Revision

AKI:

Was previously called acute renal failure. Tell me about the three phases of AKI:

- **Prerenal:**
  - Ischemia
  - Car accident
  - Loss of blood
- **Intrarenal:**
  - **When I look at the kidney biopsy under the microscope for a patient with AKI. What is the definition of AKI?**

    A sudden increase of serum creatinine and urea within hours to days.
  - **When I look under the microscope what do we see:**
    - Tubules
    - Interstitium
    - Blood vessels
    - Glomeruli
  - **Most frequent cause of AKI:**
    - **Acute tubular necrosis:**
      - Could be coming from many things:
        - Ischemic
        - Drug toxicity
        - Pigment deposition
        - Facetious
        - Idiopathic – not true
      - I can recognize where is it coming from:
        - If it was ischemia – loop of henle is affected
        - If it was toxic – Proximal convoluted tubule is affected
  - **Under the microscope what can we see?**
    - Glomeruli – crescentic glomerulonephritis
    - Blood vessels – Acute vasculitis
  - **We also talked about pigments:**
    - Hemoglobin
    - If some one got into a car accident – myoglobin
      - Some drugs give necrosis of muscle e.g. TB.
        - Streptomycin, rifampicin shown to give acute tubular necrosis sometimes due to myoglobinuria
        - Antibiotics or NSAIDS – acute tubular necrosis
  - **Now in drug induced what do we see under the microscope?**
    - Acute tubulointerstitial nephritis.

- **Postrenal:**
    - Obstruction due to:
        - Tumors
            - Benign – Prostatic hyperplasia
            - Malignant.
        - Stones

          The patients who are in the hospital will get AKI in a different pattern than those who are outpatients (car accident, trauma) as inpatients are already debilitated (diabetes, hypertension)

          Therefore, prognosis is better in patients whom are outpatients.

UTI:

- Must know what's an autosomal dominant polycystic kidney disease + autosomal recessive + renal dysplasia + stones (Which are radiopaque and which are radiolucent)
- We have Upper UT + Lower UT.

Pyelonephritis:

- **Acute:**
    - Could be very debilitating with tremors, fever and the patient is really sick so you have to give a fair amount of antibiotics + sometimes you need to hospitalize the patient.
    - We see polymorphs.
- **Chronic:**
    - Difference between them is fibrosis in chronic
    - Lymphocytes inside the interstitium.
    - Could be because of reflux, obstruction… etc.

Specific types of pyelonephritis:

- **Tuberculous:**
    - Granuloma – Caseating necrosis in the center.
        - **Formed of:**
            - Giant cells
            - Lymphocytes
            - Necrotic material
            - Epithelioid Cells (most important)
    - **Bacilli are frequently seen in the edge between the necrosis + epithelioid cells.**

- **Staghorn stones related – xanthogranulomatous pyelonephritis:**
    - Grossly – Staghorn.
    - What do wee see under the microscope?
        - Foamy histiocytes.
        - **Where also do we see foamy histiocytes?**

          In the bladder – malakoplakia – Michaelis–Guttmann bodies

How many infections are allowed for a child before you start your investigations?

- Girls: one only.
- Boys: none.
- Why? Because of genital organs (their anatomy).

Lower UTI:

Ureters are not involved frequently pathology.

Cystitis:

We spoke about its symptoms:

- Dysuria
- Frequency
- Fever, etc.

Could be:

- **Acute:**
    - Polymorphs, infiltration.
    - Hemorrhagic.
        - **Could be due to a drug:**
            - They give sometimes drugs that cause acute cystitis with hemorrhage.
            - How to treat? Inject formalin inside the bladder.
    - **Complications:**
        - Papillary necrosis
        - Pyonephrosis
        - Perinephric abscess.

- **Chronic:**
    - Whenever there is obstruction from BPH for example.
    - **It becomes chronic inflammation with:**
        - Fibrosis, scarring.
        - Thickened bladder wall
        - Trabeculation
        - Diverticula between the fibrosis the bladder is not elastic anymore it becomes thick and fibrotic.
    - Thyroidization: the tubules become flattened epithelium + the casts are like hyaline.
    - **Different types of casts + with what they are associated:**
        - Granular casts
        - Hyaline casts

Types of stones you have to know them.

Tubulointerstitial nephritis related to drugs:

- **Acute – AKI**

  Aminoglycosides (Antibiotics) can give AKI but without oliguria

  In a patient with AKI there is decreased amount of urine sometimes anuria.

- **What are the important cells in this?**
    - Eosinophils
    - Plasma cells
    - But we can see granuloma in drug toxicity as well – they rupture making body epithelioid around it but not like the one in TB.
    - So what else can give granuloma?
        - Sarcoidosis
        - TB
        - Drug toxicity
        - Wegener granulomatosis

          In malakoplakia we might see foamy histiocytes but large numbers are usually seen in xanthogranulomatous pyelonephritis.

The most important two lectures nephrotic & nephritic.

Non-neoplastic kidney diseases we have five clinical syndromes:

1- Nephrotic:

- You already know the definition of it.
- Can come from different patterns of injury (intrinsic to the kidney or systemic)
- Under the microscope the glomeruli are not very much cellular.
- **Intrinsic diseases that present as the nephrotic syndrome:**
  - **Minimal change disease:**
    - Normal glomeruli under LM
    - Specificity of EM – Diffuse effacement of epithelial cell foot processes
  - **Focal segmental glomerulosclerosis:**
    - You remember, diffuse = all.
    - Focal = some.
    - Segmental = segment abnormal
    - What do we see? Sclerosis.
    - Prognosis is better in minimal change.
  - **Membranous glomerulonephritis:**
    - Spikes + thickened membrane
    - Silver stain. Stains the membrane, we see the membrane capillary then the spikes are perpendicular to it because in between on the EM what do we see?
      - Deposits + membrane trying to engulf it.
    - Immunofluorescence what do we see?
      - IgG + C3, where? In capillaries.
  - **Systemic:**
    - Diabetes:
      - Kimmel – stein Wilson nodules
    - SLE class V.
    - Amyloid. Green birefringence under polarized light.

2- Nephritic:

- Increase cellularity in glomeruli under microscope
- Acute nephritic syndrome is different from nephrotic clinically how?
  - Hematuria
  - Proteinuria – sub-nephrotic
  - Hypertension
  - Edema
  - Nephrotic is mainly edema + normal creatinine.
  - But here we can find abnormal creatinine + C3
- **Acute post-infectious:**
  - Diffuse inflammation.
  - **What are the diseases that give us a lot of polymorphs in the glomeruli?**
    - Acute post-infectious
    - SLE class 3 + 4
- **Membranoproliferative glomerulonephritis:**
  - Double endocapillary proliferation.
  - C3 + IgG
  - Could be related to infection, like what?
    - Hepatitis C
    - Hepatitis B is usually with membranous. (More nephrotic)
  - **Could give both nephrotic and nephritic, but where are the deposits?**
    - **In membranous subepithelial but in membranoproliferative subendothelial. Why?**

      Because they made an injury to subendothelial cells then it recuperated and made double contouring.

      It's due to immune complex deposition.

      ** Like in transplant but the injury there is through the complement to endothelial cells
- The syndrome could start nephritic then moves on to RPGN.

3- RPGN:

- **What do I see under the microscope?**
  - Crescent
- **What are the three types that can give you crescentic glomerulonephritis?**
  - Anti-GBM:
    - Immunofluorescence what do we see? IgG linear capillary.
    - Lung is also affected, usually male.
  - Post-Immune complex:
    - Any of them if they developed crescent they change from their previous syndrome to RPGN.
    - **Post-infectious:**
      - What do we see? Humps. Subepithelial hump like the membranous.
      - IgG + C3 deposition.
    - Post IgA.
    - Henoch-Schönlein.
  - Pauci-immune: (no immune deposits)
    - Vasculitis:
      - Churg-Strauss syndrome
      - Wegener granulomatosis
      - Polyarteritis nodosa

4- Asymptomatic hematuria/ proteinuria

- **IgA:**
  - Mesangial disease.
  - IgA deposition
- **Alport syndrome:**
  - Thin basement membrane disease.
  - EM = basement membrane is thickened and thin– lamellated.
  - It starts thin then it becomes lamellated.

5- Chronic renal failure:

- It has all diseases. At the end the all progress to this.
- Focal global glomerulosclerosis.
- Symptoms are important to know.

Lupus nephritis:

- **Class 5: membranous – nephrotic**
- **Class 3 + 4: membranoproliferative, focal proliferative:**
  - We see subendothelial dense deposit, mesangial, and paramesangial.
  - If we see subepithelial a lot it could be either 3 or 4 + 5.

We talked about tumors:

- **Benign:**
  - **Small tumors, adenoma**
  - **Angiomyolipoma:**
    - Vessels
    - Smooth muscles
    - Fat cells
- **Malignant:**
  - **Adults:**
    - Renal cell carcinoma:
      - **Clear cell – most common:**
        - VHL – chromosome + abnormality important.
        - Syndrome associated with VHL:
          - Cerebral hemangioblastomas:

            VHL is an autosomal dominant condition involving chromosome 3 characterized by specific benign and malignant tumors with variable expressivity. Cerebellar hemangioblastoma is the most common initial manifestation, affecting patients with VHL.
      - **Papillary:**
        - Trisomy 7, hereditary
      - Chromophobe, chromophile, collecting duct… etc.
      - Cells clear + background we see thin blood vessels.
      - Sometimes it is cystic + we see one layer of clear cell at the periphery.
      - Patients on long standing dialysis are more prone to get a renal cell carcinoma.
      - **What other disease can affect a patient on dialysis for a long time?**
        - Amyloidosis. Beta 2 microglobulin – Congo red

- **Children:**
  - **Wilms:**
    - Most important thing - Anaplasia:
      - Mitosis, necrosis and pleomorphism.
    - Formed by:
      - Blastema
      - Stroma
      - Epithelium
    - Mesoblastic nephroma occurs in uterus or infancy – stromal cells + mitosis.
    - Wilms + chemotherapy = Stroma only so you have to differentiate.

Transplant:

When I speak about kidney transplant what is the most important thing?

Rejection or no rejection.

Rejection:

- **Hyperacute:**
  - Due to circulating antibodies already in his blood.
  - **Immediately attack the kidney:**
    - Hemorrhage
    - Necrosis
    - A little bit of inflammation later.
    - Polymorphonuclear cells.
- **Borderline:**
  - He has tubulointerstitial inflammation but not a lot. Where should we put it, rejection or no rejection? We follow him and check clinical signs if elevated creatinine they treat it. If not we follow up.
- **Acute:**
  - **T-cell mediated:**
    - Grade I:
      - Under microscope:
        - Tubulointerstitial inflammation + Tubulitis.
        - We graded it IA + IB depending on the severity of them.
        - A + B both have more than 25% of interstitium infiltrated but depends on how many lymphocytes you have.
    - Grade II: Endothelialitis:
      - Depends on severity of it could be A or B.

- Grade III: fibrinoid necrosis:
    - Transmural inflammation
    - We see it in antibody-mediated rejection.
- **Antibody mediated:**
    - Acute tubular injury.
    - Peritubular capillaritis:
        - We see C4D Complement.
    - Fibrinoid necrosis.
    - What will they have in blood?
        - Donor specific antibodies.
- **Chronic:**
    - Fibrosis
    - Glomerular + arterial sclerosis (obliteration of the artery).
    - **In glomeruli what can we see?**
        - Double contour (endothelial cells) – Transplant glomerulopathy.
        - Due to the injury by the C4D of the endothelial cell.

- **Infections:**
    - **Polyoma virus:**
        - In distal tubules mainly – not in glomeruli.
        - Ground glass appearance of nuclei.
        - Grey intra nuclear inclusion.
    - **Cytomegalovirus:**
        - Anywhere in the kidney.
        - Increase in size of the cytoplasm + inclusion
- **Drug toxicity:**
    - Because we give them immunosuppressants
    - Calcineurin inhibitor:
        - Isometric (same size small vacuoles) vacuolization.
            - What are other cases to see isometric vacuolization in tubules?
                - Ischemia or Mannitol perfusion. Not only one thing causes it.
        - Chronic fibrosis or hyaline nodules in the wall of blood vessels.
- **Recurrent + de novo:**
    - Disease can recur. Or de novo.