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**Continuing Education**

## ***Management of HIV/AIDS Patients in Dental Practice***

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Continuing Education Units: 4 hours

The purpose of this course is to provide awareness and a deeper understanding of the treatment options for the HIV (Human Immunodeficiency Virus) patient. Significant regulations and recommendations have been generated to lessen the chances of viral exposure. Initially, the majority of these efforts were directed in the selection and use of personal protective devices. Updated and advanced knowledge should help to remove anxiety and misconceptions, and help reduce risks for patients, practitioners and the surrounding community.

### **Overview**

The Emergence of HIV (Human Immunodeficiency Virus) Disease in June 1981 has irreversibly changed American society. The presence of infection especially within groups that have traditionally experienced discrimination has challenged American core beliefs and the manner in which we provide medical care and social services. Even today, infected persons are stigmatized, thus inhibiting prompt diagnosis and proper treatment.

By 1988, the causative viral agent was isolated and its natural history elicited, epidemiological patterns established, high-risk behaviors identified, a serologic antibody test developed and an effective anti-viral drug approved. Unfortunately, the costs of treatment and research continue to be points of contention. Even though a cure or a preventive vaccine has yet to be achieved, significant progress has been made.

In order to provide dental care in the best manner, a deeper understanding of HIV Disease is required. Updated and advanced knowledge should help to remove anxiety and misconceptions associated with the treatment of HIV-infected patients. It should also help reduce risks for patients, practitioners and the surrounding community.

## Learning Objectives

Upon the completion of this course, the dental professional will be able to:

- Identify the components of the virus that causes HIV Disease.
- List the functions various components perform in the virus' natural lifecycle.
- Explain the underlying cause of HIV Disease, namely profound immune suppression.
- Describe progression of HIV Disease.
- Recall outcomes of infection, especially oral manifestations.
- Recognize factors that favor or retard disease progression.
- Follow infection control procedures that limit/prevent disease transmission.
- Summarize socioeconomic and legal issues associated with HIV Disease.

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## Glossary

**Acute retroviral syndrome** – initial viremia that occur soon (several weeks) after initial infection; often is associated with marked flu-like symptoms.

**Acquired immunity** – resistance resulting from previous exposure to an infectious agent or antigen, may be passive or active; results from the transfer of antibodies from another person or an animal, either naturally – as from a mother to a fetus or to the newborn via breast milk or by intentional inoculation (vaccination).

**Active immunity** – protection from a disease as a result of previous exposure to the disease-causing agent or antigens; defense may also result from vaccination.

**Adaptive immunity** – see specific host defense mechanisms.

**Administrative controls** – changing how and/or when employees do their jobs.

**AIDS** – acquired immunodeficiency syndrome; final end stage or step of HIV Disease; most severe manifestation; persons with AIDS are severely immune suppressed and often have significant number of infections, weight loss, diarrhea and an unusual cancer, Kaposi's sarcoma.

**AIDS dementia complex** – also known as AIDS associated dementia; degenerative neurological condition attributed to HIV infection; group of symptoms which include loss of coordination, mood swings, loss of inhibitions and widespread cognitive dysfunction; most common central nervous system complication of HIV infection.

**AIDS related complex (ARC)** – early symptomatic HIV infection; group of common complications which include progressive generalized lymphadenopathy, recurrent fever, unexplained weight loss, swollen lymph nodes, diarrhea, herpes, oral hairy leukoplakia, thrush of mouth and throat, and the presence of antibodies against HIV; some form of immune suppression may also be present; an old term that is usually applied to people who have clinical symptoms, but do not have AIDS.

**AIDS wasting syndrome** – involuntary weight loss plus either chronic diarrhea or chronic weakness and documented fever in the absence of a concurrent illness or conditions other than HIV infection that would explain the findings.

**Antibodies** – protein-rich molecules dissolved in blood and other body fluids that can destroy antigens; members are protein class called immunoglobulins, which are produced and secreted by B cells; an antibody is specific to a given antigen.

**Antigens** – materials foreign to a human; generally can elicit an immune response by itself; usually proteins or polysaccharides, but can be any type of molecule, including small molecules (haptens) coupled to a carrier-protein.

**ARC** – AIDS related complex; an old term that is usually applied to people who have clinical symptoms, but do not have AIDS.

**B lymphocytes** – also known as B cells; cells that are transformed into plasma cells which produce antibodies; transformation occurs after interaction with various types of T cells; involved with humoral immunity (immunity of fluids).

**Capsid** – protein-rich sac that contains/holds the genetic material of a virus.

**CD** – cluster differentiating antigen group; found on some type of T lymphocytes; differentiation is made through the assignment of numbers.

**CD4** – also called CD4+ cells; cells that have type 4 (T4) cluster differentiating antigens on their surfaces; normally orchestrate the entire human immune response; the prime target cell for HIV.

**CD8** – lymphocytes with the CD8 antigen marker on its surface; also called cytotoxic T cells, T8 cells and cytotoxic T lymphocytes.

**Cell-mediated immunity** – branch of human immunity that is primarily involved with the neutralization of viruses, viral infected host cells and cancer cells; process uses T cells, macrophages and other lymphocytes rather than B cells and antibodies.

**DNA** – deoxyribonucleic acid; molecular chain found in genes within nuclei of cells; carries genetic information; principle constituent of chromosomes.

**ELISA test** – Enzyme-Linked Immunosorbent Assay; a type of enzyme immunoassay (EIA) used to determine the presence of antibodies to HIV in the blood or oral fluids; repeatedly reactive (i.e., two or more) ELISA test results should be validated with an independent supplemental test of high specificity; in the United States, the confirmation test used most often is the Western Blot assay.

**Engineering controls** - controls that isolate or remove a hazard from the workplace.

**Envelope** – outer coat of some types of viruses; composed of lipid-rich materials taken from host cell membranes; can contain mushroom-like spikes required for attachment to host cells.

**Epidemic** – a disease that spreads rapidly through a demographic segment of the human population, such as everyone in a given geographic area; epidemic diseases can be spread from person to person or from a contaminated source such as food or water.

**Epidemiology** – branch of medical science that deals with the study of the incidence, distribution and control of a disease in a population.

**Exogenous disease** – disease originating outside an organ or part.

**Genome** – complete set of genes in the chromosomes of each cell or viral particle.

**Glycoprotein** – conjugated protein in which the non-protein component is a carbohydrate.

**gp41** – glycoprotein 41; embedded in the envelope of HIV; plays a key role in viral attachment by fusing with CD4+ antigens present in T 4 (helper) cell membranes.

**gp120** – glycoprotein 120; proteins that protrudes from the surface of HIV (spikes) and binds to CD4+ T cells; gp120 allows HIV to break through

T cell membranes and then binds to host cell components; assists HIV to enter.

**gp160** – glycoprotein 160; combined entity composed of HIV proteins gp41 and gp120.

**HAART** – antiretroviral drugs are medications for the treatment of infection by retroviruses, primarily HIV; different classes of antiretroviral drugs act at different stages of the HIV life cycle, combination of several (typically three or four) antiretroviral drugs is known as Highly Active Anti-Retroviral Therapy (HAART); combined use of at least two reverse transcriptase inhibitor drugs and a protease inhibiting drug; goals are to reduce the toxic effects associated with using a single drug and to lessen the chances that drug resistant viral forms will emerge.

**Hairy leukoplakia** – see oral hairy leukoplakia

**Helper T cells** – lymphocytes bearing the CD4 marker that is responsible for many human immune functions; turns immune system “on”; central, most important immune cell.

**Helper/suppressor ratio (of T cells)** – the normal ratio of CD4 cells (helper) to CD8 (suppressor) is approximately 2:1; ratio becomes inverted in persons with AIDS (and temporarily with other diseases); abnormal ratio results in a decrease in the overall human immune response.

**Highly active antiretroviral therapy** – see HAART

**Histoplasmosis** – fungal infection usually of the lungs caused by *Histoplasma capsulatum*; a common opportunistic infection seen among persons with HIV Disease.

**HIV** – human immunodeficiency virus, type 1; the retrovirus that causes HIV Disease.

**HIV Disease** – includes all stages or steps of infection from HIV-infected asymptomatic to HIV-infected symptomatic to the final life threatening phase called AIDS; disease caused by the replication of a retrovirus called HIV and characterized by a deficiency of the immune system (acquired, persistent functional depression of CD4 T helper lymphocytes) which leads to the

development of opportunistic infections, unusual forms of neoplasms, neurological disorders and wasting syndrome.

**HIV infected** – also called HIV-positive; presence of HIV in the body, which may or may not be detected by antibody screening tests.

**Humoral immunity** – immunity of body fluids and some tissues; usually involves dissolved proteins (e.g., antibodies) that neutralize soluble foreign entities (antigens) or small cells.

**Immune deficiency** – breakdown or inability of certain components of the immune system to function, thus making a person susceptible to certain diseases that they would not ordinarily develop.

**Immune response** – activity of the immune system against foreign substances.

**Immune system** – natural human defense caused by invading foreign agents; has two aspects – innate and acquired.

**Immunity** – natural or acquired resistance to a specific disease; may be partial or complete, long lasting or temporary.

**Immunocompromised** – an immune system in which the ability to resist or fight off infections and tumors is subnormal.

**Immunodeficiency** – breakdown of immunocompetence; certain parts of the human immune system no longer function properly, which results in increased susceptibility to certain diseases.

**Immunoglobulins** – collections of various types of large molecular weight proteins that have immune potential; also known as antibodies.

**Incidence** – the number of new cases (e.g., of a disease) occurring in a given population over a certain period of time.

**Incubation period** – time interval between the initial infection with a pathogen (e.g., HIV) and the appearance of the first symptoms or signs of disease.

**Infection** – multiplication and survival of microorganisms on or in the body.

**Infection control** – controlling the spread of disease agents by performing specific procedures.

**Innate immunity** – human immunity that is present at birth; may be species specific; may involve either humoral or cell-mediated immunity or both.

**Kaposi's sarcoma** – also called KS; an AIDS-defining illness consisting of individual cancerous lesions caused by an overgrowth of blood cells on the surface of skin or the oral cavity, but can occur internally also; process can spread, change colors and affect the eyes; internal lesions may be life-threatening; caused by a virus, the infectious agent responsible for all forms of the disease is known as Kaposi's sarcoma-associated herpes virus (KSHV). Kaposi's sarcoma herpes virus of HHV-8, which is similar to the Epstein Barr virus; treated by anti-inflammation agents, radiation or chemotherapeutic drugs.

**Latency** – period in which infecting organisms is in a host, but is not producing any clinically noticeable ill effects or symptoms; in HIV Disease is usually associated with the early asymptomatic period; usually CD4 counts are normal during latency, but the HIV remains active in lymph nodes; period in which most or all HIV are in the proviral stage.

**Lymphocyte** – white blood cell; present in blood, lymph and lymphoid tissue.

**Macrophage** – large immune cell that collects and devours invading pathogens and other invaders; its activities stimulate other immune cells by presenting them with small pieces of the invader; large amounts of HIV can be harbored inside without adverse effect; serve as reservoirs of HIV.

**Non-specific host defense mechanism** – protective tissues, fluids or processes that negatively affect all types of microorganisms; example include fever, saliva, vaginal secretions, stomach pH, sweat, sebum, sneezing, coughing and vomiting.

**Opportunistic infections** – illnesses caused by certain organisms which usually do not cause disease in persons with normal immune systems; common among persons with advanced HIV Disease.

**Oral hairy leukoplakia** – whitish lesions that appear on the side of the tongue and inside cheeks; lesions appear with ribbed or hairy surfaces; usually seen in persons with declining immune competency and may be cause by a Epstein-Barr virus; not seen before the start of the HIV pandemic.

**p24** – bullet-shaped core or capsid of HIV; made of several proteins including p24 that surrounds the viral RNA with the HIV; commonly present in the blood of persons infected with HIV; used as part of the serological ELISA screening test.

**Passive immunity** – also called acquired immunity.

**Pandemic** – a disease prevalent throughout an entire country, continent or whole world.

**Persistent generalized lymphadenopathy** – chronic, diffuse, noncancerous lymph node enlargement; usually seen in persons with persistent microbial infections; for HIV the swelling involved in at least two areas for three or more months with no obvious cause save HIV Disease.

**Plasma cells** – large antibody producing cells that develop from B cells.

**PPE** – personal protective equipment, such as gloves, masks, protective eyewear and gowns, used to limit exposure to bloodborne pathogens.

**Prevalence** – a measure of the proportion of people in a population affected with a particular disease at a given point in time.

**Protease** – enzymes that break down proteins into their component peptides; HIV protease break apart proteins that eventually become part of new HIV cores.

**Provirus** – state in which the viral genome is incorporated into that of the host; viral genes will

be replicated and passed on to all host daughter cells.

**PWA** – person with AIDS; also can mean person living with AIDS.

**Regulatory T cells** – T cells that direct other immune cells to perform their special functions; chief regulatory cells – T helper and T suppressor cells.

**Retrovirus** – type of virus that, when not infecting host cells, has a genome made of single-stranded RNA molecules instead of the more usually double-stranded DNA; HIV is an example of a retrovirus; retroviruses use reverse transcriptase to convert RNA to DNA, which then become part of the host cells' genetic material.

**Reverse transcriptase** – an enzyme of HIV and other retroviruses that converts the single-stranded viral RNA into DNA; an important process that if inhibited could retard viral multiplication.

**Ribonucleic acid** – nucleic acid usually found in the cytoplasm of cells; structurally similar to DNA; genome of some viruses, such as HIV.

**Simian** – resembling an ape or monkey.

**Specific host defense mechanisms** – also known as adaptive immunity; host defense processes, such as humoral and cell-mediated immunity directed against a specific pathogen or antigen.

**Spikes** – glycoprotein-rich structures embedded in viral envelopes; usually involved with viral recognition of and attachment to host cells.

**Standard (universal) procedures** – considering all patients as being potentially infectious and therefore applying infection control procedures to the care of all patients.

**Stomatitis** – an inflammatory disease of the mouth

**Syncytia** – also called Giant Cells; dysfunctional clumps formed by cell-to-cell fusion; HIV infected cells often bind to nearby uninfected cells forming

balloon-like giant cells; result is an enhanced loss of immune function.

**Syndrome** – a group of symptoms as reported by the patients and signs as detected in an examination that together are characteristic of a specific condition.

**T cells** – types of white blood cells (lymphocytes); come from the thymus and are involved with cell-mediated immunity; some T cells are immune regulators, while others have direct biological functions.

**T helper cells** – also called T4 or CD4 cells; subset of T cells which contain CD4 markers and which are involved with the activation of B cells and the formation of other types of T cells; center piece of the human immune system; prime target/host cell for HIV.

**T suppressor cells** – also known as T8 cells; function is to slow down or stop the immune response after the need has passed.

**T lymphocytes** – also known as T cells; mature in the thymus; involved with cellular immunity through the production of biologically active T cells and/or the release of immune-related chemicals.

**Translation** – process by which HIV DNA is processed to produce proteins and enzymes.

**Viral load** – total amount of virus present in a person's blood.

**Viremia** – proliferation in the number of viral particles, often needed in order for infection to occur.

**Virion** - complete viral particle; infectious form of a virus.

**Virus** - microscopic particles that contain a genome of single or double stranded DNA or single or double stranded RNA surrounded by a protein-rich capsid coat; some viruses have an outer lipid-rich envelop covering which contain glycoprotein spikes; all viruses are obligate intracellular parasites, which have varying abilities to survive on environmental surfaces; viruses,

parasitize animals, plants, bacteria and even other viruses.

**Western blot** – confirmatory test for HIV infection; validates earlier ELISA tests; tests for antibodies against HIV using a gel migration method.

**Work control practices** – controls that reduce the likelihood of exposure by altering the manner in which a task is performed.

### **HIV/AIDS at 25**

In June 5, 1981, the Centers for Disease Control and Prevention published a report in Morbidity and Mortality Weekly Report entitled - Pneumocystis Pneumonia - Los Angeles.

The report covered the period from October 1980 through May 1981 and described the health of five active young homosexual men. Each had been treated for biopsy confirmed Pneumocystis carinii pneumonia at three Los Angeles area hospitals. Two died during the period. The five men did not know each other and had no known common contacts. None had sexual partners with similar illnesses. Three of the men had profoundly depressed T cell counts and had markedly depressed in vitro antibody responses. Lymphocyte studies were not performed on the other two men.

Pneumocystis carinii pneumonia (PCP) in the United States is almost exclusively limited to severely immunosuppressed individuals. The occurrence of pneumocystitis in previously healthy young individuals without a clinically apparent underlying immunodeficiency is unusual.

### **A Second Report**

A month later, the CDC released a report concerning Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men in New York City and California.

The CDC had followed reports of Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States among 26 homosexual men (20 in New York City and six in California). The reports began in late 1978. Ages of the men ranged from 26-51 years (average of 39). Eight of the men had died within 24 months after KS was diagnosed.

KS is a malignant neoplasm manifested primarily by multiple vascular nodules in the skin and other organs. Malignant cells are found in the tissues under the skin or mucous membranes. KS causes red or purple patches (lesions) on the skin and/or mucous membranes and spreads to other organs in the body, such as the lungs, liver, or intestinal tract.

For decades, KS was considered a rare disease that mostly affected elderly men of Mediterranean or Jewish heritage, organ transplant patients, or young adult African men. This type is called classic KS. In the last 20 years, however, most KS cases have developed in association with human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS), especially among homosexual men. This is called AIDS-related KS.

### **Age of AIDS**

These cases were later recognized as the first reported cases of acquired immunodeficiency syndrome (AIDS) in the United States. Since then; the disease has become the one of the greatest public health challenges both nationally and globally. Human immunodeficiency virus (HIV) and AIDS have infected more than 65 million people and have claimed the lives of more than 22 million persons worldwide, including more than 500,000 in the United States.

HIV/AIDS has generated an almost immeasurable amount of suffering, hardship, loss and despair. Disease spread was hastened by prejudice, denial, ignorance and even defense of freedoms associated with a sexual revolution. As HIV/AIDS moved from footnote to pandemic, our lives, attitudes and practices were challenged and then motivated to change.

In the 25 years since 1981, countless numbers of persons and multiple organizations, inside and outside the government, have mobilized to prevent and treat the disease. There have been marked successes with significant challenges remaining.

### **Prevention Programs**

During the 25 years of HIV/AIDS in the United States, there has been an unprecedented mobilization of individual, community and governmental resources directed toward slowing

and stopping the epidemic. A three-pronged approach was developed:

- preventive activities directed at persons at high risk for infection;
- HIV counseling, testing and referral services; and
- prevention schemes directed at improving the health of persons living with HIV and preventing further spread.

Dissemination of useful and correct information started in the 1980s. However, this was not enough to motivate behavioral changes among some persons at high risk. Very direct behavioral intervention packages plus training were developed. The effectiveness of such interventions has been reviewed for the last 10 years and has shown to change behavior substantially.

In 1983, HIV was identified as the cause of AIDS. Within two years, commercial HIV antibody tests were available. In 2004, 2.2 million HIV tests were performed at 11,000 CDC supported testing sites. Originally, testing required two visits about two weeks apart. Depending on setting and population, from 10 to 50 percent of the persons tested failed to return for their results. Also, drawing a blood specimen has drawbacks. The standard HIV test screens for antibodies to the virus and is called an ELISA (enzyme-linked Immunosorbent assay) test.

Since 2003, four rapid HIV tests have been approved by the Food and Drug Administration. Two have been approved for use at point-of-care sites outside of traditional laboratories. One of the tests can analyze oral fluids, whole blood or plasma. The others can test serum and plasma or whole blood. All four tests can be interpreted visually. Such tests can help reduce unrecognized infections by improving access to testing in both clinical and non-clinical sites. Results can be obtained in 30 minutes, so more of those tested will learn their results.

A reactive result from any of the four HIV tests is interpreted as a “preliminary positive,” which means that a more specific assay, typically a Western Blot (WB) or immunofluorescent assay (IFA), is required. Performing a standard ELISA screening prior to confirmatory testing is not

required. A positive WB or IFA confirms the diagnosis of HIV infection.

In the past, preventive schemes were designed to meet the needs of persons at increased risk for HIV. Now greater emphasis is placed on persons living with HIV. Current recommendations are to incorporate HIV prevention into the medical care of HIV seropositive persons. Behavior modification can be effective and lead to as much as a 43 percent relative reduction in unprotected sex and acquisition of sexually transmitted diseases.

### **Success Stories**

There have been many breakthroughs in HIV/AIDS since 1981. A retrovirus (HIV) was isolated in 1983 and identified as a causative agent of AIDS in 1984. The first antibody test (ELISA) for HIV infection was approved by the FDA in 1985. The first anti-HIV drug, AZT (zidovudine, Retrovir) was approved for use in 1987. The first confirmatory test, a WB blood test kit, was also approved in 1987.

Multiple drug therapies emerged in 1992. Potent combinations of antiretroviral drugs have been linked to adverse consequences, including metabolic complications and viral resistance. Therapeutic side effects challenge successful clinical management of HIV/AIDS. In 1994, a kit that used oral fluids instead of blood for detection of antibodies against HIV was approved. Home specimen collection kits appeared in 1995. In March, 1996, the FDA approved the first antigen test kit to screen blood donors. Such tests could prevent 25 percent of transfusion-associated cases, in which donors are infected but have not yet produced measurable antibodies. In 2003, the FDA expanded the availability of rapid HIV tests to include more than 100,000 sites, including physician offices and HIV testing centers.

One of the most notable milestones involves the reduction of perinatal HIV transmission. Observed decreases in pediatric AIDS and HIV cases likely resulted from increased identification of infected mothers and exposed infants and timely intervention to prevent perinatal HIV transmission. The need for pregnant women to know their HIV status was recognized early



in the epidemic as a key step to preventing transmission. In 1985, the CDC recommended that pregnant women at high risk be offered counseling and voluntary HIV testing.

Significant reduction of perinatal transmission of HIV infection has occurred over the last 20 years. Pediatric AIDS cases were reported as early as 1982. During 2005, an estimated 92 percent of AIDS cases reported in the U.S. among children younger than 13 were related to mother-to-child transmission of HIV. Viral spread can occur during pregnancy, labor, delivery or breastfeeding. The number of perinatal HIV infections peaked at 1,650 in 1991 and have declined to an estimated 144 to 236 per year today. Only a third of the cases of perinatally acquired AIDS were reported in children under age one.

The drop in cases can be related to several factors. These include:

- expanded and easier HIV testing;
- use of antiretroviral agents during pregnancy;
- avoiding breastfeeding; and
- scheduled cesarean delivery.

Identifying infected mothers and exposed infants combined with timely intervention can help prevent HIV transmission. As early as 1985 the CDC recommended that pregnant women at high risk be offered counseling and voluntary HIV testing. At the time, risk-based screening for HIV was recommended because no treatment was available. However, many women with HIV infection were identified with risk-based screening. In 2001, the CDC tested guidelines recommending routine HIV screening as early as possible during pregnancy with streamlined counseling and consent processes to reduce barriers to testing.

In 1994, a clinical trial demonstrated a breakthrough intervention with a 67 percent reduction of perinatal HIV transmission. It used a three-part regimen consisting of administering AZT to the mother during pregnancy and labor, and to the newborn for the first six weeks. Even greater decreases have been achieved through the use of multiple drug therapies. Maternal treatment with HAART reduced perinatal transmission to less than 2 percent of deliveries by women with HIV.

Breastfeeding was involved in 30 to 50 percent of perinatal HIV transmission. Avoiding breastfeeding is now recommended in the U.S., where safe alternatives are accessible and affordable. Several studies have confirmed that cesarean delivery performed before onset of labor and membrane rupture can reduce HIV transmission to infants whose mothers do not receive drug therapy during pregnancy or who receive only AZT.

### **Current Challenges**

There has been a marked decrease in the number of new HIV infections each year. Also, infected persons take longer to develop AIDS and persons with AIDS live longer with their immune suppression. However, people are still becoming infected. An effective preventive vaccine is needed.

HIV vaccines have been actively investigated for many years. The goal is to produce an immunization process that will produce neutralizing antibodies that protect against infection. There are a number of obstacles. One of the most important is the genetic diversity of HIV. The life cycle of HIV has two elements that cause this diversity. HIV has a marked ability to mutate. This means that even in a single individual there can be a swarm of viruses called quasi-species. Genetic diversity also exists when comparing viruses from several different people.

Much is known about HIV, including all its components and genetic codes. We know in great detail how the virus destroys the immune system. However, what is not known is which immune responses can prevent or contain an infection. The virus replicates quickly and mutates rapidly, making it difficult to know what vaccines could be effective against all types of HIV. Also, HIV has developed sophisticated mechanisms to avoid immune cell action. It can protect its surface proteins with a carbohydrate mix to shield vulnerable areas from antibody attack. The virus, like some others, can also produce proteins designed to retard the production of some types of immune cells. Other pathogens have escaped vaccine protection, including hepatitis C, TB and the malaria parasite.

Vaccine development is a top medical initiative in the United States. There are studies of persons

repeatedly exposed to HIV who never become infected. Also being studied extensively are persons who are infected, but who do not experience symptoms after 10 years or more.

## HIV Virology

All viruses are obligate intracellular parasites. This means they are dependent on their hosts for much of their metabolic (and reproductive) needs. Usually, they travel from one host cell to another as quickly as possible. Some viruses, however, can exist for extended periods of time on inert, environmental surfaces. The human immunodeficiency virus (HIV) can remain viable for short periods of time outside of its host cells, especially if held within a moist environment.

Worldwide, there are two types of HIV – HIV-1 and HIV-2. HIV-1 is far more common in the United States and usually causes more significant pathology. In this course only the term “HIV” will be used and it will represent HIV-1.

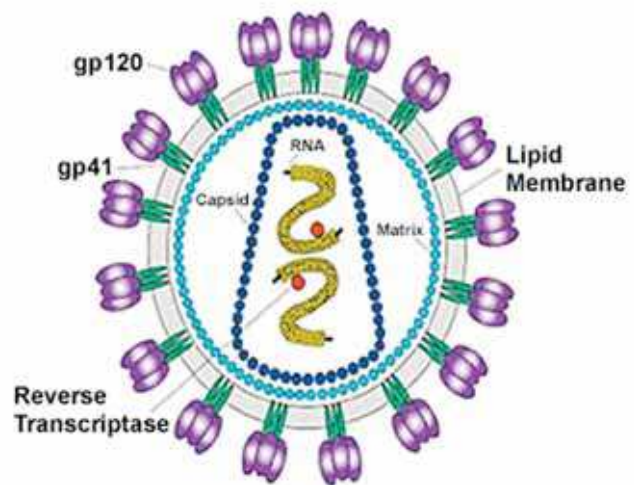
All viruses are parasitic. That means that they benefit while their hosts are damaged in some manner. Viruses steal energy and take control of the metabolic processes of their hosts. The goal is to divert host processes to the reproduction of viral particles.

Viruses are not cellular in nature; rather they form entities called particles. A complete infectious viral particle is called a virion. In some cases, infection is mild with few or even unapparent symptoms. In the case of HIV, damage is significant and is usually life threatening. Viruses do not belong to any classification kingdom (e.g., animal or plant). They are unique life forms composed of a small amount of nucleic acid held within protein-rich sacs called capsids. Some viruses have another coat, which is composed of lipid materials called an envelope. Viral genomes are composed of single or double stranded DNA or single or double stranded RNA, but not both. Usually only a limited number of viral genes are present. However, with this limited genetic material viruses are still able to locate, enter and take over host cells.

Viruses are unusually specific as to their hosts. This specificity applies not only to a desired species, but also to specific tissues and even cell types. Viral lifecycles vary greatly in

length. However, the time it takes for viruses to enter a host to the time new particles are released usually does not vary and thus is quite characteristic. However, some viruses, including HIV have very extended lifecycles lasting months to years.

Many of the most infamous human infections involve viruses. These include hepatitis B, C and D, herpes viruses, polio, measles, mumps, yellow fever, influenza and those viruses that cause the common cold. Some viral infections can be prevented by immunization. A number of viruses have been shown to be oncogenic; that is, they can over time cause cancer. Viruses not only affect animals, but they also can infect bacteria, fungi, plants and even other viruses.



### Organization of the HIV Virion

Source: NIAID. Fact Sheet - How HIV Causes AIDS. 3, 2001 and <http://www.niaid.nih.gov/factsheets/howhiv.htm>

HIV is a retrovirus. Related retroviruses cause infection in humans (a type of leukemia) and other animals, such as simians. HIV belongs to a subfamily called lentiviruses or slow viruses. Lentiviruses not only affect humans, but also cats, sheep, goats and nonhuman primates. HIV contains single stranded RNA, which exists in two pieces. Associated with the RNA is a special enzyme called reverse transcriptase. The viral capsid appears as a cone-shaped core. HIV is an enveloped virus. The envelope is primarily composed of lipid-rich materials taken from the membranes of host cells. Embedded in the envelope is a series of projectiles called spikes. Each spike is composed of two parts - gp41

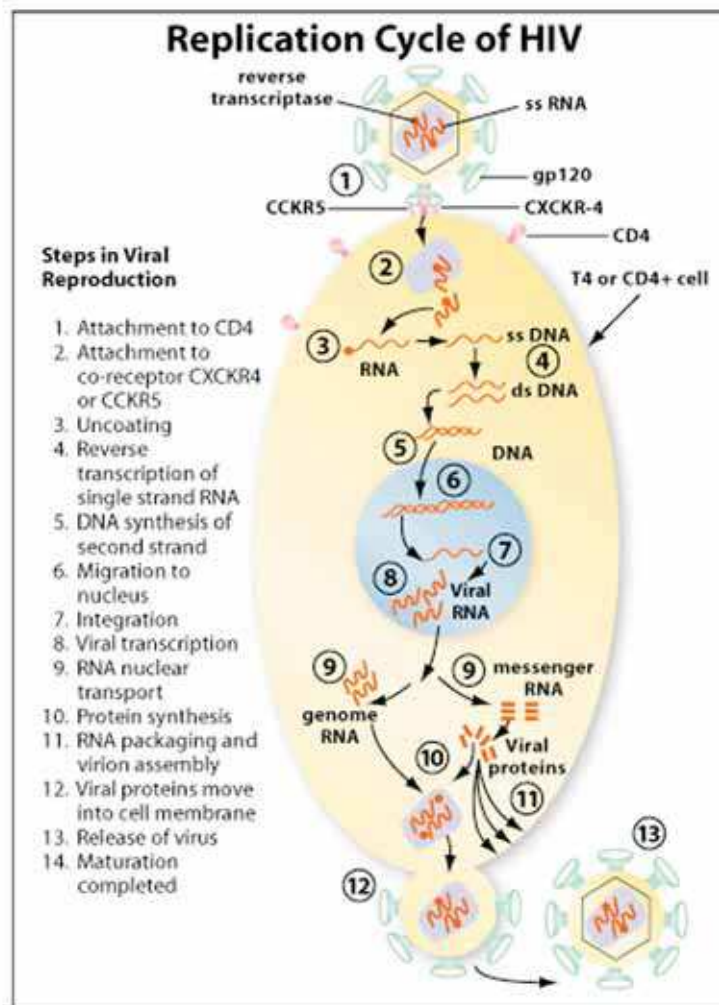
which contains a coiled up protein and gp120 (gp stands for glycoprotein). The two glycoproteins together are called gp160. The function of gp160 is to attach and penetrate specific host cells.

The genetic flow in human cells goes from DNA → RNA → proteins. The genetic message present in a small piece of DNA called a gene is transcribed into RNA, which is then translated into a protein with the help of ribosomes. However, HIV is less than two microns (10<sup>-6</sup> meters) across and is too small for ribosomes. Retroviruses reverse the genetic flow with the use of reverse transcriptase. The single stranded RNA of HIV is reverse transcribed into complementary pieces of single stranded DNA. Host enzymes then unite the RNA strands and make a complementary DNA strand with the result being a small piece

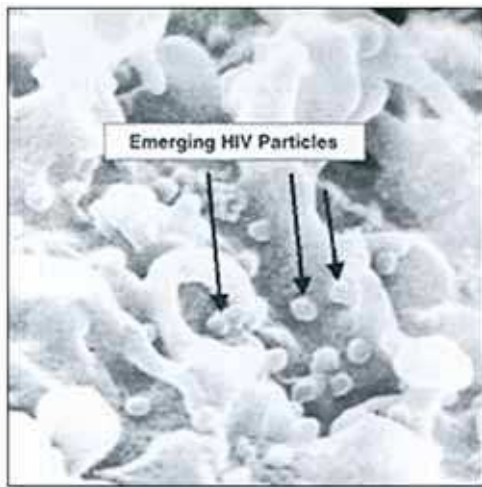
(less than 10,000 nucleotides long) of double stranded DNA (see Figure 1). This small piece of DNA migrates into the host nucleus and then integrates into the host genome.

HIV is now in its provirus state. HIV has a tendency to remain as a provirus for extended periods of time. Replication is slow and clinically it appears that the disease has gone dormant. However, HIV is multiplying at a slow rate in regional lymph nodes. The body continues to fight hard against the infection. Eventually, viral multiplication will exceed some threshold value, overwhelm the immune response and symptoms will begin.

HIV has only nine genes. Three structural genes are code for important particle components, while



**Figure 1.** Source: Stine GJ. AIDS Update 2003. 2003, Prentice Hall, Upper Saddle River, NJ, pp.56



**Figure 2.** Scanning Electron Micrograph of HIV Grown in Cultured Lymphocytes  
Source: Centers for Disease Control and Prevention

the remaining six genes are regulatory genes. These genes regulate the timing and pace of the structural gene function.

HIV uses the host cell's metabolic capacity to reproduce. The single stranded RNA pieces and the reverse transcriptase are placed within the capsid (see Figure 1). The envelope and spikes are added during the movement of the viral particles out of the host cell. Viral products are released not by bursting the host cell open, but rather through a slow release process called budding (see Figure 2).

## Immunology

Immunology is the study of the immune response. Each day humans are exposed to many foreign particles, cells and materials. It is the job of the immune system to neutralize these invaders and prevent harm to the body. Whole courses and even university majors are dedicated to the study of human immunology. However, in order to understand how HIV Disease produces pathology and to possibly develop means to prevent immune impairment, some background materials on immunology must be offered.

There are two basic forms of immunity – innate (non-specific) and specific (adaptive) immunity. Innate or non-specific immunity is the body's first line of defense. The basic function is to prevent entrance of foreign and potentially harmful materials into the body. The goal is to protect against all foreign material, not just some specific

types. Examples of innate/non-specific immunity include intact skin and mucous membranes and body fluids like saliva, vaginal secretions, stomach acid, sebum, sweat and tears. It also includes behaviors such as vomiting, spitting, sneezing or coughing. Macrophages and neutrophils are part of the innate/non-specific host defense system. These cells can engulf and kill foreign organisms without the need for antibodies.

Another line of defense is the specific/adaptive immune system that takes time to respond to a primary invasion. Specific/adaptive immunity can be divided into two responses – humoral and cell-mediated. Humoral immunity involves body fluids and some tissues. During this process B cell lymphocytes (one type of leukocyte) are stimulated by exposure to a foreign particle to become plasma cells and to form large amounts of antibodies. Antibodies are produced against a specific foreign particle, cell or chemical (also called an antigen). Antibodies are soluble proteins that bind to foreign antigens and help to remove them.

T cell lymphocytes are involved with cell-mediated immunity. T cells after exposure to foreign materials develop into biologically active cells and directly neutralize invaders. Other types of T cells differentiate into regulatory cells – cells that turn the immune response on and off (see Figure 3).

T cells that “turn on” an immune response are called T4 or T helper cells. T cells that suppress the immune response after a crisis has past are called T8 or T suppressor cells. Together they regulate (fine tuning) the entire immune response including all B and T cell activities. Cell-mediated immunity also involves the specific identification and neutralization of foreign materials, cells and organisms. In the case of viruses and tumor cells, the response is also vital to the recognition and destruction of virally infected or tumorigenic cells. The response after the first exposure to a specific foreign particle is generally slow. It may take several days to weeks for a proper (and effective) response to be accomplished. However, not all B and T cells involved in an immune response are used to directly fight the invaders. Some become memory B and T cells that replicate and persist hopefully for a lifetime. The response to a second exposure to a foreign

antigen involves already dedicated B and T cells, so the response is faster and quantitatively greater.

A properly functioning immune system is required for proper health. Problems can occur which involve a poor response or one that is too great (hypersensitivities). Sometimes the human immune system becomes confused and starts to attack host tissues and cells (autoimmunity).

HIV specifically parasitizes the central cell of the human immune system – the T4 or T helper lymphocyte (see Figure 3). As HIV takes over T4 cells it alters their growth and reproduction through a complicated process that leads to cellular death. The ration of T4 to T8 cells then changes. Normally, there are more T4 cells than T8's. In HIV infected persons, there usually is a decline in T4 counts that signals the progress of immune system deterioration. The results are debilitating. The T4 cells are not as responsive to antigen identification, macrophages become less responsive and B cells produce fewer specific antibodies and lose their normal responsiveness. The immune system is becoming dysfunctional,

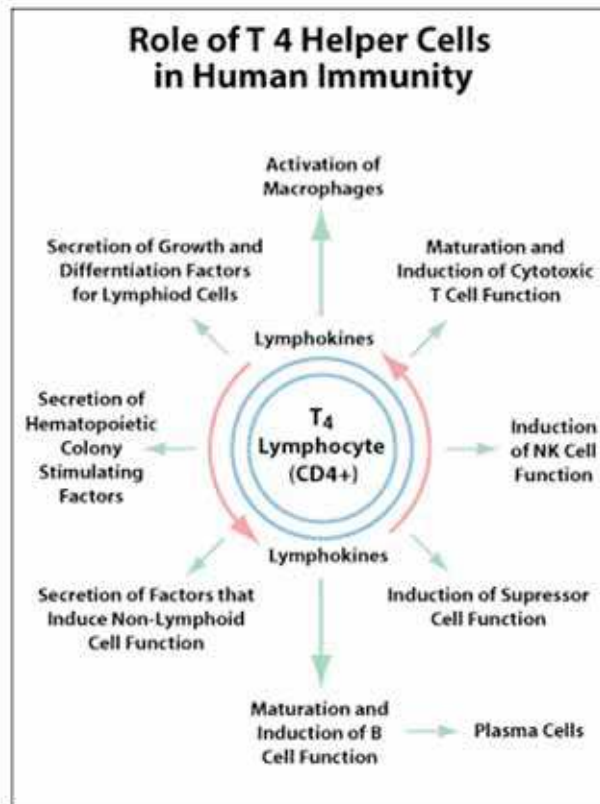
leaving the host vulnerable to attack from opportunistic infection, the development of neoplastic lesions and neurological defects.

## Viral Transmission

### Major Routes

Modes of HIV transmission depend on geographic location. In North America, HIV is spread primarily by sexual contact (homosexual and/or heterosexual), exposure to blood (and some tissues) generally through IV drug abuse and from infected mothers to their fetus (passage through the placental barrier) or newborns (via colostrums). Over 99% of all cases can be related to one or more of these risk factors. Other risk factors such as blood transfusions, transplants and hemophilia have decreased almost to zero. This is because such blood and tissues can be readily screened and the application of heat kills HIV in clotting factor concentrates without affecting agent potency.

Over the years, a number of alternative routes of transmission have been suggested. These



**Figure 3.** Source: Fauci AS. The human immunodeficiency virus: infectivity and mechanisms of pathogenesis. *Science* 239:617-22, 1988.

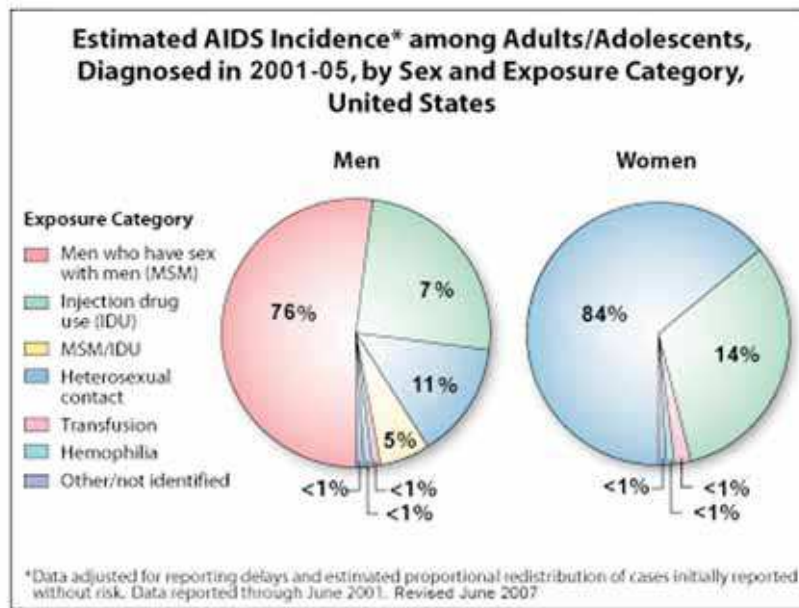


Figure 4. Source: Centers for Disease Control and Prevention

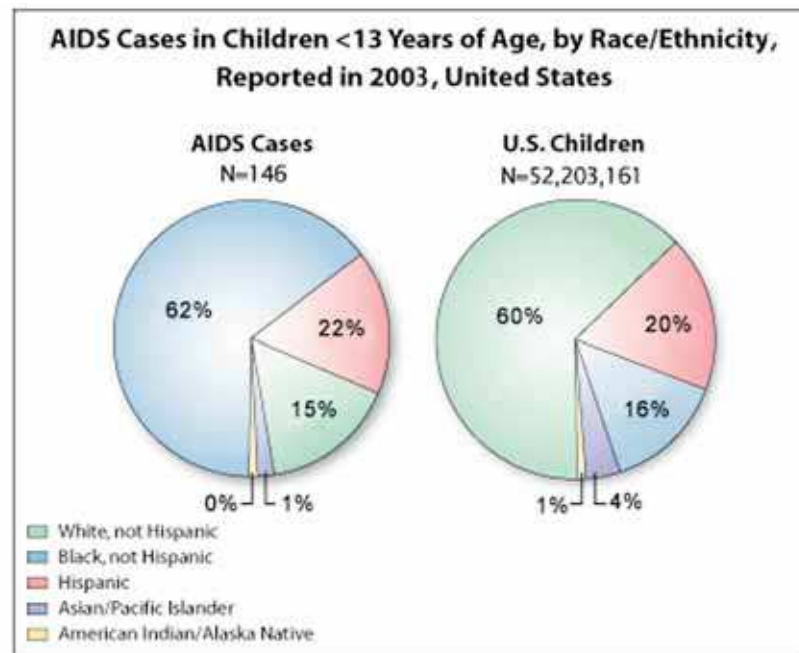


Figure 5. Source: Centers for Disease Control and Prevention

include kissing, shared use of drinking fountains, eating utensils and toilets seats. All have been proven to not be a route of transmission. Causal contact does not spread HIV. One interesting mode suggested is spread via mosquitoes. Fortunately, the acid in mosquito stomachs inactivates HIV. Mosquitoes do not transmit HIV.

Men are infected differently than women. The majority of men are still infected by having sexual

contact with other men. Almost all women are infected heterosexually or through IV drug abuse (see Figure 4). Having an infected mother is the leading risk factor for children (persons less than 13 years of age).

HIV Disease is disproportionately transmitted on the basis of race or ethnicity (see Figures 5 and 6). Although whites are more than two-thirds of the American population, they represent less

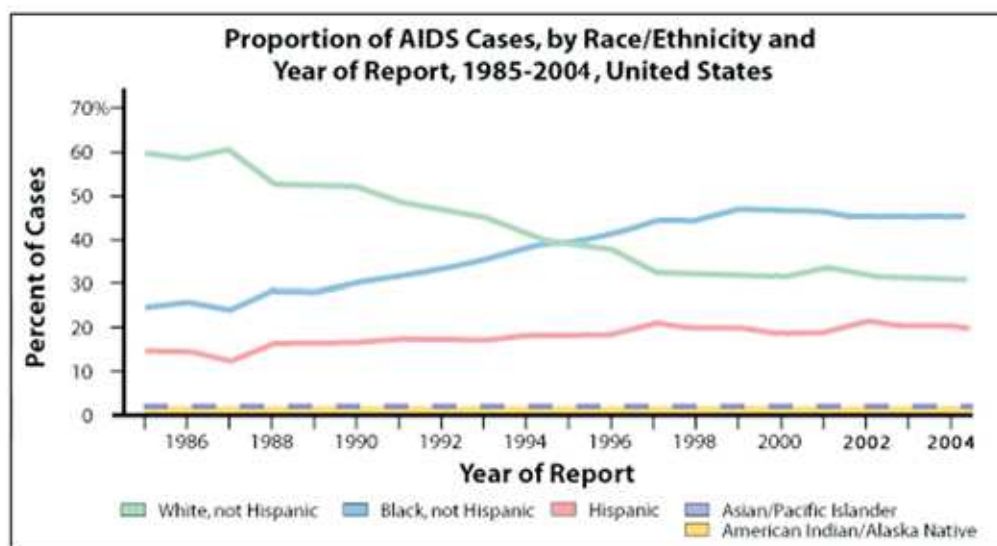


Figure 6. Source: Centers for Disease Control and Prevention

than 16% of pediatric and 28% of adult/adolescent cases. Both blacks and Hispanics have percentages greater than their presence in the population. For example, over 85% of all women with HIV Disease are minorities.

The latest reports indicate that approximately 175,000 persons in the United States (see Figure 7) are currently living with a HIV infection (infection, but not AIDS). Not all states and territories in the United States routinely report to the CDC persons diagnosed as infected. In fact, only certain areas of some states report. So the actual number of infection persons is probably closer to 750,000. Underreporting is one cause. However, many people are not tested until they start to experience symptoms. Thus, many people in America are infected, but have not been serologically screened.

Age is also a factor in HIV transmission (see Figure 7). Infection peaks in both males and females in all racial and ethnic groups from 25 to 34 years of age. It is during this period of time when high-risk behaviors are most common. However, one rapidly growing age group for HIV infection are those persons 60 years old and above.

There have been over 816,000 people in the United States that have been diagnosed with AIDS (see Figure 8). Of these, about 29% have died. Worldwide, almost 60% of persons with AIDS

have died. About 52% of all adult/adolescent cases of AIDS involve men having sex with men. Two thirds of women with AIDS were infected via heterosexual contact. Approximately 1% of AIDS cases in the United States are pediatric cases.

#### Practitioner to Patient

In July of 1990, the CDC reported the possible transmission of HIV from a Florida dentist to a female patient. Apparently, this dentist with HIV Disease infected six of his patients during the years 1987 through 1990. Investigation of the case included a comparison of the HIV genomes from the dentist and the patients. There was significant similarity among the viruses. However, the investigation did not discover the mode of virus spread. Final conclusions of the investigation suggested direct contact from the dentist to the patients was most likely rather than spread from contaminated instruments, equipment or surfaces. The dentist during the period did not routinely wear gloves.

There have been a limited number of other reports of practitioner to patient spread of HIV. All have come from outside the United States and involved invasive surgical techniques.

Fortunately, the rate of practitioner to patient infection is extremely low. Reviews of thousands of patients from approximately 75 HIV-infected dentists and physicians did not identify any cases of HIV transmission.

Transmission category	White, not Hispanic				Black, not Hispanic				Hispanic			
	2004		Cumulative through 2004 <sup>a</sup>		2004		Cumulative through 2004 <sup>a</sup>		2004		Cumulative through 2004 <sup>a</sup>	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<b>Injecting drug use</b>	341	(21)	3,513	(26)	546	(9)	6,223	(14)	368	(19)	1,816	(19)
<b>Hemophilia/coagulation disorder</b>	0	(0)	20	(0)	5	(0)	31	(0)	2	(0)	9	(0)
<b>Heterosexual contact:</b>	667	(40)	6,236	(46)	2,358	(39)	19,445	(45)	1,003	(51)	4,505	(48)
<i>Sex with injection drug user</i>	147	(9)	1,685	(12)	273	(4)	3,269	(8)	233	(12)	1,018	(11)
<i>Sex with bisexual male</i>	50	(3)	540	(4)	110	(2)	1,075	(2)	27	(1)	177	(2)
<i>Sex with person with hemophilia</i>	5	(0)	106	(1)	8	(0)	63	(0)	1	(0)	9	(0)
<i>Sex with HIV-infected transfusion recipient</i>	5	(0)	53	(0)	19	(0)	100	(0)	2	(0)	31	(0)
<i>Sex with HIV-infected person, risk not specified</i>	460	(28)	3,852	(28)	1,948	(32)	14,938	(35)	740	(38)	3,270	(35)
<b>Receipt of blood transfusion, blood components, or tissue</b>	9	(1)	144	(1)	43	(1)	332	(1)	12	(1)	62	(1)
<b>Other/risk not reported or identified</b>	646	(39)	3,772	(28)	3,144	(52)	17,254	(40)	576	(29)	3,029	(32)
<b>Total</b>	<b>1,663</b>	<b>(100)</b>	<b>13,685</b>	<b>(100)</b>	<b>6,096</b>	<b>(100)</b>	<b>43,285</b>	<b>(100)</b>	<b>1,961</b>	<b>(100)</b>	<b>9,421</b>	<b>(100)</b>

Transmission category	Asian/Pacific Islander				American Indian/ Alaska Native				Total			
	2004		Cumulative through 2004 <sup>a</sup>		2004		Cumulative through 2004 <sup>a</sup>		2004 <sup>b</sup>		Cumulative through 2004 <sup>a</sup>	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<b>Injecting drug use</b>	3	(4)	18	(5)	3	(8)	87	(28)	1,267	(13)	11,719	(17)
<b>Hemophilia/coagulation disorder</b>	0	(0)	1	(0)	0	(0)	0	(0)	7	(0)	62	(0)
<b>Heterosexual contact:</b>	30	(40)	138	(42)	17	(45)	139	(45)	4,090	(41)	30,644	(45)
<i>Sex with injection drug user</i>	3	(4)	10	(3)	2	(5)	49	(16)	666	(7)	6,063	(9)
<i>Sex with bisexual male</i>	1	(1)	7	(2)	1	(3)	10	(3)	189	(2)	1,822	(3)
<i>Sex with person with hemophilia</i>	0	(0)	0	(0)	0	(0)	2	(1)	14	(0)	182	(0)
<i>Sex with HIV-infected transfusion recipient</i>	0	(0)	1	(0)	0	(0)	0	(0)	26	(0)	186	(0)
<i>Sex with HIV-infected person, risk not specified</i>	26	(35)	120	(36)	14	(37)	78	(25)	3,195	(32)	22,391	(33)
<b>Receipt of blood transfusion, blood components, or tissue</b>	0	(0)	5	(2)	0	(0)	1	(0)	64	(1)	546	(1)
<b>Other/risk not reported or identified</b>	42	(56)	169	(51)	18	(47)	80	(26)	4,446	(45)	24,572	(36)
<b>Total</b>	<b>75</b>	<b>(100)</b>	<b>331</b>	<b>(100)</b>	<b>38</b>	<b>(100)</b>	<b>307</b>	<b>(100)</b>	<b>9,874</b>	<b>(100)</b>	<b>67,543</b>	<b>(100)</b>

**Figure 7.** Reported cases of HIV infection (not AIDS) for female adults and adolescents, by transmission category and race/ethnicity, cumulative through 2004—42 areas with confidential name-based HIV infection reporting.

Note. Includes only persons with HIV infection that has not progressed to AIDS.

Since 2004, the following 42 areas have had laws or regulations requiring confidential name-based HIV infection reporting: Alabama, Alaska, Arizona, Arkansas, Colorado, Connecticut, Florida, Georgia, Idaho, Indiana, Iowa, Kansas, Kentucky, Louisiana, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, Puerto Rico, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, West Virginia, Wisconsin, Wyoming, American Samoa, Guam, Northern Mariana Islands, and the U.S. Virgin Islands.

Connecticut has confidential name-based HIV infection reporting only for pediatric cases.

Florida (since July 1997) has had confidential name-based HIV infection reporting only for new diagnoses.

Pennsylvania (October 2002) implemented confidential name-based HIV infection reporting only in areas outside the city of Philadelphia.

Texas (February 1994 through December 1998) reported only pediatric HIV infection cases.

<sup>a</sup> Includes persons with a diagnosis of HIV infection (not AIDS), reported from the beginning of the epidemic through December 2004. Cumulative total includes 514 females of unknown race or multiple races.

<sup>b</sup> Total includes 41 females of unknown race or multiple races.

Source: Centers for Disease Control and Prevention at: <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2004report/table22.htm> (Last Modified: January 9, 2006)



Adult or adolescent exposure category	Males				Females				Total			
	2004		Cumulative through 2004 <sup>a</sup>		2004		Cumulative through 2004 <sup>a</sup>		2004		Cumulative through 2004 <sup>a</sup>	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Male-to-male sexual contact	15,607	(48)	402,722	(55)	—	—	—	—	15,607	(35)	402,722	(44)
Injecting drug use	4,564	(14)	155,872	(21)	2,355	(20)	63,181	(37)	6,919	(16)	219,053	(24)
Male-to-male sexual contact and injection drug use	1,696	(5)	60,038	(8)	—	—	—	—	1,696	(4)	60,038	(7)
Hemophilia/coagulation disorder	71	(0)	5,096	(1)	21	(0)	331	(0)	92	(0)	5,427	(1)
Heterosexual contact:	3,373	(10)	43,347	(6)	5,278	(45)	74,540	(43)	6,651	(19)	117,887	(13)
Sex with injection drug user	435	(0)	11,048	(0)	871	(0)	24,568	(0)	1,306	(0)	35,616	(0)
Sex with bisexual male	—	—	—	—	251	(0)	4,617	(0)	251	(0)	4,617	(0)
Sex with person with hemophilia	4	(0)	78	(0)	15	(0)	478	(0)	19	(0)	556	(0)
Sex with HIV-infected transfusion recipient	29	(0)	517	(0)	37	(0)	733	(0)	66	(0)	1,250	(0)
Sex with HIV-infected person, risk not specified	2,905	(0)	31,704	(0)	4,104	(0)	44,144	(0)	7,009	(0)	75,848	(0)
Receipt of blood transfusion, blood components, or tissue <sup>b</sup>	90	(0)	5,163	(1)	106	(1)	4,111	(2)	196	(0)	9,274	(1)
Other/risk not reported or identified <sup>c</sup>	7,355	(22)	85,062	(9)	4,099	(35)	29,440	(17)	11,454	(26)	94,504	(10)
<b>Subtotal</b>	<b>32,756</b>	<b>(100)</b>	<b>737,300</b>	<b>(100)</b>	<b>11,859</b>	<b>(100)</b>	<b>171,603</b>	<b>(100)</b>	<b>44,615</b>	<b>(100)</b>	<b>908,905</b>	<b>(100)</b>
<b>Child (&lt;13 yrs at diagnosis)</b>												
Hemophilia/coagulation disorder	0	(0)	223	(5)	0	(0)	7	(0)	0	(0)	230	(2)
Mother with/at risk for HIV infection: <sup>d</sup>	51	(84)	4,243	(89)	53	(87)	4,333	(94)	104	(85)	8,576	(91)
Injection drug use	12	(20)	1,653	(34)	7	(11)	1,643	(35)	19	(16)	3,296	(35)
Sex with injection drug user	6	(10)	776	(16)	6	(10)	742	(15)	12	(10)	1,518	(16)
Sex with bisexual male	1	(2)	94	(2)	1	(2)	101	(2)	2	(2)	195	(2)
Sex with person with hemophilia	0	(0)	21	(0)	1	(2)	16	(0)	1	(1)	37	(0)
Sex with HIV-infected transfusion recipient	0	(0)	11	(0)	1	(2)	16	(0)	1	(1)	27	(0)
Sex with HIV-infected person, risk not specified	17	(28)	718	(15)	11	(18)	747	(15)	28	(23)	1,465	(16)
Has HIV infection, risk not specified	15	(25)	901	(19)	25	(41)	986	(21)	40	(33)	1,887	(20)
Receipt of blood transfusion blood components, or tissue <sup>b</sup>	0	(0)	244	(5)	0	(0)	144	(3)	0	(0)	388	(4)
Other/risk not reported or identified <sup>d</sup>	10	(16)	84	(2)	8	(13)	103	(2)	18	(15)	187	(2)
<b>Subtotal</b>	<b>61</b>	<b>(100)</b>	<b>4,794</b>	<b>(100)</b>	<b>61</b>	<b>(100)</b>	<b>4,587</b>	<b>(100)</b>	<b>122</b>	<b>(100)</b>	<b>9,381</b>	<b>(100)</b>
<b>Total</b>	<b>32,817</b>	<b>(100)</b>	<b>742,094</b>	<b>(100)</b>	<b>11,920</b>	<b>(100)</b>	<b>176,190</b>	<b>(100)</b>	<b>44,737</b>	<b>(100)</b>	<b>918,286</b>	<b>(100)</b>

**Figure 8.** Reported Aids cases, by age category, transmission category, and sex, cumulative through 2004 - United States.

a - Includes persons with a diagnosis of AIDS, reported from the beginning of the epidemic through 2004. Cumulative total includes 2 persons of unknown sex.

b - AIDS developed in 47 adults/adolescents and 3 children after they received blood that had tested negative for HIV antibodies. AIDS developed in 14 additional adults after they received tissue, organs, or artificial insemination from HIV-infected donors. Four of the 14 received tissue or organs from a donor who was negative for HIV antibody at the time of donation.

c - Includes 36 adults/adolescents who were exposed to HIV-infected blood, body fluids, or concentrated virus in health care, laboratory, or household settings, as supported by seroconversion, epidemiologic, and/or laboratory evidence. One person was infected after intentional inoculation with HIV-infected blood. For an additional 424 persons who acquired HIV infection perinatally, AIDS was diagnosed after age 12. These 424 persons are tabulated under the adult/adolescent, not the pediatric, transmission category.

d - Includes 5 children who were exposed to HIV-infected blood as supported by seroconversion, epidemiologic, and/or laboratory evidence: 1 child was infected after intentional inoculation with HIV-infected blood and 4 children were exposed to HIV-infected blood in a household setting. Of the 187 children, 23 had sexual contact with an adult with or at high risk for HIV infection.

Source: Centers for Disease Control and Prevention at: <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2004report/table17.htm> (Last Modified: January 9, 2006)

## Patient to Practitioner

Fortunately, occupational acquisition for health care workers has been implicated in less than 60 cases (there are an estimated 6,000,000 health care workers in the United States). None of these individuals were infected in a dental environment. Most of the health care workers are nurses and most suffered some type of exposure to a sharp (e.g., needlestick). Occupational exposure is suspected, but not proven in an additional 120 health care worker cases. There are six dental personnel among this group.

## Epidemiology

When a population becomes infected with a contagious disease, an epidemic can occur. In order to understand how an infectious disease can spread or remain established in a population, one must consider the relationship between the infectious disease and its host population. Epidemiology is the study of disease in populations.

Some diseases are difficult to acquire, while others are almost unavoidable. HIV Disease is preventable. Transmission of HIV can be prevented. HIV is relatively difficult to contract and can be readily avoided. Unfortunately, no viable vaccine has been developed and may never be developed. Thus, the key factor in disease acquisition is behavior modification.

The first scientific evidence of HIV Disease came from blood specimens taken in Central Africa in 1959. The first clinical cases of HIV Disease started to occur in the 1960s among medical personnel from Europe who had completed extended visits to sub-Saharan Africa. By 1975 HIV had spread worldwide.

The first cases of HIV Disease in the United States were reported in the summer of 1981. They involved clusters of homosexual males in California and New York. Official recording of HIV Disease in the United States includes cases that occurred prior to 1981 with the oldest being in 1978. Diagnosis was made on the description of clinical symptoms. There is some evidence that cases occurred in New York City in 1952 and in St. Louis in 1959. Such data support the concept that HIV was present in Africa, Europe and North America over fifty years ago.

If HIV was present for over a half century, then why did the number of cases rise dramatically only in the 1980s? Sexual practices of heterosexuals changed tremendously in the United States during the 1960s. This could be related to the emergence and widespread use of birth control pills. With "The Pill", the use of condoms decreased dramatically. The 1970s was the era in which gay men and lesbians "came out the closet" and started to live openly. Increased sexual activity translated into increased exposure.

Today, better use of preventive methods and increased knowledge has led to fewer cases of HIV Disease. With improved medications, infected persons are living longer. However, the progress of HIV Disease outside First World Countries remains unchecked. In these areas the numbers of female cases equals that of males. Transmission is primarily through heterosexual contact and from infected mother to fetus or newborn. Behavioral modifications and increased knowledge have not occurred, nor are advanced screening methods and basic medical treatments readily available.

## HIV Disease

### Stages

During the initial infection, HIV comes into contact with susceptible T cells in the blood. However, the site of the first large production of the virus is local lymphoid tissue. This leads to a release of viruses and their wider dissemination to other lymphoid organs. The resulting immune response is only partially successful and some viruses escape. Eventually, increasing viral turnover leads to destruction of the immune system. HIV disease, therefore, is characterized by a gradual deterioration of immune function. During the course of infection, crucial immune cells, called CD4+ T cells, are disabled and killed, and their numbers progressively decline.

HIV Disease includes the entire spectrum of HIV infection from initial infection, asymptomatic and symptomatic periods and finally AIDS. The syndrome called AIDS is the late stage of HIV disease. AIDS is the most severe manifestation of infection. The CDC lists numerous opportunistic infections and cancers that, in the

presence of HIV infection, constitute an AIDS diagnosis. In 1993, CDC expanded the criteria for an AIDS diagnosis in adults and adolescents to include CD4+ T cell count at or below 200 cells per mL in the presence of HIV infection. In persons (age 5 and older) with normally functioning immune systems, CD4+ T cell counts usually range from 500 - 1,500 cells per mL. Persons living with AIDS often have infections of the lungs, brain, eyes, and other organs, and frequently suffer debilitating weight loss, diarrhea, and a type of cancer called Kaposi's Sarcoma.

### Testing

Even though the HIV pandemic is more than twenty years old, the majority of adults and adolescents in the United States have not been tested. Interestingly, many people (as many as 40% of persons) testing positive demonstrated signs and symptoms of HIV infection for over a year prior to being tested. Testing is still an emotional process, however it should be considered a normal component of everyday life. Instead, many people resist testing because of ignorance or denial.

Tests used to determine if a person is infected measure the presence of host antibodies to specific HIV antigens. The initial screening test is called an ELISA (enzyme linked immunosorbent assay) test. ELISA tests were first used to detect antibodies to HIV in 1983. Its use was not only to determine HIV exposure, but also to assure the safety of donated blood and tissues. Testing of the blood supply in the United States began in March of 1985. The ELISA test is now semi-automated. Again, the ELISA test determines if a person's serum contains antibodies to one or more HIV antigens, not for the presence of HIV RNA or HIV particles.

There are some problems with HIV ELISA tests. Not all persons infected with HIV will produce detectable amounts of HIV antibodies. A very limited number of persons cannot be identified by an ELISA test. Also, HIV antibodies are not usually present in sufficient amounts for periods of six to 18 weeks after infection. This "window period" allows HIV infected people to test HIV negative.

The confirmatory test for HIV infection is the Western blot. If an ELISA test is positive even after being repeated, the serum specimen is tested using a Western blot method. Collections of HIV proteins are placed onto a polyacrylamide gel (gel electrophoresis), which then gets an electrical charge. The current separates the proteins within the gel by their size and surface charges into individual bands. The protein or antigen bands within the gel are "blotted" (transferred) directly onto strips of nitrocellulose paper. After separation, serum specimens that tested ELISA positive are placed directly over the strips containing the HIV antigens. If HIV antibodies are present in the serum, an antigen-antibody reaction will occur. The strips are washed and a solution containing anti-human immunoglobulins bound to a color indicator is added. The greater the amount of antigen-antibody complexes present, the darker will be the color development. Serum results are compared to two control test strips (one positive and one negative). Detection of two or more HIV antigen bands confirms infection.

### Testing – Revised Recommendations

In September 2006, the CDC issued revised recommendations for HIV testing of adults, adolescents and pregnant women in healthcare settings. The changes apply in healthcare settings only. They do not apply to existing guidelines concerning HIV counseling, testing or referral existing guidelines in non-healthcare settings.

The goals of new recommendations are to:

1. increase HIV screening, including pregnant women in healthcare settings;
2. foster earlier detection of HIV infection;
3. identify and counsel persons with unrecognized HIV infections and
4. link identified persons with clinical and prevention services.

Identifying pregnant women will further reduce perinatal transmission of HIV in the United States.

The number of HIV infected persons in the United States is estimated to be between 1,039,000 and 1,185,000. The number unaware of their HIV infection is between 252,000 and 312,000 (24% - 27%). An estimated 40,000 persons become infected each year in the United States.

Diagnostic testing is performing an HIV test based on clinical signs or symptoms. Screening is performing an HIV test for all persons in a defined population. Also, there is targeting testing which is performing HIV tests on a subpopulation of persons at higher risk based on behavioral, clinical or demographic characteristics. An opt-out screening is the performance of an HIV test after notifying the patient that the test will be done; consent is inferred unless the patient declines. An informed consent is a communicative process between patient and provider through which the patient can participate in choosing whether or not to undergo HIV testing. HIV prevention counseling is an interactive process to assess risk, recognize risky behaviors and develop a plan to take steps that will reduce risks.

In the United States, an estimated 38% - 44% of adults aged 18 – 64 have been tested. Between 16 and 22 million persons aged 18 – 64 are tested annually. Over 44% of HIV tests are performed in a private doctor/HMO office. However, only 17% are positive. Conversely, 9% of tests are performed in community clinics (public) with over 21% being positive. Other facilities (e.g., HIV counseling/testing centers, correctional facilities and STD and drug treatment clinics) have higher rates of positive tests. In a 2003 study conducted in 16 states, 4127 persons with AIDS were first diagnosed as being HIV positive within 12 months of an AIDS diagnosis (“late testers”). Late testers were more likely to be younger (18-29 years), heterosexual, less educated and African American or Hispanic. Late testers usually are screened because they are ill. Early testers (people that were tested >5 years before an AIDS diagnosis) were more likely to submit a blood specimen because they or their partner were at risk, they wanted to know, or were required to be tested as part of a routine check up.

In 2000, 31% of persons who submitted a blood specimen at publically funded test sites that were found to be HIV positive did not return for the results. There was a definite need for immediate information or referral for treatment choices, especially in perinatal settings and post-exposure treatment facilities. The answer is a rapid HIV test, which would also be valuable in high-volume, high-prevalence settings.

For the last three years, there have been four FDA-approved rapid HIV tests (OraQuick Advance, Uni-Gold, Reveal G2 and Multispot). Only the OraQuick Advance can be used to test whole blood, plasma and oral fluids. In May 2006 the FDA approved two more rapid tests – Sure Check and Stat Pak. These tests screen for antibodies to HIV with the results obtainable in 30 minutes or less.

Rapid HIV tests take the place of the traditional ELISA (EIA) tests. They have sensitivities and specificities equal to the ELISA tests. A positive test requires a confirmatory test, a Western Blot. Rapid tests require pre- and post-screening counseling. Rapid testing offers several advantages over traditional testing such as:

- less costly for testing agencies due to fewer outreach visits to give results
- because return visits are not necessary, more people will get their results
- because results are delivered quicker, positive people get into medical care quicker
- by learning of infections earlier, potential exposures that would have occurred between traditional testing and receiving results is reduced
- post test counseling can be done with the results

Rapid HIV test play important roles including increased receipt of test results, increased identification of HIV-infected pregnant women so they can receive effective prophylaxis, increased feasibility of testing in acute care settings with same day results and increased numbers of venues where testing can be offered to high risk persons.

Rapid HIV tests are essential elements of routine screening. This can be justified based on four factors – serious health disorders could be detected before symptoms develop, treatment is more beneficial when begun before symptoms develop, the development of a reliable, inexpensive, acceptable screening test and that costs of screening are reasonable in relation to anticipated benefits. Rapid HIV testing should increase earlier screening. The earlier infection is detected, the sooner treatment and behavior modification can begin.

## Outcomes of Infection/Oral Manifestations

HIV Disease is associated with oral manifestations in 37% - 90% of patients. The development of these lesions is linked to immunosuppression and their onset is marked by a decrease in the CD4 cell count below 200 cells/mm<sup>3</sup>. Oral lesions are often predictive of worsening immunosuppression and disease progression.<sup>i</sup> The oral manifestations include bacterial, fungal, viral infections, non-specific, ulcerative or immune mediated lesions, and neoplastic diseases (Figure 9). **In some cases, the oral lesion may be the first indication that the patient has HIV infection.** Most oral lesions can be diagnosed and treated in the dental office in conjunction with the patient's primary medical care provider.

### HAART

With the development of antiviral combination medications including protease inhibitors, called highly active antiretroviral therapy (HAART), the prevalence of oral clinical lesions has changed. HAART reduces the plasma-HIV viral load and results in increased CD4 cell counts, on average 100 cells/mm<sup>3</sup>. Antiretrovirus therapy usually includes combinations of multiple types of nucleoside reverse transcriptase inhibitors and protease inhibitors with or without non reverse transcriptase inhibitors. Protease inhibitors include amprenavir, saquinavir, ritonavir, indinavir and nelfinavir mesylate. Protease inhibitors may be combined with nucleoside reverse transcriptase inhibitors including abacavir, didanosine, lamivudine, zalcitabine, zidovudine, and stavudine. Non-nucleoside reverse transcriptase inhibitors such as delavirdine, nevirapine or efavirenz may also be added to the HAART regimen. Since the development of HAART there have been significant decreases in the number of oral lesions, the prevalence of hairy leukoplakia and necrotizing ulcerative stomatitis, necrotizing ulcerative periodontitis and necrotizing ulcerative stomatitis. HIV associated salivary gland disease has significantly increased to 5%. Oral candidiasis prevalence has fallen slightly, but not statistically significant. There has been essentially no change in the prevalence of aphthous stomatitis, herpes simplex virus lesions, and Kaposi's sarcoma (Kaposi's associated herpes virus). Human papillomavirus lesions appear to be increasing. The most commonly encountered

oral manifestations of HIV infection in patients on HAART are: all lesions 37.5%, candidiasis 16.7%, hairy leukoplakia 11.4%, HIV salivary gland disease 5%, human papillomavirus lesions 4%, aphthous ulceration 3.0%, herpes simplex lesions 2.0%, necrotizing ulcerative gingivitis/necrotizing ulcerative periodontitis/necrotizing ulcerative stomatitis 1.7%, and Kaposi's sarcoma 0.3%.<sup>ii</sup>

### Dental Management of HIV Associated Oral Lesions

Oral lesions are a common occurrence in HIV infected patients. The dental management of patients with HIV associated oral lesions includes diagnosis and treatment. The oral lesions may represent the initial manifestation of the disease and parallel the development of opportunistic infections and neoplasms with worsening immunosuppression. Patients receiving HAART therapy have fewer oral manifestations overall. Those patients usually have a decrease in the incidence of some lesions, with an increase in other conditions such as xerostomia. These oral manifestations are often chronic or recurring and will require life long follow-up and treatment.<sup>iii</sup>

### Fungal Infections

Oral candidiasis is one of the most frequent infections associated with HIV.<sup>iv</sup> In fact, the development of persistent oral candidiasis can be used to predict the development of other opportunistic HIV associated infections within 3 months of onset.<sup>v</sup> The diagnosis of oral candidiasis is often based on the clinical findings of erythematous areas on the palate or tongue or the presence of loosely adherent white plaques (pseudomembrane) that can be easily wiped off leaving an erythematous or bleeding surface (see Figure 10).

An oral exfoliate cytologic preparation can be used to make the diagnosis. If the lesions respond to antifungal treatment this further establishes the diagnosis. Treatment of oral candidiasis includes topical Nystatin or clotrimazole and systemic agents ketoconazole, fluconazole,<sup>vi</sup> and itraconazole.<sup>vii, viii, ix</sup> Topical agents should be used with caution in patients with xerostomia because of high sucrose content or the decreased ability to dissolve medication in

<b>Group 1: Lesions strongly associated with HIV infection</b>
Candidiasis Erythematous Pseudomembranous
Hairy leukoplakia
Kaposi's sarcoma
Non-Hodgkin's lymphoma
Periodontal disease Linear gingival erythema Necrotizing (ulcerative) gingivitis Necrotizing (ulcerative) periodontitis
<b>Group 2: Lesions less commonly associated with HIV infection</b>
Bacterial infections: Mycobacterium avium-intracellulare Mycobacterium tuberculosis
Melanocytic pigmentation
Necrotizing (ulcerative) stomatitis
Salivary gland disease Dry mouth due to decreased salivary flow rate
Thrombocytopenic purpura
Ulceration NOS (not otherwise specified)
Viral infection Herpes simplex virus Human papillomavirus (wart-like lesions) Condyloma acuminatum Focal epithelial hyperplasia Varicella-zoster Herpes zoster Varicella
<b>Group 3: Lesions seen in HIV infection</b>
Bacterial infections: Actinomyces israelii Escherichia coli Klebsiella pneumoniae
Cat scratch disease
Drug reactions (ulcerative, erythema multiforme, lichenoid, toxic epidermolysis)
Epithelioid (bacillary) angiomatosis
Fungal infection other than candidiasis Cryptococcus neoformans Geotrichum candidum Histoplasma capsulatum Mucoraceae (mucormycosis/zygomycosis) Aspergillus flavus
Neurologic disturbances
Recurrent aphthous stomatitis
Viral infections Cytomegalovirus Mulluscum contagiosum

**Figure 9.** Revised Classification of Oral Lesions Associated with HIV Infection.

Source: EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus, 1993.



**Figure 10.** Painful oral candidiasis with atrophic glossitis in a 42-year old male patient.

Source: Dr. Susan L. Zunt



**Figure 11.** Oral hairy leukoplakia in a 28-year old male. Biopsy was positive for Epstein-Barr Virus and Candida.

Source: Dr. Susan L. Zunt

the absence of saliva. Angular cheilitis is another common oral manifestation of candidiasis. Topical clotrimazole ointment 1%, miconazole nitrate ointment 2%, ketoconazole 2%, nystatin ointment, and clotrimazole 1% - betamethasone dipropionate 0.05% ointment or cream, applied 3x daily may be helpful in controlled angular cheilitis.<sup>x</sup>

Other fungal infections such as cryptococcosis, geotrichosis,<sup>xi, xii</sup> histoplasmosis,<sup>xiii</sup> mucormycosis/zygomycosis, or aspergillosis may present as oral ulcers. Biopsy or culture is required for diagnosis. Patients with painful hairy leukoplakia may have a superimposed candidial infection. Treatment with antifungal medication may resolve the pain and usually results in a clinically less prominent lesion.

### Viral Infections

Herpes simplex infections, primary or recurrent, can usually be managed with specific antiviral therapy including acyclovir and famciclovir.<sup>xiv</sup> Valaciclovir, another commonly prescribed antiviral medication used in immunocompetent patients, should be avoided in patients with HIV infection because of the risk of hemolytic uremic syndrome. Topical penciclovir may be of benefit in the management of recurrent herpes labialis<sup>xv</sup> although its use in HIV infection has not been established. Painful recurrent herpes simplex labialis (cold sore, fever blister) is best managed with topical or systemic antiviral medications to be taken as soon as the prodromal symptoms occur to prevent/reduce viral replication. If pain is present, an analgesic may be required. Stress, depression, sunlight, menstruation, mechanical

or chemical injury may precipitate recurrences. Foscarnet has been used to treat acyclovir-resistant herpes simplex infections in patients with HIV infection.<sup>xvi</sup>

Oral hairy leukoplakia (HL) results from Epstein-Barr virus (EBV) infection (see Figure 11). The lesions are characteristically white vertical lines or elevated plaques on the lateral borders of the tongue. Often asymptomatic, the lesions may be painful, especially if there is a co-existent candidial infection. The development of HL is usually associated with CD4 counts of less than 200 cells/mm<sup>3</sup>. A clinical diagnosis may be made of HL in patients with known HIV infection. A biopsy is necessary for diagnosis in patients with unknown HIV status, as HL occurs uncommonly in HIV negative patients with or without immunosuppression. *In situ* hybridization nuclear probes for EBV DNA can be accomplished on biopsy or exfoliative cytology specimens. Treatment depends on the presence of pain, need for aesthetics and difficulty with speech or mastication especially with elevated lesions.

Oral cytomegalovirus infection can cause oral ulcers indistinguishable from herpetic infections or other ulcerative processes. Oral ulcers may be co-infected with both herpes simplex and cytomegalovirus.<sup>xvii, xviii</sup> Biopsy is required to detect the large intranuclear inclusions found in the nuclei of endothelial cells. Treatment for CMV required high dose acyclovir or ganciclovir.

### Bacterial Infections

HIV associated periodontal disease includes linear gingival erythema, necrotizing ulcerative



**Figure 12.** Chronic periodontitis in a 28-year old male subsequently diagnosed with HIV. Patient's fingers used to reflect lower lip.

Source: Dr. Susan L. Zunt

gingivitis, and necrotizing ulcerative periodontitis.<sup>xxix</sup> Linear gingiva erythema (LGE) is a band like erythematous appearance of the marginal gingiva, sometimes in the absence of local factors such as dental plaque or calculus (see Figure 12). LGE may represent an altered immune response to bacterial or response to candidal microorganisms. LGE due to *Candida dubliniensis* and responsive to ketoconazole has been reported in a child with HIV infection.<sup>xx</sup> HIV associated periodontitis has been demonstrated to be associated with a variety of human herpes viruses (HHV).<sup>xxi</sup> Treatment for the HIV associated gingival and periodontal diseases includes professional dental supragingival and subgingival plaque and calculus removal, improved oral hygiene care, use of chlorhexidine mouthwash, and antibiotics such as metronidazole. In non-responsive cases the antifungal medication fluconazole or ketoconazole is recommended.

Necrotizing ulcerative gingivitis (NUG) exhibits ulceration and necrosis of at least one interdental papillae in the absence of alveolar bone loss. NUG is characterized by pain, interdental necrosis of the gingiva papillae, bleeding and halitosis. Treatment includes antibiotics, chlorhexidine mouthwash, and debridement with careful follow-up for maintenance.<sup>xxii</sup>

Necrotizing ulcerative periodontitis (NUP) is thought to be the result of bacterial infection. The lesions are painful, exhibiting a foul odor and spontaneous bleeding. The development of NUP is associated with CD4 cell counts of 100 or less cells/mm<sup>3</sup>. NUP may be rapidly progressing and result in tooth and bone loss.

Necrotizing ulcerative stomatitis (NUS) is a destructive ulceronecrotic process specific to HIV infection. NUS may develop as a progression from necrotizing ulcerative periodontitis or it may develop without a pre-existing gingival/periodontal condition, presenting as a single ulceration. The ulcer is usually solitary and it can involve bone and adjacent soft tissue. A report of 18 cases in 13 men and 4 women, average age 37 years, range 20-52 years, found that lesions of NUS occur on the lower lip, buccal mucosa, gingiva, palate and tongue. A biopsy is required for diagnosis because fungal, viral or other infections or neoplasms also present as ulcerations.<sup>xxiii</sup> Treatment of NUS includes antibiotics and debridement with close follow-up.

### Ulcerative Conditions

Lesions that resemble minor, major and herpetiform recurrent aphthous ulcers (RAU) occur in HIV positive patients in the mouth, oropharynx and esophagus. The presence of these ulcers can cause severe discomfort. This makes it difficult for the patient to eat and results in poor nutrition. The development of major RAU in HIV positive patients has been associated with CD4 cells less than 100 cells/mm<sup>3</sup> and marks progression to severe immunodeficiency. Patients on trimethoprim/sulfamethoxazole or patients that smoked had fewer major aphthous ulcers.<sup>xxiv</sup>

Recurrent aphthous stomatitis (RAS) in HIV positive patients may be managed in a manner similar to immunocompetent RAS patients.<sup>xxv</sup> Topical corticosteroids can be used with few adverse effects. In those patients that do not respond to topical corticosteroids, a trial of systemic prednisone may be of benefit. Additionally and especially if dry mouth is present, chlorhexidine mouthwash may be of benefit in reducing the number and severity of RAS lesions and reducing the chance of candidiasis as a consequence of corticosteroid therapy.<sup>xxvi</sup> A trial of a sodium lauryl free toothpaste may be helpful in reducing the number of ulcers. For major debilitating RAU lesions that do not respond to the typical treatments for RAS, thalidomide<sup>xxvii</sup> or granulocyte colony stimulating factor<sup>xxviii</sup> have been shown to be helpful.





**Figure 13.** Kaposi's sarcoma in a 43-year old male patient. CD4 cell count was less than 20 cells/mm<sup>3</sup>.

Source: Dr. Susan L. Zunt



**Figure 14.** Biopsy confirmed benign mucosal melanosis in a 23-year old, HIV-positive, male patient.

Source: Dr. Susan L. Zunt

## Neoplasms

Oral Kaposi's sarcoma (KS) is the most common type of neoplasm encountered in the HIV positive patient (see Figure 13).

KS is of endothelial cell origin and typically multifocal. Human herpes virus type 8 has been found in the lesions and is suspected to play a role in the etiology or pathogenesis of KS.<sup>xxxix, xxx</sup> Early lesions are flat, red-purple macules. Older lesions are nodular masses. Lesions may destroy alveolar bone and result in tooth mobility. The hard and soft palate, gingiva and tongue are the most common sites for intraoral KS. Onset of KS is associated with CD4 cell count less than 100 cells per mm<sup>3</sup>. A biopsy is necessary for diagnosis as bacillary angiomatosis exhibits a similar clinical presentation (see Figure 14).

Lymphoma is also common in patients with HIV infection. These lymphomas include non-Hodgkin's lymphoma (NHL) including aggressive monoclonal B-cell Burkitt's lymphomas; large-cell lymphomas, or immunoblastic lymphomas; T-cell NHL and Hodgkin's lymphoma.<sup>32</sup>

## Xerostomia

Salivary gland hypofunction with a decrease in the salivary flow rate is associated with HIV infection. In a study of 576 HIV positive women, salivary disease as indicated by salivary gland enlargement (4.3%), tenderness (6.9%), and absence of saliva on palpation (26.6%) was more common than in HIV-negative women controls who experience rates of 1.3%, 4.6% and 13.2% respectively.<sup>xxxix</sup> The salivary gland destruction

results from CD8 lymphocytic infiltrates known as diffuse infiltrative lymphocytosis syndrome (DILS).<sup>xxxii</sup> DILS affects not only the salivary glands, but the lacrimal glands, lungs, gastrointestinal tract and kidneys. An increased incidence of salivary and lacrimal gland non-Hodgkin B cell lymphomas is associated with DILS.<sup>xxxiii</sup> A study of patients on HAART found the prevalence of xerostomia was 15.5%.<sup>xxxiv</sup>

The patient with salivary gland hypofunction is at risk of frequent or persistent candidiasis, mucosal pain, may experience difficulty in wearing dentures, difficulty with speech and swallowing, and increased risk of developing dental caries. Dry mouth symptoms can be managed by adequate intake of water, chlorhexidine mouthwash, frequent use of saliva substitutes, topical fluoride, maintaining meticulous oral hygiene, and regular dental professional care.<sup>4</sup>

(References for the Outcomes of Infection/Oral Manifestations Section appear in Appendix A.)

## HIV Disease Progression

Over the years there have been several serious efforts to classify HIV Disease. Classification is not the same as disease staging. Staging suggests a progressive sequence of events from none observable to most severe. The prognosis worsens as the disease progresses.

Dividing HIV Disease into progressive, sequential steps or stages has proven to be less than ideal. Persons infected with HIV do not follow an exact

pattern of disease progression. There is often a worsening in symptoms, followed by improvement and then worsening again. Disease progression is often uneven and resists easy categorization. In the end, the term HIV Disease was selected to include all processes and for the term AIDS to be used only for the end-stage, life-threatening part of the disease process.

Long term non-progressors are individuals who have been living with HIV for at least 7 to 12 years (different authors use different time spans) and have stable CD4+ T cell counts of 600 or more cells per cubic millimeter of blood, no HIV-related diseases, and no previous antiretroviral therapy. Data suggest that this phenomenon is associated with the maintenance of the integrity of the lymphoid tissues and with less virus trapping in the lymph nodes than is seen in other individuals living with HIV.

## Treatments

To date, there is no cure for HIV Disease and none is on the immediate horizon. A cure could involve the complete removal or inactivation of all HIV proviruses present. Alternatively, treatment could inactivate proviruses, or prevent them from developing into infectious virions causing damage, or even death. Such processes would not render a person non-infectious; however, it could offer the infected person a more normal lifespan.

The first antiretroviral drug, Zidovudine (AZT) was approved in 1987. Since then 16 other drugs have also been approved. Ten of the drugs are reverse transcriptase inhibitors, while the other seven are HIV protease inhibitors.

Within a short period, it became apparent that treatment using a single drug had serious shortcomings. Individually some of the drugs were very toxic, had to be administered every two hours and lead to drug resistant mutants. Monotherapy was stopped in 1995. It was replaced by combination drug therapy. Today, the standard for drug therapy is that HIV drugs are used in combination. The usual scheme is to use two reverse transcriptase inhibitors and a single protease inhibitor. The use of three or more drugs simultaneously is commonly referred to as HAART – highly active anti-retroviral therapy.

HIV RNA can be detected during all stages of HIV Disease. The amounts of HIV are highest soon after infection (acute retroviral syndrome) when viruses start to multiply and then are neutralized by the host's immune system. However, some virus escapes to take up residence in regional lymph nodes. Amounts of virus also rise in untreated persons when the immune system starts to decline. Increased amounts of virus (viral load) usually are associated with more advanced disease and calls for the initiation of drug therapy. Viral load can help determine the effectiveness of treatment. Ideally viral loads should be reduced as a result of drug therapy. It is thought that persons with more than 100,000 copies of HIV-RNA per mL of plasma are at high risk for HIV Disease progression. In contrast, after treatment persons with less than 10,000 HIV-RNA copies per mL are considered to be at low risk for disease progression.

Prior to 1996, scientists estimated that about half the people with HIV would develop AIDS within 10 years after becoming infected. This time varied greatly from person to person and depended on many factors, including a person's health status and their health-related behaviors. Since 1996, the introduction of powerful anti-retroviral therapies has dramatically changed the progression time between HIV infection and the development of AIDS. There are also other medical treatments that can prevent or cure some of the illnesses associated with AIDS, though the treatments do not cure AIDS itself. Because of these advances in drug therapies and other medical treatments, estimates of how many people will develop AIDS and how soon are being recalculated, revised, or are currently under study. As with other diseases, early detection of infection allows for more options for treatment and preventative health care.

With the prompt and correct use of antiviral agents and proper treatment of opportunistic infections and neoplasms, the average life span of a person with HIV Disease has been expanded to over 25 years.

## Infection Control

### Six Steps to Disease

There are six steps in the development of exogenous diseases. The exact format of each

step varies depending on the disease, the specific microorganisms involved and related environmental conditions. The basic steps described next relate to the acquisition of disease within dental environments. Prevention of disease occurs by interfering with one or more of the steps. This process is collectively called infection control, which include immunizations.

#### **Step 1.**

**The major source** of the microorganisms in dental offices is the patients' mouths. However, disease can spread from practitioners to patients. It is not possible to accurately detect which patients may indeed be harboring pathogens. To successfully prevent the spread of pathogens, infection control procedures must be applied during the care of all patients using the concept of standard (universal) procedures – considering all patients to be infectious. The importance of standard (universal) precautions is based on the understanding that asymptomatic carriers of a disease can be highly infectious. These persons are probably the most important in the spread of a disease because they are often unaware of their status and are physically able to infect others.

#### **Step 2.**

**Escape from the source:** microorganisms present in the oral cavity can be released during normal activities such as breathing, sneezing and coughing. Many dental procedures also release microorganisms. Anything removed from a patient's mouth is assumed to be contaminated.

#### **Step 3.**

**Spread of microorganisms to a new host:** transmission of disease causing microorganisms can occur in one of three routes. Spread by direct contact means touching of practitioner skin or mucous membranes to patient tissue or body fluids. Indirect contact can result from injuries with sharp items contaminated with body fluids/tissue, such as needles, instruments and dental prostheses. Transmission can also occur by droplet infection. Aerosol and spatter from patients could contact uncontacted skin or mucous membranes, which would allow direct entrance. Droplet infection may also involve inhalation of microorganisms.

#### **Step 4.**

**Entry into a new person:** microbial release does not always mean entrance into a new host. Entry involves four basic routes – 1) inhalation, 2) ingestion, 3) via mucous membranes or through 4) breaks in the skin. Proper use of infection control methods and equipment can significantly limit entrance of microorganisms. Entry can also occur because of accidents, such as needlesticks.

#### **Step 5.**

**Infection:** survival and multiplication of microorganisms on or in the body does not always mean that disease and damage to the host will occur. Humans are constantly exposed to microorganisms. Fortunately, the host's non-specific and specific defense mechanisms usually detect and neutralize invading microorganisms.

#### **Step 6.**

**Damage to the host:** sometimes continued multiplication of microorganisms can cause harm. Damage may occur quickly or over a long period of time. The human immune system and certain chemicals help to minimize the effects of disease.

Standard procedures of sterilization, disinfection and asepsis must be applied to all types of dental care to reduce the chances of cross-contamination (disease transmission) that may lead to serious infectious diseases. Cross-contamination is the spread of microorganisms from one person to another. There are four main pathways by which this may occur in dentistry – patient to patient, practitioner to patient, patient to practitioner and practice to community.

#### **Protecting Patients**

The risk of exposure to bloodborne and other pathogens is important to patients as well as practitioners. The CDC, OSHA as well as all dental professional organizations, including the ADA, specifically have recognized the importance of bloodborne pathogens.

Cross-contamination from a member of the dental team to a patient is a relatively rare event in dentistry. The overwhelming majority of patient visits do not result in infection. Chances can be reduced even further through the proper application of infection control methods. Infection

of patients by practitioners could involve hands or respiratory fluids. There have been a number of cases involving transmission of hepatitis B virus (HBV) from dentists with chronic HBV infections to patients. The last case occurred in 1985. The use of gloves has increased markedly since then and likely has reduced transmission of HBV and herpes simplex. There has been only one suspected case of spread of HIV in a dental office. Three other cases have occurred, but involved hospital situations and physicians or nurses.

Cross-contamination from one patient to another patient may occur by indirect routes through contaminated instruments, surfaces, equipment or even the hands of dental personnel. This pathway, involving improperly washed hands of a dental hygienist (in the pre-glove era), has been documented in the spread of herpes simplex virus from a herpes labialis lesion of one patient to the mouths of several other patients, resulting in herpes gingivostomatitis.

The goal of instrument processing is to prevent transfer of infectious agents to patients from contaminated dental hand instruments and handpieces and at the same time to protect the staff that must handle the items. The steps of

dental instrument sterilization are listed and described in Figure 15.

Comparison of the three heat-sterilization methods appears in Figure 16. Each of the three methods, when performed properly, yields sterilization. The ultimate goal is to consistently provide sterile instruments chairside.

### Preventing Occupational Acquisition

Cross-contamination from patient to the dental team mainly involves microorganisms present in the patient's mouth in saliva, blood, gingival crevice fluids, plaque, subgingival debris or open lesions. Exposure can occur by direct contact, through dental aerosols and body fluid spatter and by contact with previously contaminated instruments, surfaces and supplies. In the absence of adequate protective measures, the dental team is exposed to the risk of infection by oral bacteria and bloodborne pathogens present in the patient's mouth. The risks are real, dental personnel are known to acquire occupational exposures at rates much higher than the general population.

Practitioner safety can be increased by the proper sterilization of reusable instruments. Correct

Steps	Activities
<b>Transport</b>	Transport contaminated instruments to the decontamination area so that exposure of staff and the environment are minimized.
<b>Presoak &amp; Rinse</b>	Submerge in detergent solution until time is available for full cleaning.
<b>Clean, rinse &amp; dry</b>	Use ultrasonic cleaner or washer and detergent, clean and sterilize or disinfect any nondisposable instrument tray used at chairside.
<b>Package</b>	Add rust inhibitor to nonstainless steel instruments for steam sterilization, add spore tests or chemical indicators, package in proper wrap, bags, pouches or wrapped cassettes.
<b>Sterilize &amp; monitor</b>	Heat sterilize and process spore tests and check chemical indicators, record results of monitoring.
<b>Store or distribute</b>	Sterilized cassettes or packages are ready for storage or use at chairside, store in dry place in a manner that does not compress the packages.

**Figure 15.** Dental Instrument Processing.

Source: Miller CH, Palenik CJ. Sterilization, Disinfection and Asepsis in Dentistry. In: Block S.: *Sterilization, Disinfection, Preservation and Sanitation*, Fifth Edition, 2001, Philadelphia, PA, Lippincott Williams & Wilkins, pp.1049-1068.

Method	Sterilizing Conditions <sup>1</sup>	Advantages	Precautions	Spore Testing
Steam autoclave	15-30 min at 250°F or 3.5-10 min at 270°F	-Time efficient -Good penetration	-Nonstainless steel metal items corrode -Items are wet after normal cycle -Do not use closed containers -May damage plastic and rubber items -Use of hard water may leave deposits	<i>Bacillus stearothermophilus</i> strips or vented vials
Unsaturated chemical vapor	20 min at 270°F	-Time efficient -No corrosion -Items dry after cycle	-Must use special solution -Ventilation must be adequate -Pre-dry instruments -May damage plastic and rubber items -Do not use closed containers -May not be appropriate for handpieces <sup>2</sup>	<i>Bacillus stearothermophilus</i> strips
Dry heat (oven type)	60-120 min at 320°F	-No corrosion -Items dry after cycle -Closed containers may be used <sup>3</sup>	-May damage plastic and rubber items -Pre-dry instruments -Long cycle time -May not be appropriate for handpieces <sup>2</sup>	<i>Bacillus subtilis</i> strips
Dry heat (rapid heat transfer)	12 min at 375°F	-No corrosion -Items dry after cycle -Time efficient	-May damage plastic and rubber items -Pre-dry instruments -May not be appropriate for handpieces <sup>2</sup>	<i>Bacillus subtilis</i> strips

Figure 16. Dental Instrument Sterilization.

<sup>1</sup>These cycle times are representative; they do not include warm-up times, and they may vary with the brand of sterilizer. Follow the sterilizer manufacturer's directions for sterilizing conditions and confirm kill by spore testing

<sup>2</sup>Check with handpiece manufacturer

<sup>3</sup>Use spore test to confirm appropriate kill in closed containers.

Source: Miller CH, Palenik CJ. Sterilization, Disinfection and Asepsis in Dentistry. In: Block S.: *Sterilization, Disinfection, Preservation and Sanitation*, Fifth Edition, 2001, Philadelphia, PA, Lippincott Williams & Wilkins, pp.1049-1068.

disinfection and/or covering of environmental surfaces likely to be orally soiled will decrease the risks for both practitioners and patients. The proper use of personal protective equipment (PPE) can minimize exposure to bloodborne pathogens.

In the past, protection of employees from bloodborne pathogens primarily involved selection of PPE, such as gloves, masks and

protective eyewear. Although PPE is an essential component of an infection control and occupational safety program, it is not considered to be a first-line defense against occupational exposures. For example, wearing examination gloves does not fully protect employees against needlestick accidents. OSHA has indicated that engineering, work practice and administrative controls are to be used to eliminate or reduce

employee exposures. If occupational exposures remain after the application of controls, PPE should also be used.

Engineering controls are considered the most effective manner to prevent occupational exposures. Engineering controls isolate or remove a hazard from the workplace. In the case of sharps devices, safety features or engineering controls prevents sharps contaminated with patient blood from contacting employees. Examples would include sharps disposal containers, self-sheathing needles, safer medical devices, such as sharps with engineered sharps injury protections and needleless systems. Employers in dental practices must select and implement appropriate engineering controls to reduce or eliminate employee exposure.

Work practice controls reduce the likelihood of exposure by altering the manner in which a task is performed. Prohibiting two-handed recapping of contaminated needles is a work practice control. Work practices involve training employees on how to perform necessary tasks in ways that reduce their exposure to workplace hazards. OSHA required employers to identify and put into place safer work practices.

Sometimes considered part of work practice controls, administrative controls involve changing how or when employees do their jobs. Examples include scheduling work and rotating employees to reduce exposures. Although the practice of dentistry does not easily lend itself to administrative controls, changing the timing of some work tasks could reduce the numbers of employees potentially exposed to a hazard.

### **Protecting the Community**

Two other routes of microbe spread involving dental offices to community include improper handling of regulated medical waste (e.g., improper containment of contaminated medical waste, including sharps during transport) and sending orally contaminated dental impressions or appliances to a dental laboratory. Medical wastes in many areas can be treated (sterilized) in-house, decreasing the chances of cross-contamination. Or, a commercial waste hauling service could be hired. Impressions and

appliances should be disinfected properly before being sent out and upon being received back into the office.

### **Post-Exposure Protocol**

OSHA estimates that 6.1 million workers in the health care industry and related occupations are at risk of occupational exposure to bloodborne pathogens, including HIV, HBV, hepatitis C virus (HCV), and others. According to the NIOSH Alert in March of 1999, it is estimated that 600,000 to 800,000 needlestick injuries (NSIs) and other percutaneous injuries occur annually among health care workers. Studies show that nurses sustain the majority of these injuries and that as many as one-third of all sharps injuries reported have been related to the disposal process. The CDC estimates that 62% to 88% of sharps injuries can potentially be prevented by the use of safer medical devices. Needlestick injuries and other sharps-related injuries that result in occupational bloodborne pathogens exposure continue to be an important public health concern. In response to this situation, Congress passed the Needlestick Safety and Prevention Act on November 6, 2000. To meet the requirements of this act OSHA has revised its Bloodborne Pathogens Standard. Changes involve both the selection and use of safer sharps and the increased emphases on engineering and work practice controls over PPE.

Of the 56 documented cases of occupational acquisition of HIV infection, the majority involved exposure by needlestick accident. Thus, any occupational exposure to patient body fluids is important and must be dealt with immediately. The Needlestick Safety and Prevention Act requires increased reporting of events. This includes the type and brand of device involved in the incident; location of the incident (e.g., department or work area) and description of the incident.

The OSHA Bloodborne Pathogens Standard requires that dental practices generate and maintain a written Exposure Control Plan that must be reviewed and updated annually and made available to employees. The Plan addresses three major areas – exposure determination, schedule of implementation and evaluation of exposure incidence (see Figure 17).

## Post-Exposure Action Plan

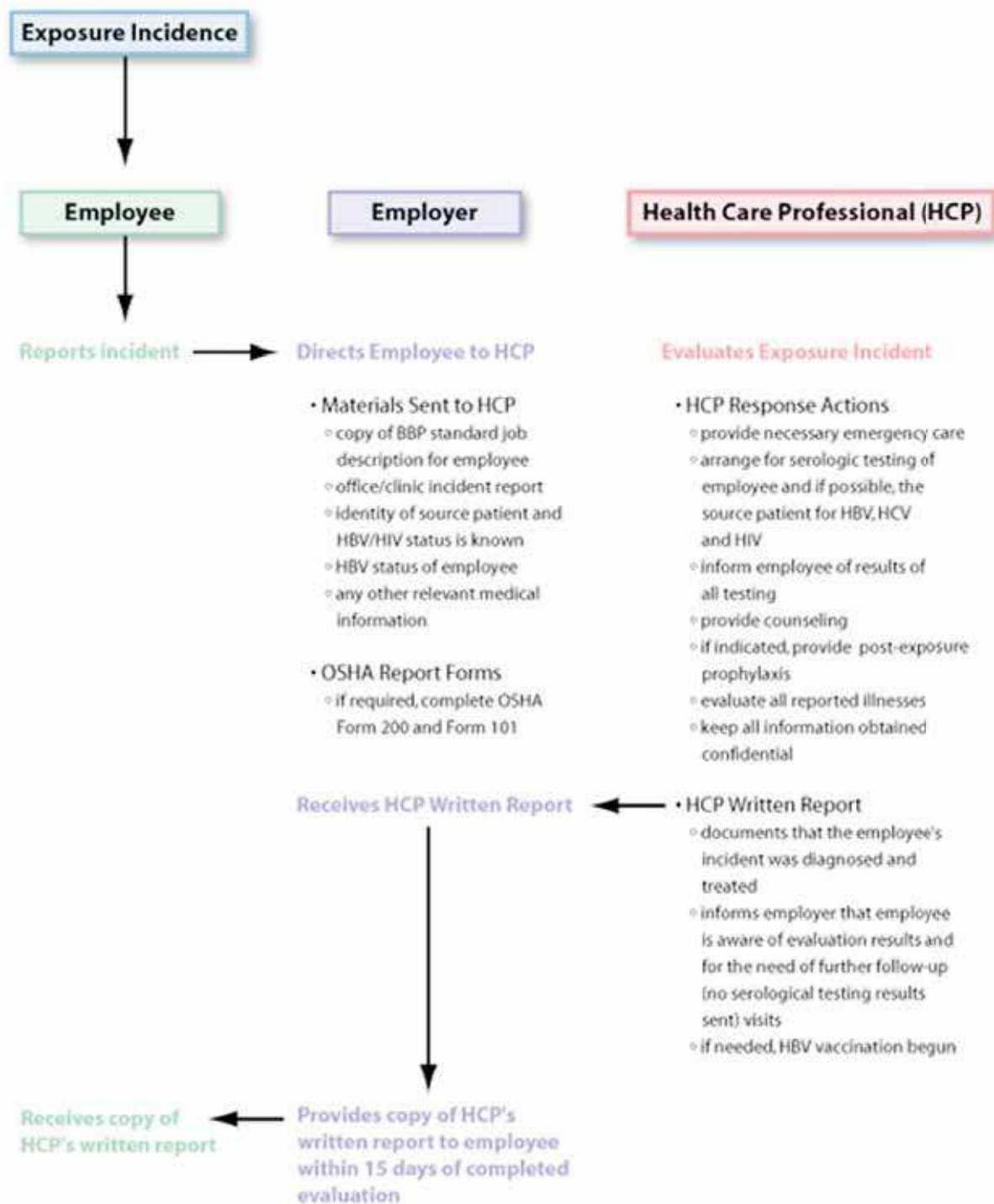


Figure 17.

Source: Palenik CJ, Miller CH. Post-exposure evaluation and follow-up. *Dental Asepsis Review* 19 (January):1-4, 1998.

Post-exposure medical evaluations and follow-up are required when an employee at work experiences an exposure incident. An exposure incident can be defined as "...any reasonably anticipated skin, eye, mucous membrane or parenteral (e.g., needlestick, cut, abrasion or puncture) contact with blood or other potentially infectious material". For the practice of dentistry, saliva is considered to be an infectious material.

Figure 17 describes a model post-exposure action plan. It is divided into a sequential series of tasks. Again, compliance involves performance that results in desired outcomes – no employee exposure to patients' body fluids. However, exposures do occur and must be reported immediately. An assessment is then made. The circumstances of the incident must be determined and if HIV post-exposure procedures are warranted, these must be initiated in the first few hours after exposure. This means that the post-exposure procedures must be applied immediately. The injured employee is transported to a proper facility where an informed evaluation can be made. If possible, the source patient (the one whose fluids were involved) is asked to join the injured employee to also be serologically evaluated.

The treatment facility must provide three services to the injured employee – post-exposure treatment and testing, counseling and an evaluation for and a report of any illnesses caused by the exposure and any follow-up visits and evaluations. All costs associated with post-exposure evaluation and follow-up the employer assumes. It is always better to have such procedures in writing and to practice them with employees. Then, when an exposure does occur the entire dental practice is better prepared to respond.

### **Outcomes of Dental Treatment**

There is limited evidence of the risks associated with the dental treatment of HIV-positive or PWA (Patients With AIDS). Most reports involve root canal therapy or extractions. In most cases, post procedure outcomes did not differ from those of persons not infected. Unfortunately, there is little or no information concerning other common dental procedures, such as prophylaxis, periodontal or orthographic surgery, scaling or root planning, or implants.

There are differing opinions on the benefit for pre-medicating persons with HIV Disease prior to dental treatment. Most persons with HIV Disease are already taking a number of medications, many of which are not common to dentistry. The dental practice must regularly update medical histories and become familiar with medications (drug-drug interactions) being taken by their HIV patients.

Persons with HIV are living longer and less symptomatic lives. Many are seeking more extensive dental treatments. From an infection control stance, such patients should not be treated any differently than patients not infected. However, from an oral medicine perspective, practices must be aware of all medications and other treatments being given and be in regular communication with the infected person's primary medical care provider.

### **Socio-Economic and Legal Issues**

Stigma has been associated with HIV/AIDS since the beginning. It continues to profoundly affect prevention efforts, leading people to deny risk, avoid testing, delay treatment and suffer needlessly. In many parts of the world, persons with AIDS are shunned and even physically harmed.

Stigma also affects Americans. It is expressed as discriminating regulations, policies and overt acts of community or individual prejudice. The greatest stigma has been linked to homosexual and bisexual men and persons with addictions, especially illicit injectable drugs. Persistent social and institutional racism and gender and economic inequities help stifle attempts at HIV/AIDS prevention.

HIV Disease seems to affect most those that have the least. Even those initially with resources tend to end up without funds, housing, insurance and the support of friends. HIV Disease tends to bankrupt the infected financially, socially and spiritually. Americans place great importance on their jobs. In time persons with HIV Disease can no longer work and soon lose their income, insurance protection and job satisfaction.

Persons with HIV Disease have received benefit of three major legal decisions. The first is the Rehabilitation Act of 1971, which prohibited



employment discrimination against individuals with disabilities in the federal sector. The Act was amended in 1992 to indicate that the term “individual with a disability” does not include an individual on the basis of homosexuality or bisexuality.

A series of rulings by federal courts in California during 1985 and 1986 held that persons with AIDS were to be delegated as “being handicapped”, rather than being considered as having an infectious disease. Infected persons who did not meet the CDC definition for AIDS were not included in the rulings. The rulings were made in response to the then growing negative feelings of American society concerning persons with AIDS. Discrimination in many phases of life (employment, insurance, medical care, housing, testing, confidentiality, of test results and credit) was increasing. AIDS was considered as a special condition that required the special protections afforded by persons having a disability.

The Americans with Disabilities Act (ADA) gives federal civil rights protections to individuals with disabilities similar to those provided to individuals on the basis of race, color, sex, national origin, age, and religion. It guarantees equal opportunity for individuals with disabilities in public accommodations, employment, transportation, state and local government services and telecommunications. The ADA was enacted in 1990.

According to the ADA an individual is considered to have a “disability” if he or she has a physical or mental impairment that substantially limits one or more major life activities, has a record of such impairment, or is regarded as having such impairment. Persons with HIV disease, both symptomatic and asymptomatic, have physical impairments that substantially limit one or more

major life activities and are, therefore, protected by the law. In 1998, the US Supreme Court ruled that the ADA protected HIV-infected people, even when they have experienced no symptoms. Such persons are to be treated as being handicapped.

Persons who are discriminated against because they are regarded as being HIV-positive are also protected. For example, the law would protect a person who was fired on the basis of a rumor that he had AIDS, even if he did not.

Moreover, the ADA protects persons who are discriminated against because they have a known association or relationship with an individual who is HIV-positive. For example, the ADA would protect an HIV-negative woman who was denied a job because her roommate had AIDS.

### Summary

Globally, HIV Disease has been disastrous. It is the leading killer among known infectious diseases. The effect on governments, economies and traditional ways of life is almost incalculable. Cruelly, the disease often affects most those with the least resources. Whole generations in many locales have been decimated. Like previous pandemics, a central theme of HIV Disease is attaching blame. By trying to assign guilt or innocence precious time has been lost and in some cases irreversible harm has occurred.

In terms of infection control, HIV Disease has been the defining event of the last 50 years. Significant regulations and recommendations have been generated to lessen the change of viral exposure. Initially, the majority of these efforts were directed in the selection and use of personal protective devices. More recently, there has been increased emphases on the identification and use of engineering and work practice controls.

## Course Test Preview

To receive Continuing Education credit for this course, you must complete the online test. Please go to [www.dentalcare.com](http://www.dentalcare.com) and find this course in the Continuing Education section.

1. \_\_\_\_\_ are the most important cells in the human immune response.
  - a. B cells
  - b. Suppressor T cells (T8)
  - c. Macrophages
  - d. Plasma cells
  - e. Helper T cells (T4)
  
2. In 2004, \_\_\_\_\_ groups were involved with 50% of diagnosed AIDS cases among adults and adolescents.
  - a. white, not Hispanic
  - b. Hispanic
  - c. Asian/Pacific Islander
  - d. black, not Hispanic
  - e. American Indian/Alaska Native
  
3. The majority of men in the United States become infected with HIV through \_\_\_\_\_.
  - a. injection drug use
  - b. high risk heterosexual contact
  - c. man-to-man sexual contact
  - d. male-to-male sexual contact and injection drug abuse
  
4. (1) The need for pregnant women to know their HIV status is a key step in preventing perinatal transmission. (2) Significant increase of perinatal transmission of HIV infection has occurred over the last 20 years.
  - a. The first statement is true. The second statement is false.
  - b. The first statement is false. The second statement is true.
  - c. Both statements are true.
  - d. Both statements are false.
  
5. \_\_\_\_\_ percent of AIDS cases in the United States are pediatric (<13 years old).
  - a. Around 1
  - b. 5
  - c. Almost 11
  - d. Approximately 15
  - e. 26
  
6. A disease of the neoplasm, \_\_\_\_\_, is indicative of AIDS.
  - a. oral hairy leukoplakia
  - b. thrush
  - c. herpes zoster
  - d. persistent generalized lymphadenopathy
  - e. Kaposi's sarcoma
  
7. A sharps container is an example of a/an \_\_\_\_\_.
  - a. administrative control
  - b. personal protective equipment
  - c. work practice control
  - d. engineering control

8. **After an occupational exposure (e.g., finger stuck with a used dental hand instrument) the injured person should be screened for antibodies to \_\_\_\_\_.**
- a. hepatitis B
  - b. HIV
  - c. HIV and hepatitis B
  - d. hepatitis B and C
  - e. hepatitis B and C and HIV
9. **Rapid HIV tests determine the presence of \_\_\_\_\_.**
- a. HIV virions
  - b. antibodies to HIV
  - c. HIV RNA
  - d. HIV provirus
10. **\_\_\_\_\_ is/are the most effective in the prevention of exposures to bloodborne pathogens.**
- a. Administrative controls
  - b. Personal protective equipment
  - c. Work practice controls
  - d. Engineering controls
11. **In a commercial on television, it was stated that last year Americans experienced over one billion colds. This number is an example of (an) \_\_\_\_\_.**
- a. prevalence
  - b. epidemic
  - c. incidence
  - d. infection
12. **(1) Lesions that resemble recurrent aphthous ulcers occur in HIV positive patients. (2) Patients on trimethoprim/sulfamethoxazole or patients that smoked had more major aphthous ulcers.**
- a. The first statement is true. The second statement is false.
  - b. The first statement is false. The second statement is true.
  - c. Both statements are true.
  - d. Both statements are false.
13. **In 1990, the CDC reported a case in which a dentist appeared to have transmitted HIV from himself to his patients. \_\_\_\_\_ mode of disease transmission was likely involved.**
- a. Droplet infection
  - b. Direct contact
  - c. Indirect contact
  - d. All of the above.
  - e. None of the above.
14. **In order to meet the CDC definition for having AIDS, a person usually has a CD4+ (T4 cell) count (number of cells per mm<sup>3</sup>) \_\_\_\_\_.**
- a. above 1000
  - b. at or near 500
  - c. of 350
  - d. of less than 200

15. **Is oral candidiasis frequently associated with HIV infections?**  
a. Yes it is.  
b. No, it very rarely seen in such people.
16. **Acyclovir is used to treat \_\_\_\_\_.**  
a. herpes simplex  
b. hepatitis B  
c. Kaposi's sarcoma  
d. persistent generalized lymphadenopathy  
e. Cryptococcosis
17. **Necrotizing ulcerative stomatitis is seen \_\_\_\_\_.**  
a. only in persons with an HIV infection  
b. only in persons who are not infected with HIV  
c. in both HIV-infected and non-infected person
18. **Diffuse infiltrative lymphocytosis syndrome has been associated with \_\_\_\_\_.**  
a. Kaposi's sarcoma  
b. oral hairy leukoplakia  
c. esophageal candidiasis  
d. xerostomia  
e. aphthous ulcers
19. **Onset of Oral Kaposi's Sarcoma is associated with a CD4 count of less than \_\_\_\_\_ cells per mm.**  
a. 200  
b. 500  
c. 100  
d. 1000  
e. 50
20. **Prohibiting two-handed recapping of contaminated needles would be an example of \_\_\_\_\_.**  
a. an engineering control  
b. personal proactive equipment selection  
c. a work practice control  
d. an administrative control
21. **To date, there have been \_\_\_\_\_ proven cases of occupational acquisition of HIV among dental health care workers in the United States?**  
a. no  
b. 1  
c. 23  
d. 56  
e. 120
22. **Does the Americans with Disabilities Act protect persons that are HIV-infected, but do not have AIDS?**  
a. Yes  
b. No

23. In \_\_\_\_\_, AIDS was first reported in the United States.
- a. 1976
  - b. 1981
  - c. 1983
  - d. 1988
  - e. 1990
24. The confirmatory test for HIV infection is \_\_\_\_\_.
- a. the ELISA test
  - b. HAART
  - c. the Western blot
  - d. called ARC
  - e. also called viral load
25. HIV RNA can be detected in the blood of a person with HIV Disease \_\_\_\_\_.
- a. only during the acute retroviral syndrome period
  - b. only when a person is experiencing clinical symptoms
  - c. when a person meets the criteria for having AIDS
  - d. during all stages of HIV Disease

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