

# CPA

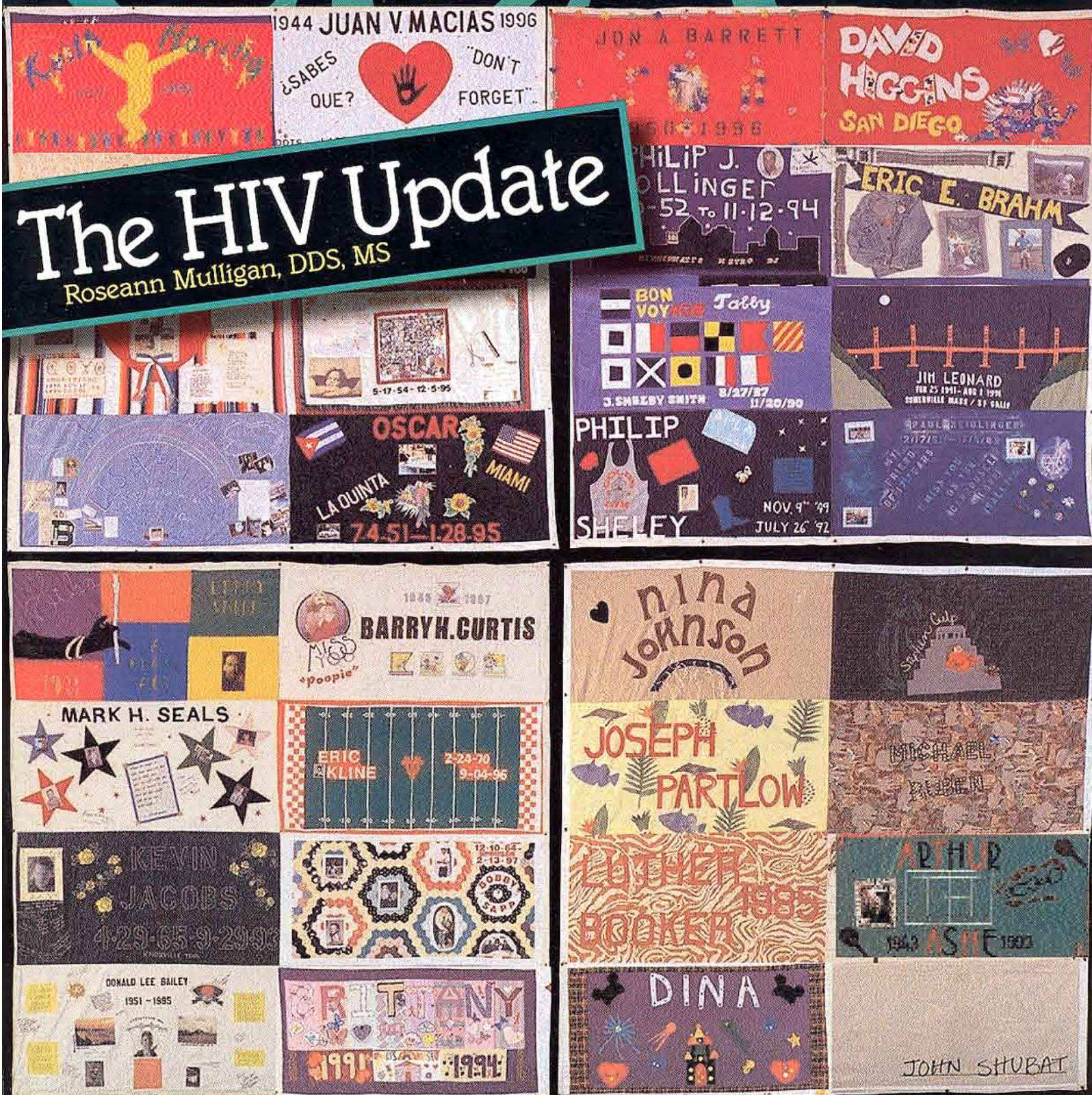
Oral Manifestations  
Oral Transmission  
Risk Assessment

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## The HIV Update

Roseann Mulligan, DDS, MS





OF THE CALIFORNIA DENTAL ASSOCIATION

# Journal

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## Getting the Job Done

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**W**e frequently hear colleagues complain that something upon which members of the profession depend has a problem or other deficiency. Complaints may arise as a result of a policy they question or from a change in philosophy in the management of benefits by third parties. Or, they may come from a supply or staffing shortage; from an increase in price, dues, or fees; or from any one of a plethora of matters that can affect the small-business owner.

There is one such problem that we have been hearing about for quite some time -- a shortage of qualified dental auxiliaries. CDA publications have received letters expressing concern about the lack of dental hygienists in particular. The shortage of both assistants and hygienists was a subject on the agenda again at the 2000 CDA House of Delegates.

Members turn to CDA for answers to this auxiliary staffing dilemma. Having said that, there are many variables that prevent a membership organization from solving a staffing shortage such as that encountered with dental hygiene for a number of years. CDA, through its volunteer efforts, can encourage school districts to favorably consider establishing a new dental hygiene training program or increase the capacity of an existing program. Dentist volunteers can consult or offer requested assistance.

But the bottom line is that CDA

cannot be expected to work miracles because staff training issues are the province of school boards and administrators. Ultimately, these individuals have the authority and responsibility to establish financial priorities for their schools or districts.

Over the years, volunteers at the American Dental Association and California Dental Association have worked tirelessly to influence or offer solutions to these kinds of problems. But, unfortunately, that is not where the real action or success is to be found. The resolutions that most colleagues demand or want are often won in the local trenches. And that is what we want to acknowledge this month by highlighting recent accomplishments of the Northern California Dental Society. I want to be quick to point out that other dental societies have also made unique contributions of time and resources to accomplish goals like the one achieved by NCDS. And, CDA, through the Board of Trustees, has approved small grants to help worthwhile component society educational projects get their starts, such as the one by NCDS.

It seems to us that the continuing complaints about auxiliary staffing shortages within the state might be addressed by others after consideration of the successful proactive efforts and accomplishments by NCDS. In our view, the NCDS approach is a real solution to problems that we frequently face as a profession. Further, it is important

that we pause to salute dentists who individually or collectively place their energies and/or resources toward solutions rather than merely complain and seek help from another authority.

The NCDS experience is straightforward. The need for a dental hygiene program was seen as necessary to resolve the staffing deficiency in that region. Leadership made contacts with several community colleges and a private school in their nine-county area. They ultimately entered into an agreement with Shasta College, committing to raise \$600,000 to start up a new program, which will graduate its first class in the spring of 2001. In addition to achieving their financial commitment, they have had an active Dental Advisory Board working with the college to develop curriculum and select the director. Their efforts required a committed leadership, starting with the board of directors of the dental society and the board of their dental foundation. One of the leaders emphasized the importance that teamwork within the society played in achieving their goal.

It is how they accomplished this goal that is impressive and important for other component societies to consider. How did a relatively small component of 215 members raise \$600,000? They established a number of avenues rather than utilizing one method. They conducted a series of fundraisers during a five-year period which members lent or contributed various assets or property that could be auctioned. Several

fundraisers netted \$50,000 each, with much of the behind-the-scenes effort coming from dental spouses. Another source of funding was built into the society dues structure. They have been conducting a "Smile Shasta" program that was underwritten by a major commercial sponsor from dental industry. And some funds came from an assessment for C.E. programs conducted by the dental society.

Finally, and perhaps as important as any of these short-term efforts, they have encouraged their membership to include their foundation's continuing scholarship and philanthropy activities into their individual estate planning. It seems clear that this dental society has made a firm commitment to develop an endowment that will contribute to the well-being of their nine-county community well into the future. Their mission, "Serving the dental and educational needs of the north state through philanthropy" should send a message to any dental society that wants to secure the highest level of respect for the dental profession in the community. I suspect that the leadership of this dental society has been able to gain significant professional satisfaction from the efforts they expended. Not only did they develop the resources to work toward resolution of a long-term staffing problem, but they have also secured considerable respect for their profession in their communities based upon their highly visible activities and contributions.

We know that there are other individuals and dental societies that

have demonstrated achievements in their communities. At a time when some dentists question the value of professional membership affiliation, it is important to reflect upon accomplishments that demonstrate the merit of professional teamwork. We salute Northern California Dental Society for *Getting the Job Done*.

## Tiniest Patients Need Care Too

BY DEBRA BELT

Mothers of young children often have similar stories about finding dentists for their children. In attempting to provide the recommended care, they call the dentist for a “first year” exam. Then the surprise comes. They are often told the visit isn’t necessary; the child is too young. Sometimes the parent is advised to bring the child in when he is older -- around 3 or so.

This situation leaves parents in limbo since, after all, they are trying to follow guidelines set by the American Dental Association, the California Society of Pediatric Dentists and the American Academy of Pediatric Dentistry.

“First-year dental visits are the recommended standard of care in pediatric dentistry,” said Ray Stewart, DMD. Stewart is currently helping draft a position paper for the California Dental Association on early childhood caries, which recommends a visit to the dentist at one year or within six months of the eruption of the first tooth.

So why do parents often have a hard time getting a dental appointment for their 1-year-olds? As in many situations, there is not a single quick answer. The scenario plays out as a result of changing ideology, supply and demand, and logistics.

“This is still a new concept,” explained Dave Perry, DDS, president-elect of the California Society of Pediatric Dentists. “Traditionally, we would wait until a child has a cavity. But with this preventive school of thought, we see a child early and talk to parents about prevention and avoiding early childhood caries. It takes a new idea such as this a while to be assimilated, and we are still in that transition period.”

As the idea continues to become more accepted and demand for early exams increases, dentistry is faced with the age-old issue of supply and demand.

“Unfortunately, the number of pediatric dentists is small compared to dentistry as a whole,” said Wayne Grossman, DDS, immediate past president of CSPD. “We are a graying population and many of us are retiring. Our resources are limited as a group, and we want to make sure general dentists provide this service or offer a referral to someone who does.”

“There aren’t enough pediatric dentists to go around,” Stewart said. “We are hoping to convince general dentists that these early exams are important so they will begin to look around for C.E. courses on what is involved in conducting these early risk assessments.”

Stewart and Grossman are not alone in their call to general dentists to become involved in helping provide this service.

“As dental health care providers, this is our best opportunity to practice truly preventive dentistry by intervening before problems are allowed to occur,” said Suzanne Berger, DDS, past president of CSPD and member of CDA’s Council on Community Health. “We must see children early, interact with parents and provide anticipatory guidance. There are not enough pediatric dentists to care for all of the children, so all dentists need to be examining young children in order to be proactive and make a difference. It’s smarter to stop decay before it starts.”

In advocating early exams, dentists familiar with the routine say there are a few basic elements involved: Attaining a medical history; conducting a risk assessment evaluating parents’ oral status and feeding habits of the baby; providing anticipatory guidance counseling; performing the oral exam; and intervening with appropriate treatments such as fluoride varnishes if necessary.

“Sometimes you have to be a little bit of politician,” said Grossman, who has been performing “well-baby” dental ex-

ams for 15 years. “You want to involve the key caregivers and sometimes that is a grandparent or another relative. There are situations where you have to get people from another generation or culture on your side.”

“The idea is for dentists to have the opportunity to talk to caregivers about several things, including their own dental care as well as feeding habits of the baby,” Stewart said. “If parents have dental decay, they can pass cariogenic bacteria on to their child during a ‘window of infectivity’ occurring between 1 and 2 years of age,” Stewart explained. “If we have the chance to talk to parents and find out when their last dental visit was and if they have decay, we can do some good with chlorhexidine rinses, brushing, and awareness of bacteria transmission.”

“We want to initiate a discussion with parents or caregivers about the many different things that can cause dental caries,” Perry said. “You want to find out if a child is sleeping with a bottle and if so ask what is in the bottle.”

Grossman said diet is one of the most important things he emphasizes. “It has the most impact on avoiding decay. I have a list of recommended snacks and Krispy Kreme doughnuts are not on the list. I suggest keeping kids away from snacks such as crackers and chips as oral bacteria thrives in an environment rich in carbohydrates.”

In performing the actual exam, dentists who routinely see young children concur on the use of the “knee-to-knee” examination technique where the baby sits on the lap of the parent and then lies back so his head is in the dentist’s lap. “The knee-to-knee is key,” Berger said. “It is comfortable and safe for the child, the dentist has better control, and the parent can see what is going on.”

This is also a good time to offer advice on how to clean the child's teeth and gums using a small soft brush or clean cloth.

In providing these preventive exams, dentists use different scheduling techniques. "It is a bit of a balancing act," said Grossman, who sets an entire morning aside to do the exams. "You have to prioritize time, energy, and staff to make it all happen. Auxiliaries can handle the discussion portion of the visit, although I tend to like to do a lot of question and answer routine myself. I do this as a service and trust that things will work out."

### U.S. Issues New Medical Privacy Rules

The U.S. government in December released the nation's first standards for protecting the privacy of Americans' personal health records. This new regulation will protect medical records and other personal health information maintained by health care providers, hospitals, health plans and health insurers, and health care clearinghouses.

"For the first time, all Americans -- no matter where they live, no matter where they get their health care -- will have protections for their most private personal information, their health records," said Donna Shalala, secretary of the Department of Health and Human Services. "Gone are the days when our family doctor kept our records sealed away in an office file cabinet. Patient information is now accessed and exchanged quickly. With these standards, all Americans will be able to have confidence that their personal health information will be protected."

The regulation was mandated by Congress when it failed to pass comprehensive privacy legislation. The new standards limit the nonconsensual use and release of private health information; give patients new rights to access their medical records and to know who else has accessed them; restrict most disclosure of health information to the minimum needed for the intended purpose; establish new criminal and civil sanctions for improper use or disclosure; and establish

### Flu Vaccine May Shoot Down Heart Attacks

Getting a flu shot may cut the risk of having a heart attack, according to research published in *Circulation: Journal of the American Heart Association*.

While recent evidence has linked various infections to heart disease, researchers have established the first link between vaccination and a reduced risk of heart attack. In a study of 218 heart attack patients, researchers linked flu vaccination to a 67 percent lower risk for a second heart attack.

Researchers at the University of Texas -- Houston Health Science Center studied heart patients during one flu season. Those who suffered a second heart attack were put in one group, while those who did not were considered controls.

Just 47 percent of patients who had second heart attacks had received a flu shot that year, compared with 71 percent of those whose hearts remained stable, the report indicates. The control group also reported a higher rate of previous flu shots. The protective effect of flu vaccination held after the researchers considered heart disease risk factors such as smoking and high blood pressure.

The findings are published in the December 19/26 issue of *Circulation: Journal of the American Heart Association*.

new requirements for access to records by researchers and others.

The Department of Health and Human Services received more than 52,000 comments on its proposed privacy rule published in 1999. The standards just released further strengthen patients' protection and control over their health information by extending coverage to personal medical records in all forms -- including paper records and oral communications. The earlier proposal had applied to electronic records and to any paper records that had at some point existed in electronic form. The final regulation provides protection for paper, oral, and electronic information, creating a privacy system that covers all personal health information created or held by covered entities.

"Comprehensive protection of personal medical records is what Congress called for in the law, and it's what American patients and their providers want and need," Shalala said. "Protection for all records is the most logical, workable, and understandable approach for patients and

providers alike."

The final rule also requires that most providers get their patients' consent for routine use and disclosure of health records, in addition to requiring their authorization for nonroutine disclosures.

### Whassup? Wasabi! Along with Tomatoes and Soybeans

Brush, floss, and eat soybean and tomato salad with wasabi dressing.

You may want to consider giving those instructions to your patients if the findings of new research are borne out by further study. Soybeans, tomatoes, and wasabi have all been found to have properties that may have positive affects in the oral cavity.

- **Soybeans:** A chemical derived from soybeans showed promising results in shrinking abnormal growth that can lead to oral cancer, according to a clinical study at the University of California at Irvine College of Medicine.
- Researchers at UC Irvine found that a

chemical called Bowman-Birk inhibitor reduced the size of precancerous oral leukoplakia in about one-third of the participants in the trial. They said the findings are among the first in humans indicating the soybean-derived inhibitor could prevent oral cancer.

- **Tomatoes:** The pigment that gives tomatoes their distinctive red color could prove to be effective in preventing and treating oral cancer, according to research results from Hebrew University of Jerusalem.

Lycoprene, which forms the pigment in tomatoes, has been linked to reduced risk of many cancers, including breast, prostate, pancreas and colorectal. When researchers added the chemical to oral cancer cells in culture as a control in an experiment on the effect of orange carrot pigment on tumor cells, the cancer cells began to die. The effects of lycoprene will next be tested on people with oral cancer.

- **Wasabi:** The powerful pale green paste used as an accompaniment to Japanese cuisine could fight cavities by preventing bacteria from lodging in the teeth and gums, according to a report.

In a test tube, Japanese researchers found that the compounds that give wasabi its flavor can block decay-causing bacteria from sticking to the teeth. This is probably because they render useless the

molecule that converts sugar to the substance that helps them stick to teeth.

Other research suggests that wasabi has a number of other health benefits, including inhibiting the growth of cancer cells in test tubes and preventing platelets from forming blood clots. In addition, wasabi has antimicrobial properties.

### Oral Piercing Can Lead to Gingival Recession

According to a report in the November issue of the *Journal of Periodontology*, piercing the tongue, lip, or cheek could cause localized gingival recession. This can lead not only to an unattractive defect, but also leaves the tooth root more vulnerable to decay and periodontal disease.

Researchers analyzed the case of a 26-year-old female who had localized gingival recession around the area of her lip piercing. The patient noticed soon after getting the oral barbell that her gums started to progressively recede in the area of the piercing. The barbell had direct contact with the area where the gums were receding. Since the patient's gingival recession was present only in the area of the oral metal device, the piercing was considered to be the cause of the gingival recession.

"Oral piercing has become a popular trend, and most people do not seek advice from a dental or medical professional pri-

or to the piercing," said Michael McGuire, DDS, president of the American Academy of Periodontology. "Another important concern is hygienic maintenance of the pierced oral area. The mouth contains millions of bacteria, and infection is a common complication of oral piercing."

Other consequences of oral piercing may include swelling, increased flow of saliva, pain, fractured teeth, interference with speech, and metal hypersensitivity.

"Many people with oral piercing do not think about the harmful effects it can have on their oral and overall health," McGuire explained. "In this particular case, the doctors were surprised that the patient had a history of mitral valve prolapse, and she was unaware of the consequences of piercing on her medical status. In fact, a case of infective endocarditis following nasal piercing has been reported."

### Correction

In the January issue of the *Journal of the California Dental Association*, Philip Wolkstein, DMD, was inadvertently left off the list of members of the Council on Peer Review. We apologize for the omission.

## Dentist Gain Spot in Annual Honesty Poll

Dentist have made up a little of the ground they have lost recently in the Gallup Organization's yearly Honesty and Ethics poll by moving up to the 8th spot for 2000, according to results released Nov. 27. Nurses took the top spot for the second year in a row.

Medical practitioners have consistently garnered high ratings for ethics according to Gallup. The honesty and ethics of elected officials, on the other hand, continue to draw skepticism from most Americans, judging by the poll results. As with every previous year, less than half the public said any elected official on Gallup's list had "very high" or "high" honesty and ethics

The top 10 in the 2000 Honesty and Ethics poll were:

1. Nurses
2. Pharmacists
3. Veterinarians
4. Medical doctors
5. Grade and high school teachers
6. Clergy
7. College teachers
8. Dentists
9. Engineers
10. Police officers

# Update on the HIV Epidemic

ROSEANN MULLIGAN, DDS, MS

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## CONTRIBUTING EDITOR

**Roseann Mulligan, DDS, MS**, is a professor and associate dean for community health programs at the University of Southern California School of Dentistry. She is also the dental director of the Pacific AIDS Education and Training Center.

*Nothing is as constant as change itself.* So wrote the Greek philosopher of Ephesus, Heraclitus (535-475 BCE).

**T**his is certainly true of the human immunodeficiency virus or HIV/AIDS epidemic. In reviewing the last *Journal of the California Dental Association* theme issue devoted to this topic (September 1993), it is clear that many changes have occurred when it comes to this epidemic. The demographic profile of the population most at risk for contracting the disease has been changing, as has our knowledge of the virus itself, its mutability, and its potential for oral transmission; the medical treatments and protocols for medications; the intraoral manifestations

being observed; and how we assess and manage our dental patients whether they have already been diagnosed with HIV infection or are demonstrating behaviors that place them at risk for acquiring the disease.

Nor does the epidemic show any signs of waning. Dr. Michael Campsmith's paper in this issue reports that the cumulative number of California AIDS cases has more than doubled in the seven-year time span since our previous report. He clearly describes the increasingly disproportionate effect this disease is having on African-Americans and Hispanics and the increasing percentage of women contracting the disease through heterosexual exposure. He also indicates that people with HIV are living longer than ever due to new treatment regimens, and

the number of people acquiring the disease is remaining constant. The net effect is that more people are living with HIV infection.

Dr. Geeta Gupta's paper on HIV pathogenesis and treatment details the steps that occur in the life cycle of HIV. The knowledge of these stages has allowed a number of new medications to be developed that specifically target a biological mechanism at that stage. The 1993 Journal issue discussed only three anti-retroviral drugs that were used to diminish HIV replication. Dr. Gupta discusses three categories of anti-retroviral drugs, specifically highlighting combination therapy or HAART (highly active anti-retroviral therapy). She notes that the combination of CD4 count and viral load testing is now used as a prognosticator of HIV disease activity and states that adherence to the medication regimen is particularly important, as mutations that may result in a drug-resistant virus are more likely when dosages are suboptimal. Dr. Gupta addresses cross-resistance sparing strategies, metabolic complications that may develop in people on protease inhibitors, and the risk of co-infections such as tuberculosis, and provides an update on recommendations for drug therapy for pregnant HIV-positive women.

Many of the common intraoral lesions discussed in 1993 are seen with considerably less frequency. Dr. Mahvash Navazesh details these changes, especially those that appear to be related to treatment of HIV infection by newer classes of medications, including HAART therapy. She discusses the relationship between CD4 counts and RNA viral load levels and the more common intraoral lesions in HIV-infected children and adults and reports on other intraoral findings that have been investigated more thoroughly over the intervening years, including

salivary gland involvement and salivary flow measurements.

The controversial topic of HIV transmission through the oral route is the subject of Dr. Fariba Younai's paper. Although transmission through casual salivary exchanges, such as via shared eating utensils, is still considered unlikely due to the antiviral properties of saliva, other oral transmission modes have been examined. Her review of the literature leads her to assert that unprotected orogenital sex may not be as safe as has been previously thought. Dr. Younai also discusses the inefficiency of local inhibitory factors in the saliva of the newborn that may be a contributing factor to the acquisition of HIV infection through breastfeeding.

Since the initial infection with the human immunodeficiency virus results in "flu-like" symptoms that resolve, followed by a 10-year incubation period, an individual may not be aware that he or she has become infected and is harboring the HIV virus. The dentist may notice a suspicious intraoral finding or become aware of the patient's involvement in behaviors that have been documented to result in HIV transmission. The paper I wrote with Ms. Sue Lemme deals with this issue by presenting a strategy of risk assessment that can be utilized by the dentist to interview the patient. This step-by-step approach in reviewing the patient's likelihood of contracting the HIV virus, in addition to providing information to the dentist, helps the patient engage in the realization of his or her potential for infection. This is an important first step to the individual's seeking HIV testing and/or ceasing involvement in hazardous behavior.

Since HIV-infected patients are living longer, many are returning to regimens of receiving routine oral health care that

might have been neglected in the past due to depleted personal, financial, and emotional resources. Dr. Ann Lyles wraps up the issue with a discussion of the likely questions that are frequently asked about caring for the oral health needs of HIV-positive patients such as: When do you need to consult with the physician; what should you ask during the consult; when should you prescribe antibiotics; and when should you refer a patient. She discusses those components of the medical history review that should receive the most attention and includes contraindications for certain drugs used in dentistry with medications used to treat HIV.

The dentist may be the first health care practitioner to interact with an undiagnosed HIV-infected person; to learn of an HIV positive patient's lack of adherence to an ongoing drug regimen; or to realize that an HIV-positive individual has dropped out of the health care system. Staying knowledgeable about the disease, so that the practitioner can reassure patients and introduce them to or induce them into the health care system, is vitally important for patients' overall well-being, including their oral health. This issue of the Journal will help you to update your knowledge base of HIV topics so that you can be more prepared to treat your HIV-positive or at-risk patients. By no means it is the last word, for the disease is likely to be with us for some time, constantly evolving. We must continue to update our knowledge and skills to assist our patients. We can count on the fact that when it comes to the HIV epidemic in particular, to use another of Heraclitus' quotes: All is flux, nothing stays still.

# Update on the Epidemiology of HIV/AIDS in the United States

MICHAEL CAMPSMITH, DDS, MPH

**ABSTRACT** During the past 20 years, the epidemic of human immunodeficiency virus and acquired immunodeficiency syndrome in the United States has continually evolved. Beginning in the mid-1990s, the numbers of annual AIDS cases and AIDS deaths have decreased, due in large measure to effective combination anti-retroviral therapies, which prolong the survival of people infected with HIV and delay progression to AIDS. This has resulted in an increase in the number of people living with HIV infection or AIDS. Increasing proportions of AIDS cases are occurring among women, racial/ethnic minorities, and people infected through heterosexual transmission. Dental care professionals are faced with the challenge of providing quality dental care to this ever-increasing population.

## AUTHOR

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In the two decades since the initial reports of opportunistic infections in previously healthy young men,<sup>1,2</sup> it has become clear that the epidemic of acquired immunodeficiency syndrome in the United States actually consists of many smaller epidemics, each with its own dynamic characteristics. First thought to affect only homosexual men, the epidemic was soon found to occur in other populations, including injection drug users,<sup>3</sup> hemophiliacs,<sup>4</sup> heterosexuals,<sup>5</sup> and children born to infected mothers.<sup>6</sup> AIDS is the end stage of a disease syndrome that begins with infection with human immunodeficiency virus. People infected with HIV can remain asymptomatic for varying lengths of time before developing the severe immune cell suppression and

opportunistic infections that currently define a diagnosis of AIDS.<sup>7</sup>

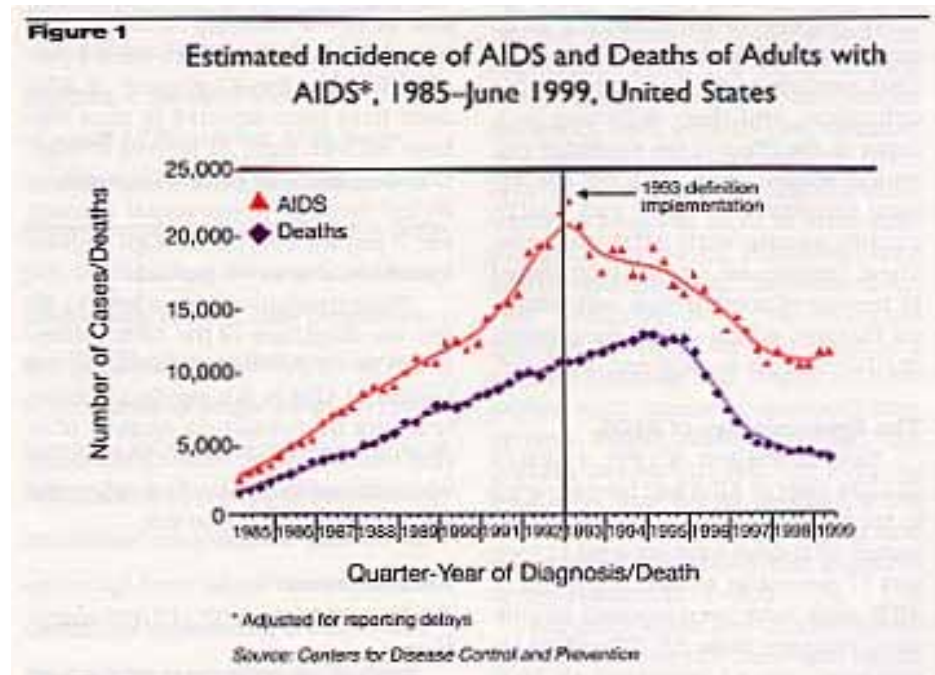
Although a number of anti-retroviral agents to treat HIV have been identified, at present there is no cure for HIV or AIDS. However, in the mid-1990s, combination anti-retroviral regimens including a protease inhibitor (termed highly active anti-retroviral therapy, or HAART) began to show promise for treating HIV infection. Due in large part to these treatment advances, there has been a sharp decline in annual deaths due to AIDS and, to a lesser extent, new cases of AIDS, since 1996. Longer survival of HIV-infected persons has resulted in an increase in the number of people living with HIV and AIDS.

This paper provides an update on the epidemiology of HIV and AIDS from 1996 through 1999. Data are provided on the

overall demographic profile of HIV and AIDS in the United States, as well as data specific for California.

### Surveillance of AIDS in the United States

Health departments in all 50 states, the District of Columbia, and U.S. dependencies (including Puerto Rico and the U.S. Virgin Islands) collect data on cases of AIDS using a uniform case definition and report form. These data are forwarded, without personal identifiers, to the Centers for Disease Control and Prevention. Surveillance data are used at the local, state, and national levels to estimate the size and scope of the epidemic, identify populations at risk, and direct resource allocation. The AIDS reporting criteria have been periodically revised as new knowledge on HIV disease and its medical treatment has been discovered. Revisions to the original case definition occurred early in the epidemic, first in 1985,<sup>8</sup> and again in 1987.<sup>9</sup> A more significant change in the case definition came in 1993, when laboratory markers of severe immune suppression (CD4+ T-lymphocyte count of less than 200 cells/F1 or percent of total lymphocytes of less than 14) were also used to define cases of AIDS.<sup>10</sup> Severe immunosuppression occurs at an earlier stage of disease than do most AIDS-defining opportunistic infections. Thus, this expanded case definition created a large increase in the reported number of AIDS cases (**FIGURE 1**), as prevalent as well as incident cases were reported. The AIDS epidemic curve (**FIGURE 1**) illustrates the rapid spread of AIDS in the 1980s, a peak in 1993 associated with the expanded case definition, and then declining incidence as the effect of the expanded definition waned. From 1996 on, the annual incidence of AIDS and deaths among people with AIDS declines. These declines are primarily attributed to the use of combination anti-retroviral therapy, which delays progression of HIV infection to AIDS and death.<sup>11-13</sup>



### The Epidemiology of AIDS

Through the end of 1999, a total of 733,374 cases of AIDS had been reported to the CDC.<sup>14</sup> Overall, 82 percent of reported AIDS cases have occurred in men and 17 percent in women; 1 percent of AIDS cases have been reported in children younger than 13. Classified by race/ethnicity, 43 percent of all AIDS cases have occurred in whites, 37 percent in blacks, 18 percent in Hispanics, and less than 1 percent each in Asian/Pacific Islanders and American Indians/Alaska natives. Mode of exposure to HIV is classified according to a hierarchical scheme; to date among people 13 and older, 47 percent of AIDS cases have been reported in men who have sex with men, 25 percent in injection drug users, 10 percent in people infected through heterosexual contact, and 2 percent infected through contaminated blood or blood products.

These cumulative figures help to define the magnitude of the AIDS epidemic in the United States. However, the burden of AIDS is not distributed equally among the population. Analysis of recent trends helps to more clearly define where the epidemic may

be heading and which groups are most at risk.

### Recent Trends

#### *Adults and Adolescents (13 and older)*

##### *Men*

Among all adults and adolescents in the United States with a diagnosis of AIDS, most have been men. Through June 1999, an estimated 610,134 cases of AIDS had been diagnosed among adult and adolescent men; of these an estimated 243,118 were still living.<sup>15</sup> The proportion of new AIDS cases diagnosed among men has decreased in recent years (**TABLE 1**). Throughout the 1980s, the majority of cases were diagnosed in white men. However, black and Hispanic men have been disproportionately affected by AIDS, and this racial disparity has increased in recent years. In 1998 blacks accounted for 11 percent of the U.S. male population and Hispanics accounted for 10 percent. From January 1996 through June 1999, an estimated 42 percent of men diagnosed with AIDS were black and 20 percent were Hispanic (Asian/Pacific Islander men

accounted for approximately 1 percent of recent AIDS cases, with less than 1 percent among Native American/Alaska native men). While the number of AIDS cases reported in 1999 was similar for white and black men, the case rate for black men was nearly eight times higher than for white men (125/100,000 vs. 16/100,000) (TABLE 2). The rate for Hispanic men was more than three times higher than for white men; rates for Asian/Pacific Islander men and Native American/Alaska Native men were similar to rates for white men.

Although the main HIV exposure risk for men has been and continues to be male-to-male sexual contact, recent estimates show this mode of transmission to be declining. Among AIDS cases diagnosed from July 1998 through June 1999, it is estimated that the proportion of cases among men who have sex with men has decreased to 53 percent. At the same time, the proportions attributed to injection drug use and heterosexual contact have increased to 27 percent and 13 percent, respectively (data adjusted for reporting delays and estimated proportional redistribution of cases initially reported without risk).<sup>15</sup>

### Women

Through June 1999, an estimated 121,528 cases of AIDS had been diagnosed among adult and adolescent women in the United States.<sup>15</sup> Of these, an estimated 61,203 were still living. The proportion of AIDS cases diagnosed among women has steadily increased, from 7 percent in 1985 to 13 percent in 1990 to 23 percent in 1999. As with men, black and Hispanic women are disproportionately affected by AIDS. Among recent AIDS cases in women, an estimated 62 percent have occurred in black women and 19 percent have occurred in Hispanic women (blacks represented 12 percent of the 1998 U.S. female population; Hispanics represented 10 percent). Similar to the pattern in men, in 1999 the AIDS case rates for black and Hispanic women were higher than the rate for white women; however, the disparities were even more

**TABLE 1. ESTIMATED AIDS INCIDENCE\* AMONG ADULTS AND ADOLESCENTS, UNITED STATES, BY SEX, THROUGH JUNE 1999**

Cumulative AIDS Incidence through June 1999			Recent AIDS Diagnoses, through June 1996	
Sex	Number	Percent	Number	Percent
Male	610,134	83	135,322	77
Female	121,528	17	40,179	23
Total	731,665**	100	175,501	100

\*Data adjusted for reporting delays.  
\*\*Includes 3 cases among people for whom sex was unknown because of missing information.

**TABLE 2. AIDS CASES IN ADULT/ADOLESCENT MEN BY RACE/ETHNICITY, UNITED STATES, REPORTED IN 1999**

RACE/ETHNICITY	CASES	RATE (PER 100,000 POPULATION)
White	12,855	16
Black	14,946	125
Hispanic	7,019	54
Asian/Pacific Islander	303	8
American Indian/Alaska Native	136	18
Total*	35,357	32

\*Includes 98 men whose race/ethnicity is unknown.

**TABLE 3. AIDS CASES IN ADULT/ADOLESCENT WOMEN BY RACE/ETHNICITY, UNITED STATES, REPORTED IN 1999**

RACE/ETHNICITY	CASES	RATE (PER 100,000 POPULATION)
White	1,924	2
Black	6,784	49
Hispanic	1,948	15
Asian/Pacific Islander	63	1
American Indian/Alaska Native	40	5
Total*	10,780	9

\*Includes 98 men whose race/ethnicity is unknown.

pronounced. Black women had a case rate nearly 25 times higher than for white women, with Hispanic women having a case rate more than seven times higher than for white women (TABLE 3).

Through 1992, the predominant HIV

exposure risk among women with AIDS was injection drug use, accounting for more than half of all cases. This has shifted in recent years, as heterosexual contact has now become the primary mode of HIV exposure for U.S. women. Among cases of

AIDS diagnosed in women from July 1998 through June 1999, an estimated 62 percent were attributed to heterosexual contact and 36 percent to injection drug use.

### Infants and Children

Through June 1999, an estimated 8,782 AIDS cases have been diagnosed among infants and children younger than 13. Of these, an estimated 3,681 infants and children with AIDS were still living. Ninety-two percent of these cases had been infected through perinatal transmission from an HIV-infected mother.

Perinatally acquired AIDS declined sharply in the 1990s as a result of the rapid implementation of the Public Health Service guidelines on the use of zidovudine (AZT) to reduce perinatal HIV transmission, as demonstrated in AIDS Clinical Trial 076.<sup>16</sup> Efforts to further reduce -- and perhaps one day eliminate -- perinatal HIV transmission include educating health care providers about the importance of offering voluntary HIV counseling and testing to all pregnant women, public information campaigns regarding prevention of perinatal HIV infection, and intensifying outreach to increase prenatal care among high-risk women.

### The Changing HIV/AIDS Epidemic in California

California was one of the first states in which a new syndrome of acquired immune deficiency was initially reported in 1981.<sup>1</sup> Through the end of 1999, the cumulative number of AIDS cases reported by the California Office of AIDS was 115,324.<sup>17</sup> This number represents more than 16 percent of all cases reported in the United States since the start of the AIDS epidemic (second only to New York, with more than 18 percent of all AIDS cases). California has had a substantially larger cumulative proportion of AIDS cases among men who have sex with men compared to the rest of the United States (71 percent vs. 47 percent). Mirroring the U.S. trend, the proportion of AIDS cases in California among men who have sex with men has been decreasing in

recent years, from 86 percent in 1990 down to 57 percent in 1999. Concurrently, the proportions due to injection drug use and heterosexual contact have increased to 13 percent and 8 percent, respectively (from 6 percent and 3 percent in 1990). Similarly to national trends, in California the proportion of recent AIDS cases among women continues to rise, accounting for 12 percent of AIDS cases reported in 1999 (up from 5 percent in 1990).

AIDS in California disproportionately affects some minority populations. Although whites still make up the largest proportion of cumulative AIDS cases (61 percent), their proportion of recent cases has been steadily declining. Among California AIDS cases diagnosed in 1998, 44 percent were in whites, 23 percent in blacks, 30 percent in Hispanics, 3 percent in Asian/Pacific Islanders and less than 1 percent in Native American/Alaska natives.<sup>18</sup> (Although the overall proportion of cases among Native American/Alaska natives is low, approximately 25 percent of all cumulative AIDS cases in Native Americans

have been reported in California.<sup>19</sup>) The number of AIDS cases diagnosed in California in 1998 and estimated incidence rates by race are shown in **TABLE 4**.

For men of all races in California, the main exposure risk continues to be male-to-male sexual contact. Among AIDS cases diagnosed in men in 1998, 65 percent were in men who have sex with men and 12 percent in injection drug users. These proportions differ by race as shown in **TABLE 5**. Among women, the trend has been toward an increasing proportion of cases attributed to heterosexual contact. For cases diagnosed in women in 1998, the main exposure modes were heterosexual contact (47 percent) and injection drug use (32 percent). As with men, these proportions differed by race (**TABLE 5**).

### Estimates of HIV/AIDS Prevalence and Incidence

CDC estimates that the prevalence of HIV infection (people diagnosed with HIV or AIDS as well as those who are infected but not yet diagnosed) in the United

**TABLE 4. AIDS CASES IN CALIFORNIA DIAGNOSED IN 1998, BY RACE/ETHNICITY**

RACE/ETHNICITY	NUMBER OF AIDS CASES DIAGNOSED	INCIDENCE (PER 100,000 POPULATION)
White	1,924	11
Black	1,023	44
Hispanic	1,325	13
Asian/Pacific Islander	110	3
Native American/Alaska Native	18	9

**TABLE 5. RISK DISTRIBUTION AMONG AIDS CASES DIAGNOSED IN CALIFORNIA IN 1998, BY RACE AND SEX**

	MALE		FEMALE	
	MSM (%)	IDU (%)	HETEROSEXUAL (%)	IDU (%)
WHITE	73	11	49	40
BLACK	53	20	40	35
HISPANIC	60	9	54	16
ASIAN/PACIFIC ISLANDER	69	5	*	*

\* Number of cases diagnosed in 1998 was too small to accurately estimate rates.

MSM = men who have sex with men

IDU = injection drug use

States at the end of 1998 was between 800,000 and 900,000 infected people.<sup>20</sup> The California Office of AIDS estimates the number of people living with HIV or AIDS in California on Jan. 1, 1996, to have been between 94,300 and 130,500.<sup>21</sup>

The CDC estimates that approximately 40,000 people in the United States are becoming infected with HIV each year;<sup>22</sup> 22 of these new infections, approximately 28,000 are in men and 12,000 are in women. Among newly infected men, approximately 50 percent are black, 30 percent are white, and 20 percent are Hispanic. An estimated 60 percent of new HIV infections in men are acquired through male-to-male sexual contact, 25 percent through injection drug use, and 15 percent through heterosexual contact. Among newly infected women, approximately 64 percent are black, 18 percent are white, and 18 percent are Hispanic. An estimated 75 percent of all new HIV infections in women are acquired through heterosexual contact and 25 percent through injection drug use.

## Summary

Data from the HIV/AIDS surveillance system in the United States have revealed these highlights about the current state of the epidemic:

- Men still account for the largest proportion of people with HIV and AIDS, but women account for an increasing proportion of infected people. Women accounted for 12 percent of AIDS cases reported in California in 1999.
- Racial/ethnic disparities among people with HIV and AIDS continue to increase. Among men with a recent AIDS diagnosis, 62 percent were black or Hispanic; among women, 81 percent were black or Hispanic. Among men in California receiving an AIDS diagnosis in 1998, 51 percent were black or Hispanic; among women, 67 percent were black or Hispanic.
- The proportion of AIDS cases attributed to heterosexual contact continues to increase, accounting for 22 percent of

all recently diagnosed cases (11 percent of cases among men and 59 percent of cases among women). Cases attributed to heterosexual contact accounted for 9 percent of AIDS cases diagnosed in California in 1998 (4 percent among men and 47 percent among women).

- Similarly, injection drug use accounts for an increasing proportion of recently diagnosed AIDS cases, with 30 percent attributed to injection drug use (27 percent of cases among men and 38 percent of cases among women). Cases attributed to injection drug use accounted for 14 percent of AIDS cases diagnosed in California in 1998 (12 percent among men and 32 percent among women).

- Perinatally acquired AIDS has declined significantly, due primarily to use of AZT.

Because of treatment advances, the number of HIV-infected people developing AIDS and dying from the disease has declined. However, the rate of new HIV infections has remained stable, with the result being more people living with HIV and AIDS every year.

In an era when effective prevention and treatment interventions are available, the HIV/AIDS epidemic will continue to evolve. Dental care professionals need to keep abreast of current recommendations for infection control practices and apply these in the treatment of all patients.<sup>23,24</sup>

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# Current Concepts in HIV Pathogenesis and Treatment

GEETA GUPTA, MD

**ABSTRACT** Over the past several years, great strides have been taken in the understanding and treatment of the human immunodeficiency virus. Death rates due to HIV have declined significantly since the introduction of protease inhibitors. Despite the advances in the field, health practitioners are still quite limited in their ability to curb this disease: 40,000 new HIV infections occur every year in the United States. This article will review the new advances in pathogenesis and treatment and discuss the limitations faced in treating the disease.

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Human immunodeficiency virus is an RNA virus that targets cells carrying the CD4 antigen. Recently, more details of the life cycle of HIV have been elucidated. After gaining entrance into the body, HIV infection primarily involves the CD4 lymphocytes but also includes macrophages, dendritic cells, microglial cells of the central nervous system, and others. The envelope protein, gp120, uses the CD4 antigen as a receptor for initial attachment. Then a conformational change occurs that requires the interaction of gp120 with a co-receptor (usually the chemokine receptor CCR5). This enables the second envelope protein, gp41, to interact with the cell membrane and allows HIV to gain entrance into the cell.

The RNA of HIV is then copied into

double-stranded DNA by the viral enzyme, reverse transcriptase. After the viral DNA is transported to the nucleus and integrated into the host genome, the infected CD4 cell begins producing viral proteins and viral RNA. New viral particles bud off the host cell membrane. The HIV protease enzyme modifies the viral proteins so that the resulting viral particle is a mature, infectious virion.

Each step of the HIV life cycle is being studied as a potential site for antiviral therapy. The current Food and Drug Administration-approved drugs target the reverse transcriptase and protease enzymes. Agents that work at the site of gp41, chemokine receptor blockers and integrase inhibitors, are under investigation.

## HIV Infection

### Acute

After initial exposure and local infection, viremia with HIV is thought to occur within five days.<sup>1</sup> Eighty to 90 percent of individuals with acute HIV infection become symptomatic approximately four weeks after exposure. The symptoms are very nonspecific and flu-like. Patients may exhibit one or more of the following: fever, headache, malaise, sore throat, anorexia, nausea, vomiting, rash, lymphadenopathy, and oral ulcers. Symptoms may last for only a few days to several weeks, but on the average they persist for two weeks.<sup>2</sup> There is no pathognomonic feature. Many patients seek medical care, but the diagnosis of HIV infection will usually be missed unless a careful history of recent risk behaviors is elicited.

During the symptoms of acute HIV infection, one finds extremely high titers of HIV in the blood. After approximately three months, the viral titers decline and remain at a relatively steady state (**FIGURE 1**). This decline is due to the host's cellular immune system, which exerts partial immunological control over HIV. HIV antibodies are often undetectable during acute HIV infection. In fact, the tests used in screening for HIV infection, the ELISA and Western blot, will often turn positive a few weeks after the symptomatic period. Therefore, if the diagnosis of acute HIV infection is suspected and the antibody screen is negative, it may be necessary to turn to an antigen test (p24 antigen or HIV-RNA testing).

### Chronic HIV Infection

After the symptoms of acute HIV infection spontaneously resolve, the patient enters the clinically asymptomatic stage. In the absence of therapy, it takes approximately 10 years before the patient will become symptomatic with AIDS-related infections or cancers. During this asymptomatic period, immune deterioration may be taking place, but because of the great reserve of the immune system, no outward signs occur.

HIV infection results in a rapid turnover of CD4 lymphocytes. The destruction of CD4 cells occurs directly and indirectly (through apoptosis). Over time, the CD4 lymphocyte count decreases, but in early disease the CD4 cell count usually remains normal. This is due to the enormous capacity of the immune system to replace these dying cells. Also, perturbations occur in the proportions of CD4 and CD8 cells (the helper:suppressor ratio). The normal ratio inverts; and as the immune deterioration worsens, this ratio becomes smaller and smaller.

When the absolute CD4 cell count falls to less than 200 cells/ml, the extent of immune deterioration is significant and the likelihood of HIV-related illnesses increase. Although many patients may still be asymptomatic, the Centers for Disease Control and Prevention uses this threshold for the categorization of Acquired Immune Deficiency Syndrome. By definition, any patient with HIV infection and a CD4 count of less than 200 cells/ml is categorized as having AIDS.<sup>3</sup>

### Monitoring of Disease

HIV is an infection of the immune system. Aside from the acute flu-like syndrome during primary HIV infection, there are few other manifestations that occur directly from the virus. Rather, the virus slowly, continuously, and silently erodes the immune system. When the immune deterioration gets to a critical level, symptoms of advanced HIV/AIDS present. Usually these manifestations are not directly caused by HIV but by opportunistic infections or cancers that the immune system can no longer control.

### CD4 Lymphocyte Cell Count

The CD4 lymphocyte cell count serves as a marker that gives information about the immune status of the HIV-infected individual. These cells are also termed T4 cells or helper cells. The CD4 cell count decreases as disease progression takes place. The normal range for the CD4 cell count is 750-1,000 cells/ml for adults. A patient with a CD4 count of more than

500 cells/ml is generally considered to have early disease. Counts from 200 to 500 cells/ml could be considered moderate disease. A patient with a count of less than 200 cells/ml would be considered in the advanced stage and meets the CDC definition of having AIDS. Those with CD4 cell counts less than 50 cells/ml are considered to be in the very advanced stage.

The CD4 lymphocyte count is used to monitor the severity of immune suppression and guides the physician as to when to administer certain antibiotic prophylaxis to prevent opportunistic infections. For example, prophylaxis to prevent *Pneumocystis carinii* pneumonia is instituted when the CD4 count falls to less than 200 cells/ml.

### Viral Load

While the CD4 cell count is the window on the immune system, the viral load provides information on the activity of the virus. The viral load test is a quantitative measurement of HIV. In the United States, the most commonly used viral load assay is the polymerase chain reaction, which tests for HIV-1 RNA. This test quantitates the number of copies of free HIV-1 RNA per milliliter of plasma (units equals copies/ml). The upper limit of the current test is 750,000 copies/ml while the lower limit is 50 copies/ml. Below this threshold, the test is not sensitive enough to detect HIV and is reported as "undetectable."

At the time of acute HIV infection, viral load testing shows extremely high viral titers, often more than 750,000 copies/ml. After three months, the viral load falls to a steady state ("set point") and then increases again in advanced infection (**FIGURE 1**). The viral set point could range from undetectable to more than 750,000 copies/ml. What determines whether the set point will be low, moderate, or high is unclear at this point. What is clear, however, is that the higher the set point, the faster HIV will progress.

Retrospective studies have documented the clinical utility of viral load testing as a prognostic marker. Using the CD4 cell count along with the viral load measurement

makes this prognostic indicator even more powerful. **FIGURE 2** shows how HIV infected patients in the Multicenter AIDS Cohort Study with a CD4 count of less than 200 cells/ml and with the highest viral loads had a 85.5 percent chance of developing AIDS-related illnesses within three years. On the other hand, patients with undetectable viral loads and a CD4 count of greater than 750 cells/ml had less than a 1 percent likelihood of progression.<sup>4</sup>

## Anti-Retroviral Therapy

### *Combination Therapy -- HAART*

During the past five years, highly potent anti-retroviral drugs have become available to treat HIV infection. When these drugs are used in combination, they have the capacity of significantly suppressing viral replication. This is evidenced by a marked decline in the viral load and is usually accompanied by an increase in the CD4 lymphocyte cell count. Combination therapy that is capable of significantly decreasing the viral load is termed highly active anti-retroviral therapy (HAART) and is commonly referred to as "cocktail" therapy.

The goal of HAART is to suppress viral replication to the lowest possible level. This would be measured on viral load testing as an "undetectable" result (less than 50 copies/ml). In the best of circumstances, HAART therapy is able to lower viral load to an undetectable level in approximately 80 percent of patients. The likelihood of success is lower in patients who have been on anti-retroviral drugs in the past, have very high initial viral loads, or have advanced disease. The duration that a particular regimen will be effective at keeping the viral load at undetectable varies per patient and can range from a few weeks to more than three years.

An undetectable viral load should not be confused with complete viral suppression or viral eradication. Research studies have shown evidence that the majority of patients with longstanding undetectable viral loads still have viral

replication taking place, however the currently available tests are not sensitive enough to measure these low values.<sup>5</sup> Also, viral load testing measures free virus in the plasma, not cell-associated virus. Since HIV is maintained in cells, if cell-associated viral DNA is measured, HIV can be detected. If therapy is stopped, the viral load rebounds. Additionally, it has been discovered that some of the HIV-infected lymphocytes are in latent stage.<sup>6</sup> These latently infected cells act as a reservoir for HIV. Even if it were possible to eradicate all free virus and cells that were actively producing HIV, when the latently infected cells would activate (months to years later), they would begin producing new virions.

Three classes of anti-retroviral drugs are approved by the FDA for use against HIV infection: nucleoside analogue reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and the protease inhibitors (**TABLE 1**). HAART is usually made up of two nucleoside analogues along with a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor. The choices of which combination to use and when to initiate therapy are individually determined with the input of the patient and physician. New data regarding anti-retroviral therapy is continually being generated and recommendations of how to use HAART are often modified. Guidelines on how anti-retroviral therapy should be prescribed have been published by the Department of Health and Human Services and the International AIDS Society.<sup>7,8</sup> These documents are regularly updated and take into consideration recent advances, theoretical concerns, and the yet unanswered questions regarding antivirals.

### *Resistance to Antivirals*

The qualities of an optimal antiviral regimen are that it

- Give potent viral suppression;
- Preserve options for future regimens in case of failure; and
- Be a regimen to which the patient will adhere.

This will usually result in clinical success. If any of these parameters is lacking, virological failure with the development of resistance becomes a concern.

Approximately one mutation occurs every time HIV replicates. On the average, in an untreated asymptomatic patient, HIV is replicating 1 billion to 10 billion times a day. Resistance to antivirals arises by specific mutations occurring in specific genes. Although most random mutations have no effect on the sensitivity of HIV to antiviral drugs, some will. In the presence of antiviral drugs, these mutations will be preferentially selected. The way to minimize or prevent the development of resistance is to maximally suppress HIV replication. If HIV is not replicating, mutations cannot develop and the virus will remain sensitive to the current regimen. If an antiviral regimen allows a significant amount of replication to take place, it is presumed that resistant mutations will inevitably develop. High-level resistance to certain antivirals has been demonstrated in less than two weeks of suboptimal therapy. Therefore, it is imperative that whenever therapy is given for HIV disease, it must be potent.

### *Adherence*

A regimen can only be effective if the patient will take it. Adherence directly influences the degree of viral suppression. One study showed that 81 percent of patients who were taking all (more than 95 percent) of their medication achieved viral load measurements of undetectable. Only 6 percent of patients who were taking 70 percent or less of their prescribed medication reached an undetectable value.<sup>9</sup>

Unfortunately, when poorly adherent patients begin complying with their regimen, many still cannot achieve undetectable viral loads. Resistance develops during the period of intermittent adherence, and reinstitution of the same regimen in full doses cannot overcome this resistance. Therefore, when initiating

a patient on an antiviral regimen, it is important for the patient to understand the significance of adherence and accept the responsibility of taking the regimen. If the patient is unable to make this commitment to therapy, it may be better to postpone therapy until he or she is ready. Many advocate the use of a placebo or candy regimen for the first few weeks of therapy so the patient can identify and solve any problems related to dosing before starting the antivirals.

Physicians often underestimate the difficulty of adherence to antivirals. The medications may cause numerous side effects in a patient who was previously asymptomatic; the number of pills ranges from five to 25 per day; some medications must be separated from others; some need to be taken on an empty stomach, some with food; etc.

### Cross-Resistance

Even with good adherence, a potent regimen may eventually fail. This is usually due to the development of viral resistance. Therefore, when initially prescribing a regimen, it is important to think one

step ahead, to what options are left for the next regimen. Unfortunately, future options can become quite limited because of the existence of a significant amount of cross-resistance. High-level resistance to one agent in the non-nucleoside reverse transcriptase inhibitor group usually results in resistance to all the other non-nucleoside reverse transcriptase inhibitors. Significant cross-resistance also exists among the protease inhibitors. Therefore, to preserve future drug options, people treating HIV use the strategy of "sparing" or excluding one class of drugs when initiating therapy. After the original HAART regimen fails, the new regimen would include an agent from the spared class. The chances that the new HAART regimen will be successful are increased since mutations conferring resistance to the spared class should not be present.

In the past few years, two types of resistance assays have been developed: the genotype analysis, which identifies specific mutations, and the phenotype analysis, which compares the drug sensitivity of the patient's virus to wild-type virus. These assays are being studied to determine

whether they can be helpful in guiding the choice of antivirals in patients who are failing HAART. Preliminary results from clinical trials show that the use of resistance assays can result in moderately lower viral loads in some situations.<sup>10-12</sup> Whether this added suppression will yield clinical benefit will only be determined with long-term follow up. In the community, these assays are often used, although they have not yet received FDA approval.

### Metabolic Complications of HAART

Anti-retroviral agents have side effects and certain toxicities that usually manifest themselves early in the course of treatment. However, over the past few years, other complications have been described that develop much later. In some patients, changes in body habitus with fat accumulation in the trunk and/or fat wasting of the extremities, face, and buttocks have been described. This is termed "lipodystrophy." Since this manifestation was noted after the availability of protease inhibitors, they were initially considered the etiology of the disorder. However, recent investigations

FIGURE 1.

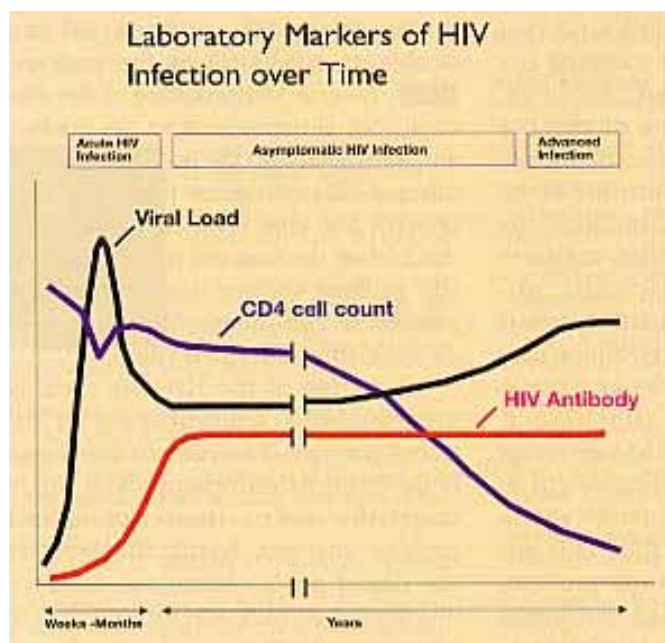
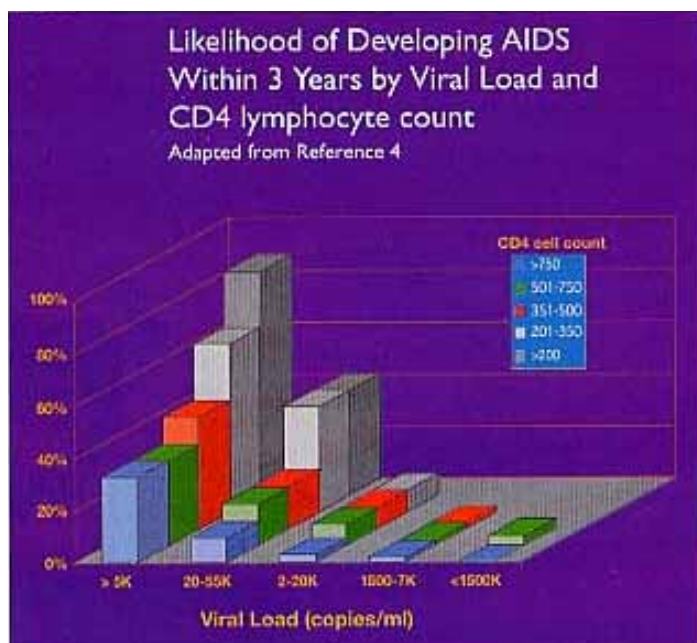


FIGURE 2.



show that although lipodystrophy is seen more commonly in patients on protease inhibitors, it can also be seen in patients on non-nucleoside reverse transcriptase inhibitors and occasionally in patients on no therapy.<sup>13</sup>

The mechanism of the disorder is not known. Observational studies have shown that the disorder may be a consequence of successful therapy, since patients with lipodystrophy are more likely to have been on long-term HAART and have viral load suppression.<sup>14</sup> Studies where patients who were on protease inhibitors were switched to another drug class have not shown resolution of the lipodystrophy.<sup>15,16</sup>

Other metabolic abnormalities that have been associated with protease inhibitors (and perhaps HAART in general) are insulin resistance and lipid abnormalities (increases in cholesterol and triglyceride levels). Mitochondrial toxicity is being theorized as the mechanism by which nucleoside analogues may give rise to certain side effects (pancreatitis, peripheral neuropathy, myopathy, hepatic steatosis and lactic acidosis).

Only when the mechanisms of these metabolic abnormalities are understood will it be possible to conclusively determine their cause. At this time, the benefit of HAART outweighs the risk of lipodystrophy, which primarily remains a cosmetic handicap. However, if pancreatitis, lactic acidosis, or hepatic steatosis occurs, therapy should be discontinued and a different regimen considered after resolution.

### Use of HAART in Pregnancy

Pregnant women who are infected with HIV have a 25 percent to 30 percent risk of transmitting HIV to their baby. Transmission usually occurs at the time of delivery, but may occur earlier. The higher the mother's viral load, the higher the risk of transmission. It has been demonstrated that treatment of the mother can decrease the risk of transmission to the baby. In 1994, the ACTG 076 study showed that AZT reduced HIV transmission by 67 percent.<sup>17</sup>

**TABLE 1. ANTIRETROVIRAL DRUGS**

#### NUCLEOSIDE ANALOGUE REVERSE TRANSCRIPTASE INHIBITORS

GENERIC NAME	CHEMICAL ABBREVIATION	BRAND NAME
Zidovudine	AZT	Retrovir
Didanosine	DDI	Videx
Zalcitabine	DDC	Hivid
Stavudine	D4T	Zerit
Lamivudine	3TC	Epivir
Abacavir	ABC	Ziagen
Zidovudine/Lamivudine	AZT/3TC	Combivir
Zidovudine/Lamivudine/Abacavir	AZT/3TC/ABC	Trizivir*

#### NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

GENERIC NAME	BRAND NAME
Nevirapine	Viramune
Delavirdine	Rescriptor
Efavirenz	Sustiva

#### PROTEASE INHIBITORS\*\*

Generic Name	Brand Name
Amprenavir	Agenerase
Lopinavir/Ritonavir	Kaletra
Indinavir	Crixivan
Nelfinavir	Viracept
Ritonavir	Norvir
Saquinavir (hard gel capsules)	Invirase
Saquinavir (soft gel capsule)	Fortovase

\*FDA approval was expected in late 2000.

\*\* Significant drug interactions occur with protease inhibitors

Since the publication of the ACTG 076 trial, the U.S. Public Health Service has recommended that all pregnant women be counseled regarding HIV. California has enacted a law that requires such counseling and the offering of an HIV test.<sup>18</sup> The California Legislature is considering enabling routine HIV testing of pregnant women.

The trials from the mid 1990s studied AZT monotherapy, however this is now considered to be suboptimal therapy. Combination therapy has become the standard of care for nonpregnant patients infected with HIV. There has been some hesitance to use combination antivirals in

pregnancy due to the unknown risks of these drugs to the fetus. Recent reports from academic centers using combination therapy in pregnancy report perinatal transmission rates of less than 2 percent. No increased fetal abnormalities have been reported, however long-term follow up is not available. Therefore, it is now recommended that a pregnant woman with HIV receive HAART therapy. This should improve the health of the mother and decrease transmission to the baby. The CDC has issued guidelines on the use of anti-retrovirals during pregnancy that are regularly updated as new information

becomes available.<sup>19</sup>

## Opportunistic Infections

Opportunistic infections occur when there is profound immune suppression. Since the widespread use of HAART, the incidence of AIDS and AIDS-related opportunistic infections has decreased. When patients with early HIV infection are put on HAART, the immune deterioration associated with HIV is delayed, so the incidence of opportunistic infections in this population has decreased. When patients with advanced disease are put on HAART, there is usually an increase in the CD4 lymphocyte count. This rise in CD4 cell count correlates with improved immune function (although it does not return to normal) and the risk for opportunistic infections declines. In patients who have low CD4 counts despite HAART, the incidence of opportunistic infections has declined because of adequate antibiotic prophylaxis.

Tuberculosis remains the most common HIV-associated infection worldwide. In the early 1990s, the incidence of TB dramatically increased in the United States. This was partially due to the increased prevalence of tuberculosis in HIV-infected patients. It is estimated that an HIV-infected individual with a positive skin test for TB is 100 times more likely to get an active TB infection compared to a person not infected with HIV. The risk of getting active TB is 7 percent to 10 percent per year whereas an HIV-negative person has a 5 percent to 10 percent risk in his or her lifetime.<sup>20</sup> Because of the large degree of overlap between these two epidemics, all patients with HIV need to be screened for TB. Conversely, any patient with active tuberculosis should be tested for HIV.<sup>21,22</sup>

The incidence of sexually transmitted diseases declined significantly from the 1980s to the mid 1990s. This was especially marked in the risk category of men who have sex with men. The lower infection rates were thought to be a consequence of increased HIV awareness and intensive educational programs that were aimed at this group. Unfortunately, over the past

few years, there has been a resurgence in STDs among men who have sex with men. Significant proportions of these patients are also infected with HIV. This higher STD rate correlates to an increase in high-risk unprotected sex. The laxity in safer sexual practices is attributed to a lower level of patient concern about contracting (and transmitting) HIV because of the availability of HAART.<sup>23,24</sup>

## Prevention

A vaccine to prevent HIV is still considered the best possible solution to curb this disease. Although much research is being done in this arena, no vaccine has yet been proven to be effective. Some of the obstacles in the way of the development of an effective vaccine include the large number of HIV strains, the ability of HIV to mutate and escape control, the difficulty of producing neutralizing antibodies, and the need for stimulation of cellular immunity.

Prevention of HIV will be the ultimate treatment of this disease. Education and behavior modification have been shown to reduce infection to an extent. Although antivirals have been a great boon; and many patients are alive because of these medications, the disease still has no cure. Patients in the Western world have been able to take advantage of HAART, but the majority of people with HIV live in poor areas of the world that have little or no access to these very expensive drugs. Worldwide, prevention rather than therapy remains the best strategy for dealing with the HIV pandemic.

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# Current Oral Manifestations of HIV Infection

MAHVASH NAVAZESH, DMD

**ABSTRACT** The oral manifestations of human immunodeficiency virus infection have changed drastically since the introduction of the highly active anti-retroviral therapy (HAART) in developed countries. Recent studies have documented significant reductions in morbidity and mortality rates among HIV-infected patients on HAART. This article focuses on the latest information about the oral manifestations of HIV infection and will discuss the impact of HAART.

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The oral manifestations of human immunodeficiency virus infection have changed drastically since the introduction of the highly active anti-retroviral therapy (HAART) in developed countries.<sup>1-3</sup> This therapy has been effective in suppressing plasma-HIV viral load below a detectable level and elevating CD4 cell counts.<sup>4</sup> Recent cohort studies have documented significant reductions in morbidity and mortality rates among HIV-infected patients on HAART.<sup>5-12</sup> This article will focus on the latest information about the oral manifestations of HIV infection and will discuss the impact of HAART on the prevalence of these conditions.

## Oral Lesions

Much has been written during the past 20 years about the association between

the HIV infection and different soft and hard tissue lesions involving the head and neck regions.<sup>13-20</sup> Although most of the original publications are based on findings in homosexual men and male intravenous drug users, recent investigations focus on women and children born to HIV-infected mothers.<sup>21-26</sup> A summary of oral lesions reported in HIV-infected children and adults is provided in **TABLE 1**.

## Common Lesions in Adults

Chronic herpetic ulcers (**FIGURE 1**), oral hairy leukoplakia (**FIGURE 2**), and Kaposi's sarcoma (**FIGURE 3**) have been identified as highly indicative of HIV infection in adults. candidiasis (**FIGURE 4**) and herpes zoster (**FIGURE 5**) infections are found to be strongly associated with HIV infection.<sup>27</sup> Saliva gland pathology including parotid enlargement (**FIGURE 6**) is found in some infected adults.

### *Common Lesions in Children*

In pediatric patients, HIV oral manifestations have been divided into three groups.<sup>26</sup> The first group includes candidiasis, herpes simplex ulcers, linear gingival erythema, parotid enlargement, and recurrent aphthous ulcers. This group is considered commonly associated with pediatric HIV infection. The second group includes papilloma, xerostomia, and periodontal diseases that are less commonly associated with pediatric HIV infection. The third group includes lesions that are strongly associated with HIV infection in adults but are rarely seen in pediatric patients. This group includes Kaposi's sarcoma, lymphoma, and oral hairy leukoplakia. More information on the oral manifestations of HIV infection and a picture gallery of clinical presentations are available at <http://www.hivdent.org>.

### *Association with Immunosuppression and Relevance to Disease Progression*

HIV disease progression is monitored by two key plasma markers: CD4 cell counts and HIV viral loads. Little is known about the relationship between HIV-associated oral lesions and viral loads.<sup>28-30</sup> However, some of the oral lesions have been well-studied and have been associated with immunosuppression as measured by CD4 counts.

### *Adults*

Some lesions are more significantly associated than others. Oral candidiasis, oral hairy leukoplakia, and Kaposi's sarcoma have been reported to be significantly associated with CD4 cell counts of less than 200 cells/ml.<sup>31-33</sup> This level of immunosuppression has also been associated with more clinical complications caused by herpes zoster infection and an increase in the number of oral lesions.<sup>34,35</sup> Necrotizing ulcerative periodontitis has been associated with CD4 cell counts of less than 100 cell/ml in one study. The mortality rate was reported to be 60 percent within 18 months of a necrotizing ulcerative periodontitis diagnosis in



**FIGURE 1.** Chronic herpetic lesions involving the midface area.



**FIGURE 2.** Hairy leukoplakia involving the lateral border of tongue in a geriatric HIV-infected patient.



**FIGURE 3.** Kaposi's sarcoma involving the palatal mucosa in an HIV-infected male.



**FIGURE 4.** Pseudomembranous candidiasis in an edentulous HIV-infected geriatric female.



**FIGURE 5.** Herpes zoster skin lesions on the forehead.



**FIGURE 6.** Parotid gland enlargement in an HIV-infected female.



**FIGURE 7.** Multiple oral papilloma lesions involving the lower lip on a young HIV-infected male.



**FIGURE 8.** Rampant cervical caries associated with HAART (courtesy of Dr. Mario Alves).

this study.<sup>36</sup> In a recent publication, the relationship of immunosuppression to pocket depth, recession, and clinical attachment level was evaluated in 316 HIV-infected dentate patients from North Carolina. Patients with CD4 cell counts of less than 200 cells/ml were 2.8 times more likely to have recession than those with higher CD4 cell counts.<sup>37</sup> Oral candidiasis has been associated with linear gingival erythema, and it has been suggested by some that it might be a better predictor of periodontitis than CD4 cell counts.<sup>38,39</sup> The prevalence of major salivary gland (parotid, submandibular/sublingual) enlargement, tenderness, and absence of saliva upon palpation was recently investigated in a U.S. multicenter national cohort of 576 HIV-infected women and 152 at-risk HIV-negative women. Unlike previous investigations that are mainly focused on parotid glands, this investigation focused on all major salivary glands and included a variety of clinical indicators of salivary gland disease. Based on the findings from this national study, the authors recommended a multidimensional approach (i.e., enlargement, tenderness and absence of saliva upon palpation) as markers for evaluation of HIV-associated salivary gland disease.<sup>21</sup> In the same cohort, the likelihood of a complaint of dry mouth and the absence of unstimulated whole saliva (flow rate equals 0 ml/min) were significantly higher in HIV-positive women than at-risk negatives. Those with CD4 counts less than or equal to 200 cells/ml were at a significantly higher risk for these conditions than those with counts greater than 500 cells/ml.<sup>23</sup>

### Children

Parotid enlargement has been associated with slower progression to AIDS in children. The median time to death has been reported as 3.4 years among patients with oral candidiasis and 5.4 years among those with parotid enlargement.<sup>25</sup> In a recent longitudinal study (1995-1998), the prevalence and prognostic significance of oral lesions were examined in 73

**TABLE 1. REPORTED ORAL LESIONS IN PEDIATRIC AND ADULT HIV-INFECTED PATIENTS**

Candidiasis
Oral hairy leukoplakia
Chronic herpetic ulcers
Papilloma
Kaposi's sarcoma
Aphthous ulcers (refractory to therapy)
Salivary gland diseases:
Xerostomia (dry mouth)
Glandular enlargement
Glandular tenderness
Diminished or absent saliva output
Cervical lymphadenopathy
Lymphoma
Periodontal diseases:
Linear gingival erythema
Necrotizing ulcerative periodontitis
Necrotizing ulcerative stomatitis

children with vertical HIV transmission who were receiving anti-retroviral medications. In this study population, cervical lymphadenopathy, xerostomia, and oral candidiasis were the most prevalent findings. Patients with severe immunosuppression had a more frequent occurrence of oral lesions during the study period. The likelihood of recurrent cervical lymphadenopathy, xerostomia and oral candidiasis was significantly higher in those with a previous (six to 18 months) diagnosis of these conditions.<sup>24</sup> In another recent study, 51 HIV-infected children were followed for two years. In this population, the presence of oral candidiasis was significantly associated with the CD4/CD8 cells ratio. Those with a CD4/CD8 ratio less than 0.5 were more prone to development of oral candidiasis.<sup>40</sup>

HIV viral load is thought to play a role in the occurrence of clinical manifestations as a reliable prognostic indicator of disease progression and anti-retroviral treatment failure.<sup>28</sup> Plasma viral load levels equal to or greater than 20,000 copies per/ml have been associated with the presence of oral candidiasis and oral hairy leukoplakia.<sup>29</sup> Recently the sensitivity, specificity, and positive predictive value of HIV-associated oral lesions for identifying immunosuppression and viral burden were investigated in 606 HIV-infected men and women in North Carolina. The concurrent presence of oral candidiasis and hairy leukoplakia had the highest (89.3 percent) positive predictive value. Oral candidiasis was significantly associated with plasma viral load equal to or greater than 20,000 copies/ml in this investigation.<sup>41</sup> Two recent publications have associated higher viral load levels with a higher likelihood of oral lesions<sup>22</sup> and salivary gland disease<sup>21</sup> in a large cohort of HIV-infected women in the United States.

### Anti-Retroviral Therapy

#### Benefits

HAART, which usually consists of a combination of three different anti-retroviral agents, has significantly decreased the progression of HIV infection to AIDS and death in the United States. The suppression of viral replication caused by HAART has increased immune function and decreased the incidence of common oral manifestations of the HIV infection. One or more drugs from the protease inhibitor class combined with nucleoside analogs and occasionally a non-nucleoside reverse transcriptase inhibitor constitute the majority of HAART regimens. In a recent study, the overall prevalence of HIV-associated oral lesions was reported to be significantly decreased because of the intervention of protease inhibitors in a cohort of HIV-infected men and women. Hairy leukoplakia, necrotizing ulcerative periodontitis, and stomatitis were among the lesions that were significantly

decreased in frequency.<sup>41</sup> Oral candidiasis has also been significantly affected by the protease inhibitor and HAART regimens.<sup>2</sup> The increase in the CD4 and neutrophil cell counts caused by protease inhibitors and HAART lead to a subsequent increase in the host defense against opportunistic agents. The occurrence of persistent major aphthous ulcers appears to be declining significantly. The management of these lesions has also been improved because of the availability of thalidomide therapy.<sup>42</sup>

### Risks

Despite this good news, there are concerns about the possible adverse effects of HAART. For example, the prevalence of oral warts has been reported to be significantly higher in HIV patients who are on protease inhibitors. An increase in oral warts from 6 percent in 1990-1991 to 26 percent in 1997-1998 is reported in HIV-positive patients evaluated at the University of San Francisco Oral AIDS Center.<sup>43</sup> Little information is available about the possible impact of anti-retroviral therapy on oral human papillomavirus. The studies of the impact of HAART on cervical human papillomavirus revealed an inability of HAART to resolve such infections.<sup>44</sup> The papilloma viruses are DNA viruses that can produce hyperplastic, verrucoid squamous, and papillomatous lesions involving the skin and mucosa. There are many human papillomavirus types. HPV 1, 2, 4, 6, 7, 11, 13, 16, 18, 32, and 57 have been found in different oral lesions. The major sites of involvement are lips, buccal and labial mucosa, and gingiva (**FIGURE 7**). The management of HPV lesions is frustrating for patients and practitioners due to the high rate of recurrences. Surgical removal and cryotherapy are the most common approaches for the management of HPV-associated lesions. Caustic agents such as podophyllin have been used with mixed results. Another concern is the possible association between protease inhibitors and dental caries. A dramatic increase in the rate of cervical and interproximal dental caries (**FIGURE 8**)

has been reported in some patients who are on protease inhibitors.<sup>45</sup> However, the exact cause-and-effect association has not established. Perioral paresthesia, dysgeusia, xerostomia, and oral ulcerations are among other possible adverse effects.<sup>46</sup> Protease inhibitors are also associated with abnormal lipid metabolism and distribution that leads to the development of lipodystrophic changes. Peripheral lipodystrophy may be manifested as enlargement of the dorsocervical fat pad (buffalo lump), enlargement of parotid glands (chipmunk face) and increased abdominal girth.<sup>47-49</sup> Pancreatitis and insulin resistance are also reported as possible adverse effects associated with HAART (See "Current Concepts in HIV Pathogenesis and Treatment" in this issue.)

### Conclusion

The oral manifestations of HIV infection have changed because of the advent of HAART. Many opportunistic infections and neoplasms have resolved or fail to occur as a result of an improved immune system. The HAART regimen is expensive and is not available in many countries. Where it is available, many HIV-infected patients may not have access to it. Therefore, the oral manifestations of HIV infection continue as in the pre-HAART era in these individuals. Oral health care providers should familiarize themselves with the oral signs and symptoms of HIV infection and recognize the significant role that these lesions play in detection, recognition, management, and transmission of HIV infection. Moreover, it is important to be familiar with the adverse effects of anti-retroviral therapy involving the head and neck area because of their impact on the quality and quantity of life for HIV patients.

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The author would be remiss in not recognizing the considerable contributions of Frank Lucatorto, DDS, MS, in the area of HIV-infected patients. He has indeed been an inspiration to the author as she

has pursued her interest in improving the quality of life for such individuals.

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# Oral HIV Transmission

FARIBA S. YOUNAI, DDS

**ABSTRACT** Although transmission of HIV through casual contact with saliva has not been shown, oral exposure to HIV-infected semen, blood, and breast milk can lead to infection. Unprotected orogenital contact, especially receptive oral intercourse, is associated with greater risk of HIV transmission than previously thought. The salivary anti-HIV properties, the local and systemic immunologic responses, the local mucosal integrity, and the level of infectious HIV present at the oral mucosal site all influence the potential for HIV infection through the oral mucosa. Although more information on the exact mechanisms of oral HIV transmission are necessary, based on the current understanding of this process, educational HIV prevention methods must focus on the potential risks associated with orogenital sexual behaviors.

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Since the onset of the human immunodeficiency virus epidemic, transmission of HIV infection through the oral route has been considered a rare phenomenon. Studies conducted in the early years of the epidemic demonstrated that nonsexual, casual contact with saliva (sharing utensils, HIV in dentistry) is not associated with an increased risk of HIV transmission.<sup>1-3</sup> As reviewed by Rothenberg et al,<sup>4</sup> from 1983 to 1994, several epidemiologic studies focused on the specific sexual behaviors that had resulted in HIV transmission. These studies also concluded that oral exposure is not considered an independent risk factor in sexual transmission of the HIV.<sup>5-21</sup> Despite these earlier studies, through

more careful epidemiologic investigations as well as anecdotal reports of HIV transmission from orogenital contact and infection of newborns through breastfeeding, it became apparent that transmission of HIV by oral mucosal exposure to infected semen, blood, and breast milk is possible.<sup>22-51</sup> As more information has become available in regard to the anti-HIV properties of saliva, there is now greater understanding of the factors that may influence the protective role of the oral environment against HIV transmission.<sup>52-54</sup> Although, casual contact with saliva remains insignificant in the spread of the HIV, the impact of oral sexual behaviors on the HIV epidemic should be given greater attention.

## HIV Epidemiology in the New Millennium

HIV is considered a predominantly sexually transmitted disease in the United States and worldwide. There are, however, significant variations in the demographics and exposure risk categories among various regions. In the United States, of the cumulative 733,374 cases of AIDS reported to the Centers for Disease Control and Prevention through December 1999, 47 percent are attributed to male homosexual and bisexual contacts; among women, heterosexual contact accounts for 40 percent of the cases.<sup>55</sup> In fact, among female groups, heterosexual transmission has surpassed the rate of parenterally acquired HIV infection.<sup>55</sup> In the second decade of the HIV epidemic, despite the enormous public educational efforts instituted at every level, surprising patterns of HIV transmission are emerging. This phenomenon may be partly related to the recent advances in the medical management of HIV infection and the steady decline in the HIV mortality rate that appear to be influencing the public's general perception of this still deadly infection. There is epidemiologic evidence that despite the general shift in the transmission patterns of the HIV infection toward women and minority populations, high-risk sexual behaviors among younger homosexual men that was on the decline remains a serious concern (this is still the largest single exposure group);<sup>55</sup> alcohol and illicit substances are becoming strongly influential in the rate and the type of sexual behaviors among high-risk groups;<sup>56-59</sup> and the spread of HIV among adolescents, especially females, has assumed an upward trend (in 1999, people age 13 to 24 accounted for 15 percent of reported new HIV cases, and women accounted for 49 percent of cases in this age group).<sup>55</sup>

In addition to the continued concern over the spread of HIV infection through homosexual and heterosexual modes, oral sexual behaviors have come into focus

in recent years. Because of the perceived relative safety of oral sex compared to other types of sexual behavior, unprotected oral sexual practices have been prevalent among many high-risk groups.<sup>60-61</sup> It has recently been realized that orogenital contact -- once considered to have an extremely low potential for infection as compared to anal intercourse or the use of contaminated intravenous devices -- may play a significantly stronger role in the future of the HIV epidemic than originally thought.<sup>46,59, 62</sup>

## Transmission of HIV Through the Oral Mucosa

Although oral transmission of HIV is considered a rare phenomenon, reports of such transmissions do exist. **TABLE 1** demonstrates a comprehensive list of the documented cases of oral transmission dating to the onset of the HIV epidemic.<sup>22-51</sup> The questionable circumstances involved with many of these cases have resulted in serious doubts concerning the true risk of HIV infection through an oral mucosal mode. For instance, the reliability of self reports of sexual practices, multiple risk behaviors, and very small numbers of seroconversions in the follow-up studies have all overshadowed the very few apparently confirmed cases of oral HIV transmission. What is common among almost all these cases is a lack of evidence for HIV transmission through saliva alone. One possible exception is a 1997 report by the CDC that described a case of potential HIV transmission between an infected man to his previously uninfected female partner through deep kissing.<sup>43</sup> In studying this report, one must note that the HIV-infected man reportedly had severe periodontal disease and gingival bleeding during tooth brushing. He reported brushing his teeth every time before engaging in a sexual relationship with his partner who also had inflamed gingival tissues according to her dental records. Therefore, because of the potential presence of

blood (of periodontal disease origin), this report also lacks strong evidence that saliva can play a significant role in HIV transmission. In fact, in terms of mode of transmission, this case is not unlike the reported cases of human bite transmission where blood contact was made by the index cases who were bitten by HIV-positive source cases.<sup>27,40</sup>

Until recently, orogenital intercourse, especially receptive oral intercourse, was believed to be associated with some but small risk of HIV transmission. In a 1993 study of the estimated risk of receptive oral intercourse, based on the HIV prevalence, sexual behaviors, and seroconversion status, the per-partner risk of seroconversion was shown to be 1 percent (range, 0.85 percent to 2.3 percent), compared to 10 percent (range, 4.2 percent to 12 percent) for receptive anal intercourse.<sup>63</sup> Other modeling studies have shown the risk for unprotected receptive anal intercourse to be eight times higher than the risk for receptive oral intercourse.<sup>64</sup> In a recent study conducted by researchers at the CDC, San Francisco General Hospital and the University of California San Francisco, the rate of HIV seroconversion related to oral sex was reported to be much higher (7.8 percent).<sup>46</sup> The study presented during the Seventh Conference on Retroviruses and Opportunistic Infections held in the early part of 2000, consisted of 102 recently infected homosexual men. Through self-administered and interviewer-administered questionnaires, clinical evaluations, partners interviews, and counselor's interventions, a process of risk assessment for six months preceding a patient's seroconversion was accomplished. Eight seroconversions (7.8 percent) were attributed to oral sex. Although a few patients recalled oral sores or periodontal disease at the time of their exposure, most did not have an apparent break in their mucosal tissues. This newly reported rate of possible oral HIV transmission has raised serious concerns over the apparent increased frequency

of unprotected oral sexual behavior, especially among young homosexual men.

In addition to the epidemiologic studies and case reports of oral HIV infection, animal studies on simian immunodeficiency virus have shown the ability of the tested virus subtypes to penetrate the oral mucosal barrier. In these studies, SIV has been successfully transmitted to neonate and adult Macaques by gently painting various viral concentrates on the dorsal aspect of the tongue.<sup>65,66</sup> In one report, the viral concentration required for transmission through the oral mucosa was shown to be 6,000 times lower than that needed for rectal infection.

All these reports point out to the likelihood of HIV transmission across the oral mucosa and raise several questions in regard to local and systemic factors, which may facilitate or hinder the transmission process. The exact mechanism of HIV transmission after exposure of oral mucous membrane surface to HIV-infected fluids is unknown. During exposure of mucosal surfaces, HIV could be transmitted by

- Entering through epithelial lesions;
- Infecting CD4 positive cells (e.g., Langerhans' cells, monocytes and macrophages;
- Infecting intact epithelial cells.<sup>67</sup>

Based on the evidence presented, it is clear that given the right circumstances, HIV is capable of infection across the oral mucosa, though the exact mode of entry is not yet clear. This is especially true if the oral exposure occurs with body fluids containing high levels of infectious HIV. One question remains and that is to what extent saliva plays a role in delivering viable viruses for infection across the oral mucosa.

### Isolation of HIV From Whole Saliva

HIV-1 was isolated from saliva in 1984.<sup>68</sup> Several studies have demonstrated a substantial number of HIV RNA or proviral DNA in saliva while others have yielded only a modest amount

(range, 15 percent to 100 percent).<sup>54,69-73</sup> There appear to be significant differences between various reports in terms of salivary collection techniques, viral isolation methods, and patient's general and oral health status, which may all have contributed to the variable results among these reports. In one quantitative study of HIV RNA in serum, semen, and saliva using an in-house competitive reverse transcriptase-polymerase chain reaction assay, a significant number of HIV viral RNA copies was shown in cell-free whole unstimulated saliva of 96 percent of the HIV-seropositive patients in the study (median of 162/ml; range: 0-72080/ml), correlating with the level of HIV in blood (mean of 14,817 copies/ml and a range of 167-254,880), and increasing with HIV disease progression.<sup>73</sup>

In a recent report, by employing a highly sensitive nucleic acid sequenced-based assay that is uninhibited by salivary components, HIV-1 RNA was detected in 42 percent of the 40 subjects tested (compared with 78 percent of plasma samples).<sup>74</sup> In that study, the mean viral load for saliva samples (2.90 log<sub>10</sub> copies/ml) was highly correlated with the plasma viral load (3.97 log<sub>10</sub> copies/ml). One interesting aspect of the study was that salivary viral load also significantly correlated with the presence of HIV-associated periodontal disease (linear gingival erythema and necrotizing ulcerative gingivitis and periodontitis) and severe gingival inflammation but not chronic periodontal disease, HIV-associated oral lesions, or presence of occult blood in saliva. The authors concluded that nonblood sources such as tonsils, salivary glands and gingival crevicular fluid may contribute to oral HIV shedding that reflects the systemic burden. A lack of association between the levels of HIV in the oral cavity and the presence of chronic periodontal disease had previously been demonstrated as well.<sup>71,75</sup> Another study had demonstrated significantly higher levels of HIV RNA in saliva of patients

with periodontitis compared to a matched control group with no periodontal disease (87.5 percent vs. 33 percent).<sup>72</sup> In that study, the level of gingival inflammation was not measured; but the HIV RNA was found in 47.6 percent of gingival crevicular fluid samples of periodontitis patients, possibly related to a higher level of inflammation.

Another factor that may play a major role in the potential for oral HIV transmission is the role of oral mucosal pathology in the rate of oral viral shedding. As described before, the Shugras and colleagues 2000 report failed to show a correlation between the levels of salivary HIV viral titer and the presence of various HIV-related oral pathologies. A previous study, however, had shown that crack cocaine-induced oral ulcers were highly correlated with the rate of oral HIV transmission among the high-risk study groups.<sup>76</sup> The discrepancies observed among these reports may be reflective of the complex mechanisms involved in oral HIV transmission. Factors influencing the likelihood of such transmission include the presence and the titer of the virus, the integrity of the oral mucosal site, mucosal and systemic immunological functions, local inhibitory factors, and the presence or absence of co-factors that are yet unknown. It must be emphasized that identification of HIV RNA in saliva is not indicative of the infectivity of the virus. Several studies have shown very low levels of infectious HIV detected in saliva (rate, 0 percent to 5 percent).<sup>68,71-73,77-80</sup> The low recovery rate of infectious HIV from saliva may be attributed to HIV inhibitory mechanisms that are endogenous to the oral environment.

### Anti-HIV Activity of Saliva

Several studies dating back to 1986 have documented an anti-HIV property in human saliva.<sup>81-91</sup> The anti-HIV-1 activity of saliva has been reported in whole saliva,<sup>81-84,88</sup> the parotid,<sup>81,88</sup> and submandibular saliva <sup>81,84,85,88</sup> and also in saliva of healthy males and females

**Table 1.**  
Case Reports and Observations on Oral Transmission

Source	Year	Report Type	Index Pt	Source	Sexual practices
Sabatini et al. <sup>22</sup>	1984	Case report	1 female	1 female	Orogenital
Marmor et al. <sup>23</sup>	1986	Case report	1 female	1 female	Orogenital; vaginal bleeding
Fischl et al. <sup>24</sup>	1987	Three-year follow-up of 45 HIV-positive patients	11 males	11 females	vaginal intercourse and repeated oral sex
Mayer et al. <sup>25</sup>	1987	Follow-up of 2,507 homosexual men, eight seroconverted	1 male	1 male	Repeated oral intercourse
Monzon et al. <sup>26</sup>	1987	Case report	1 female	Multiple	Orogenital
Anonymous <sup>27</sup>	1987	Case report	1 female	1 female	During a fight, hand bitten by IDU sister bleeding from avulsed teeth
Rozenbaum et al. <sup>28</sup>	1988	Follow-up of a cohort of homosexual men	5 males	A mean of 3.8	Oral intercourse (insertive and receptive)
Osmond et al. <sup>29</sup>	1988	Interview and testing of 117 homosexual men, 85+	2 males	Multiple	Oral intercourse and anal receptive
Goldberg et al. <sup>30</sup>	1988	Case report	1 male	1 male	Orogenital intercourse
Perry et al. <sup>31</sup>	1989	Case report	1 female	1 female	Orogenital
Detels et al. <sup>32</sup>	1989	Two-year follow-up of 2,915 men, 232 seroconverted	1 male	Multiple	Orogenital intercourse (insertive and receptive)
Spitzer et al. <sup>33</sup>	1989	Case report	1 male	1 female	Orogenital (fellatio & cunnilingus)
Quarto et al. <sup>34</sup>	1990	Case report	1 male	1 female	Orogenital (fellatio)
Lifson et al. <sup>35</sup>	1990	Prospective study of 6,705 homosexual and bisexual men	2 males	Multiple	Oral intercourse (receptive)
Murray et al. <sup>36</sup>	1991	Case report	1 male	1 male	Oral intercourse (receptive)
Lane et al. <sup>37</sup>	1991	Case report	1 male	1 male	Oral intercourse (receptive)
Keet et al. <sup>38</sup>	1992	Prospective study of 757 homosexual men, 102 seroconverted	4 males	Multiple	Oral intercourse plus an additional five men who reported both orognital and receptive anogenital intercourse
Rich et al. <sup>39</sup>	1993	Case report	1 female	1 female	Orogenital
Vidmar et al. <sup>40</sup>	1996	Case report	1 male	1 male	Finger bitten when assisting terminal AIDS patient during a grand mal seizure w/tongue laceration
Schacker et al. <sup>41</sup>	1996	Study of primary HIV infection among 46 adults	4 males	Multiple	Oral intercourse
Berry and Shea <sup>42</sup>	1997	Case report	1 male	Multiple	Oral intercourse (receptive)
Padian et al. <sup>43</sup>	1997	Case report	1 female	1 male	Oral; periodontal disease
Bratt et al. <sup>44</sup>	1997	Case report	2 males	Multiple	Oral intercourse (one insertive and one insertive and receptive with a ho/o penile skin damage)
Senterfitt et al. <sup>45</sup>	1998	Study of 30 recent HIV seroconversion	4 males	Multiple	Oral intercourse (receptive)
Dillon et al. <sup>46</sup>	2000	Study of 102 persons with	8 males	1 to multiple	Oral intercourse

as well as HIV-infected individuals.<sup>82</sup> Among the suggested mechanisms for the anti-HIV action of saliva are the salivary anti-HIV antibodies present in HIV-infected individuals<sup>85,86</sup> and aggregation of HIV-1 by large molecular-weight molecules (mucins) and thrombospondin that allow for viral clearance from the oral environment.<sup>87-89</sup> In addition, several soluble inhibitors such as lysozyme, lactoferrin, defensins, and lactoperoxidase have been suggested to contribute to the anti-HIV action of saliva.<sup>52,90-91</sup> One molecule associated with the antiviral properties of saliva against HIV is the molecule secretory leukocyte protease inhibitor.<sup>52</sup> This molecule was originally described in 1995 when McNeely and co-workers demonstrated that in vitro infection of monocytes with HIV-1 (measured by viral reverse transcriptase activity) even after one hour of exposure to saliva was suppressed for three weeks after infection. Since that original in vitro study, the in vivo effectiveness of secretory leukocyte protease inhibitor has also been demonstrated.<sup>54</sup> The exact mechanism of the HIV-1 inhibition by the protease inhibitor is not well-understood, but it appears to interact with the host cell and inhibit the HIV cell fusion process, acting early and preventing infection of the host cells.<sup>91</sup>

### HIV Transmission Through Breastfeeding

The potential for transmission of HIV by breastfeeding is well-established,<sup>47-51</sup> although the exact mechanism by which the transmission occurs has not been characterized. Secretory leukocyte protease inhibitor levels are high in both colostrum and breastmilk, as well as the saliva of the newborn immediately postpartum; only the breastmilk shows a dramatic decrease in the protease inhibitor levels over the few weeks postpartum.<sup>4</sup> Breastmilk has high levels of HIV as cell-free virus as well as infections within the milk monocytes and macrophages. These high levels of

HIV presence coupled with the relatively low levels of the protease inhibitor in milk may facilitate the viral entry in the tonsillar and intestinal crypts of the newborn and establish the HIV infection.<sup>92</sup> Therefore, it appears that the local inhibitory factors that are important in hindering the HIV oral mucosal transmission are not efficient in preventing infection of the newborn through breastfeeding. Clearly, more information about the mechanisms of HIV invasion through the oral mucosal surfaces and the exact mode of HIV entry are necessary.

### Summary

Oral mucosal exposure to infectious HIV is associated with the risk of infection. Many local and systemic factors influence the efficiency of oral HIV transmission. Although not as efficient as other sexual behaviors, unprotected oral sexual contacts do present a risk for HIV infection.

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# HIV Risk Assessment: Building on Dentistry's History of Promoting Health

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**ABSTRACT** Dentists have demonstrated a willingness to look beyond the mouth and consider the patient's overall presentation in a number of health-related areas. The HIV pandemic is another opportunity to involve the dentist in overall health issues through identification of those individuals at risk for acquiring HIV. This risk assessment activity can be facilitated through the use of a structured risk assessment algorithm that is presented in detail. The purpose of this algorithm is to encourage dentists -- when they notice specific conditions or become aware of risky behaviors -- to talk with their patients about HIV/AIDS and how the patient may be at risk. The historic success dentists have achieved in conveying information about the prevention of disease and promotion of health should bolster their resolve to expand their discussions with patients to include an HIV risk assessment.

The application of disease prevention by the dental profession to systemic conditions was first noted in the literature of the 1960s when a complete medical history review<sup>1</sup> and examination of the head and neck<sup>2</sup> area by the dentist prior to initiation of treatment and especially before giving injections of local anesthetics was called for by various authors.<sup>3,4</sup> The 1970s saw efforts to expand the dentist's role in physical evaluation<sup>5</sup> and observation of deviations from normal in the patient's gait, skin, sclera or mucosal appearance,

presence of edema, appearance of swollen joints, and breathing irregularities.<sup>6</sup> Dental education programs were noted to contain curricula to assess systemic health status and refer to physicians as appropriate.<sup>7</sup> Taking blood pressure readings as part of a dental visit was described as an "opportunity for dentists to show their commitment to total health care."<sup>8</sup>

Today dentists include in their health promotion activities counseling against tobacco use in all of its guises;<sup>9-12</sup> recognizing and reporting child abuse and/or neglect,<sup>13,14</sup> elder abuse,<sup>15</sup> and

domestic violence;<sup>16</sup> and encouraging the use of mouthguards during sports and play activities.<sup>17,18</sup> They continue to be concerned about human immunodeficiency virus as they have been since the first appearance of HIV.

### Dentistry and HIV/AIDS

For most of the past two decades, the HIV pandemic has been a focus of concern. In the beginning of the epidemic, specific intraoral lesions and symptom clusters that were unique to this infection were identified.<sup>19-22</sup> Patients who sought dental care for oral symptoms typically represented a particular demographic profile and were already diagnosed with the HIV infection, and many had already progressed to the full-blown stage of AIDS.<sup>23</sup> Their life spans were considerably shortened, and much of the oral care provided was palliative.

An HIV patient seen today may come from a variety of racial/ethnic backgrounds, be of any age, gender, or sexual preference and may not know that he or she has been infected with HIV.<sup>24</sup> Since oral lesions may be the first manifestations of HIV infection,<sup>25</sup> and since typical dental patients seek out dental care when they are feeling healthy,<sup>26,27</sup> the dentist may be the first health care practitioner who becomes aware of the possibility of a patient being infected with this life-threatening virus.

Intervention opportunities for talking with patients can occur when the oral health clinician discovers a possible manifestation of HIV.<sup>28</sup> After detecting an intraoral lesion, the dentist will need specific past medical history, behavioral activities, and additional symptomatology from the patient to add to the clinical appearance of the lesion in order to weigh the risks of possible HIV infection. There may be other signs including tattooing or piercing of various body parts indicating that patients are involved in unsafe behaviors. Such indicators warrant discussion and risk assessment by the dentist. Off-the-cuff conversations or other

comments by the patient about health or relationship issues may also trigger concerns about the patient's HIV risk.

### Structuring the Risk Assessment

In adults, HIV is transmitted in three ways: blood or blood products; shared needles, typically with other drug users; and unprotected sexual activities with an infected partner.<sup>29</sup> As has been true of the physician,<sup>30</sup> the dentist is often uncomfortable obtaining the necessary information since two of the risk factors -- use of needles and unprotected sex -- relate to topics that are taboo and not easily discussed in U.S. society. There is however a method that can be used by the dentist to systematically elicit information from the patient relative to his or her risk of HIV while encouraging the patient to feel comfortable in divulging the information and the dentist to engage in nonjudgmental inquiry into the patient's risk-taking behaviors.

The presence of a suspicious intraoral lesion or unsafe behavior should prompt a discussion that brings to the patient's conscious level his or her personal risk for HIV/AIDS. How to achieve such an understanding without precipitating panic is one of the constructs of the structured risk assessment protocol. With recent advances in HIV treatment, being tested for the virus and, if positive, receiving appropriate care as early as possible have become increasingly important. Conveying this message to the patient is another of dentistry's risk assessment goals.

### Risk Assessment Algorithm

To help structure the patient interview, the authors use an HIV risk assessment algorithm developed by Richard Call, DMD, at the Mountain-Plains Regional AIDS Education and Training Center at the University of Colorado. This algorithm addresses the three basic routes of HIV transmission: blood, shared needle use, and sex.<sup>31</sup> The branching algorithm, updated as more has been learned about HIV and the behavior that places a person

at risk for acquiring the infection, provides structure to the interview (**FIGURE 1**).

Whenever a risk behavior is identified, more complete questions are asked about that behavior before going on to the next risk area. This approach helps the health care professional structure an interview to obtain as much information as possible to assess accurately the patient's overall HIV exposure. In the training program provided as part of the Pacific AIDS Education and Training Center program for dental providers, the authors subscribe to this model by having dentist trainees role-play the interview with a standardized patient.

### Assessing a Patient's Risk for HIV

To demonstrate the algorithm, an interview model will be described that builds on the finding of a suspicious intraoral lesion. In this case, the practitioner starts by showing the patient the area that is of concern, posing the typical questions asked whenever a lesion is discovered such as: Is it painful? Is the patient aware of it? How long has it been there? Before actually beginning the questions from the algorithm, the dentist is encouraged to explain to the patient the reason for the questioning, i.e., an attempt to determine the causative factor for the oral finding, and why the dentist will be asking personal and sensitive questions. As with other diagnoses, the patient should be provided with a range of possibilities for the oral lesion, including in the differential benign explanations such as simple trauma (biting the side of the mouth, etc.), to other more systemic underlying causes. As appropriate, these could include conditions such as a drug reaction, diabetes, and sexually transmitted diseases, including HIV among other possible causes.

The patient should understand that at no time is the dentist diagnosing HIV, for that would be beyond the scope of the practice of dentistry. Rather, the goal is to collect information that may be helpful in considering the patient's relative risk for HIV. In order to facilitate open communication very early on, the dentist

must reassure the patient that what is discussed will be completely confidential and that this information will help the dentist understand the oral problem and thus be able to provide better care. Reassuring the patient of the intention to be his or her dentist regardless of the outcome of the interview is also important because discrimination against HIV-positive individuals by dental practitioners is still a concern to many. Throughout the risk assessment, the dentist should use nonjudgmental language and assiduously avoid any appearance of labeling or judging the patient.

### Blood Risks

In questioning the patient about HIV risk, it is usually helpful to begin with the least sensitive issues, usually blood-related risks, and move to those in more sensitive areas, such as needle sharing and sexual risks. As questions are asked about blood transfusions, needle use, and sexual activity, the patient's behavior as well as the behavior of past and present sexual partners<sup>32</sup> is explored. Since HIV is spread by sexual contact, sexual partners' risk behaviors are also relevant. If risky behavior is discovered, follow-up questions are asked.

Blood transfusions in the early 1980s prior to 1985 when the blood supply was routinely checked in the United States for the HIV virus would increase the risk of having acquired the infection.<sup>33</sup> Asking where a transfusion occurred is necessary as other countries did not check their blood supplies until some years later. Similar questions should be asked relative to any sexual partners of the patient. Additionally, individuals sometimes forget that major surgeries or accidents require blood transfusions. Therefore, follow-up questions about the patient and the patient's sexual partners are asked concerning whether the individuals have had surgery or been in a major accident.

### Shared Needles Risk

The questions about needles are asked in such a way as to include all possible uses of shared needles, not just those dealing with street drugs. Sharing of needles to take medications including vitamins occurs in some cultural and/or socioeconomic strata. Cleaning needles with bleach has been shown to have some effect in disinfecting needles; however, cleaning needles is not as safe as using sterile needles obtained through a needle exchange program.<sup>34</sup> Again, follow-up questions regarding the sexual partners' sharing of needles is pursued. Additional questions relating to needle use to take medications or vitamins or for body piercing or tattooing may further trigger memories of risky behaviors. Body piercing or tattooing are included in the algorithm due to the possibility of shared needles and improper cleaning between uses.<sup>35,36</sup> A history of alcohol and other drug use is also of concern since studies show that individuals participating in sex under the influence are more likely to engage in risky behaviors.<sup>37,38</sup>

### Sexual Risks

The final series of questions deals with the sexual behavior itself. Eliciting information on whether the patient is or has been sexually active and consistently applies safe sex behaviors is relevant. To determine sexual orientation without labeling, the question, "Do you have sex with men, women or both?" is asked. Questions regarding the number of sexual partners and type of sexual activities are also raised. These questions are important because the number of different sexual partners<sup>39</sup> and the type of sexual activity relate to relative risk of HIV infection with some sexual activities having a higher risk of potential infectivity than others (anal has a greater risk than vaginal, which has a greater risk than oral).<sup>40</sup> The inconsistent use of condoms, particularly with higher risk sexual activity, puts individuals at greater possibility of acquiring the disease.<sup>41</sup> Condoms should be used with

every sexual activity.<sup>42</sup> Patients should be asked if HIV testing has been performed in the past as this is often an action taken by patients who realize that they have engaged in unsafe behavior.<sup>43</sup> Determining that the patient has contracted a sexually transmitted disease other than HIV indicates a breakdown in following safe sex practices.

Pursuing a detailed HIV risk assessment not only provides information to the practitioner on the patient's relative HIV risk, it also helps patients understand how they may have put themselves at risk. Even if early in the interview the dentist determines that a patient is in danger of having acquired HIV, the dentist should continue with the entire assessment. Additional risk information is often revealed and, perhaps more importantly, the patient may learn more about his or her own behavior relative to HIV risk and be motivated to be tested.

The dentist should also be knowledgeable regarding types of HIV testing as well as testing sites so that he or she can refer the patient appropriately.<sup>44</sup> Referral to the patient's physician or to confidential or anonymous testing sites will ensure that state of California mandated counseling does occur as part of the HIV testing process. Generally keeping up with the latest information relative to the success of new medications,<sup>45</sup> the populations where the epidemic is advancing the most,<sup>46-48</sup> and issues of transmission risk during pregnancy<sup>45</sup> will help the dentist provide the patient with facts rather than myths.

### Acceptance of the Risk Assessment Model by Dentists

This risk assessment approach has been used as one segment of the authors' multiple-module HIV Training Program for Dentists for a number of years. Although dentist trainees initially have some reluctance to pursue these questions, role-play simulations using a standardized patient portraying a real patient story quickly affirm the value to the dentist

interviewer of this model of inquiry. Thirty-eight dentists trainees were asked to rate the usefulness of the knowledge or skills received in this segment of the training program. A five-point Likert scale was used with a 1 rating being "Not Useful" and 5 rating being considered "Very Useful." The Risk Assessment Workshop received an average rating of 4.5. In response to the open-ended query about the most positive experience each dentist trainee had during the entire training program, enthusiastic feedback about the Risk Assessment Workshop was received: "very useful information on a very delicate subject;" "could have used more of this," and "the risk assessment and standardized patient segments provided the most-needed areas of training."

### The Dentist's Role in Primary Care

Today's dentists routinely perform medical history reviews and physical evaluations. In addition to conveying the traditional messages about oral problems induced by the presence of plaque, they counsel their patients about the use of tobacco<sup>49,50</sup> or alcohol,<sup>49</sup> good nutrition principles,<sup>27,51</sup> the hazards of self-induced vomiting,<sup>52</sup> body piercing,<sup>53</sup> and the importance of using protective gear such as mouthguards, helmets, and seat belts during activities at high risk for injury to the orofacial complex.<sup>18</sup> Dentists often diagnose and manage intraoral side effects of medications taken for systemic diseases<sup>54</sup> or facilitate referrals of patients to physicians for diagnosis<sup>7</sup> or better control of suspected medical problems. They counsel pregnant women, or women planning on becoming pregnant, about the need for specific minerals in the diet to aid in the development of sound teeth in utero,<sup>27</sup> the capability of vitamins such as folic acid to reduce the incidence of cleft lip/cleft palate and neural tube defects in the embryo,<sup>55</sup> and the impact of the mother's periodontal disease on the birth weight of the baby.<sup>56</sup> The elderly patient is frequently advised to increase his or

her intake of calcium to 1,200 mg per day to maintain bone mass, including alveolar bone.<sup>27</sup> Dentists routinely advise patients of the side effects to medications they prescribe for managing oral disease such as the disruption of the normal flora of the gut and/or the vagina during the use of antibiotics,<sup>57</sup> the thinning of the blood during the use of aspirin-based products,<sup>54</sup> or the constipation that results from codeine-containing medications.<sup>54</sup>

### Dentistry and HIV Prevention

Although a sensitive area to broach, the prevention and control of sexually transmitted disease is a public health opportunity for all health care practitioners. Two of the five STD prevention and control concepts published in the CDC's 1998 Guidelines for Treatment of Sexually Transmitted Diseases are particularly opportune for incorporation into the dental practice: Detection of asymptotically infected people and symptomatic people unlikely to seek diagnostic and treatment services and education of those at risk in ways to decrease the possibility of becoming infected.<sup>58</sup> The dentist is in a unique position to identify and counsel patients who are unaware that they may have been infected by the HIV virus, for dentists see 62 percent of the population annually and 75 percent of individuals age 5 to 17.<sup>59</sup> Since most American males and females have had intercourse by the time they reach 16 to 18 years of age and the majority of young adults age 18 to 24 have multiple serial sex partners,<sup>60</sup> the dentist may in fact be the only health care professional regularly interacting with this younger age group who are at increasing risk of acquiring HIV.<sup>61</sup> In addition, the dentist spends more time with each patient than the median 12 minutes spent by the physician<sup>62</sup> thereby further allowing an opportunity to take note of and educate patients who are at risk for HIV.

### Conclusion

The faculty of the Pacific AIDS Education and Training Center encourage dentists to talk with their patients about HIV/AIDS and about possible risks for HIV transmission whenever patients present with an oral sign or symptom suggestive of immunologic deficiency or there are other indications of involvement in hazardous behavior. The historic success the authors have achieved in conveying information about the prevention of disease and the importance of oral health should bolster dentists' resolve to expand their preventive discussions with their patients to include preventing disease and promoting the health of the entire person. HIV infection provides dentists with the opportunity to do just that.

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# What the Dentist Should Know About a Patient with HIV/AIDS

ANN M. LYLES, DDS

**ABSTRACT** Chances are good that oral health care providers will treat someone with diagnosed or undiagnosed HIV during their careers. The Centers for Disease Control and Prevention estimate that 650,000 to 900,000 U.S. residents are living with HIV infection, more than 200,000 of whom are unaware of their infection.<sup>1,2</sup> As with any medical condition, it is possible for a dentist to do great harm by ignoring systemic manifestations of HIV. On the other hand, dentists who are ignorant of modern HIV disease management often request unnecessary medical consultations resulting in dental treatment delays. Since 1996, the growing use of highly active anti-retroviral therapy and ultrasensitive viral load testing has changed the picture of the dental patient with HIV. The goal of this article is to update and summarize information the oral health care provider needs to safely treat a person with HIV/AIDS. It is not intended to replace previous comprehensive publications on HIV and dentistry,<sup>3-5</sup> as they are still excellent resources for information. Here, simple instructions for physical evaluation of a patient with HIV/AIDS will be presented and steps for determining safe procedures explained.

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**M**any recent articles on HIV and dentistry have focused on infection control and prevention of HIV transmission from the patient to the practitioner.<sup>6-13</sup> But, for health care providers, the primary objective is to do no harm, so it is important to remember that the person with HIV needs protection from the

practitioner as well. One golden rule can be applied in every situation: Treat a person with HIV/AIDS as one would treat anyone else. In other words, HIV itself is not a valid reason to deny, delay, or alter treatment. However, medications and manifestations of HIV may affect dental treatment, and these factors should be considered carefully.

## Why dentists need to understand treatment of patients with HIV

At a time when humans are living longer than ever and people with multiple systemic diseases are common in dental practices, it would be inconsistent to refuse oral health care to those with well-controlled HIV disease. When Congress considered the Americans with Disabilities Act, it noted, "Some 43,000,000 Americans have one or more physical or mental disabilities, and this number is increasing as the population as a whole is growing older."<sup>14</sup> It also added, "The nation's proper goals regarding individuals with disabilities are to assure equality of opportunity, full participation, independent living, and economic self-sufficiency for such individuals."

In 1995, the American Dental Association took a position on treatment of people with HIV: "The American Dental Association believes that HIV-infected individuals should be treated with compassion and dignity."<sup>15</sup>

In 1998, that position was expanded in a brief to the Supreme Court supporting Sidney Abbott, a dental patient with HIV who was denied treatment solely because of her HIV status: "Patients with HIV infection may be safely treated in private dental offices when appropriate infection control procedures are employed. In addition, a decision not to provide treatment to an individual based solely on their AIDS or HIV seropositive status is unethical."<sup>16</sup>

If someone with HIV/AIDS requests dental care, it is unfair, unethical, and possibly illegal to deny treatment based solely on the person's HIV status. In *Bragdon v. Abbott*,<sup>17</sup> the Supreme Court decided that HIV may be considered a disability, depending on the situation. The Court made it clear that it was reasonable to expect dentists to treat people with HIV. It is imperative, then, that oral health care providers understand how to evaluate patients with HIV so care can be provided safely.

A more thorough discussion on dentistry, HIV, and the law can be found in

the article, "The Dentist, HIV and the Law: Duty to Treat, Need to Understand" by David Schulman.<sup>18</sup>

## The Health History Review

Medical evaluation of a patient with HIV/AIDS will help the dentist anticipate and prevent complications associated with dental care. As with all patients, a thorough medical history should be obtained, including a complete list of medications. Past and present medical conditions should be discussed and appropriate treatment modifications determined. The name and phone number of the patient's physician should be noted in the chart so the dentist may contact the physician if additional information is needed before providing dental treatment.

Some dentists indicate a reluctance to discuss HIV infection with their patients because of the sensitive nature of the disease. Patients may be just as uncomfortable discussing their HIV status because of personal or vicarious dental experiences. People with HIV/AIDS often express suspicion and fear that dentists will be judgmental and may even refuse treatment based on HIV status.<sup>19</sup> It is possible that the person with HIV/AIDS has already felt unwelcome in several dental offices. Despite the fact that it may be a violation of the Americans With Disabilities Act to refuse treatment based solely on HIV status, patients still worry that HIV will interfere with their ability to obtain dental care. If the dentist provides a good rationale for asking detailed questions, patients will be more comfortable providing personal information. For example, a dentist might explain: "I need to ask you some more questions about your medical history. Some of the questions are very personal, but I hope they don't make you feel uncomfortable. It's important for me to learn more about your health so I don't do anything that might hurt you."

Once it has been established that the primary concern is the well-being of the patient and it is clear that the

dentist intends to provide care, an honest discussion is more likely to occur. The exploration of each medical condition should be documented by noting the date of onset, the current status or level of control, and any treatment that has been rendered for that condition.

Oral health care providers should know how to probe for answers to all positive responses on medical history questionnaires. HIV/AIDS is no exception, and the same questions can be applied to the evaluation of a person who is HIV-positive as to those with other medical problems (**FIGURE 1**).

## What Was the Date of Onset or Diagnosis?

The dentist should ask how long the patient has been HIV-positive and should find out if and when an AIDS diagnosis was made. In addition to the date of the first positive HIV test, it is useful to determine when the patient became infected with HIV. This may provide a better impression of disease progression. Sometimes, this conversation will lead to a discussion of etiology (route of HIV transmission), but if not, the etiology can be discussed at the end of the conversation when the patient becomes more comfortable discussing personal information.

## What Is the Current Status or Level of Disease Control?

To determine the current status or level of HIV disease control, it may be necessary to ask several questions. Is the patient seeing a physician on a regular basis? If not, the dentist should find out why. What was the most recent T-cell or absolute CD4 count, and how does this compare with results from tests over the past year? Has the CD4 count remained stable? Is the viral load undetectable? Changes in CD4 count and viral load may indicate that the level of disease control is changing. Is the patient taking all medications as directed by the physician? Sometimes, the patient is afraid to admit failures to adhere to the treatment regimen to the physician but is willing

FIGURE 1.

**DETERMINE THE FOLLOWING FOR ANY "YES" ANSWER ON THE MEDICAL HISTORY QUESTIONNAIRE:**

- What was the date of onset or diagnosis?
- What is the current status or level of disease control?
- What treatment has been rendered for this condition, including medications?

to reveal these problems to a dentist. Adherence difficulties should be reported to the physician because disease control may suffer. These simple questions can help the practitioner determine whether the HIV disease is well-controlled.

*What Treatment Has Been Rendered for This Condition, Including Medications?*

The patient's medications should be documented, as with any patient, and potential drug interactions should be identified. Note that medical treatment for HIV may include more than traditional drugs. For example, psychological and dietary counseling can be important components of disease management. Herbal medications may be used and alternative treatment strategies such as massage therapy, meditation, or prayer may be part of the plan to control HIV infection.

*Do You Know How You Got HIV?*

As part of the medical history review, the dentist may ask how the patient became infected. However, the patient needs to know that this information request is not based in idle curiosity but is of importance because routes of HIV transmission may have implications for other health conditions. Oral health care providers need a complete medical history before deciding whether treatment modifications and referrals are necessary, such as if there is a history of a blood transfusion or IV drug use. A blood

transfusion could indicate the presence of a bleeding disorder that would affect the delivery of dental care. Treatment of any patient who is still injecting drugs can be deadly, so if this is the case, treatment should be delayed until drug use has stopped and the medical condition has stabilized. For example, several carpules of local anesthetic may be safe in the average patient, but may result in drug overdose if a patient has recently used crack cocaine. IV drug use also puts the patient at high risk for development of bacterial endocarditis, so additional information from the patient's physician might be necessary before initiating care. If HIV was contracted through unprotected sex, the dentist should make sure the patient has been counseled in ways to prevent further transmission of sexually transmitted diseases, including those that appear in the mouth. As primary health care providers, dentists have an obligation to refer patients for counseling if the mode of transmission indicates that the patient is engaging in high-risk behavior. Finally, a dentist may need to know how the patient got HIV in order to prioritize a differential diagnosis for an oral lesion because some lesions are closely associated with specific routes of HIV transmission.

During the course of a medical history review, special attention should be given to the minimum requirements for safe dental treatment:

- Ability to clot;
- Ability to recover from bacteremia;
- Ability to endure treatment in your dental care setting; and
- Absence of potential drug interactions.

**Ability to Clot**

Bleeding tendency is particularly important to discuss with patients who have HIV/AIDS for two reasons:

- If the patient acquired HIV through a blood transfusion, the dentist should find out if the transfusion was necessary because of a bleeding disorder.
- Hematologic abnormalities are

relatively common with HIV infection, either because of the HIV disease process or as consequences of drug therapy.<sup>20</sup>

Failure to detect a bleeding disorder before dental treatment could result in postoperative complications. Even "routine" care such as quadrant scaling can cause 5-10 ml of bleeding in a patient with a normal bleeding time. In a patient with a bleeding disorder, however, scaling or other invasive dental treatment could result in prolonged bleeding and possibly delayed healing and infection, so the health history questionnaire should ask about bruising or bleeding tendency. It should also ask about risk factors for prolonged bleeding, including anemia, liver disease, renal failure, gastrointestinal disease (with subsequent vitamin K deficiency), cancer and alcoholism. Since drug therapy is the most common cause of a prolonged bleeding time,<sup>21</sup> it is safest to determine all medications the patient is currently taking as well as any taken within the last six months. Prolonged bleeding can result after the ingestion of aspirin, aspirin-containing compounds, and anti-inflammatory drugs as well as anticoagulants.<sup>22</sup> Usually, antibiotics and NSAIDs do not cause a significant change in coagulation and will not interfere with routine dental treatment. However, if the patient is taking anticoagulants such as heparin or coumadin, a medical consultation should be obtained before attempting any treatment that may cause bleeding, including periodontal probing. Once the bleeding time is known, appropriate precautions can be taken to prevent complications.

Some commonly prescribed anti-retroviral medications (such as zidovudine/AZT) are known to cause anemia, but AZT-induced anemia is less common with the doses currently prescribed (500 to 600 mg/day)<sup>23</sup> and is easily managed with dose reduction or use of hematopoietic growth factors.<sup>24</sup>

Occasionally, a patient provides subjective evaluations of bleeding or

bruising tendency, rather than true medical diagnoses. It may be necessary to ask additional questions to confirm or rule out the possibility of a bleeding problem. For example, a patient may tell say, "Well, sometimes I feel a little tired, so I think I might be anemic," or, "I fell down one time and I had a big bruise on my leg for almost a week." Obviously, there is much greater concern if a patient reports three trips to the emergency room for nosebleeds that could not be controlled at home.

To assess the possibility of a bleeding tendency, the dentist may ask these additional questions:

- Do you have a bleeding disorder?
- Have you ever experienced any bleeding problems?
- Specifically, do you have trouble with excessive bleeding or bruising after an injury?
- Have you ever gone to see a doctor about bleeding that wouldn't stop?
- Has your doctor ever recommended that you take iron supplements?
- Have your blood tests ever indicated that you may have trouble clotting (low platelets)?

If the patient gives any indication of a bleeding abnormality, the physician should be asked to help determine the risk of prolonged bleeding after dental treatment. Medical monitoring of people with HIV/AIDS does not include routine testing of bleeding times, but involves complete blood counts and viral load tests. If the physician detects risk factors for prolonged bleeding such as a low platelet count or low hemoglobin, a coagulation panel may be ordered. The 1995 Journal of the American Dental Association supplement, "Dental Care for the HIV-Infected Patient," explained that dental treatment can be safely provided when platelets are greater than 60,000/mm<sup>3</sup>, hemoglobin greater than 7g/dL, and bleeding time is within two times normal.<sup>25</sup> Many dentists are uncomfortable providing dental care when the bleeding time is more than two times normal, but some feel it is safe to do limited procedures (such as local anesthetic

infiltrations and intracoronary restorations) when the bleeding time is within 2.5 times normal. Based on the coagulation panel results, the practitioner should decide whether the bleeding condition can be managed in the dental office or refer the patient to a practitioner who can safely provide care.

### Ability to Recover From Bacteremia

Occasionally, a dentist will ask if HIV is an indication for antibiotic prophylaxis before dental treatment. Perhaps the weakened immune system makes dentists concerned that they will put patients at risk for bacterial infection. For the HIV-infected patient, there are no data supporting the need for routine antibiotic coverage to prevent bacteremia or septicemia arising from dental procedures.<sup>26-28</sup>

For bacterial endocarditis prophylaxis, AHA guidelines be followed the same way for patients with or without HIV.

Neutropenia is a special case requiring consideration of antibiotic prophylaxis. In 1999, the Dental Alliance for AIDS/HIV Care in cooperation with the American Dental Association updated their recommendations for prophylactic use of antibiotics in neutropenic patients with HIV (TABLE 1).<sup>29</sup> The Dental Alliance suggests that topical antimicrobials (i.e., chlorhexidine) are indicated for all dental procedures in cases of severe neutropenia (absolute counts of less than 500/mm<sup>3</sup>), and prophylactic antibiotics should be used after a discussion with his or her physician. For moderate neutropenia (absolute counts between 500 and 1000/mm<sup>3</sup>) the Dental Alliance warns that most dental procedures will not require antibiotic prophylaxis, but more-invasive procedures may require systemic antibiotics in addition to topical antimicrobials. Patients with HIV disease and moderate neutropenia do not appear to have an increased risk for bacterial infection,<sup>30</sup> but the final decision requires the judgment of the oral health care practitioner.

Though modern drugs and lower

doses of AZT have reduced hematologic abnormalities,<sup>31-33</sup> drug-induced neutropenia may still occur in some HIV-infected individuals. This is especially true in more-advanced stages of HIV disease because drugs used to treat manifestations of HIV (gancyclovir, foscarnet, sulfa derivatives, pentamidine) can cause bone marrow suppression and neutropenia.<sup>34-37</sup> Neutropenia is more common in patients with late-stage disease and typically occurs when CD4+ cell counts are very low.<sup>38</sup> Neutrophils play an important role in the defense against bacterial infections, and immunocompromised patients are at greater risk for severe infections when the absolute neutrophil count falls below 500 cells/mm<sup>3</sup>.<sup>39,40</sup> so attempts should be made to reduce the chances of bacteremia. During dental treatment, it is possible for oral bacteria to enter the patient's bloodstream, resulting in a transient bacteremia, but there is no indication that this bacteremia puts the patient at risk for significant infections. Pretreatment chlorhexidine rinses can reduce the concentration of oral bacteria during dental treatment without posing a significant health risk to the patient.

Debate about systemic antibiotics continues because there is currently no published study supporting the idea that antibiotic prophylaxis will benefit neutropenic immunocompromised dental patients. The issue is complicated by the fact that bacteremias may occur during many routine activities such as brushing and chewing. So, transient bacteremia is not a unique consequence of dental treatment. Overprescribing of antibiotics can lead to selection of resistant bacteria, so dentists and physicians must consider this issue carefully. Perhaps the greatest concern about providing antibiotics that may be medically unnecessary is the risk of anaphylactic reaction. Immunocompromised patients have a greater incidence of drug allergy<sup>41</sup> and there is no proof that the benefit of antibiotic prophylaxis outweighs the risk of allergic reaction for this group. Some even

argue that neutropenic patients should not receive routine dental care at all, but should receive only urgent care until neutropenia is resolved..

At the very least, a pretreatment chlorhexidine rinse is recommended to reduce the chance of introducing oral bacteria into the bloodstream during treatment. Localized areas such as injection sites and periodontal pockets may be swabbed or irrigated with Betadine/povidone iodine before treatment to further reduce the chance of bacteremia. The decision about prescribing antibiotics prior to dental treatment should be made on an individual basis after discussing the patient's status with the patient's physician.

To assess a patient's ability to recover from a bacteremia, the dentist should ask the patient about the most recent CD4 count. Most immunocompromised patients follow this number closely. A CD4 count above 100 cells/mm<sup>3</sup> indicates that the immune system has some ability to fight infection and suggests that the neutrophil count is probably within normal range. The patient will probably recover from a bacteremia with no difficulty.

If the CD4 count is below 100, the patient's neutrophil count should be obtained before initiating invasive dental treatment, including periodontal probing. The patient's physician should be contacted to request the neutrophil count and to discuss consideration of antibiotic use prior to dental treatment.

### Ability to Cooperate in a Dental Care Setting

Ironically, anti-retroviral drug therapy can make it difficult to cooperate with dental treatment. Common side effects of anti-retroviral medications include fatigue, nausea, and headaches. People suffering from these adverse effects may find it difficult to keep scheduled appointments or to endure lengthy dental procedures. Patients will have to explain how the medications make them feel so the dental staff can schedule accordingly.

The oral health care team should be

**TABLE 1. SUMMARY OF ANTIMICROBIAL PROPHYLAXIS CONSIDERATIONS**

(As suggested by the Dental Alliance for HIV/AIDS Care)

- Patients with CD4+ cell counts below 100 cells/mm<sup>3</sup> and patients on long-term anti-retroviral drug therapy should be evaluated for neutropenia.
- Patients with absolute neutrophil counts below 500 cells/mm<sup>3</sup> should receive antibiotic prophylaxis before dental therapy.
- The dentist is advised to consult the physician for patients with indwelling catheters and neutrophil counts between 500 and 1000 cells/mm<sup>3</sup>.
- Bactericidal antibiotics (penicillins and cephalosporins) are the most appropriate antibiotics for prophylactic treatment.

sensitive to the fact that patients may not want to take their medications in the dental office. The bottles of pills may be large and cumbersome, side effects may occur soon after dosing, and people may wish to take their medications privately so their HIV status does not become known to others.

Dental personnel must understand that highly active anti-retroviral therapy is only effective when adherence with the treatment regimen is very high; and, as health care providers, they should encourage the greatest possible adherence. Appointments that interfere with the dosing schedule should be avoided. Some medications need to be taken with food, and others should be taken two hours before or after a meal. The patient should suggest the best time for a dental appointment so the routine is not disrupted.

Altered mental status can affect any patient's ability to receive dental care. Since advanced HIV disease can be associated with changes in mental status, the oral health care provider should determine whether the patient can comply with instructions before, during, and after dental procedures. Psychiatric conditions that may result from damage to the central nervous system include depression, dementia, anxiety/panic disorder, delirium, mania, and psychosis. The practitioner

should manage or refer dental patients with any of these conditions based on professional judgment, regardless of the patient's HIV status.

At one time, AIDS dementia was a common final state in the progression of HIV disease. Due to improved medical management, AIDS dementia is not as prevalent as previously and it no longer means that death is imminent. Many who suffered psychological damage as a result of HIV infection are now stabilized with effective drug therapies. The neurological damage remains, but the medical prognosis may be good if drug adherence is high. Whether or not a patient has HIV/AIDS, psychiatric conditions can interfere with the ability to give informed consent and cooperate with treatment. The practitioner should decide how to manage patients with psychiatric conditions on an individual basis.

### Absence of Potential Drug Interactions

None of the drugs currently used in HAART are known to interact with local anesthetics or non-narcotic analgesics. There are, however, relative contraindications to the use of some antibiotics and antifungal medications for patients taking anti-retroviral drugs. To prevent serious complications, the oral health care provider should be

**Table 2. Known Anti-Retroviral Drug Interactions in General Dentistry (as of October 2000)**

*Note: This table contains information about drugs used only in general dentistry. It does not contain all known interactions for general anesthetics used in oral surgery. The information here may serve as a guideline, but it only represents the known adverse drug reactions at this time. New drug interactions are being discovered constantly, so dentists are encouraged to check the latest information before prescribing drugs. For more complete information about all drug interactions and contraindications including general anesthetics, please consult information provided by the drug manufacturer or a recently published drug reference. Current drug information from the American Medical Association can be found by visiting <http://www.ama-assn.org/special/hiv/index.htm>.*

Nucleoside reverse transcriptase inhibitors			
Brand Name	Generic	Trade Name	Contraindications
AZT	Zidovudine	Retrovir	Relative -- Fluconazole increases AZT serum levels.
ddI	Didanosine	Videx	Relative -- Metronidazole and nitrous oxide may increase risk of peripheral neuropathy. Tetracycline may increase risk of pancreatitis and absorption may be decreased. Separate dosing of other drugs by 2 hours, esp. ketoconazole, dapsone, tetracyclines, quinolones.
ddC	Zalcitabine	HIVID	Relative -- Metronidazole may increase risk of peripheral neuropathy.
d4T	Stavudine	Zerit	Relative -- Use caution with other drugs that cause peripheral neuropathy, such as metronidazole.
3TC	Lamivudine	Epivir	None reported at this time.
AZT-3TC	Zid-Lam	Combivir	None reported at this time.
ABC	Abacavir	Ziagen	None reported at this time.
Non-nucleoside reverse transcriptase inhibitors			
Brand Name	Generic	Trade Name	Contraindications
NVP	Nevirapine	Viramune	Relative -- Antagonizes ketoconazole.
DLV	Delviradine	Rescriptor	Avoid co-administration with phenobarbital, ketoconazole, terfenadine, astemizole, midazolam. Relative -- May cause increase in plasma concentrations of clarithromycin, and sedative hypnotics (alprazolam, triazolam).
EFV	Efavirenz	Sustiva	Relative -- May cause increase in plasma concentrations of midazolam, triazolam. Serum levels of EFV are increased by fluconazole.
Nucleotide reverse transcriptase inhibitors			
Brand Name	Generic	Trade Name	Contraindications
ADF	Adefovir	Preveon	None reported at this time.
Protease Inhibitors			
Brand Name	Generic	Trade Name	Contraindications
SQVHGC	Saquinavir	Invirase	Relative -- Increased plasma levels of terfenadine, astemizole, clindamycin, itraconazole, triazolam. Saquinavir levels reduced by dexamethasone. Antagonized by dexamethasone, phenobarbital. Unpredictable absorption of ketoconazole.
SQVSGC/FTV	Saquinavir	Fortovase	Relative -- Increased plasma levels of terfenadine, astemizole, clindamycin, itraconazole, triazolam. Saquinavir levels reduced by dexamethasone. Antagonized by dexamethasone, phenobarbital.
RTV	Ritonavir	Norvir	Contraindicated with sedative hypnotics, meperidine, piroxicam, propoxyphene, astemizole and terfenadine. Relative -- Increased plasma levels of clarithromycin, fluconazole. Decreased plasma levels with dexamethasone, phenobarbital. May change levels of NSAIDs, antihistamines, antifungals.
IDV	Indinavir	Crixivan	Contraindicated with terfenadine, astemizole, triazolam, midazolam.
NLF	Nelfinavir	Viracept	Contraindicated with astemizole, triazolam or midazolam.
AMP	Amprenavir	Agenerase	Relative -- Increased plasma levels of terfenadine, astemizole, midazolam, triazolam, erythromycin, itraconazole.

familiar with possible interactions of any medications used or prescribed in the dental office (TABLE 2).

### *What Is Not Appropriate to Ask a Dental Patient*

A written health history questionnaire should not ask intrusive questions unless they are pertinent to patient care. For example, asking a dental patient to check a box indicating “sexual preference” would be inappropriate because this does not reveal information about the patient’s past or present medical conditions. Asking if the patient has ever been tested for HIV also tells a dentist nothing about the patient’s present medical status. In the context of a risk assessment, however, these questions may be quite appropriate, but only after the dentist has explained the reasoning and the patient has agreed to discuss risk factors. The results of this risk assessment should be kept confidential and should be used as a basis for medical referral, if indicated. Private information unrelated to delivery of care should be kept confidential and should not be used as a justification for refusal to treat.

Avoid asking questions in such a way as to label the patient such as, “Are you an I.V. drug user?” or “Are you gay?” because these will not provide specific information about behavior patterns and may offend patients. Questions about the way the patient got HIV will provide more useful information (i.e., from a contaminated needle, through a blood transfusion, or from a sexual partner).

### *When to Get a Medical Consultation*

If a patient cannot provide all the necessary information, the dentist will need to contact the patient’s physician by phone or using a written consultation request (FIGURE 2). It is only appropriate to request information relevant to dental treatment. Asking questions unrelated to dental care would be an invasion of the patient’s privacy.

Warning signs that more information may be needed:

- History of anemia, bruising or bleeding tendency or risk factors for bleeding problems such as long-term AZT therapy;
- Current CD4 count of less than 100;
- Recent complications of AIDS such as pneumonia or cytomegalovirus infection;
- Incomplete list of medications; and
- Reporting of lab results that seem improbable.

It may be possible to request information by calling the patient’s physician, but due to the especially sensitive nature of HIV disease, some physicians are not comfortable providing details over the phone. It is considerate to fax a written request to the physician, or at least fax a signed consent (FIGURE 3) to release medical information over the phone.

The patient should understand why personal information has been requested from the physician. Ideally, a consent form would indicate that the dentist is concerned about the patient’s feelings and recognizes the sensitivity of this information. A good consent form can also save time. If the form clearly indicates that the patient has given permission to release information related to HIV status, the physician will not hesitate before sending a response.

## **Treatment Modifications**

### *Laboratory Markers to Consider*

It is important for dental care providers to understand a few basic laboratory markers for the status or progression of HIV disease. The tests that indicate bleeding tendency and ability to combat infection are the most relevant to dental care. The results of these tests will help the practitioner determine whether treatment modifications are necessary.

Typically, every three to four months, a person with HIV/AIDS is evaluated for disease status, effectiveness of treatment, and adverse drug reactions. Periodic laboratory tests include a complete

blood count with differential and a viral RNA polymerase chain reaction or “viral load” test. A complete blood count with differential includes the absolute CD4 count and CD4 percentage. These are good indicators of immune function and stage of disease progression. CD4+ cell counts indicate the ability of the immune system to fight disease, and viral load tests indicate the activity of the virus. The two values together give a clearer picture of the status of HIV disease progression. Since the goal of HAART is to reduce the concentration of virus in the blood, viral load tests are used to evaluate the effectiveness of HAART.

## **CD4**

CD4 count (CD4+ cells per cubic mm or microliter of blood) gives a general idea of the health of the HIV-infected patient (TABLE 3). The lower the CD4 count, the more advanced the patient’s disease. A normal CD4 count in adult patients is 500-1,500. Effective anti-retroviral drugs usually increase the CD4 count, or at the very least, prevent further decreases in CD4 count.

Although a low CD4 count is a reflection of advanced disease, it should be used only as one indicator of a patient’s general health. A low CD4 count is not necessarily the same as a poor prognosis, and it is not a valid reason to withhold or delay dental therapy. It simply indicates that more information may be necessary before care can safely be provided.

## **Viral Load**

Viral load quantifies the amount of HIV in the blood. Specifically, it measures the number of copies of HIV RNA present per milliliter of plasma. Currently, the most sensitive test can measure levels as low as 50 copies/ml. Viral load levels lower than 50 copies/ml are reported as “undetectable.”

Within a couple of weeks of initial infection, viral load becomes undetectable. Then, it usually peaks within one to two months of initial infection. This peak is

**TABLE 3. CD4 COUNTS AND THEIR INDICATIONS OF GENERAL HEALTH**

CD4 Count	Classification
>500	Generally healthy, no unusual conditions likely
200-500	Mild immune suppression, moderately increased risk for some opportunistic infections
100-200	Moderate immune suppression, greatly increased risk for opportunistic infections
<100	Severe immune suppression, greatest risk for opportunistic infections. Medical consult is probably necessary.

often associated with symptoms of a flu-like syndrome (fever, headache, malaise) known as Acute Retroviral Syndrome. The viral load then declines, and plateaus at a “set point” after three to six months. The magnitude of this set point correlates with how quickly the patient’s HIV disease progresses. Patients with low or undetectable viral loads at the set point may remain asymptomatic for more than a decade, whereas patients with high viral loads progress more quickly (within a few years).

Antiviral drugs are prescribed to decrease the viral load. The goal of antiviral therapy is to get the viral load as low as possible -- ideally, to an undetectable level. This has been shown to improve clinical outcome.

Viral load is an indicator of the rate of disease progression, but it does not give information on current health status. A high viral load is not an indication to withhold or delay dental treatment.

There is a great variation in the levels of medical knowledge among dental patients. Most HIV-infected patients consider it important to keep track of their changes in viral load and CD4 count because they are good indicators of immune function and prognosis. They usually know if the viral load is undetectable because that means the disease is not progressing rapidly. Others seem less interested in the meanings of these numbers, and some don’t even understand the importance

of having these tests done on a regular basis. If a patient has not been able to give the most recent viral load or CD4 values in more than six months, the dentist should find out why. The dentist plays an important part in the health care team and can help identify obstacles to treatment and lapses in medical care. The dentist should confer with the physician to verify that CD4 and viral load tests have been done and to advise that the patient isn’t aware of their values.

### *Treatment*

The “golden rule” about dental treatment modifications for patients with HIV is that treatment modifications should be based on manifestations of HIV (or its treatment), not on HIV itself. In other words, treatment is only modified if the patient has significant physical manifestations of HIV or HAART. An asymptomatic patient with HIV should be treated the same as any other dental patient. The vast majority of dental patients with HIV require no treatment modifications.

If the patient has severe symptoms of AIDS that interfere with provision of safe treatment, pain and infection may be managed but all other dental needs should be delayed until the patient’s condition improves. Any patient with oral lesions, bleeding abnormalities, or increased susceptibility to infection should be managed using the same principles

whether or not the patient is HIV-infected.

Sometimes a symptomatic patient with HIV presents for care without all the information needed to assess the patient’s medical status. Even if the physician’s office cannot provide critical information immediately, visual and radiographic exams may be done as well as a preliminary evaluation. It would be a waste of the dentist’s time and an inconvenience to the patient to cancel the appointment until a medical consultation is obtained. Instead, the practitioner should determine the patient’s needs and request the appropriate information so treatment can be continued at the next visit. In emergency situations, antibiotics, analgesics, and even infiltrations of local anesthetic may be safely given to provide comfort until more information can be obtained from the physician.

As with any medically complex patient, possible drug interactions should be investigated before prescribing medications. Note that an outdated drug reference will not contain all of the known side effects and interactions for drugs that were recently FDA-approved. The Internet may be a more useful source of information for the rapidly changing arsenal of HIV medications. There are a number of excellent Web sites in this regard:

- <http://www.ama-assn.org/special/hiv/index.htm>
- <http://www.aidsmeds.com/>
- <http://arvdb.ucsf.edu/index.cfm>
- <http://www.ucsf.edu/warmline/drugcht/c.html>

The National HIV Telephone Consultation Service is also available for answers to questions about treatment considerations, including drug interactions of concern to dental care providers. The toll-free number is (800) 933-3413.

### *Conclusion*

With increasingly effective drug therapy and comprehensive strategies to encourage adherence with treatment regimens, the picture of the dental patient

with HIV/AIDS has changed. As people with HIV grow healthier, it becomes easier for the dentist to treat them just like everyone else. This article emphasizes the assessment and determination of when treatment should or should not be modified in light of today's changing therapies for HIV/AIDS.

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To request a printed copy of this article, please contact/Ann M. Lyles, DDS, USC School of Dentistry, 925 W. 34th St., Room 4208, Los Angeles, CA 90089-0641.

# What Color is Your Pith Helmet?

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Robert E.  
Horseman, DDS

Some of us, I suspect, are drifting in our careers. I know I am. Maybe we just fell into something 30, 40 years ago and we're still doing it. Drifting in spite of our ambition because drifting is relaxing, ambition is unsettling, and the two don't necessarily get along.

I know there are dentists who avow that the profession is the most compelling thing in their entire lives, and they could not imagine themselves in any other environment. They are lying, or have completely forgotten their earlier ambitions. What about being a fireman, eh? Or growing a fine mane of hair and emitting impassioned spittle while beating a guitar to death? I never heard of a kid who wanted to grow up to be a dentist. Nowadays, of course, a child expressing such an ambition would be promptly put on some medication and guided carefully through his formative years by expensive psychotherapists.

When I was a lad, it was my intention to become an African explorer. My role models were Osa and Martin Johnson, a ruggedly handsome couple more at home in the wilds of Africa than their hometown of Chanute, Kansas. Later, jungle adventurer Frank "Bring 'Em Back Alive" Buck came to represent everything a red-blooded American boy could aspire to, much as Pee Wee Herman did for later

generations. As soon as I could assemble a safari jacket, a pith helmet, and a gun with a larger caliber than my current Red Ryder Model II BB ordnance, I was certain my future lie along the banks of the Zambezi or in cohabiting with the Pygmies in the Congo.

How it was, then, that I found myself bent over a lab bench, eyes squinched up, carving a tooth out of wax, my whole world measured in millimeters rather than gazing rapturously out over the Serengeti from atop Kilimanjaro is a mystery. Maybe you can't see the Serengeti from the top of Kilimanjaro. Maybe you can see it more clearly from the Empire State Building with the sun rising over the crest of Annapurna. All I know is I can't glimpse it from my third-story operatory, and it has been eating at me for 50 years.

Now there is nothing wrong with drifting, but don't assume you can just drift along forever. Sooner or later you will need a plan, even if that plan is how to drift indefinitely. Ambition has a way of reasserting itself, so one of these days you may find yourself wanting to update your resume, or actually considering a change of careers. Fine! It may be time to Think Big; we are all capable of doing more than we think.

I called the Bureau of Labor Statistics to get the latest numbers.

*Me:* What are the current job opportunities for African explorers?

*BLS:* What?

*Me:* You know – African explorers. Market demand, chances for advancement, benefits, health plans -- that sort of thing.

*BLS:* Ha, ha!

My theory is that since Osa and Martin and Frank, et al. left the exploring business in the late '30s, the entire continent of Africa has been overrun by women's tour groups from the Soroptimists and Rotaryans looking to find where Clark Gable was making out with Ava Gardner in "Mogambo." A wannabe explorer would find more action at a taxidermist's.

That's the trouble with 10-year career plans, they should have been started 10 years ago. If I worked for the Bureau of Labor Statistics, I'd be recommending these growth opportunities:

- Computer nerds who come out to your house and undo the stupid things you've downloaded or deleted by mistake.
- Handyman who can fix appliances that were designed to be disposable, owned by people who can't bring themselves to throw them out.
- Llama ranching.

This business of llama ranching vaguely appeals to me in an outdoorsy

sort of way. There's a three-year apprenticeship and final exams. I'm not sure I want to be a llama rancher. I just want to fantasize that I could. Think of what a conversational ploy this would be:

*Stranger:* So, what do you do?

*Me:* I'm a dentist, but I'm thinking of moving to Peru and becoming a llama rancher up there in the Himalayas.

*Stranger:* You mean the Andes?

*Me:* Whatever.

*Stranger:* That's your dream?

*Me:* Not really.

I know I'm never going to be a llama rancher. It's probably too late anyway. I saw a llama once. It had a face like a camel and I am very frightened of camels. They spit, and as a dentist I've had quite enough of that.