Acute Kidney Injury and Key Concepts in Electrolyte Imbalance

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Fluid as a Percentage of Body Weight

- 75-80% Newborns
- 55-60% Two through Middle Age
- 45-50% Elderly

Declining percentage in elderly puts them at risk for fluid and electrolyte abnormalities.

Regulation of Fluid Balance

- Fluid intake
- Hormonal Control
  – Antidiuretic hormone
  – Aldosterone
- Fluid Output
Fluid Intake

- Fluid intake is regulated by the thirst mechanism
  1. Osmoreceptors in the hypothalamus are stimulated by an increase in osmotic pressure of body fluids and will stimulate thirst
  2. Osmoreceptors are also stimulated by a decrease in extracellular fluid volume
  3. A decrease in salivary secretions from certain medications (example – atropine) will also stimulate thirst

Clinical Implication: Those patients unable to communicate thirst need to be offered frequent opportunities for hydration.

Hormonal Control

- Antidiuretic Hormone
  - Posterior lobe of pituitary gland
  - Water conservation hormone
  - Regulates the osmotic pressure of extracellular fluid by regulating the amount of water reabsorbed in the renal tubules
  - ADH release is stimulated by an increase in osmotic pressure ► increased ADH causes dilution of blood attempting to return osmotic pressure to normal
    • Excreted urine volume will be decreased and the concentration of urine will be increased

- Aldosterone
  - Adrenal Cortex
  - Regulates extracellular fluid volume by increasing reabsorption of sodium and chloride (and water)
  - Aldosterone promotes excretion of potassium and hydrogen
  - Aldosterone production is increased in healthy persons:
    • Low fluid volume
    • Low blood sodium
    • High blood potassium
A Closer Look at Aldosterone

- Diseases causing over production of aldosterone
  - Cushing’s Syndrome

- Diseases causing under production of aldosterone
  - Adrenalectomy
  - Aids
  - Metastatic Cancer

Fluid Output

- Change in extracellular fluid result in change in intravascular volume ► change in venous return to the heart and cardiac output ► change in arterial pressure sensed by the kidneys ► change in fluid excretion by the kidneys

Fluid is also lost through:
- GI Tract
- Skin
- Lungs
Body Fluid Compartments

- **Intracellular**
  - Inside the cells
  - 40% of adult body weight

- **Extracellular**
  - Outside the cells
  - 20% of adult body weight
    - Intravascular
    - Interstitial

More About Extracellular Fluid

- **Intravascular**
  - Fluids within the blood vessels

- **Interstitial**
  - Fluid between the blood vessels and cells

Intravascular and interstitial fluids are not static as they move through capillary walls.
Movement of Fluid and Electrolytes

- Capillary Permeability
- Diffusion
- Osmosis
- Filtration
- Active Transport
- Hydrostatic Pressure
- Colloidal Osmotic Pressure

Capillary Permeability

- All capillary walls do not have the same permeability

Example: Proteins can cross membranes in the liver but not in the kidneys.
Diffusion

- The movement of solute in a solution or across a membrane. (if permeable)

- The solute can be a gas or a substance.

- The solute moves from an area of higher concentration to an area of lower concentration.

More About Diffusion

- Simple diffusion
  - Oxygen enters the intravascular compartment then goes freely into the cells by diffusion

- Facilitated diffusion
  - Requires a carrier substance such as insulin carrying glucose from the extracellular compartments into the cell
Osmosis

- Movement of a pure solvent (water) from an area less concentrated (more water) to an area more concentrated (less water)
- Passive process
- The solvent moves and not the solute because of semi permeability of membrane
- Stops when there is equal distribution

Active Transport

- When electrolytes have to move from an area of lesser concentration to an area of greater concentration against a concentration gradient

Example: Sodium / potassium pump where energy is required to move sodium out of the cell and potassium into the cell.
Hydrostatic Pressure (Pushing Pressure)

- Force of fluid pressing against vessel wall
- Determined by weight of blood and blood pressure
- Hydrostatic pressure at the arterial end of capillaries is twice as great as at venous end

Filtration

- Both solute and solvent move together in response to hydrostatic pressure

Example: Tissue perfusion where water and nutrients are exchanged as a result of differences in hydrostatic pressure between the capillaries and tissues
Osmolality

- Number of osmotically active particles active particles per kilogram of water
- Measured in milliosmoles per kilogram of water
- Extracellular osmolality determined predominantly by the concentration of sodium
  Sodium is most prevalent extracellular cation and provides 90-95% of the osmotic pressure

More about Osmolality

- Intracellular and extracellular fluid have approximately the same osmolality
- Normal serum osmolality = 280-294 mOsm/kg

Osmolarity is closely related: number of osmoles per liter of solution. (osmotic or oncotic pressure)
More about Osmolality

Closely related concepts

- Specific gravity: The weight of a solution compared to an equal amount of distilled water (can be used to estimate osmolality)
- Urine osmolality is a more specific measurement of renal function than specific gravity
  - Kidneys respond to changes in osmolality rather than specific gravity

Osmotic Pressure

- Osmotic pressure (oncotic pressure) is the pull determined by number of plasma colloids (or solute) on the concentrated side
- Determined by osmolality
- Osmotic pressure affects osmosis

Intravascular fluid has more protein than interstitial fluid so therefore has a higher oncotic pressure
Pressure Gradients

• Hydrostatic pressure at the arteriole capillary end is greater than oncotic pressure: net result is filtration of water and solutes

• Intravascular oncotic pressure is greater at the venous end than intravascular hydrostatic pressure: net result fluids are pulled in

Clinical Application

• *In heart failure leading to pulmonary edema the hydrostatic pressure in the lungs becomes increased. This increase in hydrostatic pressure exceeds the oncotic pressure in the capillaries and fluid is pushed out into the interstitial spaces of the lung.*
Extracellular Fluid Volume Deficit

- Extracellular fluid volume deficit
- Remaining fluid is more concentrated (hypertonic)
- Fluid moves out of cells (cellular dehydration)

Extracellular Fluid Volume Deficit

- Elderly at risk
  - Decrease in total body water
  - Reduced sense of thirst
  - Reduced ability of kidneys to concentrate urine
  - Also at risk: infants, those with burns or infections
- Elevated sodium (hyperosmolar hypernatremia)
- Increased urine specific gravity
- Elevated hematocrit
  - Proportion of erythrocytes to blood plasma
  - Normal
    - 35 to 45% women
    - 40 to 50% men
  - Hematocrit is elevated due to hemoconcentration
Extracellular Fluid Volume Overload

- Does not occur as primary problem unless compensatory mechanisms fail

- Normal compensation
  - Excess ECF
  - Water moves into cells
  - Osmoreceptors respond
  - Decrease ADH
  - Increased urine output

Extracellular Fluid Volume Overload

- Extracellular fluid volume excess
  - Decreased oncotic pressure
  - Fluid moves into cells
  - Cellular swelling

- Kidney disease
- Decreased cardiac output
- Excessive ADH
  - Fear
  - Pain
  - Acute Infection
  - Analgesics
  - Trauma
  - Acute Stress
Fluid Shifting

- Large quantities of fluid shift from intravascular to extravascular space
  - Increased capillary permeability allowing plasma protein to leak into interstitial spaces
  - Decreased intravascular oncotic pressure
  - Lymphatic blockage

  Can be general or localized

Phases of Fluid Shifting

- **Phase I**
  - Fluid shifts out of vascular space and symptoms resemble fluid volume deficit (circulating volume is decreased)

- **Phase II**
  - Fluid is reabsorbed and moves back into vascular space
  - Process occurs gradually and does not cause signs of fluid overload
Crystalloid IV Solutions

<table>
<thead>
<tr>
<th>Hypotonic</th>
<th>Isotonic</th>
<th>Hypertonic</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Lower concentration of salt or more water than isotonic</td>
<td>■ Like human cells or intracellular fluid</td>
<td>■ Higher concentration of salt or less water than isotonic</td>
</tr>
<tr>
<td>■ Causes movement of fluids into cells</td>
<td>■ Very little osmosis</td>
<td>■ Pulls fluid out of cells</td>
</tr>
<tr>
<td>■ .45 NS or D5W</td>
<td>■ .9NS or LR</td>
<td>■ 3% NS</td>
</tr>
</tbody>
</table>

Colloid Solutions

- Contain particles not capable of passing through semi permeable membrane
  - Retained in the vascular system
  - Increase oncotic pressure
  - Fluid is drawn into the vascular space
  - Circulating volume is increased.

- Colloidal Solutions
  - Albumin
  - Dextran
  - Hetastarch
  - Hespan

Crystalloids contain substances that can diffuse through semi permeable membranes
Anatomy and Physiology of Renal System

- Size and shape of each kidney
  - 10-12 cm long
  - 5-6 cm wide
  - 2.5 cm in depth
- Surrounded by mass of fatty connective tissue for protection
- Blood vessels, nerves, and ureters connected via the hilum
- Renal artery branches into 5 smaller arteries that enter hilus of kidney; smaller branches give rise to afferent arterioles

Renal Anatomy

- Cortex
  - Cortical area
  - Juxtamedullary area (next to medulla)
  - Contains:
    - Glomeruli
    - Proximal tubules
    - Cortical loops of Henle
    - Distal tubules
    - Cortical collecting ducts
Renal Anatomy

- **Medulla**
  - Contains renal pyramids
    - Medullary loops of Henle
    - Medullary portions of collecting ducts
      - Join to form calyces which further join to become the conduit for urine to enter the ureter
Renal Anatomy: Nephron

Nephron

- Functional unit of kidney
- Consists of glomerulus and a tubular structure
- 85% of nephrons originate in superficial part of cortex (cortical nephrons)
- 15% of nephrons originate deeper in the cortex (juxtamedullary nephrons)
  - Longer, thinner loops of Henle
  - Responsible for urine concentration
Nephron: Capillary System

- Glomerular high pressure capillary system between afferent and efferent arterioles
- Peritubular capillary system; a low system originating from the efferent arterioles
  - Surround loop of Henle

- Medullary nephrons have an additional capillary system, the vas recta, consisting of long straight capillaries following the long loops of Henle

Glomerulus of Nephron

- Tuft of capillaries emerging from afferent arterioles
- Contained within Bowman’s capsule
- Blood flows out of glomerular capillaries via the efferent arterioles
- Space within Bowman’s capsule for the filtrate: Bowman’s space
- Basement membrane of the glomerular capillary membrane determines permeability; permeable to water but not to plasma proteins
Tubular Structure of Nephron

• Proximal convoluted tubule
  – Majority of all reabsorptive and secretory processes

• Loop of Henle
  – Descending limb (thin walled)
  – Ascending limb (thick walled)
    • Impermeable to water
    • Solute are reabsorbed
    • Loop diuretics work here
    • Filtrate is diluted to allow for excretion of free water

• Distal convoluted tubule
  – Thiazide diuretics work here to inhibit sodium reabsorption
  – Aldosterone works on late distal tubule and cortical collecting tubule (below)

• Collecting tubule or duct
  – Several distal tubules drain into the collecting tubule
  – Single layer of epithelial cells
  – No further electrolyte absorption or secretion
  – Cortical collecting tubule
    • Aldosterone works here
  – Medullary collecting tubule
    • ADH (vasopressin) works here
    • Responsible for determining concentration and acidity of urine

Glomerular Filtration

• Filtration of protein free plasma through the glomerular capillaries into Bowman’s space.

• The capillary filtration pressure is approximately 60 mm Hg. (Higher pressure than other capillary beds)

• Glomerular filtration produces 125 mL of filtrate each minute.

• Constriction of the afferent arterioles decreases glomerular pressure and filtration.

• Constriction of the efferent arterioles increases glomerular pressure and filtration.

• Clinical Application
  • In shock, afferent arterioles constrict (SNS stimulation) and glomerular filtration and urine output can fall to near zero.
Compensatory Response to Decreased GFR

- Afferent arterioles: attenuation of vasoconstriction or vasodilation
- Efferent arterioles: vasoconstriction
- **Note: Afferent and efferent arterioles affected by SNS and RAAS**
- Increased tubular reabsorption of fluid
- Maintenance of cardiac output

- This means: Patients may have oliguria initially without a diagnostic rise in creatinine

Definitions

- **Azotemia**: Accumulation of nitrogenous wastes in the blood
- Prerenal azotemia: Classically defined as decreased GFR resulting from renal hypoperfusion in a structurally intact kidney, which is rapidly reversible when underlying cause is corrected
- Renal insufficiency: Reduction in glomerular filtration to 20 to 50% of normal
- Oliguria: U.O. < 400 ml / 24 hours
- Anuria: U.O. < 50 ml / 24 hours
### Diagnostic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urine Volume</strong></td>
<td>▶ Less specific&lt;br&gt; ▶ Reflects kidney perfusion</td>
</tr>
<tr>
<td><strong>Urine Specific Gravity / Osmolality</strong></td>
<td>▶ Inability to concentrate is early sign of renal dysfunction&lt;br&gt; ▶ Concentrating ability = tubular functioning</td>
</tr>
<tr>
<td><strong>BUN</strong></td>
<td>▶ Not most specific indicator&lt;br&gt; ▶ Variations exist in urea load&lt;br&gt; ▶ BUN rises in disproportion to renal function with volume depletion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum Creatinine</strong></td>
<td>▶ Specific for renal function&lt;br&gt; ▶ Rise may not be evident until 50% GFR is lost&lt;br&gt; ▶ Creatinine needs to stabilize before an accurate assessment of renal function can be made&lt;br&gt; ▶ In total loss creatinine will rise 1-2 mg/dL per day and stabilize at 12-15 mg/dL</td>
</tr>
<tr>
<td><strong>Creatinine Clearance</strong></td>
<td>▶ As GFR falls, creatinine excretion is increased and the rise in serum creatinine is less.&lt;br&gt; ▶ GFR can be overestimated (limitation of creatinine clearance)</td>
</tr>
<tr>
<td><strong>Glomerular Filtration</strong></td>
<td>▶ Glomerular filtration determined by estimation of creatinine clearance.&lt;br&gt; ▶ GFR is usually estimated with the Cockroft-Gault equation: (140-age) x weight (kg) / plasma creatinine x 72 (value multiplied by 0.85 in females)</td>
</tr>
</tbody>
</table>
Abnormal BUN or Creatinine without Kidney Injury

- **BUN**
  - Increased production
    - GI Bleeding
    - Catabolic states
    - Corticosteroids
    - Increased protein load

- **Creatinine**
  - Inhibition of tubular creatinine secretion
  - Interference with creatinine assays in the lab (false elevation)

New biomarkers of AKI are emerging that will potentially replace creatinine.

Urine output is also affected by factors other than GFR.

Acute Kidney Injury

A sudden loss of the kidneys’ ability to excrete wastes, concentrate urine, and conserve electrolytes.

New definitions and stages proposed by Acute Kidney Injury Network.
Acute Kidney Injury (AKI): Entire Spectrum of Acute Renal Failure

- The definition includes one or more of the following that occurs abruptly (*within 48 hours):
  - An absolute increase in serum creatinine of more than or equal to 0.3 mg/dL. ** - NOT in RIFLE classification
  - A percentage increase in serum creatinine of more than or equal to 50%.
  - A reduction in urine output of less than 0.5 ml/kg per hour for more than six hours *

- Occurs in approximately 13 to 20 % hospitalized patient
- Occurs is up to 67% of patients in ICUs
- Variations in statistics exist due to differences in past definitions for acute renal failure

Implications of AKI

- Often secondary to injury that causes functional or structural changes in the kidneys
- Antecedent to CKD
- Mortality is increased
  - Even with small changes in creatinine
  - O.R. for mortality 4.1 with change in creatinine of 0.3 mg/dL
  - OR 2.0 in patient’s already critically ill
  - Impact is CKD unclear

- Application of diagnostic criteria can only be applied if patient is optimally hydrated!

### Stages of Acute Kidney Injury

<table>
<thead>
<tr>
<th>Stage</th>
<th>Creatinine Criteria</th>
<th>Urine Output Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increase in serum creatinine of more than or equal to 0.3 mg/dL or increase to more than or equal to 150% to 200%</td>
<td>Less than 0.5 ml/kg per hour for more than 6 hours.</td>
</tr>
<tr>
<td>2</td>
<td>Increase in serum creatinine to more than 200% to 300%.</td>
<td>Less than 0.5 ml/kg per hour for more than 12 hours.</td>
</tr>
<tr>
<td>3</td>
<td>Increase in serum creatinine to more than 300% or serum creatinine of more than or equal to 4.0 mg/dL with an acute increase of at least 0.5 mg/dL.</td>
<td>Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours.</td>
</tr>
</tbody>
</table>

Diagnosis within 48 hours / Staging over a week.

Importance of Classification for Research

![Bar Chart showing Mortality (%) for different RIFLE categories.]

Link Between RIFLE and New Staging System

- **RIFLE “Risk”**
  - AKI Stage 1
- **RIFLE “Injury” and “Failure”**
  - AKI Stages 2 and 3

- The RIFLE “Loss” and “End Stage Kidney Disease” are considered outcomes

Over versus under estimation of AKI based on definition.
Chronic Kidney Disease Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage (protein in the urine) with normal or elevated GFR</td>
<td>90 or more</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mildly decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Kidney damage with moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Kidney damage with severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure: end-stage renal disease (ESRD). Patients who have Stage 5 disease require dialysis or transplantation to survive.</td>
<td>Less than 15</td>
</tr>
</tbody>
</table>

Research Questions

- What is the worldwide incidence of AKI?
- How can AKI be studied in different environments?
- How/when should AKI be evaluated?
- How should AKI be managed?
- **Indications/patient selection for RRT?**
- Choice of therapy?

Etiology

- Outside Hospital
  - Glomerular nephritis
  - Vasculitis
  - Obstructive Uropathy

- Inside Hospital
  - Renal hypoperfusion
  - Drug toxicity
  - Combination of hypoperfusion and drug effect

Initial Evaluation in AKI

- Contributing causes
- Clinical course including co-morbid conditions
- Assessment of volume status
- Measures to reverse or prevent worsening of functional or structural renal abnormalities.
Classifications of Acute Kidney Injury

- Prerenal – 55-60%
- Intrarenal – 35-40%
- Postrenal – < 5%

Prerenal AKI

Causes
- Decreased intravascular volume
- Decreased cardiac output
- Decreased renal perfusion
  - Sepsis and liver failure
- Renal vasoconstriction
- Pharmacological impact on GFR

Treatment
The treatment of pre-renal AKI is aimed at the rapid reversal of the underlying cause of renal hypoperfusion in order to restore adequate renal perfusion.

If sepsis – vasopressors can improve renal perfusion
Diagnostic Parameters for Prerenal AKI

- Positive response to a fluid challenge is diagnostic of pre-renal AKI.
- Oliguria.
- Urinary Sodium < 20 mEq/L.
- Concentrated urine: Urine specific gravity > 1.0150 and urine osmolality > 500 mOsm/L.
- BUN: Creatinine Ratio > 10:1 (usually closer to 20:1). Increased proximal tubular reabsorption of BUN.
- Fractional excretion of sodium (FENa) < 1%
- Fractional excretion of urea (FEurea) < 35%
- Urine Protein 0 or minimal.
- Urine Sediment: Normal or minimally abnormal; hyaline casts, no or finely granular casts.

Intrarenal AKI: Classifications

- Tubular:
  - Acute Tubular Necrosis (most common cause)
  - Tubular obstruction
- Glomerular: Glomerulonephritis and small vessel vasculitis.
- Intersitial: Interstitial Nephritis.
- Vascular: Athroembolic disease, large vessel vasculitis.
Acute Tubular Necrosis (Medullary): Etiology

- Nephrotoxic agents
- Prolonged ischemic injury
- Hemolysis or rhabdomyolysis
- Endotoxin release in sepsis
- Hypercalcemia
- Any cause of prerenal AKI that is prolonged (clinical challenge)

Nephrotoxic Agents

- Aminoglycosides
- Amphotericin B
- Chemotherapy agents
- Cyclosporine
- ACE inhibitors
- NSAIDS
- Contrast agents

**Contrast Induced Nephropathy**

- Risk potentially reduced by pretreatment with oral n-acetylcysteine
  - 24 to 48 hours before contrast exposure
  - 600 mg BID
- Risk reduced by adequate pre-procedure hydration with 0.9NS or sodium bicarbonate drip
  - 154 mEq of sodium bicarbonate/L at 3 ml/kg for 1 hour prior to procedure
  - Followed by 1 ml/kg/hr for 6 hours post procedure
  - Some evidence that sodium bicarbonate is superior to sodium chloride
ATN Pathophysiology

- Destruction of the tubular epithelial layer of cells
- Often reversible if treatment is promptly initiated.
  - If the tubular basement membrane is damaged from prolonged injury and ischemia, it cannot be regenerated.
- Oliguria develops when tubules become obstructed due to tissue swelling or cellular debris.
- A reabsorption (into circulation) of urine filtrate can occur through damaged tubular epithelium.
- Damaged tubular cells can leak ATP and potassium, and calcium can leak into the cell.
- Scar tissue can form over necrotic areas
ATN Diagnostic Parameters

- Urine Sodium > 20 mEq/L.
- Urine osmolality < 400 mOsmol/L (loss of tubular concentrating ability).
- Bun:Creatinine Ratio 10:1.
- Fractional excretion of sodium (FENa) > 2-3%.
- Fractional excretion of urea (FEurea) > 50%.
- Minimal to moderate proteinuria.
- Urine Sediment: Muddy brown casts, granular / tubular casts, renal epithelial cells.

Granular casts help differentiate between prerenal and ATN.

ATN: Treatment

- Optimizing volume status for prevention
- Avoid all nephrotoxic agents; avoid or dose adjust all medications requiring renal clearance
- A loop diuretic can be used to correct volume overload if the patient is still responsive to diuretics
  - Diuretics are controversial
  - PICARD Study
- Dopamine not indicated
  - No effect on mortality or need for RRT
  - May increase diuresis first day (may worsen function in established AKI)
  - Adverse effects
  - Fenoldopam – promising in pilot studies but not in larger studies
- Atrial natiuretic peptide (ANP) / theophyline may have role
- Treatment is supportive
  - Managing fluid and acid/base balance, electrolytes, and hematologic abnormalities
More proposed new terminology:
No more prerenal azotemia nor ATN – instead volume responsive or volume unresponsive AKI.

Volume Responsive Kidney
- Volume responsive kidney usually occurs in volume responsive patient
- Hypovolemia post important cause of volume responsive hypovolemia.

Volume Responsive Patient
- Patient may respond to volume with an increase in cardiac output but not with an improvement in kidney function.

Replacing:
Prerenal azotemia and ATN
Postrenal AKI

• Classifications
  – Mechanical
    • Urinary calculi
    • Tumor
    • Prostatic hypertrophy
    • Fibrosis
    • Blood clot
    • Retroperitoneal hemorrhage
  – Functional
    • Neurogenic bladder.
    • Ganglionic-blocking agents.

• Pathophysiology
  – Obstruction can increase renal interstitial pressure causing an increased opposing force to GFR.

• Signs and Symptoms
  – Abrupt decrease in urine output
  – Urinalysis may show hematuria.

Ultrasound can be used to rule out during initial assessment.

Progression of AKI

Onset Phase
• Hours to days
• Renal blood flow and glomerular filtration fall
• Urine output falls
• BUN: Creatinine – Normal or slight increase

Oliguric / Anuric (Maintenance)
• 8-14 days
• Decreased GFR
• Urine output < 15 ml/hr (400 cc/24 hours)
• BUN and creatinine increased
• Metabolic acidosis
• Increased potassium
• Water gain with hypertension, dilutional hyponatremia, and pulmonary congestion
• Uremia can develop: Neuromuscular irritability, seizures, coma, death
• High mortality rate
Progression of AKI

**Diuretic Phase**
- 3 to 4 weeks after onset
- Can last 1-2 weeks
- BUN and creatinine begin to decrease
  - Diuresis may occur before BUN and creatinine fall
- Urine output may exceed 3L/24 Hr: 150-200% of normal
  - Osmotic diuresis from elevated BUN
  - Tubules cannot yet concentrate
  - Fluid losses can jeopardize adequate circulating volume
- Uremic symptoms may not completely resolve because tubular function is not yet normal

**Recovery Phase**
- Recovery is shorter in non-oliguric renal failure
- Begins with stabilization of laboratory values
- Several months to one year
- BUN: Creatinine almost normal; residual dysfunction may remain
- Urine output returns to normal

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**Outcomes of AKI**

- CKD (progressive)
- Full recovery
- AKI
- AKI on CKD
- ESRD
Electrolyte Abnormalities in AKI

- Hyperkalemia – most common with oliguric AKI.
- Hyperphosmatemia.
- Hypermagnesemia.
- Hypocalcemia.
- Acidemia
  - The kidneys excrete acid.
  - Oral sodium bicarbonate is typically used to treat.
  - Negative hemodynamic effects have been associated with IV sodium bicarbonate bolus dosing
  - The treatment for severe metabolic acidosis remains controversial.

Signs and Symptoms: AKI and CKD

- Fatigue
- Confusion
- Twitching or weakness related to metabolic acidosis
- Dry skin
- Edema
- Pallor
- Uremic frost/pruritis
- Flank pain
- Infection
Uremic Syndrome

- Seen in both acute kidney injury and in chronic renal failure.
- All organs can be affected
- Signs and symptoms can include: nausea, vomiting, pruritis, bleeding, encephalopathy, and pericarditis
- Symptoms not related solely to elevated BUN or creatinine.
- Uremic symptoms warrants aggressive treatment with some type of dialysis therapy.

Review of: Treatment of Early Oliguric Kidney Injury

- Eliminate all contributing pre-renal factors
- Rule out postrenal obstructive causes
- A loop diuretic can be used to correct volume overload if the patient is still responsive to it
  - Diuretics are controversial (no osmotics)
  - PICARD study (increased mortality)
- Dopamine are not indicated
  - No effect on mortality or need for RRT
  - Adverse effects
- Atrial Natriuretic Peptide has promise in some settings
- Need higher powered studies for Theophyline
Early in AKI

OPTIMAL VOLUME MANAGEMENT IS UPSTREAM OF ALL OTHER INTERVENTIONS!

Volume management becomes more and more challenging in critically ill patients.

Increased risk of adverse pulmonary function in patients MODS if excess volume.

Treatment of Early Oliguric Kidney Injury

• Avoid all nephrotoxic agents; avoid or dose adjust all medications requiring renal clearance.
• Initiate some form of renal replacement therapy (RRT) early in severe patients
  – More research needed
  – Outcomes improved if kidney function improved
• Provide meticulous supportive care
• Avoid complications
  • Infection
  • Fluid, electrolyte, and acid/base imbalances
  • Hematologic abnormalities
  • Drug toxicity from drugs metabolized or excreted from the kidney
Treatment of Established Oliguric Kidney Injury

- Modify dose of drugs metabolized or excreted from kidney.
  - Base dose adjustment on an assumed GFR of zero.
- Limit fluid intake to avoid congestion.
- Manage electrolytes
  - Restrict potassium, phosphate, and magnesium intake.
  - Assess for hypernatremia.
- Prevent complications
  - Infection-related complications are the most common cause of death
    - Nosocomial pneumonia.
    - IV catheter infections.
    - Intra abdominal sepsis.
  - Hemorrhage
    - Uremic toxins inhibit platelets and factor VIII.
    - Factor VIII may need to be replaced.
    - Arginine vasopressin can also increase levels of factor VIII.
- Nutrition
  - Sufficient fat and carbohydrate calories to prevent protein wasting
  - Limit protein if not on dialysis
  - Folate and pyridoxine are lost through dialysis
- Avoid corticosteroids (except for interstitial nephritis and some types of renal vasculitis).
  - Catabolic effect
  - Adversely affects immune function

Nursing Considerations

- Maintain skin integrity (uremic effects - high risk for breakdown)
- Prevent infection (infection is major cause of mortality)
  - BUN > 80 to 100 mg/dL is associated with a high risk of infection.
- Nutrition
  - Patients can have accelerated protein catabolism
  - BUN > 100 mg/dL - despite routine dialysis).
  - Need higher protein intake.
- Maintain fluid restriction.
- Replace water soluble vitamins
- Monitoring of electrolytes, serum protein, albumin, hematocrit, and BUN and creatinine.
  - Low serum protein and albumin levels have an immunosuppressive effect
Criteria for RRT

- Volume overload in presence of oliguria or anuria
- Uncontrolled hyperkalemia, hyperphosphatemia, hypermagnesemia
- Life threatening acidosis
- Life threatening drug overdoses or toxicity requiring dialysis
- Symptomatic uremia
  - Nausea and vomiting
  - Bleeding
  - Pericarditis
  - Seizures, coma
- BUN 80-100 mg/dL
- Creatinine 10 mg/dL

Renal Replacement Therapy (RRT): Intermittent Hemodialysis

- Central venous access (emergency)
- Arteriovenous grafts or fistulas (chronic)
- Anticoagulation is generally required; non-heparin dialysis is also an option
- Blood pumped through an artificial kidney on one side of the dialysis membrane, while the dialysate (electrolyte) solution flows the opposite direction
- Combines adsorption, diffusion, osmosis, and ultrafiltration
  - Remove fluid and maximal amount of solute (electrolytes, metabolic products, drugs, and toxins)
  - Maximum removal allows for intermittent sessions
- Requires more hemodynamic stability than hemofiltration
- Hypotension is the most common problem
- Advances: Bicarbonate base instead of acetate based:
  - Improved cardiac stability / control of metabolic acidosis
Dialysis Equilibrium Syndrome

- From shifts in extracellular compartment
- Nausea, vomiting, confusion, seizures, coma.
- Most common in first dialysis session with high BUN.
- Treatment.
  - Decreased dialysis time.
  - Decreased dialysis flow rates.
  - Dialyzer with smaller surface area.
  - Sodium chloride, dextrose, mannitol.

RRT: SLEDD is alternative form of delivery

- Sustained low efficiency daily dialysis
  - Alternative to continuous renal replacement therapy due to the disadvantages
    - Patient immobility
    - Need for specialized equipment
    - Anticoagulation
    - Cost
  - More research needed
Renal Replacement Therapy: Peritoneal Dialysis

- Slow form of dialysis - exchange of fluids and solutes between the peritoneal cavity and peritoneal capillaries
- Utilizes diffusion
- Less efficient than hemodialysis
- No need for vascular access
- No significant hemodynamic effects
- 1 to 3 L of solution with dwell time of 30 to 40 minutes
- Osmotic gradient for fluid removal
  - Hyperosmolar glucose concentrations
- Complications
  - Abdominal distention and increased work of breathing
  - Pleural effusion
  - Hyperglycemia
  - Peritonitis

Criteria / Candidates for Continuous RRT (CRRT) (derived from data on ESKD)

- Hemodynamically unstable patients with criteria for RRT
- Patients with increased ICP who need dialysis
- Critically ill patients with early signs of AKI
  - No consensus on degree of azotemia or duration of AKI that warrants CRRT
- Nontraditional indications (CEBT):
  - Hyperthermia
  - Rhabdomyolysis
  - Systemic inflammatory response syndrome
  - Fluid management in the hemodynamically unstable patient without renal failure
CRRT: Where Do We Stand?

- No proven survival advantage over intermittent hemodialysis
  - Mortality rates high for both arms of treatment
- Limited research on timing of initiation or mode of solute clearance
- No evidence at this time to support more intensive strategies
- Different approach in CKD to AKI
  - CKD patients sodium loaded
- SLEDD (or other hybrids) may replace CRRT depending on results of future research

CRRT

**Ultrafiltration**
- SCUF – Slow continuous ultrafiltration
- Fluid moves through a semipermeable membrane via a pressure gradient (higher pressure gradient creates more fluid removal)
- Results are primarily fluid removal
- Hemofiltration, hemodialysis, and hemodiafiltration all use ultrafiltration as a component of therapy
- Adsorption is another principle involved in all 4 therapies
  - Clinging of positively charged molecules to the negatively charged membrane of the filter.
  - Filter can become clogged with molecules. The removal of these molecules from systemic circulation is a benefit of CEBT therapy.
CRRT

**Hemofiltration**
- CVVH – Continuous veno-venous hemafiltration
- Uses convection to remove solutes
  - Process of solute removal by solvent drag
  - More fluid through semi permeable membrane = more solute removed.
  - Replacement solution is used to create solvent drag
  - Faster rate of replacement solution = more solvent drag
- Convection removes medium and large molecules
- Solute removal is slow so the process must be continuous
- Fluid removal still exceeds solute removal
- Less likely than hemodialysis to produce hypotension
- Some medications are cleared via hemofiltration and require a dose adjustment
  - Dose adjusted based on an assumed creatinine clearance of approximately 14 ml/minute

CRRT

**Hemodialysis**
- CVVHD – Continuous veno-venous hemodialysis
- Uses dialysate solution to create selective diffusion of electrolytes
  - Excellent technique for the removal of small particles
- Hemodialysis removes both solutes and fluid
- Often used on patients who are chronic dialysis
- Provides more hemodynamic stability than intermittent hemodialysis
- Allows fluid overloaded critically ill patients to receive a higher caloric intake
CRRT

Hemodiafiltration
- CVVHDF – Continuous veno-venous hemodiafiltration.
- Uses both hemodialysis and hemofiltration
- Allows for the removal of small, medium, and large molecules.

CRRT
- A venous to venous connection with a double lumen venous catheter
- Jugular, subclavian, and femoral veins can be used.
- Venous-only access avoids the risk of limb ischemia associated with arterial access.
- Extra corpeal pump is used to create flow through the system.
- Filtration is ineffective when MAP fall below 60mmHg.
- Equipment
  - Blood filter, blood pumps, circuit tubing, dialysate and replacement infusion tubing, anticoagulant tubing, and a collection bag.
### CRRT

#### Hemodiafiltration

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<tr>
<th>Therapy</th>
<th>Principles</th>
<th>Replacement Solution</th>
<th>Dialysate Solution</th>
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Ultrafiltrate flow rates 35 ml/kg appear to be superior to 20 to 25 ml/kg.
Nursing Considerations in CRRT

- Hypothermia
  - Warming blankets
  - Use of warmers as part of the ECBT equipment
- Coagulation
  - Clotting versus clogging
  - Heparin most commonly used
    - Potential advantage of regional citrate
  - Alternative is to use a technique that includes the use of a replacement solution. Use of replacement solution results in continuous dilution of the hematocrit.
- Cardiac arrhythmias
  - Fluid and electrolyte imbalance
  - Equipment can cause ECG artifact that mimics cardiac arrhythmias
  - Equipment should be temporarily stopped so the patient’s rhythm can be reassessed

Electrolytes: Overview

- Abnormalities often occur in groups and symptoms can be from mixed disorders
- Treatment is focused on immediate crisis and underlying cause
- Suspect electrolyte abnormalities:
  - Renal disease
  - Endocrine disease
  - Acute change in mental status
  - Ventricular arrhythmias
Sodium

- Dominant extracellular cation
- Primary determinant of serum osmolality
- Sodium is closely related to water (regulates ECF)
- Factors to consider when assessing sodium abnormalities:
  - Serum and urine osmolality
  - Intravascular volume status / presence of edema
  - Serum albumin, lipids, and glucose
  - Medications and IV fluids
  - Renal function

Hyponatremia:
Sodium < 135 mEq/L

- S&S related to rapidness of onset and severity
  - Signs and symptoms can also be related to fluid balance.
  - Primary effects are CNS related.
- Cognitive and motor function changes @ < 125 mEq/L
- Permanent changes at levels < 110 mEq/L
- 50% mortality when < 105 mEq/L

- Muscle cramps
- Twitching / tremors
- Muscle weakness
- N&V / abdominal cramps
- Headache
- Irritability / personality changes
- Confusion
- Lethargy progressing to coma
- Seizures
Hypotonic Hyponatremia

- Most common form of hyponatremia
- Results in intracellular hypoosmolar state (creates S&S)
- Occurs as a result of excess free water in relation to sodium
- Patients can be:
  - Hypovolemic
  - Isovolemic * most common form
    - SIADH
  - Hypervolemic

Treatment for Hyponatremia

- Sodium should be corrected to an initial level of 120 to 130 mEq/L
  - Over 12 to 24 hours
  - No more than 8-12mEq / 24 hours unless life threatening symptoms
- Correct at rate proportional to development (slower rate for chronic hyponatremia)
- Free water restriction for levels > 125 to 130 mEq/L

*Caution: Osmotic demyelinating syndrome*
Hypernatremia

- **Definition:** Sodium greater than 145 mEq/L with a serum osmolality > 295 mOsm/kg. *Most cases of hypernatremia involve a hyperosmolar state.*
- **Rarely occurs in patients with:**
  - Normal ADH secretion
  - Thirst mechanism
  - Ability to consume free water
- **Almost always causes cellular dehydration.**

**Treatment**
- Correct underlying cause
- Decrease 0.5 to 1.0 mEq/L per hour
  - Replacement of free water with D5W or 0.2 or .45 NS
  - Normal saline may be used if hemodynamically unstable (adequate circulating volume is priority)
  - Loop diuretics or dialysis rarely needed
  - *Caution – Cerebral Edema*

---

### Causes
- Conditions with limited ability to consume free water (ICU setting)
- Hypertonic tube feedings
- Dehydration (burns, tachypnea, hyperthermia)
- Osmotic diuretics with excessive free water clearance.
- Diabetes mellitus
- Diabetes insipidus

### Signs and Symptoms
- Thirst (early symptom)
- Urine output decreases and urine osmolality increases due to renal water conservation
- Dry mouth and skin
- Increased body temperature
- Muscle weakness
- Headache
- Irritability and agitation
- Seizures
- Coma
**Signs and symptoms related to fluid status as well as sodium level.**

**Osmolality is determined by sodium.**

**Decrease sodium slowly to avoid cerebral edema.**

**Increase sodium slowly to avoid osmotic demyelinating syndrome.**

**Understand importance of diuretics in predisposing to hyponatremia.**

**Manifestations (neurological) of hyper and hyponatremia can be the same.**

---

**Potassium**

- 95% or > of potassium is intra cellular
- Majority of potassium contained in muscle
  - Declines with age due to decrease in muscle mass
- Dietary intake is the major source / kidneys responsible for excretion
- Ratio of extracellular to intracellular important for electrical membrane potentials
- Major body systems impacted by abnormalities:
  - GI
  - Neuromuscular
  - Cardiac

*Nerve impulse and muscular function transmission dependent on potassium.*
Hypokalemia: Causes

• K+ less than 3.5 mEq / L (total body deficit of 5-10%)

• Causes:
  – Poor K+ intake
  – Increased GI loss (not usually cause of symptomatic imbalance)
  – Increased renal loss
    • Renal tubular acidosis
    • Diuretics
    • Excess mineral or glucocorticoids (aldosterone)
    • Low magnesium
    • Certain antibiotics

  • Extracellular to intracellular shifts
    – Alkalosis (potassium exchanged for hydrogen ions)
    • also causes increased renal loss
    – Insulin
    – Treatment of DKA or H-HNK
      • Insulin
      – Beta adrenergic agonists

• Note: Does not reflect total body potassium – Correct with caution
  • Caution with hypokalemia in presence of acidosis.

Urinary K+: High with renal loss; low with other causes

Hypokalemia: Signs and Symptoms

• Symptoms occur when K+ < 3.0 mEq/L

• Severity dependent on:
  – Rapidness of onset
  – Systemic pH
  – Calcium level

• S&S related to altered membrane potentials and impaired muscle contractility
  – Increase in resting membrane potential of neuronal and muscular cells
  – Reduces excitability

• GI
• Orthostatic hypotension
• Parasthesias, weakness, fatigue and muscle cramps
  – Lower extremities are typically impacted first
• Respiratory muscle weakness, dyspnea, paralysis and arrest (< 2.5 mEq/L)
• Enhanced digitalis effect
• Severe hypokalemia can result in rhabdomyolysis
Hypokalemia: ECG Changes

- Mild hypokalemia: delays ventricular repolarization
  - ST depression, inverted T wave
  - Heightened U waves, prolonged QT interval
- Lowered threshold for ventricular fibrillation and reentrant tachycardias
- Any arrhythmia
- Severe hypokalemia
  - Increased PR interval
  - Increased QRS interval

Hypokalemia: Treatment

- Treat cause
- Correct alkalosis
- Correct hypomagnesemia
- Increased potassium intake (dietary or supplement) if potassium ≥ 3.0 mEq/L
  - Foods high in potassium: orange juice, bananas, raisins, milk, green vegetables
  - Oral supplements up to 40 mEq can be used safely several times per day.
- Add potassium to maintenance IV fluid
- IV potassium bolus for severe deficiency (less than 3.0 mEq /L if on digoxin, symptoms related to hypokalemia, or less than 2.5 mEq /L without symptoms)
  - Non glucose solution
  - Safe dosage: 10 mEq / 100 cc over 1 hour
  - May give 20 mEq over 1 hour if K+ is < 3.5 mEq / L (higher doses if life threatening)
  - Concentration should not exceed 10 mEq per 100 ml via peripheral line or 20 mEq per 100 ml if central line

Note: Replace cautiously in those with impaired ability to excrete.
### Hyperkalemia:

**K+ greater than 5.0 mEq/L**

- Rarely occurs in healthy people
- Impaired potassium management:
  - Renal Disease
  - Diabetics

#### Decreased Excretion
- Renal disease
  - Decreased renal perfusion
  - Sickle cell disease
- Decreased aldosterone
  - Addison’s
  - Diabetes
  - Drugs inhibiting aldosterone (aldactone, ACE-I, ARBs, Non steroidal antinflammatories, Heparin)

#### Increased Intake
- Salt substitutes
- Supplements
- High dose penicillin with K⁺
- Lactated ringers
- Transfusion of banked blood

### Hyperkalemia: Causes

#### Cellular disruption with leak of intracellular K⁺
- Crush injuries
- Rhabdomyolysis
- Hemolysis (blood transfusion reaction)
- Early burns
- Trauma
- Large hematoma
- Severe catabolic state
- Lysis of tumor cells (chemotherapy)

#### Intracellular to extracellular shift
- Metabolic acidosis
- Hypertonic glucose with insulin deficiency
- Hyperosmolality
- Digitalis toxicity
- Depolarizing neuromuscular blocking agents
- Beta blockers
Hyperkalemia: Signs and Symptoms

Symptoms when K+ > 6.0 mEq/L
- Skeletal muscle effects when K+ > 7.0 mEq/L
- Neuromuscular effects complicated by acidosis, low sodium, low calcium, high magnesium
- Parathesia
- Lower extremity weakness
- Hypotension

EKG Changes
- Tall narrow peaked T waves
- Wide QRS
- Prolonged PR and flattened to absent P wave

Dysrhythmias
- Bradycardia / heart block
- Sine wave pattern
- Asystole

![EKG Image]
Hyperkalemia: Treatment

- Level > 6.0 mEq/L should be treated. Urgency based on clinical manifestations.
  - Limit K+ intake
  - Volume expansion
  - K+ > 6.5 or dysrhythmias
    - Stabilize cardiac membrane with calcium chloride
      - Not if digitalis toxic
    - Shift potassium into cell
      - 50% Dextrose and insulin (50 ml and 10 units)
      - High dose inhaled beta agonists (synergistic)
      - Sodium bicarbonate to correct acidosis

Hyperkalemia: Treatment

- Kayexalate is an exchange resin
  - Exchange sodium for K+ and moves K+ out via the GI tract
  - Can be given orally or as retention enema
- Oral dose is administered in sorbitol
  - Sorbitol orally acts as osmotic laxative
- Retention enema is administered in dextrose
  - Sorbitol can cause intestinal necrosis when given by enema
- Loop diuretics if functioning kidneys
- Dialysis if renal dysfunction
Potassium is primarily inside the cell (particularly muscle).

Oral kayexalate often contains sorbitol. Caution with using sorbitol with rectal administration.

The primary systems impacted by potassium are GI, neuromuscular, and cardiac.

Administer calcium to prevent cardiac effects of hyperkalemia.

Shifts from extracellular to intracellular cause hypokalemia.

Shifts from intracellular to extracellular cause hyperkalemia.

Insulin moves potassium inside the cell.

Understand that hypomagnesemia may prevent correction of hypokalemia.

Manifestation of hyperkalemia is usually paresthesia as first symptom.

---

Calcium

- Less than 50% of dietary intake is absorbed.
- The majority of the body’s calcium is in the bone.
- Serum level regulated by parathyroid levels and vitamin D.
  - Also influenced by serum phosphate levels (inverse relationship), albumin levels, and blood pH.
  - Calcium in bone can be exchanged to maintain extracellular levels.

There are 3 types of serum calcium:
- > 40% of calcium is protein bound (mostly albumin)
- 10% is chelated (non-ionized) with substances such as citrate or phosphate
- 50% is ionized (free to leave the extracellular fluid and participate in intracellular function)

Important for several key processes:
- Muscle contraction
- Transmission of nervous system impulses
- Hormone secretion
- Blood clotting and wound healing
- Cellular function
Hypocalcemia

- Calcium < 8.8 mg/dL or ionized calcium < 4.65 mg/dL.

Common disorder in critical care.

Generally asymptomatic if development is slow or if ionized calcium remains normal.

Hypocalcemia: Causes

<table>
<thead>
<tr>
<th>Decreased calcium intake or absorption</th>
<th>Increased calcium excretion</th>
<th>Impaired ability to mobilize calcium from bone stores</th>
<th>Increased calcium binding; increased calcium chelation (decreased ionized calcium)</th>
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<td>Cushing's disease</td>
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<td>Chronic Diarrhea</td>
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<td>Hyperphosphatemia</td>
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<td>(phosphate elimination is impaired in renal failure)</td>
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Hypocalcemia: Signs and Symptoms

Most common symptoms due to neuromuscular irritability.
- Parathesias (common)
- Hyperreflexia
- Tetany (spasms of face, hands, and feet)
- **Chvostek’s sign**
  - Tapping of face over facial nerve located below the temple
  - Positive sign results in spasm of lip, nose or face.
- **Trousseau’s sign**
  - Inflate blood pressure above systolic BP and hold for 3 minutes
  - Positive sign results in contraction of fingers or hand.
- Stridor / wheezing / bronchospasm
- For severe deficit: laryngeal spasm, change in mental status, seizures
- Chronic: dry skin and hair and brittle nails; bone pain and risk of fracture
- **Cardiovascular effects:**
  - Decreased contractility
  - Hypotension
  - Prolonged QT (ST segment hugging baseline for extended period)
  - Torsades de pointes
  - Bradycardia / heart block
  - **Digitalis insensitivity**
  - Heart failure
  - Cardiac arrest

Hypocalcemia: Treatment

- **Goal:** Low-normal range
- High calcium, low phosphorous diet
- Vitamin D supplements if deficiency
- Phosphate binding antacids *
- Magnesium for hypomagnesemia
- Correct alkalosis (increases ionized Ca++)
- Thiazide diuretics (increase tubular calcium reabsorption)
- IV calcium chloride or calcium glucanate
IV Calcium Administration

- Calcium gluconate
  - Give 10 ml
  - 10 ml contains 4.5 mEq of calcium

- Calcium chloride
  - Give 3-4 ml
  - 10 ml contains 13.6 mEq of calcium

- Administer no faster than 1 ml per minute
- May cause sloughing or necrosis (central vein preferred)

Hypercalcemia

- Calcium > 10.4 mg / dL or ionized calcium > 5.26 mg / dL
- Causes:
  - Increased calcium intake (supplement or antacids)
  - Increased calcium absorption (hypophosphatemia, excessive vitamin D)
  - Increased mobilization of calcium from the bone (Vitamin D excess, immobility, hyperparathyroidism, thyroidtoxicosis, neoplasms)
  - Acidosis (increased ionized calcium)
  - Decreased calcium excretion (thiazide diuretics)
Hypercalcemia: Signs and Symptoms

- Hypophosphatemia
- Signs and symptoms related to dehydration
- Gastrointestinal symptoms (slowing of GI tract)
- Bone and flank pain / osteoporosis / pathological fractures
- Muscular symptoms: Hypotonicity / weakness / fatigue
- Neurological symptoms: Decreased mentation, agitation, comma, seizures.
- Calcium salts form at high levels
  - Pruritis from skin deposits.
  - Renal calculi and potential kidney injury
  - Deposits on the aorta, cardiac valves, and coronary arteries.

Hypercalcemia: Signs and Symptoms

- Cardiac symptoms:
  - hypertension (may be offset by co-existing dehydration)
  - cardiac ischemia
  - shortened QT segments
  - arrhythmias (conduction abnormalities)
  - digitalis toxicity.

- Life threatening signs and symptoms are rare unless calcium levels reach > 14 mg/dL.
Hypercalcemia: Treatment

- Primary Treatment: Rehydration with 0.9 NS
- Decrease calcium absorption
  - Low calcium, high phosphorous diet
  - Glucocorticoids
- Increase calcium excretion
  - Fluids (0.9NS)
  - Loop diuretics
  - Dialysis if renal failure or life threatening
  - Inhibit bone resorption (calcitonin, mithramycin, biphosphonates)
- Prevent cardiac effects
  - Calcium Channel Blockers
- Prevent renal calculi
  - Acidify urine

Calcium (serum) is found in three forms: protein bound, chelated, ionized
Assess for Chvostek’s sign and Trousseau’s sign with hypocalcemia.
Loss of calcium occurs with loop diuretics but not with thiazide diuretics
Calcium gluconate differs from calcium chloride in amount of calcium per amp
Ionized calcium is important: it can leave extracellular fluid to participate in intracellular function
Understand that low magnesium affects the absorption of calcium and release of parathyroid
Make the association between low calcium and prolonged ST segment.
Low Magnesium: < 1.5 mEq/dL

- Common disorder in hospitalized patients
- Most common causes renal and GI loss
  - Transcellular shift after hypothermia
- Low magnesium = increased digitalis effect
- EKG: Prolonged QT and Torsades de pointes
- Neuromuscular irritability and decreased ability to relax neuromuscular tone
- May induce hypokalemia and hypocalcemia
- Signs and symptoms overlap with hypokalemia and hypocalcemia (often concurrent)
- Oral magnesium can cause diarrhea and further lower magnesium levels
- IV 1 to 2 grams over 10 – 60 minutes
  - More rapidly if life threatening
  - Decrease if kidney injury present

High Magnesium: > 2.5 mEq/L

- Uncommon disorder outside kidney dysfunction
- S & S
  - Hyporeflexia.
  - Hypotension.
  - Heart block/bradycardia.
  - Muscle weakness.
  - Change in mental status.
  - Lethargy/coma.
  - Cardiopulmonary arrest.

Treat with fluids and diuretics if normal renal function.
Dialysis if renal failure.

Clinical application: SE of IV magnesium administration is hypotension.
Magnesium is drug of choice in treatment of torasades de pointes
A low level of magnesium can be associated with hypokalemia and hypocalcemia
Give IV replacement 1 to 2 grams over 10 to 60 minutes
Neuromuscular tone cannot relax with low levels of magnesium.
Especially be concerned when giving IV magnesium to patient with renal dysfunction
Signs of high magnesium include hyporeflexia and hypotension
IV magnesium administration has potential side effect of hypotension
Magnesium given orally can cause diarrhea and further lower magnesium levels

Low Phosphorous:
< 2.5 to 3.0 mg/dL
- Easily lost from RBCs and skeletal muscle but levels well preserved in cardiac muscle
- Various neuromuscular and central nervous system effects related to depleted intracellular stores
- Enteral replacement preferred if not life threatening
- Parenteral sodium phosphate or potassium phosphate if severe
  - Dose .6mg/kg/hr to .9mg/kg/hr
  - Observe for signs of hypocalcemia
  - Replace with caution since predominantly intracellular
High Phosphorous: > 4.5 mg/dL

• Causes:
  • Renal dysfunction
  • Laxatives with phosphate
  • Hypocalcemia
  • Increased cellular release

• Same clinical signs as hypocalcemia

Treat hypocalcemia
Aluminum antacids bind with phosphate
Acetazolamide to increase urinary excretion
Dialysis if due to renal failure

Gratitude!