Acute Renal Failure

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• Rapid decline in renal function
  – Rise in blood urea nitrogen (BUN)
  – Rise in serum creatinine (Cr)
  • Dependent on Baseline Cr
  • If < 3 mg/dl, Cr rise > 0.5 mg/dl
  • If > 3 mg/dl, Cr rise > 1.0 mg/dl

• Urine flow can vary
  – Decreased – oliguric or anuric
  – Normal – nonoliguric
  – Increased – polyuric

• Consequences
  – Fluid retention – volume overload
  – Electrolyte / acid-base abnormalities
  – Build up of toxins - uremia

Clinical Significance of ARF

• Hospitalized patients
• 4% of patients in medical / surgical units
• Higher incidence in certain situations
  – severe trauma, abdominal aortic aneurysm resection, cardiac surgery
  – sepsis, shock, heart failure, multi-organ failure
Clinical Significance of ARF

- Reversible – time course varies
- Treatment – renal replacement therapy (RRT)
- Mortality – high
  – Levy et al: JAMA 1996; 275, 1489

Acute Renal Failure - Causes

- Pre-renal
- Renal
Acute Renal Failure

- Post-renal (obstruction)

Diagnostic Approach

- Establish time of onset
- Review history
- Review medications
- Physical exam
  - assess volume status
  - cardiac function

Diagnostic Approach

- Examine the urine (urinalysis)
- Exclude urinary tract obstruction
- Distinguish between
  - Pre-renal disease
  - Renal disease
    • acute tubular necrosis (ATN)

Urinary Tract Obstruction (Post)

- Bilateral
  - Unless single kidney
- Urethral
- Bladder neck
  - prostate or bladder infection or cancer
    - functional: neuropathy
- Ureteral
  - Intra: crystals (sulfonamide, uric), clots, pyogenic debris, stones, edema, necrotizing papillitis
  - Extra: tumor (cervix, prostate) endometriosis, fibrosis, ligation

Urinary Tract Obstruction (Post)

- Urine flow
  - complete obstruction → anuria
  - incomplete obstruction
    • oliguria, nonoliguria or polyuria
    • alternating anuria/oliguria with polyuria
- Symptoms
  - suprapubic pain
  - urge to void
  - pain ± hematuria with ureteral stones
  - none

Urinary Tract Obstruction (Post)

- Diagnosis
  - bladder catheter
  - renal ultrasound
  - other visualizing procedure (MRI, CT)
- Treatment
  - remove obstruction
  - reversible
  - renal damage
    • ischemia
    • damage to Na conservation & concentrating mechanism
    • post-obstructive diuresis
### Pre-renal ARF

- Most common cause
- Inadequate renal perfusion
  - Hypovolemia
    - extrarenal loss: GI, skin, burns
    - obligatory diuresis: excess diuretics, osmotic diuretics, post-obstructive diuresis, lithium
    - inadequate or No fluid intake
  - Impaired cardiac function
    - CHF, MI, pericardial tamponade
  - Vascular disease
    - renal artery stenosis (bilateral, ACE inhibitor)
    - Peripheral vasodilation: bacteremia/sepsis

- If perfusion defect is corrected, renal function recovers. (Treatment)
  - ATN can occur, if perfusion not corrected
- Renin, aldosterone, ADH elevated
  - low urine volume
- Urinalysis: benign sediment, no protein
  - except CHF, high fever
- Clinical manifestations
  - 10% weight loss (if no edema) - excellent
  - orthostatic hypotension - good
  - dry skin & buccal mucosa - unreliable
- Treatment

### Hepatorenal Syndrome

- In patients with severe liver disease
- Features of pre-renal ARF except
  - inadequate response to volume expansion
  - inadequate response ↑ blood pressure
- Mechanism unknown
  - renal vasoconstriction
- Reversible if
  - hepatic function improves
  - liver transplantation

### Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Main effect - blockade of prostaglandin production
  - regulate renal blood flow – vasodilate
  - important when renal blood flow is limited
    - volume depletion, CHF, hepatic cirrhosis
- NSAIDs
  - ↓ blood flow, ↑ Na retention, ↓ K excretion, ↓ water excretion
  - hypertension, edema
  - ARF
- Idiosyncratic effect
  - Interstitial nephritis with nephrotic syndrome
Renal Artery Stenosis & Angiotensin

- Bilateral renal artery stenosis
  - limits blood flow to kidneys
  - stimulates renin-angiotensin-aldosterone axis
- Angiotensin II
  - vasoconstrictor
  - post-glomerular efferent arteriole
  - ang II maintains GFR when flow is limited
- ACEI/ARB
  - ACEI blocks generation of angiotensin II
  - ARB block angiotensin receptors
- ACEI/ARB induced ARF is reversible

Renal Causes of ARF

- Glomerular diseases: GN, lupus, Goodpasture’s syn., HS purpura, eclampsia, SBE
- Vascular diseases: vasculitis, scleroderma, malignant HTN, HUS, atheroemboli
- Intrarenal deposition: acute uric acid nephropathy
- Acute Tubular Necrosis (ATN)
  - hemodynamic
  - nephrotoxins
- Acute Interstitial Nephritis (AIN)

Acute Tubular Necrosis (ATN)

- Induced by ischemia or toxin
- Cellular debris obstructs tubules
- Tubules leak the contents
- Medulla at jeopardy (PO₂ is 10 to 20 mm Hg)
- Typically GFR < 5 ml/min and oliguria (<400 ml/day)
  - Sometimes nonoliguric
- Light microscopy reveals little damage

Urine Chemistries in ATN

- Na 30 to 90 mEq/L
- Fractional Excretion of Na or FE₅₉ > 1%
  \[ FE₅₉ = \left( \frac{U_{\text{Na}}}{P_{\text{Na}}} \right) \times \frac{\text{Cr}}{\text{U}_{\text{Cr}}} \times 100 \]
- \( U_{\text{Cr}}/P_{\text{Cr}} < 15 \)
- Loss of concentrating ability
  \( P_{\text{osm}} \approx U_{\text{osm}} \)

Acute Tubular Necrosis (ATN)

- Typically, a cause can be identified
- Urinalysis: mild proteinuria, coarse granular casts & renal tubular epithelial cells/casts

Urine in Oliguric Conditions

<table>
<thead>
<tr>
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<th>Pre-Renal</th>
<th>Renal</th>
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<tbody>
<tr>
<td>Sp. Gravity</td>
<td>&gt;1.020</td>
<td>1.010</td>
</tr>
<tr>
<td>Osmolality</td>
<td>&gt;500</td>
<td>&lt;500</td>
</tr>
<tr>
<td>Na</td>
<td>&lt;20</td>
<td>&gt;30</td>
</tr>
<tr>
<td>( U_{\text{Cr}}/P_{\text{Cr}} )</td>
<td>&gt;20</td>
<td>&lt;15</td>
</tr>
<tr>
<td>FE₅₉</td>
<td>&lt;1%</td>
<td>&gt;2%</td>
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</table>
Acute Tubular Necrosis (ATN)

- After onset, urine volume & indices change little
  - Until recovery begins
- Serum Cr rises approximately 1 mg/dl/day

Nephrotoxicity

- Kidneys susceptible
  - drugs concentrated
  - transport systems
  - renal blood flow
  - metabolism
- Mechanisms
  - vasoconstriction
    - cyclosporine, tacrolimus, amphotericin B, radiocontrast agents
  - intratubular precipitation
    - acyclovir, sulfadiazole
  - acute tubular necrosis
    - aminoglycosides, heavy metals

Aminoglycoside Toxicity

- Mechanism:
  - freely filtered, then absorbed by proximal tubular cells
    - neomycin > gentamicin > tobramycin > streptomycin
- Occurs in 10 to 20% patients
- Toxicity dependent on dose and duration
- Starts 7 or more days after initiation of tx
- Improvement begins 3 to 21 days after stopping
- Prevention
  - Avoid drug if possible
  - Adjust dose for renal function
  - Monitor blood levels

Acute Tubular Necrosis (ATN)

- Recovery
  - 1st urine output increases
  - then Cr begins to decrease
- Mortality is high
- Prevention is best
  - avoid hemodynamic instability / toxin.
- Treatment
  - control volume
  - avoid electrolyte disturbances
  - dialysis

Nephrotoxicity

- Specific tubular disorders
  - distal RTA – amphotericin B
  - proximal tubule dysfunction - streptozotocin
  - magnesium wasting - cisplatin
  - chronic interstitial nephritis / papillary necrosis - phenacetin
  - acute allergic interstitial nephritis
    - penicillins, β-lactams
    - sulfonamides
    - NSAIDs

Radiocontrast Nephropathy

- Mechanism
  - vasoconstriction
  - direct toxic effect
  - mild ↑ Cr in almost all
  - MRI agents safe
- Risk
  - Underlying renal disease (4 to 11%)
  - Diabetic nephropathy (10 to 35%)
  - CHF / decreased renal perfusion
Radiocontrast Nephropathy

- Clinical course
  - Starts immediately after administration
  - Usually self-limited
  - Mortality significantly greater
- Prevention
  - Avoid if possible
  - Avoid dehydration & NSAIDs
  - Hydrate before exposure
    - NaHCO<sub>3</sub> reduces risk
    - Acetylcysteine reduces risk

Acute Interstitial Nephritis (AIN)

- Hypersensitivity to drugs: penicillins, cephalosporins, NSAIDs.
- Patchy infiltration with lymphocytes & mononuclear cells, ± eosinophils / plasma cells
- Abrupt onset & nonoliguria
- Sometimes: “drug” rash, fever, eosinophilia, hematuria, flank pain
  - Eosinophilia occurs with atheroemboli, polyarteritis, vasculitis

Acute Interstitial Nephritis (AIN)

- Urine: WBC, WBC casts, eosinophils, protein
  - NSAIDs induce nephrotic syndrome
  - Urine indices look like ATN
- 48 h gallium scan
- Renal biopsy
- Tx: stop drug
  - Recovery usually occurs
  - Some feel steroids help

ARF

- Always think about obstruction
- Always assess the volume and cardiac status
- Always look at the urine
- Always link the diagnostic possibilities to the clinical presentation
- Prevention is the key
- Avoid complications such as hyperkalemia, GI bleeding, volume overload, pericarditis, acidosis