Renal Pathology

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Congenital Anomalies of the Kidney

- 1. Renal agenesis
  - a. Bilateral agenesis
    - i. Ultrasound: oligohydramnios
    - ii. Potter facies: flattened nose, low-set ears, and recessed chin
    - iii. Talipes equinovarus
    - iv. Pulmonary hypoplasia
    - v. Incompatible with life
  - b. Unilateral agenesis
    - i. The remaining kidney undergoes compensatory hypertrophy
    - ii. Patients often have adequate renal function
    - iii. May develop progressive glomerular sclerosis

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- 2. Hypoplasia
  - a. Failure of a kidney (usually unilateral) to develop to normal weight
  - b. There are a decreased number of calyces and lobes
- 3. Horseshoe kidney
  - a. Common; it is found in 1 in 750 autopsies
  - b. Gross: fusion of the kidneys, usually at the lower pole
  - c. Patients have normal renal function but may be predisposed to renal calculi
- 4. Abnormal locations
  - a. Most common abnormal location is a pelvic kidney
  - b. The ectopic kidney usually has normal function
  - c. Tortuosity of ureters may predispose to pyelonephritis

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Cystic Disease

- 1. Autosomal recessive polycystic kidney disease
  - a. Synonym: childhood polycystic kidney disease
  - b. Clinical features
    - i. Rare autosomal recessive disease
    - ii. Presents in infancy with progressive and often fatal renal failure
  - c. Gross
    - i. Bilaterally enlarged kidneys
    - ii. Multiple small cysts in the cortex and medulla
    - iii. The cysts are oriented in a radial fashion with their long axis at right angles to the capsule
  - d. May also have multiple hepatic cysts and congenital hepatic fibrosis

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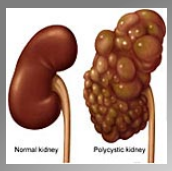

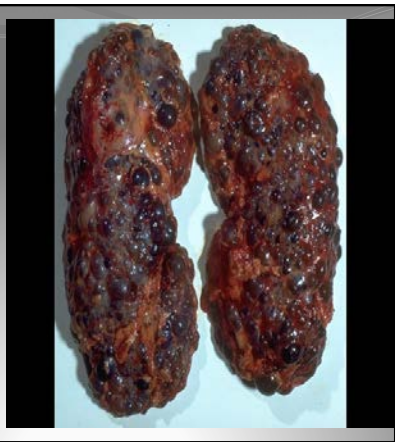

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- 2. Autosomal dominant polycystic kidney disease
  - a. Synonym: adult polycystic kidney disease
  - b. Incidence: affects 1 in 1,000 people
  - c. Genetics
    - i. Autosomal dominant inheritance
    - ii. Mutation of *PKDl gene on chromosome 16*
    - iii. The PKDl gene produces a transmembrane protein called polycystin 1
    - iv. Other mutations involve PKD2 and PKD3 genes
  - d. Clinical features
    - i. Asymptomatic with normal renal function until middle age
    - ii. Presents with renal insufficiency, hematuria, and hypertension
    - iii. Abdominal masses and flank pain
    - iv. Most patients develop end-stage renal failure by their seventh decade

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- e. Diagnosis: ultrasound and CT scans
- f. Gross
  - i. Massive bilateral kidney enlargement with large bulging cysts
  - ii. Cysts are filled with serous, turbid, or hemorrhagic fluid
- g. Micro: functioning nephrons are present between the cysts
- h. Extrarenal manifestations
  - i. Liver cysts
  - ii. Berry aneurysms of the circle of Willis
  - iii. Mitral valve prolapse
  - iv. Colonic diverticula

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Glomerular Diseases

- 1. Diagnosis of glomerular diseases
  - a. Clinical syndrome
  - b. Renal biopsy
    - i. Light microscopy (LM)
    - ii. Immunofluorescence (IF)
    - iii. Electron microscopy (EM)

Nephritic Syndrome	Nephrotic Syndrome
Hematuria (RBC casts)	Severe proteinuria (>3.5 g/day)
Hypertension	Hypoalbuminemia «3 g/dl)
Azotemia	Generalized edema
Oliguria	Hyperlipidemia
Proteinuria (<3.5 g/day)	Lipiduria

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Primary Glomerulopathies (Nephritic)

- 1. Acute post streptococcal glomerulonephritis
  - a. Synonyms: acute proliferative GN, postinfectious GN
  - b. Clinical features
    - i. Decreasing in incidence in the Western Countries
    - ii. *Children affected more frequently than adults*
    - iii. Occurs 2-4 weeks after a streptococcal infection of the throat or skin
    - iv. Organism: *Beta-hemolytic groupA streptococci*
    - v. May be caused by other bacteria, viruses, and parasites and systemic diseases (SLE and polyarteritis nodosa [PAN])
    - vi. Nephritic syndrome

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- c. Laboratory studies
  - i. Elevated antistreptolysin O (ASO) titers
  - ii. Low serum complement
- d. Light microscopy
  - i. Hypercellular glomeruli with neutrophils and monocytes
  - ii. Red cell casts in the renal tubules
- e. Immunofluorescence: *granular deposits of IgG, IgM, and C3 throughout the glomerulus*
- f. Electron microscopy: *subepithelial (humps) immune complex deposits*
- g. Treatment: conservative fluid management
- h. Prognosis
  - i. Children
    - Complete recovery in >95% of cases
    - Rapidly progressive glomerulonephritis (RPGN) (1%)
    - Chronic glomerulonephritis (2%)
  - ii. Adults
    - Complete recovery (60%)
    - RPGN/chronic renal disease (40%)

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- 2. Goodpasture syndrome (anti-GBM disease)
  - a. Pathogenesis
    - i. Production of antibodies directed against basement membrane (anti-GBM antibodies), which result in damage of the lungs and the kidney
    - ii. Goodpasture antigen is the non-collagenous component of type N collagen
  - b. Clinical features
    - i. Males> females
    - ii. Peak incidence: ages 20-40 years
    - iii. Pulmonary involvement precedes renal disease
    - iv. Present with pulmonary hemorrhage and recurrent hemoptysis
    - v. Most develop rapidly progressive glomerulonephritis (RPGN)

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- c. Light microscopy: hypercellularity, crescents, and fibrin
- d. Electron microscopy: no deposits, but there is glomerular basement membrane (GBM) disruption
- e. Immunofluorescence: *smooth and linear pattern of IgG and C3 in the GBM*
- f. Treatment: plasma exchange, steroids, and cytotoxic drugs
- g. Prognosis : poor
  - i. Pulmonary hemorrhage may be severe and life threatening
  - ii. Rapidly progressive renal failure is common
  - iii. Early aggressive treatment may prevent end-stage renal failure

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Rapidly progressive glomerulonephritis (RPGN)

- a. Synonym: crescentic glomerulonephritis
- b. Clinical feature: rapid progression to *severe renal failure in weeks or months*
- c. Occurs in several clinical settings
  - i. Following Goodpasture syndrome
  - ii. Following other forms of glomerulonephritis (post-streptococcal, SLE, Berger disease)
  - iii. Associated with vasculitis (i.e.,Wegner granulomatosis)
  - iv. Idiopathic
- d. Light microscopy
  - i. Hypercellular glomeruli
  - ii. *Crescentformation in Bowman space*

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- e. Immunofluorescence
  - i. Variable
  - ii. May show granular or linear deposits of immunoglobulin and complement
- f. Electron microscopy
  - i. Variable
  - ii. May or may not have electron-dense deposits
  - iii. GBM disruption and discontinuity is commonly seen
- g. Prognosis: poor with rapid progression to acute renal failure and end-stage renal disease

The characteristic finding in RPGN is the formation of crescents within Bowmen's space. The crescents are composed of fibrin, parietal epithelial cells, monocytes, and macrophages.

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IgA nephropathy (Berger disease)

- a. Clinical features
  - i. Most common cause of glomerulonephritis in the world
  - ii. Common in France, Japan, Italy, and Austria
  - iii. Affects children and young adults (mostly males)
  - iv. Recurrent gross hematuria
  - v. Onset may follow a respiratory infection
  - vi. Predominantly nephritic
  - vii. Associated with celiac sprue and Henoch-Schonlein purpura
- b. Pathogenesis: The mechanism is unknown. There is a possible entrapment of circulating immune complexes with activation of the alternate complement pathway.
  - There is also a possible genetic predisposition.

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- c. Light microscopy
  - i. Variable
  - ii. Normal or mesangial proliferation
- d. Immunofluorescence: *mesangial deposits of IgA and C3*
- e. Electron microscopy: mesangial immune complex deposits
- f. Prognosis: many cases slowly progress to renal failure over 25 years

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Membrano proliferative glomerulonephritis (MPGN)

- a. Types of MPGN
  - i. TypeI
  - ii. Type II (dense deposit disease)
- b. Clinical features
  - i. May be nephritic, nephrotic, or *mixed!*
  - ii. MPGN may be secondary to many systemic disorders (SLE, endocarditis), chronic infections (HBV,HCV; HIV), and malignancies (chronic lymphocytic leukemia)
- c. Lab
  - i. Decreased serum C3
  - ii. C3 *nephritic factor (MPGN type II)*

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- d. Light microscopy
  - i. Lobulated appearance of the glomeruli
  - ii. *Mesangial proliferation and basement-membrane thickening*
  - iii. *Splitting of the basement membrane ("tram-tracking") may be seen with a silver* or periodic acid-Schiff (PAS)stain
- e. Immuno fluorescence
  - i. Type I: granular pattern of C3 often with IgG, Clq, and C4
  - ii. Type II: granular and linear pattern of C3
- f. Electron microscopy
  - i. Type I: subendothelial and mesangial immune complex deposits
  - ii. TypeII: dense deposits within the GBM
- g. Prognosis
  - i. Slowly progressive course, resulting in chronic renal failure over the course of 10 years
  - ii. High incidence of recurrence in transplants

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Primary Glomerulopathies (Nephrotic)

I. Membranous glomerulonephritis

- a. Most common cause of *nephrotic syndrome in adults*
- b. Etiology
  - i. Most (85%) cases are idiopathic
  - ii. Drugs (penicillamine)
  - iii. Infections (hepatitis virus Band C, syphilis, etc.)
  - iv. Systemic diseases (SLE,diabetes mellitus, etc.)
  - v. Associated with malignant carcinomas of the lung and colon
  - vi. There may be a genetic predisposition
- c. Light microscopy
  - i. There is a diffuse *membrane-like thickening of the capillary walls*
  - ii. *Basement membrane projections ("spikes")are seen on silver stains*
- d. Immunofluorescence: granular and linear pattern of IgG and C_3
- e. Electron microscopy
  - i. *Subepithelial deposits along the basement membranes*
  - ii. Effacement of podocyte foot processes
- f. Prognosis
  - i. Variable course
  - ii. Spontaneous remission
  - iii. Persistent proteinuria
  - iv. End-stage renal disease

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II. Minimal change disease

- a. Synonyms: lipoid nephrosis, nil disease
- b. Clinical features
  - i. Most common cause of *nephrotic syndrome in children*
  - ii. Peak incidence: ages 2-6 years
  - iii. Diagnosis of exclusion
- c. Light microscopy
  - i. Normal glomeruli
  - ii. Lipid accumulation in proximal tubule cells (lipoid nephrosis)
- d. Immunofluorescence: negative; no immune complexes
- e. Electron microscopy
  - i. *Effacement of epithelial (podocyte)foot processes*
  - ii. Microvillous transformation
  - iii. No immune complex deposits
- f. Treatment: corticosteroids
- g. Prognosis
  - i. Excellent
  - ii. Dramatic response to steroids in children
  - iii. Majority have a complete recovery

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III. Focal segmental glomerulosclerosis

- a. Clinical features
  - i. African Americans> Caucasians
  - ii. Occurs in all ages
  - iii. Nephrotic syndrome
- b. Etiology
  - i. Idiopathic (primary)
  - ii. Associated with loss of renal tissue
  - iii. Superimposed on other glomerular diseases, such as IgA nephropathy
  - iv. Sickle cell anemia
  - v. Heroin abuse
  - **vi. AIDS**
  - vii. Morbid obesity
- c. Light microscopy
  - i. *focal segmental sclerosis and hyalinization of glomeruli*
  - ii. Initially affects the glomeruli along the medullary border
- d. Immunofluorescence: IgM and C_3 deposits in the sclerotic segments
- e. Electron microscopy
  - i. Nonsclerotic regions exhibit effacement of foot processes
  - ii. Sclerotic segments show increased mesangial matrix
- f. Treatment
  - i. Poor response to steroids
  - ii. High rate of recurrence in renal transplants
- g. Prognosis
  - i. Poor; children do better than adults
  - ii. Most progress to chronic renal failure

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Chronic Glomerulonephritis

- 1. Definition: the final stage of many forms of glomerular disease and is characterized by progressive renal failure, uremia, and ultimately death
- 2. Clinical features
  - a. Anemia, anorexia, and malaise
  - b. Proteinuria, hypertension, and azotemia
- 3. Gross: small, shrunken kidneys
- 4. Micro: *hyalinization of glomeruli, interstitial fibrosis, atrophy of tubules, and a lymphocytic* infiltrate
- 5. Urinalysis shows *broad waxy casts*
- 6. Treatment: dialysis and renal transplantation

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Diseases of the Tubules and Interstitium

- 1. Acute tubular necrosis (ATN)
  - a. Definition: acute renal failure associated with reversible injury to the tubular epithelium
  - b. Clinical features
    - 1. ATN is the most common cause of acute renal failure in the United States
    - 11. Oliguria and elevation of blood urea nitrogen (BUN) and creatinine
    - iii. Metabolic acidosis and hyperkalemia
    - iv. Urinalysis shows *dirty brown granular casts and epithelial casts*
  - c. Ischemic ATN
    - i. Is the most common cause of ATN
    - ii. Is due to decreased blood flow caused by severe hemorrhage, severe renal vasoconstriction, hypotension, dehydration, or shock

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- d. Nephrotoxic ATN: Caused by
  - i. Drugs (e.g., polymyxin, methicillin, gentamicin, sulfonamides)
  - ii. Radiographic contrast agents
  - iii. Heavy metals (e.g., mercury, lead, gold)
  - iv. Organic solvents (e.g., carbon tetrachloride, chloroform, methyl alcohol)
  - v. Ethylene glycol (antifreeze)
  - vi. Mushroom poisoning
  - vii. Phenol
  - viii. Pesticides
  - ix. Myoglobin
- e. Prognosis: excellent if the patient survives the disease responsible for the ATN

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Acute pyelonephritis

- a. Definition: bacterial infection involving the renal pelvis, tubules, and interstitium
- b. Pathogenesis
  - i. Ascending infection is the most common route
  - ii. Organisms :
    - Gram-negative enteric bacilli . *Escherichia coli, proteus, klebsiella, enterobacterium*
  - iii. Predisposing factors: urinary obstruction, vesicoureteral reflux, pregnancy, urethral instrumentation, diabetes mellitus, benign prostatic hypertrophy, and other renal pathology
- c. Clinical features
  - i. Females> > males
  - ii. Fever, chills, and malaise
  - iii. Dysuria, frequency, and urgency
  - iv. Costovertebral angle tenderness
  - v. Urinalysis shows pyuria and WBC casts
- d. Micro: acute inflammation of the interstitium and tubules

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Urolithiasis/Renal calculi

- a. Incidence
  - i. Occurs in up to 6% of the population
  - ii. Men are affected more often than women
- b. Stone composition
  - i. *Calcium oxalate stones (75%)*
  - ii. Magnesium ammonium phosphate ("struvite") stones
    - . Associated with infection by urea-splitting bacteria (proteus)
    - . Often form large staghorn calculi
  - iii. Uric acid stones are seen in gout, leukemia, and in patients with acidic urine
  - iv. Cystine stones
- c. Pathology
  - i. Most stones are unilateral
  - ii. Are formed in the calyx, pelvis, and bladder
- d. Clinical features
  - i. Calcium stones are radiopaque and can be seen on x-ray
  - ii. Renal colic may occur if small stones pass into the ureters
  - iii. May cause hematuria, urinary obstruction, and predispose to infection
- e. Treatment: lithotripsy or endoscopic removal

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Tumors of the Kidney

- 1. Benign tumors of the kidney
  - a. Cortical adenomas
    - i. Common finding at autopsy
    - ii. Small encapsulated cortical nodules measuring less than 3 cm
  - b. Angiomyolipomas
    - i. Hamartomas composed of fat, smooth muscle, and blood vessels
    - ii. Common in patients with tuberous sclerosis

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Renal cell carcinoma (RCC)

- a. Synonym: hypernephroma
- b. Incidence
  - i. Males> females
  - ii. They are most common from ages 50-70 years
- c. Risk factors
  - i. Cigarette smoking
  - ii. Chronic analgesic use
  - iii. Asbestos exposure
  - iv. Chronic renal failure and acquired cystic disease
  - v. Von Hippel-Lindau disease
- d. Gross
  - i. Large solitary yellow mass found most commonly in the upper pole
  - ii. Areas of necrosis and hemorrhage are commonly present
  - iii. The *tumor often invades the renal vein and may extend into the vena cava and* heart

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- e. Micro
  - i. Clear cell carcinoma
    - . Polygonal cells with clear cytoplasm
    - . Most common type
  - ii. Papillary carcinoma
  - iii. Chromophobe carcinoma
  - iv. Sarcomatoid RCC *(poor prognosis)*
- f. Clinical features
  - i. "Classic" triad (10%): hematuria, palpable mass, and flank pain
  - ii. Paraneoplastic syndromes from ectopic hormone production
    - . Polycythemia (erythropoietin production)
    - . Hypertension (renin production)
    - . Cushing syndrome (corticosteroid synthesis)
    - . Hypercalcemia (PTH-like hormone)
    - . Feminization or masculinization (gonadotropin release)
  - iii. May cause amyloidosis, a leukemoid reaction, or eosinophilia
  - iv. There is a high incidence of metastasis on initial presentation

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3. *Wilms tumor (nephroblastoma)*

- a. Peak age:2-5 years
- b. Risk factors
  - i. WAGR syndrome-Wilms tumor, aniridia, genital anomalies, and mental retardation
  - ii. Beckwith-Wiedemann syndrome
- c. Tumor suppressor genes
  - . WT-1 (llp13)
  - . WT-2 (llp15)
- d. Presents as a large abdominal mass
- e. Gross: large solitary tan mass
- f. Micro
  - i. Metanephric blastema
  - ii. Epithelial elements (immature glomeruli and tubules)
  - iii. Stroma
- g. Treatment: surgery, chemotherapy, and radiation
- h. Prognosis: excellent; long-term survival rate of 90%

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Bladder Pathology

1. Cystitis

- a. Etiology
  - i. Organisms: fecal flora *(Escherichiacoli, proteus, klebsiella, enterobacterium)*
  - ii. Radiation cystitis
  - iii. Chemotherapy agents such as cyclophosphamide (hemorrhagic cystitis)
- b. Clinical features
  - i. Females> > males
  - ii. Frequency, urgency, dysuria, and suprapubic pain
  - iii. Systemic signs (e.g., fever, chills, malaise) are uncommon
- c. Predisposing factors: benign prostatic hypertrophy, bladder calculi, and cystocele

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2. Bladder tumors

- a. Most common type: transitional cell carcinoma
- b. Epidemiology
  - i. Males> females
  - ii. Increasing in incidence
  - iii. Peak incidence is between 40 and 60 years of age
- c. Risk factors include
  - i. Cigarette smoking
  - ii. Occupational exposure to naphthylamine
  - iii. Bladder infection with *Schistosoma haematobium*
    - . Common in Egypt
    - . Tend to develop squamous cell carcinomas
- d. Clinical features
  - 1. Bladder cancer usually presents with painless hematuria
  - ii. It may also cause dysuria, urgency, frequency, hydronephrosis, and pyelonephritis
- e. Prognosis
  - i. Bladder cancer has a high incidence of recurrence
  - ii. The prognosis depends on the tumor grade and stage

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