SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME : Pharmacology Pathology and Clinical Microbiology

II nd YEAR

TOPIC : HYPERKALEMIA AND HYPOKALEMIA

Introduction

- K+ is the major intracellular ion
- Only 2% is in the ECF at a concentration of only 4 mEq/L
- K+ is taken up by all cells via the **Na-K ATPase pump**
- K+ is one of the most permeable ion across cell membranes and exits the cells mostly via K channels (and in some cells via **K-H exchange** or **via K-Cl cotransport**)

Roles of K

- Major ion determining the resting membrane electrical potential
- Changes in K concentrations (particularly in the ECF) have marked effects on cell excitability (heart, brain, nerve,muscle)
- Major intracellular osmotically active cation and participates in ICF volume regulation (exits with Cl when cells swell)
- Critical for enzyme activities and for cell division and growth
- Intracellular K participates in acid base regulation through exchange for extracellular H and by influencing the rate of renal ammonium production

Potassium homeostasis

- External potassium balance is determined by rate of potassium intake (100 meq/day) and rate of urinary (90 meq/day) and fecal excretion (10 meq/day).
- Internal potassium balance depends on distribution of potassium between muscle, bone, liver, and RBC and the ECF

Cellular K buffering

- When K is added to the ECF, most of the added K is taken up by the cells
- If K is lost from the ECF, some K+ leaves the cells, reducing the ECF K decline
- Renal reabsorption of Na+ and secretion of K+ and H+ are stimulated by **aldosterone**
- Buffering of ECF K+ through cell uptake is impaired in the **absence** of aldosterone, insulin or of catecholamines

Cont...

- Cell K exit to the ECF increases when **osmolarity increases** (as in diabetes mellitus) and in metabolic acidosis, when it is exchanged for ECF H+
- When cells die, they release their very high K content to the ECF

Renal regulation of Potassium

- In normal function, renal K + excretion balances most of the K+ intake (about 1.5 mEq/Kg/day)
- Reabsorption of Na+ and K+ in the proximal nephrone occurs at a constant rate and is not subject to hormonal regulation
- The final concentration of Na+ and K+ in the urine is varied according to the needs of the body by processes that occur in the late distal tubule and in the cortical region of the CD

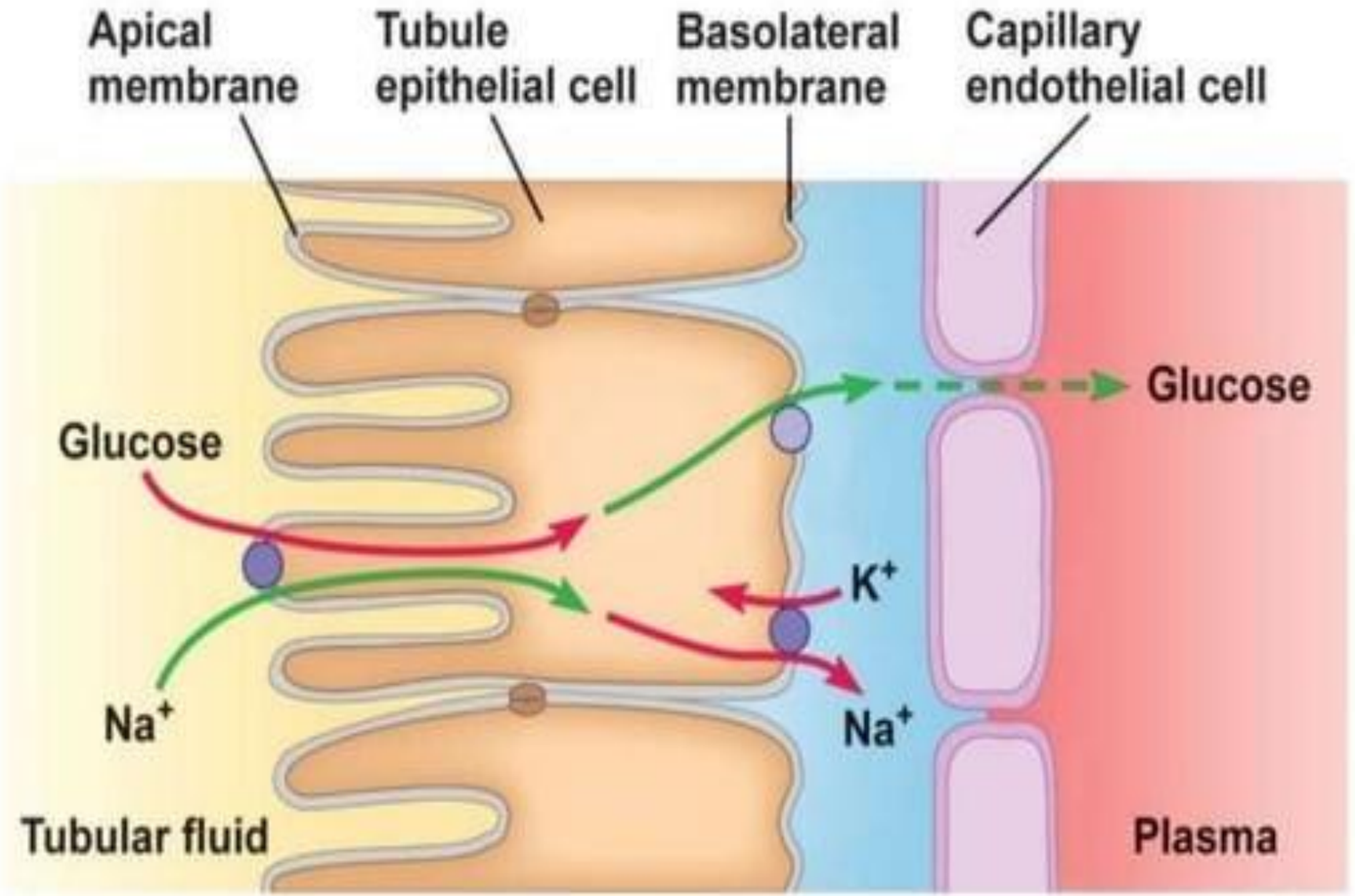
Cont...

- **Secretion** of potassium occurs in the parts of the nephron that are **sensitive to aldosterone**—that is, in the late distal tubule and cortical CD
- K+ is almost completely reabsorbed in the proximal tubule, but under aldosterone stimulation it is secreted into the cortical portion of the collecting duct
- All of the K+ in urine is derived from secretion rather than from filtration

Cont...

- In the cells of the proximal tubule, the Na+ /K+ pumps are located in the basal-lateral side of the plasma membrane but not in the apical membrane
- As a result of the action of these active transport pumps, a concentration gradient is created that favors the diffusion of Na + from the tubular fluid across the apical plasma membranes and into the epithelial cells of the proximal tubule. The Na + is then extruded into the surrounding interstitial (tissue) fluid by the Na + /K + pumps

Basolateral Na+ /K+ pumps



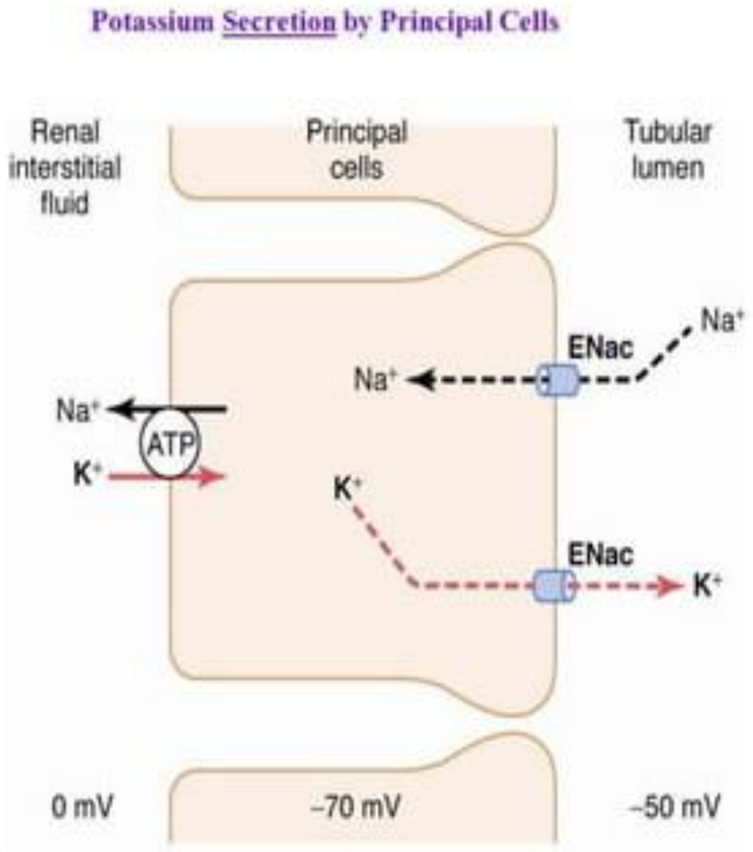
Cont...

- Along the thick ascending limb, K is reabsorbed via **Na-K-2 Cl cotransport**
- In thick ascending limb, the movement of Na+ down its electrochemical gradient from the filtrate into the cells powers the inward secondary active transport of K+ and Cl–
- This occurs in a ratio of 1 Na+ to 1 K+ to 2 Cl–
- The Na + is then actively transported across the basolateral membrane to the interstitial fluid by the Na+/K+ pumps

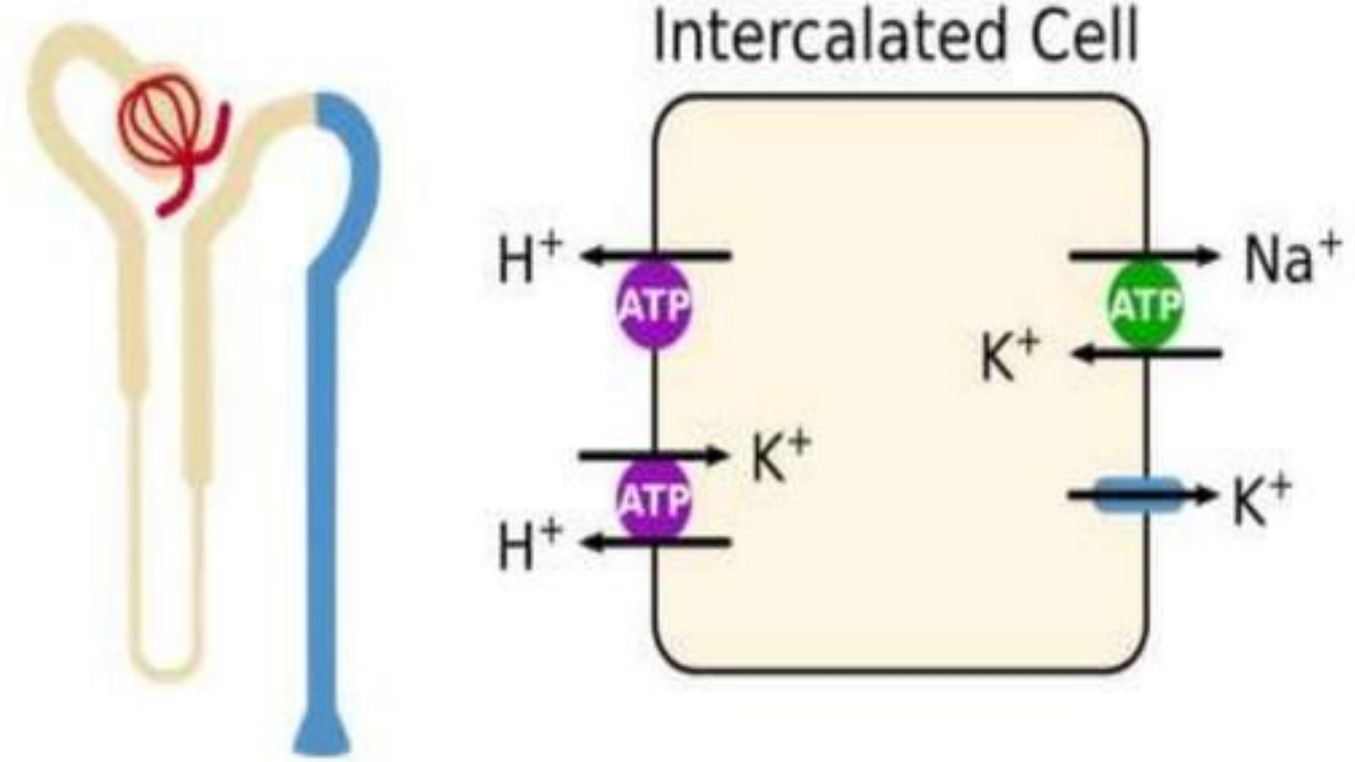
Cont...

- Cl – follows the Na + passively because of electrical attraction, and K + passively diffuses back into the filtrate
- Along the distal tubule and collecting ducts, there is net secretion of K which is stimulated by **aldosterone** and when there is **dietary K excess**
- In the CD, K+ secretion is by the **principal cells** (via luminal K+ channels and basolateral Na-K ATPase) and K+ **reabsorption** is by the alpha **intercalated cells** via a luminal **H-K ATPase**

Potassium secretion by principle cells



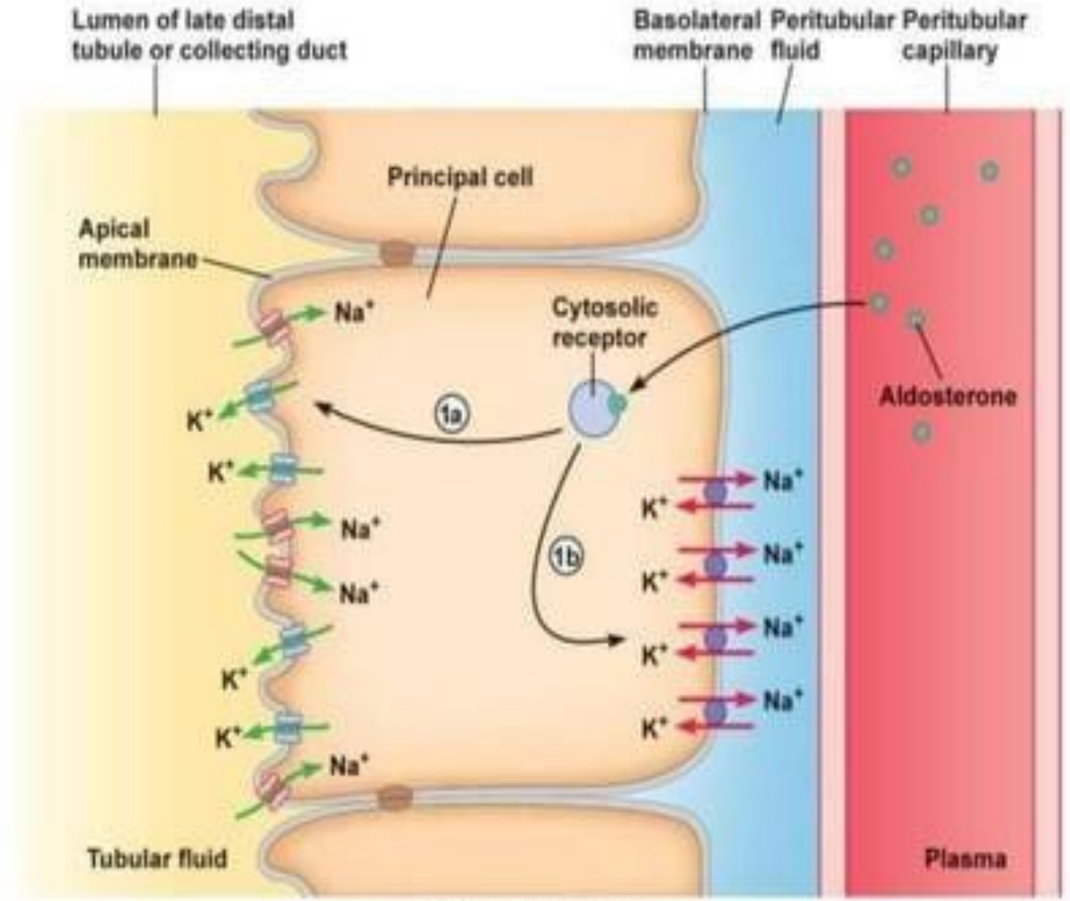
Potassium secretion by α-intercalated cells (H-K ATPase)



Determinants of K^+ secretion

- Two principal determinants of K^+ secretion are **mineralocorticoid activity (aldosterone)** and increased distal delivery of **Na^+ and water**
- Aldosterone increases intracellular K^+concentration by;
  i. Stimulating the activity of the Na^+/K^+/ATPase in the basolateral membrane
  ii. Stimulating Na^+ reabsorption across the luminal membrane, increasin the electronegativity of the lumen, thereby increasing the electrical gradient favoring K^+ secretion
  iii. Direct effect on the luminal membrane to increase K^+ permeability

Effect of Aldosterone



Potassium and blood pH

- The plasma K+ concentration indirectly affects the plasma H+ concentration (pH)
- Changes in plasma pH likewise affect the K+ conc.
- When the extracellular H+ concentration increases, some of the H+ moves into the cells and causes cellular K+ to diffuse outward into the extracellular fluid. The plasma concentration of H + is thus decreased while the K+ increases, helping to reestablish the proper ratio of these ions in the ECF

Cont...

- A similar effect occurs in the cells of the late distal tubule and cortical CD, where, positively charged ions (K+ and H+) are secreted in response to the negative polarity produced by reabsorption of Na+
- Acidosis increases the secretion of H+ and reduces the secretion of K+ into the filtrate
- Acidosis may thus be accompanied by a rise in blood K+ (hyperkalemia)

Cont...

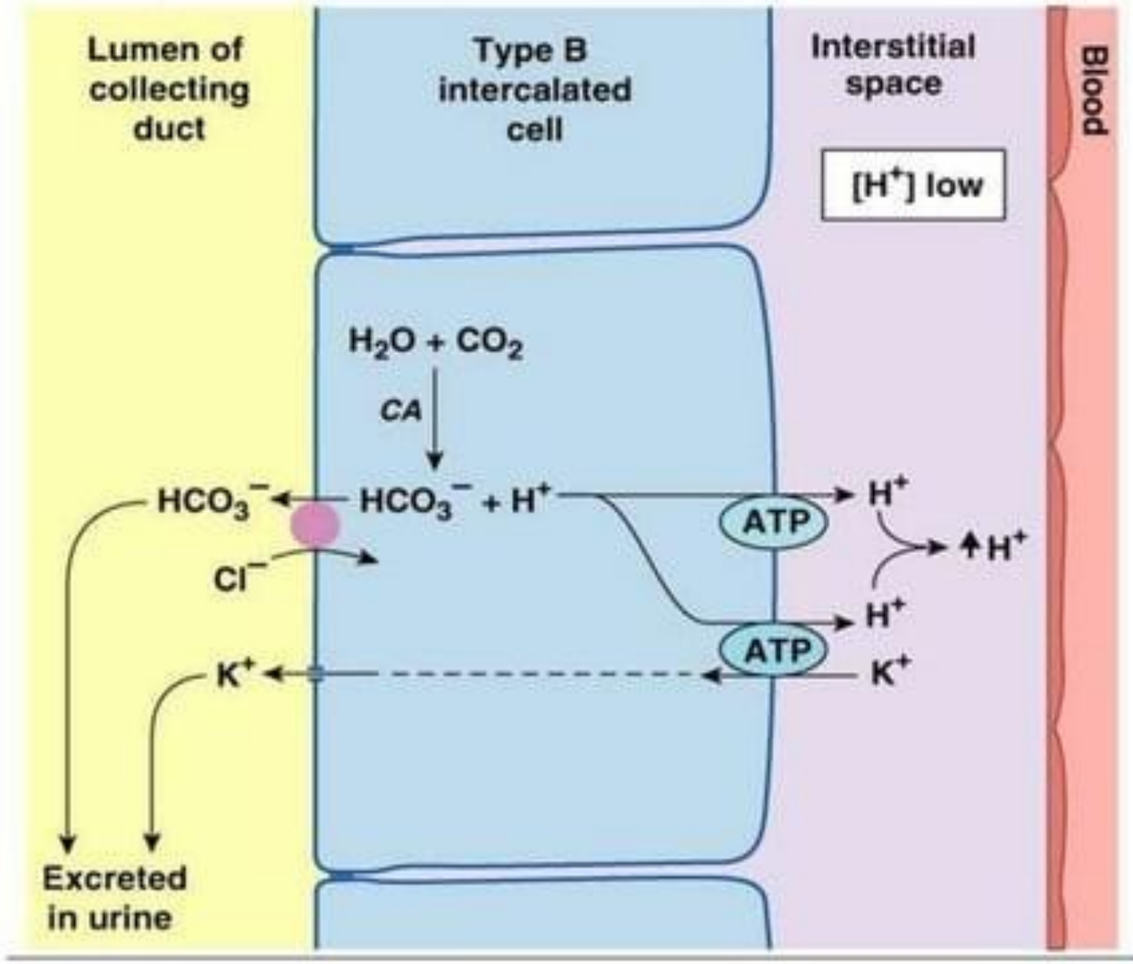
- By contrast, alkalosis (lowered plasma H + conc.) increases the renal secretion of K + into the filtrate, and thus the excretion of K + in the urine
- If, on the other hand, hyperkalemia is the primary problem, there is an increased secretion of K + and thus a decreased secretion of H +
- Hyperkalemia can thus cause an increase in the blood concentration of H + and acidosis

Cont...

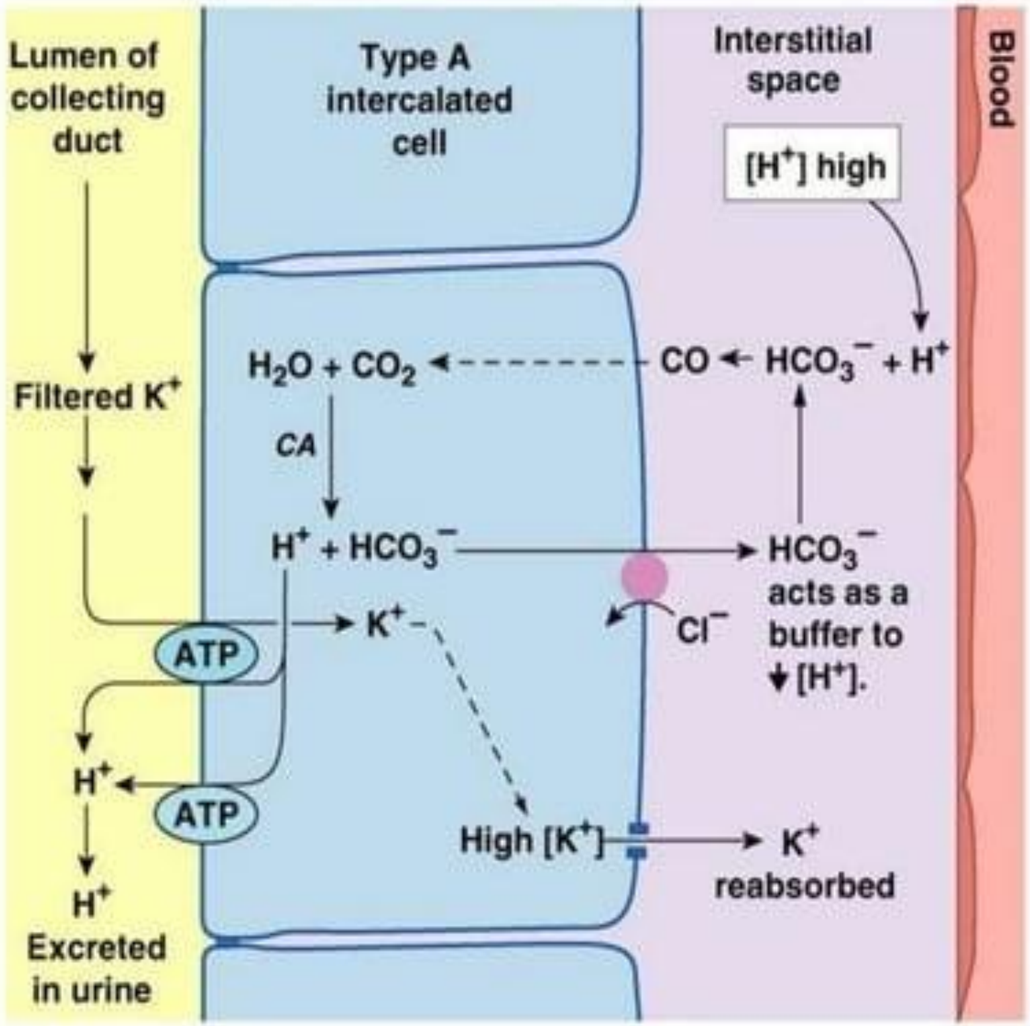
- Aldosterone indirectly stimulates the secretion of H+, as well as K+, into the cortical collecting ducts
- Therefore, abnormally high aldosterone secretion, as occurs in primary aldosteronism, or Conn's syndrome, results in both hypokalemia and metabolic alkalosis
- Conversely, abnormally low aldosterone secretion, as occurs in Addison's disease, can produce hyperkalemia accompanied by metabolic acidosis

In alkalosis;

(b) Type B intercalated cells function in alkalosis. HCO_3^- **and** K^+ **are excreted;** H^+ **is reabsorbed.**



In acidosis;


Lumen of collecting duct
Type A intercalated cell
Interstitial space
Blood
[H+] high
H2O + CO2
CO
HCO3− + H+
CA
Filtered K+
H+ + HCO3−
HCO3− acts as a buffer to ↓[H+].
Cl−
K+
ATP
H+
ATP
High [K+]
K+ reabsorbed
H+ Excreted in urine

HYPERKALEMIA

- Defined as a potassium level > **5.5 mmol/L**
- Common laboratory abnormality complicating between 1.1% and 10.0% of all hospital admissions
- Occurs in as many as 11% of patients using angiotensin-converting enzyme inhibitors (ACEIs)
- Without warning, hyperkalemia may cause nearly any dysrhythmia

Causes of Hyperkalemia

- **Excessive exogenous potassium load** (Increased Intake)
  - *Potassium supplements (IV or Oral)*
  - *Excess in diet*
  - *Salt substitutes (e.g. potassium salts of penicillin)*
- **Excessive endogenous potassium load** (Increased Production)
  - *Haemolysis*
  - *Rhabdomyolysis*
  - *Extensive burns*
  - *Tumor Lysis Syndrome*
  - *Intense physical activity*
  - *Trauma (especially crush injuries and ischaemia)*

Cont...

- **Redistribution** (Shift from intracellular to extracellular fluid)
  - *Acidosis (metabolic or respiratory)*
  - *Insulin deficiency*
  - *Drugs*
    - *Succinylcholine*
    - *Beta-blockers*
    - *Digoxin (acute intoxication or overdose)*
  - *Hyperkalemic familial periodic paralysis*

Cont...

- **Diminished potassium excretion** (Decreased Excretion)
  - *Decreased GFR (eg, acute or end-stage chronic renal failure)*
  - *Decreased mineral corticoid activity*
  - *Defect in tubular secretion (eg, renal tubular acidosis IV)*
  - *Drugs (eg, NSAIDs, cyclosporine, potassium-sparing diuretics, ACE Inhibitors)*

Causes of pseudohyperkalaemia (Factitious, spurious)

Related to collection and storage of specimen:

- Difficulty in collecting sample
- Patient clenched fist when sample was taken
- Sample was shaken or squirted through needle into collection tube
- Contamination with anticoagulant from another sample (potassium EDTA)
- Cooling
- Deterioration of specimen due to length of storage

Clinical manifestations of hyperkalemia

- Patients may have sxs related to the cause of the hyperkalemia (eg. polyuria and polydipsia with uncontrolled diabetes)
- Serious manifestations usually occur when the serum K+ is ≥7.0 meq/L (chronic hyperkalemia) or possibly at lower levels with an acute rise in serum potassium
- Cardiac manifestations;

  The progression and severity of ECG changes do not correlate well with the serum potassium concentration

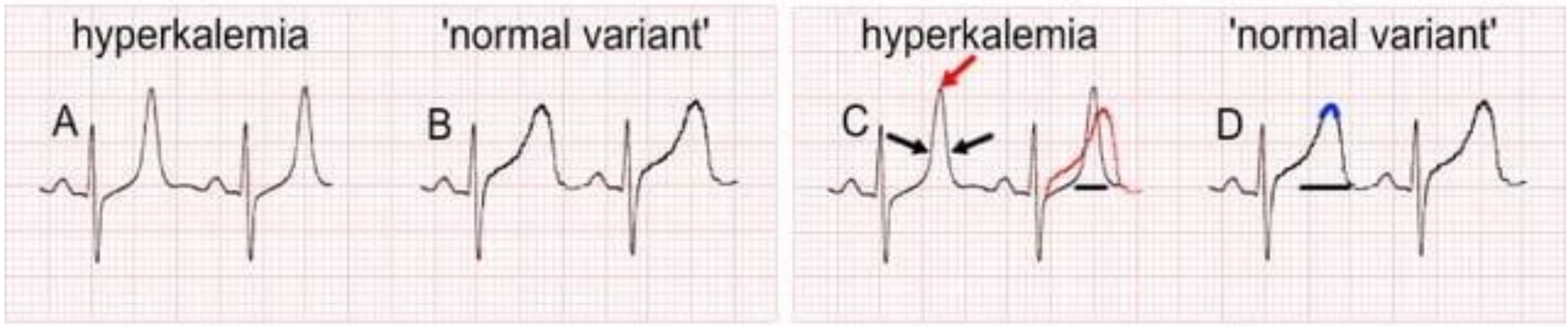
ECG changes;

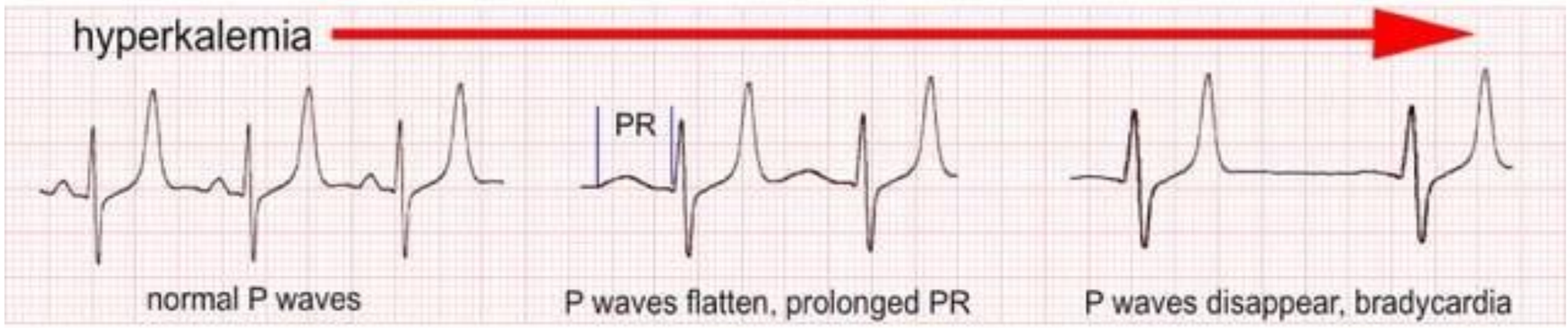
Initial changes;

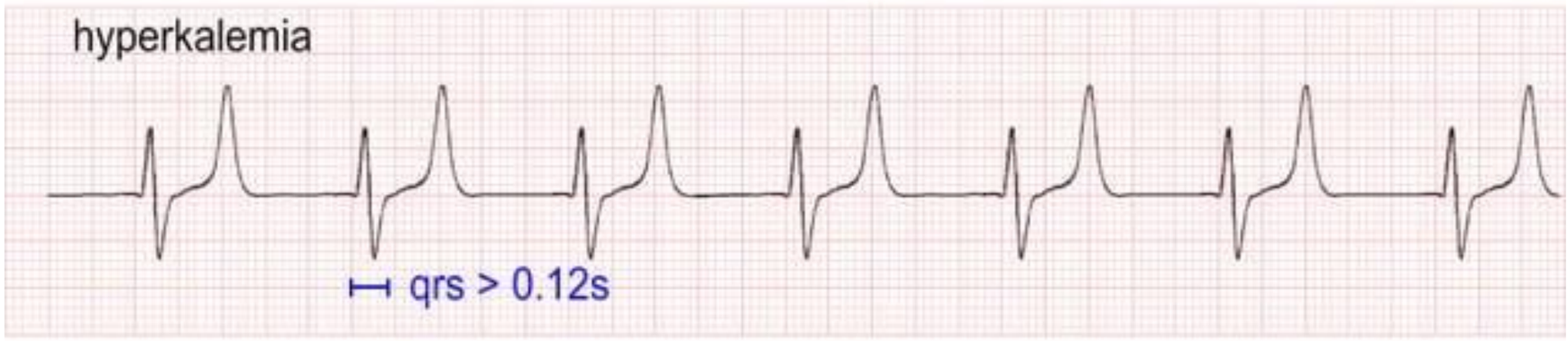
- A tall picked and symmetrical T wave with a narrow base
- Shortened QT interval
- ST-segment depression

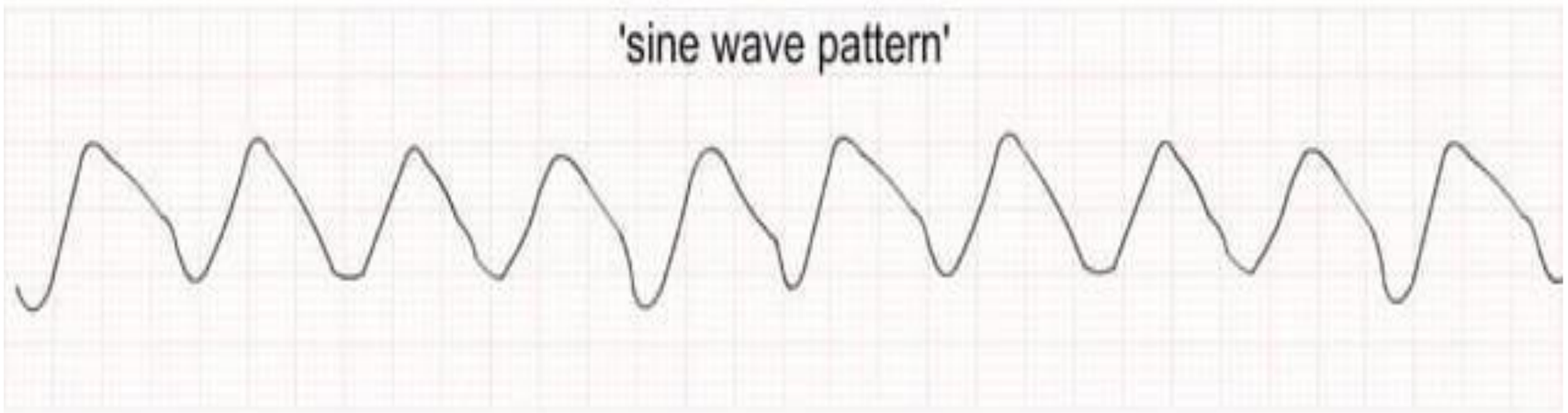
At levels > 6.5

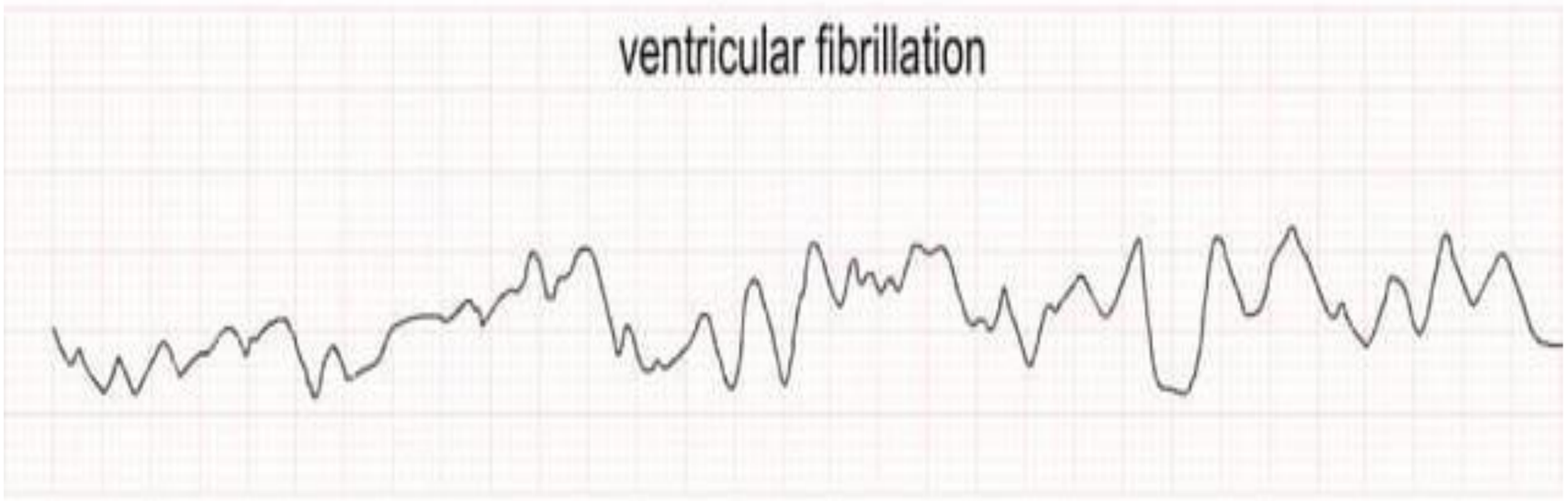
- Prolonged PR interval
- Widening of the QRS
- Amplified R wave
- Decreased or disappearing P wave
- The progressively widened QRS eventually merges with the T wave, forming a **sine wave pattern**. Ventricular fibrillation or asystole follows


hyperkalemia
'normal variant'
A
B
hyperkalemia
'normal variant'
C
D


hyperkalemia
PR
normal P waves
P waves flatten, prolonged PR
P waves disappear, bradycardia


hyperkalemia
qrs > 0.12s


'sine wave pattern'


ventricular fibrillation

Cont...

- Severe muscle weakness or paralysis;
- ✓ Ascending muscle weakness (can progress to flaccid paralysis, mimicking Guillain-Barré)
- ✓ Sphincter tone and cranial nerve function are typically intact
- ✓ Respiratory muscle weakness is rare

Treatment of Hyperkalemia

When arrhythmias are present, IV calcium is effective in treating arrhythmia

- Inhaled beta-agonists, nebulised beta-agonists, and intravenous (IV) insulin-and-glucose were all effective
- The combination of nebulised beta agonists with IV insulin-and-glucose is more effective than either alone
- Dialysis is effective

Cont...

Treatment	Usual dose	Route of administration	Onset/duration	Expected result
Calcium gluconate	1 g (4.4 mEq)	IV over 5 min	1-2/10-30 min	Reversal of cardiac toxicity
Calcium chloride	1 g (13.5 mEq)	Central IV over 5-10 min	1-2/10-30 min (Note: no effect on K+ levels)	
Insulin (regular)	1 unit/3-5 g dextrose	IV bolus or infusion	10-20 min/2-6 h	Shift of K+
Dextrose	50 mL D50W (25 g)	IV over 5 min	30 min/2-6 h	Shift of K+ intracellularly
	0.5-1.0 L D10W	IV over 1-2 h		Maintains blood glucose
				Avoid if hyperglycemic
Salbutamol/albuterol	0.5% 10-20 mg	Nebulized over 10 min (diluted)	30 min/1-2 h	Shift of K+
		Not as monotherapy		
Sodium bicarbonate	50-100 mEq	IV bolus or infusion	30-60 min/2-6 h	Shift of K+ intracellularly
		Effects unreliable		
Sodium polystyrene sulfonate	15-60 g	Orally or rectally	1-6 h/variable	Nonrenal elimination of K+
Furosemide	20-80 mg	IV bolus or infusion	5-30 min/2-6 h	Renal elimination of K+
Hemodialysis	–	–	Immediate/variable	Increased elimination of K+

HYPOKALEMIA

- Generally defined as a serum potassium level of < **3.5 mEq/L** (3.5 mmol/L)
- Moderate 2.5 – 3.0 mEq/L
- Severe < 2.5 mEq/L
- Low serum potassium concentration has been found in 10 to 40 percent of patients treated with thiazide diuretics
- The first step in the management of hypokalemia is to review the patient's drug record

Risk Factors

1. **Increased potassium excretion** (commonest mechanism)

- *Mineralocorticoid excess*

-Endogenous: Primary hyperaldosteronism, Cushing Syndrome

-Exogenous; Steroid therapy for immunosuppression, Hypomagnesemia (likely from a hypomagnesemia-induced decrease in tubular reabsorption of potassium eg; in alcoholism)

Cont...

- Hyperreninism from renal artery stenosis
- Osmotic diuresis: Mannitol and hyperglycemia
- Increased gastrointestinal losses
- Genetic disorders; Congenital adrenal hyperplasia, Bartter syndrome, Gitelman syndrome, SeSAME syndrome

Cont...

- **Drugs;**
- Diuretics: Increased collecting duct permeability or increased gradient for potassium secretion
- High-dose penicillins
- Antifungal agents (amphotericin B, azoles)
- Gentamicin
- Ephedrine
- Beta-agonist intoxication
- Verapamil

Cont...

2. A shift of potassium from the extracellular to the intracellular space

- Alkalosis (metabolic or respiratory)
- Insulin/glucose administration
- Intensive beta-adrenergic stimulation
- Hypokalemic periodic paralysis
- Thyrotoxic periodic paralysis
- Refeeding: This is observed in prolonged starvation, eating disorders, and alcoholism
- Hypothermia

Cont...

3. Inadequate potassium intake

- Eating disorders : Anorexia, bulimia, starvation
- Hospitalization: Potassium-poor TPN

NB; Renal loss Vs GI renal loss of potassium;

- **Renal loss**; Urine **K:Cr > 1.5**
- **GI loss**; Urine **K:Cr < 1.5**

  eg; dirrhoea, laxatives

Clinical presentation

- Severity is proportionate to the degree and duration of the reduction in serum potassium
- Symptoms generally do not become manifest until the serum potassium is below 3.0 meq/L (unless the serum potassium falls rapidly)
- Symptoms usually resolve with correction of the hypokalemia

Cont...

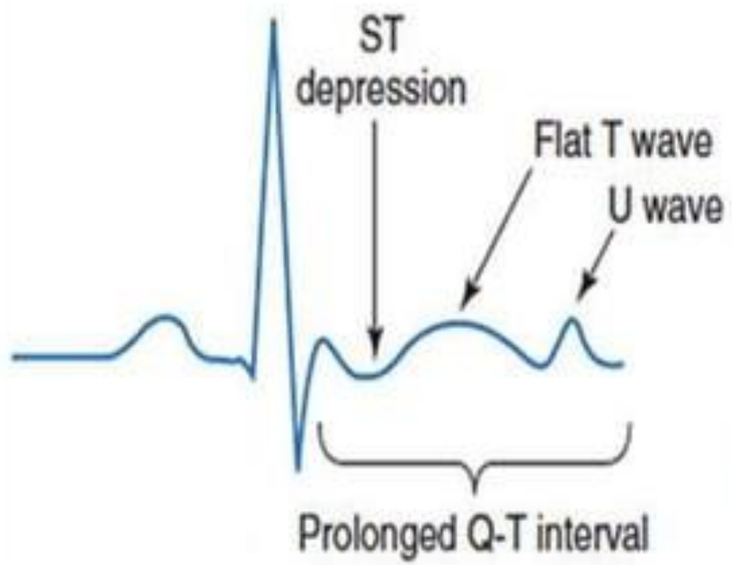
- Severe muscle weakness (ascending, and can worsen to the point of paralysis)
- Muscle cramps, rhabdomyolysis, and myoglobinuria (Decreased potassium release due to profound hypokalemia can diminish blood flow to muscles during exertion, leading to ischemic rhabdomyolysis)
- Respiratory muscle weakness (Respiratory failure)
- Involvement of gastrointestinal muscles (ileus and its associated symptoms of distension, anorexia, nausea, and vomiting)

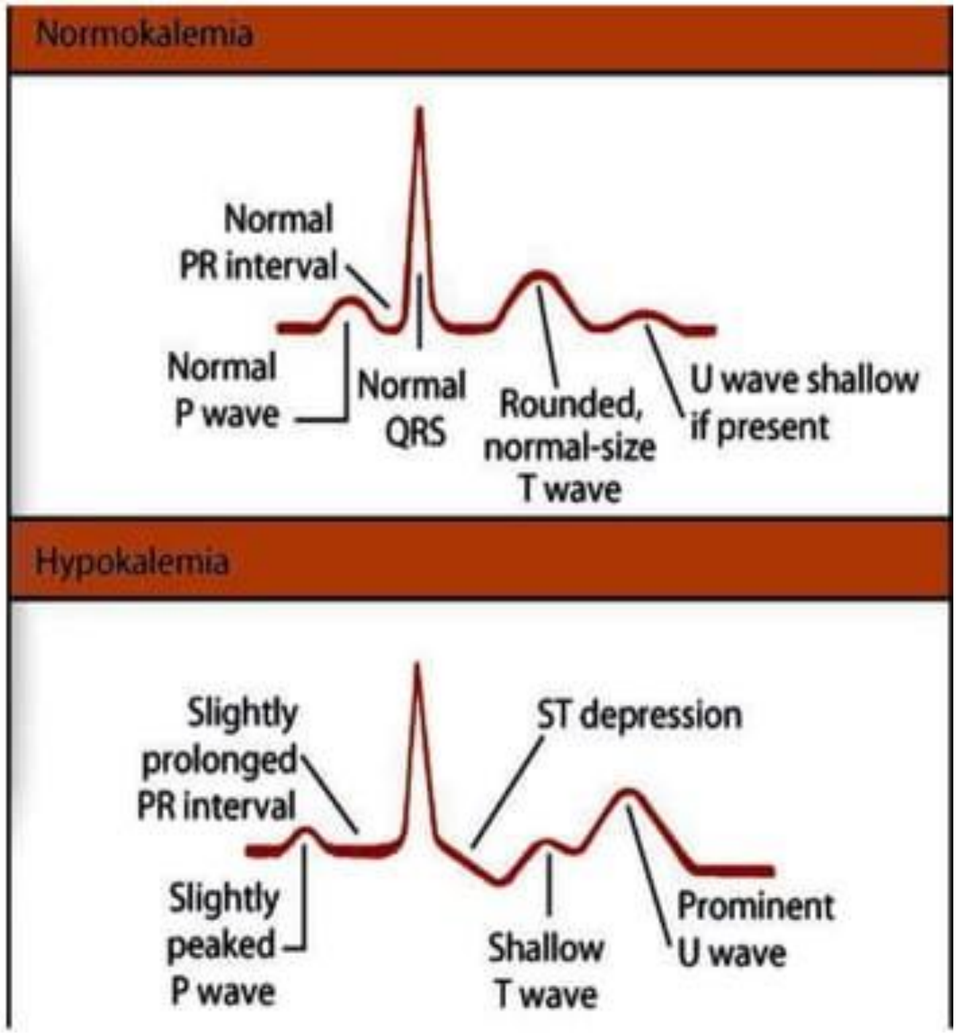
Cont...

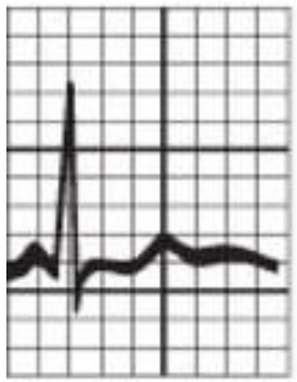
- Glucose intolerance (Hypokalemia reduces insulin secretion)
- Renal abnormalities;
  - ✓ Impaired concentrating ability
  - ✓ Increased ammonia production
  - ✓ Increased bicarbonate reabsorption
  - ✓ Altered sodium reabsorption
  - ✓ Hypokalemic nephropathy
  - ✓ Elevation in blood pressure

Cont...

- Cardiac arrhythmias and ECG abnormalities (usually at levels < ***2.5 meq/L***);
- ✓ Small or absent T waves
- ✓ Prominent U waves
- ✓ First or second degree AV block
- ✓ Slight depression of the ST segment
- ✓ Sometimes slight to marked QT-prolongation: torsades and VF can be induced


ST
depression
Flat T wave
U wave
Prolonged Q-T interval


Normokalemia
Normal
PR interval
Normal
P wave
Normal
QRS
Rounded,
normal-size
T wave
U wave shallow
if present
Hypokalemia
Slightly
prolonged
PR interval
Slightly
peaked
P wave
ST depression
Shallow
T wave
Prominent
U wave



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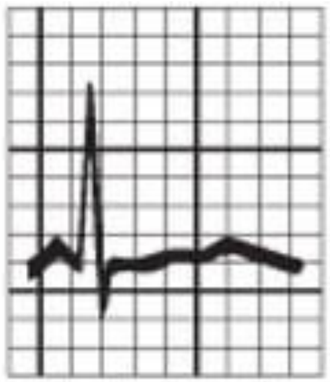

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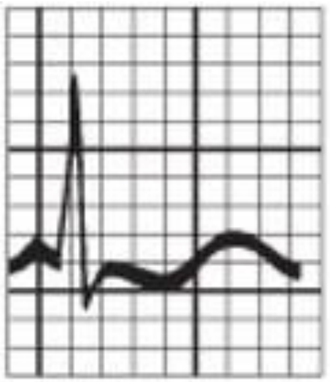

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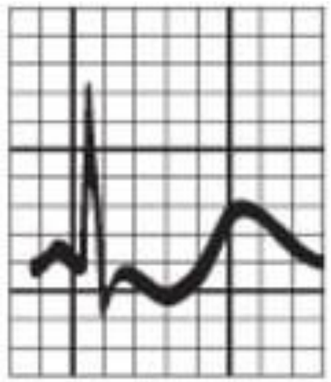

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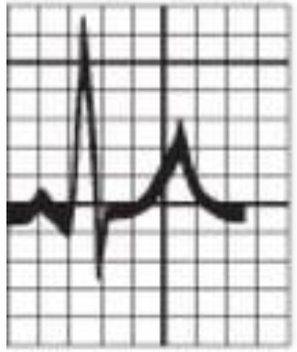
Hypokalemia



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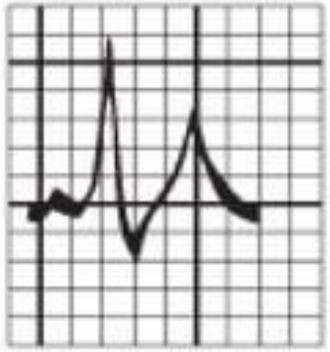

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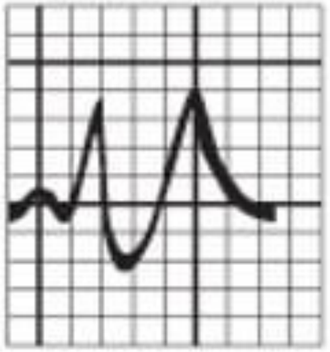

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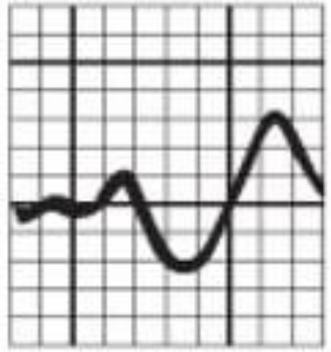

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Hyperkalemia

Management

- Oral potassium is safer, because potassium enters the circulation more slowly
- If IV, slowly, and the patient's cardiac rhythm should be monitored
- Give over a period of days to weeks to correct losses fully
- **Potassium chloride**: recommended, effective
- **Potassium bicarbonate**: only recommended when potassium depletion occurs in the setting of metabolic acidosis
- Ensure adequate dietary potassium intake

Thank You For Your Attention!!!

Foods High in Potassium