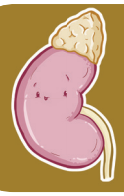

NOTES
KIDNEY DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Group of diseases involving renal system, commonly due to systemic disease/iatrogenic factors (medications, fluid management)
- Common complication of hospitalized individuals, esp. elderly with chronic disease
- Kidneys sensitive to any systemic change due to high metabolic demand
- *Classification:* pre-, intra-, post-renal causes; based on location of pathology in urinary system

SIGNS & SYMPTOMS

- Widely variable, universally includes urine abnormalities (amount, composition, color)
- May be easily evident (hematuria)/indolent (oliguria)

DIAGNOSIS

LAB RESULTS

- Blood urea nitrogen (BUN)-to-creatinine (BUN:Cr) ratio
  - Filtration/reabsorptive function
- Glomerular filtration rate (GFR)
  - Estimated value, correlates to filtration function
- Urinalysis
  - Physical, chemical, microscopic data; compare to serum concentration

Urine microscopy

- Cell/substance accumulation in tubules → casts → molds to tubular form → excreted as tubular-shaped mass
- Eosinophils, epithelial cells, erythrocytes

OTHER DIAGNOSTICS

- Medical history
  - Medication, exposure
- Physical examination
  - Systemic signs of disease
  - Limited for renal-specific disease; identify gross abnormalities of lower urinary tract

TREATMENT

- *Goal:* achieve adequate volume, composition

OTHER INTERVENTIONS

- Treat underlying systemic disease
  - Withdrawal of offending agent (e.g. medication)

ACUTE TUBULAR NECROSIS

osms.it/acute-tubular-necrosis

PATHOLOGY & CAUSES

- Disease of tubular epithelial cell death; most common cause of acute kidney injury (AKI) in hospitalized individuals; potential for permanent kidney failure
- AKA acute tubular injury (ATI)
- Death of tubular epithelial cells → disruption of basolateral cell surface → sloughing, obstruction of tubules → ↑ tubular hydrostatic pressure → ↓ GFR → filtration/reabsorption → ↓ urine output → oliguria → azotemia

MNEMONIC: LIFELESS

Differences between apoptosis and necrosis

Leaky membranes
Inflammatory response
Fate
Extent
Laddering
Energy dependent
Swell or shrink
Stimulus

CAUSES

Ischemia

- Death of tubular epithelial cells due to insufficient oxygen to meet metabolic demand
  - Most common in proximal, thick ascending tubules; most metabolically active sites across nephron due to high amounts of active sodium reabsorption
  - ↓ blood delivery to tubular epithelial cells → hypoxia → ischemia
  - ↓ blood flow → endothelial cell, ↑ vasoconstrictor release; endothelin + ↓ vasodilators release; nitric oxide (NO), prostacyclin (PGI2) → net effect of afferent arteriole constriction → ↓ glomerular filtration rate (GFR)
- Ischemic conditions/diseases
  - Shock; heart failure; renal artery stenosis; excessive gastrointestinal (GI) fluid loss; malignant hypertension; microangiopathies
  - *Systemic disease associated with thrombosis:* hemolytic-uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC)
  - Microscopic polyangiitis
  - Surgical procedures, esp. cardiac, abdominal aortic aneurysm (AAA) repair

Nephrotoxins

- Direct tubular epithelial cell injury due to toxins encountered by kidney
- Most common in proximal convoluted tubule; first tubular site in nephron for filtered toxin
- Pathophysiology
  - Direct toxic renal epithelial tubular cell injury; death
- Endogenous toxins
  - Myoglobin, hemoglobinuria; uric acid (tumor lysis syndrome); monoclonal light chains (multiple myeloma)
- Exogenous toxins
  - *Medications:* aminoglycosides (most common), cisplatin, amphotericin B, nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Heavy metals (lead); ethylene glycol; radiocontrast agents; organic solvents

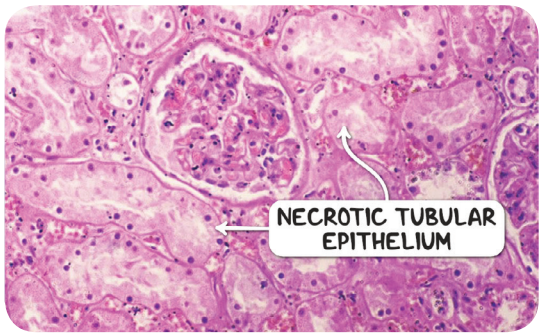

Figure 116.1 Histological appearance of acute tubular necrosis. The tubular epithelial cells are poorly demarcated and there is loss of nuclei, consistent with necrosis.

SIGNS & SYMPTOMS

- *Onset:* triggering event
- *Oliguric phase (10–14 days):* may advance to anuria if unrecognized, untreated
- *Diuretic phase (> 500ml urine per day):* due to regeneration of functional tubular epithelial cell growth, outflow of fluid overload during oliguric phase, osmotic diuresis from retained solutes
- *Recovery phase (normal urine output, concentration):* parallels full recovery of tubular epithelial cell function

DIAGNOSIS

LAB RESULTS

- Intrarenal AKI
- ↓ *BUN:Cr ratio:* < 15
- ↑ Fe_{Na}: > 2%
- *Dilute urine:* ↓ U_{osm}; < 500mOsm/kg
- ↑ K^+
- *Urinalysis:* brown granular casts
  - Sloughed-off epithelial cells in tubules, excreted as mass)

TREATMENT

OTHER INTERVENTIONS

Hydration

- Return to euvolemic fluid status/eliminate offending nephrotoxin
- 1–2 weeks for epithelial cells to regenerate

Prevention

- Identification of nephrotoxins, elimination/limitation of use
- Identification of high-risk individuals, situations for acute ↓ renal blood flow, ensure adequate intravascular volume status
- Add allopurinol in tumor lysis syndrome (TLS) cases
  - Prophylactic/therapeutic

APOPTOSIS VS NECROSIS: "LIFELESS"

	APOPTOSIS	NECROSIS
LEAKY	No	Yes
INFLAMMATION	None	Usual
FATE	Swallowed by neighbors	Eaten by phagocytes
EXTENT	Single cell	Cell groups
LADDERING	Yes	No
ENERGY DEP.	Yes	No
SWELL, SHRINK	Shrink	Swell
STIMULUS	Physiologic Pathologic	Pathologic only

KIDNEY STONES

osms.it/kidney-stone

PATHOLOGY & CAUSES

- AKA nephrolithiasis
- Stones form in kidney when solutes precipitate out as crystals in urine
- Solute supersaturated with crystalline constituents → precipitate out of solution → form crystals → further precipitation → more solutes deposit, build up → stones
- Occurs when ↑ solute, ↓ solvent, combination of both (e.g. dehydration)
- Some stones < 5mm can be passed through urinary stream within hours without intervention

TYPES

Calcium stones

- Calcium oxalate (most common)
  - Black/dark brown
  - Positively-charged calcium ion binds to negatively-charged oxalate ion in medullary interstitium
  - More likely in acidic urine
  - *Pathology:* primary hyperoxaluria (autosomal recessive disorder → excessive hepatic oxalate production); acquired hyperoxaluria (e.g. enteric oxaluria; → excessive absorption of oxalate in gut)
- Calcium phosphate
  - Dirty white
  - Calcium binds to negatively charged phosphate group
  - More likely in alkaline urine
  - *Pathology:* alteration in calcium absorption in gut/renal reabsorption → hypercalciuria

Uric acid stones

- Red brown
- Physiologic pH uric acid, proton loss → urate ion → binds sodium → forms monosodium urate → crystallizes → stones
- *Uric acid:* breakdown product of purines
- *Pathology:* excessive dietary purine → ↑ uric acid as metabolite → hyperuricosuria

Struvite stones (infection/triple stones)

- Dirty white
- Composite of magnesium, ammonium, phosphate
- Urea-splitting bacteria (e.g. *Proteus vulgaris, Staphylococci*) convert urea to ammonia → urine more alkaline → favors precipitation of magnesium, ammonium, phosphate
- Often form largest stones; can form staghorn calculi, branch into renal calyces
- *Pathology:* ammonium ions from urease-producing bacteria + alkaline urine → precipitation

Cystine stones (less common)

- Yellow/light pink
- Composed of amino acid cystine
- *Pathology:* autosomal recessive/dominant disorder → defective renal transport of cystine → ↓ renal reabsorption + increased urinary cystine excretion → cystinuria

Xanthine stones (rare)

- Brick red
- Composed of xanthine, usually found in xanthinuria
- Pathology
  - *Hereditary xanthinuria:* autosomal recessive disorder → ↓ xanthine oxidase → ↓ conversion of xanthine to uric acid → ↑ urinary excretion of xanthine
  - *Acquired:* xanthine oxidase inhibitors (e.g. allopurinol) or liver disease → ↓ xanthine oxidase

RISK FACTORS

- Genetic predisposition
  - Positive family history; genetic mutations (e.g. primary hyperoxaluria)

- Renal/urinary tract disorders
  - Vesicoureteral reflux; urinary tract infections (UTIs); congenital urinary tract malformations (e.g. horseshoe kidney); cystic kidney diseases; neurogenic bladder
- Factors associated with hyperuricemia; diet high in purines (e.g. red meat, organ meat, shellfish, anchovies); cellular depletion (e.g. leukemia, cytotoxic medications); gout
- Factors associated with increased serum calcium
  - Primary hyperparathyroidism; inflammatory bowel disease; diets high in calcium oxalate (beer, chocolate, nuts); excessive calcium supplementation
- Excessively salty foods; low fluid intake, dehydration; ↑ BMI/obesity; more common in individuals who are biologically male

COMPLICATIONS

- Gout
  - May exacerbate existing gout/cause new onset gout
- Infections
  - UTIs; pyelonephritis; urosepsis; abscess
- Scarring, stenosis; urinary fistula; obstruction of ureter → hydronephrosis; renal failure

Figure 116.2 A single calcium oxalate kidney stone.

SIGNS & SYMPTOMS

- Dull, localized flank pain in mid, lower back; one/both sides
  - Pain caused by dilation, stretching, spasm due to obstruction of ureter
  - Subsides once stone reaches bladder
- Renal colic
  - Intense bouts of pain caused by smooth muscle peristalsis against obstruction
  - Caused by sharp stone moving through ureter
- Pain on urination (dysuria); cloudy, red/brown urine
- Fever, chills (infection); nausea, vomiting

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Radiopaque
  - Calcium oxalate, phosphate
- Radiolucent
  - Uric acid stones, struvite stones, cystine stones, xanthine stones

CT scan

- Abdomen, pelvis (preferred)
- Performed without contrast (contrast ↓ sensitivity for stones < 3mm)
- Accurately detects size, location
- Density, location, appearance determines category; cannot identify type of calcium stones (e.g. oxalate/phosphate)

Ultrasound

- Preferred initial modality for pregnant individuals
- Reliably detects hydronephrosis (if stone obstructive)
- Stones detected as echodensities (with shadow effect); less sensitive than CT scan

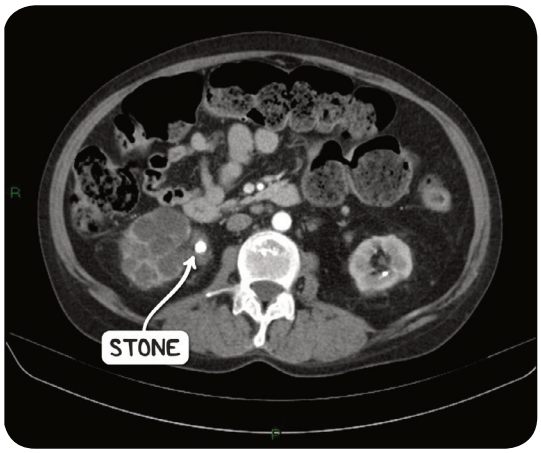

Figure 116.3 An abdominal CT scan in the axial plane demonstrating a stone in the renal pelvis. There is prominent hydronephrosis.

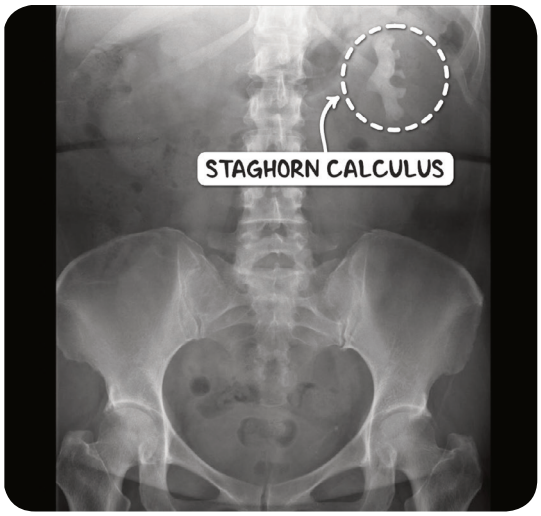

Figure 116.5 A plain abdominal radiograph demonstrating a staghorn calculus of the left kidney.

Intravenous pyelography (IVP)

- Less common
- Radiographic imaging
  - IV iodinated contrast administration
- Reliable for hydronephrosis; less sensitive, specific than CT scan for stone detection

LAB RESULTS

- Microscopic/gross hematuria
- Crystals may be present

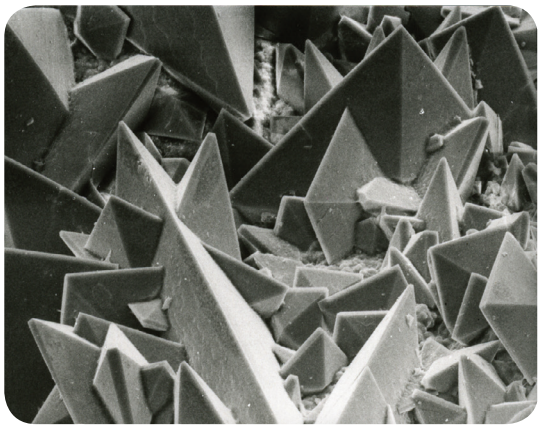

Figure 116.4 Scanning electron micrograph of the surface of a calcium oxalate stone.

OTHER DIAGNOSTICS

History

- Prior stones, colicky episodes of flank pain, passage of stone/gravel in urine

Physical exam

- Ancillary findings support etiologies/risk factors (e.g. hypovolemia, podagra of gouty arthritis)

TREATMENT

MEDICATIONS

- Analgesics
  - Treat pain
- Potassium citrate treatment
  - Makes urine alkaline, ↓ salt crystallization, ↓ stone formation
- Alpha-adrenergic blockers, calcium channel blockers
  - ↓ spasms, help stones pass through relaxed ureters, ↓ pain
- Magnesium, citrate
  - Inhibit crystal growth, aggregation; prevent kidney stones forming
- Shockwave lithotripsy
  - Noninvasive treatment; acoustic pulses travel through body to break up kidney stones into smaller fragments

SURGERY

- Surgery, endoscopic stent placement
  - For larger stones

OTHER INTERVENTIONS

- Hydration
  - Reverse precipitation, facilitate passage

TYPES OF KIDNEY STONES

	COMPOSITION	PRECIPITATION	COLOR	SHAPE	IMAGING FINDINGS	TREATMENT
CALCIUM OXALATE	Calcium	Hypocitraturia	Black, dark brown	Dumbbell/ envelope	Radiopaque	Thiazide diuretics
CALCIUM PHOSPHATE	Calcium	↑ pH	Dirty white	Wedge-shaped prism	Radiopaque	Thiazide diuretics
URIC ACID	Purines	↓ pH	Red-brown/ yellow-orange	Rosette, rhomboid, smooth	Radiolucent	Alkalinization of urine; allopurinol
STRUVITE	Magnesium, ammonium, phosphate	↑ pH	Dirty white	Staghorn; large	Radiopaque	Address infection
CYSTINE	Amino acid cystine	↓ pH	Yellow/ light pink	Hexagon	Radiolucent	Alkalinization of urine; low sodium diet
XANTHINE	Xanthine	Hypouricemia	Brick red	Variable	Radiolucent	Fluids; low purine diet

RENAL PAPILLARY NECROSIS

osms.it/renal-papillary-necrosis

PATHOLOGY & CAUSES

- Damage to renal papillary tissue, severe enough to result in cell death; multiple etiologies
- Located within renal medulla near end of vasa recta → ↑ susceptibility to ischemic damage when vascular blood supply impaired
- Both kidneys usually involved

CAUSES

- Acute interstitial nephritis, phosphate nephropathy; severe, acute pyelonephritis; renal tuberculosis (rare)

COMPLICATIONS

- Obstruction due to sloughed-off papillary necrotic tissue
- Further complicated by UTI; worsens AKI

SIGNS & SYMPTOMS

- Recent infection/immune challenge may trigger symptoms
- Colicky flank pain

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/X-ray

- Calcifications
  - Variable, due to underlying etiology

Kidney ultrasound

- Calcifications appear echodense

LAB RESULTS

- Hematuria; proteinuria (foamy urine); flecks of tissue in urine; sterile pyuria

RENAL PAPILLARY NECROSIS CAUSES

	M:F	TIME COURSE	ROLE OF INFECTION	CALCIFICATION	# OF PAPILLAE INVOLVED	PATHO-PHYSIOLOGY
DIABETES MELLITUS	1:3	10 years	80%	Rare	Several, all of same stage	Long-standing diabetes → micro-vascular disease → ischemia
ANALGESIC NEPHROPATHY	1:5	7 years	25%	Frequent	Almost all; of different stages	Direct toxicity from analgesic medication
SICKLE CELL DISEASE	1:1	Variable	+/-	Rare	Few	Sickling → ↑ viscosity → ischemia
OBSTRUCTION	9:1	Variable	90%	Frequent	Variable	Increased luminal pressure → ↓ perfusion → ischemia

M:F - male:female disease incidence

TREATMENT

SURGERY

- Remove obstruction

OTHER INTERVENTIONS

- *Specific to underlying etiology:* withdraw offending analgesic; control RBC sickling

RENAL TUBULAR ACIDOSIS (RTA)

osms.it/renal-tubular-acidosis-

PATHOLOGY & CAUSES

- Group of disorders; renal tubular cell defects unable to acidify urine → metabolic acidosis

CAUSES

RTA I (AKA distal RTA)

- Unable to secrete H^+
- Cells involved
  - Alpha-intercalated cells in distal tubule, collecting duct
- Genetic mutations
  - *H^+ ATPase, H/K ATPase on apical surface:* unable to actively secrete H^+ into tubular lumen
  - *HCO_3/Cl antiporter on basolateral cell surface:* unable to transport HCO_3 to bloodstream
- Medications
  - Lithium/amphotericin B
  - Makes cells permeable for H^+ to leak across into cell

RTA II

- Unable to resorb HCO_3; lost in urine
- *Cells involved:* brush border cells in proximal tubule
- Genetic mutations
  - *Na/HCO_3 cotransporter on basolateral surface:* ↓ HCO_3 transport → imbalance in H^+ → acidemia
- Fanconi syndrome
  - Reabsorptive disease of proximal tubular cells
  - Results in prophosphaturia, glycosuria, aminoaciduria, uricosuria, proteinuria
  - Due to genetic disease, medication (e.g. tetracyclines)
- May be no change in urinary pH
  - Intact distal tubular cell function, ability to acidify urine

RTA III (rare)

- *Cells involved:* proximal, distal tubule
- Etiology mostly unknown
- Congenital carbonic anhydrase deficiency; defect of carbonic anhydrase needed to convert $HCO_3 + H^+ \rightarrow H_2CO_3$; associated with osteopetrosis (carbonic anhydrase for bone remodeling)

RTA IV (AKA hyperkalemic acidosis)

- *Cells involved:* distal tubular cells (alpha-intercalated, principal cells)
- Aldosterone deficiency (e.g. Addison disease)
  - ↓ aldosterone-induced secretion of H+ via apical transporters in alpha-intercalated cells → ↑ cellular H^+ → H^+ moves down gradient to peritubular capillaries → acidemia
- Aldosterone resistance
  - Genetic mutation of ENac (apical cell surface of principal cells)

- Severe hypovolemia
  - ↓ intracellular Na → altered Na/K exchange → ↑ intracellular K^+ → peritubular capillaries → ↑ serum K^+ and ↓ serum Na^+ → acidemia
- Systemic lupus erythematosus (SLE)
  - Rare complication
- Medications (e.g. lithium, amphotericin B)
  - H^+ diffuses across cell into blood → acidemia

COMPLICATIONS

- Shock
  - Metabolic acidosis → dilation of peripheral arterioles → ↓ afterload, preload → ↓ effective circulating volume → distributive shock → inadequate perfusion to vital organs
- Nephrolithiasis
  - Alkalotic urine environment (pH > 6; esp. in RTA I) → hypercalciuria → precipitation of calcium stones

SIGNS & SYMPTOMS

- GI
  - ↓ appetite, vomiting, abdominal pain
- Shock
  - Tachycardia; flushing; Kussmaul breathing → ↓ CO_2 serum levels
- Nephrolithiasis (potential complication)
  - Colicky pain; hematuria; urinary frequency/hesitancy

DIAGNOSIS

LAB RESULTS

- Blood studies
  - *Metabolic acidosis:* pH < 7.35, < HCO_3
  - ↑ Cl^-
  - ↑ K^+ (in RTA IV)
- Urinalysis
  - Urinary anion gap (above 20mEq/L)
  - Acidity
  - *RTA I, II (acutely):* alkalotic (pH > 6)
  - *RTA III:* not characteristically defined
  - *RTA IV:* acidic (pH < 6)

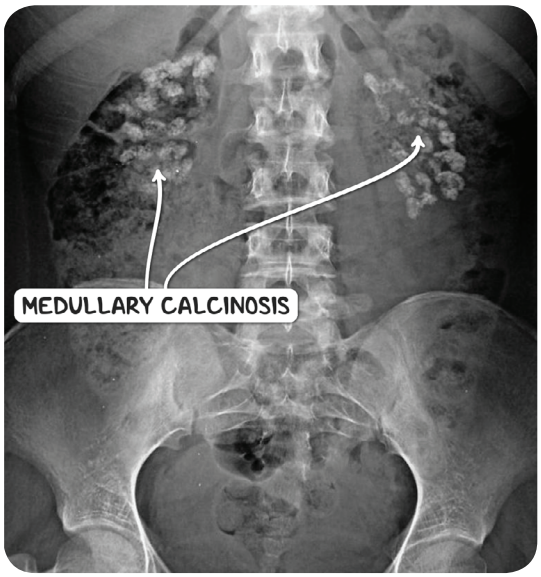

Figure 116.6 A plain kidney-ureter-bladder (KUB) X-ray demonstrating medullary calcinosis, a complication of renal tubular acidosis.

TREATMENT

MEDICATIONS

- *RTA I, II:* eplenish HCO_3, correct hypokalemia with potassium citrate
  - *RTA II:* thiazide diuretics → water loss, ↑ HCO_3 reabsorption
- *RTA IV:* treat hypoaldosteronism
  - Fludrocortisone, loop diuretics → ↑ Na^+ delivery to collecting duct → ↑ K/H exchange