ORAL SURGERY

GENITOURINARY DISEASE:

CHRONIC KIDNEY DISEASE AND DIALYSIS

Kidney disease can be caused by acute (i.e., bacterial infection, obstruction in the urinary tract, or damage to the renal parenchyma) or chronic conditions.
Progressive kidney disease can result in reduced renal function and ultimate kidney failure with effects on multiple organ systems → anemia, abnormal bleeding, electrolyte and fluid imbalance, hypertension, drug intolerance, and skeletal abnormalities.

The kidneys have several important functions:

- They regulate fluid volume
- filter waste and toxins
- maintain acid-base balance of plasma
- synthesize and release hormones (erythropoietin, 1,25-dihydroxycholecalciferol, and renin)
- responsible for drug metabolism; and serve as the target organ for parathormone and aldosterone.

About 25% of the circulating blood perfuses the kidney each minute to be filtered within the nephron, the functional unit of the kidney (The kidneys filter about 180 L/day through the function of approximately 2 million nephrons). Ultrafiltrate, the precursor of urine, is produced in nephrons at a rate of about 125 mL/min/1.73 m2.

DEFINITION

Chronic kidney disease (CKD) → abnormalities of kidney structure or function, present for 3 months or longer. It results from direct damage to nephrons or from progressive, chronic bilateral deterioration of nephrons. (Damage in CKD rarely repaired →progressive disease e.g., uremia and kidney failure) can lead to death.

The National Kidney Foundation defines a five-stage classification system for CKD based on the glomerular filtration rate (GFR).
Stage 1 is characterized by normal or only slightly increased GFR associated with some degree of kidney damage. This stage usually is asymptomatic, with a slight (10%–20%) decline in renal function.

Stage 2 is marked by a mildly decreased GFR.
Stage 3 is evidenced as a moderately decreased GFR (30–59 mL/min), with loss of 50% or more of normal renal function
Stage 4 is defined by a severely decreased GFR (15–29 mL/min).
Stage 5 is reflected by renal failure, wherein 75% or more of the approximately 2 million nephrons have lost function (GFR <15 mL/min).

With disease progression (stages 2–5)

- nitrogen products accumulate in the blood
- fewer excretory, endocrine, and metabolic functions by the kidney,
- homeostasis disturbance.
- Uremia develops→ clinical syndrome caused by renal failure, retention of excretory products, and interference with endocrine and metabolic functions

EPIDEMIOLOGY

- The early stages of CKD (stages 1–3) tend to be asymptomatic and constitute 96.5% of the disease and the rest develop end-stage renal disease (ESRD)
- More prevalent in patients older than 65 years and in those who have diabetes and hypertension.
- More common in men
- About 90% of patients with kidney failure are older than 18 years

ETIOLOGY

Main causes of ESRD

- diabetes mellitus (44%)
- hypertension (28%)
- chronic glomerulonephritis (16%)
- polycystic kidney disease (4.5%).6

PATHOPHYSIOLOGY AND COMPLICATIONS

- . The nephron includes the glomerulus, tubules, and vasculature.
- Various diseases affect different segments of the nephron at first, but the entire nephron eventually is affected (e.g., hypertension affects the vasculature first, glomerulonephritis affects the glomeruli first).
- nephrons that are lost are not replaced.
- compensatory hypertrophy of the remaining nephrons may maintain renal function for a time → relative renal insufficiency → asymptomatic
- Normal function is maintained until >50% of nephrons are destroyed

- tubular malfunction→sodium pump to lose its effectiveness,→ sodium + excessive amounts of dilute urine excreted → polyuria
- advanced renal disease → uremia (fatal if not treated). Failing kidneys→ unable to concentrate and filter the intake of sodium → drop in urine output → fluid overload → hypertension, insulin resistance, risk for severe electrolyte disturbances and cardiac disease
- The buildup of nonprotein nitrogen compounds in the blood, mainly urea due to loss of glomerular filtration function, is called azotemia level of which measured as blood urea nitrogen (BUN).
- Acids accumulate because of tubular impairment → metabolic acidosis, the →ammonia retention.
- Acidosis →nausea, anorexia, and fatigue and patients may hyperventilate
- Patients with ESRD may;
  - i- Develop anemia (due to decreased erythropoietin production by the kidney, and shortened RBC survival), leukocyte and platelet dysfunction, and coagulopathy.
  - ii- Host defense is compromised by nutritional deficiencies, leukocyte dysfunction, and depressed cellular immunity→ diminished granulocyte chemotaxis, phagocytosis, and bactericidal activity → patient is susceptible to infection
  - iii- Hemorrhagic diatheses (abnormal bleeding and bruising) due to abnormal platelet aggregation and adhesiveness, impaired prothrombin consumption, and loss of clotting factors with proteinuria.
  - iv- coronary artery blood flow is compromised due to. Congestive heart failure and hypertrophy of the left ventricle, development (because of hyperlipidemia, atherosclerosis, and fluid overload)

These complications, along with electrolyte disturbances, put patients with ESRD at increased risk for sudden death from myocardial infarction.

- v- bone disorders are seen in ESRD referred to as renal osteodystrophy. Occur due to decreased kidney function
  - a- decreased 1-α-hydroxylation of vitamin D → reduced intestinal absorption of calcium→hypocalcemia
  - b- renal phosphate excretion drops →bone buffer the acid buildup by releasing calcium and phosphates →demineralization
  - c- low levels of serum ionized calcium → ↑parathyroid hormone (PTH)→ tumor necrosis factor activation →osseous changes;

1- Adults→osteomalacia (increased unmineralized osteoid bone matrix) followed by osteitis fibrosa (bone resorption with lytic lesions and marrow fibrosis) and, finally, osteosclerosis (enhanced bone density)
2- Children → impaired bone growth, tendency for spontaneous fractures with slow healing, aseptic necrosis of the hip, and extraosseous calcifications.

CLINICAL PRESENTATION

Renal failure manifestations can involve multiple systems (e.g., >40% of patients have diabetes, and >25% have concurrent hypertension)

Signs and Symptoms

CKD Patients up to stage 3; few clinical signs

Stage 3 and beyond;

- general ill feeling, loss of appetite, and weight loss
- anemia→ pallor of the skin and mucous membranes + dizziness
- leg cramps
- insomnia
- dark urine and nocturia
- Convulsions (late manifestation) due to azotemia.
- oral ulceration and candidiasis
- bleeding diatheses → hemorrhagic episodes, ecchymoses, petechiae, gingival bleeding
- hyperpigmentation of the skin (brownish-yellow) due to retention of carotene-like pigments
- hypertension
- congestive heart failure (shortness of breath, orthopnea, dyspnea on exertion, peripheral edema), and pericarditis

LABORATORY AND DIAGNOSTIC FINDINGS

- Urinalysis (most basic test); physical, chemical, and microscopic examination of urine. This test looks for proteinuria, hematuria, cellular casts, specific gravity, and pH.
- GFR is the best measure of overall kidney function, and the most significant protein in the urine is albumin (albuminuria). T

*These two measures can determine the severity and prognosis of CKD

- Serum creatinine; measure of muscle breakdown and filtration capacity of the nephron (compares creatinine concentrations in blood)
- Blood urea nitrogen (BUN)indicator of kidney function (not as specific as creatinine because BUN is also influenced by liver function)

MEDICAL MANAGEMENT

1- stage 1 and stage 2 (Conservative Care); retard the progress of disease:
- Dietary modifications →decreasing the retention of nitrogenous waste products and controlling hypertension, fluids, and electrolyte imbalances. (Low-protein diet and limiting fluid, sodium, and potassium intake.
- Comorbid conditions (diabetes, hypertension, heart failure) should be controlled

2- stage 3; Managing anemia, malnutrition, and bone disease (e.g., hyperparathyroidism)

3- Stage 4, (by a nephrologist); preparations for renal replacement therapy

4- stage 5, or
   - when uremic features appear or
   - intractable fluid overload occurs,

dialysis is started.

Dialysis

It is the artificial filtration of blood. Dialysis becomes necessary when GFR drops below 30 mL/minute/1.73 m2 (azotemia is uncontrollable).

A- peritoneal dialysis; hypertonic solution is instilled into the peritoneal cavity through a permanent peritoneal catheter. After a time, the solution and dissolved solutes (e.g., urea) are drawn out.

1- continuous cyclic peritoneal dialysis (CCPD); older, also known as automated peritoneal dialysis (APD), uses a machine to perform three to five dialysate exchanges while the patient sleeps (for 8–10 hours).

2- chronic ambulatory peritoneal dialysis (CAPD); more common, requires shorter exchange periods. of 30 to 45 minutes four to five times per day (manually). This method allows more freedom than CCPD because the dialysate is allowed to drain into a bag strapped to the patient

The advantages of peritoneal dialysis

- relatively low initial cost

- ease of performance
- reduced likelihood of infectious disease transmission
- absence of requirement for anticoagulation.

Disadvantages;
- the need for frequent sessions
- risk of peritonitis
- frequent association with abdominal hernia
- lower effectiveness compared to hemodialysis.

hemodialysis principal use is in patients in acute renal failure or those who require only occasional dialysis. Hemodialysis is the method of choice when azotemia occurs and dialysis is needed on a long-term basis. Treatments are performed every 2 or 3 days, depending on need. Usually, 3 to 4 hours is required for each session. Hemodialysis consumes an enormous amount of the patient's time and is extremely confining. However, between dialysis sessions, patients lead relatively normal lives. Around 2/3 of the patients receive hemodialysis through a permanent and surgically created arteriovenous graft or fistula, usually placed in the forearm. Access is achieved by cannulation of the fistula with a large-gauge needle Approximately 1/3 of patients receive dialysis through a temporary or permanent central catheter while the permanent access site is healing or when all other access options have been exhausted. Patients are "plugged in" to the hemodialysis machine at the fistula or graft site, and blood is passed through the machine, filtered, and returned to the patient. Heparin usually is administered during the procedure to prevent clotting.
Hemodialysis provides about 15% of normal renal function.

complications develop
- Serum calcium concentrations require regulation (supplementation)
- Improper blood levels contribute to muscle tetany and oversecretion of PTH.
- Dialysis-related amyloidosis (dialysis for more than 5 years)→ pain and stiffness in joints and tendons.
- Anemia
- risk of hepatitis B, hepatitis C, and HIV infections
- Infection of the arteriovenous fistula →septicemia, infective endarteritis
- drugs metabolized primarily by kidney must be avoided
- abnormal bleeding (platelet destruction by mechanical trauma)

The 5-year survival rate of dialysis patients is 35%.

DENTAL MANAGEMENT

A-Patient Under Conservative Care

I-Medical Considerations

Identification.

- High-risk groups (i.e., patients with diabetes and hypertension) recommended to be screened for CKD.
- patient who has signs and symptoms of kidney disease (e.g., hematuria, repeated urinary tract infections or edema)→ referred to a physician

Risk Assessment.

- stage 1 to 3, problems generally do not arise in the provision of outpatient dental care if the patient's disease is well controlled
- stage4 or higher→ consultation before dental treatment
- presence of comorbid condition (e.g., diabetes mellitus, hypertension, systemic lupus erythematosus) → consultation before dental treatment in a hospital-like setting.

Antibiotics.

- stages 1–3 and are not receiving dialysis →do not require additional antibiotic considerations.
- invasive procedures for a patient with CKD above stage 3 → consult physician to assess the need for antibiotics.
- Alterations in dosage may be needed
- If an orofacial infection occurs →aggressive management with the use of culture and sensitivity testing and appropriate antibiotics

Bleeding.

- invasive procedure → pretreatment screening for bleeding disorders→ abnormal values →discussed with the physician.
- If bleeding is anticipated→ hematocrit levels raised using erythropoietin or RBC transfusion
- Local hemostatic agents (topical thrombin, microfibrillar collagen, absorbable gelatin sponge, suture)→ used on patients with uremia.
- Desmopressin avoided.
- Conjugated estrogens →if a longer duration of action is required

Blood Pressure.

- monitored before and during the procedure.

Capacity to Tolerate Care.

- GFR <50 mL/min → elective dental care should be delayed until patient is medically stable.
- Patients who take large doses of corticosteroids (e.g., ≥10 mg/day of prednisone)→ adrenal insufficiency (adrenal crisis!!);
  usual corticosteroid dose is taken before surgical procedures

Drug Considerations.

- drugs excreted by the kidneys are eliminated twofold less efficiently when the GFR drops to 50 mL/min → may reach toxic levels at lower GFR. →drug dosage reduced + timing of administration prolonged.
- Nephrotoxic drugs (acyclovir, aminoglycosides, aspirin, NSAID, and tetracycline) → avoided
  *NSAIDs inhibit prostaglandin synthesis→vasoconstriction and reduced renal perfusion.
  *Acetaminophen probably safer than aspirin for a short time (metabolized in the liver).
- An alternative analgesic is tramadol
- Tetracyclines, except for doxycycline, worsen renal impairment by inhibiting protein synthesis

<u>Drug frequency and dosage adjustments</u>

1- a low serum albumin value reduces the number of binding sites for circulating drugs, thereby enhancing drug effects
2- uremia can modify hepatic metabolism of drugs (increasing or decreasing clearance
3- antacids can affect acid-base or electrolyte balance, further complicating uremic effects on electrolyte balance
4- larger initial doses may be required in the presence of substantial edema or ascites, whereas smaller initial doses may be required if dehydration or severe debilitation is present
5- aspirin and other NSAIDs potentiate uremic platelet defects, so these antiplatelet agents may need to be avoided if invasive procedures are performed
6- Nitrous oxide and diazepam require little modification with ESRD → hematocrit or hemoglobin concentration measured before intravenous sedation to ensure adequate oxygenation.
7- In uremia, blood-brain barrier may not be intact, so drugs that depress the central nervous system (barbiturates, narcotics)→excessive sedation (best be avoided)
8- Opioid→dosage adjustment for CKD

9- When the hemoglobin concentration is below 10 g/100 mL, general anesthesia is not recommended

2-Oral Complications and Manifestations.

1- red-orange discoloration of the cheeks and mucosa is associated with pruritus, and deposition of carotene-like pigments
2- Salivary flow may be diminished→ xerostomia, parotid infections, Candidiasis
3- altered or metallic taste, and
4- characteristic ammonia-like odor (saliva), which results from a high urea content.
5- Poor oral hygiene, halitosis, gingivitis, periodontal disease, and tooth loss (stage 3 or higher)
6- Uremic stomatitis; rare condition, in acute renal failure and BUN levels are greater than 55 mg/dL. → red, burning mucosa covered with gray exudates and later by frank ulceration. Adherent white patches called uremic frost caused by urea crystal deposition are more common on the skin but may be seen on the oral mucosa and can resemble hairy leukoplakia.
7- Bleeding tendencies are evident as petechiae and ecchymoses on the labial and buccal mucosa, soft palate, and margins of the tongue and as gingival bleeding.
8- Tooth-specific changes
   - Enamel hypoplasia and hypocalcification (ESRD at early age).
   - In the developing dentition, red brown discoloration and a slight delay
   - erosion from persistent vomiting
   - Pulp narrowing
   - Caries, is not a feature ?? (Salivary urea inhibits the metabolic end products of bacterial plaque + increases the buffering capacity of saliva→preventing a drop in pH
9- osseous changes of the jaws
   - triad of loss of lamina dura, demineralized bone (resulting in a "ground-glass" appearance), and localized and expansile radiolucent jaw lesions (central giant cell granulomas, also called brown tumors), the latter from secondary hyperparathyroidism.
   - widened trabeculations
   - loss of cortication
   - calcified extraction sites (so-called "socket sclerosis")
   - metastatic calcifications within soft tissue and the skull.
   - Vascular calcifications of the carotid arteries

10- gingival enlargement; Patients with CKD who take
- calcium channel blocker (hypertensive)
- cyclosporine may exhibit (transplant recipients).

3-Treatment Planning Modifications.

- Oral hygiene instruction
- periodic recall appointments are important
- frequent professional prophylaxis, and antiplaque measures (chlorhexidine or triclosan rinses)→reduce the effects of drug-induced gingival enlargement in transplant recipients
- No contraindication to routine dental when there is
  - acceptable level of oral hygiene
  - proper attention to the systemic health (Dialysis Patients)

B-Patients Receiving Dialysis

1-Medical Considerations

Risk Assessment.

- the type dialysis,
- degree of kidney dysfunction,
- comorbidities
- oral health
- dental procedure planned.

For example, peritoneal dialysis presents no additional problems with respect to dental management. However, this is not the case with patients who are receiving hemodialysis. The arteriovenous fistula is susceptible to infection (endarteritis) →bacteremia,→ infective endocarditis (secondary to staphylococcal infections develop at the of the fistula, or catheter site).

2-Recommendations

Antibiotics.

American Heart Association's 2003 guidelines do not include a recommendation for prophylactic antibiotics before invasive procedures

Risk of Infection.

- More in long term dialysis patients, especially those with diabetes
- rates of tuberculosis infections are higher
- periodic testing for hepatitis (Liver function should be assessed) and HIV
- use of standard infection control procedures is important (for all patients).

Bleeding.

Hemodialysis tends to aggravate bleeding tendencies, ?? these tests should be ordered

- activated partial thromboplastin time (aPTT)
- platelet count

management modifications to reduce serious bleeding:

- Dental treatment on the day after hemodialysis
- The activity of heparin lasts for 3 to 6 hours after infusion→delay of treatment is prudent•
- Obtaining primary closure and, as needed, using pressure and local hemostatic agents (e.g., absorbable gelatin sponge, thrombin)
- Performing major surgical procedures on the day after the end of the week of hemodialysis treatment to provide additional time for clot retention before dialysis is resumed.
- Contacting the nephrologist to request that the heparin dose be reduced or eliminated during the first hemodialysis session after the surgical procedure.
- Administering protamine sulfate (usually by a physician block the anticoagulant effects of heparin.) if dental care is necessary the day of hemodialysis.

Blood Pressure.

the arm that contains the arteriovenous shunt should be protected from application of the blood pressure cuff

Capacity to Tolerate Care.

Comorbid conditions such

Dialysis patients often take several medications to control hypertension, diabetes, congestive heart failure, or hypercoagulability (i.e., anticoagulation). Dental care must be provided only when the patient is medically stable,

Drug Considerations.

Hemodialysis removes some drugs from blood→shorten the duration of effect

The chance that a given drug will be dialyzed is governed by four factors:

1- molecular weight
2- molecular size, (degree of protein binding
3- volume of drug distribution
4- endogenous drug clearance.30 For

*Example,

- larger molecule (>500 daltons) drugs are poorly dialyzed.
- Drugs with low proteins binding capacity removed during Hemodialysis
- Uremia alters protein binding →phenytoin that normally is highly protein bound exhibits lower plasma protein binding during uremia
- Drugs with high lipid affinity → high tissue binding→not available for dialysis removal.

*dosing of drugs should be tailored to occur after dialysis

3-Oral Complications and Manifestations.

- uremic odor,
- dry mouth,
- taste change
- tongue and mucosal pain

patients undergoing hemodialysis

- Petechiae, ecchymoses,
- higher plaque and calculus indices
- lower levels of salivary secretion are more common among
- Secondary hyperparathyroidism + osseous changes in the jaws
- high levels of PTH → ↑mortality

Patient With Renal Transplant; special management precautions,

- corticosteroids or antibiotic prophylaxis
- management of oral infection and gingival overgrowth caused by cyclosporine therapy