

CURRENT PERIOPERATIVE MANAGEMENT OF THE PATIENT WITH HIV

- Literature Review -

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Introduction

Human immunodeficiency virus (HIV) is a member of the lentivirus subgroup of retroviruses, and has been shown to be the cause of acquired immunodeficiency syndrome (AIDS). It is believed that HIV-1 evolved with chimpanzees and crossed over to human beings¹. Another type of the HIV virus, HIV-2, originated from the simian immunodeficiency virus (SIV) of *Cercocebus atys* in West Africa, where the virus is endemic². HIV entered the United States in the late 1970s and was first described in 1981³.

Epidemiology

Currently there are close to 1 million people infected with HIV in the United States, and there has been a steady increase in the number of infected individuals since 2001⁴. In 2003, there were an estimated 43,171 new cases of AIDS diagnosed in this country. Additionally, there was an estimated 18,017 deaths in 2003 due to AIDS, resulting in a cumulative estimated number of deaths in the United States AIDS population of 524,060⁴. In 2006 the worldwide number of deaths was 2.9 million and the total number of individuals living with HIV/AIDS is 39.5 million. The number of AIDS related deaths is decreasing in the United States due to antiretroviral therapy⁵.

HIV transmission is mediated by sexual contact or through infected blood. Neonates may be exposed directly at the time of delivery, by breast-feeding, or by transplacental spread⁶. Currently, the 3 most common routes of transmission are male-to-male sexual contact, heterosexual contact, and intravenous drug use⁴.

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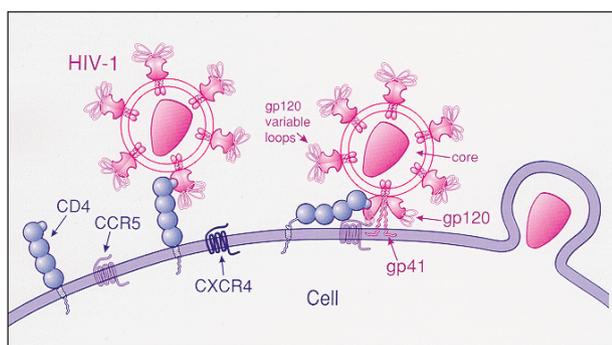
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Pathophysiology

The HIV virus is composed of single-stranded RNA, which contains a variety of genes including *gag*, *pol*, *vif*, *vpr*, *vpu*, *env*, *tat*, *rev*, and *nef*. Long terminal repeats (LTR) flank the RNA sequence at both ends⁶. The *pol* gene encodes reverse transcriptase; an enzyme necessary to copy the viral RNA to double-stranded DNA once the viral genome enters the host cell³, and integrase, an enzyme necessary for incorporation of the newly copied DNA into the host cell genome. The HIV virus is covered by a lipid bilayer that contains the envelope proteins gp120 and gp41 (Fig. 1)

Fig. 1
Pathophysiology of HIV



HIV shows marked tropism for CD4⁺ helper T cells, due to the CD4 molecule's high affinity receptor for the viral gp120 glycoprotein²; however, the CD4 molecule is not sufficient for infection. Two coreceptors have been identified as cellular targets for viral HIV. These coreceptors are CXCR4 and CCR5⁷. Macrophages and monocytes predominately carry CCR5 receptors, while T-cells carry predominately CXCR4 receptors. In the early stages of infection, the CCR5 dependent HIV viral particles predominate. As the disease progresses, a rapid decline in T-cell counts is associated with a switch from CCR5 tropic viruses to CXCR4 or CXCR4/CCR5 viruses⁷.

After the HIV viral gp120 glycoprotein binds the cell CD4 receptor, a conformational change of the gp120 glycoprotein occurs. The alteration allows the gp120 glycoprotein to bind the CCR5 or CXCR4 coreceptor. The other envelope glycoprotein, gp41, can now penetrate the host cell membrane⁶. As the HIV virus undergoes membrane fusion with the host cell, copies of its RNA genome are released into the cytoplasm of

the host cell⁸. Once the single-stranded RNA of the HIV virus is inside the host cell, reverse transcriptase can copy the viral RNA into double-stranded cDNA to be inserted into the host genome using integrase⁹. After insertion into the host cell's genome, HIV viral mRNA is transcribed using the host's own RNA polymerase. This viral mRNA is then translated into many large polyproteins, which are further cleaved by a combination of viral and host cell proteases. These polyproteins are packaged into immature virions in the cytoplasm of the cell along with viral protease. As the immature virions bud from the cell's membrane using lipid raft regions of the host cell's membrane¹⁰, the viral protease cleaves the polyproteins forming the mature HIV particle.

HIV infects CD4⁺ helper T cells, eventually killing them and suppressing cell-mediated immunity. The host becomes vulnerable to a wide variety of opportunistic infections and is predisposed to certain cancers. There are several ways in which HIV causes the net decrease in T-cells. The most common way is by viral replication and cell lysis, and the effects of a productive infection (i.e. killing by HIV-specific cytotoxic CD8⁺ lymphocytes)⁶. Persistent T-cell activation can also cause depletion of the naïve T-cell pool, leading to an overall decrease in CD4⁺ T-cell numbers¹¹. Yet another way HIV generates a net decrease in T-cells is by reducing production of CD4⁺ T-cells, a theory supported by studies demonstrating that the telomeres of CD4⁺ cells in HIV-infected cells of long-term HIV survivors are not shorter than those of uninfected CD4⁺ cells¹³.

One of the first targets of the HIV virus after infection due to sexual contact is the dendritic cell, which express CCR5 receptors. After becoming infected, these cells present the virus to CD4⁺ cells lymphocytes. Within two days of infection, virus can be detected in the draining internal iliac lymph nodes, and within five days after infection HIV can be cultured from plasma¹². Ultimately, HIV disseminates throughout the body including the central nervous system where it can hide or remain dormant for years.

During the initial infection with HIV, the plasma viral load is extremely high. This initial period is referred to as the acute stage, and usually begins 2 to

4 weeks after infection. The cell-mediated arm of the immune system helps control the infection, and thus the viral load declines. This period of decreased HIV viral load is known as the latency period, and the patient is asymptomatic during this time. The late stage of HIV infection is known as acquired immunodeficiency syndrome (AIDS), and has an average course of about 10 years¹³. Due to the high viral loads, patients in the acute stage and late stage are the most infectious

Acquired immunodeficiency syndrome is defined as a CD4+ T-cell count below 200 cells/mm³, or the development of an AIDS-defining condition. Such conditions include candidiasis, invasive cervical cancer, coccidioidomycosis, cryptococcosis, cryptosporidiosis, cytomegalovirus disease, HIV-related encephalopathy, severe herpes simplex infection, histoplasmosis, isosporiasis, Kaposi's sarcoma, certain types of lymphoma, mycobacterium avium complex, *Pneumocystis carinii* pneumonia, recurrent pneumonia, progressive multifocal leukoencephalopathy, recurrent salmonella septicemia, toxoplasmosis of the brain, tuberculosis, and wasting syndrome¹⁴. (Table 1)

Pharmacology

Several therapeutic regimes are available for the treatment of HIV infection.

Nucleoside reverse transcriptase inhibitors (NRTIs)

NRTIs remain the most commonly prescribed ARVs and are virtually always included in the initial treatment regimen. NRTIs are incorporated into the viral DNA, preventing reverse transcription and therefore inhibiting viral DNA synthesis. Viral replication is prematurely terminated and infection of new target cells is reduced. NRTIs are specific inhibitors of HIV reverse transcriptase, but also inhibit human mitochondrial DNA polymerase γ to varying degrees. Commonly used NRTIs are zidovudine, lamivudine, emtricitabine, and abacavir. Side effects commonly reported with zidovudine treatment include headache, insomnia, nausea, and vomiting. Prolonged therapy can lead to neuropathy, malaise, myalgia and myopathy with increased creatinine-phosphokinase, and pancytopenia. Peripheral neuropathy is the most common side effect of zalcitabine. It correlates with the severity of HIV infection and may affect 30% of patients treated¹⁵. Lamivudine is the least neurotoxic of the currently used nucleoside analogues. It may exacerbate preexisting neuropathy¹⁶. However, combined antiretroviral therapy was shown to improve HIV-related peripheral neuropathy¹⁷. Peripheral neuropathy generally reverses on cessation of therapy.

Table 1
Diagnostic criteria of AIDS in the patient with HIV

CD4+ T-Lymphocyte count <200 cells/ μ l	Multiple or recurrent bacterial infections
Candida of the bronchi, trachea, lungs, esophagus	Burkitt's Lymphoma
Cervical cancer, invasive	Immunoblastic lymphoma
Dissiminated or extrapulmonary Coccidioidomycosis	Dissiminated or extrapulmonary Mycobacterium avium complex or kansasii
Extrapulmonary Cryptococcosis	Mycobacterium tuberculosis
Chronic intestinal Cryptosporidiosis lasting greater than 1 month	Pulmonary or extrapulmonary Mycobacterium, any other species
Cytomegalovirus (CMV) outside of liver, spleen, lymph nodes	<i>Pneumocystis carinii</i> pneumonia (PCP)
CMV retinitis or CMV associated loss of vision	Recurrent Pneumonia
Herpes simplex virus with chronic ulcers (>1 month), bronchitis, pneumonitis, esophagitis	Progressive multifocal leukoencephalopathy
HIV-related encephalopathy	Sepsis with Recurrent Salmonella
Dissiminated or extrapulmonary Histoplasmosis	Toxoplasmosis of the brain
Chronic intestinal Isophoriasis lasting greater than 1 month	Wasting syndrome due to HIV

CDC 1993 revised classification system for HIV infection (effective after January 1993). MMWR 1992; 41:RR-17.

Non-Nucleoside reverse transcriptase inhibitors (NNRTIs)

NNRTIs act at the same step in the HIV life cycle as NRTIs, but do not require intracellular phosphorylation and thus do not inhibit human DNA polymerases. Nevirapine strongly induces CYP450 3A4 isoenzymes, while efavirenz is a mixed inducer/inhibitor of the same enzyme. The NNRTIs most commonly used are nevirapine, delavirdine, and efavirenz. Their major side effect is skin rash, including Stevens- Johnson's syndrome. Nevirapine causes cytochrome P450 enzyme induction (CYP3 A3/4) and may decrease serum levels of some anesthetic or sedative drugs (i.e., midazolam, fentanyl)¹⁸.

Protease inhibitors (PIs)

PIs function by preventing cleavage of viral precursor proteins into the subunits required for the formation of new virions. These result in the cessation of new virus production from currently infected cells. The most commonly used PIs are saquinavir, ritonavir, indinavir, and nelfinavir. Side effects are gastrointestinal symptoms, hyperglycemia, peripheral neuropathy, increased liver enzymes, and hypertriglyceridemia¹⁹. Efavirenz is a potent teratogenic drug that should be avoided during the first trimester of pregnancy²⁰. Indinavir may be associated with mild hyperbilirubinemia, hematuria, and renal failure resulting from obstructive uropathy. The PIs are metabolized by the cytochrome P450 isoenzyme cytochrome P3A4 (CYP3A4). They competitively inhibit the enzyme and may increase the effects of drugs metabolized by cytochrome P450 such as sevoflurane, desflurane, and propofol. Therefore, anesthetic drugs which are metabolized by cytochrome P450 should be titrated carefully¹⁸. Ritonavir is the most potent inhibitor of CYP3A4 and CYP2D6 and is a less potent inhibitor of CYP2C9/10²¹. Fentanyl, a synthetic opioid analgesic, is metabolized mainly by CYP3A4²¹ and to a lesser extent by other CYPs²².

Fusion Inhibitors (FIs)

Fusion (entry) inhibitors such as enfuvirtide represent a new class of antiretrovirals that effectively block viral entry into the cell and have no cross-resistance to other currently FDA-approved antiretroviral agents.

FIs must be used in conjunction with other retroviral regimens. The main side effect encountered is injection site reactions. Post injection many patients complain of pain, induration and erythema.

Side Effects and Drug Interaction with Anesthesia

Prior to administration of any anesthetic the anesthesiologist should be aware to the possible interaction of antiretroviral drugs with the anesthetics and/or toxic side effects. The presence of a myopathy or neuropathy may alter the anesthetic technique. Anemia and thrombocytopenia are major toxic side effects of zidovudine. PIs can affect glucose metabolism. Foscarnet and PIs can cause renal toxicity.

Foscarnet can also alter calcium and magnesium levels by chelating divalent metal ions thereby increasing serum calcium levels. Some side effects from other agents include ventricular arrhythmias (IV pentamidine) and bronchospasm (aerosolized pentamidine). Nevirapine is an inducer of CYP450 and therefore increased doses of anesthetic drugs may be required in patients receiving the drug¹⁸. PIs, such as ritonavir, are inhibitors of CYP450, which impair the metabolism of multiple anesthetics and analgesics, such as midazolam and fentanyl, and cardiac drugs, such as amiodarone and quinidine²¹. Etomidate, atracurium, remifentanyl and desflurane are not dependent on CYP450 hepatic metabolism, and therefore, are preferable drugs.

Due to the myriad of drug interactions, the anesthesiologist may consider regional anesthesia as the mode of anesthetic delivery. Regional anesthesia has an advantage because it does not interfere with antiretroviral drugs or the immune system. Contraindications to regional anesthesia (apart from patient acceptance and the surgical site) include sepsis, platelet abnormalities, and seeding HIV to the CNS via a bloody tap. The presence of neuropathy may reduce the appeal of regional anesthesia but there is no data suggesting contraindication. In a review of 96 HIV positive parturients, of whom 36 delivered under regional anesthesia, the advantages of regional anesthesia were confirmed²³. In 2002 the effect of spinal anesthesia was studied in 45 HIV-treated parturients who underwent cesarean delivery²⁵. No perioperative complications or changes to viral load were noted.

Perioperatively, magnetic resonance imaging (MRI) studies can be useful although not commonly done. Images of the spinal cord in 55 symptomatic HIV patients showed neurologic involvement of the spinal cord in 49 patients, mostly of infectious origin²⁴. Many compromised HIV patients are drug abusers, diabetics, postorgan transplantation recipients, and on long-term steroid treatment and develop spinal infections. They are often diagnosed too late, mostly presenting with back pain or other neurologic signs or symptoms²⁵. Prolonged epidural catheterization in such severely compromised patients may be contraindicated²⁶. However, a series of 350 cancer patients who had prolonged epidural catheterization and were monitored closely for possible infection and promptly treated had no adverse sequelae²⁷.

Common adverse effects of drug therapy

Mitochondrial toxicity can manifest as hyperlactatemia, hepatic steatosis, peripheral neuropathy, myopathy, and lipodystrophy. Although the exact pathogenesis in the HIV infected patient is debatable, the most likely culprit is NRTIs. NRTIs cause mitochondrial toxicity by inhibiting mitochondrial DNA polymerase γ . Mitochondrial toxicity is less common now, as the newer NRTIs (lamivudine, tenofovir, and abacavir) have low affinity for mitochondrial DNA polymerase γ compared with “older” NRTIs (didanosine, stavudine [d4T], zalcitabine, often referred to as “D-drugs”).

Dyslipidemia can result from antiretroviral (ARV) administration. Regular monitoring of cholesterol and triglycerides is required and lipid-lowering agents are often indicated. The metabolic syndrome, type 2 diabetes and vascular events are also complications of ARVs. An association between PI exposure and risk for increased cardiovascular events is well established. The link (although weaker) has also been demonstrated with NRTIs and NNRTIs. New ARV drugs with less effect on lipids and insulin resistance are under development.

Clinical Presentation

Initially, the acute stage of HIV infection can be subclinical or present with a mononucleosis-like prodrome of fever, sore throat, lethargy, headache,

nausea, vomiting, diarrhea, rash, lymphadenopathy, aseptic meningitis, and/or leukopenia. The number of CD4+ cells is within normal range, however, this acute stage lasts approximately 7 to 10 days. Even though the majority of HIV infections are symptomatic, many cases are initially misdiagnosed due to the similar prodrome of other viral illnesses, and the lack of detectable HIV-1 antibodies. It is essential to obtain a sexual history for high risk behavior of sexually active people who present with symptoms of viral meningitis, lymphadenopathy, sore throat, or fever²⁸. Death most often results from opportunistic infections, cancer, or wasting. These opportunistic infections occur due to the decrease in the cell-mediated immunity of the patient.

Diagnosis and Differential Diagnosis

The diagnosis of acute HIV-1 infection can be made by detection of plasma HIV-1 RNA in the plasma, in the absence of HIV antibodies. Most assays for HIV-1 RNA have sensitivities near 100%, however, approximately 2-5% of tests resulted in false positives²⁹. The false-positives yielded viral loads much smaller than those normally seen during acute infections. Upon retesting the same samples, the true-negative result was obtained²⁹. Detection of p24 has a much lower sensitivity, and lower specificity. A CD4+ T-cell count should be obtained, along with a complete blood count, chemistry profile, transaminase levels, BUN and creatinine³⁰.

Infectious mononucleosis is the most important illness in the differential diagnosis for HIV infection. Other diseases in the differential diagnosis for HIV infection include hepatitis, syphilis, influenza, and side effects of various medications.

Antiretroviral Chemotherapy

Use of current antiretroviral agents can slow the progression of HIV infection to AIDS (Table 2). Treatment should begin if the patient has a history of an AIDS-defining illness or if the patient has severe symptoms of an HIV infection irregardless of the CD4+ T-cell count. The clinician should also initiate treatment if the CD4+ T-cell count is less than 200 cells/mm³. Treatment should be offered to patients with CD4+ cell counts of 201 to 350 cells/mm³. If a patient has a cell count greater than 350 cells/mm³, and

a plasma HIV RNA level greater than 100,000 copies/ml, the decision to treat is left to the discretion of the clinician. For patients, with a CD4+ cell count greater than 350 cells/mm³, and a plasma HIV RNA level less than 100,000 copies/ml, therapy should be deferred³⁰.

Table 2
Initiation of Antiretroviral Chemotherapy

Patient Indications	Treatment Option
History of AIDS-defining illness or severe symptoms of HIV infection regardless of CD4+ T-cell count	Initiate Treatment
CD4+ T-cell count of 201-350 cells/mm ³	Offer treatment to patient
CD4+ T-cell count > 350 cells/mm ³ and plasma HIV RNA > 100,000 copies/ml	Clinician's discretion
CD4+ T-cell count > 350 cells/mm ³ and plasma HIV RNA < 100,000 copies/ml	Defer therapy

Opportunistic Infections

Opportunistic infections are a significant source of morbidity and mortality in patients infected with HIV. The use of antiretroviral therapy has helped in preventing and treating opportunistic infections. Antiretroviral therapy also increases the cell-mediated immune response, which is important for vaccinations. Vaccines elicit better immunologic responses with higher CD4+ T-cell counts. Live attenuated vaccines should not be given to HIV infected patients since this immunocompromised population may not respond as well to the vaccine and may have a greater chance of suffering from side effects of the vaccination³¹.

Early diagnosis and treatment of *Mycobacterium tuberculosis* is critical in an immunosuppressed patient to prevent acceleration of the disease. Patients with positive PPD skin tests can be treated for six months with isoniazid or rifampin. An alternate initial treatment rifabutin, pyrazinamide, or ethambutol given for 2 months followed by 4 months of treatment with isoniazid or rifampin is also acceptable³².

A very widespread and common problem for immunosuppressed patients is *Pneumocystis carinii* pneumonia. Trimethoprim-sulfamethoxazole is the first line treatment³³ and should be administered as prophylaxis if CD4+ T-cell counts decrease to less than 200 cells/mm³. Patients with a history of *Pneumocystis carinii* pneumonia should be given trimethoprim-

sulfamethoxazole for life unless antiretroviral therapy restores immune system function³³.

Toxoplasma gondii encephalitis is an opportunistic infection with the greatest risk for patients with a CD4+ cell count less than 50 cells/mm³³⁴. The drug of choice is a combination of pyrimethamine, sulfadiazine, and leucovorin.

Perioperative Anesthetic Management

The risk of contracting HIV from percutaneous exposure with an instrument infected with HIV is approximately 0.3%; however this risk increases with a rise in severity of the injury beyond a simple needlestick³¹. In order to minimize the risk to health care providers, universal precautions must be followed (Table 3). These precautions must be used for all patients:

Table 3
General Precautions for Treating HIV-infected Patients

Wear gloves	Health care workers with open lesions should avoid direct patient contact
Use caution when handling sharp objects	Use eye shields when chance of blood or body fluid exposure to the eye
Do not recap needles and dispose of used needles immediately in appropriate containers	Use appropriate equipment for cardiopulmonary resuscitation to prevent mouth-to-mouth resuscitation

1) Health care providers should wear gloves and be cautious when handling sharp objects,

2) Needles should not be recapped, and must be disposed of in the appropriate containers immediately³⁵,

3) Eye shields should be used if chance of blood/body fluid contact with the eye exists,

4) Health care workers with open lesions should avoid direct patient care,

5) Use equipment such as an ambu bag for cardiopulmonary resuscitation to prevent mouth-to-mouth resuscitation³¹.

In the event of accidental exposure, the exposed health care should be evaluated within hours and not days and should be tested for HIV at baseline³⁶. The side effects of the post exposure prophylactic medications

should be weighed against the likely risk of exposure, and patient permission to treat should be obtained. Post exposure prophylaxis should be initiated as soon as possible following an exposure. Currently, most post-exposure prophylaxis regimens involve a two drug combination; the most common regimen involves the use of zidovudine and lamivudine³⁶. Appropriate antiretroviral prophylaxis is outlined in (Table 4).

*Table 4
Chemoprophylaxis of Percutaneous Exposures to HIV-1-Infected Materials (adapted from Schooley RT. Acquired immunodeficiency syndrome. Sci Am Med 1998;1-14)*

Percutaneous Exposure

Source Material	Antiretroviral Prophylaxis	Antiretroviral Regimen
1. Blood		
Highest risk	Recommended	AZT plus lamivudine plus indinavir
Increased risk	Recommended	AZT plus lamivudine with or without indinavir
No increased risk	Offer	AZT plus lamivudine
2. Fluid containing visible blood or potentially infections fluid or tissue		
	Offer	AZT plus lamivudine
3. Other body fluids (urine, saliva)		
	Do not offer	

Mucocutaneous Exposure

Source Material	Antiretroviral Prophylaxis	Antiretroviral Regimen
1. Blood		
	Offer	AZT plus lamivudine with or without indinavir
2. Fluid containing visible blood or potentially infections fluid or tissue		
	Offer	AZT plus lamivudine with or without indinavir
3. Other body fluids (urine, saliva)		
	Do not offer	

Skin exposure (increased risk)*

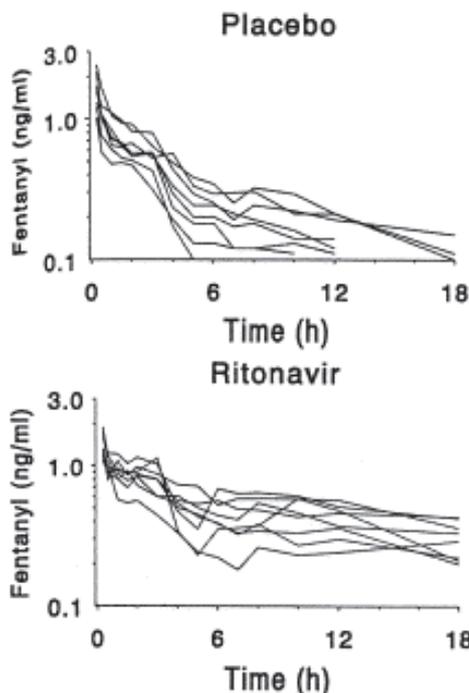
Source Material	Antiretroviral Prophylaxis	Antiretroviral Regimen
1. Blood		
	Offer	AZT plus lamivudine with or without indinavir
2. Fluid containing visible blood or potentially infections fluid or tissue		
	Offer	AZT plus lamivudine with or without indinavir
3. Other body fluids (urine, saliva)		
	Do not offer	

AZT - zidovudine; CSF -cerebrospinal fluid

* Risk is considered increased: exposure to high titers of HIV-1, prolonged contact, extensive area, an area of compromised skin integrity. For skin exposure without increased risk, the risk of drug toxicity outweighs the potential benefits.

Fig. 1

Plasma concentrations of fentanyl after an intravenous dose of 5 µg/kg fentanyl following pretreatment with oral placebo (left) or ritonavir (right) in 11 healthy volunteers. (Reprinted from Olkkola KT, Palkama VJ, Neuvonen PJ. Ritonavir's role in reducing fentanyl clearance and prolonging its half-life. Anesthesiology 1999;91:681-5; with permission.)



Preoperative assessment of the patient should include a thorough history, review of medications as well as an accurate CD4+ T-cell count. Patients with high T-cell counts (500-700 CD4+ cells/mm³) are less likely to have complications and are usually not on antiretroviral medications³. Patients with CD4+ cell counts less than 200 should have renal and liver function tests, blood counts, and clotting function tests documented. An electrocardiogram, chest radiography, and arterial blood gas may also be performed as these patients are at increased risk for cardiovascular complications³.

HIV is a systemic disease with multiorgan manifestations. The pulmonary, neurologic, cardiovascular, and hematological manifestations of HIV are of particular interest to the anesthesiologist³. *Pneumocystis carinii*, *Mycobacterium tuberculosis*, other bacteria, viral infections and fungal infections like aspergillosis and candidiasis can serve as potential pulmonary complications associated with anesthesia. These infections have the potential for impairing oxygenation. Care must be taken when placing tracheal

tubes, to avoid risk of introducing an opportunistic infection. AIDS patients may be transported with masks if the mask were to decrease the likelihood of contracting an opportunistic infection³¹. The anesthetic equipment should be treated as a potential source of infection, thus disposable anesthetic delivery circuits with bacterial filters should be considered. Both the use of masks during transport and disposable anesthetic circuits have been used in some institutions³¹.

There are several neurological complications that must be considered when treating a patient infected with HIV. Myelopathies, Guillain-Barre syndrome, peripheral neuropathies, brachial neuritis, and cauda equina syndrome are associated with the acute stage of HIV infection³⁷. In the later stages of HIV infection, neurological complications from opportunistic infections can occur. HIV-associated dementia (HAD) is another neurological complication. HAD can be controlled with antiretroviral therapy; however a less severe form of HAD can still exist³⁸.

The general side effects associated with antiretroviral medications such as hyperglycemia, hyperlipidemia, and coronary arteriosclerosis as well as the increase in life expectancy of HIV infected individuals contributes to the increase in cardiovascular complications of these patients³⁹. Protease inhibitors are associated with the dyslipidemias associated with antiretroviral therapies, putting patients at risk for future myocardial infections at a relatively young age³.

Other cardiovascular complications associated with HIV infection include cardiomyopathy, left ventricular hypertrophy, myocarditis, pulmonary hypertension, pericardial effusion, endocarditis, and malignancy⁴⁰. These complications can be due to the infection, immunosuppression, or the drug therapy. Myocarditis is a significant cause of death in adults under the age of 40, and can range in severity from asymptomatic to congestive heart failure⁴¹. The recommended therapy for myocarditis is supportive care. In the face of congestive heart failure, ionotropes, diuretics, ACE inhibitors, nitroglycerin, nitroprusside, or ventricular assist devices may be used³¹.

HIV can have hematological complications such as thrombocytopenia, leucopenia, anemia, and bone marrow suppression³. Although the thrombocytopenia

is generally not considered to be clinically important, it can worsen as the disease progresses³. Bone marrow suppression is a reversible side effect of some of the antiretroviral medications.

As mentioned earlier, there are significant side effects and drug interactions associated with antiretroviral therapy. Protease inhibitors, such as lopinavir and ritonavir, cause various dyslipidemias, increase serum aminotransferases, glucose intolerance, and inhibit cytochrome P-450 (CYP) 3A³. Due to this inhibition of the cytochrome enzyme, ritonavir has been shown to reduce the clearance of fentanyl¹⁹. Thus respiratory monitoring needs to be maintained for a longer period and dosages of fentanyl should be adjusted accordingly. Benzodiazepines and other opioids must be used with caution again due to the inhibition of cytochrome enzymes. A list of all drugs used by the patient, as well as laboratory tests, questioning the patient about side effects, and consultation with the patient's primary care provider must be obtained³.

Despite theoretical concerns of general anesthesia, it is not associated with a significant incidence of undesirable outcomes. Some transient immunologic changes have been noted, but appear to be clinically insignificant. An underlying pulmonary disease, however, is more important. A patient with repeated *P. carinii* infections, for example, may have pulmonary damage and in those cases it may be sensible to avoid endotracheal intubation. In these cases, regional anesthesia presents as a favorable option, although this consideration may apply to any patient with lung damage³.

The appropriate use of regional anesthesia, on the other hand, has been debated more frequently, as there have been reports of adverse outcomes^{3,42}. Concerns of regional anesthesia centered on the safety of spinal and epidural procedures, with fear of an extension of the HIV infection into the CNS. However, CNS infection is an early manifestation of the disease, and a failure to culture HIV in the CSF is probably due to sampling error⁴³. Furthermore, Hughes et al. have demonstrated the efficacy and safety of regional anesthesia⁴⁴. In fact, regional anesthesia for cesarean sections as well as other surgical procedures may prove beneficial. The regional approach has been associated with a decreased requirement of parenteral opioids, thus the possible

side effects cause by a protease inhibitor's effect on drug metabolism may be curtailed³.

Sepsis and platelet abnormalities are contraindications for regional anesthetics. Furthermore, the presence of neuropathy secondary to HAART therapy may diminish the appeal of regional anesthesia but currently there are no data to contradict its use. In fact, in a review of 96 HIV positive parturients, of whom 36 delivered under regional anesthesia, none of the women developed neurological sequelae, suggesting that choice of anesthesia should be based on the usual obstetric and clinical considerations. Additionally, the effect of spinal anesthesia was studied in 45 HIV-treated parturients who underwent cesarean delivery, with outcome measures including intraoperative blood pressure, heart rate, blood loss, and ephedrine requirements, and postoperative infective complications, blood transfusion, changes in blood HIV-1 viral load and lymphocyte subsets, and time to hospital discharge. The researchers found no difference in hemodynamics or postoperative complications when compared to controls⁴⁵.

Although there may be theoretical risks with an epidural blood patch (EBP), use is appropriate and safe when initiated to treat postdural puncture headache (PDPH). Acute and long-term follow-up of these patients demonstrate that there is no evidence for any unique risk from EBP in HIV-positive patients⁴⁶.

Patients with HIV related oral lesions can prove challenging. A careful inspection of the airway can reveal a variety of HIV induced lesions such as oral candidiasis with or without oropharyngeal involvement (OPC), oral hairy leukoplakia (OHL), recurrent aphthous-like ulcerations (RAU), oral Kaposi's sarcoma (OKS), orolabial herpes simplex infection (HSV), oral herpes zoster infection (VZV), intraoral or

perioral warts (HPV), and HIV-associated periodontal diseases. The lesions may cause pain, an abscess, or edema that may make for a difficult airway.

In our experience, nebulized lidocaine for 15 minutes or simply cetacaine spray can facilitate the process of an awake fiberoptic airway. Pain associated with opening the mouth decreases should a jaw thrust maneuver become necessary. An abscess or edema near the pharynx may obstruct the view of the vocal cords. In some cases involving painful oral lesions, patients may refuse to eat, thus possibly leading to malnutrition and hypoalbuminemia. In this scenario, the clinical anesthesiologist should evaluate for any signs of dehydration or electrolyte abnormalities that may need correction before surgery. Furthermore, drugs that bind to plasma proteins may be elevated, and thus may require a reduction in dosage.

Postoperatively, criteria for management of patients with communicable diseases are followed in the postanesthesia care unit. Furthermore, nurses in charge of care of these patients should not concurrently take care of other patients in the hospital⁴⁷.

Summary

Although modern medical care and current therapies save and prolong the lives of many patients with HIV/AIDS, the disease process has no cure and will continue to present itself during the perioperative period. All ages, young and old, may present with the pathology and, therefore, the anesthesiologist must have sound knowledge of the disease, treatment, complications, and multiorgan manifestations. It will be necessary to review the current treatment modalities for HIV as pharmacologic strategies are ever evolving with this disease process.

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