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This article counts towards one of the five core subjects introduced in 2007 by the GDC.

# Routine and Emergency Management Guidelines for the Dental Patient with Renal Disease and Kidney Transplant Part 2

**Abstract:** Aimed at the practitioner in Special Care Dentistry, this is the second article in a two-part series providing guidelines on the dental management of renal patients. Dentists working in Special Care Dentistry will frequently be called upon to manage dialysis patients, whether pre- or post-transplant. The following paper deals with guidance as to the assessment, work-up and management of such patients when undergoing specialist dental treatment. The key to safe treatment is careful assessment, discussion and planning with the relevant team members.

**Clinical Relevance:** This paper provides guidance to the special care dentist for the dental management of patients with renal disease, and highlights issues in patients who are either on dialysis or have a kidney transplant.

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In the dental management of renal patients, liaison with the consultant nephrologist pre-operatively is of paramount importance. The extent of the planned dental treatment, potential surgical problems that might be

encountered and the likely morbidity the patient may experience must be assessed. The names and doses of the planned drugs should also be communicated to the nephrology team. This will allow them to verify appropriateness of drug doses or suggest modifications, if necessary.

interventions or general anaesthesia; they should not be used for vascular access unless in an emergency, for example, a cardiac arrest. Patients already on dialysis may benefit from observation overnight and arrangements must be made for their dialysis treatment whilst in hospital. Patients on peritoneal dialysis (PD) may be unable to perform the dialysis themselves if compromised by sedation and analgesia, and will therefore need assistance.

A suggested process of assessment, preventive regimes and advice regarding necessary work-up when undertaking oral care procedures in renal patients are summarized in Tables 1-3.

## Dental care in pre-dialysis patients

There is no universally accepted definition of what is a pre-dialysis patient. Most people would use the term for patients in whom renal replacement therapy will be

## Treatment in a theatre environment

The special care practitioner may consider that some patients in end stage renal failure should have their oral care provided in a theatre environment where they can be monitored more closely by the medical team. Additionally, anxiety management strategy should be considered for renal patients. Discussion with a consultant anaesthetist, ideally the one who will be present at the time of treatment, should be part of the planning process.

Dialysis fistulas and grafts should be protected against pressure during lengthy

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Issue	Work-up	During Treatment/Intervention
Assessment	<p>Full medical history/ drug history.                      Current level of health.                      Establish which consultant in renal medicine involved.                      Establish renal function – renal failure can be variable in severity.                      Establish stability of BP.                      Establish allergies, especially antibiotics.</p>	
Examination and treatment planning	Radiography.	<p>Be realistic in overall treatment planning.                      Fatigue probable during treatment.                      Consider most appropriate environment for delivery of oral care.                      Consider anxiety management.</p>
Liaison with other consultants	<p>Liaise with consultant in renal medicine, outline dental needs.                      Liaise with the renal team stating your intended management work-up.                      Liaise with consultant anaesthetist additionally if treatment in theatre proposed.</p>	
Prevention	<p>Diet advice (may be on restricted fluid/salt/ potassium diet).                      Dry mouth supplements.                      Oral hygiene.                      Oral pain/discomfort.</p>	<p>Prescribe sodium fluoride toothpaste (adult 1.1%).                      Example: <i>BioXtra</i> oral gel. Care with some salivary substitutes – liaise with consultant.                      Chlorhexidine gluconate 0.2% gel or 1% rinse .                      Benzydamine hydrochloride 0.15%.</p>
Analgesia and anti-fungals	Paracetamol is safe.	<p>Avoid aspirin. Strictly avoid NSAID and COX-2 inhibitors in pre-dialysis and transplant patients.                      Oral amphotericin is safe. Avoid miconazole and fluconazole in renal transplant patients – both increase serum ciclosporin.</p>
Local anaesthetic	<p>Lignocaine may have reduced renal clearing in stage 5 renal failure.                      Other local anaesthetics, check with manufacturer.</p>	Care with dosage of local anaesthetic – risk of overdosage.
Extractions	Full Blood Count, coagulation screen to determine platelet level and INR/APTT.	Altered platelet and prothrombin function and poor haemostatic function puts patient at risk of post-operative bleeding DDAVP 0.3mcg/kg subcutaneously or IV. This needs special expertise and dentists should seek advice.
Any procedure causing gingival trauma including restorations, S&P, RCT	FBC to establish neutrophil count. Determine concomitant heart disease that would require endocarditis prophylaxis independent of the renal situation.	If WBC less than lower normal limit, may require antibiotic cover. Liaise with nephrologist.
Steroid cover and dental extractions	Determine if patient has received 10 mg of prednisolone or greater during last 3 months.	Consider IV steroid cover if patient unable to take the regular oral medication. Additional steroids, eg hydrocortisone 15 min pre-op may be required. Monitor BP during procedure.

**Table 1.** Oral management in pre-dialysis patient.

Issue	Work-up	During treatment
Establish all in Table 1	Liase with consultant nephrologist. Ideal treatment day is day after dialysis.	
AV fistula	Determine presence of AV fistula.	Do not place cannula or BP cuffs on an arm with a functioning AV fistula (AV fistula may be cannulated by non-renal personnel in cardiac arrest). Seek advice whether antibiotic cover required for protection of shunt.
Bleeding	<p>Establish whether haemodialysis (HD) or peritoneal dialysis (PD) patient.</p> <p>Consider FBC/coag screen/prior to dental extractions or other procedures.</p> <p>INR readings must be recent- ie within preceding 24 hours of treatment.</p> <p>All renal patients on a combination of anticoagulants such as clopidogrel, aspirin or warfarin should be treated in a secondary care setting.</p>	<p>HD: Avoid all dental work on haemodialysis days (heparin exposure and bleeding) and schedule dental treatment on non-dialysis days. Heparin will be cleared 12 hours after administration.</p> <p>If extraction unavoidable on dialysis day, liaise with nephrologist. Elective reduction of heparin dose during dialysis is usually possible. Patients can sometimes be dialysed with saline instead.</p> <p>Aspirin/clopidogrel/warfarin: do not stop drugs. Liaise with nephrologists or haematologist if extraction complex or multiple.</p> <p>PD: timing of dental work uncomplicated as no heparin exposure; no inherent bleeding tendency.</p> <p>Aspirin/ clopidogrel/ warfarin: Do not stop drugs Liaise with nephrologists or haematologist if extraction complex or multiple.</p>

**Table 2.** Oral care in dialysis patients.

required within a year. These patients pose a particular challenge as they are going through a phase of transition towards dialysis dependency. This brings about changes in their life pattern, possible worsening of symptoms and an impaired ability to function. Dental problems may not be a high priority for these patients and may therefore often be ignored.

Conversely, many patients with early renal failure are treated successfully in general dental practice. The main problems for the general dental practitioner are:

- Which drugs can be used safely?
- The correct dosage;
- Drugs that should be avoided; and
- Achieving adequate haemostasis post-operatively.

These issues usually occur once a patient has progressed to CKD stage 3 or beyond and further work-up may be required to ensure safety of the patient when undergoing certain dental procedures.

Nephrotoxic and non-steroidal anti-inflammatory drugs should be avoided in pre-dialysis patients. This includes COX-2 inhibitors (the Coxibs).<sup>1</sup> The use of paracetamol and local anaesthetic solution is generally safe. Mepridine should not be used as it can result in seizures in CKD patients because of the accumulation of toxic metabolites. Antibiotics are generally safe, as long as dose adjustment is made for the degree of renal dysfunction according to GFR (Table 4) and formulations containing potassium salts are avoided. Hypertension is also common at this stage and often requires a combination of three to five anti-hypertensive drugs to control blood pressure. Patients should be advised to take their morning medication before the dental procedure.

Achieving adequate haemostasis can be a concern following dental procedures. This may be multi-factorial and use of anti-coagulant drugs is often implicated. These

drugs should be temporarily discontinued only after liaison with a physician or nephrologist. Dental practitioners may wish to seek advice from a renal physician prior to elective procedures in renal patients who appear chronically ill. Uraemia-induced bleeding disorder is rare and usually only seen in CKD stage 5. Its presence is suggested by a prolonged bleeding time while INR and aPTT remain normal. This can be treated with desmopressin (DDAVP), which is usually effective for up to 4 hours. The usual dose is 0.3 mcg/kg, given subcutaneously or intravenously. This needs special expertise and dentists should seek advice.

Anaemia with haemoglobin of less than 10 g/dl may be a relative contra-indication for general anaesthesia and can be corrected within a few weeks with iron infusions and erythropoietin injections.

Endocarditis in renal patients carries a higher mortality, but the current recommendations of NICE<sup>2</sup> highlight that

Issue	Work-up	During Treatment
Establish all as per Table 1	Liaise with consultant nephrologist, as above.	
Bleeding	Many are on aspirin, clopidogrel, or warfarin.  Consider FBC/coag screen/prior to dental extractions or other procedures.	These patients have no inherent bleeding tendency, except those resulting from anticoagulant drug regime (as opposed to uraemic pre-dialysis patients).  If on aspirin and/or clopidogrel, do not stop aspirin or clopidogrel; liaise with nephrologist.
Drug dosing		Antibiotic drugs may need dose adjustment: liaise with nephrologist.
Drug interactions	Establish whether on ciclosporin or tacrolimus (both drugs most vulnerable to interaction).	Avoidazole anti-fungals in renal transplant patients – both increase serum ciclosporin and tacrolimus.  Be careful about any new drug: have a low threshold to liaise with transplant team.
Endocarditis prophylaxis	See NICE guidelines.	CG64 Prophylaxis against infective endocarditis: NICE guidance.
Gingival enlargement	Ciclosporin and Ca-channel blockers can cause gingival enlargement.	Intensive OHI necessary to restrict gingival overgrowth and chlorhexidine gluconate 0.2% oral rinse.  If severe, liaise with nephrologist: conversion of immunosuppression and withdrawal of calcium antagonists are usually very effective.
Medications	Patients will be on immunosuppressive drug regime.  May require steroid cover if oral intake of immunosuppression compromised.  Many are on aspirin, clopidogrel or warfarin.	Liaise with nephrologists as immunosuppressed re antibiotic prophylaxis prior to any procedure causing bacteraemia.  Should have low threshold for antibiotic prophylaxis if extensive dental work, even if no cardiac valvular disease.
Mouth ulcers in patients treated with mTOR inhibitors (sirolimus, everolimus)	Mouth ulcers are very common in patients taking mTOR inhibitors, such as sirolimus.	Liaise with nephrologist: sirolimus levels need to be checked; dose reduction or (severe cases) conversion of immunosuppression and withdrawal of mTOR inhibitors may be considered.
Pain	Paracetamol is safe.	Strictly avoid NSAID and derivatives as well as COX-2 inhibitors in transplant patients.

**Table 3:** Oral care in renal transplant patients.

antibiotic prophylaxis is not required for patients undergoing dental procedures. The basis for this recommendation is that no consistent association has been shown between dental procedures and increased risk of infective endocarditis (IE). The recommendation also stems from recent research that demonstrated transient bacteraemia due to normal oral

commensals, even after simple daily procedures such as brushing the teeth.<sup>3</sup> Moreover, antibiotics are not proven to reduce the risk of IE and are themselves not without side-effects and risk of anaphylaxis. The use of indwelling lines and grafts for dialysis (as opposed to native dialysis fistulas) were identified as risk factors.<sup>4</sup> There are no specific recommendations for

renal patients, although endocarditis in these patients carries high mortality rates.<sup>5</sup> We would recommend close liaison between dentist and nephrologist so that a joint decision can be made, based on the extent of the planned dental procedure as well as the individual patient profile, for example age co-morbidity and degree of immunosuppression.

DRUG	GFR 20-50	GFR 10-20	GFR <10	Peritoneal Dialysis	Haemodialysis
Amoxicillin	Normal dose	Normal dose	250 mg TDS	250 mg TDS	250 mg TDS
Clarithromycin	Normal dose	250–500 mg 12–24 hourly	250 mg 12–24 hourly	250 mg 12–24 hourly	250 mg 12–24 hourly
Clindamycin	Normal dose	Normal dose	Normal dose	Normal dose	Normal dose
Co-amoxiclav	Normal dose	Normal dose	375 mg TDS	375 mg TDS	375 mg TDS
Erythromycin	Normal dose	Normal dose	50–75% of normal dose (max 1.5 gm daily)	50–75% of normal dose (max 1.5 gm daily)	50–75% of normal dose (max 1.5 gm daily)
Fluconazole	Normal dose	Normal dose	50% of normal dose	50% of normal dose	50% of normal dose (given post-dialysis)
Fusidic acid	Normal dose	Normal dose	Normal dose	Normal dose	Normal dose
Metronidazole	Normal dose	Normal dose	Normal dose every 12 hours	Normal dose every 12 hours	Normal dose

**Table 4.** Dose adjustment of commonly prescribed antibiotics according to renal function.

### Dental care in dialysis patients

Signs and symptoms related to oral disease are common in dialysis patients, and occur more frequently in those who have diabetes as well. The high prevalence of uraemic fetor, xerostomia, saburral tongue and candidiasis could be early warning signs of the possibility of non-diagnosed advanced renal disease in diabetic patients.<sup>6</sup> Dental infections may have the potential of causing bacteraemia and thus infecting tunnelled lined and AV grafts.<sup>7</sup> However, there may be considerable variations in treatment regimes between countries, depending on the health system and how dental care is provided. In this regard, a study from the Netherlands demonstrated no difference in oral health between patients on dialysis and controls.<sup>8</sup>

The most common concern that dental surgeons have to deal with is the enhanced bleeding tendency during procedures. In patients who are on maintenance haemodialysis, uraemic platelet dysfunction should not be a major issue. However, the timing of the procedure should be carefully selected, and procedures should generally be performed on non-dialysis days. Patients are usually heparinized during dialysis to prevent blood clotting in the dialyzers. Heparin has a half-life of 1–2 hours

and the effect therefore usually wears off in 6–10 hours. Patients who are adequately dialyzed on peritoneal dialysis generally do not have enhanced bleeding tendency, and dental procedures need not be specifically timed, although liaison with the nephrologist is recommended. Patients, who normally perform peritoneal dialysis themselves at home, may temporarily need help if they are compromised by sedation or pain.

Whilst contra-indicated in pre-dialysis patients, NSAIDs can be used in dialysis patients<sup>9</sup> provided there is no ongoing issue with gastritis or peptic ulceration. However, they can still impair any residual urine output (some dialysis patients may still have good urine output, and paracetamol and opioids are therefore preferable). Other drugs, including antibiotics, can be used with dose adjustments, depending on whether the patient is on haemo- or peritoneal dialysis (Table 4).

### Dental care in kidney and kidney-pancreas transplant candidates

This is another controversial issue at the interface between nephrology and dentistry. Again, data are sparse and there are no universally accepted recommendations. Rustemeyer and Bremerich<sup>10</sup> studied 204

transplant candidates for solid organ transplantation who had been referred for dental work-up. They demonstrated that as many as 70% of transplant candidates required dental procedures prior to transplant listing; as any untreated potential focus of infection can cause problems once these patients are on immunosuppressives post-transplant. Notably, under conditions of immunosuppression post-transplant, there is an increased risk that a source of infection can flare up and lead to widespread local and systemic infection. Most transplant patients are also on corticosteroids, which may delay wound healing. As such, dental treatment should be undertaken prior to transplantation. Therefore the authors recommend that a thorough oral and radiographic examination should be a part of the pre-transplant work-up for all patients.

### Dental care after kidney and kidney-pancreas transplantation

Gingival hyperplasia is a common dental problem in transplant recipients. This has an increased prevalence in patients who are immunosuppressed with ciclosporin and is aggravated by concomitant use of calcium channel blockers for hypertension.<sup>11</sup> Counselling regarding oral hygiene and

the use of a chlorhexidine gluconate 0.2% mouthrinse is often effective in mild cases.<sup>12</sup> Stopping the calcium antagonist can be beneficial. More severe cases will need conversion of the immunosuppression to tacrolimus. However, the data on tacrolimus are controversial. The drug has been reported to increase,<sup>13</sup> as well as reduce the risk of<sup>14</sup> gingival hyperplasia. Surgical or laser excision of gingival tissue may be required for cosmetic or functional reasons.

Oral ulceration can occur frequently in patients on an immunosuppression regimen based on mammalian target-of-rapamycin (mTOR) inhibitors. These drugs, such as sirolimus and everolimus, have a unique mode of action and the occurrence of oral ulcers usually reflects high drug levels. These ulcers respond well to dose adjustment.

Another common finding is oral candidiasis. Oral candidiasis can be seen in many transplant patients. Lesions include pseudo-membranous, erythematous and chronic atrophic candidiasis.<sup>15</sup> All azole anti-fungals interact with ciclosporin as well as tacrolimus at cytochrome P450 enzymes, thus inhibiting their metabolism with a resultant increase in serum levels. As such, anti-fungals should not be prescribed without advice from a renal physician. Fluconazole may be prescribed if indicated, but the dose should be adjusted and ciclosporin levels closely monitored for a possible elevation. Amphotericin lozenges are a safe alternative in mild disease.

Amongst topical anti-fungals, clotrimazole is not absorbed from intact or inflamed skin into the circulation. Terbinafine (Lamisil) has less than 5% absorption with no significant drug interactions. Although little of miconazole (Daktarin) cream is absorbed through the skin when applied topically, miconazole (Daktarin) oral gel may be swallowed and can get into the systemic circulation in sufficient amounts to interact with, and cause a possible increase in, drug levels of ciclosporin, tacrolimus and sirolimus. Close monitoring and possible dose reduction of ciclosporin is recommended in such cases. However, an interaction with intravaginal miconazole would not normally be expected because its systemic absorption is usually very low (less than 2%).<sup>16</sup> In summary, there is little systemic absorption from these topical preparations, with the exception of miconazole oral gel. In addition, there is a potential interaction with ciclosporin and

miconazole oral gel.

Long-term immunosuppression also predisposes transplant patients to malignancies, such as squamous cell carcinoma of the oral cavity, which may develop in areas of gingival hypertrophy.<sup>17</sup> Human herpesvirus 8 (HHV-8) associated with Kaposi's sarcoma has an increased incidence in transplant recipients. Lymphoma associated with the Epstein-Barr virus is also seen in transplant patients and may occasionally affect the oral mucosa,<sup>18</sup> manifesting as hairy cell leukoplakia.<sup>15</sup> It is therefore important that there is a low threshold for biopsy if new intra-oral lesions occur in transplant patients.

Transplant patients are recommended to have an annual dermatological review owing to the increased risk of carcinoma. If a dental practitioner encounters a suspicious lesion on the face or lips of patients, an urgent referral should be made.

## Conclusion

Patients with renal failure often have a complex medical history and pose specific problems to the dental team. Many patients with mild renal disease are treated successfully in general dental practice, while patients with advanced stages of renal failure and co-morbidity may be more suitable for the specialist in special care dentistry. In these patients, the dosage of many drugs needs to be adjusted according to the residual kidney function, while other drugs, such as the NSAIDs, should be avoided altogether. The risk of endocarditis is also markedly increased compared to the general population, although specific guidelines for these patients do not exist. Dialysis patients may pose specific problems to the dental team and close liaison between renal and dental teams is recommended.

Before any dental treatment is undertaken it is important that a risk assessment of all renal patients is undertaken, as such specific problems can be identified and discussed with the nephrology team. This will enhance the patient experience and reduce the risk of possible complications.

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