Disorders of Potassium and Acid-Base Balance
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ACID-BASE DISORDERS

Physiology of Acid-Base Balance

Definitions of acid-base disorders
- Metabolic acidosis: fall in HCO$_3^-$ concentration with fall in pH
- Metabolic alkalosis: rise in HCO$_3^-$ concentration with rise in pH
- Respiratory acidosis: rise in CO$_2$ concentration with fall in pH
- Respiratory alkalosis: fall in CO$_2$ concentration with rise in pH

Compensatory response to acid-base disorders
- Metabolic acidosis: fall in pH causes increased respiration, reducing CO$_2$
- Metabolic alkalosis: rise in pH causes decreased respiration, increasing CO$_2$
- Respiratory acidosis: fall in pH causes increased renal H$^+$ secretion, raising HCO$_3^-$ concentration
- Respiratory alkalosis: rise in pH causes diminished renal H$^+$ secretion, lowering HCO$_3^-$ concentration
- See Table 1

Response to acid generation
Average 1 mEq/kg/d for typical Western diet.
- Blood buffering of newly formed acid by bicarbonate, creation of CO$_2$
- Less efficient buffering of acid by hemoglobin in red blood cells, Ca$^{2+}$ exchange in bone
- Renal handling of acid:
  - Hydrogen excretion by proximal tubule (PT) into lumen leads to reclamation and reabsorption of HCO$_3^-$
  - H$^+$ then combines with either HPO$_4^{2-}$ or HSO$_4^-$ (“titratable acids”) or NH$_3$ in tubular lumen; 10 to 40 mEq of H$^+$ excreted each day as titratable acidity, 30 to 60 mEq/d by NH$_4^+$
  - Reclamation of filtered bicarbonate occurs primarily in PT
  - Under conditions of excessive acid generation (metabolic acidosis), ammoniagenesis is required to enhance acid secretion:
    - NH$_4^+$ produced by renal tubular cells from metabolism of amino acids (primarily glutamine)
    - NH$_4^+$ reabsorbed in thick ascending loop and recycled as NH$_3$ in renal medulla
    - NH$_3$ diffuses into tubular lumen, trapped as NH$_4^+$ by secreted H$^+$
    - Glutamine metabolism enhanced by hypokalemia, inhibited by hyperkalemia

Cellular mechanisms of renal adaptation
- To respiratory acidosis:
  - Increased PT cell secretion of hydrogen ion due to decreased cell pH
  - Increased PT cell secretion of H$^+$ via Na$^+$/H$^+$ exchanger, and increased reabsorption of HCO$_3^-$ via Na$^+$/HCO$_3^-$ cotransporter on basolateral surface
- To respiratory alkalosis:
  - Decreased PT cell activity of carbonic anhydrase
  - Decreased PT cell secretion of H$^+$ and decreased reabsorption of HCO$_3^-$

Metabolic Acidosis

Causes
- Increased acid load:
  - Lactic acidosis
  - Ketoadidosis

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Ingestions:
- Salicylates
- Methanol
- Ethylene glycol
- Paraldehyde
- Sulfur
- Toluene
- Ammonium chloride
- Hyperalimentation fluids

● Extrarenal acidosis:
  - \( \text{HCO}_3^- \) losses via gastrointestinal loss:
    - Diarrhea
    - Intestinal fistula
    - Ureterosigmoidostomy

● Renal acidosis:
  - Defect in \( \text{HCO}_3^- \) reclamation:
    - Type 2 “proximal” renal tubular acidosis (RTA)
  - Defect in \( \text{HCO}_3^- \) regeneration:
    - Diminished \( \text{NH}_4^+ \) production (renal failure, hypaldosteronism-type IV RTA)
    - Diminished \( \text{H}^+ \) secretion (type I RTA)

● Utility of plasma and urine anion gap:
  - Plasma anion gap:
    - \([\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])\); normally 8 to 11 mEq/L (mmol/L)
    - Buffering of HA (proton-anion) by \( \text{HCO}_3^- \) in setting of increased acid load leads to increased unmeasured anions (\( A^- \)) and increased anion gap
  - Urine anion gap:
    - \(([\text{Na}^+]) + [\text{K}^+] \) - [Cl\(^-\)]
    - In setting of metabolic acidosis with normal plasma anion gap (“hyperchloremic metabolic acidosis”), urine anion gap is useful to distinguish between extrarenal and renal acidosis

○ Urine anion gap greater than 0 suggests failure to excrete acid load (eg, RTA)
○ Urine anion gap less than 0 suggests extrarenal bicarbonate loss (eg, diarrhea)

### Renal tubular acidosis

Hyperchloremic metabolic acidosis, normal serum anion gap, urine anion gap greater than 0.

#### Type I RTA (defect in \( \text{H}^+ \) secretion in distal tubule).

- Physiology:
  - \( \text{H}^+ \)-adenosine triphosphatase (ATPase) located in cortical collecting tubule (intercalated cells only), where \( \text{H}^+ \) secretion influenced by \( \text{Na}^+ \) reabsorption in principal cells, and in medullary collecting duct

- Pathophysiology:
  - Defect in distal \( \text{H}^+ \)-ATPase pump (Sjögren syndrome), increased collecting duct membrane permeability with back-diffusion of \( \text{H}^+ \) (amphotericin B), decreased distal delivery of \( \text{Na}^+ \) with failure to exchange for \( \text{H}^+ \) and \( \text{K}^+ \) (volume depletion), or decreased cortical reabsorption of \( \text{Na}^+ \) with net increase in luminal charges and inhibition of \( \text{H}^+ \) and \( \text{K}^+ \) secretion (“hyperkalemic type I RTA,” as in urinary tract obstruction or sickle cell disease)

  - Calcium and phosphate release from bone to buffer acidemia leads to propensity for nephrocalcinosis in type I RTA

- Diagnosis:
  - Urine pH >5.3
  - Plasma \( \text{K}^+ \) usually low or normal (except with voltage defect)

### Table 1. Formulae Quantifying the Degree of Compensation

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>( \text{CO}_2 ) decreases by 1.0-1.5 × the decrease in arterial ( \text{HCO}_3^- )</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>( \text{CO}_2 ) increases by 0.25-1.0 × the increase in arterial ( \text{HCO}_3^- )</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>( \text{HCO}_3^- ) decreases by about 1 for each 10–mm Hg increase in ( \text{CO}_2 )</td>
</tr>
<tr>
<td>Acute Respiratory acidosis</td>
<td>( \text{HCO}_3^- ) increases by about 4 for each 10–mm Hg increase in ( \text{CO}_2 )</td>
</tr>
<tr>
<td>Chronic Respiratory acidosis</td>
<td>( \text{HCO}_3^- ) decreases by about 1 for each 10–mm Hg decrease in ( \text{CO}_2 )</td>
</tr>
<tr>
<td>Acute Hyperalimentation fluids</td>
<td></td>
</tr>
<tr>
<td>Chronic Hyperalimentation fluids</td>
<td></td>
</tr>
</tbody>
</table>
- Plasma $\text{HCO}_3^-$ low (<14 mEq/L [mmol/L])
- **Treatment:**
  - $\text{HCO}_3^-$ 1-2 mEq/kg/d

**Type II RTA (defect in PT $\text{HCO}_3^-$ reclamation).**
- **Physiology:**
  - Filtered $\text{HCO}_3^-$ reabsorbed primarily in the PT after the addition of a proton in lumen ($\text{Na}^+$/H$^+$ antiporter), forming $\text{H}_2\text{CO}_3$, and conversion to CO$_2$ and H$_2$O facilitated by carbonic anhydrase
  - CO$_2$ diffuses across apical membrane and converted to $\text{HCO}_3^-$ again by carbonic anhydrase
  - $\text{HCO}_3^-$ then transported to blood by Na$^+$/3$\text{HCO}_3^-$ cotransporter
  - Distal nephron contributes a trivial amount of $\text{HCO}_3^-$ reabsorption via intercalated cell of collecting duct
- **Pathophysiology:**
  - Injury to luminal Na$^+$/H$^+$ antiporter or basolateral Na$^+$/K$^+$/H$^+$-ATPase pump (likely etiologies for type II RTA in multiple myeloma, Fanconi syndrome, ifosfamide therapy) or deficient/inhibited carbonic anhydrase (cystinosis, acetazolamide therapy)
  - Acidosis milder than type I RTA due to intact reabsorption of $\text{HCO}_3^-$ in distal nephron
- Often evidence of generalized PT dysfunction is present, with glycosuria, aminoaciduria, and phosphaturia
- **Diagnosis:**
  - Urine pH >5.3 if above reabsorptive threshold, <5.3 in steady state, plasma K$^+$ usually low, plasma $\text{HCO}_3^-$ 14 to 20 mEq/L (mmol/L)
- **Treatment:**
  - $\text{HCO}_3^-$ 10 to 15 mEq/kg/d

**Type IV RTA (aldosterone deficiency or resistance).**
- **Physiology:**
  - Aldosterone promotes distal Na$^+$ reabsorption, K$^+$ and H$^+$ secretion
  - Direct effects of aldosterone on Na and K channels in luminal membrane of principal cells in cortical collecting tubule, increased Na$^+$/K$^+$/H$^+$-ATPase pump activity in basolateral membrane, and H$^+$-ATPase pump activity in intercalated cells in cortical collecting duct, medullary collecting tubule cells
- Indirect effects of aldosterone in H$^+$ secretion secondary to electrochemical gradient induced by Na$^+$ reabsorption
  - **Pathophysiology:**
  - Decreased adrenal aldosterone production (heparin, tuberculosis, adrenal insufficiency)
  - Decreased activity of renin-angiotensin system (diabetes, renal insufficiency, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers)
  - Resistance to aldosterone (potassium-sparing diuretics, trimethoprim, pseudohypoaldosteronism)
  - Acidosis exacerbated by hyperkalemia-induced inhibition of glutaminase with diminished ammoniagenesis
- **Diagnosis:**
  - Urine pH <5.3, plasma K$^+$ high, plasma $\text{HCO}_3^-$ 14 to 20 mEq/L (mmol/L)
- **Treatment:**
  - Correct hyperkalemia, $\text{HCO}_3^-$ 1 to 2 mEq/kg/d

**RTA of renal insufficiency (reduction in nephron mass).**
- **Physiology:**
  - Under normal conditions, ammonium excretion increases in response to an acid load, as described earlier in the Physiology/Response to Acid Generation subsection; this increase can be up to 3 to 4 times normal, but is limited by glomerular filtration rate (GFR)
- **Pathophysiology:**
  - Fibrosis that occurs with chronic kidney disease leads to diminished functional nephron number and diminished capacity for ammoniagenesis
  - At GFR less than 40 to 50 mL/min (0.67 to 0.83 mL/s), total ammonium excretion diminishes
  - H$^+$ is retained but a reduction in $\text{HCO}_3^-$ is stabilized at serum levels of 12 to 20 mEq/L by calcium buffering from bone
- **Diagnosis:**
  - Measurement of GFR
Treatment:

- **NaHCO<sub>3</sub>** therapy can be used to minimize bone buffering of acidemia and delay development of osteopenia, but this benefit must be weighed against risks of sodium retention.

- **Indications for use of alkali include:**
  - Dyspnea/inability to maintain respiratory compensation
  - Chronic kidney disease in children (at risk of growth retardation)
  - Severe acidosis with plasma HCO<sub>3</sub><sup>-</sup> less than 12 mEq/L (mmol/L)

**Treatment**

**Anion gap acidosis.**
- Treat underlying disease process
- With saline hydration, NaCl + HA → kidney excretes NaA rather than NH<sub>4</sub><sup>+</sup>
- Transition from “anion gap” to “nonanion gap” acidosis in the hydrated patient during treatment

**Lactic acidosis and ketoacidosis.**
- Treat underlying disease process
- Controversies surround use of bicarbonate-containing fluids in ketoacidosis and lactic acidosis due to potential risk of worsening intracellular acidosis and lack of clinical benefit

**Ingestions.**
- Competitive inhibition of alcohol dehydrogenase with ethanol or fomepizole for alcohol ingestions
- Indications for hemodialysis treatment under conditions of ethylene glycol, methanol, and salicylate ingestion

**Rhabdomyolysis.**
- Enhancement of myoglobin excretion with alkalization of urine with bicarbonate-containing fluids, hemodialysis

**Renal tubular acidosis.**
- Identify type of RTA by urine pH, serum potassium
- Calculate bicarbonate deficits, replacement needs, and maintenance dosing of bicarbonate in cases of RTA types I, II, and IV

**Metabolic Alkalosis**

**Causes**

- Two phases of metabolic alkalosis:
  - **Generation phase.**
    - Factors that generate a metabolic alkalosis:
      - Loss of hydrogen due to gastrointestinal losses:
        - Gastric suction
        - Vomiting
        - Antacid therapy
        - Chloride-losing diarrhea
      - Renal losses:
        - Diuretics
        - Mineralocorticoid excess
        - Hypercalcemia/milk-alkali syndrome
        - Low chloride intake
      - H<sup>+</sup> shift into cells:
        - Hypokalemia
        - Refeeding
      - Retention of bicarbonate:
        - Massive blood transfusions
        - NaHCO<sub>3</sub> administration
      - Contraction alkalosis:
        - Diuretics
        - Sweat losses in cystic fibrosis
  - **Maintenance phase.**
    - Factors that permit maintenance of metabolic alkalosis:
      - Decreased GFR (due to volume depletion or renal failure) or
      - Increased tubular reabsorption of HCO<sub>3</sub><sup>-</sup> (due to volume depletion, chloride depletion, hypokalemia, hyperaldosteronism)

**Urinary chloride measurement in diagnosis of metabolic alkalosis.**
- Urine Cl<sup>-</sup> < 10 mEq/L (mmol/L):
  - Vomiting
  - Nasogastric suction
  - Diuretics
- Urine Cl<sup>-</sup> > 20 mEq/L (mmol/L):
  - In hypertension:
    - Cushing syndrome
    - Primary hyperaldosteronism
    - Hypokalemia
    - Glucocorticoid remediable aldosteronism
    - Conditions of apparent mineralocorticoid excess
  - With normal/low blood pressure:
    - Bartter syndrome
    - Gitelman syndrome

**Treatment**
- Metabolic alkalosis with low urinary chloride:
Normal saline or ½ normal saline lowers plasma HCO₃⁻ by reversing the stimulus to renal Na⁺ retention, permitting NaHCO₃ excretion, and increasing distal Cl⁻ delivery, which promotes HCO₃⁻ secretion (“saline-responsive alkalosis”)

Metabolic alkalosis with high urinary chloride:
- Treatment of underlying disorder (eg, adrenal adenoma resection) and repletion of potassium

Respiratory Acidosis

Causes
- Inhibition of respiratory drive:
  - Opiates
  - Anesthetics
  - Sedatives
  - Central sleep apnea
  - Obesity
  - Central nervous system lesions
- Disorders of respiratory muscles:
  - Muscle weakness:
    - Myasthenia gravis
    - Periodic paralysis
    - Aminoglycosides
    - Guillain-Barré syndrome
    - Spinal cord injury
    - Acute lateral sclerosis
    - Multiple sclerosis
  - Kyphoscoliosis
- Upper airway obstruction:
  - Obstructive sleep apnea
  - Laryngospasm
  - Aspiration
- Lung disease:
  - Pneumonia
  - Severe asthma
  - Pneumothorax
  - Acute respiratory distress syndrome
  - Chronic obstructive pulmonary disease
  - Interstitial lung disease

Renal adaptation
- Elevated PCO₂ in PT leads to decreased intracellular pH, enhances H⁺ secretion in PT, leading to increased HCO₃⁻ generation over 5 days (3 to 5 mEq/L [mmol/L] HCO₃⁻ for every 10–mm Hg increase in PCO₂)

Treatment
- Ventilatory support
- NaHCO₃ therapy controversial in this disorder:
  - Perhaps beneficial in severely acidemic patient (eg, status asthmaticus) versus
  - Hazards of therapy in patients with reversible hypercapnea (eg, chronic obstructive pulmonary disease in which respiratory drive is depressed)

Respiratory Alkalosis

Causes
- Hypoxemia
  - Pulmonary diseases:
    - Pneumonia
    - Interstitial fibrosis
    - Emboli
    - Edema
  - Congestive heart failure
  - Anemia
- Stimulation of the medullary respiratory center:
  - Hyperventilation
  - Hepatic failure
  - Septicemia
  - Salicylate intoxication
  - Pregnancy
  - Neurologic disorders
- Mechanical ventilation

Symptoms
- Lightheadedness
- Paresthesias
- Cramps
- Carpopedal spasm

Renal adaptation
- Decreased PCO₂ in PT leads to increased intracellular pH, inhibits H⁺ secretion in the PT, leading to decreased HCO₃⁻ generation over 5 days (reduces serum concentration of HCO₃⁻ 3 to 5 mEq/L [mmol/L] for every 10–mm Hg decrease in PCO₂)

Treatment
- Correction of underlying disorder
- Increasing PCO₂ in inspired air (breathing into paper bag) in setting of acute respiratory alkalosis
Mixed Acid-Base Disorders

Diagnosis
- Identified by inappropriate or inadequate correction using the formulae for renal and respiratory compensation described in Table 1

Common scenarios
- Mixed respiratory acidosis and metabolic alkalosis (eg, chronic obstructive pulmonary disease and diuretic therapy)
- Mixed metabolic acidosis and metabolic alkalosis (eg, ketoacidosis and vomiting)
- Mixed respiratory alkalosis and metabolic acidosis (salicylate intoxication)

Change in serum anion gap (ΔAG)
- Use of ΔAG to determine if mixed acid-base disturbance is present
- The ΔAG = measured anion gap – expected anion gap
- The ΔAG is most useful to distinguish concomitant metabolic alkalosis and anion gap metabolic acidosis
- If ΔAG + measured bicarbonate is greater than physiologic bicarbonate concentrations (eg, 21 to 27 mEq/L [mmol/L]), an underlying metabolic alkalosis is present

ADDITIONAL READING


DISORDERS OF POTASSIUM (K)

Physiology of K Balance
Total body K determined by internal and external K balance:

Internal balance
Factors that regulate:
- Acid-base/metabolic acidosis: differences between organic (limited K shifts) and inorganic hyperchloremic acidosis
- Insulin: K moves from extracellular to intracellular sites
- Tonicity: hyperglycemia, mannitol moves K from intracellular to extracellular sites
B₂ adrenergic receptor: Catecholamines through B₂ adrenergic receptor move K into cells; ß adrenergic receptor prevents K movement from extracellular to cellular compartments

Clinical correlate: “stress hypokalemia”

External balance
Renal K physiology:
- K freely filtered
- Filtered K reabsorbed in proximal convoluted tubule and proximal straight tubule
- K added to distal loop of Henle (at least in deep glomeruli) so that, at tip of loop, fractional excretion of K (FE_K) 150% of filtered load
- K reabsorbed in ALH (Na, K2Cl cotransporter) so that, at beginning of distal convoluted tubule, FE_K 15% of filtered load
- K added to lumen of cortical collecting tubule so that, at end of this tubule, FE_K 100% of filtered load
- K secretion mediated by Na reabsorption through Na channel followed by Na extrusion by basolateral Na, K ATPase, resulting in increases in cell K and K extrusion into the lumen through K channels
- K secretion regulated by aldosterone secretion (regulated by angiotensin II and total body K) and action (regulated by 11 B-OH steroid dehydrogenase and mineralocorticoid receptor) as well as distal nephron Na delivery and concentration
- K reabsorbed by collecting tubule, through K/H exchange (regulated by decreases in total body K)
- K added to distal loop of Henle (at least in deep glomeruli) so that, at tip of loop, fractional excretion of K (FE_K) 150% of filtered load
- K reabsorbed in ALH (Na, K2Cl cotransporter) so that, at beginning of distal convoluted tubule, FE_K 15% of filtered load
- K added to lumen of cortical collecting tubule so that, at end of this tubule, FE_K 100% of filtered load
- K secretion mediated by Na reabsorption through Na channel followed by Na extrusion by basolateral Na, K ATPase, resulting in increases in cell K and K extrusion into the lumen through K channels
- K secretion regulated by aldosterone secretion (regulated by angiotensin II and total body K) and action (regulated by 11 B-OH steroid dehydrogenase and mineralocorticoid receptor) as well as distal nephron Na delivery and concentration
- K reabsorbed by collecting tubule, through K/H exchange (regulated by decreases in total body K)
- Urine K is independent of GFR above 30 mL/min (0.50 mL/s)
- Increases in urinary K are due to increases in K secretion or decreases in K reabsorption

Hypokalemia

Definition
- Serum K less than 3.5 mEq/L (mmol/L)

Causes

Normal total body K/transcellular shift.
- Alkalemia
- Insulin excess
- “Stress” (eg, asthma attack, acute coronary syndrome, drug intoxication [cocaine] or withdrawal [alcohol], ß₂ adrenergic drugs)
- Hypokalemic periodic paralysis
- Thyrotoxicosis
- Refeeding syndromes
- Barium
- Cesium hypothermia

Decreased total body K.
- Decreased K intake, or
- Increased K losses:
  - Gastrointestinal
  - Renal

Spurious.
- Extreme leukocytosis

Diagnostic approach
To decreases in total body K: use of urine K concentration, 24-hour urine K, transtubular K gradient:
- Low 24-hour urine K (<20 mEq [mmol]/d):
  - Extrarenal losses.
    - Metabolic acidosis: gastrointestinal losses
    - Normal pH: decreased intake, gastrointestinal losses
    - Metabolic alkalosis: gastrointestinal losses
  - Renal losses.
    - Metabolic alkalosis:
      - Low urine chloride (<10 mEq [mmol]/d): vomiting, diuretics
      - High urine chloride (>20 mEq [mmol]/d): hypertension:

ADDITIONAL READING
“Normal” aldosterone: Cushing syndrome, Liddle syndrome, apparent mino.
aldosteronid excess syndrome
High aldosterone: primary aldosteron.
ism, glucocorticoid remediable aldo.
steronism
Normal or low blood pressure: diuret.
ic (during therapy), severe K deple.
tion, Bartter syndrome, Gitelman syndrome

Variable pH:
- Magnesium depletion
- Anionic drugs
- Metabolic acidosis
  - RTA types I and II

Clinical manifestations
- Cardiovascular:
  - Arrhythmias
  - Digitalis toxicity
- Neuromuscular:
  - Smooth muscle:
    - Ileus
  - Skeletal muscle:
    - Weakness
    - Paralysis
    - Rhabdomyolysis
- Endocrine:
  - Glucose intolerance
- Renal/electrolyte:
  - Vasopressin resistance
  - Increased ammonia production
  - Metabolic alkalosis
- Structural changes:
  - Renal cysts
  - Interstitial changes
  - PT dilation, vacuolization

Treatment
- Estimate of K deficit: serum K may not reflect total body K
- Reverse source of K loss
- Symptomatic: intravenous K (rate, compli.
cations)
- Asymptomatic:
  - Metabolic acidosis:
    - K plus citrate, or
    - HCO3
  - Metabolic alkalosis:
    - K plus NaCl (chloride responsive)
- Role of spironolactone, amiloride (chloride resistant)
- Importance of magnesium therapy

ADDITIONAL READING
  (vol 1; section 1, Disorders of Water, Electrolytes and
  Acid-Base). Philadelphia, Current Medicine, 1998, pp 2-17
2. Weiner ID, Wingo CS: Hypokalemia: Consequences,
  11:369-375, 2000

Hyperkalemia

Definition (mmol/L)
- Serum K ≥5.0 mEq/L (mmol/L)

Causes
- Normal total body K: transcellular shift.
  - Exercise, especially in setting of β adrenerg.
ic receptor blockade and mineral acidosis
  - Hyperchloremic metabolic acidosis
  - Insulin deficiency
  - Hypertonicity
  - α adrenergic receptor stimulation
  - Tissue breakdown or ischemia, for ex.
  ample:
    - Rhabdomyolysis
    - Gastrointestinal
    - Brain
- Increased total body K.
  - Increased intake: rare as sole cause
  - Decreased renal K excretion
- Spurious.
  - Thrombocytosis
  - Leukocytosis
  - Ischemic blood draw

Diagnostic approach
To increases in total body K: use of urine K concentration, 24-hour urine K, and/or transt tub.
ular K gradient (SK/Urinal K ÷ Sosm/Uosm):

Normal to high 24-hour urinary K (>40 to 60 mEq [mmol]/d):
- Relative increase in K intake

Low 24-hour urinary K (<20 to 40 mEq [mmol]/d):
- Decrease renal K excretion:
  - GFR >20 mL/min (0.33 mL/s):
Decreased distal nephron Na delivery
Decreased mineralocorticoid production or action
Decreased total body Na
Increased total body Na:
- heart failure
- cirrhosis
Decreased production:
- Addison disease
- Isolated hypoaldosteronism (hereditary, acquired, drugs [angiotensin-converting enzyme inhibitors, heparin, nonsteroidal anti-inflammatory drugs, COX2 inhibitors], infection [human immunodeficiency virus], chronic kidney disease [diabetes, tubular interstitial diseases, others])
Decreased action:
- Hereditary (pseudohypoaldosteronism types I and II)
- Acquired (drugs [angiotensin receptor blockers, amiloride, spironolactone, triamterene] and pseudohypoaldosteronism [hereditary, acquired: sickle cell disease, renal allograft disease, obstruction])

GFR <20 mL/min (0.33 mL/s):
- Endogenous or exogenous K
- Drugs that impair K excretion

Clinical manifestations
- May be disproportionately greater than level of serum K
- Cardiovascular:
  - T-wave abnormalities
  - Lengthened segments
  - Bradycardia
- Neuromuscular:
  - Ileus
  - Paresthesias
  - Weakness
  - Paralysis
- Renal/electrolyte:
  - Decreased ammonia production
  - Metabolic acidosis

Treatment
- Who requires emergent therapy:
  - Electrocardiogram abnormalities
  - Ileus
  - Paralysis
- Emergent therapies:
  - Doses, pharmacology
  - Stabilize cell membrane: Ca
  - Shift K from extra to intracellular compartments:
    - Insulin (± glucose)
    - HCO3
    - Albuterol (B2 adrenergic receptor agonist)
  - Decrease total body K
    - K exchange resin (oral or rectal)
    - Hemodialysis
- Prevention of hyperkalemia:
  - Importance of diet
  - Recognition of drugs that decrease K secretion
  - Role of adequate distal Na delivery
  - K exchange resins

Additional reading