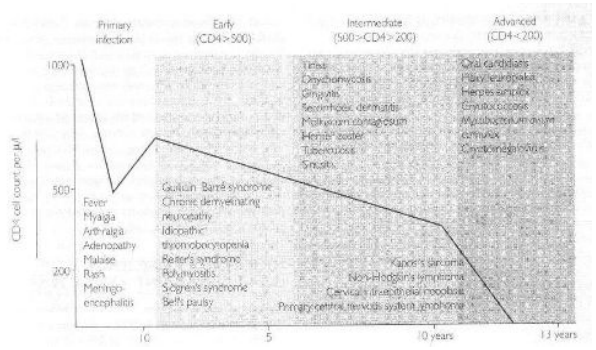
# HIV [created by Paul Young 02/10/07]

## general

- AIDS is a worldwide epidemic with greater than 20 million deaths worldwide by the end of 2004, and three million deaths in 2004 alone
- In the last 10 yrs, our perception of HIV infection and AIDS has changed from an almost uniformly fatal disease into a manageable chronic illness with introduction of HAART
- A few studies indicate that in the era of HAART, ICU admissions for PCP have declined, and overall outcomes seem to be improved. Respiratory failure is still the commonest reason for admission to ICU

## progression of illness




## CXR changes associated with HIV

**Focal infiltrates**
- Bacteria
- *Mycobacterium tuberculosis*
- *Pneumocystis jiroveci* (uncommon)

**Diffuse opacities**
- *P. jiroveci*
- *M. tuberculosis*
- Kaposi's sarcoma
- Bacteria
- Disseminated fungal infection
- Cytomegalovirus

**Diffuse nodules**
- Kaposi's sarcoma (large nodules)
- *M. tuberculosis* (miliary nodules)
- *P. jiroveci*
- Fungi (small nodules)

**Pneumothorax**
- *P. jiroveci*

**Mediastinal lymphadenopathy**
- *M. tuberculosis*
- Nontuberculous mycobacteria
- Kaposi's sarcoma
- Lymphoma
- Fungi

**Pleural effusion**
- Bacterial (parapneumonic or empyema)
- *M. tuberculosis*
- Kaposi's sarcoma
- Lymphoma
- Fungi
- Cardiomyopathy
- Hypoproteinaemia

**Cavitation**
- *M. tuberculosis* (high $CD4^+$)
- *Pneumocystis carinii* (low $CD4^+$)
- *Pseudomonas aeruginosa* (low $CD4^+$)
- *Rhodococcus equi*
- Fungi

### mucocutaneous infections in HIV

- Herpes zoster (varicella-zoster virus infection)
- Mucosal candidiasis
- Oral hairy leukoplakia (Epstein-Barr virus infection)
- Seborrhoeic dermatitis (*Pityrosporon* spp. yeast infection)
- Molluscum contagiosum (poxvirus infection)
- Genital and cutaneous warts (human papillomavirus infection)
- Fungal infections of the skin and nails
- Recurrent mucocutaneous herpes simplex virus infections
- Folliculitis (*Staphylococcus aureus*, *Pityrosporon* spp.)

## PCP

General:
- Pneumonia caused by Pneumocystis jiroveci (formerly classified Pneumocystis carinii) has always been a major cause of illness and death in patients with HIV infection.
- Once thought to be a parasite, genomic analysis revealed that P. jiroveci is in fact a fungus that infects only humans, whereas P. carinii is pathogenic only in immunodeficient rats.

Diagnosis:
- The diagnosis of PCP is established by identification of the organism in specimens obtained from the respiratory tract, either in sputum induced by inhalation of hypertonic saline or by bronchoscopy

Treatment:
- Trimethoprim-sulfamethoxazole is the preferred treatment for PCP in patients who have not had an adverse reaction to this drug
- Patients with severe PCP who do not respond or who are intolerant of this medication are usually given pentamidine, although this drug is associated with more adverse reactions
- Gas exchange typically deteriorates during the first few days of anti-Pneumocystis therapy when corticosteroids are not given; corticosteroids may attenuate lung injury caused by the inflammatory response to killed organisms, allowing the patient to survive to receive more antimicrobial therapy

Prognosis:
- Before the availability of HAART, patients who survived mechanical ventilatory support for PCP rarely lived for >1 yr.
- With the use of HAART, the prospects for long term survival are considerably more hopeful, especially if the patient has not yet received antiretroviral therapy

## Hep C

- HIV infected persons tend to have more severe liver disease and liver-associated mortality than HCV-infected persons without HIV disease.
- Death rates from HCV increased after the introduction of HAART, and the prevalence of HCV-associated cirrhosis is four times higher in patients with HIV infection compared with HIV seronegative persons
- It seems that impaired cellular immunity from HIV infection leads to accelerated HCV reproduction, with an eight-fold increase in HCV replication in HIV-infected persons compared with HIV-seronegative persons.
- HCV also accelerates the progression of HIV disease
- Management of co-infection with HIV and HCV should include agents active against both viruses, but the timing and optimal combinations present problems related to pharmacodynamics and toxicity.

## outcomes

- it seems that critically ill patients with HIV infection have similar short-term outcomes as other patients with a comparable severity of illness

## HIV drugs

**Reverse transcriptase inhibitors**

*Nucleoside analogues*
- Abacavir (ABV)
- Didanosine (ddI)
- Lamivudine (3TC)
- Stavudine (d4T)
- Zalcitabine (ddC)
- Zidovudine (AZT)
- Combivir (AZT + 3TC)*
- Trizivir (AZT + 3TC + ABV)*

*Nucleotide analogues*
- Tenofovir

*Non-nucleoside reverse transcriptase inhibitors*
- Delavirdine
- Efavirenz
- Nevirapine

**Protease inhibitors**
- Amprenavir
- Indinavir
- Lopinivir (+Ritonavir)**
- Nelfinavir
- Ritonavir
- Saquinavir

## management of prophylaxis and HAART in critically ill patients

When to start prophylaxis:
- If an HIV-infected patient develops a critical illness, prophylaxis against opportunistic pathogens like P. carinii should be started or continued unless it is otherwise indicated

When to start HAART:
- the decision to start HAART during critical illness or a severe infection is problematic. Proponents of early institution of HAART, even in critically ill patients, hold that prompt treatment of underlying HIV infection is the most important determinant of long-term survival and that an improved immune system would facilitate the resolution of an active infection.
- these drugs are often difficult to administer to critically ill patients. Only zidovudine is available in an intravenous preparation
- All of the antiretrovirals may have significant interactions with other medications that may be used to treat the critical illness, and drugs may impose new toxicities in patients not well enough to withstand them.
- immune reconstitution after antiretroviral therapy may lead to a new life-threatening accelerated inflammatory response to active or resolving infection, as in the cases of respiratory failure after institution of HAART in patients recovering from PCP
- most clinicians defer starting HAART until the acute illness has resolved or improved significantly.
- Patients already receiving HAART should continue to receive these drugs whenever possible, as discontinuing therapy is associated with viral replication and the emergence of resistance.

## toxic effects of HAART

General:
- HAART may carry the risk of life-threatening toxicities that prompt admission to the ICU

Protease Inhibitors:
- can cause pancreatitis [very rare], which may be severe.
- Protease inhibitors also cause a syndrome of lipodystrophy, insulin resistance, and hyperlipidemia

Nucleoside reverse transcriptase inhibitors:
- may cause lactic acidosis by disrupting mitochondrial DNA replication by selective inhibition of DNA polymerase.
- Mild hyperlactemia occurs commonly; severe lactic acidosis occurs at a rate of 1.3 cases per 1,000 person years of nucleoside exposure and may be life threatening
- If severe hyperlactemia or lactic acidosis is found, then the nucleoside analog reverse transcriptase inhibitor should be stopped immediately, and standard supportive care should be given.
- Because patients may also develop severe lactic acidosis due to sepsis, empirical antibiotics are administered pending the results of a bacteriologic evaluation.

Abacavir:
- is a nucleoside analog that is used in HAART regimens.
- associated with hypersensitivity reactions within a few weeks of treatment in around 3% of patients, and rechallenge often leads to life-threatening anaphylaxis. The initial hypersensitivity reaction is characterized by fever, chills, nausea, diarrhea, and rash. The rash is not always present, sometimes misleading the clinician into diagnosing an infection

## immune reconstitution syndromes

General:
- When HAART inhibits viral replication, there is a corresponding increase in the population of memory and naïve T cells, enhancement of lymphoproliferative responses, increased interleukin-2 receptor expression, and reduced production of some plasma cytokines
- These proinflammatory effects underlie newly recognized syndromes associated with immunologic reconstitution
- IRIS has also been described after or during infection with Mycobacterium avium complex, cryptococcosis, cytomegalovirus,herpes zoster, hepatitis B and C viruses, and the agent that causes progressive multifocal leukoencephalopathy.

Diagnostic Criteria:
1. the diagnosis of AIDS,
2. treatment with anti-HIV medications, symptoms consistent with an infectious or inflammatory condition that occurred while receiving antiretroviral therapy
3. symptoms that cannot be explained by a newly acquired infection or by the expected clinical course of the disease or side effects of therapy.

Clinical features:
- In the lung, some patients develop a granulomatous disorder that resembles sarcoidosis, whereas others \with latent or active mycobacterial infection may develop fever, lymphadenopathy, and opacities on the chest radiograph 2–8 wks after starting treatment with HAART

Treatment:
- discontinuation of HAART, reintroduction of corticosteroids, or both.