Oral and Dental Aspects of Chronic Renal Failure

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(1) INTRODUCTION

The incidence of chronic renal failure (CRF) continues to rise worldwide (Ansell and Feest, 2002; McDonald and Russ, 2002; US Renal Data System, 2002), and, as a consequence, increasing numbers of individuals with such disease will probably continue to require oral health care. CRF and its treatment have systemic and oral manifestations. There are few detailed reports of the oral and dental disease manifestations, and of the relevant treatment needs of patients with CRF. Likewise, there are no systematic reviews of the treatment of oral disease in patients with CRF. The present report reviews current information published in peer-reviewed journals or available from relevant nationally (e.g., within the US or UK) or internationally recognized sources—that the oral and dental aspects of renal disease, highlighting the variable impact of CRF upon the mouth, and provides guidance for the dental treatment of patients with CRF.

(II) CHRONIC RENAL FAILURE

Chronic renal failure (CRF) is defined as a progressive decline in renal function associated with a reduced glomerular filtration rate (GFR, as measured clinically by the creatinine clearance rate). The most common causes are diabetes mellitus, glomerulonephritis, and chronic hypertension. In older individuals, the most commonly diagnosed cases of CRF are renovascular disease and diabetes mellitus, although other conditions cause poly cystic kidney disease and pyelonephritis (Ansell and Feest, 2002; McDonald and Russ, 2002; US Renal Data System, 2002).

(III) EPIDEMIOLOGY

Data on the epidemiology of CRF are available in many countries, although different sampling techniques are used in each country, and units in some regions (e.g., the UK) are not obliged to report patient figures. The reported incidence of CRF is 337, 90, 107 and 95 per million population (pmp) in the USA, Australia, New Zealand, and the UK, respectively. The incidence increases with age, and males are more commonly affected than females. Incidence also varies with ethnicity. For example, in the USA, Caucasians and Black Americans have higher incidences than Asians and Native Americans. However, in the UK, the incidence of CRF is higher in Asians and Afro-Caribbeans than in Caucasians (Roderick et al., 1994).

The death rate is 178, 189, 217, and 209 per 1000 patient years (pyr) in the USA, Australia, New Zealand, and the UK, respectively (Table 1). These figures suggest that the USA has a lower death rate than the UK, but the USA data do not include deaths in the first 90 days following the onset of chronic renal failure. However, the UK death rate at 1 year and 90 days (188/1000 pyr) is comparable with that in the USA. There are only slight differences in the death rates between genders. Ethnicity also affects death rate: in the USA, it is lowest in Asians (130/1000 pyr) and highest in Caucasians (193/1000 pyr).

Survival rates vary with ethnic origin and the underlying cause of renal failure. In the USA, for example, the five-year survival rate
for Caucasians is lower than that for Black Americans (34.7% compared with 46.8%). The prognosis for individuals with diabetes mellitus and/or hypertension is worse than that for individuals with glomerulonephritis (30.9% and 36.5%, compared with 59.9%). A comparison of these figures with the five-year survival rate (62%) for all cancers in the USA highlights the poor prognosis for individuals with chronic renal failure (US Renal Data System, 2002).

The most common cause of death is cardiac failure, followed by infection and malignancy (Ansell and Feest, 2002; McDonald and Russ, 2002; US Renal Data System, 2002). Diabetes mellitus and hypertension greatly increase this risk (Santiago and Chanzan, 1989).

(IV) CLINICAL FEATURES

The clinical signs and symptoms of renal failure are collectively termed 'uremia'. CRF affects most body systems, and the clinical features are dependent upon the stage of renal failure and the systems involved. For example, early features are typically nocturia, polyuria, and anorexia. Tables 2 and 3 outline the signs, symptoms, and clinical features of CRF (Stein and Wild, 2002).

(V) TREATMENT OF CHRONIC RENAL FAILURE

The treatment of CRF includes dietary changes, correction of systemic complications, and dialysis or renal graft receipt.

Dietary and fluid restrictions may be required to accommodate the reduced excretory capacity of the kidneys. Acidosis and increased levels of potassium can be treated by reducing dietary intake of potassium-rich foods, such as bananas, and sodium restriction can aid the control of hypertension. It is sometimes necessary to reduce protein consumption to minimize nitrogenous waste products. Despite this treatment, most patients progress to end-stage renal failure (ESRF), requiring dialysis or transplantation.

(a) Dialysis

There are two types of dialysis: hemodialysis and peritoneal dialysis (PD). In each case, the patient's blood is separated from the dialysis fluid (dialysate) by a membrane which allows water and toxins, but not blood cells, to pass out of the blood. In PD, the peritoneal membrane acts as the filter, whereas, in hemodialysis, the membrane is within the dialysis machine. Individuals commonly commence with PD and may progress to hemodialysis if renal function deteriorates further.

Most affected patients receive hemodialysis for up to 4 hrs, 2 or 3 times each week (Ansell and Feest, 2002). Arteriovenous fistulae in the arm are required for regular vascular access via wide-bore needles. The fistula is usually fashioned from a native vein; however, it is sometimes necessary to use animal or synthetic grafts if the local anatomy is unsuitable (Werner and Spa, 1999). Hemodialysis increases the risk of viral transmission (such as HIV and hepatitis B and C; Pol, 1995) and is costly.

In comparison of the cost-effectiveness of hemodialysis and PD, one finds that the latter has less initial cost, but the long-term cost of the two techniques is similar. Although the two techniques are equally effective and appropriate for most patients, it is common, at least in the UK, to begin with PD, since the veins will be available should the technique fail and hemodialysis become necessary (Stein and Wild, 2002).

For PD to take place, a catheter is placed into the peritoneum through which the dialysis fluid is exchanged. Continuous ambulatory peritoneal dialysis (CAPD) requires 4 exchanges of approximately 2 liters throughout the day. An alternative method is automated peritoneal dialysis (APD), in which the dialysis fluid exchanges are carried out automatically by machine, during the hours of sleep (for 8-10 hrs).
(b) Renal Transplantation
Renal allografts may be cadaveric or from living donors, either related or non-related (although those from living relatives give rise to the best prognosis). Cadaveric organs are allocated on the basis of HLA tissue-typing, ABO compatibility, and the age and size of the donor and recipient.

In the UK, during 2001, 1743 (29.6 per million population) kidney transplant operations were performed (http://www.uktransplant.org.uk/statistics/ transplant_activity/, http://www.statistics.gov.uk/census2001/pop2001/ united_kingdom.asp). These consisted of 1385 cadaveric and 358 living donor renal transplants. The majority (263) of the living donors were relatives. The one-year success rate is presently 86% for cadaveric and 95% for living-donor-transplanted kidneys (www.uktransplant.org.uk/). The principal cause of allograft failure is rejection, although adverse drug side-effects may also be a contributing factor.

Immunosuppressant therapy is required to minimize the risk of allograft rejection. Commonly used agents are prednisolone, azathioprine, cyclosporin, and, more recently, tacrolimus. Cyclosporin has been associated with potentially serious side-effects, including nephrotoxicity (Grinloy and Cruzado, 2004), hepatotoxicity, neurotoxicity, hypertrichosis, and diabetes mellitus (Ota and Bradley, 1983; Svirsky and Saravia, 1989; Pirsch et al., 1997; Al-Zayer et al., 2001). Tacrolimus has adverse side-effects similar to those of cyclosporin, such as nephrotoxicity and neurotoxicity (Mihatsch et al., 1998); however, diabetes is a more frequent complication (Zuckermann et al., 2003) and occurs in up to 37% of patients receiving tacrolimus (McDonald and Russ, 2002). Hypertension and cytomegalovirus infection are less common with tacrolimus than with cyclosporin therapy. In addition to immunosuppressants, recipients of renal allografts require an array of medications, some of which can give rise to oral side-effects (see below).

(VI) ORAL MANIFESTATIONS OF CHRONIC RENAL FAILURE AND RELATED THERAPIES

(a) Gingival Enlargement
Gingival enlargement secondary to drug therapy is the most-reported oral manifestation of renal disease. It can be induced by cyclosporin and/or calcium channel blockers. It principally affects the labial interdental papillae, although it can become extensive, involving the gingival margins and lingual and palatal surfaces (Somacerrara et al., 1994; Kennedy and Linden 2000).

(i) Cyclosporin-induced Gingival Enlargement
The prevalence of gingival enlargement in individuals taking cyclosporin is unclear, and reportedly has a wide range—from 6 to 85% (Seymour et al., 1987; Slavin and Taylor, 1987; Pan et al., 1992; Perriu et al., 1992; King et al., 1993; Thomason et al., 1993; Allman et al., 1994; Somacerrara et al., 1994). It can be evident within 3 mos of the initiation of cyclosporin therapy (Savage et al., 1987; Thomason et al., 1996). Children and adolescents may be more prone to this drug-induced gingival enlargement than adults. If oral hygiene is poor, older individuals are also prone to gingival enlargement (Seymour and Smith, 1991).

Improvement in oral hygiene and professional cleaning results in a reduction in cyclosporin-associated gingival enlargement (Thomason et al., 1993, 1996; Somacerrara et al., 1994; Fu et al., 1997). However, this may be due to reduction in plaque-related inflammation rather than any drug-associated gingival enlargement (Seymour and Smith, 1991). There are conflicting reports on the association between gingival enlargement and cyclosporin dose (Porter and Scully, 1994), but the extent of the gingival enlargement does not seem to be related to the function of the allograft (Thomas et al., 2001).

Regular clinical monitoring of cyclosporin-related gingival

<table>
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<th>Table 3. Clinical Features of Chronic Renal Disease</th>
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enlargement is essential, since squamous cell carcinoma (Varga and Tyldesley, 1991) and Kaposi’s sarcoma have been reported within such gingival lesions (Qutibi et al., 1988; Farge, 1993).

(ii) Calcium Channel-blocker-induced Gingival Enlargement

Calcium channel blockers are prescribed to renal allograft recipients to reduce hypertension and cyclosporin-induced nephrotoxicity (Morales et al., 1994). There are many reports of nifedipine, amldipine (Seymour et al., 1994; Ellis et al., 1999), diliazem (Colvard et al., 1986; Giustinianni et al., 1987; Bowman et al., 1988; King et al., 1993), verapamil (Cucchi et al., 1985; Perne et al., 1989), oxicpine, felodipine, and nitrendipine (Hassell and Heft, 1991; Rees and Levine, 1995) causing this gingival enlargement. The reported prevalence of nifedipine-induced gingival enlargement is variable and occurs in 10-83% of treated patients (Seymour et al., 1987; Barclay et al., 1992; Ellis et al., 1999). There are no data on the frequency of gingival enlargement with the other calcium channel blockers.

The presence of dental plaque may predispose to nifedipine-induced gingival enlargement (Nishikawa et al., 1991), but is not essential to its development (Morisaki et al., 1993). The dose or duration of treatment is not related to the prevalence of gingival enlargement (Barclay et al., 1992; Ellis et al., 1993). Some studies have reported a reduction in gingival enlargement following a change to an alternative calcium channel blocker (Ledermark et al., 1984; Cebec et al., 1996), but these drugs can still cause some gingival enlargement (Westbrook et al., 1997).

(iii) Combined Cyclosporin and Calcium Channel-blocker Therapy

There may be an increased incidence (Thomason et al., 1995, 1996; Mariggiotta et al., 1996; McKaig et al., 2002) and severity (King et al., 1993, 1994; Thomason et al., 1993, 1995, 1996; O’Valle et al., 1995; Mariggiotta et al., 1996; McKaig et al., 2002) of gingival enlargement when cyclosporin and nifedipine are prescribed together. In contrast, the combination of verapamil with cyclosporin does not seem to increase the frequency or severity of drug-induced gingival enlargement significantly (Cebec et al., 1996).

(iv) Tacrolimus

Tacrolimus has been reported both to cause (Adams and Famili, 1991; Spencer et al., 1997) and to lessen (Asante-Korang et al., 1996; Cox and Freese, 1996) gingival enlargement, although in a recent study of children with renal allografts, while 41% of those receiving cyclosporin had gingival enlargement, the majority of those receiving tacrolimus did not have this problem (Sheehy et al., 2000). Cyclosporin-associated gingival enlargement may reduce or resolve when cyclosporin is replaced by tacrolimus (Dodd, 1997; Badar et al., 1998; Basque et al., 1998; Hernandez et al., 1998, 2000; James et al., 2000; Kennedy and Linden, 2000).

(v) Other Gingival Changes

The gingiva in individuals with CRF can be pale due to anemia (Loehr and Schwaeb, 1991; London and Drueke, 1997), with possible loss of the demarcation of the mucogingival junction (Buckley et al., 1986), and when there is platelet dysfunction, the gingiva may bleed easily (Opaty, 1997).

(b) Oral Hygiene and Periodontal Disease

The oral hygiene of individuals receiving hemodialysis can be poor. For example, only 15% of 45 individuals receiving hemodialysis from 4 centers in Virginia, USA, had a good standard of oral hygiene (Naugle et al., 1998). Deposits of calculus may be increased (Epstein et al., 1980; Jaffe et al., 1986; Gavalda et al., 1999).

There is no good evidence of an increased risk of periodontitis (Brown et al., 1989; Thorstensson et al., 1996; Naugle et al., 1998), although premature tooth loss has been reported (Loesey et al., 1986). Localized suppurative osteomyelitis, secondary to periodontitis, was observed in one individual receiving hemodialysis (Tomaseilli et al., 1993).

(c) Xerostomia

Symptoms of xerostomia can arise in many individuals receiving hemodialysis (Eigner et al., 1986; Gavalda et al., 1999; Kho et al., 1999; Kao et al., 2000; Klassen and Krasko, 2002). Possible causes include restricted fluid intake, side-effects of drug therapy, and/or mouth-breathing. Long-term xerostomia may predispose to caries and gingival inflammation and can give rise to difficulties with speech, denture retention, mastication, dysphagia, sore mouth, and loss of taste (Porter et al., 2004).

It also predisposes to caries and infections such as candidosis and acute suppurative sialadenitis (Porter et al., 2004).

(d) Oral Malodor/Bad Taste

Uremic patients may have an ammonia-like oral odor (Eigner et al., 1986; Kho et al., 1999), which also occurs in about one-third of individuals receiving hemodialysis (Kho et al., 1999). Chronic renal failure can give rise to altered taste sensation, and some patients complain of an unpleasant and/or metallic taste (Levy, 1988), or a sensation of an enlarged tongue (Levy, 1988; Ray, 1989; Kho et al., 1999).

(e) Mucosal Lesions

A wide range of oral mucosal lesions, particularly white patches and/or ulceration, has been described in individuals receiving dialysis and allografts (Table 4). In particular, lichen-planus-like disease (sometimes termed lichenoid disease) can arise, sometimes, but not always, as a consequence of the associated drug therapy (e.g., diuretics, beta-blockers) (Chau et al., 1984; Hogan et al., 1985; Markizien et al., 1986; Torrelo et al., 1990). Similarly, oral hairy leukoplakia can occur secondary to drug-related immunosuppression (Greenspan and Greenspan, 1989; King et al., 1993, 1994), although clinically and histopathologically similar lesions lacking Epstein-Barr virus (EBV) have been observed with uremia (McCreary et al., 1997). Of note, this latter lesion may resolve with correction of the uremia.

**Table 4. Oral Mucosal Lesions Reported in Chronic Renal Disease**

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Description</th>
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<tr>
<td>White patch</td>
<td>Macules/nodules</td>
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<tr>
<td>Erythematous patch</td>
<td>Fibro-epithelial polypsis</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Geographic tongue</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Black hairy tongue</td>
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<tr>
<td>Oral hairy leukoplakia</td>
<td>Papilloma</td>
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<tr>
<td>Uremic stomatitis</td>
<td>Pyogenic granuloma</td>
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</table>
Uremic stomatitis may manifest as white, red, or grey areas of the oral mucosa. The erythropsulataceous form consists of grey pseudomembrane overlying painful erythema patches, while an ulcerative form is red with a 'pustulate' covering (Levy, 1988; Ross and Salisbury, 1994). There are no good historical descriptions of uremic stomatitis; thus, it is difficult to define the cause of this unusual oral mucosal change. It has been suggested, but never definitively demonstrated, that uremic stomatitis may be due to chemically based trauma from elevated levels of nitrogenous compounds (Larato, 1975; De Rossi and Glick, 1996; McCready et al., 1997).

In some instances, the mucosal surface may become erythematous or ulcerate (King et al., 1994; Kho et al., 1999; Klassen and Krasko, 2002). Oral mucosal macules and nodules have also been described in 14% of individuals receiving hemodialysis (Klassen and Krasko, 2002). Other lesions that can occur intra-oraly in allograft recipients are listed in Table 4 (King et al., 1994).

(f) Oral Malignancy
The risk of oral squamous cell carcinoma in patients receiving hemodialysis is generally similar to that of otherwise healthy individuals in the general population (Lee and Gissler, 1978; Bradford et al., 1990), although there have been reports suggesting that therapy following renal transplantation predisposes to epithelial dysplasia and carcinoma of the lip (Rege et al., 1992; Thomas et al., 1993). Perhaps unsurprisingly, Kaposi's sarcoma (KS) can occur in the mouths of immunosuppressed renal transplant recipients (Farge, 1993). There have been reports of squamous cell carcinoma (Varga and Tylleskot, 1991) and KS (Quinbi et al., 1988) arising within areas of cyclosporin-induced gingival enlargement. Any increased risk of oral malignancy in CRF probably reflects the effects of iatrogenic immunosuppression, which increases liability to virally associated tumors, such as Kaposi's sarcoma or non-Hodgkin's lymphoma. The inconsistent association between oral epithelial dysplasia and oral squamous cell carcinoma is in accord with the low risk of such disease in individuals with other, more significant, immunosuppressed states—for example, HIV disease.

(g) Oral Infections

(i) Candidosis
Angular cheilitis has been described in up to 4% of hemodialysis and renal allograft recipients (King et al., 1994; Klassen and Krasko, 2002). Other oral candidal lesions—such as pseudomembranous (1.9%), erythematous (3.8%), and chronic atrophic candidosis (3.8%)—have been reported in allograft recipients (King et al., 1994). These figures may underestimate the increased susceptibility of immunosuppressed allograft recipients to fungal infection, since systemic anti-fungal agents are commonly prescribed prophylactically (Quirk et al., 1995).

(ii) Viral Infection
Prior to the availability of appropriate anti-viral drugs (e.g., acyclovir, gancyclovir, and valacyclovir), about 50% of renal allograft recipients, who were seropositive for herpes simplex, experienced recurrent, severe, and prolonged HSV infections (Korsager et al., 1975; Armstrong et al., 1976; Naraqi et al., 1977). However, in recent years, the use of effective anti-herpetic regimes has significantly reduced the frequency of such infection (Kletzmyer et al., 2000; Ljungman, 2001; McGavin and Goa, 2001; Squilliet and Legendre, 2002). Long-standing post-allograft immunosuppression may predispose subjects to human herpesvirus 8 (HHV-8) and associated Kaposi's sarcoma (Leao et al., 2000).

(h) Dental Anomalies
Delayed eruption of permanent teeth has been reported in children with CRF (Woodhead et al., 1982; Koppang et al., 1984; Sampson and Meister, 1984; Wolff et al., 1985; Carl, 1987; Levy, 1988; Jaffe et al., 1990). Enamel hypoplasia of the primary and permanent teeth (Wolff et al., 1985; Kho et al., 1999; Koch et al., 1999; Al Nowaiser et al., 2003) or without brown discoloration (Bottomley et al., 1972; Woodhead et al., 1982; Wolff et al., 1985; Eiger et al., 1986; Carl, 1987; Levy, 1988) can also occur.

Narrowing or calcification of the pulp chamber of teeth of adults with chronic renal disease can occur (Kelly et al., 1980; Spolnik et al., 1981; Wysocki et al., 1983; Nasstrom et al., 1985, 1993; Galli et al., 1991; Nasstrom, 1996; Gudejevic, 2000). The exact cause of this dental change is not known. Renal allograft recipients have significantly more narrowing of the pulp chamber than those receiving hemodialysis (Nasstrom et al., 1985). There is no consistent association between corticosteroid therapy and narrowing of the pulp chamber (Galli et al., 1991).

Increased (Loosey et al., 1986) and decreased rates of dental caries (Woodhead et al., 1982; Sampson and Meister, 1984; Wolff et al., 1985; Jaffe et al., 1986; Levy, 1988; Klassen and Krasko, 2002; Al Nowaiser et al., 2003) have been observed in groups of patients with CRF. However, there is no evidence of a significantly increased risk of caries in patients with CRF. Although patients may have xerostomia, there would seem to be no increased risk of cervical caries, as might be expected (Porter et al., 2004).

Non-carious tooth tissue loss is more prevalent in individuals with CRF than in the general population (Levy, 1988). This may be due to xerostomia (Levy, 1988), esophageal regurgitation, or induced vomiting in bulimia nervosa (if a patient finds the restricted diet unpleasant) (Levy, 1988; Klassen and Krasko, 2002).

(i) Bone Lesions
A wide range of bony anomalies can arise in chronic renal disease. These reflect a variety of defects of calcium metabolism, including: loss of hydroxylation of 1-hydroxycholecalciferol to active vitamin D (1,25-dihydroxycholecalciferol); decreased hydrogen ion excretion (and resultant acidosis); hyperphosphatemia; hypocalcemia and resultant secondary hyperparathyroidism; and finally, interference in phosphate biochemistry by dialysis (Nadimi et al., 1993).

Secondary hyperparathyroidism affects up to 92% of patients receiving hemodialysis (Massry and Ritz, 1978). Hyperparathyroidism may present as a maxillary brown tumor (Okada et al., 2000), enlargement of the skeletal bases (Nadimi et al., 1993; Phelps et al., 1994; Michiaki et al., 1996; Damm et al., 1997b; Vigneswaran, 2001), or tooth mobility (Carmichael et al., 1995).
Table 5. Orofacial Features of Renal Osteodystrophy—Bony Features

- Bone demineralization
- Decreased trabeculation
- Decreased thickness of cortical bone
- Ground-glass appearance of bone
- Metastatic soft-tissue calcifications
- Radiolucent fibroelastic lesions
- Radiolucent giant cell lesions
- Lytic areas of bone
- Jaw fracture (due to trauma or during surgery)
- Abnormal bone healing after extraction

Table 6. Orofacial Features of Renal Osteodystrophy—Tooth and Periodontium

- Delayed eruption
- Enamel hypoplasia
- Loss of the lamina dura
- Widening of the periodontal ligament
- Severe periodontal destruction
- Tooth mobility
- Drifting
- Pulp calcifications
- Pulp narrowing

Orofacial features of renal osteodystrophy due to hyperparathyroidism are listed in Tables 5 and 6 (Sampson and Meister, 1984; Lockey et al., 1986; Carl, 1987; Levy, 1988; Molpus et al., 1991; Nadimi et al., 1993; Michiawaki et al., 1996; Damm et al., 1997; Ganibegovic, 2000; Okada et al., 2000; Klassen and Krasko, 2002).

Table 7. Drugs Commonly Used in Dentistry That May Have Implications for Patients with Renal Disease

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<th>Drug</th>
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<td><strong>Antibiotics</strong></td>
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<tr>
<td>Amoxicillin, ampicillin</td>
<td>Reduce dose, rash more common</td>
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<tr>
<td>Erythromycin</td>
<td>Maximum 1.5 g daily (ototoxicity)</td>
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<tr>
<td>Tetracyclines</td>
<td>Avoid—use doxycycline or minocycline if necessary (avoid excessive doses)</td>
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<tr>
<td>Cefalexin, cefradine</td>
<td>Reduce dose</td>
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<td>Probenecid</td>
<td>Avoid (ineffective, increased toxicity)</td>
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<td><strong>Antifungals</strong></td>
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<tr>
<td>Amphotericin</td>
<td>Use only if no alternative</td>
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<tr>
<td>Fluconazole</td>
<td>Usual initial dose then halve subsequent doses</td>
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<tr>
<td>Miconazole</td>
<td>Increases plasma-cyclosporin concentration</td>
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<tr>
<td><strong>Antivirals</strong></td>
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<tr>
<td>Acyclovir</td>
<td>Reduce dose</td>
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<td><strong>Analgesics</strong></td>
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<tr>
<td>Aspirin</td>
<td>Avoid (sodium, water retention; deterioration in renal function; risk of gastric hemorrhage)</td>
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<tr>
<td>Ibuprofen, diflunisal</td>
<td>Avoid if possible/use lowest effective dose (sodium, water retention; deterioration in renal function)</td>
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<tr>
<td>Dihydrocodeine, pethidine</td>
<td>Reduce dose/avoid (increased and prolonged effect, increased cerebral sensitivity)</td>
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<tr>
<td><strong>Other drugs</strong></td>
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<tr>
<td>Carbamazepine</td>
<td>Caution (reduces plasma-cyclosporin concentration)</td>
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<tr>
<td>Nitrazepam, temazepam</td>
<td>Start with small doses (increased cerebral sensitivity)</td>
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<tr>
<td>Povidone-iodine</td>
<td>Avoid regular application to inflamed or broken mucosa</td>
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<tr>
<td>Ephedrine</td>
<td>Avoid (CNS toxicity)</td>
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(VII) DENTAL MANAGEMENT OF PATIENTS WITH CHRONIC RENAL FAILURE

Untreated dental infection in immunosuppressed individuals can potentially contribute to morbidity and transplant rejection (Greenberg and Cohen, 1977). Thus, there is a need for detailed assessment and provision of good dental care following the diagnosis of CRF. Regular clinical review is important for the early identification of oral complications of renal disease (Bottomley et al., 1972; Naylor et al., 1988). Regular, nonsurgical, periodontal treatment is indicated (Bottomley et al., 1972; Potter and Wilson, 1979; Naugle et al., 1998). However, several studies have found that individuals receiving dialysis have unmet restorative dental need (Potter and Wilson, 1979; Naugle et al., 1998). In addition, despite sometimes having high levels of dental need, the attendance by affected patients for dental care is no better than that of those without renal disease (King and Thornhill, 1996; Naugle et al., 1998; Klassen and Krasko, 2002).

It has been recommended that patients requiring a renal transplant have a detailed oral assessment and treatment prior to surgery (Kirkpatrick and Morton, 1971; Somers, 1982; Eigner et al., 1986; Naylor and Fredericks, 1996; Ferguson and Whyman, 1998), perhaps highlighting a need for appropriately trained oral health professionals to collaborate with renal physicians. The dental examination should be timed appropriately to allow any necessary dental treatment to be carried out in a planned manner (Klassen and Krasko, 2002). Most transplant centers worldwide have a dental check in their pre-transplant protocol (Yamalik et al., 1993).
However, Klassen and Krasko (2002) found that pre-transplant oral care was not meticulous. There is no evidence that poor oral hygiene or consequent dental disease significantly affects the morbidity or mortality associated with CRD. Nevertheless, there have been occasional reports of the severe local and systemic spread of odontogenic infection in renal transplant recipients (Reyna et al., 1982; Wilson et al., 1982).

There may be a bleeding tendency in hemodialysis recipients, due to anti-coagulants or platelet dysfunction, but its effects can be minimized if dental treatment is carried out on the day following dialysis (Stewart, 1967; Dobkin et al., 1978; Precious et al., 1981; Sowell, 1982; Mannucci et al., 1983; Buckley et al., 1986; Eshach and Adamson, 1989; Jamieson and Wiegmann, 1990; De Rossi and Glick, 1996; Naylor and Frederick, 1996). This is a practical solution, since the patients will still be in the hospital.

To minimize the risk of adrenal crisis in individuals who have been large doses of corticosteroid (10 mg prednisolone daily or equivalent during the preceding 3 mos) and undergoing major surgical procedures (such as extraction of more than one tooth), appropriate corticosteroid cover should be administered (Seymour et al., 1994). In the past, large doses were used (up to 200 mg hydrocortisone), but more recent guidelines have recommended lower physiological doses (25 mg intravenous hydrocortisone per-operatively) (Nicholson et al., 1998).

Impaired renal function can result in high blood levels of drugs or their metabolites (Perneger et al., 1994); thus, it may be necessary to reduce the dosage of many drugs or use alternative agents (Bennett et al., 1983). Potential medication complications are listed in Table 7 (British National Formulary, 2002).

Infective endocarditis, affecting previously healthy cardiac tissue, has been reported in individuals on hemodialysis (Leonard et al., 1973). In countries such as the USA and New Zealand, bacteremia-producing antibiotic prophylaxis prior to dental procedures is recommended for individuals receiving renal dialysis and allografts, since there is a risk of infective endocarditis or infection of the vascular access site (Levy, 1988; Hay et al., 1992; Hall et al., 1994; Naylor and Frederick, 1996; Werner and Saad, 1999). The British Society for Antimicrobial Chemotherapy (BSAC) guidelines (Simmons, 1993) do not recommend antibiotic prophylaxis for individuals with renal disease who require dental procedures that are likely to give rise to a bacteremia. Klassen and Krasko (2002) have stressed that good oral health lowers the risk of oral infection, and, therefore, the risk of septicaemia, endocarditis, or endarteritis at the site of vascular dialysis access. There is, thus, no simple answer to the need for antibiotic prophylaxis for the bacteremia-producing dental procedures in patients with chronic renal disease. Nevertheless, there are instances where antibiotic prophylaxis may be important—for example, mitral valve prolapse and mitral valve regurgitation are common in patients with polycystic kidney disease type 1 (Lumiaio et al., 2001).

The ideal management of drug-induced gingival enlargement is to substitute another drug (Khocht and Schneider, 1997), but this may not always be possible. Meticulous oral hygiene (Daley et al., 1986; Hassell and Hefti, 1991; Nishikawa et al., 1991; Seymour and Smith, 1991; Hancock and Swan, 1992; Somacerrera et al., 1996, 1997; Hall, 1997; Westbrook et al., 1997; Bader et al., 1998; Oettinger-Barak et al., 2000) can lessen any plaque-related gingival disease, but may still be some drug-associated gingival enlargement. Single case reports have advocated the use of antimicrobial agents (Nash and Zaltzman, 1998; Winsberger et al., 1998) such as metronidazole (Wong et al., 1994) to lessen the gingival enlargement, but metronidazole may also increase the cyclosporin concentration and the potential for nephrotoxicity (Seymour et al., 1997). Sculpel or laser excision of the gingival enlargement is necessary if the excess gingival tissue is unsightly and/or interferes with mastication, speech, or oral care (Khocht and Schneider, 1997). Recurrence is common, especially when the oral hygiene is inadequate (Seymour et al., 1994; Hall, 1997), highlighting the need for long-term effective plaque control and consideration of additional anti-plaque measures such as topical chlorhexidine gluconate or triclosan preparations.

**CONCLUSION**

The prevalence of chronic renal failure (CRF) is increasing worldwide. Oral and systemic complications can occur as a result of CRF or its treatment. In recent years, the pattern of oral manifestations has changed, principally as a consequence of the adverse oral side-effects of drug therapy and immunosuppressant drugs. The incidence of gingival enlargement may fall as tacrolimus (and related agents) is used in place of cyclosporin. The dental management of patients with CRF is complicated by some systemic consequences of CRF, in particular, anemia, liability to bleeding, and cardiovascular or endocrine disease, but with the use of well-supervised treatment protocols, the dental management of individuals with chronic renal failure can be effective and safe.

**REFERENCES**


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