

# Oral consideration and dental management in organ transplant patient

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## **Abstract:**

Organ transplantation is now a widely undertaken procedure. Life expectancy of patients who have undergone heart, lung, kidney, liver or bone marrow transplantation has improved dramatically over the past 10 to 20 years. The increase in the number of organ transplant patients has also had an impact on oral and dental services. Oral and dental problems that arise in these patients are usually consequences of drug induced immunosuppression.

The successful management of various oral lesions associated with organ transplantation patients necessitates close co-operation of dental physician with the various transplant teams. This will also ensure general well being of these patients.

*Key words:* Organ transplantation; complications; dental management.

## **Introduction:**

Transplantation has become a treatment of choice for restoration of body functions in the end stage organ diseases. Development of the immunosuppressive agents has reduced the morbidity associated with organ transplantation (OT) but at the same time has resulted in the appearance of several oral lesions.

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Patients who have undergone organ transplantation can present with a variety of oral lesions that appear to be related either directly to their medication or arise as a consequence of drug induced immunosuppression (1, 2).

### ***Historical background:***

Dr. Joseph E. Murray performed the first successful human organ transplantation between identical twin brothers in 1954.

In 1962 first kidney cadaver transplant was done.

In 1966 pancreas transplantation was performed successfully.

In 1967 first human heart transplant was done.

In 1968 first human liver transplantation with 13 months survival rate done.

In 1968 genetically related bone marrow transplantation, hematopoietic cell transplantation was done.

In 1990 lung transplantation with 60% survival of 5 years was done.

### ***Etiology:***

The signs and symptoms of disease necessitating transplantation are advanced cardiac and coronary artery disease, end stage renal disease, advanced liver diseases, diabetes mellitus, bone marrow transplantation, leukemia and immune deficiency syndromes (3).

### ***Classification of organ transplantation:***

There are two types of transplantations.

1] Solid organ/ tissue transplantation : examples heart, lung, kidney, liver, intestine, pancreas, skin, eye component.

2] Hematopoietic cell transplantation (HCT). The transplanted cell, tissue or organ is referred to as the graft and the types of transplants are shown in table 1.

### ***Transplantation immunology:***

It is the study of human immune response to alloantigen expressed by the donor organ/ tissue. After allogenic transplantation T-cells are activated. These T-cells interact with major histocompatibility complex (MHC) of donor cells to initiate reaction. MHC system is divided into two and it identifies self and nonself. MHC class I includes HLA- A, B, C, E, F, G. These antigens are expressed on most of the nucleated cells and red blood cells. MHC class II includes HLA-DR, DQ, DP, DO are present on antigen presenting cells (APCs) like macrophages, B-cells, dendritic cells and endothelial cells. The expression of these MHC gene products on a cell surface is regulated by various cytokines such as Interferon gamma (IFN- $\gamma$ ), Tumor necrosis factor (TNF). T- cells can be activated either by the donors or recipients APCs resulting in expression and production of lymphokines and cytokines, T-cell, NK-cells. This results in direct tissue damage and damage to the vascular endothelium of the graft which may ultimately result in graft rejection (3).

**Table 1: Types of transplants :**

Type of graft	Procedure	Description
Autograft	Autologous	Transplantation from self
Isograft	Syngeneic	Transplantation between genetically identical individual, monozygotic twin
Allograft	Allogenic	Transplantation from genetically different individual of the same species
Xenograft	Xenogenic	Transplantation between different species

**Table 2: Laboratory findings in advanced liver and renal diseases :**

Advanced Liver Disease	Advanced Renal Disease
↑se in Aspartate aminotransaminase	↑ se in Serum creatinine
↑se Alkaline phosphatase	↑ se in Blood urea nitrogen
↑ se Prothrombin time	↑ se in specific gravity of urine, proteinuria
↑ se Serum bilirubin	↓ sed Hematocrit
	Prolonged partial thromboplastin time
	↓ sed WBC count

**Table 3: Types of rejection:**

Type of rejection	Description
Acute	Occurs within days to weeks due to primary activation of the T-cell response
Chronic	Occurs in months to years after transplantation; probably occurs by continued, albeit muted, cell mediated toxicity.
Hyperacute	Occurs in minutes to hours after transplantation and is caused by preformed antidonor antibodies activating complex.

### **Laboratory findings before transplantation:**

Pre-operative assessment should include bleeding time (BT), hamatocrit, total WBC count, differential count, platelet count, prothrombin time (PT), partial thromboplastin time (PTT), serum bilirubin, alkaline phosphatase, blood urea nitrogen, serum creatinine, aspartate amino transferase, urine analysis for protein and specific gravity of urine. Laboratory findings in advanced liver and renal diseases are given in table 2.

### **Complications:**

Complications are broadly classified as

- 1] Complications caused by rejection shown in table 3
- 2] Complications caused because of the side effects of immunosuppressive drugs shown in table 4.
- 3] Medication induced complications like neurotoxicity, hepatotoxicity, bone marrow suppression, gastrointestinal disturbances, fever, chills, edema and thrombosis.
- 4] Complications related to oral cavity

Oral Lesions can be categorized into infectious process and non infectious process. Immunosuppressed OT patients are more susceptible to oral infections especially bacterial, viral and fungal infections. Severity mainly depends on level of immunosuppression. Bacterial infections like dentoalveolar abscess, dental caries and periodontal abscesses are more common and need proper culture and sensitivity tests and antibiotic prophylaxis. Viral infections like CMV (75%) of organ transplant patient are seropositive. HSV 50%, EBV, varicella

zoster are most common viral infections and can be treated by Acyclovir 1g/day or 200mg/3-4 time daily (4).

Oral hairy leukoplakia, which is usually associated with HIV, can occur in organ transplant and chronic immuno suppressed patients. Fungal infections like candidiasis and deep fungal infections are common in these patients. Combination of medications have significant higher incidence of candidiasis than that of the single regimen used as immunosuppressants and can be treated with topical antifungal agents like nystatin and amphotericin B (5, 6, 7).

Oral mucositis: Oral mucositis is induced by radiation therapy and chemotherapy, and is characterized by mild mucosal damage to extensive ulcerations and affects non keratinized surfaces. It begins by 6 to 12 th day and resolve by 14-18 days (8, 9).

Oral bleeding may occur during profound thrombocytopenia either due to active disease in patients with acute leukemia at diagnosis or secondary to chemotherapy induced myelosuppression (2).

Periodontal problems: Most of periodontal problems that occur in these patients are mainly because of long term use of immunosuppressive drugs. Gingival overgrowth associated with long term use of cyclosporine and calcium channel blockers. Overgrowth occurs within three months and the labial gingiva appears to be a predilection site. Better oral hygiene and the removal of plaque-retentive factors will improve the patients gingival health and it has been reported that systemic metronidazole (400 mg b.d. for 7 days) can

resolve cyclosporine-induced gingival  
Oral malignancy: Organ transplant patients appear to be more susceptible to the development of malignant neoplasms. Secondary malignancies like lymphoproliferative disorders, hematopoietic malignancies, solid tumors are most frequently observed in post transplant period (2, 8, 11).

GVHD (Graft versus host disease): It is caused by reaction of donor derived immunocompetent cells against the recipient tissues. Severity depends on the difference in histocompatibility, number of donor T-cells and use of immunosuppressant medication. Acute GVHD occurs in < 100 days after stem cell transfer and is characterized by apoptosis, necrosis and ulcerations of skin and oral cavity. Chronic GVHD occurs in > 100 days after stem cell transfer and it typically manifests as lichenoid changes, painful ulcerations, hyposalivation and hypersensitivity of teeth (12, 13).

Salivary gland changes and dry mouth: Xerostomia is common after HCT. There is a reduction in secretion of IgA after the transplantation and its level returns to normal after six months (14, 15).

Taste alteration: Hypogeusia or ageusia is common in organ transplant patients. In addition, cyclosporin and tacrolimus may induce metallic, salty, sour or bitter taste and can last for days to months (8).

Osteoporosis and bone loss: Long term corticosteroid therapy contributes to loss of bone density. Bisphosphonate leads to musculoskeletal pain and increased risk of osteoradionecrosis in the jaw (16).

changes (2, 10).

### ***Medical management:***

Pre-transplantation management of the transplant candidate mainly focuses on successful prevention of rejection and depends on high doses of chemotherapy, immunosuppressive agents and radiation therapy to prevent graft versus host diseases. So blood and tissue typing, standard ABO and Rh blood typing is performed to prevent red blood cell (RBC) agglutination and cross matching is done (3).

Post Transplantation Medical management includes three stages:

1. Immediate post transplant period: For the first three months after transplantation, patient should be on immunosuppressive therapy to prevent cytotoxic T-cells from destroying the graft. Patients are at greatest risk for technical complications, acute rejection and infection during this period. In this period only emergency dental treatments are carried out and elective procedures should be postponed.
2. Stable transplant period: Three months after transplantation when the graft is stable and functional. Medical considerations during this stage are related to the effect of immunosuppressive agents. Patients are susceptible to infections in case of overimmunosuppression and risk of acute rejection in case of underimmunosuppression.
3. Chronic Rejection Period: This is a period of total rejection. During this period, only emergency medical treatment should be provided (3).

**Table 4 Immunosuppressive agents and their side effects.**

<b>Drugs</b>	<b>Major side effects</b>
Azathioprine	Bone marrow suppression resulting in leucopenia, thrombocytopenia and anemia. Hepatotoxicity
Cyclosporine	Hepatotoxicity, nephrotoxicity, elevation of blood pressure, gingival hyperplasia, hirsutism, gynaecomastia,
Tacrolimus	Hepatotoxicity, nephrotoxicity, neurotoxicity, elevation of blood pressure, post transplant diabetes mellitus,
Mycophenolate mofetil	Immunosuppression, rejection leukopenia
Sirolimus	Hyperlipidemia, hypertriglyceremia
Muromonab – CD3	Cytokine Release Syndrome
Corticosteroids	Hypertension, diabetes mellitus, osteoporosis, improper healing, mental depression, psychosis, increase risk of infection

**Table 5: Recommended Standard Prophylactic Regimen For Dental Oral Procedures:**

<b>MEDICATION</b>	<b>REGIMEN</b>
Amoxicillin + metronidazole	2g + 500mg orally 1 hr before procedure
Amoxicillin, penicilline allergy	
Vancomycin	1g IV infused slowly over 1 hr preoperatively
Patients Unable to take medication:	
Ampicillin + metronidazole	2g + 500mg IV infused slowly over 1 hr preoperatively

***Dental management:***

Dental management during pre-transplantation or preconditioning phase should include oral/ dental evaluation by clinical radiography and identification of the foci of infection. All nonrestorable, nonvital and teeth with advanced periodontal diseases should be extracted. An active and effective oral hygiene programmes should be initiated. It should include tooth brushing, flossing, diet modification if necessary, topical fluoride application, plaque control and use of chlorhexidine and revidine mouth washes (1, 8).

Patient receiving dental treatment including dental prophylaxis needs medical consultation like degree of organ failure, need of antibiotic prophylaxis, selection of drug and modification of doses and precautions to avoid excessive bleeding. Laboratory tests such as assessment of current BT, PT, activated partial thromboplastin time (APTT), platelet count, WBC, differential count should be carried out before planning various surgical procedures.

Dental considerations in post transplant patient have three stages:

Immediate post transplant period (first six months)- During this period avoid routine dental treatment and continue oral hygiene procedures. Keep oral tissues, including lips moist. Avoid trauma and assess oral cavity for infection and bleeding. Consider sugarless chewing gums, salivary substitute, or sialogogues in patients with oral dryness.

Emergency dental care should be provided under medical consultation (1, 3).

Stable post transplant period: Maintenance of effective oral hygiene procedures and screening tests- BT, PT APTT, platelet count. Medical consultation regarding patient status, management and control of infection. Oral mucosal diseases must be diagnosed and treated at the earliest. Consideration of antibiotic prophylaxis and supplemental corticosteroid (steroid bust) and monitoring the oral cavity for oral complications (17, 18, 19).

Chronic rejection period: Render immediate or emergency dental treatment. Patients are very ill as they are immunosuppressed and have organ failure (1, 3).

***Conclusion:***

The field of organ transplantation is developing rapidly. Oral considerations in the transplantation population are many and new treatment strategies warrant continuous adaptation of oral care regimens to the changing scope of oral complications. A dentist needs an exceptionally strong knowledge base in medicine to minimize adverse outcome secondary to provision of oral health. It is incumbent on the dental practitioner to expediently diagnose and treat any oral infections. Patient's medical history should be updated with every dental appointment. Close coordination with transplantation physician is necessary as the patients medical condition can change quickly. Dentists must continue to inform

themselves of their role in the care of their patients.

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