Chronic Kidney Disease



Definitions

- **Chronic kidney disease (CKD):** Kidney structure or function abnormality for **≥ 3 months** (irrespective of cause)
- **Kidney damage:** Structural abnormality OR lab evidence (e.g., albuminuria) for **≥ 3 months**
- **Decreased kidney function: eGFR < 60 mL/min/1.73 m²** (G3a–G5) for **≥ 3 months**
- **End-stage kidney disease (ESKD):**
  - **eGFR: < 15 mL/min/1.73 m²**
  - **Plus:** Manifestations of uremia requiring chronic renal replacement therapy

CKD Criteria (KDIGO)

- **Markers of kidney damage (≥ 1 for ≥ 3 months):**
  - **Albuminuria: AER ≥ 30 mg/24 h** OR **ACR ≥ 30 mg/g**
  - **Urinary sediment abnormalities:** e.g., abnormal casts
  - **Tubular disorders:** Electrolyte/other abnormalities due to tubular dysfunction
  - **Pathology:** Pathologic abnormalities
  - **Imaging:** Structural abnormalities detected by imaging
  - **History:** Kidney transplantation
- **Markers of decreased function (≥ 3 months):**
  - **eGFR: < 60 mL/min/1.73 m²**

Staging of CKD (CGA: Cause–GFR–Albuminuria)

GFR categories

- **G1: ≥ 90 mL/min/1.73 m²** (normal/high)
- **G2: 60–89 mL/min/1.73 m²** (mildly decreased)
- **G3a: 45–59 mL/min/1.73 m²** (mild–moderate)
- **G3b: 30–44 mL/min/1.73 m²** (moderate–severe)
- **G4: 15–29 mL/min/1.73 m²** (severely decreased)
- **G5: < 15 mL/min/1.73 m²** (kidney failure)

Albuminuria categories

- **A1: < 30 mg/24 h** OR **< 30 mg/g** (normal–mildly increased)
- **A2: 30–300 mg/24 h** OR **30–300 mg/g** (moderately increased)
- **A3: ≥ 300 mg/24 h** OR **≥ 300 mg/g** (severely increased)

Etiology

- **Common causes:** Diabetic nephropathy, hypertensive nephropathy, glomerulonephritis
- **Other causes:** Polycystic kidney disease, analgesic misuse, amyloidosis
- **Diabetic nephropathy + hypertension** = commonest cause of ESKD

Uremia

- **Definition:** Accumulation of uremic toxins due to ↓ renal excretion
- **Examples:** Urea, creatinine, **β_2-microglobulin**
- **Key point:** Many CKD manifestations are due to uremic toxins (e.g., nausea, vomiting, hiccough, pruritus)
- **Clinical pattern:** Patients often remain asymptomatic until late stages (high compensatory capacity)

Clinical Presentation and Complications (High-Yield)

Volume Status

- **Hypervolemia:** Due to impaired sodium and water handling
- **Clinical relevance:** Drives hypertension, edema, pulmonary edema, heart failure

CKD–Mineral and Bone Disorder (CKD-MBD)

- **Core components:** Abnormal metabolism + bone turnover/mineralization + extra-skeletal calcification
- **Metabolic abnormalities (mechanisms):**
  - **Phosphate (P):** ↑ due to ↓ **renal excretion**
  - **FGF23:** ↑ in response to ↑ phosphate
  - **Vitamin D (calcitriol):** ↓ due to ↑ **FGF23 (main cause)** + loss of functioning kidney mass → ↓ renal hydroxylation
  - **Calcium (Ca^{2+}):** ↓ due to phosphate retention + ↓ active vitamin D → ↓ intestinal Ca^{2+} absorption
  - **PTH:** ↑ (secondary hyperparathyroidism) due to ↑ P/FGF23 + ↓ Ca^{2+}/calcitriol
  - **Tertiary hyperparathyroidism:** Later; parathyroid hyperplasia with autonomous PTH secretion
- **Renal osteodystrophy (bone biopsy classification):**
  - **High turnover:** Osteitis fibrosa cystica (↑ PTH → ↑ bone resorption)
  - **Low turnover:**
    - **Adynamic bone disease:** Over-suppression of PTH (vitamin D analogs, calcium-based binders) or post-parathyroidectomy → ↓ bone formation
    - **Osteomalacia:** Vitamin D deficiency → insufficient mineralization
  - **Mixed uremic osteodystrophy:** Mixed pattern
- **Extra-skeletal calcification:**
  - **Vascular calcification:** e.g., coronary artery calcification → ↑ cardiovascular risk
  - **Calciphylaxis:** Arterioles/capillaries in dermis/subcutaneous tissue (later)
  - **Other:** Soft tissue, valvular calcification
- **Gold standard:** Bone biopsy for diagnosis/classification of bone disease

Cardiovascular Abnormalities

- **Hypertension causes:** Salt/water retention
- **LVH causes:** Volume overload + systolic hypertension
- **Ischemic vascular disease risk factors:**
  - **Traditional:** Hypertension, diabetes, atherosclerosis, dyslipidemia, obesity, smoking
  - **Non-traditional (CKD-specific):** Systemic inflammation, albuminuria, MBD/vascular calcification, hyperuricemia, oxidative stress
- **Heart failure causes:** Myocardial ischemia, LVH, cardiomyopathy, salt/water retention
- **Arrhythmias causes:** Electrolyte disturbances, volume overload, sympathetic overactivity, acidosis
- **Pericardial disease:** Uremic pericarditis/pericardial effusion
- **Key point:** CVD is leading cause of morbidity/mortality at every CKD stage (often die from CVD before reaching ESKD)

Hematologic Abnormalities

- **Anemia definition (adults):**
  - **Male:** Hb < 13 g/dL
  - **Female:** Hb < 12 g/dL
- **Typical type:** Normocytic normochromic (unless iron deficiency → microcytic; B12 deficiency → macrocytic)
- **Etiology (multifactorial):**
  - **EPO deficiency:** Main cause
  - **Uremic toxins:** Bone marrow suppression + ↓ RBC lifespan
  - **Bleeding tendency:** ↓ iron stores
  - **Folate/Vit B12 deficiency**
- **WBCs:** Leukocyte dysfunction → ↑ infection risk
- **Platelets:** Abnormal adhesion/aggregation → ↑ bleeding tendency
- **(Hb ~10 g/dL in CKD): Serum ferritin** (iron status assessment)

Dermatologic Abnormalities

- **Pigmentation:** Due to failure to excrete beta-melanocyte stimulating hormone
- **Pallor:** Due to anemia
- **Uremic pruritus**
- **Bullous dermatoses**
- **Calcific uremic arteriolopathy (calciphylaxis)**
- **Nephrogenic systemic fibrosis:** Seen in CKD exposed to gadolinium (MRI contrast)

Respiratory Abnormalities

- **Pleurisy:** Due to uremia
- **Pulmonary edema:** Multifactorial (hypoalbuminemia + hypervolemia + heart failure)
- **Pneumonia (± TB):** Due to impaired immunity

Neuromuscular abnormalities

- **Uremic encephalopathy:** Early impaired mental status → seizures/coma if untreated
- **Asterixis**
- **Somatic neuropathy:** Sensory > motor; lower > upper; distal > proximal
  - **Sensory neuropathy clue:** Restless legs syndrome
- **Autonomic neuropathy:** Sympathetic overdrive + ↓ parasympathetic function
- **Uremic myopathy**
- "Myelopathy" is not a typical neuromuscular complication of uremia (vs encephalopathy/neuropathy/myopathy/myoclonus)

GIT and nutrition

- **Uremic fetor:** Ammonia/urine-like breath odor from urea → ammonia in saliva; often metallic taste
- **Glossitis:** Nutritional deficiencies (iron, B12, folate)
- **GERD / esophagitis:** Delayed gastric emptying
- **Gastritis / delayed gastric emptying / peptic ulcer**
- **Constipation**
- **Protein-energy wasting (PEW):** Common in advanced CKD/dialysis; associated with ↑ morbidity/mortality
  - **Contributors:** Poor intake (anorexia/nausea/vomiting), metabolic acidosis (catabolism), dialysis losses, endocrine disorder (insulin resistance), blood loss

Glucose metabolism in CKD

- **Both:** Hyperglycemia and hypoglycemia can occur
- **Hyperglycemia (more common):** Insulin resistance associated with CKD
- **Hypoglycemia causes:** ↓ renal insulin clearance + ↓ renal glucose release + malnutrition

Acute on chronic kidney disease (ACKD)

- **Definition:** Acute (often reversible) decline in kidney function occurring in patient with pre-existing CKD

Predictors of progressive CKD

Non-modifiable

- **Age:** Older age
- **Gender:** Worse in males
- **Ethnicity:** Worse in non-Caucasian
- **Genetics:** Worse in ADPKD with **PKD1** genotype; RAAS gene polymorphisms

Modifiable

- **Comorbidities:** Hypertension, diabetes
- **Lifestyle:** Obesity, smoking, alcohol intake
- **Lab changes:** Proteinuria/albuminuria (A3 = faster progression), hyperuricemia
- **RAAS dysfunction**
- **Medications:** Nephrotoxic drugs, herbal agents
- **Others:** Metabolic syndrome, insulin resistance, dyslipidemia
- **Most significant predictors (lecture):** Degree of impaired kidney function at presentation + hypertension control + severity of proteinuria/albuminuria

Investigations

Functional decline

- **Serum markers:** ↑ creatinine and BUN OR ↑ cystatin C
- **Chronic vs acute clue (lecture):** If relatively well with normal urine volume plus:
  - **BUN: > 140 mg/dL**
  - **Creatinine: > 13.5 mg/dL**
  - **Blood urea: > 300 mg/dL**
- **eGFR:** Decreased
- **eGFR estimation:** CKD-EPI, MDRD; cystatin-based eGFR

Structural renal damage (laboratory + biopsy)

- **Electrolytes:**
  - **Na^+ retention:** Occurs once GFR severely reduced with unchanged sodium intake
  - **K^+ level initially maintained:** By (1) cellular shift (ECF→ICF), (2) ↑ renal excretion, (3) ↑ colonic secretion
  - **Hyperkalemia:** When protective mechanisms fail at GFR **~20–15 mL/min**
  - **Hypokalemia (less common):** Vomiting or ↑ diuretic use
  - **Ca^{2+}:** ↓ (see CKD-MBD)
  - **P:** ↑
- **ABG:** Metabolic acidosis
  - **Mechanism:** Accumulation of acidic waste + ↓ NH_4^+ production + ↓ HCO_3^- regeneration
- **Urine studies:**
  - **Albuminuria: AER ≥ 30 mg/24 h** OR **ACR ≥ 30 mg/g**
  - **Dipstick:** Hematuria or proteinuria
  - **Microscopy:** Abnormal sediments (e.g., waxy casts)
  - **Broad casts** suggest chronic renal failure
- **Renal biopsy (not routine):**
  - **Indications:** Rapid/unexplained decline in eGFR OR need to confirm etiology (e.g., GN) before disease-specific therapy

Imaging

- **Renal ultrasound: 1st-line** technique for kidney structure assessment
- **US findings suggesting chronic kidney damage:**
  - **Kidney length: < 9 cm**
  - **Parenchymal thickness: < 1 cm** (± cortical thickness reduction)
  - **Cortical echogenicity:** Increased
  - **Other:** Multiple cysts, calcifications, renal scarring
- **US findings suggesting specific etiology:**
  - **Obstruction:** Ureteral/renal pelvic dilatation
  - **PKD:** Bilaterally enlarged kidneys with multiple cysts
- **Kidney size :**
  - **In CKD:** Kidneys are bilaterally shrunken **EXCEPT** in **DM, PKD, amyloidosis, hydronephrosis**
  - **Small kidneys clue:** Late renal artery stenosis; late reflux nephropathy (irregular small kidneys)
  - **Large kidneys not present in:** Renal artery stenosis
- **Helpful test to differentiate acute vs chronic: Renal ultrasonography**
- **CT/MRI/angiography:** As indicated

MANAGEMENT OF CKD PATIENTS

TREAT AND CONTROL THE CAUSE

- **Examples:** Diabetes mellitus, hypertension

SUPPORTIVE CARE

- ☑ **Medications (safety + dose adjustment)**
  - **Potentially nephrotoxic substances:**
    - **If risks > benefits:** Avoid and replace with safer drug
    - **Example: Acetaminophen** instead of **NSAIDs** for pain
    - **Contrast imaging:** Avoid when possible; if needed, use with caution
  - **Renally cleared medications:** Adjust dosing based on **eGFR**
- ☑ **Volume overload**
  - **Dietary salt restriction**
  - **Diuretics:** Loop diuretics (± metolazone)
- ☑ **Electrolytes**
  - **Hypernatremia:** Na restriction
  - **Hyperkalemia:** Dietary K restriction + kaliuretic diuretics
- ☑ **Acid-base disturbance (metabolic acidosis)**
  - **Alkali supplementation:**
    - **Agent:** Sodium bicarbonate
    - **Route:** Oral
    - **Benefits:** Kidney protective (↓ oxidative damage) + improves protein nutrition (↓ protein catabolism) + protects against hyperkalemia
  - **Diet:**
    - **Low-protein diet:** ↓ acid production
    - **Base-inducing fruits/vegetables:** ↑ serum HCO_3^-
    - **Caution:** Fruits/vegetables may increase hyperkalemia risk
- ☑ **Mineral and bone disorder (targets: normalize phosphate, calcium, PTH)**
  - **Hyperphosphatemia correction:**
    1) **Diet control:** Restrict phosphate (cola, canned food, fast food)
    2) **If still high:** Oral phosphate binders ↓ dietary phosphate absorption
    - Oral **calcium carbonate** can lower serum phosphorus
  - **Vitamin D supplementation (if** 25-OH vitamin D < 30 ng/mL**):**
    - **Daily: 1000** or **2000 IU**
    - **Monthly: 50,000 IU**
  - **Avoid hypocalcemia:**
    - **Step:** Correct hyperphosphatemia + treat vitamin D deficiency
    - **Dietary calcium:** Increase to **1500 mg** elemental calcium daily
  - **Avoid hyperparathyroidism:**
    - **Correct:** Ca^{2+}, phosphate, vitamin D
    - **Parathyroidectomy:** Last line if medical therapy fails
  - **Adynamic bone disease clue:** Low PTH in long-term hemodialysis patient with fractures

- ☑ **Cardiovascular abnormalities (hypertension)**
  - **Target BP: < 130/80 mmHg**
  - **Non-pharmacological:**
    1) Healthy weight
    2) Lower salt intake (**< 5 g NaCl/day**)
    3) Regular exercise (if not contraindicated)
    4) Stop smoking and alcohol
  - **Pharmacological (first-line depends on proteinuria):**
    - **Proteinuria present:** RAAS blocker (ACEIs/ARBs)
      - **Uses:** First-line to ↓ proteinuria and slow CKD progression; can be used even if normotensive
      - **Caution:** Avoid dual RAAS blockade; follow creatinine and potassium
      - **antiproteinuric drug: Captopril** (ACEI)
    - **Proteinuria absent:** Consider calcium channel blocker and/or thiazide/thiazide-like diuretic
  - U-shaped SBP curve (very low or very high SBP associated with faster eGFR decline)
- ☑ **Hematological abnormalities (anemia)**
  - **Why treat:** ↑ quality of life + improves cardiovascular health (↓ LVH/angina; ↓ COP)
  - **Options:**
    1) Iron therapy
    2) Check and treat vitamin B12/folate deficiency
    3) **Erythropoiesis-stimulating agent:** Best option
    4) Blood transfusion (avoid when possible)
  - **Blood transfusion cautions:** ↑ infections + iron overload + alloimmunization (if transplant candidate)
  - **Indication for transfusion:** Urgent rapid correction (e.g., acute hemorrhage)
- ☑ **Dermatological abnormality (pruritus)**
  - **Topical:** Skin emollients
  - **Systemic:** Gabapentin; antihistamines not recommended
  - **Phototherapy:** UVB
- ☑ **Glycemic control (diabetic CKD)**
  - **Target HbA1c: ≤ 7%**
  - **If limited life expectancy/comorbidities/high hypoglycemia risk:** Target may be **> 7%**
  - **Insulin caution:** Reduced eGFR increases hypoglycemia risk
- ☑ **Lifestyle and nutrition**
  - **Protein:** Low protein diet **0.8 g/kg/day** (unless on dialysis)
  - **Calories: 25–35 kcal/kg IBW/day**
  - **Salt:** Restricted (**< 5 g/day**) to correct hypervolemia and hypertension
  - **Fluid:** Balance to avoid volume overload
  - **K^+:** Restrict to correct hyperkalemia
  - **Phosphate:** Restrict to correct hyperphosphatemia
  - **Ca^{2+}:** Allowed within dietary recommendations

- **Smoking cessation (why):** Dose-dependent progression of kidney disease + ↑ hyperfiltration/proteinuria + diabetic nephropathy-like glomerulopathy
- **Obesity (why weight reduction):** ↑ CKD risk; associated with glomerulopathy, FSGS, proteinuria

☑ **Dyslipidemia (KDIGO recommendations)**

- **Non-dialysis:**
  - **Age ≥ 50 years:** Start statin
  - **Age 18–49 years + cardiovascular risk:** Start statin
- **Dialysis:** Starting statin is not recommended

Retarding CKD progression (goals)

- **Proteinuria goal:** Reduce ideally to **< 500 mg/day**
- **GFR decline goal:** Slow ideally to **~1 mL/min/year** (aging-related decline)

Renal replacement therapy

Non-operative options

- **Hemodialysis**
- **Peritoneal dialysis**

Indications to initiate dialysis (KDIGO: consider if ≥ 1 persists)

- **Persistent kidney failure symptoms:** Serositis (e.g., pericarditis), acid-base disturbance, electrolyte abnormalities, pruritus, anorexia, neurologic signs attributable to uremia
- **Persistent inability to control volume status**
- **Persistent inability to control blood pressure**
- **Persistent malnutrition not responsive to dietary interventions**
- **Persistent cognitive impairment**
- **clinical trigger:** Pericardial rub = dialysis indication
- **Urgent dialysis trigger:** Serum K **~7.2 mEq/L** with relevant ECG changes

Operative option

- **Kidney transplantation:** Treatment of choice when possible for ESKD