**Acute renal failure**

1) What is the differential diagnosis of acute renal failure (ARF)?
   - Prerenal / Postrenal / Intrinsic renal injury
   - Use of clinical features and urinary findings to differentiate acute tubular necrosis (ATN) from other causes of intrinsic renal injury
   - Role of renal biopsy
2) How do you distinguish ATN from prerenal azotemia?
   - Effect of volume challenge (beware risk of volume overload in ATN)
   - Urinary findings

| | **Prerenal azotemia** | **ATN** |
|---|---|---|
| **BUN/Creatinine ratio** | > 20 | 10-15 |
| **Urine sodium ($U_{Na}$ in mEq/L)** | < 20 | > 40 |
| **Urine osmolality ($U_{Osm}$ in mOsm/kg)** | > 500 | < 350 |
| **Fractional excretion of sodium ($FE_{Na}$)** | < 1% | > 2% |
| **Urine sediment** | Normal<br>Occasional nonspecific casts | Renal tubular epithelial cells<br>Muddy brown casts |

3) How do you calculate fractional excretion of sodium?
   $FE_{Na}$ = (urine sodium × plasma creatinine) / (plasma sodium × urine creatinine)
4) What are the causes of ATN?
   - Ischemia/ hypoperfusion
   - Nephrotoxins (aminoglycoside antibiotics, hemoglobin or myoglobin, contrast agents etc.)
5) What are the mechanisms of decreased glomerular filtration rate (GFR) in ATN?
   - Casts of necrotic/sloughed tubular epithelial cells (↑ $P_T$)
   - Backleak (wasted GFR)
   - Possible ischemic/nephrotoxic effects on glomerulus (↓ $K_f$)
   - Tubuloglomerular feedback (↓ $P_{GC}$) "acute renal success"
6) What determines the susceptibility of the kidney to ischemia?
   - Paradoxical vulnerability of kidney to hypoperfusion
   - Heterogeneity of oxygen delivery to renal parenchyma
     (medulla operates on the "brink of anoxia"
   - High oxygen demand in medullary tubules (pars recta proximal tubule and thick ascending limb of Henle) make these segments particularly vulnerable
     - Tubular epithelial oxygen demand is GFR (transport work) dependent
     - No capacity for anaerobic glycolysis in proximal tubule
7) What is the usual clinical course of ATN?
   - Initiation (ischemic or nephrotoxic tubular damage)
   - Maintenance phase (low GFR from effects of tubular injury; established renal failure)
   - Recovery phase (rising GFR; recovering tubules)
     - Dangers of hypovolemia and hypokalemia in the diuretic phase
     - Tubular regeneration usually able to restore renal function if patient survives trauma/sepsis etc. (depends on intact tubular basement membranes)