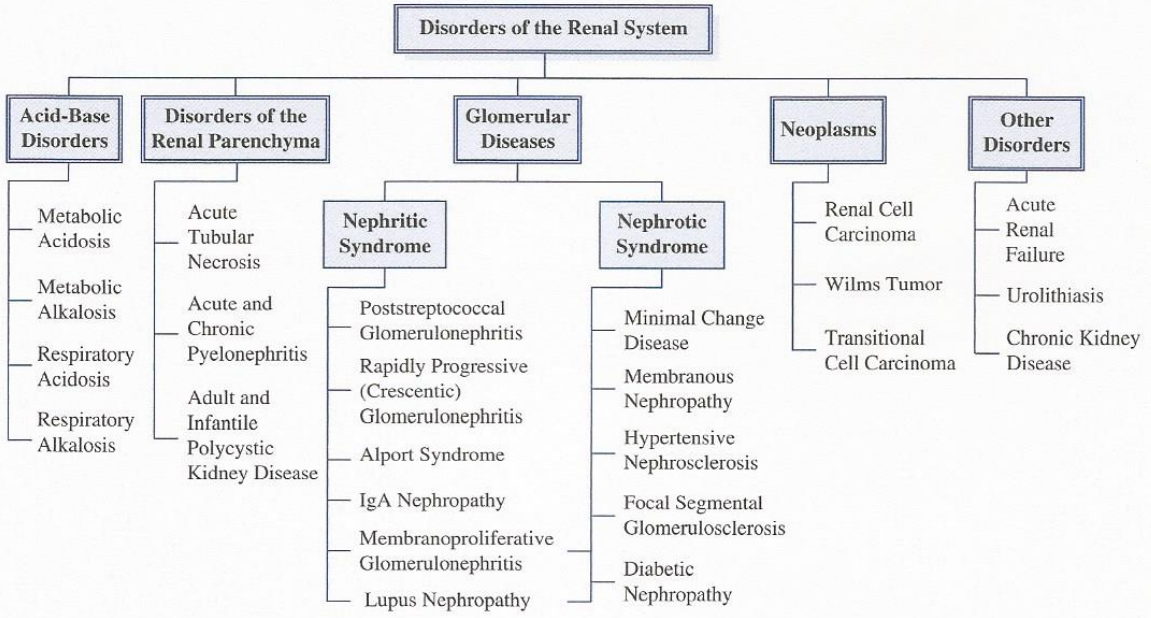

RENAL SYSTEM

GLOMERULAR FILTRATION

Filtration Barrier

- Composed of the fenestrated capillary endothelium, the fused GBM, and the podocyte foot processes epithelial layer.
- The capillary endothelium serves as a size barrier while the basement membrane contains heparin sulfate, which leads to a negative charge barrier preventing protein filtration.

Glomerular Filtration Rate (GFR) and Filtration Fraction

- GFR can be estimated by the clearance of creatinine ($C_{creatinine}$).
- The effective renal plasma flow (RPF) can be estimated by the clearance of para-aminohippuric acid (C_{PAH}).
- The filtration fraction (fraction of RPF filtered across glomerular capillaries) is equal to GFR/RPF.

CLINICAL MANIFESTATIONS OF NEPHROTIC AND NEPHRITIC SYNDROME

Nephrotic Syndrome

- *Proteinuria:* due to disruption of glomerular charge barrier
- *Hypoalbuminemia:* due to proteinuria
- *Edema:* due to decreased plasma oncotic pressure from proteinuria
- *Hyperlipidemia:* due to increase in lipoprotein synthesis
- *Hypercoagulability:* due to increase in urinary excretion of antithrombin

Nephritic Syndrome

- *Oliguria and Azotemia:* due to renal inflammation
- *Hypertension:* results from decreased clearance of sodium and water
- *Hematuria:* due to leakage of blood into Bowman capsule

A 3-year-old boy presents to the emergency room with a 1-week history of generalized edema and fatigue. Your history reveals that he suffered from a viral URI 1 week before this visit. Serum and urine studies reveal massive proteinuria, hyperlipidemia, and hypoalbuminemia. You suspect that a renal biopsy would show normal-appearing glomeruli on electron microscopy except for fusion of the epithelial foot processes and you begin the child on prednisone.

Minimal Change Disease (Lipoid Nephrosis)

Etiology and Epidemiology	Etiology unknown, but usually occurs following a viral URI so it is hypothesized that circulating T cells may be responsible for secreting a cytokine that subsequently damages the glomerulus; also has been associated with Hodgkin disease and hypersensitivity reactions. Most often seen in **young boys**, but can occur in girls, older children, and adults.
Pathology	*Light microscopy:* **Normal-appearing glomeruli**; can see **lipid accumulation** in renal tubular cells. *Electron microscopy:* **Fusion of epithelial foot processes.**
Clinical Manifestations	**Nephrotic syndrome** with edema, hypertension, and malaise. Complications include infection by gram-positive organism, thromboembolism, shock, and protein malnutrition.
Treatment and Prognosis	**Prednisone**; cyclophosphamide or cyclosporine for steroid-resistant cases; ACE inhibitors to reduce proteinuria. Prognosis is excellent, especially in steroid-responsive patients.
Notes	Minimal change disease is the prototype of the nephrotic syndrome.

A 40-year-old white woman with a history of SLE presents to your nephrology office with a chief complaint of increased swelling in her legs. She had been referred by her primary-care physician, who suspected an illness, which may be related to her lupus. Recent laboratory studies show proteinuria, hypoalbuminemia, and hyperlipidemia. You suspect that a renal biopsy would demonstrate immune complex deposition on electron microscopy as well as a "spike and dome" appearance on silver methenamine stain.

Membranous Nephropathy

Etiology and Epidemiology	An immune complex disease of unknown etiology. Secondary disease seen in 10% of SLE patients (type V lupus nephritis) and is sometimes associated with infections (eg, hepatitis B and C, syphilis, malaria), drugs (eg, gold salts, penicillamine, NSAIDs), or solid-organ malignancy. **Incidence is highest in adults.**
Pathology	*Light microscopy:* Diffuse capillary wall thickening and basement membrane thickening. *Immunofluorescence:* Granular pattern of IgG or C3 deposits (lumpy-bumpy). *Electron microscopy:* Electron-dense **immune complex deposition** in **subepithelial locations** within the basement membrane of glomerular capillary walls. *Silver methenamine stain:* A **spike-and-dome appearance** resulting from the extension of basement membrane between and around the immune deposits (spikes = basement membrane, domes = immune complex deposits).
Clinical Manifestations	**Nephrotic syndrome** with edema, proteinuria, and anorexia often accompanied by **azotemia**. Hematuria can also be seen in 50% of patients. Complications include **renal vein thrombosis** and higher incidence of occult neoplasms of the lung, stomach, and colon.
Treatment and Prognosis	Up to 70% of patients will experience spontaneous remission; otherwise, cyclosporine or other immunomodulators can be used; ACE inhibitors (reduce urinary protein loss); renal transplant for severe cases. Prognosis is good, especially in patients who spontaneously remit or respond to medications.
Notes	Membranous nephropathy is a common cause of adult nephrotic syndrome.

A 40-year-old HIV-positive man is admitted to the hospital complaining of generalized edema and fatigue. A complete history reveals that he is a habitual IV drug user. Laboratory studies show hypoalbuminemia, hyperlipidemia, proteinuria, and microscopic hematuria. You suspect that his current presentation is related to his HIV and you prepare the patient for a renal biopsy to determine the exact diagnosis.

Focal Segmental Glomerulosclerosis

Etiology and Epidemiology	Often idiopathic, but also has been associated with heroin use, morbid obesity, reflux nephropathy, and HIV infection. Most often occurs in older patients.
Pathology	*Light microscopy:* Sclerosis within capillary tufts of deep juxtaglomerular glomeruli with **focal distribution** (involves some, but not all, glomeruli) and **segmental distribution** (involves only a part of the glomerulus); hyalinosis (deposition of hyaline masses) also seen. *Immunofluorescence:* IgM and C3 seen in sclerotic lesions. *Electron microscopy:* Fusion of epithelial foot processes.
Clinical Manifestations	**Nephrotic syndrome** with edema and proteinuria; more severe disease is seen in HIV and IV **drug users**. *Lab findings:* 80% have microscopic **hematuria** at presentation.
Treatment and Prognosis	Corticosteroids; in steroid-resistant patients, treatment with immunomodulators such as cyclosporine or tacrolimus can be considered; ACE inhibitors (reduce urinary protein loss). Most patients tend to progress to ESRD in 5-10 years, although the course is variable.
Notes	

A 10-year-old girl presents to the clinic complaining of eye swelling. You note that the child was seen 3 weeks ago in clinic for a chief complaint of sore throat. Upon taking a history and performing a physical, you find that the patient has pronounced periorbital edema, has been urinating very little despite adequate fluid intake, and has a blood pressure of 150/90 mm Hg. Laboratory findings include azotemia, hematuria, red cell casts in the urine, and an elevated ASO antibody titer. You reassure the parents that their child's condition will likely resolve on its own.

Poststreptococcal Glomerulonephritis (Acute Proliferative Glomerulonephritis)

Etiology and Epidemiology	Most frequently seen in **children** following infection with nephritogenic strains of **group A β-hemolytic streptococci**.
Pathology	*Gross pathology:* Characterized by **intense inflammatory reaction** involving all glomeruli in both kidneys, resulting in **punctate hemorrhages** on kidney surfaces. *Light microscopy:* Enlarged, hypercellular, swollen glomeruli with proliferation of mesangial and endothelial cells; normal GBM thickness. *Electron microscopy:* **Electron-dense humps** on the epithelial side of the basement membrane **(subepithelial localization)**. *Immunofluorescence:* Coarse granular immunofluorescence for IgG or C3 **(lumpy-bumpy)**.
Clinical Manifestations	**Nephritic syndrome** with hypertension and periorbital edema. *Lab findings:* **Urinary RBCs** and/or red cell casts, decreased serum C3, elevated ASO antibody titer (evidence of recent streptococcal infection); **azotemia**.
Treatment and Prognosis	Usually resolves spontaneously.
Notes	Poststreptococcal glomerulonephritis is an **immune complex disease** with the antigen-antibody complex being of streptococcal origin and is the prototype of the nephritic syndrome.

A 45-year-old white woman with a 15-year history of SLE presents to the nephrologist after her primary-care physician found hematuria and proteinuria on a routine urinalysis. The patient has edema of the ankles on physical examination and she is experiencing a SLE flare-up with an extensive malar rash visible over her face. A renal biopsy is obtained and examination by light microscopy reveals wire-loop abnormalities. You examine the patient's current immunosuppressive therapy to see what additional therapies should be added.

Lupus Nephropathy

Etiology	Renal component of **SLE**.
Pathology	Five distinct renal histologic patterns: **(1) Type I:** normal; **(2) Type II** *(mesangial form):* focal and segmental glomerular involvement with increase in mesangial matrix; **(3) Type III** *(focal proliferative form):* involves less than half of glomeruli, causing extensive damage to individual glomeruli; **(4) Type IV** *(diffuse proliferative form):* most severe form involving all glomeruli with marked inflammation, mesangial proliferation, and scarring. *Light microscopy:* **wire-loop abnormality** caused by immune complex deposition and gross thickening of GBM. *Electron microscopy:* **endothelial cell proliferation**. *Immunofluorescence:* marked **subendothelial immune complex deposition**. **(5) Type V** *(membranous form):* similar to membranous glomerulonephritis.
Clinical Manifestations	**Type I:** No clinical findings. **Types II and III:** Mild to moderate proteinuria and hematuria. **Type IV:** Combination of **nephrotic and nephritic** syndromes. **Type V: Nephrotic syndrome**.
Treatment	**Types I and II:** No treatment. **Types III, IV, and V:** Immunosuppression (corticosteroids, cyclophosphamide, and/or azathioprine); transplant or dialysis for severe cases.
Notes	Renal lesion severity often determines overall prognosis of SLE patients.

A 40-year-old white man is admitted to the hospital with complaints of blood in his sputum and urine. A thorough history also reveals fever, malaise, and a 10-lb weight loss over the past month. On physical examination, you find that his blood pressure is 160/95 mm Hg and that he has several abnormal lung sounds. A urine dipstick demonstrates hematuria. CXR reveals several nodular lesions, and blood tests show significantly elevated BUN and creatinine levels, the presence of c-ANCA, and an elevated ESR. You start the patient on a high dose of corticosteroids and you suspect that a renal biopsy would demonstrate crescent-moon shapes between the Bowman capsule and the glomerular tuft.

Rapidly Progressive (Crescentic) Glomerulonephritis

Etiology	**Type 1:** Idiopathic or **Goodpasture syndrome**. **Type 2 (immune complex):** Idiopathic; postinfectious causes; SLE; **IgA nephropathy**; **Henoch-Schönlein purpura**. **Type 3 (pauci-immune type):** Idiopathic; **Wegener granulomatosis**; microscopic polyangiitis.
Pathology	*Light microscopy:* Formation of **crescent-moon shape** between Bowman capsule and glomerular tuft, resulting from deposition of fibrin in the Bowman space and from proliferation of parietal epithelial cells of the Bowman capsule.
Clinical Manifestations	**Nephritic syndrome** with hematuria, hypertension, and azotemia. Signs and symptoms are specific to each etiology (eg, hemoptysis and anti-GBM antibodies in Goodpasture syndrome).
Treatment and Prognosis	Treat with diuretics and ACE inhibitors; immunosuppression with steroids or cytotoxic agents as appropriate for underlying cause; may require dialysis or transplant. Patients generally have a rapid course to end-stage renal failure requiring dialysis.
Notes	Rapidly progressive glomerulonephritis (RPGN) refers to a syndrome associated with severe and progressive glomerular injury. It encompasses many different etiologies.

A 10-year-old boy presents to the clinic complaining of a red tinge to his urine. A more detailed history reveals that he was diagnosed with mild nerve deafness 2 years earlier and that he also developed posterior cataracts 1 year ago. Laboratory studies confirm hematuria as well as the presence of erythrocyte casts. You begin to wonder if his conditions may be related to a genetic disorder.

Alport Syndrome

Etiology	Genetic disorder with heterogenous inheritance (usually X-linked dominant) that results in the mutation of α_5-chain of **type IV collagen**.
Pathology	*Electron microscopy:* Irregular foci of thickening or attenuation in the GBM with **longitudinal splitting** of the lamina densa.
Clinical Manifestations	Triad of **nephritis**, **nerve deafness**, and various eye disorders (**cataracts**, lens dislocation, corneal dystrophy); often initially presents with hematuria and erythrocyte casts.
Treatment	ACE inhibitors; consider renal transplant for severe cases.
Notes	

A 25-year-old woman with a history of SLE is admitted to the hospital with generalized edema, malaise, and fatigue. You take a thorough history, which reveals that she had cold symptoms 2 weeks earlier. Laboratory studies show hypoalbuminemia, hypercholesterolemia, proteinuria, and low complement levels. When a renal biopsy shows reduplication of the basement membrane and a "tram track" appearance of the capillary loops on light microscopy, you adjust the patient's current corticosteroid dose and decide to add an antiplatelet drug to her regimen.

Membranoproliferative Glomerulonephritis

Etiology and Epidemiology	Associated with inherited complement component deficiency. **Type I** is seen in SLE, hepatitis B and C, and involves classic and alternative pathway activation. **Type II** involves only alternative pathway activation. Most affected patients are aged < 30.
Pathology	**Types I and II:** *Light microscopy:* reduplication of basement membrane **(splitting)** and expansion of mesangial matrix into the capillary loops (**tram track** appearance). **Type I:** *Electron microscopy:* subendothelial electron-dense deposits. **Type II:** *Electron microscopy:* characteristic **dense deposit** of homogeneous material within GBM.
Clinical Manifestations	**Type I:** Commonly presents with **nephrotic** syndrome. **Type II:** Commonly presents with **nephritic syndrome** with hematuria and chronic renal failure. *Lab findings*: Decreased C3 levels, **elevated BUN and Cr, RBCs and/or RBC casts in urine.**
Treatment and Prognosis	Corticosteroids and immunosuppression if appropriate for underlying cause. Slowly progresses to renal failure with a high recurrence rate after transplant.
Notes	

A 15-year-old Asian American boy presents to the emergency room complaining of blood in his urine. Upon taking a complete history, you learn that he has also been suffering from fevers, myalgias, and arthralgias for the last 2 days. Laboratory studies confirm the presence of red blood cells in the urine, but also reveal increased serum IgA levels and normal serum complement levels. You begin him on prednisone and you suspect that he is afflicted with the most common form of acute glomerulonephritis in the United States.

IgA Nephropathy (Berger Disease)

Etiology and Epidemiology	Primary renal disease of **IgA deposition** in the glomerular mesangium that can manifest after infection (viral URI, GI infection, flu-like syndrome) or can be a component of **Henoch-Schönlein purpura**. Most commonly seen in children and young adults with men affected more often than women.
Pathology	*Light microscopy:* Focal proliferative glomerulonephritis with diffuse mesangial widening. *Electron microscopy:* **Mesangial deposits of IgA**.
Clinical Manifestations	Presents with **recurrent hematuria** (red or cola-colored urine) 1-2 days after an upper respiratory or GI infection. Hypertension, fatigue, and mild proteinuria may be present. *Lab findings:* Increased serum IgA level (50% of cases), normal serum complement levels, RBCs in urinalysis.
Treatment and Prognosis	ACE inhibitors for proteinuria; steroids or immunosuppressants for selected cases. 20%-30% of patients progress to end-stage renal failure over 20-30 years.
Notes	Berger disease is the most common form of acute glomerulonephritis in the United States and is also prevalent in Asia.

A 60-year-old man is admitted to the ICU with hypotension and severe sepsis. His hypotension gradually resolves with aggressive fluid resuscitation and pressor support. Over the next couple of days, he becomes progressively oliguric. Laboratory studies reveal worsening renal failure and hyperkalemia. His urine sediment demonstrates muddy brown casts. You worry that this patient may need temporary or permanent dialysis to manage his volume status and electrolyte levels.

Acute Tubular Necrosis

Etiology	Precipitated by **renal ischemia** (eg, prolonged hypotension, shock), **crush injury** (eg, intense exercise, myoglobinuria), **contrast** or **nephrotoxic drugs** (eg, aminoglycosides).
Pathology	*Kidney:* **Focal tubular epithelial necrosis**; rupture of basement membranes; eosinophilic hyaline casts in collecting ducts; interstitial edema; **evidence of epithelial regeneration** (flattened epithelial cells with mitotic figures).
Clinical Manifestations	Presents with signs of acute renal failure. Death caused by arrhythmia from hyperkalemia can occur during the initial oliguric phase. *Lab findings:* **Oliguria**, elevated urinary sodium (> 40 mEq/L), azotemia, **tubular epithelial cell casts** (**muddy-brown casts**) in urine, hyperkalemia.
Treatment and Prognosis	Loop diuretics for diuresis; electrolyte and fluid level management (may require dialysis). May recover renal function or may lead to ESRD.
Notes	**Acute drug-induced interstitial nephritis** is caused by a hypersensitivity reaction to certain antibiotics (eg, methicillin, sulfa drugs), NSAIDs, or diuretics. It presents with fevers, eosinophilia, hematuria, and proteinuria of varying degrees a few days after exposure to the offending agent. On pathology, it is characterized by a mononuclear infiltrate in the interstitial space with sparing of the glomeruli. Resolution generally occurs after withdrawal of drug.

A 40-year-old woman presents to the emergency room complaining of colicky abdominal pain and flank pain radiating toward her groin. After taking a complete history, you learn that she has seen blood in her urine in recent weeks and that she has a history of recurrent UTIs. You order a plain abdominal film and find that there is a large staghorn calculus. As you prepare to admit the patient to the hospital, you call the urology service for evaluation of treatment for her condition.

Urolithiasis (Kidney Stones)

Etiology	**Calcium oxalate and/or calcium phosphate stones** (80%-85%): Hypercalcemic conditions (eg, hyperparathyroidism, vitamin D intoxication, sarcoidosis). **Ammonium magnesium phosphate (struvite) stones** (10%): Urease-positive bacteria (eg, *Proteus vulgaris*). **Uric acid stones** (5%): Diseases with increased cell proliferation and turnover (eg, leukemia, myeloproliferative disorders) or hyperuricemia. **Cystine stones** (< 5%): Cystinuria (hereditary impaired reabsorption of cystine).
Pathology	*Kidney:* Presence of stone within renal calyces, pelvis, or bladder. Urolithiasis can also result in other pathologic conditions such as **renal colic** (painful ureter distention), **hydronephrosis**, and **pyelonephritis**.
Clinical Manifestations	**Flank pain** radiating toward the groin and **hematuria**. *Imaging:* Calcium stones and ammonium magnesium phosphate (struvite) stones are **radiopaque**; uric acid and cystine stones are **radiolucent**. Complications include recurrence of stones (calcium) and increased incidence of UTIs (struvite).
Treatment	Most stones pass spontaneously with **hydration and pain control**, although surgical removal or lithotripsy may be necessary in selected cases; consider hydrochlorothiazide for recurrent calcium stones; consider allopurinol with alkaline diuresis for uric acid stones.
Notes	**Hydronephrosis** refers to the dilation of the renal pelvis and calyces. It is caused by urinary outflow obstruction and is associated with progressive atrophy of the kidney if left untreated.

A 70-year-old man presents to the emergency room because he is unable to urinate. After taking a detailed history, you learn that he has had increasing urinary hesitancy and decreased force of his urine stream for several months. He also complains of a sensation of incomplete bladder emptying. On rectal examination, you find a smooth, firm, elastic enlargement of the prostate. Examination of the lower abdomen reveals signs of a distended bladder. You order laboratory studies that show increased urinary sodium excretion and an elevated BUN and creatinine. You determine that the patient requires prompt urethral catheterization to help reverse his renal failure.

Acute Renal Failure (Pre-, Intra- and Postrenal Azotemia)

Etiology	**Prerenal:** Caused by decreased effective arterial volume (ie, CHF, hypovolemia, systemic vasodilation [sepsis]), or renal vasoconstriction (NSAIDs, ACE inhibitors, RAS). **Intrarenal:** Caused by acute tubular necrosis, acute interstitial nephritis, glomerulonephritis, and thrombotic microangiopathy. **Postrenal:** Caused by kidney stones, BPH, neurogenic bladder, and neoplasia.
Pathology and Pathophysiology	**Prerenal:** Renal hypoperfusion leads to decreased GFR, resulting in sodium and water retention. **Intrarenal:** Characterized by patchy tubular necrosis, which leads to tubule obstruction and fluid backflow across the necrotic tubule and a resulting decrease in GFR. **Postrenal:** Only develops with bilateral outflow obstruction, which results in elevation of ureteral pressure, which is transmitted to nephrotubules, resulting in decreased GFR.
Clinical Manifestations	Oliguria; **azotemia**; hyperkalemia. *Lab findings:* **(1) Prerenal:** urinary $Na^+ < 10$, urine osmolality > 500, Fe $Na^+ < 1\%$, **BUN/Cr > 20**; **(2) Intrarenal:** urine osmolality < 350, Fe $Na^+ > 2\%$, urinary **epithelial/granular casts**; **(3) Postrenal:** urinary $Na^+ > 40$, Fe $Na^+ > 4\%$; BUN/Cr > 20.
Treatment	**Pre- and intrarenal:** Fluid and electrolyte management; reversal of underlying cause; dialysis if necessary. **Postrenal:** Treatment of obstruction.
Notes	

A 72-year-old man presents to your nephrology clinic for follow-up of his kidney disease. His past medical history is significant for coronary artery disease, type 2 diabetes for which he takes insulin, and hypertension. On physical examination, you note bilateral crackles in the lung fields as well as 2+ pitting edema in both lower extremities. Laboratory studies are notable for a potassium level of 6.2 mmol/L and a creatinine level of 5.3 mg/dL. You tell the patient that it is likely time to initiate dialysis for his condition.

Chronic Kidney Disease

Etiology	Associated with **diabetes**, **hypertension**, glomerular diseases (eg, RPGN), vasculitides (eg, Wegener granulomatosis), renal artery stenosis, drugs (eg, lithium, sulfa drugs), infection or autoimmune diseases (eg, SLE).
Pathophysiology	As GFR decreases, the kidney is unable to maintain appropriate electrolyte balances (eg, **potassium excretion is impaired**, resulting in hyperkalemia; **sodium and water handling is impaired**, leading to volume overload) or pH balance (eg, failing kidney cannot produce enough ammonia to bind with endogenous acid and be excreted as ammonium, resulting in metabolic acidosis). Anemia results from decreased synthesis of EPO by failing kidney.
Clinical Manifestations	Asymptomatic in early stages, but as chronic kidney disease (CKD) progresses, patients present with **edema** and **dyspnea** (from volume overload), fatigue, and weakness. Complications include cardiac arrhythmias (from electrolyte abnormalities), encephalopathy, platelet dysfunction, renal osteodystrophy, and pericarditis. *Lab findings:* Anemia; **elevated BUN and creatinine**; metabolic acidosis; hypocalcemia; hyperphosphatemia; **hyperkalemia**.
Treatment and Prognosis	ACE inhibitors and diuretics; monitor electrolytes; phosphate binders; control underlying disease; progressive disease will require dialysis or transplant. Patients on chronic dialysis for CKD have a 5-year survival rate of 35%.
Notes	Indications for dialysis initiation in CKD include metabolic disarray (eg, acidosis; hyperkalemia), management of volume overload, progressive uremic encephalopathy or other symptoms of uremia (malnutrition; pericarditis or pleuritis).

A 60-year-old man presents to the clinic with cola-colored urine and flank pain. After taking a careful history, you find that the man has had a low-grade fever over the last few weeks and that he has lost 10 lb over the past month. He is a chronic smoker (a pack of cigarettes a day for the last 30 years). On physical examination, you feel a large mass in the left flank area. Laboratory findings demonstrate secondary polycythemia. You suspect that an abdominal CT scan will show a solid renal mass and possible metastasis to regional lymph nodes.

Renal Cell Carcinoma

Etiology and Epidemiology	Associated with **von Hippel-Lindau disease**, deletion on chr 3 and cigarette **smoking**. Most common among **men** (2:1 male:female ratio) in sixth decade of life (usually age 50-70).
Pathology	*Kidney:* Characterized by **polygonal clear cells** (demarcated only by cell membranes, nuclei pushed to the sides), which are derived from the tubular epithelium. **Invades IVC and spreads hematogenously** to the lungs, bones, and other sites.
Clinical Manifestations	Manifests with **hematuria**, **palpable abdominal mass**, **flank pain**, long-standing fever, and weight loss; associated with **paraneoplastic syndromes** (ectopic EPO, ACTH, PTHrP, prolactin, gonadotropins, renin). *Imaging:* Solid renal mass evident on CT. *Lab findings:* Secondary polycythemia due to increased EPO production.
Treatment	Radical nephrectomy for localized disease; chemotherapy/radiation if invasive/distant disease.
Notes	Renal cell carcinoma is the most common renal malignancy.

A 60-year-old man presents to the clinic with painless hematuria. A full history reveals that he worked in a factory that used aniline dyes for 20 years before retiring 10 years ago and that he also has smoked a pack of cigarettes per day for the last 30 years. You order serum and urine studies that demonstrate hematuria, exfoliated normal and abnormal urothelial cells in the urine, and anemia. You fear that this patient may be suffering from a neoplastic condition.

Transitional Cell Carcinoma

Etiology and Epidemiology	Associated with **smoking**, alcohol use, exposure to **aniline dyes**, prior **cyclophosphamide** treatment, and phenacetin abuse. Most common in men aged > 40.
Pathology	*Gross:* Varies from flat to papillary and from noninvasive to invasive; can occur anywhere in urinary tract system (renal calyces, renal pelvis, ureters, bladder) and may spread by local extension to adjacent tissue. *Microscopic:* **Multiple grades of carcinoma**; histopathology varies from well-differentiated tumor cells resembling normal transitional cells to anaplastic tumor cells with giant cells and multiple mitoses.
Clinical Manifestations	Most often presents with **painless hematuria**; may also present with **irritative voiding symptoms** (if concurrent infection is present), palpable mass on bimanual examination, hepatomegaly, or supraclavicular lymphadenopathy (if metastasized).
Treatment and Prognosis	Chemotherapy, radiotherapy, and transurethral resection or radical cystectomy for bladder cancer (often recurs after removal). Prognosis is dependent on stage and grade.
Notes	**Squamous cell carcinoma (SCC)** of the bladder accounts for 3%-7% of bladder cancers in the United States and is associated with schistosomiasis and other causes of chronic bladder infection.

A 3-year-old boy is brought to the emergency room by his mother because he is experiencing abdominal pain after accidentally falling onto a toy truck that hit his abdomen. On physical examination, you can feel a huge, palpable flank mass on his left side. Urinalysis reveals microscopic hematuria. When a CT scan reveals a large enhancing mass originating from the kidney, you begin to suspect that this child's condition is related to a gene deletion on chromosome 11 and is not related to his mishap with the toy truck.

Wilms Tumor

Etiology and Epidemiology	Caused by deletion of **WT-1 gene** (tumor suppressor) on short arm of **chr 11**. Most commonly seen in **early childhood** (ages 2-5).
Pathology	*Gross:* Large, solitary, **well-circumscribed renal mass**; originates from primitive metanephric tissue. *Microscopic:* Immature stroma with primitive tubules and glomeruli; presence of mesenchymal elements (eg, bone, cartilage, connective tissue).
Clinical Manifestations	Most often presents as a huge, nontender **palpable flank or abdominal mass** in a **young child**; may also be associated with fever or abdominal pain; can be associated with unilateral muscular hypertrophy (hemihypertrophy). *Lab findings:* **Microscopic hematuria**.
Treatment and Prognosis	Surgery to remove tumor; radiotherapy and chemotherapy with actinomycin D and vincristine. There is an excellent survival rate.
Notes	Wilms tumor can be associated with the **WAGR complex** (*W*ilms tumor, *a*niridia [absence of iris], *g*enitourinary malformation, mental-motor *r*etardation).

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A 25-year-old woman presents to the emergency room with fevers, vomiting, and severe right-sided flank pain. After taking a complete history, you find that she is sexually active and has had a 1-week history of burning pain while urinating and increased urinary frequency. Urinalysis reveals white cell casts in the urine and a urine sample is sent for culture. While you await the culture results, you start her on broad-spectrum antibiotics.

Acute and Chronic Pyelonephritis

Etiology and Epidemiology	**Acute:** Caused by infection of renal parenchyma; more frequent among women. **Chronic:** Results from chronic urinary tract obstruction and recurrent UTIs.
Pathology	**Acute: Affects renal cortex with sparing of glomeruli**; neutrophilic infiltration and abscess formation within renal interstitium; abscesses may rupture introducing WBCs into tubular lumen. **Chronic: Asymmetric corticomedullary scarring**; tubules contain eosinophilic, proteinaceous casts resulting in gross appearance reminiscent of thyroid follicles **(thyroidization of the kidneys)**; in later stages, results in tubular atrophy and interstitial fibrosis.
Clinical Manifestations	**Acute: Fever**; **flank pain with CVA tenderness**; polyuria and dysuria; nausea, vomiting, and diarrhea. **Chronic:** Recurrent episodes of acute pyelonephritis can lead to renal hypertension and ESRD. *Lab findings:* **WBC and/or WBC casts in urine**.
Treatment	**Acute:** Antibiotics and fluids. **Chronic:** Renal transplant if progresses to ESRD.
Notes	**Renal papillary necrosis** is a complication of acute pyelonephritis in diabetics or chronic phenacetin users and is characterized by ischemic necrosis of tips of renal papillae. **Diffuse cortical necrosis** is an acute generalized infarction of renal cortices (medulla is spared) usually because of a combination of DIC and end-organ vasospasm in association with obstetric catastrophes or septic shock.