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HIV and Anaesthesia

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INTRODUCTION

Worldwide, it is estimated that there are 36 million people who are infected with HIV. In the 2005 National HIV Survey, 10.8% of all South Africans above 2 years old were living with HIV, the highest prevalence being females between 25-29yrs living in KZN.

Estimated HIV prevalence among South Africans aged 2 years and older, by sex and race and by province

Sex and Race	Number surveyed	Prevalence %
Male	6,342	8.2
Female	9,509	13.3
African	9,950	13.3
White	1,173	0.6
Coloured	3,382	1.9
Indian	1,319	1.6
National	**15,851**	**10.8**

Province	Number surveyed	Prevalence %
KwaZulu-Natal	2,729	16.5
Mpumalanga	1,224	15.2
Free State	1,066	12.6
North West	1,056	10.9
Gauteng	2,430	10.8
Eastern Cape	2,428	8.9
Limpopo	1,570	8.0
Northern Cape	1,144	5.4
Western Cape	2,204	1.9
Total	**15,851**	**10.8**

Estimated HIV prevalence among South Africans, by age

Age (years)	Male prevalence %	Female prevalence %
2-4	4.9	5.3
5-9	4.2	4.8
10-14	1.6	1.8
15-19	3.2	9.4
20-24	6.0	23.9
25-29	12.1	33.3
30-34	23.3	26.0
35-39	23.3	19.3
40-44	17.5	12.4
45-49	10.3	8.7
50-54	14.2	7.5
55-59	6.4	3.0
60+	4.0	3.7
Total	8.2	13.3

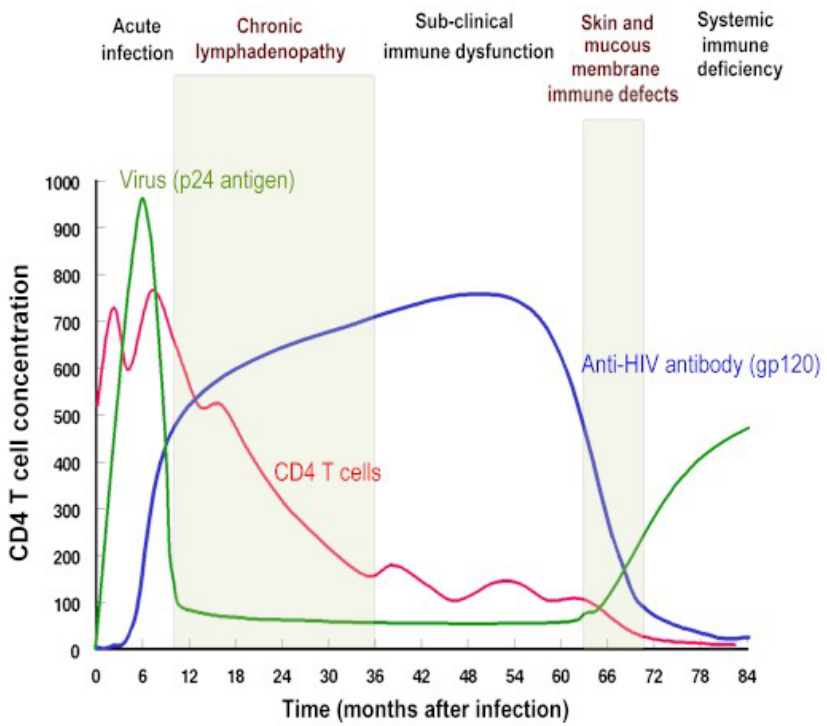
Amongst national antenatal clinic attendees, 28% were HIV positive.

Estimated HIV prevalence among antenatal clinic attendees, by province

Province	2001 prevalence %	2002 prevalence %	2003 prevalence %	2004 prevalence %	2005 prevalence %	2006 prevalence %	2007 prevalence %
KZN	33.5	36.5	37.5	40.7	39.1	39.1	37.4
Mpumalanga	29.2	28.6	32.6	30.8	34.8	32.1	32.0
F/State	30.1	28.8	30.1	29.5	30.3	31.1	33.5
Gauteng	29.8	31.6	29.6	33.1	32.4	30.8	30.3
N/West	25.2	26.2	29.9	26.7	31.8	29.0	29.0
E/Cape	21.7	23.6	27.1	28.0	29.5	28.6	26.0
Limpopo	14.5	15.6	17.5	19.3	21.5	20.6	18.5
N/Cape	15.9	15.1	16.7	17.6	18.5	15.6	16.1
W/Cape	8.6	12.4	13.1	15.4	15.7	15.1	12.6
National	24.8	26.5	27.9	29.5	30.2	29.1	28.0

With the dramatic success of highly active antiretroviral treatment (HAART), the anaesthesiologist is ever more likely to encounter HIV infected patients as part of routine practice.

COURSE OF HIV INFECTION



The course of HIV is variable. Following infection with HIV, there is a latent period of about 8-12 weeks during which there may be an intense viraemia. This period is followed by seroconversion when the antibodies to HIV appear in the serum. There is also a rapid fall in viraemia, suggesting that the immunological response has contained the infection. At this stage one third of individuals have a brief illness lasting about 2 weeks – symptoms here include fever,malaise,arthralgia,rash and lymphadenopathy. There then follows an asymptomatic phase of variable duration-average time being 10-11 years before AIDS develops.

STAGING OF HIV

Table 1. CDC Classification System for HIV-Infected Adults and Adolescents

CD4 Cell Categories	Clinical Categories		
	A Asymptomatic, Acute HIV, or PGL	B Symptomatic Conditions,#* not A or C	C AIDS-Indicator Conditions*
(1) ≥500 cells/µL	A1	B1	C1
(2) 200-499 cells/µL	A2	B2	C2
(3) <200 cells/µL	A3	B3	C3

Key to abbreviations: CDC = U.S. Centers for Disease Control and Prevention; PGL = persistent generalized lymphadenopathy.
For symptomatic conditions, see Table 2 .
* For AIDS-indicator conditions, see Table 3 .

Table 2. CDC Classification System: Category B Symptomatic Conditions

Category B symptomatic conditions are defined as symptomatic conditions occurring in an HIV-infected adolescent or adult that meet at least 1 of the following criteria:

a) They are attributed to HIV infection or indicate a defect in cell-mediated immunity.

b) They are considered to have a clinical course or management that is complicated by HIV infection.

Examples include, but are not limited to, the following:

Bacillary angiomatosis
Oropharyngeal candidiasis (thrush)
Vulvovaginal candidiasis, persistent or resistant
Pelvic inflammatory disease (PID)
Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
Hairy leukoplakia, oral
Idiopathic thrombocytopenic purpura
Constitutional symptoms,such as fever (>38.5°C) or diarrhea lasting >1 month
Peripheral neuropathy
Herpes zoster (shingles), involving ≥2 episodes or ≥1 dermatome

Table 3. CDC Classification System: Category C AIDS-Indicator Conditions

Bacterial pneumonia, recurrent (≥2 episodes in 12 months)
Candidiasis of the bronchi, trachea, or lungs
Candidiasis, esophageal
Cervical carcinoma, invasive, confirmed by biopsy
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1-month duration)
Cytomegalovirus disease (other than liver, spleen, or nodes)
Encephalopathy, HIV-related
Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1-month duration)
Kaposi sarcoma
Lymphoma, Burkitt, immunoblastic, or primary central nervous system
Mycobacterium avium complex (MAC) or *M kansasii* , disseminated or extrapulmonary
Mycobacterium tuberculosis , pulmonary or extrapulmonary
Mycobacterium , other species or unidentified species, disseminated or extrapulmonary
Pneumocystis jiroveci (formerly *carinii*) pneumonia (PCP)
Progressive multifocal leukoencephalopathy (PML)
Salmonella septicemia, recurrent (nontyphoid)
Toxoplasmosis of brain
Wasting syndrome due to HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥2 loose stools per day ≥1 month) or chronic weakness and documented fever ≥1 month

WHO CLINICAL STAGING :

This clinical staging and case definition for HIV is for resource limited settings. Staging is based on clinical findings and does not require a CD4 count.

Table 4. WHO Clinical Staging of HIV/AIDS for Adults and Adolescents

Primary HIV Infection
Asymptomatic
Acute retroviral syndrome
Clinical Stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical Stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)
Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrheic dermatitis
Fungal nail infections
Clinical Stage 3
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhea for >1 month
Unexplained persistent fever for >1 month (>37.6°C, intermittent or constant)
Persistent oral candidiasis (thrush)
Oral hairy leukoplakia
Pulmonary tuberculosis (current)
Severe presumed bacterial infections (eg, pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)
Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis
Unexplained anemia (hemoglobin <8 g/dL)
Neutropenia (neutrophils <500 cells/µL)
Chronic thrombocytopenia (platelets <50,000 cells/µL)

Clinical Stage 4

HIV wasting syndrome, as defined by the CDC (see Table 3, above)
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month or visceral herpes at any site)
Esophageal candidiasis (or candidiasis of trachea, bronchi, or lungs)
Extrapulmonary tuberculosis
Kaposi sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Cryptococcosis, extrapulmonary (including meningitis)
Disseminated nontuberculosis *Mycobacteria* infection
Progressive multifocal leukoencephalopathy
Candida of the trachea, bronchi, or lungs
Chronic cryptosporidiosis (with diarrhea)
Chronic isosporiasis
Disseminated mycosis (eg, histoplasmosis, coccidioidomycosis, penicilliosis)
Recurrent nontyphoidal *Salmonella* bacteremia
Lymphoma (cerebral or B-cell non-Hodgkin)
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy
Symptomatic HIV-associated cardiomyopathy
Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis

AIDS DEFINING ILLNESSES (1993 CDC revised classification):

1. Candidiasis of bronchi, trachea or lungs
2. Candidiasis of the oesophagus
3. Coccidiomycosis , disseminated or extrapulmonary
4. Cryptococcosis , extrapulmonary
5. Cryptosporidiosis, chronic intestinal (> 1 month duration)
6. CMV disease (excl. Liver, spleen, or lymph nodes)
7. CMV retinitis (with loss of vision)
8. Encephalopathy (HIV related)
9. Herpes simplex; chronic ulcer (> 1 month); bronchitis; pneumonitis; or oesophagitis

10. Histoplasmosis, disseminated or extrapulmonary
11. Isosporidiosis , chronic intestinal (> 1 month)
12. Kaposi's sarcoma
13. Burkitt's lymphoma
14. Immunoblastic lymphoma
15. Primary lymphoma of the brain
16. Mycobacterium avium complex or M.Kansasii, disseminated or extrapulmonary
17. Mycobacterium TB (pulm * or extrapulm)
18. Mycobacterium, other species/ unidentified species, dissem or extrapulm)
19. Pneumocystis carinii pneumonia
20. Pneumonia, recurrent*
21. Progressive multifocal leukencephalopathy
22. Recurrent salmonella septicaemia
23. Toxoplasmosis of the brain
24. Wasting syndrome due to HIV
25. Invasive cervical CA *
26. HIV with CD4< 200

*Requires lab confirmation of HIV

ORGAN INVOLVEMENT IN AIDS

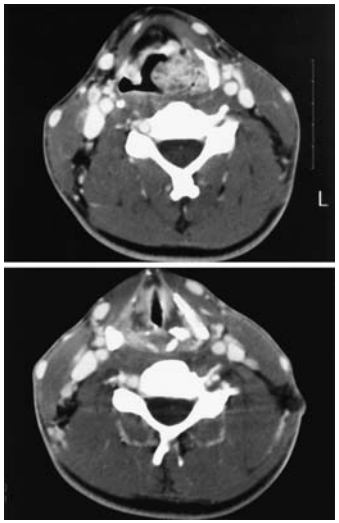
Organ involvement is widespread. These affectations may be caused by:

- HIV itself
- Opportunistic infections
- Neoplasms
- Antiretroviral drugs

1. THE AIRWAY

Kaposi's sarcoma is the commonest malignancy affecting AIDS patients. Two thirds of those with Kaposi's Sarcoma have affectation of the head and neck. The commonest part of the airway affected is by far the supraglottis.There have been several reported cases of Kaposi's Sarcoma affecting the airway. It should be emphasised that these patients don't always present with stridor and vigilance is required especially in patients with cutaneous manifestations of Kaposi's Sarcoma.

Below is a CT Scan showing Kaposi's Sarcoma affecting the supraglottic structures. The problem was discovered on direct laryngoscopy on a patient presenting for surgery. Endotracheal intubation and surgery was abandoned because of the risk of fatal haemorrhage. In this case the patient was sent for radiotherapy and chemotherapy to debulk the tumour prior to theatre. (Ref: Anest.& Analg)



2. PULMONARY MANIFESTATIONS

Pulmonary involvement is caused mainly by opportunistic infections, the most common of which is Pneumocystis Carinii. Those patients with CD4 counts less than 200 are particularly at risk. Other common diseases affecting the lung include:

Tuberculosis
Strep. Pneumonia
Haemophillus influenza
Staph. Aureus
Kaposi's Sarcoma
Gram negatives
Rare involvement of the lungs occurs with:
Herpes simplex
Candida
Cryptococcus
Lymphoma
Drug reactions

Neuraxial blocks, if sufficient, may be preferable in these cases although a high motor block with intercostal muscle weakness may not be tolerated in severe cases.

3. CARDIAC MANIFESTATIONS

Postmortem studies show cardiovascular involvement in up to 40% of AIDS patients. The following have been described:

Pericardial Effusion

The causative factors in HIV are:

Table 1. Causative Factors Associated With Pericardial Effusion in Patients With the Human Immunodeficiency Virus

Source, y	Factor
Flum et al,[18] 1995 and Decker and Tuazon,[19] 1994	*Staphylococcus aureus*
Karve et al,[20] 1992	*Streptococcus pneumoniae*
Holtz et al,[25] 1985	*Nocardia asteroides*
Ferguson et al,[26] 1993	*Listeria monocytogenes*
Lee-Chiong et al,[27] 1995 and Legras et al,[28] 1994	*Rhodococcus equi*
Kroon et al,[29] 1989	*Chlamydia trachomatis*
Sunderam et al,[21] 1986	*Mycobacterium tuberculosis*
Woods and Goldsmith,[30] 1989 and Choo and McCormack,[31] 1995	*Mycobacterium avium*
Moreno et al,[32] 1994	*Mycobacterium kansasii*
Zuger et al,[22] 1986	*Cryptococcus neoformans*
Zakowski and Ianuale-Shanerman,[33] 1993	*Histoplasma capsulatum*
Guerot et al,[34] 1995	*Toxoplasma gondii*
Nathan et al,[35] 1991	Cytomegalovirus
Freedberg et al,[36] 1987	Herpes simplex
Stotka et al,[24] 1989	Kaposi sarcoma
Flum et al,[18] 1995	Lymphoma and adenocarcinoma
Eisenberg et al,[23] 1992	Postmyocardial infarction

Myocarditis

Myocarditis is a common and important cause of ventricular dysfunction in AIDS patients. It is present in one third of all AIDS patients. Common causes include:

1. Opportunistic infections – toxoplasma gondii, mycobacterium TB, cryptococus neoformans
2. HIV itself
3. Immune mediated response to HIV – due to release of cytokines from T cell activation OR due to increased immunoglobulin production from B cell differentiation

Dilated cardiomyopathy

Occurs late in HIV and is associated with a low CD4 count. It carries a poor prognosis. Possible pathogenic mechanisms include:

1. Direct HIV mediated cardiac injury
2. Immune mediated cardiac injury
3. Associated selenium deficiency esp. in children

Endocarditis

In HIV, the most commonly involved valve is the tricuspid valve. Marantic endocarditis is associated with malignant neoplasms and a hypercoagulable state. Infective endocarditis usually involves Strep. Viridians and Staph. Aureus.

Pulmonary Hypertension

The incidence of pulmonary hypertension is higher in the HIV population than in the general population. It tends to occur at a younger age in HIV population and these patients have a better functional capacity than those in the general population. Postulates of pathogenesis include:

1. Primary pulm. Hypertension – HIV induced release of endothelin 1 from macrophages; HIV induced release of TNF and proteolytic enzymes from alveolar macrophages which enhance adherence of leukocytes to endothelium and promotes endothelial proliferation.
2. Secondary causes – talc granulomas in IV drug abusers; portal hypertension; thromboembolism; lung disease

Cardiac neoplasms

Kaposi's sarcoma usually involves the visceral pericardium and subepicardial fat resulting in pericardial effusion and cardiac tamponade.

B cell lymphoma involving the heart has also been described.

Coronary artery disease

Pathogenesis in HIV incl:

1. Angitis secondary to HIV
2. Cytokine release from monocytes and macrophages resulting in altered leukocyte adhesion to endothelial cells
3. Atheromas secondary to dyslipoproteinaemias caused by HAART especially protease inhibitors.

Drug induced cardiotoxicity

This may be due to antiretroviral drugs or drugs used to treat opportunistic infections.

Table 2. Cardiotoxicity of Medications Used in HIV Patients*

Medications	Treatment	Cardiovascular Adverse Effects
Amphotericin B	Antifungal	Dilated cardiomyopathy, hypertension, and bradycardia
Doxorubicin	Kaposi sarcoma	Cardiomyopathy
Epoetin alfa	Anemia	Hypertension
Foscarnet sodium	CMV	Cardiomyopathy
Ganciclovir	CMV	Ventricular tachycardia
Interferon alfa	Antineoplastic, antiviral, and immunomodulator	Arrhythmia, myocardial infarction or ischemia, cardiomyopathy, sudden death, AV block, and congestive heart failure
Pentamidine	*Pneumocystis carinii*	QT prolongation and Torsades de pointes
Pyrimethamine	Toxoplasmosis	QT prolongation
Trimethoprim-sulfamethoxazole	*P carinii*	QT prolongation and Torsades de pointes
Zidovudine	Antiretroviral	Myocarditis and dilated cardiomyopathy

**HIV indicates human immunodeficiency virus; CMV, cytomegalovirus.*

4. NEUROPATHY

Peripheral neuropathy is the most frequent neurological complication of HIV infection. Five forms of peripheral neuropathy are recognised:

1. Distal symmetric polyneuropathy- occurs late in HIV. Causes include HIV itself, CMV, Vit B12 deficiency and antiretrovirals esp. zidovudine and zalcitabine. Patients present with a glove and stocking sensory loss and depressed ankle reflexes.
2. Inflammatory demyelinating polyneuropathy-occurs early in HIV.Causes include autoimmune destruction and CMV.Patients present with progressive muscle weakness, areflexia and mild sensory loss.
3. Mononeuritis Multiplex - the early form is self limited and due to autoimmune mechanisms. The late form is progressive and due to CMV. Patients present with multifocal cranial and peripheral neuropathies especially foot and wrist drop and facial weakness.

4. Progressive polyradiculopathy-occurs late in HIV. Causes include CMV and neurosyphillis. Patients present with flaccid paralysis and saddle distribution anaesthesia with sphincter dysfunction.
5. Autonomic neuropathy-occurs late in HIV. A variety of factors contribute to autonomic neuropathy including central and peripheral nervous system abnormalities, dehydration, malnutrition, medication such as tricyclic antidepressants and vincristine. Patients present with orthostatic hypotension, resting tachycardia, sweating dysfunction, urinary dysfunction and impotence.

As the CNS is the first crucial organ to be affected by anaesthetic drugs, early diagnosis of HIV deserves careful evaluation of cognitive and neurologic dysfunction. Patients with AIDS are more sensitive to opioids and benzodiazepines. The probable mechanism is based on an increase in IL-1 levels causing an increase in gamma amino butyric acid production
HIV infection, opportunistic infections and intracranial masses may cause raised intracranial pressure. Hence the measures for reducing intracranial pressures should be employed and the use of neuraxial anaesthesia would be precluded in these patients.

5. GASTROINTESTINAL TRACT

In advanced AIDS, reflux oesophagitis is common. This may increase the risk of pulmonary aspiration on induction of general anaesthesia.

The histological pattern of liver injuries can be divided into 5 categories:

1. Hepatitis B, C
2. Granulomatous lesion-TB
3. Mass lesion – Kaposi's Sarcoma, lymphoma
4. Vascular-Kaposi's Sarcoma
5. Hepatotoxic medication-HAART

It is important to note that liver disease may be associated with a decrease in metabolic ability of the liver and coagulation abnormalities. This requires modification of anaesthetic technique and use of anaesthetic drugs.

6. HAEMATOLOGICAL MANIFESTATIONS

A wide spectrum of haematological abnormalities in HIV is very common and may appear at any stage of the disease. Of interest to the anaesthetist is the hypercoagulable state and thrombocytopenia associated with HIV.

HYPERCOAGULABLE STATE

Various abnormalities leading to a hypercoagulable state have been detected in HIV individuals. These include:

1. Antiphospholipid antibodies
2. Lupus anticoagulant
3. Increased levels of Von Willebrand factor
4. Decreased levels of protein c, s and antithrombin 3.

These abnormalities correlate with the severity of HIV associated immunosupression as evidenced by the CD4 counts. The causes of these abnormalities in HIV are:

1. Direct effect of infectious agents (eg.CMV) on blood vessels
2. Interference with the synthesis and metabolism of proteins involved in the haemostatic pathway
3. Release of procoagulant factors from AIDS neoplasms
4. Low grade DIC secondary to HIV

THROMBOCYTOPENIA

The incidence of thrombocytopenia in HIV individuals is between 5-15%. Of these, 6-24% have severe thrombocytopenia. It has been described in asymptomatic HIV infection and AIDS patients. Platelet abnormalities are quantitative rather than qualitative. Possible mechanisms of thrombocytopenia are:

1. ITP-immune destruction by antiplatelet antibodies or by immune complexes.
2. Decreased production-HIV infection of megakaryocytes expressing the CD4 molecule.

7. ENDOCRINE AND METABOLIC EFFECTS

ADRENAL INSUFFICIENCY

Adrenal insufficiency is the most serious endocrine abnormality in HIV infection. The prevalence of adrenal insufficiency in asymptomatic HIV individuals is 5-10%.

Pathogenesis:

Primary – adrenalitis due to CMV , MAI , MTB , Cryptococcus, Histoplasmosis, Toxoplasmosis ,Pneumocystis carinii , HIV itself or malignancy.

Secondary – CMV or Toxoplasmosis of the pituitary gland
Drug induced –ketoconazole inhibits adrenal steroidogenesis
Phenytoin and rifampicin accelerate the degradation of cortisol

Clinical suspicion is difficult as symptoms of fatigue, weight loss, anorexia and nausea are all too common. However, one should consider the diagnosis if these symptoms are accompanied by unexplained hyponatraemia, hyperkalaemia and postural hypotension.

LIPID METABOLISM

HIV is associated with hypertriglyceridaemia. The pathogenesis is twofold:
-decreased levels of lipoprotein lipase in HIV
-increased hepatic synthesis of fatty acids

The use of protease inhibitors results in protease inhibitor associated lipodystrophy.The features of this syndrome include lipodystrophy , hypertriglyceridaemia, hyperinsulinaemia, deposition of visceral abdominal adipose tissue. The exact aetiology of this syndrome is unknown. The median time interval from initiation of protease inhibitor therapy to lipodystrophy is 10 months.

PREDICTORS OF OPERATIVE OUTCOME IN HIV PATIENTS

Multiple studies were done to determine predictors of operative morbidity and mortality in HIV patients. The following factors were predictive of operative outcome in terms of morbidity (infection, anaemia, bleeding, hypertension, bradycardia):

1. Post op % CD4 count – a count between 15-21% were predictive of increased risk of morbidity.
2. % change in CD4 count from pre-op values
3. Pre-op CD4 count

In a study of 68 HIV positive patients who underwent orthopaedic or gastrointestinal tract surgery it was found that both pre-op CD4 counts and the type of operation influenced post-op infection rates:

CD4 COUNT	PROBABILITY OF POST OP INFECTION (%)	
	Contaminated op	Clean op
500	21	6
400	31	11
300	43	18
250	49	22
150	61	32
100	67	38
50	72	44

From the above, it is evident that when deciding to operate on HIV positive patients, both the CD4 counts and type of operation need to be considered. Studies also revealed the predictors of post –op mortality to be:

1. pre-op WBC count
2. pre-op % lymphocyte count – a count of 13-17% indicates a high risk of mortality
3. post-op plasma viral loads- a count of 32000-114000 molecules/ml indicates a high risk of mortality
4. post-op CD4 count – a count of 15-21% indicates a high risk of mortality

PRE-OPERATIVE CLINICAL ASSESSMENT

A common misconception is that majority of HIV positive patients would be categorized as ASA3/4 at pre-anaesthetic assessment and hence would be easily identified. However, a recent study done in Johannesburg showed the opposite. In a study of 350 patients (of which 103 were HIV positive) majority of the HIV infected patients were classified either as ASA 1or 2 rather than ASA 3/4. Furthermore, majority of the HIV positive patients whose CD4 counts were < 200 were classified as ASA1/2 rather than ASA3/4. This shows that those severely immunocompromised patients could easily be missed at pre-anaesthetic evaluation without further investigations being done. Further studies are needed to determine what the consequences could be.

EFFECT OF ANAESTHESIA ON THE IMMUNE SYSTEM

There have been a number of contradictory studies on the effect of anaesthesia on the immune system.

Nashina et al in 1998 showed that both thiopentone and midazolam suppress phagocytosis and neutrophil chemotaxis at clinically relevant concentrations. Later studies done by Marcia et al in 2001 showed that

antibody responses of patients given either a general anaesthetic or epidural or in the control group were not altered significantly following in vivo testing. Here, general anaesthesia was induced with thiopentone and maintained with isoflurane, air and oxygen. No surgery was done on the subjects.

There have been various studies showing the effect of volatiles on natural killer cell activity in mice. Studies done by Markovic et al in 1993 have shown that both halothane and isoflurane directly or indirectly inhibit natural killer cell activity

Opiates have time and again been shown to decrease phagocytic killing properties and superoxide anion production in polymorphonuclear leukocytes and macrophages. However, the effect of short term opiates is unclear and there isn't enough clinical data to justify its avoidance.

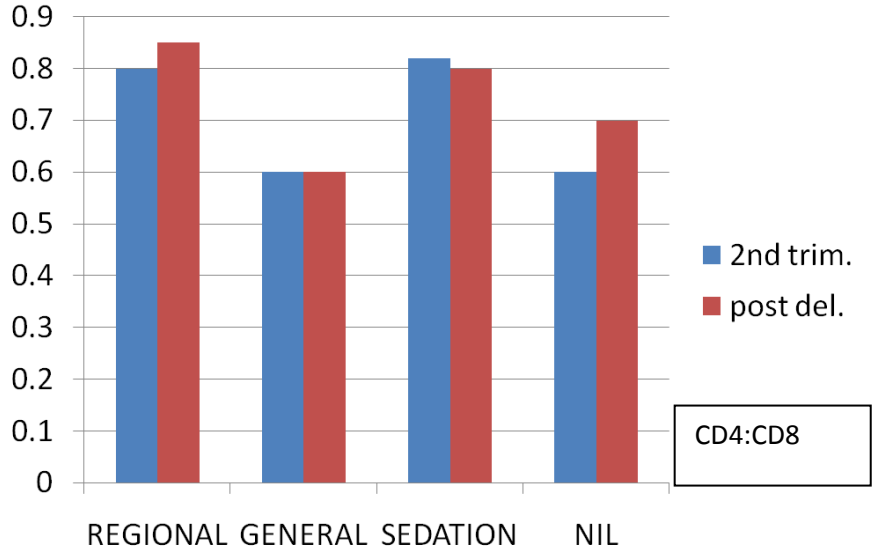
It has been proven that surgery itself results in both immune modulation and immune stimulation. It is the cell mediated arm of immunity that is paralysed due to release of the powerful endogenous immune suppressant PgE2 and the associated increase in Th2 cells and the decrease in Th1 cells.

Considering the above effects of general anaesthesia and surgery on the immune function, we would expect progression of HIV in such patients. However, there is very little data, if any, that suggest this. In fact, a retrospective study done by Manning –Williams et al compared HIV positive parturients who had regional anaesthesia, general anaesthesia or no anaesthesia for delivery showed that there were no difference in the 24-48 hr and 4-6 week complication rates between the groups. Furthermore, these groups showed no worsening of their CD4/CD8 T cell ratios post delivery in the 3 groups.

HIV AND PREGNANCY

Pregnancy alters both cell mediated and humoral mediated immunity. Several investigations have shown a decrease in CD4 cell counts during normal pregnancy , the nadir occurring in the third trimester usually returning to normal approximately 3 months post-partum. The CD8 count increases as pregnancy approaches term suggesting that the parturients cell mediated immunity is suppressed. It has been hypothesised that AIDS may progress rapidly in the parturient especially if they received general anaesthesia.

A study done by Manning-Williams and Gershan compared the clinical outcome and and peripartum complications of HIV infected parturients undergoing general anaesthesia, regional anaesthesia or no anaesthesia for delivery. They found no difference in the clinical outcome and peri-partum complications of HIV parturients undergoing general anaesthesia, regional anaesthesia or no anaesthesia.Furtermore, CD4:CD8 ratios were measured in the second trimester and 48hrs post partum. The CD4:CD8 ratios remain stable pre-partum and post partum. A limitation of the study was that majority of the 30 patients studied had CD4 counts above 200 and hence patients with advanced disease may show a different outcome. It should be borne in mind that all these studies were conducted on healthy HIV positive individuals. There are, as yet, no studies on individuals with advanced disease.



(Ref: Int.J.Obst.Anesth.)

There had been some concern that regional anaesthesia could possibly introduce HIV into the CNS resulting in rapid neurological deterioration. However, in 1995, Hughes and colleagues studied 30 HIV positive parturients of which 18 received neuraxial blocks. A six month post-partum follow up of these patients revealed no neurological and immunological sequelae. The CD4, CD8 and p24 antigen counts remained stable pre-delivery, in the peri-partum and 6 month follow up period

The recommendation for HIV positive parturients is that regional anaesthesia is the method of choice. However certain precautions exist:

- Need to exclude CNS space occupying lesions
- Be aware of peripheral neuropathies
- AIDS dementia makes co-operation impossible
- Platelet count must be known

Concerns have been expressed over the use of epidural blood patches to treat post dural puncture headaches in hiv positive patients. Tom and colleagues investigated 6 HIV positive patients who received an epidural blood patch to treat post dural puncture headaches. No adverse sequelae over a 2 year follow up period were reported.

ANTIRETROVIRAL THERAPY

Highly active antiretroviral therapy (HAART) or triple therapy is considered the standard of care in treatment of HIV infected individuals.
According to the KZN health department, indications for antiretroviral therapy are as follows:

-CD4 count less than 200 irrespective of stage

OR

-WHO stage 4 AIDS defining illness irrespective of CD4 count

AND

Willingness and readiness to take antiretrovirals adherently

RECOMMENDED REGIMENS IN ADULTS:

Regimen	Drug
1A	Stavudine, Lamivudine & Efavirenz
1B	Stavudine, Lamivudine & Nevirapine
2	Lopinavir, Ritonavir, Didanosine & Zidovudine

Regimen 1a and 1b are first line therapy for adults. Regimen 1b is for women who are at risk of pregnancy. Regimen 2 is second line therapy for patients who fail first line therapy.

WOMEN WHO FALL PREGNANT WHILST ON ANTIRETROVIRALS :
(DEPT. OF HEALTH GUIDELINES)

Women who fall pregnant whilst on efavirenz must be counselled about the potential teratogenicity. If they decide to continue pregnancy,efavirenz must be stopped and nevirapine started.
Women who fall pregnant on regimen 1b should continue therapy throughout pregnancy.

Women who fall pregnant on regimen 2 should continue their antiretrovirals.

SIDE EFFECTS OF ANTIRETROVIRALS:

Nucleoside reverse transcriptase inhibitors

Zidovudine	Anaemia,neutropenia,pancytopenia,headache , neuropathy,myopathy
Didanosine	Peripheral neuropathy,pancreatitis,GIT disturbance
Stavudine	Peripheral neuropathy ,pancreatitis,lactic acidosis
Zalcitabine	Peripheral neuropathy,pancreatitis
Abacavir	GIT disturbance,rash,myalgia
Lamivudine	Peripheral neuropathy,rash,GIT disturbance, lactic acidosis
Adefovir	GIT disturbance,increased liver enzymes,renal toxicity

Non nucleoside reverse transcriptase inhibitors

Nevirapine	GIT disturbance,increased liver enzymes,rash,p450 enzyme induction
Efavirenz	Rash,GIT disturbance,increased liver enzymes
Delavirdine	Rash,GIT abn,increased liver enzymes

Protease inhibitors :

Saquinavir	GIT disturbance,hyperglycaemia,lipodystrophy,inhibits cyt P450 enzyme
Indinavir	GIT disturbance, hyperglycaemia, skin rash , nephrolithiasis,renal failure, unusual distribution of fat, inhibits cyt P450
Ritinovir	GIT disturbance, hyperglycaemia, increased liver enzymes, lipodystrophy, inhibits cytochrome 450
Nelfinavir	GIT disturbance, hyperglycaemia, lipodystrophy, inhibits cyt P450
Amprenavir	Rash, inhibits cyt P450

DRUG INTERACTIONS OF RELEVANCE TO THE ANAESTHETIST

Protease inhibitors ,particularly ritinovir,are inhibitors of cytochrome P450 resulting in decreased metabolism of multiple drugs.Ideally, such drugs should be avoided and alternatives sought or dosage adjustments made. In contrast, nevirapine is an inducer of cytochrome P450 and therefore increasing doses of these drugs may be required.
Drugs whose metabolism is affected by induction/inhibition of cytochrome P450 :

1. Analgesics – fentanyl ,pethidine,dextropropoxyphene, ? other opiates
2. Cardiac drugs – amiodarone, fleicanide, quinidine
3. Sedating agents – midazolam ,diazepam , clonazepam, flurazepam, triazolam
4. Anti TB – rifampicin ,rifabutin

CONCLUSION

Numbers of HIV infection are increasing across the globe. With the evolution of HAART, HIV has changed from a fatal condition to a chronic condition.Most patients whom the anaesthetist encounters will be healthy , but all warrant thorough assessment to tailor appropriate analgesic and anaesthetic techniques.General anaesthesia is considered safe , but drug interactions and their impact on various organ systems should be considered pre-operatively. Regional anaesthesia is often the technique of choice. Yet, one must consider the presence of neuropathies, local infection and blood clotting abnormalities.

REFERENCES

1. Sande Volberding, The Medical Management of AIDS, 6th edition
2. Center for Disease Control and Prevention , 1993 Revised Classification System for HIV infection and Expanded Surveillance Case Definition for AIDS Amongst Adults , www.cdc.gov
3. World Health Organisation, WHO case definition of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults, 2007, www.who.int
4. Pairoj et al, Arch. Int. Med. 2000; 160; 602-608.
5. Hoang et al, American J.of Surgery; Sept 2000; 180;228-233.
6. AC Lundgren et al, SAMJ; July 2008; 98;545-548.
7. Savioz et al, Europ. J. Of Surg. 1998; 164; 483-487.
8. Shmuel et al, Anesth. Analg; 2004; 98; 503-511.
9. Hignett et al, Anesthesiology Clinics 2008; 26;127-143.
10. Manning-Williams et al, Int.J.Obst.Anesth.1997; 6; 76-81.
11. Hughes SC et al ,Anaestesiology 1995; 82; 32-37.
12. Marcia et al , Anesth.Analg. 2001; 93;460-465.
13. Nashina et al , Anesth.Analg. 1998; 86; 159-165.
14. Markovic et al , Anesthesiology 1993; 78; 700-706.
15. National Dept. Of Health Guidelines 2004 ; National Antiretroviral Treatment Guidelines ; www.doh.gov.za