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VARIATIONS IN ORAL PRESENTATION OF HIV

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A thesis submitted in partial requirement
for the

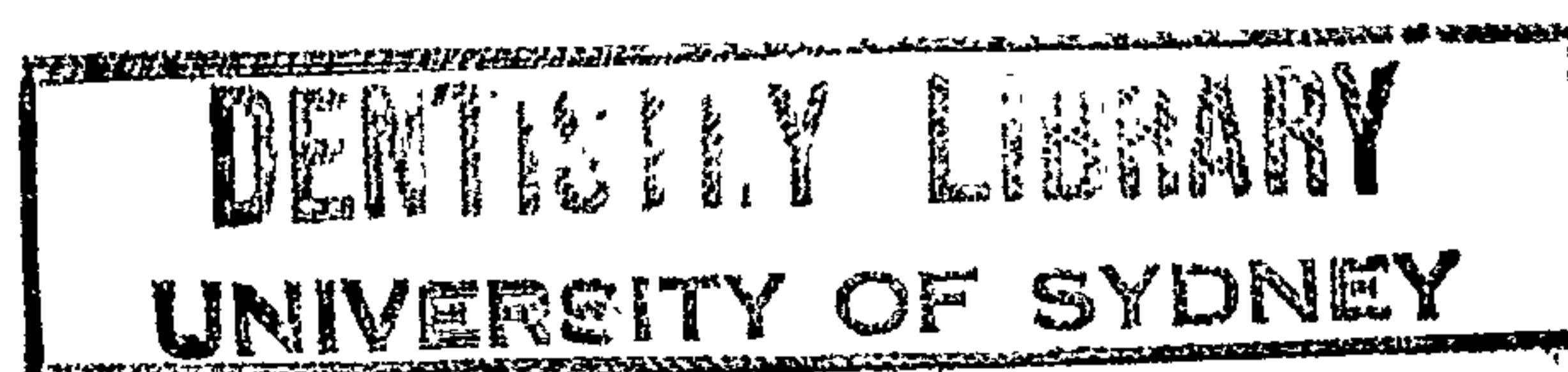
DIPLOMA IN PUBLIC HEALTH DENTISTRY

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SUMMARY

The HIV pandemic has touched the entire fabric of our society and in little over a decade has become a major public health problem. The need for dental professionals to recognise the oral symptoms of HIV infection is strongly recommended.

An overview of the epidemiology of the HIV pandemic is broadly outlined. Cases have been reported from most continents, however there appears to be considerable variations with regard to the numbers reported. Global patterns and current and projected estimates for cases is provided. Routes of transmission especially the risk of transmission in the health care setting is discussed.

A review is made of the scientific etiologic and immunologic principles and the nature of the viral agent to provide the reader with a framework for understanding the particular havoc wrecked by HIV. Methods to test for presence of HIV are also addressed. Current case definition for AIDS and suggested classification systems for HIV-associated diseases are listed.

The thesis is centred on the oral manifestations of HIV infection. Updated classifications of oral lesions associated with HIV infection and suggested diagnostic criteria are included. Particular emphasis is given to the varying presentations of oral lesions. The lesions are grouped and described as strongly associated, less commonly associated and possibly associated with HIV infection. Illustrations are provided for many of the oral lesions. A survey of oral changes in HIV infection was carried out to observe the spectrum of oral lesions seen in Australia.

The results of the study are clearly outlined. Comparison is made of the survey results with those obtained from earlier studies.

Further, emphasis is placed on the early detection of the precursors of symptomatic HIV positive patients which is in the best interest of both the patient and the provider.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ANUG	Acute necrotising ulcerative gingivitis
ARC	AIDS-related complex
ARV	AIDS-associated retrovirus
CDC	Centers for Disease Control (Atlanta, Georgia, USA)
CMV	Cytomegalovirus
EBV	Epstein-Barr virus
ELISA	Enzyme-linked immunoabsorbent assay
GPA	Global Programme on AIDS - World Health Organization
HBLV	Human B-lymphotropic virus
HIV	Human Immunodeficiency Virus
HIV-1	Human Immunodeficiency Virus type 1 (=HIV)
HIV-2	Human Immunodeficiency Virus type 2 (=HTLV-4, LAV-2)
HIV-G	HIV-associated gingivitis
HIV-P	HIV-associated periodontitis
HIV-SGD	HIV-associated salivary gland disease
HL	Hairy leukoplakia
HPV	Human papilloma virus
HSV	Herpes simplex virus
HTLV-3	Human T-cell lymphotropic virus type 3
HTLV-4	Human T-cell lymphotropic virus type 4 (=HIV-2, LAV-2)
IDU	Injecting drug users
KOH	Potassium hydroxide stain
KS	Kaposi's sarcoma
LAV	Lymphadenopathy-associated virus
LIP	Lymphoid interstitial pneumonitis
MMWR	Morbidity and Mortality Weekly Report
MCOI	Mucocutaneous opportunistic infections
NHL	Non Hodgkin's lymphoma
PAS	Periodic acid-schiff stain
PCP	<i>Pneumocystis carinii</i> pneumonia
PCR	Polymerase chain reaction
PGL	Persistent generalised lymphadenopathy
PLH	Pulmonary lymphoid hyperplasia
RAU	Recurrent aphthous ulceration
RIPA	Radioimmune precipitation assay
SIV	Simian immunodeficiency virus
SFI	Surveillance, Forecastings and Impact Assessment Unit (World Health Organization)
VZV	Varicella-zoster virus
WHO	World Health Organization

1 INTRODUCTION

In June 1981, the Morbidity and Mortality Weekly Report (MMWR) printed by the Centers for Disease Control (CDC) reported five previously healthy, young homosexual men treated for biopsy-confirmed as *Pneumocystis carinii* pneumonia (PCP). This was the first documented report on what is known as Acquired Immune Deficiency Syndrome (AIDS)-an epidemic which has attained global importance.

AIDS is a complicated disorder of the defence system of the body.

Acquired means contracted/transmitted as opposed to inherited.

Immunodeficiency implies poor body defence mechanisms against infections.

Syndrome is a grouping of illnesses which helps to identify a particular disease, in this case AIDS.

AIDS is caused by a virus called Human Immunodeficiency Virus (HIV). Once the virus is "acquired" the individual harbours it for life. AIDS is the end stage of HIV infection. HIV attacks the sophisticated structure of immunity leaving the person infected by this virus susceptible to organisms with which the system had previously lived in relative harmony. These so-called opportunistic infections do not occur in healthy people. The breakdown in immunological surveillance system in HIV infection also predisposes the individual to the development of otherwise rare cancers such as Kaposi's sarcoma and lymphomas. These are life threatening illnesses for persons with a suppressed immune system. The body is now deemed to have acquired an immune deficiency that, together with other

physiological changes, constitutes a syndrome given the acronym "AIDS". It is irrelevant whether an HIV infected person is asymptomatic or has progressed to AIDS with multiple opportunistic infections as there is potential for transmission of the virus at any stage of HIV disease, by unprotected heterosexual or homosexual activity, needle sharing by injecting drug users (IDUs), transfusion with contaminated blood and occupational exposure in specific circumstances.

AIDS is a 100 percent lethal disease, and it is thought, that most HIV infected individuals will eventually develop AIDS. There is very little evidence to support the concept that HIV infection is reversible (Polk et al 1987). Although the time between infection with HIV and diagnosis of AIDS varies, studies estimate a median incubation period of about nine to ten years (Bacchetti, Moss 1989, Lemp et al 1990). Considering that there is a long latency between acquisition of viral infection and the development of clinical AIDS, cohort studies of incidence of AIDS among seropositive persons must be of long duration.

Survival varies considerably being dependant upon disease/s at diagnosis, age, race, risk group, availability of treatment and unidentified variable biologic host factors. From the patient perspective, early intervention with antiretroviral drugs and prophylactic therapy for selected opportunistic infections has each contributed to a significant lengthening of life expectancy (Stewart 1993). It has been shown that survival time after a definitive diagnosis of AIDS increases for patients treated with antiretroviral drugs such as zidovudine (Fisch et al 1987).

Australian data show that mortality within two years of diagnosis of AIDS fell from 83.5 percent in 1986 to 47.6 percent in 1990 with therapeutic management (The National AIDS Registry 1992a).

In many ways the epidemic of AIDS has become the ultimate challenge to public health. In just over a decade it has grown from a trickle of rare illnesses with no known cause or even a name to become a tidal wave of disease which is gaining momentum as it unfolds on every corner of the globe.

Knowledge of HIV infection has become a critically important requirement for professionals who are responsible for oral health care delivery. The possibility of transmission to those having patient contact, dental workers and patients has created great emotional concerns, as well as the impact on infection control techniques and costs. HIV infected individuals actively seek consultation and care for oral health. In many instances treatment may be provided by the dentist unaware of a patient's HIV seropositive status.

Oral manifestations of HIV associated diseases can often constitute the earliest clinical expressions of the disease. In fact up to 70 percent of patients with AIDS exhibit an oral lesion (Silverman et al 1986, Barr, Torrosian 1986). This high prevalence of oral lesions in HIV infected individuals is presumably secondary to compromised oral defence factors (Yeh et al 1988). These lesions interfere with the normal health status of the individual, making it necessary to seek treatment which is best provided by those trained in oral health care services.

The diagnosis of HIV infection is missed too often, with significant costs to patients and the community. In Western Australia, more than 30 percent of people with AIDS became aware of their HIV infection only at the time of their AIDS-defining illness (Gillieatt et al 1992). They would have unknowingly carried HIV for about nine years. All would have consulted a doctor/dentist for an HIV-related disorder during that time; almost all would have developed an HIV-induced lesion of skin or mucous membrane well before their AIDS-defining illness. In Australia, nearly one in five still learn of their HIV status at the time of, or less than three months before developing AIDS; these figures are the lower limits of late detection as some people must have died from undetected HIV/AIDS (Stewart 1993).

The oral cavity can mirror the progression of HIV infection. The dental clinician must therefore check not just the teeth and periodontal tissues but all other oral structures as part of an initial or periodic examination. These lesions may lead to further immune-suppression which could result in the patient's premature death if not correctly identified and treated. Owing to the rapid developments in the entire field of HIV infection, there is every likelihood of newer drugs being developed which may indefinitely delay the progression of HIV infection to AIDS. Then the dental profession's inability to recognise oral lesions associated with HIV infection may allow progression beyond a point where early intervention medical treatment may have had some efficacy (Foltyn 1992).

In the western industrialised countries, laboratory based immunological markers correlate with the disease progress and help to determine the point at which therapeutic intervention is required. This is not always practical in the developing countries and almost unheard of in many of the underdeveloped countries. Again with the latter groups, stigma follows revelation of one's HIV status. Those who are infected are frequently shunned by society and instead of receiving much needed support are subjected to ostracism, public hostility and may even be refused health care when it is most needed. This often leads to many patients concealing his/her HIV seropositive status even when known to them. It is here that the clinician may have to depend on the clinical findings to assess disease progression.

The medical profession in general has not had the training to be able to easily identify the often subtle changes in texture, tone and colour that distinguish healthy oral tissues from diseased oral tissues.

The World Health Organization has been largely responsible for tracking the AIDS crisis through its Global Programme on AIDS. The WHO-Oral Unit is presently conducting a survey to monitor the changing profile of oral manifestations possibly associated with HIV infection. Examiners from several countries are taking part in the study. The writer had the opportunity to participate as an investigator in the study being conducted in Sydney. The data is collected using a recording form for individuals infected with, or suspected of being infected with HIV. Information requested is collected by a combination of

questioning the individual, oral examination and review of medical/ dental records. The forms will be summarised and only the summary data, not individual patient data, will be released.

Limited Australian data on oral manifestations associated with HIV infection is available at present. There is a need for dental healthcare workers to have an update on the varying presentation of oral lesions associated with HIV infection. There is also need to assist the clinician in suspecting HIV infection in the absence of access to routine blood examination when the patient's status is unknown. The writer's experience from the study conducted and easy access to current literature enabled a better understanding of recent developments in this field.

The specific aims of the thesis are -

- (1) To provide a comprehensive review of all available literature on oral manifestations in HIV infection.
- (2) To ascertain if the spectrum of HIV related oral lesions in Australia is similar to that reported from other countries.

2 EPIDEMIOLOGY

" Epidemics have often been more influential than statesmen or soldiers in shaping the course of political history and diseases may also colour the moods of civilisation."

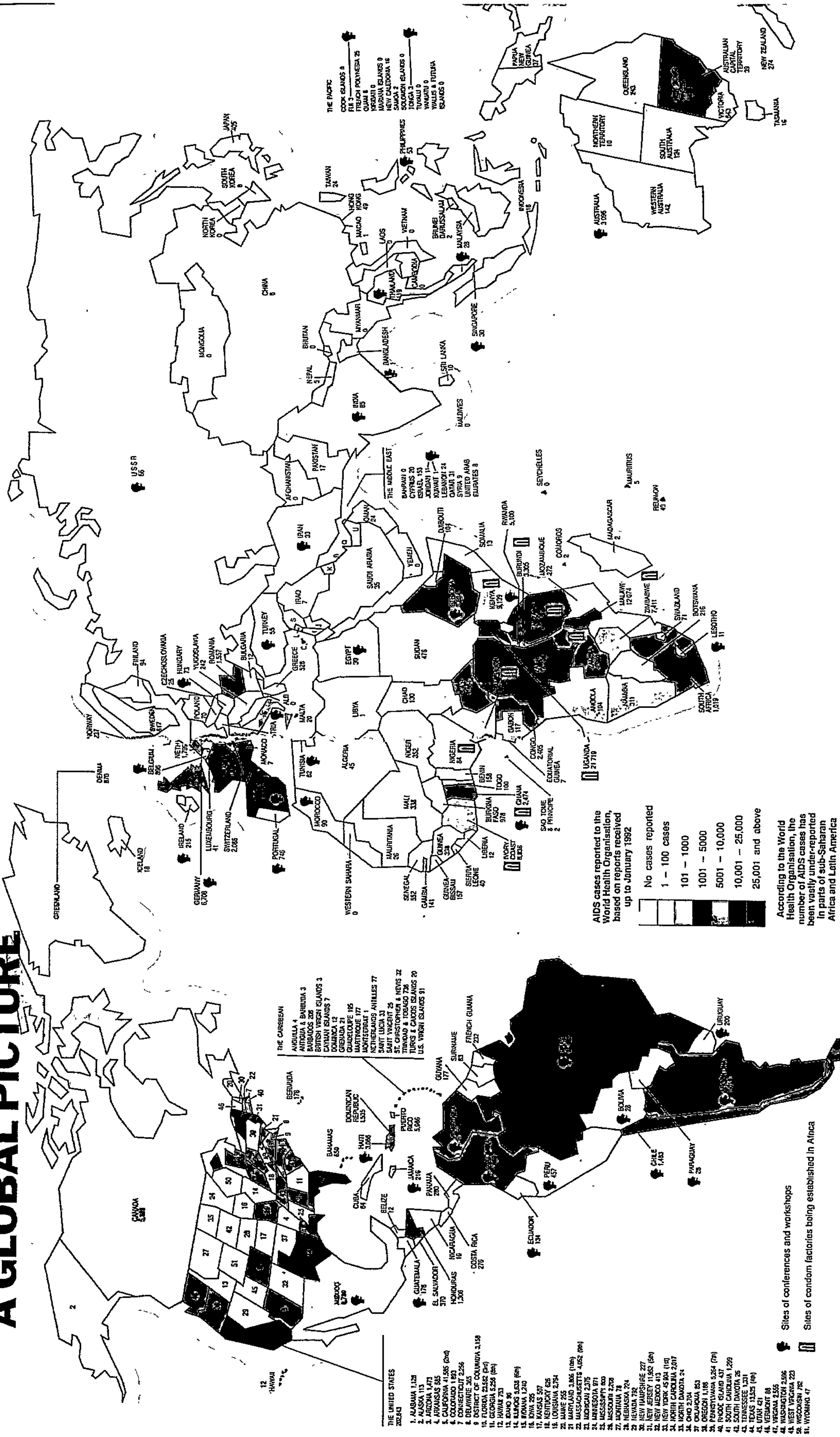
- Rene and Jean Dubos, in *The White Plague* (1987).

At the beginning of the last decade, most infectious diseases had been eliminated as important causes of morbidity and mortality in Western countries. The first description of AIDS in 1981, followed two years later by its etiology being confirmed as a new retrovirus, has enabled epidemiologists to describe the course and extent of this new communicable disease problem facing human populations.

As of December 1992, a cumulative global total of 611,589 cases of AIDS from 173 countries has been reported to the Surveillance, Forecasting and Impact Assessment Unit (SFI) of the World Health Organization (WHO). Large numbers of cases have been reported from North America, Latin America, Oceania, Western Europe and areas of Central, Eastern and Southern Africa (**Figure 1**). Taking into account under-diagnosis, under-reporting and delays in reporting, WHO estimates that about 2 million people, including more than half a million children have developed AIDS since the beginning of the epidemic (WHO 1992).

AIDS is the late stage of infection with HIV. Considering the long latency period, the current number of AIDS cases thus reflects the HIV infections acquired a decade ago.

A GLOBAL PICTURE



For a realistic picture of the epidemic today, one must look not at AIDS cases but at the number of people infected with HIV. WHO estimates that at least 10-12 million people to date have been infected with HIV.

Global estimates of HIV infection at this time based upon the best estimates available to the WHO - Global programme on AIDS (1992) are as follows -

Europe	1/2 million
N.America	1 million
S.America	1 million
Africa	6 million
Middle East	30,000
Asia	1/2 million
Australasia	30,000

2.1 ORIGIN

Soon after the identification of AIDS, a number of cases were reported among Haitians, indicating Haiti as a possible source of the disease. Later, it was suggested that Haitians working in Africa contracted the disease there, then homosexual men from New York who visited Haiti perhaps became infected and carried the disease back to the USA.

In 1983-1984 a T cell lymphotropic retrovirus was isolated by different groups of investigators and is now known to be the cause of AIDS. The virus was named lymphadenopathy-associated virus (LAV) by the French team led by Montagnier (Barre-Sinoussi et al 1983). A year later it was isolated and named human T cell lymphotropic virus-III (HTLV-III) by Gallo (Gallo et al 1984) and AIDS associated retrovirus (ARV) by Levy (Levy et al 1984).

Isolation of the retrovirus was an important event as it meant that blood tests could be developed to see whether an individual had been infected and a nations' blood supply could be screened to detect contamination. By May 1985, the Australian Red Cross was able to announce that blood supply in Australia had been rendered safe through systematic screening of blood and blood donors.

In 1986 an international committee proposed the name HIV, which has become universally accepted (Coffin et al 1986). The original form of HIV is now known as HIV-1 while the similar virus, endemic to West Africa as the cause of AIDS is known as HIV-2 (Kanki et al 1987).

Investigations have as yet revealed neither the origin of HIV nor the length of time it has been present in human populations. Serologic studies suggest that

HIV-1 may have been present as early as 1959 in some African patients whose sera were in long-term storage. The very high prevalence of infection in Africa has suggested that the human immunodeficiency virus might have arisen in that continent. It has now become evident that AIDS is what was known in Africa for many years as '*slim disease*'. Furthermore, the similarity of HIV-2 to a virus endemic to African green monkeys, Simian immunodeficiency virus (SIV), fuelled speculation that the human retrovirus might have evolved from its simian relative. Alternatively, both might have derived, during primate or human evolution, from a common ancestral precursor. Furthermore, the possibility has not been excluded that monkey virus arose from the human virus (Perry 1988). Another study places the divergence of HIV-1, HIV-2 and one form of SIV as recently as 140-160 years ago (Sharp, Li 1988). In his book, '*Plagues and People*', William McNeill (1977) wrote -

" When a transfer of a virus from animals to humans does take place, the microbe may make people extremely ill. At first human bodies cannot fight off the virus as their immune system is just not ready to cope with it. This is why so many people die in the beginning of epidemics. It is not in the interest of the microbe to kill off all its potential hosts, because this would eliminate its own possibility of survival. In time, either the microbe goes through genetic changes or humans acquire new defences to deal with the microbe."

Theoretically this could happen to HIV in future. It could mutate and/or our bodies will adapt and learn to live with it. But because this may take hundreds of years, it is no comfort to us right now as we watch in horror the mounting casualties.

2.2 GLOBAL ASPECTS OF THE EPIDEMIC

Since HIV infection precedes the development of AIDS by an average of 10 years, an optimal understanding of the current patterns of AIDS must be based upon an analysis of both HIV seroprevalence data as well as reported AIDS cases (Table 1). From such analysis the WHO has recognised **four different patterns** for the division of the AIDS epidemic (Chin, Mann 1989). The explanation for the existence of these patterns includes the apparent date of HIV entry and/or period when HIV began to spread extensively in the population, the relative importance of the modes of transmission, and details of sexual and other social risk behaviours in the population.

Table 1 **AIDS cases reported to WHO by continent as of 23 Dec. 1992.**
Source: WHO - Global programme on AIDS - SFI (1992).

Continent	Number of cases	Number of Countries or Territories Reporting		
		to WHO	Zero cases	1 or more cases
AFRICA	211032	53	1	52
AMERICAS	313083	45	0	45
ASIA	2582	41	8	33
EUROPE	80810	31	0	31
OCEANIA	4082	22	10	12
Total	611589	192	19	173

2.2.1 Pattern I

Pattern I comprises countries where most cases occur among homosexual or bisexual men and injecting drug users (IDU) in cities. Heterosexual spread is limited but increasing. Transmission due to blood and blood products occurred between the late 1970s and 1985 but now been largely controlled through self-exclusion of persons with known risk factors or behaviours and by routine blood screening for HIV antibody. The male/female sex ratio ranges from 10-15:1 and to date perinatal transmission is uncommon. Overall population seroprevalence is estimated to be less than 1% but has been measured to be over 50% in some groups practising high-risk behaviours. This pattern is typical of industrialised countries with large numbers of reported AIDS cases, including North America, many Western European countries, Australia (Table 2), New Zealand, and many urban areas in Latin America.

Table 2 Cumulative cases of AIDS and deaths from AIDS in Australia by sex and State/ Territory in which diagnosis was made, diagnosed and reported to 30 November 1992.
Source: National AIDS Registry, Australian HIV Surveillance Report (1992).

State/ Territory	Male	Cases Female	Total	Male	Deaths Female	Total
ACT	41	2	43	34	1	35
NSW	2077	69	2149	1372	43	1416
NT	14	0	14	6	0	6
QLD	329	12	342	205	8	214
SA	143	8	151	87	2	89
TAS	21	2	23	13	1	14
VIC	755	14	771	521	9	531
WA	172	8	180	107	3	110
Total	3552	115	3673	2345	67	2415

2.2.2 Pattern II

Pattern II comprises countries where most cases occur among heterosexuals. The male/female ratio is approximately 1:1, and as a result mother-to-infant transmission is common. Transmission through IDUs and homosexual men are not believed to be major factors. In a number of countries, overall population seroprevalence is estimated at more than 1% and in some urban areas up to 15% of the sexually active age group is infected. Transmission through blood and blood products has been a significant problem and continues in those countries that have not yet implemented nationwide donor screening. In addition, the use of unsterile needles and syringes for injection is considered an important public health problem. This pattern is presently observed in sub-Saharan Africa and in the Caribbean. The hardest hit by the epidemic is sub-Saharan Africa where figures are expected to be a lot higher than those reported, as many countries in Africa do not have the equipment and facilities for making a correct diagnosis of AIDS (Pindborg 1992).

2.2.3 Pattern III

Pattern III comprises countries where only a small number of cases have been documented. Cases have generally occurred in persons who have travelled to Pattern I or II areas and as a result of use of imported blood products. Homosexual and heterosexual transmission have only recently been documented. Pattern III is mainly found in Eastern Europe, North Africa, the Middle East, Asia, and most of the Pacific (excluding Australia and New Zealand). Ever since AIDS cases were first reported to the WHO, the incidence rates have been

extremely low in Eastern Europe, mainly because these countries had made homosexuality a criminal offence. Asian incidence rates are also surprisingly very low. This fact may be explained by a delayed appearance of the epidemic in this continent. Reports from Thailand indicate a dramatic increase in the number of HIV-infected IDUs, in whom AIDS will eventually develop (Smith 1990). In Japan, the majority of AIDS cases are found among haemophiliacs.

2.2.4 Pattern I/II

In many Latin American countries HIV transmission among heterosexuals who have had multiple sexual partners has increased since the mid-1980s to the extent that this mode of transmission has become predominant. As a result of this shift, the WHO has reclassified Latin America as Pattern I/II (Sato et al 1989).

2.2.5 Predictions for future cases

The Global Programme on AIDS (GPA) of the WHO periodically reviews and updates its projections for the HIV/AIDS epidemic for the year 2000. Projections of the course of the AIDS epidemic for the year 2000 obtained by the Delphi questionnaire survey method estimates a cumulative total of AIDS cases in adults to reach 5-6 million (Sato et al 1989). In light of the continuing rise in HIV infections in all continents, WHO now projects that by the year 2000, some 30-40 million men, women and children will have been infected with HIV since the beginning of the epidemic.

In the next few years, HIV infection will become a major drain on health

resources in most countries. During the present decade, prevention and control programs are projected to be potentially capable of preventing almost one-half of the new cases of AIDS which may occur between now and the year 2000 (WHO 1989). On the other hand, more than one-half of the projected increase will occur regardless of how effective prevention efforts may be since these will be developing in those persons already infected with HIV (WHO 1989). It is clear that the epidemic is destined to continue to grow and extend in the foreseeable future, particularly among ethnic minorities, women and children. Much concern has been expressed about the spread of HIV among indigenous population groups eg. aborigines owing to added risk factors such as poor general and genital health, poor education, poor sex structure and increased alcohol consumption. The epidemic of AIDS has rapidly progressed to a pandemic level.

2.3 TRANSMISSION OF HIV

HIV is transmitted in 3 ways: through sexual contact; as a result of parental exposure to infected blood or blood products; and perinatally from mother to neonate. Sexual contact with exchange of body fluids constitutes the major risk factor for transmitting or contracting HIV infection. Sharing of needles by IDUs is also a major risk factor. There are however, rare examples of transmission through artificial insemination and organ transplantation, but at the present time no other common routes of transmission have been identified. In particular, the evidence argues strongly, perhaps unequivocally, against transmission through casual or social contacts which do not involve any of the activities listed above (Jaffe, Lifson 1988).

HIV has been isolated from blood, semen, vaginal secretions, saliva, tears, breast milk, cerebrospinal fluid, amniotic fluid, and urine and probably will be isolated from other body fluids, secretions and excretions. However, epidemiological evidence has implicated only blood, semen, vaginal secretions, and breast milk in transmission (CDC 1987a).

Although HIV has been isolated from saliva (Groopman et al 1984), so far no cases of transmission have been documented via this route in casual or household contact situations (Friedland et al 1986, Jaffe, Lifson 1988). Even in a case in which an HIV-infected child had bitten several relatives, no contacts became seropositive (Shirley, Ross 1989). The low risk of transmission of HIV via saliva may be related to the low concentration of the virus in the saliva of infected individuals (Levy, Greenspan 1988). In addition, it appears that saliva can reduce the ability of HIV to infect lymphocytes (Fox et al 1988).

2.3.1 Sexual transmission

HIV can be transmitted from man to man, from man to woman, from woman to man and from woman to woman. The majority of HIV cases in the western industrialised countries continue to be among homosexual men. Among them, the most significant risk factor is sexual behaviour in the form of receptive anal intercourse. Man-to-woman transmission is also well documented (Padian et al 1987). In both cases, the number of sexual partners is also of significance. Woman-to-man transmission is not uncommon (Padian 1987). In all forms of sexual transmission, genital ulceration is an important additional risk factor. Woman-to-woman transmission has been reported in a few cases (Monzon, Capellan 1987). People with HIV are most infectious when their viral load is highest, which occurs at two points in the chronology of infection: around the time of seroconversion, and years later, at the time of advanced immunodeficiency (Stewart 1993). It is not clear what other factors determine whether or not HIV is transmitted during sexual activity.

2.3.2 Perinatal transmission

Transmission of HIV from mother to offspring appears possible during three periods, during pregnancy, during delivery or immediately after birth. HIV has been detected in foetal tissues (Sprechers et al 1986). Postpartum transmission can also occur through breast feeding (Ziegler et al 1985)

2.3.3 Transmission via blood

Donor blood is not tested for HIV in all countries and so a significant number of cases of transfusion-associated HIV infection and AIDS will probably continue to occur. In the industrialised countries, blood products administered to haemophiliacs and those with bleeding disorders are all rendered free of HIV. Transmission of HIV infection through the use of contaminated needles, shared by IDUs, is a major and growing route of transmission in the United States and Western Europe.

2.3.4 Risk of HIV transmission in the health-care setting

Risk of transmission to health-care workers

Occupational exposure to HIV has been an issue of major concern to all health-care workers since the virus was first recognised. Early in the epidemic, it was assumed by some that since contact between dental-care professionals and persons infected with HIV was frequent and often involved bleeding, risk of transmission might be high. Dental community concern about occupational risk was heightened by studies that demonstrate a higher incidence of blood and saliva-borne infections, such as hepatitis B, in dental professionals than other health-care workers. Because in the absence of barrier protection, dentists have frequent skin and mucous membrane contact with saliva and blood from patients, fear developed that HIV could be transmitted to dental professionals as frequently as hepatitis B virus (Council on Dental Therapeutics 1976, West 1984).

Contrary to this assumption, transmission from the patient to dental staff appears to be practically nonexistent (Scully, Porter 1991). Seroprevalence rates among dentists are lower than the background level of seroprevalence in the general population (Verrusio 1989).

The modes of HIV transmission from infected patients to health-care workers include needlestick and sharps exposures, extensive contact with blood or other body fluids and direct skin and/or mucous membrane exposure to blood (CDC 1987b).

Several prospective studies of health-care workers with documented percutaneous or mucous membrane exposures to HIV-infected blood or fluids have been conducted. The combined data from these studies indicate that of the 1,948 health-care workers with 2,042 parental exposures to blood or blood containing body fluids from patients with HIV infection, only six (0.29%) of the exposures resulted in seroconversion. In addition, 1,051 mucous membrane exposures were documented in these studies, and none resulted in seroconversion. The risk of being infected with HIV as a result of a percutaneous injury is estimated at less than 0.3 percent and infection resulting from skin or mucous membrane exposure is even lower (McCray 1986, Marcus 1988, Henderson et al 1990). The size of the inoculum of blood appears to be critical for predicting the likelihood of infection following a needlestick injury (Napoli, McGowan 1987).

Occupational exposure to HIV for the dental profession is one that is occasioned by way of needlestick or suture injury, scalpel cut, scaler point or elevator, which may break the skin. Exposure may also be through contact by blood or blood stained saliva to mucous membranes or skin by blood or blood stained saliva which may be non-intact, chapped, abraded, affected by dermatitis or prolonged contact such as in a glove tear with blood pooling on the skin.

Anonymous HIV-antibody testing, conducted as part of the Health Screening Program at the Annual Session of American Dental Association since 1986, has screened a total of 6,235 dentists, many of whom practised in areas with a high prevalence of HIV infection. Only two dentists without other risk factors, have tested positive for HIV antibody. One case has been identified by the CDC as occupationally acquired; in the other there is insufficient evidence to attribute the dentist's seropositivity to occupational exposure (Verrusio et al 1989).

The publicity given to the AIDS problem overshadows the fact that the dentist is at far greater risk from the hepatitis B virus than HIV.

Risk of transmission to patients

Diseases caused by bloodborne pathogens can be transmitted in any circumstances in which the exchange of blood and body fluids is possible. Hence it has always been acknowledged that there is a theoretical risk that an infected health-care provider could transmit HIV infection to a patient, although it is felt that the risk is significantly smaller than that for transmission from the patient to dentist.

Currently, there is no scientific evidence to indicate that HIV-positive health-care providers pose an identifiable risk of HIV transmission to their patients. To date, there has been only one documented case of transmission from an HIV-infected health-care provider (dentist) to patients during the past 11 years of experience with AIDS, an indication that the risk is infinitesimal (CDC 1991).

Studies reported on continuing investigation of 15,795 patients treated by 32 HIV infected health-care workers in the United States have identified 84 HIV infected patients (1 in 188). However no health-care worker to patient link was established. Risk factors such as multiple sex partners, injecting drug use, blood transfusions and prior HIV infection were attributed to the infection identified. The findings of seropositive patients in the investigations is to be expected because an estimated one in 250 persons in the United States is infected with HIV (CDC 1992).

Strict adherence to universal precautions and recommended infection control practices remain essential for minimising the risk of HIV transmission in the workplace (CDC 1987, CDC 1989). Dentists should strive to minimise the **real risk** of HIV transmission by adhering to infection control practices as put forth by the CDC, thereby reducing the **perceived risk** of HIV infection in patients and increasing the level of **acceptable risk** (Greer 1991).

3 VIROLOGY AND IMMUNOPATHOLOGY

Viruses are the simplest form of life. They are little more than a cluster of genes packaged in a protein coat. There is even some controversy as to whether they are truly alive, since they lack the three conditions which generally characterise living things: they are unable to feed on their own, grow on their own or reproduce themselves. A virus can only reproduce by entering a living cell and exploiting the metabolic machinery of the host cell to make replicas of itself. Viruses often have a preference for a particular species and for a particular type of cell within the organism.

Identification of the virus responsible for AIDS resulted in a rapid expansion of knowledge about both the virus and the disease. The modern tools of molecular biology have helped to unravel rapidly the structure and biology of the virus and to classify it by identifying homologies with other viruses.

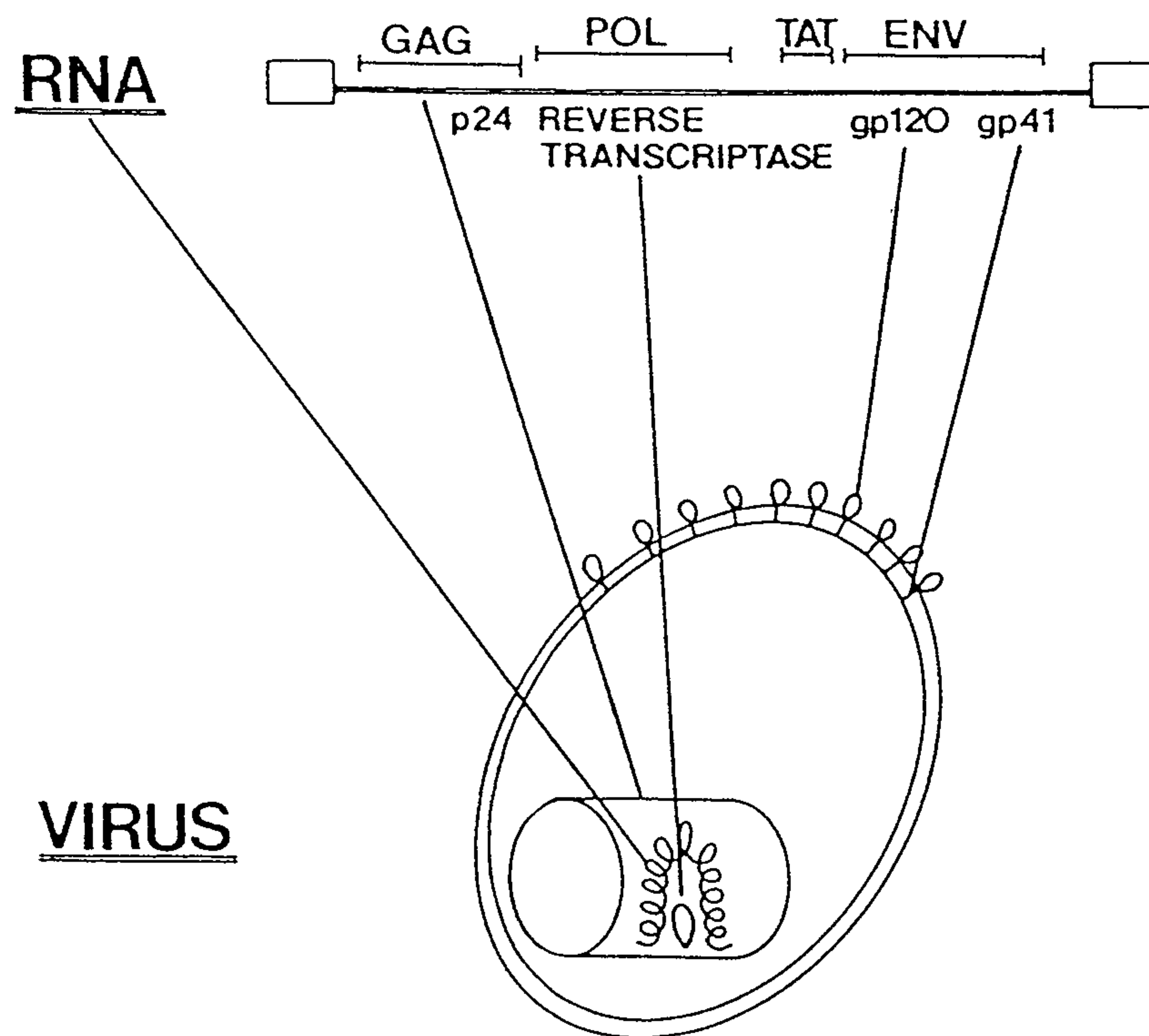
Human immunodeficiency Viruses (HIVs), the putative cause of AIDS, belongs to the retrovirus family (Coffin et al 1986). "*Retro*" is an abbreviation of reverse transcriptase, a unique collection of enzymes which allows the retrovirus to make DNA copies of its RNA. These DNA copies can then be integrated into the host chromosomes where they influence cell function and replicate freely (Levy 1985).

The complete sequence of several isolates of the viral RNA has been established through gene cloning in bacteria. There is wide variation in RNA sequences from different isolates, leading to concern that, as with influenza, a single source of vaccine may not be sufficient to immunise against all such variants (Francis, Petricciani 1985). Comparison of these sequences with other viruses has suggested that HIV should be classified in the lentivirus sub-family (Gonda 1985).

3.1 GENOME OF HIV

The genome of HIV shares many features with other retroviruses (Marx 1986). HIV consists of two relatively small fragments of RNA joined end to end. These are surrounded by a protein core and associated with reverse transcriptase (Cunningham 1989) (**Figure 2**). The major core protein p24, has a unique cylindrical shape that is surrounded by a lipid envelope. The envelope glycoproteins (gp41 and gp120) are inserted into the lipid and represent the interface of the virus with its environment. The genome of HIV reflects the structural components and contains three major genes: **gag**, **pol** and **env** (Benn 1985, Haseltine 1988).

Figure 2 Diagram of HIV and its RNA showing the regions for structural proteins and the enzyme, reverse transcriptase.
Source: Cunningham (1989).



The **gag** encodes the core protein, **pol** encodes the enzymes, including reverse transcriptase, while **env** encodes the envelope glycoprotein. The gene products of **pol** direct the synthesis of a cDNA copy of the viral RNA, thus reversing the usual method of reduplicating genes. Other parts of the HIV genome are regulatory in function: the **tat** (transactivating region) is capable of causing marked, even explosive, replication of HIV; the **nef** appears to function by regulating host cellular factors from its location just inside the cell membrane, thus inhibiting the replication of HIV. The **tat**, **nef** and other regulatory genes appear to provide an exquisitely subtle means of controlling the latency and replication of HIV (Levy 1988, Haseltine et al 1988).

Characteristics of HIV-2

HIV-2 shares a number of characteristics with HIV-1, but their antigenic properties are different, sera containing antibodies against HIV-2 do not react with HIV-1 envelope antigens gp120 and gp41 (Clavel et al 1986).

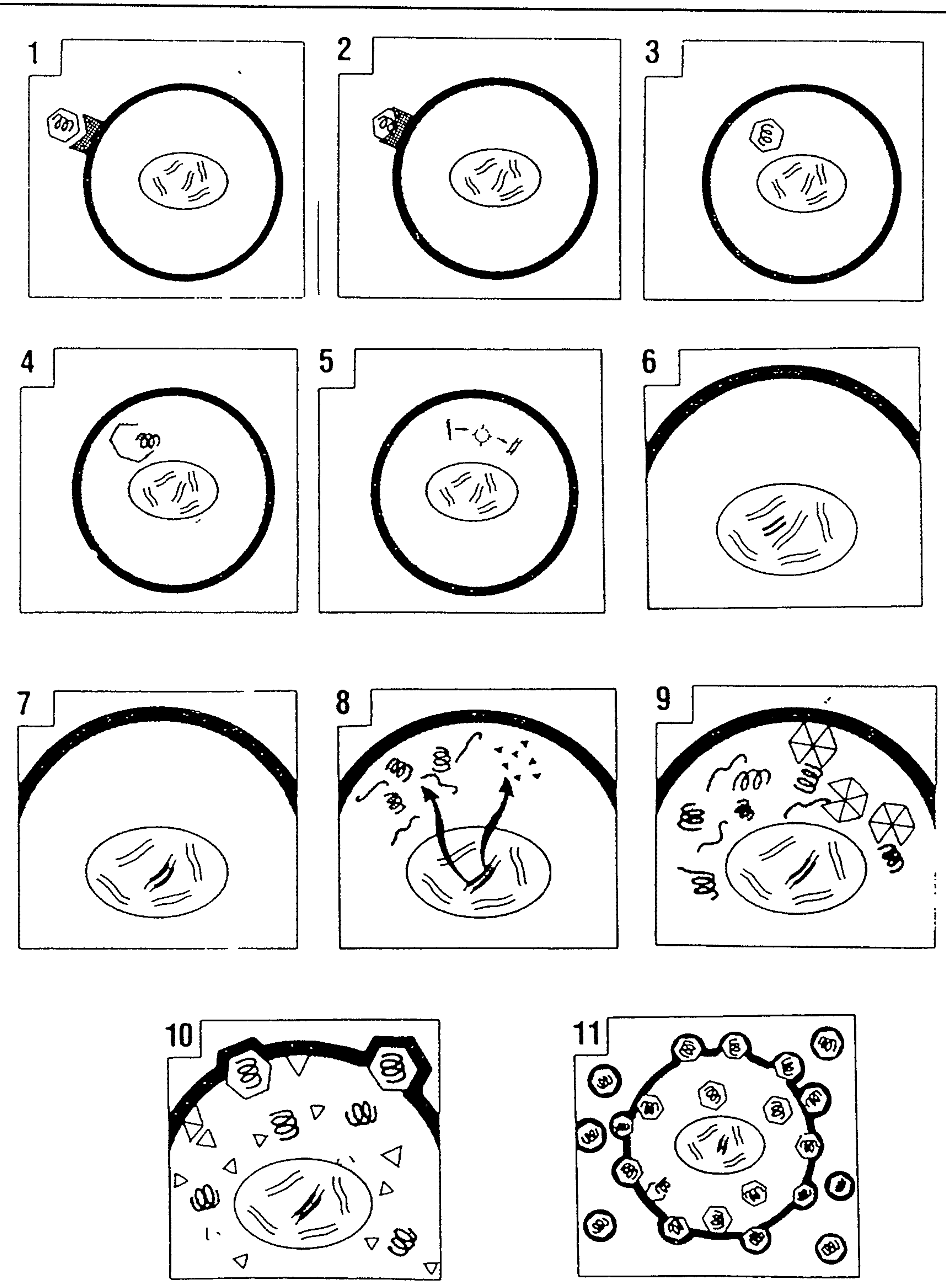
3.2 LIFE CYCLE OF HIV

Once inside the host, the virus binds to the CD4 molecule of the T-helper cells and other target cells like the bone marrow stem cells, macrophages, endothelial cells, glial cells, lymph node, dendritic cells, cervical epithelium and possibly Langerhans cells. However it is the effects of HIV on T-helper cells which probably play a major role in the pathogenesis of HIV disease and AIDS. Binding of HIV to CD4+ target cells involves interaction of the external envelope glycoprotein molecule gp120 with the CD4 molecule, although other cell receptors may be involved. This interaction can involve free viral particles but direct cell-to-cell spread of HIV may also occur (Rabson 1988). The virus enters the target cell, or is internalised, through fusion of the viral envelope with the target cell membrane (Suzuki 1989) (Figure 3).

After penetration of the cell membrane, HIV uncoats and the viral RNA is subject to reverse transcription. This involves the production of a single-strand DNA copy of the viral RNA and destruction of the viral RNA. A second strand of DNA is then synthesised. The linear double stranded DNA becomes circular and is translocated from the cytoplasm to the nucleus, where it is integrated into the host cellular DNA. The integrated piece of viral genome is now called integrated proviral DNA. HIV can remain latent for long periods sometimes for the lifetime of the host cell. Alternatively, upon activation viral genomic RNA is synthesised and transported into the cytoplasm. By action of messenger RNA (m RNA), and other factors, viral proteins are synthesised, processed and assembled. The formation of the full virion involves budding of the virion core through the

cellular membrane, whereby HIV acquires a coat containing envelope glycoproteins and is now an extracellular mature HIV virion.(Haseltine 1988, Rabson 1988)

Figure 3 Life cycle of HIV.
Source: Suzuki (1989).



3.3 PATHOGENESIS OF HIV DISEASE

Every living thing, from a one-celled bacterium to a many celled mammal, has evolved a way of protecting itself from outside threat. This protective mechanism is the immune system. The immune system, part of the body's host defence mechanisms, is a highly sophisticated, integrative system designed to help protect the host against the ravages of infectious microorganisms, environmental toxins and cell mutations. This function can be adequately performed because the immune system has the ability to distinguish 'self' from 'non-self' and to react in various ways to eliminate the threat represented by 'non-self'.

In principle, one would expect the immune system to respond to HIV in much the same way it does to any other virus. But HIV outsmarts the body's immune defences. It does this by attacking the immune system itself. Not only does it target the immune system, but it goes for the very heart of it: the helper T cell, the cell responsible for orchestrating the entire immune response.

3.3.1 HIV and the immune system

HIV selectively infects the T4 (or CD4+) cell (Bowen et al 1985, Gallo 1987). Interestingly, HIV-2 also infects T4 cells (helper cells) and uses, like HIV-1, the CD4 molecule as part of its receptor (Clavel et al 1987). HIV is cytopathic for infected cells, eventually leading to their destruction. The result is a quantitative defect in T4 cells (Bowen et al 1985, Laurence 1985, Margolick, Fauci 1987).

Persons who are immunologically normal have between 600 and 1200 T4

cells/mm³. Asymptomatic HIV-infected individuals often have a lower than normal number of T4 lymphocytes while persons with AIDS generally have from 0-500 T4 cells/mm³ (Laurence 1985). The number of T4 cells seems to correlate with the clinical course of the disease. Persons with very low T4 cell counts tend to have more clinical problems, especially infection, than those with higher T4 cell counts (Lane, Fauci 1987). Due to a low number of T4 cells, the individual is also usually lymphopenic (low total lymphocyte count), with low T4/T8 cells ratio (normally 2:1). The number of T8 cells is generally normal (Laurence 1985, Lane, Fauci 1987).

Besides an abnormal number of T4 cells, the function of infected T4 cells is also defective. This includes:

1. decreased ability of T4 cells to release lymphokines,
2. decreased cytotoxicity,
3. decreased T cell help to B cells for Ig synthesis and
4. decreased ability of T cells to proliferate in mixed lymphocyte cultures.

Possibly the most significant finding is that T4 cells are unresponsive or less responsive to specific antigen and therefore lack all of the antigen induced T4 cell functions. Defective cell-mediated immunity is manifested clinically as opportunistic infections and tumours (Bowen 1985, Margolick, Fauci 1987). Studies have also demonstrated that activated T4 lymphocytes are more easily infected and more productive of virus than resting T4 cells. There are several immune stimulators that activate lymphocytes and therefore could be co-factors

necessary for active infection and disease. Theoretical possibilities include: other infectious agents (such as cytomegalovirus (CMV), Epstein-Barr virus (EBV), parasitic infections), environmental antigens, drugs, toxic substances and genetic factors (Lane, Fauci 1987, Margolick, Fauci 1987).

Humoral immunity or B cell abnormalities seen in AIDS may be due to the aforementioned lack of induction and regulation by the T cell; to direct activation of the B cell by HIV, EBV, or CMV; or possibly to an excess secretion of lymphokines that stimulate B cells (Margolick, Fauci 1987). Whatever the cause, B cells in AIDS are polyclonally activated, which results in a hypergammaglobulinemia (high levels of circulating IgG, IgA, IgM) and increased levels of circulating immune complexes and autoantibodies (Seligman et al 1987). At the same time, B cells will not mount an antibody response to a new antigen (Laurence 1985).

Monocytes/macrophages in HIV infection have also been shown to be abnormal.

In vitro tests show:

- (1) decreased intracellular killing following phagocytosis,
- (2) decreased chemotaxis,
- (3) decreased expression of class II HLA antigens (Seligman et al 1987).

These defects may be due to a lack of gamma interferon and other monocyte stimulating lymphokines from the T4 cell, as well as direct infection of monocyte/macrophages with HIV (Laurence 1985).

The immunological abnormalities reported in association with HIV infection are summarised in Table 3.

Table 3 **Immunologic abnormalities in HIV infection.**
Source: Seligman et al (1987).

Characteristic abnormalities

- Depletion of T4 cells
- Decreased proliferative response to soluble antigens
- Impaired delayed-type hypersensitivity reactions
- Polyclonal B cell activation with increased immunoglobulin production

Consistently detected abnormalities

- Lymphopenia
 - Decreased proliferative response to T cell mitogens and alloantigens
 - Decreased proliferative response to specific B cell mitogens
 - Decreased interleukin-2 production
 - Decreased cytotoxicity to virally infected cells
 - Increased immune complex formation
 - Decreased natural killer cell activity
 - Decreased monocyte chemotaxis
 - Decreased major histocompatibility complex class II antigen expression on monocytes and macrophages
-

All of the mechanisms by which by which HIV causes damage to the immune system are not fully understood (Levy 1988). Recent evidence has confirmed that there are other important mechanisms by which HIV does damage to the immune system. According to the hypothesis of clonal deletion, the immune system initially contains cells that have the potential to attack the body's tissues, but these cells are somehow eliminated before they can do any harm. This elimination is called clonal deletion (Duffin 1992). It has been suggested that HIV may somehow reactivate the mechanism of clonal deletion against useful or potentially useful CD4 cells instead of just potentially harmful CD4 cells (Duffin 1992). More recent experiments are re-examining "*autoimmunity*" as a potential mechanism of HIV damage.

4 TESTING FOR HIV INFECTION

"Testing for presence of HIV infection is an integral part of any sound national strategy for combating the AIDS epidemic. It should therefore be carried out within a system designed to ensure optimal quality control, access to support services and confidentiality of results."

(Basten 1988, Third National Conference on AIDS - Australia)

Methods to test for presence of HIV are important for epidemiologic and public health surveillance purposes, for diagnosis and management of individual patients and also for investigations of the properties and biology of the virus.

The goals for HIV testing are three fold: (Basten 1988)

- (1) To protect the community.
- (2) To assist in diagnosis and management.
- (3) To create a national data base for prevalence of infection in order to monitor its spread, to gauge the efficacy of preventive measures and to provide information for future planning.

The most frequently used assays determine the presence of one or more antibodies to HIV, produced by the immune system of the host. The development of tests for the detection of antibodies to HIV which could be utilised on a large scale was one of the major breakthroughs in the attempts to control the AIDS epidemic. Such tests have been commercially available since March 1985. Most countries use repeated tests and/or two different tests in order to minimise false positive and false negative results.

Antibodies to HIV are usually detected in the first two to six weeks of illness (Boyle et al 1993). The "window period", in which patients infected with HIV may not test positive for anti-HIV antibodies, but may be capable of transmitting the virus is generally limited to this two to six weeks, although a period of up to three months is given to include a level of safety (Boyle et al 1993). In rare cases, it has been reported that infection may occur at least 35 months before antibodies can be detected (Imagawa, Lee, Wolinsky 1989).

The importance of antibody testing is that patients with antibodies to HIV (seropositives), in contrast to what is known of many other viral diseases, are considered to be infected with HIV. Thus, a positive antibody status suggests that the person in question can transmit the disease. The final proof that the virus is actually present is established by growing the virus in tissue cultures where it transforms lymphocytes by inducing multinucleate cells. The virus is further identified by electronmicroscopy and by its reverse transcriptase activity. However, many of these assays are laborious, time consuming and expensive and cannot be used on a large scale. Antibody tests are therefore the method of choice for screening purposes. Studies using these HIV antibody tests have provided the data upon which is based almost all of our current understanding of the epidemiology of HIV infection.

4.1 HIV CULTURE

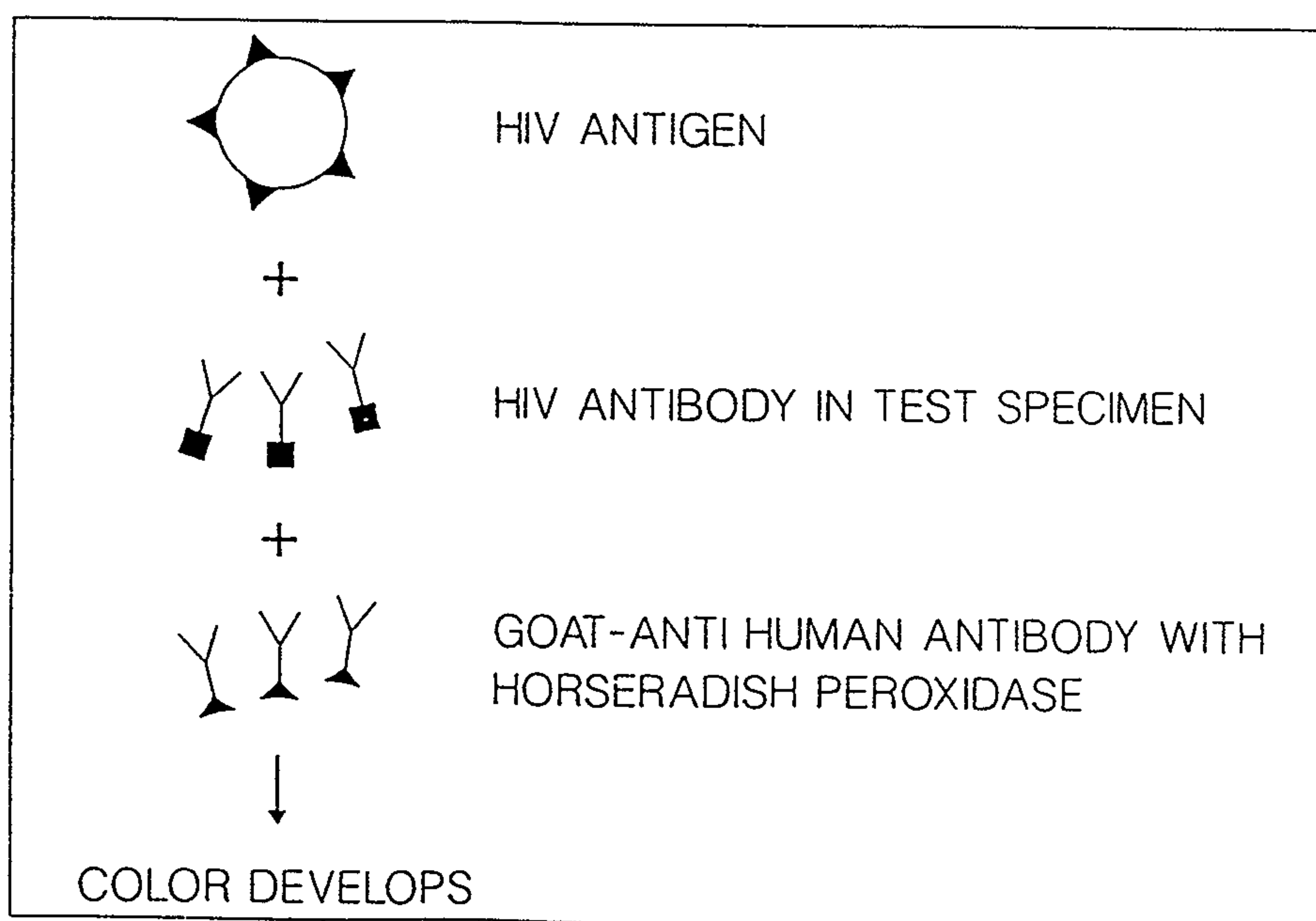
Direct identification of infectious HIV originally involved separation of the patient's peripheral blood mononuclear cells (PBMC), stimulation with the

mitogen phytohemagglutinin (PHA) and subsequent cultivation of cells for up to 30 days (Barre-Sinoussi et al 1983, Gallo et al 1984). Newer approaches involve cocultivation of patient's PBMC with PBMC from seronegative persons. This gives positive results in over 90% of seropositives (Levy 1988). The HIV recovered is identified using reverse transcriptase, immunofluorescence or immunoblot assays, or electron microscopy.

4.2 HIV ANTIBODY ASSAYS

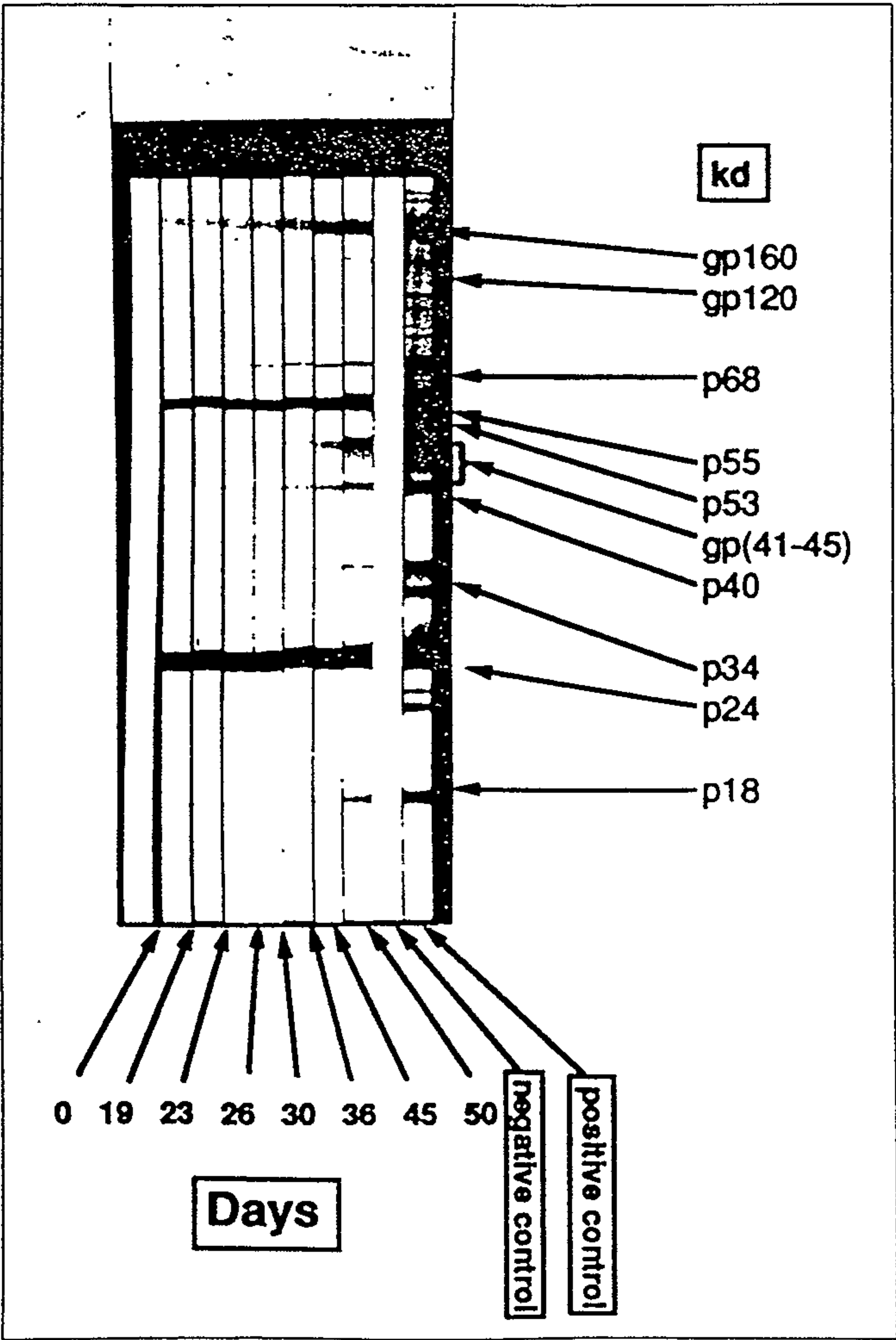
The most widely used test is **enzyme-linked immunosorbent assay (ELISA)**. This is an automated procedure requiring little time or expense. HIV proteins obtained from cultures, are attached to wells of plastic plates or to beads (Fig. 4).

Figure 4 ELISA assay.
Source: Greenspan et al (1990).



Patient or other serum is exposed to these and any binding of anti-HIV antibodies is detected colorimetrically using an enzyme-linked antihuman antibody (Cooper, Tindall 1989). False-positive reactions may occur because of non-specific bindings or cross-reactivity, and so a second confirmatory ELISA may be appropriate. However purer HIV antigens produced by recombinant technology are now available and should reduce the false-positive rate (Greenspan et al 1989). Because of the excellent specificity and sensitivity as well as ease of automation, the ELISA test is currently being used as a major screening test at teaching hospitals and blood banks in Australia (Cooper, Tindall 1989).

Figure 5 **Western blot.**
Source: Boyle et al (1993).



A more accurate antibody assay is the **Western blot** (Tsui et al 1988). These utilise gel electrophoresis to separate viral antigens and thus antibodies to individual proteins can be detected (**Figure 5**).

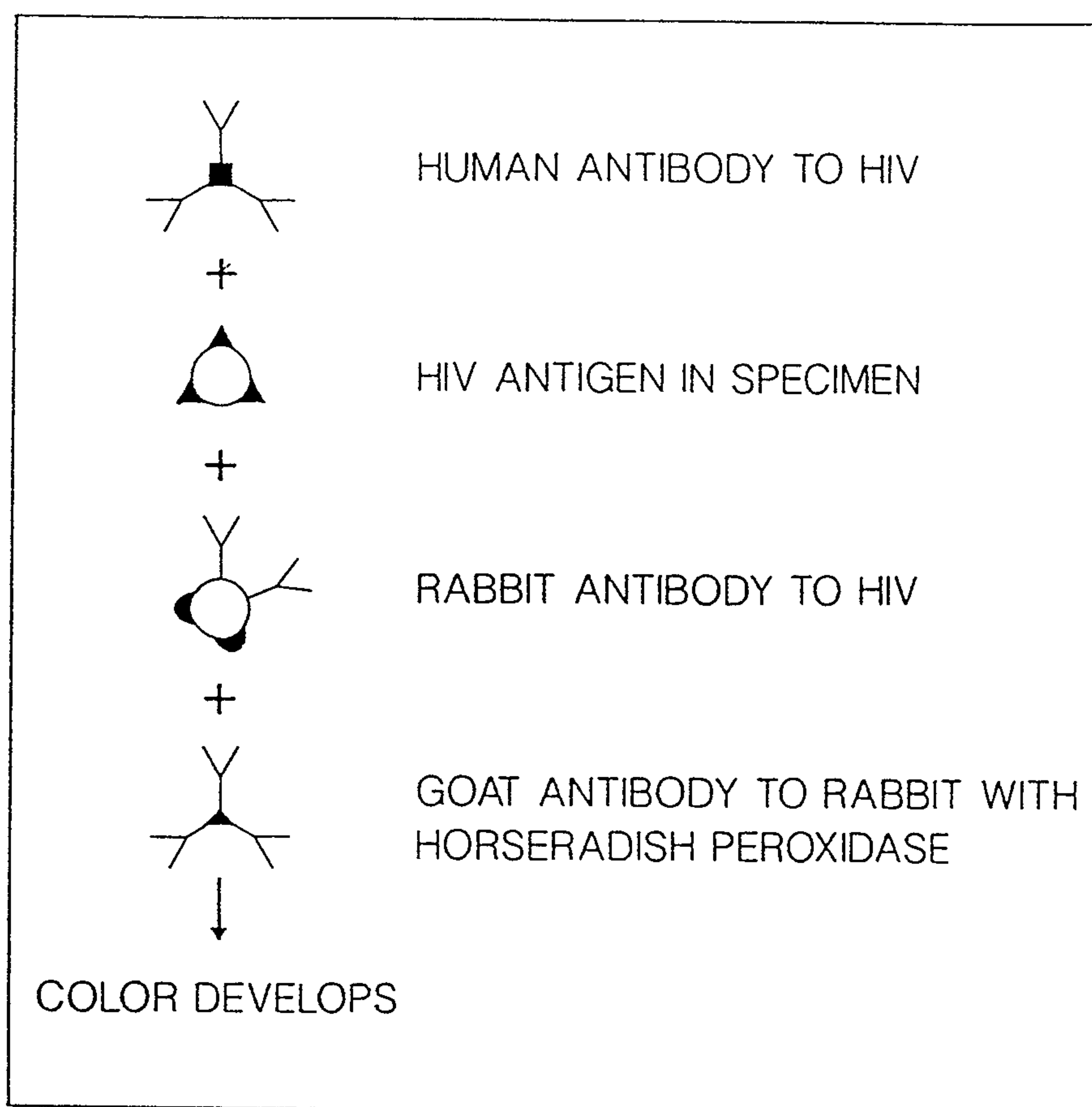
The Western blot method involves electrophoresis of disrupted HIV virions on slab gels. Most viral antigens can thus be individually detected (Greenspan et al 1990). Cells in a malignant T cell line infected with HIV are lysed and the lysate is centrifuged and placed in wells on a polyacrylamide gel slab. Electrophoresis then separates the various proteins by molecular weight and charge. When this is complete the slab gel is placed adjacent to a nitrocellulose sheet and the viral proteins are "blotted" upon it again using electrophoresis. The patient's serum is then added to the nitrocellulose sheet and if HIV antibodies are present they will react with the viral antigens. After washing, labelled antihuman immunoglobulin is then applied and the Western blot of the viral proteins is visualised (Tsui et al 1988). The Western blot permits identification of antibodies to individual HIV proteins (Boyle et al 1993).

Other antibody assays include the radioimmune precipitation assay (**RIPA**), radioimmune and neutralisation assays which have applications in specific areas of HIV research.

4.3 HIV ANTIGEN ASSAYS

Of the two approaches currently available, the more frequently used is the **sandwich assay** (Allain et al 1987). Here antibodies to HIV are attached to a plastic dish or beads (**Figure 6**). The test specimens (cell culture, blood or other fluids, cell or tissue extracts), exposed to this solid phase, produce attachment of HIV protein to the antibodies. The reaction is revealed using a labelled second anti-HIV protein antibody (Diggs 1988).

Figure 6 HIV antigen test.
Source: Greenspan et al (1990).



In the **competition assay**, plates containing antiviral antibodies are exposed to biotin-labelled HIV protein. If fluid containing HIV or HIV proteins is added, competition occurs between the test antigen and the labelled antigen so that a quenching of the reaction is seen (Homsy et al 1988). Antigen assays are extremely sensitive and have been used to show evidence for the presence of HIV well before seroconversion to monitor the effects of therapy for HIV (Ranki et al 1987). Antigen assays have also been investigated as indicators of prognosis (Lelie et al 1988).

4.4 POLYMERASE CHAIN REACTION (PCR)

The polymerase chain reaction (PCR) is a relatively newer method by which even a few molecules of DNA, which might otherwise go undetected, can be amplified many times and thus produce a measurable reaction. This method offers the most sensitive approach to the detection of specific sequences of DNA, including those of HIV and other viruses (Greenspan et al 1990).

A specific sequence of HIV proviral DNA is selected and "*primers*" or short pieces of DNA, are synthesised to have sequences complementary to the DNA on each side of the target sequence. On heating of the test sample, the two strands separate and the primers are able to bind to the flanking sequences one on each strand. Furthermore in the presence of DNA polymerising enzyme, the primers start the synthesis of two new strands complementary to the original two. Cycles are repeated with consequent amplification of the target DNA sequence by many orders of magnitude. This amplified DNA can then be detected and analysed using molecular biological methods (Ou et al 1988)

Since HIV can remain latent as DNA integrated into the host chromosomes, PCR offers a particularly important approach to detection of HIV (Loche, Mach 1988). Although very demanding and as yet fairly expensive, this method is under review at present as it is quicker and cheaper than culture of HIV.

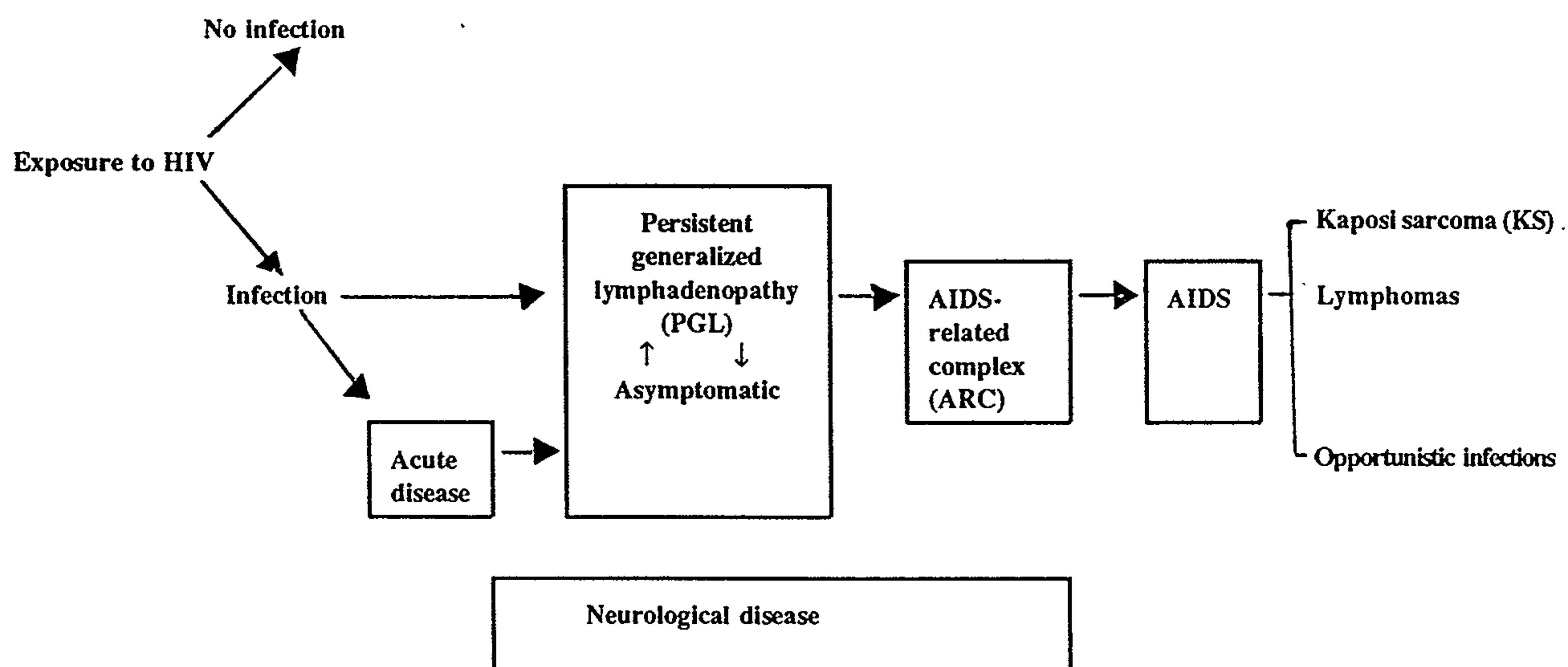
5 NATURAL HISTORY OF HIV INFECTION

Exposure to HIV may or may not result in infection. **Figure 7** is a schematic depiction of clinical responses to HIV in adults. Among those who are infected, **seroconversion** is asymptomatic in many individuals and the first clinical manifestations may not develop for several years. About 53 to 93 percent of cases experience acute HIV infection (primary HIV infection) at the time of seroconversion (Tindall, Cooper 1991). The symptoms of acute HIV infection include maculopapular rash, fever, myalgia, arthralgia, headache, diarrhoea and sore throat, and also neurological manifestations which disappear after a few weeks (Boyle et al 1993). Oral manifestations of acute HIV infection include erythema of buccal and palatal mucosa and ulcers in addition to the sore throat (Gaines 1989).

Some of these patients, as well as some of those without acute symptoms, develop **persistent generalised lymphadenopathy (PGL)**. A small minority of cases may exhibit PGL with some constitutional symptoms. Some patients with PGL (5-10%) may revert to an asymptomatic state (Tindall, Cooper 1991). In both asymptomatic and PGL subjects, the condition may progress to '**AIDS-related complex**' (ARC), characterised by long-lasting fever, weight loss, persistent diarrhoea, oral candidiasis, herpes zoster and /or hairy leukoplakia (Greenspan et al 1990). Some patients with ARC, as well as an incremental number of asymptomatic carriers and PGL patients, progress to develop **full-blown AIDS** characterised by opportunistic infections and/or Kaposi's sarcoma (KS) or Non Hodgkin's lymphoma (Weismann et al 1988). Neurologic disease characterised by encephalopathy, myelopathy or peripheral neuropathy may also be seen (Lane,

Fauci 1987). AIDS may however present denovo in a previously clinically well asymptotomatically infected individual (Moss, Bacchetti 1989).

Figure 7 Schematic description of clinical responses to HIV in adults.
Source: Weismann et al (1988).



Clinical Predictors

Persistent lymphadenopathy, which often appears early in HIV infection, was originally thought to predict progression to AIDS in HIV-infected patients but now appears not to be a predictor of progression (Moss 1988). The most commonly reported clinical predictors of progression to AIDS are herpes zoster, oral candidiasis, hairy leukoplakia and "constitutional symptoms" like sustained weight loss or fatigue, night sweats and persistent diarrhoea (Moss 1988).

5.1 WHO/CDC CASE DEFINITION FOR AIDS

The full syndrome (AIDS) is the more extreme expression of HIV infection. At the other end of the spectrum are those who have been exposed to HIV and are infected, who carry antibodies and usually also the virus itself, but who are healthy. Between these two extremes fall a large number of cases showing a wide variety of clinical and immunologic effects of HIV. The WHO/CDC definition (CDC 1987c), remains the most comprehensive, accepted listing and is therefore reproduced. The CDC definition specifies that a case of acquired immune deficiency syndrome (AIDS) is an illness characterised by:

I. Without laboratory evidence for HIV infection

If laboratory tests for HIV were not performed or gave inconclusive results and the patient had no other cause of immunodeficiency listed in Section I.A below, then any disease listed in Section I.B indicates AIDS if it was diagnosed by a definitive method.

A. Cause of immunodeficiency that disqualifies diseases as indicators of AIDS in the absence of laboratory evidence for HIV infection

1. High-dose or long-term systemic corticosteroid therapy or other immunosuppressive/ cytotoxic therapy 3 months before the onset of the indicator diseases
2. Any of the following diseases diagnosed 3 months after diagnosis of the indicator disease: Hodgkin's disease, non-Hodgkin's lymphoma (Other than primary brain lymphoma), lymphocytic leukemia, multiple myeloma, any other cancer or lymphoreticular or histiocytic tissue, or angioimmunoblastic lymphadenopathy
3. A genetic (congenital) immunodeficiency syndrome or an acquired

immunodeficiency syndrome atypical of HIV infection, such as one involving hypogammaglobulinemia

B. Indicator diseases diagnosed definitively

1. Candidiasis of the oesophagus, trachea, bronchi or lungs
2. Cryptococcosis, extrapulmonary
3. Cryptosporidiosis with diarrhoea persisting ≥ 1 month
4. Cytomegalovirus disease of an organ other than liver, spleen, or lymph nodes in a patient ≥ 1 month of age
5. Herpes simplex virus causing a mucocutaneous ulcer that persists longer than 1 month; or bronchitis, pneumonitis, or oesophagitis for any duration affecting a patient ≥ 1 month of age
6. Kaposi's sarcoma affecting a patient ≤ 60 years of age
7. Lymphoma of the brain (primary) affecting a patient ≤ 60 years of age
8. Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia (LIP/PLH complex) affecting a child ≤ 12 years of age
9. *Mycobacterium avium* complex or *M. Kansaii* disease, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
10. *Pneumocystis carinii* pneumonia
11. Progressive multifocal leukoencephalopathy
12. Toxoplasmosis of the brain affecting a patient ≥ 1 month of age

II. With laboratory evidence of HIV infection

Regardless of the presence of other causes of immunodeficiency (I.A), in the presence of laboratory evidence of HIV infection, any disease listed above (I.B) or below (II.A or II.B) indicates a diagnosis of AIDS.

A. Indicator diseases diagnosed definitively

1. Bacterial infections, multiple or recurrent (any combination of at least two within a 2-year period), of the following types affecting a child ≤ 13 years of age:

- Septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media or superficial skin or mucosal abscesses), caused by *Haemophilus*, *Streptococcus* (including *Pneumococcus*), or other pyogenic bacteria
2. Coccidioidomycosis, disseminated (at a site other than, or in addition to lungs or cervical or hilar lymph nodes)
 3. HIV encephalopathy (also called "HIV dementia", "AIDS dementia", or "subacute encephalitis due to HIV")
 4. Histoplasmosis, disseminated (at a site other than, or in addition to lungs or cervical or hilar lymph nodes)
 5. Isosporiasis with diarrhoea persisting ≥ 1 month
 6. Kaposi's sarcoma at any age
 7. Lymphoma of the brain (primary) at any age
 8. Other non-Hodgkin's lymphoma of B-cell or unknown immunologic phenotype and the following histologic types:
 - a. Small non-cleaved lymphoma (either Burkitt or non-Burkitt type)
 - b. Immunoblastic sarcoma (equivalent to any of the following although not necessarily all in combination: immunoblastic lymphoma, large-cell lymphoma, diffuse histiocytic lymphoma, diffuse undifferentiated lymphoma, or high-grade lymphoma)
 9. Any mycobacterial disease caused by mycobacteria other than *M. tuberculosis*, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
 10. Disease caused by *M. tuberculosis*, extrapulmonary (involving at least one site outside the lungs, regardless of whether there is concurrent pulmonary involvement)
 11. Salmonella (non-typhoid) septicemia, recurrent
 12. HIV wasting syndrome (emaciation, "slim disease")

B. Indicator diseases diagnosed presumptively

1. Candidiasis of the oesophagus
2. Cytomegalovirus retinitis with loss of vision
3. Kaposi's sarcoma
4. Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia (LIP/PLH complex) affecting a child ≤ 13 years of age
5. Mycobacterial disease (acid-fast bacilli with species not identified by culture), disseminated (involving at least one site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
6. *Pneumocystis carinii* pneumonia
7. Toxoplasmosis of the brain affecting a patient ≥ 1 month of age

III. With laboratory evidence against HIV infection

With laboratory test results negative for HIV infection, a diagnosis of AIDS for surveillance purposes is ruled out unless:

A. All the other causes of immunodeficiency listed above in Section I.A are excluded and

B. The patient has had either:

1. *Pneumocystis carinii* pneumonia diagnosed by a definitive method or
2. a. Any of the other diseases indicative of AIDS listed above in Section I.B diagnosed by a definitive method and
 - b. A T-helper/inducer (CD4) lymphocyte count $\leq 400/\text{m}^3$

A case of AIDS is defined as a reliably diagnosed opportunistic disease in an adolescent or an adult at least moderately indicative of underlying cellular immunodeficiency and with no other known cause of underlying cellular immunodeficiency or any other reduced resistance reported to be associated with an opportunistic disease, including secondary immunodeficiencies associated with immunosuppressive therapy, lymphoreticular malignancy, or starvation (CDC 1987c).

5.2 CLASSIFICATIONS OF HIV INFECTION

CDC Classification

In May, 1986, the Centers for disease control presented a classification system for HIV infection primarily applicable to public health purposes, including disease reporting and surveillance, epidemiologic studies, prevention and control activities, and public health policy and planning (CDC 1986).

The system classifies the manifestations of HIV infection into four mutually exclusive groups, designated by Roman numerals I - IV (Table 4). The classification system applies only to patients diagnosed as having HIV infection.

Table 4 **Summary of classification system for HIV-associated disease.**
Source: CDC (1986).

Group I.	Acute infection
Group II.	Asymptomatic infection *
Group III.	Persistent generalised lymphadenopathy *
Group IV.	Other disease
Subgroup A.	Constitutional disease
Subgroup B.	Neurologic disease
Subgroup C.	Secondary infectious diseases
Category C-1.	Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS †
Category C-2.	Other specified secondary infectious diseases
Subgroup D.	Secondary cancers †
Subgroup E.	Other conditions

* Patients in group II and III may be subclassified on the basis of a laboratory evaluation.

† Includes those patients whose clinical presentation fulfils the definition of AIDS

Group I includes patients with transient signs and symptoms that appear at the time of, or shortly after, initial infection with HIV as identified by laboratory studies. Defined as a mononucleosis like syndrome.

Group II includes patients who have no signs or symptoms of HIV infection. Patients in this category may be subclassified based on whether haematologic and/or immunologic laboratory studies have been done and whether results are abnormal in a manner consistent with the effects of HIV infection.

Group III includes patients with persistent generalised lymphadenopathy, but without findings that would lead to classification in Group IV. Patients in this category may be subclassified based on the results of laboratory studies as in Group II

Group IV includes patients with clinical signs and symptoms of HIV infection other than or in addition to lymphadenopathy. Patients in this group are assigned to one or more subgroups based on clinical findings.

In subgroup C, the patients are divided further into two categories:

Category C-1 includes patients with symptomatic or invasive disease due to one of the 12 specified secondary infectious diseases listed in the surveillance definition of AIDS.

Category C-2 includes patients with systematic or invasive disease due to one of six other specified secondary infectious diseases: **oral hairy leukoplakia**, multidermatomal herpes zoster, recurrent *Salmonella* bacteremia, nocardiosis, tuberculosis or **oral candidiasis**.

Walter Reed classification

The Walter Reed classification system is based on the presence or absence of a combination of clinical and laboratory parameters (Table 5). It relies on the T4 cell count and function as an indicator of a patient's stage of HIV disease (Redfield et al 1986).

Table 5 **Walter Reed classification system.**
Source: Redfield et al (1986).

WR Stage	HIV (antibody or antigen)	Chronic lymph- adeno-pathy	T4 / mm ³	Delayed hypersensitivity skin test	Thrush	Oppor- tunistic infection
0	Negative	Absent	>400	Normal	Absent	Absent
1	Positive	Absent	>400	Normal	Absent	Absent
2	Positive	Present	>400	Normal	Absent	Absent
3	Positive	Varies	<400	Normal	Absent	Absent
4	Positive	Varies	<400	Partial anergy	Absent	Absent
5	Positive	Varies	<400	Complete anergy and/ or thrush		Absent
6	Positive	Varies	<400	Partial or complete anergy	Absent/ Present	Present

The number of T4 cells declines gradually over the years after HIV infection. In association with this drop in T4 cells, and especially when the T4 count falls below 400 per mm³ the patients may show a decreased reaction on skin test. When the T4 cell number drops further, clinical symptoms appear. These include, initially, skin and mucous membrane lesions (Weismann et al 1988). Later, more severe opportunistic infections qualifying for the diagnosis of AIDS may occur. Thus the clinical course of HIV infection is highly associated with the underlying status of the immune system (Redfield et al 1986).

6 ORAL MANIFESTATIONS OF HIV INFECTION

The spectrum of oral lesions found in the HIV-infected population forms a diverse group of opportunistic conditions all of which may be seen in non HIV-infected patients (Jordan, Main 1991). Many of the oral signs of HIV disease are the same common diseases which occurs in people without HIV infection, for example, oral candidiasis (thrush) which commonly affects malnourished babies and the elderly in many third world countries. A diagnosis of HIV disease therefore, cannot be made on oral signs alone.

However, the relevance of oral examination of HIV infected patients has been widely accepted (Cook 1990). For instance, the presence of oral candidiasis, hairy leukoplakia, or oral Kaposi's sarcoma strongly influences the grouping of HIV-infected patients in the CDC classification (Schulten et al 1990). People with HIV infection often develop diseases of the mouth before any other visible signs develop (van der Waal et al 1991). With the continuing increase in HIV-positive individuals, it is important that dentists become familiar with the clinical features of HIV-associated oral diseases (Silverman 1991). Early detection of the precursors of symptomatic HIV-positive patients is in the best interests of both patient and the provider (Jordan, Main 1991).

In 1986, the European Economic Community took the initiative to establish a classification of the oral manifestations of HIV infection. Over 30 different oral lesions and diseases known to be associated with HIV infection were included in the initial classification and later amended (Pindborg 1989) (Table 6).

Table 6 Oral lesions associated with HIV infection.
Source: Pindborg (1989).

FUNGAL INFECTIONS	VIRAL INFECTIONS
Candidiasis	Caused by:
Pseudomembranous	Herpes simplex virus
Erythematous	Cytomegalovirus
Hyperplastic	Epstein-Barr virus
Angular cheilitis	Hairy Leucoplakia
Histoplasmosis	Varicella-zoster virus
Cryptococcosis	Herpes zoster
Geotrichosis	Varicella
	Human papilloma virus
	Verruca vulgaris
BACTERIAL INFECTIONS	Condyloma acuminatum
HIV-necrotizing gingivitis	Focal epithelial hyperplasia
HIV-gingivitis	
HIV-periodontitis	NEOPLASMS
Caused by:	Kaposi's sarcoma
Mycobacterium avium intracellulare	Squamous cell carcinoma
Klebsiella pneumoniae	Non-Hodgkin's lymphoma
Enterobacterium cloacae	
Escherichia coli	
	UNKNOWN ETIOLOGY
Actinomycosis	Recurrent aphthous ulceration
Cat scratch disease	Progressive necrotizing ulceration
Sinusitis	Toxic epidermolysis
Exacerbation of apical periodontitis	Delayed wound healing
Submandibular cellulitis	Idiopathic thrombocytopenia
	Salivary gland enlargement
NEUROLOGIC DISTURBANCES	Xerostomia
Trigeminal neuropathy	Melanotic hyperpigmentation
Facial palsy	

Mucocutaneous opportunistic infections (MCOI) are frequent and of diagnostic value in HIV disease. A classification was proposed by Schoefer et al (1989).

Class I MCOI	Almost pathognomonic for immune deficiency Herpes exulcerans, hairy leukoplakia.
Class II MCOI	Important indicators of immune deficiency Oral candidiasis, herpes zoster, molluscum contagiosum.
Class III MCOI	Less important indicators of immune deficiency Folliculitis, Human papilloma virus infection (HPV), bacterial abscesses.

An updated classification (Table 7) has been proposed by the EEC-Clearinghouse on oral problems related to HIV infection and the WHO Collaborating Centre on oral manifestations of HIV (1991) in which three groups of lesions are recognised.

Table 7 **Updated classification of oral lesions associated with HIV infection.**
Source: EEC-Clearinghouse on oral problems related to HIV infection and WHO Collaborating Centre on oral manifestations of HIV (1991).

Group 1. Lesions strongly associated with HIV

Candidiasis

- Erythematous
- Hyperplastic
- Pseudomembranous
- Angular cheilitis

Hairy leukoplakia

HIV-gingivitis

HIV-necrotizing gingivitis

HIV-periodontitis

Kaposi's sarcoma

Non-Hodgkin's lymphoma

Group 2. Lesions less commonly associated with HIV

Atypical ulceration

Salivary gland diseases

- Dry mouth due to ↓ salivary flow rate
- Unilateral/bilateral swelling of major salivary glands

Thrombocytopenic purpura

Viral infections (other than Epstein-Barr virus)

- Cytomegalovirus
- Herpes simplex virus
- HPV (warty-like lesions)
 - Condyloma acuminatum
 - Focal epithelial hyperplasia
 - Verruca vulgaris
- Varicella-zoster virus
 - Herpes zoster
 - Varicella

Group 3. Lesions possibly associated with HIV

Bacterial infections (excl. gingivitis/periodontitis)

- Actinomyces israelii*
- Enterobacter cloacae*

Escherichia coli

Klebsiella pneumoniae

Mycobacterium avium intracellulare

Mycobacterium tuberculosis

Cat-scratch disease

Drug reactions

- (ulcerative, erythema multiform, lichenoid)

Exacerbation of apical periodontitis

Fungal infection other than candidiasis

- Cryptococcus neoformans*
- Geotrichium candidum*
- Histoplasma capsulatum*
- Mucoraceae (Mucormycosis)*
- Aspergillus flavus*

Melanotic hyperpigmentation

Neurologic disturbances

- Facial palsy
- Trigeminal neuralgia

Osteomyelitis

Sinusitis

Submandibular cellulitis

Squamous cell carcinoma

Toxic epidermolysis

A fourth group of lesions consisting of lesions associated with the use of drugs has been considered, but not definitely accepted. The writer has used this categorisation because it strongly emphasises the relative importance of the various oral lesions.

Investigations into the oral manifestations of the AIDS pandemic has been hampered by lack of agreement on definitions and diagnostic criteria for the common oral lesions seen in association with HIV infection. With this in view, a set of definitions and criteria for use by dental professionals has been proposed and is reproduced (Greenspan et al 1992).

DEFINITIONS

I. CANDIDIASIS

A. Pseudomembranous candidiasis

1. Presumptive: Yellow-white, loosely adherent (wipeable) plaque located anywhere in the mouth.
2. Definitive: As noted above, plus positive morphologic verification (including potassium hydroxide [KOH], periodic acid-Schiff (PAS)-stained, or Gram- stained preparation).

B. Erythematous candidiasis

1. Presumptive: Erythematous macular patches on mucosal surfaces. When dorsum of the tongue is involved, area is depapilated (smooth).
2. Definitive: As noted above, plus positive morphologic Verification (including KOH, PAS-stained, or Gram-stained preparation).

C. Angular cheilitis

1. Presumptive: Fissures or linear ulcers at the corners of mouth.
2. Definitive: As noted above, plus positive morphologic verification (including KOH, PAS-stained, or Gram-stained preparation).

II. GINGIVITIS/PERIODONTITIS

A. HIV-associated gingivitis

1. Presumptive: Erythematous marginal gingival band that can extend into adjacent attached and alveolar mucosa.
2. Definitive: As noted above; also, lesion does not respond to removal of dental plaque and calculus and oral hygiene measures.

B. HIV-associated periodontitis (necrotizing periodontitis)

1. Presumptive: Severely destructive lesion characterised by soft tissue ulceration and necrosis with rapidly progressive, non-self-healing loss of periodontal attachment and bone. Deep pain and spontaneous bleeding are or may have been associated with lesion.
2. Definitive: As noted above, plus documented progression of rapid tissue loss (within 4 weeks) and exclusion of other causes of periodontal (soft and hard tissue) destruction.

III. NECROTIZING STOMATITIS (presumptive and definitive)

Localised acute, painful ulceronecrotic lesion of oral mucosa that exposes underlying bone or penetrates or extends into contiguous tissues. Margins are sharply defined and undermined, and specific laboratory studies, including biopsy, are not useful in identifying etiologic agents or processes.

IV. HERPES SIMPLEX

A. Intraoral form

1. Presumptive: Solitary, multiple, or confluent lesions that may be noted together with vesicles on keratinised mucosa, including hard palate, attached gingiva, and dorsum of the tongue. Occasionally, nonkeratinised mucosa may be involved. Round to slightly irregular margins with minimal to no erythematous halos are present.
2. Definitive: As noted above, plus demonstration of virus by use of tests such as immunohistochemical analysis and culture.

B. Perioral Form

1. Presumptive: Single or multiple vesicles or ulcers with crusting on vermillion portion of lips and adjacent facial skin.

2. Definitive: As noted above, plus demonstration of virus by tests such as immunohistochemical analysis and culture.

V. CYTOMEGALOVIRUS (presumptive and definitive)

Oral ulcer from which cytomegalovirus can be identified immunohistochemically or by culture of biopsy tissue.

VI. VARICELLA-ZOSTER VIRUS (presumptive and definitive)

Unilateral vesiculoerosive eruption of skin and oral mucosa along distribution of branch or branches of trigeminal nerve, often preceded or accompanied by pain. Its unique clinical presentation is definitive without laboratory confirmation.

VII. APTHOUS ULCERATION (presumptive and definitive)

A. Minor apthous ulcer

Single or multiple recurrent, well-circumscribed, painful ulcer(s) on nonkeratinised tissue, measuring 0.2 to 0.5 cm with border, from which no etiologic agent can be identified.

B. Major apthous ulcer

Solitary or multiple, nonhealing, painful ulcers, greater than 0.5 cm in diameter, from which no etiologic agent can be identified.

C. Herpetiform apthous ulcers

Multiple recurrent crops of painful ulcers on nonkeratinised mucosa, less than 0.2 cm in diameter, which may coalesce and from which no etiologic agent can be identified.

VIII. HAIRY LEUKOPLAKIA

1. Presumptive: Vertically corrugated, slightly elevated white surface alteration of lateral or ventral tongue margin, that does not wipe off. May also be seen at other oral sites, usually in conjunction with tongue lesions.
2. Definitive: As noted previously, plus confirmation of presence of herpes-type viral particles by electron microscopy or demonstration of EBV by molecular biologic or immunocytochemical techniques

IX. HIV SALIVARY GLAND DISEASE

1. Presumptive: Enlargement of major salivary glands and/or complaint of xerostomia in absence of xerogenic agents, medications, and diseases known to cause xerostomia.
2. Definitive: As noted previously, plus either labial or major salivary gland biopsy evidence of periductal focal sialoadenitis with predominant CD8+ infiltrate, or reduced stimulated salivary flow rate.

X. ORAL KAPOSI'S SARCOMA

1. Presumptive: Brown, red, blue, or purple macule, papule, or nodule. Has predilection for hard palate and attached gingiva but can appear on other mucosal sites.
2. Definitive: As noted above, plus confirmation by tissue biopsy.

XI. ORAL WARTS/PAPILLOMA

A. Papilloma

1. Presumptive: Papillary outgrowths of oral mucosa.
2. Definitive: As noted above, plus biopsy and routine histopathologic analysis to differentiate wart from papilloma not otherwise specified.

B. Focal epithelial hyperplasia

1. Presumptive: Multiple small papules with granular surface features and irregular margins that tend to coalesce.
2. Definitive: As noted above, plus biopsy and routine histopathologic analysis.

It is anticipated that the presumptive diagnosis will be adequate for use in epidemiologic surveys when large numbers of patients are examined briefly, to determine the prevalence and incidence of these conditions in a given population. The definitive diagnosis will be useful in clinical care, in pathogenesis and therapy studies.

6.1 LESIONS STRONGLY ASSOCIATED WITH HIV INFECTION

6.1.1 Candidiasis

The commonest oral fungal disease seen in association with HIV infection is candidiasis (Greenspan D, Greenspan JS 1991). Candidiasis is an infection due to yeasts of the genus *Candida*, which is a member of the family *Cryptococcaceae*. Oral candidiasis was included in some of the earliest descriptions of AIDS and HIV infection (Klein et al 1984). Oral candidiasis is often the initial manifestation of symptomatic infection with HIV (Gottlieb et al 1981, Silverman et al 1986, Samaranayake, Scully 1989). Further it may imply the concurrent presence of oesophageal candidiasis (Tavitian et al 1986, Tindall et al 1989). Oral candidiasis is also a predictor of likelihood of other opportunistic infections (Chandrasekar, Molinari 1985, Morfeldt-Manson et al 1989). Oral candidiasis has been used as a marker of disease severity in classifications of HIV infection (Redfield et al 1986). Concurrent xerostomia in HIV disease may well add to the development of candidiasis. Particularly in young men, the development of oral candidiasis without a local cause, such as xerostomia, or therapy with antimicrobials, corticosteroids or other immunosuppressive drugs is strongly suggestive of HIV infection (Scully et al 1991a).

A number of clinical variants of oral candidiasis are now recognised. Traditionally, the disease was classified as acute pseudomembranous (thrush), acute atrophic, chronic atrophic and chronic hyperplastic varieties, with a subsequent addition of *Candida*-associated angular cheilitis (MacFarlane, Samaranayake 1989). However, there has been a need to revise this classification

in the light of newer findings, particularly with respect to oral candidiasis in HIV infection (Holmstrup, Axell 1990). The variety of clinical types of oral and systemic candidiasis is matched by a variety of causative yeast species. *Candida albicans* is the best known and by far the most common pathogen of the group, although several other species such as *Candida glabrata* and *Candida tropicalis* are infrequently isolated from oral lesions (MacFarlane 1990).

In order to understand the pathogenesis of oral candidiasis, it is important to realise the commensal existence of this fungus intraorally in some 20-50 percent of healthy individuals (Samaranayake 1989). The transformation of this innocuous commensal to the harmful parasite is dependent on a number of factors although by far, the most important factor would appear to be the health of the host (Odds 1988). Hence, the often used aphorism "*Candidiasis is a disease of the diseased.*"

Epidemiology

From the earliest periods of the AIDS epidemic, oral candidiasis was recognised as an important sign of disease progression. In the first report on the disease, which later became known as AIDS in homosexual men, oral candidiasis was described as part of the disease in four of the five patients described (Gottlieb et al 1981). Unexplained oral candidiasis was prominently featured in persons in whom AIDS eventually developed (Masur et al 1982). Klein et al (1984), early in the AIDS epidemic, focused the attention of clinicians worldwide on this disease entity by demonstrating its value as a predictor of full-blown AIDS in adults.

A substantial body of epidemiologic data now emphasises its high prevalence in HIV-infected persons (Phelan et al 1987, Coleman et al 1989). The frequency of *Candida* isolation and clinical signs of oral candidiasis increases with advancing HIV infection (Torssander et al 1987). In 22 reported investigations of prevalence of oral candidiasis in a total of 3387 patients infected with HIV, the prevalence ranges from 11 to 96 percent. The mean frequency of oral candidiasis weighted according to the number of subjects in each study is 36.5 percent indicating that, in general, oral candidiasis may develop in one-third to one-half of HIV-infected persons (Samaranayake 1992).

Clinical variants

Oral candidiasis, in connection with HIV infection, comprises four major types:

(1) **pseudomembranous**, (2) **erythematous (atrophic)**, (3) **hyperplastic**, (4) **angular cheilitis** (Greenspan et al 1990). The four clinical variants occur with varying frequency in patients with AIDS, ARC, and healthy seropositives and it is therefore important to distinguish among these types (Pindborg 1989). Recent studies have shown that both erythematous and pseudomembranous candidiasis are equally important with regard to the subsequent development of AIDS with the median time to development of AIDS in both groups being approximately 25 months (Greenspan D, Greenspan JS 1991). The pseudomembranous form is apparently more common in patients with full-blown AIDS while the erythematous form seems to be the most common expression of oral candidiasis in HIV infected patients not yet fulfilling the criteria of AIDS (Van der Waal et al 1991). Angular cheilitis has also been commonly reported (Porter et al 1989, Schulten et al 1989, Wanzala et al 1989). Another noteworthy feature of oral

candidiasis in HIV infection is the frequent presentation of the disease in multiple oral sites (Cahn et al 1989).

The **erythematous or atrophic** form of oral candidiasis may well be the most common early oral manifestation of HIV infection (Cahn et al 1989), and most often appears clinically as a red lesion. The colour intensity may vary from fiery red to a hardly discernible pink spot (Greenspan et al 1990). The sites most frequently affected are the palate and the dorsum of the tongue (**Figure 8**). In the latter location the erythema is associated with loss of filiform papillae. Erythematous candidiasis may also appear as spotty areas of the buccal mucosa. This is a very characteristic feature of HIV infection, but quite often overlooked as erythematous candidiasis is usually without disturbing clinical symptoms. In one study (Greenspan, Overby et al 1989) the lesion was present on the hard palate in 60 percent, on the soft palate in 17 percent, and on the dorsum of the tongue in 57 percent of 66 patients with erythematous candidiasis. In another African survey (Wanzala et al 1989) the lesions of the tongue and palate were reported in 63 percent and 50 percent, respectively, of 31 HIV-positive women. Before the AIDS era, erythematous candidiasis, then called acute atrophic candidiasis, was infrequently observed in patients after broad-spectrum antibiotic therapy or rarely during corticosteroid therapy. The erythematous appearance was believed to be a secondary consequence of shedding of the plaque of pseudomembranous candidiasis, which was the primary event (Cawson 1978). On the contrary, in HIV infection the erythematous type appears to precede the pseudomembranous variety (Pindborg, Nielsen 1989), although prospective surveillance studies are warranted to confirm this observation.

As opposed to erythematous, **pseudomembranous candidiasis** classically presents as semiadherent, whitish yellow, soft, creamy, drop-like or sometimes confluent membranes removable from the mucosa by wiping with a gauze swab, which leaves a red and slightly bleeding surface. The disease is usually acute, but in HIV-infected patients it may, if untreated, persist for several months during which the course of the infection appears to be chronic rather than acute. Pseudomembranous lesions may involve any area of the oral mucosa, most frequently the tongue, hard and soft palate, and buccal mucosa (Greenspan et al 1990) (**Figures 9 & 10**). In a study of 106 AIDS patients with this condition, 48 percent and 42 percent of the lesions were seen on the dorsum and lateral surface of the tongue, respectively: 20 percent on the hard palate, 19 percent on the soft palate, and 15 percent on the buccal mucosa (Greenspan, Overby et al 1989).

The **hyperplastic** type in HIV-infected patients is most often seen bilaterally on the buccal mucosa and rarely in the retrocommissural area, which is the classic presentation site in HIV-negative persons. The lesions are characterised by whitish yellow patches which cannot be removed by scraping. The lesions have been related to tobacco smoking (Greenspan et al 1990). This is the least common variant of oral candidiasis in HIV positive patients. This form and angular cheilitis each constitute approximately 10 percent of oral candidiasis seen in HIV infection (Samaranayake 1992). The chronic hyperplastic candidal variant in HIV-positive or AIDS patients should be clearly distinguished from hairy leukoplakia lesions (Samaranayake, Pindborg 1989).

Angular cheilitis (angular stomatitis) is a disease of multifactorial etiology, and it may be infective or non infective in origin. AIDS and HIV infection should now be added to the list of causative factors of angular cheilitis, because cumulative data from a number of studies indicate that one in 10 patients with HIV infection may have angular cheilitis (Porter et al 1989, Schulten et al 1989). Before the advent of HIV infection, these lesions were most commonly seen in elderly persons as a complication of denture induced stomatitis (chronic atrophic candidiasis), due to anaemia, loss of occlusal vertical dimension or vitamin deficiency, and the disease was relatively rare among younger age groups. However, today it should be remembered that, when observed in young individuals, angular cheilitis could be the first indication of HIV infection (Greenspan et al 1990). Clinically, the lesion is characterised by fissures radiating from the angles of the mouth often associated with small white plaques (**Figures 11 & 12**). The lesions manifest as red, fissured crusts with or without ulceration and could be accompanied by subjective symptoms such as soreness, tenderness, or burning or pain (Ohman et al 1985). Although the infection is generally caused by *Candida* species and/or *Staphylococcus aureus* (Greenspan et al 1990), the extent of involvement of the latter organisms in HIV-induced angular cheilitis remains to be determined.

Another type of oral candidiasis, the **papillary variant**, has also been described by some workers. Characteristically manifesting in the hard palate, they appear as erythematous papillary nodules similar to those observed in denture induced papillomatosis. In two German studies, this variant was found in 6 percent and 11 percent of 262 and 110 HIV-positive and AIDS patients respectively (Reichart et al 1987, Langford et al 1988).

6.1.2 Hairy Leukoplakia

Since the original description of oral hairy leukoplakia (HL) among homosexual men with HIV infection in San Francisco (Greenspan et al 1984), this white lesion of the tongue has been seen in all risk groups worldwide (Rindum et al 1987, Greenspan, Mastrucci et al 1988, Barone et al 1990). HL is probably due to opportunistic infection by Epstein-Barr virus (EBV) in association with HIV infection. The association of EBV with HL has been confirmed by using Southern blot hybridization for EBV DNA and by *insitu* hybridization (Greenspan et al 1985).

HL is found almost exclusively in persons with HIV infection and indeed may be commoner than oral candidiasis (Greenspan D, Greenspan JS 1992). Very rarely cases of hairy leukoplakia have been described in other conditions which are not associated with HIV-infection (Syrjänen et al 1989, Greenspan et al 1989). The prevalence and incidence of HL are not yet fully documented, but reports give a range of from 20 percent point prevalence in those with otherwise asymptomatic HIV infection in the United States (Feigal et al 1988) to 36 percent in patients in Tanzania with full-blown AIDS (Schiødt et al 1990). A recent study in Europe observed a prevalence rate of 29.5 percent confirming that HL is frequently seen in symptomatic patients with HIV infection (Ramuel et al 1992). In one study in Africa the clinical presence of HL was found to have a predictive value for the presence of AIDS or HIV infection of 100 percent and 95 percent respectively (Schiødt et al 1990).

A significant proportion of patients with HL and without AIDS subsequently progress to AIDS fairly rapidly (Katz et al 1992). In a study of 198 cases of HL, the median time to AIDS was 24 months and the median time to death was 41 months (Greenspan et al 1991).

Clinical features

Oral hairy leukoplakia is a white lesion of the tongue, and occasionally of other parts of the mouth and pharynx, that is due to epithelial hyperplasia (Greenspan D, Greenspan JS 1992). Clinically, the lesion presents as a white patch that is often corrugated or even hairy, usually occurring on the lateral margins of the tongue often bilaterally. It may be very small (**Figure 13**), consist of several patches that run together, or be extensive (**Figure 14**), even covering the dorsal surface of the tongue. Occasionally it may spread downwards onto the ventral surface of the tongue where it usually has a flat appearance (Greenspan et al 1990). HL is rarely seen on the buccal mucosa, labial mucosa, floor of the mouth, soft palate and oropharyngeal mucosa (Kabani et al 1989). HL has not been described in the oesophagus, larynx, anal/vaginal mucosa or skin (Hollander et al 1986). The lesions of HL are white, often corrugated and sometimes so prolific as to produce a shaggy, carpet like appearance. However, the size and severity of the lesion cannot be used to predict the stage of HIV infection, including the presence or absence of AIDS (Schiødt et al 1987).

Although usually asymptomatic, the lesion may sometimes cause discomfort if superinfected with *Candida*. Patients may, sometimes complain of its unsightly appearance and also of a "cotton-wool" feeling in the mouth (Greenspan D, Greenspan JS 1991) (**Figure 15**).

Candida can be identified in more than 50% of HL lesions by smear, culture or histopathologic study. However, the lesion is not eliminated even when all traces of the fungus are removed by aggressive antifungal therapy (Schiødt et al 1987, Greenspan D, Greenspan JS 1991).

6.1.3 HIV-gingivitis (HIV-G)

HIV-associated gingivitis (HIV-G) occurs as lesions confined to soft tissues that show distinctive patterns of erythema affecting the gingival margin, attached gingiva, and alveolar mucosa, even in patients with excellent oral hygiene and little or no plaque accumulation (Greenspan et al 1990). Profound erythema of the gingival margins is observed in essentially all sites of HIV-G (Figure 16). In most cases this erythema has an intensely red linear band that affects both facial and proximal tissue and extends 2 to 3 mm apically from the gingival margin (Winkler et al 1988). In addition, both punctate and diffuse erythema are seen in about 75 percent of affected patients (Winkler et al 1988). The unusual punctate or speckled areas of erythema may involve the entire attached gingiva from the gingival margin to the alveolar mucosa. The punctate areas resemble the speckled appearance seen on some mucosal surfaces with atrophic candidiasis, although *Candida* has not been confirmed as the causative agent in gingival biopsies of these lesions (Winkler, Robertson 1992). In some regions these punctate areas appear to coalesce and give a bright red appearance to the affected tissues. The coalescing regions may also contribute to a more diffuse pattern of erythema that extends from the gingival margin deep into the vestibular fornix (Winkler et al 1988). In a number of cases the HIV-infected patient may present with swollen interdental papillae irregularly distributed (Greenspan et al 1990).

These HIV-G lesions most frequently involve the entire mouth and are usually distributed equally to all quadrants. About 15 percent of HIV-G-affected sites show gingival bleeding on probing, and 11 percent exhibit spontaneous bleeding (Winkler et al 1989). Gingival pain is a frequent but not consistent finding in patients who have only signs of HIV-G (Winkler et al 1988).

In general, HIV-G does not respond to intensive scaling and root planing and improved plaque control measures alone (Greenspan et al 1990). Characteristics of HIV-G are summarised in Table 8.

Table 8 Characteristics of HIV-associated gingivitis (HIV-G).
Source: Winkler et al (1988).

Bleeding on brushing or spontaneously
Red marginal zone
Swollen interdental papillae
Poor response to conventional therapy

Studies have demonstrated that the predominant microflora of sites with HIV-G include *Candida albicans*, *Proformalis gingivalis*, *Bacteroides intermedius*, *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum*, and *Wolinella recta* (Murray et al 1988). Cultivable *C. albicans* was identified in about 50 percent of HIV-G sites compared with 26 percent of unaffected sites in HIV-positive patients and 3 percent of healthy sites in HIV-negative patients (Murray et al 1988). The percentage of sites that were positive by DNA probe detection in

HIV-G sites of HIV-positive patients and in matched gingivitis sites of HIV-negative patients for *A. actinomycetemcomitans* (23%, 7%), *B. gingivalis* (52%, 17%), *B. intermedius* (63%, 29%), and *W. recta* (50%, 14%) suggested a microbiologic profile similar to conventional periodontitis but substantially different than conventional gingivitis (Murray, Grassi, Winkler 1989).

6.1.4 HIV-necrotizing gingivitis

Acute necrotizing ulcerative gingivitis (ANUG) results from an infiltration of the host gingiva by endogenous microflora. The development of ANUG seems to follow conditions such as physical and/or emotional stress, lack of sleep and malnutrition, i.e., conditions that produce a lowered host resistance. AIDS is a disease in which immune responsiveness is drastically compromised. Necrotising gingivitis as a periodontal complication of HIV infection was first described by Dennisson et al (1985). Later studies describing ANUG in HIV-infected patients have corroborated this initial description (Winkler et al 1987, Pindborg, Holmstrup 1987, Schulter et al 1989, Porter et al 1989).

Clinical features

Necrotizing gingivitis may be superimposed on or precede HIV-G or HIV-associated periodontitis. In general, HIV infected patients with ANUG has the classic symptoms of ulceration and necrosis affecting primarily interproximal gingiva, gingival bleeding, gingival pain and halitosis (Winkler et al 1987, Schiødt, Pindborg 1987). Because of gingival necrosis, there is little deep

pocketing (Rosenstein et al 1989). The onset is either sudden or insidious with bleeding on toothbrushing, pain and a characteristic foetor ex ore (halitosis). Symptoms may subside gradually over 3-4 weeks but the condition often recurs. The gingiva appears fiery red and swollen (**Figure 17**), and both the margin of the gingiva and the top of the interdental papillae is the seat of a yellowish-greyish necrosis which bleeds easily (Pindborg, Holmstrup 1987).

ANUG is observed primarily in proximal areas of the lower anterior teeth and rarely traverses the mucogingival junction (Winkler, Robertson 1992).

6.1.5 HIV-periodontitis (HIV-P)

HIV-associated periodontitis (HIV-P) has all the gingival features of HIV-G and additionally manifests severe deep pain, gingival bleeding, soft tissue necrosis, and rapid destruction of the periodontal attachment apparatus (Greenspan et al 1990). The lesion is progressive, and spontaneous resolution is rare and does not respond to conventional periodontal therapy (Winkler et al 1988).

A history of severe pain is a distinguishing feature of HIV-P and the chief reason many patients seek dental treatment. Unlike the pain associated with ANUG, in which pain is localised to the gingivae, the pain associated with HIV-P is usually described as localised in the jaw bone or as a deep aching pain. Frequently patients say that their *"teeth are hitting the jaw bone when they chew."* In many cases this deep pain precedes the development of the clinically obvious HIV-P lesion and diminishes after sequestration of alveolar bone (Winkler et al 1988).

Essentially all HIV-P sites bleed to probing, and about 50% of sites show spontaneous bleeding as evidenced by the presence of blood clots at the affected soft tissue-tooth interface or by frank bleeding in response to light external pressure or air drying (Winkler et al 1988). Nocturnal gingival bleeding is not uncommon (Winkler, Murray 1987). Areas affected by HIV-P frequently do not show deep pocket formation, because severe gingival necrosis usually coincides with loss of crestal alveolar bone. The rapid apical progression of this soft tissue necrosis may lead to exposure of crestal and interseptal alveolar bone and to subsequent bone sequestration. Loss of more than 90 percent of the alveolar housing has been observed in as little as a few weeks (Winkler, Robertson 1992).

Although severe cases of HIV-P can affect all the teeth and surrounding periodontium, HIV-P is usually seen as a localised lesion, resulting in islands of a severely involved periodontium surrounded by areas of HIV-G or relatively normal tissue (Winkler et al 1988). Frequently only one surface of a tooth is severely involved with HIV-P, whereas remaining surfaces are only slightly affected. However there is no evidence of site specificity and all regions of the mouth appear to have similar chances of being affected. Halitosis and fever are not consistent features of HIV-P, even in the most severe cases (Winkler et al 1988).

The clinical presentation of HIV-P shows considerable variation. Initial lesions show little radiographic evidence of bone loss, minimal tooth mobility, and necrosis limited to the alveolar crest (Greenspan et al 1990). Moderate HIV-P

usually involves the entire attached gingiva with exposure and partial sequestration of bone to the mucogingival line. Tooth mobility is common. Severe HIV-P shows extensive radiographic evidence of bone loss, and necrosis of soft tissue and underlying alveolar bone extends well past the mucogingival line. Mobility may be so profound that the teeth are at risk for frank exfoliation (Winkler, Robertson 1992).

Microbiologic studies suggest that the microbial profile of sites associated with HIV-P are similar to that of conventional periodontitis. Notable exceptions include higher proportions of *C. albicans* and *W. recta* in HIV-P. Moreover, the qualitative microbiologic profiles of HIV-G and HIV-P are essentially the same, and only *W. recta* shows major quantitative differences (Zambon 1988).

HIV-P as well as ANUG may in some cases progress into **necrotizing stomatitis**. Necrotising stomatitis is characterised by an acute, massively destructive ulcerative and necrotizing lesion of the gingiva that extends into contiguous mucosal and osseous tissues. The infection may lead to extensive denudation and eventual sequestration of bone (Williams et al 1990). Necrotizing stomatitis represents the most severe form of periodontal infection seen in association with HIV, which may resemble noma or cancrum oris and is one of the more serious oral infections of HIV disease (Winkler, Robertson 1992).

6.1.6 Kaposi's sarcoma

Prior to the 1980s, Kaposi's sarcoma (KS) was a rare lesion found almost exclusively in three groups of patients: (1) Older males of eastern Mediterranean and Jewish descent (Bingham 1985); (2) Africans, especially in Zaire and Uganda (Taylor et al 1971); (3) Patients undergoing immunosuppressive therapy (Penn 1979). In these patients, the lesions of KS occurred, mainly on the skin of the lower extremities and were only rarely reported to involve the oral cavity (Bayer et al 1978).

Occurrence of KS in HIV infection

Since the beginning of the AIDS epidemic, Kaposi's sarcoma has been recognised as a common feature of the syndrome (Safai et al 1985). It is estimated that 34 percent of all patients with AIDS have KS diagnosed during the course of their disease (Santucci et al 1988) and that it is the initial clinical manifestation of the disease in 30 percent of cases (Safai et al 1985, Dodd et al 1991), but its overall prevalence in HIV infection appears to be decreasing (Gallo 1990). There is increasing evidence that KS may be a sexually transmitted disease (Beral et al 1990, Dodd et al 1991). The lesion is found more frequently in homosexual men with AIDS than those from other risk groups (Safai et al 1985), and it has been suggested that there is a transmissible agent prevalent in the homosexual population. Cytomegalovirus (CMV) infection have been suggested as a cofactor, because CMV is more prevalent among homosexuals (Lifson 1990). The decreasing rate of KS in patients with AIDS is in part related to a broader definition of AIDS that includes other diseases (Beral et al 1990, Lifson 1990).

However, the principal explanation may be related to the fact that homosexual men, who are mainly afflicted with KS, now represent a smaller proportion of AIDS patients because of the dramatic spread of HIV into the heterosexual population by IDUs and HIV-seropositive sexual partners (Epstein, Silverman 1992).

The concept of KS as a neoplasm has been questioned lately, as studies suggest that HIV may induce an angioproliferative factor, possibly a protein. Thus, it cannot be excluded that KS is a result of vascular proliferation rather than a true neoplasm (Salahuddin et al 1992). Patients with KS have a median survival time of less than 2 years and less than 10 percent survive 5 years (Payne et al 1990).

Oral manifestations of KS

KS involves the oral cavity in up to 55 percent of HIV infected patients (Silverman et al 1986, Phelan et al 1987, Ficarra et al 1988, Lifson et al 1990, Epstein, Silverman 1992). Oral KS may occur in any mucosal site but most commonly involves keratinised and attached oral mucosa (Ficarra et al 1988, Barret et al 1988, Epstein, Scully 1991). The palate is most commonly involved followed by the gingiva (Barret et al 1988, Epstein, Scully 1991) (**Figures 18 & 19**). In some cases the oral cavity is the only site of KS (Dodd et al 1991). One third of patients with oral KS may have multiple sites of involvement (Epstein, Silverman 1992). Although descriptions of oral KS vary (**Table 9**), the essential description is of a flat or raised pigmented lesion (Daly et al 1989).

Table 9 **Appearance of intra-oral Kaposi's sarcoma as described by various investigators.**
Source: Daly et al (1989).

Investigators	Appearance of Oral KS
Lozada et al (1983)	Flat, bluish, vascular lesions; exophytic pigmented lesions.
Green et al (1984)	Flat, pigmented lesions; raised or exophytic, pigmented lesions.
Marcusen et al (1985)	Bluish, angiomatous lesions.
Wofford and Miller (1985)	Red, violet, pink or purple macules, papules or nodules.
Silverman et al (1986)	Flat, asymptomatic, vascular-like discolourations; exophytic growths.

Lesions at early stages present as flat, blue -purple or red-purple discolourations that do not blanch with pressure and must be differentiated from benign vascular lesions, ecchymosis, or salivary gland abnormality (Epstein, Silverman 1992). Later stage lesions become raised and nodular (**Figure 20**). Non-pigmented KS has also been reported in the oral cavity (Daly et al 1989).

Tissue biopsy is required for definitive diagnosis, which can be readily obtained with the patient under local anaesthesia (Green et al 1984). Fine-needle aspiration cytology has also been described as diagnostic (Barret et al 1988, Daly et al 1989). However, oral KS in a subject at risk for HIV infection is usually clinically characteristic, so that biopsy is often a formality.

In Australia, up until early 1992, KS has been the AIDS defining diagnosis in 17.2 percent of people diagnosed with AIDS making it the second most common AIDS defining diagnosis behind *Pneumocystis carinii* pneumonia (PCP) (The National AIDS Registry 1992b). Although not necessarily the most threatening to the patient's health, KS lesions are the most visible of all manifestations of AIDS. The implications of this cannot be ignored. The uninformed public's fear of AIDS and the severe social reactions KS patients can experience are often more painful and harmful than the early stages of the malignancy (Volberding 1989).

6.1.7 Non-Hodgkin's lymphoma (NHL)

High grade non-hodgkin's lymphomas (NHL) are the second most common malignancy in HIV infection (Epstein, Silverman 1992). Following the first reports on NHL in homosexual men (Lozada et al 1982, Zeigler et al 1982), the incidence of NHL is rapidly increasing (Levine 1987, Kristal et al 1988). Lymphomas are primarily found in IDUs who are HIV positive (Ahmed et al 1987, Roithmann et al 1990). Because the number of IDUs is escalating, this may partly explain the rapid increase of NHL in HIV-associated malignancy (Scully et al 1991b). An additional risk factor is the longer survival of immunosuppressed patients with HIV disease (Epstein, Scully 1992). The lymphomas in patients with AIDS tend to be aggressive, high -grade lymphomas, and survival is measured in months from diagnosis (Hiddemann 1989, Kaplan 1990).

The most common presentation of NHL in HIV is extranodal disease; central nervous system involvement is frequently seen (Zeigler et al 1984, Kaplan 1990). Oral lymphomas, almost exclusively of the non-hodgkin's type and B cell lineage, are now a recognised complication of HIV infection (Scully et al 1991). Intraoral NHL presents most often as rapidly growing masses involving the gingiva (**Figure 21**) and palate (Zeigler et al 1984, Silverman et al 1986, Green, Eversole 1989, Kaugars, Burns 1989, Brahim et al 1988). Studies have also reported oral NHL characterised by soft tissue tumefactions with underlying bone as the seat of destruction (Kaplan et al 1989).

The relation between NHL and EBV has been documented by many investigators (Levine 1987, Green, Eversole 1989, Hamilton 1989, Gallo 1990). However, the findings that not all B cell lymphomas demonstrate EBV DNA suggest that other mechanisms resulting in polyclonal stimulation may also be important (Hamilton 1989, Kaplan 1990). The present hypothesis of the pathogenesis of HIV-associated NHL suggests that it is the result of a complex interaction of EBV infection, antigenic stimulation, and T-cell dysfunction (Yarchoan et al 1986).

? figures reversed ?

Figure 8 Erythematous candidiasis.
Source: Survey of oral changes in HIV infection (1992).



Figure 9 Pseudomembranous candidiasis.
Source: Foltyn (1993).



Figure 10 Pseudomembranous candidiasis under a unilateral removable partial denture.
Source: Foltyn (1993).



Figure 11 Angular cheilitis.
Source: Survey of oral changes in HIV infection (1992).

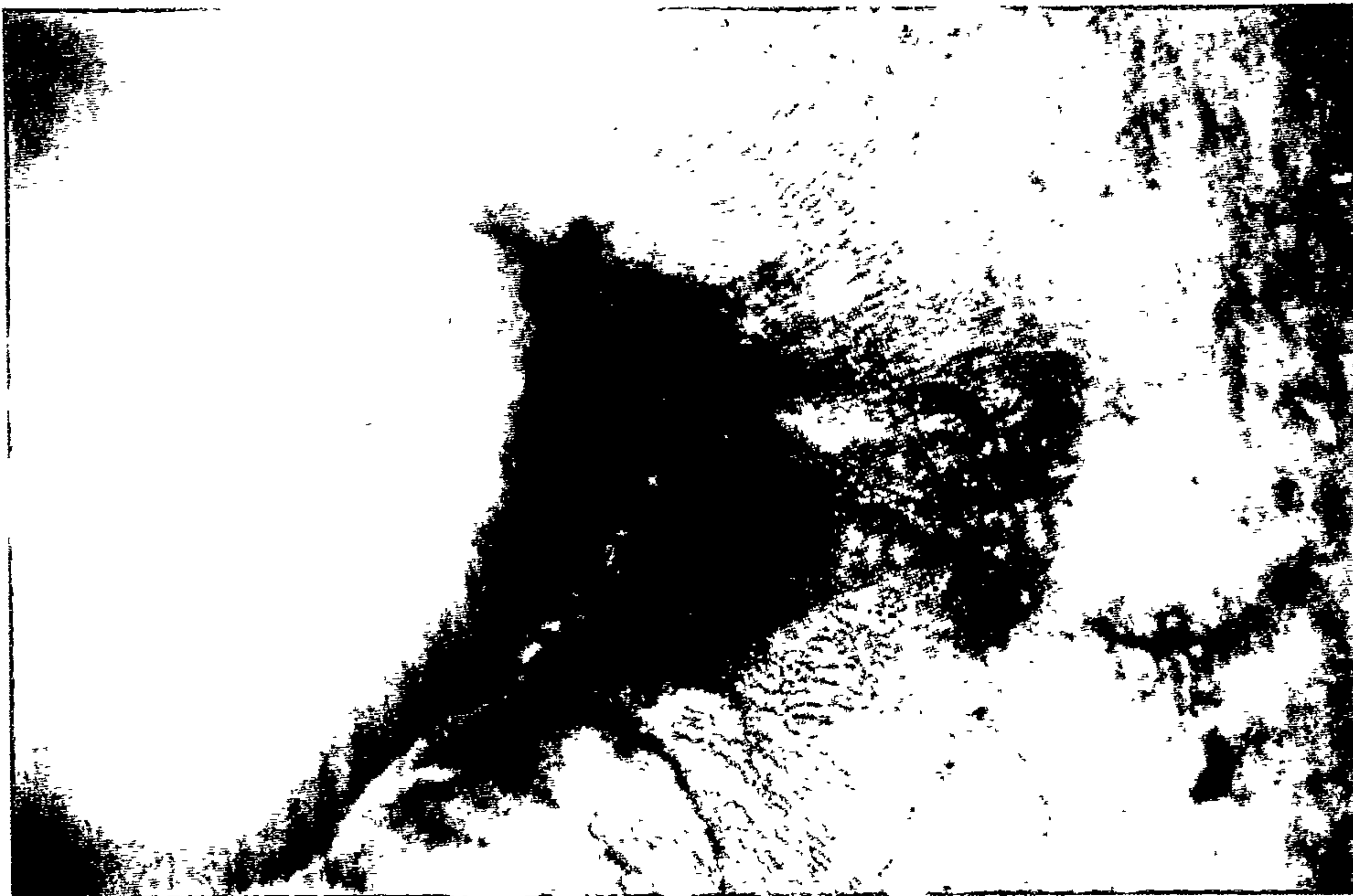


Figure 12 Angular cheilitis without visible colonisation by *Candida*.
Source: Foltyn (1993).

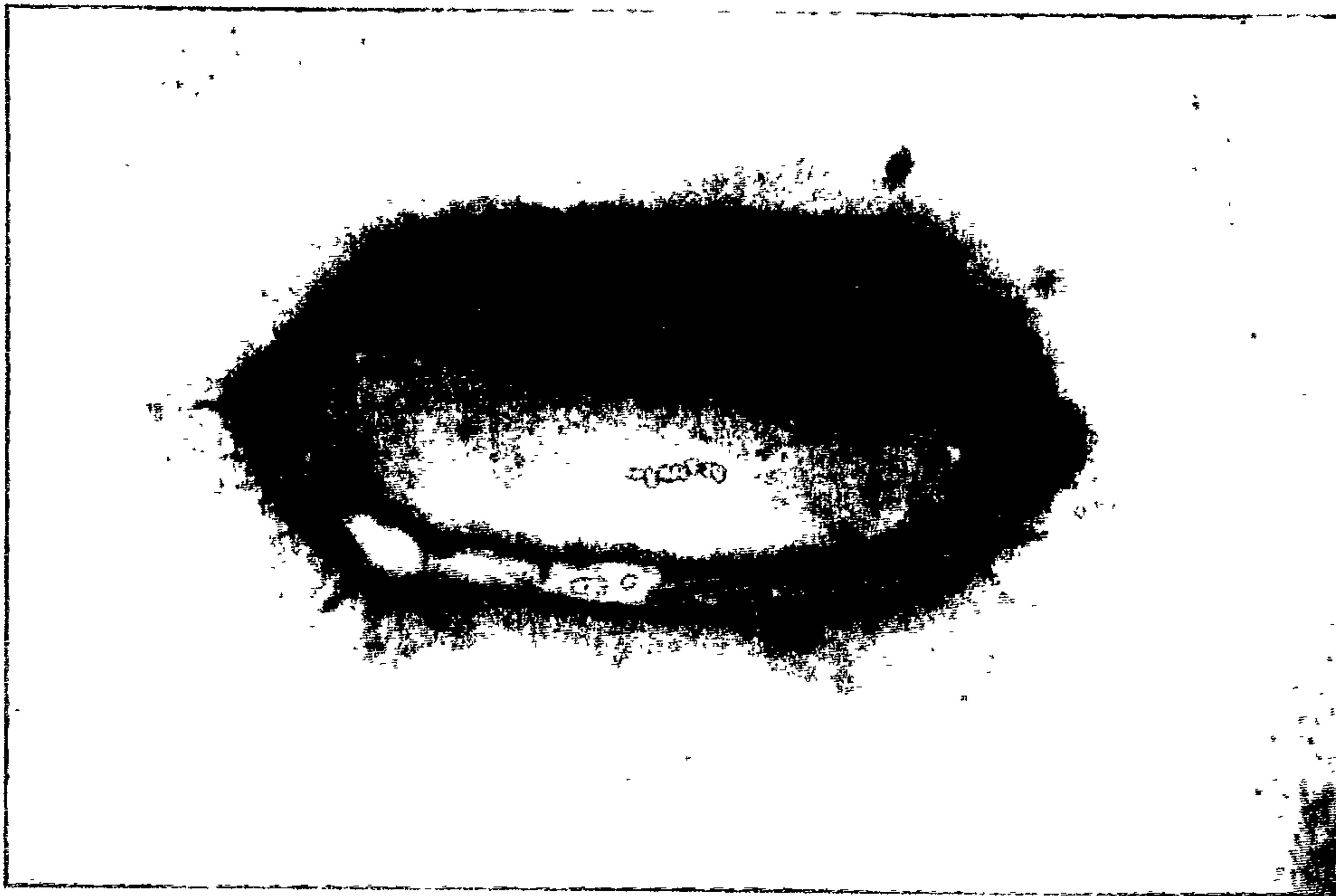


Figure 13 Early hairy leukoplakia - discrete patch on the side of the tongue.
Source: Foltyn (1993).



Figure 14 **Advanced hairy leukoplakia.**
Source: Foltyn (1993).



Figure 15 **Extensive hairy leukoplakia - corrugated white lesions on the tongue.**
Source: Survey of oral changes in HIV infection (1992).



Figure 16 HIV-gingivitis.
Source: Survey of oral changes in HIV infection (1992).

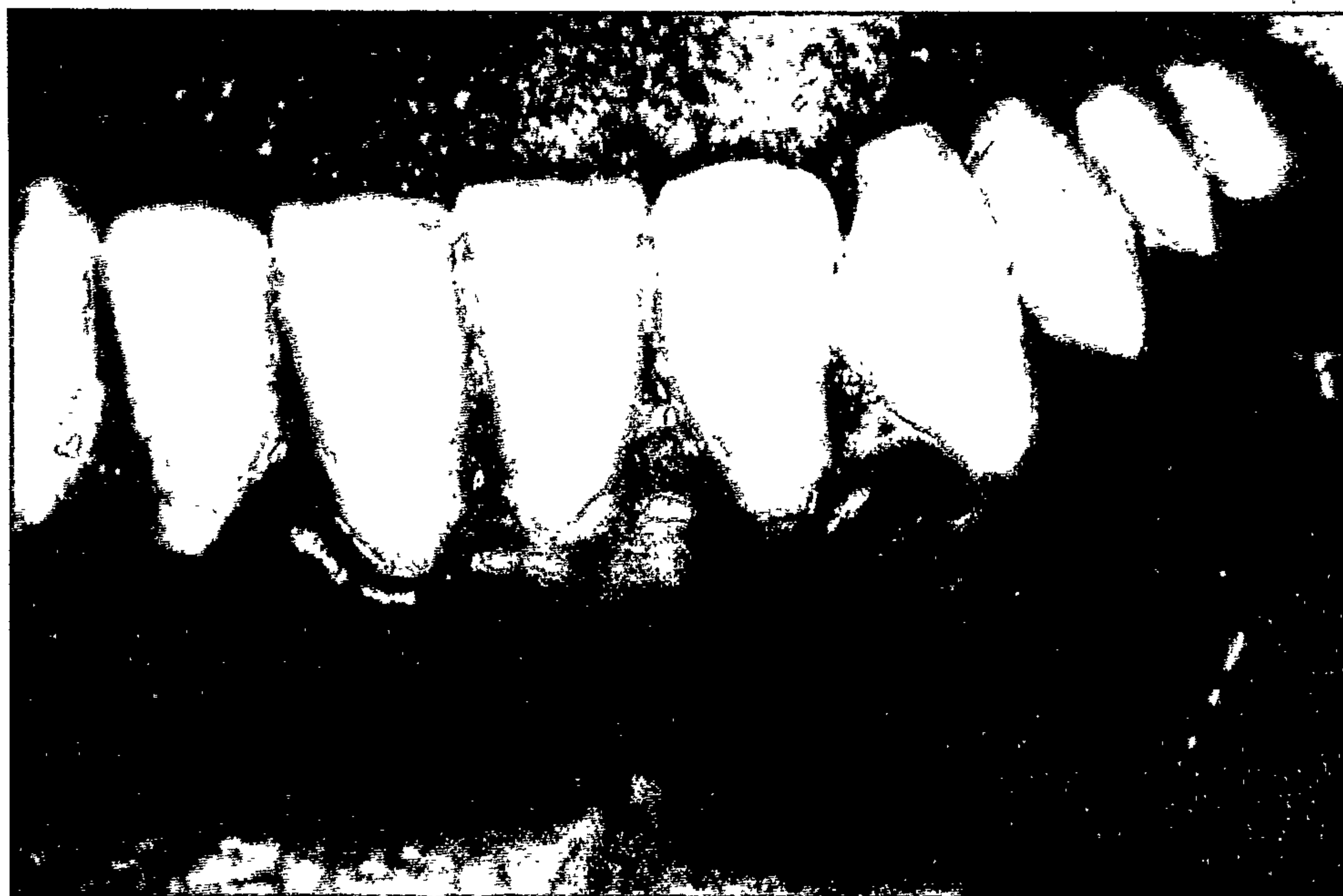


Figure 17 HIV-related acute necrotising ulcerative gingivitis (ANUG) around mandibular anterior teeth.
Source: Foltyn (1993).



Figure 18 Kaposi's sarcoma-palate.
Source: Foltyn (1993).

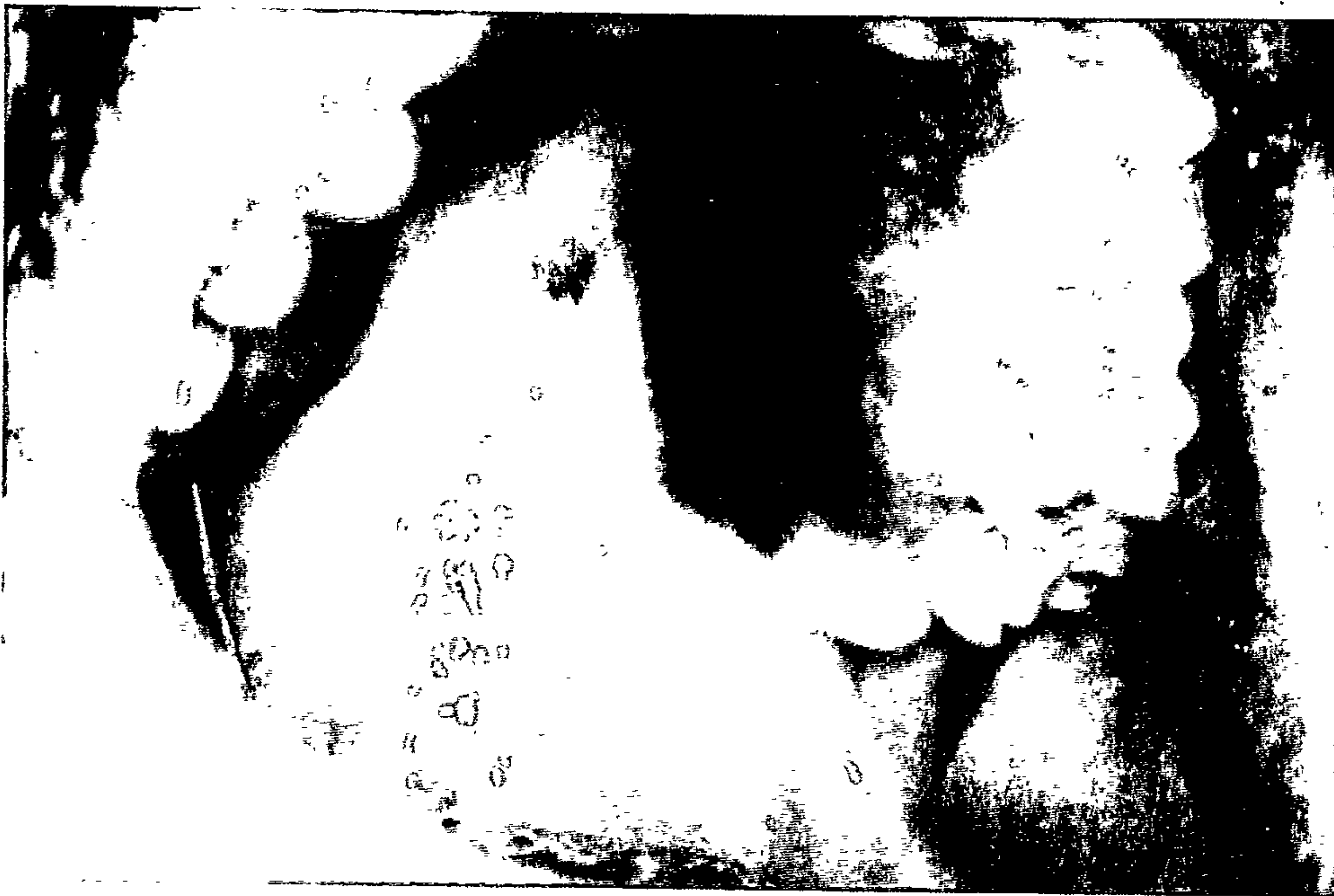


Figure 19 Kaposi's sarcoma-labial gingiva.
Source: Foltyn (1993).



Figure 20 Kaposi's sarcoma-nodular lesion on palate.
Source: Survey of oral changes in HIV infection (1992).



Figure 21 Non-Hodgkin's lymphoma on gingival margin of mandibular teeth.
Source: Foltyn (1993).



Figure 22 **Aphthous-like ulceration.**
Source: Survey of oral lesions in HIV infection (1992).



Figure 23 **Oral ulceration associated with cytomegalovirus (CMV) infection.**
Source: Foltyn (1993).



Figure 24 Herpes simplex virus (HSV) infection.
Source: Survey of oral changes in HIV infection (1992).



Figure 25 Human papilloma virus (HPV) infection - with healing lesion of herpes labialis.
Source: Survey of oral changes in HIV infection (1992).



6.2 LESIONS LESS COMMONLY ASSOCIATED WITH HIV INFECTION

6.2.1 Atypical ulceration

Oral ulcers of non-specific origin have been described in association with HIV (Bach et al 1988, MacPhail et al 1991, Phelan et al 1991). The clinical appearance and behaviour of these non-infectious or ^{non-}neoplastic ulcerations is similar to recurrent oral ulcers of minor, major and herpetiform type, but with increased severity and frequency (Reyes-Teran et al 1992). These aphthous-like ulcers may first be seen during the acute illness associated with HIV seroconversion (Gaines 1989), and can be associated with pharyngeal and/or oesophageal ulcers (Bach et al 1988). In a study by Silverman et al (1986), 8 percent of the 375 homosexuals (comprising AIDS, ARC, high-risk, contact and healthy groups) had aphthae. Because recurrent aphthous ulceration (RAU) is commonly encountered in most populations, it is difficult to evaluate whether the prevalence of RAU is truly heightened among patients with HIV infection (Pindborg 1989).

The etiology and pathogenesis of RAU are unknown. Current hypotheses implicate a defect in immune regulation (Greenspan et al 1990) or a cryptic role for herpes simplex virus (Eglin et al 1982). Humoral and cell mediated immunity against oral streptococcal antigens and human oral mucosa appear to be features of RAU (Donatsky 1978). An apparent increase in the frequency of RAU has been seen in the AIDS risk groups. Perhaps the local and systemic host defects in HIV infection cause these ulcers in this group of patients. The sites most commonly involved include the tonsillar area, soft palate, labial and buccal mucosa, floor of the mouth, ventral aspect of tongue and oesophagus (Bach et al 1988, Phelan et al 1991).

The ulcers may have the typical appearance of RAU, with well circumscribed ulcers in crops, each showing an erythematous margin (MacPhail et al 1991) (Figure 22). Some are of the minor RAU type, less than 5 mm in diameter, a few appear as crops of tiny 1-2 mm ulcers which may coalesce (herpetiform ulcers). More commonly seen is the third variety, major RAU (Scully et al 1991b). This condition has also been known as "*Sutton's aphthae*" and "*peradenitis mucosa necrotica recurrens*" (Pindborg 1981). Major RAU appear larger (10 mm or more), more painful and persistent than the minor variety, being one to ten in number and leading to interference with mastication and swallowing. These ulcers tend to heal with the formation of scars, may show raised borders and a crateriform appearance (Reyes-Teran et al 1992). Some of the larger persistent major RAU require biopsy to exclude lymphoma, carcinoma, and other conditions (Greenspan et al 1990).

6.2.2 Salivary gland diseases (HIV-SGD)

Patients with HIV infection, both adults and children, may have parotid swelling and/or xerostomia (Silverman et al 1986, Porter et al 1989, Schiødt et al 1989, Greenspan et al 1990). The etiology can be multifactorial and may involve an autoimmune reaction, viral and bacterial infection, acute and chronic inflammation and tumours (Schiødt et al 1989, Greenspan et al 1990).

Studies have described a new clinical entity in HIV-infected patients that they named "diffuse infiltrative CD8 lymphocytosis syndrome" (Itescu et al 1990). This disorder, which clinically resembles Sjögren's syndrome is characterised by persistent circulating CD8 lymphocytosis and diffuse lymphocytic infiltration of salivary and lacrimal glands, gastrointestinal tract and lungs (Ficarra 1992). The minor salivary glands present focal lymphocytic infiltrate as in Sjögren's

syndrome, but the infiltrate is constituted predominantly by CD8 cells. HIV does not appear to directly cause the salivary gland damage (Schiødt et al 1989) and neither Epstein-Barr virus nor cytomegalovirus appear causal. A major histocompatibility complex antigen, HLA-DR5, is implicated in the pathogenesis of this syndrome (Itescu et al 1990).

Dry mouth due to decreased salivary flow

Preliminary reports suggest that xerostomia may occur in 10-13 percent of patients with AIDS (Silverman et al 1986, Schiødt, Pindborg 1987). Xerostomia was also found in patients with early stages of HIV infection (Schiødt et al 1989). Although there is no difference in the average salivary flow rate between groups of patients with and without AIDS (Yeh et al 1987), some HIV infected patients suffer from severely reduced flow rates (Greenspan et al 1990). Phelan et al (1987) reported cases of xerostomia among AIDS patients in whom medications may have been casual. However it is now clear that parotid and submandibular salivary flow rates are diminished and that there are sialochemical alterations (Atkinson et al 1989). The potential causes of xerostomia in HIV-infected patients are summarised in Table 10.

Table 10 **Potential causes of xerostomia in HIV-infected patients.**
Source: Ficarra (1992).

Sicca syndrome (diffuse infiltrative CD8 lymphocytosis syndrome)
Salivary gland infection (CMV, bacteria, others)
Emotional distress
Anaemia (AZT)
Nutritional deficiencies
Anticholinergic drugs
Radiation therapy (for lymphomas, oral KS)
HIV-related nephropathies (polyuria)
Dehydration

Enlargement of major salivary glands

AIDS associated swelling of the parotid glands was initially reported in children but is now also recognised in adults. Parotid gland enlargements occurred in 10 percent of children with AIDS, in one study (Pahwa et al 1986). More recently, enlargement of the major salivary glands have been noted in adult patients with AIDS, ARC and otherwise asymptomatic HIV infection (Colebunders et al 1988, Schiødt et al 1989). Clinically, the salivary gland enlargement is asymptomatic, can be unilateral but often bilateral and appears as a diffuse soft swelling (Ficarra 1992).

6.2.3 Thrombocytopenic purpura

Thrombocytopenic purpura is a relatively frequent complication of infection with HIV. Previous reports suggests a prevalence of 3-9 percent, depending on the risk group studied (Kaslow et al 1987, Ratner 1989, Karpatkin 1990). This disorder has been observed in almost every risk category and in all stages of HIV infection. A temporary acute thrombocytopenia can be associated with acute HIV infection (Tindall, Cooper 1991). It should be pointed out that in IDUs, thrombocytopenic purpura may develop as the result of the use of intravenous heroin and cocaine (Adams et al 1978).

HIV-related thrombocytopenic purpura shows some differences from the classic autoimmune thrombocytopenic purpura with respect to the presence of circulating immune complexes, increased platelet associated IgG, and C3 and C4 (Ficarra 1992). The pathogenesis appears to be related to the deposition of immune

complexes on platelets or an antibody specific for platelet membrane antigens (Stickler et al 1985, Karpatkin 1990).

Oral lesions caused by this immunopathologic disorder may appear in both early and late stages of HIV infection. The oral lesions may be seen as the initial presentation or may appear after skin lesions have occurred. In the oral cavity, the lesions appear as small blood-filled purpuric lesions (petechiae) or large ecchymosis and are sometimes associated with spontaneous gingival bleeding (Reichart et al 1987). Rarely, gingival bleeding may be confused with HIV-G (Greenspan et al 1990). Severe bleeding can also be a complication of oral surgical procedure (Ficarra 1992).

6.2.4 Viral infections (other than Epstein-Barr virus)

While HIV infection predisposes to opportunistic infections, certain viral opportunists are capable of facilitating dissemination and expression of HIV while concomitantly adversely affecting the immune response. Most of the viral agents that infect the orofacial tissues of HIV seropositive patients are latent endogenous herpes group viruses (**herpes simplex virus**, **Epstein-Barr virus**, **cytomegalovirus**). As the opportunists become pathogenic, HIV infection may be augmented with heightened immunosuppression, further complementing opportunism by the herpes group viruses. Occasionally, **varicella zoster virus** and **human papilloma virus** may be associated with oral lesions in HIV-positive patients (Eversole 1992).

Cytomegalovirus (CMV) infections

Oral mucosal involvement by cytomegalovirus is uncommon although this virus is regularly excreted into the saliva in AIDS patients (Marder et al 1985). When infection of the oral tissues occurs, large, sharply demarcated oral ulcers lacking rolled margins, which are often multiple and painful are present (Andriolo et al 1986, Kanas et al 1987, Langford et al 1990) (**Figure 23**). Biopsy discloses granulation tissue with typical CMV inclusions identifiable in endothelial cells and other connective tissue cells. These lesions occur despite high antibody titres and a robust CD4 and CD8 (Eversole 1992). In two of the four patients reported by Langford et al (1990), Two died of disease, and at autopsy both had disseminated CMV disease. Thus it is assumed that oral CMV ulceration is a harbinger of disseminated disease (Eversole 1992).

Herpes simplex virus (HSV) infections

Herpes simplex virus (HSV) causes primary and recurrent disease. The HSV infections are particularly severe and persistent but rarely disseminate (Scully et al 1991a). In the HIV-positive immunocompromised host, oral lesions are encountered in approximately 10 percent of individuals (Silverman 1986, Phelan 1987). It should be noted that this figure is not appreciably different from that of the general population. The point prevalence of oral HSV infection among HIV-positive and HIV-negative patients was found to be on a parity by Melnick et al (1989). Importantly, although HSV recurrent disease may not be more prevalent, the clinical course is dramatically altered in the HIV-seropositive patient; the lesions are more widespread, occur in atypical distribution patterns, and may persist for weeks or even months.

Most oral and perioral HSV infections are caused by HSV-1, but there are occasional reports of HSV-2 associated lesions in HIV-infected persons (MacPhail et al 1989). HSV infections can be clinically seen as either vesicles or ulcers on the palate, gingival margins and elsewhere on the oral mucosa and the vermilion border of the lips (Foltyn 1993a) (**Figure 24**).

In infants, HSV infections has been reported to involve the oral mucosa in 3 of 15 paediatric AIDS cases (Scott et al 1984). Herpetic stomatitis in HIV-infected patients is somewhat different from the classic form of herpetic gingivostomatitis. The stomatitis, especially in AIDS, is more severe with extensive lesions and marked crust formation on the vermilion borders (Greenspan et al 1990). Among adults, recurrent herpes labialis has been commonly reported in homosexual men. The labial lesions progress rapidly and eventuate in diffuse weeping ulcers that extend onto the facial skin and persist for many weeks (Zimmerli et al 1988). Numerous cases of intraoral herpetic lesions that are not merely confined to the palatal gingiva; rather, clustered vesicles and erosions involving the entire hard palate, the lower labial mucosa or the buccal mucosa unilaterally have also been reported (Eversole 1992). It should be noted that the CDC case definition of AIDS includes patients who are HIV seropositive and harbour orofacial herpetic lesions that have persisted for more than one month (CDC 1987).

Human papillomavirus (HPV) infections

Benign epithelial wart-like proliferation of the oral mucosa of various configurations such as verruca vulgaris, condyloma acuminatum and focal

epithelial hyperplasia have been reported in some HIV-positive persons and are associated especially with human papillomavirus (HPV) type 7 or other HPVs including types 13, 18, 32 and a novel HPV type (Greenspan, de Villiers et al 1988, de Villiers 1989). However, oral papillomas are not common in HIV-infected persons (Silverman et al 1986).

Clinically, HPV-associated lesions are papillary, sessile, or pedunculated lesions or they may be papular; most oral condylomas are multiple and involve many mucosal sites, including the gingiva, tongue, buccal and labial mucosae (de Villiers 1989) (Figure 25).

Varicella-zoster virus (VZV) infections

Reports of oral infection with varicella-zoster virus (VZV) in HIV infection are not common in the dental literature, although oral chicken pox and zoster have been recorded (Schiødt, Rindum, Bygbert 1987). Nevertheless, herpes zoster may herald poor prognosis (Friedman-Kien 1986, Murray, Godbold et al 1989). Murray, Godbold et al (1989) found that after 3.5 years AIDS developed in 54 percent of patients who initially had herpes zoster. In a retrospective study of AIDS patients with KS, 8 percent had prior zoster (Friedman-Kien 1986). In this same report the authors prospectively followed 35 subjects who were HIV positive but did not have AIDS. In seven of these patients AIDS developed from 1 to 28 months after zoster.

6.3 LESIONS POSSIBLY ASSOCIATED WITH HIV INFECTION

6.3.1 Bacterial infections (excluding gingivitis/periodontitis)

Mycobacterium avium intracellulare, an acid-fast bacillus, seldom caused disseminated disease in adults before the advent of the HIV pandemic. It has been known to cause localised lung disease. However, in HIV infection, *Mycobacterium avium intracellulare* infection is relatively common and is characterised by fever, weight loss and debilitation (Greenspan et al 1990). Oral manifestations in the form of ulcerated lesions on the palate, with firm borders and necrotic centres extending down to bone have been reported (Volpe et al 1985).

Klebsiella pneumoniae and *Enterobacter cloacae* have been reported in association with oral lesions in patients undergoing cancer chemotherapy (Peterson 1983). Similar lesions have been described in the mouths of immunosuppressed homosexual men (Greenspan et al 1990). Although infection with *Mycobacterium tuberculosis* is common in HIV disease, especially in drug abusers and in Africa; there have been very few reports of oral lesions (Scully et al 1991b). Rare opportunistic oral infections with *Actinomyces israelii*, *Escherichia coli* have been described in HIV-positive persons (Silverman et al 1986, Cohen, Kurzrock 1987, Schiødt, Pindborg 1987).

6.3.2 Cat-scratch disease

Oral vascular lesions (epithelioid angiomatosis) which may be clinically and histologically similar to Kaposi's sarcoma, but which are infective in origin have

been reported in HIV-disease (Cockerell et al 1987) and shown to be related to cat-scratch disease caused by the CSD bacillus (Le Boit et al 1988). More recently, epithelioid angiomatosis has been described as affecting the oral cavity as a first sign of HIV infection (Speight et al 1991).

6.3.3 Drug reactions

Lichenoid reactions involving the oral mucosa have been described in HIV disease (Silverman 1989). There are also occasional reports of oral ulcers and other reactions after the use of various drugs used in HIV disease, including foscarnet and interferon (Gilquin et al 1990). The cytidine analog 2,3-dideoxycytidine produces mouth ulcers in nearly two thirds of patients (McNeeley et al 1989). These ulcers resolve by the third week of therapy at latest, or if the drug is withdrawn, and they do not develop in patients given low doses (McNeeley et al 1989).

6.3.4 Exacerbation of apical periodontitis

Periapical exacerbation associated with HIV infection was first reported by Herlen & Gerner (1984) on a 27-year old bisexual man who had experienced intermittent pain and swelling during and after endodontic treatment carried out by his local dentist. Radiographs showed periapical radiolucencies. Endodontic revision was complicated by repeated exacerbations. In the course of the treatment, the patient had to seek medical attention, which led to the diagnosis of AIDS. Delayed healing of apical periodontitis after endodontic treatment of several teeth in an AIDS patient has also been reported (Gerner et al 1988).

6.3.5 Fungal infections other than candidiasis

Among the opportunistic infections characteristic of AIDS is one caused by *Cryptococcus neoformans*, however it was only in 1987 that the first cases of oral infection were reported (Lynch, Naftolin 1987). Cases with persistent ulcers of the tongue or hard palate with pseudomembrane centrally and marked induration extending beyond the border of the ulcer and which may be painful to palpation have been reported (Lynch, Naftolin 1987, Glick et al 1987).

Infection with *Histoplasma capsulatum* causes fungal infection known as histoplasmosis. The disease is endemic to the Ohio River Valley in the USA as well as to the Caribbean and parts of Central and South America (Follansbee 1988). However, the organism is a common opportunistic pathogen causing localised or disseminated disease in immunocompromised patients, as with HIV infection where the presence of histoplasmosis is diagnostic of AIDS (Follansbee 1988). Although histoplasmosis usually presents with persistent fever, weight loss and pulmonary symptoms, it can occasionally present with oral or skin lesions (Greenspan et al 1990).

Geotrichium candidum is a common soil fungus and cases of disseminated geotrichosis have been described in immunosuppressed individuals (Schuster 1980). Lesions may depict florid gingivitis involving the maxillary and/or mandibular gingiva associated with pain, soreness and bleeding (Schuster 1980). Rare opportunistic oral infections with *Mucoraceae* and *Asperigillus flavus* have been described in HIV-positive persons (Scully et al 1991b).

6.3.6 Melanotic hyperpigmentation

Brownish or brown-black macular oral hyperpigmentation, typically associated with intraleukocytic melanin or pigment in the basal cell layer or lamina propria, with premature melanosomes, has been described in HIV-infected patients (Langford et al 1989). However, in a study from Florence the prevalence of oral hyperpigmentation in HIV-seropositive patients did not appear higher in HIV-seropositive patients when compared with a control group of HIV-seronegative persons (Ficarra et al 1990). Proliferative melanocytic disorders including melanoma and eruptive dysplastic naevi have also been reported (Moore, Cook 1985, Gupta, Imam 1987).

The cause of melanotic hyperpigmentation in HIV-seropositive patients relates to multiple factors (Table 11). Oral melanotic hyperpigmentation may also develop in HIV-positive persons, especially in those with dark-pigmented skin, with no apparent reason (Langford et al 1989, Ficarra 1992). In these cases it can be hypothesised that oral hyperpigmentation may be caused by HIV. So far, there is no evidence that melanocytes harbour HIV; nevertheless, HIV may stimulate melanogenesis as a result of direct or indirect interference with the production of epithelial growth factors (Ficarra 1992).

Table 11 **Possible etiology of melanotic mucocutaneous pigmentations in HIV-seropositive patients**
Source: Ficarra (1992)

Antibacterial drugs (clofazimine)
Antifungal drugs (Ketaconazole)
Pyrimethamine
Fixed drug eruption (heroin)
Zidovudine (AZT)
Adrenal insufficiency
Postinflammatory hyperpigmentation
HIV (?)

Clinically, oral pigmentations may appear well circumscribed in some cases and diffuse in others. In some patients they may progress and recur after surgical excision (Ficarra et al 1990).

6.3.7 Neurologic disturbances

Neurologic disorders are a significant source of morbidity in patients with HIV infection. It has been estimated that in at least 50 to 60 percent of patients with HIV infection, neurologic dysfunctions develop during the course of the disease (Ficarra 1992). HIV is neurotropic and neurologic manifestations due to direct effects of HIV on the central nervous system include dementia, neuropathy and other changes (Price, Brew 1988). Peripheral neuropathy involving the oral structures may affect the motor function (facial nerve) or the sensory function (trigeminal nerve) and can be observed during all stages of HIV infection (Langford-Kuntz et al 1988). It has been reported that in HIV-positive patients the peripheral nervous system may be involved in 90 to 95 percent of cases (De Girolami et al 1990).

Facial nerve palsy has been reported in association with acute/primary HIV infection and the clinical presentation seems highly variable (Piette et al 1986, Wiselka et al 1987). Most cases start as Bell's palsy, an isolated unilateral peripheral facial paralysis of sudden onset and unknown origin (Ficarra 1992). This may also cause pain, but most patients recover or improve within a few weeks (Belec et al 1989).

Trigeminal neuralgia has not been documented as a result of direct HIV infection. However such symptoms may occur due to invasion by local tumours, which may occur associated with HIV infection (Milan et al 1986).

6.3.8 Osteomyelitis

Osteomyelitis has been rarely reported in association with HIV disease (Pindborg 1989).

6.3.9 Sinusitis

A report mentioned that chronic sinusitis may occasionally be found in patients with AIDS (Marcusen, Sooy 1985).

6.3.10 Submandibular cellulitis

Odontogenic infections associated with HIV infection may fail to resolve or spread to produce submandibular cellulitis (Pindborg 1989). Studies have reported on ten in Central Africa who presented with acute gangrenous cervicofacial cellulitis (Vuillecard et al 1989). All of them resulted from untreated dental infection. Nine of the ten patients were positive for HIV antibody without any other symptoms or confirmation of AIDS. Bacteriologic investigations failed to show bacteria responsible for the condition but all patients healed after surgical treatment and antibiotics (Vuillecard et al 1989).

6.3.11 Squamous cell carcinoma

Oropharyngeal squamous cell carcinoma has been reported in patients with HIV disease (Lozada et al 1982, Silverman et al 1986, Jacobs 1987), however, prevalence rates and risks have not been established. Nevertheless, a recent extensive survey of American men at risk during the AIDS epidemic has not confirmed a significant increase in oral carcinoma (Biggar et al 1989). In HIV-positive patients squamous cell carcinoma is seen in a younger age group and often in persons lacking the common risk factors associated with squamous cell carcinoma. Evidence to suggest a heightened risk of oral squamous cell carcinoma in HIV disease is assumed from the difference in mean age of squamous cell carcinoma in the general population (60 years) and in HIV disease (32 years) (Lozada et al 1982, Silverman 1990).

6.3.12 Toxic epidermolysis

Toxic epidermolysis (Lyell's syndrome) has been more frequently observed in paediatric AIDS patients with oral involvement (Pindborg 1989) but is also seen in adults. Reichart et al (1987) described two HIV-seropositive patients who had toxic epidermolysis involving the oral mucosa. Whether this disease is more prevalent in HIV infection is unknown. It has not been reported in other studies.

7 SURVEY OF ORAL CHANGES IN HIV INFECTION

7.1 METHOD

7.1.1 Study population

The first 40 consecutive HIV positive patients attending the Dental Clinic at St. Vincents Hospital in Sydney and a private dental practice, also in Sydney, were studied to note variations in oral presentations. A wide range of HIV infected patients are seen in these clinics. Participants were recruited starting July 1992. The sample was extracted from a survey, which is at present continuing, where it is planned to include at least 500 HIV-positive patients in the next one year in order to analyse the association between various oral lesions in HIV infection and the immunological marker CD4+ cell count. It is anticipated that, on completion, the outcome of the study would be of value in future patient management.

Inclusion criteria for the study population were a confirmed HIV-positive status and written informed consent. Exclusion criteria were HIV-negative status, unwillingness to participate in the study and those patients already included in the study.

7.1.2 Data collection

The data was collected by completing one patient questionnaire and one proforma dental examination. Participants were requested to complete a questionnaire to obtain data regarding past and present medical, dental and HIV history in addition to general information such as date of birth, sex, country of birth and residence, ethnic origin and reason for dental visit. The dental history included questions on

current oral discomfort/interference with oral functions, number of dental visits in the past 3 years with month and year of the last visit and disclosure of HIV status at the last dental visit. HIV history included time since first aware of HIV seropositivity, HIV risks, stage of HIV infection. Past and present medication taken, smoking history and current T4 cell count were also included.

The oral cavity was examined for mucosal lesions. All patients were examined under optimal conditions, using a dental chair, adequate illumination, mouth mirrors and gauze squares for tongue extension. A dental examination proforma was completed by the dentist at examination. Diagnostic criteria as suggested by Greenspan et al (1991) were used for the recognition of oral lesions in the study. However, the charting was based solely on the presenting clinical features of the oral lesions. The dental conditions noted by the examiner are shown on Table 12, the survey form used.

Table 12 Oral examination form.
Source: Survey of oral changes on HIV infection (1992).

SURVEY OF ORAL CHANGES IN HIV INFECTION - ORAL EXAMINATION

Study number • visit number □□□□ • □□

Today's date:..... |_|_|_|_|_|_|_|
D D M M Y Y

Examiner's initials |_|_|

Are any oral lesions or conditions
present today? Y/N |_|

If yes, please tick the appropriate box for all lesions present (refer to attached
WHO diagnostic criteria).

Please also record site of lesions on one or more of the pro-forma examination
sheets (as appropriate).

	Present and patient aware	Present and patient unaware	Previously present (not now)
Candidiasis			
pseudomembranous ...	☐	☐	☐
erythematous	☐	☐	☐
angular Cheilitis	☐	☐	☐
atrophic	☐	☐	☐
Erythematous gingival banding	☐	☐	☐
Necrotizing gingivitis	☐	☐	☐
Necrotizing periodontitis	☐	☐	☐
non HIV-related periodontal conditions	☐	☐	☐

Table 12 Oral examination form (page 2).

Ulcerations

recurrent herpes labialis	☐	☐	☐
recurrent aphthous ulceration	☐	☐	☐
atypical oral ulcerations	☐	☐	☐
Hairy leukoplakia	☐	☐	☐
Oral Kaposi's sarcoma	☐	☐	☐
Non-Hodgkin's lymphoma	☐	☐	☐
Other (specify) _____	☐	☐	☐
Other (specify) _____	☐	☐	☐
Unknown oral lesion	☐	☐	

Colour of unknown lesion	red ☐	white ☐
Topography	raised ☐	flat ☐

HIV-related **FACIAL** lesion(s)

(specify)	☐	☐
.	☐	☐
.	☐	☐
.	☐	☐

7.2 RESULTS

The sample included 36 males (90%) and 4 females (10%) with a mean age of 37.6 years. Thirty-two patients (80%) attended the clinic for routine dental care, 5 (12%) for emergency dental care and 3 patients were referred for evaluation of HIV oral problems. Twenty-five patients (62%) had visited the dentist on more than 3 occasions in the past 3 years (Table 13).

Table 13 Dental visits in past 3 years.
Source: Survey of oral changes in HIV infection (1992).

Dental visits	Number	Percentage
Nil	5	12.5
1	4	10
2	6	15
3	12	30
4	4	10
5 or more	9	22.5

While 30 patients (75%) told their dentist of their HIV-seropositivity, 5 patients (12%) preferred not to. Five patients were not aware of their HIV-positive status at their last dental visit. The majority of the patients were homosexual men (Table 14).

Table 14 Distribution of 40 HIV-seropositive patients by risk groups.
Source: Survey of oral changes in HIV infection (1992).

HIV risks	No.	%
Male to male sex	35	87.5
Male to female sex	3	7.5
Injecting drug use	1	2.5
Receipt of contaminated blood products	1	2.5
Birth to an infected mother	0	-
Unknown	0	-

The group included patients at different stages of infection, from symptomless ‘carriers’ to AIDS (Table 15).

Table 15 Distribution of patients by stage of HIV infection.
Source: Survey of oral changes in HIV infection (1992).

Stage of HIV infection	No.	%
Early with no signs or symptoms (groups II and III)	12	30
ARC (group IV but not AIDS)	4	10
AIDS	19	47.5
Unsure	2	5
Not answered	3	7.5

The results of the oral examination are presented in Table 16. In the total group of patients, 15 patients (38%) were free from oral disease on examination, but many gave a history of some oral lesion in the past. Eleven patients (28%) had multiple oral mucosal lesions.

Candidiasis was the most common oral infection, observed in 14 patients (35%). Pseudomembranous candidiasis was more frequently seen [9 patients (64%)]. Further, 16 patients (40%) gave a history of candidiasis in the past which had resolved due to antifungal therapy.

Hairy leukoplakia was diagnosed in 11 patients (28%), while 3 patients had experienced HL in the past. Only 1 patient (2%) presented with oral Kaposi's sarcoma with lesions in the palatal mucosa.

Periodontal disease, ranging from HIV-G to necrotizing periodontitis was noted in 7 patients (18%). Non HIV-related periodontal conditions were noted in 10 patients. Other oral mucosal changes observed included warts, xerostomia, petechiae and non-HIV leukoplakia.

Table 16 Oral changes in 40 HIV-infected patients.
Source: Survey of oral changes in HIV infection.

Oral changes	Present & patient aware		Present & patient unaware		Previously present (not now)	
	No.	%	No.	%	No.	%
CANDIDIASIS						
Pseudomembranous	8	20	1	2.5	15	40
Erythematous	2	5				
Angular cheilitis	3	7.5			1	2.5
Atrophic/Hyperplastic						
HIV-G	1	2.5				
HIV-P	2	5				
Necrotizing gingivitis						
Necrotizing periodontitis	2	5	2	5		
Non-HIV related periodontal conditions	8	20	2	5	2	5
Ulcerations						
Recurrent herpes labialis					1	2.5
Recurrent aphthous ulceration					6	15
Atypical oral ulcerations					2	5
HAIRY LEUKOPLAKIA	9	22.5	2	5	3	7.5
KAPOSI'S SARCOMA	1	2.5				
Non-Hodgkin's lymphoma						
Others	(1) HPV-wart (lower lip). (2) Xerostomia (3) HPV-wart (tongue, lips, gingival margins)		(1) Petechiae-tongue/palate (2) Non-HIV leukoplakia (smoking related) (3) Unknown oral lesion		(1) Shingles	

8 DISCUSSION AND CONCLUSIONS

A wide range of oral manifestations of HIV have been reported, the more common of which were observed in the present group. Although the spectrum of HIV-related oral lesions is similar to that reported in other countries, there appears to be substantial differences in the prevalence of oral mucosal lesions.

Studies by Schulten et al (1989) on 75 HIV seropositive patients reported 76 percent of the patients with one or more oral lesions while similar studies by van der Waal et al (1991) on 100 HIV-positive patients reported 80 percent with one or more oral lesions. In contrast, only 62 percent of the patients in the present study exhibited an oral lesion on examination. Similarly there also appears to be differences in prevalence rates of individual oral lesions. Studies by Schulten et al (1989) cited prevalence rates of 52 percent for oral candidiasis, 16 percent for periodontal disease, 16 percent for HL and 4 percent for KS; studies by Porter et al (1989) on a group of 44 British patients infected with HIV reported prevalence rates of 36 percent for oral candidiasis, 32 percent for periodontal disease, 15 percent for HL and 2.3 percent for oral KS while studies by van der Waal et al (1991) cited prevalence rates of 56 percent for candidiasis, 27 percent for periodontal disease, 15 percent for HL and 4 percent for KS.

However in the present sample of 40 HIV-positive patients, candidiasis, although the most common oral infection was observed in 35 percent, periodontal disease in 18 percent, HL in 28 percent and oral KS in 2 percent. Surprisingly, in spite of the large proportion of patients with AIDS (19 patients, 48%), only 1 case of

KS was observed. Also worth mentioning is the increased prevalence of HL in this study when compared with earlier reports. These differences in prevalence rates may be explained by a number of factors.

First, different populations and clinical settings possibly account for these variations e.g., all the patients in the present sample were examined under optimal conditions and almost 80 percent of the present sample of patients reported to the clinic for routine oral examinations. In contrast, in the study by Schulten et al (1989), up to 33 percent of the patients were bedridden at the time of oral examination.

Previous studies have also included subjects with, variously, AIDS, ARC and asymptomatic HIV infection (Lozada et al 1983, Marcusen et al 1985, Silverman et al 1986, Porter et al 1989); therefore prevalence rates should be carefully interpreted. Different geographic distribution of high-risk groups may also account for different reported prevalence (Phelan et al 1987).

Other influencing factors could include the sample size, examiner's knowledge of the patient's serologic status and/or possible risk factor(s), investigatory conditions, number of oral examinations and the use of different diagnostic criteria (Schulten et al 1989). Since the sample in the present study included only the first 40 cases seen, it remains to be seen if prevalence of oral lesions is greatly different in the final sample.

The decreased prevalence rates of oral changes in this study could also possibly be attributed to the fact that most participants in the study were already on some form of antiretroviral and prophylactic therapy (Foltyn 1993b).

Clinically, some HIV-related oral lesions show substantial variation and may be difficult to distinguish. In particular, hairy leukoplakia needs to be carefully differentiated from a number of white lesions unrelated to HIV but also occurring on the tongue (Table 17).

Table 17 **Differential diagnosis to oral hairy leukoplakia.**
Source: Greenspan et al (1990).

Lesions due to restorative materials
Idiopathic leukoplakia
Smoker's leukoplakia
Smokeless tobacco lesions
Lichen Planus
Chronic hyperplastic candidiasis
White sponge nevus
Geographic tongue
Frictional keratosis
Tongue and cheek biting

Similarly, conditions like salivary gland enlargements although relatively less common in HIV infection need to be differentiated from lymphomas, Sjögren's syndrome, salivary gland infections, salivary gland tumours and KS (Greenspan et al 1990).

We in dentistry are now standing amid considerable public controversy over the twin issues of HIV testing and HIV transmission in the clinical setting. As health care providers dentists assume certain professional responsibilities. Dental professionals are involved in this pandemic because of the need to provide dental care without discrimination. It is the writer's belief that the dental care of patients with HIV infection or those at risk for HIV infection can be provided by the medically competent dental practitioner. The dentist may be the first health care professional to suspect an incipient case of HIV infection and the diagnostic acumen required mandates knowledge of epidemiologic factors and oral and clinical manifestations of HIV infection. The dental practitioner should be prepared to accept the responsibility of being able to make, or at least to suspect, an early diagnosis of HIV-related oral lesions. The tentative diagnosis can often be made on clinical grounds only, especially when the HIV status is known to the dentist. In other cases a culture or a biopsy may be required.

When confronted with a patient of whom the serological status is unknown, the dentist faces the problem of whether to discuss the possible underlying disease with the apparently healthy patient. Owing to ethical and cultural differences that exist between the various countries of the world, there is no uniform answer to this important question.

The fears among dentists of treating HIV infected patients have focused on patients with the frank syndrome AIDS. However it is worth mentioning that patients with other expression of HIV disease, including ARC and apparently

healthy individuals with antibodies of HIV are probably all carriers of that virus and may also pose a potential threat. Therefore adequate infection control measures must be taken routinely, for all patients and for all procedures, to prevent transmission of infectious agents.

To conclude, the writer wishes to emphasise that -

- (1) Dentists should be encouraged to participate more fully in the diagnosis of HIV infection. Dentists committed to service will find increasing expression of their talent and new roles of responsibility in dealing with HIV-infected patients.
- (2) A thorough oral examination of all patients is mandatory. Part of dealing rationally with the anxiety that surrounds the HIV issue is recognising just what is and what is not HIV related. Whereas a variety of oral lesions are linked to HIV infection, most are not. An appropriate diagnostic approach is required to sort out the vast majority of non-HIV related lesions from the relatively few that are. Recognising the clinical features is part of that approach.
- (3) HIV-infected patients do not present unusual problems as regards the provision of routine dental care. The majority of regular dental care for the HIV-infected population can and should be provided by the dental practitioner without fear of untoward complication. Referral for specialist dental care should be based on the same criteria as are used for all other patients.

- (4) Universal infection control procedures should be adopted and strictly adhered to at all times, treating each patient as potentially infectious and thus also minimising the risk of transmission or cross-contamination.
- (5) An important consideration in oral HIV care is appropriate consultation with the patients physician. The development of an effective working relationship, based on mutual respect for the other's expertise, may be extremely important in reducing suffering and morbidity and can contribute extraordinarily to the patients well being.

The dentist armed with a knowledge of immune principles and protected by the consistent use of barrier techniques and universal infection control procedures, is in an ideal position to be of service not only to the individual patient but to the scientific community at large. As the pandemic grows, dental practitioners must anticipate seeing both knowingly and unknowingly HIV infected patients and diagnosing and caring for their oral lesions. Dental care is not a privilege of the healthy, and the HIV infected patient is one among myriad other ill patients who will benefit from timely diagnosis and treatment.

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