PULMONARY COMPLICATIONS OF HIV
PULMONARY COMPLICATIONS OF HIV

1. HIV AND AIDS
2. HIV AND LUNG DEFENCES
3. CASE DEFINITION OF AIDS AND CLASSIFICATION INTO CLINICAL CATEGORIES
4. PROGRESSIVE IMMUNOSUPPRESSION
5. CHEST RADIOGRAPH FINDINGS IN PATIENTS WITH HIV INFECTION
6. INFECTIOUS AND NON INFECTIOUS RESPIRATORY TRACT COMPLICATIONS OF PATIENTS WITH HIV INFECTION
7. CLINICAL EVALUATION OF A PATIENT WITH HIV INFECTION AND RESPIRATORY DISEASE
Human immunodeficiency virus
Human immunodeficiency virus

- **Group:** Group VI (ssRNA-RT)
- **Family:** Retroviridae
- **Genus:** Lentivirus
- **Species:** Human immunodeficiency virus 1 & 2
HIV - 1

M (MAJOR) WORLD-WIDE

O (OUTLIER) WEST AFRICA

N (MINOR) RARE, HIGHLY DIVERGENT

Further divided into subtypes or clades - subtype C found in India
HIV AND AIDS

AIDS – first recognised in 1981
– when the U.S, C.D.C reported the occurrence of pneumocystis carinii pneumonia in 5 previously healthy homosexual men.

AIDS & PULMONARY COMPLICATIONS

- 70% of patients with HIV have pulmonary complications during life
- additional pulmonary pathology is often an autopsy finding
## Global summary of the HIV and AIDS epidemic, December 2004

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td><strong>Number of people living with HIV in 2004</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>37.2 million</td>
<td>(33.8 – 41.7 million)</td>
</tr>
<tr>
<td>Women</td>
<td>17.6 million</td>
<td>(16.3 – 19.5 million)</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>2.2 million</td>
<td>(2.0 – 2.6 million)</td>
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<tr>
<td><strong>People newly infected with HIV in 2004</strong></td>
<td>4.9 million</td>
<td>(4.3 – 6.4 million)</td>
</tr>
<tr>
<td>Adults</td>
<td>4.3 million</td>
<td>(3.7 – 5.7 million)</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>640 000 (570 000 – 750 000)</td>
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<tr>
<td><strong>AIDS deaths in 2004</strong></td>
<td>3.1 million</td>
<td>(2.8 – 3.5 million)</td>
</tr>
<tr>
<td>Adults</td>
<td>2.6 million</td>
<td>(2.3 – 2.9 million)</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>510 000 (460 000 – 600 000)</td>
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</table>

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.
About 14,000 new HIV infections a day in 2004

- More than 95% are in low and middle income countries
- Almost 2,000 are in children under 15 years of age
- About 12,000 are in persons aged 15 to 49 years, of whom:
  - almost 50% are women
  - about 50% are 15–24 year olds
Adults and children estimated to be living with HIV/AIDS as of end 2003

Total: 34 – 46 million
The 1993 AIDS Surveillance Case Definition of the U.S. Centers for Disease Control and Prevention
A diagnosis of AIDS is made whenever a person is HIV-positive and:

- he or she has a CD4+ cell count below 200 cells per microliter OR
- his or her CD4+ cells account for fewer than 14 percent of all lymphocytes OR
- that person has been diagnosed with one or more of the AIDS-defining illnesses listed below.
Clinical categories of HIV infection
Clinical categories of HIV infection are defined as:

- **Category A** consists of one or more of the conditions listed below in an adolescent or adult (> 13 years) with documented HIV infection. Conditions listed in Categories B and C must not have occurred.

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute (primary) HIV infection with accompanying illness or history of acute HIV infection
**Category B**

- consists of symptomatic conditions in HIV-infected adolescent or adult, not included in Category C & that meet at least one of the following criteria:
  - The conditions are attributed to HIV infection or indicate a defect in CMI.
  - The conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection.
Examples of conditions in clinical Category B include, but are not limited to:

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal: persistent, frequent, or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical CIS
- Constitutional symptoms, eg. fever (38.5°C) or diarrhea >1mth
- Hairy leukoplakia, oral
- Herpes zoster – at least 2 distinct episodes or >1 dermatome
- Idiopathic thrombocytopenic purpura
- Listeriosis
- Pelvic inflammatory ds, esp tubo-ovarian abscess
- Peripheral neuropathy
Category C

- includes the clinical conditions listed in the AIDS surveillance case definition.

- For classification purposes, once a Category C condition occurs, the person will remain in Category C.
AIDS Defining Conditions
AIDS Defining Conditions

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
AIDS Defining Conditions contd

- CMV disease (other than liver, spleen, or nodes)
- CMV retinitis (with loss of vision)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis chronic intestinal (>1 month's duration)
AIDS Defining Conditions - contd

- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- MAIC or M. kansasii, disseminated or extrapulmonary
- M. tuberculosis, any site (pulmonary or extrapulmonary) Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
AIDS Defining Conditions—contd

- Pneumocystis carinii pneumonia
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV
Additional Illnesses That Are AIDS-Defining in Children, But Not Adults

- Multiple, recurrent bacterial infections
- Lymphoid interstitial pneumonia/ pulmonary lymphoid hyperplasia
1993 Revised Classification System for HIV Infection and AIDS
1993 Revised Classification System for HIV Infection and Expanded AIDS Surveillance Case Definition for Adolescents and Adults

<table>
<thead>
<tr>
<th>CD4+ T cells</th>
<th>Clinical Categories</th>
</tr>
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<tbody>
<tr>
<td>(1) &gt;500/mL</td>
<td>(A) Symptomatic, Acute (Primary) HIV or PGL*</td>
</tr>
<tr>
<td>(2) 200-499/mL</td>
<td>(B) CD4+ T cells Symptomatic, Not (A) or (C) Conditions</td>
</tr>
<tr>
<td>(3) &lt;200/mL</td>
<td>(C) AIDS-Indicator Conditions</td>
</tr>
<tr>
<td>AIDS-Indicator T-cell count</td>
<td>A1</td>
</tr>
<tr>
<td></td>
<td>A2</td>
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<td></td>
<td>&gt;A3</td>
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PGL-persistent generalized lymphadenopathy. Clinical Category A includes acute (primary) HIV infection.
The three CD4+ T-lymphocyte categories are defined as follows:

**Category 1**: >500/mL

**Category 2**: 200-499/mL

**Category 3**: <200/mL

These correspond to CD4+ T-lymphocyte counts per mL of blood & guide clinical & therapeutic actions in mgnt of HIV-infected adolescents and adults. The revised HIV classification system also allows for the use of the percentage of CD4+ T cells.
Disease progression is influenced by viral characteristics and individual host factors.

CD4 Cell Counts (cells/mm³) (normal range if uninfected = 500–1,600)

- Antibodies produced (seroconversion), median 25 days
- Viral burden ‘set point’ <1,000–1,000,000
- AIDS diagnosis <200 CD4 cells

Early Symptoms
- Generalized lymphadenopathy, oral hairy leukoplakia, diffuse histiocytic lymphoma, dermatologic changes, herpes zoster, tuberculosis

Opportunistic Infections
- Bacterial, viral, fungal, parasitic infections

Neoplastic Diseases
- Kaposi’s sarcoma, lymphoma, invasive cervical cancer

Neurologic Manifestations
- Dementia; changes in gait, concentration, memory, affect, peripheral neuropathy

Primary HIV infection, mononucleosis-like illness (fever, rash)

After the primary infection period, a higher viral burden predicts more rapid disease progression and a higher risk of transmission from pregnant women to offspring.

Wasting, opportunistic infections, neoplastic diseases, and neurologic manifestations occur more frequently in late HIV/AIDS and may become chronic.
Revised WHO Clinical Staging of HIV/AIDS For Adults and Adolescents (2005)
• Primary HIV infection
  • Asymptomatic
  • Acute retroviral syndrome

Clinical stage 1
• Asymptomatic
• Persistent generalized lymphadenopathy

Clinical stage 2
• Moderate and unexplained weight loss (<10% of presumed or measured body weight)
• Recurrent respiratory tract infections (sinusitis, bronchitis, otitis media, pharyngitis)
• Herpes zoster
• Recurrent oral ulcerations
• Papular pruritic eruptions
• Angular cheilitis
• Seborrhoeic dermatitis
• Fungal finger nail infections
Clinical stage 3

**Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations**

- Unexplained chronic diarrhoea >1mth
- Unexplained persistent fever (intermittent or constant >1mth)
- Severe weight loss (>10% of presumed or measured body wt)
- Oral candidiasis
- Oral hairy leukoplakia
- Pulmonary TB diagnosed in last two years
- Severe presumed bacterial infections (e.g. pneumonia, empyema, meningitis, bacteraemia, pyomyositis, bone or joint infection)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

**Conditions where confirmatory diagnostic testing is**
Clinical stage 4

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe or radiological bacterial pneumonia
- Chronic herpes simplex infn >1mth (orolabial, genital or anorectal)
- Oesophageal candidiasis
- Extrapulmonary Tuberculosis
- Kaposi’s sarcoma
- CNS toxoplasmosis
- HIV encephalopathy
Clinical stage 4

**Conditions where confirmatory diagnostic testing is necessary**

- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tubercullosis mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Candida of trachea, bronchi or lungs
- Cryptosporidiosis
- Isosporiasis
- Visceral herpes simplex infection
- CMV infection (retinitis or of organ other than liver, spleen or lymph nodes)
- Disseminated mycosis (histoplasmosis, coccidiomycosis, penicilliosis)
- Recurrent non-typhoidal salmonella septicaemia
- Lymphoma (cerebral or B cell NHL)
- Invasive cervical carcinoma
- Visceral leishmaniasis
Pulmonary complications in patients with HIV infection

- infectious
- non infectious
<table>
<thead>
<tr>
<th>Infections</th>
<th>Neoplasia</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pneumocystis jiroveci</strong></td>
<td></td>
<td>-LIP, -NSIP, -BOOP, Pulmonary Hypertension, -COPD, Bronchial hyperreactivity</td>
</tr>
<tr>
<td><strong>Bacterial pneumonia</strong></td>
<td>Kaposi's sarcoma</td>
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<tr>
<td>S. pneumoniae</td>
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<tr>
<td>S. aureus</td>
<td>Non-Hodgkin's lymphoma</td>
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<tr>
<td>H. influenzae</td>
<td>Hodgkin's lymphoma</td>
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<td>B. catarrhalis</td>
<td>Bronchial carcinoma</td>
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<td>P. aeruginosa</td>
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<td>Rhodococcus equi</td>
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<tr>
<td>Nocardia asteroides</td>
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<td><strong>Mycobacteria</strong></td>
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<td>M. tuberculosis</td>
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<tr>
<td>Atypical mycobacteria</td>
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<tr>
<td><strong>Fungal pneumonia</strong></td>
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<tr>
<td>Aspergillus spp.</td>
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<tr>
<td>Cryptococcus neoformans</td>
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<tr>
<td>Histoplasma capsulatum</td>
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<td></td>
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<tr>
<td>Coccidioides immitis</td>
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<tr>
<td><strong>Viral pneumonia</strong></td>
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<td></td>
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<tr>
<td>CMV, Herpes simplex,Varicella zoster</td>
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</tbody>
</table>
INFECTIOUS PULMONARY COMPLICATIONS IN HIV
• **Infectious**
  • Upper respiratory infections
  • Acute bronchitis
  • Acute sinusitis (viral, bacterial, fungal)

• **Bacterial pneumonia**
  • S. pneumoniae
  • S. aureus
  • H. influenzae
  • B. catarrhalis
  • P. aeruginosa
  • Rhodococcus equi
  • Nocardia asteroides
Mycobacteria
- M. tuberculosis
- Atypical mycobacteria

Fungal pneumonia
- Pneumocystis jiroveci
- Aspergillus spp.
- Cryptococcus neoformans
- Histoplasma capsulatum
- Coccidioides immitis
Protozoal infections
- Strongyloides stercoralis,
- Toxoplasma gondii,
- Cryptosporidium parvum

Viral pneumonitis
- CMV,
- Herpes simplex,
- Varicella zoster
NON-INFECTIONOUS PULMONARY COMPLICATIONS IN HIV
MALIGNANCIES

- Kaposi’s sarcoma
- Non hodgkin’s lymphoma
- Hodgkin’s lymphoma
- Adenocarcinoma lung

Others

- Lymphocytic interstitial pneumonitis
- Non-specific interstitial pneumonitis
- Bronchiolitis obliterans organizing pneumonia
- Primary pulmonary hypertension
- Pulmonary embolism
CHEST RADIOGRAPH FINDINGS IN PATIENTS WITH HIV INFECTION
Without pathological findings

- Pneumocystis Carinii Pneumonia,
- Asthma,
- Kaposi Sarcoma of the trachea
Pleural effusion

- Bacterial pneumonia,
- Mycobacteriosis,
- Kaposi Sarcoma,
- Lymphoma,
- Cardiac insufficiency
Pneumothorax

Pneumocystis Carinii Pneumonia
Miliary image

- Mycobacteriosis
- Fungi
Bilateral hilar lymphadenopathy

- Mycobacteriosis
- KS
- Sarcoidosis
Diffuse infiltrates

- PCP (centrally pronounced)
- CMV,
- KS,
- LIP,
- cardiac insufficiency,
- fungi
Focal infiltrates

- Bacterial pneumonia,
- Mycobacteriosis,
- Lymphoma,
- Fungi
Cystic lesions

- PCP,
- fungi
Chest x-ray

- Multifocal infiltrates - Bacterial pneumonia, mycobacteriosis, PCP, KS

- Cavernous lesions - Mycobacteriosis (CD4 > 200), bacterial abscess (Staph...
Cigarette Smoking in HIV Infection
Cigarette Smoking in HIV Infection

- cigarette smoking induces a compartmentalized, suppressive lung inflammatory environment in HIV-positive individuals.

- associated with a marked depression in both the percentage and absolute numbers of lung lymphocytes. Lung CD4+ and lung CD8+ cell numbers were suppressed by smoking, and lung CD4+/CD8+ cell ratios trended toward lower values in smokers.

- HIV-infected smokers had increased numbers of AM recovered by BAL and showed suppressed spontaneous production of the proinflammatory cytokines IL-1 and TNF. These compartmentalized changes in the lung contrast with the lack of a defect in peripheral blood CD4+ cells in cigarette smokers.
EFFECTS OF HIV IN THE LUNG

- HIV infection of lung cells
- HIV and lung host defenses
HIV infection of lung cells
HIV infection of lung cells

- HIV entry into lung cells is mediated by the CD4+ molecule on the cell surface.

- HIV infection of human alveolar macrophages is preferentially mediated by the CCR5 receptor.
HIV AND LUNG DEFENCES
HIV and lung host defenses

- Progressive HIV infection decreases numbers of lung CD4+ T cells
- Causes intense infiltration of CD8+ T cells in the interstitium and alveolar spaces.
- Called as LYMPHOCYTIC ALVEOLITIS
- Pronounced in patients with early to middle stage disease
- Caused by compartmentalisation of HIV specific cytotoxic T cells
PROGRESSIVE IMMUNOSUPPRESSION
PROGRESSIVE IMMUNOSUPPRESSION

- Spectrum of respiratory diseases changes as immunodeficiency develops
- In case of normal CD4+ count and undetectable or low HIV-RNA in blood – risk of opportunistic infection is low
- More virulent organisms cause problems earlier in the natural history of HIV infection
<table>
<thead>
<tr>
<th>CD4+ cell count (× 10⁶ cells l⁻¹)</th>
<th>Pulmonary pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>Bacterial pneumonia</td>
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<tr>
<td></td>
<td>TB (re-infection)</td>
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<td></td>
<td>Lung carcinoma</td>
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<tr>
<td>200–500</td>
<td>Bacterial pneumonia</td>
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<tr>
<td></td>
<td>TB (re-infection)</td>
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<td></td>
<td>Lung carcinoma</td>
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<tr>
<td>50–200</td>
<td>Bacterial pneumonia</td>
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<td>TB (primary)</td>
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<td>Lung carcinoma</td>
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<td>PCP</td>
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<td>KS</td>
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<td>MAC</td>
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<td>CMV</td>
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On 22 September 2003, the leaders of UNAIDS, WHO, and the Global Fund to Fight AIDS, Tuberculosis and Malaria joined together to declare the lack of access to antiretroviral drugs to be a global health emergency. In response, the "Treat 3 Million by 2005" (3 by 5) Initiative was launched.
TO CONCLUDE..

Although, most of the pulmonary complications of HIV infection are not unique to the disease, the variability and non-specificity of clinical and radiological findings in these patients frequently complicate their diagnosis.