

HIV/AIDS Cancer and Impact on Surgical Practice: Implication for the Surgeon

A. Z. Sule

SUMMARY

Background: The most recent UNAIDS report on the global epidemic estimated the total number of people living with HIV in 2008 to be 33.4 million (31.1-35.8 million) world wide, two-third of known carriers of HIV are living in sub-Saharan Africa. Although HIV prevalence appears to be stable, much remains uncertain about the direction of the epidemic. In the developed countries, the increased cancer risk among immunocompromised persons with HIV/AIDS (PHA) is well observed. Now a person diagnosed with HIV as a young adult in a resourcerich country can expect to live for 30 or 40 years after infection because of public health education and community awareness in conjunction with advances in antiretroviral therapy. In recent, large scale cohort studies, the incidence of non-AIDS morbidity and mortality rivals that related to AIDS and these non-AIDS conditions including cancer occur at higher rates in those with on-going HIV replications and lower CD₄ cell count.

Data Sources/Study selection: Information was obtained by searches of medical journals, examination of reference lists and web resources. Peer-reviewed articles on HIV/AIDS cancer and its impact on surgical practice from references were obtained.

Data Synthesis/Conclusion: The severe immunodeficiency cause by advanced HIV infection has been recognized as capable of causing three types of malignancies: Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL) and cervical cancer. Kaposi's sarcoma and non-Hodgkin's lymphoma occur at exceptionally high incidence with relative risk being hundred-fold above those in uninfected populations. Cervical cancer is an AIDS-defining cancer when it occurs in HIV-infected woman and the relative risk is 5 to 10-fold. Although these are the only forms of cancer that have been designated as AIDS-defining, several other malignant diseases have been reported to occur more frequently following HIV infection than in its absence. The distribution of these cancers varies with the socio-demographic characteristics of the population studied indicating risk factors for cancer differs amongst populations. There remain some controversies as to why cancers occur at increased rates. In immunosuppressed PHA, risk of AIDS-related cancer generally increased with degree of immunosuppression. In Hodgkin's lymphoma, incidence has an inverse relationship with CD₄ count. Some tumours are observed more frequently in PHA

.....
From: Department of Surgery, Jos University Teaching Hospital.

Correspondence: Dr. A. Z. Sule

because of lifestyles that expose them to specific carcinogens such as lung cancer. Other tumours have been reported to have marginal or inconsistent increases in PHA, and their associations are still controversial.

Over the past 20years, AIDS has been transformed from a disease that was almost inevitably fatal to a chronic condition that is manageable. The longer survival will likely increase the importance of cancer as a clinical problem. In recognition of the increasing importance of cancer as a cause of mortality and morbidity in PHA, managing persons affected according to standard practices regardless of HIV status is stressed. These practices should emphasize helping PHA avoid high-risk lifestyles such as smoking and screening for early detection of cancers. Paying detail attention to safety survival practices and appropriating the right choice of procedures for HIV related cancer surgeries in addition to identification of preoperative chronic conditions such as diabetes and hypertension, etc. is important. With the population's geographic and social diversity, Nigeria also presents unique research opportunities relating to cancer for the surgeon that can be embedded in programs targeting HIV/AIDS.

Niger Med J. Vol. 51, No. 3, July–Sept., 2010: 101 – 108.

Key words: HIV/AIDS, cancer, surgical practice

INTRODUCTION

In June 1981 the Centres for Disease Control published a report of 5 patients with pneumocystic carinii.¹ A month later, an article published by the New York Times stated: "Doctors in New York and California have diagnosed among homosexual men 41 cases of rare often rapidly fatal form of cancer (Kaposi sarcoma). The cause of the outbreak is unknown, and there is as yet no evidence of contagion."² These reports marked the beginning of Human Immunodeficiency Virus (HIV) or Acquired Immune Deficiency Syndrome (AIDS), a major epidemic in the last half of the twentieth century and it is on the threshold of its third decade of existence. The most recent UNAIDS report on the global pandemic estimated the total number of people living with HIV in 2008 to be 33.4 million (31.1-35.8 million) worldwide, two-thirds of known carriers of HIV are living in sub-Saharan Africa.³

HIV-1 is the etiological agent of this epidemic and has a cell-surface protein (gp120) which recognizes and binds to receptors on several types of human cells. In particular, HIV binds to the CD₄ receptor which is carried in high density on the surface of the CD₄+ lymphocytes (helper T-lymphocytes). The

extent of depletion in immune function correlates with loss of CD₄⁺ helper T-cells. Functional impairment of CD₄⁺ lymphocytes results in disorder of antibody production, delayed hypersensitivity and macrophage function. In addition, secretory immune deficiency occurs in the gut with depletion of immunoglobulin A (IgA) containing jejunal and rectal plasma cells. This results in vulnerability to many opportunistic infections, an increased risk of cancer development and malnutrition due to reduction in nutrient absorption and malnutrition.

The severe immunodeficiency caused by advanced HIV infection has been recognized as capable of causing three types of malignancy: Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL) and cervical cancer.⁴ These cancers that occur at AIDS onset or during the AIDS course are the only forms of cancers that have been designated as AIDS-defining. The risk of these AIDS-related cancers generally increased with the degree of immunosuppression. Over the past 20 years, AIDS has been transformed from a disease that was almost inevitably fatal to a chronic condition that is manageable.⁵ The evolution began modestly in the early 1990s with the introduction of protease inhibitors and highly active antiretroviral therapy (HAART). Between 1996 and 1998, HIV related morbidity and mortality decreased by 60% in the United States.^{6,7,8} As of December 2008, approximately 4 million in low and middle-income countries were receiving antiretroviral therapy – a 10-fold increase over 5 years (World Health Organization, UNCF, UNAIDS 2009)³

A person diagnosed with HIV as a young adult in a resource-rich country and those in low and middle income countries who have access to HAART can be expected to live for 30 or 40 years after infection.⁴ In most individuals, it appears likely that profound immunodeficiency can be kept at bay for decades. Thus the focus of HIV medicine has shifted to the occurrence of disease in people with mild or moderate immune deficiency. In recent large scale cohort studies, the incidence of non-AIDS morbidity and mortality rivals that related to AIDS and these non-AIDS conditions occur at higher rates in those with ongoing HIV replication and lower CD₄⁺ cell count.^{9,10} If people are likely to live for 40 years what then will this mean for cancer incidence? It has been known for about a decade that a wide range of cancers occur at increased rate in people with AIDS.⁴ More recently there has been a growing appreciation that this applies to HIV before AIDS diagnosis and that a range of mainly infection related cancer occurs at increased rates.^{11,12}

It has been estimated that 10% of all HIV/AIDS patients will go on to develop cancer.¹³ In Nigeria with over 3 million people affected by HIV/AIDS, this means that HIV/AIDS is responsible for an additional 300,000 cases of cancer that would not have been there. Increased access to affordable highly active antiretroviral therapy to control HIV replication and drugs to treat infectious complication has reduced the effects of competing mortality and the importance of cancer in person with HIV/AIDS (PHA) has likely amplify. This report describes the state of knowledge about cancer pattern in PHA and its impact on surgical practice.

Data Sources/Study selection

Information was obtained by searches of medical journals, examination of reference lists and web resources. Articles on HIV/AIDS cancer and its impact on surgical practice from peer-reviewed and references were obtained.

Data Synthesis

HIV/AIDS Cancer Incidence

In developed countries cancer incidence in PHA is driven largely by Kaposi's sarcoma in homosexual men, a group commonly co-infected with the Kaposi's sarcoma associated herpes virus (KSHV). Kaposi's sarcoma (KS) and non-Hodgkin's lymphoma occur at exceptionally high incidence with a relative risk being 100s-fold above those in uninfected population.^{14,15} Cervical cancer has a relative risk increase of 5 to 10-fold.^{14,15} Hodgkin's lymphoma though not yet accepted as an AIDS-defining cancer in HIV-positive person, its risk is increased 10 to 15-fold.^{14,15} In immunosuppression¹⁶ some tumours are observed to have marginal or inconsistent increases in PHA and their association with level of HIV/AIDS immunosuppression is still controversial.^{17,18,19} such cancers include: Lung cancers, squamous cell carcinoma of the conjunctiva, mekel cell carcinoma of the skin, stomach cancer, testicular cancer and melanoma, leukaemia, multiple myeloma and liver cancer.

Aetiology of HIV/AIDS Cancer

The reasons for the observed increase in the mainly infectious-related cancers in PHA remains unresolved. Although researchers do not know the exact reasons for the increased risk of developing some of these cancers, there are several theories as to why HIV-positive people are susceptible, such as increased life expectancy due to antiretroviral drug;²⁰ weakened immune system related to the virus or the effects of antiretroviral and the likelihood of increased high risk behaviour in people living with HIV.²¹ Apart from a real association between HIV and cancer, it is important to consider the possibility that increased medical surveillance in people with HIV may have led to the diagnosis of cancer that would otherwise remain inapparent.²² This effect is expected to be greatest for those forms of cancers with a long latency that may be detected by screening and for those that are most clinically apparent such as cutaneous cancers. A well known researcher recently wonders if antiretroviral would be cancerogenic. People with HIV have high rates of smoking, alcohol consumption and exposure to oncogenic sexually transmitted and blood-borne viruses. It is certainly likely that these confounding life-style cancer risk factors make some contribution to increased cancer risk in this population.

The recent finding that immune suppressed transplant recipient share a similar pattern of increased cancer risk with PHA strongly suggest the hypothesis that immune deficiency is responsible.¹¹ Increased cancer rates have been documented in both populations for those cancers related to infection with Epstein-Barr Virus (non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma), human herpes virus 8 (Kaposi's sarcoma), human papilloma virus (anogenital and head/neck cancers), helicobacter pylori (stomach), hepatitis B and C (liver cancer) and

polyomavirus (Merkel cell carcinoma). If cancer is related to immune deficiency, then it is, at least possible that improving immune function through HAART will reduce cancer incidence. This has been conclusively demonstrated for Kaposi's sarcoma and non-Hodgkin's lymphoma in which cancer are closely linked to CD₄+ cell count and begin to decrease within months of the institution of HAART.^{23,24} The picture is much less clear for non-AIDS-defining cancers as studies have mostly simply described time trend in rates rather than studying the association between HAART, or CD₄+ cell count and risk of cancers at the level of the individual. For two of the most common cancers related to HIV infection, Hodgkin's lymphoma and anal cancer, there is no evidence of any recent decrease in rates among HIV infected individuals, and in the case of anal cancer, incidence may actually be increasing.¹² Nevertheless, at an individual level, lower CD₄+ cell count was shown to predict increased risk of non-AIDS-defining cancer in a cohort of individual starting HAART.²⁵

A likely reason we have not seen striking reduction in non-AIDS-defining cancers in cohorts of HIV-infected individuals is that for these cancers, risk is clearly less strongly associated with profound immune deficiency than are Kaposi's sarcoma and non-Hodgkin's lymphoma. This knowledge has been established in AIDS-defining cancers where the introduction of HAART led to massive decline in the incidence of primary brain lymphoma but little if any in rates of Burkitt's lymphoma.²⁶ It is quite possible, although unproven, that further improvement in immune function associated with HAART use will result in declining risk for important non-AIDS-defining cancers such as anal cancer and Hodgkin's disease and further reduction in AIDS-defining cancers. If a CD₄+ cell count of 350, then this could be an important factor to take into account in question of when to start HAART and in determining the optimal goal of HAART.

To determine the association of immune deficiency and HAART with non-AIDS-defining cancer we need data on cancer occurrence from large observational prospective studies which collect regular data on CD₄+ cell count. The relative rarity of each specific cancer type means that large international pooling efforts will likely be required to answer these questions.

FEATURES OF HIV/AIDS CANCER TYPES

Kaposi's Sarcoma (KS)

This is a multifocal angiosarcoma derived from proliferating capillary vessels and perivascular connective tissue. There are a number of different types of kaposi sarcoma. An indolent slow-growing form is seen mainly in Jews, Italians and Africans especially the Bantus of Uganda and Zaire who are about 45 years. An aggressive highly malignant epidemic form related to AIDS is seen in HIV positive patients irrespective of race in their third decade.

Over 95% of Kaposi' sarcoma, irrespective of their source are infected with the human Herpes Virus 8 also known as Kaposi's sarcoma-associated Herpes virus (KSHV). Specific KSHV antibodies are present in 70-90% of Kaposi sarcoma (KS) patients and in 100% of the immuno-compromised patients.^{14,15}

Patients with KS tend to develop a second malignancy, most often Hodgkin's lymphoma. In developed countries, cancer incidence is driven largely by KS in homosexual males; a group commonly co-infected with the KSHV.^{14,15} KSHV infection is required for KS to develop, and population variation in KS incidence seems to reflect differences in the prevalence of KSHV. Although KS can occur with severe immuno-suppression, the risk increases progressively as CD4+ cell count decline. In developed countries, KSHV occurs predominantly in men who have sex with men (30% infected compared to 1-3% infected in other groups).^{14,15} There is fatal outcome from AIDS in 9-12 months.

The disease begins as nodules or plaques predominantly in the skin of the limbs but the nodules may be found in many internal organs such as the intestine, mesentery, lungs, liver, lymph nodes and rarely the brain in HIV positive patients. The treatment of HIV/AIDS-related KS usually cannot cure the cancer, but it can help relieve pain or other symptoms. Treatment of HIV/AIDS with highly active antiretroviral drugs can effectively control the virus in most patients. This can then be followed by palliative care for KS. The efficacy of taxanes (e.g. paclitaxel, docetaxel) and anthracyclines, as agents with anti-angiogenic properties has been shown for patients with AIDS-associated KS and in those with refractory or life threatening KS with HIV infection.

Non-Hodgkin's Lymphoma (NHL)

HIV/AIDS-related non-Hodgkin's lymphoma (NHL) is the second most common cancer associated with HIV/AIDS after KS. There are different subtypes of NHL. The most common subtypes of NHL in people with HIV/AIDS are primary central nervous system lymphoma (affecting the brain and spinal cord), found in 20% of all NHL cases in people with HIV/AIDS, primary effusion lymphoma (causing fluid to accumulate around the lungs or in the abdomen) or intermediate and high-grade lymphoma. More than 80 percent of lymphoma in people with HIV/AIDS are high-grade β -cell lymphoma, while 10 percent to 15 percent of lymphoma among people with this cancer who do not have HIV/AIDS are of this type. It is estimated that between 4 percent and 10 percent of people with HIV/AIDS developed NHL. Human herpes virus-8 infection is associated with primary effusion lymphoma while Epstein's Barr Virus (EBV) is a herpes-related virus that is associated with primary central nervous system lymphoma, high-grade β -cell lymphoma and primary effusion lymphoma.

The two main treatment modalities of HIV/AIDS-related non-Hodgkin lymphoma are chemotherapy and radiotherapy. Previously, chemotherapy treatment for HIV/AIDS-related NHL was given at lower doses due to the person's weakened immune system. However, with improving antiretroviral agents, patients with AIDS-related NHL are usually treated with the same doses of drugs given to people with lymphoma who do not have HIV. Rituximab (Rituxan) is a monoclonal antibody that is directed against the β -lymphocytes and is used in combination with chemotherapy for most patients. For people with HIV/AIDS-related lymphoma, radiation therapy may or may not be given

along with chemotherapy.

HIV/AIDS Cervical Cancer

Women with HIV/AIDS have a higher risk of developing cervical intraepithelial neoplasia (CIN), a precancerous growth of cells of the cervix. CIN occurs in 11 to 29 percent of women with AIDS and may be associated with human papillomavirus (HPV) infection.²¹ High-grade CIN can turn into invasive cervical cancer, and women with AIDS are at higher risk for developing this type of cancer. The risk of invasive cervical cancer in women with AIDS does not correlate with the degree of immunosuppression.²⁷ The explanation is that women in areas with limited medical care have a higher competing mortality and die before dysplasia can progress to cervical cancer. As people with HIV/AIDS (PHA) survive longer, these cancer could become increasingly important making screening in PHA for precancerous lesions a highly public health priority.

Treatment for women with the precancerous condition CIN are generally not as effective for women with HIV/AIDS due to weakened immune system. Often, the standard treatment for HIV/AIDS can reduce the symptoms of CIN. Women with invasive cervical cancer and whose HIV/AIDS is well controlled by medication are generally treated similarly to women who do not have HIV/AIDS.

HIV/AIDS Anal Cancers

Individuals infected by the human immunodeficiency virus (HIV) have a high risk of infection by human papilloma virus (HPV) as well as a high incidence of anal intraepithelial neoplasia (AIN) and anal cancer caused by HPV.²⁸ The potentialization of the effect of HIV by HPV is not fully understood.²⁹ These changes may be due to a deficient response of the immune system to HIV or direct interaction between HIV and HPV. In anal cancer patients, the frequency of detection of high-risk HPV's ranges from 70 to 100 percent, depending on origin, location, sexual orientation and HIV status.³⁰ Anal cancer has similar biological and epidemiological properties to cervical cancer. Like the cervix, the anal canal has a transformation zone in which the columnar epithelium of the rectum joins the squamous epithelium of the anus. As the cervical transformation zone, the ano-rectal junction is common site of anal HPV infection and development of AIN, a potential precursor of anal cancer. Anal intraepithelial and cervical neoplasias present the same histological patterns and are associated with the same types of HPV. Transmission and acquisition of HPV infection occurs through the mucocutaneous epithelial tissue. As a result in the incidence of cervical cancer after the implementation of oncotoc cytology in recent decades, anal examination of high-risk groups such as HIV-positive patients has been recommended for the detection of anal cancer. The examination for the detection of premalignant lesion is done by anoscopy under coloscopic vision and histology. This is better than anal cytology for the diagnosis of these lesions.³¹

Hodgkin's Lymphoma

Hodgkin lymphoma incidence has an inverse relationship with CD₄ + cell count in which moderate decrease in CD₄ + cell

count greatly increase risk but risk decrease with severe immunodepression.²¹

HIV/AIDS Neck/Head Cancers

Evidence of an association is weak. The increases are mainly at buccal/palatal site and are specifically associated with chewing tobacco and bettle nut rather than at pharyngeal and tonsillar sites which are human papillomavirus associated.²¹

Other HIV/AIDS Cancer

Cancer risks at other or unexpected sites appear to have little increase. When such increase are reported, much of the association is likely to be because of confounding rather than a direct HIV or immuno-suppression effect.^{17,18} The 2-fold higher risk of lung cancer is likely explained by an increased frequency of smoking. Marginally significant increase in liver cancer risk may be because both HIV and Hepatitis B and C are transmitted through needle sharing in drug and blood product use. Conjunctival tumour risk could be increased because for reasons of occupation and ultraviolet light exposure is more common in PHA. The excess risk of other rare tumours is small. It is therefore, difficult to determine if exposure in PHA might be different from those in the general population because their etiologies are not known.¹⁷ Recently, an association between Merkel cell carcinoma and polya virus established in PHA demonstrates the potential for discovering new viral associations.²¹

HIV/AIDS Cancer and Impact on Surgical Practice

The longer survival of patients with HIV/AIDS will likely increase the importance of cancer as a clinical problem as incidence rises exponentially with age. Surgical involvement in the care of HIV-positive patient diagnosed with cancer will grow with procedure ranging from diagnostic to palliative. It is anticipated that there will be a corresponding increase in surgical workload since a surgeon plays a principal role in the orchestration of the cancer patient care. The surgical curriculum has undergone a change to ensure surgeons are knowledgeable with regard to their much reduced, although still important role in contemporary treatment of AIDS.³² However, there is limited specific information concerning the overall impact of HIV/AIDS-related malignancy on surgical practice. Surgeons need to be aware of the disease when deciding on the course of surgery.

SURGERY

Anaesthesia

Twenty to 25 percent of HIV-Positive patients will require surgery during their illness.³³ Anaesthesiologists and surgeons need to be aware of the disease when deciding on course of anaesthesia and surgery. This multi-organ disease may be complicated either by opportunistic infections, substance abuse or antiretroviral therapeutic drugs which can have an impact on anaesthesia.

Central and Peripheral Nervous System

Some 30% of adults and 50% of children suffering from AIDS will develop neurological disorders.³⁴ In the early stage of infection, headache, photophobia, meningoencephalitis,

depression, irritability, Guillain-Barré-like syndrome or cranial and peripheral neuropathy can be observed. The latent phase of the disease is associated with demyelinating neuropathy and cerebrospinal fluid pathology, while the late period may witness meningitis, focal and diffuse encephalopathy, myelopathy, myopathy and peripheral neuropathy. As the central nervous system is the first crucial organ to be affected by anaesthetic drugs, preoperative evaluation of cognitive and neurologic dysfunction is important. Patients with AIDS are more sensitive to opioids and benzodiazepines. The probable mechanism is based on increased interleukin-1 levels causing an increase in amino butyric acid mediator production.³⁵ HIV infection and its complication such as intracranial masses or opportunistic infections may cause cerebral oedema, cerebral haemodynamic disturbances and increased intracranial pressure (ICP) and generally preclude the use of neuroaxial anaesthesia.

Pulmonary Abnormalities

Pulmonary manifestations are caused mainly by opportunistic infections. The most common was pneumocystic carinii but recently pulmonary tuberculosis is seen increasingly among young women of childbearing age. It may be complicated by pneumatoceles, pneumothorax or respiratory failures. Computer tomography and not conventional x-ray may reveal bilateral haziness of both lungs in this condition.

Cardiac Manifestation

In the advanced stage of HIV-infection, myocarditis is common and is caused by opportunistic infection. Pulmonary hypertension, accelerated coronary arteriosclerosis, a decrease in left ventricular contractibility and myocardial infarction are reported in young HIV patients.³⁶ Preoperative cardiovascular monitoring of these patients is of crucial importance.

Gastrointestinal Abnormalities

In advanced AIDS, oesophageal reflux is common which may increase the risk for pulmonary aspiration on induction of anaesthesia. Abnormal liver function test are also common in advanced AIDS and reflect the decreased metabolic and secretory ability of the liver in addition to coagulation abnormalities. Electrolyte abnormalities are caused by diarrhea and decreased oral intake resulting from dysphagia or nausea.

Haematological Abnormalities

Bone marrow involvement and coagulation abnormalities may result from HIV infection, HAART, nutritional factors or neoplastic diseases. Thrombotic episodes and various predisposing abnormalities related to a hypercoagulable states that correlate with the severity of HIV disease are reported in the literature. The co-existence of HIV related illness such as malignancy and autoimmune disease as well as antiretroviral drug therapy may also predispose these patients to thromboembolic events.

Renal Abnormalities

HIV patients are at risk for developing renal disease caused by HIV-infection, viral hepatitis drug abuse, antiretroviral

drugs and dehydration. The HIV-associated nephropathy is a distinct clinico-pathological syndrome and presents as a nephritic syndrome. Its progression to end-stage renal disease can be slowed down by the use of steroid and angiotensin-converting enzymes inhibitors.

Endocrine and Metabolic Abnormalities

Primary or secondary adrenal insufficiency is the most serious endocrine abnormality in HIV patients. Thyroid function test in AIDS patients may be abnormal, but clinical hypothyroidism is rare. Hypocalcaemia caused by islet cell damage and resulting from pentamidine treatment is another metabolic abnormality. Hypoglycaemia may also result from hyperinsulinaemia in association with hypopituitarism or as a complication of protease inhibitor treatment.

HIV Therapy Interaction with Anaesthesia

More than 14 drugs have been used in HIV/AIDS therapy. Most of them produce side effects that interact with anaesthetic drugs. Non-nucleoside reverse transcriptase inhibitor, nevirapine causes cytochrome p₄₅₀ enzyme induction and may decrease serum levels of some anaesthetic or sedative drugs (i.e Midazolam, fentanyl). Protease inhibitors are metabolized by cytochrome p₄₅₀ isoenzyme, cytochrome p_{3a4}. They competitively inhibit the enzyme and may increase the effects of drugs metabolized by cytochrome p₄₅₀.

Anaesthetic Management

Prior to surgery, healthcare providers should perform a physical examination, detail medical history and laboratory testing to determine the patients' overall health. Assessment of risk and co-existing diseases during preoperative evaluation should focus on the patient's status type of surgery and anaesthesia, which combined with the Centres for Disease Control stage of HIV infection, immunologic status (CD₄+ cell count) and the existent opportunistic infection and malignancy, should allow a good prediction for the perioperative risk of the HIV-patient to be construed.

Advanced HIV infection, when accompanied with opportunistic infection or malignancies, may complicate the perioperative course and management. The CD₄+ cell count/mortality relationship is useful in risk assessment as it falls below a critical level increases the peri-postoperative mortality and morbidity. Preoperative assessment should therefore, include evaluation of opportunistic infections, treatment with antiretroviral or anti-opportunistic drugs and laboratory work-to include complete blood count, clotting functions, and glucose, liver and renal function tests. Verification of the immunological status i.e the CD₄+ lymphocyte cell count and viral load during the previous 3months is important. Patients with a history or signs of cardiac or pulmonary dysfunction should under a more thorough evaluation (blood gases, pulmonary function test, echocardiography, cardiac effort test and radioactive cardiac scanning or even cardiac catheterization in addition to the usual electrocardiography and chest radiography routine done.)

Anaesthetic Techniques

General anaesthesia is considered safe, but drug interaction and their impact on various organ systems should be considered preoperatively. Regional anaesthesia is often the technique of choice. Yet, one must consider the presence of neuropathies, local infection or blood clotting abnormalities.

SURGICAL PROCEDURES AND HIV/AIDS CANCER

Risk and Implications of Surgical Transmission of HIV

Surgical intervention has become a common component in the management of patients infected with the HIV or suffering from the clinical consequences of AIDS. At the onset of the AIDS epidemic in 1984, pessimism was pervasive regarding operative treatment of the HIV/AIDS patient because of poor surgical outcomes and concern about accidental exposure and infection with the virus.³² Current and accurate knowledge about the modes and degree of risk transmission has lessened apprehension but not caution in the operating room. All surgical team members must routinely practice safe techniques. This caution has become more appropriate since risk with percutaneous exposure to HIV is greater where body fluids contain higher titre of HIV as in AIDS with co-existing AIDS-related cancer.

Prophylaxis after Exposure

Occupational exposure should be considered as urgent medical conditions to ensure timely post exposure management and administration of Hepatitis B immunoglobulin, Hepatitis B vaccine and/or antiretrovirals. Recommendations for HIV post exposure prophylaxis include a basic 4-week regimen of two drugs. The combination of agents for HIV exposure are zidovudine and lamivudine; lamivudine and stavudine or didanosine and stavudine. An expanded regimen that includes the addition of a third drug is recommended for HIV exposure that pose an increased risk for transmission. In special circumstance (e.g delayed exposure report, unknown source persons, pregnancy in the exposed person, resistance of the source virus to antiretroviral agents or toxicity of the prophylaxis regimens), consultation with local experts is advised.

Surgical Complications

It has been suggested that HIV patients may have an increased risk of surgical complications (especially bleeding, nerve damage and infection), because they have weakened immune system. Regardless of surgical procedure, there is a 13.3% mortality rate 6 months postoperatively when the CD₄+ count is <50/mm³ and a 0.8% mortality rate when the CD₄+ count is more than 200/mm³.³⁷ Late diagnosis and delayed surgical exploration in HIV/AIDS patients have resulted in increased morbidity and mortality risk (57-87%), while elective procedure carried a 43% mortality rate.^{38,39} These poor outcomes prompted suggestions that operative procedure in AIDS provided little benefits. However, with new anti-viral therapy the operative mortality is 11% to 19% for emergency abdominal surgery and the risk-benefit analysis is more in favour of laparotomy.^{39,40,41}

However, there is currently no scientific data on the prevalence of surgical complication for HIV patients compared

to non-infected patients. Though operative outcomes are now more favourable with mortality and morbidity rates similarly to patients without HIV infection, the coexistence of cancer and HIV infection may, however, expose a patient to significant risk of peri-postoperative complication and the risk benefits analysis becomes an important consideration.

It is evident that HIV/AIDS poses an unusual and challenging surgical problem. Advances in medical technology will no doubt continue to witness a surge in the application of minimally invasive procedure and devices such as cutting diathermy and stapling machine in HIV/AIDS cancer surgical procedure to limit the risk of transmissions.

PREVENTION OF HIV/AIDS CANCERS

Early Detection

As people with HIV/AIDS (PHA) live longer most may develop cancer lesions during the course of their HIV infection. The time interval between the onset of the precursor lesion and the onset of invasive cancer can be exploited to reduce their incidence. Cancer treatment can be very hard on the immune system of people with HIV. So it is important for people with HIV to prevent cancer and find cancer in its early stages.

PHA should have regular medical check-ups. Such tests as pap smear, colon or rectal examination, oral examination by dentist every six months, mammography should be taken regularly. Warning signs of cancer that may be observed at self-examination include:

- a Sore-throat that does not heal. Also look for new growths on the skin ovary changes in the size, color or shape of moles or words.
- b A lump or hardness in the skin, especially in female breasts and in the male testicles and groin area.
- c. Oral examination: should determine the presence of sores; check the inside of the mouth, lips, gum and tongue for swelling or bleeding, white patches, scab or cracks.
- d. Changes in bowel or bladder habits.
- e. Heartburn or trouble swallowing that does not go away.

Healthy Living to Prevent Cancer

- i Quitting smoking: this can greatly reduce the risk of cancer of the mouth, throat, lungs, stomach and liver.
- ii. Take all your HIV medications on schedule: A stronger immuno system is the best protection against many types of cancer.
- iii. Protection from other viruses: HIV, HPV, Hepatitis and herpes are passed through sex or sharing needles or other equipment used to inject drugs. The use of condom the right way every time is advised during sex. Never share needles or drug works.
- iv Eat healthy foods: Foods such as mineral, vitamins and fibres, vegetables, fruits, rice, bean can lower risk of cancers of the stomach, colon, breast, rectum and prostate.
- v. Get plenty of exercise and stay a health weight '
- vi Avoid drugs and alcohol: Drugs and alcohol hurts the immune system
- vii Protection from the sun: Wear a hat , sunglasses and

clothing

Research

Studies in place where environment exposure differ greatly in different population offer new opportunities to identify novel association between HIV/AIDS and cancer or clarify risk factors. Finding new association is of general scientific interest. The recent finding of a polyomavirus associated with marked cell carcinoma, an HIV/AIDS related tumour demonstrate the potential for new viral association. In PHA, reducing mortality from preventable infection like tuberculosis and candida is the primary priority. Success in these goals will reveal new clinical challenges including cancer. Thus the world stands at a crossroads where knowledge about cancer in PHA is likely to contribute to understanding cancer itself and may also provide data to develop public health responses to the emergent problem. The renewed focus on HIV/AIDS care makes cancer monitoring and research in PHA timely. In this context systematic gathering of treatment outcome data for cancer in PHA and comparing response is essential. This data that will determine the association of immune deficiency and HAART with non-AIDS-defining cancer ought to come from large observation prospective studies that collect data on CD₄⁺ cell count.

The relative rarity of each specific cancer type means that large international pooling efforts will likely be required to answer these questions. Nevertheless, as cancer incidence rises exponentially with age, we can expect to see many more cases of cancer. Such data will allow the development of treatment regimens that might best be suited to PHA and permit the investigation in antiretroviral therapy to be meaningful to all PHA. Research can provide practical as well as academic benefits, informing both healthcare and the public health planning. These studies also encourage the development of epidemiologic and laboratory capability. Researchers should focus on the advantages conferred by undertaking studies that might be uniquely done in their own context and are likely to have public relevance to their environment.

CONCLUSION

The focus of HIV medicine is shifting as AIDS is gradually being transformed from a disease that was almost inevitably fatal to a chronic condition that is manageable. The longer survival is increasing the importance of cancer as a cause of morbidity and mortality in PHA, clinical practices that encourage screening for early detection of cancer and changes of high-risk lifestyle for cancer are advocated. Surgeons need to be aware of HIV/AIDS cancer and its course during anaesthesia and surgery. As reasons for the observed increase in the mainly infectious-related cancer in PHA remain unresolved research to identify novel association between HIV/AIDS, CD₄⁺ cell count and HAART or clarify risk factors is of scientific interest. Such knowledge can provide practical and academic benefit that will better health services tremendously.

REFERENCES

1. Centres for Disease Control. Pneumocystic pneumonia. *MMWR Morb Mortal Wky Rep.* 1981; **30**: 250–252.

2. Aitman L. Rare cancer seen in 41 homosexuals. *The New York Times.* New York July 3, 1981. Available at <http://www.mytimes.com/1981/07/03/health/03AIDS.html>. Accessed May 1, 2004.
3. UNAIDS. Report on global HIV/AIDS epidemic. Geneva: UNAIDS, 2008.
4. Antiretroviral therapy cohort collobartion. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: A collobarative analysis of 14 cohort studies. *Lancet* 2008; **372**: 293–299.
5. Sepkowitz. AIDS–The first 20 years, *N Engl J Med.*, 2001; **344**: 1764–72 [PMID: 1139644].
6. Palella F. J Jr, Delaney K. M., Moorman A. C., Loveless M. O. fuhrer J., Satten G. A. *et al.* Delcining morbidity and mortality among patients with advanced human immuno-deficiency virus infection. HIV outpatient study investigations. *N Engl J Med.* 1998; **338**: 853–60 [PMID: 9516219].
7. Jones J. L., Hanson D. L., Dworkin M. S., Alderton D. L., Fleming P. I., Kaplan J. E. *et al.* Surveillance for AIDS-redefining opportunistic illnesses, 1992-1997. *MMWR CDC Surveill Summ.* 1999; **48**: 1–22 [PMID: 12412613]
8. Centres for Disease Control and Prevention. Trends in annual age-adjusted rate of death due to HIV diseases, USA 1987-2002. Atlanta: Centres for Disease Control and Prevention; last updated 27th June 2005.
9. Lewden C., May T., Rosenthal E. *et al.* Changes in causes of death among adults infected by HIV between 2000 and 2005: The mortalities 2000 and 2005 surveys (ANRS EN 19 and Motavic). *J. Acquir Immune Deiiic Syndr.* 2008; **48**: 590–598.
10. Palella F. J. Jr., Bakar R. K., Moorman A. C. *et al.* Mortality in the highly antiretroviral therapy era: Changing causes of death and disease in the HIV outpatient study. *J. Acquir Immune Deiiic Syndr.*, 2006; **43**: 27–34.
11. Grulich A. E., Van Leeuwen M. T., Falster M. d., Vajdic C. M. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: A meta-analysis. *Lancet* 2007; **370**: 59–67.
12. Patel P., Hanson D. L., Sullivan P. S. *et al.* Incidence of types of cancers among HIV-infected persons compared with the general population in the United States 1992-2003. *Ann Intern Med* 2008; **148**: 728–736.
13. Joint United Nations Programme on HIV/AIDS (UNAIDS): Report on the Global AIDS Epidemic. UNAIDS/08 25EJC151E. Geneva; 2008.
14. Biggar R. J. Epidemiology of malignancies in HIV/AIDS: In AIDS-related cancers and their treatment. Edited by Feigal E., Levine A. M., Biggar R. J. New York Marcel Dekker; 2000: 25–58.
15. Frisch M., Bigger R. J., Engels E. A., Goedert J. J. AIDS-cancer match registry study group. Association of cancer with AIDS-related immunosuppression in adults. *JAMA* 2001; **285**: 1736–45.
16. Biggar R. J., Chaturved A. K., Goedert J. J., Engel E. A. HIV/AIDS cancer march study. AIDS-related cancer and severity of immunosuppression in persons with AIDS. *J. Natl Cancer Inst.* 2007; **99**: 962–72.
17. Waddell K. M., Lawallen S. B., Atonyi A. C., Harrington C. S., Liomba G. Carcinoma of the conjunctiva and HIV infection in Uganda and Malawi. *Br. J. Ophthalmol* 1996; **80**: 503–8.
18. Chaturvedl A. K., Pfeiffer R. M., Chang L., Goedert J. J., Engel E. A. Elevated risk of lung cancer among people with AIDS. *AIDS* 2007; **21**: 207–13.
19. Guech-Ongey M., Engel E. A., Goedert J. J., Biggar R. J.,

HIV/AIDS CANCER AND IMPACT ON SURGICAL PRACTICE

- Mbulalteye S. M. Elevated risk for squamous cell carcinoma of the conjunctiva among adults with AIDS in the United States. *Int J. Cancer* 2008; **122**: 2590–3.
20. Andrew E. Grulich. Living longer with HIV: What does it mean for cancer risk? *Current opinion in HIV and AIDS* 2009; 41–2.
 21. Robert J., Biggar, Anil K., Chaturvedl, Kishor Bhatia and Sam M., Mbulalteye. Cancer risk in persons with HIV/AIDS in India. A review and future directions for research.
 22. Andrew E. Grulich, Xinan Wan, Matthew G. Law, Marylon Coates and John m. La;dor. Risk of cancer in peoples with AIDS. *AIDS* 1999; **13**: 839–843.
 23. Franceschi S., Maaol L. D., Rickenbach M. *et al.* Kaposi's sarcoma incidence in the Swiss HIV Cohort study before and after highly active antiretroviral therapy. *BJ Cancer* 2008; **99**: 800–804.
 24. Polesel J., Clifford GM, Rickenbach M. *et al.* Non-Hodgkin Lymphoma incidence in the Swiss HIV Cohort Study before and after highly active antiretroviral therapy. *AIDS* 2008; **22**: 301–306.
 25. Baker J. V., Pang G., Rapkin J. *et al.* CD₄⁺ count and risk of non-AIDS disease following initial treatment for HIV infection. *AIDS* 2008; **22**: 841–848.
 26. International collaboration on HIV and cancer. Highly active antiretroviral therapy and incidence of cancer in human immunodeficiency virus-infected adults. *J Natl Cancer Inst* 2000; **92**: 1823–1830.
 27. Wabinga M. R., Parkin D. M., Wabwire Mangen J. W. Cancer in Kampala, Uganda in 1989–91: Changes in incidence in the era. *AIDS Int. J. Cancer* 1993; **54**: 26–36.
 28. Chin-Hong P. V., Palefsky I. M. Human papillomavirus anogenital in HIV-infected individuals. *Dermatologic therapy* 2005; **18**: 67–76.
 29. Palefsky J. M., Holly E. A. Immunosuppression and co-infection with HIV. *J. Natl Cancer Inst Monogr* 2003; **3**: 41–6.
 30. Steenbergeen R. D., De Wilde J., Wilting S. M. *et al.* HPV-mediated transformation of the anogenital tract. *J. Clin Virol* 2005; **325**: 525–533.
 31. Araiz C. P., Hefoisa L., Ramualda C. B. Diagnostic methods for prevention of anal cancer and characteristics of anal lesions caused by HPV in men with HIV/AIDS. *BJID* 2008; **12**: 293–299.
 32. Darin J. S., Russell A. W., Dimitri V. G. and Samuel E. W. The surgeon and AIDS: Twenty years later. *Arch Surg* 2005; **140**: 961–967.
 33. Eichler A., Eiden U., Kessler P. AIDS and anaesthesia. *Anaesthetist* 2000; **49**: 1006–17.
 34. Prince R. W. Understanding the AIDS dementia complex (ADC). The challenge of HIV and its effect on the central nervous system. *Res Pub Assoc Res Nerv Ment Dis* 1994; **72**: 1–45.
 35. Miller L. G., Galpern W. R., Dunlap K. *et al.* Interleukin-1 augments gamma-aminobutyric acid-A4 receptor in brain. *MOI Pharmacol* 1991; **39**: 105–8.
 36. Mesa R. A., Edell E. S., Dunn W. F. *et al.* Human immunodeficiency virus infection and pulmonary. *Mayo Clinic Proc* 1998; **73**: 37–45.
 37. Farizo K. M., Buehler J. W., Chamberland M. E. *et al.* Spectrum of disease in persons with human immunodeficiency virus in United States. *JAMA* 1992; **267**: 1798–805.
 38. Robinson G, Wilson S. E., Williams R. A. Surgery in patients with AIDS. *Arch Surg* 1987; **122**: 170–175.
 39. Wexner S. D., Smithy W. B., Trillo G, Hopkins B. S., Dailey T. H. Emergency colectomy for cytomegalovirus ileocolitis in patients with AIDS. *Dis Colon Rectum* 1988; **31**: 755–761.
 40. Yii M. K., Saunders A., Scott D. F. Abdominal surgery in HIV/AIDS patients: Indications, operative management, pathology and outcome. *Aust N Z J Surg* 1995; **65**: 320–326.
 41. Tran H. S., Moncure M. *et al.* Predictors of operative outcomes in patients with HIV-infection and AIDS. *Am J Surg* 2000; **180**: 228–233.