Acute and Chronic Renal Failure
Last Lecture 10 (13/4/2015)
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Renal failure:
Is of two types:
- Acute RF (Acute Kidney Injury AKI): from days → weeks.
- Chronic RF (CKD): months → years.

*Cause of AKI:
1. Prerenal  
2. intrarenal  
3. postrenal
   - 90% of causes are of the first two types (pre-and-intrarenal).

*Cause of chronic Kidney Disease are:
1. Uncontrolled hypertension  
2. Uncontrolled diabetes  
3. Infections
Acute Kidney Injury AKI

**Epidemiology of AKI:**
- 0.1% population **good prognosis** (85% recovery)
- 3-7% hospitalized
- 25-30% ICU **poor prognosis** (mortality can reach 45-75%)
**Pre-renal** (causes reside in the decrease in RBF):

- Hypovolemeia: Fluid loss or blood loss → Shock: (excessive diuretics use, vomiting diarrhea, bleeding)
- **hepatorenal syndrome** in which renal **perfusion** is compromised in **liver failure**
- vascular problems, such as **atheroembolic disease** and **renal vein thrombosis**
Intrarenal (damage to the kidney itself):

- Prerenal can be converted to intra-renal if not treated properly. The most common cause is acute tubular necrosis ATN. Less common is pyelonephritis and glomerulonephritis. In ATN: causes can be prolonged ischemia, heavy metals, or nephrotoxic drugs etc. Usually the tubular injury in ATN is reversible.

- Toxins or medications (e.g. NSAIDs, aminoglycoside antibiotics, iodinated contrast, lithium, etc.

- Rhabdomyolysis (breakdown of muscle tissue) - the resultant release of myoglobin in the blood affects the kidney; it can be caused by injury (especially crush injury and extensive blunt trauma), etc.

- Hemolysis - the hemoglobin damages the tubules; acute glomerulonephritis
Post-renal (obstructive causes in the urinary tract) due to:

- medication interfering with normal bladder emptying.
- benign prostatic hypertrophy or prostate cancer.
- kidney stones.
- due to abdominal malignancy (e.g. ovarian cancer, colorectal cancer).
- obstructed urinary catheter.
Staging Of AKI

**Risk**: GFR decrease >25%, serum creatinine increased 1.5 times or urine production of < 0.5 ml/kg/h for 6 hours

**Injury**: GFR decrease > 50%, doubling of creatinine or urine production < 0.5 ml/kg/h for 12 hours
**Failure**: GFR decrease > 75%, tripling of creatinine (> 4 mg/dl) OR urine output below 0.3 ml/kg/h for 24 hours or anuria for 12 hours.

**Loss**: persistent AKI or complete loss of kidney function for more than 4 weeks

**End stage renal disease**: need for renal replacement therapy (RRT) for more than 3 months
### Classic laboratory findings in AKI

<table>
<thead>
<tr>
<th>Type</th>
<th>$U_{Osm}$</th>
<th>$U_{Na}$</th>
<th>Fe$_{Na}$</th>
<th>BUN/Cr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prerenal</td>
<td>$&gt;500$</td>
<td>$&lt;10$</td>
<td>$&lt;1%$</td>
<td>$&gt;20$</td>
</tr>
<tr>
<td>Intrinsic</td>
<td>$&lt;350$</td>
<td>$&gt;20$</td>
<td>$&gt;2%$</td>
<td>$&lt;15$</td>
</tr>
<tr>
<td>Postrenal</td>
<td>$&lt;350$</td>
<td>$&gt;40$</td>
<td>$&gt;4%$</td>
<td>$&gt;15$</td>
</tr>
</tbody>
</table>
# BUN:Cr Ratio as a tool

<table>
<thead>
<tr>
<th>Location</th>
<th>BUN:Cr</th>
<th>Urea:Cr</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prerenal</strong></td>
<td>&gt;20:1</td>
<td>&gt;100:1</td>
<td>BUN reabsorption is increased. BUN is disproportionately elevated relative to creatinine in serum. Dehydration is suspected.</td>
</tr>
<tr>
<td><strong>Intrarenal</strong></td>
<td>&lt;10:1</td>
<td>&lt;40:1</td>
<td>Renal damage causes reduced reabsorption of BUN, therefore lowering the BUN:Cr ratio.</td>
</tr>
<tr>
<td>Normal or <strong>Postrenal</strong></td>
<td>10-20:1</td>
<td>40-100:1</td>
<td>Normal range. Can also be postrenal disease. BUN reabsorption is within normal limits.</td>
</tr>
</tbody>
</table>
MAJOR CONSEQUENCES OF AKI.

(Problems we might face in AKI):

1. Daily increase in creatinine and urea.
   Plasma Urea: In complete renal shutdown
   Urea: it rises by about 5 mmol/L per day.
   Creatinine rises by 1 mg/dl daily.

2- Hyperkalemia…might need dialysis

3- M. Acidosis

4- Extracellular volume expansion → Malignant hypertension, pulmonary edema (can be fatal)
Prevention Of Acute Renal Failure

Why should we prevent ARF?

- The kidneys are susceptible to the adverse effects of medications because the kidneys are repeatedly exposed to substances in the blood.
- The kidneys receive a large blood flow (23% of the cardiac output at rest; the entire blood volume circulates through the kidneys about 14 times/minute).
- The kidney is the major excretory organ for many toxic substances & during the normal urine concentration process, these substances increase in concentration & can be toxic to the kidneys.

How to prevent ARF?

- In patients taking nephrotoxic medications (gentamicin, vancomycin), renal function should be monitored closely.
- Serum BUN & creatinine levels should be obtained for 24 hours after initiation of these medications & at least twice a week while the patient is receiving them.
- Closely monitor dosage & Duration of use.
- Provide adequate hydration to patients at risk for dehydration:
  - Pre- intra- post- operative patients
  - Patients with neoplastic disorders or those receiving chemotherapy
  - Treat hypotension.
- Continually assess renal function (urine output, laboratory values) when appropriate.
- Prevent & treat infections (infections can produce progressive renal damage).
- Give meticulous care to patients with indwelling catheters to prevent infections of urinary tract. Remove catheters as soon as possible.
Chronic Renal Failure: Chronic kidney disease (CKD)

Introduction-

- Chronic kidney disease (CKD), is a progressive loss in renal function over a period of months or years.
- Chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with high blood pressure or diabetes.
- It is differentiated from acute kidney disease in that the reduction in kidney function must be present for over 3 months.
- Chronic kidney disease is identified by a blood test for creatinine.
- Higher levels of creatinine indicate a lower GFR and as a result a decreased capability of the kidneys to excrete waste products.
Pathophysiology

- In CKD, reduced clearance of certain solutes principally excreted by the kidney results in their retention in the body fluids.

- CKD leads to progressive decline in renal function.

- Reduction in renal mass leads to hypertrophy of the remaining nephrons with hyperfiltration, and the GFR in these nephrons is transiently increased, placing a burden on remaining nephrons.

- leading to progressive glomerular sclerosis and interstitial fibrosis.
The **hyperfiltration and hypertrophy** of residual nephrons, although beneficial it is major cause of progressive renal dysfunction (this is an example of positive feed back...destruction breeds more destruction).

The increased glomerular capillary pressure may damage the capillaries, leading to **glumeriolosclerosis**
Etiology Of CRF

Causes of chronic kidney disease (CKD) include the following:

- Diabetic kidney disease.
- Hypertension.
- Vascular disease (Angina & MI).
- Glomerular disease.
- Tubulointerstitial disease (nephritis affecting the interstitium of the kidneys)
- Urinary tract obstruction or dysfunction
- Recurrent kidney stone
Pathophysiology of diabetic nephropathy

- When the level of **blood glucose rises** beyond the kidney's capacity to reabsorb glucose from the renal ultrafiltrate
- Glucose remains diluted in the fluid, raising its **osmotic pressure** and causing more water to be carried out, thus, increasing the excreted urine volume.
- The increased volume dilutes the sodium chloride in the urine, signalling the release of more **renin** causing **vasoconstriction** >> passing less blood through the kidneys. Because the kidney is **nurtured** exclusively by the blood it filters, the vasoconstriction also reduces the nutrients supplied to it, causing **infarct** of its tissues and reduction of renal function which results in
- Glomerular **sclerosis**.
MAJOR CONSEQUENCES OF CKD

- Metabolic acidosis
- Salt and water retention
- Anemia
- Uremia
- Endocrine disorder
- Disorder of mineral metabolism
Chronic Failure:

With 4 phases:

Described earlier as an example of using GFR as a tool to stage CRF (Lecture 1 or 2):

1st phase: Decrease renal reserve:
  in which 50% of GFR is only there.
  Homeostasis is perfectly maintained
  Urea and creatinine levels are within normal range.

2nd phase: Renal insufficiency:
  20-50% of GFR is maintained only.
  The earliest sings is isosthenuria or polyuria with isotonic urine. Azotemia, anemia, and hypertension appear too.

3rd phase: Chronic RF:
  20-5% of GFR.
  All signs and symptoms of uremia
  Pt may enter a viscous circle, less functional nephrons → more pressure on already working so on and so forth.

4th phase: End-stage Renal Failure
  Can't survive without dialysis or kidney transplantation
Another Classification for CKD

- **Stage 1**  Slightly diminished function; kidney damage with normal or relatively high GFR (≥90 ml/min/1.73 m²): Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine test or imaging studies.
- **Stage 2**  Mild reduction in GFR (60–89 ml/min/1.73 m²)
- **Stage 3**  Moderate reduction in GFR (30–59 ml/min/1.73 m²)
- **Stage 4**  Severe reduction in GFR (15–29 ml/min/1.73 m²) Preparation for renal replacement therapy.
- **Stage 5**  Established kidney failure (GFR <15 ml/min/1.73 m²) permanent renal replacement therapy, or end-stage renal disease.
Dialysis

- Dialysis is primarily used to provide an artificial replacement for lost kidney function. It aims to restore the composition of the body's fluid environment toward normal.

1) **Hemodialysis**: In this type the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semipermeable membrane. The cleansed blood is then returned via the circuit back to the body; **all in all it is a complicated procedure done for** (4-6) **hours, 3 times per week and needs an A-V shunt**
Dialysis

2) Peritoneal dialysis: In this procedure a sterile solution containing minerals (even potassium at LOW concentrations) and glucose is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a semipermeable membrane. The dialysate is left there for a period of time to absorb waste products, and then it is drained out through the tube and discarded...this procedure needs a long time (may reach 24 hours).
Hemodialysis
Table 31-7

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Normal Plasma</th>
<th>Dialyzing Fluid</th>
<th>Uremic Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrolytes (mEq/l)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>142</td>
<td>133</td>
<td>142</td>
</tr>
<tr>
<td>K⁺</td>
<td>5</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>3</td>
<td>3</td>
<td>2</td>
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<tr>
<td>Mg²⁺</td>
<td>1.5</td>
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<tr>
<td>Cl⁻</td>
<td>107</td>
<td>105</td>
<td>107</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>24</td>
<td>36</td>
<td>14</td>
</tr>
<tr>
<td>Lactate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPO₄⁻</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nonelectrolytes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>100</td>
<td>125</td>
<td>100</td>
</tr>
<tr>
<td>Urea</td>
<td>26</td>
<td>0</td>
<td>200</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
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</table>
Good Luck