chest pain & dyspnoea occur in 50% of patients.
- S/S may be limited to respiratory tract with high CD4 count & localized pulmonary histoplasmosis.

DIAGNOSIS:
- Histoplasma Ag can be detected in BAL fluid in patients with pulmonary involvement.
- Detection of Histoplasma Ag in blood is sensitive method for diagnosis of disseminated histoplasmosis.

TREATMENT:
- Disseminated histoplasmosis: I/V Amphotericin B for 3-10 days followed by oral Itraconazole.
Chest radiograph of patient who had pulmonary histoplasmosis.
ASPERGILLOSIS

ETIOLOGY:
- Caused by *Aspergillus fumigatus*

RISK FACTORS:
- Neutropenia
- Low CD4 count
- Corticosteroid use
- Exposure to broad spectrum ATB
- Previous pneumonia or lung disease
- Patients with HIV associated aspergillosis have low CD4 count i.e < 50/µL

CLINICAL FEATURES:
Two major syndromes are:
- Respiratory tract disease (either semi invasive pseudomembranous tracheitis or invasive pneumonitis)
- Diffuse meningoencephalitis syndrome
SEMI-INVASIVE PSEUDOMEMBRANOUS TRACHEITIS:

- Associated with fever, cough, dyspnoea, stridor or wheezing caused by airway obstruction
- Bronchoscopy: confluent, exudative pseudomembrane adherent to tracheal wall

INVASIVE PNEUMONITIS:

- Associated with fever, cough, dyspnoea, chest pain, hemoptysis & hypoxemia
- Chest X-ray: diffuse interstitial pneumonitis or localized wedge shaped dense infiltrate representing pulmonary infarction
There are areas of bronchiectasis. In addition there is a large thick walled cavity in the periphery of the left mid zone. This appearance is typical of a mycetoma in a cavity.
DIAGNOSIS:

- Clinical S/S with histopathological demonstration of organisms in biopsy specimens of involved sites

TREATMENT:

- Invasive aspergillosis is Voriconazole. Amphotericin B is alternative drug.
HPE showing A. fumigatus
CRYPTOCOCCOSIS

ETIOLOGY:
- HIV associated cryptococcal infections are caused by Cryptococcus neoformans var neoformans
- Infection occurs when CD4 count < 50/µL

CLINICAL FEATURES:
- Cryptococcosis is most common cause of meningitis in AIDS patients
- Disseminated disease is common manifestation with or without meningitis. Approx. half of patients with disseminated disease have pulmonary involvement
- S/S of pulmonary infection are cough, fever, dyspnoea, & hemoptysis
- Chest Xray: focal or diffuse interstitial infiltrate in > 90%
- Lobar disease, cavitary disease, pleural effusion, hilar or mediastinal LAP can be seen
X-ray showing pulmonary cryptococcal infection [right upper lobe].
C. neoformans with Methamine silver stain
**DIAGNOSIS:**
Cryptococcus Ag is detected in CSF with India ink stain

**TREATMENT:**
Amphotericin B plus Flucytosine for 2 wks followed by fluconazole for 8 wks
COCCIDIODOMYCOSIS

**ETIOLOGY:**
- Caused by Coccidiodes immitis

**EPIDEMIOLOGY:**
- Incidence is 2-5% in south west Asia where it is endemic.
- Increased risk is associated with extensive exposure to disturbed soil.
- Both localized pneumonia & disseminated infection occurs in patients with CD4 count < 200/µL.
CLINICAL FEATURES:
- Localized pneumonia with cough & fever
- Disseminated disease with generalized LAP, skin nodes, ulcers, bone & joint involvement.
- Localized meningeal disease
- Chest X-ray: Diffuse reticulonodular infiltrates

DIAGNOSIS:
- Culture of C. immitis from clinical specimens or demonstration of typical spherule in HPE of involved site.

TREATMENT:
- For nonmeningeal pulmonary or disseminated disease, Amphotericin B is preferred
HRCT shows numerous, bilateral, small, well-defined nodules, randomly distributed throughout the lung in an AIDS patient with disseminated coccidioidomycosis.
VIRAL PNEUMONIA

CYTOMEGALOVIRUS DISEASE:
CMV is ds DNA virus in Herpes family that reactivates to cause disseminated or localized end organ disease in patients with advanced HIV i.e. CD4<50/µL

CLINICAL FEATURES:
- Retinitis is most common clinical manifestation of CMV
- Colitis is second most common clinical feature
- Esophagitis caused by CMV occurs in < 5-10% f ti t ith AIDS
CMV pneumonitis is uncommon but when it occurs it presents with:

- Shortness of breath
- Dyspnoea on exertion
- Non productive cough
- Hypoxemia
- Chest X-ray: interstitial infiltrates
DIAGNOSIS OF CMV PNEUMONITIS:
- Chest X-ray: pulmonary interstitial infiltrates
- Identification of multiple CMV inclusion bodies in lung tissue, BAL & induced sputum

TREATMENT:
- I/V Gancyclovir or Foscarnet for 21-28 days

HERPES SIMPLEX VIRUS PNEUMONITIS & VARICELLA ZOSTER VIRUS PNEUMONITIS:
Both occur in HIV infection but are less common than CMV pneumonitis
- VZV pneumonitis is severe complication of HIV infection in children & is accompanied by vesicular rash
- Treatment of HSV & VZV pneumonitis: i/v Acyclovir
IDIOPATHIC INTERSTITIAL PNEUMONITIS

LYMPHOID INTERSTITIAL PNEUMONITIS:
- Occurs mostly in children as a result of immunological reaction to HIV or EBV within lung

CLINICAL FEATURES:
- Nonspecific or progressive dyspnoea

DIAGNOSIS:
- Benign lymphocytic infiltrate on TBLB or open lung biopsy

TREATMENT:
- Usually self limited. Severe case treated with short course glucocorticoid
NON SPECIFIC INTERSTITIAL PNEUMONITIS:

- Occurs mostly in adults with HIV infection

CLINICAL FEATURES:

- Nonspecific or fever with nonproductive cough & mild chest discomfort

DIAGNOSIS:

- Interstitial infiltrates of lymphocytes & plasma cells in lung biopsy

TREATMENT:

- Usually self limited by appropriate management of underlying HIV infection
All the best..