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Management of the Dental Patient with Renal Disease

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The kidneys are essential organs responsible for a multitude of bodily functions. One of the most important roles involves the regulation of intravascular volume and concentration of fluids in the body by producing urine. In addition, the kidneys are involved in regulation of blood pressure, detoxification of harmful substances, secretion of hormones, the control of acid/base balance and concentration of several electrolytes, and many other functions. This article provides the dental practitioner with a review of the renal system, associated pathology, and how one must alter their management to provide effective and safe treatment.

The kidneys are retroperitoneal organs (ie, located behind the peritoneum) situated on the posterior wall of the abdomen on each side of the vertebral column, at about the level of the twelfth rib. The left kidney is slightly superior in the abdomen than the right, due to the presence of the liver displacing the right kidney inferiorly. The kidneys receive blood directly from the aorta via the renal arteries; blood is returned to the inferior vena cava via the renal veins. Urine is excreted from the kidneys into the renal pelvis, through the ureters, and then collects in the bladder. The bladder (the detrusor muscle) is capable of distending to accept urine without increasing the pressure inside. This means that large volumes can be collected (700–1000 mL) without high-pressure damage to the renal system. When urine is passed, the urethral sphincter at the base of the bladder relaxes, the detrusor contracts, and urine is voided via the urethra.

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Renal anatomy

Each kidney contains approximately 1 million subunits called nephrons. Each nephron consists of an initial filtering component, called the renal corpuscle, and a tubule that extends from the renal corpuscle. The kidney anatomically consists of an outer cortex and an inner medulla. The outer cortex contains all of the renal corpuscles while the inner medulla contains the tubules. The renal corpuscle contains a compact tuft of interconnected capillary loops called the glomerulus. Each glomerulus is supplied with blood by an afferent arteriole. The glomerulus protrudes into a fluid-filled capsule called Bowman's capsule. The combination of a glomerulus and a Bowman's capsule comprises a renal corpuscle.

As blood flows through the glomerulus, a portion of the plasma filters into Bowman's capsule. As the blood is filtered, the fluid that enters the renal corpuscle is free of cells and proteins. This filtrate then leaves the renal corpuscle and enters the tubule, at which point substances are added or removed. The remainder of the blood supplied to the glomerulus by the afferent arteriole exits by way of the efferent arteriole. The efferent arteriole continues into the peritubular capillary and eventually into the venous system. Along its entire length, each tubule is surrounded by the peritubular capillaries. As will be discussed, this intimate relationship between the tubule and peritubular capillaries provides for basic renal function.

Blood in the glomerulus is separated from the filtrate in Bowman's space by a barrier consisting of three layers: (1) a single-celled capillary endothelium, (2) a noncellular proteinaceous layer of basement membrane, and (3) a single-celled epithelial lining of Bowman's capsule. The last layer of epithelium has a unique set of cells called podocytes. The podocytes possess a number of extensions, or foot processes, which are embedded in the basement membrane. Fluid filters first through the capillary endothelium, then through the basement membrane, and finally between the negatively charged foot processes of the podocytes [1]. The loss of this negative charge is seen in many glomerular diseases and leads to proteinuria, as will be discussed later in this article.

Once the filtrate has passed through these three layers, it then travels toward the renal tubule, which is continuous with Bowman's capsule. This tubule consists of a single layer of epithelial cells, which differ in structure and function along the length of the tubule. The first portion is called the proximal tubule. Fluid continues to a portion of the tubule called the loop of Henle, which consists of a descending limb and an ascending limb. Lastly, the flow of filtrate continues to the distal convoluted tubule and finally terminates in the collecting duct system. Multiple collecting ducts merge and the urine drains into a central cavity of the kidney, which is called the renal pelvis. The renal pelvis is contiguous with the ureter, which empties into the bladder.

The end of each ascending limb of the loop of Henle passes between and contacts the afferent and efferent arterioles. At the end of the ascending

limb is a unique set of cells called the macula densa. These cells are involved in the detection of changes in the sodium concentration of the filtrate. The macula densa is in contact with a group of specialized secretory cells, which are a part of the afferent arteriole, called the juxtaglomerular cells (Fig. 1). The combination of the macula densa and juxtaglomerular cells is known as the juxtaglomerular apparatus. The juxtaglomerular cells secrete the hormone renin [1]. The role and importance of this hormone will be discussed later in this article.

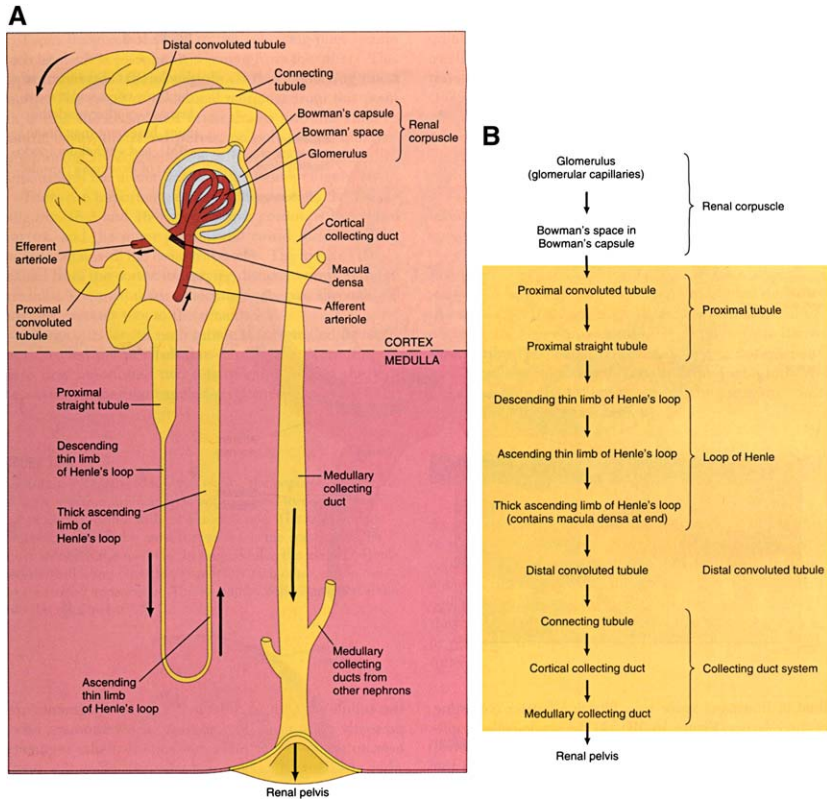

Fig. 1. Basic structure of a nephron. (*A*) Anatomical organization. The macula densa is not a distinct segment but a plaque of cells in the ascending loop of Henle where the loop passes between the arterioles supplying its renal corpuscle of origin. The orange (outer) area is called the cortex and the dark pink (inner) the medulla. (*B*) Consecutive segments of the nephron. All segments in the screened area are parts of the renal tubule; the terms to the right of the brackets are the most commonly used combination terms for several consecutive segments. (*From* Vander A, Sherman J, Luciano D. The kidneys and regulation of water and inorganic ions. In: Kane K, editor: Human Physiology, 10th edition. New York: McGraw-Hill; 1998. p. 505; with permission.)

Basic renal function

As previously mentioned, the glomerular filtrate is cell-free and contains the same substances as plasma but excludes proteins. There are three basic components of renal function: (1) glomerular filtration, (2) tubular reabsorption, and (3) tubular secretion.

The glomerular filtration rate (GFR) is the rate at which plasma is filtered into Bowman's capsule. There are four factors that affect filtration: (1) hydrostatic pressure in glomerular capillaries, (2) oncotic pressure of the plasma, (3) hydrostatic pressure in Bowman's capsule, and (4) oncotic pressure in the capsule. The hydrostatic pressure in the glomerular capillaries drives filtration into Bowman's capsule. The oncotic pressure of the plasma changes with the concentration of plasma proteins. An increase in this pressure promotes reabsorption. The hydrostatic pressure within the capsule opposes filtration. This pressure is usually low and does not affect filtration except in cases of downstream blockage or pathology. Finally, the oncotic pressure within the capsule is virtually zero; little if any protein is present within the capsule. Adding the opposing vectors, it is clearly seen that in normal renal function there is a positive net pressure in favor of filtration. The GFR is not a fixed value but changes with physiologic regulation. This is achieved by neural and hormonal input to the afferent and efferent arterioles.

Tubular reabsorption is based on two types of active reabsorption. The first uses a transport maximum system, and the second is based on a gradient time system. Transport systems in the renal tubule have a limit to the amounts of material they can transport per unit time. Transport systems involve almost all natural organic and some inorganic substances. These substances include glucose, amino acids, small peptides and proteins, ketone bodies, calcium, and phosphate. An exception with respect to natural organic substances is urea. Transport systems have carriers that are easily saturated and have high affinity for the substrate. The second mechanism, the gradient-time system, has carriers that cannot be saturated and have low affinities for the substrate. Examples of this type of mechanism are sodium, potassium, chloride, and water.

Tubular secretion also uses a transport system. This transport system secretes substances from the peritubular capillaries into the tubular lumen. The most important substances secreted by the tubules are hydrogen ions, potassium, creatinine, and foreign chemicals, such as penicillin.

The renal clearance of any substance is the volume of plasma from which that substance is completely removed by the kidneys per unit time. A number of substances can be used to provide an approximate measure of GFR. However, many of these substances need to be administered and then monitored in the urine to provide an accurate measure of the GFR. Clinically, the creatinine clearance is used to approximate GFR. Creatinine is a waste product of muscle, which is filtered and not reabsorbed, with minimal

secretion. In clinical practice, the creatinine clearance overestimates the GFR, but is close enough to be highly useful.

Each portion of the tubule has specific functions. The first portion is the proximal tubule. Once the ultrafiltrate enters this region, approximately two thirds of the filtered sodium is reabsorbed. Also, about two thirds of the filtered water, potassium cations (K^+), and chloride anions (Cl^-) follow the sodium.

Metabolites, such as carbohydrates, proteins, peptides, amino acids, and ketone bodies, are reabsorbed via secondary active transport, linked to sodium. Carbonic anhydrase inhibitors, such acetazolamide, are diuretics that act in the proximal tubule by inhibiting the reabsorption of filtered bicarbonate anions (HCO_3^-). The ultrafiltrate continues to travel down the descending limb and up the thick ascending limb of the loop of Henle. The ascending limb is impermeable to water and thus only sodium is reabsorbed here. This is also the site of action of the loop diuretics, such as furosemide. The ultrafiltrate enters the early distal tubule, which reabsorbs sodium but continues to be impermeable to water. This is also the site where thiazide diuretics, such as hydrochlorthiazide, take their effect. Movement is then into the late distal tubule and finally to the collecting duct. Here variable amounts of sodium cations (Na^+), K^+, and water are secreted or reabsorbed.

The late distal tubule and collecting duct have special features that will be discussed separately. Within this region is a set of cells called the principal cells. They are involved in reabsorption of sodium and water, and secretion of potassium. Aldosterone, a steroid hormone produced in the adrenal gland, increases sodium reabsorption and potassium secretion. Also, antidiuretic hormone (ADH) produced in the hypothalmus increases water permeability by directing the insertion of water channels into the principal cells [2].

Electrolyte balance

The total body water is approximately 60% of one's body weight. The percentage varies slightly in newborns and women, but for this discussion our example will be a 70-kg male. Fluid within cells (intracellular fluid) is two thirds of total body water. The major intracellular cations are K^+ and magnesium (Mg^{2+}) while the major anions are proteins. Fluid outside the cells (extracellular fluid) is one third of total body water. The major extracellular cation is Na^+ and the major anions are Cl^- and HCO_3^-. Of the extracellular fluid, one quarter is plasma containing proteins, such as albumin. The other three quarters of the extracellular fluid is interstitial fluid. This fluid is an ultrafiltrate of the plasma and hence has little protein. The body attempts to maintain equilibrium between these compartments. As volume and osmolarity change secondary to various situations, such as diarrhea, vomiting, or adrenal insufficiency, water will shift between extracellular and intracellular compartments in an attempt to correct this change.

A number of changes that take place within the nephron that also attempt to re-establish equilibrium through secretion and reabsorption. We have mentioned the major cations and anions that reside in their respective compartments, as one can imagine movement of fluid also leads to movement of electrolytes. Movement of electrolytes between compartments can lead to serious and sometimes life-threatening situations. Table 1 is a summary of some signs and symptoms that may be seen in these patients.

Sodium regulation

Because Na^+ is the major extracellular solute, changes in total body Na^+ result in similar changes in the extracellular volume. Through a number of processes, changes in the extracellular volume changes cardiovascular pressures, leading to changes in blood pressure. A brief example will give us a better understanding of this system. If a patient loses Na^+ and water due to diarrhea, the body will have an initial reflex to increase sympathetic activity on the renal system, which will slow the GFR to promote Na^+ and water reabsorption. The body also activates a slower but more complete response via the hormone aldosterone. Aldosterone is a complicated hormone that acts on the cortical collecting ducts and, through protein synthesis, induces Na^+ reabsorption. Aldosterone is one end point in a complicated pathway termed the renin-angiotensin system. A description of this pathway

Table 1
Signs and symptoms of renal disorders

Disorder	Signs and symptoms
Hypernatremia	Lethargy, weakness, irritability
	Can cause seizures or lead to a coma
Hyponatremia	Can cause seizures, nausea, vomiting, stupor, or coma
Hyperkalemia	Neuromuscular and cardiac sequelae (heart block, ventricular fibrillation, asystole)
	ECG changes: peaked T waves, flattened P waves, wide QRS complex
Hypokalemia	Also causes cardiac changes and instability, ventricular tachycardia
	ECG changes: depressed T waves
Hypercalcemia	Altered mental status, muscle weakness, constipation, nausea, vomiting
	Nephrolithiasis
Hypocalcemia	Paresthesias, tetany, seizures, weakness, mental status changes
	QT interval prolonged
Hypermagnasemia	Lethargy, weakness
	Paralysis; decreased blood pressure, heart rate
Hypomagnesemia	Hyperreflexia and tetany
	Ventricular fibrillation, atrial tachycardia, atrial fibrillation
	QRS widening; PR, QT intervals prolonged
Hyperphosphatemia	Soft tissue calcification
	Heart block
Hypophosphatemia	Diffuse weakness and flaccid paralysis

must be simplified, since a detailed explanation would be beyond the scope of this article. Renin, an enzyme secreted by the kidney, initiates the cleavage of a protein in the blood. This protein is called angiotensinogen. Through a number of steps, angiotensinogen eventually forms angiotensin II. Angiotensin II has many effects, including the secretion of aldosterone and constriction of renal arterioles. Thus angiotensin II, by increasing secretion of aldosterone, will also increase reabsorption of Na^+ and water and secretion of K^+.

During the sympathetic reflex due to decreased extracellular volume, the secretion of vasopressin (ADH) is also stimulated. ADH is secreted from the hypothalamus, which is stimulated by baroreceptors in the cardiovascular system and osmoreceptors in the hypothalamus. ADH increases water permeability of the principal cells of the late distal tubule and collecting duct by stimulating the insertion of aquaporins, which are essentially water channels.

Potassium regulation

As we have previously discussed, K^+ is mostly intracellular. However, changes in such extracellular concentrations can lead to detrimental effects, such as cardiac arrythmias. The control of renal function is the major mechanism by which body K^+ is regulated. Intake of K^+ regulates the secretion of K^+ via the hormone aldosterone.

Calcium regulation

Extracellular calcium concentration normally remains relatively constant. Regulation of plasma calcium concentration occurs through the gastrointestinal tract, bone, and kidneys. This regulation is mediated by hormones, mainly parathyroid hormone and the active form of vitamin D_3 (1, 25-dihydroxyvitamin D_3). Parathyroid hormone stimulates kidney tubular reabsorption of calcium, release of calcium from bone, and formation of the hormone 1, 25-dihydroxyvitamin D_3, which acts on intestinal absorption of calcium. Vitamin D_3 is formed in the skin or ingested, and then undergoes hydroxylation in the liver and kidney; the latter is stimulated by parathyroid hormone to become the active form 1, 25-dihydroxyvitamin D_3 [1].

Acid–base regulation

Metabolic reactions occur throughout the body and are extremely sensitive to the hydrogen-ion concentration. Small changes in the pH can cause conformational changes in proteins. A number of mechanisms buffer small changes in pH within the body. The major extracellular buffering system is the carbonic-acid-bicarbonate system, involving carbon dioxide and HCO_3^-, and the major intracellular buffers are proteins and phosphates.

The kidneys and the respiratory system are the homeostatic regulators of plasma hydrogen-ion concentration. The kidneys maintain a stable plasma hydrogen-ion concentration by excreting excess hydrogen ions while still regulating plasma bicarbonate concentration. The kidneys can either excrete bicarbonate when the body is in a state of alkalosis or contribute new bicarbonate during times of acidosis. Acid–base disorders are a complicated set of disorders that are the result of differing pathologies. The body has an acute response to correct these changes by using the bicarbonate system, and a chronic response that involves the use of renal and respiratory mechanisms. The details of these disorders are beyond the scope of this article.

Other renal functions

Erythrocyte production

Erythrocyte production is directly controlled by the secretion of a hormone called erythropoietin. Erythropoietin is secreted into the blood by a group of cells in the kidney. This hormone acts on the bone marrow to stimulate the proliferation of erythrocyte progenitor cells and their differentiation into erythrocytes. The secretion of erythropoietin increases during such situations as heart failure, lung disease, anemia, and exposure to high altitude [1]. Without this hormone, patients develop severe anemia, as seen in end-stage renal failure.

Gluconeogenesis

Gluconeogenesis is the biosynthesis of new glucose. This function is mostly dedicated to the liver. However, the kidney also participates in this function. The importance of the kidney's role in this function is currently under investigation, and kidney disease could impact glucose homeostasis and possibly lead to hypoglycemia.

Kidney function tests

As previously discussed, the kidneys are involved in numerous homeostatic functions. Injury to the kidneys can lead to an impairment of these functions. Unlike many other organs, a large portion of the kidney has to be lost before there are noticeable changes in the body. End-stage renal disease is when the GFR is $<25\%$ of normal, renal insufficiency is 25% to 40% of normal GFR, and decreased renal reserve is 60% to 75% of normal GFR. When kidneys are injured, the first signs of injury are usually chemical changes seen in the blood and urine. As renal function diminishes below 20% of normal, patients require dialysis to maintain normal homeostasis.

Blood urea nitrogen

As protein is broken down into amino acids, ammonia is produced. The ammonia is carried to the liver, where it combines with carbon dioxide to form urea. This urea is the major nitrogenous waste product of protein catabolism. Normally, the urea is excreted by the kidneys. As kidney function begins to decrease, urea builds up in the blood. This uremia can result in a syndrome of vomiting, anorexia, nausea, pruritus, irritability, and asterixis. This can progress to multi-organ failure, encephalopathy, and death, termed uremic syndrome, which will be discussed further in this article. The normal reference range of blood urea nitrogen (BUN) is 10 to 20 mg/dL. Deviations from this range are not always caused by renal pathology. Dehydration, blood in the intestinal tract, or even a large meal of meat can cause the concentration of urea in the blood to elevate. An elevation of BUN over 100 mg/dL will begin to cause a qualitative platelet dysfunction, and must be considered before any surgical procedures.

Creatinine

Creatinine is a breakdown product of muscle metabolism. Unlike BUN, the level of creatinine in the blood is not affected by protein-rich meals or blood in the intestinal tract. The normal reference range of blood creatinine is 0.3 to 1.5 mg/dL.

These two values are usually considered as a ratio. This ratio allows one to evaluate the filtering function of the kidney and body hydration. A normal BUN/creatinine ratio is 10:1. In times of dehydration, this ratio can rise to 20:1 or higher. This ratio may be increased secondary to certain kidney diseases, breakdown of blood in the intestines, or poor blood flow to the kidneys. The BUN/creatinine ratio may be decreased in certain types of kidney and liver disease.

Urinalysis

Urinalysis is used to measure kidney output function and problems with the collecting system. This test evaluates the urine's pH, color, specific gravity, and determines if there are leukocytes, nitrates, proteins, red blood cells, ketones, or bacteria present in the urine. These parameters help in screening for various renal system pathologies. The use of these tests is not useful for diagnosing a particular disease. Rather the tests are used as indicators of possible underlying pathology and should be followed up with further testing.

Renal pathology

The list of renal diseases is long. Thus, this section is important not for details about these diseases, but for the impact the diseases have on the body and as a basis for understanding how these changes can affect the

dental treatment of patients. The following renal diseases will be grouped into categories based on underlying pathology.

Congenital diseases

With few exceptions, congenital diseases result from a developmental defect arising during gestation rather than a hereditary defect.

Kidney agenesis

On one end of the spectrum is total bilateral renal agenesis, which is incompatible with life. A unilateral agenesis is compatible with life. However, the lone kidney often becomes hypertrophied, leading eventually to chronic renal failure [3].

Hypoplasia

Hypoplasia refers to failure of the kidneys to develop to a normal size. Hypoplasia may occur bilaterally and lead to renal failure in early childhood. However, it is seen more commonly as a unilateral defect.

Ectopic kidneys

Ectopic kidneys lie either above the pelvic brim or may lie within the pelvis. Kidney function is normal. However, secondary to the tortuosity of the ureters, these patients may have an increased predisposition to urinary tract infections.

Horseshoe kidney

Horseshoe kidney results from fusion of the upper or lower kidney poles. Kidney function remains normal.

Cystic kidney diseases

This group of disorders contains a large variety of diseases. We will only discuss the most common of the group.

Adult polycystic kidney disease

Adult polycystic kidney disease is a hereditary disorder characterized by multiple expanding cysts of both kidneys. The cysts ultimately destroy the renal parenchyma and cause renal failure [3]. The likelihood of developing renal failure increases as the patient ages but usually does not become clinically apparent until 40 to 60 years of age. This disease involves many other organ systems, such as the liver, spleen, and cerebrovascular system.

Childhood polycystic kidney disease

Childhood polycystic kidney disease can occur at birth or can span up to early childhood. These children can also develop hepatic fibrosis, which can lead to portal hypertension alongside renal failure [3].

Glomerular diseases

Glomerular diseases involve glomeruli that have been attacked by a variety of causes, some of which include systemic diseases, hereditary disorders, infectious causes, and drugs. To understand this group of diseases, we must first divide them into two broad categories: nephritic syndrome and nephrotic syndrome. Below is a summary (Table 2) that helps differentiate the two syndromes based on clinical findings.

Nephritic glomerulonephropathies

Acute poststreptococcal glomerulonephritis. Acute poststreptococcal glomerulonephritis usually occurs 2 to 4 weeks after a streptococcal infection of the throat or skin and is most often caused by *B*-hemolytic group A streptococci. There is a good prognosis in children with complete recovery in most patients. Complete recovery is seen in over half of adults, but the remainder may develop chronic renal disease.

Rapidly progressive glomerulonephritis. Rapidly progressive glomerulonephritis can develop following many glomerulonephritis disorders. Patients rapidly develop severe renal failure in weeks to months. These patients have a poor prognosis and many develop end-stage renal disease.

Goodpasture syndrome. Patients with Goodpasture syndrome produce antibodies that attack the basement membrane of the kidney and lungs. Most of these patients develop rapidly progressive glomerulonephritis leading to renal failure.

Berger disease. Berger disease (IgA nephropathy) affects young adult males primarily and the pathogenesis of this disease is unclear. These patients may slowly develop renal failure over 25 years.

Nephrotic glomerulonephropathies

Membranous glomerulonephritis. Membranous glomerulonephritis is the most common cause of nephrotic syndrome in adults. It is caused by a wide variety of insults. The course of this disease is irregular. Disease progression can resolve spontaneously, or progress to end-stage renal disease.

Table 2
Clinical findings of nephritic syndrome and nephrotic syndrome

Nephritic syndrome	Nephrotic syndrome
Variable proteinuria	Severe proteinuria (>3.5 g/d)
Hematuria (blood in the urine)	Hypoalbuminemia (protein in the blood)
Azotemia (accumulation of nitrogenous wastes)	Generalized edema
Hypertension	Hyperlipidemia
Oliguria	Lipiduria

Minimal change disease. Minimal change disease is the most common cause of nephrotic syndrome in children. The prognosis is excellent and in most cases there is a complete recovery.

Progression of the above diseases eventually leads to chronic glomerulonephritis. These patients develop chronic renal failure. Patients develop a large spectrum of complaints such as nausea, vomiting, weakness, and loss of appetite. In addition, they often become hypertensive and uremic, and unless treatment is instituted in the form of dialysis or kidney transplant, these patients usually die from this disease.

Renal tubular diseases

Renal tubular diseases affect the renal tubules and the surrounding interstitium.

Acute tubular necrosis

Acute tubular necrosis (ATN) is defined as acute renal failure secondary to reversible injury to the tubular epithelium. This damage to the tubular cells can be caused by a number of different insults. One common cause is inadequate blood flow to the kidneys causing ischemia. Examples include blood loss secondary to hemorrhage, dehydration, and shock. The other major cause of ATN is toxic damage to the tubule cells. The toxic damage occurs secondary to nephrotoxic medications, environmental toxins, or poisons. As mentioned earlier, this is a potentially reversible injury and hence the kidneys may recover. However, recovery depends on what caused the damage initially and the severity of the damage.

ATN is the most common cause of acute renal failure (ARF). Traditionally ARF has been divided into prerenal, intrarenal, and postrenal causes. These categories are used to identify where in the renal system the pathology lies. For example, ATN is due to damage to tubular cells and hence is a cause of intrarenal ARF.

Acute pyelonephritis

Pyelonephritis is caused by an infectious source that affects the renal pelvis, tubules, and interstitium. Affected patients normally present with fever and have tenderness in the costovertebral angle. This infection can be treated and cured with antibiotics.

Chronic renal failure and end-stage renal disease

In contrast to ARF, chronic renal failure (CRF) is a slowly progressive condition characterized by irreversible reduction in GFR. This irreversible damage can be seen in virtually all of the diseases discussed. The progression of CRF begins with asymptomatic decrease in kidney function and

eventually leads to end-stage renal disease. During this decline in kidney function, multiple organ systems are affected. Patients develop symptoms directly related to the kidneys' dysfunctions. End-stage renal disease, also known as uremic syndrome, is the final stage of CRF. Uremia is defined as symptomatic renal failure associated with metabolic events and complications [4]. Table 3 summarizes the effects of uremia on the body.

Management of end-stage renal disease

Over 200,000 patients in the United States now suffer from end-stage renal disease; over 75% of these patients require dialysis to maintain normal homeostasis. There are three modalities for the treatment of renal failure. The first is conservative medical management. This is reserved for the

Table 3
Effects of uremia on the body

Body system	Effect
Cardiovascular	Hypertension
	Congestive heart failure
	Pericarditis
Neurologic	Fatigue
	Impaired cognition
	Irritability
	Drowsiness
	Peripheral neuropathy
	Encephalopathy
Musculoskeletal	Renal osteodystrophy
	Growth retardation
Hematologic	Anemia
	Bleeding tendency due to platelet dysfunction
	Susceptibility to infections
Metabolic	Hyperglycemia
	Hyperuricemia
	Acidosis
Endocrine	Hypothyroidism
	Hyperparathyroidism
Dermatologic	Pruritus
	Yellow skin
	Brittle hair
Ocular	Retinopathy
Gastrointestinal	Nausea
	Vomiting
	Anorexia
	Gastrointestinal bleeding
Reproductive	Infertility
	Impotence
	Amenorrhea
	Delayed puberty
Respiratory	Pulmonary edema
	Pleuritis

patients with renal insufficiency. The second is dialysis, which is for the end-stage renal patient. The third is kidney transplantation.

Conservative medical management for those patients with renal insufficiency consists of dietary restrictions, specifically restricting fluid intake to 1.5 to 2.0 L/d, restricting protein to 0.7 to 1.2 g/kg/d to minimize the increase in BUN, restricting sodium chloride and potassium chloride to 2 g/d, and altogether avoiding magnesium, phosphorus, and aluminum. Patients are typically prescribed loop and thiazide diuretics to maintain appropriate fluid balance and calcium carbonate (300–2500 mg by mouth 30 minutes before meals and bedtime) to control serum calcium and phosphorus levels. Sodium bicarbonate is reserved to control metabolic acidosis, and is administered intravenously in a monitored hospital setting [5]. When medical management fails, these patients progress toward dialysis.

Dialysis removes fluid and wastes and equilibrates electrolytes and acid–bases via diffusion and osmosis across a semipermeable membrane. There are two forms of dialysis: hemodialysis and peritoneal dialysis. Peritoneal dialysis (PD) is accomplished through the infusion of dialysate, which is composed of electrolytes and different concentrations of dextrose (1.5%, 2.5%, and 4.0%). A dialysis catheter is surgically placed into the peritoneum, which is a semipermeable membrane and is used for access. This form of dialysis is performed by the patient four to five exchanges a day, whereby 2 to 3 L of dialysate is infused over 30 minutes, allowed to dwell within the peritoneum for 2 to 4 hours, and then allowed to drain. Typically the last exchange of the day is left to dwell overnight. Complications of PD include peritonitis, which can cause membrane failure; PD catheter obstruction or infection; obesity secondary to the caloric absorption of dextrose; hernias; and back pain.

Hemodialysis uses vascular access through a primary arteriovenous fistula, a polytetrafluoroethylene graft, or percutaneous intravenous catheters. Hemodialysis uses an artificial kidney that circulates blood along a semipermeable membrane. This process typically requires a low dose of heparin to prevent clotting within the circuit. Dialysate flows in a countercurrent direction on the opposite side of the membrane. The concentration gradient created allows solutes to diffuse. The pressure gradient can be manipulated to remove fluid if the patient presents with volume overload. Hemodialysis is typically performed three times a week; each session is for about 4 hours. Complications associated with hemodialysis include issues with access, such as clotting and infections. For this reason, practitioners should avoid using blood pressure cuffs or intravenous needles with patients on hemodialysis. Other complications include hypotension, dyspnea, and bleeding.

Complications of end-stage renal disease

Volume

Patients with end-stage renal disease do not produce urine. Therefore their fluid balance is depends on dialysis or fluid restriction. If these patients

become volume overloaded they can develop pulmonary edema, hypertension, congestive heart failure, and peripheral edema. Conversely, if too much fluid is removed following dialysis, volume depletion can lead to hypotension, orthostasis, and syncope. Ideally, patients should be euvolemic. During dental treatment, continuous blood pressure should be performed in the nonaccess arm.

Electrolytes

Disturbances with potassium, magnesium, phosphorus, and calcium can occur. This is why a basic metabolic panel is checked following dialysis. Hyperkalemia can lead to dysrhythmias and heart block, and is one of the indications for emergent dialysis. Hypomagnesaemia results in generalized muscle weakness resulting in ventilatory collapse hypotension and bradycardia. Hypocalcaemia and hyperphosphatemia are common in renal failure due to the decreased excretion of phosphate and production of vitamin D.

Acid–base

Patients with end-stage renal disease are at risk for developing a metabolic acidosis because they are unable to clear accumulated hydrogen ions. The body initially tries to compensate for this through hyperventilation, as previously discussed. However when this mechanism fails, the patient develops lethargy, confusion, nausea, and vomiting. This can progress to cardiovascular collapse, coma, and death. One of the common causes of metabolic acidosis is renal failure, and is one of the other reasons for emergent dialysis.

Anemia

Anemia is a common issue in patients with end-stage renal disease, mainly due to hemolysis secondary hemodialysis, and also from the lack of production of erythropoetin. A complete blood count should be checked before any dental procedures to check the hemoglobin and hematocrit. Many renal failure patients also have other comorbid diseases, such as coronary artery disease and diabetes. These patients need to be treated with caution. The combination of anemia and a stressful clinical setting (eg, dental procedure) can increase the myocardial oxygen demand, leading to a cardiac event. Stress-reducing measures, nitrous oxide or supplemental oxygen, and profound local anesthesia should be employed for minor procedures. Any extensive dental procedures requiring sedation should be performed in an inpatient setting with an anesthesiologist.

Bleeding

Bleeding typically occurs because of the use of heparin for anticoagulation during dialysis, or because of a qualitative platelet dysfunction secondary to uremia. The half-life of heparin is approximately 3 to 4 hours, and the treatment of platelet dysfunction due to uremia is dialysis. For these reasons, any elective dental procedures should be coordinated on nondialysis

days. This will allow any residual effects of heparin to resolve, and the uremia can be corrected the day before the procedure. If heparin cannot be used (eg, when there is risk of heparin-induced thrombocytopenia), other anticoagulant alternatives can be used, such as argatroban or lepirudin. Argotroban is synthetically derived, inhibits thrombin, and is metabolized by the liver. Lepirudin, which derived from the saliva of medicinal leeches, also inhibits thrombin and is metabolized by the kidney [6]. Patients on hemodialysis or with renal insufficiency will require the doses of lepirudin adjusted accordingly [7]. Patients with end-stage renal disease should have their prothrombin time, partial thromboplastin time, international normalized ratio, BUN, and creatinine checked before any surgical procedures.

Infections

There is a higher rate of infection in patients with end-stage renal disease and in renal transplant patients compared to the immunocompetant population. Patients with end-stage renal disease and renal transplant patients require aggressive treatment of any odontogenic infection. Many of these patients require hospital admission, surgical drainage of the abscess, removal of the source of infection, and adjuvant intravenous antibiotics. Dental practitioners should avoid treating these infections with oral antibiotics alone, since transplant patients are immunocompromised and odontogenic infections can spread rapidly. Many authors recommend the use of prophylactic antibiotics to prevent infections of synthetic arteriovenous grafts before any routine dental procedures. However, there presently is not sufficient data in the literature to support this practice.

Drug clearance

Because many drugs are metabolized or excreted via the kidney, renal dosing needs to be performed to account for the drug's extended half-life or active metabolites. One of the most common drugs prescribed by the dental practitioner is penicillin, which exists as either a sodium or potassium salt (eg, penicillin V). Potassium salts should be avoided due to the potential of hyperkalemia. Other alternative drugs, such as clindamycin or erythromycin, which are metabolized by the liver, can be considered. Nonsteroidal anti-inflammatory drugs, because of their nephrotoxic effects, should be avoided in patients with the renal insufficiency. However, nonsteroidal anti-inflammatory drugs can be used once these patients progress to end-stage renal disease and no longer have any residual renal function. Local anesthetics can be used without having to adjust the dosage. However, a vasoconstrictor should be used conservatively because of underlying hypertension related to the renal disease. Many narcotics can be used in patients with end-stage renal disease. However, narcotics should be used cautiously due to prolonged effects. The one narcotic that should always be avoided is meperidine because it has active metabolites that can accumulate and result in seizures [8].

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