HIV INFECTION
AND
DENTAL PRACTICE

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DEDICATION

I dedicate this treatise to my loving wife, Jenny, in recognition of the immense support she has given me.
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PREFACE

The Human Immunodeficiency Virus (HIV) has had a profound effect on the medical and dental professions as well as the general community. In regard to dental practice, there is no way that contact with known and unknown carriers can be avoided, short of ceasing practice, and it is likely that this occupational hazard will become increasingly regular. Concern over acquiring HIV in the dental setting is well founded, given that Hepatitis B Virus (HBV) is transmitted in a similar fashion and has been shown to be transmitted occupationally to dental healthcare workers. Further concern regarding HIV transmission to dentists arises from poor prognostic outcomes of infection, the social stigma infection entails and the general lack of directives both from governments and professional organizations concerning both management and complex medicolegal issues. Added to this is the limited, but rapidly expanding, knowledge of the virus and its effect.

However, this concern should not be confused with fear. This epidemic has challenged the medical and dental professions alike, leading to an expanded knowledge of oral medicine and infection control, as well as the development of closer working relationships between dental and medical specialities and the general dental practitioner. This virus will force both professions to reappraise various ethical and legal concerns and procedures to prevent disease transmission. There is no reason, given the ability of healthcare professionals to adapt to previous infectious diseases, such as Hepatitis B Virus, that the dental profession cannot adequately adapt to HIV.

Therefore, it is the aim of this treatise, in three chapters, to show that concern, and not fear is warranted in the dental setting. The aim of Chapter One is to examine the essential clinicopathological features of HIV infection. This is achieved in the context of, firstly, its status as a global epidemic and, secondly, in relation to its impact on those groups inherently at-risk from the infection, including those providing healthcare services. Chapter Two provides a structured evaluation of the frequently unique oral manifestations associated with HIV-induced immunosuppression which have significantly broadened the field of oral medicine. The aim of Chapter Three is to provide an evaluation of the principal issues affecting the provision of dental services generally to HIV infected patients, including an assessment of the risks involved in providing this care. This chapter also seeks to focus on the underlying medicolegal implications for dental practice raised in this epidemic.

This treatise is based on information available to June 1990, and I anticipate that, in the future, significant advances will occur in several key areas: medicolegal issues, the actual numbers of those infected, management options, new emerging trends with various risk groups and the development
of a suitable vaccine. A particular challenge to the dental profession in the future will be keeping abreast of developments in the Human Immunodeficiency Virus epidemic and adapting where necessary.
CHAPTER ONE

THE CLINICOPATHOLOGICAL STAGING AND
EPIDEMIOLOGY OF HIV INFECTION
1.1: AN INTRODUCTION TO INFECTIOUS DISEASES AND THE HIV EPIDEMIC

Infectious disease epidemics have afflicted both rural and urban populations ranging from the plagues of medieval times to the influenza and poliomyelitis epidemics of the twentieth century. They have always been a major cause of mortality and morbidity as man has attempted various means of suppressing their effect.

Oliver Wendell Holmes Snr and Ignaz Semmelweiss could be regarded as the pioneers in attempting to prevent disease transmission by implementing practical infection control procedures. Semmelweiss introduced revolutionary infection control procedures into hospitals in 1847 that enabled a tenfold reduction in maternal mortality over a two year period at the Vienna General Hospital.

The germ theory of 1857 paved the way for combatting infectious diseases utilizing scientifically based methods. This discovery by the French biochemist, Louis Pasteur, was concerned with the underlying mechanism of the disease process, something poorly understood previously.

Surgical practice was revolutionized in 1868 by the formulation of the theory of sepsis and antisepsis by Joseph Lister, a breakthrough made possible only by the work of Pasteur. The introduction of the disinfectant
phenol by Lister dramatically reduced mortality and morbidity due to infectious diseases and marked the beginning of man’s struggle to control these diseases, a struggle that has continued until present times. The impact of these discoveries on infectious diseases such as smallpox, typhoid and poliomyelitis can be seen in their low incidence in developed countries.

One characteristic of epidemics is their ability to spread. It took only four years from the first case in Marseilles, in 1347, for the Black Death to invade the whole of Europe, killing nearly a third of the population. Four years after the first reporting of what became known as the Acquired Immune Deficiency Syndrome (AIDS), cases had been reported in forty countries on five continents. A combination of migratory and travel patterns and the social, sexual and drug abusing behaviour of humans has aided its rapid spread. The rapidity of reporting of the first ten thousand cases of AIDS is a sober reminder of the twenty four million deaths due to Black Death. Insignificant as these cases of AIDS may seem in comparison to those of Black Death, it must be remembered that AIDS represents only the tip of the iceberg (Refer below). With an estimated ten million carriers worldwide (63; 64; 70; 220; 235), we may be faced with an epidemic of comparable proportions and social impact.

The first account of a new infectious disease epidemic was reported in June 1981 (69; 73; 70; 180; 310) by the
Centers for Disease Control (CDC). Five previously healthy young homosexual men had been treated for Pneumocystis carinii pneumonia (PCP) at three different hospitals in Los Angeles between October 1980 and May 1981 (69). This infection was previously confined to severely immune suppressed individuals, such as those receiving ongoing immunosuppression following allogenic organ transplants. Several weeks after these reports of PCP a number of cases of Kaposi's sarcoma (KS), a previously rare tumour also observed in immune suppressed individuals, were similarly reported in young homosexual men in New York City, as well as California (73). Although the majority of cases occurred in the United States of America (USA), by September 1982, there were 41 similar case reports from ten other countries (70).

By late 1982, the disease was being called by its present name: **Acquired Immune Deficiency Syndrome (AIDS)**. The alarming death rate was obvious early in the epidemic; by September 1982 the CDC had received reports, mainly from three major American metropolitan areas (San Francisco, New York City and Los Angeles) of 593 cases with 243 deaths over the first 15 months (42%) (220). The first Australian case of AIDS was described in December 1982 (393); however, retrospective analyses of stored sera of Australian homosexual men, following the introduction of serological screening methods, have shown that the virus was present in 1981, although limited evidence suggests it was not apparent prior to
that (335). Apparently, seropositivity in this cohort rose rapidly from 5% to 32% in only one year (335). The first Australian case, to be accepted by the CDC as meeting the strict criteria for a diagnosis, occurred in 1983 in an American man resident in Sydney (310).

Initial cases of AIDS in the USA were clustered around the above major metropolitan areas; however, from mid 1984 an increasing proportion have been reported from relatively smaller cities and rural areas. To illustrate this point, relatively smaller metropolitan areas (populations <500,000) reported 10% of all AIDS cases in the United States, prior to 1985, compared with 19% in 1988 (79). Australia appears to be following the same pattern, albeit on a smaller scale (286).

The origin of Human Immunodeficiency Virus (HIV), later discovered to be the causative agent for AIDS, and when it first began to spread remains unclear. One definitive method of pin-pointing the origin would involve the evaluation of stored blood by current serological methods. Anecdotal case reports from Africa have identified HIV in sera stored from Zaire in 1959 (55; 56; 318). On superficial analysis, it seems that the virus was present nearly two decades prior to the first report of AIDS (70), although the possibility of false positives and perhaps less sensitive early confirmatory assays may cast some doubt on these findings. The methods and reliability of the storage of this sera over twenty years may also be influential.
Notwithstanding these comments, it is difficult to ignore the work of Saxinger and colleagues (426), who reported up to 65% of samples taken from a study of Ugandan children indicated HIV infection, as early as 1972. The above observations, however, do not date the earliest origin of the virus. Furthermore, in the absence of large-scale retrospective analyses of sera from the United States and Europe, in particular, there is also no clue to its geographic origin.

The work of Saxinger, along with other studies (55; 318), do suggest that the spread of HIV within urban areas of Central Africa began to increase markedly during the late 1970's. These studies correlate with a marked increase of AIDS indicator diseases throughout Africa in the late 1970's and early 1980's (55; 56; 318). A similar increase in these indicator diseases were also evident in the USA during this period (70; 79).

The idea of a transmissible agent being responsible for AIDS was suggested when initial reports were confined to intravenous drug abusers (IVDA's) and homosexual males. The appearance of the disease in haemophiliacs and blood transfusion recipients, with no other risk factors in lifestyle, corroborated the idea of a transmissible and probably viral agent analogous to Hepatitis B. Definitive confirmation came when the virus was discovered and serologically identified, whether by
antigen or antibody presence, in infected individuals confined to certain risk groups.

The major breakthrough in understanding the disease was the isolation of the virus, independently, by Montagnier and Gallo. In May 1983, a research group at the Pasteur Institute in Paris reported the isolation of a Human T-Lymphotropic retrovirus from a patient at risk for AIDS (180; 343). Due to its association with lymphadenopathy, the agent was named Lymphadenopathy Associated Virus (LAV-1). Around the same time, Gallo and co-workers (1983) (157; 327), from the National Cancer Institute in the United States of America (USA), reported on a large series of similar viral isolates (Human T-cell Lymphotropic Virus Type-III (HTLV-III)).

In 1984, AIDS related retroviruses (ARV) were repeatedly isolated from AIDS patients in San Francisco, thus consolidating the aetiological link. Subsequent studies have shown that LAV, ARV and HTLV-III are all variants of the one virus strain. In order to avoid different nomenclatures, in 1987, these retroviruses were officially designated as the Human Immunodeficiency Virus, to be known in abbreviated form as HIV. Intensive work on HIV has now identified more than one thousand serologically different isolates (327).

The identification of a similar virus from African green monkeys, Simian Immunodeficiency Virus (SIV), suggested primates as a possible origin of HIV.
However, infection with SIV leads to a chronic infectious state in macaques rather than the progressive clinical deterioration observed in advancing HIV immunosuppression in humans. Cross reactions of sera from West Africans to HIV and SIV led to the identification by Montagnier and colleagues (318) of another human retrovirus, HIV-2, in 1985. The genomic sequence of HIV-2 is approximately 40% identical to that of HIV-1 and 70% identical to SIV (318). At this stage HIV-2 is essentially confined to Africa, and it is uncertain whether it will cause the same pattern of disease as HIV-1. Despite the cross reactivity in some African patients between HIV and SIV, a common link between the two viruses remains uncertain.

In the United States, when widespread serological testing of supposed risk groups was undertaken, it became clear that HIV infected patients could demonstrate a spectrum of clinicopathological findings, ranging from otherwise normal individuals to those with advanced AIDS. An iceberg phenomenon has been described with the vast majority (90%) being relatively or completely asymptomatic (220). This is best illustrated by the estimate of ten million people being infected with HIV (63; 64; 70) worldwide to the end of 1989, as compared to the nearly 200,000 reported cases of AIDS (63; 64; 220; 235). The situation appears to follow the same pattern in Australia, where an estimated 30,000 to 50,000 people are infected, as compared to only 1,745 reported cases of AIDS to February, 1990 (45).
Reported AIDS cases probably substantially underestimates the actual number of cases in many areas due to problems in recognizing, diagnosing and testing the disease. Even in countries with sophisticated surveillance systems and advanced medical technology, such as the USA, it has been suggested that only 70% to 90% of all HIV-related deaths are reported to the CDC (79). The situation appears to be worse in Africa, where the limited access of large segments of the population to health care facilities capable of diagnosing the disease, the poor efficiency of surveillance systems and a general reluctance of governments to officially recognize the existence of AIDS prior to 1987 have all contributed to an underreporting of actual cases.

Throughout the epidemic, the vast majority of reported cases of AIDS in the USA, Europe and Australia have been confined to certain risk groups. These groups are essentially homosexual or bisexual men and intravenous drug abusers (87% to 92% of all reported cases) (41; 63; 64; 70). There has been a male predominance in reported cases, ranging from 7.5:1 to 98:1 across the United States (average 28:1) (63; 64; 70; 82). This wide range of reported ratios illustrates two points. Firstly, the ratio of 98:1 reported from San Francisco in 1986 (64) still reflects closely the pattern of transmission (between homosexual males) in the initial stages of the epidemic. Secondly, while this trend was also true of
studies performed in the early stages in New York City (70), the figure of 7.5:1, suggested by the CDC in 1986 (64), indicates well the possible emerging trends in the epidemic.

The increasing number of female AIDS victims reflected in this ratio of 7.5:1 is significantly influenced by two factors:

1. The increasing incidence of heterosexual venereal transmission to females from infected male sexual partners; and

2. An increasing number of children infected in utero or perinatally by infected mothers. On this latter point, paediatric AIDS victims boosts the number of females by contributing an approximately equal number of male and female cases.

In order to illustrate the possible emerging trends, an increase in heterosexually acquired HIV infection among females from 1% in 1986 to 4.9% in 1988 (77) has been reported in the USA. As a result of in utero and perinatal transmission, it was suggested that in New York City, one in every 80 children will be born to HIV infected mothers in 1989 (120).

This trend may be symptomatic of a potential direction that this epidemic may take in the future. A major influence on the future direction of the AIDS epidemic in western society is heterosexual venereal transmission.
In order to show that HIV infection is breaking into the heterosexual community, between 6.8% (19) and 70% (103) of steady heterosexual partners of HIV infected individuals have themselves seroconverted (44; 77; 170; 270; 320). Of these cases, 70% of index partners have been intravenous drug abusers (IVDA's) and 18% have been bisexual men (102), suggesting a bridge for infection to pass from homosexual males to the general community.

Studies by Luzi (251) and Redfield (326), in 1985, have already confirmed this direction, indicating the possibility of an exponential rise within the heterosexual community. The efficacy of heterosexual venereal transmission is best illustrated by the African experience of AIDS, where male to female ratios approximate 1:1 (270). While many cases of AIDS in Africa are of yet undetermined cause, there is ample evidence to suggest the predominant method is by heterosexual venereal transmission. Reported HIV seropositivities of 61% (318) and 51% (321) among African prostitutes, in the absence of known blood transfusions, injections or anal intercourse, is suggestive of this mode of spread.

Society has yet to face the full consequences of the HIV epidemic. The long-term cost, in terms of health care and social welfare provisions, and economic loss to nations at this time is inestimable. The challenge posed to the dental profession includes participating in
the recognition and management of infected individuals, and in the prevention of transmission of infection. These issues will be addressed in Chapters Two and Three.
1.2: DEFINITIONS AND CLINICOPATHOLOGICAL STAGING OF HIV INFECTION

This section is devoted to three separate aspects of HIV infection:

1. Definitions and revised classifications.
2. Principal systemic manifestations of HIV infection.
3. The natural history of HIV disease progression.

1.2.1: DEFINITIONS AND REVISED CLASSIFICATIONS

Six different definitions and classifications of HIV infection and AIDS have been proposed:

A: The original definition (1982).
C: WHO/CDC case definition (1986).
D: New classification CDC (May 1986).
E: Case definition for paediatric HIV infection (September 1987).
F: Revised case definition (September 1987).

With progressive experience of the epidemic, classification criteria have necessarily been modified. Earlier definitions and classifications related exclusively to AIDS, but with further knowledge the classifications first included intermediary conditions
(AIDS Related Complex (ARC)), then allowed for not only the reporting of children and asymptomatic individuals, but also eventually the full clinical spectrum associated with HIV infection, from seroconversion to full blown AIDS.

A. **THE ORIGINAL DEFINITION (1982)**

(Refer Appendix 1A)

The original definition of AIDS was offered by the CDC as 'an unusual infection or unusual cancer which affected somebody who had previously been in good health' (18). Obviously this definition was far too broad, and for epidemiological purposes it allowed for the over-reporting of abnormal findings as a possible case of AIDS, and reflected the uncertainty of what disease process was being dealt with. No hint had been given to the multitude of infections or neoplasms possible, or towards a possible cause of these abnormalities.

B. **SIMPLE DEFINITION (1984)**

(Refer Appendix 1B)

The isolation of LAV-I, HTLV-III and ARV in 1983 and 1984 meant that the original definition could now be improved. Although serological tests were not yet required to provide a definitive diagnosis of AIDS, it was known that the infection causing this unique immunosuppression was a retrovirus. No attempts had yet
been made to include specific infectious diseases or neoplasms in the definition, as a comprehensive list had not been compiled. No significant changes in reporting occurred with the introduction of this definition, the only changes being the isolation of several supposed causative agents.

C. **THE WHO/CDC CASE DEFINITION FOR AIDS (1986)**

(Refer Appendix 1C)

(WHO Wkly Epidem Rec 1986; 61:69-76.)

By 1986, the identification of various protozoal, fungal, bacterial and viral infections known to be associated with the unique immunosuppression of AIDS had been identified. Similarly, general manifestations such as chronic diarrhoea, pulmonary diseases and neoplasms had been identified as being indicative of immune deficiency. The discovery of serum antibody testing and culturing, specific to the causative agent, meant that people could be diagnosed as having AIDS when certain diseases were present in combination with a positive identification of the virus or viral antibodies.

The knowledge that HIV affected the T lymphocytes and the clinical and laboratory findings seen over the early stages of the epidemic allowed for determinations of absolute T lymphocyte numbers and ratios of T-helper to T-suppressor lymphocytes to evaluate various rates of immunosuppression. Where previously reported cases of AIDS only required presumed immunosuppression in
conjunction with the possible risk of infections or malignancies; the definitive identification of HIV infection by laboratory studies, serum testing and culture meant that there was a slight drop in the rate of new AIDS cases reported in Australia and the USA (Refer Section 1.7; Tables 1.7.6 and 1.7.7).

Furthermore, the recognition of an intermediary phase of infection, AIDS Related Complex (ARC), allowed for the proposal of a spectrum of disease from seropositive asymptomatic individuals, through ARC, to AIDS.

D. NEW CLASSIFICATION OF MAY 1986 (135)

(Refer Appendix 1D)

By 1986, the designation Human Immunodeficiency Virus (HIV) had been proposed as the appropriate name for the retroviruses that had been implicated as the causative agent of AIDS. This designation was proposed to avoid the use of different nomenclatures for the various viruses that had been previously isolated.

On May 23 1986, the CDC presented a classification system for HIV infection, primarily applicable to public health purposes, including disease reporting and surveillance, epidemiologic studies, prevention and control activities, public health policy and planning (135; 164). This system was adopted in Australia in January 1988. The system classifies the manifestations of HIV infection into four mutually exclusive groups,
designated by Roman Numerals I-IV (Refer Appendix 1D), and applies only to patients serologically proven to have HIV infection. Classification in a particular group is not explicitly intended to have prognostic significance, nor to designate the severity of illness.

The implications of this increasingly complex classification meant that only people with serologically proven HIV infection were now reported. Furthermore, the classification involved the full spectrum of HIV disease, from the acute febrile illness coincident with seroconversion (Group I), through the stages of asymptomatic seropositivity and symptomatic disease (Groups II and III), to findings suggestive of AIDS (Group IV). Where previously, AIDS was only diagnosed in conjunction with a multitude of infectious diseases and neoplasms, now a diagnosis could only be made if the patient could be included in Group IV, subgroups C1 and D. Closer scrutiny of reported cases and stricter diagnostic criteria meant that there was a slight reduction in the exponential trends of reported cases (Refer Section 1.7; Tables 1.7.3, 1.7.6, and 1.7.7).

**Group I: Acute infection**

Group I classifies the acute febrile illness, described by Cooper and co-workers (428) as a mononucleosis-like syndrome that has since been shown (455; 462) to precede seroconversion for HIV antibody. Although this classification only applies to people diagnosed as
having HIV infection, it must be noted that serological testing is usually negative at the onset, and remains that way for one to three months before becoming positive. This illness has been noted in between 10% (428) and 50% (17; 455) of newly infected individuals.

The first report of this acute illness by Cooper and co-workers (428), in a group of homosexual and bisexual men, suggested an illness of sudden onset, lasting from three to fourteen days. Seroconversion to HIV antibody was also associated with fevers, sweats, malaise, lethargy, anorexia, nausea, myalgia, arthralgia, headaches, sore throat, diarrhoea, generalized lymphadenopathy, macular erythematous eruptions, and thrombocytopenia. These findings have since been supported by similar reported incidents arising from work related accidents in healthcare workers (25).

Immunological changes during seroconversion involve inverted T4:T8 ratios, as set out in the previous WHO/CDC classification (Refer Appendix 1C). These changes result from increasing numbers of circulating T8 cells rather than the depletion of absolute T4 cell numbers more commonly seen in the latter stages of HIV infection.
Group II: Asymptomatic infection

These people have formed antibodies to HIV but are otherwise well, with no apparent illness, and are known as asymptomatic seropositive individuals. Reclassification may be carried out based on whether laboratory studies are abnormal in a manner consistent with the effects of HIV infection.

Studies of absolute numbers of T cells and ratios of T-helper to T-suppressor lymphocytes have been used since the early stages of the epidemic, and remain the most effective method of testing immune function. In addition to these, many other tests may be used to suggest immune dysfunction, some of which have been set out in the previous WHO/CDC classification (Refer Appendix C). The most commonly used immune function tests and the values found in people with both normal immune systems and pronounced immunesuppression are outlined in Table 1.7.9 (Refer Section 1.7). It must be remembered that these tests of immune function become more pronounced with advancing HIV-induced immunesuppression.

Group III: Persistent generalized lymphadenopathy

(PGL)

This group allows for the classification of infected individuals who have developed persistent and usually generalized lymphadenopathy, but are otherwise
asymptomatic. Further reclassification occurs as a result of laboratory studies (Refer Section 1.7; Table 1.7.9) or other diseases, that allow for inclusion in Group IV.

**Group IV: Other diseases**

Patients within this group have clinical symptoms and signs of HIV infection other than or in addition to lymphadenopathy. These people have HIV-related disease that may be classified as constitutional, neurologic, infectious, neoplastic or other diseases thought to be attributable to HIV infection. A diagnosis of AIDS is given only when a person is diagnosed with infectious disease or neoplastic disorders, as set out in subgroups C1 and D. Each subgroup may include people with mild symptoms, as well as those who are severely ill.

**Subgroup A : Constitutional disease**

Classification within this subgroup is based upon generalized findings, in the absence of concurrent findings other than HIV infection. These findings are chronic fever and diarrhoea of more than one month duration, and involuntary weight loss of greater than 10% of baseline, in conjunction with a positive test for HIV.
Subgroup B: Neurologic disease

Incorporation under this subgroup implies generalized neurologic disorders associated with HIV infection, such as dementia, myelopathy and peripheral neuropathy, and still pertain only to HIV-related disorders, and not a diagnosis of AIDS.

Subgroup C: Secondary infectious diseases

Classification under subgroup C involves the diagnosis of an infectious disease known to be associated with HIV infection and/or at least moderately indicative of a cell mediated immune defect. Patients are further classified, depending on the type of infectious disease and its possible relationship to HIV infection, into Category C-1 and Category C-2. This subclassification conveniently categorizes patients as having AIDS (Category C-1), and separates them from those with other HIV-related diseases (Category C-2).

Category C-1

Infection by various organisms known to cause symptomatic or invasive disease in HIV infected individuals allows for a diagnosis of AIDS. Principal among these diseases are Pneumocystis carinii pneumonia, toxoplasmosis, cryptococcosis, cytomegalovirus of various
organ systems, chronic mucocutaneous and/or disseminated herpes simplex infection and oesophageal, bronchial or pulmonary candidiasis.

**Category C-2**

The identification of these particular infections, in conjunction with HIV seropositivity, is not diagnostic for AIDS but suggests an association with HIV-induced immunosuppression. Of particular interest to the dental profession among this category are oral candidiasis and hairy leukoplakia (HL). Previous classifications have identified oesophageal, bronchial and pulmonary candidiasis as being diagnostic for AIDS, without making any mention of oral candidiasis. The identification of oral candidiasis in association with HIV infection (133; 234; 264; 368) has led to its inclusion in this category, as being indicative of HIV-induced immunosuppression. Similarly, HL has been included on the basis of its association with HIV infection. Although it has been claimed to have prognostic significance in determining disease progression (132; 134; 142; 179; 181; 226; 331), it is not considered diagnostic for AIDS (Refer Section 2.2.3.c).
Subgroup D: Secondary cancers

Previous classifications (Refer Appendix 1C) have included Kaposi’s sarcoma (KS), lymphoma and squamous cell carcinoma (SCC) as being diagnostic for AIDS. This classification continues to include KS and lymphoma as being diagnostic for AIDS, further specifying the types of lymphoma known to occur in the advanced stages of HIV infection, as being small, non-cleaved non-Hodgkin’s lymphoma, immunoblastic sarcoma or primary lymphoma of the brain.

Inconclusive evidence relating squamous cell carcinoma to people with AIDS has meant that this lesion is no longer considered diagnostic. This represents a major change to previous classifications. Identification of this lesion may lead to inclusion under subgroup E, as a lesion indicative of HIV-related disease.

Subgroup E: Other conditions

This subgrouping provides scope for the classification of new lesions not previously classified, since shown to be associated with HIV-infection, as well as other lesions and infectious diseases classified previously, that have since been associated with HIV-induced immunosuppression.
E. CASE DEFINITION FOR PAEDIATRIC HIV INFECTION

(September 1987)

(Refer Appendix 1E)

This definition recognizes the different presentations of HIV infection in children as compared to adults. Major changes to the adult classification include the introduction of "lymphoid interstitial pneumonitis" as a separate subclass under symptomatic infection (Class P-2, subclass C), as recognition of its incidence in infected children (420; 421; 425; 427). Once the cause of pneumonitis is identified, further classification in subclass D or subclass F may be carried out.

The diagnosis of AIDS in children continues to be based upon the infectious diseases and secondary cancers, as specified in subgroup C, category C-1 and subgroup D of the previous adult classification (Refer Appendix 1D). Grouping under asymptomatic infection in children is further subclassified, depending on tests of immune function (Refer Section 1.7, Table 1.7.9), in order to differentiate positive serological tests due to maternal HIV antibody, as opposed to true HIV infection.

The recognition of maternal antibody in children has meant the provision of two definitions for HIV infection, for children up to the age of 15 months and one for children between the ages of 15 months and thirteen years. Differentiation between these two ensures that reported cases of children under 15 months
of age have both abnormal immune function tests (Refer Section 1.7, Table 1.7.9) and other diseases, in association with serologically proven HIV infection. Older children need only a positive HIV test, regardless of signs, symptoms or immunologic abnormalities.

F. REVISED CASE DEFINITION (1987)
(Refer Appendix 1F)

Revision of the case definition, by the CDC in September 1987, meant that a positive test for HIV antibody was not necessarily required for a diagnosis of AIDS in all cases. The principal reason for this novel departure from earlier classifications resulted from the realization that the clinical expertise and knowledge of clinicopathological manifestations of HIV infections were comprehensive. As a result, AIDS may be diagnosed in the presence of certain 'indicator diseases' (Refer Appendix 1F) while waiting for definitive serum confirmation of infection. The range of diseases listed are essentially the same, although more specific diagnostic clinicopathological detail is given.

The diagnosis of AIDS without serologically proven HIV infection provided a significant increase in the reporting of new AIDS cases (77; 240; 286; 318). In areas such as Africa, where testing resources are limited, cases could now be reported in the absence of serological testing. Similarly, in other countries,
cases could now be reported before serological proof of HIV infection.

This rapid influx of newly reported cases was reflected in the figures from the U.S.A., Australia and Africa. The ability to report cases without serologically proven HIV infection had special relevance in Africa, where the percentages of reported African AIDS cases, in relation to total reported cases worldwide, rose from 3% in early 1987 (343) to 12% in December of that year (Refer Section 1.7, Table 1.7.3) (318). The impact of this revision within Australia contributed to a 92% increase in total reported AIDS cases from July to November 1987 (286). Consistent rises of cases of less than 10% over the preceding months prior to these revisions are a direct result of the exponential increase in newly reported Australian AIDS cases. The immediate rise of 37% in September 1987, therefore, was significantly due to the coincident implementation of these revisions.

1.2.2: PRINCIPAL SYSTEMIC MANIFESTATIONS OF HIV INFECTION

The principal systemic manifestations of HIV infection may involve many organ systems simultaneously, depending on the stage of HIV-induced immunosuppression. Multisystem involvement is usually displayed in individuals with advanced immunosuppression. The following organ systems will be addressed: mucocutaneous, neurologic, gastrointestinal tract,
respiratory, neoplastic and ocular. Involvement of any system may be due to a number of various causes, but all are fundamental to HIV infection. Orofacial manifestations of HIV infection will be addressed in detail in Chapter 2.

1. Mucocutaneous manifestations.
2. Neurologic manifestations.
3. Gastrointestinal tract manifestations.
4. Respiratory manifestations.
5. Neoplastic manifestations.
6. Ocular manifestations.

1. MUCOCUTANEOUS MANIFESTATIONS OF HIV INFECTION

A wide variety of mucocutaneous lesions have been observed in association with HIV infection. These lesions may be broadly classified as being due to neoplastic processes, infectious processes or other causes. Laurence et al. (243) have suggested that those lesions due to infectious processes tend to become more recurrent or intractable in conjunction with HIV infection, although this evidence remains anecdotal.

A review of suggested mucocutaneous manifestations reveals some very imprecise entities, such as gingivostomatitis, viral rashes and desquamation (17). Other disorders that have been reported, such as dandruff, rhinorrhcea, catarrh (17), anogenital carcinoma, granuloma annulare, squamous cell carcinoma
and basal cell carcinoma (343) are difficult to suggest without further evidence. In addition to some of the lesions mentioned previously, lesions due to human papillomavirus, molluscum contagiosum and various other infections may result more from the lifestyle of infected individuals rather than being due directly to HIV. No evidence to support the claimed association of geographic tongue (17) to HIV-induced immunesuppression can be found. Regardless of these reports, many neoplasms, infections and other lesions have been closely associated with HIV-induced immunesuppression.

a. **Neoplasms**

The most common neoplastic disorder observed is Kaposi's sarcoma (KS), being reported in up to one third of all cases of advanced infection (343). KS commonly affects multiple organ systems, probably as a result of multifocal rather than disseminated disease. Early lesions may present as firm, painless swellings with large variations in size. Variations in clinicopathological findings of oral lesions have been outlined in Section 2.3.1, with similar variations being observed in other locations. Anecdotal cases of anogenital carcinoma, squamous cell carcinoma (Refer Section 2.3.3), basal cell carcinoma, and non-Hodgkin's lymphoma (Refer Section 2.3.2) have been reported (343), although further evidence is required to accurately evaluate their connection with HIV.
b. **Infections**

Mucocutaneous signs usually involve non-specific dermatitis, vasculitis or abscess formation. These signs may be attributable to various fungal, bacterial and viral infections, however, the exact aetiology may remain obscure or result from a combination of multiple infectious agents.

The most common fungal infection in HIV infected individuals results from Candida albicans. In addition to oral lesions, candidiasis may occur in the oesophagus, pharynx and lungs, and occasionally spread to the skin. Possible symptoms of candidal oesophagitis, for example, may include vague substernal pain or burning sensations and dysphagia. In addition, Cryptococcus neoformans (Refer Section 2.2.1.b.i) and Histoplasma capsulatum (Refer Section 2.2.1.b.ii) have been implicated in ulcerative lesions of the skin and oral cavity, but reported infrequently.

Mucocutaneous lesions arising from bacterial infections have also been reported relatively infrequently. Anecdotal reports of skin lesions due to Mycobacterium avium intracellulare (432; 433) and *Staphylococcus aureus* (440; 459), for example, do not necessarily suggest an increased susceptibility to bacterial infections.
Viruses represent the most common reported causes of mucocutaneous lesions. Herpes simplex virus (HSV) has caused extensive rectal, perirectal, genital and oesophageal ulceration. Cytomegalovirus (CMV) infection, resulting from either reactivation of a latent stage or as a primary infection, may lead to extensive ulcerations of the skin and oesophagus. Both localized and disseminated varicella zoster virus infection have been noted, presenting as vesicular mucocutaneous eruptions, followed by crusting and confluent ulcerations. Papular or nodular lesions due to HPV occur with similar prevalence rates in HIV infected and non-HIV infected homosexuals, probably indicating a direct link to the homosexual lifestyle rather than HIV itself. Rare urticarial and maculopapular eruptions and angioedema have been associated with Hepatitis B Virus (HBV) infection in HIV infected individuals, but seem to be coincidental findings.

c. Other Causes

The exact aetiology of many mucocutaneous lesions remains unknown. The identification of multiple potentially infecting microorganisms from some lesions raises the question of whether individual isolates contribute to, or are contaminants of, an infective lesion. Boudreau and co-workers (44) reported in 1988, the simultaneous identification of Staphylococcus aureus, cytomegalovirus and acid fast bacilli in
multiple dermal abscesses. The relative contributions, if any, of each of the three potentially infecting microorganisms was undetermined.

Consistent reports of seborrhoeic dermatitis, roseola, dry scaly skin and allergic reactions suggest a close association with HIV-induced immunosuppression. More evidence is required, though, to confirm an association for other lesions, such as granuloma annulare, ichthyosis, telangiectasia and desquamation.

Adverse cutaneous drug reactions are apparently more common in HIV infected individuals (436; 456; 458). Most of these reactions result from the use of Trimethoprim-Sulphamethoxazole, a regime used to treat Pneumocystis carinii pneumonia (PCP) (436). It has been suggested that severe drug-induced maculopapular rashes, similar to those observed in Stevens-Johnson Syndrome and toxic epidermolysis, occur ten times more commonly in association with HIV infection than in non-infected individuals undergoing an identical regime, who also have no history of drug allergies or atopic illness (436).

2. **NEUROLOGIC MANIFESTATIONS**

Neurologic involvement of HIV infected individuals was first reported early in 1982, and is thought to be due to a combination of opportunistic infections, neoplastic disorders and/or direct cytopathic effects of HIV on the
glial cells of the central nervous system. Although clinical neurologic dysfunction has been suggested in up to 70% of people with advanced HIV infection (222), it has also been noted coincident with seroconversion (49; 288). Whether there is a general decline in neurological performance as disease progresses, and whether any significant differences occur between seropositive and uninfected individuals are still not known (222; 288).

HIV-associated neurological disorders may result from involvement of either the central nervous system or peripheral nervous system.

a. **Central Nervous System**

Central nervous system involvement predominantly affects subcortical structures, and symptoms include global cognitive impairment (forgetfulness, confusion and slowness of thought), motor impairment (loss of balance, handwriting deterioration), behavioural changes (apathy, regression, psychosis and mood swings), headaches and seizures (375).

Spinal cord myopathy, caused by progressive demyelination of the lateral and posterior columns, produces leg weakness (222), unsteadiness and difficulty in walking (375). Neuromuscular complications of advanced HIV infection, such as proximal muscle weakness
and fatigue, are considered to result from direct HIV-induced muscle fibre atrophy (222).

b. **Peripheral Nervous System**

Involvement of the peripheral nervous system, manifested as inflammation and demyelination of neural tissue, is due to a combination of direct viral effects and infected immune cells. Symptoms, including peripheral tingling, weakness in the limbs and severe burning sensations in the feet, become more pronounced as infection progresses. Other suggested signs and symptoms of HIV-induced neurologic disorders include pyrexia, malaise, myalgia, irritability, mood changes, forgetfulness and confusion. Recovery from the physical symptoms is usually complete; although depression, irritability and lethargy may remain (49; 222).

Although HIV has been directly implicated in neurological disorders by infecting glial cells and macrophages (49), many other causes have been suggested. Progressive multifocal leukoencephalopathy, toxoplasmosis, cryptococcal, herpes simplex and cytomegalovirus infection, and non-Hodgkin's or primary lymphoma have all been shown to produce neurological dysfunction (49; 138; 205; 209; 232; 246; 256; 324).

Degenerative involvement of the nervous system conveys certain physical and social consequences, as well as placing certain constraints on healthcare systems.
Psychoses and motor impairment of infected individuals could place the general public at an increased risk of injury. In addition, the drain of managing these disorders will tend to increase the occupancy rates of public hospitals and place undue pressure on specialist neurologic treatment centres and staff.

3. **GASTROINTESTINAL MANIFESTATIONS**

Gastrointestinal manifestations have been attributed to a combination of neoplastic disorders, bacterial, viral, fungal and protozoal infections and may appear anywhere from the oral cavity to the anus. The most common gastrointestinal disorders involve dysphagia, hepatitis or chronic diarrhoea.

a. **Dysphagia**

Common causes of dysphagia include oesophageal candidiasis, infection by herpes simplex virus or cytomegalovirus, non-specific oesophagitis, Kaposi’s sarcoma and lymphoma.

b. **Hepatitis**

Hepatitis has been noted in all stages of HIV infection, by moderately elevated serum transaminases. While this may be attributable to HIV infection, other causes of hepatitis should be excluded; especially Hepatitis B infection (HBV). Lymphomas of histiocytic
origin and Kaposi’s sarcoma can both involve the gastrointestinal tract, and present as bleeding per rectum.

c. **Chronic diarrhoea**

Mild, intermittent diarrhoea frequently cannot be attributed to any one particular pathogen, but has claimed to be a direct effect of HIV infection (256). It may be due to a number of factors; various viral, enteric protozoal, fungal and bacterial infections (256).

Infection by enteric protozoa is a common cause of chronic diarrhoea, with Cryptosporidium species, Entamoeba histolytica, Giardia lamblia and Isospora belli being the most common pathogens. Cryptosporidium species can cause chronic, profuse, watery diarrhoea, in addition to infecting the gall bladder, intrahepatic and extrahepatic bile ducts. Isospora belli causes disseminated infection leading to chronic diarrhoea and extraintestinal lymphadenopathy (256).

Chronic diarrhoea in patients with AIDS may also be caused by a variety of bacteria; including Salmonella, Strongyloides, Shigella, and Campylobacter species. Additional causes are fungi, cytomegalovirus (CMV) Kaposi’s Sarcoma (KS), and non-Hodgkin’s lymphoma (NHL).
4. RESPIRATORY MANIFESTATIONS

As a result of direct suppression of the immune system, advanced HIV infected individuals are susceptible to a range of respiratory pathogens, the acquisition of which depends on those endemic to the geographical area. In addition to the various bacterial, viral and fungal pathogens, respiratory symptoms may also result from neoplastic disorders.

Diffuse pneumonitis may be caused by Pneumocystis carinii, Cryptococcus neoformans, cytomegalovirus (CMV), Mycobacterium avium intracellulare (MAI) and Legionella bacteria (138). By far the most common opportunistic pathogen is Pneumocystis carinii being identified in 63% of all cases of AIDS (180). Pneumocystis carinii pneumonia (PCP) may have an insidious onset and patients present with a dry cough and dyspnoea, frequently in the setting of other concomitant opportunistic infections (138). Treatment difficulties, recurring infection and the high rate of mortality due to this pathogen underline the importance of rapid and accurate disease recognition. KS may also affect the lungs and pleura, and may be associated with bloodstained pleural effusions and occasional massive intra-alveolar haemorrhage.
5. **NEOPLASTIC MANIFESTATIONS**

The most commonly reported neoplasms displaying an increased incidence in association with HIV-induced immunosuppression are non-Hodgkin's lymphoma (NHL) and Kaposi's sarcoma (KS) (Refer Section 2.3). Anecdotal case reports of other neoplasms suggest a possible association with HIV infection, although further evidence is required.

NHL, of B lymphocyte origin, may produce multisystem involvement, involving the central nervous system, orbit, pharynx and jaw, intestine, liver, kidney, bone marrow, and muscle (256). Lymphoma of this type may also present with rapidly enlarging, painful lymph nodes and associated systemic signs (177). These signs, including lymphadenopathy and hepatosplenomegaly, may mimic the clinical and haematological features of chronic lymphocytic leukaemia. These lymphomas are often architecturally diffuse and of the undifferentiated small non-cleaved or large cell subtypes. High grade malignancy and poor prognosis are not uncommon.

Before KS appeared in these patients, most cases of this essentially rare, vasculoproliferative tumour were localized to the lower extremities of elderly men of Mediterranean extraction (Ashkenazic Jews). The pattern of dissemination suggests a multicentric origin, rather
than haematogenous metastatic spread from a single primary site (256; 370).

Although preponderant in homosexual males, KS has now been reported among all known risk groups for HIV infection (19; 75; 109; 322; 402). Although this has led to attempts to correlate the homosexual lifestyle to the development of KS, its preponderance in this risk group may simply reflect the high prevalence of infection within homosexuals.

KS most frequently appears in one or more mucocutaneous sites anywhere on the body. Depending on the stage of disease these painless, palpable, erythematous to violaceous lesions may appear as macules, infiltrative plaques or nodules. Within the oral cavity, lesions may occur at any site but have been reported to appear most commonly in the palate (80% to 95% of all lesions), then the gingivae and buccal mucosa. Other reported sites include the lips, tonsils, tongue, oropharynx, masseter muscle, parotid glands and epiglottis (Refer Section 2.3.1.) (70; 141; 180; 249; 301; 406).

KS has also been found in the heart, liver and lungs, centring its neoplastic growth around areas of high vascularity. Lesions of the gastrointestinal tract may appear in the oesophagus, stomach, small and large intestines, appendix and rectum, as flat to nodular vascular lesions. Other sites include the spleen, gallbladder, pancreas, kidney, adrenal gland, testis,
epididymis, palpebral conjunctivae, adventitia of aorta and large vessels, and perineural connective tissue (256). With such a wide range of reported sites and clinicopathological findings, it becomes obvious that KS may be found anywhere, and is typically variable in its presentation.

The development of squamous cell carcinoma (SCC) (Refer Section 2.3.3) of the epiglottis (18) and oropharynx (316), and cloagenic carcinoma of the anorectum (256) have also been reported, but only rarely. Although originally thought to be closely associated with HIV infection, inconsistent reportings have meant that SCC is no longer considered diagnostic for AIDS (Refer Appendix 1D and 1F). It has not been found to consistently occur more commonly in advanced HIV infection, although it has appeared in age groups not normally at-risk for its development.

6. **OCULAR MANIFESTATIONS**

HIV-induced immunosuppression allows for the viral, bacterial and fungal infection of various ocular components, as well as the development of neoplastic disorders. Ocular disorders have been consistently reported in patients with advanced stages of HIV infection (92; 138). Common findings include multiple foci of white granular lesions on the retina, known as "cotton wool spots" (chorioretinitis), and reported in up to 50% of AIDS cases (92), retinal haemorrhage and
vasculitis, coagulative necrosis and atrophy of the retina. Possible causes of chorioretinitis are cytomegalovirus, toxoplasmosis (92; 138) and candidal infection. HIV has also been directly implicated in these lesions due to its isolation from the retina of infected individuals (92). KS of the conjunctiva (92), inferior fornix and eyelid have also been noted.

1.2.3: THE NATURAL HISTORY OF DISEASE PROGRESSION

Much interest has centred on two distinct phases of HIV infection; the time interval from initial infection to a diagnosis of AIDS (incubation period for AIDS), and the period from AIDS to death. Attempts have been made to elicit differences between the various risk groups, and between adult and paediatric cases of HIV infection, within these two stages of the disease.

A. The time from initial infection to advanced HIV infection leading to a diagnosis of AIDS (incubation period for AIDS)

The terms "incubation period" and "latent period" have been used loosely in many studies attempting to describe the progression of HIV infection. **Incubation period** will be used in this treatise to denote the full period involved from a definitive date of infection with HIV to a diagnosis of AIDS, as set out in Appendix 1F.
There are five difficulties inherent in attempting to evaluate the incubation period for AIDS:

i. Most studies cannot definitively identify a date of infection in individuals with the possible exceptions being blood transfusion recipients, children infected perinatally and some healthcare workers infected by needlestick injuries. Where there is more than one transfusion or needlestick injury, accurate determinations of infection dates become increasingly difficult.

ii. Even where dates of infection are determined as being due to transfusions, needlesticks or perinatal transmissions, the possibility of other unknown or undisclosed risk factors may be of relevance (for example, heterosexual venereal transmission).

iii. The short history of the epidemic where unknown proportions of infected individuals may not have seroconverted, may never seroconvert or may have remained asymptomatic for the duration of the epidemic.

iv. There are a limited number of people suitable to study because the vast majority of infected individuals, in the form of homosexual and bisexual men and intravenous drug abusers, have unknown dates of infection. In these latter groups, repetitive exposures, sexually transmitted diseases, seminal plasma antigen and drugs may also influence disease progression.
v. The evolution of classification systems, meaning that lesions that led to a diagnosis previously are now not necessarily considered to be diagnostic for AIDS (for example; SCC). Similarly, variations in diagnostic criteria and disease reporting between countries make true comparisons of these periods exceedingly difficult.

The window period for HIV infection will be used in this treatise to describe the period of time involved from infection to overt seroconversion for HIV antibody. This is a period in which, although the individual may be potentially infectious (Refer below), serological testing proves to be inconclusive. This is of particular relevance when assessing the use of blood and blood products for transfusions and haemophiliacs, or the use of organs for transplantation.

Evidence suggests that the time that may elapse between infection with HIV and antibody production demonstrates considerable variation (25; 270; 299; 425; 428; 450; 455; 461; 462). Transfusion of HIV contaminated plasma to chimpanzees produced an active antibody response three to twelve weeks after exposure (270). In man, definitive estimations of the window period arise from well documented case reports of individuals with known dates of infection, in the absence of any other risk factors. Difficulties do arise, however, in pin-pointing exact dates for seroconversion to HIV antibody.
The hallmark case for the window period came from the nosocomial infection of a nurse with HIV infected blood, in which seroconversion occurred between 27 and 49 days after accidental injection (25). Other reports of parenteral exposure to HIV (270; 289; 299; 425; 428; 450; 455; 462) have similarly confirmed a likely period of 28 to 49 days for the development of antibodies. Reports definitively determining the window period in cases of sexual transmission are essentially limited, due to the previously outlined difficulties in determining actual dates of infection, with the main complicating factor being possible repetitive exposures.

In the majority of people with known HIV exposure, who have been followed prospectively, detectable antibody has developed within six months. Anecdotal reports, such as that by Imagawa et al. (461), have reported HIV infection for as long as 35 months without detectable antibody, however, methods of isolation and continual extensive high risk activity cast doubts on these suggestions.

The modelling of cases of HIV infection with known exposure, in published reports up to September 1989, have provided a median estimate of 2.1 months for the window period (462). Furthermore, 95% of the reported cases seroconverted by conventional serological screening methods within 5.8 months after exposure. In this way, HIV infection for longer than six months without detectable antibody seems uncommon.
Attempts to correlate this laboratory identification of HIV with clinical observations were attempted by Cooper et al. (428), who suggested that an acute febrile illness, observed in a cohort of homosexual men, could be used as clinical criteria for possible HIV infection. The sudden onset of a mononucleosis-like syndrome that lasts from three to fourteen days, was retrospectively identified in 92% of cases in this study (428). Subsequent studies have confirmed this illness, however, it apparently appears in 10% to 50% of infected individuals (17; 75; 427; 428).

This acute illness appears to occur approximately 2 weeks after infection with HIV (25; 270; 428; 450), and has been reported to precede serological detection of HIV antibody by between 2 weeks (428) and 25 weeks (25; 270; 299; 425; 428; 450; 455; 462). The period involved from infection to this illness seems to be related to the size of inoculum, with other, as yet undetermined, factors possibly playing a role.

A deep intramuscular injection, involving the exchange of infected blood in a nurse, has been reported to produce this acute illness within 13 days (25). In cases where transmission has reportedly involved a superficial needlestick injury (299), or a small quantity of infected material (289), the acute illness occurred 25 days (299) and 56 days (289) after exposure, respectively. Further studies are required to assess the variations in this period, the factors involved,
and the precise relationship between infection, the acute illness and overt seroconversion.

Recent studies have further complicated the issue of the window period by suggesting that HIV infection can be detected prior to both seroconversion and the onset of this acute illness. A negative antibody test during this window period does not necessarily infer an individual is not infected. This result may also mean that antibody levels are insufficient for detection by current serological methods (444).

HIV can be detected by more sensitive tests, such as Polymerase chain reaction (PCR), tests for HIV p24 antigen or HIV proteins (Refer Section 1.5), and the evaluation of CD4 and CD8 lymphocyte numbers. Ranki et al. (455) have suggested that HIV infection can be detected between 6 and 14 months prior to seroconversion. This suggestion challenges the belief that most cases of infection have led to seroconversion within 6 months (25; 270; 299; 425; 428; 450; 455, 462).

In real terms, the possibility of the late serological detection of HIV antibody, and the suggestions of an infectious seronegative state within the window period have serious implications for the risks involved in receiving blood transfusions, blood products and organ transplants. Ludlam et al. (444) hinted at an infectious seronegative state in haemophiliacs, who were possibly infected by a single contaminated batch of factor VIII,
but fell short of comparing the lack of antibody detection with viral identification or isolation from lymphocytes.

Confirmation of an infected seronegative state was provided by viral isolation in 4 out of 96 seronegative blood donors by Feorino and co-workers (140), and in 4 out of 235 homosexual and bisexual men by Ranki et al. (455). Since no reported cases of defined exposure to HIV that has led to infection has occurred without the eventual development of HIV antibody, it seems that the above reports represent a transitional stage to seroconversion.

Regardless of whether the infected individual does produce antibodies, the finding of a seronegative infected state does raise the possibility of transmission during this stage. Unfortunately, recipients of blood transfusions are not routinely tested, so it is unclear how many of these may have been infected as a result of a donor's seronegative infected state.

Anecdotal reports have suggested that seronegative infected donors of organs and blood products are capable of transmitting HIV infection to recipients. Hilgartner (472) has noted seroconversion to occur in a transfused individual as a result of infected red blood cells, which were seronegative at the time of donation. Similarly, a cadaveric organ donor, found to be negative
for HIV antibody two days prior to donation, transmitted HIV infection to both surviving recipients (123). These reports suggest that seronegative infected individuals may be infectious prior to seroconversion.

The detection of this infectious state has serious implications for the risks involved in transfusions and organ transplants. Added to this is the possible non-detection of HIV antibody post seroconversion, as borne out in a study of 88 AIDS patients (452), where only 82% were found to be HIV antibody positive by conventional screening methods. The isolated nature of reports of HIV infection in these recipients may be due to the donor exclusion criteria, heat and solvent detergent treatment or the use of ultraviolet light on blood and organs.

It has been hypothesized that the incubation period (period involved from infection with HIV to a diagnosis of AIDS) could differ from one risk group to another. Because dates of infection are difficult to determine in most risk groups, other than some cases of transfusion recipients, haemophiliacs, accidental percutaneous and perinatal transmissions, the study of this period is limited to these individuals. Furthermore, no data are available on the number of persons infected via these methods who have not yet developed AIDS. Therefore, the proportions of these infected individuals who will ultimately develop AIDS, and the upper limit of the incubation period cannot be estimated at this time.
All studies of adult cases of HIV infection within the USA attributable to the transfusion of blood products, with known dates of infection (ie. single transfusions), suggest a mean incubation period of between 27.5 and 31 months (102; 104; 138; 140; 170; 270; 447). Ranges of 15 months to 57 months for this period have also been reported (140). Variations between adults and children, in terms of the incubation period, may be attributable to a larger inoculation of HIV relative to body weight and the presence of an immature immune system in children. In comparison to the mean incubation period for adults (27.5 to 31 months), this period was only 14 months for all paediatric cases of transfusion-acquired AIDS in the USA to 1986 (102; 138; 140; 425).

This period seems to be even smaller in cases of HIV infection acquired perinatally, where the majority of cases of AIDS, and often death, are reported within the first year of life (421; 425; 427; 448). Mean incubation periods of all perinatally acquired cases in the USA have been determined to be between 3 and 8 months (42; 421; 427).

Anecdotal reports concerning transfusions in children suggest that incubation periods far in excess of the mean incubation periods quoted above may occur. Maloney et al. (447) reported a case in 1989 of a child transfused at birth who was diagnosed some five and a half years later in the absence of any other known risk factors. A more recent report, by Guarino et al. (466)
in 1990, suggested that a girl who received a single transfusion at 7 months of age had seroconverted, but had still not acquired clinical features diagnostic for AIDS, some 11 years later.

There are two points to make from these reports. Firstly they show that, as the duration of the epidemic increases, more prolonged incubation periods are reported. This would seem to suggest that more time is needed to determine the upper limit of this period. Secondly, these reports suggest the possibility of some infected individuals never progressing to AIDS.

A comparison of these actual incubation periods from transfusion cases with other risk groups remains inconclusive. Regardless of this fact, many studies of haemophiliacs (170; 223; 270; 443; 444), homosexual and bisexual men (50; 102; 103; 170; 179; 180; 181; 183; 219; 223; 270; 352; 399), intravenous drug abusers (102) and other individuals, without known dates of infection, have suggested incubation periods for AIDS, and have attempted to draw comparisons. However, it must be stressed that these suggestions may not truly predict this period for the following three reasons:

1. The first indication of HIV infection in individuals without known dates of infection essentially revolves around the serological identification of HIV antibody. The assumption in the aforementioned studies is that seroconversion
occurs within weeks of supposed infection with HIV and that this time is short in relation to the actual incubation period. However it has previously been pointed out that seroconversion may not occur for a period of 6 months (25; 270; 289; 299; 428; 450; 462), and possibly even up to 35 months (461) after infection.

2. Furthermore, the detection of antibody to HIV in these studies may not necessarily occur coincident with overt seroconversion. With a known protracted latent period of infection, where individuals remain asymptomatic although infected, serological detection may occur many months later.

3. Inaccuracies also occur because these same studies assume that seroconversion occurs at a mid-point between a negative and positive serological test. Protracted periods between serological testing and the possibility of false negative and false positive results cast even more doubt on the accuracy of these reports.

Regardless of these inaccuracies, these studies may be used to suggest possibly underestimated periods of incubation in those individuals without known dates of infection. The largest study, attempting to evaluate the rates of progression of these adult risk groups, studied cohorts of seropositive homosexual men, haemophiliacs and IVDA's over a three year period (170). A total of 725 individuals, from cohorts of homosexual men in New York City, Washington and Denmark; haemophiliacs from
Hershey, Pennsylvania, and intravenous drug abusers from New York City, were studied. Results showed that 34.2% of the homosexual men from New York City progressed to AIDS over the 3 year period, compared to only 14.9% (range 8.0% to 17.2%) of the other 4 cohorts.

At best, this study (170) remains anecdotal for three reasons:

1. Although all individuals were seropositive at the time of the study, known dates of infection and, therefore, duration of infection is not known.
2. No mention is made of the clinical status of any of the individuals in any of the cohorts, specifically, what proportion of each group were close to developing AIDS.
3. The study only involved a 3 year period.

To further amplify the difficulties involved in assessing the data of these individuals, an anecdotal report by Greenspan et al. (183) suggested that homosexual men have a mean incubation period of only seven and a half months. However, these seropositive individuals had been infected and had seroconverted for an unknown period of time. In addition, all individuals had symptomatic HIV-associated disease, in the form of hairy leukoplakia, at the time of being studied. At best, this seven and a half month period can therefore be considered an underestimation of the true incubation period. Other anecdotal studies have also probably
underestimated the true incubation period, suggesting periods of up to 9 years (102; 140; 170; 270; 280; 330; 421).

Despite these impediments, attempts have been made to rank the various risk groups according to the risk of developing AIDS. Disregarding perinatal transmission, it has been hypothesized that transfusion-acquired AIDS has the shortest incubation period of all the risk groups (102; 104; 140; 170; 270), ranging up to 57 months. At the other end of the scale, the haemophiliacs are supposed to display the slowest rate of progression to AIDS (170; 270; 443; 444), with suggested mean incubation periods exceeding 8 years. Other risk groups have been hypothesized to have intermediary mean incubation periods. Studies of homosexual and bisexual men have suggested a maximum estimate of the mean incubation period as 7.8 years (446), with a range of between 4.2 and 15 years.

Due to the reasons mentioned previously, these comparisons cannot be considered accurate. In addition to these, not all of the seropositive individuals in any of the studies had progressed to AIDS. This further amplifies the possibility of infected individuals never progressing to AIDS, or that the upper limit of the incubation period may well exceed the duration of the epidemic to date. These possibilities are supported by anecdotal case reports of individuals with transfusion-acquired HIV infection, presumably the mode of
transmission exhibiting the most rapid progression to AIDS, who still have not been diagnosed up to 11 years post-infection (466).

Until a definitive determination of infection in these individuals can be determined, no accurate comparisons can be made. Furthermore, while still in the initial stages of the epidemic, information relevant to our understanding of HIV will remain limited.

B. The period involved in the transition from a diagnosis of AIDS to death

Estimations of the period involved from a diagnosis of advanced HIV infection (AIDS) to death primarily depend on the time at which a definitive diagnosis is made. Due to problems mentioned previously in regard to the late recognition and reporting of AIDS cases, estimations from Africa are unusually short, with only 7.5% of all cases surviving more than 3 months (Plummer. D, Written Communication, National AIDS Bulletin; December 1989).

The mean survival time of all reported AIDS cases in the USA for this period (diagnosis to death), have been estimated at 29 months in adults (180) and between 11 and 15 months in children (41; 180); reflecting the earlier identification and better medical care in the more developed countries. A shorter period in children
is consistent with earlier suggestions of a more rapid natural progression of HIV disease.

In the USA up until December 1987, 60% of all reported paediatric cases of AIDS and 49% of all reported adult cases had died (421). Within Australia to March 1990, 55% of all reported adult cases of AIDS and 67% of all reported paediatric cases had died (286). These figures would suggest a death rate, for the epidemic to date, in the order of 50% to 60%. Although only limited cases were reported in Australia prior to 1985 (50 cases of AIDS), the fact that 96% of these have died suggests that the death rate in Australia may reach 100% (Refer Section 1.7, Table 1.7.2).

It seems probable that the period involved from a diagnosis of AIDS to death will progressively lengthen for the following three reasons:

1. With increased awareness, many infected individuals are seeking testing by self referral. As a result, the majority of AIDS cases will be detected earlier.

2. Many drugs have been shown to suppress the effects of HIV on the immune system (Refer Section 1.6.1). In addition, these drugs are now being used during stages of advancing immunosuppression, rather than after a diagnosis of AIDS.

3. More is now known about the various indicator diseases for AIDS, resulting in an earlier
diagnosis. With increasing knowledge and experience, more efficient treatment methods may be implemented at earlier stages.

To demonstrate the probable contributions of these three factors within Australia, 36% of all AIDS cases diagnosed in the preceding twelve months to October 1987 had died, as compared to only 21% of the same in the twelve months preceding March 1990 (286).

C. Other differences in the presentation of HIV infection between adults and children

In addition to the different rates of disease progression between adults and children, the following differences may also be seen:

i. Clinical abnormalities.

ii. Modes of transmission and risk groups.

iii. Ratios of male to female cases of AIDS.

i. Clinical Abnormalities

The clinical abnormalities seen in HIV infected children are summarized in Table 1.7.10 (Refer Section 1.7). These manifestations are similar to those seen in HIV infected adults and children with primary T-cell and phagocytic cell defects (420). True comparisons of manifestations between adults and children are difficult
because of age differences and a lack of sufficient detail to fully evaluate these variations.

It is known, however, that children usually die as a result of opportunistic infections, and reach this stage of HIV disease more rapidly than adults. This may help explain a lower incidence of Kaposi's sarcoma and hairy leukoplakia, and an absence of reports of B-cell lymphomas and squamous cell carcinomas. In addition, a lack of reported cases of various venereal infections and lesions is likely to be a direct result of a lack of sexual contact. Anecdotal reports suggesting an increased incidence of parotid enlargement in children (20% of cases) (420) as compared to adults (5% of all seropositive homosexual men) (421), require more detail to fully evaluate.

As a direct consequence of being infected during foetal development, infected children have been shown to display certain physical abnormalities. These physical traits, seemingly unique to HIV infection, have been termed "foetal AIDS syndrome". Although Marion and co-workers (442) have observed this HIV embryopathy in 75% of children infected perinatally, more evidence is required.

The syndrome is reportedly characterized by a small head, prominent forehead, flat nasal bridge, short nose with flattened columella, long palpebral fissures with an upward slant, prominent triangular philtrum, growth
failure with associated microcephaly and very prominent eyes with a bluish tint in the sclera (421).

ii. **Modes of transmission and risk groups**

As mentioned previously, HIV infection in adults in Europe, USA and Australia predominantly affects homosexual and bisexual men and IVDA’s (87% to 92% of all cases). Mainly due to age, no cases of paediatric HIV infection have been attributed to any of these routes.

Although the absolute risk groups for HIV transmission in children are the same for the USA and Australia, variations in the relative contributions of these groups may reflect the emerging filtration of HIV into the heterosexual community in the USA. As a result, 80% of paediatric AIDS cases in the USA to January 1990 involved perinatal transmission (421), as compared to only 20% of those in Australia to that time (286).

The predominant method of infection in Australia involves the receipt of infected blood via transfusion, accounting for 67% of all AIDS cases in children (286). In contrast, this method only accounts for 12% of cases in the USA (421). Most cases of HIV infection in children occur before the age of 5, with the main method of transmission being perinatal (USA) or via transfusions (Australia). For those children infected between the ages of 5 and 13 in these countries,
haemophilia poses the most significant risk (286; 421).

Within countries with the second and third epidemiological pattern (for example; Africa and Eastern Europe - Refer Section 1.3.2), blood transfusions, the use of unsterilized needles and perinatal transmission account for the vast majority of cases. An anecdotal report by Patrascu et al. (471) has suggested that the lack of sterile medical supplies may play an important role in spreading HIV infection among children. Of 1025 samples of sera taken from Romanian children, 35.8% were seropositive to HIV. With only 3% of mothers of these infected children also being seropositive, these findings suggest that the lack of disposable needles and medical supplies, in these countries, may cause widespread HIV infection in children.

iii. **Ratios of Male to Female Cases of AIDS**

Differences in the ratio of male to female cases between adults and children reflect the differences in the modes of transmission. Ratios in adults vary considerably, from 1:1 in Africa (270) to 98:1 in San Francisco (64) at various stages of the epidemic. On the other hand, ratios in children essentially approximate birth ratios (1:1) (421).
1.3: **GLOBAL EXTENT AND EPIDEMIOLOGICAL ASPECTS**

This section is devoted to three separate epidemiological aspects of HIV infection:

1.3.1 Global extent and incidence of HIV infection.
1.3.2 Epidemiological patterns of HIV infection.
1.3.3 Aspects of HIV infection within Australia.

1.3.1: **GLOBAL EXTENT AND INCIDENCE OF HIV INFECTION**

As of 1 May 1990, 254,078 cases of AIDS had been reported from 156 countries, with the Americas (60%) and Africa (25%) being the major contributors (286). The United States alone contains 126,127 cases, or 50% of the worldwide total of reported AIDS cases. Although Africa had reported 63,842 cases, or 25% of the total (286), the number is thought to be five to ten times higher (56; 70; 103). Accurate surveillance in Africa is almost impossible due to the limited access of large segments of the population to a minimal number of health care facilities capable of diagnosing advanced HIV infection, and a low efficiency of current surveillance systems.

Another possible explanation for the underreporting in Africa is that cases of advanced HIV infection (AIDS) have been characterized by sudden and dramatic wasting, persistent fevers and chronic diarrhoea. Malnutrition,
fevers, infant mortality, pulmonary diseases and
diarrhoea are so generally widespread in Africa that
many cases of AIDS have been and will continue to be
missed (56; 70; 103).

With such a widespread underestimation of HIV
infection, it is not difficult to imagine that cases of
AIDS are similarly under-reported. Even areas with
accurate surveillance systems, such as the USA, are
estimated to only report up to 90% of all cases of AIDS
(79). Obviously, lesser developed countries will
contribute significantly more. As a result, precise
comparisons between countries is exceedingly difficult,
if not impossible.

No concrete conclusions or trends can be drawn from
such heterogeneous data, and projections into the future
can only be considered as hypotheses. Regardless of
this, it has been suggested by the CDC (433) that
reported cases of advanced HIV infection (AIDS) probably
represents less than half of the actual cumulative total
to the end of 1989, a total which may well approach
400,000 (433). Later predictions by the World Health
Organization (WHO) (286) suggest that, as of 1 May 1990,
there are an estimated 650,000 cases of AIDS.
Furthermore, they suggest that more than 6,500,000
people worldwide are infected with HIV, the vast
majority of which come from Africa (3,500,000) (286).
HIV infection is a global problem, due mainly to the ability of the virus to produce widespread infection before the onset of symptomatic disease, the sexual promiscuity of certain groups of human beings, and the ease of international travel, which have all contributed greatly to the rapid spread of HIV.

The global extent of HIV infection has variously been estimated at between 6.5 and 10 million people (77; 286). More than half (54%) of all these people are estimated to occur in Africa, which contains only 12% of the world’s population (398), meaning that a disproportionately high percentage of individuals are infected. Reported cases of AIDS in Africa have accounted for between 17% (1989) and 25% (1990) of the world total (286; 398), due to the problems mentioned previously (Refer Section 1.7, Table 1.7.3).

The most advanced areas, in terms of the spread of HIV, are the Congo Basin and parts of East and Southern Africa. In countries like Zaire, Zambia, Uganda and Tanzania it has been speculated that 10% of the entire population is infected (318). In the sexually active age groups, and in urban areas, this proportion seems to be even higher (318). Most of the remaining people infected with HIV are thought to be in the developed world of North America, Europe, Australia and New Zealand, which between them have about 22% of the world’s population. It has been suggested that the United States has up to 2.5 million HIV infected people,
a figure approximating 1% of the entire population (286). Similarly, it is estimated that Africa contains more than 3.5 million HIV carriers (286).

In order to show the incidence of HIV infection throughout the world, both the increases in reported cases and the reported increases in seroprevalence rates within various cohorts can be studied. Following the initial reports in the United States (69; 73), 70 additional cases were identified within the next six weeks. These initial cases could be backdated to 1978, and so, only five years later (by February 1983), the first 1000 cases had been reported (180). By December of that year, only nine months later, the second 1000 cases had been identified in America, showing an exponential increase. The number of new cases reported worldwide, increased from 80 per week in 1985 to over 400 a week in early 1988 and 500 a week in 1990 (318).

In much the same way, increasing rates of seroprevalence can be used to show the rapid spread of HIV-1 infection throughout the world (Refer Section 1.7, Table 1.7.4). A sero-survey of blood stored within the USA since 1978, for 6,875 homosexual men (219), showed that the prevalence of antibodies to HIV-1 increased from 4% in 1978 to 35% in 1981 and 73% in 1985. Table 1.7.4 (Refer Section 1.7) shows the prevalence of antibody to HIV-1 in several other cohorts throughout the world. These cohorts included homosexual men, intravenous drug abusers, haemophiliacs, prostitutes and
their male clients, and show that all risk groups from various geographic areas exhibited similar rates of increasing HIV infection.

1.3.2: EPIDEMIOLOGICAL PATTERNS OF HIV INFECTION

To date, three different epidemiological patterns of HIV infection have been proposed (312), due to differences in geographical location, risk groups and the possible dates and duration of viral exposure. It is not currently known whether disease progression differs between these three patterns:

a. First epidemiological pattern (Western Europe, North America, parts of South America, Australia and New Zealand).

b. Second epidemiological pattern (Africa, Caribbean and some areas of South America).

c. Third epidemiological pattern (Asia, the Pacific region (excluding Australia and New Zealand), Middle East, parts of Eastern Europe and some rural areas of South America).

a. The first epidemiologic pattern

The first epidemiological pattern has occurred in Western Europe, North America, some areas of South America, Australia and New Zealand; areas in which the
epidemic was initially found in homosexual men, then bisexual men, haemophiliacs, intravenous drug abusers (IVDA’s) and blood transfusion recipients. The virus seems to have been introduced to these areas in the mid to late 1970’s and began to spread extensively through the late 1970’s and early 1980’s (69; 70; 73; 180; 286; 318).

Homosexual transmission remains the predominant group in most areas, accounting for up to 90% of the cases from any one region (125). As a result, young adult males (25-44 years of age), living in urban areas, are predominantly affected. The second highest group are IVDA’s (0-10% of all AIDS cases) (102; 103; 241; 318); although in some areas of Southern Europe, such as certain regions of Italy, this mode of transmission has accounted for between 20% and 70% of reported AIDS cases from that region (294), and may represent the predominant risk group. This regional variation may be a result of greater proportions of IVDA’s from any one region.

Heterosexual transmission is essentially limited when compared to other geographic areas, but is continually increasing. The transmission of HIV from contaminated blood or blood products seems to no longer be a major problem in these developed countries, due to a combination of serological screening and donor exclusion criteria, although tens of thousands of individuals have been infected by this latter method, prior to 1985.
Perinatal transmission is becoming an increasing problem. The index cases of perinatally infected children in the USA have involved mothers who are IVDA's (53%), have had sexual intercourse with an IVDA (20%) or bisexual man (20%), or mothers who have come from geographic areas where heterosexually acquired HIV infection is endemic, such as Africa (301; 349).

b. Second epidemiological pattern

The second epidemiological pattern is that evident in Africa, the Caribbean and some areas of South America. In this pattern, the virus has predominantly affected heterosexuals and persons who have been treated with blood transfusions and other injections. Up to 25% of the 20 to 40 year age group in some urban areas of Africa are infected. Similarly, it has been suggested that up to 90% of female African prostitutes, and 30% of their male contacts are similarly infected (318). A study of Nairobi prostitutes (318) from a low socioeconomic area in 1986 adequately displays the contribution of heterosexual transmission within Africa. In the absence of any other known risk factors, the rise in seroprevalence from 8% in 1981 to 61% in 1985 can be directly attributed to heterosexual venereal transmission. Further evidence of the contribution of this mode of transmission may be gained from the finding that, of the male sexual contacts of these prostitutes, the seroprevalence rose from 0% to 17% in the same period (318).
The virus seems to have been introduced to these countries in the early to mid 1970's and begun spreading rapidly throughout the 1970's. The precise nature and extent of the epidemiological pattern of HIV infection in these areas is difficult to assess, due to the problems of recognition and reporting outlined previously. Homosexual transmission does not appear to be a major factor in these areas, although transfusion of HIV infected blood is a major public health problem. Non sterile needles and syringes have accounted for an undetermined proportion of HIV infection (318).

The disease has infected young adults of both sexes in this pattern, in both rural and urban areas. Because similar numbers of men and women are infected by the virus, more pregnant women are infected. This has meant that HIV is more prevalent amongst infants and young children. An anecdotal study by Saxinger and colleagues (426) revealed, retrospectively, that 65% of Ugandan children were seropositive in 1972, suggesting that large numbers of children from these areas may be infected.

c. Third epidemiological pattern

The third epidemiological pattern of transmission may be a variant of the second one, and is found in Asia, the Pacific region (excluding Australia and New Zealand), the Middle East, parts of Eastern Europe and some rural areas of South America. In this pattern, the
incidence of reported infection to date is relatively low (Refer Section, Table 1.7.3). Initial studies indicate that those most at-risk of transmission are prostitutes and those who have received blood products from endemic regions.

Both homosexual and heterosexual transmission have been documented (318), but the prevalence remains relatively low even in individuals with multiple partners. The majority of infected individuals are also young adults in their economically productive and child-bearing years, however, the epidemic has been too short lived at present for perinatal transmission to have become a major problem. In some countries, such as Hong Kong and French Polynesia, infected individuals are predominantly male, while in others, like the Philippines, they are predominantly female. The virus seems to have been introduced to these regions in the early to mid 1980’s, probably from more endemic areas, such as the United States, Australia and Europe.

Countries with the first and second epidemiological pattern were only alerted to the presence of HIV years, maybe even decades, after it had entered and begun spreading through the population. With infected individuals remaining asymptomatic for an as yet unspecified length of time, HIV was able to spread extensively before identification. It was only when HIV caused symptomatic disease that a new epidemic was identified. The fact that HIV was able to spread
extensively before specific detection was possible has had important social ramifications.

Because AIDS affects men and women in their procreative years, and their offspring, it will drastically reduce the rates of population growth in certain urban populations of Central and East Africa, where 5% to 30% of women of child bearing age have been shown to be HIV-1 seropositive (318). Loss of skilled manpower may be important in countries where the educated elite have a higher incidence of infection (318).

Further studies in Africa have demonstrated that HIV-1 is primarily a heterosexually transmitted disease and that the main risk factor for acquisition is the degree of sexual activity with multiple partners, rather than sexual orientation. With widespread heterosexual venereal transmission, HIV has spread through the general community in Africa, and is beginning to do the same in the USA and Europe. Transmission to females and children may serve to eliminate a great proportion of the young generation in endemic areas.
1.3.3: ASPECTS OF HIV INFECTION WITHIN AUSTRALIA

The HIV epidemic within Australia is comparable to that in the USA in terms of the following aspects of the disease:

a. The rate of increase of reported cases of AIDS and HIV infection.
b. The groups of individuals at-risk.
c. The ages of known infected individuals.
d. The geographical location of infected individuals (urban vs. rural).
e. The male to female ratios of reported cases of AIDS.
f. The progression of disease including death rates.
g. Future likely trends.

a. The rate of increase of reported cases of AIDS and HIV infection

Following the first case of AIDS in 1982 (393), Australia confirmed five cases in 1983 (310; 393), all in homosexual men, who had probably acquired the infection while visiting the USA. December 1983 saw the first apparent report of indigenously acquired AIDS, in a bisexual man who had never travelled outside of Australia (310). These were followed by 42 cases in 1984, 112 in 1985, and 220 cases to the end of 1986
(286). These cases predominantly involved homosexual men.

It took 25 months for the first fifty cases of AIDS in Australia to be reported, but only six weeks for the seventh group of fifty cases (393). This rapidity may be due to a combination of increasing infection, better identification, and more efficient and rapid reporting of AIDS cases. This exponential pattern is similar, albeit on a smaller scale, to that experienced by the USA (Refer Section 1.7, Table 1.7.3).

Limited studies of seropositivity within cohorts of Australian homosexual men, displaying an increase from 0% in 1980 to 32% in 1982 (335), showed similar rates of infection to various North American studies (103; 109; 196; 270; 318) (Refer Section 1.7, Table 1.7.4). The later recognition of seropositivity within Australia, as compared to other countries, may suggest that HIV spread from these countries to Australia. Further evidence of this comes from the fact that initial Australian cases of AIDS occurred in homosexual men who had all travelled to the United States (393; 310).

b. The groups of individuals at-risk

The spread of HIV infection within Australia has been similar to that in the USA with respect to both the actual groups of individuals at-risk and the stability of the percentages of these risk groups within each
country throughout the epidemic (Refer Section 1.7, Tables 1.7.3, 1.7.4, 1.7.5 and 1.7.6). Differences between developed countries do occur, however, in respect to the relative contribution of each of these risk groups (102; 103; 119; 219; 280; 393).

Transmission by IVDA alone is apparently greater in the USA (17%) compared to Australia (2.5%), possibly as a result of the presence of "shooting galleries", widespread needle sharing and increased drug availability. A further 2.8% of cases (286) in Australia and 7.7% of cases (127) in the USA occur in homosexual or bisexual men who also abuse intravenous drugs. In these cases, it remains unknown as to which risk behaviour was responsible for infection. Similarly, cases attributable to IVDA may have been infected by heterosexual venereal transmission.

The proportion of AIDS cases attributable to IVDA is larger again in Italy (60%), where seroprevalence ranges from 20% to 70%, and more, depending on the geographical region (294). It has been hypothesized that these figures are due to an alarming rate of IVDA amongst Italian prostitutes (294). The actual contribution of IVDA to these figures cannot be gauged due to the presence of additional risk behaviours, such as homosexual and heterosexual venereal transmission.
Although most of the risk groups in Australia have maintained similar relative percentages of AIDS cases throughout the epidemic, the exception is those infected by blood transfusions. The rates for this mode of transmission have dropped from 10% (December 1985) to 3.2% (November 1989), due mainly to the lack of newly acquired transfusion-associated cases since the screening of blood began in 1985 (286). The current relative contributions of transfusion-acquired AIDS are similar, accounting for 3% of cases in the USA (102), 1.8% of cases in the United Kingdom (UK) (262) and 3% of those from Europe (102). With problems of reporting, the situation in less developed countries, such as Africa, remains unclear.

Homosexual and bisexual men constitute the group at most risk for AIDS in all developed countries except Italy. These individuals have currently accounted for up to 88.8% of all Australian cases (286), 85% of cases within the UK (9; 11; 241; 242), and up to 84% of all cases in the USA and Europe (56; 79; 318). Slight ranges of 80% to 89.4% for all cases that may be attributed to these behaviours are a result of the emergence of infection in other risk groups, with subsequent spread to the general community.

Nearly 1,500 cases of AIDS in children under 13 years of age have been reported in the USA (102), with just over 100 in Australia (286). The main mode of transmission in Australian paediatric cases is the
receipt of blood transfusions (66.7%), then perinatal infection (20.0%) and haemophilia (13.3%) (286). The situation is not the same in the USA, with between 68% and 76% of cases being due to perinatal infection, 12% to 14% due to blood transfusion and 16% were haemophiliacs (102).

The greater percentages of perinatal transmission in the USA may be related to the larger proportions of AIDS cases being attributed to IVDA in the USA (up to 25%), as compared to Australia (up to 4%)(286). Widespread HIV infection in these individuals has been suggested in several anecdotal studies, where seropositivity can range from 5% to 20% in west coast cities, and up to 50% in New York City (301). The correlation between IVDA and HIV infection in children has been demonstrated by studies showing that perinatal infection occurs mainly via mothers acquiring HIV through IVDA or from sexual intercourse with men who abuse drugs (301).

Heterosexual venereal transmission varies greatly, from an estimated 70% of all reported AIDS cases in Africa (55) to 0.8% in Australia (286). It is obvious from Australian data that heterosexual transmission is not yet as great a problem as it is in areas with the second and third epidemiological patterns (286) (Refer Section 1.3.2).
c. **The ages of known infected individuals**

Up to 88.2% of all reported AIDS cases in Australia have occurred in the 20 to 49 year age group, with this group accounting for up to 86% of all AIDS related deaths in this country (285). These findings are similar to the USA (75% occurring in the 25-44 year age group) (102); Sweden (90% less than 45 years of age) (203); Africa (80% in the 15-35 year age group) and Europe (70% in the 20-39 year age group) (102), showing that AIDS is predominantly a disease of the young adult age group.

d. **The geographical location of infected individuals (urban vs rural)**

The majority of cases of AIDS within Australia, until December 1989, have occurred in New South Wales (62% of all national cases), followed by Victoria (22%) and Queensland (6.5%) (286). The highest cumulative number of cases per million of total population is also recorded by New South Wales (150 per million in December 1989). These findings are in accordance with those of the USA, where the majority of cases are clustered in areas of denser population (79; 220). There is also a greater proportion of cases involving homosexual or bisexual men, and up to 70% of all transfusion-acquired cases have occurred in these urban areas, displaying the relationship between HIV transmission and the receipt of blood products from HIV endemic areas (286).
The migration of HIV infection from major metropolitan to less densely populated areas in the USA (79) is similar to the trends evident in Australia, where more cases are recently being reported from Tasmania and the Australian Capital Territory. These latter areas respectively account for 1.3% and 1.1% of all reported AIDS cases in Australia up until February 1990 (286).

e. The male to female ratios of reported cases

Ratios of male to female cases are also similar for all countries with the first epidemiological pattern. The ratio in Australia has ranged from 25:1 (March 1988) to 32:1 (November 1989) (286), the USA is currently 10.5:1, and Europe 8.5:1 (318). Ratios within the USA may vary markedly, depending on the relative contributions of homosexual and heterosexual venereal transmission. The ratios in third world countries and Asia also reflect the degree of heterosexual transmission, with Africa and Asia approximating the same (1:1) (56; 318).

f. The progression of disease including death rates

In January 1989; 48.2% of all AIDS cases in Australia had died, ranging from 13.3% of heterosexuals, to 40% of IVDA's and 80.7% of transfusion recipients. By September 1989, the number of deaths had risen to 52.5% for all Australian AIDS cases, ranging from 27.8% of IVDA's, 39% of heterosexuals and 86% of transfusion recipients. Only three months later (December 1989),
the deaths had risen further to 54.4%, and the number of transfusion related deaths had also risen to 90%, a reflection of the lack of newly acquired infection via this route (286). These death rate figures of between 50% and 55% for all reported AIDS cases are similar to those of the USA (102).

Current Australian statistics suggest that essentially all people with AIDS will die within seven years of diagnosis. As of May 1990, 96% of the 50 people diagnosed with AIDS prior to 1985 have died, and of those cases diagnosed in 1985 alone 97.2% have died (286). Of the cases diagnosed in the last six months of 1988, 44.1% have died, as have 18.9% of those diagnosed in the last six months of 1989 (286).

g. **Future likely trends**

There has been a gradual shift in the distribution of reported AIDS cases from homosexual males to other groups, (for example, women and children), which had previously enjoyed lower prevalence rates in Australia and the USA. Growing numbers of apparently healthy individuals may be infected and unknowingly transmit the disease during pregnancy and childbirth. It is estimated that in 1991, in the USA alone, between 10,000 and 20,000 children will have symptomatic HIV infection, with most of these being infected at birth. This represents a 10 to 20 fold increase over the number of affected newborns to the end of 1988 (301).
Current reported AIDS cases do not demonstrate the actual numbers of people presently infected with HIV; therefore, to what extent rates of infection in various risk groups will change is unclear, in particular the extent to which the general heterosexual community may become infected.

It still remains, however, that AIDS is a disease predominantly affecting the homosexual and bisexual community (89% of Australian cases) (286; 102). An upsurge in heterosexually acquired AIDS within Australia, to mirror what is happening in certain parts of Europe, Asia and the USA has been forecast. It was suggested in 1988 that by the end of 1991 Australia will have 3,000 cases of AIDS with 1,500 deaths; as compared to 300,000 cases and 180,000 deaths in the USA (121). Later estimations (WHO - May 1990) suggested that a more realistic figure for cases of AIDS in the USA, as of May 1990, would be 375,000 (286).
1.4: RISK GROUPS

1.4.1: INTRODUCTION AND FACTORS INVOLVED IN TRANSMISSION

The later identification of initial AIDS cases (393) and the lack of detection of HIV by retrospective analysis within Australia prior to 1981 (335), seems to suggest that HIV was introduced to Australia some years later than the USA and Europe. As a result, we have the benefit of learning from epidemiological studies, which have clearly defined certain groups of individuals at high risk of contracting HIV. Initial cases were confined to homosexual and bisexual men, but soon it became obvious that HIV was analogous to Hepatitis B Virus (HBV), and could be transmitted by the exchange of certain body fluids.

HIV has been isolated from most bodily fluids (131); including blood (154; 206; 386), semen (206; 219; 326), vaginal and cervical secretions (45; 206; 211; 219; 313; 326), saliva (131; 146; 147; 148; 151; 155; 156; 170; 186; 191; 208; 326), tears (17; 476), breast milk (318; 372), cerebrospinal fluid (205; 207; 222; 324), amniotic fluid and urine (167). However; epidemiologic evidence has only directly implicated blood, semen, vaginal secretions and, possibly, breast milk in transmission. The transmissibility of HIV due to contact with saliva remains unclear, although suggestions of inhibitory salivary components (148; 170), a lack of definitive
cases of occupationally acquired HIV in dentists, and an absence of transmission from non-sexual casual contact would suggest a minimal role (Refer below).

The isolation of HIV from most bodily fluids would suggest that these fluids may potentially act as vectors for HIV transmission. With so many possible vectors, it is obvious that a multitude of mechanisms may lead to infection. Some of these include:

1. Possible blood to blood transmission (IVDA; heterosexual and homosexual venereal transmission; transfusion of blood and blood products; perinatal transmission; and needlestick injuries).

2. Possible saliva to blood transmission (heterosexual and homosexual venereal transmission; casual contact, such as biting and the sharing of toothbrushes and razor blades; occupational transmission).

3. Possible semen to blood transmission (heterosexual and homosexual venereal transmission).

The exact contribution of each bodily fluid in transmitting HIV is difficult to ascertain because of the often multiple exchanges of many possibly infected bodily fluids.
Difficulties in separating out the relative contributions of these various body fluids makes it exceedingly difficult to evaluate the role that saliva may play. However, transmission via saliva (Refer Section 1.4.8) seems to be relatively ineffective for the following reasons:

1. Studies suggesting the presence of HIV inhibitory components within saliva (146; 148).
2. The limited number of cases of presumed occupationally acquired infection in dentists and other healthcare workers (201; 233; 266; 360; 381; 473; 495).
3. A lack of transmission due to non-sexual household contact, where toothbrushes, razor blades and toys have been shared (151).

However, the situation remains unclear because:

1. Dentists are not routinely tested, and as such, both the seroprevalence rates and the relative contribution of saliva remains unclear.
2. Even if these rates were known, additional risks may be valid, such as the contact with blood via needlestick injuries.
3. It is unclear whether cases of venereal transmission (heterosexual and homosexual) arise from the contact of infected blood, infected saliva or other infected body fluids.
Evidence suggests that the greatest risk of HIV infection involves contact with infected blood (IVDA, heterosexual and homosexual venereal transmission, blood transfusions). A slightly smaller risk has been suggested for semen, vaginal and cervical secretions. The risk for saliva and breast milk appears to be less, with the transmission via urine, tears, cerebrospinal fluid and amniotic fluid being merely theoretical possibilities, until proven otherwise.

The isolation of HIV in a body fluid does not prove that the fluid or tissue represents a mode of transmission. Instead, the successful transmission of HIV to a susceptible host relies on many factors, the relative contributions of each being unclear due to the multiplicity of these factors in the transmission process. These factors are:

1. The concentration of intact HIV circulating in the vehicle of spread of the carrier.
2. The actual volume of the infective vehicle transferred into the susceptible host.
3. The mode of escape from the carrier reservoir and transfer to the host, which may influence the number of surviving virus particles.
4. The mode and site of entry of the virus into the host, such as frank percutaneous inoculation versus possible transepithelial transmission.
5. The possibility of repetitive exposures to infective material, such as in multiple sexual
partners, multiple transfusions and needlestick injuries.

6. The relative effectiveness of the host immune response.

7. The possibility of other co-factors that may facilitate transmission, such as drug use, the presence of blood and tears in the mucosa.

Among each of the major groups at high risk in the USA, that is homosexual and bisexual males and persons who take drugs by intravenous contaminated injections, their relative contributions to reported AIDS cases have remained similar. The main differences between the risk groups are a decrease in the cases of AIDS attributable to the transfusion of blood and blood products, and a concomitant increase in heterosexual and perinatal transmission (351; 93). Although female to female homosexual transmission has been reported in one case, this frequency would seem to be very low in comparison to the well documented modes of male to male, male to female, and female to male transmission (102). The situation is the same for most parts of Europe and Australia (93; 12).

In addition, the actual contribution of specific risk activities to HIV infection (seroprevalence rates and reported AIDS cases), and the number of exposures needed to cause infection remains unclear. Difficulties arise from the possibility of repetitive exposures and additional risk behaviours.
1.4.2: **THE GENERAL POPULATION**

Suggestions of the prevalence of HIV infection in the general population have been based on studies with varying degrees of selection bias. These studies have involved:

2. Recruits for military service.
3. Selective populations that have voluntarily presented for screening.

Seroprevalence studies of blood donors probably most closely approximates the situation in the general population (0.001% HIV+ in Australia) (14; 232; 331). However, the exact situation remains unclear because, although age ranges and sex distribution of blood donors are similar to those of the general community, exclusion criteria ensures that homosexual males, IVDA's and haemophiliacs are actively deterred from donating blood. With this in mind, these studies would suggest an underestimation of true national rates of HIV infection.

Studies of military recruits (0.14% to 0.15% prevalence of HIV) (58; 56; 102; 335) are difficult to extrapolate to the general community for reasons of the same exclusion criteria. Further bias is provided by a limited age range (predominantly 16 to 20 years of age) and a predominance of male recruits, factors that would
appear to correlate with an increased HIV prevalence in these individuals.

Notwithstanding these exclusion criteria, studies of blood donors and military recruits in the USA (232; 335) show more than 92% of seropositive individuals with recognized risk factors other than heterosexual transmission as a probable cause. With many possibly infected individuals excluded from these cohorts (due to the bias mentioned above), the suggestion of 8% of cases being due to heterosexual venereal transmission could overestimate its true contribution.

Of even less relevance to the general community are studies of selective populations that voluntarily present for screening, such as a study of 12,000 people (to 1990) by the Albion Street Aids Centre (Sydney) (Plummer D, Written Communication, National AIDS Bulletin; June 1990) suggesting that 1,600 individuals were seropositive for HIV. Difficulties in extrapolating these seroprevalence rates to the general community arise for the following three reasons:

1. These individuals presented voluntarily for screening due to possible past exposure to HIV, engaging in risk activities or fear of infection. In this way, no individuals who did not engage in any risk activities presented for screening.
2. The selection bias meant that a disproportionate number of homosexual and bisexual men, IVDA's and prostitutes were screened.

3. With young adults being most at risk for HIV infection, the presentation of larger proportions of these individuals in this study means that a resulting higher prevalence of infection than the general population may occur.

As a result, the finding of 13% of these individuals being seropositive to HIV almost certainly overestimates the true seroprevalence rate within the general community. Various attempts have been made to extrapolate seroprevalence rates of selected cohorts to the general community, however, due to selection bias, the exact situation remains unclear. Unless routine HIV testing on a major scale is introduced, as suggested by Gordin et al. (441), there would be no way of accurately determining rates of infection within the general community.

1.4.3: HOMOSEXUAL AND BISEXUAL MEN

Reported cases of AIDS among adult Australian homosexual males is at least 10,000 times that among the non-high-risk general population, confirming the extent
to which HIV infection has been primarily concentrated in one segment of the population in those countries with the first epidemiological pattern (125) (Refer Section 1.3.2). Homosexuality and bisexuality accounts for 88.8% of all Australian AIDS cases (286), and with the additional risk of IVDA, constitute a further 2.7% of cases to February 1990 (286). It is uncertain, though, whether these cases can be attributed to the exchange of infected blood, semen, saliva, or a combination of these fluids.

Cases of AIDS due to male to male venereal transmission constitute between 60% and 100% in most countries (except Africa, Asia and the Pacific region) (57). Those countries with less than 50% of reported cases of AIDS due to this mode have either widespread heterosexually acquired infection (for example; Africa, Asia and Pacific region) or an apparently high proportion of IVDA’s in the general community, especially among prostitutes (for example; Italy, Greece, Belgium and Spain) (57; 102; 206; 318).

Seroprevalence rates among homosexual and bisexual men have ranged from 10% to 70% in the USA, with the majority of studies between 20% and 50% (102). These rates have shown rapid increases, as suggested by a study of 378 homosexuals in New York City, where the seropositivity rose from 6.6% in 1979 to 43.7% in 1984 (363); and in another study of 6,875 homosexuals in San
Francisco, where seroprevalence rates rose from 4% in 1978 to 73% in 1985 (24; 180; 270).

Within Australia, homosexual and bisexual men still constitute the group at highest risk for AIDS, although seroprevalence rates seem to be below those of the USA and most European countries. An anecdotal study of homosexual and bisexual men attending a Sydney STD clinic, suggested the prevalence of antibody to HIV rose from 5% to 32% between 1981 and 1982 (335). Other Australian studies have shown similar seroprevalence rates ranging from 3% to 35% (14; 393).

Women engaging in receptive anal intercourse potentially face the same risk experienced by homosexual males in a similar situation, especially where bleeding or mucosal tears occur, or where there is genital ulceration (14). While it may theoretically be possible that one such episode could lead to infection, it has been suggested that the chance of becoming infected after ten to fifty such episodes with an infected male is about 48% (14). Similar anecdotal studies, such as that by De Gruttal et al. (438), have suggested a 0.5% to 3% chance of infection for every such receptive male to male sexual contact.

The prevalence rates of other diseases in HIV infected homosexual and bisexual men, such as syphilis and gonorrhoea (73%), HBV (54%), herpes simplex (11%) and herpes zoster virus (5%) (352), strongly suggest the
possibility of these patients being infected by a multitude of other various infections.

1.4.4: **INTRAVENOUS DRUG ABUSERS (IVDA's)**

Intravenous drug abuse per se does not constitute a risk for HIV infection, rather it is the sharing of needles that permits viral transmission. Boughton and Hawkes (14) and Paine et al. (14) have suggested that more than 90% of all Australian IVDA's have shared needles. This is in accordance with other studies from around the world, that show between 75% and 90% of all IVDA's share needles (56; 105; 109; 110; 278; 294; 330).

The exact contributions of IVDA in cases of HIV infection (including AIDS), and true comparisons between studies, are difficult to determine due to the possibility of additional risk behaviours, such as homosexual and heterosexual venereal transmission. In this way, suggested cases may overestimate the actual contribution of this mode of transmission.

IVDA has been implicated in transmitting HIV in up to 25% of American AIDS cases (142); 30% in New York City (64); 14% of all European cases (56; 318), 66% of Italian cases (142); 60% of cases in Spain (2); but only up to 4.1% of all Australian AIDS cases (286) to February 1990.
A smaller percentage of AIDS cases in Australia being attributed to IVDA may result from:

1. Less additional risk factors.
2. A shorter duration of the epidemic in this country and the relatively earlier introduction of needle exchange programmes.
3. Lower proportions of IVDA’s in the general community.

The apparent rarity of HIV infection in healthcare workers (HCW’s) due to needlestick injuries, with an estimated < 1% chance of seroconverting from percutaneous injection of HIV infected sera (6; 13; 16; 76; 78; 81; 218), suggests that this mode of transmission may be relatively ineffective. This may be a result of the decreased frequency of inoculation and size of inoculum, when compared to the situation in intravenous drug abuse.

Seroprevalence rates vary greatly between countries; with up to 83% of IVDA’s in cohorts in the USA being seropositive (303). In addition, up to 70% of these individuals in Spain, France and Italy (142; 294); 30% in Florence (142); and 40% of IVDA’s in Bangkok are reported to have been infected with HIV (14). Several studies have suggested a plateau in seroprevalence rates at about 60% in cohorts of IVDA’s in the USA (109; 110; 349). Possible explanations for this plateau are the
entry of new IVDA’s for insufficient times to have seroconverted, and the simultaneous introduction of safe sex practices and needle exchange programmes that have effectively reduced the incidence of HIV infection.

An excellent example of the efficacy of transmission by infected needles has been provided by Patrascu et al. (471), in a study of 1,025 children in Romania, showing that 35.8% were seropositive to HIV. At the most, perinatal transmission may have accounted for 1% of these cases of infection. In the absence of any other known risk factors, except the nosocomial use of contaminated needles, 99% of cases of HIV infection could be directly attributed to blood to blood transmission.

IVDA also constitutes the primary source for heterosexual and perinatal transmission of HIV in the USA, Europe and Australia (102; 109; 251; 349). In this way, IVDA’s may act as a channel, or bridge, to pass HIV onto the general community. As reported earlier, 53% of all perinatal infections in the USA occurred in children born to female IVDA and 20% have involved children born to sexual partners of male IVDA’s (349). Additionally, significant proportions of IVDA’s support their habits by prostitution, meaning that not only spouses and children may be infected, but also a disproportionately large number of their sexual contacts (14).
1.4.5: **RECIPIENTS OF BLOOD AND BLOOD PRODUCTS**

It seems that the introduction of donor screening, serological testing and heat treatment have significantly reduced the transmission of HIV by the transfusion of blood and blood products. Donor exclusion criteria were implemented in Australia late in 1983, while the routine serological testing for HIV antibodies and the heat treatment of donated blood was introduced in April 1985. The effect of these changes can be seen in the seroprevalence rates of blood donors. HIV prevalence in blood donors has declined from 0.035% in 1985 (56; 318) to < 0.015% in 1987 in the USA (102), and 0.001% in Australia (14; 331).

To date, no cases of transfusion-associated HIV infection have been reported in Australian patients, who received blood or blood products after the introduction of serological screening in April 1985 (14; 393). However, this is not the case in the USA, where anecdotal reports have suggested the transmission of HIV from blood (93; 472) and organs (123) taken from seronegative individuals. A seemingly seronegative infectious state (Refer Section 1.2.3) suggests the possibility of further cases of HIV infection as a result of blood transfusions.

In order to quantify a risk, Curran and co-workers (102) cited Mosley et al. as reporting that 89% of recipients of HIV-positive transfusions became infected,
and Ward et al. as suggesting that, once a donor transmitted HIV to a recipient, all subsequent recipients of that donors blood became infected.

The production of one batch of human factor concentrate requires the use of blood from hundreds to more than one thousand donors (333). There is a risk of transmission of HIV if only one of these donors is infected with the virus. Often, one batch is used for the treatment of many haemophiliacs, and if a batch is infectious, most of the haemophiliacs may seroconvert. However, the introduction of heat treatment of these human factor concentrates has essentially removed this risk of transmission.

Studies have suggested that the prevalence of HIV amongst haemophiliacs in the USA may range from 34% to 94% (19; 270; 333). Similar rates of up to 82% (14) have been reported within Australia. These higher seroprevalence rates may indicate:

1. A larger proportion of severe cases of haemophilia within a cohort. These more severe cases are at a greater risk of HIV infection due to the increased frequency and number of factor infusions.

2. The possibility of widespread infection via blood due to an increased number of at-risk individuals donating blood prior to the introduction of donor exclusion criteria and serological screening.
3. The utilization of blood products from areas of higher HIV prevalence.

Seroprevalence rates in haemophiliacs are dependent on the severity of the disease, and therefore, the number or frequency of factor infusions. The use of factor VIII concentrates made from pooled blood from thousands of donors, especially originating in the USA, has been associated with both the development of AIDS and seropositivity among patients with haemophilia A. Patients with haemophilia B, who have exclusively used factor IX concentrate, are also at-risk but both the number of reported AIDS cases and suggested seroprevalence rates have been lower than those reported for patients for haemophilia A (453).

HIV incidence rates in haemophiliacs for the period from June 1983 to May 1984 in the USA, of 298.5 for severe cases and 43.2 for mild cases of haemophilia per 100,000 people receiving transfusions, confirm these findings (453). Similarly, repetitive exposures in blood transfusion recipients increase the risk of HIV infection. The incidence rate for HIV infection in American adults for the same period, rose from 0.15 in those individuals receiving less than 10 units in that year, to 4.83 for those receiving more than 10 units for the same period (453). More significant differences are evident in the paediatric population in the USA over the same period with incidence rates being 0.84 (less than
10 units) and 22.48 (greater than 10 units) per 100,000 people receiving transfusions (453).

1.4.6: INFANTS

The potential transmission of HIV to a foetus or infant may occur whenever there is contact, by the child, with body fluids known to be infected with HIV (for example, blood, vaginal and cervical secretions, amniotic fluid and breast milk). Perinatal transmission has been implicated in 78% of all paediatric AIDS cases in the USA, compared to only 20% of the same in Australia (63; 64; 80; 286; 393). These differences may be due to differences in the proportions of IVDA's, the increased prevalence of HIV infection, and longer duration of the epidemic in the USA. The transmission of HIV from seropositive mothers to their children has been reported to occur in 30% to 65% of cases (114; 312). It has also been speculated that this transmission is more likely to occur during stages of viraemia, for example, at initial infection with HIV, or in the later stages of HIV-related illness (17; 211).

Perinatal transmission has been suggested to occur at three stages of pregnancy; in utero, during labour and postnatally. The acquisition of HIV in utero appears to be the most frequent mechanism of transmission from mother to child, with anecdotal evidence suggesting that HIV can cross the placenta, causing infection, as early as the fifteenth week of gestation (17; 362).
The exact contribution of transmission during labour and delivery is difficult to gauge due to problems in serologically testing infants pre and post partum, and the complicating presence of maternal antibody. Postnatal transmission of HIV may occur by blood transfusion (318; 372) or via the breast milk. A report by Ziegler et al. (434) suggesting that transmission from a mother, infected postnatally by transfusion, to an infant via breast milk, indicates this possibility of transmucosal spread of HIV.

However, these modes are considered to be small incremental risks when compared to in utero transmission. Difficulties in determining the exact stage of pregnancy responsible for transmitting HIV arise due to three reasons:

1. Unknown latent periods and window periods for HIV infection in adults, further complicated by a lack of information on these periods in unborn children.
2. Problems of definitively detecting antibody to HIV in unborn infants due to the presence of maternal antibody.
3. The presence of multiple opportunities for transmission to occur.

1.4.7: HETEROSEXUALS

Infection by heterosexual venereal transmission, like homosexual venereal transmission, may result from
several sexual practices that involve the exchange of many potentially infected bodily fluids. Possibilities for HIV transmission may often involve:

1. Oral contact, such as kissing, where there is the exchange of infected saliva and possibly blood.
2. Orogenital contact (oral sex), where potentially infected semen, saliva, blood, vaginal and cervical secretions may all be exchanged.
3. Anogenital or vaginogenital contact (sexual intercourse), where there may be the exchange of the same bodily fluids described above.

Due to the common combinations of these three possibilities for transmission in most sexual acts, it cannot be determined which of the bodily fluids are instrumental in transmitting infection. With the majority of acts of sexual intercourse also involving the exchange of saliva, it is theoretically possible, but not likely, that this body fluid may be the most important vector for HIV transmission.

Most people identified as presumably having been infected by venereal means are presumed to have contracted the virus through sexual intercourse, a presumption that is probably correct in the majority of cases. However, genital contact is often preceded by kissing, and it is a mistake to assume that infection always results from this genital contact rather than
orogenital or oral contact, unless these three routes can be adequately separated.

Even disregarding oral transmission, the suggestion by Cunningham et al. in 1985 (471), that HIV can be transmitted by atraumatic methods such as artificial insemination, indicates the possibility of transmucosal spread during sexual intercourse. Similar reports of perinatal infection and transmission via breast milk (372; 434) suggest that this mode of spread may be an important method of infection in heterosexually acquired HIV infection.

Cases of HIV infection are only classified as attributable to heterosexual venereal transmission in the absence of all other identifiable risk factors. The actual contribution of heterosexual venereal transmission is unclear due to an apparent under-reporting of AIDS cases attributable to this mode. This under-reporting may occur for two reasons:

1. Where there are multiple risk factors, as there often is, the case will be recorded in the highest risk category in the classification hierarchy.
2. Individuals classified as being infected by an undetermined risk behaviour may have been infected by heterosexual venereal transmission.

At present there seems to be a very low incidence of transmission by heterosexual intercourse, where both
partners have no other risk factors (2.3% of AIDS cases in the USA (102); 0.8% of all AIDS cases in Australia (286)). There is a relatively higher risk when one partner is a bisexual man, haemophiliac, blood transfusion recipient prior to 1985 or IVDA (56; 102; 128; 318). Approximately 70% of index partners for these heterosexually acquired AIDS cases in the USA were IVDA's and 18% were bisexual men (102). Studies have suggested that seropositivity in heterosexual men and women is higher in areas where HIV seroprevalence is also high amongst IVDA's and prostitutes (102; 318).

Attempts to evaluate the actual risk of infection from heterosexual venereal transmission need to be based on individuals with no other risk factors. Suggestions of the contribution of this mode are provided by both reported cases of AIDS and African studies, as well as studies of blood transfusion recipients and haemophiliacs from the USA and Australia. The exact contribution, however, cannot be gauged due to the possibility of other risk factors.

Heterosexual venereal transmission has been suggested by the identification of HIV in semen (219; 326), vaginal and cervical secretions (45; 206; 211; 219; 313; 325; 407), and the development of HIV-related illnesses in female sexual partners of men with AIDS (191; 320). An efficient spread of HIV by heterosexual venereal means is strongly suggested by the equal numbers of infected males and females in reported cases of AIDS.
from Africa (47; 89; 236; 325). Anecdotal studies of African prostitutes have suggested further evidence, with a higher prevalence of HIV among female prostitutes (88%) and their male clients (28%), than among female controls (12%) (122; 404).

Other studies in Africa have shown that between 34% and 65% in the Congo and 51% of the prostitutes in Kenya (17; 56; 318) are seropositive to HIV, and that the virus is efficiently transferred to up to 43% of their male clients (465). It has also been suggested that other sexually transmitted diseases, genital ulceration (45; 236; 296), oral contraceptives and non-circumcision (296; 318), may further increase this risk of transmission.

Blood transfusion recipients seem to have no other risk factors for HIV transmission. In this way, studies of monogamous heterosexual partners of infected blood transfusion recipients, showing seroprevalence rates of up to 70% (19; 44; 77; 103; 170; 270; 320) are suggestive of this mode. Similar studies, involving the transmission of HIV from infected haemophiliacs, have reflected a 6.8% (19) to 10% (170; 211; 270; 311) rate of infection in heterosexual partners. The actual risk of HIV infection in these two groups due to heterosexual intercourse, however, is difficult to ascertain due to previously reported problems. Notwithstanding these comments, anecdotal studies have suggested that a woman who has vaginal intercourse with an infected male
between ten and fifty times has a 17% to 33% chance (mean 26% chance) of being infected (14).

With 90% of AIDS cases occurring in males in Australia and the USA (56; 286), it is more likely for heterosexual females to come into contact with an infected male. This is reflected in the increased prevalence of heterosexually acquired HIV infection in females rather than males in these countries, with male to female ratios for this mode of infection currently being 1:3 (56; 286; 318).

Although AIDS and HIV infection have been identified since 1981, no more than 1% of cases in Australia have been attributed to heterosexual contact. Even taking into account the apparent under-reporting of cases due to this mode, it seems that the prevalence of heterosexually acquired infection may not attain the same levels seen in homosexuals. However, recent studies suggest that increases are inevitable, with IVDA's, prostitutes and sexually promiscuous individuals being at the highest risk of acquiring and transmitting HIV (103).

1.4.8: DENTISTS AND HEALTHCARE WORKERS

The seroprevalence of HIV amongst dentists is unclear because of a lack of mass screening. As a result, possible rates can only be extrapolated from studies of other healthcare workers. Dentists are potentially
at-risk of HIV infection for the following three reasons:

1. There is constant contact with body fluids known to be infected with HIV, such as blood (56; 154; 206; 386) and saliva (146; 147; 148; 155; 156; 191; 208; 326).
2. The not infrequent reporting of a low compliance with recommended infection control procedures (6; 30; 160; 354; 361; 364).
3. An apparently high number of needlestick injuries (56; 147; 154; 155; 191; 206; 326).

Other potential cases of HIV infection in dentists may result from additional risk factors, such as heterosexual and homosexual venereal transmission. Cases of AIDS among healthcare workers (HCW’s) result primarily from HIV infections that occur outside of the healthcare setting. However, a small number of HCW’s have been infected with HIV through occupational exposures. Case reports in the USA (to 1988) have confirmed occupational HIV transmission to twenty five HCW’s and presumed occupational transmission to a single dentist (78; 218; 233).

Seroconversion due to needlestick injuries in the work environment have been documented in superficial (360; 388; 394) and deep inoculations (25; 365), mainly in nurses. These HCW’s were reported to have become HIV-positive after sustaining percutaneous injuries.
However, these studies remain anecdotal for the following two reasons:

1. None of these individuals had serum samples drawn before or soon after the injury, making it difficult to attribute seropositivity directly to the injury (25; 201; 360; 388; 394).

2. No data is forwarded on the frequency of exposures in these individuals, nor the number of exposures that may be required to result in seroconversion.

While the issue of occupational transmission of HIV in healthcare workers is generally discussed in relation to percutaneous transmission, limited information exists concerning the relative risk of transmission by transmucosal spread. The concept of this mode of spread involves the transfer of virus from an infected individual to the mucosal surfaces or skin of a susceptible host, with subsequent passage of the virus through an intact epithelial surface.

Such exposures are relevant in the setting of an analytical laboratory, operating theatre or dental surgery, whereby the eyes, mouth, skin or oral cavity of healthcare workers may be inadvertently contaminated by splashes of infected material. This raises the question of the possible risks involved in transmission of HIV from splashes of these surfaces by body fluids, such as blood and saliva in healthcare workers.
It is generally held that the transmission of HIV by saliva appears to be ineffective, although there is conflicting evidence. Studies of the experimental transmission of any body fluids across intact skin have not yet been described in the literature, and until routine screening of all healthcare workers (particularly dentists) is undertaken, the issue will remain relatively unclear.

The possibility of transmucosal spread has special relevance to dentistry, suggesting the additional risk of occupational infection via various fluids containing HIV (for example, blood and saliva), that have contaminated eyes, skin or the mouth via splashes. However, it is still uncertain whether these mucous membranes and skin represent intact surfaces. Allen and Organ (20) have demonstrated frequent minute breaks in the integrity of these surfaces in dentists, suggesting that the concept of true transmucosal spread may be complicated by possible inapparent percutaneous transmission.

The body of literature available on the transmission of HIV does not go into any depth on transmucosal spread, but the general feeling is that it is not transmitted in this manner. In direct support of this notion are the recommendations for safe sex practices, that operate on the grounds of a lack of direct and indirect evidence to support this claim.
These suggestions seem to be based on the evidence against transmucosal spread, provided by several studies of cohorts of extensively exposed non-sexual household contacts of infected individuals (43; 151), demonstrating an absence of transmission. In these studies, contact included the sharing of eating utensils, toys, toothbrushes and razor blades, and they suggest that this form of transmission appears to be relatively ineffective.

Similarly, the reporting of only one case of presumed occupational transmission of HIV to a dentist, to date (78; 218; 233), in the presence of possible inapparent percutaneous and needlestick transmission, further suggests that this mode of spread may be ineffective. However, the efficacy of transmucosal spread remains unclear due to a lack of studies of healthcare workers investigating this mode of transmission.

While this may suggest that transmission of HIV across intact epithelial surfaces is not effective, two points are brought to mind:

1. The difficulty in separating out multiple practices.
2. Anecdotal cases that suggest that this mode of infection is possible via saliva, semen, breast milk and blood (102; 434; 470; 477).
Of particular relevance to dentistry is the commonly overlooked suggestion of transmucosal spread via saliva by Salahuddin et al. (477). In this case, a male acquired HIV by transfusion during abdominal aortic surgery. This surgery left him impotent, meaning that the sole risk activity between him and his wife involved the exchange of saliva via kissing. Subsequent transmission of HIV to his wife would suggest one seemingly valid example of the transmucosal spread of HIV via saliva.

Similar anecdotal reports, by Cunningham et al. (470), of transmission by atraumatic artificial insemination and by Ziegler et al. (434), of definitive postnatal transmission via breast milk further support the possibility of this mode of spread. Yet more anecdotal evidence is provided by the suggestion by Weiss et al. (102), that three healthcare workers in the USA have been infected through non-needlestick exposures to blood, involving the inoculation of skin lesions and/or mucous membranes.

While this evidence remains anecdotal, the possibility of this form of transmission in an emergency setting, and during invasive procedures, cannot be overlooked. This has implications for laboratory technicians, dentists, medical officers, ambulance officers and nurses in both the prevention and active treatment of splashes of infected material. With a suggested risk involved, the prevention of infection should involve the
routine use of gloves, eyewear, gowns and masks (Refer Section 3.1.2). Active treatment of splashes should involve serological testing, washing of the infected mucosa and the possibility of prophylactic AZT. The relevance of a possible risk in relation to dentistry and the precautions to be observed are detailed in Chapter Three.

1.4.9: PRISONERS

Suggested seroprevalence rates in prisoners (up to 25% of all Spanish prisoners (2)) that exceed those of the general community may be due to two factors:

1. The relatively high proportion of IVDA in these individuals, with reports suggesting that 13% to 55% of all prisoners have engaged in IVDA (402; 14). The limited availability of sterile needles and syringes suggests that the majority of these individuals shared needles (14).

2. The practise of consensual and coercive homosexuality with apparently limited adherence to safe sex practices. Between 30% and 50% of prisoners are suggested to have admitted to homosexual practices (402).

With increased seroprevalence rates in prisoners, the difficulty in controlling the spread of HIV infection is further compounded by the constant fluctuation of the prison population due to work release, weekend
sentencing and similar programmes (14). Studies are needed to determine seroprevalence rates among all prisoners, and the possibility of this infection spreading to the general community.

1.4.10: ETHNIC GROUPS

Studies have suggested that the risk of HIV infection in heterosexuals and blood transfusion recipients is dependent on the prevalence of HIV from that region (101; 277; 278; 305; 331). In this way, patients from areas of widespread HIV infection (for example; Africa and the USA) may constitute a greater risk for occupational transmission than the general local population, because of higher seroprevalence rates from within their community. Several Asian, Pacific and East European countries consider this risk to be sufficient to serologically screen all tourists from endemic areas (14; 17).

In the USA, certain ethnic groups display an increased prevalence of HIV and HIV-related illness. Blacks account for 25% of adult and 56% of paediatric AIDS cases, while only representing 11.6% of the total population (102). Similarly, Hispanics account for 13% of adult and 20% of paediatric AIDS cases while only representing 6.5% of the total population (102). This seemingly increased prevalence of HIV infection in the black and Hispanic communities may reflect higher rates of IVDA, and subsequent perinatal infection, or a longer
duration of infection. Anecdotal reports have suggested that Haitians provided a channel for the initial spread of HIV from Africa to the USA and Europe (180; 308), although an exact association, and its present influence on the epidemic remains unclear.

In addition, rates of HIV infection are dependent upon various socioeconomic and educational factors, habits, and customs and the availability of treatment. Increased rates can be seen in lower socioeconomic groups, with a similarly lower level of education, availability of treatment, and poor receptiveness of interventional education. This is especially the case with those minority groups mentioned above, namely Hispanics and blacks.

1.4.11: OTHER PEOPLE AT INCREASED RISK

a. Recipients of organ transplants

HIV-related immunosuppression may be masked by the drug-induced immunosuppression seen in transplant recipients. Anecdotal reports of AIDS after renal transplantation have been described in Australia (91; 295); although transfusion of blood both per- and post-operatively, in each case, makes it difficult to determine the precise source of HIV infection. Similar reports of kidney transplant recipients (295; 91; 123) seroconverting after receiving organs from infected individuals, underlines the need for the routine
screening of all organ donors. This risk may not be totally removed, as suggested by the CDC, where a seronegative cadaveric donor infected both living recipients during a possible seronegative infectious stage (Refer Section 1.2.3) (123).

b. artificial insemination

Studies reporting the transmission of HIV by the artificial insemination of infected semen (91; 123; 295; 470) suggests that heterosexual venereal transmission may not require genital ulceration or other predisposing factors. Definitive confirmation of the contribution of semen in the transmission of HIV was provided by an Australian report, by Cunningham et al. in 1985 (470), where 50% of seronegative women who were artificially inseminated with infected semen, in the absence of other known risk factors, subsequently seroconverted.

c. siblings and casual contact

The transmission of HIV to children during pregnancy (120; 235; 301; 362), childbirth (120; 235; 301; 400) and breastfeeding (120; 235; 301; 372) appears to be statistically significant. In contrast, the risk of transmission by normal casual contact appears to be very low or non-existent (41; 65; 64; 70; 76; 79; 83; 119; 151; 233; 286; 301; 360). In support of this view is the indirect evidence that AIDS has remained confined, almost exclusively (96% in USA and Australia), to the
risk groups initially described (286). Further evidence arises from the absence of transmission to non-sexual household contacts of infected individuals in at least eight prospective cohort studies (17; 151; 199; 362). In each of these studies contact included the sharing of household items, such as toothbrushes and razors, eating utensils, facilities, as well as hugging and kissing. This lack of evidence of transmucosal spread of HIV, suggested by Friedland et al. (151) may indicate that, although theoretically possible, this mode of spread is not efficient.
1.5: **SEROLOGICAL SCREENING FOR HIV INFECTION**

The definitive diagnosis of HIV clearly rests with the direct identification of the virus in host tissues. Viral isolation techniques, however, currently lack sensitivity and are not readily available. Individuals should be considered both infected and infective where antibodies are repeatedly identified by Enzyme Linked Immunosorbent Assay (ELISA) and supplemental confirmatory tests, such as Western Blot (WB) and Immunofluorescence Assay (IFA). ELISA was introduced in April 1985 in most developed countries for seroepidemiological studies, blood bank screening programmes, and the screening of individuals considered to be at high risk for HIV infection. This test was widely advocated because it is rapid and economical, and has proved to be highly sensitive and specific when screening the different high risk groups from Europe and the USA (270).

Before discussing the implications of serological screening and the questions it raises, the various testing methods will be discussed. The possible methods for detecting HIV infection may involve:

b. Testing for HIV by viral culture.
c. Testing for HIV antigen.
d. Testing for HIV DNA.
a. Testing for HIV Antibody

Tests detecting antibody to HIV have been widely used to serologically screen for HIV infection because they are generally considered specific, sensitive, rapid and economical. However, these tests can only be considered to detect the majority of infected individuals. Tests for HIV antibody may not detect all individuals infected with HIV, for the following four reasons:

1. The presence of a seronegative infectious state, previously discussed (Refer Section 1.2.3), where overt seroconversion usually takes up to six months after infection to occur. Anecdotal reports (461), suggesting protracted periods of up to 35 months for this window period, cast even more doubt on the efficacy of these tests in detecting all infected individuals.

2. Anecdotal suggestions that detectable antibody to HIV may disappear after a period of two and a half years (172).

3. The possibility of low titres of antibody levels, even though overt seroconversion has occurred.

4. The possibility of false positive and false negative results (Refer below).

The most commonly used test, ELISA, is considered to be 99% accurate. It has been shown to be both highly specific (98.6%) and highly sensitive (97.3%), when dealing with individuals of the different risk groups
within Europe and the USA (452). Screening of individuals from Africa and from low risk groups have shown substantial non-specific reactivity, meaning that this test should be supplemented by more specific confirmatory tests, such as Western Blot (WB) or Immunofluorescence Assay (IFA), in order to validate positive test results.

An ELISA that finds no HIV antibodies is regarded as suggesting that the blood tested has not been infected by the virus, and the test is not generally repeated. A positive result is repeated at least once, and if it then turns negative, is assumed to be HIV free but not suitable for blood transfusions. Tests that are repeatedly positive are then retested by more specific, more reliable confirmatory assays (such as WB or IFA).

Rather than detecting HIV antibodies collectively, as ELISA does, WB detects the individual antibodies against the major antigenic proteins of HIV, in particular the p24 core antigen and gp41 transmembrane glycoprotein of the viral envelope. This means that WB is more specific, and further evidence indicates that it is also more sensitive (17). Due to the time involved with overnight incubation and higher costs, this method is used only as a confirmatory test, rather than for mass testing.

The latex agglutination test is a less specific but rapid and simple test developed specifically for large
scale screening in places, such as Africa, where technological aids are limited. It is a cheaper and more economical means of testing large numbers of individuals from less developed countries. The IFA and SKBSL are new tests that have not yet been approved for widespread use, although they are currently used as a second choice behind WB as confirmatory assays.

b. **Testing for HIV by viral culture**

The classic method for detecting viral infection is the growth of virus from the tissues of a person suspected of being infected. Culturing HIV is a highly specific, time consuming, labour intensive and expensive procedure, usually reserved for studying the effects of antiviral agents and vaccines on HIV. Viral culture is considered the most accurate means of identifying infection early in individuals and may be of benefit in determining initial infection during the previously discussed seronegative infectious stage. Additionally, viral culture may be used to detect HIV in patients whose clinical presentation is strongly suggestive for HIV infection, yet have repeatedly negative HIV antibody assays.

c. **Testing for HIV antigen**

The most common assay for HIV antigen detects the p24 antigen (p24 core protein) which is often detectable in a person’s serum early, and transiently, following
primary infection with HIV. Therefore, the test is useful for the early definitive diagnosis of HIV infection before the appearance of antibodies. As antibody levels increase, antigen usually becomes undetectable.

In the late stages of infection there appears to be an association between the reappearance of HIV p24 antigen and evidence of advancing immunosuppression (17; 281). This suggests that the presence of p24 antigen in the serum of HIV-positive individuals may be of prognostic significance, by indicating an accelerating immunosuppression. As antigen testing is more specific and more sensitive than antibody assays and is capable of detecting HIV earlier it would be ideal to use these assays universally, however, higher costs ensure they are not readily available.

Testing for HIV p24 antigen would enable the determination of the infection status of patients prior to overt seroconversion. This would be of value, not only to test blood and organ donors prior to donation, but also for other healthcare workers in order to ascertain infection early. In this way, relevant precautions and early preventive management (for example; AZT therapy) may be implemented.
d. **Testing for HIV DNA**

Tests to measure viral DNA, incorporated into human genes, have been developed and can detect HIV infection prior to the sufficient production of antigen to evoke an antibody response. In this way, these tests represent the earliest possible identification of HIV infection in individuals. The Polymerase Chain Reaction (PCR or gene amplification) is a recent discovery that could prove to be the most sensitive of all tests for HIV infection. The increased specificity of these techniques means that they have the potential to definitively determine infection prior to overt seroconversion for HIV antibody.

Several studies (455; 477) of seropositive individuals have shown that PCR was able to detect all cases of HIV infection, up to 14 months prior to positive antibody assays. By detecting all cases prior to confirmatory antibody assays, this test has displayed similar sensitivity to conventional antibody tests. In addition, without any known false positive results from either antibody assays or PCR, it can be concluded that these tests also exhibit similar specificities.

The Cetus test uses an enzyme that can 'amplify' DNA sequences from HIV present in white blood cells, thus allowing the monitoring of both drug regimes and the clinical course of infection. To date, its efficacy in detecting infection is unknown, although it has the
potential to provide rapid and accurate detection of HIV infection.

Although the screening of blood by current antibody assays has been shown to be both highly specific and highly sensitive, the preceding evidence indicates that not all cases of HIV infection are detected by these assays. In addition, when infection is detected by routine conventional antibody assays, it is commonly later than more specific, laboratory based methods, such as PCR and viral culture. This raises the question of the current risk of receiving a blood transfusion, especially while blood is still screened by conventional antibody assays.

By extrapolation of the number of transfusion-associated cases of AIDS in the USA with the total number of people in that country receiving transfusions, a relative risk of 0.0006% has been suggested, prior to the introduction of serological screening (104). This risk would seem to be even smaller when considering that many of the individuals who were transfused received units from multiple donors (for example, trauma, haemophiliacs). Even further reduction in this risk has been provided by serological screening and donor exclusion criteria.

Earlier suggestions of false negative results during the seronegative infectious phase and the later identification of HIV by antibody assays indicates that
there is still a real risk of acquiring HIV by blood transfusion. This risk appears to be very small, with only isolated cases of post-transfusion seroconversion from seronegative donors (93; 472). An exact determination of this risk remains unclear, however, as blood transfusion recipients are not routinely tested for HIV.

Although serological testing of individuals to detect HIV infection has been beneficial, the main complicating factor is the possibility of false positive and false negative results. Additionally, its introduction has had profound social and legal implications, raising the complex issues of mass screening, counselling, informed consent and HIV disclosure.

The benefits of the serological screening of at-risk individuals have been:

1. A reduction in cases of HIV infection in blood transfusion recipients and haemophiliacs due to the combination of serological screening of blood donors and donor exclusion criteria.

2. The ability to definitively determine HIV infection in individuals has allowed for the determination of risk activities known to place an individual at an increased risk of infection. In addition, this has allowed for the implementation of safe sex procedures, needle exchange programmes and
infection control procedures, all aimed at reducing the transmission of disease.

3. An ability to attempt to directly correlate an incident (such as a needlestick injury or sexual assault) to the acquisition of HIV. This is achieved by determining a seronegative state prior to the accident with subsequent seroconversion, in the absence of other known risk factors.

The possibility of false positive and false negative results has serious implications for both the healthcare profession and the general community, and are the main complicating factors in suggestions for large-scale screening. Severe psychosocial consequences have been noted, including suicide (209), when individuals are falsely informed of a positive result; while a false negative result may cause healthcare workers and infected individuals to abandon various methods for preventing HIV transmission, thereby possibly spreading the disease.

As with all forms of medical screening, testing for HIV antibody yields a certain number of false results. Although the false positive rates suggested in blood donors (0.0006%) (254) and military recruits (0.0007%) (58) are only low, the mere presence of these results shows that serological screening cannot accurately determine all individuals infected with HIV. This is especially the case when taking into account the additional problems of false negative results that may
occur during the previously discussed seronegative infectious phase.

When properly performed on individuals at high risk for HIV infection, the combination of ELISA and confirmatory assays are considered to accurately determine 99% of all infected individuals (17; 281). However, in populations at a lower risk for HIV infection, such as the general community, there would be relatively fewer true cases of infection. In this way, there will be a higher ratio of false positive results to genuine positive results than there would be in high risk groups. The mass testing of individuals at lower risk for HIV infection, therefore, would yield a greater percentage of false positive results.

The ability to detect HIV infection in individuals has raised the question of the feasibility of mass serological screening. Suggestions range from testing the whole general community, to those who may present for medical and/or dental treatment. Other suggestions include the screening of groups of individuals that seem to be at a low risk for HIV infection (for example, HCW's), although the exact risk remains unclear.

The main advantage of large-scale screening of any of those groups above, is to gain an idea of the extent of HIV infection. Similarly, the relative contributions of various risk behaviours and possible vectors for transmission could be assessed, particularly in relation
to the risks involved in occupational transmission for healthcare workers. As discussed previously, the only way to assess the risk of occupational transmission is by the determination of seroprevalence rates in these individuals. However, due to difficulties of logistics and cost, and the added problems of informed consent and confidentiality, it seems that mass screening may not be introduced. An added problem may be the greater proportion of false positive results due to the testing of individuals at a lower risk for HIV infection.

However, it still remains that the only way to presently control infection is to ascertain all HIV infected individuals by mass screening and promote behavioural change. The question is then raised as to how often these tests must be repeated in order to determine newly acquired infections. With progressive infection and obvious spread of HIV into the general community, individuals are becoming more aware and more likely to personally know infected individuals. With an increasing concern for possible HIV infection, the possibility of mass screening may become a reality. Development of a preventive vaccine and the necessity to determine an individual’s infection status prior to vaccination may herald the introduction of mass screening.

Patient counselling has an important role in the HIV epidemic. For professional patient counsellors, such as some AIDS physicians, clinical psychologists and social
workers, counselling may involve considerable interactive and far-reaching discussions with the patient, both before and after serological screening for HIV. This is designed to help the individual accept and adapt to the implications of a positive result (both genuine and false), and to encourage change where necessary. It is primarily concerned with preventing infection in those not already infected, and to prevent disease transmission from those infected to others.

Medical and dental practitioners, in addition to the clinical care of potentially infectious patients, have a clear-cut role in providing a sound basis to obtain informed consent for HIV testing. The practitioner must exercise caution in the case of confirmed positive tests in entering into aspects of patient counselling outside of their sphere of expertise. Referral to experienced counsellors where necessary is an important aspect of patient care. Of particular concern is the possibility of an inexperienced counsellor raising a false positive result with a patient prior to confirmation by further testing, as this has led to suicide in some patients (209).

A summary of aspects that may be raised by the patient’s physician and/or non-clinical counsellor include the following:

1. Basic education as to why the individual may have been exposed to HIV and therefore requiring a
test. This involves the recognition of needle sharing, unsafe sexual practices or other risk behaviours.

2. Basic knowledge concerning HIV and AIDS, and the need for preventing its transmission. This involves a discussion of how testing is undertaken, what it determines and the accuracy of the test. The individual needs to voluntarily agree to testing, on the basis of the information provided, in order to fulfill the requirements of informed consent.

3. The concept of confidentiality needs to be addressed, as well as the means by which it is assured. Warning of the notification procedures required by health authorities and the possible implications of a positive result are needed.

4. These individuals should be aware that sexual activity is the major mode of spread, and that potential transmission exists wherever there is the exchange of body fluids; such as semen, blood, saliva, vaginal and cervical secretions, faeces or urine. This risk may be reduced by monogamous relationships (especially between HIV seronegative persons), the constant use of safe sex procedures (for example, condoms) and a reduction in the number of sexual contacts.

5. People at high risk should not share needles for parenteral drug injection.
6. People at high risk should not donate blood, semen or organs, and remove the word "donor" from their driver’s licence if it is present.

7. If infected, individuals must inform all healthcare professionals, so that appropriate blood and body fluid precautions and appropriate clinical evaluations may be performed.

8. Infected individuals should be made aware that approximately 65% of infants born to infected mothers have been infected with HIV (235; 346).

9. Infected individuals are urged to refer persons with whom they have high risk sexual activity or have shared needles, in order to reduce the spread of HIV and to supply appropriate testing and counselling services.

10. Despite the fact that casual household transmission does not readily transmit HIV (43; 151), infected individuals are advised not to share toothbrushes and razor blades, due to the potential risk of transmucosal spread (Refer Section 1.4.8).

11. Adequate warning should be given concerning the signs and symptoms of progressive HIV disease; cough, fever, dyspnoea, lymphadenopathy, unexplained weight loss, profound fatigue, persistent skin lesions, unexplained diarrhoea and persistent headaches.

12. A healthy lifestyle should be advocated, including adequate diet, sleep and exercise, as well as an avoidance of deleterious substances (for example, drugs, cigarettes and alcohol).
Serological testing of individuals raises the possibility of four results:

1. Antibody negative with no possibility of future seroconversion (for example; previous blood transfusion).
2. Antibody negative, which may include the seronegative infectious state and false negative results.
3. Antibody positive and infected (genuine positive result).
4. Antibody positive but not infected (false positive result).

Regardless of the outcome, individuals need to fully understand the implications and meaning of these results. In the case of a negative result, counselling aims to ensure the individual remains free of HIV by appropriate educational intervention. For positive results, maintenance of health, prevention of disease transmission by educational intervention and appropriate referrals are paramount.
1.6: FUTURE TRENDS

The emerging trend in the USA is the reduction of reported AIDS cases in some predominant risk groups, such as homosexual and bisexual males and blood transfusion recipients. This relative reduction is compensated for by the concomitant increase in heterosexual venereal and perinatal infection, indicating that HIV has spread further into the general community (77; 79; 80; 102). Similar trends appear to be emerging in Australia (286; 393).

These trends are a direct result of attempts to curb the HIV epidemic, by a combination of the following:

1. Educational intervention, in the form of safe sex practices, needle exchange programmes and continuing educational programmes for healthcare workers, primarily aimed at the prevention of disease transmission from at risk individuals.

2. Improved sterilization and disinfection techniques employed by healthcare workers (Refer Section 3.1.2), also aiming to prevent disease transmission.

3. The evolution of more specific, more sensitive and more reliable serological tests to enable earlier detection of HIV infection (Refer Section 1.5).

The advances mentioned above have managed to curb HIV infection, however, the only valid strategy for halting
the HIV epidemic clearly rests with the management of already infectious individuals by antiviral drug therapy and the prevention of HIV infection by widespread vaccination.

1.6.1: **ANTIVIRAL DRUG THERAPY**

There is now a convincing body of evidence to show that early intervention may delay the progression of HIV-induced immunosuppression. Unfortunately, most drugs suggested are unable to match their in vitro effects with those in vivo. The only approved and commercially marketed drug with demonstrated efficacy, both in vitro and in vivo, against HIV is Zidovudine (AZT).

Initial research on AZT has demonstrated alterations in the normal course of retroviral illness in animals (202). Further anecdotal studies have suggested that AZT may be a potent inhibitor of HIV replication, thereby slowing the progression of disease. These suggestions have led to its introductory use as a prophylactic regime in occupational HIV exposures, and as a regulator of immunosuppression, primarily in asymptomatic infected individuals (202).

Results of AZT trials in Australia (presented at the Third National Conference on AIDS, Hobart; August 1988) suggested a prolonged span of relatively good health, where HIV-related disease had already developed. Of
those people receiving AZT for AIDS, 50% were reported to have died within 80 weeks of diagnosis, as compared to a 44 week duration from diagnosis to death, for half of the AIDS patients not receiving drug therapy. Without the availability of the data from clinical trials, particularly the opportunity to assess clinical variables and statistical methods, it is difficulty to assess the roles of AZT; however, the suggestion of improved survival time is at least encouraging.

Although the reported side effects of AZT therapy may be severe (202), they are generally considered to be of less relevance to the more severe effects of HIV-induced immunosuppression. These side effects appear to be less severe in basically healthy people, providing a strong argument for early drug intervention.

Compound Q (GLQ223) is thought to selectively kill HIV infected macrophages, rather than just preventing replication of the virus, and is being trialled extensively in the USA. The question remains, however, whether this action may cause increased concentrations of free HIV to readily infect other macrophages. Dextran Sulphate, CD4 protein treatment, ddc, Alpha Interferon, Suramin, Acyclovir, Ribavirin, Trisodium Phosphonotomate, Ansamycin, Imreg and Antimoniotungstate have all been trialled extensively in the USA, but seem to be unable to match their in vivo effects with those in vitro.
It must be emphasized that these drugs serve only to prolong the period between diagnosis and death, and as such, are in no way meant to cure people. Australian statistics suggest that the vast majority, if not all people, will die from HIV infection, with the only current feasible method of preventing infection being by direct educational intervention. Future methods of controlling HIV will revolve around the successful application of an HIV vaccine. For already infected individuals, vaccination may play a role in preventing disease progression, in addition to the effects of antiviral drug therapy (137; 220).

1.6.2: VACCINES

Vaccination of at-risk individuals has eradicated smallpox, and significantly reduced the incidence of poliomyelitis, measles, mumps and rubella in developed countries. Similar effects have been demonstrated more recently by a vaccination for Hepatitis B, rabies and Varicella virus. Similarly, the only feasible method for preventing HIV infection also involves widespread vaccination, whether that be of at-risk individuals or the general community.

Vaccination with live attenuated retroviruses in animals has been shown to have the potential to cause infection and even to induce malignancies (137), the latter being due to the oncogenic properties of these viruses. Therefore, research has centred on genetic
engineering, aimed at identifying the main immunogenic viral proteins, in order to produce purified protein subunit vaccines.

However, there are currently three obstacles to developing and testing a vaccine to prevent HIV infection:

1. An inability, to date, to delineate the viral components that induce protective immunity in the host (137). In this way, antibodies induced by vaccination may be specific for different antigenic proteins than those expressed by in vivo HIV infection (149).

2. The chimpanzee is currently the only animal that can readily be infected with HIV (137), leading to a chronic infectious state, with apparently similar immune responses to humans. However, the very limited availability of these animals for research purposes, at these preliminary stages of vaccine evolution, seriously limit progress.

3. Studies on efficacy may be complicated by individuals who may be infected at the time of vaccination but are seronegative (seronegative infectious state). Seroconversion may then be due to a pre-existing infection with HIV rather than vaccine failure.

Therefore, methods of distinguishing viral from vaccine-induced antibody formation would need to be
developed. Perhaps distinguishing antibody subtypes may be one answer. Clearly it would be necessary to determine the infection status of individuals prior to vaccination perhaps by employing more specialized techniques, such as those above, in addition to conventional existing antibody assays.

The ideal vaccine to prevent HIV infection needs demonstrated safety and efficacy, while at the same time minimizing the time required for approval. In this way, Francis et al. (149) have proposed three stages to evaluate a vaccine for HIV:

1. To test the ability of a candidate vaccine to induce specific antibodies in animals and test the effect of these antibodies on viral replication in vivo and in vitro.

2. Once this candidate vaccine has been demonstrated to be effective in these ways, and after major pre-clinical safety issues have been resolved, the vaccine can be administered to small groups of human volunteers to gain preliminary information on the short term safety and immunogenicity.

3. Gain data on the immunogenicity, ideal doses and spacing of these doses.

The question of whether efficacy should be established in animal models prior to human testing has provided a dichotomy of thought. Although the efficacy of several HIV vaccines are being tested in chimpanzees, mice, cats
and macaques, phase one trials of at least four
different HIV candidate vaccines are currently being
undertaken in humans. Regardless of the methods used to
determine efficacy, successful vaccination of
individuals is the key to the future halting of the HIV
epidemic.
### 1.7 TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Prurigo, dry skin.</td>
</tr>
<tr>
<td>2.</td>
<td>Seborrhoeic conditions: perioral, periorbital dermatitis, otitis externa, dandruff.</td>
</tr>
<tr>
<td>3.</td>
<td>Psoriasis.</td>
</tr>
<tr>
<td>4.</td>
<td>Candidiasis.*</td>
</tr>
<tr>
<td>5.</td>
<td>Other dermatophyte infections eg. tinea pedis, tinea cruris, pityriasis versicolour.</td>
</tr>
<tr>
<td>6.</td>
<td>Gingivostomatitis.*</td>
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<tr>
<td>7.</td>
<td>Pyogenic infections eg. furuncles, folliculitis, bullous impetigo, abscess.</td>
</tr>
<tr>
<td>8.</td>
<td>Herpes simplex virus (HSV).*</td>
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<tr>
<td>9.</td>
<td>Varicella zoster virus (VZV).*</td>
</tr>
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<td>10.</td>
<td>Warts.</td>
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<td>12.</td>
<td>Molluscum contagiosum.</td>
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<td>'Viral' rashes.</td>
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<tr>
<td>14.</td>
<td>'Geographical' and other tongue signs.*</td>
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<td>15.</td>
<td>Atopic dermatitis.</td>
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<tr>
<td>17.</td>
<td>Rhinorrhoea, catarrh.</td>
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<tr>
<td>18.</td>
<td>Desquamation (palms, soles).</td>
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<tr>
<td>20.</td>
<td>Telangiectasia.</td>
</tr>
</tbody>
</table>

* Denotes mucocutaneous lesions of special relevance to dentistry.
### TABLE 1.7.2: SIX MONTHLY NATIONAL AIDS CASE FATALITY RATES
(July 1982 - February 1990) (286)

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>No. of known deaths</th>
<th>Case fatality rate (%)</th>
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<tbody>
<tr>
<td>1982</td>
<td>July-Dec</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1983</td>
<td>Jan-June</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1983</td>
<td>July-Dec</td>
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<td>5</td>
</tr>
<tr>
<td>1984</td>
<td>Jan-June</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>1984</td>
<td>July-Dec</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
<td>1985</td>
<td>Jan-June</td>
<td>64</td>
<td>58</td>
</tr>
<tr>
<td>1985</td>
<td>July-Dec</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>1986</td>
<td>Jan-June</td>
<td>92</td>
<td>79</td>
</tr>
<tr>
<td>1986</td>
<td>July-Dec</td>
<td>129</td>
<td>111</td>
</tr>
<tr>
<td>1987</td>
<td>Jan-June</td>
<td>183</td>
<td>152</td>
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<td>1987</td>
<td>July-Dec</td>
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<td>135</td>
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<td>1988</td>
<td>Jan-June</td>
<td>211</td>
<td>119</td>
</tr>
<tr>
<td>1988</td>
<td>July-Dec</td>
<td>286</td>
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<td>1989</td>
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<td>45</td>
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<tr>
<td>1990</td>
<td>Jan-June</td>
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1760 978 55.6
### TABLE 1.7.3: THE GLOBAL EXTENT OF AIDS

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<th></th>
<th>NOV86</th>
<th>DEC87</th>
<th>MAY88</th>
<th>JUL89</th>
<th>AUG89</th>
<th>NOV89</th>
<th>MAY90</th>
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<tr>
<td>Americas</td>
<td>(343)</td>
<td>(318)</td>
<td>(379)</td>
<td>(240)</td>
<td>(77)</td>
<td>(286)</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>85</td>
<td>75</td>
<td>74</td>
<td>70</td>
<td>68</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>Europe</td>
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<td>8775</td>
<td>11445</td>
<td>22609</td>
<td>23459</td>
<td>25698</td>
<td>33896</td>
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<td>%</td>
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<td>13</td>
<td>13.5</td>
<td>14</td>
<td>14</td>
<td>13</td>
</tr>
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<td>Africa</td>
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<td>10992</td>
<td>30064</td>
<td>30244</td>
<td>31512</td>
<td>63842</td>
</tr>
<tr>
<td>%</td>
<td>3</td>
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<td>12</td>
<td>18</td>
<td>17.6</td>
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<td>25</td>
</tr>
<tr>
<td>Asia</td>
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<td>406</td>
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| Total  | 34448 | 73747 | 91905 | 167373| 172143| 185463| 254078|
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TABLE 1.7.5: DEATH RATES OF RISK GROUPS IN AUSTRALIA (286)
(Shown as a percentage of total AIDS cases)

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**RISK GROUP**

**Homosexual & Bisexual men**

|      | 42  | 46  | 44  | 52  | 53  | 50.2| 49.3| 46.9| 47.1| 51.7| 53.8| 55.2|

**Intravenous Drug Abusers**

|      | 0   | 67  | 50.0| 33.3| 40.0| 33.3| 27.8| 27.8| 25.0|

**Homosexual & Bisexual men who abuse intravenous drugs**

|      | 100 | 100 | 43  | 50  | 53  | 54.1| 58.3| 53.3| 48.5| 45.0| 50.0| 47.9|

**Blood Transfusion recipients**

|      | 70  | 69  | 87  | 81  | 86  | 84.7| 83.3| 80.7| 77.7| 85.7| 90.0| 82.5|

**Haemophiliacs**

|      | 50  | 100 | 100 | 67  | 67  | 62.5| 50.0| 50.0| 46.6| 53.3| 53.3| 52.6|

**Heterosexuals**

|      | 50  | 100 | 75  | 20  | 25.0| 22.2| 13.3| 16.6| 39.1| 28.6| 46.7|

**Under Investigation**

|      | 25  | 50  |     |     |     |     |     |     |     |     |     |     |

**None of the Above**

|      | 83  | 83.3| 85.7| 66.6| 66.6| 66.6| 61.5|

**TOTAL**

|      | 45  | 48  | 50  | 54  | 55  | 52.5| 51.1| 48.3| 48.0| 52.5| 54.4| 55.5|

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<td>1.2</td>
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<td>1.4</td>
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<td>1988</td>
<td>3. Homosexual &amp; Bisexual men who are IVDA</td>
<td>2</td>
<td>1.5</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
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<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>1989</td>
<td>4. Blood Transfusion recipients</td>
<td>10</td>
<td>8.5</td>
<td>7</td>
<td>7</td>
<td>8</td>
<td>6</td>
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<td>5.0</td>
<td>4.5</td>
<td>4.4</td>
<td>4.1</td>
<td>3.9</td>
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<td>2</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
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<td>1.3</td>
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<td>1.0</td>
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</tr>
<tr>
<td></td>
<td>6. Heterosexual</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
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<td></td>
<td></td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>8. None of the above</td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<td>0.7</td>
<td>0.6</td>
<td>0.7</td>
<td>0.6</td>
<td>0.9</td>
<td>1.6</td>
<td>1.9</td>
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<td>98</td>
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<td>306</td>
<td>373</td>
<td>470</td>
<td>622</td>
<td>795</td>
<td>943</td>
<td>1101</td>
<td>1168</td>
<td>1301</td>
<td>1451</td>
<td>1547</td>
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### TABLE 1.7.7: AUSTRALIAN AIDS CASES TO 31.12.89: number of cases by sex, transmission category and state as a proportion of total cases for each year (286)

<table>
<thead>
<tr>
<th></th>
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<td>115</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>100</td>
<td>100</td>
<td>97.6</td>
<td>93.0</td>
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<td>95.4</td>
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<td>PERCENTAGE BY STATE/TERRITORY:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NSW</td>
<td>100</td>
<td>50</td>
<td>66.7</td>
<td>70.4</td>
<td>70.4</td>
<td>66.4</td>
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<td>0</td>
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<td>5.6</td>
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<tr>
<td>TAS</td>
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<td>0</td>
<td>0</td>
<td>0.9</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>1.3</td>
</tr>
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<td>1.7</td>
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<td>ACT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
<td>0.8</td>
<td>1.6</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>PERCENTAGE BY TRANSMISSION CATEGORY:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homo-/Bisexual</td>
<td>100</td>
<td>66.7</td>
<td>73.8</td>
<td>86.1</td>
<td>87.9</td>
<td>87.8</td>
<td>89.7</td>
<td>88.4</td>
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<td>Hetero/ IVDA</td>
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<td>0.5</td>
<td>2.1</td>
<td>1.7</td>
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<td>0</td>
<td>33.3</td>
<td>2.4</td>
<td>0</td>
<td>5.8</td>
<td>1.9</td>
<td>2.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Haemophilia</td>
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<td>0</td>
<td>4.8</td>
<td>0.9</td>
<td>0.4</td>
<td>1.4</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
<td>0</td>
<td>1.4</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>0</td>
<td>0</td>
<td>19.1</td>
<td>10.4</td>
<td>4.9</td>
<td>5.4</td>
<td>1.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Undetermined</td>
<td>0</td>
<td>0</td>
<td>1.7</td>
<td>0</td>
<td>1.6</td>
<td>2.1</td>
<td>3.4</td>
<td></td>
</tr>
</tbody>
</table>
Those people who should be tested due to an increased risk of HIV infection are:

1. **All** persons engaging in homosexual intercourse, especially those who have been sexually active since HIV was first detected.

2. **All** haemophiliacs who have received factor VIII infusions, especially prior to 1985.

3. **Everyone** who has had a transfusion of blood or blood products between 1978 and April 1985, when antibody testing of all blood donors was introduced. Some countries, such as Africa and Eastern Europe, do not routinely screen donors, meaning that there still exists a risk of transfusion-acquired HIV infection.

4. **All** individuals who have had sexual intercourse (especially anal intercourse) with prostitutes, particularly from areas where heterosexually acquired infection is endemic, such as Africa, Asia or the USA.

5. **All** male and female prostitutes.

6. **All** intravenous drug abusers who have ever shared a needle, or syringe, or whom you suspect have shared.

7. **All** sexual partners of IVDA’s.

8. **All** children born to HIV infected mothers.

9. **All** donors for sperm banks, organ transplants and blood.

10. **All** prisoners, especially those who have engaged in any of the above risk activities.

11. **All** members of the armed forces, especially those who have engaged in any of the above risk activities.

12. **All** diplomatic personnel sent to, or returning from, areas where AIDS is a major problem and/or the blood supply is not screened.

13. **Anyone** who is worried about possible infection for any reason. A test is often needed to dispel unwarranted fears.
TABLE 1.7.9:  Typical immunological profile of uninfected individuals and those with advanced HIV infection

<table>
<thead>
<tr>
<th>Laboratory tests/studies</th>
<th>Advanced immune suppression</th>
<th>Non infected individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lymphocyte count</td>
<td>&lt; 1000/mm³</td>
<td>1500/mm³</td>
</tr>
<tr>
<td>Total T-lymphocyte numbers</td>
<td>&lt; 1000/mm³</td>
<td>1200/mm³</td>
</tr>
<tr>
<td>Total helper-inducer T-lymphocytes (T4+,Leu-3+)</td>
<td>&lt; 400/mm³</td>
<td>800/mm³</td>
</tr>
<tr>
<td>Total suppression-cytotoxic T-lymphocytes (T8,Leu-2+)</td>
<td>&lt; 400/mm³</td>
<td>400/mm³</td>
</tr>
<tr>
<td>Helper/suppressor ratio (T4:T8,Leu-3:Leu-2)</td>
<td>&lt; 1.0</td>
<td>&gt; 1.0</td>
</tr>
<tr>
<td>Skin test reactivity</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>

In vitro lymphocyte function

| Blast transformation to phytomagglutinin A       | < 25,000cpm*                | 50,000cpm*               |
| Natural killer cell activity                    | < 20% lysis                 | 40% lysis                |

Immunoglobulin levels

| IgG                                             | 2000mg/dl                   | 1200mg/dl                |
| IgA                                             | 350mg/dl                    | 240mg/dl                 |
| IgM                                             | 190mg/dl                    | 190mg/dl                 |

Other serological abnormalities

| Circulating alpha interferon                    | Present                     | Absent                   |
| Alpha, thymosin                                 | > 1000pg/ml                 | < 500pg/ml               |
| Beta 2 microglobulin                            | > 5.0mg/dl                  | < 2.5mg/dl               |

* cpm = counts per minute

TABLE 1.7.10: Clinical abnormalities in infants with Acquired Immunodeficiency Syndrome

(421; 426)

Findings reported in > 90%
* Poor growth / failure to thrive.
* Chronic interstitial pneumonitis.
* Hepatosplenomegaly.

Findings reported in 50% - 90%
* Diffuse adenopathy.

Findings reported in 10% to 50%
* Protracted or recurrent diarrhoea.
* Thrombocytopenia.
  * Birth weight < 2500g.
  * Eczematoid rash.
  * Recurrent otitis media.
  * Development failure.
  * Microcephaly.

Findings present in < 10%
* Kaposi's sarcoma.
* Chronic parotid swelling.
CHAPTER  TWO

ORAL MANIFESTATIONS OF
HIV INFECTION
2.1: **INTRODUCTION**

Initial reported cases in the USA of what was to become known as AIDS, included the intraoral findings of Kaposi's sarcoma and candidiasis in homosexual males (69; 73; 94; 152). As early as 1982, oral lesions due to herpes simplex virus (HSV) and cytomegalovirus (CMV) infection were also identified as being associated with the profound immunosuppression, later found to be caused by HIV. In this way, initial cases of AIDS suggested a common occurrence of oral manifestations and indicated that dentists may play an integral part in the identification and management of these lesions.

The identification of oral lesions, in conjunction with HIV infection, is relevant to both the practice of oral medicine and dentistry. It raises five main implications for the practice of oral medicine in relation to these oral changes:

1. Although studies had demonstrated a wide variety of prevalence rates of oral manifestations in certain risk groups at different stages of the disease (from seropositive asymptomatic to AIDS), it is not uncommon to find oral lesions in the majority of these individuals at some stage of HIV infection. Earlier studies suggesting that oral lesions were relatively uncommon have not been confirmed by later studies. More recent studies have shown that
oral manifestations seem to be more common for three reasons:

a. An increased awareness of the variability of the clinical presentation of these lesions.

b. The more widespread use of specific diagnostic aids that have evolved.

c. Variations in incidence levels may be due to the heterogeneous nature of many studies where individuals were studied, from different risk groups and geographical regions, with different stages of HIV infection. Further variation may be due to the reporting by clinicians whose clinical expertise and diagnostic criteria itself varied greatly.

2. A large range of changes have been identified and these changes may be multiple. It is unsure whether some of these lesions are a direct consequence of HIV, an indirect consequence of HIV-induced immunosuppression, or represent supervening infection or coincidental findings. Large reported ranges of oral changes may be due to the reasons given above in (1).

3. Of these common and often multiple changes, some lesions are rare or unique. In this way, the practice of oral medicine has been extended by the common identification of seemingly rare lesions
(for example; KS), and unique lesions (for example; CMV, MAI).

4. Due to the multiplicity, incidence and recurrent nature of many of these oral lesions, there are two main problems in terms of management. Firstly, there are the actual management problems of many of these oral lesions, due to the profound underlying immunesuppression. For example, the management of recurrent infections due to Candida species and HSV. Secondly, management problems give rise to a genuine need for a close dual relationship between medical and dental specialities due to the unique nature of the disease.

5. The identification of these oral lesions raises the importance of research, directed at three major areas:

a. The identification of oral manifestations (including, as yet unrecognized lesions), and the most suitable and efficient method to manage them. There is a genuine need for the prospective study of individuals prior to the implementation of drug therapy (for example, prophylactic antifungal therapy).

b. Determining the relationship between the development of oral lesions as prognostic signs for the terminal stages of HIV (AIDS) and death.
c. To distinguish the exact aetiology of many lesions; determining whether they arise directly due to HIV, indirectly due to HIV advanced immunosuppression or represent unrelated lesions.

Additional to having relevance to the practice of oral medicine, the identification of oral manifestations and their management incurs special relevance to general dental practice. With studies suggesting a 43% to 93% incidence of oral manifestations in AIDS patients, and up to a 93% incidence in seropositive individuals (316), it is obvious that oral lesions are common in relation to HIV infection. Added to this is the identification of rare or unique lesions that are often multiple, and may precede or preclude a diagnosis of AIDS. In this way, the dentist is ideally situated to not only diagnose HIV infection and AIDS but also to work closely in conjunction with medical specialities in managing these complications. As a result, the role of the dentist in relation to HIV infection may be summarized as being:

1. To identify individuals at-risk for HIV infection (Refer Section 1.4).
2. To utilize serological testing, with due respect to the implications it raises, in order to determine cases of HIV infection (Refer Section 1.5).
3. To diagnose oral manifestations of HIV infection that may precede or preclude a diagnosis of AIDS (Refer Chapter 2).

4. To prevent the transmission of HIV by educating those individuals at-risk of infection. (Refer Section 1.5).

5. To provide routine dental care to both HIV infected and at-risk individuals without risk of disease transmission (Refer Sections 3.1.1 and 3.1.2).

6. To liaise with medical specialities in the management of HIV infected patients, in particular the management of oral lesions that may arise in relation to immunesuppression (Refer Chapter 2).

The fundamental aims of the chapter, therefore, are twofold:

1. To demonstrate the important role that the dental practitioner plays by providing information regarding the range, incidence, clinical presentation, management and difficulties in diagnosis of the many oral manifestations seen in association with HIV infection.

2. To attempt to assess the aetiology of these oral lesions and attempt to attribute them directly or indirectly to HIV infection.

In order to fulfill these aims, oral manifestations of HIV infection have been essentially categorized into two principal groups; infections and neoplasms. A third
group, comprising a range of sometimes ill-defined, and possibly unrelated, conditions and symptoms will undergo continued assessment and revision as further clinical research is performed in these patients. The same revision process will also continue for the above mentioned two principal groups.

The classification used in this chapter represents a variation of that proposed by Pindborg in 1986 and 1989 (316). Amendment has been necessary in order to further subcategorize lesions, and to incorporate oral findings reported subsequent to Pindborg's original classifications.
2.2: INFECTIONS

2.2.1: FUNGAL INFECTIONS

A number of different fungal infections have been associated with HIV infection, with candidiasis being not only the earliest identified, but also easily the most consistently reported oral fungal infection. Infection by Candida species was recognized from the initial cases of what became known as AIDS, and probably represents the most preventable oral manifestation of HIV infection. Reported incidence and prevalence levels of all of these fungal infections are directly related to the prophylactic use of antifungal therapy. Other less common fungal infections, such as those caused by Cryptococcus species, Histoplasma and Geotrichum species, have been reported infrequently. With only isolated anecdotal reports, the question is raised of possible contaminant infection even though they appear to be related to HIV infection.

Variations in the reported incidence and prevalence of these oral fungal infections may be due to the following:

1. Most studies report the intraoral findings of individuals at only one point in time.
2. In many of the later studies, the possibility of concomitant prophylactic antifungal therapy in
individuals, at the time of study, cannot be ruled out.

3. Many cohorts contain individuals with differing rates of immunesuppression (from seropositive asymptomatic to AIDS), making meaningful comparisons difficult.

4. Lower incidence levels may result from the improved treatment methods that have evolved with increasing clinical expertise.

5. Both within and between studies, different diagnostic tests have been used on individuals (for example; cytological smear, biopsy and response to antifungal therapy).

2.2.1.a: **CANDIDA SPECIES**

Candida albicans may be detected in between 40% and 60% of asymptomatic, clinically normal individuals, and is a common inhabitant of the oral cavity, gastrointestinal tract and vagina (350). Clinical oral candidiasis may occur in healthy individuals with changed oral conditions. Two factors that may alter the oral environment in favour of candidal overgrowth are:

1. The selective depression of normal bacterial flora by the use of broad spectrum antibiotics.

2. The presence of poor denture hygiene.

In addition, clinical oral candidiasis may occur as a result of abnormal health, due to either congenital
immunesuppression (for example, diabetes or neutrophil dysfunction) or acquired immunesuppression, such as is seen in individuals undergoing marrow suppressive therapy (chemotherapy), kidney grafts or virally induced HIV immunesuppression.

The identification of oral candidiasis is relevant to the practice of dentistry in terms of:

1. Local significance; whereby these lesions may provide the first sign or symptom of HIV infection.
2. Systemic significance; where the appearance of oral candidiasis in prospectively followed HIV infected individuals may denote an advancing immunesuppression. Oral candidal infection may then act as a focus for further candidal colonization that may lead to disseminated infection. The need to prevent disseminated infection raises the question of preferred treatment options.
3. The overall predictive outcome of these lesions, in terms of progression to terminal stages of HIV infection (AIDS) and death.
4. Other principal aspects of management of these lesions.
5. The various forms of candidiasis prevalent in the oral cavity of HIV infected individuals.
1. Local significance

In the first instance, reports suggesting that various forms of oral candidiasis may be seen in up to 94% of all HIV infected individuals at some stage of the disease process (315; 368), indicates that dentists may be able to diagnose this fungal infection in patients otherwise unaware of their HIV infection status. In this way, the development of oral candidiasis, especially the florid pseudomembranous form, in previously healthy individuals with no other reasons for fungal overgrowth should be investigated. This becomes even more important for individuals who belong to any of the recognized risk groups for HIV infection (Refer Section 1.4).

Secondly, the diagnosis of oral candidiasis may be suggestive of an advancing immunesuppression. One report by Tavitian and colleagues (369) has suggested that oral candidiasis may be a marker for oesophageal candidiasis, and hence technically speaking, a diagnosis for AIDS. Although only studying ten patients with oral candidiasis, they found that all ten of these asymptomatic individuals had endoscope confirmed oesophageal involvement and therefore a possible diagnosis of AIDS as defined by the CDC (62; 72; 75).

This raises the question of whether more significance should be placed on oral candidiasis as an indicator disease for AIDS in the absence of other more
established conditions such as Pneumocystis carinii pneumonia or Kaposi's sarcoma. Considering up to 94% of individuals may be identified at some stage of HIV infection with oral candidiasis (315; 368), and considering asymptomatic oesophageal involvement could also present in a significant number, if the trend identified by Tavitian and co-workers (369) holds true, it raises the possibility of assigning a great many more cases as AIDS, much earlier than may be the case if symptomatic oesophageal candidiasis remained the definitive diagnostic criterion, as outlined by the CDC in 1986 (Refer Appendix 1C).

It would be necessary, therefore, to exercise caution in establishing a diagnosis of AIDS in a patient with oral candidiasis, without due consideration for the clinical severity of oesophageal candidiasis, if present, and the extent of immunosuppression, as assessed by objective laboratory means.

2. **Systemic significance**

The systemic significance of the identification of oral candidiasis may be seen as:

1. It raises the possibility of a need to search for HIV on an ad hoc basis.
2. The identification of oral candidiasis in infected patients, with prior serological confirmation, may be indicative of advancing immunosuppression.
3. The presence of oral candidiasis, according to Tavitian and colleagues (369), raises the possibility of oesophageal involvement.

4. Involvement of the oesophagus, particularly in cases of an aggressive oesophagitis, raises the diagnosis of AIDS and also the possibility of disseminated infection and death, if not properly diagnosed and adequately treated.

As a result of these possible systemic complications, the following points are relevant in regard to the management of oral candidiasis:

1. The patient needs to be questioned carefully concerning any possible symptoms of oesophageal involvement such as dysphagia.

2. The work of Tavitian and co-workers (369) raises the question of the need to perform endoscopy on all patients with oral candidiasis, or on the other hand, whether all oral lesions should be considered to give rise to oesophageal involvement.

3. On the basis of this work by Tavitian et al. (369), the question is raised as to whether one should rely on topical or systemic antifungal therapy, in the absence of symptoms suggestive of oesophageal involvement.

No specific guidelines are provided in the available literature regarding the use of topical or systemic antifungal therapy. With oral candidiasis being so
common, and since there is an apparent rarity of disseminated candidiasis in HIV infected individuals, there is no overriding mention made in the literature to use systemic antifungal therapy as a first line of treatment. However, due to the difficulty of clinically diagnosing candidal infection ante-mortem in other immune suppressed individuals, and the lack of definitive post-mortem studies of those with HIV infection (389), the true role of systemic antifungal therapy in the management of oral candidiasis, in general, remains uncertain.

As a result, a reasonable suggestion on the management of these individuals, based on the available literature, revolves around the use of topical antifungal therapy and careful monitoring, with certain exceptions. In certain circumstances, systemic antifungal treatment, either taken orally or by intravenous infusion, should be used. These circumstances may include:

i. Individuals with a history of advanced immunosuppression and associated symptoms, seen by recent indicator diseases for AIDS and laboratory tests of immune function.

ii. Individuals with a history of intermittent oral candidal infections and, in particular, a history of previous oesophageal candidal infection.

iii. Individuals who have previously been treated with topical antifungal therapy where candidal overgrowth rapidly recommenced.
iv. Individuals who the clinician feels requires a systemic approach due to personal preference.

3. **Overall predictive outcome in terms of progression to AIDS and death**

The majority of early studies suggested that the incidence of oral candidiasis increased during the course of HIV infection. Further to these studies, reports by Chandrasekar et al. (86), Tavitian et al. (369) and Klein et al. (234) have all suggested that oral candidiasis may predict the appearance of advanced stages of HIV infection, that is, the appearance of opportunistic infections and other disease processes.

In the study by Klein and co-workers (234), two suggestions as to the predictive value of oral candidiasis were forwarded:

1. That 59% (13/22) of individuals with oral candidiasis acquired a major opportunistic infection or KS within a median time period of three months (range 1 to 23 months), as compared to 0/20 of similar individuals, without oral candidal infection, who were followed for 12 months.

2. Of the 15 individuals with both oral candidiasis and T4:T8 ratios of less than or equal to 0.51, 12 of these (80%) progressed to AIDS within a median period of three months. This compared to none of the four (0/4) individuals with similar T cell
ratios but no evidence of candidal infection, who were followed for a 12 month period.

This study, however, is difficult to interpret for the following three reasons:

1. There is no mention of the various types, severity or location of candidiasis in any of these individuals, making true prognostic outcomes difficult.

2. This prospective study attempted to compare disease outcomes between the study group, who were followed up for 23 months and the control group, who were only studied for 12 months. This raises the question of the true situation at 12 months and 23 months in both groups. Without this information, true comparisons are impossible.

3. Definitive predictive outcomes cannot be based on a study of only twenty two individuals with oral candidiasis. Similarly, suggestions that T cell ratios do not indicate advancing immunosuppression have been based on only four individuals.

Although suggestive of oral candidiasis being of predictive value, the following three factors demonstrate that the exact situation remains unclear:

1. Although oral candidiasis has been found in up to 94% of HIV infected individuals (315), this disease has also been found in normal individuals.
Clinical oral candidiasis has been found in up to 50% of seronegative homosexual males (34; 315).

2. Although early studies suggested an increased incidence of oral candidiasis during the course of HIV infection, later studies (34; 190; 234; 258; 315; 327; 334; 352) have suggested significant differences in incidence rates throughout the various stages of HIV infection. These ranges (29% to 94%) of the prevalence of oral candidiasis may be due either to the heterogeneous nature of the studies or the fact that the prevalence of oral candidiasis may be typically variable. These variations may be due to:

a. Figures collated from retrospective, prospective and once-up studies, with variable follow-up periods.

b. The reporting of individuals at different stages of the disease, with similar variations in age, sex and dentate status.

c. The effect of prophylactic antifungal therapy that may have been administered prior to entry to the study, thus eliminating or changing the clinical expression of oral candidiasis.

3. Autopsy findings by Welch and colleagues (389) have suggested, retrospectively, that only 81% of all individuals displayed oral candidiasis at some stage of HIV infection. Additionally, oral candidal infection has been shown to occur at any stage of HIV-induced immunosuppression, with apparently no predilection for any one stage.
Therefore, any suggestions of predictive value for oral candidiasis will remain unclear until further definitive studies are undertaken. Until this time, it seems that T4:T8 ratios represent a more efficient method of assessing immunosuppression. Definitive prospective studies over long periods of time need to be primarily aimed at two areas:

1. The changes in the clinical appearance of oral candidiasis during both antifungal therapy and the different stages of HIV infection.
2. To assess whether the different forms of oral candidiasis (Refer below) are specific for the different stages of HIV infection and, therefore, of any predictive value.

In order to be definitive, these further studies will need to fulfill the following three criteria:

1. Careful descriptions are needed of the diagnostic methods used to detect candidal infection (for example, swabs, histologically proven biopsy specimens, clinical diagnosis or response to antifungal therapy). Preferably, a single diagnostic method should be used within each study.
2. Careful accurate clinical descriptions should be given of the types, location and severity of candidal lesions, with due concern to the possibility of additional causes or co-factors.
3. Large-scale prospective studies of age and sex matched HIV infected individuals and non-infected individuals are needed, with similar dentate status and risk behaviours.

4. **Other principal aspects of management of these lesions**

Asymptomatic, chronic oral candidiasis requires careful monitoring, with particular attention being paid to the signs and symptoms of an acute exacerbation; such as a proliferation of the lesions, burning sensation, metallic taste, odynophagia and/or dysphagia (180; 343). Control of these lesions basically involves the combination of optimal oral hygiene, mouthwashes and appropriate antifungal therapy. Suggestions as to the choice of systemic or topically antifungal therapy have been given in the section relating to the systemic significance of oral candidal infection (Refer Section 2.2.1.a.2). Response to antifungal therapy is usually good with complete clinical resolution of candidal infection; however, relapse is common once therapy is completed.

Possible side effects of systemic antifungal therapy are generally considered secondary to the possibility of disseminated thrush; however, complications such as liver toxicity, bone marrow suppression and hypersensitivity reactions due to Ketoconazole, and the cariogenic effects of Clotrimazole (22; 180) may need to
be considered. An additional consideration for the intravenous infusion of systemic antifungal drugs is the need for a four to five week period of hospitalization.

Regardless of these possibilities, systemic therapy may prevent possible haemorrhagic oesophagitis or oesophageal perforation. Definitive antifungal therapy needs to be rapidly instigated to prevent the possibility of further candidal colonization of the oesophagus and respiratory tract.

5. *The various forms of oral candidiasis*

The various forms of oral candidiasis seen in normal people, cases of HIV infection and AIDS patients are listed below, roughly in order of their prevalence. Pseudomembranous candidiasis (thrush) is easily the most common form identified and appears to be directly linked to HIV-induced immunosuppression. The relationship of the other four forms, however, remains unclear.

i. Pseudomembranous form (Thrush).
ii. Chronic atrophic form (Erythematous).
iii. Chronic hyperplastic form.
iv. Angular cheilitis.
v. Papillary variant.
i. **Pseudomembranous candidiasis (Thrush)**

Pseudomembranous candidiasis is classically an acute condition, however, in association with HIV infection this lesion may persist for several months in a chronic state (22; 28; 180; 343;). This form seems to predominantly affect individuals with AIDS, being found in between 14% and 32% of these patients (85; 357).

Clinically, the lesions are characterized by creamy white or yellowish, slightly elevated plaques on a reddened or normal mucosal base. These plaques, resembling 'milk curd', may be scraped away leaving a raw mucosal surface that is erythematous and bleeds easily. These lesions are commonly widespread with confluent plaques involving most of the oral mucosa. Individual reports have involved the buccal and labial mucosa (180; 234; 343; 350), tongue (180; 343; 350), the hard and soft palate (180; 234; 343; 350), the gingiva (343; 350), pharynx (180) and floor of the mouth (180; 343). With progressive immunosuppression, HIV infected individuals commonly present with confluent plaques covering the entire oral cavity.

ii. **Chronic atrophic candidiasis (Erythematous)**

This form of candidiasis seems to be prevalent in all known stages of HIV infection, but has been suggested to be more common in asymptomatic seropositive individuals, and coincident with seroconversion (85; 180; 357).
Reports have suggested this form in between 13% and 35% of people with AIDS (303; 357), and in 30% of HIV positive individuals (180). The true prevalence of this form of oral candidiasis remains unclear, however, as studies make no mention of the dentate status of those studied. This raises the question of how many individuals were suffering from a traditional denture stomatitis, totally unrelated to HIV infection.

Erythematous candidiasis in association with HIV infection may occur either as a sequela to acute pseudomembranous candidiasis, or it may originate de novo. The lesions are red or erythematous, thus resembling the pseudomembranous form where the plaques have been wiped off (180; 303; 357). Common reported locations include the palate (180; 234; 343), with characteristic erythema and atrophy being evident, highly suggestive of denture stomatitis. Involvement of the buccal mucosa, dorsum of tongue and pharynx have also been infrequently reported (180; 234; 350).

iii. Chronic hyperplastic candidiasis

This type of lesion has been reported in between 6% and 13% of people with AIDS (85; 357), with the clinical presentation ranging from isolated areas of infection to a widespread infection of the entire oral cavity and gastrointestinal tract (180; 343; 350). It is characterized by firm, white, persistent and apparently keratotic plaques, commonly found bilaterally on the
buccal mucosa, lips and tongue (180; 350; 343), with only rare involvement of the retrocommissural areas (180). Similar clinical characteristics to the pseudomembranous form raise the possibility of past misdiagnosis on the part of clinicians. In this way, some of the lesions thought to be this form may really represent pseudomembranous candidiasis.

iv. **Angular cheilitis**

This form of candidiasis is characterized by a feeling of dryness and a burning sensation at the corners of the mouth. Clinically, the epithelium at the commissures appears wrinkled and macerated, with deep fissures that ulcerate, tend to bleed, and contain a superficial exudative crust. These fissures do not involve intraoral tissues, but stop short of or at the mucocutaneous junction (180; 350).

Anecdotal reports suggest it occurs in 5% to 7% of people with HIV-related illness (85; 357). However, other possible causes of this condition, such as reduced vertical dimension or vitamin deficiency, are not identified, and no data regarding the ages or medical condition of the individuals within the cohorts are provided. As a result, it is difficult to associate this lesion directly to HIV-induced immunesuppression.
v. Papillary variant

A papillary variant of candidiasis has been suggested in up to 11% of people with AIDS (85; 343; 357). It is characterized by erythematous papillary nodules of the hard palate, and may be associated with chronic atrophic candidiasis (denture stomatitis). With insufficient information regarding the dental status of these individuals, particularly the presence of dentures, it is also difficult to directly associate this papillary variant with HIV infection.

2.2.1.b: OTHERS

i. CRYPTOCOCCUS SPECIES

Previous reports of oral cryptococcal infection in the immune suppressed were limited to those with chronic lymphocytic leukaemia (CLL). Although generalized cryptococcal infection has been identified in between 7.5% and 26% of all HIV infected individuals at various stages of the disease (166), only three cases of oral cryptococcal lesions have been reported (112; 166; 252). All reported cases of oral cryptococcal lesions have involved persistent ulceration of various intraoral sites, namely the middle posterior portion of the palate (166), the tongue (252) and the maxillary right quadrant (112).
The identification of Cryptococcus species in these oral lesions raises two possibilities:

1. Disseminated cryptococcal infection that enables the contamination of ulcers due to unrelated causes. On initial analysis, the report by Lynch et al. in 1987 (116) may provide some support for this kind of infection, where ulceration of the tongue was directly adjacent to a badly broken down molar in a patient with disseminated cryptococciosis, suggesting the possible contaminant infection of a traumatic ulcer. An alternative explanation, however, is possible (Refer below).

2. The possibility that Cryptococcus species is the direct cause of these ulcerative lesions, and may then act as a possible source of disseminated infection.

Each of the three definitive reports of oral cryptococcal lesions (116; 252; 112), including that of Lynch and co-workers (116), could suggest a direct causal relationship of this fungus with the ulcerative lesions. This suggestion arises from the following findings in these reports:

1. In all three cases, Cryptococcus species were confirmed by incisional or excisional biopsy and appropriate staining.
2. In two out of three of these cases (166; 252), swabs of the lesion transferred to Sabaroud’s Agar definitively grew Cryptococcus species.

3. Resolution of the lesion, in one case (112), occurred with Amphotericin B and Ketoconazole therapy.

4. In all three cases, a definitive diagnosis of disseminated cryptococcal infection was made either just prior to death or at post-mortem.

Oral Flucytosine and intravenous Amphotericin B have both been proven effective in controlling oral ulceration due to Cryptococcus species, and are often used simultaneously (252). Problems of the emergence of mutant strains and toxic side effects may limit their usefulness (166; 252). Oral Ketoconazole appears to be less effective in managing these lesions (252).

These studies raise the possibility that oral ulceration may be directly caused by Cryptococcus species. It is unknown whether these lesions are exceedingly rare or reported rarely, and further research is required to clarify this issue.

ii. **HISTOPLASMA SPECIES**

There have been only two reports (145; 180), to date, of oral lesions possibly due to infection by Histoplasma capsulatum. These cases have involved individuals with AIDS, and have presented as ulceration of the floor of
the mouth (180) or an ulcerative lesion of the palate that led to palatal perforation (145).

The first case, Dr. David Lewis’s case, cited by Greenspan and co-workers (180), cannot be interpreted due to an inability to analyze the patient’s condition, other possible causes of the lesion and the methods of detection of histoplasmosis. A report by Fowler et al. in 1989 (145), is suggestive of a direct causal association between histoplasmosis and an ulcerative lesion of the palate, that led to palatal perforation. This association is suggested by the positive identification of this fungus from biopsy specimens of the oral lesions and from culture, and slight regression of these lesions with appropriate Ketoconazole therapy. However, the possibility of local contamination of an unrelated lesion cannot be ignored.

These two reports are suggestive of a possible relationship between Histoplasma species and ulcerative lesions in HIV infected individuals. If such an association exists then lesions due to this species are either exceedingly rare or infrequently reported.

iii. GEOTRICHUM SPECIES

Oral infection by organisms of the Geotrichum species have only been reported in one patient (180). In this case, the lesions were identical to those seen in acute pseudomembranous candidiasis, with a white, velvety
patch-like covering of the oral mucosa (180). This report, by Greenspan and colleagues (180), also cited by Schiodt and Pindborg (343), however, did not provide any clinical or laboratory details.

2.2.2: **BACTERIAL INFECTIONS**

The most commonly reported bacterial infections of the oral cavity in HIV infected individuals are confined to the periodontium, and seem to be closely associated with HIV-induced immunesuppression. The relationship of other less frequently reported bacterial infections of the oral cavity, such as those due to Mycobacterium avium intracellulare (MAI) and enteric pathogens remains unclear.

2.2.2.a: **PERIODONTAL INFECTIONS**

Periodontal manifestations have consistently been reported in association with HIV-induced immunesuppression. However, the majority of studies poorly describe the exact clinical presentation of these periodontal lesions. A wide clinical diversity of these lesions, dependent on the extent of HIV-induced immunesuppression, is aptly demonstrated by the substantial number of terms used to describe these distinctive lesions.
Although reports have used a vast number of terms, these lesions have been broadly categorized in order of severity into:

1. HIV-Gingivitis (HIV-G); where changes are confined to the soft tissues.
2. HIV-Periodontitis (HIV-P); where the lesion extends into the periodontal apparatus with subsequent loss of attachment and bone. This categorization includes the appearance of Acute Necrotizing Ulcerative Gingivitis (ANUG). The majority of cases of periodontal manifestations seem to involve a classical ANUG superimposed on a rapidly progressive periodontitis.

In addition to these, the exacerbation of apical periodontitis in endodontically treated teeth and necrotizing stomatitis have also been reported (215; 395; 478). Recent confirmatory reports of this necrotizing stomatitis (478) suggest that it may represent a further progression of HIV-P, due possibly to advanced stages of immunesuppression. With better treatment methods meaning that HIV infected individuals have improved survival times, the possibility exists that reports of necrotizing stomatitis may become more frequent.

Preliminary studies of these manifestations suggest subtle changes in the subgingival microflora and colonization patterns (1; 352; 353; 478), with an
increased number of anaerobic pathogens, such as Bacteroides species, Fusibacterium species, Actinobacillus Actinomycetemcomitans and Peptostreptococcus micros being consistently identified. This finding raises the question of whether these bacteria are the cause of the lesions, or represent contaminant infection. In the majority of studies, the actual contribution of various bacteria remain unclear for the following reasons:

1. The common use of empirical antibiotics prior to clinical presentation in many of these HIV infected individuals.
2. An inability to exclude other possible causes or co-factors of the disease process.
3. The identification of bacteria by swabbing does not necessarily indicate a causative role.
4. A lack of definitive prospective studies demonstrating the induction of periodontal manifestations, due to biopsy confirmed aetiological bacteria, in the absence of other possible factors. In addition, resolution of the disease process by specifically sensitive antibiotics may be indicative of a causative role.

Most important to the general dental practitioner is the need to understand the subtle differences between periodontal infections in HIV infected and non-infected patients. Arising from this is a consideration of the
relevance of these lesions, preferred treatment options and differential diagnoses.

Generally speaking, there are four main differences between the clinical presentation of HIV induced periodontal manifestations and the periodontal lesions seen in non-HIV-infected patients:

1. The full range of periodontal complications in association with HIV-induced immunosuppression commonly affects individuals at a younger age (20 to 35 years of age) than non-infected individuals (1; 5; 180; 337; 343; 352; 353; 478; 479). In addition, these lesions are more prevalent in infected individuals, with severe HIV-associated periodontitis being seen in 29%, and HIV-associated gingivitis in up to 51% of all HIV infected individuals (334; 352). The prevalence of periodontitis and gingivitis in the general non-infected population appears to be much less than this.

2. These lesions commonly occur in HIV infected individuals with pristine oral hygiene who attend for regular dental treatment, as well as those individuals with less adequate oral hygiene. In this way, HIV-associated periodontal problems may only be indirectly related to oral hygiene status, but more closely associated with the degree of immunosuppression.
3. These lesions have a more rapid onset with similarly rapid rates of progression in HIV infected individuals. They tend to be more episodic, with not only more severe but also more rapid bone and attachment loss (22; 315; 337; 352; 353). This rapidity has been demonstrated by two reports of the loss of 90% and more hard and soft tissue attachment in only three to six months (1; 396).

4. These lesions often represent a more acute condition, with severe pain and widespread destruction of oral tissues and underlying bone. Common presenting features are a severe, deep aching pain due primarily to exposed alveolar bone and spontaneous, often profuse, gingival bleeding (315; 337).

As suggested earlier, various terms have been proposed to describe the distinctive periodontal complications seen in HIV infected patients. With advanced HIV-induced immunosuppression it has been suggested that these lesions become more severe. Similarly, the following three descriptions may correspond with distinct stages of general immunosuppression, however, further definitive studies are needed to accurately delineate this association. In the present author's opinion, the following three terms should be retained to describe the distinctive periodontal lesions seen in association with HIV infection.
1. **HIV associated gingivitis (HIV-G)**

As the name implies, HIV-G is confined to the soft tissues. It differs from the traditional gingivitis seen in non-infected individuals in the following ways:

a. It is often more widespread, causing distinctive erythema not only of the free gingiva, but also of the attached gingiva and alveolar mucosa. HIV-G is also commonly more severe with punctate or diffuse gingival erythema being reported in up to 75% of cases involving the entire attached gingiva from the free gingival margin to the alveolar mucosa (396).

b. HIV-G is more prevalent (51% of seropositive individuals) (334; 479) than gingivitis in non-infected individuals with no immunosuppression.

c. Although gingivitis in both HIV infected and non-infected individuals is usually generalized, HIV-G may also commonly affect many localized areas (396). An anecdotal report by Winkler et al. (396) suggests that there is commonly a lack of response to the removal of plaque and calculus. Conventional gingivitis is fully reversible, yet after extensive oral hygiene instruction, scaling and prophylaxis in HIV infected patients, HIV-G frequently shows little response and may progress to HIV-P. This has been confirmed by further suggestions that these lesions are difficult to manage and may occur in the absence of plaque (1; 337; 396).
The clinical presentation of HIV-G is not exclusive to any one stage of HIV infection; however, it is more commonly seen in the earlier stages of immunosuppression (396; 479). It is seen as the predominant periodontal lesion.

2. HIV associated periodontitis (HIV-P)

HIV-P has all of the above features, in addition to severe soft tissue necrosis, and rapid destruction of the periodontal attachment and bone. Most cases of HIV-P represent a classical Acute Necrotizing Ulcerative Gingivitis (ANUG), superimposed on a rapidly progressive and severe periodontitis (396).

General differences in the presentation of periodontal problems between HIV infected and non-infected individuals have been outlined previously. However, HIV-P specifically differs from classical periodontitis in the following ways:

a. It is more prevalent, being suggested in up to 29% of all HIV infected individuals (334; 352).

b. HIV-P can occur in well managed dentitions, in the apparent absence of aetiological factors, such as plaque and calculus (334).

c. HIV-P has a more rapid onset and rate of progression. Loss of attachment and bone occurs rapidly, as demonstrated by anecdotal reports
suggesting a loss of 90% of tissue attachment in only three to six months (1; 396).

d. The condition is more acute with severe pain and profuse, often spontaneous, gingival bleeding commonly reported (315; 337). Pain is thought to result from interdental necrosis with subsequent dissolution and, occasionally, sequestration of interseptal bone (396).

e. Although many cases of HIV-P may be generalized, it more frequently affects several localized areas with interspersed regions of apparently normal tissue (396).

f. HIV-P is more episodic than classical periodontitis with recurrent exacerbations being increasingly acute. Due to the HIV-induced immune-suppression, HIV-P also seems to be more intractable.

Of those individuals reported in detail with severe HIV-P, the level of immune-suppression appears biased towards the severest end of the spectrum, being predominantly reported in patients with AIDS (1; 165; 395; 396; 478).

3. **HIV associated necrotizing stomatitis (HIV-NS)**

Reports of an HIV-associated necrotizing stomatitis, focused around a periodontal origin, may represent a more severe form of HIV-P. On the other hand, it may represent a periodontal expression of another lesion described later (Refer Section 2.4.1), as progressive
necrotizing ulceration (PNU). HIV-NS may share similar inherent mechanisms with PNU, reported by Pindborg and others (29; 315; 180; 316; 343) to occur at other mucosal sites throughout the oral cavity, essentially at advanced stages of HIV-induced immunesuppression.

To distinguish HIV-NS from severe cases of HIV-P, the denudation of alveolar, in addition to interceptal, bone has been arbitrarily chosen as the differentiating factor. HIV-NS represents a progression of necrosis beyond the mucogingival junction and into contiguous palatopharyngeal, buccal or lingual tissues with the exposure of underlying alveolar bone, in addition to interceptal bone as seen in HIV-P.

The identification of any of these distinctive lesions in individuals not thought to be infected with HIV should prompt the general dental practitioner to perform serological testing. In addition, these manifestations in HIV infected patients may denote varying stages of immunesuppression and host response factors.

Due to the severity, rapidity and known persistence of these lesions, definitive therapy must be instigated immediately. The key to avoiding widespread necrosis of oral tissues involves prompt recognition and rigorous interceptive and preventive therapy. The primary goal in therapy is complete resolution without the need for more radical forms of treatment, such as resective surgery.
a. **Interceptive therapy**

The immediate goal in this phase of therapy, similar to the treatment of acute and non-acute periodontal infections in uninfected patients, involves the elimination of potentially aetiological microflora (1; 396). This may be achieved by a combination of:

i. The complete removal of plaque and calculus from the root surface by prophylaxis and scaling.

ii. Thorough debridement of necrotic tissues by curettage and root planing. The need for aggressive debridement seems to be more important than the possibility of delayed wound healing (112; 316).

iii. Intensive oral hygiene instruction aimed at maintaining low levels of plaque.

iv. There may be a need for suitable samples to be taken for appropriate antibiotic sensitivity tests. One particular instance where these may be used is intractable, severe cases where conventional interceptive therapy does not promote periodontal resolution. Whether or not the routine culturing of periodontal pockets, in these cases, would be beneficial remains unknown.
The issue of whether adjunctive parenteral antibiotic therapy may be of use in association with HIV-induced periodontal complications needs to be addressed. Anecdotal reports suggesting the value of Amoxycillin, Metronidazole and Tetracycline have prompted many clinicians to routinely administer these drugs, for short periods (5 to 7 days), in conjunction with conventional periodontal therapy \((1; 337; 396)\). However, the actual contribution of individual drug regimes, in these reports, is unclear due to the simultaneous use of interventional periodontal therapy (in the form of scaling and root planing), oral hygiene maintenance, antimicrobial mouthwashes and the common use of multiple antibiotic regimes, simultaneously, for the treatment of these periodontal infections \((1; 337; 396)\).

In this way, any possible suggestion of the use of any antibiotic regime cannot be interpreted due to a difficulty in separating out their effects from other factors, such as the removal of possibly aetiological microflora via plaque and calculus removal. Therefore, without tangible support for the role of adjunctive antibiotic therapy and antimicrobial mouthwashes (for example, Chlorhexidine) in both HIV infected and non-infected patients, the clinical suggestion is that the routine periodontal treatment outlined above should be the basis for therapy.
Definitive evidence of the effect of antibiotic therapy, in the absence of other forms of therapy, with special reference to possible additional side effects (for example, resistant strain selection) in the severely immune suppressed, such as those infected with HIV, need to be undertaken before their use is advocated.

b. Preventive therapy

This is aimed at the maintenance of low levels of microbiota in order to prevent recurrent exacerbations, and generally involves periodic review of the patient. At these reviews, the following steps may be undertaken:

i. Further debridement of hard and soft tissues.

ii. Detailed evaluation and examination of the entire oral cavity to determine additional manifestations of HIV infection and/or recurrent exacerbations of pre-existing lesions.

iii. The maintenance of optimal oral hygiene.

With such a wide clinical variation of these lesions, a differential diagnosis must include a large number of possibilities. Some of these may include; herpetic gingivostomatitis, pericoronitis, apical periodontitis, chemical or physical trauma, progressive necrotizing ulceration, recurrent aphthae, and ulceration due to
cytomegalovirus, herpes simplex virus, Epstein-Barr virus and Kaposi's sarcoma.

2.2.2.b: OTHERS

i. MYCOBACTERIUM AVIUM INTRACELLULARE (MAI)

Although generalized infection with MAI has been detected in between 25% and 50% of individuals with AIDS at autopsy (26; 389), a single report by Volpe and co-workers (383) has suggested MAI as the cause of intraoral lesions. This single report (383) identified lesions of the anterior palate and edentulous portion of the right maxilla initially, followed by disseminated invasion of the maxillary, frontal, sphenoid and ethmoid sinuses. Severely reduced immune function, evidenced by severely depleted laboratory values, may have been a major predisposing factor in allowing the infection to advance from marginal tissue into palatal bone within only five days.

There are three important points arising from this report:

a. This report definitively identified MAI as the possible causative agent of oral lesions in a patient already diagnosed with AIDS. A possible direct causal association of MAI results from the identification of this bacterium from a biopsy of oral lesions, and its subsequent culture from these
tissues. A reported increase in the size and severity of these lesions whilst undergoing recommended optimal antimicrobial chemotherapy merely suggests an inability to control the disseminated MAI infection.

b. The individual reported in this case had previously been diagnosed with AIDS, according to current CDC classification criteria (Refer Appendix 1), due to oesophageal candidiasis and disseminated MAI infection. As the development of oral lesions were subsequent to the diagnosis of AIDS, the lesions seem to have resulted from the disseminated MAI infection.

c. The isolated nature of this report suggests that although oral lesions due to MAI seem to be associated with HIV infection, they are either exceedingly rare or reported infrequently. As with previous sections involving Histoplasma and Cryptococcus species, the question of whether secondary contamination or superinfection of unrelated lesions have occurred, still remains.

ii. ENTERIC PATHOGENS

Despite an apparent conviction that enteric organisms may give rise to oral lesions (180; 315; 316; 343; 353), there is a conspicuous absence of detailed prospective clinical studies in HIV infected individuals to support this. To attempt to determine a causative effect of these bacteria in the immune suppressed, studies of
individuals with similar immunosuppressive states, such as those with acute leukaemia, may be of use (410; 501).

Infections due to enteric gram negative bacilli have been described by Dreizen and colleagues (501) as primary pathogens causing lesions of the oral mucosa and/or perioral skin in myelosuppressed individuals. However, more definitive studies, such as that performed by Barrett (410), have failed to prospectively identify any of these lesions. Furthermore, when these pathogenic bacteria were isolated from swabs of existing lesions, where an alternative aetiology could be readily identified, there was no suggestion that these microorganisms had initiated the lesions, changed the lesion's existing behaviour or disseminated as a result of colonization. These findings suggest the lack of an aetiological role for enteric pathogens in oral lesions in myelosuppressed individuals. It is unclear whether these rules similarly apply to HIV.

Due to infrequent reporting and the lack of definitive confirmation of an aetiological role in oral lesions, at best, enteric pathogens may be considered to cause contaminant infection. Reports of lesions due to these bacteria in HIV infected individuals make no mention of the methods of bacterial sampling nor the specific behavioural patterns of the lesions, making accurate interpretation impossible. As such, the suggestion by Barrett (410) that the mere presence of bacteria on
swabs and in sputum is not indicative of a causative role in leukaemic individuals may be of relevance here.

The apparent infrequency of reports of oral lesions possibly due to enteric pathogens may be due to the empirical administration of antibiotics for other purposes in these individuals, thereby possibly suppressing clinical signs and prematurely terminating infections related to the dental structures. Similarly, HIV induced disordered local inflammatory responses may have been responsible for the lack of clinical signs and symptoms in HIV infected patients.

The preceding evidence indicates that enteric pathogens may provide contaminant infection of pre-existing, unrelated lesions. The isolated nature of reports due to these microorganisms suggests that they are either rare occurrences or rarely reported. It remains unclear whether the infrequency of reports of bacterial orofacial infections is a reflection, at least in part, of the improved overall control of bacterial colonization and infection as more clinical experience is gained in the management of individuals with HIV-induced immunosuppression.

2.2.3: **VIRAL INFECTIONS**

The unique immunosuppression produced by HIV infection commonly makes these individuals susceptible to a wide range of viral infections. Easily the most commonly
identified oral viral lesion involves infection with the human herpes group of viruses, in particular herpes simplex types 1 and 2 (HSV-1 and HSV-2). HSV-1 and HSV-2 appear to be directly associated with HIV induced immunosuppression, with the other viruses of the herpes group also, most probably, being directly related. However, the association of other viral lesions such as hairy leukoplakia (HL) and those due to human papillomavirus (HPV) are less clear.

The identification of these viral lesions in the oral cavity raises several possibilities to the dental practitioner:

1. These lesions may prompt the use of serological screening to test for HIV infection.
2. In those patients where the HIV status is already known, the identification of certain viral lesions of more than one month duration, such as those due to HSV and cytomegalovirus (CMV), may be diagnostic for AIDS.
3. It has been suggested that HL is of prognostic value in determining disease outcome (175; 179; 181; 180; 184; 333; 343).
4. The possibility of cross-infection of not only HIV but also other viral diseases between patients and healthcare workers.
5. Due to the often severe, intractable and rapidly recurring nature of these lesions, adequate management may pose a problem.
2.2.3.a: HERPES GROUP OF VIRUSES

At present there are six of the herpes group of viruses that have been identified as human pathogens: herpes simplex type 1 (HSV-1), herpes simplex type 2 (HSV-2), varicella-zoster Virus (VZV), cytomegalovirus (CMV), Epstein-Barr Virus (EBV), and only discovered in 1986; human B-lymphotropic virus (HBLV) (304). The first five of these viruses have been directly implicated in lesions of the oral cavity in cases of HIV infection (276).

i. HERPES SIMPLEX TYPES 1 and 2 (HSV-1 and HSV-2)

Orofacial mucocutaneous infection by HSV in immune competent individuals has been identified as a distinct clinical entity for over 250 years. The two serotypes of HSV (HSV-1 and HSV-2) were originally thought to cause, respectively, oral and genital ulcerations. Further research has shown that these two serotypes share approximately 50% of their genetic information, cause virtually the same infections, cross react immunologically due to shared antigenic material, and produce similar antibody responses.

In this way, it is difficult to separate out the effects of HSV-1 and HSV-2 on oral lesions in both HIV infected and non HIV infected patients. When HSV infection occurs in these individuals, the question of
whether it represents primary or recurrent infection is raised. The majority of reported orofacial HSV lesions in cases of HIV infection contain a prior history of recurrent HSV lesions, suggesting that the majority arise from the recurrent exacerbation of the virus that remains dormant in sensory nerve ganglia (39; 136; 225; 276; 304).

Although orofacial HSV infection is seen commonly in all cases of HIV infection, and seems to be directly associated with the immunosuppressive state, it is not considered pathognomonic for AIDS, as it is also seen in patients with suppressed or normal immune systems in the absence of HIV infection. The issue of orofacial HSV infection in association with HIV may be looked at in terms of its clinical presentation and management.

**Clinical Presentation**

With advancing immunosuppression one would expect orofacial HSV lesions to be more prevalent, however, reports suggest this is not the case. It has been estimated that 80% to 90% of the adult non-HIV-infected population have been exposed to HSV, with approximately 20% to 40% of these experiencing recurrent orofacial exacerbations (39; 225; 276; 304). In contrast, the prevalence of HSV antibodies, denoting prior infection in HIV infected individuals, ranges from 50% to 80%, with studies suggesting that between 4% and 9% exhibit orofacial infections (34; 258; 315; 327; 352).
On initial analysis, these figures would seem to contradict the widely held theory that immunosuppression makes HIV infected patients more susceptible to various infectious processes, for example HSV. However, many of these individuals, especially those in the advanced stages, commonly receive systemic Acyclovir to guard against genital herpes. Therefore, the possible effect of prophylactic antiviral therapy in diminishing the true HSV prevalence rates of those infected with HIV cannot be overlooked.

The study of individuals from all stages of HIV infection raises the question of whether the severity or prevalence of orofacial HSV corresponds to any particular staging of the disease. The majority of studies in this field (327; 352) have suggested that orofacial HSV infection is more prevalent during the middle stages of HIV-induced immunosuppression. Their finding that these lesions are less common at the severest end of the disease spectrum may also be due to the possible effect of systemic antiviral drug therapy.

For the majority of immune competent non-HIV-infected individuals, recurrent HSV represents a painful experience. However, in relation to HIV, infection with HSV means that these acute problems may be life threatening (38; 39; 253; 336; 343). However, the literature does not appear to contain detailed definitive accounts of cases of HIV infection in which dissemination of orofacial HSV has been a principal or
sole source of death. Additionally, there is an apparent absence of these reports in similarly immune suppressed individuals, such as leukaemic patients.

In the absence of these studies, the majority of authors propose that orofacial HSV in HIV infected patients has a distinctive clinical appearance, being more severe and difficult to manage. However, recent reports by MacPhail and colleagues (357) illustrate well the variety of clinical presentations that these lesions may adopt.

The classical HSV lesions in these individuals represent yellowish fluid filled vesicles that quickly rupture forming shallow, painful ulcers with a grey pseudomembrane and erythematous border. Several smaller ulcers often coalesce to form expansive lesions, which may fulfill the criteria set down by the CDC (Refer Appendix 1) for a diagnosis of AIDS, if they persist for longer than four weeks (253; 343; 62; 72).

With the strong possibility of encountering multiple oral complications in HIV infected patients, it may be difficult at times to distinguish herpetic lesions from other forms of ulceration and, when raised white plaque formation occurs, from candidiasis. In order to confirm typical cases and as an aid in diagnosing those cases which do not fit the classical presentation mentioned above, cytopathology is an efficient method of distinguishing HSV lesions from others (39; 136; 225;
304). The serological detection of HSV antibody may be of questionable value in cases of HIV infection due to background impaired immune responses. The culture of HSV from swabs denotes the presence of the virus, but is not necessarily diagnostic of a causative role. Continual excretion of the virus and the possibility of disseminated infection raises the possibility of the contaminant infection of unrelated lesions, similar to other infectious processes mentioned previously (for example, Cryptococcus and Histoplasma species - Refer Section 2.2.2).

**Management**

The possibility of acquiring ocular and digital HSV infections, in addition to HIV or other viral diseases, underlines the need to implement strict infection control procedures (Refer Section 3.1.2). In addition to the acquisition of HSV from patients, the possibility of cross-infection also exists. This possibility was confirmed by Manzella and co-workers (257) in 1984, who traced an outbreak of HSV-1 gingivostomatitis directly to a dental operatory, where a hygienist had an uncovered herpetic whitlow.

Normally, reactivated HSV infections are rapidly controlled by the human host response in immune competent individuals, with lesions being essentially small and self limiting and confined to the vermilion border of the lower lip, if they occur at all. Many
authors claim that, in association with HIV, reactivation of HSV leads to severe, frequent lesions which are long lasting and extensive (38; 39; 253; 336). However, detailed prospective studies are not available for critical analysis.

While these studies are not available, anecdotal case reports, such as that provided by MacPhail and colleagues (253), suggest the possibility of distinctive widespread necrosis of orofacial tissues by HSV in advanced stages of HIV infection. The chronic, indolent nature of these lesions, presumably due to the resistance to Acyclovir therapy, raises the need for the definitive control of HSV in those infected with HIV. With the elimination of latent HSV being impossible, management involves a combination of antitherpetic medication and appropriate palliative care.

Fortunately, Acyclovir has proved to be effective against HSV in both immune competent and immune suppressed individuals. Without similar definitive studies with regard to HIV, the efficacy of systemic or topical Acyclovir therapy can only be gauged by case reports that suggest its effectiveness (39; 253; 304). However, the persistence of Acyclovir resistant HSV lesions in one anecdotal report (357), in an individual at the severest end of the disease spectrum, raises the possibility of increased viral resistance due to prolonged prophylactic exposure to Acyclovir. This then
raises the need for the development of other effective antiviral agents.

Oral prophylaxis with Acyclovir is often needed because of the frequency and severity of recurrent genital herpes in association with HIV-induced immunosuppression. The issue of prophylactic Acyclovir has been studied prospectively in the myelosuppressed and shown to be both effective and well tolerated with generally minimal toxicity for therapeutic periods of up to six months (340). However, there is general concern regarding its prolonged use.

ii. **VARICELLA-ZOSTER VIRUS (VZV)**

Several reports indicate that VZV infection, either in the form of widespread, if not disseminated, chicken pox or as infection confined to specific dermatome(s), may occur in between 7% and 8% of all HIV infected patients (180; 316; 327; 343; 352). The majority of these reports do not distinguish between these two clinical presentations. Intraoral involvement has been mentioned in four such cases, but it generally remains unclear whether this occurred in the setting of trigeminal or disseminated VZV infection.

In relation to VZV infection generally, suggestions of a poor prognosis (243; 269) may merely correlate with a relationship between VZV and advanced stages of HIV-induced immunosuppression. This is supported by a
report by Friedland and co-workers (243), indicating
that the prevalence of clinical VZV infection in
individuals with KS (advanced stages of HIV infection)
was seven times that of age matched non-HIV-infected
controls. The infrequency of reported orofacial VZV
lesions suggests that they are relatively uncommon, and
may seem to be associated with the severest end of the
disease spectrum.

iii. CYTOMEGALOVIRUS (CMV)

Despite the prevalence of CMV carriage in some HIV
groups, particularly homosexual males (90% to 100%)
(136; 259; 352; 353), its association with oral lesions
appears to be extremely uncommon in the setting of
HIV-induced immunesuppression. Only one definitive case
of oral ulceration, reported by Kanas and co-workers
(227), is evident in the available literature, where
confirmation of a specific CMV aetiology appeared likely
as a result of biopsy, supplemented by cultures. A
possible response to Acyclovir therapy may also support
a direct aetiology in this case.

In addition to the definitive report by Kanas and
colleagues (227), describing painful broad ulcerated
necrotic lesions of the palatal gingiva, Andriolo and
co-workers (22) have reported ulcerative lesions of the
tongue and buccal mucosa due to CMV. However, this
latter suggestion is difficult to interpret due to a
lack of clinical and diagnostic information. With only
one definitive report, therefore, some scepticism exists as to whether primary CMV infections of the oral mucosa exist in AIDS (41; 316; 327; 343; 352).

Similar considerations regarding the possibility of viral contamination of a pre-existing unrelated lesion are raised, as with other infections (for example; Cryptococcus and Histoplasma species and enteric pathogens - Refer Section 2.2.1 and 2.2.2). As disseminated CMV infection was identified by Kanas et al. (227) subsequent to the detection of oral ulceration, the possibility exists that dissemination arose from a primary oral mucosal lesion. The alternative explanation suggests an oral lesion that is part of an established disseminated CMV infection.

The second association of CMV with oral lesions comes in the form of a possible aetiological link between CMV and the development of Kaposi's sarcoma (KS), a lesion present in the oral cavity in 44% (352) of patients with AIDS, for which KS was the diagnostic criterion. The evidence for a direct CMV link with KS comes in the form of studies confirming the virus in tumour cells, detected by reassociation kinetics, in situ hybridization and anticomplement immunofluorescence.

Many authors suggest that CMV may be directly involved in the neoplastic transformation of endothelial cells, leading to the induction of KS in HIV infected
individuals (106; 117; 232; 290; 350). A possible aetiological role arises from:

1. Suggestions that the reported prevalence of KS in homosexual males with AIDS (up to 51%) may be related to the prevalence of CMV in these individuals (90% - 100%) (136; 176; 180; 259; 334; 352; 353). This is confirmed by reports suggesting that 100% of patients with KS similarly display CMV infection (334; 339).

2. The definitive identification of CMV DNA, CMV RNA and CMV determined antigens in endothelial cells derived from biopsies and cultures of KS lesions (56; 117; 237; 350).

However, the possibility that CMV directly causes neoplastic transformation is questionable due to an inability to consistently identify CMV inclusions, antigens, DNA or RNA by various techniques in all KS tumour lesions (range of 0% to 40%) (117; 141; 237; 290; 350). These inconsistent findings suggest that either latent CMV is reactivated after neoplastic transformation, thereby infecting some endothelial cells or that CMV is a dormant passenger.

Without consistent evidence for CMV infection in all KS tumour lesions and an apparent lack of reports of KS in non-HIV-infected homosexual men, it seems that CMV plays no direct aetiological role. It appears that KS requires the setting of HIV-induced immunesuppression,
which may well account for the apparent absence of this lesion in homosexual males who are not seropositive for HIV, but who do have serological evidence for CMV infection.

iv. **EPSTEIN-BARR VIRUS (EBV)**

EBV may have an association with the oral lesion hairy leukoplakia (Refer below), observed frequently in HIV-induced immunosuppression. Except for its association with African Burkitt’s lymphoma (177; 276) and nasopharyngeal carcinoma in non-HIV-infected individuals, EBV infection has generally been considered relatively innocuous. The initial description of hairy leukoplakia (HL), by Greenspan and colleagues (179) in 1984, represented the first oral epithelial lesion reported to display evidence of EBV infection. In addition to this possible association with HL (Refer Section 2.2.3.c), EBV has since been associated with non-Hodgkin’s lymphoma (NHL) (Refer Section 2.3.2.) (177; 276) and thymic carcinoma (276) in the immune suppressed, including those with HIV. Preliminary research revolved around the thought that EBV was a co-factor in the development of AIDS (276), although no direct evidence has supported this claim.

EBV can be consistently identified in seropositive individuals and studies suggest strongly, yet do not prove, a direct role for EBV in the pathogenesis of NHL among HIV infected and similarly immune compromised
individuals (177; 276). In developed countries, between 75% and 80% of the general non HIV infected population ultimately become infected with EBV, with evidence suggesting that access and replication occurs in the epithelial cells of the oropharynx (39). This finding raises the question that if EBV is directly associated with HL, then why does this lesion predominantly appear on the lateral border of the tongue (Refer Section 2.2.3.c)?

2.2.3.b: **HUMAN PAPILLOMAVIRUS (HPV)**

HPV infection of the oral cavity in the form of verruca vulgaris, condyloma acuminatum and focal epithelial hyperplasia have been reported in HIV infected individuals, primarily in homosexual men (87; 180; 224; 315; 352; 367). Suggested prevalence rates of 29% for venereal lesions (352) and up to 4% for the above mentioned oral lesions due to HPV (315; 352) in HIV infected individuals, do not necessarily suggest that these lesions are common in association with HIV.

The majority of these studies contain essentially limited clinical information regarding the clinical presentation of these lesions, the diagnostic methods used and the stages of disease progression of those studied. Similarly, variations in suggested prevalence rates in these individuals may merely indicate varying proportions of venereally acquired and non venereally acquired HIV infection. In this context, it should be
noted that the suggested prevalence of HPV in seropositive homosexual men is apparently no greater than in male homosexuals as a group.

As such, the identification of oral HPV lesions may be indicative of risk behaviours conducive to the acquisition and transmission of HIV, and in no way associated with HIV-induced immunosuppression. In this way, it seems that HPV infection causes several distinctive lesions (mentioned above) that may be linked to lifestyle. On the other hand, Greenspan and co-workers (179) have proposed a direct association of HPV with HIV-induced immunosuppression by virtue of the identification of HPV within epithelial cells of hairy leukoplakia (HL) via immunohistochemistry and electronmicroscopy. High HPV carriage and the preponderance of HL in homosexual men may provide further evidence of this association.

While this concept was originally held, it is now generally debated due to the inconsistent identification of HPV in HL. Studies suggesting that between 73% and 100% of HL lesions contain HPV (179; 181; 182; 183; 184) involved the evaluation of homosexual men, while the identification of HPV in between 0% and 5% of HL lesions (132; 228) were seen in non-homosexual or predominantly non-homosexual groups; suggesting a direct link to the homosexual lifestyle. In this way, it seems that HPV plays no direct aetiological role, but by virtue of possible contaminant infection of HL lesions in
homosexual men, may be related to HIV-induced
immunesuppression.

2.2.3.c: **HAIRY LEUKOPLAKIA (HL)**

Since the first description, by Greenspan et al. in
1984 (179), of a "white lesion of the lateral border of
the tongue" in a seropositive homosexual male, hairy
leukoplakia has been recognized as a common oral
manifestation in HIV infected individuals. Although
initially reported exclusively among homosexual males
(179; 180; 234), subsequent reports suggested that HL
also affected those from other risk groups, such as
haemophiliacs (182; 333; 343), blood transfusion
recipients (182; 333; 345), intravenous drug abusers
(343; 345), and female sexual partners of seropositive
men (182; 343; 345; 439). Its identification in other
risk groups suggested that, although the lesion
preferentially affects homosexual males, it may be due
to the direct action of HIV. However, reports of HL in
seronegative renal transplant recipients (429) indicated
that this lesion results more from immunesuppression,
rather than by any direct HIV action.

Hairy leukoplakia will be discussed in terms of its
suggested prevalence, histopathological presentation,
possible aetiology and specific relevance to the dental
practitioner. Before discussing this lesion,
familiarization with the different descriptive terms
used in the literature must be undertaken. In addition
to the conventional term "hairy leukoplakia", many reports describe this lesion as "oral hairy leukoplakia". This seems to be a tautologous term when considering that HL has only been found in the oral cavity (Refer below). In 1986, Eversole and co-workers (132) proposed the term "condyloma planus" due to the possible initial association of HPV to this lesion, and its close pathological similarity to the flat venereal warts of the genital tract. Similarly, Green et al. (175) tentatively proposed the term "pseudo-hairy leukoplakia" to describe lesions that clinically and histologically resembled HL but lacked the necessary diagnostic criteria of the identification of EBV DNA within epithelial cells of the lesion. In this treatise, the term hairy leukoplakia (HL) will be used in preference to the other proposed terms.

Studies suggesting the prevalence of HL in HIV infected individuals (with a range of 4% to 49%) (74; 181; 182; 183; 184; 315; 334; 352; 354), mainly involving homosexual men, are difficult to interpret for the following reasons:

1. The majority of studies contained not only different relative proportions of the various risk groups but also individuals at varying stages of HIV-induced immunosuppression, from seropositive individuals to full blown AIDS (181; 182; 183; 184; 315; 334; 352; 354).
2. These same studies have distorted prevalence levels by virtue of the fact that unspecified, probably large, numbers of individuals included in these prevalence studies were specifically referred for the management of HL.

3. The common use of poor diagnostic criteria to identify HL. In support of this is a claim by Rosenberg and colleagues (334) that 49% of HIV infected individuals displayed HL, based purely on the identification of "a white oral lesion". With such a broad definition for HL, lesions due to HSV, Candida species and various other causes may have been included in suggested prevalence levels for HL.

4. The possibility that subclinical or non-detected HL may have occurred due to the possible regression and recurrence of the lesion in those undergoing prophylactic Acyclovir therapy (142; 153).

Due to a lack of detailed definitive prospective studies, true prevalence rates for HL cannot be gauged, however, the lesion is thought to be commonly associated with HIV-induced immunosuppression, leading to its inclusion since 1986 in CDC classifications as an HIV-associated disease (62; 72; 75) (Refer Appendix 1).

The histopathological presentation of HL is well documented. The characteristic findings are acanthosis and hyperparakeratosis, with the formation of extensive hair-like kerratin projections colonized with
microorganisms. Also evident are ballooned prickle cells with pyknotic nuclei, the so-called koiocytes, often with perinuclear halos. There also appears to be an absence of or minimal inflammation seen, even in those cases infected by Candida species (132; 179; 180; 182; 184; 234; 333; 343). The majority of cells near the epithelial surface show dense aggregates of nuclear chromatin material margined along the nuclear membrane, termed inclusion bodies, and typically found in cells infected by the herpes group of viruses.

Within the epithelial cells of this lesion, the majority of the cytoplasm has a "ground glass appearance" with either viral inclusion bodies due to EBV, or an even distribution of two distinct viral particles, presumably EBV and HPV. These viruses may be identified by various means, including in situ hybridization, immunocytochemistry, reassociation kinetics and ultrastructural observations. The identification of EBV, usually by virtue of the presence of distinctive inclusion bodies, has been considered necessary, by Green et al. (175), for a diagnosis of HL.

Since the initial recognition of HL as a unique clinical entity, various studies have attempted to implicate HIV, Candida species, HPV and EBV in the aetiology of the lesion. Further studies seem to indicate that, of these infectious agents, only HPV and EBV may be directly associated with HL, with only EBV potentially playing any aetiological role.
i. **HIV**

Suggestions that HIV may play an aetiological role arose from the initial identification of HL exclusively in association with HIV infection and the regression of the lesion by antiviral therapy, such as Acyclovir and AZT. However, an inability to disclose HIV antigens in HL (345), the predominance of the lesion in homosexual men rather than being common in all risk groups, and the identification of HL in a seronegative renal transplant recipient (429) casts significant doubt on any direct aetiological role. An indirect role, however, may be suggested by virtue of the induction of immunesuppression by HIV that allows for the formation of HL.

ii. **Candida species**

The implication of this fungus in the aetiology of HL arose from similarities in the clinical presentation and the identification of candidal hyphae in up to 83% of all lesions of HL (142; 175; 342). However, a lack of response to antifungal therapy, as opposed to antiviral therapy, suggests secondary colonization of Candida species rather than an initiating influence (41; 132).

iii. **HPV**

The possibility of an aetiological role for HPV in HL has been discussed previously (Refer Section 2.2.3.b).
Weight of evidence would suggest no direct aetiological role for HPV, although, by virtue of the possible contaminant infection of these lesions in homosexual men, it does suggest risk behaviours conducive to HIV infection.

iv. EBV

Current evidence suggests a possible causal association of EBV in the aetiology and pathogenesis of HL (Refer Section 2.2.3.a). Identification of EBV may be performed by means of electronmicroscopy, immunocytochemistry, in situ hybridization of cells harvested from the surface of the lesion. This possible association has been suggested by the following:

a. The lack of effect of antifungal drug therapy and the observation that HL may regress during the administration of Acyclovir, possibly due to the direct effect of this drug on EBV (142; 153).

b. The fact that, prior to October 1986, HL had not been reported in the English literature among any risk group other than homosexual males, a group of individuals with an exceedingly high prevalence of EBV infection.

c. The consistent isolation of EBV from the epithelial cells of HL, but not the adjacent mucosa (153; 234), is more suggestive of an aetiological role rather than contaminant infection. Prevalence rates of EBV infection in these lesions have
consistently ranged between 62% and 100% (135; 184; 228).

d. Evidence provided by Eversole et al. (175) that EBV can infect oral epithelial cells, demonstrated by the presence of EBV receptor sites on these cells. This association may be due to a decreased local immunity, as demonstrated by the decreased number of Langerhan’s cells at the site of occurrence, or to an increase in the receptor sites for EBV on the lateral margins of the tongue.

e. Subsequent findings by Daniels and co-workers (134) that the absence of these mucosal antigen-processing cells may permit EBV infection. Furthermore, the observation of Langerhan’s free interzones along the surface of normal tongue epithelium suggests that EBV may infect these sites preferentially. These findings may help explain the apparent predilection of HL for the lateral margins of the tongue, and have been confirmed by subsequent studies (175; 345).

f. The ability of EBV to produce some of the characteristic histopathological features of HL. In 1989, Kabani and colleagues (226) proposed that the combination of HIV-induced immunosuppression and high concentrations of EBV allows this virus to readily infect oral epithelium, leading to hyperplasia. Subsequently, direct interference of normal cell metabolism by EBV enhances the retention of keratin. In this way, it was suggested that EBV may produce some of the
characteristic features of HL; hyperplasia, hyperparakeratosis and ballooned prickle cells (226).

Recently, however, El-Labban and colleagues (481) have raised significant doubt, at least from the view-point of ultrastructural analysis, on a possible aetiological role for EBV by electronmicrographic examination of single and serial sections of HL lesions. This study suggested that the membrane-bound structures found in epithelial cells of HL, previously referred to as EBV, possibly represent various levels of sectioning of transversely cut cell processes.

Although a direct aetiological role may be possible, contaminant infection in the same manner as for other infectious processes cannot be overlooked. This possibility has been raised by an anecdotal report detecting EBV DNA in the epithelial cells of the parotid gland by in situ hybridization (345), thereby providing a persistent source of EBV for salivary contamination. However, the situation remains unclear due to a lack of definitive studies concerning salivary gland EBV infections in individuals with HL.

The dental practitioner needs to be aware of the uniqueness of HL, its clinical presentation and possible prognostic value, the differential diagnosis and methods of management. HL is a unique lesion in that it is confined to the oral cavity, with efforts to identify
the lesion on mucosa other than the oral mucosa proving inconclusive. Therefore, of relevance to the provision of dental care is a lesion, unique to the oral cavity, that has been included in the CDC classification for HIV-associated disease (Refer Appendix 1) (62; 72; 75).

The clinical presentation of HL has been clearly described in the literature. A clinical diagnosis can be made on the identification of three distinctive features:

a. Its uniqueness to the oral cavity and increased prevalence in HIV infected homosexual males.
b. It exhibits a common predilection for the lateral and ventral surfaces of the tongue (134; 175; 179; 226; 333; 342; 343).
c. The common presentation involves white patches with a heavily corrugated or hairy appearance.

Although early reports of HL proposed a distinctive clinical appearance, the variety of clinical presentations that these lesions may adopt has been well illustrated by subsequent studies. These variations include:

d. Although commonly affecting the tongue, anecdotal reports have suggested additional mucosal sites in 6% to 14% of all HL lesions (132; 134; 175; 179). Although rare, these sites have included the soft palate, buccal mucosa and floor of the mouth.
e. Although initially suggested to be corrugated in appearance, smooth flat lesions similar to other keratotic lesions have been reported (226; 333; 342).

f. Variations in the extent of the lesion have been reported from tiny, nearly invisible lesions with delicate vertical striations or corrugations to extensive, poorly demarcated thick white patches with heavy corrugations (179; 226; 333; 342; 343).

g. HL is usually asymptomatic, found bilaterally in up to 80% of cases (175), and does not rub off (226).

h. The possibility of widespread HL has been suggested by a recent anecdotal report of two cases, by Kabani and colleagues (226), where marked oral involvement extended into the pharyngeal mucosa. The extent of HL is not considered to be prognostically significant though, with smaller lesions thought to exhibit similar prognostic value for the subsequent development of AIDS as extensive ones (342; 343).

Many authors suggest that the identification of HL may accurately determine the period involved in the progression to advanced stages of HIV disease (AIDS) (175; 180; 181; 183; 184; 226; 333; 343). Various studies have suggested the development of AIDS in 48% after 16 months, 83% after 30 months (175; 180; 184; 333; 343), 22% after 33 months (179), 30% after 36 months and 57% after 48 months (181). However, these
prognostic estimates remain anecdotal for various reasons:

a. HL has been identified inconsistently in all stages of HIV infection, predominantly in homosexual men. With the lesion seemingly not specifically related to any one stage of HIV-induced immunosuppression, prognostic estimates are difficult.

b. With no mention of drug regimes, the possibility exists that regression and recurrence of HL occurred in individuals undergoing intermittent Acyclovir therapy for other reasons. In this way, it is possible that the first identification of lesions, and hence inclusion in the above studies, may have been subsequent to its initial presentation.

c. These studies have involved individuals at varying stages of the disease. Without any clinical or laboratory information regarding the stages of immunosuppression in these people, it is possible that many already had AIDS at entry to the study.

Without further long-term follow-up, it is not clear yet whether these lesions may accurately predict the eventual development of AIDS in those studied. Furthermore, these studies involved homosexual males, and as such it is thus far unknown in the absence of further studies whether HL in other risk groups carries any prognostic implications (333).
The diagnosis of HL is frequently made on the basis of direct clinical observation with or without biopsy. Some authors, however, propose that the formal identification of EBV in biopsy specimens, as suggested by Greenspan et al. (181), be required in "questionable cases" or, in the opinion of Green and colleagues (175), is required in each case to confirm HL. While the proposal by Green and colleagues (175) may be an overreaction, this must be balanced against the knowledge that HL may, at times, resemble other unrelated oral lesions. Some of these specific lesions may include; ideopathic leukoplakia, tobacco-induced lesions, lichen planus, frictional keratosis, geographic tongue, galvanic lesions, severe leukoderma, white sponge naevus, chronic hyperplastic and pseudomembranous candidiasis. Due to the similarity of HL with candidal lesions, and the consistent identification of Candida species from these lesions, probably in the form of contaminant infection, non-resolution with antifungal therapy may also be of diagnostic value.

Limited information is available regarding the management of HL, probably due to its asymptomatic nature. However, in cases producing an unsightly appearance or periodic discomfort, management may occasionally be required. Possible management regimes have been suggested by case reports and prospective studies, and have essentially centred on antifungal and antiviral therapy. Initial interest on management, based on the identification of Candida species in these
lesions, revolved around the use of systemic or topical antifungal therapy. However, these drugs have only been shown to reduce the size of HL in some cases, without complete clinical and histological regression (181). Non resolution with antifungal therapy may be considered highly suggestive of HL due to the general consensus that Candida species causes contaminant infection rather than playing any initiating influence. The majority of studies involving antiviral agents specifically aimed at eliminating EBV, the possible causative virus of HL, have been promising. The oral or topical administration of such agents as Acyclovir, Desciclovir and Ganciclovir have been associated with regression in a number of reports (142; 153; 181), however, recurrence is a common finding.

Although a study by Friedman-Kien et al. (153) based regression on the clinical absence of the lesion due to Acyclovir, this was not supported by laboratory evidence to confirm the absence of EBV. However, a double blind placebo controlled trial by Greenspan and co-workers (181) reported not only a clinical regression of HL, but a subsequent absence of EBV as determined by in situ hybridization, following Ganciclovir therapy. This latter study provides some evidence for both a causative role for EBV and for the use of Ganciclovir in selected cases.

A recent study by Phelan and Klein (cited by Greenspan (181)) raises the possibility that AZT, possibly by
virtue of its potent inhibition of HIV replication (202), may be useful in the management of HL. The partial remission of HL during AZT therapy, in this case, most probably resulted from a slight restoration of immune function by HIV inhibition, rather than being suggestive of a causative role for HIV in the induction of HL. Due to the isolated nature of these studies, definitive long term prospective studies are required with evidence of clinical and histological regression of HL in order to prove the efficacy of such drugs as Acyclovir, its derivatives, or AZT.
2.3 NEOPLASMS

The effect of HIV infection on the immune system predisposes infected individuals to various neoplastic processes, with Kaposi's sarcoma (KS) being by far the most common. Lymphoma, usually of the non-Hodgkin's type, and squamous cell carcinoma have also been reported but appear less commonly. These neoplasms are directly associated with an advanced HIV-induced immunosuppression, with KS and lymphoma possibly being diagnostic for AIDS, as set out by the CDC (Refer Appendix 1) (62; 72; 75). Although originally considered diagnostic, SCC is now classified under Group IV subgroup E as an HIV-related disease (75).

2.3.1: KAPOSI'S SARcoma

Prior to 1981, the classical or endemic form of Kaposi's sarcoma (KS), described by Moricz Kaposi in 1872, was a rare lesion found almost exclusively in older males of Eastern Mediterranean or Ashkenazic Jewish descent (106; 135; 249), Africans (especially from Zaire and Uganda) (232; 249; 371), and individuals undergoing immunosuppressive therapy such as renal transplant recipients. A review of reports of KS, prior to 1975, identified the majority of lesions as occurring on the skin of lower extremities (152), with only eight cases involving the oral cavity (106; 192).
This classical or endemic form differs from the epidemic form of KS, seen in association with HIV infection, in the following ways:

a. Prior to the HIV epidemic, KS was a rare neoplasm with an annual incidence of 0.02 to 0.06 per 100,000 in North America and Europe (152; 298). In contrast, epidemic KS currently accounts for 90% of all malignancies in association with HIV infection, with up to 51% of those patients with KS displaying oral lesions (135; 141; 152; 180; 237; 339; 382; 392).

b. Although the endemic form of KS affected older males of essentially rural descent, the epidemic expression of this neoplasm classically affects young homosexual males (range 25 to 50 years with mean age of 39 years), predominantly from major metropolitan areas (135; 141; 152; 237; 339).

c. Rather than behaving in an indolent fashion, as seen with the endemic form, HIV infected patients display an aggressive, rapidly disseminating and frequently multicentric neoplastic process with a more generalized anatomic distribution (37; 176).

Initial cases of epidemic KS shared a number of distinctive characteristics; they were all identified in young homosexual males who were sexually promiscuous, used both prescription and recreational drugs, and had a history of multiple sexually transmitted diseases (64;
As the duration of the epidemic increased, this form has predominantly affected homosexual males, although it has also been identified in intravenous drug abusers, Haitians, haemophiliacs and children of seropositive individuals (135; 141; 152; 237; 339). Of possible significance is the apparent absence in any of the available literature of epidemic oral KS in cases of heterosexually acquired HIV infection.

Individual studies of the prevalence of generalized KS in AIDS patients have ranged from 15% (406) to 51% (34; 176; 180; 258; 334). One anecdotal study by Silverman and colleagues (352), suggesting that 80% of all individuals with AIDS had KS lesions, does not accurately predict prevalence levels because of the large numbers of individuals included in this study who were specifically referred for the management of this lesion. A review of all cases of AIDS suggests a constant prevalence rate for KS of 22% for those in Australia (106) and between 20% and 30% for those in the USA at various stages throughout the epidemic (64; 141).

With knowledge of the prevalence of KS in HIV infected individuals, the question is raised as to the prevalence of oral lesions in these people. The study by Silverman and colleagues (352), whilst not being able to accurately indicate the prevalence of KS in patients with AIDS, does give some suggestion as to the
prevalence of oral lesions in those individuals with epidemic KS. In this way, the finding that 44% of all patients with KS displayed oral involvement is significant. This initial finding has been confirmed by subsequent studies that show up to 51% of patients with KS display oral involvement (176; 180).

Within the oral cavity, studies of KS consistently agree as to the common sites of involvement, with the palate being the most common (between 80% and 95% of all intraoral KS lesions), followed by the gingiva. Subsequent reports have suggested that KS may occur on any mucosal surface (37; 106; 135; 141; 176; 249; 339; 352; 353).

The presentation of KS in unusual sites, suggested by isolated reports involving the masseter muscle (141) and parotid gland (141; 301; 406), proposes the need for general dental practitioners to be fully aware of the varied clinical presentations (Refer below). This becomes even more important when considering that the oral cavity has often been the only (8%), or initial site (20%) of KS in these individuals (41; 70; 141; 180; 249).

The predominance of KS in young homosexual males and the common presentation of clustered lesions, mainly involving the rectum and oral cavity, gave rise to the speculation that a transmissible agent may directly inoculate the anal and oral mucosa (141). Most interest
has centred around attempts to implicate HIV or CMV in the induction of the epidemic form of KS (106; 117; 141; 232; 237; 290; 334).

HIV was initially thought to induce neoplastic transformation by virtue of its predominance in homosexual males, the group most commonly affected with KS. However, an aetiological role is considered unlikely because of a failure to show the presence of HIV sequences in tumour lesions (141). It is still not known whether under certain conditions HIV is capable of inducing KS or if, as is thought more likely, KS has a different aetiological basis that is permitted expression in the setting of HIV-induced immunosuppression.

The possibility of an aetiological role for CMV in the induction of KS has been raised previously (Refer Section 2.2.3.a.iii). This suggestion arose from the known CMV carriage in homosexual males (334; 339), a group predominantly affected with KS. Evidence came in the form of viral confirmation by various methods within tumour cells of the lesion (106; 117; 141; 232; 290; 334). However, inconsistent findings (56; 141; 237) are suggestive of no direct aetiological link between KS and CMV in all tumour lesions. It seems that there are two possible roles for CMV; either latent CMV is reactivated after neoplastic transformation, thereby infecting endothelial cells, or that CMV is a dormant passenger.
There have been two main classification systems proposed for the staging of KS in association with HIV infection, based on either a clinical or histopathological presentation. The initial classification, proposed by Eversole and co-workers (135), was based on the clinical presentation of these lesions and involved grouping of KS as representative of a macular, plaque or nodular stage. Further research indicated that KS could be more conveniently categorized according to histopathological presentation, with Green et al. (175) proposing two distinct stages; one representing early lesions and the other late or tumour stage lesions. Furthermore, it has been suggested that, although classifying lesions as early or late, each stage does not carry different prognostic significance (339; 175).

a. **Early lesions:** These lesions are located in the lamina propria and are characterized by atypical vascular channels, haemosiderin deposits, a chronic inflammatory process and eosinophilic bodies.

b. **Late/tumour stage lesions:** These lesions consist of well-defined nodules with diffuse involvement of the lamina propria. In addition to those characteristics of the early lesion, prominent spindle cell proliferation in conjunction with atypical vessels and mitotic figures are commonly seen. A chronic inflammatory process is essentially absent,
and vessels are either absent, or detectable only at the peripheries (237).

The majority of cases of KS have generally been described as "a flat or raised pigmented lesion" (106), of rapid onset and appearing as either macules, infiltrative plaques or nodules. A yellowish tinge around the peripheral aspects of rapidly enlarging lesions seems to be due to a combination of red blood cell lysis and haemosiderin release (392).

While the classical form of KS presents as a pigmented lesion, the following descriptions of definitively confirmed KS lesions that presented in a non-pigmented form show the clinical variability of these oral lesions in association with HIV infection. Barrett et al. (37) noted the development of three focal oral ulcerations in a 35 year old homosexual male who was seropositive for HIV. The use of swabs and biopsy confirmed the absence of any concomitant fungal, bacterial or viral involvement that may have changed the character of the lesion. Therefore, this non-pigmented ulcerative form of KS was suggestive of an atypical presentation which corresponded histopathologically to an early rather than late form of tumour development, as classified by Green et al. (175).

A second example of an atypical presentation of KS, in the form of a non-pigmented, painless, fluctuant swelling of the palate in a homosexual man, who had
previously been diagnosed with AIDS, was proposed by Daly and colleagues (106). This non-pigmented lesion was histopathologically consistent with a late or tumour stage lesion, according to the criteria of Green and co-workers (175). Table 2.5.1 (Refer Section 2.5) illustrates well the variety of clinical descriptions that have been applied by different authors for oral KS lesions.

KS represents an end-stage of HIV infection, where immunosuppression is sufficient to allow subsequent tumour development and a possible diagnosis of AIDS (Refer Appendix 1) (62; 72; 75). Suggestions of survival times are based on the diagnosis of KS "at initial presentation", an identification that may occur at any stage; from discrete lesions detected at regular follow ups, to disseminated tumour lesions detected due to the presenting signs and symptoms of advanced HIV-induced immunosuppression.

A review of all cases of AIDS, to date, demonstrate that individuals diagnosed with KS in Australia have a mean survival time of only 12 months, compared with 17.3 months in the USA and 21 months in the UK (141; 286; 437). The reasons for the regional differences in these survival times are not clear but may include variability in the recognition, detection and management of KS and opportunistic infections. Greater survival times, for example, in the USA and UK as compared to Australia, may be a reflection, in part, of relatively larger numbers
of patients, with perhaps many enjoying the benefits of enhanced patient care and, therefore, prolonged survival in more recent times.

It seems that the presence of an opportunistic infection at the time of diagnosis of KS reduces survival times. The mean survival time is reduced from 14 months, for those diagnosed solely with KS, to 6.9 months for a simultaneous diagnosis of KS and an opportunistic infection (141).

Individuals with KS are in the terminal stages of HIV infection and, as such, definitive treatment may only be required in selective cases for cosmetic reasons, pain, bleeding or due to functional impairment. Prior to treatment, a definitive diagnosis must be based on the identification of previously discussed distinctive histopathological changes evident in biopsy specimens. As these changes occur deep in connective tissue, without involving the epithelium, adequacy of biopsy specimens becomes critical (106; 176). The possibility of delayed wound healing does not negate the need for biopsies of a sufficient size to form a diagnosis. However, this is not to mean that biopsies are required to confirm these tumours in cases of previously diagnosed disseminated KS or those already known to be in the final stages of AIDS.
This concern for the potential lack of healing may be outweighed by the need to definitively identify KS as the cause of oral lesions for the following reasons:

a. The histopathological identification of KS, and hence a diagnosis of AIDS, allows for suitable categorization of HIV disease progression and the implementation of further tests of immune function and treatment modalities (Refer below).

b. This diagnosis suitably excludes the presence of swellings associated with periapical dental infection, or other tumours.

With such clinical diversity (Refer Section 2.5; Table 2.5.1), KS should be suspected in the differential diagnosis of all ulcerative, non-pigmented and pigmented oral lesions, swellings and unusual lesions in patients with known or possible HIV infection. A differential diagnosis should include lesions due to infectious diseases such as Mycobacterium and herpes simplex, squamous cell carcinoma and lymphoma (383; 399; 352). For the pigmented form; haematomas, vascular tumours; such as haemangioma, lymphangioma, angiofibroma, haemangiopericytoma, hamartomas, pyogenic granuloma (especially if present on the dental alveolus), multiple foci of ecchymoses, thrombocytopenia, malignant melanoma and subepithelial deposits of amalgam restorative material, should all be considered in the differential diagnosis (37). Predominantly early lesions
may similarly be confused with localized gingival or periodontal lesions, or a granulomatous disorder (312).

The definitive management of oral KS depends on the size and extent of lesions; but may involve chemotherapy, radiotherapy, laser resection, or combinations thereof. While radiotherapy is generally considered the most effective and practical method, reports suggest mixed results. This form of therapy is usually reserved for lesions of the oropharynx that are symptomatic or interfere with normal function.

The majority of authors (23; 37; 141) agree that resolution, in the form of total disappearance, of the lesion or residual flat pigmentation is common, regardless of total dose and fractionation used. Total dose may be of the order of 1,500 Rads with fractions ranging from 150 to 400 Rads (141). In support of this is the finding by Ficarra and colleagues (141) that 92% of individuals had complete regression of KS lesions and resolution of symptoms, which in all cases remained stable until their demise. However, suggestions that radiotherapy had no effect on KS lesions (135) and the need by Barrett et al. (37) to discontinue therapy due to severe radiation-induced oral and oropharyngeal mucosal toxicity cloud the issue.

Cytotoxic drugs, such as Vinblastine or Bleomycin are sometimes used either systemically or as intralesional injections. Systemic chemotherapeutic agents are
generally used to manage widely disseminated KS or rapidly progressive lesions. As is the case with radiotherapy, results are mixed with the consensus of opinion suggesting resolution (106; 141; 246; 382). However, severe reactions to these drugs (37) and the non-resolution of lesions (37; 135) have been reported.

The third option for the management of oral KS involves laser resection. This method is generally more effective in cases of exophytic lesions, which are small and discrete, rather than invasive KS lesions. Although laser resection has the benefits of decreased post operative pain and better haemostasis, the combination of possible delayed wound healing and the multicentric nature of KS ensures it has very limited indications.

In addition to the treatment of actual KS lesions, general consideration should be given to monitoring the individual for oral complications unrelated to KS (which may include candidal or HSV infection or mucosal ulceration due to therapy), nutritional support and pain control. Adequate management of these individuals is multifaceted and usually requires the combined management of different healthcare groups (for example, physicians, clinical counsellors, oncologists and radiotherapists).
2.3.2: LYMPHOMA

People with HIV-induced immunosuppression are apparently predisposed to the development of EBV containing lymphomas, due possibly to a combination of abnormally high numbers of EBV infected B cells in the circulation and profound HIV-induced T cell defects (49). Higher incidences of NHL, of the undifferentiated small non-cleaved (Burkitt's and non Burkitt's) or large cell (histiocytic) subtypes have been reported (48; 256; 316; 408), with up to 2% (352) of AIDS cases displaying these tumours. These tumours were reported infrequently in the early stages of the epidemic, however, with further clinical expertise they are either becoming more common or are being more commonly reported.

Before the advent of AIDS, NHL of the oral cavity was uncommon. The tumour had a mean age of 63 years, with no reported cases occurring in individuals younger than 39 years of age. Between 20% and 32% of intraoral cases were reported to occur on the palate, with only 35% of oral tumours demonstrating bony involvement (231). In contrast, HIV-associated NHL has different clinical characteristics and a more dire prognosis. The age group of affected individuals ranges from 20 to 61 years of age with a median age of 37, 2 years less than any reported cases of non-HIV-associated NHL (231; 408). Whereas 35% of NHL previously involved bone, now up to 45% of oral tumours have been reported to involve bone (231).
These figures suggest a more aggressive behaviour of the lymphomas and a greater frequency in young individuals infected with HIV. However, with limited numbers suitable for effective statistical analysis and the possibility that, prior to the AIDS epidemic, less interest may have been expressed in the form of publication of cases of oral lymphomas in younger patients, these suggestions are difficult to assess accurately.

Additional to the above suggested clinical differences, the natural history and prognosis of HIV-associated NHL has been suggested to be less favourable. This suggestion was provided in the form of a report, by Ziegler and colleagues (408), of 90 homosexual men with NHL, where 62% of lymphomas were high grade, 21% intermediate and only 7% were low grade tumours. Apart from a predominance of high grade malignancy, other factors that may reduce survival time for patients infected with HIV include progressive immunosuppression and the attendant risk of diseases, such as opportunistic infections (for example; PCP).

Although a possible aetiological role for EBV has been raised, there is a paucity of definitive information. A possible link has been suggested by the following findings:

a. Individuals with similar immune-deficient states causing defects in immunity to EBV, such as
allograft recipients, have only rarely been reported to acquire these tumours (177). The increased prevalence of these tumours in HIV infected individuals may be due to the known EBV carriage in homosexual males, the predominant group at-risk for HIV.

b. With the majority of HIV infected individuals being homosexual males, many of these have increased numbers of EBV infected B cells. Subsequent neoplastic transformation and chromosomal aberrations are thought to result from the longevity and increased rate of cell division in these EBV infected cells.

c. The histological identification of EBV DNA by virtue of in situ hybridization techniques, evident in up to 75% of all cases of oral NHL (177).

A recent report by El-Labban and co-workers (481), however, casting doubt on the aetiological role of EBV in HL, similarly raises the possibility that previous studies detecting EBV in lymphomas may have mistakenly diagnosed these membrane-bound structures thought responsible for viral replication (481). Instead, these structures may represent various levels of transversely cut cell processes. Although a direct link has been suggested, it is not clear whether EBV directly induces neoplastic change or whether it infects these cells post-transformation. Further long-term definitive studies are required to ascertain an aetiological role.
From limited information available, it appears that NHL is not commonly seen in the oral cavity (180; 231; 316; 394), with most of these cases already being diagnosed with HIV infection or AIDS prior to the identification of these tumours. Only two reported cases (249; 352) have identified intraoral NHL (of the left retromolar area and gingiva) as the initial manifestation of HIV-related disease. The favoured intraoral sites seem to be the palatal mucosa and bone (231; 316; 394). The gingivae are considered to be a rare site with only four cases reported (316; 394). Other isolated reports have identified lesions of the retromolar area (231; 249), hard palate (231) and recent extraction socket (177), displaying a wide clinical variability. These cases suggest that NHL may present anywhere in the oral cavity.

An anecdotal report (246) of the simultaneous occurrence of disseminated KS and NHL in a homosexual man, that involved the oral cavity, suggests the wide clinical variability of these lesions in association with HIV. The diagnosis of NHL was made after the patient’s death, at which time lesions thought to be KS due to their clinical similarity to previously diagnosed lesions of this type were found to be either pure deposits of lymphoma or collision tumours of KS and NHL. This report further emphasizes the clinical variability of NHL.
The management of intraoral NHL involves specialist referral to an oncologist or haematologist for clinical staging, especially when considering its propensity for extranodal involvement. Treatment may involve radiotherapy and/or chemotherapy depending on the stage of the lesions, although cure rates for all such lymphomas in these patients appears very low (394; 408). From the work of Ziegler and colleagues (408) in 90 homosexual males, 35 of 66 individuals (53%) had complete responses to combination chemotherapy or radiotherapy or both, with 19 (54%) of the 35 having had a relapse. These figures would suggest that 50 (80%) individuals had lymphoma that either showed partial or no response to therapy or relapsed. Of these 50 individuals, 38 (76%) had died as a result of progressive lymphoma or other complicating diseases. These figures clearly indicate the difficulty in managing HIV infected patients with lymphomas and the generally poor prognosis of such individuals.

2.3.3: SQUAMOUS CELL CARCINOMA

Initially considered diagnostic for AIDS by the CDC (Refer Appendix 1C), further classifications indicate that oral SCC may be related more to the advanced HIV-induced immunosuppression, hence its listing as an HIV-associated disease (Refer Appendix 1D). This change in classification arose from the limited number of case reports of oral SCC in association with HIV. These isolated reports have identified SCC of the buccal
mucosa (18; 249), arytenoid cartilage (18), floor of mouth (352) and tongue (352; 316).

It seems that the inclusion of SCC as a diagnostic criterion in the early stages of the epidemic was based solely on two studies, by Lozada-Nur and co-workers (249) in 1983 and Silverman and colleagues (352) in 1986. The first study (249) reported two cases of SCC, of the floor of the mouth and tongue in 53 individuals; while Silverman et al. (352) reported seven cases in a study of 375 homosexual males, with all lesions occurring in the same sites. These authors concluded that these were not coincidental findings for two reasons:

a. The incidence of oral carcinoma is only seven cases out of 100,000 of the general population per annum.

b. These lesions presented in an age group not commonly affected, with a mean age of only 36 years.

However, these studies (249; 352) make no mention of the age, alcohol consumption or drug habits of those studied, making a direct association with HIV difficult. Also, while the average age of these patients (mean age 36 years) is less than that expected of oral SCC in the general population (average age 60 years (483)), possibly suggesting an association with HIV, small numbers and the likelihood that individuals entered both
studies because of oral pathology may incorrectly associate a higher incidence. Further suggestive of a lack of association with HIV comes in the form of more recent studies (315; 327; 334), involving a combined total of 297 individuals, which have failed to identify any cases of oral SCC. The inconsistency of these findings casts significant doubt on a possible direct relationship with HIV infection.

Previous suggestions of oral SCC in younger individuals (mean age 36 years) with HIV infection may merely reflect the predominant ages of those individuals infected by HIV. In a study by Krolls and colleagues (482) of 14,253 individuals of the general population, 3.5% of oral SCC were found to occur in those less than 30 years of age, indicating that the presentation of these lesions in young individuals is not extremely rare. This finding also indicates that oral SCC may not necessarily be associated with HIV infection.

Furthermore, the study by Krolls and co-workers (482), in addition to that by Rich and colleagues (483), have both indicated an increasing trend towards a rising number of cases in younger individuals of the general population. With 11% (1,039 out of 9,775) of individuals up until 1976 exhibiting oral SCC, it seems that the finding of only nine cases in HIV infected patients (249; 352), with a mean age of 36 years, may have no statistical significance nor directly associate this lesion with HIV.
2.4: **OTHER REPORTED FINDINGS**

Many authors have attempted to directly associate lesions that have been reported infrequently with HIV infection, leading to the provisional inclusion of an assortment of apparently unrelated conditions in current classification systems, such as that proposed by Pindborg (316). It is unclear whether the setting of HIV-induced immunosuppression allows the development of such lesions, or whether they would have occurred in the absence of HIV.

In this way, isolated reports in HIV infected individuals of the following lesions of the oral cavity; toxic epidermolysis (327), granuloma annulare (178), oral hyperpigmentation (239; 262; 316), epithelioid angiomatosis (90; 158; 244; 316), infection by Actinomycosis species (316; 405), facial palsy (397), odontalgia (272), severe sinusitis (258; 316; 384), and erythema multiforme (265) have been suggested as being associated with HIV infection. However, these lesions also occur in those individuals not infected with HIV and, without adequate prevalence studies, may not appear to present with any greater frequency in association with HIV-induced immunosuppression.

Oral lesions due to various venereal diseases, such as syphilis and gonorrhoea (334; 349; 352), have been noted in seropositive patients. These lesions have been confined to homosexual males and seem to be directly
related to lifestyle practices. In this way, these oral lesions are indicative of a lifestyle conducive to HIV infection, thereby representing a possible marker for HIV. Salivary disturbances have been noted in between 6% and 13% of those at varying stages of the disease (316; 334; 343; 352), but does not appear to be directly related to HIV. Disturbance of salivary flow may be due to involvement of salivary glands by CMV, HIV, venereal diseases or KS, or may result from drug therapy, chemotherapy or radiotherapy.

Although the above reported findings are difficult to directly associate with HIV-induced immunesuppression, the findings of a progressive form of necrotic ulceration and delayed wound healing seem to be suggestive of lesions that arise directly due to the diminished host response.

2.4.1: **PROGRESSIVE NECROTIC ULCERATION (PNU)**

Initial reports of oral ulceration described these lesions as major aphthae (352) or gangrenous stomatitis (165; 395). Several reports of an HIV-associated necrotizing stomatitis or HIV periodontitis (Refer Section 2.2.2.a), exhibiting an ulcerative nature, may represent a periodontal expression of PNU. A possible association with HIV-induced immunesuppression was suggested by reports of extensive and non-specific progressive ulceration in between 2% and 10% of all seropositive individuals, where not accounted for by
other definitive causes (180; 316; 334; 343; 352). This form of ulceration has been reported to occur anywhere in the oral cavity; including the buccal mucosa, gingiva, palate, tongue and periodontal tissues, with severe cases involving the hypopharynx and oesophagus (29; 315; 316; 352).

A differential diagnosis must include a consideration of other previously discussed lesions of the oral cavity seen in association with HIV infection (for example; KS, SCC, lymphoma, lesions due to CMV, Cryptococcus and Histoplasma species and herpes simplex virus). PNU is a clinically descriptive term that does not indicate aetiology. Biopsy with special stains and culture for opportunistic pathogens plays an important role in identifying these lesions - a diagnosis made essentially by exclusion.

Accumulating evidence (29; 165; 316; 395) can be found to suggest that there is an entity which is of unclear aetiology, prolonged and progressive in nature and frequently requiring intensive palliative pain relief and nutritional support. Further identification and study of these lesions may indicate the underlying mechanism; perhaps based on grossly disordered local inflammatory and repair processes. This particular lesion may well be retained in future classification systems.
2.4.2: DELAYED WOUND HEALING

Delayed wound healing is considered relatively common due directly to a diminished host response resulting from HIV infection. It has been observed, usually at advanced stages of HIV infection, after simple and surgical extractions, periodontal therapy, osteotomies and biopsies (106; 316; 327; 343). The general dental practitioner needs to consider the possibility that the delayed wound healing of any extraction socket or intraoral wound may be indicative of an HIV-induced immunosuppression. Further research may indicate that the underlying mechanism(s) is similar to that of PNU.

The above is a summary of those lesions affecting the oral cavity which are closely associated with HIV-induced immunosuppression or thought to have some connection. The following main points are clear:

a. The uniqueness of some of these lesions.

b. The challenge many of these lesions pose to diagnosis.

c. The problems of management primarily due to the underlying disturbance of host response factors.
Further investigation may provide the following:

a. The range of lesions that can be definitively connected with HIV will be extended.

b. An elimination of the direct connection of some of these lesions.

c. The probable extension of the range of possible clinical presentations of any one particular lesion.
2.5: **TABLES**

**TABLE 2.5.1: CLINICAL PRESENTATION OF ORAL KAPOSI’S SARCOMA**

<table>
<thead>
<tr>
<th>Investigator (Reference)</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lozada et al. (249)</td>
<td>Flat, bluish, vascular lesions. Exophytic pigmented lesions.</td>
</tr>
<tr>
<td>Eversole et al. (135)</td>
<td>Violaceous plaques, red or purple tumefactive nodules.</td>
</tr>
<tr>
<td>Marcusen et al. (258)</td>
<td>Bluish, angiomatous lesions.</td>
</tr>
<tr>
<td>Nickles et al. (293)</td>
<td>Reddish area.</td>
</tr>
<tr>
<td>Silverman et al. (352)</td>
<td>Flat, asymptomatic vascular-like discolorations; exophytic growths.</td>
</tr>
<tr>
<td>Green et al. (176)</td>
<td>Flat, pigmented lesions; raised or exophytic, pigmented lesions.</td>
</tr>
<tr>
<td>Wofford and Miller (399)</td>
<td>Red, violet, pink or purple macules, papules or nodules.</td>
</tr>
<tr>
<td>Daly et al. (106)</td>
<td>Painless, non-pigmented soft swelling.</td>
</tr>
<tr>
<td>Barrett (37)</td>
<td>Ulcerative, non-discoloured lesions.</td>
</tr>
</tbody>
</table>
CHAPTER THREE

THE DENTIST'S ROLE IN
THE MANAGEMENT OF
HIV INFECTION
The treatment of HIV infection in the dental operatory raises many clinical, ethical and medicolegal issues. The main aim of the dental practitioner may be seen as providing an ethical standard of care to all individuals, whether carrying any infectious disease or not, and the prevention of disease transmission by appropriate educational intervention and infection control procedures. As a professional healthcare worker, the dental practitioner has a responsibility to both the patient and the community.

The direct responsibility of the dental practitioner to patients in relation to HIV may be seen as follows:

a. To provide early intervention by the identification of HIV infection within the dental surgery. This is achieved by an evaluation of risk behaviours (Refer Section 1.4) or oral manifestations suggestive of HIV infection (Refer Section 3.1.1.3 and Chapter 2).

b. To provide comprehensive, often multidisciplinary care (Refer Sections 3.1.1.1 and 3.1.1.2), with due concern to the complex issue of confidentiality (Refer Section 3.1.1.4).

c. The provision of care may involve the establishment of links with centres for further management and testing, and the establishment of a close working relationship with a network of other healthcare workers. This interaction may primarily involve infectious disease physicians and clinical
immunologists, with adjunctive interaction with oncologists, radiotherapists, respiratory physicians, palliative care physicians, counsellors, clinical nursing specialists, social workers, pharmacists, dieticians and clergy (Refer below).

d. Prompt and early recognition of both HIV and its various oral manifestations (Refer Chapter 2) allows for early intervention and prompt management. These, coupled with an increasing standard of care, management of opportunistic infections and nutritional support, allows for increased survival rates for those infected with HIV.

In addition to these responsibilities to the patient, the dental practitioner also has an important responsibility to the general community:

a. To provide a form of surveillance, principally in the form of clinical examination, histories and special investigations, of the general population that seek routine dental care. In this way, the dental practitioner performs an important clinically-based screening method for a large proportion of the population. The fact that up to 95% of all HIV infected individuals, as suggested by Marcussen and colleagues (258), develop oral manifestations at some stage of HIV infection
underlines the importance of this form of surveillance of the general community.

b. The dental practitioner has an ethical obligation to treat seropositive patients who present for dental care within their scope of training and expertise and, where specifically indicated, to refer these patients for adjunctive specialist dental and/or medical opinion (Refer Section 3.1.1).

c. To provide a safe working environment in order to prevent the transmission of HIV between patients and staff (Refer Sections 3.1.2 and 3.2.2).
3.1: CLINICAL ASPECTS

Without the utility of mass serological screening, the dental practitioner cannot be certain of a patient’s infectivity in the majority of cases (161). This uncertainty is further compounded by the following:

a. Anecdotal reports suggesting a seronegative infectious period, lasting up to 35 months (461) before detectable antibody is produced, further questions the efficacy of serological screening in identifying cases of HIV infection (Refer Section 1.2).

b. The inability of medical histories and oral examinations to identify all cases of HIV infection. It has been suggested by Gerbert and co-workers (161) that up to 90% of those infected with HIV are unaware of their seropositive state. Even less cases of HIV infection may be identified in an emergency setting, especially in cases of multiple trauma and head injuries.

c. With seemingly limited cases actually being recognized, it raises the possibility of the transmission of other viral diseases such as HBV, HSV and CMV.

These difficulties in definitively assessing the infectious status emphasizes the need to consider all individuals as potentially infected with HIV and/or blood-borne pathogens, and to adhere rigorously to
widely recommended infection control procedures (12; 13; 16; 36; 40; 65; 66; 68; 76; 78; 96; 98; 221; 287; 361), as set out in Section 3.1.2 and Appendix 3A, for minimizing the risk of exposure to potentially infected blood and body fluids.

These guidelines, widely endorsed by the National Health and Medical Research Council (NH & MRC) and the Centers for Disease Control (CDC), and referred to as "universal blood and body fluid precautions", should be used in the care of all patients, with special emphasis placed on the provision of care where the HIV status is unknown (for example, emergency settings and where serological testing is refused) (12; 13; 16; 36; 40; 65; 66; 68; 76; 98; 287; 401).

The provision of dental treatment to those possibly infected with HIV enforces the need for dental practitioners to perform the following functions, in addition to those outlined previously:

a. To establish and maintain optimum standards of infection control that should have the maximum potential to prevent the spread of infectious diseases, including HIV, between patients and staff. Unfortunately this optimum standard is difficult to achieve in the setting of general dental practice (Refer Section 3.1.2), mainly because equipment is designed poorly in terms of preventing disease transmission. Therefore, it is
not possible to achieve the same standards of infection control provided in the setting of an operating suite.

b. The need for continuing voluntary education on the part of dental healthcare professionals, especially in relation to the nature and prevention of infectious diseases. These may take the form of postgraduate courses, journals, tutorials, seminars, text books and video tapes. The efficacy of educational intervention has been suggested by Gerbert and colleagues (161; 163), who attempted to relate an increase from 21% (1986) to 31% (1988) of practitioners willing to treat AIDS patients directly to educational programmes.

c. The need to constantly review standards of care and infection control in dental practices via an inbuilt quality assurance systems.

In relation to these matters, the representative dental organizations (in particular, the Australian Dental Association and Universities) have a strong role, if not obligation, to fulfill in the provision of ongoing education. As a result of increased education concerning HIV in the general community, patients are now expecting to see active evidence of rigid infection control procedures in dental operatories. Visible evidence of attempts to prevent disease transmission reflects a concern for the patient’s welfare and may aid in building a practice. This notion of patients seeking signs of infection control has been suggested previously
by Gerbert and colleagues (164) and Bowden and colleagues (414).

3.1.1: **THE PROVISION OF CARE TO HIV INFECTED INDIVIDUALS**

The important responsibility the dental practitioner bears to the patient and the community has been outlined previously (Refer Section 3.1). The management of patients who are infected with HIV will be addressed under the following four headings:

3.1.1.1. The provision of multidisciplinary care.
3.1.1.2. The extent of routine dental treatment offered.
3.1.1.3. The identification of cases of HIV infection.
3.1.1.4. The issue of confidentiality.

3.1.1.1: **THE PROVISION OF MULTIDISCIPLINARY CARE**

In addition to routine dental care afforded by the general dental practitioner, further management may be provided by specialist dental and medical practitioners and physicians. This raises the need for the provision of an adequate referral system that may include interaction not only with those healthcare workers mentioned above but also with specialists in the fields of oral medicine, oral and maxillofacial surgery and periodontics. With advanced HIV-induced
immunesuppression there is an increasing potential for multidisciplinary management, that is combined dental and medical consultation and management. As a result of increasing mucosal disease (Refer Chapter 2), oral care may become polarized towards the specialized fields of oral medicine and periodontics, for example, rather than the discipline of routine restorative dentistry.

Practitioners must identify treatment that is beyond their sphere of expertise or experience and provide appropriate referral where specifically indicated (Refer below). Many practitioners, unwilling to treat those infected with HIV, refuse treatment (Refer Section 3.2.1) or provide referral to a limited number of willing practitioners in private and public hospital practice. This attempt to transfer the burden of the HIV epidemic has been suggested by several studies from the USA showing that between 69% and 79% (161) of dental practitioners would not treat HIV infected individuals and that between 63% (163; 195) and 74% (162), in other studies, would rather refer these patients.

Dental practitioners have an ethical imperative to treat patients, including those with HIV infection. A common reason given for declining treatment is an inability to guarantee the prevention of transmission of infectious diseases. This would seem to suggest that the dental practitioner is also unable to prevent the transmission of HIV for the 90% (161) of infected individuals treated in the dental operatory whose
serological status is unknown. In this way, the practitioner cannot give any such guarantee to any patient. This then raises the question of whether adequate safety, in terms of infection control, can be assured for all dental patients and, therefore, whether such practitioners should continue in the provision of dental care.

There are two direct consequences of the referral of cases of HIV infection to selected practitioners in private practice or public hospital settings:

a. There is an increased risk of HIV transmission in the referring practitioner’s surgery because they believe, that by excluding known HIV infected individuals, they have rid their practice of HIV infection. Resulting from this belief, there would be a declining awareness of proper infection control procedures with a concomitant increased risk of HIV transmission.

b. The burden of managing HIV infected patients would then fall on a limited number of willing practitioners in private practice or public hospitals, where resources are already stretched. Confining the management of large numbers of these individuals to only a small number of practitioners would also increase the relative risk of accidents, such as needlestick injuries.
However, the dental practitioner may decline treatment to HIV infected patients under certain circumstances and may need to arrange appropriate referrals, where specifically indicated, in order to provide multidisciplinary medical and dental care. Such circumstances may include the following:

a. Where the patient requests extensive elective treatment (for example, crown and bridge work) that is not warranted.

b. Where severe medical complications related to HIV make management in a private practice setting difficult. In this way, conditions such as thrombocytopenia, secondary to bone marrow suppression, either as a consequence of drug therapy or HIV, would be more suitably managed in a hospital setting.

c. Where the treatment required is beyond the experience and expertise of the dental practitioner, as in the case of the need for specialist oral medicine, oral and maxillofacial surgery or periodontic opinion.

3.1.1.2: **THE EXTENT OF ROUTINE DENTAL TREATMENT OFFERED**

Specific guidelines outlining the extent of dental treatment to HIV infected patients cannot be found, with the majority of literature being primarily concerned with the diagnosis and management of the various HIV
related oral manifestations. However, the following factors may cause modification of dental treatment plans for those infected with HIV:

a. Factors that would cause similar modifications of treatment in non-HIV-infected patients, such as specific contraindications, an inability to pay, poor oral hygiene or motivation.

b. The presence of HIV-associated medical and oral complications, some examples of which are:
   * HIV-associated periodontitis (HIV-P) or HIV-associated necrotizing stomatitis (HIV-NS).
   * Debilitated states which may restrict the use of general anaesthetics or the ability of patients to undergo complex and prolonged treatment.

c. The immediate and long-term prognosis of the patient ascertained by appropriate clinical and laboratory evaluation (Refer Chapters 1 and 2).

Without specific treatment directives set down for dental practitioners to follow some general, if not provisional, guidelines must be addressed. In the present author’s opinion, management from a dental perspective may be no different from that of non-infected patients, except in the advanced stages of HIV infection. The underlying theme throughout management revolves around the prevention of disease transmission (Refer Section 3.1.2 and Appendix 3A).
Modification in treatment occurs in the latter stages of HIV-induced immunosuppression in much the same way that other medical conditions, such as congestive cardiac disease, poorly controlled diabetes and immunosuppressive drug therapy may modify treatment.

At the better end of the spectrum, with no hint of advanced immunosuppression, HIV infected patients may be treated in the same manner as those not infected, with special care taken to prevent disease transmission. It is reasonable to assume that currently dental practitioners willingly provide routine dental care to the majority of the suggested 90% (161) of HIV infected individuals who are unaware of their HIV status. Suggestions of a variable incubation period for AIDS (Refer Section 1.2.3) and anecdotal evidence that infected individuals may not proceed to advanced stages for periods up to 11 years, as suggested by Guarino and colleagues (466), underlines the need to provide routine dental care to those patients without advanced stages of HIV disease.

Modification becomes necessary when there are clinicopathological signs of significant deterioration. In this way, simplification of the treatment plan may be required, in addition to a need to construct a close confidential working relationship with medical colleagues, in particular, the patient's physician.
Therefore, in advanced cases of HIV infection the treatment objectives may be seen as:

a. To maintain the individual in relative comfort by the elimination of pain without further compromising the patient’s health.

b. To tailor treatment in such a way as to address the most urgent needs and refrain from performing elective treatment.

c. The elimination of any possible source of oral infection that may lead to systemic complications, within the patient’s ability to tolerate necessary dental care.

d. Careful periodic evaluation and examination of the oral cavity to monitor disease progression.

3.1.1.3: THE IDENTIFICATION OF CASES OF HIV INFECTION

The dental practitioner currently relies on two methods of screening to identify cases of HIV infection:

a. Detailed clinical examination aimed at detecting oral, perioral and systemic manifestations suggestive of HIV infection, as set out in Chapters 1 and 2.

b. Thorough and comprehensive medical histories, in the form of continually updated direct questioning or signed questionnaires. Primarily aimed at evaluating risk (behavioural) factors (Refer
Section 1.4), enquiries should be made of generalized symptoms (Refer Section 1.2.2) and a history of infectious disease suggestive of HIV infection, in particular multiple sexually transmitted disease and Hepatitis B.

Possible cases of HIV infection, as suggested by these two clinical methods, can be confirmed by judicious serological screening with due concern for informed consent (Refer Section 1.5), counselling procedures (Refer Section 1.5) and confidentiality (Refer Section 3.1.1.4). However, this form of surveillance cannot identify all cases of HIV infection, indeed, even mass serological screening may not identify all cases given the possibility of a seronegative infectious state (Refer Section 1.2.3). However, with only isolated anecdotal reports of seroconversion following seronegative blood donations, considerable support for continued screening remains.

The following points also raise doubts as to the efficacy of identifying cases of HIV infection by current screening methods:

a. In the case of Hepatitis B, it has been shown by Goebel (169) and other authors (76; 277; 364) that a medical history alone cannot identify all at-risk patients. Presumably the same applies to those at-risk for HIV infection.
b. The inadequacy of medical histories has been suggested by Stevenson and Higgins (364), where 7% of all dental practitioners in New South Wales seldom obtain any form of history and only 28% attempted to identify any of the risk behaviours conducive for HIV transmission.

c. A survey of dental schools worldwide suggested that cases of HIV infection do not represent a high priority, with only 13% of these dental schools screening patients from high risk groups. The situation seems to be slightly better in Australia with 60% of Australian dental schools screening those patients from high risk groups (277). This attitude in teaching institutions is reflected in the abovementioned inadequacies of medical histories.

In the absence of mass serological screening, the dental practitioner must primarily rely on combining detailed clinical examination and medical histories with serological confirmation to identify cases of HIV infection. However, an inability to detect all such cases by these methods emphasizes the need for the practitioner to consider all patients as potentially infectious.

3.1.1.4: THE ISSUE OF CONFIDENTIALITY

As outlined previously, the dental practitioner has clear cut ethical and legal responsibilities to both the
patient and the general community. With the advent of HIV infection the issues of confidentiality have become increasingly complex. This is due partly to the fact that HIV has brought an infectious disease, more characteristic of epidemics of other centuries, into the mainstream of modern medicine and society. It is the first infectious disease to occur during the era of human rights, with regulated guidelines and laws setting aside the rights of the individual and the expectation of a safe working environment that is free of avoidable risk.

In so far as routine dental treatment is concerned, there is generally no conflict between the practitioner's ethical and legal responsibilities. However, HIV raises the clear-cut potential of infecting other individuals, in particular sexual partners and physicians. This raises the question of when dental practitioners may breach the ethical confidentiality of a doctor-patient relationship on a need-to-know basis.

Possible disclosures must be evaluated on a perceived risk/benefit ratio. The benefit of highly selective dissemination of information regarding a patient's seropositivity, on a strict need-to-know basis, can be seen as the notification of inherent risks involved for physicians and sexual contacts. On the other hand, possible risks of such disclosure may be seen as loss of employment, insurance coverage, refusal of medical and dental services and the disruption of relationships with
family and friends. Legal advice (PC1: Refer Personal Communications) suggests that informed consent, preferably in written form, should be the basis of possible disclosures outside of the doctor-patient relationship.

Informed consent relies on mutual co-operation between the patient and physician to ensure that disclosure is selectively performed to those who need-to-know. In this way, there are two scenarios depending on the degree of co-operation:

a. Full co-operation.

  b. Lack of co-operation.

a. **Full co-operation.**

In this scenario, the patient may agree to personally divulge his/her HIV status or give informed consent, in written or verbal form, to the physician or dental practitioner for such disclosure. The benefits of this situation may be seen as:

i. The infected patient can be suitably managed in light of their HIV status.

ii. Informed parties, in the form of physicians or sexual partners, are made aware of inherent risks and can utilize necessary risk reduction procedures in order to prevent disease transmission.
iii. The referring physician has ethically fulfilled all obligations to the community and is legally allowed to selectively divulge required information due to informed patient consent.

b. **Lack of co-operation**

Without co-operation, the infected patient is reliant on the dental practitioner's code of ethics to maintain confidentiality. With a clear-cut potential of infecting other individuals (in the form of unwitting sexual partners or attending physicians), the responsibility is raised of a preventable disease that the practitioner tries, in the first instance, to remedy by direct educational means aimed at gaining co-operation in the form of informed consent. Failing this, the ethical responsibility remains and suggests the need for others who may be placed at-risk to be properly informed. In this way, the physician or dentist needs to wrestle with various ethical and legal considerations concerning disclosure, which are complicated by limited legislation and a lack of legal precedence regarding the disclosure to other individuals on a need-to-know basis. Therefore, choosing to disclose a patient's seropositivity on ethical grounds to another physician, in light of limited legislation, may constitute a breach of confidentiality and form a legal precedent.
This raises the question of how best to manage seropositive patients in the dental operatory while attempting to maintain the confidentiality of the dentist-patient relationship. The following recommendations, based on current legal advice (PC1: Refer Personal Communications), seem appropriate:

i. Written informed consent, resulting from the mutual co-operation of all parties, forms the ideal basis for any possible disclosure. The value of verbal consent in litigation cases is less certain, with no legal precedent having been set in connection with HIV confidentiality. In this way, appropriate education aimed at highlighting the benefits of selective disclosure to seropositive patients in order to gain written consent cannot be underestimated.

ii. In order to prevent indiscriminate disclosure to other patients, there are two important considerations. Firstly, dental staff should be carefully selected and educated regarding the legalities of potential breaches of confidentiality. Secondly, treatment could be rescheduled at such a time, either at the beginning or end of the day, to prevent any suspicion of added precautions or detailed questioning.

iii. In cases where mutual co-operation is not achieved, the individual practitioner must decide on the need to breach the doctor-patient relationship. If this is considered necessary on ethical grounds, there
are two possibilities open to the practitioner. The first option, made available by New South Wales (NSW) Department of Health Guidelines (491), allows for such disclosure to the Chief Health Officer, who may then act in the interests of all parties by placing certain restraining powers on the seropositive individual. This option allows the practitioner to fulfill his/her ethical and legal responsibilities to both their patient and the general community.

The second option involves the disclosure of information directly to other practitioners. In the USA, legislation allows such disclosure in 17 states (221; 485; 486; 487); however, like Australia there is currently no legal precedence in this area. Therefore, although the practitioner may seem to be acting on sound ethical considerations, subsequent court action may find a breach of confidentiality. In this regard, learned legal advice from barristers, fully conversant with HIV legislation, should be sort before any possible breach is performed.

The position of the dental practitioner in relation to confidentiality, as it applies to HIV, is not well defined but should be based on that which applies to medical practitioners because the ethical and legal responsibilities to the individual and the community for both professions are similar. There are several options
open to the general dental practitioner in the situation where a patient is found to be or admits to being HIV positive, but states a clear-cut unwillingness for this information to be disclosed beyond the bounds of the immediate dentist-patient relationship. In such a case, those at potential risk could include fellow healthcare workers (HCW’s) or sexual partners of the patient. In the latter case, the unsuspecting wife of a bisexual man raises a particular problem for the dental practitioner in terms of defining his/her ethical responsibility to that third party, and by inference, to the community at large.

In essence, the dentist has the choice of confining his/her ethical framework simply to the immediate dentist-patient relationship, which removes any ethical obligation to inform the third party. The second alternative is to accept the responsibility to redefine their personal ethical parameters to include notification of potentially at-risk third parties. Current legal advice (PC1: Refer Personal Communications) and a lack of legislation to the contrary would appear to permit disclosure to other HCW’s involved in the patients management on a strict need-to-know basis.

However, in the case of a sexual partner of a patient so infected, two options open to the dental practitioner may include non-disclosure or disclosure to the Chief Health Officer, as provided by current New South Wales
(NSW) Department of Health Guidelines (491). Under the present legislation, a dental practitioner could notify the chief health officer from NSW of the risk an infected patient may pose to others. The steps that may follow such notification include attempts at rectification by direct educational means and, if such measures fail, a written warning of the possibility of confinement if risk behaviour does not cease. Confinement remains a last resort but has been evoked recently in NSW.

Disclosure through a third option, that is direct disclosure to the third party (in this case, the sexual partner) or indirect disclosure via this individual’s physician, has no basis in legislation (PC2: Refer Personal Communications). Furthermore, this course of action may expose the dentist to medicolegal challenge, as action may generally be perceived to have been taken outside of the normal ethical boundaries of general dental practice.

In light of possible litigation, it is the present author’s opinion, based entirely on a personal ethical imperative to prevent disease transmission within the community and to provide early educational and therapeutic intervention, that it is within the dental practitioner’s ethical parameters to disclose the HIV status of an individual to others who are unknowingly placed at-risk. This disclosure must be made with the full knowledge that it may be considered beyond the
boundaries of general dental practice and lead to subsequent medicolegal precedent.

In summary, while personal notification of a third party at-risk represents a valid option, in the opinion of the present author, intervention through the Chief Health Officer (491) appears to be the preferred option. This preference is made given current legislation designed to protect the interests of the general community in carefully selected instances of at-risk behaviour that has not been rectified by conventional educational means. Future legislation, however, may well modify these available options.

3.1.2: THE PREVENTION OF HIV TRANSMISSION

Preventing the transmission of infectious disease has always been an important consideration in dental practice. The key to effective infection control, regardless of the microorganisms concerned, remains the establishment and maintenance of high standards of general clinical hygiene for all patients (13; 16; 36; 40; 65; 98; 99; 100; 364).

Hepatitis B virus (HBV) is the target disease when discussing issues of infection control because of its modes of transmission, virulence, infectivity and epidemiology within both the general population and HCW's. Therefore, guidelines set down to prevent the transmission of HBV are applicable to HIV. The
guidelines suggested by the NH & MRC (Refer Appendix 3A) provide the most accurate and expedient method of preventing HIV transmission and are similar to other suggested protocols for infection control (13; 16; 36; 40).

Any guidelines for infection control must fulfill the following criteria:

a. They should be simple in concept and as practical as possible.

b. They should be generally applicable to all patients with infectious disease encountered in dental practice (for example, HSV, HIV, HBV, CMV and delta hepatitis).

c. They should be readily applicable to both general and hospital practice.

d. They should be compatible with the present practise of dentistry and undergo constant evaluation to incorporate improved suggestions and future developments.

Effective infection control may be separated into two different aspects:

3.1.2.1. The prevention of contamination.

3.1.2.2. The elimination of contamination.
3.1.2.1: THE PREVENTION OF CONTAMINATION

Effective infection control should be based on preventing contamination rather than eliminating it once established. This prevention of contamination may be achieved in four ways:

a. Limited surface contamination.

b. The use of disposable equipment and materials where necessary.

c. Personal hygiene.

d. Personal protection.

3.1.2.1.a: Limited surface contamination

(Refer Appendix 3A; Section A1)

Limiting those items or areas that may be contaminated, within a predetermined zone of contamination, is consistent with the principles of "motion economy" and represents the most fundamental method of preventing disease transmission (36; 40; 287). Its application reduces the areas requiring subsequent elimination procedures after each patient. The use of autoclavable handpieces and triplex syringes has been widely recommended, often with the use of plastic wrap around handpiece connections (Refer Appendix 3A; Section A.1.10.2). The disinfection of work destined for the laboratory (for example, dentures and impressions) eliminates the possibility of cross-infection (Refer Appendix 3A; Section A.1.12).
3.1.2.1.b: The use of disposable equipment and materials where necessary

(Refer Appendix 3A; Section A2)

All materials, equipment and instruments used in the dental operatory should ideally be either disposable or heat sterilizable, however, with present day equipment this is not possible. For those items that are not heat sterilizable or disposable, predispensing of materials (Refer Appendix 3A; Section A.1.7) and the use of effective antiviral disinfectants become important.

3.1.2.1.c: Personal Hygiene

(Refer Appendix 3A; Section A3)

Personal hygiene in the form of routine glove use changed after each patient (Refer below and Section A.4.1) and frequent, thorough hand washing with povidone-iodine scrub is an effective simple method of preventing contamination.

3.1.2.1.d: Personal Protection

(Refer Appendix 3A; Section A4)

Due to the nature of our work, dental healthcare professionals are prone to ocular injuries from fragments of amalgam. Apart from a possible loss of sight, the possibility of the transmucosal spread of HIV from splashes in the eye has been suggested previously
(Refer Section 1.4.8), by reports of transmission via breast milk and during artificial insemination (434; 470). It remains unclear whether HIV is able to cross the ocular epithelial barrier, however, the transmission of HBV has been implicated in this manner in hospital workers (503) and duplicated experimentally in a chimpanzee, as noted by Jakush et al. (221).

Additionally, dental practitioners are prone to both percutaneous injuries from needles and sharp instruments and inapparent frank percutaneous inoculation by the droplet contamination of inapparent cuts on the face and hands. Therefore, the routine use of gloves, face masks, protective eye wear and clothing that provides maximum coverage are necessary.

The routine use of gloves are recommended for the treatment of all patients, including those that may not be infected with any infectious disease. This form of personal protection is not meant to prevent such accidents as needlestick injuries, but forms an effective barrier from the possibility of transmucosal and inapparent frank percutaneous transmission.

The efficacy of routine glove use has been demonstrated by Allen and Organ (20), where over 80% of dental practitioners displayed occult blood impaction under the finger nails after performing routine dental treatment not involving surgery. Even after frequent hand washing over a five day period, more than 30% of practitioners
still displayed blood impaction. Furthermore, all practitioners were found to have cuts on their hands (range 1 to 11; average 4) that could potentially act as channels for HIV transmission via inapparent percutaneous means.

Current NH and MRC guidelines recommending the use of double gloves (Refer Appendix 3A; Point A.4.1) are in accordance with the recommendations of other authors and professional organizations (12; 13; 16; 36; 65; 66; 68; 74; 75; 76; 96; 126; 173). Underlining their importance is the recommendation by specialists in the field of endodontics, a practice requiring complete tactile sensation, for the use of double gloves for all patients with infectious disease (99; 100).

Mitchell (275) found that gloves were sufficiently durable for repeated dental procedures and sterilization, and could be completely rid of all bacterial flora by the use of 10% povidone-iodine solution. Similar studies agree that surgical gloves could be washed completely free of bacteria (143; 168; 173). The reuse of gloves, though, must be coupled with the knowledge of potential hazards, including punctures of the rubber surface. An evaluation of several types of surgical gloves found that "pin holes occurred randomly and were independent of glove use or sterility". All brands of gloves tested had pin holes ranging from 1.7% to 9% (168). The use of disposable gloves, with replacement between every patient is ideal,
even though several authors (168; 275) have suggested that washing gloved hands effectively removes more bacteria than the washing of ungloved hands.

Without routine testing of both dental patients and dental healthcare workers there is no evidence suggesting that gloves do not prevent HIV transmission. However, it is logical to assume they do provide an effective barrier, based on the documented efficacy of gloves in preventing the transmission of HBV from carrier dentists to their patients (229; 503).

The current NH and MRC guidelines (Refer Appendix 3A), allowing for the careful resheathing of dental hypodermic syringes (Refer Appendix 3A; Point A.4.5), is in direct contravention of previous guidelines (116; 284; 371; 378; 388). This change in recommendations has been as a result of:

a. A realization that dental practice involves the careful handling of many sharp instruments, including needles.

b. An unsheathed syringe will require disassembly at some stage, and disassembly using haemostats or leaving it unsheathed on the bracket table are both undesirable.

c. A realization that the syringes used in dental practice differ from those used in medical practice (Refer Appendix 3A; Special notes; Point 8).
3.1.2.2: **THE ELIMINATION OF CONTAMINATION**

The elimination of contamination, the second principle of infection control, relies on the often combined use of chemical and physical methods. It is generally considered that physical means, mainly in the form of autoclaving are ideal (12; 65; 115; 126; 287); however, the design of current dental equipment and an inability of many instruments to withstand these methods means that chemicals may need to be used either solely or in combination with physical elimination (13; 15; 16; 36; 40; 287).

a. **Physical Methods**

Physical methods, principally in the form of autoclaving and dry heat sterilization, are widely accepted as the most effective methods of eliminating contamination (12; 13; 15; 16; 36; 40; 287). Martin and colleagues (260) conclusively showed that "the use of boiling water" was "totally inadequate for instrument sterilization in general dental practice". However, a study by Stevenson and Higgins (364), displaying similar results to other studies (99; 115), showed that regardless of this fact, 25% of NSW dental practitioners still use this method routinely to sterilize instruments.

The physical removal of serum residues and debris is also an important method of maintaining the efficiency
of both physical and chemical elimination methods. This removal may take the form of washing instruments by hand or in an ultrasonic cleaner prior to elimination procedures, as suggested by Simpson and co-workers (354). Christensen and co-workers (496) conclusively showed the diminished effect of chemical sterilants-disinfectants due to residues of blood (Refer Appendix 3A; Section 4.5).

b. Chemical Methods

Being a retrovirus, HIV is regarded as being quite labile against environmental influences, losing its infectivity within a short period of time outside of a natural host (494). Doubts about this hypothesis arose because, under experimental conditions, infectious cell free virus could be recovered from dried material after up to 15 days at room temperature (329; 493). However, it must be realized that the concentrations of HIV used in these studies were much greater than those commonly encountered in patient derived specimens (for example; fresh blood). It is clear though, from these studies and that by Martin et al. (261) that viral particles, possibly including HIV, may be present in a dental operatory, on surfaces such as benches, floors and handpieces. Fortunately, HIV behaves similarly to other enveloped retroviruses regarding its sensitivity to chemical sterilants and detergents (260; 261; 329). All officially recommended chemical sterilizing agents effective against HBV have since been shown to be
effective against HIV (260; 261; 329; 401; 496). More significantly, any chemical with active ingredients such as sodium hypochlorite, formaldehyde, glutaraldehyde and phenol have been shown to kill HIV at concentrations much less than those used in general dental practice (261).

Chemical sterilants-disinfectants may be used for the elimination of contamination on surfaces that cannot be heat sterilized, such as benches, cabinets and handles. Similarly, they may be used as immersion agents for dental instruments and materials not able to withstand heat sterilization, and designated by Jakush (221) as "semi-critical" or "non-critical" items. Present guidelines from both the AIDS Task Force and the NH & MRC (12; 13; 15; 16; 36; 40; 287) permit the use of chemical sterilants-disinfectants in the decontamination of dental handpieces between patients.

Glutaraldehyde (as a 2% or 1% solution) has been widely recommended as a suitable decontaminant for semi-critical and non-critical instruments and work surfaces, irrespective of the presence of blood and body fluid contamination. The AIDS Task Force in Australia advocate a 2% glutaraldehyde solution, even though they state that lower concentrations are effective against HIV (12; 13; 15; 16). Due to the toxicity of its vapours, glutaraldehyde must be used in well ventilated areas with the provision of appropriate protective
apparel (13; 15; 16) (Refer Appendix 3A; Special notes 1).

Although several authors (12; 13; 15; 16; 97) have proposed the use of 0.5% sodium hypochlorite, its use is not advocated by current NH & MRC guidelines (Refer Appendix 3A; Point 1.9.3 and Special notes 3). Although considered effective, the demonstrated corrosion of dental equipment (238; 267), irritation to skin and eyes, a reduced efficiency in the presence of organic matter (496) and unpleasant odour severely limit its use.

The efficacy of alcohol solutions in eliminating HBV have been controversial. Most authors discussed this form of chemical disinfection due to initial studies by Bond and co-workers (497), however, subsequent studies, including two by these same authors, have demonstrated that a 70%-80% alcohol solution was an effective disinfectant against HBV after an exposure time of two to ten minutes. The promising aspect of a study by Christensen and co-workers (496) was the superiority of alcohols as surface disinfectants over glutaraldehyde, iodophors and chlorine containing compounds. However, the poliovirus and four bacteria tested are of no clear clinical significance to dentistry, which raises the question of whether these results can be directly applied to HIV.
3.1.2.3: SPECIAL CONSIDERATIONS

Current equipment design often precludes effective decontamination procedures. Despite the use of autoclavable instruments (for example; handpieces, scalers and triplex syringes) in some dental operatories, current equipment design means that after use, when these are replaced in the bracket holder, both the line and holder will become contaminated. This problem may be addressed, in part, by the chemical sterilization of all instruments and possibly the line before replacement in the bracket holder (Refer Appendix 3A; Section 1.10). However, a better solution would be design modifications that take into account infection control principles. Triplex syringes pose a problem because the nozzles are often permanent fixtures that may only be decontaminated by wiping with chemical agents. In the absence of design improvements, the use of cotton wool pledgets and tweezers may suffice.

There is a genuine need for the design of X-ray film packets with completely waterproof outer plastic envelopes, which could be removed after exposure to allow the scout nurse to process each film packet individually. Failing this, the use of plastic wrap as an outer protective disposable layer may serve as an interim measure.

Further areas of concern, due to current equipment design revolves around retraction valves. These valves
create a negative pressure in the waterline and prevent water from dripping onto the patient whenever the high speed handpiece is removed from the mouth. It has been hypothesized, by Bagga and colleagues (30), that these valves aspirate up to 0.9 mls of infected material into the water lines, thereby acting as a possible source of subsequent cross-infection. Sterilizing the handpiece between patients would not totally eliminate this problem as 95% of the oral fluid aspirated into the dental unit passed via the handpiece into the water cooling line. Similarly, check valves may reduce the amount of material aspirated, but not eliminate any possible risks of transmission. While the risk of transferring infectious material in this way is uncertain, the water cooled handpieces should run over a sink for approximately 30 seconds after each patient is treated, so that potential pathogens are flushed away prior to sterilization procedures.

Similarly, the present design of the dental syringe poses an area of concern for possible transmission, as it does not lend itself to easy removal of the needle unless it is first recapped. It is during this recapping phase that the greatest potential for needlestick injuries may occur, as is the case in medical practice with the recapping of wholly disposable syringes and needles. Although the current NH & MRC guidelines (Refer Appendix 3A, Point 4.5) allow for the careful recapping of dental syringes, the onus must finally rest with the manufacturers, as suggested by
Stevenson and Higgins (364), in designing needles with a single sharp end that may be pushed from the reusable syringe rather than being unscrewed (59; 116; 377; 378).

The provision for recapping dental syringes within the current NH & MRC guidelines (Refer Appendix 3A; Section 4.5 and Special notes 8) is in direct contravention of previous recommendations (13; 16; 116; 284; 361; 371; 388). This is primarily due to the fact that initial guidelines were formulated by medically orientated personnel who based their assumptions on experiences with the recapping of disposable syringes. However, it has since been realized that dental and medical syringes differ. In addition, there has been recognition of a genuine need to protect the needle that potentially poses the threat of percutaneous injury whilst lying on the bracket table during dental procedures. Therefore, it is often considered necessary to recap dental syringes, preferably with the aid of needleguard holders, haemostats or tweezers (54; 116; 377; 378).

A further area for concern involves the use of protective clothing. Although widely advocated in the literature, between 13.6% and 57% of dental practitioners, in various studies in the USA and Australia (162; 248; 364), wore gloves routinely, while up to only 70% routinely wore masks (162; 163; 271; 319; 364).
The disposal of waste presents a further problem of possible disease transmission (Refer Appendix 3A; Special notes 2; 4 and Point 1.12). The Public Health Division of the Department of Health must be contacted as the disposal of contaminated waste and needles through domestic waste services exposes many people to a risk of HIV infection. Of concern then is the suggestion, by Stevenson and Higgins (364), that 89% of the NSW dental practices surveyed utilized local council refuse disposal services, with only 9% disposing of those contaminated items via professional firms or incineration.

The need to disinfect all items destined for the laboratory (Refer Appendix 3A; Points A.1.12 and B.1.1) raises the question of which chemical sterilants may be used effectively, whilst maintaining the dimensional stability of currently used impression materials. The dimensional stability of zinc oxide eugenol, silicone rubber, alginate and polysulphide impression materials has been demonstrated following 16 hours of exposure to glutaraldehyde (107; 126; 374). For all dental materials where glutaraldehyde is not widely recommended (for example, polyether, hydrocolloid and compound), dimensional stability has been demonstrated with the use of chlorine containing disinfectants, such as sodium hypochlorite (107; 126). The sterilization of casts and fixed and removable prostheses may be achieved by various chemical means, however ethylene oxide sterilization seems to be more effective (374). In
order to achieve sterilization, it is imperative that all impressions, models and prostheses are rinsed to reduce debris, serum residues and residual microorganisms (107; 126; 374).

The advent of HIV infection has placed two demands on the dental profession. In the first instance is a genuine need to reinforce and reappraise general infection control procedures in both private practice and public health settings, with special emphasis being placed on certain possible problem areas (Refer Section 3.1.2.3). Secondly, and following on from the first demand, is a need for professional organizations (for example; the ADA) and teaching institutions to interact and widen their knowledge of various aspects of HIV, with efficient communication of this information to the general dental practitioner.

3.1.3: ASSESSMENT OF THE RISK TO DENTAL HEALTHCARE WORKERS

As of March 14 1988, 5.4% of all AIDS cases in the USA had occurred in healthcare workers, a similar number to the proportion of the US labour force employed in healthcare services (5.7%). This suggests that the risk to healthcare workers may be no greater than that of the general population. However, these cases are not purely occupationally acquired cases, therefore in order to quantify the actual risk of occupational transmission, risk behaviours need to be delineated.
It has been suggested previously that dental healthcare workers are at-risk of occupational transmission by three possible means:

i. Transmucosal spread via splashes of intact epithelial surfaces such as the eye, suggested by anecdotal reports of transmission by saliva (477), breast milk (434) and artificial insemination (470) (Refer Section 1.4.8).

ii. Inapparent frank percutaneous inoculation via splashes of non-intact epithelial surfaces (such surfaces may include the eyes, hands and face where minute breaks in the integrity of the epithelium occur) (Refer Section 1.4.8).

iii. Frank percutaneous transmission, demonstrating the greatest risk, in the form of needlestick injuries or other injuries involving sharp instruments (Refer Section 1.4.8).

It seems reasonable to expect that dental healthcare workers may be at a significant risk of occupational acquisition when the following points are taken into consideration:

i. There is a general lack of adherence to widely recommended infection control procedures, as suggested by several studies (20; 162; 188; 271; 319; 380), even though there is constant occupational contact with potentially infected body fluids.
ii. Following on from this is the fact that dental healthcare workers commonly operate without the routine use of gloves, masks and protective eyewear, which raises the possibility of transmission via inapparent open cuts or, less likely in the setting of dental practice, intact epithelium (Refer Section 1.4.8).

iii. Dental healthcare workers routinely work with sharp instruments (including needles) which frequently cut patient's tissues and give rise to the possibility of percutaneous transmission (Refer Section 1.4.8).

However, current large scale prospective studies (43; 160; 220; 387; 388; 473; 490; 495) suggest a real but minimal risk for healthcare workers, in particular dental healthcare workers. Concern over HIV transmission in dental practice is well founded considering that between 13% and 27% of dental practitioners have been found to have serological evidence of past or occasionally current Hepatitis B (HBV) infection predominantly as a result of occupational transmission (41).

A serological survey of 1231 dentists and dental hygienists in the USA, in 1987, represents the only large-scale study of dental healthcare workers (220; 76). It found that, although many of these practitioners cared for numerous HIV-positive patients, only one dentist (0.1%) had serological evidence of HIV
infection. He apparently had no additional risk factors nor certain accidental exposures to HIV contaminated materials; however, he wore gloves irregularly when treating patients and gave a positive history of multiple needlestick injuries and other trauma to his hands. Therefore, it must be assumed that transmission occurred via the percutaneous inoculation of breaches in the skin or needlestick punctures by infected saliva and/or blood. There is no doubt that other practitioners were similarly exposed but do not seem to be infected.

To further clarify the possible risk of occupational HIV transmission in the dental surgery, two large-scale prospective studies of healthcare workers in general must be evaluated (160; 473). Unfortunately, the cases of HIV infection reported in these studies are those that have not been excluded as a result of an identification of other risk behaviours (for example; possible homosexual venereal transmission). The first of these studies, that provided by Gerberding (160), indicates that the rate of nosocomial HIV transmission in over 1,000 individuals for every accidental exposure is less than 0.1% (four cases resulting from over 4,000 accidental exposures).

These findings are similar to those of Barnes (473) who found that 16 (<1%) of over 2,200 healthcare workers (including clinicians, nurses and laboratory workers), inadvertently exposed to HIV contaminated blood and
other body fluids were infected. Exposure in these cases were a result of, often multiple, needlestick injuries and overt mucosal splashes of such surfaces as the eyes and mouth. For both of these studies (160; 473), when needlestick injuries were examined alone, less than 0.5% of subjects had seroconverted. This is in direct contrast to the situation with Hepatitis B (HBV), where infection rates following such exposures range from 2.5% to 30% (41).

Nonetheless, the potential for occupational transmission is very real and, although there are no such cases to date documented in Australia, the CDC has indicated that as a result of prospective epidemiologic studies of injured healthcare workers and reasonably substantiated individual case reports, 22 cases of occupationally infected healthcare workers in the USA had been identified to the end of 1988 (81). However, without routine testing of dental personnel and their patients the real risk of bilateral transmission remains unknown. A review of the literature did not reveal any significant commitment (including the CDC) to prospectively screen healthcare workers and their patients in order to establish the actual risks.

Perhaps more significant than the absolute number is the wide variety of healthcare workers who have been infected (physicians, home healthcare providers, nurses, research laboratory workers, technicians, a phlebotomist and dentist), and the means of acquisition, principally
involving needlestick injuries, but also the contact of blood (and possibly other body fluids) with open cuts, non intact skin and intact mucous membranes (81). The vast majority of these healthcare workers who have become infected were exposed to body fluids of known HIV infected patients. This is relevant because it has been suggested that enhanced healthcare worker protection will result from the identification of all possibly infected individuals. However, there is growing evidence that a substantial percentage of these patients deny any risk behaviours, especially in acute emergency care situations. This has been demonstrated by some studies of acute emergency patients in the USA (441; 31) where incidental findings of the order of 3.7% being seropositive, yet mostly denying any HIV risk factors were reported. The question is raised, though, whether these individuals concealed their seropositivity purposely, were unaware of their HIV status or unable to divulge any information due to their condition.

Regardless, these suggestions further emphasize the need to consider all patients as potentially infectious (Refer Section 3.1.1.3). A definite risk of occupational transmission in the dental setting raises the question of how best to manage such accidental parenteral, mucous membrane or cutaneous exposures to uncertain and known infected bodily fluids.

In the case of an accidental exposure, the source patient should be serologically tested for HIV with due
regard to the issues of informed consent and confidentiality. Where the source patient has AIDS, is seropositive or refuses the test, the healthcare worker should be counselled regarding the risk of infection and evaluated clinically and serologically both immediately after the incident and at six-weekly intervals thereafter. It is generally unclear how long intermittent testing should continue given that the time taken to seroconvert is on the average six months (270; 299; 425; 428; 455; 462), it may take as long as 35 months, as described by anecdotal reports (461) (Refer Section 1.2.3). Although current research evaluating the prophylactic use of AZT in occupational exposures is encouraging, prevention of these accidents in the first instance is of primary importance.
3.2: MEDICOLEGAL ASPECTS OF HIV INFECTION

From the medicolegal view-point, there are several outstanding issues (other than the more prominent issue of confidentiality (Refer Section 3.1.1.4)) that need to be addressed in the provision of dental care in the era of the HIV epidemic:

3.2.1. Refusal to treat.
3.2.2. Transmission in the dental operatory.
3.2.3. Carrier dentists.

3.2.1: REFUSAL TO TREAT

The ongoing debate within the medical and dental professions regarding the duty to treat people infected with HIV demonstrates that both professions are divided as to the correct ethical position. While several studies indicate an unwillingness or reluctance to treat infected patients (161; 162), there is no way of knowing the extent to which patients are refused treatment on the grounds of HIV infection. We do know, however, that clinicians in large public health settings who act on various HIV committees, are approached by patients and dentists who report either an unwillingness in the sense of won’t treat or, on the part of patients, a denial of treatment (502).

Studies have suggested that, in the USA, the number of dental practitioners willing to care for known
seropositive patients was only 21% in 1986 and 31% in 1988 (163; 380). It seems reasonable to assume that these figures would roughly correspond to the current situation in Australia. It has been suggested by Hazelkorn and others (195; 218) that the course of action for some dentists involves an initial examination followed by some seemingly logical but pedantic excuse to preclude the need for additional appointments.

Ethically and legally, a dentist in most situations can decline treatment to new prospective patients (89). There are, however, special circumstances in which a dentist could be risking ethical and legal problems if treatment is refused, especially in an emergency setting. If the individual with an infectious disease, such as HIV, is a patient of record, additional ethical and legal concerns must be considered. A dental practitioner may face a charge of abandonment of an existing patient if he/she flatly refuses to assist that patient further. "Abandonment" in the legal sense implies a "breach of duty" and is a cause for possible professional liability in the USA (248). A healthcare provider may be legally liable if a provider-patient relationship has been established, then broken, without ensuring properly that competent substitute care can be provided. However, the exact situation is unclear at present, in relation to HIV and dentistry in Australia, as no legal precedent has been set (89).
The refusal to treat patients, on the part of the practitioner, with known HIV infection raises four main concerns:

i. The most common explanation for not being able to treat seropositive individuals is that the dental practitioner cannot ensure that transmission will not occur. In this way, many dentists believe that by excluding known HIV infected patients from their operatory (in the form of refusing treatment or referrals), they will keep their practices free of HIV infection. If adequate prevention of transmission from known seropositive patients cannot be assured, presumably where adherence to recommended infection control procedures are maximal, the question is raised of the prevention of HIV transmission when providing routine dental care to patients whose serological status is unknown to the dental team.

ii. With only 10% of seropositive patients being aware of their HIV status, as suggested by Gerbert and colleagues (161), the unwise decision of rejecting a patient who benefits the dental practitioner by confiding his/her seropositivity is stressed.

iii. The risk of HIV transmission is not eliminated as rejected patients will most likely seek another dentist with the added possibility of now concealing their HIV status for fear of further rejection. Of particular concern to the refusing dentist is the potential of becoming unknowingly
exposed to more infected patients due to concealment of this information by patients who have been warned by acquaintances who have previously been refused treatment.

iv. The rejection of known HIV-positive patients and the misuse of referrals means that the burden of the HIV epidemic is not shared, but falls on the shoulders of those dental practitioner's who are willing to provide treatment.

In the USA, Logan (248) has suggested that many States have made an official declaration that AIDS is a handicapping condition. As a result, refusal to treat is prohibited under current anti-discrimination laws. Some States have gone further so as to rule that extra charges cannot be made for treatment to HIV-positive individuals, even though increased costs may be incurred.

In summary, it is the responsibility of the dental practitioner to provide routine dental treatment to patients, irrespective of their HIV status. Refusal to treat a patient on the basis of HIV infection alone is professionally, ethically and possibly legally irresponsible. However, in certain circumstances (Refer Section 3.1.1.1) the provision of care may not be undertaken in a private practice setting, especially where treating patients at the advanced stages of HIV infection. In this way, appropriate referrals where specifically indicated may be required. At present in
NSW there is no formal legal requirement to prevent
dentists from refusing treatment to patients infected
with HIV (PC2: Refer Personal Communications); however,
a legal precedent where a dentist is found to unjustly
refuse treatment to such a patient could be established
at any time.

3.2.2: TRANSMISSION IN THE DENTAL OPERATORY

It has previously been demonstrated (Refer Sections
1.4.8 and 3.1.3) that there is a potential for HIV
transmission in the dental setting. This potential is
supported by one reported case of probable occupational
transmission in a dentist (76; 220). Given this, there
is no reason to suggest it is not possible for
transmission to occur between patients via contaminated
dental equipment, as has been demonstrated to be the
case with Hepatitis B virus (HBV). Furthermore, this
possibility is supported by reports of the bilateral
transmission of HIV in medicine, such as that by
Patrascu and co-workers (471). Therefore, it would not
be surprising for the two-way transmission of HIV to be
demonstrated (dentist to patient and patient to
dentist), perhaps principally via contaminated equipment
(in particular; the reuse of needles and via injuries),
as has been demonstrated to be the case with Hepatitis
B Virus.

With the potential for HIV transmission, the question
is raised as to the medicolegal implications for
preventing transmission, in terms of the roles of the
dentist and staff and the infected patient. The dental
practitioner has a clear-cut legal and professional
obligation to provide a safe working environment for
themselves, their staff, and patients. This environment
is ensured by a legal obligation to abide by documented
infection control practices designed for the protection
of both parties.

There is no legislation in NSW requiring a patient to
disclose their HIV status to their dental practitioner
or other healthcare workers (PC1 and PC2: Refer Personal
Communications). In contrast, disclosure of this
information to their healthcare providers is mandatory
in two States of the USA (485; 486). This is in
addition to a further 15 States where it is legal for
one healthcare worker to disclose a patient’s
infectivity to another on a need-to-know basis (248).

It is unclear whether future Australian legislation
will follow the emerging trend in the USA. Regardless
of any future direction, currently the onus is placed
directly on the dental practitioner to prevent disease
transmission and consider all patients as potentially
infectious. As discussed previously (Refer Section
3.1.1.4) the dentist can, in the absence of legislation
to the contrary, disclose a patient’s carrier status to
other healthcare providers on a strict need-to-know
basis, as part of an overall strategy of infection
control. Given that there is a potential for HIV
transmission in the course of routine dental treatment, and the patient has no current medicolegal obligations to disclose their infectivity, the onus of prevention rests with the dental practitioner. This raises the question of a dentist’s legal liability in cases where dental staff become infected, the dentist is infected by a patient and a patient is infected from the dental operatory (not from infectious staff members per se (Refer Section 3.2.3)).

3.2.2.a: Dental staff infected occupationally

If a civil law action or workers compensation claim following occupational HIV infection of a dental staff member were to be successful, it would appear necessary to demonstrate the staff member’s HIV status at the time of documented work related transmission, with subsequent seropositivity in the absence of additional risk (behavioural) factors.

Although current legal advice (FC1: Refer Personal Communications) suggests that the judicial system in the USA and NSW are different, a lack of current legislation and legal precedence means that comparisons must be drawn from the situation in the USA. Logan (248) suggests that, in the absence of legal precedence in the USA, the ground work has nevertheless been laid for future legal challenges in that country. The basis for successful legal challenge in the USA will probably revolve around the complex issue of informed consent.
Logan (248) predicted that if legal action were taken against the employing dentist by an infected staff member, that the matter would probably be decided on medicolegal precedent rather than on the dentist's provision of accepted infection control precautions. There would seem to be no defence possible for a dental practitioner who could be demonstrated not to have followed accepted guidelines, with perhaps the most indefensible breach of infection control being the reuse of contaminated needles.

Logan (248) has raised the possibility, on the other hand, that a practitioner may seek an adequate defence in the form of obtaining informed consent from prospective employees. Informed consent in this sense would probably involve signed acknowledgement of the clearly written potential risk involved in the provision of dental care for patients who knowingly or unknowingly carry infectious diseases, such as HBV or HIV.

Based on the situation in the USA, current legal advice (PC1: Refer Personal Communications) suggests that the same position would apply in NSW to infected staff members, from a workers compensation or civil litigation point of view. Similarly, with no recourse for dentists to force patients to undergo serological testing and a lack of current legislation requiring such disclosure (PC2: Refer Personal Communications), the onus of prevention rests with the dental practitioner. As such, any possible cases of HIV transmission to staff members,
not informed, may find the dentist at fault. The profession awaits the outcome of future legal challenge.

3.2.2.b: **Dental practitioner infected by a patient**

In the case of a dental practitioner becoming infected with HIV during the normal course of dental treatment, perhaps by accidents such as needlestick injuries, there is no legal recourse for the dentist given that no legislation exists in NSW requiring a patient to disclose their HIV status (PC2: Refer Personal Communications). Even where transmission occurred in the presence of adequate precautions, the patient would not be liable given the absence of current legislation in NSW. A similar situation appears to exist in the USA; however, in the two States that require seropositive individuals to notify their healthcare provider, failure to do so, in the setting of transmission to a dentist, could provide a basis for successful legal challenge by the practitioner. As yet, no precedent has been set.

Recovery via workers compensation legislation, if the practitioner is so covered, may be successful provided that there is documented seroconversion post-accident, an absence of additional risk (behavioural) factors and the routine implementation of barrier precautions.
3.2.2.c: Patient infected from dental operatory

The patient may potentially acquire HIV in the dental surgery via the dental staff (Refer Sections 3.2.2.a and 3.2.3) or via dental equipment. Two scenarios are possible; either the patient tries to subsequently equate transmission to the dental surgery, in the absence of any other risk factors, or there is an obvious accident that occurred in the dental setting, such as an accidental percutaneous injury to dental staff that introduced blood into the patient’s oral cavity. The chances of successful litigation against the dental practitioner, on behalf of the patient, are increased by the following:

i. An absence of risk (behavioural) factors other than dental treatment on the part of the patient.

ii. Documentation of seronegativity prior to dental treatment with subsequent seroconversion.

iii. Evidence that infection control procedures in the dental surgery were breached, probably in the form of testimonial evidence given by staff members (for example, the reuse of needles).

iv. Definitive confirmation of HIV infection in the dental practitioner or staff member.
However, current legal advice (PC2: Refer Personal Communications) suggests that successful litigation would appear very difficult, if not impossible, for the following reasons:

i. There is no legal recourse on the part of newly infected patients to force a dental practitioner or staff member to be serologically tested.

ii. The long incubation period of AIDS means that the tracing of the alleged source takes place after an extended period of time, a situation that has similarly complicated the tracing of HBV infection.

iii. The testimonial evidence would need to be very strong and definitive.

iv. Even if the dental practitioner was forced to undergo serological testing, as may be evoked by public health officials under current legislation in NSW (491), following suspected transmission to patients, it may still be very difficult to directly attribute transmission to the infected dentist.

Therefore, in summary, it seems that the basis for preventing the transmission of HIV in the dental surgery revolves around the rigid implementation of recommended infection control procedures. This is especially important when considering that patients are not legally required to divulge their HIV status and that successful litigation in NSW would seem to revolve around the confirmation of a breach of such precautions.
3.2.3: CARRIER DENTIST

The prevalence of HIV infection in dental practitioners is presently unknown. With one documented case of probable occupational transmission in over 1,200 dental HCW’s tested (76; 220) the suggestion is that the prevalence may be low; however, without further screening this cannot be accepted as true of the whole profession. An important consideration is that dental practitioners represent a cross-section of the community, and as such may share individuals with the same risk (behavioural) factors for HIV acquisition as the community generally. It is probable, therefore, that the potential for transmission to patients from infected dentists is already a real issue.

Any definitive guidelines regarding HIV carrier dentists may lead to significant controversy. This controversy may occur at two levels. Firstly, where inadequacies may be demonstrated, perhaps following medicolegal challenge; and secondly, where controversy arises from the tightening of guidelines requiring significant alterations to, or restrictions on, the conduct of general dental practice. These aspects will be discussed below.
The possibility of the transmission of HIV from carrier dentists in the setting of general practice raises three main controversies:

1. The need for informed patient consent.
2. The need for retrospective and/or prospective follow-up of patients treated by infected dentists.
3. The need for placing restrictions on the clinical practice of infected dental practitioners.

Of central importance to these considerations is the fact that the "stakes" associated with HIV acquisition are far greater than those of HBV. It is clear with HBV that more than 90% of those infected will fully recover (39). With HIV infection it is possible that 100% may die (286). This potential difference raises concern that guidelines suggested for HBV carrier dentists may need to be evaluated more strictly before application to HIV infected dentists.

Past CDC guidelines (71; 83; 503), based on Hepatitis B carrier dentists (who have not been shown to infect patients), do not require informed patient consent. However, these guidelines stipulate that where transmission to patients is demonstrated, there is a need for the dentist to obtain signed informed consent from future patients. Further demonstration of HBV transmission, regardless of adherence to relevant
infection control precautions, would lead to suspension of practice under these guidelines (71; 83; 503).

Before translating these guidelines to HIV infected dentists, several points need to be weighed up. Firstly, there is evidence to demonstrate that, in the case of Hepatitis B, patients may become infected inadvertently, despite adherence to the recommended clinical procedures inherent in these guidelines (504). When this is coupled with the potential outcome of HIV infection, the lack of information concerning HIV prevalence in dentists and the lack of information concerning the potential for transmission of HIV to patients in the dental setting, serious consideration should be given, in the opinion of the present author, to applying stricter guidelines in the case of HIV carrier dentists. Specifically, these guidelines should include:

1. Routine informed patient consent.
2. Routine serological follow-up of patients treated by the HIV infected carrier dentist.

While accepting that this may severely limit a practitioner’s ability to continue viable dental practice, it appears, given the potential risks and uncertainties involved, the only way of ensuring the safety of dental patients. On the positive side, follow-up of patients over, for example 1 to 2 years, without evidence of transmission may negate the need to
continue with these stricter guidelines in the case of the dentist concerned. Similar information from other HIV carrier dentists may lead to a general easing of guidelines and establish in the minds of dentists and their patients that the provision of dental care via dental practitioners so infected is safe from the risks of HIV transmission. Furthermore, it is the opinion of the present author that a single case of HIV dentist to patient transmission should be sufficient grounds for the dentist to cease practice.

Apart from the above guidelines, and the obvious option of ceasing practice altogether, HIV carrier dentists could confine patient care to other HIV carriers, however, it is acknowledged that both the dentist and patients, under these circumstances, may be increasingly exposed to the risk of acquisition of opportunistic infections, such as Pneumocystis carinii pneumonia.

Whatever guidelines are applied to the HIV carrier dentist, it is essential that principal sectors of the dental profession (particularly, the universities and dental associations in concert with medicine) should liaise with the intention of establishing carefully conceived guidelines and with the intention of monitoring their efficacy. Of particular concern for the dental profession is the possibility that, if it fails to provide adequate safeguards in relation to HIV carrier dentists then abrupt and unilateral government legislation may ensue.
PERSONAL COMMUNICATIONS
PERSONAL COMMUNICATIONS

PC1: Mr. P. Zacharatos (LL.B.).
Solicitor; Marsdens Solicitors, Sydney.
Recommended by the Albion Street AIDS Centre, Sydney.
Multiple discussions May to August 1990.

PC2: Mr. R. O'Donahue (B.A.Dip.Ed.).
Education officer; Occupational Health and Safety issues.
AIDS Bureau; New South Wales Department of Health.
Multiple discussions May to August 1990.
APPENDICES

APPENDIX 1
DEFINITIONS AND CLASSIFICATIONS OF HIV INFECTION AND AIDS.

APPENDIX 3
INFECTION CONTROL PROCEDURES
APPENDIX 1A: THE ORIGINAL DEFINITION (1982)

"An unusual infection or unusual cancer which affected somebody who had previously been in good health" (18).

APPENDIX 1B: THE SIMPLE DEFINITION (1984)

"AIDS: caused by a chronic infection of the T-Lymphocytes (especially the helper sub-type) by a novel human retrovirus". A diagnosis could be made when "this infection had caused damage sufficient to increase the risk of malignancies and opportunistic infections" (164).
APPENDIX 1C: THE WHO/CDC CASE DEFINITION FOR AIDS (1986)

(WHO Wkly Epidem Rec 1986; 61:69-76)

Acquired Immune Deficiency Syndrome (AIDS) is an illness characterized by:

1. One or more of the opportunistic diseases listed below (diagnosed by methods considered reliable) (Refer below) that are at least moderately indicative of underlying cellular immunodeficiency; and

2. Absence of all known underlying causes of cellular immunodeficiency (other than HTLV-III/LAV/HIV infection) and absence of all other causes of reduced resistance reported to be associated with at least one of those opportunistic diseases.

Despite having the above, patients are excluded as AIDS cases if they have negative results on testing for serum antibody to HIV, do not have a positive culture for HIV and have both a normal or high number of T-helper lymphocytes, and a normal or high ratio of T-helper to T-suppressor lymphocytes.

Diseases that are at least moderately indicative of an underlying immunodeficiency as mentioned in 1. above

a. Protozoal and helminthic infections

1. Cryptosporidiosis; causing diarrhoea for more than one month.
2. Pneumocystis carinii pneumonia.
3. Strongyloidosis; causing pneumonia, central nervous system infection, or disseminated infection.
4. Toxoplasmosis.

b. Fungal infections

1. Candidiasis; causing oesophagitis (by histological, microscopic, autopsy or endoscopic findings, and not by culture alone).
2. Cryptococcosis; causing central nervous system or other infection, disseminated beyond lungs and lymph nodes.

c. Bacterial infections

1. Mycobacterium avium intracellulare (M. avium complex or MAI) or M. kansaii, causing infection disseminated beyond the lungs and lymph nodes.
d. Viral infections

1. Cytomegalovirus (CMV); causing infection in internal organs other than the liver, spleen, or lymph nodes.
2. Herpes simplex virus (HSV); causing chronic mucocutaneous infection with ulcers persisting more than one month or pulmonary, gastrointestinal tract (beyond mouth, throat, or rectum) or disseminated infection.

e. Cancers

1. Kaposi’s sarcoma (KS).
2. Lymphoma limited to the brain.

f. Other opportunistic infections with positive tests for HIV

In the absence of any of the above opportunistic diseases, any of the following diseases are considered indicative of AIDS if the patient has a positive test for HIV.

1. Disseminated histoplasmosis (culture, histology or cytology).
2. Bronchial or pulmonary candidiasis.
3. Isosporiasis, causing chronic diarrhoea.

g. Pneumonitis

1. Chronic lymphoid interstitial pneumonitis.

h. Lymphoma

1. Non-Hodgkin’s lymphoma with a positive test for HIV.

Additional to classifying AIDS, the CDC in collaboration with the NIAID Working Group proposed a prodromal phase of AIDS, called AIDS Related Complex (ARC) (Refer below). To satisfy the definition for ARC, a person must have any two (or more) signs/symptoms and any two (or more) abnormal laboratory values.
AIDS RELATED COMPLEX (ARC)

I. **Clinical signs and symptoms**: unexplained chronic condition present for three months or longer.

A. Lymphadenopathy for at least three months duration in the absence of any current illness or drug known to cause lymphadenopathy. The lymphadenopathy must be found at more than two non-inguinal sites.

B. Weight loss of more than seven kilograms (> 15 pounds) or more than ten percent (> 10%) normal body weight.

C. Fever that is intermittent or continuous and exceeds 38 degrees Celsius.

D. Diarrhoea.

E. Fatigue and/or malaise.

F. Night sweats.

II. **Laboratory studies**

A. Decreased number of T-helper cells.

B. Decreased ratio of T-helper to T-suppressor lymphocytes.

C. Anaemia or leukopaenia or thrombocytopenia or lymphopaenia.

D. Increased serum globulin levels.

E. Decreased blastogenic response of lymphocytes to mitogens.

F. Cutaneous anergy to multiple skin test antigens.

G. Increased levels of circulating immune complexes.
APPENDIX 1D: NEW CLASSIFICATION SYSTEM FOR HIV ASSOCIATED INFECTION (1986)

(CDC MMWR 1986; 35:334-339)

Group I  Acute infection *
Group II  Asymptomatic infection*
Group III  Persistent Generalized 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 Groups I and II may be subclassified on the basis of a laboratory evaluation.
^ Includes those patients whose clinical presentation fulfills the definition of AIDS used by CDC for national reporting.

GROUP I: ACUTE INFECTION

Defined as a mononucleosis-like syndrome associated with seroconversion for HIV antibody. About 50% of persons newly infected with HIV exhibit this acute transitory illness, characterized by a self limited glandular fever-like syndrome of short duration and possibly symptoms of aseptic meningitis. Tests for antibodies to HIV are usually negative at the onset and remain that way for one to three months before becoming positive. All patients in this group recover from this illness and are then reclassified into Groups II and III.

GROUP II: ASYMPTOMATIC INFECTION

The patients in this group have been infected by HIV and have formed antibodies to the virus, but are otherwise well and have no apparent illness. Subclassification may be carried out based on whether haematologic and/or immunologic laboratory studies are abnormal in a manner consistent with the effects of HIV infection.
GROUP III: PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL)

Included in this group are patients with persistent generalized lymphadenopathy, but without findings that would lead to classification in Group IV. It may be defined as palpable lymphadenopathy (lymph node enlargement of one centimetre or greater) at two or more extra-inguinal sites persisting for more than three months in the absence of a concurrent illness or condition other than HIV infection to explain the findings. Patients in this group may be reclassified or subclassified based on the results of laboratory studies as in Group I.

GROUP IV: OTHER DISEASE

This group includes patients with clinical symptoms and signs of HIV infection other than or in addition to lymphadenopathy. Each subgroup may include patients who have mild symptoms, as well as patients who are severely ill.

Subgroup A: Constitutional disease

Defined as one or more of the following:

i. Fever persisting for more than one month.
ii. Involuntary weight loss of greater than ten percent (>10%) of baseline.
iii. Diarrhoea persisting for more than one month.
iv. Absence of a concurrent illness or condition other than HIV infection to explain the above findings.

Subgroup B: Neurologic disease

Defined as one or more of the following:

i. Dementia.
ii. Myelopathy.
iii. Peripheral neuropathy.
iv. Absence of a concurrent illness or condition other than HIV infection to explain the findings.

Subgroup C: Secondary infectious diseases

Defined as the diagnosis of an infectious disease associated with HIV infection and/or at least moderately indicative of a defect in cell mediated immunity. In this subgroup, patients are divided further into two categories:

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

a. Pneumocystis carinii pneumonia.
b. Chronic cryptosporidiosis.
c. Toxoplasmosis.
d. Extra-intestinal strongyloidosis.
e. Isosporiasis.
f. Candidiasis (oesophageal, bronchial or pulmonary).
g. Cryptococcosis.
h. Histoplasmosis.
i. Mycobacterial infection with Mycobacterium avium complex or M. kansasii.
j. Cytomegalovirus infection.
k. Chronic mucocutaneous or disseminated herpes simplex virus (HSV) infection.
l. Progressive multifocal leukoencephalopathy.

Category C-2 - includes patients with symptomatic or invasive disease due to one of six other specified secondary infectious diseases:

a. Oral hairy leukoplakia.
b. Multidermatomal herpes zoster.
c. Recurrent Salmonella bacteraemia.
d. Nocardiosis.
e. Tuberculosis.
f. Oral candidiasis.

Subgroup D: Secondary cancers

Defined as the diagnosis of one or more kinds of cancers known to be associated with HTLV-III/LAV/HIV infection as listed in the surveillance definition of AIDS (Refer Appendix 1C) and at least moderately indicative of a defect in cell-mediated immunity. This subgroup includes those patients with one or more of the specified cancers listed whose clinical presentation fulfills the definition of AIDS as used by the CDC for national reporting.

a. Kaposi’s sarcoma.
b. Non-Hodgkin’s lymphoma (small, non-cleaved lymphoma or immunoblastic sarcoma), or primary lymphoma of the brain.
Subgroup E: Other conditions

Defined as the presence of other clinical findings or disease, not classified above, that may be attributed to HTLV-III/LAV/HIV infection and/or may be indicative of a defect in cell mediated immunity.

Included within this subgroup are patients with:-

a. Chronic lymphoid interstitial pneumonitis.

b. Signs and symptoms that could be attributed to HIV infection or to another coexisting disease not classified elsewhere.

c. Other clinical illness, the course or management of which may be complicated or altered by HIV infection.

Examples include:-

1. Patients with constitutional symptoms not meeting the criteria for subgroup IV.A.

2. Patients with infectious diseases not listed in subgroup IV.C.

3. Patients with neoplasms not listed in subgroup IV.D.
APPENDIX 1E:  CASE DEFINITION FOR CHILDREN UNDER 13 YEARS OF AGE (September 1987), (426; 421)

A. Infants and children with perinatal infection up to 15 months of age

Infection in infants and children up to 15 months of age who were exposed to infected mothers in the perinatal period may be defined by one or more of the following:-

1. Identification of the virus in blood or other tissues; and/or
2. The presence of HIV antibody as indicated by a repeatedly reactive screening test (ELISA) plus a positive confirmatory test (WB or IFA) in an infant or child with a normal immunologic test results indicating both cellular and humoral immunodeficiency, and meeting the requirements of one or more of the subclasses listed under P-2 (Refer Appendix 1F, section C); and/or
3. Any child who meets the previously published CDC case definition for AIDS.

The infection status of other perinatally exposed seropositive children up to 15 months of age who lack the above immunologic and clinical criteria is indeterminate. These infants should be followed for HIV-related illnesses and tested at regular intervals for persistence of antibody to HIV. Infants and children who: become seronegative; are virus culture negative (if performed); and continue to have no clinical or laboratory abnormalities associated with the HIV infection are unlikely to be infected.

B. Older children with perinatal infection and children with other modes of transmission

HIV infection in these children is defined by one or more of the following:-

1. The identification of the virus in blood or tissues; and/or
2. The presence of HIV antibody (positive screening test plus confirmatory test) regardless of whether immunologic abnormalities or signs or symptoms are present; and/or
3. Any child who meets the previously published CDC case definition for AIDS.

These definitions apply to children under 13 years of age. It is recommended that HIV infection in adolescents be classified according to the adult classification system (Refer Appendix 1D and 1E).
C. **Classification of HIV infection in children under 13 years of age (421)**

**Class P-0**  Indeterminate infection

**Class P-1**  Asymptomatic infection
- Subclass A  Normal immune function
- Subclass B  Abnormal immune function
- Subclass C  Immune function not tested

**Class P-2**  Symptomatic infection
- Subclass A  Non specific findings
- Subclass B  Progressive neurologic disease
- Subclass C  Lymphoid interstitial pneumonitis
- Subclass D  Secondary infectious diseases
  - Category D-1  Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS (Refer Appendix 1D)
  - Category D-2  Recurrent serious bacterial infections
  - Category D-3  Other specified secondary infectious diseases (Refer Appendix 1D)

**Subclass E**  Secondary cancers
- Category E-1  Specified secondary cancers listed in the CDC surveillance definition for AIDS (Refer Appendix 1D)
- Category E-2  Other cancers possibly secondary to HIV infection

**Subclass F**  Other diseases possibly due to HIV infection
APPENDIX 1F:  REVISED CASE DEFINITION

In September 1987 the CDC revised the case definition for AIDS for surveillance purposes (266). A positive test for HIV antibody is no longer required for a diagnosis. While waiting for definitive serum confirmation, AIDS may be diagnosed in the presence of an 'indicator disease' (Refer below) given that other causes of immunodeficiency (steroid therapy, immunosuppressive therapy, cytotoxic therapy, or genetic immunodeficiency syndrome) are ruled out.

List of indicator diseases

Candidiasis of the oesophagus, trachea, bronchi or lungs.

Cryptococcus, extrapulmonary.

Cryptosporidiosis with diarrhoea persisting for more than one month.

Cytomegalovirus disease of an organ other than the liver, spleen, lymph nodes in a patient more than one month of age.

Herpes simplex virus infection causing a mucocutaneous ulcer that persists longer than one month; or bronchitis, pneumonitis, or oesophagitis for any duration affecting a patient more than one month of age.

Kaposi's sarcoma affecting a patient less than sixty years of age.

Lymphoma of the brain (primary) affecting a patient less than sixty years of age. Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child less than thirteen years of age.

Mycobacterium avium complex or Mycobacterium kansaii, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes).

Pneumocystis carinii pneumonia.

Progressive multifocal leukoencephalopathy.

Toxoplasmosis of the brain affecting a patient less than one month of age.
APPENDIX 3A: Guidelines for dental treatment of patients with infectious diseases (NH & MRC)

A. PREVENTION

1. Limited Surface Contamination

1.1 Clearly designate those surfaces in the operatory where infective material CAN be placed ('dirty' surfaces) and those where contaminated material should NOT be placed ('clean' surfaces).

1.2 Disposable plastic backed paper should be placed over 'dirty' surfaces and changed between patients.

1.3 Non disposable and non sterilizable material (e.g. charts, radiographs and bulk materials) should be placed ONLY on 'clean' surfaces (this includes the interior of cabinets and drawers).

1.4 One sink should remain non contaminated for personal use ('scrub sink'). A second sink should be allocated for immersion of contaminated instruments and for disposal of contaminated liquids ('flush sink').

1.5 Pre-set light and chair positions and determine instrument needs BEFORE contact with patient.

1.6 If adjustments in chair and light positions must be made DURING treatment, confine handling of this equipment to clearly defined points of contact. Cover these points with disposable plastic wrap where possible and change between patients. Disposable plastic bags may be useful as covers for chair control (particularly if located in headrest) and for x-ray units. Light sources should be contacted only by their handles.

1.7 Predetermine materials and dispense PRIOR to patient contact. Use disposable mixing surfaces and disposable or sterilizable mixing instruments.

1.8 Use a 'scout' nurse to dispense further materials or instruments if necessary once treatment is commenced. Non sterilizable auxiliary equipment (e.g. amalgamators) should be operated by the 'scout' nurse. If a 'scout' nurse is unavailable the assisting nurse should deglove, dispense and then reglove (new gloves).
1.9 When using conventional integrated dental suction units:

1.9.1. Ensure intermittent thorough flushing through of suction lines with water DURING treatment, to PREVENT blood and saliva coagulation in suction lines. Sufficient water can be kept at chairside in large disposable (milkshake container size) waxed paper or plastic cups which should be disposed of between patients.

1.9.2. Encourage patients not to rinse and spit out mouthwashes into spittoons. Use two paper cups (one with water/one empty) and dispose of liquids into ‘flush’ sink immediately.

1.9.3. Avoid hypochlorite solutions (see below).

1.10 When requiring handpieces, triplex syringes and ultrasonic scalers:

1.10.1. Use autoclavable handpieces.

1.10.2. Place disposable plastic wrap securely around connection of handpiece to air/water lines.

1.10.3. Determine full extent of need for high and low speed handpieces BEFORE patient contact.

1.10.4. Use each handpiece ONCE and decontaminate with glutaraldehyde impregnated environmental wipe BEFORE relocating back in bracket table. Later sterilize all burs and bur changers.

1.10.5. Similar measures can be applied to ultrasonic scalers and scaler tips. Scaling with hand instruments avoids the problem of decontamination of many ultrasonic scalers; however, special care should be exercised with these sharp hand instruments.

1.10.6. Avoid using triplex syringes that cannot be removed in their entirety for sterilization. The use of cotton wool pledges and tweezers, as well as disposable plastic syringes containing water may be a suitable compromise.

1.10.7. To confine contamination the importance of effective suction, and the use of rubber dam where practical, is emphasized.

1.11 Use enclosed ‘self developing’ x-ray films (e.g. Phil X-30) and rinse in ‘flush’ sink.

1.12 With ALL materials (e.g. dentures / impressions) destined for the laboratory:

1.12.1. Decontaminate BEFORE materials leave the surgery (see below).

1.12.2. Ensure that containers for transport are not contaminated in the surgery. Place ALL disposable SOFT materials in a large plastic bag and ALL sharp materials in a rigid walled plastic container.
2. Disposable Equipment

2.1 Disposable equipment must be used wherever possible and discarded between patients. This applies particularly to hypodermic needles.

2.2 Use of items of equipment which are not disposable and unable to be sterilized should be avoided where possible. When not possible special measures may be used. In the case of light cured restorative materials, the surfaces of the light emitter handled by the operator should be carefully covered with plastic wrap and decontaminated PRIOR to returning to stand.

3. Personal Hygiene

3.1 Do not contaminate ‘scrub’ sink with contaminated material. Following removal of disposable gloves, wash hands thoroughly with soap and water in this sink.

3.2 Use liquid soap dispensers and paper towels. Avoid linen towels and the reuse of bar soap.

4. Personal Protection

4.1 Wear two pairs of disposable surgical gloves for all infective patients. Discard between patients.

4.2 Wear protective spectacles, disposable hair cover and surgical masks. Spectacles should be decontaminated following treatment (see below).

4.3 Staff should wear disposable waterproof paper or plastic gowns (or surgical sterilizable gowns if available) preferably with long sleeves able to be overlapped by gloves.

4.4 All sharp objects (e.g. needles, scalpel blades, glass ampoules) should be disposed of in a rigid walled plastic container.

4.5 Hypodermic needles SHOULD BE RESHEATHED WITH CARE using tweezers or a haemostat following injection. (Note: there are MANY sharp dental instruments and equal care should be exercised, particularly during clean up procedures following treatment).

4.6 Nursing staff should discard top layer of gloves (see 4.1) after procedure and add heavy duty rubber gloves for instrument collection and decontamination.
B. **ELIMINATION**

Following completion of clinical procedure the suggested sequence of decontamination is:

1.1 Nurse to place materials (e.g. impressions and dentures) into one per cent stabilized glutaraldehyde solution for one hour in a disposable or autoclavable container.

1.2 Nurse to discard top layer of gloves into waste bag and place heavy duty pair over inner pair.

1.3 Draw detergent solution through suction system, followed by water and then one per cent stabilized glutaraldehyde.

1.4 Place sharp objects in rigid walled container and seal with lid.

1.5 Carefully agitate hand instruments under water in 'flush' sink to dislodge gross contamination and allow to soak.

1.6 Discard all disposable objects used during the procedure into waste bag.

1.7 Wipe down all 'dirty' surfaces with one per cent glutaraldehyde environmental wipes.

1.8 Remove gross contamination from soaking instruments and transfer to autoclave tray along with handpieces. Swab 'flush' sink with one per cent glutaraldehyde and rinse with water.

1.9 Remove top (heavy duty) gloves and discard into waste bag.

1.10 Remove mask, haircover and gown and place in wastebag, followed by inner pair of gloves.

1.11 Protective spectacles should be decontaminated separately (from impressions etc.) in glutaraldehyde.

1.12 The wastebag should be tied off and placed inside a second non contaminated heavy duty plastic bag which would also be securely tied. Sharp objects must NOT be placed in these bags unless in sealed intact rigid plastic containers.

1.13 Non disposable linen should be laundered in hot water with commercial laundry bleach.
Special Notes

1. Ensure decontaminating solutions of glutaraldehyde and hypochlorite are used in WELL VENTILATED AREAS.

2. If contaminated fluids (such as blood) are spilled, one per cent hypochlorite solution (10,000 ppm available chlorine) should be placed over the spill for 30 minutes. Mop spillage with paper towels and dispose of these in wastebags using protective apparel. Swab area with commercial detergent, now that virus is inactivated, to remove residual hypochlorite.

3. Hypochlorite solutions, even in low concentrations, cannot be recommended at this stage for passage through integrated dental suction units. The long term damage to equipment is not yet sufficiently clear even at low levels.

4. Contact Public Health Division of Department of Health to obtain advice concerning disposal of contaminated waste in different municipalities.

5. There is no evidence to suggest aerosols are effective means of transmission of viruses such as HBV and HTLV-III. Clinicians are advised, however, to wear protective spectacles, employ effective high volume suction and rubber dam where applicable to confine contaminated fluids and prevent eye injury from particulate matter.

6. Decontamination of high and low speed handpieces, their bracket holders and air/water lines remain difficult due to equipment design. The potential for contamination can be reduced by definitive use of each handpiece ONCE during each clinical procedure, followed by immediate chemical surface disinfection and subsequent autoclaving of handpieces where possible, or by chemical disinfection if a handpiece cannot be autoclaved.

7. Underlying these guidelines is the essential requirement that PRACTICAL TREATMENT PLANNING be exercised in each case. This would probably involve the provision of basic emergency care in the vast majority of cases.

8. Resheathing of hypodermic needles is generally NOT recommended in medical practice. The design of both dental syringes and their double tipped, threaded hypodermic needles, however, differs from the conventional plastic disposable syringe and single tipped, friction fitted needles used in general medical practice. Resheathing of hypodermic needles following injections in dental practice is not advised, but if, in particular instances, it is considered necessary by the clinician, it should be carried out with care (perhaps with the aid of haemostats or tweezers).
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