What are the special clues in symptoms and lab findings that will help you determine which disease you're dealing with?

1. **Prerenal AKI:**
    - Mostly outpatients.
    - Caused by any condition decreasing renal blood flow.
    - Could be drug induced.
2. **Intrarenal AKI:**
    - Mostly inpatients.
    - Happens from inside the kidney itself.
3. **Postrenal AKI:**
    - Obstruction of urine flow (Kidney stones or BPH)
4. **Acute tubular injury:**
    - Damaged tubular epithelial cells.
    - Could be due to:
        - Ischemia
        - Toxins:
            - Endogenous → Crush injury or Hemoglobinopathy.
            - Exogenous → Drugs, metals and Radiocontrast dye.
5. **Cystic renal dysplasia:**
    - Commonest cystic renal disease in children.
    - Caused by disorganized renal development.
    - Often associated with poorly formed ureter.
6. **Autosomal dominant polycystic kidney disease:**
    - Progressive distention of kidney by enlarging cysts.
    - Caused by mutation in two genes PKD1 (85% of cases: chromosome 16) and PKD2 (155 cases, chromosome 4) (also PKD3 in rare cases).
7. **Autosomal recessive polycystic kidney disease:**
    - Gene on chromosome 6.
    - Liver is always affected.
    - Large kidneys at birth
8. **Medullary sponge kidney**
    - Dilated collecting ducts give "spongy" appearance.
    - May present with renal infections in adult life.

9. Renal papillary necrosis:

- Ischemic necrosis of the tips of the renal papillae.
- Usually associated with diabetes mellitus.
- Eosinophils.

10. Acute drug included interstitial nephritis:

- Usually triggered by penicillin derivatives or NSAIDs & diuretics.
- Eosinophils are characteristic.
- Resolves on cessation of the inciting drug.
- Type I hypersensitivity.
- T cell–mediated (type IV) hypersensitivity reaction.
- The abnormalities in acute drug-induced nephritis are in the interstitium.
- With some drugs (e.g., methicillin, thiazides, rifampin), interstitial non-necrotizing granulomas with giant cells may be seen.
- The glomeruli are normal except in some cases caused by nonsteroidal anti-inflammatory agents, in which the hypersensitivity reaction also leads to podocyte foot process effacement and the nephrotic syndrome.

11. Pyelonephritis:

- Ascending infection. E-coli most commonly
- Could be hematogenous – TB
- Systemic evidence of infection.
- White cell casts.
- Complications of acute Pyelonephritis:
  1- Papillary necrosis.
  2- Pyonephrosis.
  3- Perinephric abscess.
- **When is it considered chronic?**
  - When there is scaring and fibrosis.
- **When is it called obstructive?**
  - When there is obstruction
- **When is it called reflux nephropathy?**
  - When it's caused by a vesicoureteric reflux or intrarenal reflux

12. Stones:

- **Calcium stones:**
  - CALCIUM OXALATE and PHOSPHATE
  - They are radiopaque
  - They are associated with hypercalciuria
- **Ammonium magnesium phosphate stones:**
  - Magnesium ammonium phosphate (15-20%) - (Struvite stone).
  - These stones are formed in alkaline urine
  - They are radiolucent. But if they were mixed with calcium phosphate, they become radiopaque.
  - They can form large staghorn.
- **URIC ACID & URATE (5-10%).**
  - Uric acid stones are associated with hyperuricemia
- **Cysteine stone:**
  - Associated with cystinuria or genetically determined aminoaciduria.

13. Cystitis:

- Microorganisms in the bladder
- **When is it associated with malakoplakia?**
  - When there are Michaelis-Gutmann bodies.

14. Nephrotic syndrome:

- Heavy proteinuria
- **Minimal change disease:**
  - Diffuse Epithelial Cell Disease
  - Young children.
  - LM → Normal under the microscope.
  - EM → Effacement of epithelial foot processes
  - Good response to corticosteroid therapy
- **Focal segmental glomerulosclerosis:**
  - Sclerosis within capillary tufts.
  - Increased matrix
  - Obliteration of capillary lumina
  - Higher incidence of hematuria & hypertension.
  - Poor response to corticosteroid therapy.

- **Membranous glomerulonephritis:**
  - Azotemia
  - Spike and dome appearance
  - Deposits of IgG or C3
  - Thickened capillary walls
  - Mostly caused by autoantibodies that cross-react with antigens expressed by podocytes.
- **Diabetic nephropathy:**
  - Kimmelstiel-Wilson nodules
  - EM → thickness of glomerular basement membrane
- **Renal amyloidosis:**
  - Mesangial amyloid deposits
  - Congo red stain
  - Crisscross fibrillary pattern
  - Apple green birefringence under polarized light
- **Lupus Nephropathy:**
  - Deposition of DNA and anti DNA complexes within the glomeruli.
  - Spike and dome pattern by silver methanamine (jones) stain

  - Class one: Normal.
  - Class two: Mesangial lupus glomerulonephritis. Immune complex deposits in the mesangium.
  - Class three: Focal proliferative lupus glomerulonephritis. Swelling and proliferation of endothelial and mesangial cells with neutrophilic infiltration or fibrinoid deposits and capillary thrombi.
  - Class four: Diffuse proliferative lupus glomerulonephritis. Similar to class 3 but more diffuse. Immune complexes depositions create an overall thickening of the capillary walls, which resembles rigid "wire loops" on LM.
  - Class five: Membranous lupus glomerulonephritis. The patients have severe nephrotic syndrome and there is thickening of the capillary walls due to deposition of basement membrane like material as well as immune complexes.

15. Nephritic syndrome:

- Increase cellularity.
- Proliferation of cells.
- Pigmented granular casts.
- **Poststreptococcal glomerulonephritis (acute proliferative glomerulonephritis):**
    - Infection
    - Nephritogenic strains of group A B-hemolytic streptococci.
    - Urinary red cells and red cell casts
    - Decreased serum C3
    - Increased titers of anticationic proteinase (ASO)
    - EM → Humps.
    - Immunofluorescence → Lumpy bumpy.

16. RPGN:

- Progresses rapidly to renal failure
- Crescentic
- Severe glomerular injury.
- EM → ruptures in GBM
- Immunofluorescence → IgG and C3
- **Type I, anti-GBM disease: (Good pasture syndrome)**
    - Nerve deaflines and ocular disorders
    - Hereditary nephritis
    - Clinically manifested as the nephritic syndrome
    - Hemorrhagic pneumonitis
    - Caused by mutation in the gene for the 5-chain type IV collagen
- **Type II, Immune Complex-Mediated Crescentic Glomerulonephritis:**
    - Granular ("lumpy bumpy") pattern of staining
    - Severe injury in the form of segmental necrosis
    - Immunofluorescence → **Granular pattern** of immune complex disease
    - EM → demonstrates discrete deposits.
- **Type III, pauci immune (ANCA-associated)**
    - RPGN is without immune complex deposition or antiglomerular basement membrane antibodies.
    - Associated with ANCAs.
    - Segmental necrosis
    - Oliguria and azotemia are more pronounced
    - **Wegener's granulomatosis/ microscopic polyangiitis:**
        - Transmural necrosis.

- **Membranoproliferative glomerulonephritis**
    - Endocapillary proliferation and glomerular basement membrane splitting (double contour) "tram-track" appearance.
    - Lobular appearance.
    - GBM thickened.
    - **Type I:**
        - **Caused by circulating immune complexes**.
        - Association with **hepatitis B and C antigenemia**.
    - **DDD:**
        - **Excessive complement activation.**
        - Mutations in the gene encoding the complement regulatory protein **factor H.**
        - Membranoproliferative pattern
        - DDD carries worse prognosis than type I..
- **Asymptomatic hematuria/proteinuria:**
    - Microscopic hematuria with red cell casts
    - **Alport syndrome:**
        - Alternating areas of extreme thinning of the glomerular basement membrane
        - Thick, irregular areas with basket weaving are shown.
    - **IgA nephropathy (Berger disease):**
        - Benign recurrent hematuria (gross or microscopic) – stays for several days then subsides only to recur once again.
        - Deposition of IgA in the mesangium
        - Abnormality in IgA1 production
        - Increased frequency in individuals with celiac disease.
        - Can be a component of the Henoch- Schonlein vasculitis disease.
        - Children + Young adults.
        - Focal glomerulonephritis may be the presenting feature

17. Chronic kidney disease:

- Results from any type of kidney disease
- It's the result of **progressive scarring**
- **It leads to end-stage kidney disease.**

18. Adenoma:

- Benign, Small, Asymptomatic
- Derived from the renal tubules

19. Angiomyolipoma:

Benign, It is often associated with the tuberous sclerosis syndrome.

20. Oncocytoma:

- It's a benign tumor that arises from the intercalated cells of collecting ducts.
- Associated with genetic changes— loss of chromosomes 1, 14, and Y.

21. Renal cell carcinoma:

- Most common malignant tumor.
- More common in men, cigarette smoking.
- Gene deletion in chromosome 3
- Associated with VHL disease
- Arises in the renal poles (upper more frequently)
- Polygonal clear cells + primitive tubule formation.
- Three common forms:
    - Clear cell carcinoma:
        - Solitary, large and spherical.
        - Arises anywhere in the cortex.
        - Cystic softening or hemorrhage.
        - Direct invasion to the perinephric fat and adrenal gland may happen.
        - May appear almost vacuolated or solid.
    - Papillary renal cell carcinoma
        - Exhibit papilla formation with **fibrovascular** cores.
        - They tend to be **bilateral and multiple.**
        - They also show **necrosis**, hemorrhage, and cystic degeneration.
        - The cells may have clear or, more commonly, **pink cytoplasm**
    - Chromophobe renal carcinoma.
        - The least common
        - They arise from intercalated cells of collecting ducts.
        - Stain more darkly, so they are less clear than cells in clear cell.
        - Shows extreme **hypodiploidy**, by losing entire chromosomes, including chromosomes 1, 2, 6, 10, 13, 17, and 21.
        - **Grossly, they tend to be** tan-brown.
        - The cells usually have clear, flocculent cytoplasm with very prominent, distinct cell membranes,
        - Good prognosis

22. Wilms tumor (nephroblastoma):

- Most common renal malignancy of early childhood.
- Associated with deletions of the short arm of chromosome 11
- Characteristics are varied with immature stoma, primitive tubules and glomeruli, and mesenchymal elements such as fibrous connective tissue and cartilage bone
- In most lesions, triphasic combination of blastemal, stromal and epithelial cell types is observed.
- The tumor is large, solitary, and well-circumscribed mass.
- Nephrogenic rests are precursor lesions of Wilms tumors.
- The WT-1 and WT-2 genes localized to this chromosome are cancer suppressor genes.
- The presenting feature is palpable flank mass,
- The disease can be part of the AGR (or WAGR) complex:

  This set of anomalies is associated with deletion of the WT-1 tumor suppressor and other nearby genes.
- It can also be associated with Beckwith-Wiedemann syndrome:

  Associated with deletion of the WT-2 gene.
  - The gene involved in these patients are 11p15.5 "WT2"
  - Focal anaplasia which is restricted within the nephrectomy → prognosis is good
  - Diffused anaplasia → have the least favorable outcome"

- **Denys Drash syndrome (DDS):**
  - This syndrome is characterized by gonadal dysgenesis and renal abnormalities.
- **Both WAGR and DDS** are associated with abnormalities **of Wilms tumor 1 gene (WT1)** located on 11p13.

23. Transitional cell carcinoma

- Most common tumor of the urinary collecting system.
- Multifocal
- Associated with phenacetin abuse
- The presenting feature is **hematuria.**
- **May recur.**

24. Squamous cell carcinoma constitutes a minority of urinary tract malignancies.

- This cancer may result from **chronic inflammatory processes**, such as chronic bacterial infection or Schistosoma haematobium infection.
- It can also be associated with renal calculi.

25. Transitional Cell Carcinoma:

- Macroscopically (fronded and seaweed-like to solid)
- Microscopically (well differentiated and papillary to poorly differentiated and widely muscle-invasive)
- **Squamous metaplasia of the urothelium**
- Deletions of the short (p) or long (q) arm of chromosome 9 and deletions of 17p (which involves the p53 gene).

Types of rejection:

26. Hyperacute:

- Hyperacute under the microscope (antibody mediated):

1- Necrosis 2- Hemorrhage 3- Polymorph nuclear cells infiltrate

27. Acute rejection:

1. **Acute T cell mediated**:
   - Grade 1 will look like tubulointerstitial inflammation and
   - If it got more severe the wall of the vessels will thicken and endothelialitis and is grade 2.
   - If really severe inflammation, thickening endothelialitis and fibrinoid necrosis type 3 may be t cells or antibody mediated.
   - The T cell mediated has a better prognosis than the antibody mediated
2. **Acute Antibody mediated rejection to diagnosis we need 3 criteria:**
   - **1- Cellular injury:**
     - Dilatation of the peritubular capillaries and polymorph or lymphocytes within them.
     - Acute tubular injury and necrosis no inflammation or anything else but is c4d positive or lastly blood vessels fibrinoid necrosis and inflammation and infiltration.
   - **2- C4d positive in immunofluorescence.**
   - 3- **Circulating antibodies:** not as high as in the hyperacute.

28. Chronic:

- Fibrosis and sclerosis of blood vessels.
- Antibody or t cell mediated
- **All in t cell:**
  - Borderline changes will need clinical investigation (creatinine).
  - Grade 1 A or 1 B: depending on the tubulointerstitial inflammation severity between both.
  - Grade 2: endothelialitis we see a few lymphocytes beneath the endothelium and thick wall.
  - Grade 3: may be t cell mediated or antibody mediates more severe than the rest.

29. Chronic allograft nephropathy:

- Fibrosis, arterial sclerosis, and scarring.
- May be from rejection, drug toxicity (cyclosporine) or other things
- We see double contouring in the glomeruli
- In capillary we also see narrowing of the lumen and atherosclerosis like in hypertension to differentiate between them we do silver stain and if we see silver elastic multilayering it is hypertension if not then it is chronic allograft nephropathy.

30. Transplant glomerulopathy:

- Chronic lesion more than a hundred days and 2 double contouring.

31. Drug toxicity:

Cyclosporine toxicity:

→ Acute we see the isometric vacuolization in the tubules.

→ If chronic we see strip fibrosis or nodules in the wall of the blood vessels hyaline nodules.

32. Most important infection:

- **Polyoma** virus:
  - In chronic transplant because they are taking a lot of immunosuppressants.
  - We can see inclusion in the nuclei ground glass appearance and gray.
  - It is mainly in the tubule.
- **Cytomegalovirus:**
  - It makes the cells big and is in the glomeruli and nuclei (everywhere not specific).