

1. Acute Renal Failure

- Simultaneous, rapid hit to nephrons
- Usually reversible
- Most commonly caused by renal hypoperfusion (shock), as kidney has fragile blood supply. May also be caused by dehydration.
 - Hypoperfusion causes drop in GFR, “prerenal azotemia,” BUN:Cr>10
 - More prolonged hypoperfusion, or toxic renal assault (e.g. gram negative sepsis, gentamicin) may cause acute tubular necrosis—the most common cause of acute renal failure.
 - Postrenal azotemia usually caused by obstruction

2. Chronic renal failure

- Progressive loss of nephrons, chronic scarring
- Remaining nephrons must compensate, so they hypertrophy and increase their GFR (hyperfiltration)
- Immediate solution, proves detrimental in the long run

Consequences of chronic renal failure:

- ↓renal perfusion→renin secretion by JGA→fluid and NA retention→edema
- Hyperkalemia→arrhythmias
- Decreased erythropoietin production→anemia
- Unfiltered toxins in blood→uremia
 - N/V, loss of appetite
 - Inflammation→pericarditis, mucosal ulceration
 - Platelet dysfunction→bleeding diathesis
 - Altered nerve conduction→peripheral neuropathy, altered nerve conduction
- Increased PO₄ retention→renal osteodystrophy

3. Treatment

ESRD—expensive, poor quality of life with dialysis

Major cause=diabetic nephropathy; others include hypertensive nephrosclerosis, chronic glomerulopathies, pyelonephritis/obstruction, and PKD

Dialysis—Patient’s blood equilibrated with dialysis solution, semi permeable membrane, removal of metabolic wastes

Hemodialysis=blood circulated externally through machine

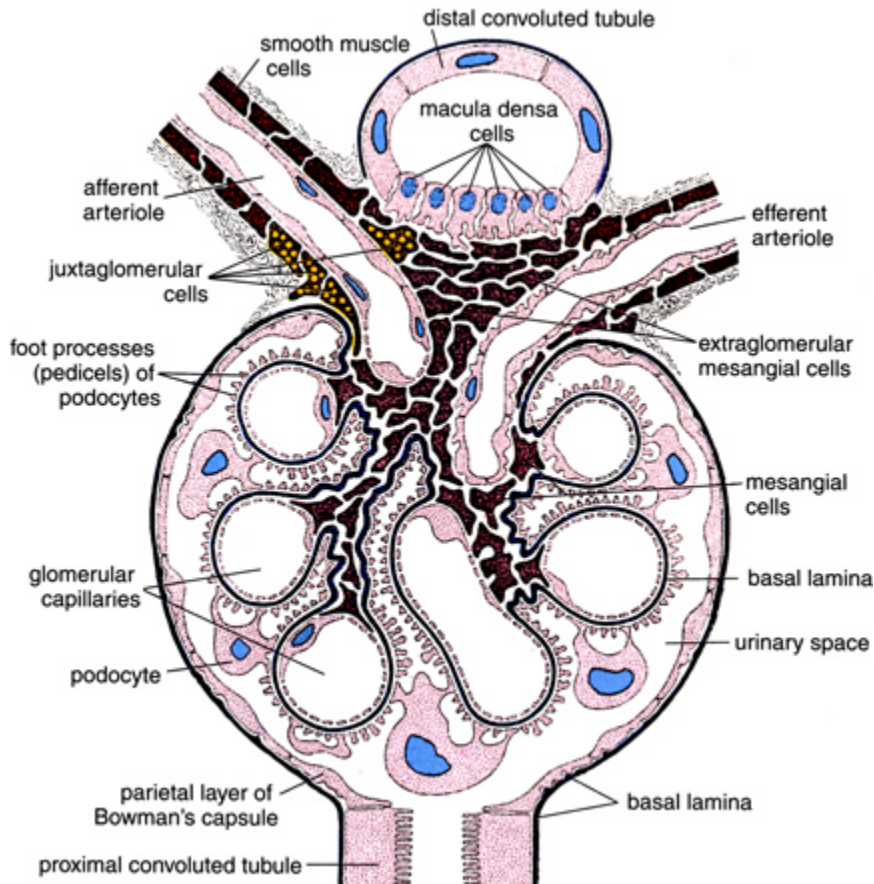
Intraperitoneal=Solution infused into peritoneum, equilibrates, and removed

Overall 25% mortality per year

Also give EPO to help anemia

Transplant—Much better QOL and survival, but shortage. Also graft rejection, chronic use of immunosuppressants which leads to infection.

The Glomerulus



Podocytes (visceral epithelial cells)—interdigitating processes embedded in lamina rara externa
 Form foot processes with filtration slits
 Mesangial cells—support glomerular tuft, embedded in mesangial matrix. Contractile, proliferative, and phagocytic. Capable of laying down matrix, collagen, and biologically active mediators
 Juxtaglomerular apparatus—
 Consists of juxtaglomerular cells (renin), macula densa cells (sensitive to NA concentration and BP)
 Basement membrane—thick electron dense layer (lamina densa), surrounded by thinner peripheral layers (lamina rara interna and externa). Composed of type IV collagen.
 Inner, fenestrated layer of endothelial cells

Glomerulus—fenestrated epithelial cells line an anastomosing network of capillaries.

Two endothelial layers

Glomerular barrier function—*Size and charge* determine permeability qualities. Smaller (radius <40-45 Å), positively-charged or neutral molecules permeate the GBM and are filtered and reabsorbed in the proximal tubule. Albumin is excluded because the GBM is negatively-charged, and albumin is repelled. Injury to the glomerulus allows passage of proteins and RBCs into urine, therefore injury is characterized by proteinuria and hematuria.

Tamm-Horsfall protein—TAL, secreted into tubule (Excretion), unknown function but marker of disease when it forms cellular casts in urine.

Normal urine protein— <150 mg/day, 2/3 is Tamm-Horsfall

- Dipstick screens for abnormal urinary protein
 - Negative
 - 1+ (15-30 mg/dL urine)
 - 2+ (40-100 mg/dL)

- 3+ (150-350 mg/dL)
- 4+ (>500)
- Urinary protein:Creatinine
 - Estimates 24-hour urine protein excretion from random urine sample
- Definitive test—measure 24-hour collection

Abnormal urinary protein excretion

- Glomerular pattern-albumin
- Tubular pattern-smaller proteins, injured tubules can't reabsorb and filter proteins, especially B2 microglobulin
- Bence-Jones-plasma cell dyscrasia, monoclonal light chains, *dipstick will not detect*

Important things to remember

- Proteinuria not specific to glomerular injury
- May result from increased levels of exercise or fever (transient)
- May result from orthostasis—benign
- If persistent, >2g/day—high grade, injury to glomerular capillary loop
- If >3.5 g/day, within nephrotic range, most patients will exhibit signs of nephrotic syndrome

Nephrotic Syndrome

Group of conditions characterized by increased basement membrane permeability, permitting loss of plasma proteins via urine, especially low molecular weight proteins (e.g. albumin)

- Massive proteinuria (>4 g/day)
- No RBCs in urine!
- Hypoalbuminemia→decreased oncotic pressure→generalized edema
- Hypoalbuminemia→increased hepatic protein synthesis→hypercholesterolemia, hyperlipidemia
- Hyperlipidemia→lipiduria with oval fat bodies

Diseases associated with nephrotic syndrome

1. Minimal change disease
 - a. Most often in young children, but can be seen in adults
 - b. Normal-appearing glomeruli on LM
 - c. EM shows effacement of foot processes
 - d. Responds to steroids
2. Focal Segmental Glomerulosclerosis
 - a. Clinically similar to MCD, but occurs in older patients
 - b. Sclerosis within capillary tufts of deep JG cells, with focal or segmental distribution (focal=some, but not all glomeruli; segmental=only part of glomerulus). Extensive epithelial damage with ECM deposition.
 - c. Mostly idiopathic, may have some hematuria
 - d. Respond poorly to steroids, may progress to chronic GN (50% develop ESRD within 10 yrs)
 - e. Immunofluorescence shows deposition of IgM and complement

3. Membranous glomerulonephritis
 - a. Major primary cause of nephrotic syndrome in adults
 - b. Immune complex disease, unknown etiology
 - c. Nephrotic syndrome + azotemia
 - d. Thickened capillary walls on LM and EM, thickening of BM
 - e. Immune complexes in intramembranous and subepithelial locations within and upon BM—mimicked in animal model with repeated injections of foreign protein. “Spike and dome” appearance from extension of BM between and around immune deposits.
 - f. Granular immunofluorescence of IgG and complement.
 - g. Slowly progressive, little response to steroids.
 - h. Also associated with HBV, gold salts, penicillamine, SLE