Acute Renal Failure

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Acute Renal Failure

• 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

Acute Renal Failure

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

Acute Renal Failure

• Consequences
  – Fluid retention – volume overload

Acute Renal Failure

• Consequences
  – 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

Pre-renal ARF

• ↑ renal vascular resistance / renal ischemia
  – hepatorenal syndrome
  – NSAIDs

Pre-renal ARF

• 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

Hepatorenal Syndrome

• Diagnosis
  – Clinically, appears volume depleted
    • urinary indices consistent with pre-renal ARF
    • Edematous: ascites, anasarca
    • if not edematous, fluid challenge may be indicated
• Treatment
  – Dialysis indicated if
    • hepatic transplant possible
    • hepatic function likely to recover

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 FE_Na > 1%
- U_Cr/P_Cr < 15
- Loss of concentrating ability
  \( P_{\text{osm}} \approx U_{\text{osm}} \)

Urine in Oliguric Conditions

<table>
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<tr>
<th>Pre-Renal</th>
<th>Renal</th>
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<tbody>
<tr>
<td>UA</td>
<td>hyaline casts</td>
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<tr>
<td>Sp. Gravity</td>
<td>&gt;1.020</td>
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<tr>
<td>Osmolality</td>
<td>&gt;500</td>
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<tr>
<td>Na</td>
<td>&lt;20</td>
</tr>
<tr>
<td>U_Cr/P_Cr</td>
<td>&gt;20</td>
</tr>
<tr>
<td>FE_Na</td>
<td>&lt;1%</td>
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</tbody>
</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, sulfathiazole
  – 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 interstial 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
    - NaHCO₃ 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
  - Eosinohilia 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