

PERITONSILLAR ABSCESSSES
IN HIV POSITIVE PATIENTS

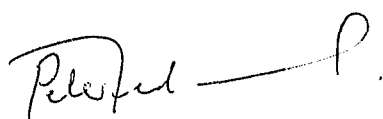
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A Research Report submitted to the
Faculty of Health Sciences of the University of the Witwatersrand, Johannesburg
in partial fulfilment of the requirements
for the degree of Master of Medicine in the Branch of
Otolaryngology

Johannesburg 1998

DECLARATION

I, Peter Leon Friedland, hereby declare that this research report is my own work and has not previously been presented for any degree of any university.



PETER LEON FRIEDLAND

31 January 1998

Johannesburg
South Africa

DEDICATION

To my wife Linda,
for her incredible support, understanding and patience
and in recognition of all that she means to me

and

To my children Gavriel, Leora, Yael and Aharon
for the wonderful gifts they are.

and

To my mother Selma
for her support and understanding

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Data from this research report formed the basis of a paper presented
at the XVI World Congress of Otorhinolaryngology, Head and Neck
Surgery, Sydney, Australia, 2 - 7 March 1997

Friedland P.L., Cleaton-Jones P, McIntosh W.A. Peritonsillar
abscesses in HIV positive South Africans

ABSTRACT

HIV positivity rates are high in South Africa. By August 1996 some 2,5 million individuals were estimated to be positive. (21) At least 70% of such HIV positive individuals present with head and neck manifestations, which include infection, inflammation and tumour, which are often the only and initial presenting sign.

There has been no documented study detailing association between HIV positivity and peritonsillar abscesses. The aim of this study was to investigate the immune status and HIV seropositivity in a series of patients with peritonsillar abscesses. The study sample consisted of all individuals with peritonsillar abscesses who presented to 5 academic hospitals in the Johannesburg/Soweto metropolitan complex over 7 months, and who gave informed consent to participate and have their HIV status measured.

In the study period 96 patients, aged 20 to 49 years presented with peritonsillar abscesses, 57 of whom fulfilled the inclusion criteria. The clinical signs were recorded, as well as HIV status, CD4 and CD8 lymphocyte counts. The data were analysed using SAS. Ten of the 57 (18%) were HIV positive. Mean (SD) CD4 counts were HIV positive 0,448 (0,124), HIV negative 0,899 (0,134); while CD8 results were HIV positive 0,865 (0,546), and HIV negative 0,546 (0,250).

General linear models analysis showed statistically significant effects of HIV status on the CD4 ($P < 0,0001$) and CD8 counts ($P < 0,01$). Clinically all patients had similar presentations. All showed no clinical signs of HIV disease and all were unaware of

their HIV status. The HIV positive rate in the study sample (18%) was higher than the HIV positive rate in the general heterosexual South African population (12%) for this region at the time of the study. This small sample of HIV patients suggests that peritonsillar abscess may be an early presenting sign of HIV infection.

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CHAPTER 1 - INTRODUCTION

1.0 General remarks

It has been estimated that 40 - 70% of patients with Human Immunodeficiency Virus (HIV) infection present with a symptom or physical finding in the head and neck region. (1-3) These manifestations include various types of infection, inflammation or tumour (2,4) Many of these symptoms or signs are the initial and often the only manifestations of HIV infections. (1,5) Doctors working in the Ear, Nose and Throat Department at the five teaching hospitals in the Johannesburg area have noticed in recent years that some patients presenting with peritonsillar abscess (PTA) have also been HIV positive but often are asymptomatic from the AIDS defining disease as documented by the World Health Organisation (WHO) (6) and the Centre for Disease Control (CDC) in Atlanta. (7) Since the association between HIV disease and PTA has not been defined the current study was undertaken.

In published articles, the terms AIDS and HIV are used interchangeably and inconsistently. In this report the term HIV infection has been used to encompass both HIV positivity and its full clinical spectrum.

1.1 Review of literature

1.1.1 History of HIV infection

HIV infection is one of the most devastating and important diseases of the 20th century. In December 1997 the Joint United Nations Program on HIV/AIDS and the World Health Organisation estimated that there are 30 million adults and children living with HIV infection (8).

Cases of AIDS were first reported in 1981 in previously healthy homosexuals who presented with *Pneumocystis carinii* pneumonia. (9) Soon thereafter, in another group, many cases were reported of similar illnesses, including Kaposi's sarcoma. (10) Around the same time AIDS was noted in haemophiliacs, intravenous drug users and infants born to intravenous drug users, and the first cases of AIDS associated with blood transfusions were reported. (11)

While AIDS was recognised as a distinct clinical entity it was only in 1984 that the causative agent, a T lymphotropic virus was discovered. (12-13) This was termed human immunodeficiency virus (HIV-1). A year later, in 1985, a reliable serological diagnostic test, the enzyme-linked immunoabsorbent assay (ELISA) was developed. This was a highly sensitive test and when combined with the highly specific Western blot test was greater than 99 % accurate. (14)

Since the initial infections several classification systems for HIV disease based on clinical features and laboratory values have been proposed including those of WHO and CDC. (7,15-16) The WHO clinical classification for HIV infection (6) is universally used in South Africa. (Table 1.1)

Table 1.1 : WHO clinical staging of HIV infection (6)

Clinical stage 1

1. Acute retroviral infection
2. Asymptomatic
3. Persistent generalised lymphadenopathy (enlargement of the lymph nodes).
Performance scale 1 : asymptomatic, normal activity.

Clinical stage 2

4. Weight loss, <10% of body weight.
5. Minor mucocutaneous manifestations (seborrhoeic dermatitis, prurigo (chronic itchy skin), fungal nail infections, recurrent oral ulcerations, angular cheilitis (inflammation of the corners of the mouth.))
6. Herpes zoster (shingles), within the last 5 years.
7. Recurrent upper respiratory tract infections (i.e. bacterial sinusitis).

And/or performance scale 2: symptomatic, normal activity.

Clinical stage 3

8. Weight loss, >10% of body weight.
9. Unexplained chronic diarrhoea, >1 month.
10. Unexplained prolonged fever (intermittent or constant), > 1 month.
11. Oral candidiasis (thrush).
12. Vulvovaginal candidiasis, chronic (>1 month) or poorly responsive to therapy.
13. Oral hairy leukoplakia (thickening of the dorsal surface of the tongue).
14. Pulmonary tuberculosis, within the past year.
15. Severe bacterial infections (e.g. pneumonia).

And/or performance scale 3: bed-ridden, <50% of the day during the last month.

Clinical stage 4

(AIDS - defining conditions)

16. HIV wasting syndrome, as defined.
17. Pneumocystis carinii pneumonia.
18. Toxoplasmosis of the brain.
19. Cryptococcosis, with diarrhoea, > 1 month.
20. Cryptococcosis, extrapulmonary.
21. Cytomegalovirus (disease of an organ other than liver, spleen or lymph nodes).
22. Herpes simplex virus infection, mucocutaneous > 1 month, or visceral any duration.
23. Progressive multifocal leuko-encephalopathy (selective destruction of the central nervous system).
24. Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis).
25. Candidiasis of the oesophagus, trachea, bronchi or lungs).
26. Atypical mycobacteriosis, disseminated.
27. Non-typhoid salmonella septicaemia.
28. Extrapulmonary tuberculosis
29. Lymphoma.
30. Kaposi's sarcoma.
31. HIV encephalopathy, as defined.

And/or performance scale 4: bedridden, >50% of the day during the last month

1.1.2 The HIV virus and transmission

HIV-1 is a retrovirus with the unique ability to convert its own diploid, single stranded RNA to double stranded DNA for incorporation into the host cell genome. This is made possible by the viral polymerase enzyme, reverse transcriptase. HIV-1 is one of four retroviruses that have been associated with human disease. These retroviruses are subdivided into 2 subfamilies, the lentiviruses and the oncornaviruses. HIV-1 and HIV-2 are lentiviruses. HIV-2 is a related but distinct viral species that causes a similar illness to HIV-1. It was first isolated in 1985 in West Africa and is the predominant HIV type in many areas in that region (18).

The principle target of HIV-1 is the CD4 lymphocyte (T helper cell) which expresses large numbers of CD4 receptors on its membrane. Other cells that bear CD4 receptors, such as macrophages and monocytes are also targets. The CD4 lymphocytes are pivotal to the overall function of the immune systems, including cell mediated and humoral immunity. HIV infection leads to a gradual decrease in T lymphocyte helper cells (CD4), which leads to a change in the ratio of T helper to T suppressor cells (CD8). By decreasing the number of T cells, the virus makes infected individuals susceptible to opportunistic infections including other viruses, fungi, bacterial and protozoa. (19)

The virus is transmitted by transfer of body fluids, principally by three main modes: sexual intercourse especially through receptive an intercourse, transfusion of infected blood products and perinatal transmission. (20) Although the initial patients diagnosed with HIV were homosexual men, intravenous drug users and haemophiliacs, the overwhelming majority of HIV infections have been in the heterosexual individuals as a result of sexual intercourse. (8-11,20)

1.1.3 Global HIV infection

By December 1997 it was believed that 30 million adults and children were living with HIV infection (8) which is 1 in every 100 sexually active adults world wide. By the year 2000 the number will soar to 40 million if current transmission rates hold steady. The United Nations Program on Aids (UNAIDS) and WHO estimate that 5.7 million people were infected in 1997 at a rate of 16 000 new infections every day. This includes 590 000 new infections among children. (8) Table 1.2 is a summary of the HIV/AIDS epidemic.

Table 1.2 : Global summary of the HIV/AIDS epidemic, December 1997 (8)

People new infected with HIV in 1997	Total	5.8 million
	Adults	5.9 million
	Women	2.1 million
	Children - 15 years	590 000
No. of people living with HIV/AIDS	Total	30.6 million
	Adults	29.5 million
	Women	12.1 million
	Children - 15 years	1.1 million
AIDS deaths in 1997	Total	2.3 million
	Adults	1.8 million
	Women	820 000
	Children - 15 years	460 000
Total no. of AIDS deaths since the beginning of the epidemic	Total	11.7 million
	Adults	9.0 million
	Women	4.0 million
	Children - 15 years	2.7 million
Total no. of AIDS orphans (1) since the beginning of the epidemic		8.2 million

Defined as HIV-negative children who lost either their mother or both parents to AIDS when they were under the age of 15

Because over 90 % of people with HIV live in the developing world, where there are few facilities for voluntary testing and counselling, UNAIDS estimates conservatively that 9 out of 10 HIV positive people have no idea that they are infected. Regional estimates and modes of transmission are summarised in Table 1.3

Table 1.3 : Regional HIV/AIDS statistics and features, December 1997 (8)

Region	Epidemic started	Adults & children suffering with HIV/AIDS	Adult prevalence rate (1)	Cumulative no of orphans(2)	Percent of HIV-positive adults who are women	Main mode(s) of transmission (3) for adults living with HIV/AIDS
Sub-Saharan Africa	late '70s - early '80s	20.8 million	7.4 %	7.8 million	50 %	Hetero
North Africa & Middle East	late '80s	210 000	0.13 %	14 200	20 %	IDU, Hetero
South & South-East Asia	late '80s	6.0 million	0.6 %	220 000	25 %	Hetero
East Asia & Pacific	late '80s	440 000	0.05 %	1 900	11 %	IDU, Hetero, MSM
Latin America	late '70s - early '80s	1.3 million	0.5 %	91 000	19 %	Hetero, MSM
Caribbean	late '70s - early '80s	310 000	1.9 %	48 000	33 %	IDU, MSM
Eastern Europe & Central Asia	early '90s	150 000	0.07 %	30	25 %	IDU, MSM
Western Europe	late '70s - early '80s	530 000	0.3 %	8 700	20 %	MSM, IDU
North America	late '70s - early '80s	360 000	0.6 %	70 000	20 %	MSM, IDU, Hetero
Australia & New Zealand	late '70s - early '80s	13 000	0.1 %	300	5 %	MSM, IDU
TOTAL		30.6 million	1.0 %	8.2 million	41 %	

1. The proportion of adults living with HIV/AIDS in the adult population (15 to 49 years of age).
2. Orphans are defined as HIV-negative children who lost their mother or both parents to AIDS when they were under 15
3. MSM (men who have sex with men, IDU (injecting drug users), Hetero (heterosexual transmission).

In sub-Saharan Africa, an alarming 7.4% of all Africans aged between 15 and 49 years are now thought to be infected with HIV. Levels of infection vary, however, widely across the continent. South Africa continues to be the worst affected area. By early 1997, the Government of South Africa had estimated that 2.4 million South Africans were living with HIV. (21) In Beit Bridge, a major city on the South African border with Zimbabwe, the proportion of pregnant women infected shot up from 32 % in

1995 to 59 % in 1996. In Botswana, the number of adults infected with HIV has doubled over the last five years, now reaching 25 % to 30 % of the adult population. In Zimbabwe, infection was estimated at one in five adults in 1996 and, in one town with a large population of migrant workers, seven pregnant women in 10 were already testing HIV-positive in 1995. (8)

In Botswana, life expectancy, which rose from under 43 years in 1955 to 61 years in 1990, has now fallen to levels previously found in the late 1960s. Already a quarter more infants are dying in Zambia and Zimbabwe than would be the case if there were no HIV. On current trends, Zimbabwe's infant mortality rate can be expected to rise by 138 % by the year 2010 because of HIV infection, and its under-five mortality rate by 109 %. (8)

In Asia, the epidemic is more recent than in Africa, and only a few countries in the region have developed sophisticated systems for monitoring the spread of HIV. In India, the infection rate of under 1 % of the total adult population, is still low by the standards of many countries. At the end of 1996, the Chinese government estimated that up to 200 000 people were living with HIV but some estimates indicate that this figure may have already doubled. In Latin America and the Caribbean, the HIV epidemic is taking a heavy toll, especially on men who have sex with men and injecting drug users. Drug injection is behind the dramatic surge in HIV infection in several Eastern European nations, accounting for the majority of the 100 000 new infections estimated to have occurred in 1997. (8)

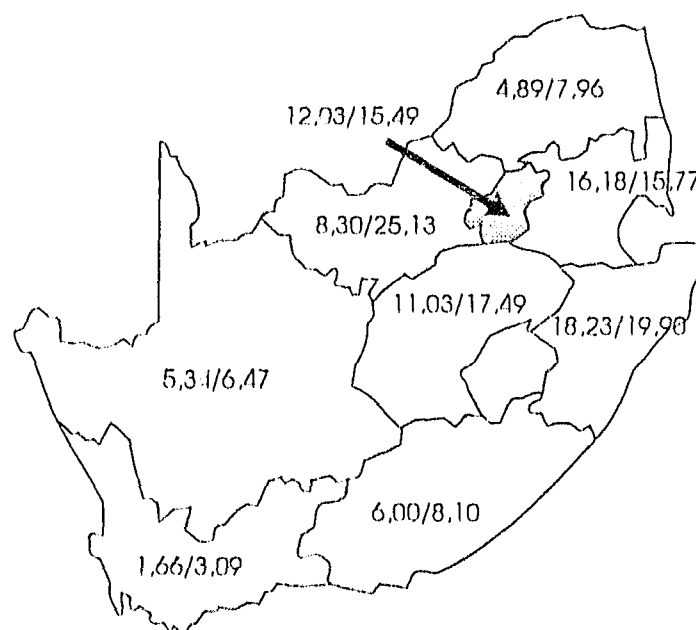
1.1.4 HIV in South Africa

The most recent and reliable figures available are from the 7th National HIV survey of women attending public health service antenatal clinics in South Africa in October and November 1996. These data were only released in June 1997. (21) Based on this survey it was estimated that some 2,4 million individuals were HIV positive by August 1996. The 8th National HIV Survey was completed in October and November 1997 but the results will only be ready for publication in June 1998. The 1996 study, based on a sample of 15 044 specimens screened, estimated that 15,07 % of women attending ante-natal clinics (ANC) nationally, were infected with HIV by the end of 1996 an increase on the 10,44 % the prevalence level of HIV in this group in 1995. (Table 1.4)

Table 1.4 : National HIV surveys in women attending ante-natal clinics, South Africa, 1995 and 1996 (21)

	Est(HIV+)	1996 (95% confidence interval)		Est(HIV+)	1995 (95% confidence interval)	
		Lower limit	Upper limit		Lower limit	Upper limit
South Africa	15,07	13,35	14,79	10,44	9,86	11,02
Province						
Western Cape	3,09	1,06	2,24	1,66	0,94	2,38
Eastern Cape	8,10	6,92	9,28	6,00	4,89	7,11
Northern Cape	6,47	5,05	7,89	5,34	4,10	6,58
Free State	17,49	15,57	19,41	11,03	9,44	12,62
KwaZulu - Natal	19,90	17,68	22,12	18,23	16,31	20,15
Mpumalanga	15,77	14,34	17,20	16,18	14,40	17,96
Northern Province	7,96	6,24	9,68	4,89	4,00	5,78
Gauteng	15,49	13,58	17,40	12,03	10,36	13,70
North West	25,13	22,31	27,95	8,30	6,67	9,92
Age Group						
<20	12,78	11,33	14,23	9,50	8,15	10,85
20 - 24	17,52	16,28	18,76	13,12	11,97	14,27
25 - 29	15,21	16,28	18,76	11,03	9,81	12,25
30 - 34	12,13	10,67	13,59	8,05	6,79	9,31
35 - 39	9,67	7,85	11,49	7,37	5,47	9,28
40 - 44	9,94	5,76	14,12	4,36	1,96	6,76
45 - 49	5,83	2,25	9,41	7,45	0,00	19,36

The highest rate of HIV infection was between the 20 and 29 years with a rate of 17,52 % in the 20 - 24 and 15,21 % in the 25 - 29 year age groups. Just more than 12 % of the under 20 and 30 - 34 year groups were HIV positive, while almost 10 % of the 35 - 44 group tested positive for HIV. The estimated rates of HIV infection in the provinces in 1995 and 1996 are shown in the following Figure 1.1



Estimated percentage rates 1995/1996

Figure 1.1 Geographic distribution of HIV positivity results (21)

The results of the national antenatal clinic surveys have been used to estimate the number of South Africans probably infected based on the following assumptions:

1. The prevalence rate of HIV infection in all pregnant women in South Africa is the same as the prevalence rate in women attending antenatal clinics of the public health services.
2. The prevalence rate of HIV infection in all women aged 15 - 49 years is the same as the prevalence rate in pregnant women.
3. The male to female ratio of HIV positives is 0,73 : 1
4. The transmission rate of HIV infection from mother to child is 0,3 (30 %)

The results in a particular population can be estimated by applying the above assumptions. For example to estimate the HIV positivity rate for males in Gauteng between 15 and 49 years of age, the ANC rate of 15,49 is multiplied by 0,73 to produce an estimate of 11,3 %.

1.1.5 HIV monitoring

HIV infection progression is monitored using a combination of clinical and laboratory parameters. The clinical features used in South Africa are based on the WHO clinical staging of HIV infection listed in Table 1.1. This describes an early seroconversion illness, asymptomatic phase, and period of generalised lymphadenopathy which progresses to a stage of weight loss, mucocutaneous manifestations and recurrent upper respiratory infections. The next clinical stage includes oral hairy leukoplakia, oral candidiasis, prolonged unexplained fever, chronic diarrhoea and pulmonary tuberculosis. The final clinical stage includes

many diseases (known as AIDS defining conditions), such as *Pneumocystis carinii* pneumonia and Kaposi's sarcoma.

Several laboratory markers have been described to monitor progression and immune status in HIV infection. (22) These include viral load, CD4 lymphocyte counts, p24 antigen, B2 microglobulin and total lymphocyte count. In developed countries quantitative viral load and CD4 lymphocyte counts are used to predict HIV disease progression and initiate the effects of therapy. (23) This therapy and viral load monitoring are unavailable in the public sector in South Africa. Second line markers include B2 microglobulin and p24 antigen which are not used frequently. B2 microglobulin has poor specificity and the p24 antigen test is expensive.

The CD4 lymphocyte count is a clinically useful measure of immune function and is recognised as an important prognostic marker in the progression and staging of HIV infection. (22,24-25) This is because the CD4 lymphocytes are the main target of HIV infection and their number tends to decline over time. Increasing viral load and a worsening clinical course of HIV infection is associated with a progressive decline in CD4 lymphocyte count. Specific complications of HIV infection can roughly be anticipated to occur at four levels of CD4 count and HIV infection can be staged according to this count (22,24-25) as illustrated in Table 1.5.

Table 1.5 : The staging of HIV disease based on the CD4 cell count (21,24-25)

CD4 cell count	Stage	Comment
> 500	Early	Risk of disease low. Response to routine immunisations and PPD skin testing reliable.
200 - 500	Middle	Risk of minor signs and symptoms high; risk of opportunistic disease moderate. May benefit from antiretroviral therapy.
50 - 200	Late	Risk of opportunistic disease high. Benefit from <i>Pneumocystis</i> prophylaxis and antiretroviral therapy.
<50	Advanced	Risk of opportunistic disease and death high. Benefit from <i>Pneumocystis</i> , <i>Mycobacterium avium</i> complex, and fungal prophylaxis. May benefit from antiretroviral therapy.

T lymphocytes in the peripheral blood are comprised predominantly of CD4 cells with the remainder being mostly CD8 T cells. Flow cytometry is the gold standard method for measuring CD4 counts. (28-29)

The basic principles of flow cytometry are as follows:

Cells are incubated with specific antibodies (eg CD4) which are conjugated to different coloured fluorochromes (eg phycoerythrin [PE]). The cells are passed single file through a laser beam (Argon laser emitting blue light at a wavelength of 488nm) and the energy imparted to the fluorochromes by the laser is emitted shortly afterwards at a specific wavelength (eg PE always emits light at a wavelength of 575nm which is an orange-red colour) which is detected by a detector (called a photomultiplier tube) and the information transmitted to a computer. The computer stores information for each cell such as the number of signals from each cell and the different colours encountered on that specific cell.

If all CD4 antibodies are labelled red and all CD8 antibodies labelled green then it is possible to tell for each cell 1) if they have a red or green signal or both and 2) how many red or green signals there are per cell. From this information, the CD4 percentage is calculated. It is the percentage of lymphocytes (whether they are B or T lymphocytes or natural killer cells) in the peripheral blood sample that are CD4. This percentage is then multiplied by the total absolute lymphocyte count to give an absolute CD4 count. The latter is obtained by multiplying the total white cell count by the percentage of lymphocytes in the peripheral blood.

Adult reference ranges are fairly broad and the local range is from 500 to 2000 x $10^6/l$ (at the South African Institute for Medical Research laboratories). Other quoted reference ranges are CD4 percentages of 28-57% with absolute CD4 counts ranging from 300-1400 x $10^6/l$. (29-31)

Studies have suggested that a low total lymphocyte count is an important marker of disease progression and can be used to initiate cotrimoxazole therapy for *Pneumocystis carinii* if CD4 counts are not available. (31) In most developing countries, especially in Africa, the technology, expertise and finance necessary for CD4 count measurements is not available so a total lymphocyte count (TLC) derived from a full blood count (FBC) may be used. (32) The WHO has formulated a laboratory staging system for HIV infection based on CD4 lymphocyte and total lymphocyte counts (Table 1.6) which may be used in

conjunction with the WHO clinical staging system (Table 1.1) to provide useful prognostic information.

Table 1.6 : Laboratory assessment of HIV infection (8)

WHO laboratory stage	CD4 lymphocyte count/mm ³	Total lymphocyte count
A	>500	> 2 000
B	200 - 500	1 000 - 2 000
C	<200	< 1 000

A WHO Laboratory Stage A corresponds with asymptomatic individuals in the WHO Clinical Stage 1. Stage B corresponds to Clinical Stages 2 and 3 and includes patients with weight loss, prolonged fevers, recurrent upper respiratory tract infections, oral candidiasis and severe bacterial infections. Stage C describes those patients with AIDS defining conditions (WHO Clinical Stage 4) and with a CD4 lymphocyte count below 200 or a TLC count below 1000, and prophylactic treatment for *Pneumocystis carinii* would be advocated. In one study of 831 HIV positive patients, a TLC below 1250 which correlated with a CD4 count below 200 preceded the development of *Pneumocystis carinii* pneumonia or cerebral toxoplasmosis in 76 % of patients. (31)

1.2 Otolaryngological manifestations of HIV infection

While patients with HIV infection are susceptible to any conditions of the head and neck, and while these conditions present in the same way as they do in patients who are not HIV positive certain conditions appear to be more characteristic. (1,2,4)

1.2.1 Oral and oropharyngeal manifestations

The oral cavity is one of the most common sites of HIV infection and may be the initial site of symptoms and signs (3,4). Several oral lesions have been associated with HIV infection specifically and the time between infection with the virus and the manifestation of these oral sequelae is not predictable. The most frequent presentation in patients with HIV infection is oral, pharyngeal and oesophageal candidiasis (5) with a reported prevalence up to 90%.

The candidiasis usually presents as a painful, diffuse, thick, white membrane (thrush) but may also present in a hyperplastic form and an erythematous (atrophic form). Angular cheilitis, which appears as a fissuring and inflammation of the epithelium at the angle of the mouth is another form. As early as 1984, Klein et al (32) reported oral candidiasis in high risk patients as the initial manifestation of HIV infection.

Another very common condition seen in this region is Kaposi's sarcoma which has been reported on the palate, buccal mucosa, gingival mucosa and posterior pharyngeal wall. The lesion appears as it does elsewhere as a raised or flat reddish blue nodule. Herpes simplex virus presents in a more virulent manner in AHIV infected patients. The lesions are usually 1 - 3 cm in diameter and can occur anywhere throughout the mouth and lips. Hairy oral leukoplakia, verrucae, non-Hodgkin's lymphoma, acute necrotising ulcerative gingivitis (ANUG), cytomegalovirus infections and aphthous ulcers have also been commonly reported in AIDS patients. (1,2,4,5)

In children recurrent adenotonsillitis and hypertrophy causing obstructive sleep apnoea (OSA) have been observed in the HIV positive patients (33). Follicular tonsillitis has been documented in both adults and children, however, no data exist comparing the prevalence of OSA or follicular tonsillitis in non-HIV infected and HIV infected children or adults. Similarly, to date there are no published studies comparing the prevalence of peritonsillar abscesses (PTA) in HIV infected and non-HIV infected patients.

1.2.2 Nasal and sinus manifestations

HIV infected patients are susceptible to the usual agents which cause sinusitis as well as uncommon bacteria, viruses, fungi and parasites. (34) Giant herpetic nasal

ulcers have been reported in HIV infected patients. These ulcers begin in the vestibule and can extend onto the septum and facial skin. Non-Hogkin's lymphoma and Kaposi's sarcoma have been reported in the nasal vestibule although the latter often presents on the tip of the nose. (34)

1.2.3 Otological manifestations

HIV infected patients can present with outer, middle and inner ear infections. The skin of the external ear may be involved with Kaposi's sarcoma which manifests in similar fashion to other skin areas. Pneumocystis infection can present as subcutaneous external ear masses or aural polyps. Otitis externa and media have also been documented with similar aetiologies and pathogenesis as non-HIV infected patients. Sensorineural hearing loss ranges from 20,9 % to 49 %; vertigo and facial nerve palsy are not uncommon inner ear manifestations. (35-37)

1.2.4 Laryngeal manifestations

Epiglottitis has occurred in several AIDS patients and Kaposi's sarcoma involving the upper airway is a common complication. (1)

1.2.5 Salivary gland manifestations

Xerostomia and cystic parotid enlargement of unknown aetiology are frequently presenting signs in HIV patients. (38,39)

1.2.6 Cervical manifestations

Persistent generalised lymphadenopathy was one of the earliest reported manifestations of HIV infection. (1-2,33) This is a non tender enlargement of lymph nodes in the anterior and posterior triangle of the neck present for longer than 3 months. Other causes of lymphadenopathy in HIV positive patients are metastatic Kaposi's sarcoma and non-Hodgkin's lymphoma and mycobacterial infection. (39)

1.3 Peritonsillar abscess

Peritonsillar abscess (PTA) or quinsy as it is commonly termed, is the most common complication of acute tonsillitis as well as the most common deep infection of the head and neck. (40-41) PTA is a collection of pus that develops between the fibrous tonsillar capsule at its upper pole and the superior constrictor muscle of the pharynx. Although incidence data of PTA in South Africa are not available, Fagen and Wormald (42) reported on their management of 51 patients presenting to Groote Schuur Hospital with PTA between the ages 16 and 40 years

oropharyngeal swelling and accumulation of saliva. The patient will often complain of dysphagia for solids and difficulty in coping with their own saliva.

Examination usually reveals an ill-looking patient with pyrexia and trismus. There is almost a classical appearance of the oropharynx. There is asymmetry of the soft palate with a unilateral peritonsillar swelling and oedema displacing the ipsilateral tonsil to the midline. The cervical examination reveals tender lymph nodes in the jugulodigastric region.

The differential diagnosis includes any condition causing swelling and oedema of the soft palate. The most likely condition to be confused with a typical quinsy is an abscess of an upper molar tooth. A less common condition is a carcinoma of the oropharynx. In such instances the typical age group for oral carcinoma is the 5th to 7th decade. For example, Green et al (43) reported an elderly, debilitated patient with a metastatic renal carcinoma presenting mistakenly as a PTA. Usually a careful history and examination will lead to the correct diagnosis.

1.3.3 Management

Diagnosis is confirmed with needle aspiration of pus. Treatment includes admission to hospital, intravenous antibiotic treatment with penicillin or an appropriate alternative. Aspiration of pus with or without incision and drainage of the PTA is performed under local anaesthesia. Although several studies have

indicated the clinical efficacy of aspiration alone many doctors perform an incision and drainage of the abscess. (40) The majority of otolaryngologists advise a patient to have an interval tonsillectomy (IT) 6 weeks later to avoid a recurrence. (40,44-45) Follow up studies of PTA patients have revealed a recurrence in only 20% of cases (12,46) at most and therefore IT is only appropriate for those patients who have documented recurrent follicular tonsillitis. A second quinsy is regarded as stronger, if not absolute, indication for tonsillectomy. (41,44-45)

The alternative method of managing a PTA is to perform an immediate quinsy tonsillectomy (QT) under general anaesthesia. The advantages are that an incision and drainage is avoided and only one hospital admission is necessary but this assumes that a tonsillectomy is necessary to prevent a recurrent PTA which is not supported by the 20% recurrence figures. Another advantage of QT is the immediate relief of pain compared to gradual pain relief over a few days in IT. The disadvantages are a theoretical risk of increased bleeding which is not supported in the literature. (40,47-48) Increased anaesthetic risk due to abscess rupture or difficult intubation is said to be a concern.

QT are not routinely performed in South Africa and needle aspiration with or without incision and drainage is the most common form of management.

1.3.4 Complications

PTA is a potentially lethal condition. Increasing oedema and spread of infection can cause upper airway swelling and respiratory obstruction. Spread of infection through the constrictor muscles of the pharynx can lead to a parapharyngeal abscess which may involve the carotid sheath leading to jugular vein thrombosis and fatal carotid artery haemorrhage. (13)

1.4 Study objectives

The preceding literature review has shown that large number of people are HIV positive, particularly in South Africa. There is also a local anecdotal belief that PTA may be an early presentation in HIV infected individuals. No objective evidence for this belief exists. The current study was designed to investigate the association between HIV and immune status in patients with PTA using CD4 and CD8 lymphocyte counts to indicate immune status.

A possible benefit of the study is that PTA may prove to be a marker for HIV infection in asymptomatic patients and help with earlier diagnosis. This will lead to earlier counselling and treatment.

CHAPTER 2 - MATERIALS AND METHODS

2.1 Study design and ethics

The investigation was a descriptive prospective study approved by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand (Clearance 950505) and heads of ENT departments at the five academic hospitals. [Appendix A] These hospitals were the Johannesburg, Hillbrow, J.G. Strydom (now Helen Joseph), Coronation and Baragwanath (now Chris Hani Baragwanath) Hospitals which serve an estimated population of 3 million people. The exact population number is not known and the 1996 Census figures have not yet been made public.

2.2 Study population

All patients spontaneously presenting to, or referred to, the ENT Clinics at the five academic hospitals in the Johannesburg area, comprised the study population. Each of these hospitals run ENT out patient (OPD) clinics on 2 or 3 days of the week at which approximately 35 - 100 patients are seen, depending on the hospital. On days where no OPD clinics were scheduled, and after hours, patients with PTA would be referred to and examined in the ENT wards examination and procedure rooms. Typically, at Baragwanath and Hillbrow Hospitals approximately 4 patients with PTA are likely each week while Johannesburg, J.G. Strydom and Coronation ENT departments would see approximately 3 patients per week with PTA. Although patients with follicular tonsillitis would be referred to OPD, most would be treated as an outpatient.

2.3 Study sample

The sample studied was all patients presenting consecutively to the ENT Outpatients or wards at the five academic Hospitals with a confirmed diagnosis of PTA over an eight month period commencing July 1995. The patients usually presented with a typical history of preceding sore throat, inability to swallow saliva adequately, referred ear pain and a 'plummy' voice. Clinically they were mostly pyrexial, exhibited trismus and had the typical unilateral swelling the in the peritonsillar area, displacing the affected tonsil medially. The diagnosis was confirmed by needle aspiration of pus under local anaesthesia.

The study began as soon as ethical clearance was obtained, questionnaires printed and ENT Registrars trained and briefed about the study. It was not timed to coincide with any particular period or season of the year.

2.4 Inclusion and exclusion criteria

Any patient presenting with PTA for the first time was considered for inclusion. Such individuals were included if they gave informed consent. (Figure 2.1) The diagnosis was confirmed by history, examination and attempted needle aspiration of pus. A sterile size 16 or 18 gauge 'Jelco' needle (Critikon - Johnson & Johnson, Midrand, South Africa) attached to a 20 ml syringe was inserted into the peritonsillar area. This area had been anaesthetised with Xylocain 10 % topical spray (Astra Pharmaceuticals, Sweden) and or infiltrated with 0,5 cc of 2 % Xylotox E80-A (Adcock Ingram, Johannesburg, South Africa) solution for injection. The peritonsillar area was

illuminated by a head light worn by the doctor and the tongue depressed with a metal or wooden spatula. A nursing sister in attendance restrained the patient's head.

Patients who presented with conditions having a similar clinical picture but no definite PTA were excluded. These were patients with severe follicular tonsillitis and those with a history of previous PTA, patients with soft palate and palatoglossal swelling and cellulitis due to other causes such as suspected oral carcinoma. Immunocompromised patients from other causes other than HIV for eg chemotherapy for malignancies were also excluded.

Consenting patients with incomplete questionnaires and incomplete or missing blood tests were also excluded from the final data analysis group.

2.5 Data collection

2.5.1 Clinical information

A standardised questionnaire was produced to be completed by the ENT Registrar to whom the patient first presented. The questionnaire was pretested in a pilot study on 6 patients with PTA in order to minimise ambiguity. Experience from this pilot run indicated how Registrars should be instructed to complete the questionnaire. Because the five hospitals participating were spread over a vast distance and ENT OPD's were scheduled many times on the same week days at these different hospitals it was logistically impossible for the investigator to complete all questionnaires, collect blood samples and manage the PTA patients personally. This was performed by the

Registrars at the various hospitals. The investigator was responsible for training the Registrars, collecting the completed questionnaires, tracing the blood results and collating the data. The questionnaire (Figure 2.2, 2.3) was divided into 3 Categories : demographic, brief patient history and clinical documentation by doctor. The questionnaire sought basic patient information regarding age, gender, marital status, occupation and sexual preference. It included patient symptoms, previous PTA or tonsillitis and treatment thereof. Also required was clinical information regarding the site of the quinsy, whether pus was aspirated and whether an incision and drainage of the PTA was performed.

2.5.2 Blood tests

HIV and CD4 and CD8 lymphocyte count blood tests were taken on admission with appropriate counselling. This was performed according to the guideline of the Faculty of Health Sciences of the University of the Witwatersrand "Procedures for obtaining informed consent for HIV testing in Adults." [Appendix B]

All HIV tests performed at Baragwanath, Hillbrow, J.G. Strydom and Coronation were processed by the central laboratory at the South African Institute for Medical Research (SAIMR). HIV tests for Johannesburg Hospital were processed at the National Institute of Virology (NIV). The protocol for the SAIMR and NIV differ slightly although all testing was done according to the 3-ELISA approach in keeping with the WHO recommendation of screening of populations with a seroprevalence of 10 % (49-50) WHO recommends a combination of 3 ELISA's based on different antigens and differing test principles to be performed in a sequential fashion.

Dear Patient

I am Dr Peter Friedland, who works in the EAR NOSE and THROAT DEPARTMENT of the UNIVERSITY OF THE WATWATERSRAND. I am completing a Masters degree in Medicine and am required to do research.

You have been referred to us because of an abscess or infection in and around your tonsils. This is called a QUINSY. Doctors in our department have noticed that some patients that have been referred to us with Quinsies have also been previously infected with the HIV virus.

We are asking you to participate in a research study which will help us learn whether this is true and scientifically significant. We wish to estimate the number of patients referred to us with quinsies who also have the HIV virus and the strength of their immunity.

If you agree to participate in this study you will receive the standard and routine treatment which we give all our patients with Quinsies. This includes admission to our ward, intravenous antibiotics and drainage of your QUINSY. In addition your consent will be asked for 2 blood samples, which are for an HIV test and a CD4 count which estimates the strength of your immunity. Should your HIV test be positive, you will be referred for counselling to the HIV clinic who have experts in this field.

We also wish you to answer a short questionnaire which your doctor will ask you. The blood results and answers to your questionnaire are completely confidential. Confidentiality is assured by the coding system we use.

Permission to do this study has been obtained from the educational authorities and from the University of the Witwatersrand committee for research on human subjects.

Participation is voluntary and you are free to participate or withdraw your consent and discontinue participation at any time. If you decline to take part in this study it will not affect your regular treatment in any way.

If you are happy to participate in this study please sign the relevant portion below.

Yours sincerely

DR PETER FRIEDLAND

I AGREE TO PARTICIPATE IN THE STUDY OUTLINED ABOVE:

PATIENT : NAME :

SIGNATURE :

GUARDIAN : NAME :

SIGNATURE :

Figure 2.1 Informed Consent

QUESTIONNAIRE

PATIENT

DATE: _____

HOSPITAL: _____

NAME: _____

HOSPITAL NUMBER: _____

AGE: _____

GENDER: _____

MARITAL STATUS: _____

OCCUPATION: _____

SEXUAL PREFERENCE: _____

HOME LANGUAGE: _____

CODE

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Figure 2.2 Study Questionnaire (page 1)

CODE

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WHEN DID YOUR SYMPTOMS OF TONSILLITIS BEGIN? _____

HAVE YOU RECEIVED ANY ANTIBIOTIC TREATMENT FOR YOUR TONSILS IN THE LAST FEW DAYS ? _____

HAVE YOU HAD TONSILLITIS BEFORE? _____

IF YES, HOW MANY TIMES PER YEAR? _____

HAVE YOU HAD A QUINSY BEFORE? _____

IF YES, HOW MANY TIMES? _____

HAVE YOU EVER HAD A TONSILLECTOMY? _____

HAVE YOU EVER BEEN ADMITTED TO HOSPITAL BEFORE FOR TONSILLITIS?

DO YOU KNOW YOUR HIV STATUS? _____

IF YES: _____ [POSITIVE/NEGATIVE]

CODE

--	--	--	--

CLINICAL DOCUMENTATION (DOCTOR)

SITE OF QUINSY? LEFT RIGHT BILATERAL

PUS ASPIRATED? YES NO

INCISION & DRAINAGE YEST NO

PLEASE LIST ANY OPPORTUNISTIC INFECTIONS PRESENT

Figure 2.3 Study Questionnaire (page 2)

At the Baragwanath, Hillbrow, J.G. Strydom and Coronation Hospitals a Capillus HIV1/HIV2 Rapid Test (Cambridge Biotech LTD, Galway, Ireland) was performed initially as a screening test. If this was positive serum was sent to the central laboratory at the SAIMR where two confirmatory tests were performed. These were the AxSYM HIV-1/HIV-2 microparticle enzyme immunoassay (EIA) (Abbott Diagnostics, Illinois, USA) and the Access HIV-1/HIV-2 chemoluminescent enzyme immunoassay (Sanofi Diagnostics Pasteur Marnes - La Coquette, France).

HIV samples from the Johannesburg General, which were sent to the NIV, were first screened using the Biotest anti-HIV-1/HIV-2 EIA (Biotest AG, Germany). Reactive samples were tested in the following two tests, Pasteur Genelavia MIXT HIV-1/HIV-2 EIA (Sanofi Diagnostics Pasteur, France) and the Murex Wellcozyme HIV-1+2 EIA (Murex Diagnostics Ltd, England).

Serum reactive (i.e. HIV positive) on all three tests was considered HIV antibody positive. Serum that was non-reactive on the first test was considered HIV negative as was serum that was reactive on the first test and non reactive on the second test. Serum that was reactive on the first and second tests and non reactive on the third test was considered to be an equivocal (borderline) result. A Western blot test or P24 antigen test was then performed to confirm or reject HIV positivity.

All CD4 and CD8 counts, CD4 and CD8 percentages and ratios from all the hospitals were performed at the SAIMR laboratory at the Johannesburg Hospital. The CD4 counts were performed as follows:

A 5 ml specimen collection was done in EDTA anticoagulant and the sample processed within 24-36 hours of collection. At the laboratory instruments were standardised on a daily basis to ensure quality control according to international recommendations. T cell subset analysis was performed using a whole blood lysis method. Fifty microlitres of whole blood was incubated with the triple antibody combination of CD4 PE/CD8 FITC/CD3ECD (Coulter Corporation, Hialeah, Florida, USA) according to the recommendations of the manufacturer. Q-prep reagent (Coulter Corporation, Hialeah, Florida, USA) was used to lyse the red cells. Data was acquired on the Epics XL Flow Cytometer (Coulter Corporation, Hialeah, Florida, USA) and reports printed. The automated analyser used for cells counts was the Technikon H3 (Bayer, Germany) and manual differentials were performed only when an automated count could not be obtained from the instrument.

2.5.3 Patient treatment

All patients with PTA irrespective of their inclusion in or exclusion from the study were managed in a similar fashion. Patients were admitted to the ENT wards at the relevant hospital. Medical management included intravenous antibiotics, usually penicillin or another appropriate antibiotic if the patient was allergic to penicillin. The abscess was aspirated by needle (Section 2.4). Incision and drainage was performed depending on a registrar's clinical judgement at the time.

2.6 Implementation of tasks

2.6.1 Registrar on duty at a hospital

Each ENT registrar worked according to the following steps:

1. Confirm diagnosis of PTA according to definition provided.
2. Obtain consent from patient to participate in study and have HIV test.
3. Conduct interview and complete questionnaire.
4. Perform standard and routine treatment for PTA.
5. Submit samples to SAIMR Laboratory for HIV, CD4 and CD8 blood tests.

2.6.2 Researcher

The investigator collated the questionnaire, traced blood results at the central laboratory of the SAIMR, NIV and Johannesburg Hospital SAIMR laboratory, and collated data and statistics.

2.6.3 Hospitals

HIV, CD4 and CD8 blood tests were paid for by the individual hospitals to the SAIMR and NIV. These are part of the current standard work up of all suspected HIV infected patients.

2.7 Data Analysis

The questionnaire was coded and the data captured on a Sun SPARCcentre 2000 computer on Wits network and analysed using SAS (51). Descriptive statistics comprised demographic data frequencies, CD4 and CD8 frequencies, means standard deviations and 95% confidence intervals. Analytical statistics used a general linear models analysis multivariate analysis. This is not appropriate for discrete variables which did not have a normal distribution and were not continuous. For these a two way contingency table, Chi square Test and Fisher's exact test was utilised. The critical level of statistical significance was set at $P < 0,05$.

CHAPTER 3 - RESULTS

3.1 Sample studied

Over the 7 month period 96 patients aged 20 - 49 presented with peritonsillar abscesses at the hospitals. Fifty seven (59,4 %) patients completely fulfilled the inclusion criteria. Thirty nine patients (41%) were excluded due to missing or incomplete blood results. HIV tests from Baragwanath, Hillbrow, J.G. Strydom and Coronation Hospitals were transported to Central SAIMR laboratory in Hillbrow. The Johannesburg General HIV blood tests were tested at the NIV in Sandringham, Johannesburg. All flow cytometry (CD4 and CD8) was performed at SAIMR laboratory at the Johannesburg General. Specimens therefore had to be transported from the five hospitals to three laboratories from one end of Johannesburg to the other. Loss in transport evidenced by non-arrival of specimens in the test laboratories is the explanation for the frustrating high loss of blood specimens and results. It proved impossible to collect repeat specimens. The final study sample for this report is therefore 57, 10 of whom (18 %) were HIV positive.

3.2 Demographic data

3.2.1 Gender

The study sample consisted of 31 females (54,4 %) and 26 males (45,6 %), a female to male ratio of 1.2 to 1. Among the 10 HIV positive patients the gender ratio was 4F:1M. (Table 3.1) There was no statistically significant difference in HIV status between the genders.

Table 3.1 : HIV status by gender

HIV status	Female	Male	Total
Negative	23	24	47
Positive	8	2	10
Total	31	26	57

Fisher's exact P-value = 0,092

3.2.2 Marital status

Most patients were married (72 %). Only one HIV positive was single. (Table 3.2)

Table 3.2 : HIV status by marital status

HIV Status	Single	Married	Total
Negative	15	32	47
Positive	1	9	10
Total	16	41	57

Fisher's exact P-value = 0,25

3.2.3 Sexual preference

Forty-six of the 57 patients answered this question. Forty-five (95%) were heterosexual and one (2 %) was homosexual. (Table 3.3)

Table 3.3 : HIV status by sexual preference

HIV status	Heterosexual	Homosexual	Total
Negative	37	1	38
Positive	8	0	8
Total	45	1	46

Fisher's exact P-value = 1,00

3.2.4 Language

Table 3.4 lists the eight home languages of the 56 patients who responded to the question. The three most frequent languages were, in descending order, Zulu, Xhosa and Sotho. The same preponderance was present among the HIV infected patients. (Table 3.4)

Table 3.4 : HIV status by home language

HIV Status	A	E	N	S	Sh	T	X	Z	O	Total
Negative	3	2	0	9	1	6	8	17	1	47
Positive	0	0	1	2	0	0	2	5	0	10
Total	3	2	1	11	1	6	10	22	1	57

A = Afrikaans, E = English, N = Ndebele, S = Sotho, Sh = Shangaan, T = Tswana, X = Xhosa, Z = Zulu, O = No Response

3.2.5 Employment and occupation

Unemployment was high in the sample comprising 25 (43,8%) patients. (Table 3.5) The individual occupations which were almost all unskilled in type showed no particular pattern. No less than 70 % of the HIV infected group were unemployed. Of the remaining three, their occupations were cleaner, painter and scholar.

Table 3.5 : HIV status by employment status

HIV status	Unemployed	Employed	Total
Negative	18	29	47
Positive	7	3	10
Total	25	32	57

Fisher's exact P value = 0,087

3.2.6 Hospital admissions

The majority of patients 31 (54 %) were admitted to Hillbrow Hospital. Six PTA cases were admitted to the Coronation and 1 PTA case to the J.G. Strydom Hospitals. However, all the patients from the these two hospitals were excluded due to missing blood results. (Table 3.6) The proportions of HIV infected patients were similar at Baragwanath and Johannesburg hospital.

Table 3.6 : HIV status by hospital admission

HIV status	Baragwanath	Hillbrow	Johannesburg	Total
Negative	11	26	10	47
Positive	3	5	2	10
Total	14	31	12	57

Chisquare = 0,20 on 2df, P=0,91

3.2.7 Age

The age distribution of the HIV infected patients and non HIV infected patients is shown as box and whisker plot in Figure 3.1 and as scattergram Figure 3.2. Thirty six patients (63 %) were between the age 20 and 34, of whom 18 (31,5 %) were between 20 and 24 and, 16 (28 %) were aged 25 - 34 years. Fourteen patients (25 %) were between 35 and 44 years and 6 (10,5 %) were between 45 - 49. An age-matched general linear models analysis showed no significant effects for HIV status ($P=0,90$) and gender ($P=0,66$).

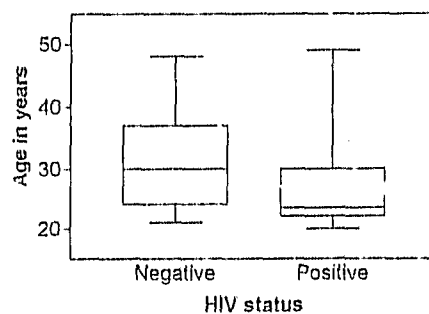


Figure 3.1 Box and whisker plot for HIV status by age

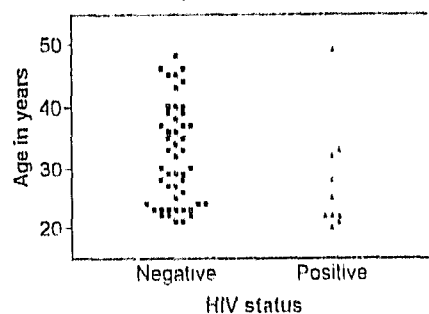


Figure 3.2 Scattergram for HIV status by age

3.3 Clinical data

3.3.1 Symptom duration

Forty patients (70 %) had symptoms of 5 days or less before presenting to hospital. Twenty one patients (36 %) had symptoms for 3 days or less and only 5 patients (8 %) had symptoms of 10 days or more. The distributions by HIV status are shown in Figures 3.4 and 3.5. A general linear models analysis showed no statistically significant effects for HIV status ($P=0.19$) or gender ($P=0.33$) on symptom duration.

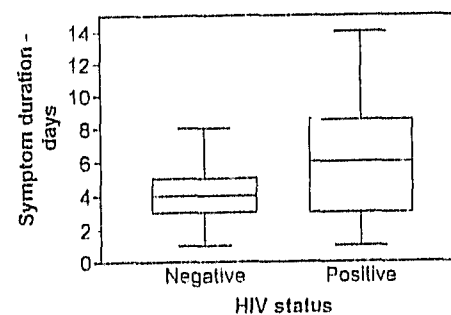


Figure 3.4 Box and whisker plot for HIV status by symptom duration

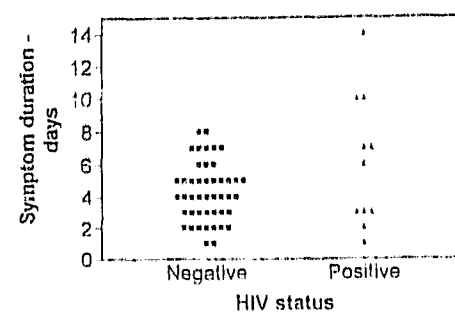


Figure 3.5 Scattergram for HIV status by symptom duration

3.3.2 Antibiotic usage before admission

Thirty seven patients (65 %) did not receive antibiotics prior to admission which included 9 (90 %) HIV positive and 28 (49 %) HIV negative patients. Only 20 patients (35 %) received antibiotics. (Table 3.7) There was no statistically significant difference in usage between the HIV status groups.

Table 3.7 : HIV status by antibiotic use before admission

HIV status	No	Yes	Total
Negative	28	19	47
Positive	9	1	10
Total	37	20	57

Fisher's exact $P = 0,082$

3.3.3 Previous episodes of tonsillitis

More patients presented with PTA without a previous episode of tonsillitis, 37 (65 %) did not have a history of previous tonsillitis, 20 (35 %) did. (Table 3.8) No statistically significant difference in rate of previous tonsillitis was found. Nine HIV positive patients (90 %) had never had tonsillitis prior to this admission. Of the 20 patients (35 %) with a previous tonsillitis, 13 (65 %) had two previous episodes.

Table 3.8 : HIV status by previous episodes of tonsillitis

HIV status	No	Yes	Total
Negative	28	19	47
Positive	9	1	10
Total	37	20	57

Fisher's exact $P = 0,082$

3.3.4 Previous episodes of quinsy

Eleven patients (19 %) had had a previous PTA but half of the HIV positive patients had had PTA before. (Table 3.9) A previous quinsy was significantly more common among the HIV infected patients. Table 3.10 shows that the frequency of previous episodes was also higher in the HIV infected group.

Table 3.9 : HIV status by previous quinsy

HIV status	No	Yes	Total
Negative	41	6	47
Positive	5	5	10
Total	46	11	57

Fisher's exact = $P=0,0165$ (statistically significant)

Table 3.10 : HIV status by number of previous quinsies

HIV status	1	2	3	4	Total
Negative	4	2	0	0	6
Positive	2	1	1	1	5
Total	6	3	1	1	11

3.3.5 Previous tonsillectomy

There was only 1 previous tonsillectomy so this was not investigated.

3.3.6 Quinsy management

Patients with PTA were managed by aspiration and/or incision and drainage of the abscess. In 34 (60 %) of the patients pus was aspirated and only 27 patients (47 %) incision and drainage was performed

3.3.7 Site of quinsy

The sites of the quinsy are listed in Table 3.11. There was a left sided preponderance and only 2 (3,5 %) patients had bilateral PTA.

Table 3.11 : HIV status and site of quinsy

HIV status	Left	Right	Bilateral	Total
Negative	24	21	2	47
Positive	7	3	0	10
Total	31	24	2	57

3.3.8 Patient knowledge of their HIV status

Most patients, 53 (95 %) had no knowledge of their HIV status. All who were aware of their status, believed it to be negative including 1 patient who was HIV positive on testing.

3.4 Laboratory data

3.4.1 CD4 counts and percentages

The general linear models analysis of the CD4 count showed a highly significant effect for HIV status ($P=0,0001$) but not for gender ($P=0,83$). The F value for gender is <1 - the variability in CD4 counts attributed to gender differences is smaller than the "error" (unexplained background) variability therefore gender was not important in determining variability in the CD4 counts. F value for HIV is much greater than 1 - so much of the variability in CD4 counts can be attributed to HIV status therefore HIV status did statistically significantly ($P=0,0001$) affect the CD4 counts. (Table 3.12) In Table 3.13 the mean and median CD4 counts for the HIV positives are shown as considerably lower than in the HIV negative group.

Table No 3.12 : General linear models analysis results for CD4 count

Source	df	SS	MS	F	Pr>F
Gender	1	0.003	0.003	0.05	0.831
HIV	1	1.823	1.823	22.04	0.0001
Error	52	4.303	0.082		
Total	54	6.10			

Table 3.13 : HIV status by CD4 count

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	45	0.898	0.314	0.81	0.99	0.86
Positive	10	0.448	0.124	0.37	0.53	0.48

Results for the CD4 percentages are listed in Tables 3.14 And 3.15. The same explanation for the general linear models analysis as above applies showing a highly statistically significant effect for HIV status ($P=0.0001$) but not for gender. The mean and median CD4 percentages were much lower in the HIV positive group.

Table 3.14 : General linear models analysis results for CD4 percentage

Source	df	SS	MS	F	Pr>F
Gender	1	354.09	354.09	3.23	0.0782
HIV	1	2076.8	2078.81	18.93	0.0001
Error	52	5704.4	109.7		
Total	54	8135.3			

Table 3.15 : HIV status by CD4 percentage

HIV status	N	Mean	SD	95% CI		Median
				Lower	Upper	
Negative	45	44.89	10.579	41.80	47.98	44
Positive	10	27.80	9.554	21.88	33.72	26

3.4.2 CD8 counts and percentages

The general linear models analysis showed a significant effect on CD8 count of HIV status ($P=0.011$) but not for gender ($P=0.257$) (Table 3.16). This significant effect was not as large as for the CD4 count and CD4 percentage. Table 3.17 lists the CD8

count results. The trend is the opposite to CD4, CD8 mean and median counts are higher in the HIV positive group.

Table 3.16 : General linear models analysis results for CD8 count

Source	df	SS	MS	F	Pr>F
Sex	1	0,136	0,136	1,31	0,257
HIV	1	0,715	0,715	6,86	0,011
Error	52	5,422			
Total	54	6,274			

Table 3.17 : HIV status by CD8 count

HIV status	N	Mean	SD	95% CI		Median
				Lower	Upper	
Negative	45	0,345	0,250	0,47	0,62	0,492
Positive	10	0,864	0,546	0,53	1,20	0,705

The CD8 percentage results (Tables 3.18 And 3.19) show the same trends as for the CD8 absolute counts namely a significant effect of HIV status ($P=0,001$) but not of gender ($P=0,71$).

Table 3.18 : General linear models analysis results for CD8 percentage

Source	df	SS	MS	F	Pr>F
Sex	1	15,66	15,66	0,14	0,71
HIV	1	2656,21	2656,21	23,70	0,001
Error	52	5,422			
Total	54	8499,52			

Table 3.19 : HIV status by CD8 percentage

HIV status	N	Mean	SD	95% CI		Median
				Lower	Upper	
Negative	45	27,33	9,927	24,43	30,23	24
Positive	10	45,1	13,253	36,89	53,31	41,5

3.4.3 CD4:CD8 ratio

The general linear models analysis showed a highly statistically significant effect on the CD4:CD8 ratio for HIV status ($P=0,0003$) but not for gender ($P=0,274$) (Table 3.20 and 3.21).

Table 3.20 : General linear models analysis for CD4:CD8 ratio

Source	df	SS	MS	F	Pr>F
Gender	1	0,815	0,815	1,22	0,274
HIV	1	9,855	9,855	14,75	0,0003
Error	54	36,074	0,668		
Total	56	46,745			

Table No. 3.21 : HIV status by CD4:CD8 ratio

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	47	1,878	0,850	1,63	2,12	1,783
Positive	10	0,741	0,558	0,40	1,09	0,591

3.4.4 White cell count (WCC)

No statistically significant effects of WCC were found for either HIV status ($P=0,229$) or gender ($P=0,221$) (Table 3.22).

Table 3.22 : General linear models analysis result for WCC

Source	df	SS	MS	F	Pr>F
Gender	1	433,78	433,7	1,53	0,221
HIV	1	417,6	417,6	1,48	0,229
Error	54	15276,7	282,903		
Total	56	16128,2			

The white cell counts were much lower in the HIV positive group but the very high standard deviation and 95 % confidence intervals in the HIV negative group indicates too much variation to show a significant effect within the sample size (Table 3.23).

Table 3.23 : HIV status by WCC

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	47	5,82	18,594	0,51	11,14	0,7
Positive	10	0,63	0,313	0,44	0,82	0,8

3.4.5 CD3 counts and percentages

The general linear models analysis showed no statistical significant effects on CD3 counts for HIV status ($P=0,353$) and gender ($P=0,302$) (Table 3.24 and 3.25).

Table 3.24 : General linear models analysis result for CD3 count

Source	df	SS	MS	F	Pr>F
Sex	1	0,261	0,261	1,09	0,302
HIV	1	0,210	0,210	0,88	0,353
Error	54	12,992	0,240		
Total	56	13,464			

Table 3.25 : HIV status by CD3 count

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	47	1,486	0,458	1,36	1,62	1,353
Positive	10	1,373	0,639	0,98	1,77	1,34

The CD3 percentage results (Table 3.26 and 3.27) show the same trends as for the CD3 absolute counts, namely a statistically insignificant effect of HIV status ($P=0,201$) and for gender ($P=0,489$).

Table 3.26 : General linear models analysis result for CD3 Percentage

Source	df	SS	MS	F	Pr>F
Sex	1	52,09	52,09	0,48	0,489
HIV	1	179,31	179,31	1,67	0,201
Error	54	5800,73	107,42		
Total	56	6032,14			

Table 3.27 : HIV status by CD3 percentage

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	47	72,76	10,589	69,74	75,79	72
Positive	10	76,7	9,104	71,06	82,34	77,5

3.4.6 Lymphocyte counts

No statistically significant effects on lymphocyte counts were found for either HIV status ($P=0,134$) or gender ($P=0,145$) (Tables 3.28 and 3.29).

Table 3.28 : General linear models analysis result for Lymphocyte count

Source	df	SS	MS	F	Pr>F
Sex	1	1,258	1,258	2,18	0,145
HIV	1	1,333	1,333	2,31	0,134
Error	52	30,0	0,577		
Total	54	32,596			

Table 3.29 : HIV status by Lymphocyte count

HIV status	N	Mean	SD	95 % CI		Median
				Lower	Upper	
Negative	45	2,063	0,785	1,33	2,29	1,87
Positive	10	1,774	0,725	1,32	2,22	1,685

CHAPTER 4 - DISCUSSION

4.1 Collection of sample

4.1.1 Investigator and registrars

This was a difficult study to complete as patients were entered into the study at all 5 academic hospitals and the ENT Registrars completing the questionnaires and managing the patients were rotating hospitals every few months. Continual motivation and supervision was needed to ensure the completion of the data. The heavy clinical work load, theatre lists, emergencies and after hours work made the completion of the questionnaires an additional burden. When the investigator travelled to these hospitals to collection questionnaires, he discovered occasional patients with PTA who were not entered into the study. The patients were usually seen after hours or on a busy weekend, where the above factors discouraged the registrars from entering these patients into the study. Approximately ten patients were not entered into the study for these reasons.

Thirty-nine patients (41 %) with PTA were excluded due to incomplete and missing blood results. Of these 31 patients (79,4 %) were HIV negative and 8 patients (20,6 %) were HIV positive. The major problem arose with the transport of specimens and sera from Baragwanath, J.G. Strydom, Coronation and Hillbrow Hospitals to the SAIMR Central Laboratory for confirmation of HIV status and then onto the Johannesburg Hospital SAIMR laboratory for flow cytometry for CD4 and CD8 counts. Most of these patients had incomplete flow cytometry results. It was disappointing that 41 % (39 patients) had to be excluded for the above reasons. This left the study sample of 57 patients of which 47 (82 %) were HIV negative and 10 (18 %) were HIV positive. Because of the exclusion of PTA patients with incomplete results the absolute presentation rate of PTA at the academic hospitals is inaccurate. However, relative comparisons may be made. Fortunately, the ratio of HIV positive to HIV negative patients in the excluded patients was almost the same as in the included patients.

4.2 Demographic Data

Although there were no statistically significant results for the demographic data when matched for HIV status and gender, there are some trends that need further investigation, other variables may be dropped from future studies.

4.2.1 Gender

The ratio of males to females in the study was 0,83:1 compared to the South African statistic of 0,73:1 in the general population based on the 1991 census figures. (21) A larger sample of PTA is needed to establish any gender effect.

4.2.2 Marital status

Forty-one patients (72 %) were single, which included 9 (90 %) of the HIV positive patients. While marital status is unlikely to have any role in PTA, the possibility of multiple sexual partners in the unmarried group must increase risk of HIV infection.

4.2.3 Sexual preference

Forty-five patients (95 %) of those who answered the question were heterosexual. Only one patient was homosexual and he was HIV negative. This correlates with the fact that HIV disease in South Africa is predominantly a heterosexually spread infection. (8,20)

4.2.4 Occupation and language

Twenty-five patients (43,8 %) were unemployed and 22 (38,5 %) were Zulu speakers. The next largest groups of 11 (19 %) and 10 (17 %) patients were Xhosa and Sotho speakers respectively. Recent census figures for these groups are not available. There is no reason to suspect that either occupation or language influence the rate of PTA.

4.2.5 Hospital admissions

The majority of patients 31 (54,5 %) were treated at Hillbrow hospital. There are two factors that may account for this. Firstly, Hillbrow is the most densely populated area in South Africa and secondly the workload of the ENT Registrars at that hospital (now closed) was not as demanding as the Baragwanath and Johannesburg hospitals. This may have given more time for questionnaire completion. The 7 patients treated at J.G. Strydom and Coronation hospitals were excluded due to incomplete blood results.

The only other recent report on PTA in South Africa is from Cape Town. (42) No breakdown of demographic variables was provided, therefore no direct comparison can be made to prevalence in the present study.

4.2.6 Age

Nine HIV positive patients (90 %) were between ages 20 and 34, the one exception was 49 years old. This is a higher proportion compared to the 7th National HIV Survey, 1996 (21) in which approximately 45 % of HIV positive women were between ages 20 - 34. The present study percentage positivity may be inaccurate due to small sample size or may reflect the natural peak incidence of PTA in the second and third decades of life. (40,41)

4.3 Clinical Factors

None of the clinical data were found to be statistically significant when matched for HIV status and gender.

4.3.1 Symptom duration

Forty patients (70 %) had symptoms of sore throat, dysphagia, fever for 5 days or less before presenting to hospital and this correlates with the general history of PTA. (31,41,46-47) This confirms that patients were referred and treated promptly at the ENT departments at the various hospitals.

4.3.2 Antibiotic usage prior to admission

Most patients (65 %) did not receive antibiotics prior to admission which included 9 (90 %) of the HIV positives. This also confirmed the principle that PTA occurs in patients who are inadequately treated for tonsillitis. (40,41) A large proportion of patients (43,8 %) were unemployed and financial constraints may have influenced their lack of treatment or attendance at public or private health facilities.

4.3.3 Previous episodes of tonsillitis and PTA

The majority of patients 37 (65 %) did not report previous recurrent tonsillitis and it was interesting that the majority of patients 37 (65 %) did not receive antibiotics prior to admission in spite of symptoms. Based on these figures it would appear that inadequately treated acute tonsillitis as opposed to recurrent chronic tonsillitis is the major factor predisposing to PTA in this study. Forty six (86 %) of the HIV negatives and 5 (50 %) of the HIV positives had no previous PTA. The 20 % PTA recurrence rate in HIV negatives certainly reflects the figure of 20 % quoted in the world literature. (26,12) Recurrent PTA was statistically significant in the HIV positives ($P=0,0165$). This may be inaccurate because of small sample size or may reflect increased susceptibility to PTA as a result of depressed immunity. There is no current literature to compare HIV positivity and PTA.

4.3.4 Patients knowledge of HIV status

Fifty-three patients (93 %) had no knowledge of their own HIV Status. This mirrors the WHO and UNAIDS HIV/AIDS estimate that 90 % of people living in Africa have no idea of their HIV status. (8) Only 3 patients admitted to knowledge of their HIV status but when asked to respond whether they were HIV positive or not, 9 patients added that they were HIV negative. In a study in urban Kenya of 63 randomly chosen women who tested HIV positive, just one was already aware that she was infected. (8) In developed countries patients knowledge of their HIV status is much higher. For example in Germany, CDC estimates that 75 % of HIV infected patients were aware of their infection in 1996 before a diagnosis was made. (8)

4.4 Laboratory Data

The WCC, CD3 count and lymphocyte count was not found to be statistically significant when matched for HIV status and sex. However, the CD4 ($P = 0,0001$) CD8 ($P = 0,011$) and CD4:CD8 ratios ($P = 0,003$) were statistically significant.

4.4.1 CD4 counts and percentages

The CD4 counts in HIV positive patients were considerably lower than in HIV negative patients. The CD4 count below 500 and greater than 200 correlates with the early and middle stage of HIV disease (Table 1.5) in which the patient is generally asymptomatic and with risk of minor signs and symptoms high and the risk of opportunistic disease moderate. This also correlates with WHO Laboratory Stage B (table 7). A total lymphocyte count mean (SD) of 1,774 (0,725) for HIV positives also places the patient in WHO Lab Stage B. The HIV positives had a CD4 % mean (SD) 27,8 (9,554) which is just below the quoted reference ranges for normal CD4 percentages is 28 - 75 %. (27-28) Unfortunately comparisons cannot be made as no other studies of PTA and tonsillitis related to HIV status and CD4 counts exist, however these levels correspond to the head and neck clinical manifestations described in stages 2 and 3 of WHO classification of HIV infection. (Table 1.1)

4.4.2 CD8 counts, percentages and CD4:CD8 ratio

The CD8 counts in HIV infected patients were mean (SD) 0,864 (0,546) approximately double the CD4 counts in HIV positives. This reflects the nature of the T lymphotropic HIV virus which depletes CD4 (T helper) lymphocyte and causes and increase in CD8 (T-suppressor) lymphocytes, leading to an inverse ratio of CD4:CD8 of 1:2. (18,24,31) This confirms the immune compromise characteristic of HIV infection. (25-26)

4.5 Summary

The clinical and laboratory data reflect that although the patients in the current study sample were generally healthy and exhibited no signs of HIV disease, (WHO Clinical Stage 1) the HIV positive patients had clear statistically significant laboratory evidence of immunocompromise, (WHO Laboratory Stage B). It was even more interesting that the majority of these patients were unaware of their HIV status.

The HIV positivity rate of 18 % was higher than the general heterosexual population positivity rate of 12 % for this region during the time period of the study. (21) This is higher than the estimated adult heterosexual prevalence rate in sub-Saharan Africa of 7.4 %, and almost thirty times higher than the 0.6 % prevalence ratio in the heterosexual, homosexual and drug user population in North America.

4.6 Suggested further research

The current study is the first report of association between PTA and HIV infection. It would be prudent to repeat the study on a larger sample in order to confirm the current findings. A potentially useful addition would be to investigate the infecting bacteria to see if a particular bacterium is significantly associated with HIV infection when PTA is present.

In order to do this a very large sample would be needed so a multicentre study would be best. At the same time a reliable system of blood specimen transport would be required and sufficient researchers to cope with the work load.

4.7 Conclusion

This study has shown that in 57 patients with PTA an HIV positivity rate of 18 % was present, higher than the 12 % rate in the general population for the study region at the time of the investigation. This, coupled with the absence of HIV/AIDS symptoms and a significantly higher rate of previous quinsy among HIV infected patients supports the

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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)

Ref: R14/49 Friedland

CLEARANCE CERTIFICATE

PROTOCOL NUMBER M 950505

PROJECT

Peritonsillar cellulitis and abscesses
in HIV positive patients

INVESTIGATORS

Dr P Friedland

DEPARTMENT
Hospital

Ear Nose and Throat, Johannesburg

DATE CONSIDERED

950526

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE

950531

CHAIRMAN. (Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Professor W A McIntosh
Dept of Ear Nose and Throat, Medical School

=====

DECLARATION OF INVESTIGATOR(S).

To be completed in duplicate and ONE COPY returned to the Secretary at Room 10001, 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.

DATE...16.7.95.....SIGNATURE

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL CORRESPONDENCE

APPENDIX A

MINIMUM PROCEDURE FOR OBTAINING INFORMED CONSENT FOR HIV TESTING OF ADULTS.

This document has been prepared for use in the teaching hospitals and associated health care facilities of the University of the Witwatersrand.

PART 1: EXPLANATORY NOTES FOR HEALTH CARE WORKERS

1. *What is informed consent?*

Informed consent is the legal requirement that is necessary before a doctor or other health care worker may examine, investigate or manage a patient.

2. *Informed consent to HIV testing must be specific and explicit.*

Consent to HIV testing is not covered by the usual contractual agreement which is implied when a patient consults a doctor. The reason is that the implications of a positive test in the present social climate may be extreme. (This may change as attitudes to and knowledge and understanding of HIV infection change).

3. *What does informed consent imply in the context of HIV testing?*

Informed consent implies that the patient has received a minimum of pre-test information and understands the following:

- 3.1 the reasons or purpose for which the test is being performed;
- 3.2 the potential advantages and disadvantages of having his/her HIV status determined;
- 3.3 the influence the result of the HIV test may have on his/her treatment;
- 3.4 the possible psycho-social impact of a positive test.

4. *Post-test counselling*

The principle of informed consent implies that once the patient's test is known (positive or negative) appropriate counselling will follow. The health care worker should therefore ensure that the HIV-positive patient is directed to appropriate facilities where he/she will receive counselling and care, and if possible, sexual partners and family will be counselled.

5. *Documentation*

It is recommended that a note be made in the patient's file/record that informed consent for HIV testing has been obtained.

APPENDIX B

**PART II : MINIMUM PROTOCOL FOR OBTAINING INFORMED
CONSENT FOR HIV TESTING OF ADULTS.**

1. I/We/the doctor(s) wish(es) you to be tested for HIV infection.
2. This is a test on your blood which will establish whether or not you have been infected with the virus which causes AIDS
3. The reason/s I want this test to be performed is/are:
(Indicate appropriate option(s) chosen)
 - 3.1 to help me diagnose your illness;
 - 3.2 to help me give you proper treatment;
 - 3.3 because you may need to have an operation where the health care workers may wish to know your HIV status;
(Health care workers should be aware that pre-operative HIV testing is condoned only where certain well-defined high risk or exposure-prone surgical procedures are contemplated, as set out in SAMDC Guidelines)
 - 3.4 because you have asked to be tested for HIV infection.
4. If the test is positive, your treatment may have to be modified in your own interests.
(Treatment should not be sub-optimal because of any perceived potential risk to the health care worker)
5. You should realise now that if the test shows you to be HIV positive, this means that :
 - 5.1 you may be able to make changes to your lifestyle which will improve your quality of life;
 - 5.2 you will in all likelihood eventually develop AIDS, which at present can be treated but can not yet be cured;
 - 5.3 you may need to change your sexual behaviour to avoid infecting other persons;
 - 5.4 your result will be treated confidentially, but should it become known you may suffer discrimination in obtaining work, insurance and medical aid cover.
6. A negative test is not an absolute guarantee that you have not been infected.

Note : In the case of a minor or a non-competent adult, the consent of a parent, or guardian must be obtained

[A separate protocol is available for children (minors)]

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