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

<table>
<thead>
<tr>
<th></th>
<th>Prerenal azotemia</th>
<th>ATN</th>
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</thead>
<tbody>
<tr>
<td>BUN/Creatinine ratio</td>
<td>&gt; 20</td>
<td>10-15</td>
</tr>
<tr>
<td>Urine sodium ((U_{Na}) in mEq/L)</td>
<td>&lt; 20</td>
<td>&gt; 40</td>
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<tr>
<td>Urine osmolality ((U_{Osm}) in mOsm/kg)</td>
<td>&gt; 500</td>
<td>&lt; 350</td>
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<tr>
<td>Fractional excretion of sodium ((F_{ENa}))</td>
<td>&lt; 1%</td>
<td>&gt; 2%</td>
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<tr>
<td>Urine sediment</td>
<td>Normal</td>
<td>Renal tubular epithelial cells</td>
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<tr>
<td></td>
<td>Occasional nonspecific casts</td>
<td>Muddy brown casts</td>
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3) How do you calculate fractional excretion of sodium?
   \[ F_{ENa} = \frac{\text{urine sodium} \times \text{plasma creatinine}}{\text{plasma sodium} \times \text{urine creatinine}} \]

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 (\(\uparrow P_T\))
   • Backleak (wasted GFR)
   • Possible ischemic/nephrotoxic effects on glomerulus (\(\downarrow K_t\))
   • Tubuloglomerular feedback (\(\downarrow P_{GC}\)) "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)