KIDNEY DISEASES

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Kidney Diseases

- Renal failure (acute & chronic)
- Glomerular Syndromes
- Interstitial Diseases
- Vascular Disease
- Nephrolithiasis
- Urinary obstructions
- Asymptomatic urinary abnormalities
Acute Renal Failure

- Sudden interruption of kidney function resulting from obstruction, reduced circulation, or disease of the renal tissue
- Results in retention of toxins, fluids, and end products of metabolism
- Usually reversible with medical treatment
- May progress to end stage renal disease, uremic syndrome, and death without treatment
Acute Renal Failure

• Causes
  • Prerenal
    • Hypovolemia, shock, blood loss, embolism, pooling of fluid d/t ascites or burns, cardiovascular disorders, sepsis
  • Intrarenal
    • Nephrotoxic agents, infections, ischemia and blockages,
  • Postrenal
    • Stones, blood clots, BPH, urethral edema from invasive procedures
Acute Renal Failure

- **Stages**
  - **Onset** – 1-3 days with \(^{\text{^BUN}}\) and creatinine and possible decreased UOP
  - **Oliguric** – UOP < 400/d, \(^{\text{^BUN,Crest, Phos, K,}}\) may last up to 14 d
  - **Diuretic** – UOP \(^{\text{^to as much as 4000 mL/d but no waste}}\) products, at end of this stage may begin to see improvement
  - **Recovery** – things go back to normal or may remain insufficient and become chronic
Acute Renal Failure

- Subjective symptoms
  - Nausea
  - Loss of appetite
  - Headache
  - Lethargy
  - Tingling in extremities
Acute Renal Failure

- **Objective symptoms**
  - Oliguric phase –
    - vomiting
    - disorientation,
    - edema,
    - ^K+
    - decrease Na
    - ^ BUN and creatinine
    - Acidosis
    - uremic breath
  - CHF and pulmonary edema
  - hypertension caused by hypovolemia, anorexia
  - sudden drop in UOP
  - convulsions, coma
Acute Renal Failure

- Objective systems
  - Diuretic phase
    - Increased UOP
    - Gradual decline in BUN and creatinine
    - Hypokalemia
    - Hyponaturmia
    - Tachycardia
    - Improved LOC
Acute Renal Failure

- Diagnostic tests
  - H&P
  - BUN, creatinine, sodium, potassium. pH, bicarb. Hgb and Hct
  - Urine studies
  - US of kidneys
Background---CKD

- chronic kidney disease (CKD) as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of <60 mL/min/1.73 m² for 3 or more months.
Chronic Renal Failure

- **Objective symptoms**
  - **Skeletal**
    - Muscle and bone pain
    - Bone demineralization
    - Pathological fractures
    - Blood vessel calcifications in myocardium, joints, eyes, and brain
  - **Skin**
    - Yellow-bronze skin with pallor
    - Puritus
    - Purpura
    - Uremic frost
    - Thin, brittle nails
    - Dry, brittle hair, and may have color changes and alopecia
Chronic Renal Failure

- Other abnormal findings
  - Metabolic acidosis
  - Fluid imbalance
  - Insulin resistance
  - Anemia
  - Immunological problems
K/DOQI CKD Staging

Requires 2 or more GFR, 3 or more months apart

GFR 90  60  30  15

Other markers kidney disease: proteinuria, hematuria, anatomic
Complications Possible
Complications Evident
Renal Replacement

Stage 1  2  3  4  5
Kidney Failure is the Tip of the Iceberg...

Prevalence of Chronic Kidney Disease (CKD):

- **Stage 5**: Kidney Failure/End-stage kidney disease (GFR <15): 400,000
- **Stage 4**: GFR 15–29: 300,000
- **Stage 3**: GFR 30–59: 7,400,000
- **Stage 2**: Kidney damage & GFR 60–89: 5,700,000
- **Stage 1**: Kidney damage & GFR >90: 5,600,000

19 million Americans with CKD
8 million Americans with GFR<60


http://www.unckidneycenter.org/kcpp/i
Pathophysiology

- Regardless of the etiology of renal injury, with progressive destruction of nephrons, the kidney has an innate ability to maintain GFR by hyperfiltration and compensatory hypertrophy of the remaining healthy nephrons.

- The residual nephron hyperfiltration and hypertrophy, although beneficial for the reasons noted, has been hypothesized to represent a major cause of progressive renal dysfunction. This is believed to occur because of increased glomerular capillary pressure, which damages the capillaries and leads initially to focal and segmental glomerulosclerosis and eventually to global glomerulosclerosis.
Pathophysiology

- Factors other than the underlying disease process and glomerular hypertension that may cause progressive renal injury include the following:
  - Systemic hypertension
  - Acute insults from nephrotoxins or decreased perfusion
  - Proteinuria
  - Hyperlipidemia
  - Hyperphosphatemia with calcium phosphate deposition
Hyperkalemia

- when GFR falls to less than 20-25 mL/min.
- It can be observed sooner
  - ingest a potassium-rich diet
  - if serum aldosterone levels are low, such as in type IV renal tubular acidosis
    - Diabetes
    - ACE inhibitors & ARB
    - NSAIDs
- extracellular shift of potassium
  - acidemia
  - lack of insulin
Metabolic acidosis

- CKD stage 5
  - Unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium.
  - In CKD stage 5, accumulation of phosphates, sulphates, and other organic anions are the cause of the small anion gap.
Fluid overload

- Extracellular volume expansion and total-body volume overload
- GFR falls to less than 10-15 mL/min,
  - Peripheral edema
  - Pulmonary edema
  - Hypertension
Ca & P

- Secondary hyperparathyroidism
- Hypocalcemia
- Decreased renal synthesis of 1,25-Dihydroxycholecalciferol
- Hyperphosphatemia
Osteodystrophy

- severe CKD

  Osteitis fibrosa (high–bone turnover PTH↑)

- Osteomalacia (aluminum accumulation )

- Adynamic bone disease

- Dialysis-related amyloidosis
  - Beta2-microglobulin accumulation
  - Chronic dialysis for at least 8-10 years .
Anemia

- Normochromic normocytic anemia
  - Decreased renal synthesis of erythropoietin
  - RBC survival is decreased
  - Tendency of bleeding
    - platelet dysfunction
Diagnostic Workup in HTN

- Assess risk factors and comorbidities
- Reveal identifiable causes of HT
- Assess presence of target organ damage
- Thorough history and physical
- Labs: UA, glucose, Hct, lipids, K⁺, Cr, Ca, uric acid,
- Optional: TSH
- EKG
Acute nephritic syndrome

- 1–2 g/24 h of proteinuria,
- hematuria with red blood cell casts,
- pyuria,
- hypertension,
- fluid retention,
- rise in serum creatinine associated with a reduction in glomerular filtration.
IMMUNE COMPLEX MARKERS

- ANA....... LUPUS GN

- ASO TITER..... POSTSTREPT. GN

- OTHER INFECTIVE MARKERS ...AntiHCVAb, HBsAg
ANCA + GN

pauci-immune glomerulonephritis

- No Extra Renal disease..... ANCA associated crescentic GN
- Extra renal disease....
  1. Systemic vasculitis...
     Microscopic polyangitis
  2. Respiratory granulomas...
     Wegener’s Granulomatosis
  3. Asthma+ Eosinophilia...
     Churg strauss syndrome
- Low serum C3:
  - cryoglobulinemia,
  - systemic lupus erythematosus,
  - bacterial endocarditis,
  - shunt nephritis,
  - membranoproliferative
  - poststreptococcal glomerulonephritis

- Normal serum C3:
  - polyarteritis nodosa, ANCA Asociated GN
  - visceral abscess,
  - Goodpasture syndrome, Anti GBM Dis
  - Henoch-Schönlein purpura, and IgA nephropathy.
### Albominuria-Proteinuria

<table>
<thead>
<tr>
<th></th>
<th>24-Hour Albumin&lt;sup&gt;a&lt;/sup&gt; (mg/24 h)</th>
<th>Albumin&lt;sup&gt;a&lt;/sup&gt;/Creatinine Ratio (mg/G)</th>
<th>Dipstick Proteinuria</th>
<th>24-Hour Urine Protein&lt;sup&gt;b&lt;/sup&gt; (mg/24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>8–10</td>
<td>&lt;30</td>
<td>–</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30–300</td>
<td>30–300</td>
<td>–/Trace/1+</td>
<td>–</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>&gt;300</td>
<td>&gt;300</td>
<td>Trace–3+</td>
<td>&gt;150</td>
</tr>
<tr>
<td>Type</td>
<td>Frequency in office practice</td>
<td>Pathophysiology</td>
<td></td>
<td></td>
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<tr>
<td>-------------------------------------------</td>
<td>----------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
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<tr>
<td><strong>Exclude first</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Transient proteinuria secondary to stress such as fever or heavy exercise</td>
<td>4 percent of men 7 percent of women</td>
<td>Possibly transient angiotensin II or norepinephrine-mediated alterations in glomerular permeability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthostatic proteinuria</td>
<td>2 to 5 percent of adolescents Uncommon over age 30</td>
<td>Not clear; ? neurohumoral or altered glomerular hemodynamics</td>
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<tr>
<td><strong>Hemodynamic causes</strong></td>
<td></td>
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<tr>
<td>Heart failure; renovascular hypertension</td>
<td></td>
<td>Possibly angiotensin II and, in heart failure, norepinephrine-mediated increase in glomerular permeability</td>
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</tr>
<tr>
<td><strong>Glomerular proteinuria</strong></td>
<td>Major cause when above disorders excluded; responsible for all causes of nephrotic syndrome</td>
<td>Abnormalities in glomerular capillary wall</td>
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<tr>
<td>Glomerular diseases</td>
<td></td>
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<tr>
<td>Diabetic nephropathy</td>
<td>Increasing frequency with prolonged duration of diabetes</td>
<td></td>
<td></td>
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<tr>
<td>Reflux nephropathy and other tubulointerstitial diseases</td>
<td></td>
<td>Secondary glomerular injury due to hemodynamic and structural changes resulting from nephron loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overflow proteinuria</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Multiple myeloma with cast nephropathy</td>
<td>Uncommon</td>
<td>Overproduction of light-chains, leading to tubular obstruction; suspect if acute renal failure, bland urine sediment, negative dipstick for protein, and positive sulfosalicylic acid test, indicating nonalbumin proteinuria</td>
<td></td>
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EVALUATION OF PROTEINURIA

URINE DIPSTICK + PROTEINURIA

Quantify 24-h excretion, or spot morning protein/creatinine ratio (mg/g)

30-300 mg/d or 30-350 mg/g
- Microalbuminuria
  - Consider
    - Early diabetes
    - Essential hypertension
    - Early stages of glomerulonephritis (especially with RBCs, RBC casts)

300-3500 mg/d or 300-3500 mg/g
- RBCs or RBC casts on urinalysis
  - In addition to disorders listed under microalbuminuria consider
    - Intermittent proteinuria
    - Postural proteinuria
    - Congestive heart failure
    - Fever
    - Exercise

> 3500 mg/d or > 3500 mg/g
- Nephrotic syndrome
  - Diabetes
  - Amyloidosis
  - Minimal change disease
  - FSGS
  - Membranous glomerulopathy
  - MPGN
  - Go to Fig. 45-2

Go to UPEP

UPEP

Glomerular
- Selective (mostly albumin; e.g., minimal change disease)
- Nonselective (reflects all plasma proteins; e.g., FSGS, diabetes)
- Tubular injury, any cause
  - Hypertension
  - Chronic renal failure

Tubular
- Tamm-Horsfall
- β2-microglobulin

Abnormal proteins
- Light chains (κ or λ)
- Plasma cell dyscrasias
Hematuria

- Hematuria is defined as two to five RBCs per high-power field (HPF)
- It can be detected by dipstick.
- Common causes of isolated hematuria stones, neoplasms, tuberculosis, trauma, and prostatitis.
- Gross hematuria with blood clots is almost never indicative of glomerular bleeding
Historical clues — hematuria

- Concurrent pyuria and dysuria, : urinary tract infection, may also bladder malignancy.

- A recent upper respiratory infection: postinfectious glomerulonephritis or IgA nephropathy.

- A positive family history of renal disease: hereditary nephritis, polycystic kidney disease, or sickle cell disease.

- Unilateral flank pain, which may radiate to the groin, : ureteral obstruction due to a calculus or blood clot, occasionally malignancy.
Historical clues — hematuria

- Symptoms of prostatic obstruction in older men such as hesitancy and dribbling: (BPH)
- Recent vigorous exercise or trauma.
- History of a bleeding disorder or bleeding from multiple sites due to excessive anticoagulant therapy
Distinguishing extraglomerular from glomerular hematuria

<table>
<thead>
<tr>
<th></th>
<th>Extraglomerular</th>
<th>Glomerular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color (if macroscopic)</td>
<td>Red or pink</td>
<td>Red, smoky brown, or &quot;Coca-Cola&quot;</td>
</tr>
<tr>
<td>Clots</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>&lt;500 mg/day</td>
<td>May be &gt;500 mg/day</td>
</tr>
<tr>
<td>RBC morphology</td>
<td>Normal</td>
<td>Dysmorphic</td>
</tr>
<tr>
<td>RBC casts</td>
<td>Absent</td>
<td>May be present</td>
</tr>
</tbody>
</table>
EVALUATION OF HEMATURIA

HEMATURIA

Proteinuria (>500 mg/24 h), Dysmorphic RBCs or RBC casts

Pyuria, WBC casts

Urine culture
Urine eosinophils

Serologic and hematologic evaluation: blood cultures, anti-GBM antibody, ANCA, complement levels, cryoglobulins, hepatitis B and C serologies, VDRL, HIV, ASLO

Hemoglobin electrophoresis
Urine cytology
UA of family members
24 h urinary calcium/uric acid

IVP +/- Renal ultrasound

As indicated: retrograde pyelography or arteriogram, or cyst aspiration

Renal biopsy

Cystoscopy

Biopsy and evaluation

Renal CT scan

Open renal biopsy

Follow periodic urinalysis
HEMATURIA & AGE

Transient unexplained
Urinary tract infection
Stones
Exercise
Trauma
Endometriosis
SS/SA hemoglobin
Polycystic kidney disease
Cancer
- Bladder
- Kidney
- Prostate
- BPH
Intrinsic glomerular disease

Age
10 20 30 40 50 60 70 80
Pyuria

- *Isolated pyuria* is unusual
- Inflammatory reactions in the kidney or collecting system are also associated with hematuria.
- The presence of bacteria suggests infection, and white blood cell casts with bacteria are indicative of pyelonephritis.
- White blood cells and/or white blood cell casts may also be seen in tubulointerstitial processes such as interstitial nephritis, systemic lupus erythematosus, and transplant rejection.
Nephrotic Syndrome

- Massive proteinuria (> 3.5 gms, for 1.73 m² body surface/24 hours in urine) - glomerular permeability problem
- Pathogenesis: varies with disease; most are immune complex deposition
- Laboratory and Clinical:
  - Hypoalbuminemia, generalized edema, Hyperlipidemia, lipiduria, fatty casts and oval fat bodies in urine.
Nephrotic Syndrome

• Complications
  • Generalized edema (anasarca)-massive amounts of albumin in urine, hypoalbuminemia
  • Susceptibility to hypercoagulation due to loss of antithrombin III in urine and increases in fibrinogen, increased platelet aggregation; bilateral renal vein thrombosis can occur
  • Susceptibility to infections due to Loss of immunoglobulins and complement in urine (infections-Staphylococcus aureus and Streptococcus pneumoniae; spontaneous bacterial peritonitis due to Strep. pneumoniae)
  • Protein malnutrition
Nephrotic Syndrome

- Complications
  - Iron resistant microcytic hypochromic anemia due to loss of transferrin
  - Hypocalcemia and secondary hyperparathyroidism due to vitamin D deficiency with enhanced urinary excretion of cholecalciferol-binding protein
  - Depressed thyroxine levels due to loss of thyroxine-binding globulin
Primary Causes of Nephrotic Syndrome

- Minimal change disease (nil disease; lipoid nephrosis)
- Focal segmental glomerulosclerosis
- Idiopathic membranous glomerulonephritis
- Membranoproliferative glomerulonephritis
**Diabetic Nephropathy-clinical course**

- After the onset of proteinuria >500 mg/24 h, renal function declines, with 50% of patients reaching renal failure in 5–10 years;

- thus, from the earliest stages of microalbuminuria, it usually takes 10–20 years to reach end-stage renal disease.
FIGURE 125-1  Stages of diabetic nephropathy. GFR = glomerular filtration rate.
Clinical Case 1

- S.E. is a 10 year-old with acute lymphocytic leukemia receiving chemotherapy
- Has fever, neutropenia and thrombocytopenia
- UOP is 1.2 cc/kg/hour
- On clinical exam she has very moist mucus membranes
- BUN and creatinine are 110 and 0.7. Albumin is 3.5
Assessment of case #1

- Is she in renal failure?
  - Creatinine is normal, so NO!
- Why is BUN so high?
Use of plasma BUN: Cr ratio

- In pre-renal BUN:Cr > 20 usually
- However, BUN may be increased disproportionately with blood products, excess amino acids in TPN, GI or other bleed; increased catabolism (treatment with steroids, fever).
Clinical Case #2

- CE is a 15 yo male who presented with URI symptoms, then headache, vomiting, abdominal pain, knee pain, edema, and a purpuric rash on his legs. He had not voided for 24 hours.
- What is diagnosis?
  - HSP
Physical exam and labs

- BP was 152/94. He had anasarca. Heart and lung exams were normal.
- A urinalysis revealed hematuria and proteinuria. BUN and Creatinine were 76 and 8.0. Albumin was 3.1
- He has aggressive HSP nephritis