PREOPERATIVE CLINICAL STATUS IN HIV-POSITIVE PATIENTS PRESENTING FOR ANAESTHESIA, AND THE CORRELATION WITH THE CD4-COUNT

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesia

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DECLARATION

I, Phillipa Rae Penfold, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Anaesthesia in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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Signature

_____ day of _____ month, 2008

For Natasha

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS STUDY

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ABSTRACT

BACKGROUND

HIV infection is common in South Africa. The disease often remains clinically latent, despite the patient having severe immune compromise. Clinical preoperative assessment may result in patients with this severe systemic disease going unnoticed.

OBJECTIVES

The primary objective was to determine the relationship between the preoperative physical status of HIV-positive patients presenting for anaesthesia and the CD4-count. The secondary objectives were to determine the prevalence of HIV infection in this group of patients, to determine the prevalence of HIV infection in selected subgroups, to ascertain what proportion of patients presenting for anaesthesia know their HIV status, and to ascertain what proportion of HIV-positive patients are receiving highly active antiretroviral therapy (HAART).

METHOD

A sample of 350 adult patients presenting for anaesthesia at Chris Hani Baragwanath Hospital was selected. Patients were interviewed preoperatively and were examined, and in doing so their ASA physical status grading was determined. Blood was sampled, and in those who were confirmed HIV-positive,

a CD4-count was checked. Further data were collected: age, gender, the type, nature, urgency and time of day of surgery, the patient's knowledge of their HIV status, and whether the patient was receiving HAART or not.

RESULTS

HIV-positive patients were more likely to be classified as ASA 1 or 2 than ASA 3 or 4 (OR 2.1). HIV-positive patients with CD4-counts above 200 cells.mm^{-3} were also more likely to be ASA 1 or 2 than ASA 3 or 4 (OR 3.88). However, within the group of HIV-positive patients with CD4-counts below 200 cells.mm^{-3}, significantly more patients were classified as ASA 1 or 2 than ASA 3 or 4 ($p<0.0001$). Three patients with CD4-counts below 50 cells.mm^{-3} were classified as ASA 1 or 2. The overall prevalence of HIV infection was 29.4%. Within the various subgroups, the groups with higher disease prevalence rates were females, patients presenting for obstetric surgery, and the younger age groups. The highest prevalence of HIV infection was found in patients aged 30-39 years (43.0%), and the lowest prevalence was found in patients aged 60 years or older (7.7%).

CONCLUSIONS

Routine clinical preoperative assessment in patients from a population with a high HIV prevalence rate may result in asymptomatic, severe immune compromise secondary to HIV infection being missed in a significant number of patients. Further study into the perioperative outcomes of these patients is warranted.

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CHAPTER ONE – INTRODUCTION

Countries in Sub-Saharan Africa carry the highest prevalence of HIV infection worldwide, with a rate of 7.2%, and South Africa ranks highly within this group[1].

Patients are assessed preoperatively in order to determine their physical fitness, for both the planned surgery and the planned anaesthetic. Anaesthetists will take a history from the patient and examine them clinically. These findings are often summarised in a more objective format, such as a grading according to the American Society of Anesthesiologists (ASA) physical status grading system, which is a score from 1-5 and denotes risk of perioperative mortality. Following this, anaesthetists will order appropriate investigations in order to ascertain the level of risk associated with proceeding with surgery, and to guide any preoperative optimisation of function that may be required[2].

HIV infection remains clinically latent for a variable length of time. An infected individual may only present with signs or symptoms once they are already severely immune compromised, and may appear clinically 'normal' despite marked levels of immune suppression[3]. As a result, there is a concern that a patient who is clinically well on physical examination, with no features which may prompt further investigation, may in fact be HIV-positive with a significant level of immune compromise. The implications of this are still unclear, as few studies have focussed on this subgroup of patients in the perioperative period.

According to the available literature reviewed, no similar study has been published.

1.1 Problem statement

HIV-positive patients presenting for anaesthesia at Chris Hani Baragwanath Hospital (CHBH) may be classified preoperatively as being clinically well, despite being markedly immune compromised.

1.2 Aim

The aim of this study is to investigate whether the preoperative clinical condition, as indicated by the ASA physical status grading, of a patient presenting for anaesthesia at CHBH correlates with subsequent laboratory testing for HIV infection and level of immune compromise, as denoted by the CD4-count.

1.3 Objectives

1.3.1 Primary objective:

To determine the association between the ASA physical status grading of HIV-positive patients presenting for anaesthesia and the CD4-count of those patients.

1.3.2 Secondary objectives:

(a) To determine the prevalence of HIV in the patient sample.

(b) To determine and compare the prevalence of HIV in the following subgroups of patients:

- different age groups
- male and female patients
- patients presenting for obstetric and non-obstetric surgery
- patients presenting for elective and emergency surgery
- patients presenting for clean and septic procedures

(c) To determine how many patients presenting for anaesthesia are aware of their HIV status.

(d) To determine how many patients presenting for anaesthesia are receiving highly active antiretroviral therapy (HAART).

1.4 Research assumptions

1.4.1 Definitions:

The following definitions were used in this study:

Type of surgery: the category of surgery for which the patient is presenting.

- Obstetric surgery: any procedure relating to a pregnancy, for example caesarean section, uterine evacuation, laparotomy for ectopic pregnancy.

- Non-obstetric surgery: any procedure not relating to pregnancy. All other surgical disciplines are included in this group, for example maxillofacial surgery, urological surgery, neurosurgery and orthopaedic surgery.

Urgency of surgery: denotes how much time the anaesthetist had for the preoperative assessment.

- Elective surgery: a procedure that was booked on the day prior to surgery, allowing the anaesthetist sufficient time for full preoperative assessment and patient optimisation, for example total hip replacement, mastectomy, repair of an uncomplicated hernia.
- Emergency surgery: a procedure that was booked on the same day as surgery, not allowing the anaesthetist sufficient time for full preoperative assessment and optimisation, for example appendicectomy for acute appendicitis, exploratory laparotomy for blunt abdominal trauma, caesarean section for foetal distress.

Nature of surgery: denotes the level of contamination associated with the surgery.

- Clean surgery: procedures associated with minimal levels of contamination, for example open reduction and internal fixation of a fractured ankle, laparoscopic cholecystectomy, uterine evacuation for retained products of conception.
- Septic surgery: procedures associated with significant levels of contamination, for example incision and drainage of a Bartholin's

abscess, debridement of an infected diabetic foot, frontal ethmoidectomy for severe sinusitis.

Time of day of surgery: denotes during which shift the procedure was booked for.

- Office hours: procedures booked to be done from Monday-Friday during the time period from 08h00-16h00.
- After hours: procedures booked to be done when only emergency anaesthesia staff are present, namely from Monday to Thursday from 16h00 until 08h00 the next morning, and from 16h00 on a Friday until 08h00 on a Monday morning.

1.5 Study design

This is a prospective cross-sectional relational observational study.

1.6 Ethical considerations

1.6.1 Ethical clearance:

The study has been approved by the regional Ethics Committee – the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand (**Appendix A**).

1.6.2 Post-Graduate approval:

The study has been approved by the Post-Graduate Committee of the University of the Witwatersrand, Faculty of Health Sciences (**Appendix B**).

1.6.3 Site approval:

Permission has been granted by the Superintendent of Chris Hani Baragwanath Hospital (**Appendix C**).

1.6.4 Patient approval:

Patients were invited to participate in the study. Patients received a printed document (**Appendix D**) explaining the reason for the study, exactly what their involvement in the study would be, their right to refuse to participate without any repercussions on their care, and their right to withdraw from the study at any time. A 24-hour contact number was supplied should they have required further information. The printed information was provided in English. The researcher and a translator provided verbal information in a language that the patient could understand if they couldn't understand English, or were not able to read the document. Written consent was obtained from all patients agreeing to participate (**Appendix E**). The counselling form (**Appendix F**) was signed as confirmation that the patients had received appropriate pre-test counselling.

1.6.5 Declaration of Helsinki:

The research was conducted according to the principles described in the Declaration of Helsinki[4].

1.7 Summary of methodology

A sample of 350 adult patients was selected using modified consecutive sampling. A trained counsellor gave pre-test counselling, and informed consent was obtained.

All patients were interviewed and examined by the principal investigator. The ASA physical status grading was determined. Secondary data were recorded regarding their age group, gender and ASA physical status grading, as well as the type of surgery they had been booked for, the urgency of the procedure and the nature of the surgery. The knowledge of HIV status was also recorded, and whether they were receiving HAART or not.

Patients who did not know their HIV status had blood sampled for HIV testing and CD4-count. Patients who were known to be HIV-positive had blood sampled for CD4-count only. The blood samples were sent for Rapid HIV Antibody testing. Those samples that tested positive were sent for confirmatory HIV ELISA testing, and the results were recorded. The samples for CD4-count were only sent for testing in those patients whose status was confirmed to be HIV-positive.

The patients were given their test results postoperatively with appropriate post-test counselling, unless they had chosen not to receive them. Patients that had tested HIV-positive were referred to the Department of Infectious Diseases for ongoing management of their condition, including ongoing counselling. The patients were not followed up postoperatively.

The data was analysed using Stata statistical software package. The association between the ASA physical status grading and HIV status as well as CD4-count (in those patients that tested HIV-positive) was described. Logistic regression analysis and the Mantel-Haenszel combined odds ratio were used to adjust for the presence of confounding variables. The prevalence of HIV infection was determined in the total sample as well as in the various subgroups, and these were compared using the chi-squared test, Fisher's exact test or the continuity correction. The knowledge of HIV status was recorded and described, as was the use of HAART.

1.8 Significance of study

A positive relationship between the preoperative physical status of HIV-positive patients and their degree of immune compromise will indicate that clinical examination of patients preoperatively is a sufficient means of detecting the presence of immune compromise. It will indicate that the severity of HIV-infection can be clinically assessed in patients who present for anaesthesia and have not tested for HIV, or who have tested HIV-positive but have not been assessed with regard to their level of immunity.

However, if there is no relationship between the preoperative physical status of HIV-positive patients and their degree of immune compromise, this will indicate that clinical examination is an insufficient means of assessing HIV-positive patients. Patients with severe immune compromise may be assessed as clinically normal. The current practice is that patients who are assessed as clinically

normal are not investigated further unless there are questions raised by their history. Patients who are unaware of their HIV status will not be suspected of having impaired immunity, and will therefore present for anaesthesia and surgery without having their degree of immune compromise determined. The implications of this remain unclear, although available literature provides some speculation as to the negative impact that this may have on patient outcome. If this is so, the results of this study may encourage the formation of new policies regarding the preoperative assessment of patients, which may include more widespread testing of patients for HIV infection, as well as determining the level of immune function in HIV-positive patients. This knowledge will allow for the appropriate management strategy to be selected for the care of the patient.

Determining the prevalence of HIV infection in the population of patients presenting for anaesthesia will allow anaesthetists to be aware of the magnitude of the HIV burden in the patients they manage. If the prevalence is high, then the management of this subgroup of patients can be prioritised. This will help to improve the quality of care that these patients receive, and will improve patient safety. This may also encourage improvements to be developed in ensuring the safety of operating theatre staff. This may also direct further research into this subgroup of patients.

Determining how many patients are aware of their HIV status will allow anaesthetists to realise how many patients will be able to give an accurate history that will arouse suspicion of underlying immune compromise. If the majority of patients are aware of their HIV status, the potential need for more widespread

preoperative HIV testing will be less than if very few patients know their HIV status.

Determining how many HIV-positive patients presenting for anaesthesia are receiving HAART will allow anaesthetists to ascertain how many patients are accessing appropriate healthcare for their condition. These patients would be regularly having their level of immunity assessed and managed. If this applies to most HIV-positive patients, then the potential need for perioperative investigation into the degree of immune compromise will be less than if most HIV-positive patients are unaware of their level of immunity.

1.9 Limitations of study

1.9.1 Study period:

The data collection was done over a six-week period in December and January. Some elective lists are closed for one or two weeks during this period. The patients presenting during this time could have been scheduled for more emergent procedures than at other times of the year.

1.9.2 Patient categorisation:

Patients were categorised on the basis of the type of operating theatre in which they were booked, whether clean or contaminated, elective or emergent. Occasionally, cases that are inappropriate for that type of operating theatre are still booked to be done in them.

1.9.3 Quality of data collection:

This was a single observer study. Only the researcher was involved in the categorisation of patients, in order to minimise the subjectivity inherent in the ASA physical status grading. The researcher may have been stricter or more lenient in grading patients than other anaesthetists.

Data was captured using double entries, and the complete data set was checked by a biostatistician.

1.9.4 Contextuality:

This study was done in the context of patients presenting for anaesthesia at CHBH. Generalisation to other populations may be limited.

1.10 Research report outline

This research report will comprise the following chapters:

Chapter One – the introduction to the study, including the aim and objectives of the study, and a brief summary of the methodology used.

Chapter Two – a review of the literature pertinent to topics raised by the study.

Chapter Three – an in-depth description of the methodology used for the study.

Chapter Four – the results of the study.

Chapter Five – an interpretation of the results of the study, and a discussion of the questions and answers raised by the results.

Chapter Six – a summary of the study, and conclusions drawn from the study.

CHAPTER TWO – LITERATURE REVIEW

2.1 History and epidemiology of the HIV/AIDS pandemic

2.1.1 The global scenario

The history of the Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) pandemic began in 1981 with the isolation of the virus and its causal link to the syndrome[5]. Prior to this, the commonest features of the syndrome were grouped under a variety of terms, for example slim disease[6] or idiopathic lymphadenopathy syndrome[7]. The aetiological virus was named either human T-cell lymphotropic virus type III (HTLV-III), lymphadenopathy-associated virus (LAV) or AIDS-associated retrovirus (ARV)[7]. Following this discovery, the clinical features as well as the natural history of the HIV infection have undergone extensive study and now form a well-defined disease entity[8].

The spread of HIV infection is through body fluids, with the three commonest routes initially being sexual transmission, transmission through sharing of hypodermic needles amongst intravenous drug users and transmission via infected blood transfusions[8]. The high prevalence amongst homosexual men resulted in a mistaken assumption that this group were at higher risk for transmission, but it is now known that the burden of infection can be even higher in heterosexual populations[9]. With the advent of the pandemic came widespread screening of donated blood products, as well as strict criteria for acceptance of blood donors[10]. This has lead to transmission via infected blood products being

extremely uncommon, and the spread of the infection into the heterosexual population has resulted in mother-to-child-transmission (MTCT), or peripartum, infection becoming one of the commonest routes of infection today[11].

2.1.2 The South African scenario

The epidemiology of the HIV infection in South Africa is quite different to that in developed countries. Historically, the black population was relocated into remote parts of the country, forcing a major increase in migrant labour[3]. Men (and on occasion women) moved to work in cities and towns, and could only return to their families when on leave. Traditional communities were largely patriarchal, and women stayed at home to look after the children. Concurrently, education of the black people was substandard. The sex trade flourished as women were forced to earn a living, and men were separated from their families for prolonged periods of time.

Today, despite changes in government policy and the abolition of apartheid, the legacy of this regime remains[12 13]. Migrant labour and the associated use of the sex trade continues (especially in the trucking community[14]), and while education standards have improved, poverty and unemployment are still high[15]. Access to healthcare is often limited[16], and may even be discouraged by community members who advocate traditional health practices[17]. Many societies are still male-dominant, and empowerment of women to make choices for themselves is severely lagging[18]. An environment is thus created wherein the spread of HIV infection amongst heterosexual people continues largely unabated.

South Africa carries the dubious honour of having one of the highest prevalence rates of HIV infection in the world, with an estimated adult rate of 18.8% (16.8-20.7)[19]. HIV is not a notifiable disease, and as such, all statistics have been based on estimates and models. Initially, the prevalence rates were based on extrapolation of test results of women attending antenatal clinics[20]. At this stage, the prevalence of HIV ranged from 15.4% to 40.7%, depending on the province. In 2002, the first national level household survey was undertaken using a random sample of males and females aged 2 years and older[21]. This revealed a total prevalence of 11.4%. In 2005, the survey was repeated, this time estimating the prevalence at 10.8%[22]. However, these single-figure numbers are often unhelpful: within the samples, the prevalence differed greatly depending on age group, geographical area, gender and race – ranging from 0.6% (white people in 2005) to 16.5% (people in Kwazulu-Natal province in 2005). This indicates the complexities involved in assigning risk of infection to a population group. Moreover, an individual has the right to refuse testing[23]. This results in prevalence rates which are skewed and thus potentially inaccurate.

Despite all these issues, what pervades is that the epidemic is large, and also present in every part of society in South Africa. It affects mainly heterosexual people, although as in developed countries, there is still a contribution to the prevalence rate from homosexual male groups and intravenous drug users. The infection of children is also high, as can be expected following the obvious increase in MTCT[8].

2.2 Management of HIV infection

2.2.1 Principles of management

Management of HIV infection involves a multidisciplinary approach. With the lack of an outright cure or vaccination, attention is focussed on maintaining clinical latency, that is, stopping disease progression[24]. Efforts are made to maintain a good state of health and nutrition, and to stop reinfection from other sources. Once the disease has progressed to a level wherein the individual is significantly immune compromised, pharmacotherapy is considered.

Highly active antiretroviral therapy (HAART) comprises a combination of drugs which act at different stages of the viral infective process. The drugs act together to suppress viral replication and thereby to lower to viral load, ideally to undetectable levels. The South African guidelines stipulate that HAART should be started in an infected individual once their CD4-count is below 200 cells.mm^{-3}, or if they show severe clinical disease (WHO clinical stage 4, see **Table 2.1**), whichever happens earlier[25]. This practice has been criticised[26 27]. It appears that, once the CD4-count drops below 350 cells.mm^{-3} then the decision to start HAART should probably be made sooner than it is currently made[24 28 29].

Table 2.1 World Health Organisation Adults HIV and AIDS Staging System

WHO Stage 1	Seroconversion illness Asymptomatic infection Persistent generalised lymphadenopathy Performance status 1 (fully active and asymptomatic)
WHO Stage 2	Less than 10% unintentional weight loss Herpes zoster within the last 5 years Minor mucocutaneous manifestations (eg seborrhoea, prurigo, fungal nail infections, oral ulcers, angular cheilitis) Recurrent upper respiratory tract infections (eg bacterial sinusitis) Performance status 2 (symptomatic but near fully active)
WHO Stage 3	More than 10% unintentional weight loss Chronic diarrhoea for > 1 month Prolonged fever for > 1 month Oral candida Vulvovaginal candidiasis > 1 month with poor response to therapy Oral hairy leukoplakia Severe bacterial infection (pneumonia, pyomyositis) Pulmonary tuberculosis within the last year Performance status 3 (bedridden <50% of past month)
WHO Stage 4	Extrapulmonary tuberculosis *Pneumocystis jeroveci* pneumonia Cryptococcal meningitis Herpes simplex virus ulcer > 1 month or visceral infection Oesophageal or pulmonary candidiasis CNS toxoplasmosis Cryptosporidiosis plus diarrhoea > 1 month Isosporiasis plus diarrhoea > 1 month Cytomegalovirus infection other than liver, spleen or lymph node HIV wasting syndrome HIV encephalopathy (AIDS-dementia complex) Kaposi's sarcoma Progressive multifocal leukoencephalopathy Disseminated mycosis Atypical disseminated mycobacteriosis Non-typhoid *Salmonella* bacteraemia Lymphoma Recurrent pneumonia Invasive cervical carcinoma Performance status 4 (confined to bed >50% of past month)

However, for HAART to be effective it requires excellent compliance on the part of the patient. Viral resistance results in treatment failure – a problem for both the

patient and whoever may be infected by that patient in the future. HAART has several severe side-effects, which may even be fatal[30 31]. Usually three drugs are prescribed, resulting in a complicated treatment regimen. Subsequently, the decision to start HAART in an individual is not taken lightly, and careful follow-up and ongoing counselling is required[24].

It has been shown that there is a period in the natural history of the disease where HAART has optimal effect[29]. Early HAART increases the risks of developing long-term drug toxicity and viral resistance. This means that when the patient becomes symptomatic, the options available for treatment are fewer and even more toxic. If HAART is delayed for too long, significant immune recovery may not occur[32]. The number of CD4-positive T-lymphocytes increases, but the function of these cells may be diminished. The patient is at higher risk of developing adverse reactions and immune reconstitution illnesses[33 34]. There is also the concern that they are at higher risk for developing cancer in the long-term.

2.2.2 South African controversies and stigma

The management of the epidemic in South Africa has attracted global interest[35]. Some political leaders have denied that HIV infection results in AIDS[36], in stark contrast to evidence from international literature. HAART has only been in use in South Africa for the past few years, despite it being well accepted in other countries since the 1990's[25 37]. This delayed rollout of essential drug therapy has occurred as a result of a lack of political will in accepting the role that this therapy

plays, in favour of more traditional and dietary regimens which have not enjoyed acceptance elsewhere[38]. Now that HAART is available, the rollout continues to be hampered by administration and resource failings[39]. In 2005, only 30 000 HIV-positive people had accessed HAART, out of approximately 1 650 000 HIV-positive people meeting the criteria for commencement of therapy[40].

A further complication arises from the ongoing stigma attached to the HIV infection[41]. Poor education, mixed messages from government, and misinformation from community leaders has resulted in groups of people who refuse to believe in the existence of the infection, and subsequently refuse testing[42]. People are afraid to admit their HIV status, even after extensive counselling, which naturally leads to ongoing viral transmission and delayed access to healthcare services in the face of failing health. Principles expounded by education campaigns (for example condom use, faithfulness to a single partner and sexual abstinence[43]) are slow to be accepted. In addition, women are not empowered to make choices, or to insist on their partners changing their behaviour[18]. With the rollout of HAART, patients accessing treatment have often not informed family members of their status, and often have infected family members and spouses that refuse testing, even in the face of successful management[42]. Following on from these reasons, many people accessing healthcare are unaware of their HIV status and are reluctant to have their blood tested.

At hospital level, a person can only be tested for HIV if they have given informed consent. This involves comprehensive counselling before the test is taken (pre-

test counselling) and also after the result has been given (post-test counselling)[3]. This time-consuming process often requires trained counsellors, which is a limiting factor in performing research into HIV prevalence in smaller, more specific population groups – research which would help delineate which sections of the population carry high levels of disease burden.

2.3 Preoperative assessment for anaesthesia

2.3.1 The perioperative environment

Anaesthetists work in the operating theatre environment, and as such are quite removed from what happens in the ward and in the community. Surgeons will book an operating list the previous day, and as a result the anaesthetist will have a limited period of time in which to assess the patient's condition before surgery.

This preoperative assessment is crucial to ensuring safe delivery of anaesthesia. The patient is interviewed and examined, in order to determine the level of risk associated with the ensuing anaesthetic. This short period of time is the only window of opportunity that the anaesthetist has to ascertain whether the patient has any special needs, or any areas in which there is cause for increased concern. Eliciting as much accurate information as possible will guide the anaesthetist in their decision making, in terms of type of anaesthetic chosen, drugs used, monitors required, possible complications to prepare for, as well as the nature of post-operative care necessary to arrange for the patient.

2.3.2 Use of the ASA physical status classification

The American Society of Anaesthesiologists (ASA) physical status classification (**Table 2.2**) is used to grade patients in terms of the possibility of perioperative problems as a result of preoperative physical status[44]. Patients with chronic diseases tend to have a higher score assigned to them, depending on their level of disease control and the impact the disease has on their daily functioning. This scoring system has been widely in use since its original reporting in 1941, and subsequent modification in 1961[45]. It has been criticised for being subjective[46 47], as well as not accounting for multiple pathologies, however it has been shown repeatedly to correlate with perioperative mortality and morbidity[48-51].

Table 2.2 ASA physical status grading[44]

ASA Physical Status Grading	Description	Expected perioperative mortality rate
1	A normal, healthy patient.	0.06-0.08%
2	A patient with mild systemic disease and no functional limitations.	0.27-0.4%
3	A patient with moderate to severe systemic disease that results in some function limitation.	1.8-4.3%
4	A patient with severe systemic disease that is a constant threat to life and functionally incapacitating.	7.8-23%
5	A moribund patient who is not expected to survive 24 hours with or without surgery.	9.4-51 %
E	Indicates 'emergency'.	

This correlation, as well as the ease with which it is used, has meant that, despite its faults, it is a score accepted by many anaesthetists who use it every day to

guide their decision-making in terms of investigating patients preoperatively. ASA 1 and 2 patients are seldom investigated further following the interview and examination, as they are deemed essentially healthy with minimal functional limitation. ASA 3, 4 and 5 patients are often subject to extensive investigation prior to surgery, so that the exact degree of functional curtailment can be determined and possibly optimised in order to improve the outcome for the patient. In addition, they may be more intensively monitored intraoperatively.

Hence it is clear that being able to accurately distinguish between ASA 1 and 2 patients and ASA 3, 4 and 5 patients is of paramount importance if this scoring system is to be used (as it often is) to determine preoperative and intraoperative management plans.

2.3.3 Pitfalls in the use of the ASA physical status classification

The shortfall of this system occurs in two situations. Firstly, an ASA 3 patient may be investigated unnecessarily, incurring cost, inconvenience and possible discomfort for poorly founded reasons. The results of the investigations may have no impact of further management of the patient. Secondly, an ASA 1 or 2 patient may not be investigated at all, thus running the risk of having vital information not being diagnosed. This latter scenario is of interest – we rely on interview technique and clinical acumen to determine whether a patient is healthy or not, and if deemed healthy, nothing further is done. Comorbidities that are subclinical are thus potentially undetected, with the assumption that if the comorbid entity is not causing clinical disease or functional limitation, it is not worth investigating.

2.3.4 Ordering special investigations

After the initial interview and examination, the anaesthetist may choose to order blood tests, x-rays, cardiology or respiratory assessments or other investigations. The purpose of these is to aid the anaesthetist in ensuring perioperative safety for the patient. Typical examples are determinations of the initial haemoglobin concentration in a patient awaiting a total hip replacement, or having an electrocardiogram (ECG) done in order to determine the presence of ischaemic heart disease in a diabetic patient with poor effort tolerance.

Previously, patients would be 'tested routinely', and all patients having surgery would often come to theatre armed with blood results, a chest x-ray and an ECG. This practice is expensive and unnecessary, and has thus fallen away[52-54]. The ASA set up a task force to help formalise this, and also produced a set of guidelines[2]. From this, investigations were suggested to be appropriate if they fulfilled one of three criteria (although not only limited to these):

1. The discovery of a disease or disorder that may affect perioperative anaesthetic care.
2. The verification or assessment of an already known disease, disorder, medical or alternative therapy that may affect perioperative anaesthetic care.
3. The formulation of specific plans and alternatives for perioperative anaesthetic care.

As a consequence, it has been left up to the individual anaesthetist to decide what is appropriate for an individual patient. Seemingly healthy patients seldom

require further investigation. However, patients with various comorbid conditions and clinical features of systemic disease will be subject to further testing in order to determine whether they will be able to endure anaesthesia and surgery, as well as to plan which anaesthetic and surgical technique will be the most appropriate for them.

Investigations should only be requested if the results will have an impact on the management of the patient. Detecting a low preoperative haemoglobin level in a patient is deemed appropriate if there is an expectation of blood loss during the surgery so that the necessary blood products are ordered. Checking the platelet count in a pre-eclamptic parturient will guide the anaesthetist in terms of selecting the more commonly employed neuraxial anaesthetic technique or general anaesthesia, which is safer in patients with bleeding diatheses[55]. Decisions regarding proceeding with surgery can also be made based on judicious use of investigations. A patient with ischaemic heart disease and a strongly positive cardiac stress test may be referred for a coronary revascularisation procedure rather than proceeding with the planned elective surgical procedure[56]. If HIV infection is subclinical, it may only be detected if the patient's blood is sent for testing. If this is not done, there may be some important implications. These are discussed later in this report.

2.3.5 Concerns with the extrapolation of guidelines

Understandably, all these recommendations come from experience with patients with a wide range of common conditions. Panels of experts compile guidelines which individual practitioners then extrapolate (within reason) to apply to a specific clinical situation[2 56]. This method of practising is not without fault. Different populations display different burdens of disease, and guidelines created in the developed world may not always be applicable in developing countries. HIV infection is an example here - developed countries have prevalence rates that are generally low[19]. As a result, the presence or absence of HIV infection in a patient is seldom used to direct guidelines regarding clinical practice. It is debatable whether such guidelines can be used blindly in a population that is vastly different, such as in South Africa where the prevalence rate of HIV infection is high.

2.4 Implications of the natural history of HIV infection on perioperative management

An HIV-positive person is one who has undergone seroconversion following exposure to HIV. The initial acute process may have clinical manifestations which are usually non-specific and transient, but it is most often asymptomatic. This is followed by a period of clinical latency, which can last from several months to several years. During this time, the immune system of the infected person gradually declines, as viral replication occurs at the expense of CD4-positive T-lymphocytes. Eventually, this depletion results in clinical manifestations of

immune compromise, which start as non-specific signs and progress to the more well-known features of the Acquired Immune Deficiency Syndrome (AIDS)[3 57]. This is illustrated in **Figure 2.1**.

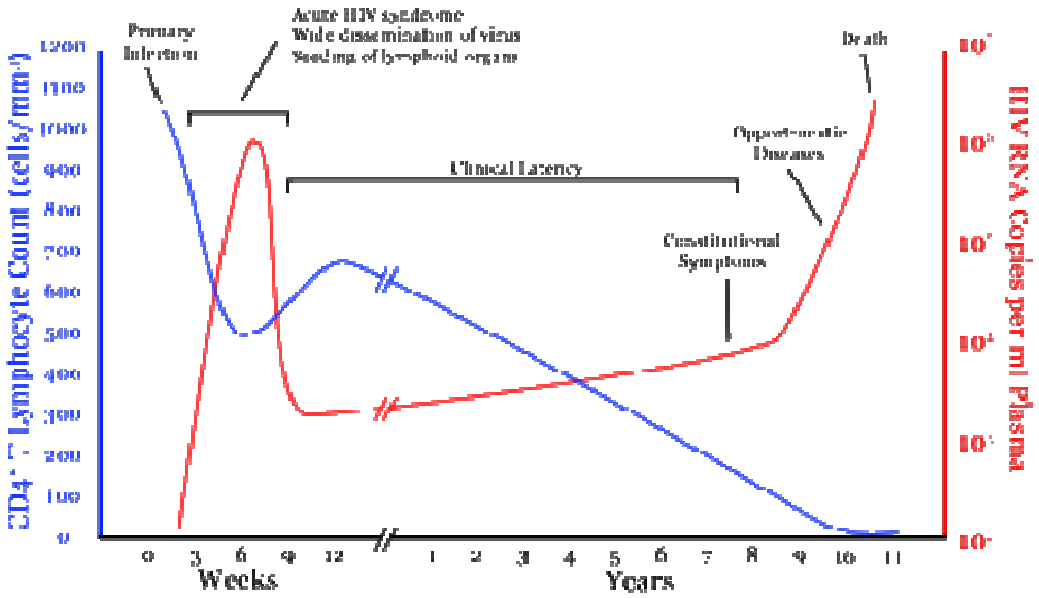

Figure 2.1 The relationship of CD4-count and viral load over time in HIV infection[58]

The World Health Organisation (WHO) clinical staging system is used in South Africa[59] (**Table 2.1**).

Having looked at all this, making a diagnosis of HIV infection purely on clinical grounds is difficult. Early features of infection are usually ignored or dismissed as insignificant, and the latent period is asymptomatic. The rate of progression from infection to AIDS is based on a number of factors, and is often impossible to predict. Many infected people are clinically well for long periods of time despite severe immune compromise. Monitoring the CD4-count of HIV-positive people is

the most widely used screening method of assessing prognosis and assigning risk of clinical disease.

Using the model wherein clinically well patients are not investigated preoperatively, patients that are asymptomatic and are as such deemed 'clinically well' may indeed be harbouring HIV infection. This would go undetected if no investigations were performed. This may not be a problem in its own right. Many anaesthetists would argue that HIV infection alone is not a reason to change the management plan of the patient. However, not detecting HIV infection may well prove to be problematic in the group of patients that are asymptomatic despite having significant degrees of immune compromise; for example the group of patients who most likely will begin to develop features of AIDS within the next few months.

2.5 The immune system and the operating environment

2.5.1 Anaesthesia and the immune system

The implications of anaesthetising immune compromised patients are not fully elucidated. Reproducible evidence shows how anaesthesia in itself suppresses immunity[60 61], in the context of lowering the typical physiological response to surgery. It has been suggested that anaesthesia alone causes a transient response[62]. However, the effects of the combination of surgery and anaesthesia on the level of immunity of a patient are indisputable[63 64].

Different anaesthetic agents and different anaesthetic techniques have different effects on the immune system. Inhalational anaesthesia has been compared with intravenous as well as neurolept anaesthesia[65]. Different induction agents have been compared with each other, and the use of regional techniques has been looked at. The use of a propofol infusion as total intravenous anaesthesia (TIVA) has been shown to have less deleterious effect that balanced inhalational anaesthesia[66 67]. Propofol has been shown to be the safest induction agent[68]. Sevoflurane may have properties that alleviate the immunosuppressive effects of thiopentone and nitrous oxide[69]. Fentanyl has also been shown to have effects on immunity, raising the question of the safety of opioid-based anaesthesia[70]. Short-acting opiates are safer than longer-acting morphine. The use of epidural analgesia postoperatively has also been shown to minimise the immune insult[71].

This knowledge can easily be compiled, and, with further research, anaesthetists could develop 'immune-friendly' techniques. These could be put to good use in a patient known to be HIV-positive (and thus heavily reliant on what remains of their immune function), especially when the CD4-count is low, or is unknown.

2.5.2 Surgery and the immune system

The surgical literature has explored the implications of operating on markedly immune compromised patients. A patient who presents with immune compromise before being operated on is clearly at a higher risk for poor postoperative immune function[60 72-74]. This results in an even higher risk for postoperative complications, especially in a resource-limited setting[75-82]. It appears prudent to find and employ

methods to boost the immune system before embarking on surgery. With the advent of HAART, surgeons have been looking at whether attempts should be made to raise the CD4-count in HIV-positive patients before operating[83-85] on them . Orthopaedic surgeons have shown the greatest interest in this, as the development of sepsis around implantable foreign material carries grave implications[86-89]. Surgeons have suggested that raising the CD4-count to above 200 cells.mm^{-3} before undergoing elective surgery would be beneficial to the patient, although this remains to be definitively proven. Some surgeons even go so far as to delay surgery until the CD4-count is above 500 cells.mm^{-3} [90].

While delaying surgery in order to initiate HAART may be appropriate in some instances, the advent of HAART has had other implications as well. Previously, HIV infection was an absolute contra-indication to patient selection for some procedures, such as organ transplantation. With HAART, HIV infection is being viewed more as a chronic disease than a preterminal condition, and HIV-positive people are starting to be considered for procedures such as solid organ transplantation and cardiac surgery[91-95]. Research has also shown that HIV-positive patients with viral control on HAART have the same prognosis as HIV-negative patients in the critical care setting. Thus, HIV-positive patients are no longer denied admission to the Critical Care Unit on the basis of their HIV status alone[96]. Diagnosing HIV infection can thus change the management of many patients.

Surgical techniques are constantly being modified. The development of minimally invasive techniques has resulted in a greater awareness of the effect that surgery

has on the whole body. Laparoscopic techniques have been compared with open techniques, and have been consistently shown to cause a lesser degree of immune compromise[97-101]. Endovascular procedures have been shown to have similar effects[102-105]. Some cardiac surgery can be performed 'off-pump', thus avoiding the immune compromise associated with cardiopulmonary bypass[106]. These newer methods have been shown to decrease the length of hospital stay, decrease cost (after the initial outlay for equipment), and shorten the time taken for recovery in the majority of patients[107].

Some endoscopic and endovascular procedures can be performed under conscious sedation, or a light level of anaesthesia using a mask. Postoperatively, the fluid shifts seen after traditional open surgery are much less apparent, and the recovery of patients is smoother and requires less nursing care. This is particularly relevant in the frail patient, as well as those with severe immune compromise and less organ function reserve as is seen in the patient with AIDS.

2.5.3 Implications for postoperative recovery

Both changes in surgical and anaesthetic technique could be employed in patients with low immunity in order to ensure swift uncomplicated postoperative recovery. Postoperative immune suppression puts a patient at a much higher risk of developing sepsis, a major cause of morbidity and mortality[108]. A large proportion of research into care of the critically ill involves finding methods to minimise the incidence of sepsis. Systemic sepsis and wound sepsis both result in compromised patient outcome, further postoperative complications, delayed

discharge and increased cost[109]. If severely immune compromised patients are currently recovering poorly, and thus requiring higher care facilities, then improved management strategies based on the preoperative detection of their disease may move forward in alleviating this problem.

2.6 Further implications of the lack of knowledge of HIV status

2.6.1 Public Health and access of healthcare

The stigma associated with HIV infection in South Africa has already been discussed. Patients presenting for anaesthesia are usually unaware of their HIV status. Patients presenting for elective surgery are often clinically well, and as such would not be subject to preoperative investigations. These patients, having accessed healthcare for other reasons, namely the surgical pathology, would miss a potential screening opportunity which would enable access to the appropriate clinic to assess their HIV status and thus to initiate HAART.

2.6.2 Opportunities for ongoing research

There is very little literature available describing anaesthesia in HIV-positive patients. Most of the global HIV burden is carried by poorer developing countries[110]. Conversely, most significant research is conducted in wealthier developed countries, usually as a result of increased financial and human resources. Research into the effects that HIV has on anaesthesia (or vice versa) would require a sizeable database of HIV-positive patients presenting for

anaesthesia. This is unlikely in countries with a low disease burden, and in South Africa this is hampered by both the need for informed consent and counselling before testing and the lack of financial resources in the public sector. The information available regarding HIV and anaesthesia is largely expert opinion. Few clinical trials having been conducted, and there have been few randomised controlled trials published[111-113].

2.6.3 Implications for operating theatre staff safety

Attention has been focussed on the dangers that blood-borne infections may pose on the anaesthetist, and on whether or not universal precautions for the prevention of transmission of blood-borne pathogens are adhered to in the operating theatre[114]. A list of these precautions is given in **Table 2.3**. Compliance is generally poor, but has been shown to increase if the patient in question is known to be HIV-positive[115].

Table 2.3 Universal precautions for the prevention of transmission of blood-borne pathogens[116]

Universal precautions for the prevention of transmission of blood-borne pathogens
1. Take meticulous care to prevent injury when using, cleaning or disposing of sharp materials – needles, scalpels and other sharp instruments.
2. Do not resheath needles, do not remove needles from syringes by hand, do not bend, break or otherwise manipulate needles by hand.
3. Place used disposable syringes and needles, scalpel blades, suture needles or other sharp items in puncture-resistant containers. Keep the containers as close to the place of use as possible.
4. Use protective barriers (gloves, eyeglasses, waterproof aprons and waterproof footwear) to prevent exposure to blood and body fluids.
5. If hands or other skin surfaces are contaminated with blood or body fluids containing blood or other potentially infectious body fluids, wash immediately and thoroughly (as soon as patient safety permits).

2.7 Available literature and the need for further study

The obstetric population has been investigated. Regional anaesthesia has been shown to be safe in HIV-positive mothers, and remains the treatment of choice[117]. Very little information is available about the effects that anaesthesia has on the HIV-positive patient in other settings. It is unclear whether surgery and anaesthesia affect the prognosis of the HIV-positive patient, or whether there are methods available to minimise any deleterious effects.

Literature from the South African setting is even more scant. Guidelines regarding preoperative workup of patients do not include HIV status in their list of conditions to test for. No study has investigated the relationship between the level of immunity of a patient and the preoperative physical status associated.

Estimating the prevalence in the patients presenting for anaesthesia is problematic. On the one hand, people coming to hospital are less healthy than the general population, so it would seem likely that the prevalence may be higher. On the other hand, patients are often only given the option of having elective surgery if they are indeed healthy, so the prevalence may be lower. In addition, a large proportion of patients present for emergency procedures, including trauma-related, obstetric and gynaecological. Lastly, the population served by one department is specific to that hospital, both geographically and in terms of social demographics. All this contributes to the inhomogeneous nature of the sample in question. There has been no study determining the prevalence of HIV infection in patients presenting for anaesthesia in any Southern African context.

CHAPTER THREE - METHODOLOGY

3.1 Study design

The study was a prospective cross-sectional relational observational study.

Prospective: only individuals giving written informed consent will be included in the study. They will then be followed forward in time until the required data is collected.

Cross-sectional: data will be collected from participants at a single given period. There will be no follow-up of participants following data collection.

Relational: part of the data will be analysed in order to determine the presence or absence of a relationship between two subsets of the data.

Observational: the data will be collected without any intention of intervening in any aspect of the management of the participants.

This study design was chosen because it will provide an appropriate means of conducting a survey of the current status of patients presenting for anaesthesia at Chris Hani Baragwanath Hospital (CHBH). By accurately assessing the problems pertaining to the current practice of preoperative clinical assessment of patients, plans and policies can be made for future improvements in the management of patients.

3.2 Study site

The study was conducted at Chris Hani Baragwanath Hospital (CHBH), in Soweto, Johannesburg. CHBH is a 2800-bed tertiary public hospital, which services a predominantly black population in the low-income bracket

3.3 Study population

The study population comprised all patients presenting for anaesthesia during the study period.

3.4 Study period

The study took place over a period of six weeks, from 1 December 2005 until 16 January 2006. Permission to perform the study was granted by the Hospital Chief Executive Officer, and ethical clearance was granted by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand (**Appendix A**). Four trained counsellors were employed for pre-test and post-test counselling, as well as to assist in referring the patient to the necessary healthcare providers as deemed appropriate. Patients signed the counselling form to confirm they had received appropriate pre-test counselling (**Appendix F**).

3.5 Sample population and sampling method

In consultation with a biostatistician, a sample of 350 patients was selected. This number was chosen so that a two-sided 95% confidence interval for a single proportion (using the large sample normal approximation) would extend 0.05 (setting significance at below 0.05) from the observed proportion for an expected proportion of 35%.

Modified consecutive sampling was used. The hospital runs daily elective surgical lists from Monday to Friday, and has seven emergency theatres that run 24 hours a day. A daily list of all patients that were scheduled for anaesthesia was compiled, and all patients that had had emergency anaesthesia the day before was added to this list. A second list comprising every third patient on the first list was then drawn up, and these patients were approached for the purposes of the study. The selection processed stopped once 350 patients had been recruited.

The hospital does cater for out-patient surgery, although the majority of patients spend at least one night in hospital before and one night after the surgery. These out-patients were also approached, if they had been included in the second list. They were given the option of waiting for their results or of coming back to the hospital at a later stage to get their results and post-test counselling.

3.6 Exclusion criteria

The following patients were excluded from the study:

1. Any patient under the age of 18 years, or otherwise unable to give informed consent.
2. Any patient who refused to participate, after having received appropriate pre-test counselling, or chose to withdraw their name from the sample after they had already been tested.
3. Any patient presenting for anaesthesia that was to be administered by someone other than an anaesthetist (for example procedures performed under local anaesthesia, procedures requiring conscious sedation administered by a nursing assistant)
4. Any patient that had already been included in the study population (for example those patients coming for repeat surgery).

3.7 Data collection

Once the final list had been compiled, the patients were approached. The study was explained to them in a language that they could understand, by either the researcher or a translator. Patients received a written information sheet, detailing all aspects of the study. The information sheet was written in English (**Appendix D**).

Patients were then given pre-test counselling by a trained counsellor. All explanations were done in a language that the patient could understand, in terms

of the National Health Act of 2003. Patients were allowed to withdraw their participation at any time, and at no time was a patient coerced into participation.

If the patient consented (and signed the consent and counselling form – **Appendix E** and **Appendix F**), the patient was interviewed and examined. If the patient was previously proven to be HIV-negative, no blood samples were taken. The patient was required to show some sort of recent documentation of their HIV status in this instance. If the patient was known to be HIV-positive, a single blood sample was taken to be sent for a CD4-count. If the status of the patient was unknown, two blood samples were taken. The first sample was sent for Rapid HIV Antigen testing, using the Determine® HIV-1/2 rapid diagnostic test (Abbott Laboratories). This is a visually read, rapid immunochromatographic test for the detection of antibodies to HIV-1/2 in human serum, plasma and whole blood. This has a sensitivity of 99.9%, and a specificity of 97.8%, and is considered an acceptable test for use in clinical practice[118]. If this tested positive, the remainder of the specimen was sent for HIV ELISA testing, using an Elecsys 2010 HIV Combi® fourth generation HIV ELISA (Roche Diagnostics). This ELISA detects both HIV-1/2 antibodies and the p24 antigen, and is widely used as a confirmatory test for the presence of both early and established HIV infection. It has a 100% sensitivity and a 98.8% specificity[119]. If this confirmed the status of the patient to be HIV-positive, then the second sample was sent for CD4-count testing, using CD45-assisted pan-leucogating. This is an accurate, robust method of CD4 T-cell enumeration, and has been well validated[120]. These second samples were kept in appropriate laboratory conditions while waiting for the HIV

test results. If the first sample tested HIV-negative, the second sample was discarded.

Once the HIV results were known, the counsellors approached the patients again and gave them their results, with the appropriate post-test counselling, unless the patient had requested not to know their HIV test result. The patients were referred to the appropriate healthcare facilities as necessary, for ongoing management of their condition, as well as ongoing counselling.

Patient confidentiality was maintained at all times. Ward staff were not informed of the nature of the interviews, and results were not made available to anyone except the patients and their relevant counsellor. Patients were assigned a numerical code, and this was the only identifying feature on the data sheet. The codes were listed with the names and contact details of the patients on a separate sheet. This was kept locked away for the duration of the study, and remains available only to the researcher. The purpose of this list of details is to allow those patients that chose not to receive their results opportunity to change their mind in the future, because their results would not be available by any other method.

Data capture was managed by entering values onto a separate page for each patient, as well as onto a spreadsheet. The details of the collected data are as follows:

1. Age – the patients were allocated to 1 of 5 randomly chosen age groups:
    i. 18-29 years
    ii. 30-39 years
    iii. 40-49 years
    iv. 50-59 years
    v. Over 60 years
2. Gender (male or female)
3. ASA physical status grading (from 1-5). The 'E' (denoting emergency) was omitted because the urgency of the procedure was noted separately. The specific guidelines used for patient classification in this study are tabulated in **Table 3.1**. Patients who were known to be HIV-positive were not graded differently on the basis of this knowledge alone. The grade was only changed if the patient had clinical features of immune compromise, or if the patient was already taking HAART.
4. Knowledge of HIV status (known or unknown)
5. HIV status (positive or negative)
6. CD4-count (in those that tested HIV-positive, or were known to be HIV-positive) which was grouped into 1 of 5 groups. The following groups were chosen because they represented clinically significant categories (significance in brackets):
    i. 500 cells.mm^{-3} or more (normal)
    ii. 350-499 cells.mm^{-3} (still immune competent)
    iii. 200-349 cells.mm^{-3} (where initiation of HAART is considered in some countries)

iv. 50-199 cells.mm^{-3} (criterion for diagnosis of AIDS, and where initiation of HAART occurs in South Africa)
v. Less than 50 cells.mm^{-3} (critically immune compromised, requiring fast-tracking of HAART)

7. Management – whether those known to HIV-positive were taking HAART or not.
8. Type of surgery – this was divided into obstetric surgery and non-obstetric surgery.
9. Urgency of surgery (elective or emergency), based on whether the procedure had been booked or an elective or an emergency list.
10. Nature of surgery (clean or contaminated), based on whether the procedure had been booked on a list of clean or contaminated (septic) procedures.
11. Time of day of surgery (office hours or after hours) – this only impacted on emergency procedures, as elective surgery was only done during office hours. This detail was chosen to try to determine whether more HIV-positive patients presented when anaesthetic staffing was at a minimum or not. If it were determined that there was a proven benefit to determining the HIV status of patients prior to surgery, this would increase the workload of staff (in terms of preoperative assessment, investigations and counselling), which would have greatest impact when staff numbers were lowest.

Table 3.1 HIV/AIDS-related criteria used in this study for classification according to the ASA Physical Status Grading System

ASA Physical Status Grading	Examples of criteria used for categorisation
1	Asymptomatic No previous long-term illnesses Clinically normal
2	Persistent generalised lymphadenopathy Features of WHO clinical stage 2 Past history of significant illness, eg pulmonary tuberculosis fully treated more than one year previously with no subsequent limitations of function Patients on HAART with full viral suppression
3	Features of WHO clinical stage 3 Still able to function in a limited capacity Patients on HAART with suboptimal viral suppression
4	Features of WHO clinical stage 4 Not expected to die within the next 24 hours
5	Life-expectancy less than 24 hours (No patient in the study met this criteria)

Measures to minimise error were employed. Data was captured using double entries, that is, it was entered on two separate sheets which were checked against each other. The complete data set was checked by a biostatistician for errors and missing data.

3.8 Data analysis

The data were analysed using the Stata statistical software package. The association between the ASA physical status grading and HIV status as well as the CD4-count was determined using logistic regression modelling and the Mantel-Haenszel combined odds ratio (thus adjusting for confounding variables). Disease prevalence in each group was also determined by logistic regression modelling, and patient groups were compared using the Chi-squared test, Fisher's exact test and the continuity correction. Statistical significance was set at $p \leq 0.05$.

3.9 Funding

The study was funded by means of a research grant from the Jan Pretorius Fund, provided by the South African Society of Anaesthesiologists.

CHAPTER FOUR – RESULTS

4.1 Sample and patient refusal

A total of 369 patients were approached. Nineteen patients (5.1%) refused to participate. Reasons for refusal included not wanting to have more blood taken in patients who had been in hospital for some time), fear of receiving the result, fear of not recovering from the surgery because of additional stress, and not feeling the need to have blood tested, on the basis of being sure of being HIV-negative (older patients and patients who were no longer sexually active).

4.2 Prevalence in total sample

In the total sample of 350 patients, 103 were confirmed to be HIV-positive, giving an overall prevalence of 29.4% (95% CI 24.9 – 34.4).

4.3 Distribution of sample according to ASA physical status grading

The total sample distribution according to ASA grade and HIV status is shown in **Table 4.1**. Patients classified as ASA 1 or 2 comprised 82.6% of the total sample. Of these, 31.8% were HIV-positive, and 68.2% were HIV-negative. Patients classified as ASA 3 or 4 comprised the remaining 17.4% of the sample, and of these, 18.0% were HIV-positive and 82.0% were HIV-negative.

Table 4.1 Distribution of sample according to ASA grade and HIV status

	Total (%)	HIV-positive (%)	HIV-negative (%)
ASA 1 or 2	289/350 (82.6)	92/289 (31.8)	197/289 (68.2)
ASA 3 or 4	61/350 (17.4)	11/61 (18.0)	50/61 (82.0)

Within the total sample, the classification of ASA grade was most affected by age, regardless of HIV status. Using logistic regression analysis, younger patients were more likely to be classified as ASA 1 or 2 than older patients ($p<0.0001$).

Within the HIV-positive group, the likelihood of being classified as ASA 1 or 2 was analysed. Confounders were found to be the nature of surgery (clean or septic) and the urgency of surgery (elective or emergency). After adjusting for these, using the Mantel-Haenszel combined odds ratio, patients were more likely to be ASA 1 or 2. The adjusted odds ratio (OR) of 2.1 ($p<0.05$).

4.4 Relationship between ASA physical status grading and CD4-count

The distribution of data according to ASA grade and CD4-count in the HIV-positive group is shown in **Table 4.2**. No patient met the criteria for classification as ASA 5. There were 92 HIV-positive patients who were classified as ASA 1 or 2. Of these, 26.1% had a CD4-count of 500 cells.mm^{-3} or greater, 16.3% had a CD4-count of 350-499 cells.mm^{-3}, 34.8% had a CD4-count of 200-349 cells.mm^{-3}, 19.6% had a CD4-count of 50-199 cells.mm^{-3}, and 3.3% had a CD4-count below 50 cells.mm^{-3}. There were 11 HIV-positive patients who were classified as ASA 3

or 4. Of these, 2 patients had a CD4-count of 500 cells.mm^{-3} or greater, 3 patients had a CD4-count of 200-349 cells.mm^{-3}, 3 patients had a CD4-count of 50-199 cells.mm^{-3}, and 3 patients had a CD4-count below 50 cells.mm^{-3}.

Table 4.2 Association between ASA physical status grading and CD4-count in HIV-positive patients

		ASA 1 or 2 (%) (n=92) (%)	**ASA 3 or 4 (n=11)**
CD4-count (cells.mm^{-3})	**<50**	3 (3.3)	3
	50-199	18 (19.6)	3
	200-349	32 (34.8)	3
	350-499	15 (16.3)	0
	500+	24 (26.1)	2

Patients were more likely to be ASA 1 or 2 if their CD4-count was above 200 cells.mm^{-3} (crude OR 3.88, $p<0.05$). However, within the group of patients with CD4-counts below 200 cells.mm^{-3} (n=27), 21 patients (77.78%) were also classified as ASA 1 or 2, which represented a significant majority ($p<0.0001$). Moreover, there were 3 patients with a CD4-count of below 50 cells.mm^{-3} that were also classified as ASA 1 or 2.

4.5 Prevalence in different patient subgroups

The prevalence of HIV in the different subgroups is summarised in **Table 4.3**.

Table 4.3 Differences in HIV prevalence in different demographic subgroups

		HIV-POSITIVE/TOTAL (%)
GENDER	**Male**	29/142 (20.4)
	Female	74/208 (35.6)
AGE (YEARS)	**18-29**	49/152 (32.2)
	30-39	34/79 (43.0)
	40-49	14/56 (25.0)
	50-59	4/37 (11.1)
	60+	2/26 (7.7)
TYPE OF SURGERY	**Obstetric**	51/137 (37.2)
	Non-obstetric	52/213 (24.4)
NATURE OF SURGERY	**Clean**	87/300 (29.0)
	Septic	16/50 (32.0)
URGENCY OF SURGERY	**Emergency**	71/221 (32.1)
	Elective	32/129 (24.8)
TIME OF DAY	**Office hours**	65/215 (30.2)
	After hours	38/135 (28.1)

The male subgroup had an HIV prevalence of 20.4%, while the female subgroup had an HIV prevalence of 35.6%. Therefore, female patients had a higher prevalence of HIV than males ($p<0.005$).

In the different age groups, 32.2% of patients aged 18-29 years were HIV-positive, 43.0% of patients aged 30-39 years were HIV-positive, 25.0% of patients aged 40-49 years were HIV-positive, 11.1% of patients aged 50-59 years were HIV-positive, and 7.7% of patients aged 60 years and older were HIV-positive.

Patients presenting for obstetric surgery had an HIV prevalence of 37.2%, while those presenting for non-obstetric surgery had an HIV prevalence of 24.4%. Therefore, patients undergoing obstetric procedures had a higher prevalence than those undergoing non-obstetric procedures ($p<0.05$).

Patients presenting for clean procedures had an HIV prevalence of 29.0%, while those presenting for septic procedures had an HIV prevalence of 32.0%. This difference did not achieve statistical significance.

Patients presenting for emergency surgery had an HIV prevalence of 32.1%, while those presenting for elective surgery had an HIV prevalence of 24.8%. This difference did not achieve statistical significance.

The subgroup with the highest prevalence was patients aged 30-39 years (43.0%), and the lowest HIV prevalence was found in patients aged 60 years and older (7.7%).

4.6 Patient knowledge of HIV status and patients on HAART

Only 103 patients (29.4%) were aware of their HIV status. Of these, 38 (36.9%) were HIV-positive, which represented 10.9% of the total sample. Only 4 patients in this group (10.5%) had been started on HAART – this represented 3.8% of the total HIV-positive group. This was despite the fact that although 11 patients (28.9% of the group that knew they were HIV-positive) met the criteria for initiation of HAART (on the basis of having a CD4-count below 200 cells.mm^{-3}).

CHAPTER FIVE - DISCUSSION

5.1 The problem of patient refusal

Some difficulties were encountered while collecting the data for this study. Patient refusal was known to be a possibility, and as shown, 5.1% of patients approached refused to participate. This is not a high proportion of the total, and considering that the patients who refused were from different groups and refused for different reasons, it is unlikely to have had much impact on the validity of the results. Patient refusal was for both reasons that may have indicated that they were at high risk for testing HIV-positive, and for reasons that suggested that they were low risk for testing HIV-positive. The worst scenario would have been if all those that refused had been HIV-positive – this would have increased the total prevalence from 29.4% to 33.1%. If all 19 had tested HIV-negative, the overall prevalence would have dropped from 29.4% to 22.8%.

5.2 Potential biases in this study

5.2.1 Study period

The data collection was done over a six-week period in December and January. Some elective lists are closed for one or two weeks during this period. The patients presenting during this time could have been scheduled for more emergent procedures than at other times of the year. Some of the elective

theatres may have been used for procedures normally booked in emergency theatres.

5.2.2 Patient categorisation

Patients were categorised on the basis of the type of operating theatre in which they were booked, whether clean or contaminated, elective or emergent. In most instances, this can be assumed to be a reasonable way of deducing the nature and urgency of the planned procedure. However there may have been times when this did not hold true.

The theatres used for clean surgery are all scrubbed down at the end of the day, and as a result some surgeons occasionally take the opportunity of adding contaminated cases onto the end of a clean list. Similarly, it may happen that an emergency case is done on an elective list if the delay for the emergency theatre is too long, or if the elective list has been completed earlier than expected.

Patients are booked on emergency lists at the hospital for all manners of procedures, and with varying level of urgency. The categorisation of patients as ‘emergency’ in this study thus simply denotes that the patients were most likely to have been seen by the anaesthetist for the first time outside theatre, with no opportunity to investigate the patient further or suggest alternative management strategies. This may not always have been true – patients presenting for elective caesarean sections are booked on the same list as those for emergency caesarean sections, and patients presenting for elective termination of

pregnancies are booked on the same list as those presenting for uterine evacuation for unexpected and incomplete miscarriages. These elective patients on emergency lists are still not seen before they arrive in theatre. It is very seldom that any further work-up is requested before operating. They are, however, kept starved, unlike many other emergency cases.

5.2.3 Quality of data collection

This was a single observer study. There was assistance for some of the data collection, however only the researcher was involved in the decision-making process. The ASA physical status grading is quite a subjective classification – this bias was thus minimised by the fact that only one person (the researcher) decided which grade a patient was assigned. This fact on its own, however, is another source for bias – the researcher may have been stricter or more lenient in grading patients than other anaesthetists. A list of inclusion criteria for each grading (tabulated previously – see **Table 3.1**) was referred to in order to minimise this.

5.2.4 Contextuality

The study was conducted at CHBH, a large tertiary state hospital servicing a population of predominantly low-income black patients from Soweto and surrounding areas, in Johannesburg. It may not be possible to generalise the results of this study to other population groups.

5.3 Clinical evaluation in HIV

Distributing the sample across different ASA grades yielded interesting results. Younger patients were more likely to be classified as ASA 1 or 2 than older patients, regardless of HIV status. This showed that age is a much more significant variable in predicting 'wellness' than any other variable studied. Within the HIV-positive group, the nature of surgery (clean or contaminated) was discovered to be a confounder, which is expected. Patients presenting with localised or systemic sepsis are certainly more likely to be more ill than those presenting to the clean theatres. The urgency of surgery was also found to be a confounder. Reasons for this are less clear, as many emergency cases are still graded as ASA 1 or 2. Possible reasons could be the high burden of septic emergencies that present to the hospital, or the ages of patients presenting to the emergency theatres. The latter reason is less likely, in view of the high caseload of trauma and obstetric emergencies seen at the hospital – these usually involve younger patients. After adjusting for these confounders, HIV-positive patients were still more likely to be classified as ASA 1 or 2 (adjusted odds ratio OR 2.1). In other words, more HIV-positive patients presenting for theatre will appear well than those appearing unwell.

As has already been discussed, HIV infection remains asymptomatic for a varying length of time, with many infected individuals only manifesting clinical features once they have reached a significant level of immune compromise. This was supported by the findings in the study population. Patients grouped as ASA 1 or 2 were frequently found to have low CD4-counts. More than half (57.6%) had CD4-

counts below 350 cells.mm^{-3}, and 22.8% met the National Criteria for initiation of HAART (CD4-count below 200 cells.mm^{-3}). As expected, patients with higher CD4-counts were more likely to be classified as ASA 1 or 2 than those with lower CD4-counts (crude OR 3.88). However, what was interesting was that even within the group of patients with CD4-counts below 200 cells.mm^{-3}, 77.78% of patients were still classified as ASA 1 or 2. This is a significant majority. There were even patients with CD4-counts below 50 cells.mm^{-3} who met the same criteria – all appearing well with a normal functional capacity, despite clear laboratory evidence of significant immune compromise. These patients are unlikely to have been tested for HIV on clinical grounds alone, and as such their underlying deficiency would have certainly been missed.

These results were found despite the potential for bias, because of a single observer classifying patients into ASA physical status grades, where the observer specifically looked out for AIDS-related signs. In the non-research environment, patients presenting for emergency procedures may not be examined as thoroughly as those presenting electively, and the more subtle signs of immune compromise may be missed. In this study, patients with clinical features of significant immune compromise were usually graded as ASA 3 or 4 (based on their functional capacity).

5.4 Prevalence and high-risk groups

The total prevalence found in the sample population is higher than that of the general population. It is more in line with the figures generated by the seroprevalence studies of women attending antenatal clinics. This helps to show the heterogeneity of the population that present for anaesthesia.

Clearly, women are more at risk than men of testing HIV-positive. This is shown by the prevalence differences between female and male patients (35.6% compared to 20.4%). It is further illustrated by the differences between patients presenting for different types of surgery: 35.9% in patients presenting for obstetric and gynaecological procedures, compared to 25.0% in patients presenting for other types of surgery. This is in keeping with national statistics, where female gender has consistently been shown to be a factor for increased risk of infection.

Differences in prevalence between the different age groups are also in keeping with what has been found in previous studies. The highest prevalence has always been found to be in those of reproductive age, or from 25-35 years of age. In this study, the highest prevalence of all was in patients aged 30-39 years (43.0%). The older groups had the lowest prevalence, with those patients aged 60 years and older being at the lowest risk (7.7%).

Patients presenting for contaminated procedures were at no significantly higher risk for testing HIV-positive than those presenting for clean procedures (32.0% compared with 29.0%). This could emphasise just how many patients who were

HIV-positive were indeed asymptomatic. HIV-positive patients are at higher risk for septic complications if they are more severely immune compromised, so if more HIV-positive patients in the sample had been clinically unwell on the basis of their HIV infection, this difference might have been greater.

Patients presenting for emergency procedures had slightly increased likelihood of testing HIV-positive than those presenting for elective procedures (32.1% compared with 24.8%), although this also did not achieve significance. If this result was borne out in a larger sample, it may show that healthier patients are selected for elective surgery, and that the larger proportion of the HIV infection burden is carried by those who do not present in time for preoperative workup. In the future, it may become definitively clear that HIV-positive patients would benefit from initiation on HAART before having some types of surgery. This result shows that there would still need to be practices in place in which to manage an HIV-positive patient who has not yet been started on HAART.

Investigating the time of day of patient presentation also yielded no significant differences. Of patients presenting for anaesthesia during office hours, 30.2% tested HIV-positive, compared with 28.1% of those who presented after hours. This means that if it is shown to be of benefit to test patients prior to having anaesthesia, then there will be a need for an after-hours laboratory service. At CHBH, a 24-hour emergency laboratory is equipped with facilities for Rapid HIV Antibody testing. In addition, most hospitals are staffed by the minimum number of healthcare providers after hours. Testing at this time would then only be feasible if it were simple to do, requiring the minimum number of people.

Adequate counselling facilities are usually not available. The protocols drawn up for HIV-testing would need to be revised in order to address this problem, perhaps allowing for testing to be done anonymously before surgical intention, and allowing the patient to receive the required counselling and result on the following day.

The groups shown to be at a higher risk for HIV infection are identified based on comparison with the groups with lower prevalence. However, it is clear that all groups are at a higher risk for HIV infection when compared with the rest of the world. The lowest prevalence shown (7.7%) is already significantly higher than the prevalence in other research populations. If it is shown that testing patients preoperatively would result in a change of anaesthetic practice which would benefit the patient, this would imply that all patients at CHBH would benefit from this, not only those in the higher risk groups.

5.5 Knowledge of HIV status

If a significant proportion of patients had been found to already know their HIV status (whether HIV-positive or HIV-negative), preoperative HIV testing would be less of a pressing issue. The anaesthetist could select a management plan based purely on the history taken from the patient. However, only 29.4% of the patients studied knew their status. In the group that knew, 36.9% were HIV-positive, and 28.9% of these met the criteria for initiation of HAART. However, only 4 of the HIV-positive patients in the study (3.8%) had been started on the therapy by the time they presented for anaesthesia.

All women attending antenatal clinic are offered HIV testing. This was initiated so that HIV-positive mothers could be given nevirapine, an antiretroviral drug used to help prevent mother-to-child transmission of HIV. The drug is given to the mother approximately four hours before delivery of the infant, and then a second dose is given to the infant the following day. Subsequently, the majority of patients presenting for anaesthesia for obstetric procedures knew their status. Very few of them had had a CD4-count taken though, and some of them were found to have marked immune suppression. The emphasis in the management of these women appears to be more towards stopping the transmission of HIV to the infant, and less towards the maintenance of good health in the mother. Pregnant women are tested quite late in their pregnancy, and most of the patients presenting for obstetric procedures in early pregnancy did not know their HIV status.

Some patients that knew their status had only recently been tested, during their current admission. This was done for several reasons. Patients sometimes request testing, or are tested at the suggestion of the healthcare provider. HIV-positive patients from this group occasionally knew their CD4-counts as well, which had been taken after their status had been confirmed. Patients are seldom started on HAART while they are admitted for acute illnesses, especially those not related to HIV infection. The knowledge of their status could have been used to formulate the safest management plan (both anaesthetic and surgical) for them.

5.6 Concerns regarding preoperative HIV testing

One of the primary concerns for embarking on preoperative testing of any sort is the potential for harm. As with any decision, the benefits of testing need to be weighed against the associated risks.

The actual testing process is not considered to be harmful, as it involves simple blood sampling. This is much more of a concern in children, where painful procedures are kept to a minimum. The delay of waiting for test results is also unlikely to be much of a concern, as the Rapid Antigen test can be completed in 15 minutes. If this short delay is too long, then the planned procedure is likely to be of such an emergent nature as to preclude many options available for anaesthesia in any event. In this case, the benefit of the HIV result would be less evident.

The implications associated with the HIV test results are more of a cause for concern. The stigma associated with HIV infection, as well as a general lack of education regarding the options available for the management of the infection, have already resulted in too few people volunteering to find out their status. This problem has improved slightly with the roll-out of HAART in South Africa, however it remains a hurdle.

The spread of HIV in South Africa is largely by sexual transmission, and this social element to the disease often gives rise to feelings of guilt, as well as assigning blame to a sexual partner. Patients may react to a positive test result in

varying ways, for example with denial, anger, fear or depression. For this reason, results should only be given once the patient has been adequately counselled. This is possible in the elective situation, but becomes problematic prior to more urgent procedures. If adequate counselling is not provided before operating, then the patient should only receive their test results once the procedure is completed. Patients are often anxious before surgery. Postoperative disclosure would also prevent additional preoperative anxiety resulting from the possibility of a positive test result.

The stigma associated with HIV may not be confined to patients only. Healthcare providers may also show stigma, which may not be based on scientific evidence. The roll-out of HAART has affected the medical disciplines more than the surgical ones, and surgeons and anaesthetists may not be well versed in the management of patients taking unfamiliar drugs. Knowing that a patient is HIV-positive may trigger the unnecessary cancelling of procedures, or the presumed need for additional investigations or specialist referrals. Adopting more regular preoperative HIV testing should therefore be undertaken with this in mind, and theatre staff education should become a priority.

5.7 Potential benefits of preoperative HIV testing

Knowing the HIV status of a patient before operating can have many benefits. The primary benefit is that the management of the patient could be altered in a way that would result in the best outcome. Surgery and anaesthesia both result in immune suppression, which is exacerbated by pre-existing immune compromise.

An HIV-positive patient with significant preoperative immune compromise could be considered for initiation of HAART, with the option to delay elective surgery until there is some degree of return of immune function.

There are often instances where the risks of starting HAART or delaying surgery are greater than the benefit that this return of immunity would confer. In these cases, the type of surgery planned could be changed – for example, to a minimally invasive technique, and the mode of anaesthesia could be tailored. An anaesthetist may choose to anaesthetise the patient using total intravenous anaesthesia (TIVA) by means of a propofol infusion, which may confer less of an insult to the immunity of the patient, or they may choose to insert an epidural catheter for intra- and postoperative analgesia. The patient may be considered for postoperative recovery in a high-care setting where this would not have been considered otherwise.

There are other benefits to preoperative HIV testing, which may be secondary to the primary concern of the patient in question, but nevertheless warrant attention.

The South African public sector is a resource-limited environment. Research, which often requires considerable funding, is given much less of a priority than service delivery. Subsequently, healthcare providers are often forced to rely on evidence obtained in very different settings, which cannot always be appropriately extrapolated to the South African hospital setting. There is very little data available regarding HIV and anaesthesia in general, and even less pertaining specifically to South African healthcare. Determining the HIV status of patients

presenting for anaesthesia would provide an invaluable resource in terms of further study into safer anaesthesia. This benefit could be carried over into the realm of critical care as well as pain management. Epidemiological studies could also be facilitated.

There is also a potential benefit from a Public Health perspective. In a setting where the disease prevalence in the general population is high, any access to healthcare should be seen as an opportunity to screen for HIV. Earlier education and intervention regarding regular follow-up, 6-monthly CD4-counts, counselling, diet and lifestyle changes is preferable at all stages of HIV infection. The timely introduction of HAART is far superior to starting therapy later, as has been discussed.

Lastly, the operating theatre is a high-risk area for disease transmission to all healthcare workers. While it is prudent to comply with universal precautions regardless of the disease profile of the patient, compliance has been shown to increase if the patient is known to be HIV-positive. This knowledge may also encourage the development of more ergonomic methods to ensure compliance with universal precautions. This is often not seen as needing high priority in a resource-limited setting.

5.8 Preoperative testing and other diseases with high prevalence

Guidelines drawn up by professional and expert bodies play a large role in ensuring safe anaesthetic practice. However, it is important to use these

guidelines in the most appropriate way for the population in question. Healthy individuals presenting for surgery may not need any form of preoperative testing, but in a setting where there is a high prevalence of a disease which may not be clinically manifest, this disease should be screened for, if it has the potential to change perioperative management.

5.9 Further research

There are many unanswered questions regarding HIV and safe anaesthetic practice.

The trials investigating different anaesthetic techniques and their effects on the immune system should be repeated in HIV-positive patients. HIV-positive patients with varying levels of immune compromise should be studied in terms of the effect of anaesthesia and surgery on their individual immune systems.

Long-term effects of anaesthesia and surgery on the natural history and prognosis of HIV infection should be determined, and the results in patients not taking HAART should be compared with those taking HAART.

Cost-effectiveness studies should be conducted in the setting in which widespread HIV testing will be taking place.

The effects of anaesthesia on HIV-positive patients taking HAART should be evaluated, in order to determine whether there is any change in their response to

the therapy. Research into the safety of anaesthetising a patient taking HAART should also be conducted. This information should be used in conjunction with surgical findings in order to determine the benefits and risks of delaying surgery in HIV-positive patients in order to initiate HAART.

The attitudes of patients and healthcare providers to the results of an HIV test should be investigated. This could help determine the effect that stigma and lack of education would have on patient care should HIV testing be made a more frequent preoperative investigation.

CHAPTER SIX – SUMMARY AND CONCLUSIONS

6.1 Summary

The majority of HIV-positive patients in the sample were classified as ASA 1 or 2, in other words, essentially asymptomatic with no clinical signs. A significant proportion of these had markedly low CD4-counts, signifying considerable immune compromise. This shows that HIV infection and the ensuing immune compromise cannot be reliably diagnosed on clinical grounds alone.

Patients presenting for anaesthesia at Chris Hani Baragwanath Hospital have a high prevalence of HIV infection. Groups at higher risk for infection are females, patients presenting for obstetric procedures, and patients in younger age groups. However, all patients are a significantly higher risk for infection than those from population groups in other parts of the world.

Most patients did not know their HIV status. Very few of the HIV-positive patients, including those that knew their status, had been started on HAART.

6.2 Conclusions

The results of this study bring into question the manner in which HIV-positive patients presenting for anaesthesia are managed. Preoperative HIV testing at CHBH should be encouraged, because it has been shown that HIV infection is often not detected clinically. Patients that test HIV-positive should be further

investigated as to their level of immunity, as this is also not always clinically apparent. The high prevalence of HIV at CHBH emphasises that this should be made a priority.

Sufficient evidence exists to suggest that there are numerous ways in which we could minimise the immune insult created by surgery and anaesthesia. These practices could be applied to HIV-positive patients, especially those with a significant degree of immune compromise. Knowing the HIV status of patients will provide a means for anaesthetists and surgeons to formulate and adopt more appropriate management plans which would directly benefit the patient.

HIV-positive patients could be referred to the appropriate facility for management of their condition, and the initiation of HAART if necessary. Presentation for anaesthesia and surgery should be seen as a vital opportunity for accessing healthcare, and holistic patient management would be facilitated.

Further research into improved management plans for HIV-positive patients presenting for anaesthesia could be conducted. More widespread testing for HIV infection would facilitate sampling for such studies.

The safety of operating theatre staff should also be prioritised, in view of the high prevalence of HIV infection in the patients arriving in theatre. Accessible, feasible protocols could be developed for the ease of implementation of universal precautions in theatre, in order to minimise accidental exposure to HIV infection.

LIST OF REFERENCES

1. World Health Organisation AIDS Epidemic Update December 2005. *www.who.int/hiv/epi-update2005_en.pdf (accessed November 2006)*.
2. Practice advisory for preanesthesia evaluation: a report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. *Anesthesiology* 2002;96(2):485-96.
3. Wilson D, Naidoo S, Bekker L, Cotton M, Maartens G. Handbook of HIV Medicine: Oxford University Press Southern Africa, 2002:1-60.
4. World Medical Association Declaration of Helsinki - Ethical principles for medical research involving human subjects. October 2000.
5. Horowitz HW, Telzak EE, Sepkowitz KA, Wormser GP. Human immunodeficiency virus infection, Part I. *Dis Mon* 1998;44(10):545-606.
6. Mugerwa RD, Marum LH, Serwadda D. Human immunodeficiency virus and AIDS in Uganda. *East Afr Med J* 1996;73(1):20-6.
7. Frazer IH, Sarngadharan MG, Mackay IR, Gallo RC. Antibody to human T cell leukaemia virus type III in Australian homosexual men with lymphadenopathy. *Med J Aust* 1984;141(5):274-6.
8. Adler MW. ABC of Aids: Development of the epidemic. *Bmj* 2001;322(7296):1226-9.
9. Grant AD, De Cock KM. ABC of AIDS. HIV infection and AIDS in the developing world. *British Medical Journal* 2001;322(7300):1475-8.
10. Galel SA, Lifson JD, Engleman EG. Prevention of AIDS transmission through screening of the blood supply. *Annu Rev Immunol* 1995;13:201-27.
11. Van de Perre P. The epidemiology of HIV infection and AIDS in Africa. *Trends in Microbiology* 1995;3(6):217-222.
12. Madhavan S, Schatz EJ. Coping with change: household structure and composition in rural South Africa, 1992 - 2003. *Scand J Public Health Suppl* 2007;69:85-93.
13. Wittenberg M, Collinson MA. Household transitions in rural South Africa, 1996-2003. *Scand J Public Health Suppl* 2007;69:130-7.
14. Ramjee G, Gouws E. Prevalence of HIV among truck drivers visiting sex workers in KwaZulu-Natal, South Africa. *Sex Transm Dis* 2002;29(1):44-9.
15. Dias R, Posel D. Unemployment, Education and Skills Constraints in Post-Apartheid South Africa. *Trade and Industrial Policy Strategies* 2006.
16. Lalloo R, Myburgh NG, Smith MJ, Solanki GC. Access to health care in South Africa--the influence of race and class. *S Afr Med J* 2004;94(8):639-42.
17. Ojikutu B, Jack C, Ramjee G. Provision of antiretroviral therapy in South Africa: unique challenges and remaining obstacles. *J Infect Dis* 2007;196 Suppl 3:S523-7.
18. Dunkle KL, Jewkes RK, Brown HC, Gray GE, McIntryre JA, Harlow SD. Gender-based violence, relationship power, and risk of HIV infection in women attending antenatal clinics in South Africa. *Lancet* 2004;363(9419):1415-21.
19. UNAIDS. 2006 Report on the global AIDS epidemic: Executive summary. 2006.
20. National HIV and Syphilis Sero-Prevalence Surveys of Women Attending Public Antenatal Clinics in South Africa. *www.doh.gov.za/docs (accessed March 2006)*.
21. Nelson Mandela/HSRC Study of HIV/AIDS South African National HIV Prevalence, Behavioural Risks and Mass Media Household Survey 2002.
22. Nelson Mandela/HSRC Study of HIV/AIDS South African National HIV Prevalence, Behavioural Risks and Mass Media Household Survey 2005.
23. van Wyk C. AIDS: some medico-legal aspects. *Medicine and Law* 1991;10(2):139-53.
24. Deeks SG. Antiretroviral treatment of HIV infected adults. *Bmj* 2006;332(7556):1489.

25. National Department of Health SA. National Antiretroviral Treatment Guideline. 2004.
26. Sterling TR, Chaisson RE, Keruly J, Moore RD. Improved outcomes with earlier initiation of highly active antiretroviral therapy among human immunodeficiency virus-infected patients who achieve durable virologic suppression: longer follow-up of an observational cohort study. *J Infect Dis* 2003;188(11):1659-65.
27. Kress KD. HIV update: emerging clinical evidence and a review of recommendations for the use of highly active antiretroviral therapy. *Am J Health Syst Pharm* 2004;61 Suppl 3:S3-14; quiz S15-6.
28. Ahdieh-Grant L, Yamashita TE, Phair JP, Detels R, Wolinsky SM, Margolick JB, et al. When to initiate highly active antiretroviral therapy: a cohort approach. *Am J Epidemiol* 2003;157(8):738-46.
29. Palella FJ, Jr., Deloria-Knoll M, Chmiel JS, Moorman AC, Wood KC, Greenberg AE, et al. Survival benefit of initiating antiretroviral therapy in HIV-infected persons in different CD4+ cell strata. *Ann Intern Med* 2003;138(8):620-6.
30. Barbaro G. Metabolic and cardiovascular complications of highly active antiretroviral therapy for HIV infection. *Curr HIV Res* 2006;4(1):79-85.
31. Abrescia N, D'Abbraccio M, Figoni M, Busto A, Maddaloni A, De Marco M. Hepatotoxicity of antiretroviral drugs. *Curr Pharm Des* 2005;11(28):3697-710.
32. Garcia F, de Lazzari E, Plana M, Castro P, Mestre G, Nomdedeu M, et al. Long-term CD4+ T-cell response to highly active antiretroviral therapy according to baseline CD4+ T-cell count. *J Acquir Immune Defic Syndr* 2004;36(2):702-13.
33. Jevtovic DJ, Salemovic D, Ranin J, Pesic I, Zerjav S, Djurkovic-Djakovic O. The prevalence and risk of immune restoration disease in HIV-infected patients treated with highly active antiretroviral therapy. *HIV Med* 2005;6(2):140-3.
34. Stoll M, Schmidt RE. Immune restoration inflammatory syndromes: apparently paradoxical clinical events after the initiation of HAART. *Curr HIV/AIDS Rep* 2004;1(3):122-7.
35. Montaner JS, Hogg RS. Hungering for HAART. *Ann Intern Med* 2007;146(8):609-10.
36. Asser M. Analysis: Mbeki and the AIDS sceptics. *BBC News* 2000.
37. Treating AIDS patients at the heart of the problem. *http://www.doctorswithoutborders.org/publications/ar/12004/southafrica (accessed November 2007)*.
38. Baleta A. "Dr Beetroot" sidelined in South Africa. *Lancet Infect Dis* 2006;6(10):620.
39. Ndlovu N, Daswa R. Monitoring AIDS treatment rollout in South Africa: lessons from the Joint Civil Society Monitoring Forum (JCSMF). *www.idasa.org.za (accessed November 2007)*.
40. HIV/AIDS in South Africa. *www.aids.org.za/hiv.htm (accessed November 2007)*.
41. Gruskin S. Bangkok 2004. Current issues and concerns in HIV testing: a health and human rights approach. *HIV AIDS Policy Law Rev* 2004;9(3):99-103.
42. Skinner D, Mfecane S. Stigma, discrimination and the implications for people living with HIV/AIDS in South Africa. *Sahara J* 2004;1(3):157-64.
43. Murphy EM, Greene ME, Mihailovic A, Olupot-Olupot P. Was the "ABC" approach (abstinence, being faithful, using condoms) responsible for Uganda's decline in HIV? *PLoS Med* 2006;3(9):e379.
44. Morgan GE, Mikhail MS, Murray MJ. Clinical Anesthesiology, Third Edition. 2002:8-9.
45. Miller RDE, Cucchiara RF, Miller ED. Anesthesia, Fourth Edition. 1994:809-10.

46. Mak PH, Campbell RC, Irwin MG. The ASA Physical Status Classification: inter-observer consistency. American Society of Anesthesiologists. *Anaesth Intensive Care* 2002;30(5):633-40.
47. Sidi A, Lobato EB, Cohen JA. The American Society of Anesthesiologists' Physical Status: category V revisited. *J Clin Anesth* 2000;12(4):328-34.
48. Voney G, Biro P, Roos M, Frielingsdorf B, Shafighi M, Wyss P. Interrelation of peri-operative morbidity and ASA class assignment in patients undergoing gynaecological surgery. *Eur J Obstet Gynecol Reprod Biol* 2007;132(2):220-5.
49. Woodfield JC, Beshay NM, Pettigrew RA, Plank LD, van Rij AM. American Society of Anesthesiologists classification of physical status as a predictor of wound infection. *ANZ J Surg* 2007;77(9):738-41.
50. Froehner M, Koch R, Litz R, Heller A, Oehlschlaeger S, Wirth MP. Comparison of the American Society of Anesthesiologists Physical Status classification with the Charlson score as predictors of survival after radical prostatectomy. *Urology* 2003;62(4):698-701.
51. Castellano P, Lopez-Escamez JA. American Society of Anesthesiology classification may predict severe post-tonsillectomy haemorrhage in children. *J Otolaryngol* 2003;32(5):302-7.
52. Mantha S, Roizen MF, Madduri J, Rajender Y, Shanti Naidu K, Gayatri K. Usefulness of routine preoperative testing: a prospective single-observer study. *J Clin Anesth* 2005;17(1):51-7.
53. Finegan BA, Rashiq S, McAlister FA, O'Connor P. Selective ordering of preoperative investigations by anesthesiologists reduces the number and cost of tests. *Can J Anaesth* 2005;52(6):575-80.
54. Munro J, Booth A, Nicholl J. Routine preoperative testing: a systematic review of the evidence. *Health Technol Assess* 1997;1(12):i-iv; 1-62.
55. Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, et al. Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). *Reg Anesth Pain Med* 2003;28(3):172-97.
56. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *J Am Coll Cardiol* 2007;50(17):e159-241.
57. Mindel A, Tenant-Flowers M. ABC of AIDS: Natural history and management of early HIV infection. *Bmj* 2001;322(7297):1290-3.
58. HIV therapy information.
59. Proposed 'World Health Organization staging system for HIV infection and disease': preliminary testing by an international collaborative cross-sectional study. The WHO International Collaborating Group for the Study of the WHO Staging System. *Aids* 1993;7(5):711-8.
60. Schneemilch CE, Schilling T, Bank U. Effects of general anaesthesia on inflammation. *Best Pract Res Clin Anaesthesiol* 2004;18(3):493-507.

61. Brand JM, Kirchner H, Poppe C, Schmucker P. The effects of general anesthesia on human peripheral immune cell distribution and cytokine production. *Clin Immunol Immunopathol* 1997;83(2):190-4.
62. Procopio MA, Rassias AJ, DeLeo JA, Pahl J, Hildebrandt L, Yeager MP. The in vivo effects of general and epidural anesthesia on human immune function. *Anesth Analg* 2001;93(2):460-5, 4th contents page.
63. Delogu G, Moretti S, Antonucci A, Marcellini S, Masciangelo R, Famularo G, et al. Apoptosis and surgical trauma: dysregulated expression of death and survival factors on peripheral lymphocytes. *Arch Surg* 2000;135(10):1141-7.
64. Salo M. Effects of anaesthesia and surgery on the immune response. *Acta Anaesthesiol Scand* 1992;36(3):201-20.
65. Corsi M, Mariconti P, Calvillo L, Falchi M, Tiengo M, Ferrero ME. Influence of inhalational, neuroleptic and local anaesthesia on lymphocyte subset distribution. *Int J Tissue React* 1995;17(5-6):211-7.
66. Pirttikangas CO, Salo M, Mansikka M, Gronroos J, Pulkki K, Peltola O. The influence of anaesthetic technique upon the immune response to hysterectomy. A comparison of propofol infusion and isoflurane. *Anaesthesia* 1995;50(12):1056-61.
67. Schneemilch CE, Ittenson A, Ansorge S, Hachenberg T, Bank U. Effect of 2 anesthetic techniques on the postoperative proinflammatory and anti-inflammatory cytokine response and cellular immune function to minor surgery. *J Clin Anesth* 2005;17(7):517-27.
68. Salo M, Pirttikangas CO, Pulkki K. Effects of propofol emulsion and thiopentone on T helper cell type-1/type-2 balance in vitro. *Anaesthesia* 1997;52(4):341-4.
69. Schneemilch CE, Hachenberg T, Ansorge S, Ittenson A, Bank U. Effects of different anaesthetic agents on immune cell function in vitro. *Eur J Anaesthesiol* 2005;22(8):616-23.
70. Brand JM, Frohn C, Luhm J, Kirchner H, Schmucker P. Early alterations in the number of circulating lymphocyte subpopulations and enhanced proinflammatory immune response during opioid-based general anesthesia. *Shock* 2003;20(3):213-7.
71. Volk T, Schenk M, Voigt K, Tohtz S, Putzier M, Kox WJ. Postoperative epidural anesthesia preserves lymphocyte, but not monocyte, immune function after major spine surgery. *Anesth Analg* 2004;98(4):1086-92, table of contents.
72. Albaran RG, Webber J, Steffes CP. CD4 cell counts as a prognostic factor of major abdominal surgery in patients infected with the human immunodeficiency virus. *Arch Surg* 1998;133(6):626-31.
73. Ferrero S, Bentivoglio G. Post-operative complications after caesarean section in HIV-infected women. *Arch Gynecol Obstet* 2003;268(4):268-73.
74. Ragni MV, Crossett LS, Herndon JH. Postoperative infection following orthopaedic surgery in human immunodeficiency virus-infected hemophiliacs with CD4 counts < or = 200/mm3. *J Arthroplasty* 1995;10(6):716-21.
75. Bjorklund K, Mutyaba T, Nabunya E, Mirembe F. Incidence of postcesarean infections in relation to HIV status in a setting with limited resources. *Acta Obstet Gynecol Scand* 2005;84(10):967-71.
76. James J, Hofland HW, Borgstein ES, Kumiponjera D, Komolafe OO, Zijlstra EE. The prevalence of HIV infection among burn patients in a burns unit in Malawi and its influence on outcome. *Burns* 2003;29(1):55-60.
77. Jjuuko G, Moodley J. Abdominal wound sepsis associated with gynaecological surgery at King Edward VIII Hospital, Durban. *S Afr J Surg* 2002;40(1):11-4.

78. Khwaja S, Rosenbaum DH, Paul MC, Bhojani RA, Estrera AS, Wait MA, et al. Surgical treatment of thoracic empyema in HIV-infected patients: severity and treatment modality is associated with CD4 count status. *Chest* 2005;128(1):246-9.
79. Lin PH, Bush RL, Yao Q, Lam R, Paladugu R, Zhou W, et al. Abdominal aortic surgery in patients with human immunodeficiency virus infection. *Am J Surg* 2004;188(6):690-7.
80. Maiques-Montesinos V, Cervera-Sanchez J, Bellver-Pradas J, Abad-Carrascosa A, Serra-Serra V. Post-cesarean section morbidity in HIV-positive women. *Acta Obstet Gynecol Scand* 1999;78(9):789-92.
81. Tran HS, Moncure M, Tarnoff M, Goodman M, Puc MM, Kroon D, et al. Predictors of operative outcome in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. *Am J Surg* 2000;180(3):228-33.
82. Paiement GD, Hymes RA, LaDouceur MS, Gosselin RA, Green HD. Postoperative infections in asymptomatic HIV-seropositive orthopedic trauma patients. *J Trauma* 1994;37(4):545-50; discussion 550-1.
83. Consten EC, Slors FJ, Noten HJ, Oosting H, Danner SA, van Lanschot JJ. Anorectal surgery in human immunodeficiency virus-infected patients. Clinical outcome in relation to immune status. *Dis Colon Rectum* 1995;38(11):1169-75.
84. Savioz D, Chilcott M, Ludwig C, Savioz M, Kaiser L, Leissing C, et al. Preoperative counts of CD4 T-lymphocytes and early postoperative infective complications in HIV-positive patients. *Eur J Surg* 1998;164(7):483-7.
85. Thurer RJ, Jacobs JP, Holland FW, 2nd, Cintron JR. Surgical treatment of lung cancer in patients with human immunodeficiency virus. *Ann Thorac Surg* 1995;60(3):599-602.
86. Goddard NJ, Rodriguez-Merchan EC, Wiedel JD. Total knee replacement in haemophilia. *Haemophilia* 2002;8(3):382-6.
87. Harrison WJ, Lewis CP, Lavy CB. Wound healing after implant surgery in HIV-positive patients. *J Bone Joint Surg Br* 2002;84(6):802-6.
88. Luck JV, Jr. Orthopaedic surgery on the HIV-positive patient: complications and outcome. *Instr Course Lect* 1994;43:543-9.
89. Young WF, Axelrod P, Jallo J. Elective spinal surgery in asymptomatic HIV-seropositive persons: perioperative complications and outcomes. *Spine* 2005;30(2):256-9.
90. van Marle J, Tudhope L, Weir G, Botes K. Vascular disease in HIV/AIDS patients. *S Afr Med J* 2002;92(12):974-8.
91. Ragni MV, Belle SH, Im K, Neff G, Roland M, Stock P, et al. Survival of human immunodeficiency virus-infected liver transplant recipients. *J Infect Dis* 2003;188(10):1412-20.
92. Neff GW, Bonham A, Tzakis AG, Ragni M, Jayaweera D, Schiff ER, et al. Orthotopic liver transplantation in patients with human immunodeficiency virus and end-stage liver disease. *Liver Transpl* 2003;9(3):239-47.
93. Roland ME. Solid-organ transplantation in HIV-infected patients in the potent antiretroviral therapy era. *Top HIV Med* 2004;12(3):73-6.
94. Roland ME, Adey D, Carlson LL, Terrault NA. Kidney and liver transplantation in HIV-infected patients: case presentations and review. *AIDS Patient Care STDS* 2003;17(10):501-7.
95. Trachiotis GD, Alexander EP, Benator D, Gharagozloo F. Cardiac surgery in patients infected with the human immunodeficiency virus. *Ann Thorac Surg* 2003;76(4):1114-8; discussion 1118.

96. Morris A, Masur H, Huang L. Current issues in critical care of the human immunodeficiency virus-infected patient. *Crit Care Med* 2006;34(1):42-9.
97. Sylla P, Kirman I, Whelan RL. Immunological advantages of advanced laparoscopy. *Surg Clin North Am* 2005;85(1):1-18, vii.
98. Buunen M, Gholghesaei M, Veldkamp R, Meijer DW, Bonjer HJ, Bouvy ND. Stress response to laparoscopic surgery: a review. *Surg Endosc* 2004;18(7):1022-8.
99. Bolla G, Tuzzato G. Immunologic postoperative competence after laparoscopy versus laparotomy. *Surg Endosc* 2003;17(8):1247-50.
100. Wichmann MW, Huttl TP, Winter H, Spelsberg F, Angele MK, Heiss MM, et al. Immunological effects of laparoscopic vs open colorectal surgery: a prospective clinical study. *Arch Surg* 2005;140(7):692-7.
101. Endres JC, Salky BA. Laparoscopy in AIDS. *Gastrointest Endosc Clin N Am* 1998;8(4):975-90.
102. Pearson S, Hassen T, Spark JI, Cabot J, Cowled P, Fitridge R. Endovascular repair of abdominal aortic aneurysm reduces intraoperative cortisol and perioperative morbidity. *J Vasc Surg* 2005;41(6):919-25.
103. Sweeney KJ, Evoy D, Sultan S, Coates C, Moore DJ, Shanik DG, et al. Endovascular approach to abdominal aortic aneurysms limits the postoperative systemic immune response. *Eur J Vasc Endovasc Surg* 2002;23(4):303-8.
104. Arko FR, Hill BB, Olcott C, Harris EJ, Jr., Fogarty TJ, Zarins CK. Endovascular repair reduces early and late morbidity compared to open surgery for abdominal aortic aneurysm. *J Endovasc Ther* 2002;9(6):711-8.
105. Boyle JR, Goodall S, Thompson JP, Bell PR, Thompson MM. Endovascular AAA repair attenuates the inflammatory and renal responses associated with conventional surgery. *J Endovasc Ther* 2000;7(5):359-71.
106. Bittner HB, Fogelson BG. Off-pump coronary artery bypass grafting in a patient with AIDS, acute myocardial infarction, and severe left main coronary artery disease. *J Cardiovasc Surg (Torino)* 2003;44(1):55-7.
107. Al-Rashedy M, Dadibhai M, Shareif A, Khandelwal MI, Ballester P, Abid G, et al. Laparoscopic gastric bypass for gastric outlet obstruction is associated with smoother, faster recovery and shorter hospital stay compared with open surgery. *J Hepatobiliary Pancreat Surg* 2005;12(6):474-8.
108. Angele MK, Faist E. Clinical review: immunodepression in the surgical patient and increased susceptibility to infection. *Crit Care* 2002;6(4):298-305.
109. Weigand MA, Horner C, Bardenheuer HJ, Bouchon A. The systemic inflammatory response syndrome. *Best Pract Res Clin Anaesthesiol* 2004;18(3):455-75.
110. Mezzaroma I, Carlesimo M, Pinter E, Alario C, Sacco G, Muratori DS, et al. Long-term evaluation of T-cell subsets and T-cell function after HAART in advanced stage HIV-1 disease. *Aids* 1999;13(10):1187-93.
111. Avidan MS, Jones N, Pozniak AL. The implications of HIV for the anaesthetist and the intensivist. *Anaesthesia* 2000;55(4):344-54.
112. Evron S, Glezerman M, Harow E, Sadan O, Ezri T. Human immunodeficiency virus: anesthetic and obstetric considerations. *Anesth Analg* 2004;98(2):503-11.
113. Hughes SC. HIV and anesthesia. *Anesthesiol Clin North America* 2004;22(3):379-404, v.
114. Tait AR, Tuttle DB. Prevention of occupational transmission of human immunodeficiency virus and hepatitis B virus among anesthesiologists: a survey of anesthesiology practice. *Anesth Analg* 1994;79(4):623-8.

115. Picheansathian W. Compliance with universal precautions by emergency room nurses at Maharaj Nakorn Chiang Mai Hospital. *J Med Assoc Thai* 1995;78 Suppl 2:S118-22.
116. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. *Am J Infect Control* 2007;35(10 Suppl 2):S65-164.
117. Gershon RY, Manning-Williams D. Anesthesia and the HIV infected parturient: a retrospective study. *Int J Obstet Anesth* 1997;6(2):76-81.
118. Arai H, Petchclai B, Khupulsup K, Kurimura T, Takeda K. Evaluation of a rapid immunochromatographic test for detection of antibodies to human immunodeficiency virus. *J Clin Microbiol* 1999;37(2):367-70.
119. Kwon JA, Yoon SY, Lee CK, Lim CS, Lee KN, Sung HJ, et al. Performance evaluation of three automated human immunodeficiency virus antigen-antibody combination immunoassays. *J Virol Methods* 2006;133(1):20-6.
120. Glencross D, Scott LE, Jani IV, Barnett D, Janossy G. CD45-assisted PanLeucogating for accurate, cost-effective dual-platform CD4+ T-cell enumeration. *Cytometry* 2002;50(2):69-77.

APPENDICES

APPENDIX A Ethics approval certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Penfold et al

CLEARANCE CERTIFICATE **PROTOCOL NUMBER M040230**

PROJECT Prospective study to determine prevalence of HIV/AIDSin patients presenting for anaesthesia at CH Baragwanath over a 4 week period.

INVESTIGATORS	Dr P R Penfold et al
DEPARTMENT	Anaesthetic
DATE CONSIDERED	04.02.27
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 04.04.07 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof A C Lundgren

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX B Post-Graduate Committee approval

Faculty of Health Sciences
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
7 York Road PARKTOWN Johannesburg 2193 Telegrams WITSMED Telex 4-24655.SA
FAX 643-4318 TELEPHONE 717-2075/2076
E-MAIL healthpg@health.wits.ac.za

DR PR PENFOLD
33 NILE STREET
KENSINGTON
2094

APPLICATION NUMBER 9401973H
STATUS (DEG 27) (MMA00) PZZ

2004-11-11

Dear Dr Penfold

Approval of protocol entitled Prospective study to determine the prevalence of HIV/AIDS in patients presenting for anaesthesia at Chris Hani Baragwanath Hospital

I should like to advise you that the protocol and title that you have submitted for the degree of Master Of Medicine (In Anaesthesia) have been approved by the Postgraduate Committee at its recent meeting. Please remember that any amendment to this title has to be endorsed by your Head of Department and formally approved by the Postgraduate Committee.

Dr AC Lundgren has/have been appointed as your supervisor/s. Please maintain regular contact with your supervisor who must be kept advised of your progress.

Please note that approval by the Postgraduate Committee is always given subject to permission from the relevant Ethics Committee, and a copy of your clearance certificate should be lodged with the Faculty Office as soon as possible, if this has not already been done.

Yours sincerely

S Benn (Mrs)
Faculty Registrar
Faculty of Health Sciences

Telephone 717-2075/2076

Copies - Head of Department_____Supervisor/s

APPENDIX C Permission from Hospital Superintendent

Gauteng Department of Health

CHRIS HANI BARAGWANATH HOSPITAL

PERMISSION FOR RESEARCH

DATE: 9 February 2004

NAME OF RESEARCH WORKER: Dr P R PENFOLD

TITLE OF RESEARCH PROJECT: PROSPECTIVE STUDY TO DETERMINE THE PREVALENCE OF HIV/AIDS IN PATIENTS PRESENTING FOR ANAESTHESIA AT CHRIS HANI BARAGWANATH OVER A FOUR WEEK PERIOD

OBJECTIVES OF STUDY (Briefly or include a protocol): See attached proposal.

METHODOLOGY (Briefly or include a protocol): See attached proposal

CONFIDENTIALITY OF PATIENTS MAINTAINED: YES

COSTS TO THE HOSPITAL: NIL

APPROVAL OF HEAD OF DEPARTMENT: YES (PROF A.C. LUNDGREN)

APPROVAL OF CRHS OF WITS UNIVERSITY: PENDING

SUPERINTENDENT PERMISSION: Dr. A. Narilo Senior Clinical Executive

Signature: _____ Date: 2004/2/9

Subject to any restrictions: * No additional cost hospital (eg Non routine pre op lab test)
* Ethics Approval

APPENDIX D Patient information sheet

INFORMATION SHEET

Good morning/afternoon. My name is Dr Penfold. I am a registrar in the Department of Anaesthesia of this hospital.

You are going to have an operation that is going to require an anaesthetic. I am doing a study on all patients that receive anaesthetics in this hospital, and I would like to invite you to be a part of this study.

Firstly, have you ever heard of HIV or AIDS ?

HIV is an infection that is common in South Africa. It is spread in body fluids, so people can be infected during sexual intercourse, sometimes a pregnant mother can give it to her unborn child, and people can get it from some forms of contact with contaminated blood.

HIV is a virus, in other words a germ. It attacks the body's ability to fight other germs. Over time, a person infected with HIV becomes unable to fight infection caused by germs that would not normally make a person sick. At this stage, we say the person has AIDS.

At the moment, there is no cure for HIV or AIDS. However, there are some medicines available that can slow down the progress of the disease. The treatment cannot get rid of the HIV in the patient, but it can help to get them back to the stage where they are not as sick as they were before. These medicines are available for free at this hospital.

I am doing a study to find out how many patients receiving anaesthetics are HIV-positive, and how many have AIDS. I also want to see how unwell the patients with HIV and AIDS look, to see if we can see that they have the virus without testing for it. In order to find this out, I need to test every patient coming for an anaesthetic for HIV. I want to make it clear that I have no reason to suspect that you either HIV-positive or HIV-negative, I simply want to test everyone.

The results of this study will show how many patients coming for operations should be receiving the medicine that helps to fight HIV. This will help these patients know that they need to go to the clinic where the treatment is given. It will also help us to know we need to do more studies to see if we are treating these patients in the safest way for them. We may start to test more people for HIV, based on these results – especially if the patients that are found to be HIV-positive look so well that we don't suspect HIV in them.

If you agree to be part of my study, I will send a trained counsellor to come and talk to you about what it means to have an HIV test. If you still agree to be tested, I will come and take two tubes of blood from you – about two teaspoons full. This will require an injection, which can be painful.

The first tube will be tested for HIV using the quick test that we use. If the quick test shows that the blood is HIV-positive, the rest of that tube will be sent for another HIV test that will double-check the result. If the second test also shows that the blood is HIV-positive, then I will send the second tube for a test called a CD4-count. This test helps to show how far the HIV infection has progressed. If it is a very low number, then it means that the HIV has killed a lot of cells that help to fight infection, and it might mean that you will need to go on treatment.

If the quick test shows that the blood is HIV-negative, then we won't need to double check, and the second tube of blood will be thrown away.

All the results will be kept confidentially – only I will know the results. Not even your name will be kept with the results – I will keep your name and contact number on a separate paper, in case you want to get hold of me. The results will be kept under a secret code.

I will also look at your hospital file to get some more information about you. I will need to write down your age, sex, what type of operation you are going for, how urgent your operation is, whether your operation is clean or septic, and what time of day you are going to have your operation. I will also ask you some questions about your general state of health, and I will examine you to see how healthy you are.

You can choose whether you would like to receive your results or not. If you choose to receive your results, a counsellor will come again to give you the results as well as more information to help you with the results. You can also choose to receive your results at a later stage. Test results take about two days to be ready.

If you do not agree to be part of the study, this is absolutely fine. The care you receive in the hospital will not change at all, and I will fully accept your decision. If you agree to be part of the study but then you change your mind later, you can contact me and I will immediately remove all information about you out of the study.

If you agree to be part of the study, I will need you to sign a form stating that I have explained the study well, and that you understand how you will be involved. I will also need you to sign another form after you have received counselling, to say that you have been fully counselled.

Do you have any questions to ask me ?

If you have any questions at a later stage, or if you want to contact me for anything regarding the study, you can contact me at any time of the day at 082 771 8296.

Thank you for giving up your time to hear about the study.

APPENDIX E Informed consent form

I, _____, agree to participate in the study that Dr Penfold has explained to me.

I understand that I will have counselling, then I will have two tubes of blood taken from me. One tube will be tested for HIV, and if the blood is HIV-positive, then the other tube will be sent for a CD4-count.

I understand that I can choose whether or not to receive my test results. My results will be kept confidentially, and my name will not be kept with my results. I will receive counselling if I choose to receive my results.

I understand that Dr Penfold will take some information from my file – my age and sex, and information about the operation I am going to have: what type of operation it is, how urgent it is, whether it is clean or septic, and what time of day I am going to have the operation.

I understand that Dr Penfold is going to ask me questions about my general health, and that she is going to examine me.

I understand that I can choose to pull out of the study at any time, and I have Dr Penfold's contact number.

_____ _____

Signature Date

APPENDIX F Counselling form

I, _____, have received pre-test counselling as part of my agreement to participate in Dr Penfold's study.

☐ I would like to receive my test results, and I have made arrangements with my counsellor to meet for post-test counselling

☐ I would not like to receive my test results at this stage. If I change my mind in the future, I know that I can contact Dr Penfold at any time to arrange to receive my results with post-test counselling.

_____
Signature of patient

_____
Signature of counsellor

_____
Date