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 with introduction of HAART. 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.

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

Protease Inhibitors:
- can cause pancreatitis (very rare), which may be severe.
- Protease inhibitors also cause a syndrome of lipoatrophy, 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.

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.

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- 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.

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 if it is otherwise indicated.

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Diagnosis:
- The diagnosis of PCP is established by identification of the organism in specimens obtained from the respiratory tract, either by induced 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 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 antimicrobial therapy.

- HIV-infected persons tend to have more severe liver disease and liver-associated mortality than HIV-infected persons without HIV disease.
- Death rates from HDV increased after the introduction of HAART, and the prevalence of HDV-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 HDV reproduction, with an eight-fold increase in HDV replication in HIV-infected persons compared with HDV-seronegative persons.
- HDV 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.