

**PRACTICE GUIDELINES FOR THE
TREATMENT OF
HIV PATIENTS IN GENERAL DENTISTRY**

(4th Edition)

Endorsed by
Oral Health Advisory Group of the Pacific AIDS Education and Training Center
formerly the Dental Steering Committee

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Foreword

We wish to thank Roseann Mulligan, DDS, MS, Chair, Oral Health Advisory Group of the Pacific AIDS Education and Training Center, for her help and guidance in collaborating to update this current revision of Practice Guidelines for the Treatment of HIV Patients in General Dentistry.

This document is an update to three previously published versions of guidelines and is intended to supplement the following resource related to the dental treatment of HIV-infected patients:

American Academy of Oral Medicine Clinician's Guide to
Treatment of Patients with HIV & Other Communicable Diseases
Fourth Edition. 2013
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The Oral Health Advisory Group of the Pacific AIDS Education and Training Center approved the adoption of this document as general guide for treatment of HIV-infected patients. The field of HIV therapy undergoes constant change. Therefore, the Los Angeles Commission on HIV has requested that the Oral Health Advisory Committee of the Pacific AIDS Education & Training Center regularly update this supplement

Our knowledge of HIV manifestations, diagnosis and treatment will continue to grow and change over time. It is for this reason that dental care providers are encouraged to continually educate themselves about HIV disease and associated oral health treatment considerations.

Disclaimer

This executive summary is not intended to set out any standards of care. It is intended to serve as a helpful source of up-to-date information to assist dental practitioners in making informed decisions about the care they provide. Dentists should always exercise their own professional judgment in any given situation, with any given patient. No information contained in this document should be construed as legal advice. Dentists must consult with their own lawyers for legal advice.

Oral Health Advisory Group

These recommendations for treatment were assembled and reviewed by the Pacific AIDS Education & Training Center's Oral Health Advisory Group. The members of this committee are individuals professionally involved with ensuring the best possible dental care for HIV infected patients. This group includes faculty and administrators from dental schools, Pacific AIDS Education and Training Center faculty and staff, dental and medical clinic directors, and attorneys all involved in providing service to individuals who are HIV positive.

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Patient Assessment

A. Medical Assessment

In general, the medical assessment of a patient with HIV infection includes the same elements as any other patient. It is the standard of care to ask about all health conditions and to collect information about the status of each condition at baseline (first visit) and periodically thereafter, especially during annual updates. The patient's medication list should also be completed and updated as well, listing dosages and regimens that are subject to change during the course of HIV disease management.

When to Contact the Patient's Physician? The decision on when to contact the patient's physician is up to the dental care provider, based on his or her assessment of the patient's medical conditions and oral treatment needs, and whether additional information is needed from the patient's physician prior to initiating treatment. This is handled the same way as for any other medical condition. Some examples are:

- To obtain the necessary laboratory test results

- When there is any doubt about the accuracy of the information provided by the patient (i.e. inconsistent or illogical answers to questions about medical history) and more accurate information is needed to ensure patient's safety in the course of dental treatment

- If patient reports a change in his/her general health or signs and symptoms and considering the nature and severity of the condition and any impending medical treatments, it is necessary to determine the need for dental treatment modifications.

- The dental health provider should use the medical history and the laboratory test results to decide if treatment should occur in a hospital setting. Such a decision should be made in consultation with the patient's physician

B. Oral Health Assessment

Oral Health Assessment of the HIV sero-positive patient is the same as any other dental patient. Every patient must undergo a baseline dental and periodontal assessment even if they do not occur on the same first visit. The dental record must clearly indicate the patient's chief complaint and its history. In addition, the patient's previous dental history, including all past treatments, complications and frequency of recall and hygiene visits should be obtained. A full mouth series of radiographs is necessary for diagnosis and treatment planning. If the patient is edentulous or impacted teeth are noted, a panoramic radiograph should be taken. A complete head and neck and extra oral examination including the cutaneous tissues, the regional lymph nodes, all major salivary glands, the cranial nerves, the temporomandibular joints and the muscles of mastication should be performed. This should be followed with an intraoral assessment of all oral and pharyngeal mucosal tissues, gingivae and the dentition. A full record of decayed and missing teeth as well as all existing restorations and prostheses and their time of placement should be documented. Periodontal charting should include examination and recording of the following: measurements of pocket depths, attachment loss, mobility, bleeding on probing and suppuration.

A comprehensive treatment plan should be formulated based on the collected information and phased in terms of priority of care (addressing pain, eliminating infections, restoration of diseased teeth and periodontal tissues and oral hygiene instruction and education). The plan should be reviewed with the patient presenting different treatment options and signed by both the doctor and the patient. The patient has the right to refuse the dental care provider's recommendations; risks of non-treatment should be explained and patient's refusal should be documented and signed by the patient. The patient's treatment plan should be updated on an annual basis even if care is still ongoing and the original plan has not been completed.

In the course of dental treatment, the dentist should prescribe all the necessary medications that address the patient's dental and periodontal needs. For oral conditions that require care by a specialist in a particular dental field (i.e., oral and maxillofacial surgery, periodontics, prosthodontics, orofacial pain, oral medicine, etc.), the dental care provider should make the necessary referral and follow-up.

If at any point during the dental treatment, the dental care provider notices oral soft tissue lesions or salivary gland conditions that directly or indirectly indicate HIV disease progression, a referral should be made to the oral health specialist who can assist in diagnosing and treating the oral condition and at the same time the patient's physician should be notified of the referral, the reasons for the referral, the possible implications related to the HIV infection (if any) and the need for follow-up.

The dental care provider must have a contingency plan for responding to patients with emergencies that occur after office hours, on weekends, during holidays or office vacation schedules.

Diagnostic Tests in the Evaluation of the HIV Infected Patient

The CD4 cell count and the viral load are the two laboratory markers that are used to monitor HIV infection. The CD4 cells are a subset of lymphocytes (synonyms are the T4 cell count or helper cells), which correlates with the patient's immune status. The normal value for adults is 750 – 1000 cells/ml. Patients with values less than 200 cells/ml are considered to have advanced immunosuppression and are defined as having AIDS. Those with a value of less than 50 cells/ml are considered to be in a very advanced stage and are usually symptomatic. Patients with low CD4 cell counts (less than 200 cells/ml) are at risk for developing the diseases associated with AIDS (opportunistic infections and cancers.) Those with high counts (greater than 350 cell/ml) usually manifest no AIDS related illnesses.

The viral load is a test, which measures the amount of viral RNA in a milliliter of plasma. It represents how much the virus is replicating and the magnitude of the viral burden in the body. The viral load test is also used as a prognostic indicator: the higher the value, the higher the risk of a declining CD4 count and clinical progression. With lower values, one expects a slower progression of disease.

Depending on the test kit used, the minimum viral load value is 20 – 50 c/ml. Below this value, the test is usually reported as “undetectable.” The goal of therapy with antiviral drugs is to reduce the viral load to an “undetectable” value. The significance of an “undetectable” viral load is that very little viral replication is occurring. This means that there is little risk of the virus being able to mutate which can result in drug resistance and treatment failure. Reduction of the viral load to “undetectable” levels usually results in an improvement in the immune system (the CD4 cell count rises). Many patients are unable to reduce their viral load to undetectable. For these patients the goal is to reduce the viral load as much as possible.

In interpreting the viral load, it is important to know that patient fluctuation plus lab variation can be as much as three fold. So a value of 50,000 c/ml followed by a value of 70,000c/ml may be within the lab variation. But a value of 5,000 c/ml followed by a value of 50,000 c/ml shows a significant increase. This might indicate drug failure or that the patient has stopped taking medications.

For the dentist, the CD4 cell count indicates the immune status of the patient. The magnitude of the viral load is not an indicator to withhold dental treatment for the patient. High viral loads may be present in a patient with early asymptomatic disease, while low viral loads can be seen in very advanced patients on suppressive antiviral therapy. Knowledge of these markers can tell the dentist the general health of the patient and the risk of progression. The dentist can play an important part in reminding patients of the need for regular follow up and monitoring of these markers.

Most commonly, the CD4 cell count and viral load determinations are to be performed every three to six months depending on the past history of HIV infection and level of suppression achieved.

Lab Values to Track HIV/AIDS Progression

CD4 Cell Count: Assesses the level of CD4 or T-helper cells, which help the immune system to fight infections. Decreases in this number indicate an increased risk of infection. The CD4 can be listed as CD4 or the number may be listed as T4 (CD3+CD4) count. In children under age 5 years, CD4 percentage is

preferred for monitoring immune status because of age related changes in absolute CD4 count in this age group; however, CD4 count can be used in older children.

Viral load (VL) or HIV-1RNA: This represents the copies/ml of the virus in the blood plasma. The goal is to reach an undetectable level of copies. Increasing viral load levels while on antiviral therapy can indicate the development of resistance. The level of viral load does not determine dental care treatment modifications. Treatment modifications are based on the clinical presentation and laboratory indicators. The CD4 cell count correlates with the immune status of the patient

Platelets: Platelets are necessary, along with other factors, for blood to clot. If thrombocytopenia occurs, the risk of bleeding may be so severe as to delay elective and even some emergency therapy until the platelets can be replaced. There is a critical value (see below) which, if not reached, places the patient at risk for severe bleeding.

Absolute neutrophils: Neutrophils may be reported as segmented cells, granulocytes, polymorphonuclear cells, polys, or PMNs. The neutrophils are a special class of white cells that are important for fighting infections. If their numbers decrease, the risk of infection increases.

Critical Laboratory Test Values

Critical laboratory test values are the values that necessitate a change in dental management. It is essential to monitor the lab values that have a direct impact on the ability to safely treat dental patients. All of the HIV/AIDS patients require monitoring of their neutrophils and platelets for invasive treatment, but comorbidities may require monitoring of other labs such as those for liver function or diabetes.

Absolute Neutrophil Count (ANC)

Less than 500 cells/mm³ (Normal values 1,800 – 8,000 cells/mm³): An ANC below 500 cells/mm³ (<about 20 % Neutrophils) represents a risk of infection due to severe neutropenia and necessitates prophylactic antibiotics prior to invasive procedures that will precipitate bacteremia using the AHA guidelines. Consider a therapeutic regimen of post-treatment antibiotics concurrent with invasive procedures and after consultation with the physician.

Platelets

For most care, the platelet count should be above 50,000 cells/ml³. (Normal adult values: 150,000-450,000 cells/mm³). A low value represents thrombocytopenia. **Less than 50,000 for adult patients or less than 75,000 for pediatric patients.** When an extensive and/or invasive procedure is planned with risk of bleeding, consult with the physician and recommend intervention to boost platelets prior to such procedures. The physician may elect to give a platelet infusion to increase the platelet count. **The dentist must receive laboratory confirmation of the platelet count immediately (1-2 days) before invasive procedure.** Delay elective dental procedures until the platelet count improves.

CD4 T-Lymphocytes (Helper cells) (absolute)

Less than 50 cells/mm³ (normal values 590-1120 cells/mm³) **or less than 15% CD4 percentage for children under 5 years (normal value is CD4 percentage \geq 25%):** Evaluate patient for severe opportunistic disease and treatment plan them realistically considering their degree of disease. Even

patients with severely diminished CD4 levels may tolerate definitive dental care rather than only palliative treatment; this must be individually considered for each patient with close consultation with the physician to determine stage of disease. At or below 200 cells/mm³: the patient is considered to have AIDS due to the increased risk of opportunistic infections. Emphasize good oral care and have them contact you immediately if oral problems start.

Viral Load

The viral load does not have an impact on dental treatment planning. The number of viral copies is indicative of disease, but any modification of dental treatment would be based on the other laboratory test results (discussed previously) and not on the viral load. A significantly high viral load is taken as a predictor of more rapid disease progression and should be correlated with the patient's CD4 count. However, for a very high viral load (eg. 1 million), a consult is warranted and treatment deferred until it improves.

Suggested Frequency of Obtaining Lab Reports

The issue of how frequently laboratory tests need to be obtained is primarily dependent upon the patient's CD4 T-helper cell count, whether the patient is on antiretroviral therapy (cART), and the length of time of viral suppression during cART.

Laboratory tests are important to monitor the patient's health. The suggested frequency of tests is listed below and is based on the patient's prior CD4 test results and medical stability. cART can independently play havoc with blood values regardless of the CD4 count so the patients who are taking this therapy require frequent monitoring: usually every six months or less, depending upon critical values that may need more follow-up. Current laboratory test results are very important for invasive dental procedures. At the same time, clinical judgment is necessary as most dental procedures need not be delayed just because the laboratory results are older than ideal.

Additional Tests Based on Clinical Scenario

Like any patient, the clinical scenario may direct the provider to order additional tests. The indication and interpretation of these laboratory tests would not differ in HIV infected patients. The following are some examples of labs that may be ordered in specific situations:

- complete blood count (CBC) including red blood cell count (RBC), white blood cell count (WBC) and differential count (Diff), platelet count (PLT), hemoglobin level (Hb) and hematocrit (Hct) in patients with history of anemia, thrombocytopenia, advanced HIV disease and prior to surgical procedures to determine if the patient is at risk for post-operative complications such as infection or poor healing
- metabolic panel in patients with a history of kidney disease, hepatitis B/C or other liver diseases as the dentist may need to adjust the dosage of analgesics or antibiotics prescribed
- INR or prothrombin time (PT) and partial thromboplastin time (PTT) for patients with advanced liver disease, those who are taking prescription anticoagulants or when history or physical findings indicate a need to assess bleeding potential
- Hemoglobin A-1C in diabetic patients to determine the patient's level of glycemic control and their risk for post-operative complications such as infection or poor healing

- Assessment of tuberculosis status in patients with a history of recent exposure to or symptoms of TB, they may include skin PPD testing, blood Quantiferon Assay or chest x-ray

It should be emphasized that although having access to laboratory tests for HIV positive patients is helpful to the dental provider, it is not always necessary for many routine procedures.

The dentist can also be instrumental in encouraging the patient to adhere to their medication regimen. The most common cause for drug failure is the patient taking his/her medications inconsistently. Missing just a few doses a month can result in the virus becoming resistant.

Antibiotic Prophylaxis

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. In fact, patients with AIDS have shown a higher incidence of allergic reactions to antibiotics and other medications, so it may endanger the patient's health by over-prescribing antibiotics.

Prophylactic antibiotics should not be prescribed routinely for the dental visit when the HIV infection is well controlled. Routine antibiotic coverage prior to procedures likely to cause bleeding and bacteremia is not recommended. Many patients at an advanced stage of HIV disease are already taking antibiotics to prevent opportunistic infection, so the dentist should not prescribe additional medications without contacting the physician.

- If a patient with a neutrophil count below 500 cells/mm³ requires procedures likely to cause bleeding and bacteremia and is not already taking antibiotics for prophylaxis against opportunistic infections, the physician should be contacted regarding the need for antibiotic prophylaxis for dental procedures. Therefore, it is important to check with the physician for the most current CBC with differential.
- The regimen for prevention of bacterial endocarditis is the same in HIV patients as it is for non-infected patients. The American Heart Association guidelines for antibiotic prophylaxis should be followed as with any patient. Consult the patient's physician to determine the need for antibiotic prophylaxis for the patient with multiple co-morbidities and with prosthetic joint replacements or intravascular devices.
- As with any patient, it is the standard of care to investigate all possible drug interactions before prescribing antibiotics or any other medications for patients with HIV infections.

Treatment Considerations

Modifications of Dental Therapy

There is no justification to modify dental treatment based on the fact that the patient is infected with the HIV virus. However, if the patient's medical status is complex, treatment adjustments may be necessary as would be the case with any medically compromised patient. After performing a thorough assessment the dentist should determine any needed treatment modifications. **IT IS ESSENTIAL FOR ALL PRACTITIONERS TO UNDERSTAND THAT MOST HIV PATIENTS, EVEN IF SYMPTOMATIC, CAN BE TREATED SAFELY IN A TYPICAL DENTAL OFFICE OR CLINIC.**

- Bleeding tendencies may determine whether or not to recommend full mouth scaling and root planning or multiple extractions in one visit. In conjunction with establishing a history of excessive bleeding and the appropriate laboratory tests, a tooth-by-tooth approach to assess bleeding tendencies could be used as a clinical method to evaluate the patient's risk of hemorrhage.
- In patients who are at risk for increased bleeding, deep block injections should be avoided. In these patients intraligamentary or local infiltration may be an appropriate alternative.
- When performing dental extractions on patients who are at risk for increased bleeding, local measures such as primary closure after surgery and the use of local thrombotic agents such as gelfoam or topical thrombin are helpful in controlling the bleeding.
- In patients who are taking oral anti-platelet drugs or anticoagulants, the decision to discontinue these agents prior to dental procedures must be made in conjunction with the patient's physician and after careful consideration of the patient's risk of bleeding versus their risk for thromboembolism.
- For patients who are taking antiplatelet agents such as aspirin, clopidogrel (Plavix), ticlopidine (Ticlid), and dipyridamole/aspirin (Aggrenox) there is no need to discontinue the anticoagulant for dental and most surgical procedures. For extensive surgical procedures, consult the patient's physician to see if these agents may be discontinued prior to the planned procedure. Typically these drugs must be withheld one week before the procedure.
- Restorative and simple tooth extractions may be performed on patients who take warfarin anticoagulant (Coumadin) with INR values of 3.5 or lower. For extensive surgical procedures or when the INR values are higher, consult with the patient's physician to see if warfarin may be discontinued. It should be noted that many patients who take warfarin are at risk for a thromboembolic event and therefore, it is preferred to discontinue warfarin in conjunction with heparin bridging. This is accomplished by stopping warfarin 5 days before the scheduled surgery and replacing it with low molecular weight heparin (Lovenox). In extreme cases, where the patient's risk of thromboembolism is very high, hospitalization, warfarin reversal and heparinization may be necessary.

- For patients who are taking the increasingly popular novel anticoagulants such as Dabigatran (Pradaxa), rivaroxiban (Xarelto) and apixaban (Eliquis), there is no need to discontinue these agents for dental procedures or routine dental prophylaxis. For extractions and surgical procedures, discontinuation of these agents 24 hours before the planned procedure is adequate to reduce the risk of bleeding.
- In severe cases of profound thrombocytopenia (platelets < 50,000) or anemia (Hb < 10 g/dL), depending on the invasiveness and extent of treatment needed, patients may be treated more safely in a hospital environment where blood or platelet transfusions are available.
- The ability to withstand treatment for an extended amount of time should be ascertained.
- The ability to return for sequential visits should be determined when a treatment plan is prepared or when a dental procedure is being initiated.
- A pre-treatment antibacterial mouth rinse will reduce intraoral bacterial load, especially for those patients with periodontal disease.
- A six-month recall schedule should be instituted to monitor any oral changes. If the patient is severely immunosuppressed i.e. (CD-4 count of <100), a shorter recall period such as a three-month interval should be considered.
- Patients exhibiting oral lesions should be assessed in a timely manner.
- When salivary hypofunction is present, the patient should be closely monitored for caries, periodontitis, soft tissue lesions and salivary gland disease.
- Fluoride supplements in the form of a rinse and/or toothpaste should be encouraged for those with increased caries and salivary hypofunction.
- Oral hygiene is important in a medically compromised patient, as poor hygiene may be responsible for more rapid progression of oral disease. A proactive attitude and an emphasis on prevention should be encouraged. Dental treatment should also be prioritized based on the patient's health and circumstances (e.g. ability to tolerate long appointments, ability to perform oral hygiene etc.).

Nutrition Counseling

Because of certain oral conditions, the HIV patient may have difficulty consuming a balanced diet. The patient may suffer from changes in taste and decreased ability to chew and swallow because of drug-induced salivary hypofunction. Medications can also lead to GI upset and nausea, further inhibiting the intake of a balanced diet. It is the role of the dentist to recognize oral manifestations that are associated with nutritional deficiencies resulting in intraoral manifestations due to low levels of vitamin B 12, folic acid, etc. Nutritional supplements or referral to the patient's physician or a registered dietitian may be necessary. Some areas to be aware of include:

- Poor oral intake of food or fluid
- Difficulty chewing and swallowing due to continuous mouth sores resulting from candidiasis, herpes simplex, aphthous ulcers, etc.

- Severe dental caries
- Changes in perception of taste or smell
- Patient complaints of economic inability to meet caloric and nutrient needs

Patient education and Referrals for Substance Abuse including Tobacco Usage

As part of patient education about oral self-care and the importance of regular dental and maintenance visits, the dental care provider should provide information to the patient about the negative impact of smoked and smokeless tobacco, e-cigarettes, marijuana and illicit substances such as crystal methamphetamine on oral tissues. As necessary, the patient should be provided with the appropriate referrals for recovery, counseling and risk reduction programs.

HIV Testing

Just like the materials and processes used in dentistry have improved in the past decade, so too has the testing and treatment for HIV. In fact, the field of HIV testing has improved dramatically in recent years. Using the same premise of screening using a sensitive test and reflexing to a more specific test, the HIV tests currently recommended by the CDC are extremely sensitive and specific because these tests ascertain both antibody (IgM and IgG) and antigen (p24). This makes these tests far more accurate and allows detection of HIV earlier in the disease process. The 4th generation tests allow detection of infection at the acute stage of infection, between 2-3 weeks, well before the former standard Western Blot test would detect infection. The 4th generation tests also have a far shorter processing time, and can be run in most lab settings in 60 minutes, for a preliminary result. For these reasons, the Western Blot is no longer considered a confirmatory test.

It is important to refer to the CDC's website for the most current recommendations; currently the latest were released in 2014 and can be found at

<http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf>

The current testing recommendations call for the use of a 4th generation test, reflexed if positive to HIV 1/2 antibody differentiation test and an RNA/Nucleic Acid Test (NAT).

If people test positive, it is important to assure they are linked to medical care. Early detection of HIV infection provides many opportunities for health professionals to intervene and help prevent further transmission to others. Use of antiretroviral medications shortly after infection can reduce the viral load set point, reduce the onset of opportunistic infections and assure connection to medical care.

Physicians who regularly care for HIV patients also will have access to community resources, including testing for partners, Pre-Exposure Prophylaxis for partners, and medication assistance. The Affordable Care Act has made insurance more widely available, so that more people can get tested for HIV. The US Preventive Services Task Force has given HIV testing a Grade A, which means insurance providers will reimburse it.

Hepatitis B and C

Hepatitis B

According to the CDC, Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, October 25, 2013, if one has been vaccinated and has developed immunity, there is virtually no risk for infection following an exposure. For an unvaccinated person, the range of infection varies from 6% to 30% and depends on the hepatitis B e antigen (HBeAg) status of the source individual. If this person is both e antigen positive and surface antigen (HBsAg) positive, he or she will have more virus in the blood and are more likely to transmit HBV.

Standard Precautions, formerly known as Universal Precautions, are now the minimum infection prevention processes to be followed in the dental operator as many patients and their healthcare providers may be unaware of their HBV status. It is important to consistently follow routine barrier precautions and safely handle needles and other sharps. Blood contains the highest HBV titer of all body fluids. It is the most important vehicle of transmission in the health-care setting. In the dental setting, the gingival sulcus has the greatest concentration of hepatitis B. The hepatitis B virus is also found in other body fluids, including saliva. However, saliva is not an efficient vehicle of transmission because it contains low quantities of infectious HBV. HBV has been demonstrated to survive in dried blood on surfaces for at least one week when at room temperature.

All healthcare providers must be offered the hepatitis B vaccine by their employer, free of charge within 10 days of potentially being exposed to body fluids. (Title 8 Cal OSHA) The vaccine is indicated for people who have an occupational risk of exposure to blood or other blood-contaminated body fluids. The employee has the right to refuse the hepatitis B vaccine. A hepatitis B declination statement must be signed and witnessed. The vaccine consists of three doses. The second dose is given 1-2 months after the first; and the third dose is 4-6 months after the first. A blood test to determine antibody titers should be done 30-60 days after the last dose. A titer level >150 indicates that the person is immune for life. A person must have a titer >10 to be immune. If a person has a titer level <10 after immunization, the entire series must be repeated. If the person continues to have a low titer level, they are considered primary non-responders. If this person has an exposure, counseling is advised, as the person should get an immunoglobulin injection to help boost immunity.

Hepatitis B is 100 times more infectious than HIV. Prior to the introduction of the HBV vaccine, healthcare providers had a prevalence of HBV infection approximately 10 times higher than the general population.

For more information go to: <http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm#overview>

Hepatitis C

According to the CDC (May 30, 2015), approximately 3.2 million people in the United States have chronic hepatitis C virus (HCV), with those born during 1945-1965 having the highest prevalence. It is the most common chronic blood borne infection in the United States. HCV is spread in the dental office by percutaneous or mucosal exposures to infected blood. **For HCV, the risk of infection after**

a needlestick or cut is approximately 1.8%. The risk following a blood splash is unknown; however, HCV infection from such an exposure has been reported. Injection drug users have the highest risk of HCV and account for 60% of cases. Sexual exposure accounts for approximately 15% of cases, whereas an additional 5% of exposures are from a combination of hemodialysis patients, those employed as a health care workers (HCW), or infants infected by their mother during birth. 20% have no known recognized source. Co-infection with HIV and HCV is common (50% to 90%) among HIV-infected injection drug users. Co-infection is also common among persons with hemophilia who received clotting factor concentrates before 1987.

It is important to note that percutaneous exposure to blood through tattooing; body piercing and acupuncture can transmit HCV. There are a number of serologic tests currently approved by the FDA that can measure antibodies to HCV. Though these tests cannot distinguish between acute, chronic or resolved infections.

Health care workers (HCWs) are at occupational risk for acquisition of HCV through a blood exposure. About 25-50% of HIV-infected individuals in the United States are also infected with hepatitis C virus. The latest Centers for Disease Control and Prevention and the U.S. Public Health Service/Infectious Disease Society of America recommendations are to screen all HIV-infected persons for HCV infection.

According to the CDC guidelines, post-exposure prophylaxis should not be used after occupational exposure to HCV. The guideline (<http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm#section1>) recommendations are:

- Serologic testing of source patient
- Determination of baseline values of HCV for the person exposed (anti-HCV and ALT activity)
AND
- Follow-up testing four-six months after exposure for anti-HCV and ALT
- Confirmation of all anti-HCV results reported as positive by enzyme immunoassay

In the United States the therapeutic regimens that have been approved for treatment of chronic hepatitis C include: alpha interferon, pegylated interferon, and the combination therapy of interferon and ribavirin with possible addition of boceprevir and telaprevir. In 2013 two new drugs for treatment of HCV were approved by the FDA. These drugs, simprevir and sofosbuvir in combination with other medications depending on the HCV genotypes involved, may reduce the treatment time but are very expensive.

There are no current recommendations to restrict an individual who is infected with HCV from working. Universal precautions and strict aseptic techniques, which include hand washing, use of personal protective barriers and proper care in the use and disposal of needles and sharps, should be employed.

Medications Used in Patients with HIV

Knowledge of antiretroviral drugs is constantly growing, but it should be emphasized that long-term clinical data on drug interactions does not exist for many of the newer medications. Patients taking some of these drugs are likely to suffer from salivary hypofunction. Use of prescription medications such as pilocarpine, cevimeline, and bethanechol as salivary gland stimulants should be considered. Excellent oral hygiene home care, topical fluoride and frequent hygiene recall visits, as well as nutritional counseling and saliva enhancers (sugarless gum, water, saliva substitutes) will be critical for prevention of periodontal disease and dental caries. Patients should also be assessed for consumption of unexpected sources of sugar such as over the counter medications including products like antacids (e.g. Tums, Rolaids); cough drops; suspensions (e.g. Nystatin); and, fungal troches (e.g. Mycelex). All of these may contribute to dental caries.

Currently, there are no known drug interactions between antiretrovirals and local anesthetics used in general dentistry. There are, however, several drugs that are prescribed by dentists or used in the office that may be contraindicated in patients taking antiretroviral medications. It is recommended that the dental care provider consult a reference that thoroughly discusses drug side effects and interactions prior to prescribing any medications or dispensing in the dental office. Combination anti-retroviral therapy (cART) regimens can change rapidly and constant updating of the patient's medication list is necessary. As with most medications, cART can often result in salivary hypofunction.

See Appendix A—Antiretroviral Drugs

Post-Exposure Prophylaxis (PEP)

Most occupational HIV exposures do not result in the transmission of HIV. There have been no documented reports of occupational transmission from a dentist to a patient. Documentation of the event and assessment of risk remain important. The person who is exposed should be referred immediately to a physician who can provide counseling, testing and appropriate medications. The interval within which PEP should be initiated for optimal efficacy is not known, however, “as soon as possible” is recommended. This exposure should be treated as a medical emergency.

For updated recommendations: see the October 2014 New York State Department AIDS Institute, www.aidsinstitute.org.

Management of Occupational Blood Exposure

- Wash wounds and skin with soap and water
- Flush mucous membranes with water
- The incident should be reported to a supervisor if applicable and should be documented in an injury/exposure log
- Report to a medical provider for testing, and access to post-exposure protocol
- New testing algorithms include the combo Antibody/Antigen test with confirmation by Multispot.

Basic Overview:

Determine whether high or low risk depending on source

- Low titer exposure
- Higher titer exposure

Medications

- Start within hours of exposure (as soon as possible)
- Triple therapy for 4 weeks

Baseline Labs to Monitor for Adverse Reactions

- Pregnancy test if applicable
- Complete Blood Count with differential and platelets
- Urinalysis
- Renal Function Tests (BUN and Serum Creatinine)
- Liver Function Tests (Aspartate and Alanine Aminotransferase, Alkaline Phosphatase, Total Bilirubin)

Monitor

- Baseline
- If fourth generation testing is used, blood should be tested every 6 weeks and 16 weeks.
- If third generation testing is used, test at 6 weeks, 12 weeks and 24 weeks.
(Note: fourth generation testing is generally used now)

The National Clinicians' Post-Exposure Prophylaxis Hotline is the PEP line. This is an excellent resource for questions and it is open 24 hours a day, 7 days a week. Their number is (888) 448-4911.

Legal and Privacy Issues

Testing for HIV infection and reporting HIV test results are governed by California statute. Protection of information regarding HIV status, handling of public health records containing information about HIV or AIDS and personally identifying information, and federal and state rules governing protected health information and medical records, all limit disclosure by medical care providers. Additionally, people living with HIV (“PLWH”) are entitled to a host of legal protections. Both federal and state constitutions promise a right to privacy which applies to HIV status. These laws, in addition to federal and state laws prohibiting discrimination against PLWH, are key considerations when serving this community.

Informed Consent for HIV Testing¹

Before a medical care provider, including a dentist, may test a patient for HIV infection, the provider must inform the patient that the test is planned. Medical care providers must also provide information about the test, inform the patient that there are numerous treatment options available for a patient who tests positive for HIV and that a person who tests negative for HIV should continue to be routinely tested. The medical care provider must also inform the patient that he or she has the right to decline the test. If a patient declines the test, the medical care provider shall note that fact in the patient’s medical file.

HIV Testing for Occupational Exposure²

In some limited instances, healthcare workers, including dentists, may be exposed to blood borne pathogens as part of their occupation. Thus, occupational exposure may give rise to HIV testing. In these cases, the law requires following strict protocols that balance the needs of the healthcare workers with the privacy interests of PLWH. Even in the context of occupational exposure, HIV testing of a patient cannot be mandated by a healthcare worker. Post-exposure prophylaxis for HIV exposure is available for occupational exposure and should be considered where appropriate.

Notification of HIV Test Results³

A patient who is tested for HIV infection should receive timely information and counseling from the medical care provider. An explanation of the results as well as the implications of those results to the patient’s health should be explained.

If the patient tests positive for HIV infection, the medical care provider shall inform the patient that there are numerous treatment options available and identify follow-up testing and care that may be recommended. That information must also include contact information for medical and psychological services to ensure proper linkages to HIV care. If the patient tests negative for HIV infection and is known to be at high risk for HIV infection, the medical care provider shall advise the patient of the

¹ California Health and Safety Code § 120990.

² California Health and Safety Code § 120262.

³ California Health and Safety Code § 120990(h).

need for periodic retesting due to limitations of testing technology and the six month “window period” for verification of results.⁴ Medical care providers may also offer prevention counseling or a referral to prevention counseling to the patient.

Electronic notification of test results for HIV infection is only permitted if requested by the patient and the medical care provider considers such notification “most appropriate.”⁵ Prior consent from the patient must be obtained for any electronic notification and the medical care provider must view the results prior to the patient accessing such results. Telephone communication is not considered electronic communication. Regardless of the type of notification, protocol with regard to dispensing post-test information, as described above, still applies.

HIV Reporting⁶

In 2006, California, along with a number of other states, moved from codes-based reporting to names-based reporting for HIV/AIDS. This was in response to new funding requirements of the Ryan White CARE Act, requiring federal funding allocations to states be calculated according to the number of HIV-positive individuals identified by name. Surveillance data from previously identified individuals living with HIV could not be imported to the new system and had to be re-identified and validated under the new system.

Dentists, as health care providers, are required to report cases of HIV infection to the local health officer using patient names on a form developed by the state Department of Public Health. Laboratories are also required to submit HIV case report forms to the local health officer. Once the local health officer is able to eliminate duplicate reports, they are submitted to the state Department of Public Health. The state, in turn, removes any personally identifying information and submits required reporting to the federal Centers for Disease Control.

Confidential Public Health Records⁷

Because HIV reporting has shifted to a names-based reporting system, there are legal protections that generally prohibit disclosure of public health records containing information regarding HIV or AIDS and personally identifying information, either developed or acquired by the local public health agency, the state, or an agent thereof. A few exceptions do apply, including written authorization of the person who is the subject of the record or a guardian or conservator of that person or use of public health records containing such information by state and local health officers in conducting research in the investigation, control and surveillance of the disease.⁸ Unauthorized disclosure, ranging from negligent to willful, may result in civil penalties up to \$25,000 per actionable offense.⁹

⁴ See California Department of Public Health, *HIV Testing Information and Resources for California Clinicians*, <http://www.cdph.ca.gov/programs/aids/documents/ctthivtestinfoforclinicians.pdf> (last accessed March 17, 2015) (explaining “window period”).

⁵ California Health and Safety Code § 123148.

⁶ California Health and Safety Code § 121022(a).

⁷ California Health and Safety Code § 121025.

⁸ California Health and Safety Code § 121025 (a)-(b).

⁹ California Health and Safety Code § 121025 (e).

Disclosure of HIV Test Results¹⁰

Unauthorized disclosure of HIV test results linked to individually-identifying information is generally prohibited from disclosure. Including the results of an HIV test in a patient's medical records is not considered disclosure. Written authorization is required for each separate disclosure of HIV test results and must identify to whom such disclosure can be made. Unauthorized disclosure, ranging from negligent or willful, may result in civil penalties up to \$25,000 per actionable offense.

Privacy and Confidentiality of Medical Records¹¹

Federal law governing protected health information under the Health Insurance Portability and Accountability Act also protects records containing information regarding HIV or AIDS and personally identifying information. Unauthorized disclosure is generally prohibited unless it falls within specific permitted use such as coordinating care and treatment of the patient, as part of administrative processes to obtain payment for care provided, for public health purposes, and in response to criminal justice processes, including specific circumstances where court orders or warrants demand disclosure. Unauthorized disclosure is subject to administrative penalties and criminal penalties for anyone who knowingly obtains or discloses individually identifiable personal health information. This law offers individuals no private right to legal action.

State law governing confidential medical information under the Confidentiality of Medical Information Act applies to any licensed or certified health care provider, which includes dentists. Medical records include charts, records, notes, laboratory results, and pharmacy and prescription histories.

Unauthorized disclosure is generally prohibited unless it falls within specific exceptions such as coordinating care, treatment, payment of services for the patient, for public health purposes, and in response to legal processes, including specific circumstances where court orders or warrants demand disclosure. Unauthorized disclosure is subject to a private right of action including provisions for civil penalties (including nominal damages and actual damages) as well as administrative fines up to \$250,000 per violation.

Legal Standards for Treating PLWH¹²

Federal and state constitutions protect the fundamental right to privacy. In California, that fundamental right extends to HIV status.¹³ In addition to these constitutional rights, PLWH are protected by non-discrimination mandates which can be found in the federal Americans with Disabilities Act¹⁴, Section 504 of the federal Rehabilitation Act, and California's Unruh Civil Rights Act and Disabled Person's Act.¹⁵ These laws prohibit discrimination against all PLWH in public accommodations.

¹⁰ California Health and Safety Code § 120980.

¹¹ Health Insurance Portability and Accountability Act, HIPAA Privacy Rule, 45 CFR § 164.500 et. seq. (2000); Confidentiality of Medical Information Act, California Civil Code § 56.10 et seq. (1981).

¹² U.S. Const. amend. IV.

¹³ CA Const. art. I, § 1.

¹⁴ *Bragdon v. Abbott*, 524 U.S. 624 (1998) (finding that the Americans with Disabilities Act applies to all people living with HIV, regardless of their stage of infection).

¹⁵ Americans with Disabilities Act of 1990, 42 U.S.C. §§ 12181-12189 (1990); Rehabilitation Act of 1973, § 504 (1973); Unruh Civil Rights Act, California Civil Code § 51 et. seq. (2003); California's Disabled Persons Act, California Civil Code § 54.1 (1996).

Dentists, as medical care providers providing health services to the public, are required to comply with non-discrimination provisions applying to public accommodations. This means dentists must serve PLWH and any considerations when making exceptions to serving a patient living with HIV must be based on reasonable judgments informed by current medical knowledge and not based on stereotypes or irrational fears. Given that the risk of HIV infection to dental staff or other patients is remote and can be further reduced by implementing already required universal safety precautions applying to all blood borne pathogens, any argument which relies on this particular risk will be legally insufficient.¹⁶

The community standard of practice requires that dentists be as familiar with basic HIV medical care as they are with other common medical conditions. A referral to other general practitioners because the dentist is ignorant about basic HIV medical care is a violation of community dental practice norms. Referrals to a specialist or to a hospital setting must always be based on the clinical needs of the patient, not the ignorance or fear of the dentist, staff or other patients. The legal obligation of the dental provider is to refer patients for testing and follow-up. For example, a dentist may be held legally liable if a patient who has a lesion with unknown etiology needs a referral in order to rule out possible HIV etiology, and the referral for testing and counseling is not done.

Ethical Standards for Treating PLWH

Ethical standards of the California Dental Association, American Dental Association, and World Dental Federation also make clear that it is unethical to refuse to care for PLWH because of fear of the risk of infection.

Best Practices for Treating PLWH

Any decision to deny dental services to PLWH should be done with an abundance of caution. Typically, any policies and practices that result in differential treatment and care of HIV-positive patients, including blanket refusals to treat HIV-positive patients and blanket referrals of all HIV-positive patients to “specialists” have been found to be scientifically unwarranted, and courts have found such blanket practices and policies to constitute unlawful discrimination against PLWH.

PLWH have reported facing discrimination in accessing dental services.¹⁷ Given this particular history, dentists must understand that some PLWH may choose not disclose their HIV status. For this reason, any effort to help patients feel comfortable and confident in disclosing their HIV status is vital to serving this vulnerable population.

Staff must receive appropriate training on the specific protections which apply to the privacy and confidentiality of HIV status. Because patient information must be kept confidential to the extent possible, unauthorized disclosures of HIV or AIDS-related information coupled with personally identifiable information, or medical records of patients living with HIV, should be monitored. Given that unauthorized disclosures can lead to significant awards for damages, utilizing a uniform written authorization form that includes specific mention of HIV/AIDS-related information, the party with

¹⁶ See United States Department of Justice, Civil Rights Division, *DOJ HIV/AIDS Enforcement*, http://www.ada.gov/aids/ada_aids_enforcement.htm (last accessed March 17, 2015)(citing two recent dental discrimination cases settled on behalf of PLWH).

¹⁷ See Brad Sears, Christian Cooper, Fariba S. Younai, and Tom Donohoe. HIV Discrimination in Dental Care: Results of a Discrimination Testing Study In Los Angeles County (2011), <http://williamsinstitute.law.ucla.edu/wp-content/uploads/Sears-HIV-Discrimination-Dental-Care-Dec-2011.pdf> (last accessed March 17, 2015).

whom such information can be shared, and the patient's signed consent would help to safely facilitate any necessary exchange in information.

Selected Websites for HIV/AIDS Information for Dentists

General Sites of Particular Interest to Dentists:

- American Dental Association – legal, regulatory, ethical issues, evidence-based dentistry
<http://www.ada.org/>
- California Dental Association – extensive resources on practice management
<http://www.cda.org>
- HIVdent – extensive information on oral manifestations, infection control, medications, picture gallery, and other resources: <http://www.hivdent.org>

Federal Government-Sponsored Websites:

- Aids.gov – overview of federal resources—<http://www.aids.gov>
- Centers for Disease Control and Prevention (CDC) (www.cdc.gov):
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
<http://www.cdc.gov/nchstp/hiv-aids/dhap.htm>
CDC National Prevention Information Network (NPIN)--<http://cdcnpin.org>
- Health Resources and Services Administration (HRSA):
HRSA Target Center – Tools for the Ryan White Community
[http://careacttarget.org/library/guide-hivaids-clinical-care-oral health](http://careacttarget.org/library/guide-hivaids-clinical-care-oral%20health)
AIDS Education Training Centers (AETCs) – HIV Education for Healthcare Professionals, with listing of regional AETC’s resources and training opportunities—<http://aidsetc.org/>
- National Institutes of Health (NIH)
AIDS Info – Guidelines in use of antiretroviral agent—<http://aidsinfo.nih.gov>
National Institute for Dental and Craniofacial Research—<http://www.nidcr.nih.gov/>

Clinical Resources for Dentists:

- HIVdent – Comprehensive site with resources for oral healthcare—<http://www.hivdent.org>
- American Academy of Oral Medicine – Publisher of Clinicians Guides Series, which includes “Clinician’s Guide to Treatment of Patients with HIV & Other Communicable Diseases, 4th ed, 2013.” <https://maaom.memberclicks.net/clinicians-guides>
- Mountain Plains AETC – publications include “Oral Health Care for the HIV-Infected Patient”
<http://www.mpaetc.org/Products>

General Clinical Resources:

- HIV Insite (UCSF) – comprehensive up-to-date information on HIV/AIDS
<http://hivinsite.ucsf.edu/>
- HIV Insite Database of Antiretroviral Drug Interactions
<http://hivinsite.ucsf.edu/insite?page=ar-00-02>
- John Hopkins AIDS Guide – available for mobile devices and web
<http://www.hopkinsguides.com/Hopkins.up>
- University of Liverpool –free drug interaction apps for HIV and Hepatitis C
<http://www.hiv-druginteractions.org/>
<http://www.hep-druginteractions.org/>
- Infectious Disease Society of America - HIVMA/IDSA Primary Care Guidelines for the Management of Persons Infected with Human Immunodeficiency Virus
<http://www.hivma.org/home>
- DrugBank – comprehensive database with over 6,800 drug entries—<http://www.drugbank.ca/>

Infection Control:

- Organization for Safety, Asepsis and Prevention (OSAP) – mission is safe and infection-free delivery of oral healthcare – <http://www.osap.org>
- American Nursing Association Safe Needles Save Lives – many resources on needlestick safety and prevention – www.needlestick.org

Post-Exposure Prophylaxis:

- The National Clinician's Hotlines:
Post-Exposure Prophylaxis Hotline – http://www.nccc.ucsf.edu/about_nccc/pepline/
PEpline 888-448-4911 – national clinician’s PEP telephone hotline
Warmline 800-933-3413 – national HIV telephone consultation service
- Florida Caribbean AETC – resources include printed summary guidelines for PEP and many other topics, <http://fcaetc.org/treatment-guidelines.php>

International Issues in HIV/AIDS:

- AIDS Education Global Information System (AEGIS) – information and resources for global AIDS epidemic – <http://www.aegis.com/>
- World Dental Federation (FDI)<http://www.fdiworlddental.org>

Known Antiretroviral Drug Interactions In General Dentistry

NOTE: The information here may serve as a guideline, but it only represents some of the known drugs and the adverse drug reactions *at this time* (2015). New drugs and 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, please consult information provided by the drug manufacturer or a recently published drug reference. **Some good sources include: American Academy of Oral Medicine 2012, and Medical Management of HIV Infection 2013. Latest updates can also be found on various websites-see Selected Websites for HIV/AIDS information as a guide. Summary information on antiretroviral drug interactions is available in a free app for Apple and Android devices from the University of Liverpool. This app can be downloaded from the website: hiv-druginteractions.com.**

The human immunodeficiency virus (HIV) must insert its genetic material into a susceptible cell to replicate and release more virions. This process involves a number of steps that present opportunities for therapeutic intervention. HIV mutates rapidly in response to single drug therapy and quickly develops resistance to individual drugs. Antiretroviral (ARV) drugs delivered in combination therapy were found to be far more effective in suppressing HIV replication. This is now the standard of care for anti-HIV drug therapy and it allows those who respond favorably to therapy to have a more normal life span. However, this comes with a price. There is direct toxicity from the drugs themselves and drug-drug interactions are frequent. These effects can have serious consequences, and can be difficult to predict. The current ARV drugs are far more effective and easier to tolerate than earlier drugs, but they are all toxic to varying degrees. Clinicians prescribing these drugs always have to weigh hoped-for benefits against potential negative consequences from adverse effects of the individual drugs and unintended interactions between all the medications a given patient is taking.

Six major classes of ARV drugs have been developed to treat HIV/AIDS, however no drugs have been developed to date that cure the HIV infection. The drugs currently available in each of these classes are discussed below. ARV drugs may be cited by an abbreviation, a pharmaceutical name, and/or a brand name, so all these names are presented. Many drugs, including a number of ARVs and other commonly prescribed drugs, interact with the Cytochrome P450 (CYP450) enzyme system in the liver and intestine that is responsible for much drug metabolism. An individual drug may be a substrate (i.e. be metabolized by) these enzymes; it may also inhibit or induce the metabolism of another drug. An individual drug may be a substrate, inhibitor, and/or inducer all at the same time depending on the individual CYP450 enzymes it interacts with and how these affect other involved drugs. This can greatly complicate the spectrum of drug-drug interactions and make them difficult to predict.

Drug interactions in dental practice are not as voluminous as they are in medical practice because most dental-related drug therapy is short-term and the number of drug classes is small in comparison. Dentists do need to be aware of the potential for interaction between drugs they may prescribe and the

ARV and other drugs that patients are taking concurrently. There may be interactions involving drugs not prescribed by the dentist that can have clinical consequences for dental practice. As an example, drugs that inhibit the metabolism of warfarin could increase bleeding tendency and dentists should have recent INR values for such patients before performing invasive procedures. The app for mobile devices from the University of Liverpool that gives information on potential ARV drug interactions with other drugs is particularly easy to access and understand. This app is a free download from the website: hiv-druginteractions.com.

Fortunately for dentists, their most commonly used drugs are local anesthetics, which have very low potential for drug-drug interactions with ARVs. Commonly used amide anesthetics are metabolized by the CYP450 system but adverse drug-drug interactions with ARVs have not been noted. Systemic toxicity from local anesthetics can occur from excessive dosage or inadvertent intravascular injection. Care should be taken when administering local anesthetics to patients with compromised liver function because toxic dose levels may be lower in such persons. Other drugs that dentists may prescribe, including some antibiotics, antifungals, anxiolytics, sedatives and topical steroids, have the potential for interactions with certain ARVs. In the following list of currently-approved ARVs (with FDA approval dates), each drug has a section on Contraindications with potential drug-drug interaction concerns for general dentists listed first, followed by other potential interactions that dentists should be aware of, and then a summary of adverse reactions to the drugs themselves.

Regarding the adverse reactions listed, the more common ones are abbreviated with the key as follows: D – diarrhea, F – fever, GI – gastrointestinal, HA – headache, N – nausea, R – rash, V – vomiting.

1. NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI)

NRTIs prevent the conversion of viral RNA into double-stranded DNA so it can insert into the genome of the cell. This was the first class of ARV medications discovered. These drugs are the backbone of antiretroviral therapy, and are commonly prescribed in three-drug regimens that contain two NRTIs and a third drug chosen from one of the NNRTI, PI, or INSTI classes. NRTIs are not extensively metabolized before being eliminated by the kidneys. Therefore, significant interaction with enzymes involved in drug metabolism are unlikely. However, drug-drug interactions from other causes can occur. Adverse effects from NRTI drugs themselves are common and can be severe. These include mitochondrial toxicity, lactic acidosis, hepatic steatosis, myelosuppression with cytopenia, cardiomyopathy, and many others.

<u>ABBREVIATION</u>	<u>BRAND NAME</u>	<u>CONTRAINDICATIONS</u>
AZT Approved 1987	Zidovudine Retrovir	Dental - Fluconazole increases AZT serum levels General – Do not prescribe with other drugs that cause bone marrow suppression Adverse reactions - GI side effects, bone marrow suppression and anemia, N, V, HA, F, R, malaise, bleeding gingiva, oral ulcers, taste perversion
ddI Approved 1991	Didanosine Videx	Dental - Metronidazole and nitrous oxide may increase risk of peripheral neuropathy, so use with caution. Avoid

tetracycline as it may increase risk of pancreatitis and absorption may be decreased. Separate dosing of other drugs for 2 hours, especially ketoconazole, quinolones. Adverse reactions - peripheral neuropathy, cardiovascular risk, anemia, leucopenia, xerostomia, sialadenitis

d4T Approved 1994	Stavudine	Zerit	Dental - Metronidazole and nitrous oxide may increase risk of peripheral neuropathy, so use with caution. Adverse reactions – peripheral neuropathy, which may range in severity from mild to disabling, pancreatitis, anemia, neutropenia, thrombocytopenia
3TC Approved 1995	Lamivudine	Epivir	Dental - interactions unlikely, possible exception is midazolam General – clinically significant drug interactions with lamivudine appear to be uncommon. Adverse reactions – HA, N, V, stomatitis
ABC Approved 1998	Abacavir	Ziagen	Dental – interactions unlikely General - Clinically significant drug-drug interactions uncommon. However, simultaneous initiation of abacavir with drugs likely to cause systemic reactions or rash (such as sulfonamides, other NRTIs, or fosamprenavir) may complicate the evaluation of possible hypersensitivity reactions Adverse reactions – hypersensitivity reaction, R, N, V, D, fatigue, pharyngitis, oral ulcers
TDF Approved 2001	Tenofovir	Viread	Dental – interactions unlikely General – Clinically significant drug-drug interactions unlikely Adverse reactions - renal toxicity, possible effects on bone metabolism, N, V, flatulence.
FTC Approved 2003	Emtricitabine	Emtriva	Dental – interactions unlikely General - Clinically significant drug-drug interactions unlikely. Adverse reactions – HA, N, V, nasopharyngitis

FIXED DOSE COMBINATIONS WITH NRTIs ONLY:

For drug-drug interaction potential and adverse reactions, see discussion of individual drugs

AZT-3TC
Approved 1997

Combivir (zidovudine + lamivudine)

AZT+3TC+ABC Approved 2000	Trizivir (zidovudine + lamivudine + abacavir)
ABC+3TC Approved 2004	Epzicom (abacavir + lamivudine)
TFD+FTC Approved 2012	Truvada (tenofovir + emtricitabine)

2. NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)

NNRTIs prevent the conversion of viral RNA into DNA similar to the NRTIs, but they have a different mechanism of action. These drugs have an affinity for the CYP450 enzyme system. NNRTIs may be metabolized by these enzymes as well as inhibit or induce them whether or not they are a substrate for metabolism. These properties greatly increase the potential of NNRTIs for serious drug-drug interactions. Serious adverse effects of the drugs themselves include drug hypersensitivity (including Stevens-Johnson Syndrome), lipid disorders, serious skin rash, and liver toxicity.

<u>ABBREVIATION</u>	<u>BRAND NAME</u>	<u>CONTRAINDICATIONS</u>
NVP Approved 1996	Nevirapine Viramune	Dental - NVP is both a substrate and inducer of CYP450 enzymes, affecting the levels of many co-administered drugs, and those that inhibit CYP3A activity, such as ketoconazole, cimetidine, and macrolide antibiotics, can increase NVP levels. Risk of hepatotoxicity with fluconazole General – increases metabolism of warfarin and may decrease INR below therapeutic levels. Adverse reactions - hepatotoxicity, R, stomatitis
DLV Approved 1997	Delviradine Rescriptor	Dental - avoid co-administration with Phenobarbital and ketoconazole, increases plasma concentrations of clarithromycin, midazolam, alprazolam, and triazolam. General – DLV inhibits metabolism by CYP450 enzymes, affecting the levels of many co-administered drugs. Adverse reactions – R, F, HA, fatigue, conjunctivitis, muscle aches, changes in fat distribution in the body (lipodystrophy), stomatitis, oral ulcers, xerostomia, taste perversion
EFV Approved 1998	Efavirenz Sustiva	Dental - increases plasma concentrations of midazolam, triazolam. Serum levels of EFV are increased by fluconazole. EFV interacts with CYP450 enzymes, affecting the hepatic metabolism of many co-administered drugs, including many antiretrovirals.

Adverse reactions – CNS effects, hypersensitivity reaction (including Stevens-Johnson Syndrome), lipodystrophy, D, V, R, hyperlipidemia, insomnia, vivid dreams, stomatitis

ETV Etravirine Intelence
Approved 2008

Dental - antifungal agents increase ETV concentrations, whereas ETV decreases itraconazole and ketoconazole concentrations. It increases serum levels of alprazolam, diazepam, and warfarin, which may increase INR. Erythromycin increases ETV concentration.
General - ETV may act as a substrate, inhibitor, or inducer of multiple CYP450 enzymes. It has therapeutically significant interactions with many medications, including a number of antiretroviral agents, and may have effects that are difficult to predict.
Adverse reactions – erythema multiforme, N, R, HA, stomach pain, blurred vision, dizziness, mouth ulcers

RPV Rilpivirine Edurant
Approved 2011

Dental - macrolide antibiotics and azole antifungals may increase RPV levels. RPV may affect the levels of other medications. It decreases serum levels of ketoconazole.
General - An acidic gastric environment is necessary for absorption of RPV. Medications that increase gastric pH substantially reduce serum RPV concentrations. It is a substrate of CYP450 enzymes, so drugs that induce or inhibit this system may alter serum RPV levels. Adequate pharmacokinetic data and clinical correlates are not yet available for many potential interactions.
Adverse reactions – CNS effects, depressive disorders, HA, insomnia, R, increased lipids, hepatotoxicity

FIXED DOSE COMBINATIONS WITH NRTIs and NNRTIs:

For drug-drug interaction potential and adverse reactions, see discussion of individual drugs

TDF+FTC+EFV Atripla (tenofovir + emtricitabine + efavirenz)
Approved 2006

TDF+FTC+RPV Complera (tenofovir + emtricitabine + rilpivirine)
Approved 2011

3. PROTEASE INHIBITORS (PI)

PIs block the enzyme necessary to produce mature virions that propagate the HIV infection. PIs have a high barrier to development of drug resistance, but also have a propensity to bad metabolic effects,

including GI disturbances, dyslipidemia, insulin resistance, and changes in fat distribution in the body (lipodystrophy). Similar to NNRTIs, PIs have a strong affinity to CYP450 enzymes and consequently a strong potential for serious drug-drug interactions. All PIs inhibit the most prominent CYP enzyme. The strong inhibitory properties of ritonavir are actually exploited by combining it with other PIs so that the other PI drug can be effective when administered in smaller doses.

<u>ABBREVIATION</u>	<u>BRAND NAME</u>	<u>CONTRAINDICATIONS</u>
SQV Approved 1995	Saquinavir Invirase	Dental - increased plasma levels of clindamycin, itraconazole, ketoconazole, triazolam, midazolam. Increased metabolism of dexamethasone. General - SQV is metabolized by the CYP450 enzyme system, and alters the concentrations of other drugs metabolized by this pathway. Similarly, drugs that induce or inhibit these enzymes, such as ketoconazole, may cause therapeutically significant alterations in SQV levels. Drug formulation of SQV is boosted with ritonavir. Adverse reactions – D, N, V, dizziness, hyperlipidemia, lipodystrophy, neutropenia, thrombocytopenia,
IDV Approved 1996	Indinavir Crixivan	Dental - contraindicated with triazolam, midazolam. Increased blood levels of clarithromycin. Reduce dose when given with ketoconazole. General - IDV is an inhibitor of CYP450 enzyme system and may alter serum concentrations of other drugs metabolized by this pathway. Because IDV is also metabolized by CYP450 enzymes, drugs that affect this enzyme system, such as ketoconazole, may significantly affect IDV levels. Adverse reaction – increased insulin resistance, kidney stones, hyperbilirubinemia, N, HA, V, D, stomach pain
RTV Approved 1996	Ritonavir Norvir	Dental - contraindicated with sedative hypnotics (alprazolam, diazepam, midazolam), meperidine, propoxyphene. Increases plasma levels of clarithromycin, fluconazole. Decreased plasma levels of ritonavir may occur with dexamethasone. Changes levels of NSAID's, antihistamines, antifungals. General - In current practice, ritonavir is used almost exclusively at subtherapeutic doses solely to maintain therapeutic serum levels of other protease inhibitors used in combination, i.e., as a pharmacokinetic enhancer of other protease inhibitors. Ritonavir is a potent inhibitor of CYP450 enzymes. Coadministration with ritonavir therefore causes clinically significant serum alterations of a variety of drugs.

			Adverse reactions – D, N, V, hepatotoxicity, pancreatitis, hyperlipidemia, taste perversion, may cause perioral paresthesia
LPV/r Approved 2000	Lopinavir/r	Kaletra	Dental – it may increase metabolism of warfarin and thereby decrease INR. Items listed above for ritonavir apply for this combination drug as well. General - The ritonavir component of lopinavir/ritonavir is a potent inhibitor of CYP450 enzymes. Coadministration with lopinavir/ritonavir therefore causes clinically significant alterations in serum levels of a variety of drugs. Adverse reactions – D, N, V, hyperlipidemia, glucose intolerance, hepatotoxicity, GI intolerance, xerostomia
NLF Approved 1997	Nelfinavir	Viracept	Dental – coadministration with some benzodiazepines can alter serum levels (alprazolam, diazepam, flurazepam). Should not be administered with midazolam. Drugs that affect the CYP450 enzyme system (e.g. ketoconazole) affects NLF levels. General - NLF is a substrate and inhibitor of CYP450 enzymes and significantly interacts with many drugs. Adverse reactions – D, flatulence, GI disturbances, R, fatigue, liver effects, oral ulcers, pharyngitis
FPV Approved 2003	Fosamprenavir	Lexiva	Dental – co-administration with some benzodiazepines can alter serum levels (alprazolam, diazepam, flurazepam). Should not be administered with midazolam. General - FPV is both a substrate and inhibitor of CYP450 enzymes and alters the concentrations of other drugs metabolized by this pathway Adverse reactions – increased lipids, cardiovascular disease, R, D, N, V, HA, fatigue, itching of face and mouth
ATV Approved 2003	Atazanavir	Reyataz	Dental – coadministration with azoles could increase ATV and also increase itraconazole and ketoconazole. Could reduce efficacy of codeine and increase serum concentration of alprazolam, diazepam, midazolam. General - ATV is a substrate and inhibitor of certain CYP450 enzymes, and alters serum concentrations of other drugs metabolized by this pathway. Adverse reactions – heart rhythm changes, renal changes, increased bilirubin, depression, dizziness, SOB, N, V R, oral ulcers

TPV Approved 2005	Tipranavir	Aptivus	<p>Dental – increases concentration of benzodiazepines, and should not be administered with midazolam or triazolam. Increases serum concentrations of macrolide antibiotics, including erythromycin. It can inhibit metabolism of warfarin and increase bleeding</p> <p>General - TPV both inhibits and induces CYP450 enzymes. It must be coadministered with ritonavir, and its net effect is inhibition. TPV also induces other metabolic processes. Thus, TPV alters the concentrations of many other drugs metabolized by these pathways, in ways that may be complex and difficult to predict.</p> <p>Adverse reactions – D, N, V, HA, fatigue, hyperglycemia, increase lipids</p>
DRV Approved 2006	Darunavir	Prezista	<p>Dental - DRV increases metabolism of warfarin thereby decreasing INR. It increases serum concentrations of the benzodiazepines midazolam and triazolam, and antifungals itraconazole and ketoconazole.</p> <p>General - Darunavir is a substrate for and inhibits CYP450 enzymes, and it must be coadministered with ritonavir. Darunavir has clinically significant interactions with many medications, including other antiretrovirals.</p> <p>Adverse reactions – hyperlipidemia, lipodystrophy, stomach pain, N, V, D, R, HA, xerostomia, pharyngitis</p>

FIXED DOSE COMBINATIONS WITH PROTEASE INHIBITORS AND DRUG METABOLISM INHIBITOR:

For drug-drug interaction potential and adverse reactions, see discussion of individual drugs

ATV + COBI Atazanivir + Cobisistat
Approved 2015

DRV + COBI Darunivir + Cobisistat
Approved 2015

4. FUSION AND ENTRY INHIBITORS

Entry inhibitors interfere with the viral ability to enter the cell. The two currently available entry inhibitors are in different drug classes and have markedly different metabolic profiles as discussed below.

<u>ABBREVIATION</u>	<u>BRAND NAME</u>	<u>CONTRAINDICATIONS</u>
T-20 Enfuvirtide (Fusion inhibitor)	Fuzeon	General - Enfuvirtide is catabolized by proteolytic enzymes; it is not metabolized by CYP450 enzymes.

Approved 2003

There are no known clinically significant interactions between enfuvirtide and other medications.

Adverse reactions – It must be injected and pain, redness, itchiness at injection sites are common. Other common reactions are F, R, dizziness, anxiety, abdominal pain, myalgia, xerostomia, taste perversions

MVC Mariviroc Selzentry
(Entry Inhibitor)
Approved 2007

Dental – concurrent azole antifungals (itraconazole and ketoconazole) and erythromycin may increase MVC serum concentrations.

General – MVC is a substrate of CYP450 enzymes and p-glycoprotein, and has therapeutically significant interactions with many medications. It neither induces nor inhibits CYP450 enzymes, thus MVC does not appear to cause significant changes in concentrations of other drugs.
Adverse reactions – liver dysfunction, N, R, dizziness, stomach pain, loss of appetite

5. INTEGRASE STRAND TRANSFER INHIBITORS (INSTI) -

Integrase strand transfer inhibitors (INSTI) block the enzyme necessary to integrate the viral DNA into the DNA of the cell. They are generally well tolerated, although they are also prone to development of drug resistance and cause insomnia and headaches.

ABBREVIATION

BRAND NAME

CONTRAINDICATIONS

RAL Raltegravir
Approved 2007

Isentress

Dental – Not clinically significant with drugs commonly prescribed by dentists are noted.

General - RAL does not interact with the CYP450 enzyme system and thus has a lower risk of significant drug-drug interactions. It is metabolized primarily by glucuronidation and inducers or inhibitors of this system may affect serum levels of RAL.

Adverse effects – skin reaction, R, liver problems, allergic reaction, muscle pain, D, HA, dizziness

EVG Elvitegravir Vitekta
Approved 2012

Dental – Coadministration with many drugs used by dentists has not been studied with EVG. Azole antifungal drugs appear to increase EVG concentrations.

General - Elvitegravir is primarily metabolized by CYP450 enzymes, so drugs that induce or inhibit the actions of these enzymes may affect serum levels of EVG. Elvitegravir is only available coadministered with other drugs (such as Stribild) and the formulation will have the effects of all its pharmaceutical components.

Adverse effects – These are still being studied but appear to be few. D and R have been noted.

DTG Dolutegravir Tivicay
Approved 2013

Dental – Coadministration with many drugs used by dentists has not been studied.

General - Dolutegravir is metabolized primarily by glucuronidation, and CYP450 enzymes. Inducers or inhibitors of these enzymes affect serum levels of dolutegravir. It needs to be taken with a pharmacologic booster.

Adverse reactions – dolutegravir appears to have a more favorable adverse effects profile but has been noted to cause N, D, HA, R, insomnia, fatigue and has the potential for allergic reactions.

FIXED DOSE COMBINATION WITH NRTI AND INSTI ARVs:

For drug-drug interaction potential and adverse reactions, see discussion of individual drugs

ABC + DTG + 3TC Abacavir + Dolutegravir + Lamivudine
Approved 2014

6. PHARMACOKINETIC ENHANCERS

Pharmacokinetic enhancers have no activity against HIV but they enhance the activity of ARV medications that are given concurrently. One drug in this class is approved as of 2014.

<u>ABBREVIATION</u>	<u>BRAND NAME</u>	<u>CONTRAINDICATIONS</u>
COBI Cobisistat Approved 2012	Tybost	COBI is a pharmacokinetic enhancer that has no activity against HIV. COBI is a substrate and inhibitor of CYP450 enzymes and other metabolic systems. It is intended to boost the antiretroviral effects of ARVs that are metabolized by these enzymes. Thus, COBI causes clinically significant alterations in serum levels of a variety of other drugs that are metabolized by or are substrates of these systems. Management of most of these interactions has not been established. Azole antifungals and clarithromycin may increase serum COBI concentrations (and COBI may simultaneously increase serum levels of the coadministered antimicrobial). Adverse reactions – D, N, HA, lipidemia, decreases kidney function

FIXED DOSE COMBINATION WITH ARV INHIBITORS AND DRUG METABOLISM INHIBITOR:

For drug-drug interaction potential and adverse reactions, see discussion of individual drugs

EVG+FTC+TDF+ COBI Approved 2012	Stribild	EVG (Elvitegravir) – integrase inhibitor FTC & TDF – NRTIs COBI (Cobicistat) – ARV drug metabolism inhibitor
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It is best to consult a drug reference before prescribing any medications to determine if there are any contraindications.

A NOTE ON HEPATITIS C:

Hepatitis C (HCV) is a viral infection that has many of the same risk factors as HIV. Approximately one-fourth of the HIV-positive individuals in the US are believed to be coinfecting with both viruses (i.e. about 250,000-300,000 persons). Older HCV drug regimens did not have high cure rates and did not contain direct acting antiretroviral drugs. Direct-Acting Antiviral agents (termed DAAs) for HCV were introduced in 2011 and are much more effective at curing the disease in shorter time frames. However, drug interactions in the coinfecting are very complex and will become more so as more HCV drugs are released. A major concern for dentists is the infectivity of HCV from an occupational blood borne exposure. HCV is considered to be approximately 10 times more infective than HIV from a blood borne exposure and no post-exposure prophylaxis (PEP) has been available to date (2015). The current hope is that the advent of DAAs for HCV will result in an effective PEP for HCV to be developed in the near future. The University of Liverpool has also developed an app for mobile devices that identifies drug interactions with HCV drugs. It can be downloaded at **hep-druginteractions.com**.