Incidence of TB: HIV (+) vs HIV (-)

Active Tb disease after TB infection

- HIV (+)
  - TB Infection
    - 3-13% every year
    - >30% (40/60%) lifetime

- HIV (-)
  - 5% first 2 years
  - 10% lifetime

*Increased risk of TB disease in HIV*
More difficult to treat TB disease

- Adverse drug reactions
- May increase *default rates* in TB programs
- May increase overall *mortality rate* in TB programs
More difficult to diagnose TB in HIV

• TB infection
  – False positives and false negatives from tuberculin skin test in HIV

• TB disease
  – Classical symptoms may be missing
  – Sputum smear may be negative
  – Chest x-rays may be normal or atypical
More extra pulmonary TB in case of HIV co-infection.

PTB, pulmonary TB
EPTB, extrapulmonary TB
LNTB, lymph node TB
MTB, miliary TB
DTB, disseminated TB
TBM, meningeal TB
ABDTB, abdominal TB
GU TB, genitourinary TB

The global answer to TB/HIV: Collaborative activities
Cascade of infections and cancers that develop as immune function is depleted.

HIV/AIDS prevention and treatment. NIH Stefano Bertozzi and coll.
<table>
<thead>
<tr>
<th>CD4+ cell count (× 10^6 cells l^{-1})</th>
<th>Pulmonary pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>Bacterial pneumonia</td>
</tr>
<tr>
<td></td>
<td>TB (re-infection)</td>
</tr>
<tr>
<td></td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td>200–500</td>
<td>Bacterial pneumonia</td>
</tr>
<tr>
<td></td>
<td>TB (re-infection)</td>
</tr>
<tr>
<td></td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td>50–200</td>
<td>Bacterial pneumonia</td>
</tr>
<tr>
<td></td>
<td>TB (primary)</td>
</tr>
<tr>
<td></td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td></td>
<td>PCP</td>
</tr>
<tr>
<td></td>
<td>KS</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Fungal infections</td>
</tr>
<tr>
<td></td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td></td>
<td>Bacillary angiomatosis</td>
</tr>
<tr>
<td>&lt;50</td>
<td>Bacterial pneumonia</td>
</tr>
<tr>
<td></td>
<td>TB (atypical appearances)</td>
</tr>
<tr>
<td></td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td></td>
<td>PCP</td>
</tr>
<tr>
<td></td>
<td>KS</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Fungal infections</td>
</tr>
<tr>
<td></td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td></td>
<td>Bacillary angiomatosis</td>
</tr>
<tr>
<td></td>
<td>MAC</td>
</tr>
<tr>
<td></td>
<td>CMV</td>
</tr>
</tbody>
</table>

TB, Tuberculosis; PCP, Pneumocystis carinii pneumonia; KS, Kaposi's sarcoma; MAC, Mycobacterium avium complex; CMV, cytomegalovirus.
Cambodia:

Vietnam: similar but very few fungal infections, no atypical mycobacteriae or anguillulosis

Dakar and Bangui: very few PCP more pneumoninae with *S pneumoniae* and *H influenzae*, Kaposi, more severe illnesses with no diagnosis…

*ANRS* study on lung diseases and AIDS in East Asia and Africa

*French national agency for scientific research in AIDS*
The respiratory diseases are frequent (80% of the cases) and severe during the course of HIV infection.

- They can occur at every phase of the evolution: from the beginning of AIDS until death.
- The respiratory diseases are numerous:
  - infectious <= immunodepression
  - tumourous
  - others
- The ARV have modified the situation in wealthy countries, and also in developing countries, but, in these countries, lung diseases associated with AIDS remain frequent and severe, and their diagnosis and treatment continue to be difficult.
HIV and lungs: infections are the most important problem

Lung = target for many and severe infections with high incidence of death

- This natural evolution can be modified by:
  - prophylactic treatment => effective on some pathologies (ex: cotrimoxazole and pneumocystosis or toxoplasmosis)
  - The use of antiretroviral treatments: they are very effective against HIV and can remain effective for a long time if the treatment is correctly adapted and if the patient is compliant.
VIH and lungs: 3 situations

- No prophylaxis against lung diseases and no ARV treatment
- No ARV treatment but possible access to prophylaxis (ex: prophylaxis of pneumocystosis by cotrimoxazole)
- ARV treatment is possible: mortality by infectious disease drastically decreases
3 pathologies for 80% of pulmonary infectious diseases in AIDS:

- Tuberculosis
- Pneumocystosis
- Bacterial pneumoniae
Respiratory diseases in patients not receiving ARV

Infectious diseases

- Pneumocystosis (PCP)
- Tuberculosis
- Bacterial Pneumoniae
- Parasitic pneumoniae
- Fungal pulmonary diseases
- Atypical mycobacteriae
- Viral diseases
Respiratory diseases in patients not receiving ARV

*Infectious diseases*

- Pneumocystosis
- Tuberculosis
- **Bacterial pneumonias**
- Parasitic pneumonias
- Fungal pneumonias
- Atypical mycobacteria
- Viral diseases

- *Strepto pneumoniae*
- *H. influenzae*
- **others**
  - *Staph. aureus*
  - *Ps. aeruginosa*
  - Legionnaires’ disease
  - *Nocardia asteroides*
  - *Rhodococcus equi*....
Respiratory diseases in patients not receiving ARV

Infectious diseases

- Pneumocystosis
- Tuberculosis
- Bacterial pneumonia
- Parasitic pneumonias
- Fungal pneumonias
- Atypical mycobacteria
- Viral diseases

- Toxoplasmosis
- Anguillulosis
- Leishmaniosis
- Cryptosporidiosis
- Strongiloïdiasis...
Respiratory diseases in patients not receiving ARV

Infectious diseases

- Pneumocystosis
- Tuberculosis
- Bacterial pneumonia
- Parasitic pneumoniae
- Fungal pneumoniae
- Atypical mycobacteriae
- Viral diseases

- Cryptococciosis
- Aspergillosis
- Histoplasmosis
- Coccidioïdomycosis
- Penicilliosis
- Coccidioidomycosis
Respiratory diseases in patients not receiving ARV

**Infectious diseases**
- Pneumocystosis
- Tuberculosis
- Bacterial pneumoniae
- Parasitic pneumoniae
- Fungal pneumoniae
- Atypical mycobacteriae
- Viral diseases
Respiratory diseases in patients not receiving ARV

**Infectious diseases**

- Pneumocystosis
- Tuberculosis
- Bacterial pneumoniae
- Parasitic pneumoniae
- Fungal pneumoniae
- Atypical mycobacteriae

**Viral diseases**

- CMV
Possible etiologies according to radiological appearance:

**Focalised condensation**

**Frequent pathology**
- common bacterial infection

**possible pathology**
- Tuberculosis
- Mycosis (aspergillosis, cryptococcosis…)
- Non TB mycobacteria
- others bacterial infections (*Nocardia, Actinomyces, Rhodococcus equii*…)

**rare pathology**
- lymphoma
- toxoplasmosis

**differential diagnosis**
- lung cancer

courtesy of Mayaud in Girard, Katlama, Pialoux “VIH 2001”, éd. Douin Paris
Possible etiologies according to radiological appearance

Diffuse lesions

**Frequent pathology**
- pneumocystosis
- Kaposi’s disease
- tuberculosis

**Possible pathology**
- mycosis (aspergillosis, histoplasmosis, cryptococcosis)
- mycobactérioses atypical mycobacteries
- others infections (toxoplasmosis...)
- usual bacterial infections

**Rare pathology**
- interstitial lymphoïd pneumonia

**Différential diagnosis**
- pulmonary œdema
- iatrogenic pneumopathy

courtesy of Mayaud in Girard, Katlama, Pialoux “VIH 2001“, éd. Douin Paris
Possible etiologies considering radiological aspect:
Normal chest Rx with clinical respiratory signs

Frequent pathology
- Bacterial infection of superior airways
- Opportunistic infection at the beginning (Pneumocystosis)

Possible pathology
- bronchial tuberculous infection or TB miliary at the beginning
- other opportunistic infections at the beginning (aspergillosis)
- endo-bronchial tumour
- lymphocytic interstitial pneumonia (T CD8 in BAL)

Rare pathology
- HTAP

Differential diagnosis
- pulmonary embolism
- bronchospasm
- lactic acidosis (ARV complications)

With courtesy of Mayaud in Girard, Katlama, Pialoux “VIH 2001 “, éd. Douin Paris
Chest X ray  TB HIV(-)  
and HIV+ CD4≥200

- more frequent in superior lobes
- caverns
- typical nodular infiltrates (in the apex and more or less excavated)

Chest X ray  TB HIV+  
( CD4 < 200 )

- cavitation is rare
- Frequency of TB pneumoniæ and adenopathies (often associated)
- Lesions in inferior and superior lobes
- Frequency of miliaries
- Frequency of extra pulmonary TB
CXR in case of patients TB/ HIV+

not too severe immunodepression
CD4>200

Severe immunodepression
Male 30 years old
Soldier HIV +

Pneumonia of right superior and middle Lobes
Hilar adenopathies
AFB x3 negative

Bronchial aspiration and BAL : AFB+ +

Bronchial endoscopy
Aspect of fistula from adenopathy
TB bilateral pneumonia and mediastinal adenopathies in a patient with AIDS. CD4 level: 50/mm3. No excavation.
TB, HIV+: double tuberculous pneumonia; middle lobe and left superior lobe. Mediastinal adenopathies
Bilateral pneumonia + mediastinum and hilar adenopathies + HIV context = TB
Bilateral tuberculous pneumonia, in a patient with AIDS. Rapidly deteriorating condition.
CD4 level: 35/mm³
HIV+ AFB pos.
TB pneumonia associated with mediastinum adenopathies
Left lower lobe TB pneumonia
(negative silhouette sign with cardiac left edge)

Bulky hilar adenopathy
(positive silhouette sign with Aortic arch)
R L lobe and middle lobe TB pneumonia in context of severe immunodepression

Inferior lobe TB are not rare in case of AIDS
Middle lobe, right upper lobe and left upper lobe pneumonia. Mediastinum enlargement (probable mediastinum adenopathies. IN HIV context, TB is highly probable
TB of middle or inferior lobes pneumonii are common in cases of AIDS.
Tuberculous miliary: HIV+ young woman,
CD4 level: 60/mm3
Mediastinal adenopathies are frequent in AIDS cases.

Endobronchial fistula with bronchogenic dissemination is possible.
Immune reconstitution inflammatory syndrome: 4 clinical exemples
Male HIV +, CD4 level: 50/mm3
October 2006. AFB (-)
Dec 2006: AFB + in sputum. Beginning of TB treatment
Beginning of anti retroviral treatment.
Chest X-ray on 28/02/2007 (After 3 weeks of ARV treatment)
Chest X ray on 04/04/2007: 7 weeks of antiretroviral and TB treatment. (Favourable issue after few weeks of associated cortico-steroid)
TB, VIH+, beginning of TB treatment

Case 2
Beginning of ARV treatment after 2 months of TB treatment
severe pericarditis few weeks later
Pericardic drainage and continuation of the TB and ARV treatment
D12 of ARV treatment

Left increase opacities and pneumothorax
D 20 after drainage of the pneumothorax
Man, 37 years old, refugee from Congo. Diarrhea, worsening condition, cough and weight loss. HIV positive. CD4 level: 14/mm3.

Beginning of ARV treatment the 30/12/2008
X chest radio 3 weeks later. Dyspnea, cough, fever, delirium and headache...

TB miliary with BK positive in sputum (PCR technique)
intra-cérébral tuberculous granulomas
Tuberculous abdominal adenopathies
Paradoxical reactions in the immune reconstitution inflammatory syndrome

- Fever
- Adenopathies
- Ascites
- Pleural or pericardic effusion
- Pulmonary infiltrate or pneumoniae
- Encephalic diseases (tuberculoma)

- Beginning soon after introduction of ARV
- The severity is correlated with the initial Immunodepression (CD4 level)
Several micro-organisms are responsible for lung diseases in AIDS. Therefore, differential diagnosis of TB in HIV patients are many, and especially pneumocystosis.
Pneumocystoses which clinical data?

- HIV infection not known before (80% of cases)
- No prophylaxy with *bactrim* *(100% of cases)*
- Fever: 38° - 40°C
- Normal pulmonary auscultation (90% of cases)
- No extra-pulmonary signs (90% of cases)
- *Interstitial/alveolar diffuse opacities* (100% of cases)
- **Hypoxemia** *(SaO2 < 90%)* 100% of cases

Courtesy of Chan Sarin ANRS1260
Interstitial picture: ground glass attenuation image
Male, HIV +, severe dyspnea, normal auscultation, SaO$_2$ 86%
interstitial and alveolar diffuse lesions
Bilateral alveolar and Interstitial opacities without excavation
Bilateral alveolar and interstitial opacities without excavation
Man 25 years old. Increasing dyspnea and non productive cough. Fever 38° C.

First line antibiotic by doxycycline: no improvement.

Emergency room: Sa O2 88%, normal auscultation. Positive test for HIV.

Bronchio alveolar lavage: pneumocystosis
Male 42 years old, cough, exertional dyspnea, SaO2 92 %; HIV+
BAL: pneumocystosis
Chest X ray: could be considered as normal. Possible ground glass attenuation image
HIV+ context, exertional dyspnea, non-productive cough, normal pulmonary auscultation, CD4 level 150/ mm3.
Endoscopy with BAL: *P. jirovecii*

Pneumocystosis at the beginning of the evolution
Man 55 years old. Retired soldier, divorced for 10 years dyspnea, cough, SaO2 85%. Normal auscultation. Positive test for HIV. CXR considered as normal.

Pneumocystis in the bronchio-alveolar lavage.
CT scan of the previous patient

Normal CT scan
interstitial and diffuse pneumonia with ground glass attenuation

+ Hypoxemia \( \text{SaO}_2 < 90\% \)

Without cotrim. prophylaxy

Cotrimoxazole +/-cortisone + oxygen are mandatory to prevent death

The pulse oxymeter is a very useful tool, yet expensive
But cheaper and cheaper (less than 100 dollars)

If no oxymeter, remember that polypnea is proportional to hypoxemia
National TB Program strategy for TB case finding

Respiratory +/- general symptoms → AFB-sputum X 3 (2 days)
If negative → antibiotic (amoxycillin) X 10 days
If patient not improved and new smears negative
↓
CXR (after 2 or 3 weeks)

*If it was PCP, the patient is dead*

In HIV infected patients, CXR must be performed early
non TB bacterial pneumoniae are fréquent in case of HIV infection

- *Streptococcus pneumoniae*
- *H. influenzae*
- autres
  - *Staph. aureus*
  - *Ps. aeruginosa*
  - Légionellose
  - *Nocardia asteroides*
  - *Rhodococcus equi*....

Mild Immunodépression

Severe immunodepression
Non TB bacterial pneumonia are frequent in HIV infection with moderate immunodepression: *Streptococcus pneumoniae*, *Hemophilus*....

They are often bilateral
Pneumopathy to pseudomonas aeruginosa. Context of worsening condition and cachexia. (CD4 level: 40/mm3)
bilateral opacities
With excavated nodules

Nocardiosis

Infectious disease and aids ward. khmero russian hospital
PhnomPenh
One can also see fungal infections:
Cryptococcosis
Histoplasmosis
*Penicillium marneffei*
Invasive aspergillosis
Disseminated histoplasmosis to *H. capsulatum* in an HIV+ patient

BAL: fungal microorganisms in the macrophages
W. 20y. HIV+, cough, dyspnea, t° 38°5C
Miliary

AFB -

BAL : Histoplasmosis
Sometimes in AIDS: poly-pathology
Soldier 25 y. old
Confusion, obnubilation with quick onset,
Vomiting then coma
t° 40°C. HIV+

Bronchio alveolar
lavage: *P. carinii*  
*and S. aureus*
Very severe dyspnea in HIV context
Not able to produce sputum. Endoscopy with BAL…
Very severe dyspnea in HIV context
Not able to produce sputum. Endoscopy with BAL…
Kaposi illness: various lesions on chest Xray

- Diffuse micro or micronodules
- Alveolar condensation, lower lobes predominant
- Pleural effusion
- Possible mediastinal adenopathies
- Frequent (but not constant) association with cutaneous or mucositis lesions, which can help for diagnosis

Possible confusion with TB
Kaposi illness
Courtesy of Dr Difenthal. Tanzania
Lymphocitic interstitial pneumonias:
- 2 to 5 years old HIV children (20% of HIV+ children in developed countries)
- Less frequent in adults. The diagnosis is difficult: One must eliminate opportunistic infection (Bronchial-alveolar lavage and lung biopsy)
Lymphoma

Courtesy Dr. Jaffer Dharsee. Tanzania
Lymphoma

- Rarely confined to chest only

- When seen in the chest it presents as typical mediastinum nodal enlargement, or mass in the anterior mediastinum (as in the previous slide) pleural or pericardial effusion, pulmonary infiltrates or pulmonary mass
In cases of acute respiratory disease in AIDS with AFB(-) in sputum, Bronchial endoscopy and BAL (broncho alveolar lavage) are useful for diagnosis if a reliable bacteriological laboratory is available…

Conclusion (1) :
BAL is feasible even in low income countries

100 cc

Slowly injection

Slowly aspiration

> 50 cc collected
Conclusions (2)

- VIH infection increases risk of developing very severe TB
- TB treatment is the same in HIV(+) and HIV(-) cases but with more risk of complications and more risk of associated opportunistic infections
- Collaboration between National TB program and HIV/AIDS program is crucial in countries with high TB/VIH prevalence
- Mortality rate of lung disease in AIDS stay at a high level
TB is yet the more frequent lung disease in AIDS and the more frequent cause of death

CXR can give informations for diagnosis especially if AFB neg

Diagnostic of opportunistic infections can be difficult and needs sophisticated explorations (need of financement and training)

Reference hospital should have special pulmonology ward with bronchoscopy and BAL available

Physicians working in TB program or in TB field must be correctly trained to CXR interpretation