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**HIV INFECTION.
MANIFESTATIONS
IN THE ORAL CAVITY**

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МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
2-я КАФЕДРА ТЕРАПЕВТИЧЕСКОЙ СТОМАТОЛОГИИ

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**ВИЧ-ИНФЕКЦИЯ.
ПРОЯВЛЕНИЯ В ПОЛОСТИ РТА**

**HIV INFECTION.
MANIFESTATIONS IN THE ORAL CAVITY**

Учебно-методическое пособие



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MOTIVATIONAL CHARACTERISTIC OF THE THEME

Total time: 65–70 minutes.

Dentists can often detect early manifestations of systemic diseases in the oral cavity and may function as gatekeepers in the healthcare system by referring patients to physicians and nurse practitioners for evaluation and treatment. Advances in the biotechnology of oral fluid testing and the direct accessibility of the oral cavity to examination may change the scope of dental care whereby the dentist can promote public health, advocate needed changes in health policy, and align dentistry more closely with medicine and nursing. That alignment was not fully realized generations ago when dentistry was largely isolated from its allied health professions and focused almost exclusively on the restoration of teeth. Advances in oral fluid testing received widespread attention when antibodies to HIV infection could be detected from oral transudate, and forever changed the erstwhile, relatively tranquil landscape of dental practice. Dentistry was catapulted into the center of the HIV/AIDS crisis. Dentists saw a major shift in their role as oral diagnosticians testing for HIV antibodies. That shift also necessitated an in-depth understanding of bioethical principles and their judicious application in clinical management. The principles of biomedical ethics from medical practice have now become even more important and integrated into dental practice.

The purpose of the seminar: to define the role of the dentist in the evaluation of HIV infection, to integrate the knowledge of students on the principles and measures of HIV prevention in the course of provision of dental care to patients.

Seminar Objectives:

1. To study the specific clinical manifestations of HIV infection in the oral cavity.
2. To learn the techniques for a dentist to follow in the evaluation of HIV infection and HIV-infected patients.
3. To master the principles and measures for the prevention of HIV infection.

Requirements for the initial level of students' knowledge:

- in microbiology, virology, immunology: general characteristic of retroviruses, modern methods of microbiological and immunological testing;
- in therapeutic dentistry: principles of clinical examination and treatment planning for the patients with oral mucosal diseases;
- in infection diseases: etiology, pathogenesis, transmission routes, clinical manifestations of HIV, HIV prevention methods;
- in general dentistry: dental office management, aseptic and antiseptic requirements.

Checklist of related disciplines:

1. Brief characteristics of retroviruses.
2. Methods of immunological testing.
3. Elements of oral mucosa lesions.
4. Basic principles of infectious disease prevention.

Test questions:

1. Etiology, pathogenesis and epidemiology of HIV infection. HIV transmission routes.
2. Clinical stages of HIV infection.
3. The classification of oral lesions associated with HIV infection.
4. Features of clinical manifestations of HIV infection in the oral cavity.
5. HIV infection evaluation techniques for dentists.
6. Modes of dental treatment of HIV-infected patients.
7. Prevention of HIV infection.

The first report on what is known as AIDS (Acquired Immune Deficiency Syndrome) appeared in 1981. The full syndrome (AIDS) is a more radical manifestation of HIV infection. The Center for Disease Control and Prevention (CDC) reports that the virus attacks the immune system, eventually making the body prone to multiple infections of different types. The CDC estimates that approximately 1.1 million people are currently living with HIV or AIDS.

1. With the development of antiviral strategies, AIDS is now a chronic disease. Highly active antiretroviral therapy has significantly reduced deaths and people with HIV can now survive more than 20 years with the disease. This means that more HIV-infected individuals are likely to seek dental advice over time.

2. Approximately one of five (20 %) HIV-infected persons does not know that he/she is infected.

CLINICAL STAGES OF HIV INFECTION

I. Acute infection. In this stage patients have transient signs and symptoms that appear at the time of, or shortly after, primary HIV infection as identified by laboratory tests. Defined as a mononucleosis-like syndrome acute infection occurs within two to four weeks of initial infection with HIV. The symptoms of acute infection are similar to a bad flu or, as people describe it, “the worst flu in a lifetime”. According to AIDS.gov, during the acute infection phase, large amounts of virus are being produced in the body, which attack CD4 T cells, a type of cells making up the immune system. Eventually the body brings the virus back to low levels, and the CD4 T cell number increases.

II. Asymptomatic infection. In this stage patients have no manifestations and symptoms of HIV infection. Patients in this stage may be subclassified based on whether hematologic and/or immunologic laboratory tests have been done and whether the results are abnormal in terms of the effect of HIV infection. After a few weeks of acute infection the amount of virus present in the body decreases as the immune system attempts to fight off the infection. This stage may last for many years and is marked by a slow decline in CD4 positive T-cells. A person is considered infected with HIV in case of a positive HIV test. Additionally, a patient may have enlarged lymph nodes. This stage may persist for a period of eight years or longer.

III. Generalized lymphadenopathy syndrome. This stage is characterized by typical lymph node swelling of over 1cm in diameter in at least two sites apart from the groin. The lymphadenopathy should have persisted for three months or longer and have been explained by no other cause. The patient may suffer from mild symptoms such as skin rashes, fatigue, night sweating, a slight weight loss and fungal skin and nail infections. The National Institute of Allergy and Infectious Diseases (NIAID) reports that headaches and fatigue are also common symptoms of this stage of AIDS.

IV. AIDS-related complex. In this stage patients have clinical symptoms or signs of HIV infection other than or in addition to lymphadenopathy: oral hairy leukoplakia, multidermatomal herpes zoster, recurrent Salmonella bacteremia, nocardiosis, tuberculosis or oral candidiasis, etc.

V. Terminal stage, or AIDS. When the patient's CD4⁺ T cell count declines to a very low level, the diagnosis of AIDS is made. Advanced AIDS is associated with opportunistic infections which may make the infected person consistently and often severely sick. These infections include Mycobacterium avium complex disease (caused by fungi), Pneumocystis carinii pneumonia (caused by bacteria), and cytomegalovirus (caused by viruses). A severe chronic diarrhea, intense night sweating, memory loss, depression and other disorders of the brain may occur in case of advanced AIDS.

DEFINITION OF AIDS-RELATED COMPLEX

To satisfy the definition a person must have any two (or more) signs/symptoms and any two (or more) abnormal laboratory values.

I. Clinical signs: chronic condition present for 3 months or longer, unexplained

1. Lymphadenopathy > 2 non-inguinal sites.
2. Weight loss 10 % normal body weight.
3. Fever > 38 °C, intermittent or continuous.
4. Diarrhea.
5. Fatigue/malaise.
6. Night-sweat.

II. Laboratory studies:

1. Decreased number of T-helper cells.
2. Decreased ratio of T helper: suppressor lymphocytes.
3. Anemias or leucopenia or thrombocytopenia or lymphopenia.
4. Increased serum globulin levels.
5. Decreased blastogenic response of lymphocytes to mitogens.
6. Cutaneous anergy to multiple skin test antigens.
7. Increased levels of circulating immune complexes.

CHARACTERISTICS OF HIV

HIV belongs to a group of retroviruses which are characterized by the ability to transfer their genetic information into the DNA of the host cell. The virus itself is an RNA virus and uses an enzyme called reverse transcriptase to copy its genome into DNA, which is subsequently integrated in the genome of the host cell. Therefore, in addition to the replication of the host cell DNA during cell division, the viral genome is replicated as well. Once infected, the host will thus harbor the virus for the rest of its life.

An HIV molecule is about 1/20th the size of *E. coli* and 1/70th the size of a typical white blood cell. The virus is surrounded by a membrane made of fatty materials dotted with small spikes made of proteins. The viral genetic material is inside the membrane. The virus also contains several proteins necessary for replication (fig. 1).

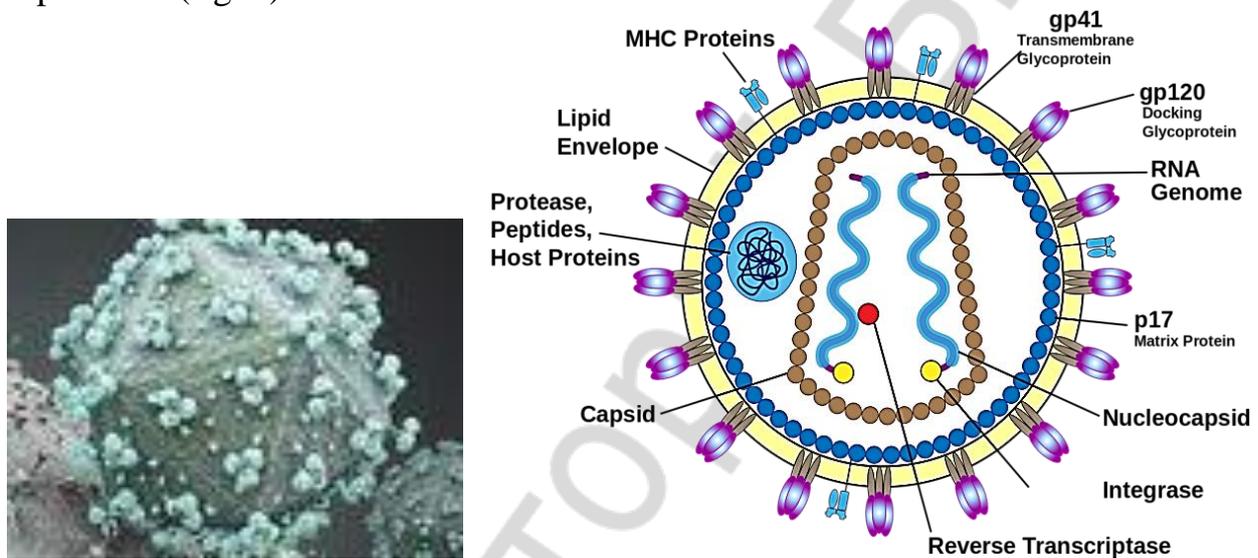


Fig. 1. Structure of HIV

The human immunodeficiency virus, which is transmitted via unprotected sex and contaminated blood, weakens the immune system and eventually leads to acquired immunodeficiency syndrome. Because of the weakened immune system, the body is unable to fight off the infection.

TRANSMISSION

HIV is transmitted via contaminated body fluids, explains the Patient Education Institute, a publisher of health information. It can be contracted as a result of exposure to semen, vaginal fluids, breast milk or blood. It cannot be transmitted via sweat, saliva, tears or insects. The highest levels of HIV are usually found in the blood, though the most common route of transmission is unprotected sex. It is also commonly spread via contaminated needles.

ORAL MANIFESTATIONS OF INFECTIOUS DISEASES

Group I — Lesions strongly associated with HIV infection:

- Candidiasis;
- Pseudomembranous;
- Erythematous;
- Hyperplastic;
- Oral Hairy leukoplakia;
- Kaposi's sarcoma;
- Non-Hodgkin's lymphoma;
- HIV associated periodontal disease.

Group II — Lesions commonly associated with HIV infection:

- Atypical ulcerations;
- HIV associated salivary gland diseases;
- Thrombocytopenia;
- Viral infections: *Herpes simplex virus infection*, *Human papilloma virus infection*, *Cytomegalovirus infection*;
- Zoster virus infection: *Shingles*, *chickenpox/Varicella*.

Group III — Lesions uncommonly associated with HIV infection:

- Bacterial infections: *actinomyces israeli*, *Escherichia coli*, *Klebsiella pneumonia*, *Mycobacterium avium*, *Mycobacterium tuberculosis*;
- Melanotic hyper pigmentation;
- Cat scratch disease;
- Drug reactions;
- Bacillary epitheloid angiomatosis;
- Fungal infections other than candidiasis;
- Neurological disturbances;
- Recurrent aphthous ulcerations: *Viral infections*, *Molluscum contagiosum*.

ORAL CANDIDIASIS

Oral candidiasis is a very prevalent feature, occurring in about 75 % of AIDS patients. The clinical features of candidiasis vary according to the type of lesion.

Pseudomembranous candidiasis has previously been described as acute. However, in association with AIDS this type of lesion may persist for months. Clinically it is characterized by the presence of creamy white or yellowish single or confluent plaques on a red or normal colored oral mucosa. Easily rubbed off leaving the underlying mucosa bleeding. This type of candidiasis may involve any part of the oral mucosa (fig. 2).

Erythematous (atrophic) candidiasis appears clinically as a red lesion. The common locations are palate and dorsum of the tongue. Erythematous candidiasis in association with AIDS is usually chronic. The lesion on the tongue is characteristically located along the midline and filiform papillae are atrophic (fig. 3).



Fig. 2. Pseudomembranous candidiasis



Fig. 3. Erythematous candidiasis

Hyperplastic candidiasis in HIV-infected patients is usually found bilaterally on the buccal mucosa. This type of lesion is more rarely presented in AIDS patients and may be related to tobacco smoking (fig. 4).



Fig. 4. Hyperplastic candidiasis

In addition to the intraoral lesions, **angular cheilitis** may occur.

The diagnosis of candidiasis relies on the clinical features and the presence of Candida hyphae on smears. Additional diagnostic tests involve culture on specific media. However, if other lesions are suspected, biopsy may be necessary.

ORAL HAIRY LEUKOPLAKIA

Oral hairy leukoplakia locations are lateral borders of the tongue. However, it may sometimes spread to cover the entire dorsal surface. The surface may be smooth, corrugated or markedly folded with thick, hair-like projections. Hairy leukoplakia can also appear on the buccal mucosa, on the floor of mouth and palate. The patients are usually asymptomatic. The origin of the disease is associated with the high levels of replication of Epstein–Barr virus in the cells of the tongue epithelium.

The diagnosis of Hairy leukoplakia is an indication of immunodeficiency and exposure to the AIDS virus. Preliminary reports indicate that approximately one-third of Hairy leukoplakia cases will develop into AIDS (fig. 5).



Fig. 5. Hairy leukoplakia

PERIODONTAL DISEASES

Linear gingival erythema. The onset is sudden with spontaneous gingival bleeding. Symptoms may subside gradually over 3–4 weeks but the condition often recurs. Linear gingival erythema is presented as a distinctive linear band of erythema that involves the free gingival margin and extends 2–3 mm apically. The anterior gingiva is most commonly affected (fig. 6).



Fig. 6. Linear gingival erythema

Necrotizing ulcerative gingivitis. The onset is sudden with bleeding on toothbrushing, pain, and halitosis. Symptoms may subside gradually over 3–4 weeks but the condition often recurs. The gingiva appears fiery red and swollen,

and both the margin of the gingiva and the tips of the interdental papillae are the seat of a yellowish-grayish necrosis which bleeds easily. The anterior gingiva is most commonly affected. It appears that necrotizing ulcerative gingivitis, in some HIV patients, has a rather destructive course leading to the loss of soft tissue and bone as well as the formation of sequester (fig. 7).



Fig. 7. Necrotizing ulcerative gingivitis

Necrotizing ulcerative periodontitis. An aggressive form of the periodontal disease has been observed in the risk groups for AIDS and in AIDS patients. The disease is accompanied with irregular generalized destruction of supporting tissues and bone. When treating these patients the response may not be the same as in healthy patients.

ORAL MANIFESTATIONS OF NEOPLASMS

Kaposi's Sarcoma. Multifocal neoplasm of vascular endothelium initially begins with a single, or more frequently, multiple, pink, red or violet macules, papules or nodules on the skin or mucosal surfaces. The skin lesions are frequently located on the trunk, arm, and head and neck, in contrast to the distribution of lesions on the legs in classic KS. The skin lesions often become dark and larger.

Kaposi's sarcoma:

- most common neoplasm in HIV/AIDS;
- male to female ratio 20 : 1;
- occurs in all risk groups;
- more frequent in whites;
- more frequent in homosexuals;
- may not be a malignancy;
- doesn't blanch with pressure.

Oral Manifestations of Kaposi's Sarcoma. Kaposi's sarcoma usually appears first on the skin. The favorite location is the palate. The oral lesions may appear as bluish, blackish, or reddish macules which are usually flat in the early stages. In later stages the lesions may become darker, elevated, often lobulated and ulcerated. The oral lesions are usually non-tender before they become ulcerated. The gingival mucosa is also frequently involved. In some patients the gingival manifestation of Kaposi's sarcoma may have the form of an epulis (fig. 8).

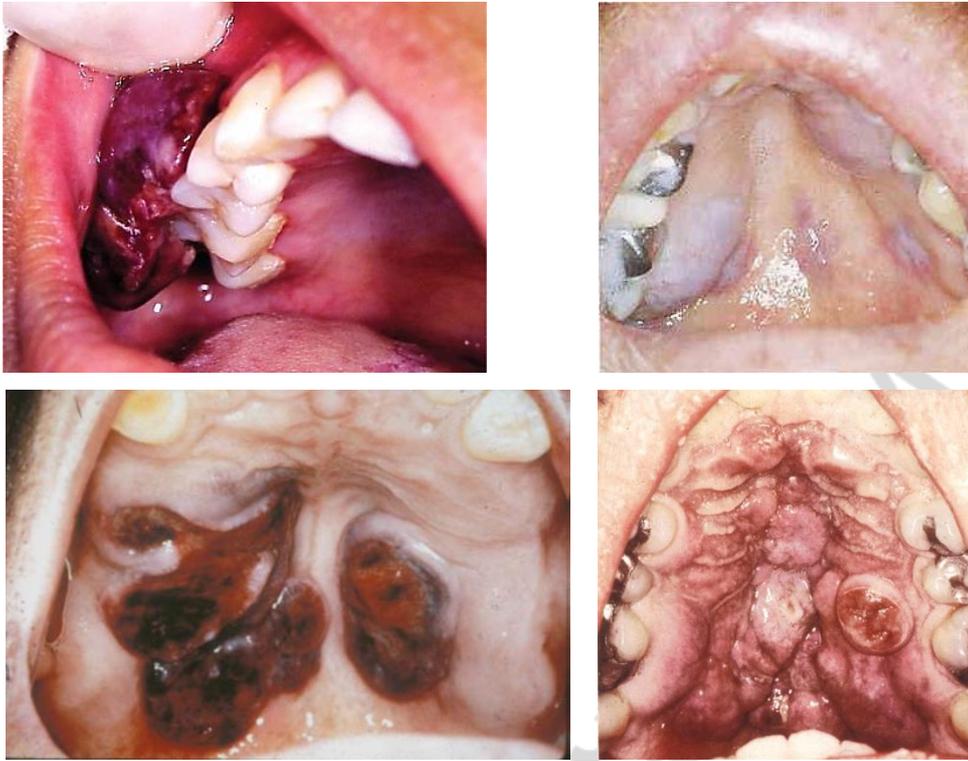


Fig. 8. Kaposi's sarcoma

Non-Hodgkin's Lymphoma. It is the second most common malignancy in AIDS. Lymphomas of B cell phenotype are a well-known complication of long-term immunosuppressive therapy. In HIV infection, suppression of cell-mediated immunity is accompanied with the evidence of increased B cell activity. Soft tissue masses are frequently affected by ulcerations and may resemble Kaposi's sarcoma. Treatment: chemotherapy, radiotherapy or a combination of both (fig. 9).



Fig. 9. Non Hodgkin's Lymphoma

METHODS OF DIAGNOSIS OF HIV INFECTION

Diagnosis of HIV infection is based on a comparison of epidemiological, clinical and laboratory data.

HIV Tests:

I — Antibody tests: Elisa or EIA; Western blot.

II — Viral test: RNA tests.

If HIV infection is suspected it is best to refer the patient for medical evaluation and laboratory assessment based on the appropriate screening tests. The standard recommended CDC screening test for HIV infection is the *EIA* or enzyme immunoassay which evaluates the presence of HIV antibodies. This test is performed on a blood draw which is a procedure not typically provided in the dental setting. Two tests are required to confirm a positive diagnosis.

GENERAL TREATMENT PRINCIPLES OF OPPORTUNISTIC INFECTIONS OF THE MOUTH IN HIV-INFECTED PATIENTS

- The success of treatment depends on the timely and correct diagnosis.
- Treatment of HIV-infected patients is more effective if it is provided on top of the highly active antiretroviral therapy.
- Treatment and prevention of a dental disease in such patients should be provided under the condition of strict compliance with the rules of administration of an adequate hygienic oral care.
- When conducting causal therapy the use of topical antibiotics is not recommended to avoid suppression of the resident oral microflora.
- Local treatment should be as non-traumatic as possible.
- Avoid the use of immunomodulators and immunostimulants of various types.
- Administered drugs should have minimal side effects.
- Surgical procedures should be carried out under the blood coagulability screening test.

Dental care to HIV-infected out-patients should be provided at the district public health organizations. Some HIV-infected patients may seek private medical advice. Accordingly, every dentist should be ready to provide medical assistance to this category of patients.

It should be noted that a HIV-positive status does not affect the treatment plan. However, the dentist dealing with a HIV-positive patient should consult with the patient's consulting doctor to have a more complete overview of the patient's condition and coordinate the treatment plan.

Necessary attention should be paid to the prevention of diseases in the oral cavity: hygienic education of patients, the use of fluoride preparations for topical application in the form of toothpastes and mouthwashes.

Administration of antibacterial drugs for pretreatment is recommended (metronidazole orally for a week, irrigation of the mouth with a chlorhexidine solution).

Treatment of HIV-gingivitis and HIV-periodontitis should include proper individual oral hygiene, professional hygiene and general antibiotic therapy. In addition to systemic administration of antibiotics chlorhexidine rinsing is recommended before and after periodontal treatment (for three days). In case of HIV-necrotizing gingivitis antifungal drugs are prescribed.

Local anesthesia should be of infiltration or intraligamentary type. Patients with blood coagulation disorders should not be given conduction anesthesia.

To prevent possible complications of endodontic treatment, antibiotics, and nonsteroidal drugs are recommended. Biological therapies are ineffective, since they presuppose good general and local resistance of the body.

Antimycotic agents are prescribed in the form of suspensions or solutions for topical treatment of mild forms of candidiasis. Antifungal creams are used for angular cheilitis. Systemic treatment of moderate and severe forms of the disease includes a 14-day course of fluconazole, voriconazole and itraconazole.

Treatment of Kaposi's sarcoma without highly active antiretroviral therapy is not effective. Local treatment includes X-ray therapy, cryotherapy, and chemotherapy. Surgical treatment can provoke the appearance of subsidiary associated lesions.

The rules of medical ethics are to be strictly followed while providing treatment to HIV-infected patients. Disregard or disapproval of these patients is unacceptable. Medical confidentiality must be observed. Disclosure of the fact of HIV/AIDS diagnosis of a patient is forbidden, otherwise the doctor may be held criminally liable.

PERSONAL PROTECTIVE EQUIPMENT

1. Latex or vinyl gloves must be used if there is a risk of contact with blood, blood-contaminated saliva, or mucous membranes (gloves should be worn for all procedures and for all patients).

2. Hand washing is necessary before putting on gloves and when changing gloves between patients. Old gloves are to be discarded. Washing or attempts at disinfection or sterilization of previously worn gloves are not allowed as these efforts are ineffective, may destroy the integrity of the gloves and cause cross contamination easily.

3. Chin-length plastic face shields or surgical masks and protective eyes shields are to be worn to protect the eyes from splatter during dental treatment. Masks are to be changed between patients and in the course of patient care if they become wet or moist. Face/eye shields should be washed with an appropriate cleaning agent.

4. Protective reusable or disposable gowns, laboratory coats, or uniforms must be worn when treating patients. It is recommended that reusable protective clothing be washed using a normal laundry cycle and changed daily if visibly dirty.

5. Waterproof paper, aluminum foil, or plastic covers should be placed on light handles or X-ray unit heads and other equipment where cleaning and disinfection is problematic. These materials should be removed, discarded and replaced between patients.

6. Rubber dams, high-velocity air evacuation, and proper patient positioning is recommended to reduce the formation of salivary particles and aerosols during treatment.

7. Splash shields are to be used in the dental laboratory.

SHARP INSTRUMENT AND NEEDLE MANAGEMENT

1. Potentially infective needles, burs, scalpel blades, files and other sharp instruments must be handled very carefully.

2. A one-handed “scoop” technique or a mechanical device designed for holding the needle sheath during recapping is the recommended approach for recapping. All needles are to be recapped after use or when re-placing on the operative tray or prior to disposal. Syringes and needles, scalpel blades and other sharp items must be placed in puncture-resistant containers for later disposal. Needles should not be bent or broken prior to disposal.

INJURIES AND HIV EXPOSURE

Sharp force injuries and other forms of exposure may occur during dental treatment and if the patient is known to be HIV-infected, appropriate post exposure management is critical.

• **If the contact with blood or other body fluids occurred with the damage of the skin (prick, cut), the victim must:**

- remove the gloves working surface inside;
- squeeze the blood out of the wound;
- treat the damaged area with one of the disinfectants (70 % alcohol, 5 % tincture of iodine for cuts, 3 % hydrogen peroxide solution for needle sticks, etc.);
- wash your hands in running water with soap, and then sponge the hands with 70 % alcohol;
- apply a patch on the wound, put on a finger cot;
- put on new gloves — continue the work if necessary.

• **In case of contamination with blood or other biofluid without skin damaging:**

- treat the skin with one of disinfectants (70 % alcohol, 3 % hydrogen peroxide, 3% chloramines solution);
- rinse the contaminated area thoroughly with soap sponge with alcohol again.

• **In case of contact of the biomaterial with mucous membranes:**

- mouth — rinse with 70 % alcohol;
- nose — instill 30 % Albucidum drops;
- eyes — rinse with water (clean hands), instill 30 % Albucidum drops.

• **In case of contact of the biomaterial with a dressing gown, clothing, footwear:**

- gloves are to be disinfected;
- in case of minor contamination with the biofluid, put off the clothes and place them into a plastic bag, then send the clothes for laundry without preliminary treatment or disinfection;

- in case of heavy contamination the clothes are to be soaked in a liquid disinfectant (excluding 6 % hydrogen peroxide and calcium hypochlorite neutral, which destroy fabrics);
- personal clothing contaminated with body fluids is to be washed in hot water (70 °C) and detergent;
- the skin of the hands and other body parts under the contaminated clothing is to be sponged with 70 % alcohol, then washed with soap and water and sponged with alcohol again;
- contaminated shoes are twice wiped with a rag soaked in a disinfectant solution.

Any exposure case should be immediately reported and medical treatment should be quickly provided (within one to two hours). Even with exposure by a percutaneous needle stick, there is a small risk of contracting AIDS (within 0.32 % as estimated in a number of studies) Mixed risk results are reported for mucous membrane exposure with one source indicating an estimated risk of 0.09 % and another less than 0.03 %.

Reported factors that increase the risk of HIV infection following exposure include: deep penetrating injury, visible blood on the injury device, injury from a needle placed in a patient's artery or vein and inoculation by a terminal HIV-related patient not on therapy or with a very high viral load.

It is important to note that the risk of contracting the infection through a needle sticks injury while providing dental aid to an untreated HIV-infected patient is low and if the patient is on HAART and has minimal HIV virus at the time of the needle stick injury, it may be considered virtually impossible. Further, it should be appreciated that pure saliva not contaminated by blood has not been implicated in the transmission of HIV. The virus, however, has been isolated from subgingival biofilm in HIV-infected patients. Hence, to be on the safe side the above precautions should be used in case of any type of exposure involving contact with oral fluids.

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