



National Institute of Dental and Craniofacial Research

Dental Management of the Organ or Stem Cell Transplant Patient

Notify the patient's physician if you notice signs of marked immunosuppression. In some cases, the dosage of anti-rejection agents prescribed for patients may need to be reduced. This may help control the opportunistic infections and other oral complications. However, there will be patients who must be maintained on high-dose immunosuppression. Treatment of oral opportunistic infection is necessary in any transplanted patient.

Common immunosuppressive drugs and their side effects include:

- **Cyclosporine:** Changes in liver/kidney function, hypertension, bleeding problems, and poor wound healing are among the adverse effects of this potent agent, which also interacts with a number of other drugs. Gingival hyperplasia occurs in some patients. Calcium channel blockers, for example, may exacerbate the problem. Children tend to be more susceptible to gingival overgrowth than adults. Emphasize conscientious daily oral hygiene to all patients.
- **Tacrolimus:** An immunosuppressive drug used increasingly in place of cyclosporine, tacrolimus causes less gingival overgrowth but is associated with oral ulcerations and numbness or tingling, especially around the mouth.
- **Azathioprine:** Bone marrow suppression and related complications such as stomatitis and opportunistic infections are significant side effects of this drug. A decrease in white blood cell counts and excessive bleeding may occur.
- **Mycophenolate mofetil:** This immunosuppressive drug is commonly used as an alternative to azathioprine. Adverse effects include decreased white

cell counts, opportunistic infections, and gastrointestinal problems.

- **Corticosteroids:** Steroid drugs increase the risk of oral and systemic infection, and at the same time, they may mask the typical signs of infection occurring in the mouth. Hypertension, high blood glucose (steroid-induced diabetes), poor wound healing, and changes in mood are other side effects of these drugs. If your patient has cushingoid facies (moon face), you may find oral lesions resulting from cheek and tongue biting. In addition, adrenal suppression may occur, making invasive dental and medical procedures more difficult for your patient.
- **Sirolimus:** Side effects of this immunosuppressive drug can include hypertension, joint pain, low white blood cell count, and hypercholesterolemia. In addition, because oral ulcers can result from high levels of sirolimus, refer a patient with oral ulcers to the transplant team for drug titration.

Chronic Graft-versus Host Disease

In patients who receive a stem cell transplant from a donor, an autoimmune-like disease called chronic graft-versus host disease (cGVHD) may develop, usually within two years of transplantation. cGVHD may affect multiple organ systems, including the mouth, and you should screen stem cell transplant patients at every dental visit because treatment and supportive care for pain, sensitivity, and dry mouth are important.

Oral cGVHD has three components: mucosal involvement, sclerotic involvement of the mouth and surrounding tissues, and salivary gland involvement:

- **Mucosa:** The oral mucosa presents with the classic findings in cGVHD, including lichenoid changes, erythema, ulcerations, hyperkeratotic patches, and mucosal atrophy.
- **Musculoskeletal tissue:** Limited mouth opening and limited tongue mobility may be caused by involvement of the temporomandibular joints or by sclerotic changes in the perioral tissues.
- **Salivary glands:** Salivary gland dysfunction may result from medication, inflammation, and fibrosis of the major and minor salivary glands.

Treatment and supportive care for the oral effects of cGVHD should be coordinated with the patient's medical team. Patients may need artificial saliva for dry mouth; topical immunosuppressive agents, such as steroid rinses, to manage their oral disease; and palliative agents, such as lidobenalox rinse or viscous lidocaine, to manage oral pain.

Oral Cancer

The long-term use of immunosuppressive drugs and other treatments puts transplant patients at risk of developing cancers, including cancers of the oral cavity. Squamous cell carcinoma, especially of the tongue, salivary gland, lip, or throat; oral Kaposi's sarcoma; and lymphoma are among the malignancies that sometimes occur in transplant patients. Because early detection of oral cancer is essential for effective treatment, screen patients at every appointment, and biopsy new oral lesions that lack a clear etiology.

Organ Rejection

If a patient's body begins to reject a transplanted organ, only emergency dental care may be provided. Before dental treatment, talk with the patient's physician about antibiotic prophylaxis or other special needs.

ADDITIONAL READINGS

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KEY POINTS

- Before and after organ or stem cell transplantation, patients require specialized dental management.
- Optimal dental management can play an important role in a transplant patient's quality of life.
- Work with the transplant patient's medical team and tailor dental treatment plans to meet the patient's special needs.

PATIENT POPULATION

According to the Health Resources and Services Administration, nearly 29,000 solid organ transplants and more than 6,300 stem cell transplants from unrelated donors were performed in the United States in 2013. Thousands more patients received stem cell transplants from their family members and far more than that received transplants from their own stem cells. Stem cell transplants are a treatment for life-threatening leukemia, lymphoma, or other diseases.

Of those who received a solid organ transplant in 2013, most (about 17,000) people received a kidney, usually because of end-stage kidney failure resulting from severe diabetes or high blood pressure. About 6,000 livers were transplanted, most often for people with hepatitis C virus or alcoholic liver disease. Other organs transplanted were the heart, lung, pancreas, and intestine.

Because the immune system of a transplant patient is compromised, the patient is at increased risk of oral and systemic infections and other complications and requires specialized dental care delivered by general dentists in collaboration with the medical team. Optimal management of the patient's oral health requires communication between the dentist and the medical team.

MANAGING ORAL HEALTH BEFORE TRANSPLANTATION

Before treating a prospective transplant recipient, obtain and review the patient's medical and dental histories, perform a noninvasive initial oral examination (without periodontal probing), and obtain radiographs. After the examination, discuss with your patient's physician the current status of your patient's overall health and immune system. Decisions about the timing of treatment, the need for antibiotic prophylaxis, precautions to prevent excessive bleeding, and the appropriate medication and dosage should be considered during your discussion.

Whether a patient can tolerate dental treatment is a crucial concern. For some patients, it will be safer to undergo extensive dental treatment after their overall health improves after transplantation.

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Preparing for Dental Treatment

Before starting your patient's dental treatment before transplantation, consider several factors:

- **Antibiotic prophylaxis:** Consult with the patient's physician to determine whether antibiotic prophylaxis is required to prevent systemic infection from invasive dental procedures. Unless advised otherwise by the physician, the American Heart Association's standard regimen to prevent endocarditis (<http://www.heart.org/>) is an accepted option.
- **Oral infection:** If the patient presents with an active oral infection, such as a purulent periodontal infection or an abscessed tooth, antibiotics should be given to the patient before and after dental treatment to prevent systemic infection. Confirm the choice of antibiotic with the patient's physician. Before transplantation, the active oral infection must be eliminated.
- **Excessive bleeding:** Several factors can cause bleeding problems in transplant candidates, such as the disease itself or medications. For example, patients may have a decreased platelet count or be on anticoagulant medications. Patients with end-stage liver disease may have excessive bleeding because the liver is no longer producing sufficient amounts of clotting factors. Before treatment, assess the patient's bleeding potential with the appropriate laboratory tests and take precautions to limit bleeding.
 - Consult with your patient's physician about whether antifibrinolytic drugs, vitamin K, fresh frozen plasma, or other interventions are appropriate for critical dental procedures. The physician also may decide to temporarily decrease the patient's level of anticoagulation before extensive dental surgeries.

Because of bleeding risk, some patients are suitable for surgery only in a hospital setting or dental offices designed to handle emergency medical situations.

- Use aggressive suctioning techniques when performing extractions or other invasive procedures to prevent your patient from swallowing blood. In a small number of patients with advanced liver disease, swallowed blood may increase risk for hepatic coma.
- Manage bleeding sites with careful packing and suturing techniques.
- **Medication considerations:** Patients preparing to undergo organ or stem cell transplantation may be taking multiple medications. These include anticoagulants, beta blockers, calcium channel blockers, diuretics, and others. Be aware of the side effects of these medications, which range from xerostomia and gingival hyperplasia to orthostatic hypotension and hyperglycemia, and their interactions with drugs that you might prescribe.

Likewise, use caution when prescribing medication to patients with end-stage kidney or liver disease. Many medications commonly used in dental practice, including NSAIDs, opiates, and some antimicrobials, are metabolized by these organs and are not removed from circulation as quickly in patients with markedly reduced kidney or liver function. Before dental treatment, consult the patient's physician on appropriate drug selection, dosage, and administration intervals.

- **Other medical problems:** Patients with end-stage organ failure may have other major medical conditions. A person with

end-stage kidney disease, for example, may have diabetes or significant pulmonary or heart disease. Carefully review your patient's medical history to determine what additional treatment considerations your patient may have.

Dental Treatment

Whenever possible, all active dental disease should be eliminated before transplantation, since post-operative immunosuppression decreases a patient's ability to resist systemic infection.

- Eliminate or stabilize sites of oral infection. Patients with active dental disease who can tolerate treatment should receive indicated dental care. Depending on the patient's condition, temporary restoration may be appropriate until his or her health improves.
- Extract nonrestorable teeth.
- Consider removing orthodontic bands or adjusting prostheses if a patient is expected to receive cyclosporine after transplant because some people taking this drug will develop gingival hyperplasia. The overgrowth can be minimized with good plaque control, and removing orthodontic bands may make it easier to maintain good oral hygiene.
- Conduct dental procedures on days that your patient with end-stage renal disease does not undergo hemodialysis.
- Pay special attention to your patient's anxiety and pain tolerance.
- Counsel the patient about oral health. Explain that effective oral hygiene is crucial before and after transplantation. The patient may experience fewer oral and dental problems after transplantation by reducing the number of oral bacteria and inhibiting their proliferation.

- Instruct patients to bring a current list of their medications, including over-the-counter drugs, to every appointment and note those medications that may be problematic.

MANAGING ORAL HEALTH AFTER TRANSPLANTATION

Except for emergency dental care, patients who receive organ or stem cell transplants should avoid dental treatment for at least 3 months. Dosage of immunosuppressive drugs is highest in the early post-transplant period, and patients are at greatest risk for serious complications, such as rejection of the transplanted organ, during that time. Once the graft has stabilized (which typically occurs within 3 to 6 months of the transplant procedure) and the medical team clears the patient for dental treatment, patients can be treated in the dental office with proper precautions.

Preparing for Dental Treatment

Treatment after transplantation requires consultation with your patient's physician. The medical consult can help you understand your patient's general health and ability to tolerate treatment. Post-transplant patients vary widely in their ability to endure dental treatment and heal following invasive procedures. Your discussion needs to address whether your patient requires antibiotic prophylaxis and if the physician will need to adjust other medications before treatment.

- **Infection:** Patients who have had a transplant procedure are at increased risk for serious infection. Bacterial, viral, and fungal infections are more common, especially immediately after the procedure. The decision to premedicate for invasive dental procedures and selection of the appropriate regimen should be done in consultation with the patient's physician.

- **Medication considerations:** Your transplant patient may be taking one or more medications that affect dental treatment. Immunosuppressive drugs can cause gingival hyperplasia, poor healing, and infections and may interact with commonly prescribed medications. Anticoagulant medications may contribute to excessive bleeding problems, whereas a patient taking steroids is at risk for acute adrenal crisis. The patient's physician may want to adjust these medications several days before an invasive dental procedure.

Dental Treatment

All new dental disease should be treated after the patient's transplant has stabilized.

- Check your patient's blood pressure before you begin treatment. Know baseline levels for each patient and call his or her physician immediately if blood pressure exceeds accepted thresholds. Do not treat a patient when this problem is present.
- Know your patient's bleeding potential and take appropriate steps to manage excessive bleeding.
- Prescribe an antimicrobial rinse when appropriate.
- Recommend saliva substitutes and fluoride rinses if your patient has dry mouth.
- Advise your patients to follow a conscientious oral hygiene routine and emphasize the importance of oral health.
- Examine the patient's mouth thoroughly for dental infection, since immunosuppressive drugs can hide signs of a problem. As a result, infections are

often more advanced than they appear when detected. Treat all infections aggressively.

- Watch for signs of adrenal insufficiency with surgical stress in patients taking steroids. These patients may require hydrocortisone replacement therapy at the time of extensive dental procedures to avoid adrenal insufficiency syndrome. A person experiencing this condition may become hypertensive, weak, feverish, and nauseated and should be transported immediately to a hospital for treatment.
- Exercise care in prescribing medications to avoid potentiating the renal and hepatic toxicities of immunosuppressant drugs. Consult the patient's physician to ensure proper drug selection and dosing.

Side Effects of Immunosuppressive Drugs

Immunosuppressive drugs are associated with side effects and oral complications. These adverse reactions are among the most frequent oral health problems affecting transplant recipients, and the clinical presentation of oral lesions may differ from that observed in immunocompetent patients.

Several complications associated with immunosuppression manifest in the mouth, including bacterial infections, oral candidiasis, reactivation of herpes simplex virus, uncommon viral and fungal infections, hairy leukoplakia, and aphthous ulcers. Oral ulcers may be caused by herpes simplex virus reactivation or side effects of systemic immunosuppression, and in stem cell transplant patients, oral ulcers may be a sign of graft-versus-host disease. In addition, progressive periodontal disease, delayed wound healing, and excessive bleeding may become problems for these patients.