HYPERKALEMIA

APPROACH & MANAGEMENT

Dr UMAR

PHYSIOLOGY

- Potassium is a major intracellular cation
- Total body K+ content in a normal adult -**3000-4000mEq**
- 98% Intracellular , 2% in ECF
- Normal homeostatic mechanisms maintain the serum K level within a narrow range (3.5-5.0 mEq/L).

- The primary mechanisms maintaining this balance are the buffering of ECF potassium against a large ICF potassium pool (via the Na-K pump)

- Na-K ATPase pump actively transports Na+ out of the cell and K+ into the cell in a 3:2 ratio

- **Renal excretion – Major route of excess K+ elimination**
- Approx 90% of K+ excretion occurs in the urine,

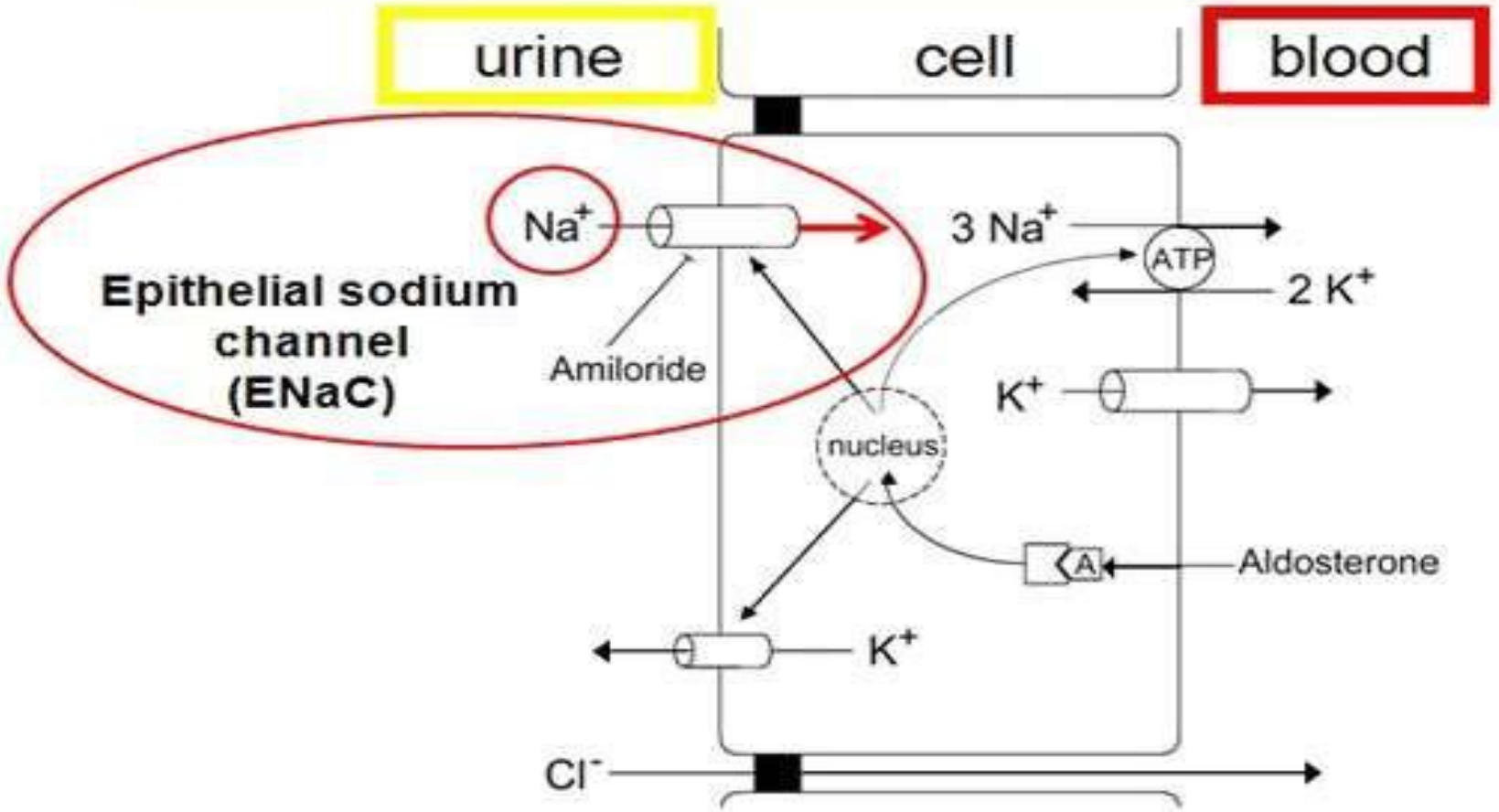
- less than 10% excreted through sweat or stool.

- Within the kidneys, K+ excretion occurs mostly in the principal cells of the cortical collecting duct (CCD).

- Urinary K+ excretion depends on :

1. **luminal Na+** delivery to the DCT and the CCD,
2. effect of **Aldosterone** and other adrenal corticosteroids with mineralocorticoid activity.

Aldosterone-sensitive distal nephron



Factor	Effect on Plasma K^+	Mechanism
Aldosterone	Decrease	Increases sodium resorption, and increases K^+ excretion
Insulin	Decrease	Stimulates K^+ entry into cells by increasing sodium efflux (energy-dependent process)
Beta-adrenergic agents	Decrease	Increases skeletal muscle uptake of K^+
Alpha-adrenergic agents	Increase	Impairs cellular K^+ uptake
Acidosis (decreased pH)	Increase	Impairs cellular K^+ uptake
Alkalosis (increased pH)	Decrease	Enhances cellular K^+ uptake
Cell damage	Increase	Intracellular K^+ release
		Cell membrane

HYPERKALEMIA

- Defined as a plasma potassium level of >5.5 mEq/L

- **Severe hyperkalemia when serum potssium Levels are >6.0meq/L**

decrease in renal excretion is the most frequent cause

- PSEUDOHYPERKALEMIA
- Artificial increase in serum potassium during or after venipuncture
- Mainely occurs due to marked increase in muscle activity durin venipuncture
- Marked increase in cellular elements(thrombocytosis,leucocytosis,erythrocytosis)
- Cooling of blood followin venipuncture is another cause
- Genetic causes causing increase in passive potassium permeability for erythrocytes

II. Intra- to extracellular shift

- **Acidosis** – Uptake of H+, efflux of K+
  NAGMA

- **Hyperosmolality**; hypertonic dextrose, mannitol, - Solvent Drag effect

- **β2-Adrenergic antagonists** (noncardioselective agents)
  Suppresses catecholamine stimulated renin release- in turn aldosterone synthesis

- **Digoxin** and related glycosides (yellow oleander, foxglove, bufadienolide)- Inhibits Na/K ATPase

- Hyperkalemic periodic paralysis- Episodic attack of muscle weakness asso with Hyper k+. Na Muscle channelopathy

- Lysine, arginine, and ε-aminocaproic acid (structurally similar, positively charged)

- Succinylcholine; depolarises Muscle cells, Efflux of K+ through AChRs . Contraindicated in thermal trauma, neuromuscular injury, disuse atrophy, mucositis, or prolonged immobilization- upregulated AChRs

- Rapid tumor lysis / Rhabdomyolysis

- III. **Inadequate excretion**

- A. **Inhibition of the renin-angiotensin-aldosterone axis**;

  (↑ risk of hyperkalemia when these drugs are used in combination

- Angiotensin-converting enzyme (ACE) inhibitors

- Renin inhibitors; aliskiren

  (in combination with ACE inhibitors or angiotensin receptor blockers [ARBs])

- Angiotensin receptor blockers (ARBs)

- Blockade of the mineralocorticoid receptor:
  - spironolactone, eplerenone,

- Blockade of the epithelial sodium channel (ENaC): amiloride, triamterene, trimethoprim, pentamidine, nafamostat

B. **Decreased distal delivery**

- Congestive heart failure

- Volume depletion

C. Hyporeninemic hypoaldosteronism

- Tubulointerstitial diseases:
  SLE, sickle cell anemia, obstructive uropathy
- Diabetes, diabetic nephropathy
- Drugs: nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase 2 (COX2) inhibitors, β-blockers, cyclosporine, tacrolimus

- Chronic kidney disease, advanced age

- Pseudohypoaldosteronism type II: defects in WNK1 or WNK4 kinases, Kelch-like 3 (KLHL3), or Cullin 3 (CUL3)

In The above said conditions –most Pt will be volume expanded- secondary increse in circulating ANP that inhibit both Renal renin release and adrenal aldosterone release

D. **Renal resistance to mineralocorticoid**

- Tubulointerstitial diseases:

  SLE, amyloidosis, sickle cell anemia, obstructive uropathy, post–acute tubular necrosis

- Hereditary:

  pseudohypoaldosteronism type I; defects in the mineralocorticoid receptor *or the epithelial sodium channel (ENaC)*

E. **Advanced renal insufficiency**

- Chronic kidney disease
- Acute oliguric kidney disease

PRIMARY ADRENAL INSUFFICENCY

- Autoimmune: Addison's disease, polyglandular endocrinopathy
- Infectious: HIV, cytomegalovirus, tuberculosis, disseminated fungal infection
- Infiltrative: amyloidosis, malignancy, metastatic cancer
- Drug-associated: heparin, low-molecular-weight heparin
- Hereditary: adrenal hypoplasia congenita, congenital lipoid adrenal hyperplasia, aldosterone synthase deficiency
- Adrenal hemorrhage or infarction, including in antiphospholipid syndrome

pesudoHypoaldosteronism type1

DISEASE OF INFANCY

AUTOSOMAL RECESSIVEFORM

mutations in epithelial sodium channels (opposite to liddles syndrome)

AUTOSOMAL DOMINANT FORM

mutations affecting the mineralocorticoid receptors

SYMPTOMS

- Hyponatrenia,volume depletion,hyperkalemia

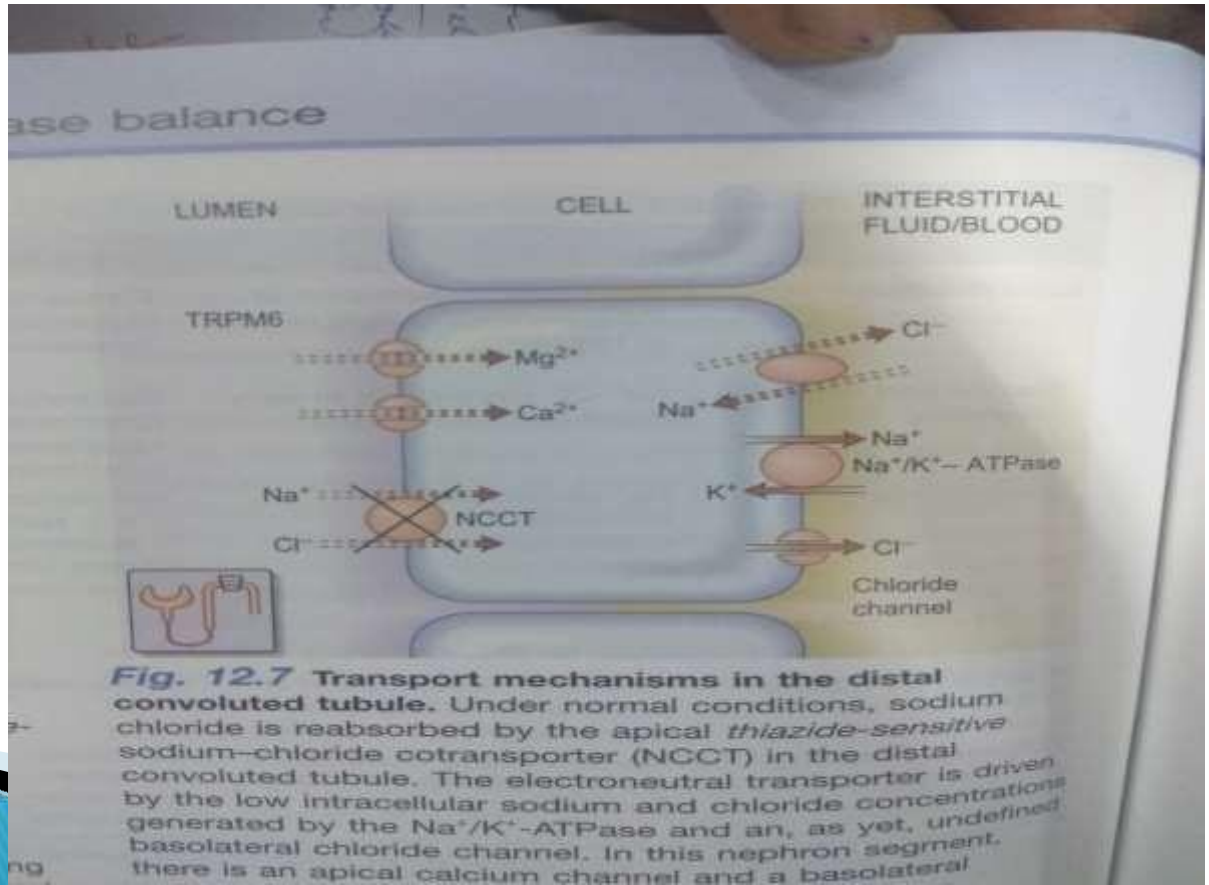


Fig. 12.7 **Transport mechanisms in the distal convoluted tubule.** Under normal conditions, sodium chloride is reabsorbed by the apical *thiazide-sensitive* sodium–chloride cotransporter (NCCT) in the distal convoluted tubule. The electroneutral transporter is driven by the low intracellular sodium and chloride concentrations generated by the Na^+/K^+-ATPase and an, as yet, undefined basolateral chloride channel. In this nephron segment, there is an apical calcium channel and a basolateral

pseudoHypoaldosteronism type2(gordons syndrome)

- Opposite to gittlemans syndrome
- Increased sensitivity of sodium reabsorption to thiazide sensitive sodium chloride cotransporter(NCCT)
- SYMPTOMS
- Retension of sodium causing hypertension,volume expansion,low renin aldosterone,hyperkalemia,metabolic acidosis

- **Clinical Features**
- **Most of Hyperkalemic individuals are asymptomatic.**

- If present - symptoms are nonspecific and predominantly related to muscular or cardiac functions.

- The most common - weakness and fatigue.
- Occasionally, frank muscle paralysis or shortness of breath.

- Patients also may complain of palpitations or chest pain.
- Arrythmias occur- Sinus Brady, Sinus arrest, VT, VF, Asystole

- Patients may report nausea, vomiting, and paresthesias

- **ECG Changes**

- ECG findings generally correlate with the potassium level,

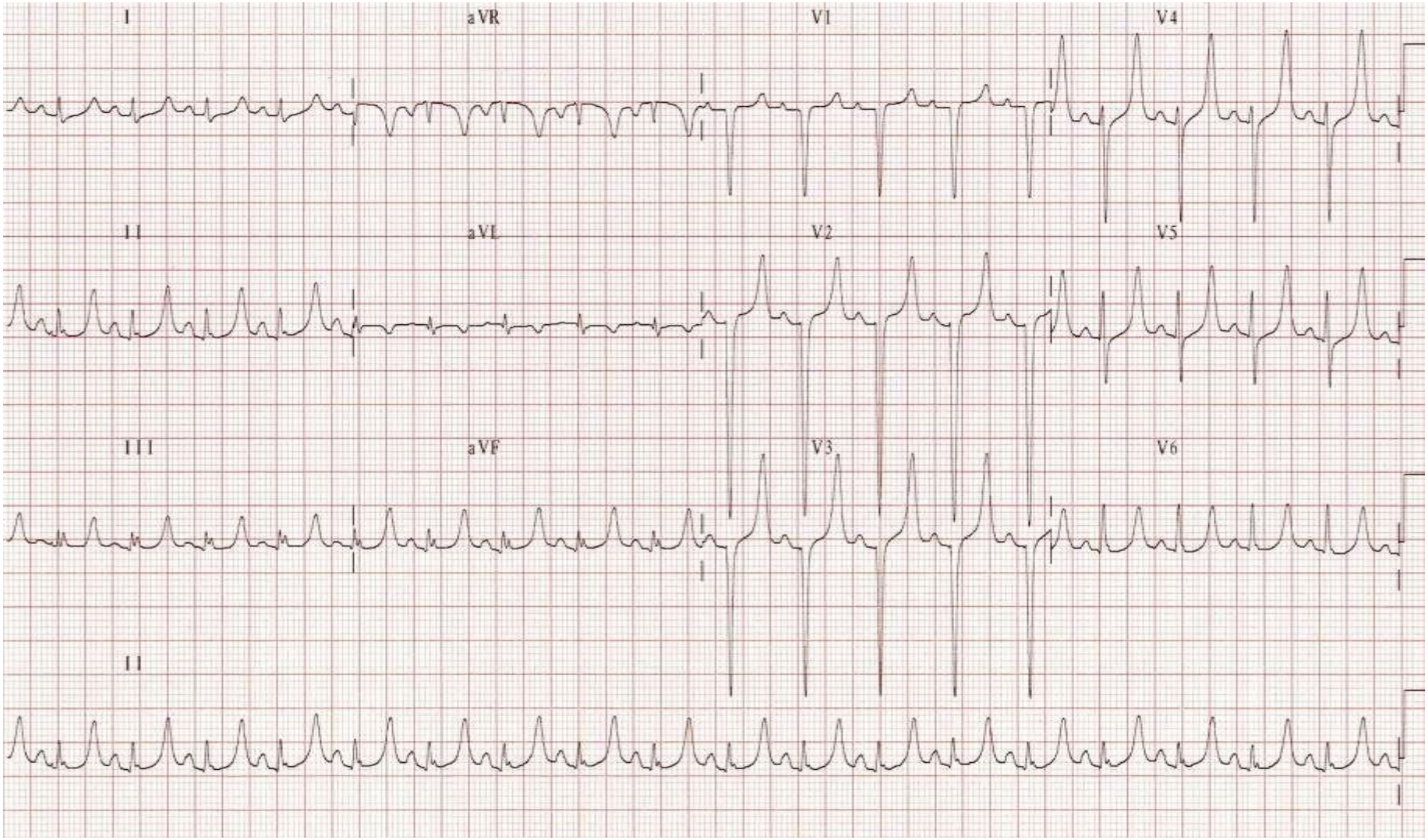
- Potentially life-threatening arrhythmias - occur without warning at almost any level of hyperkalemia.

- In patients with organic heart disease and an abnormal baseline ECG, bradycardia may be the only new ECG abnormality.

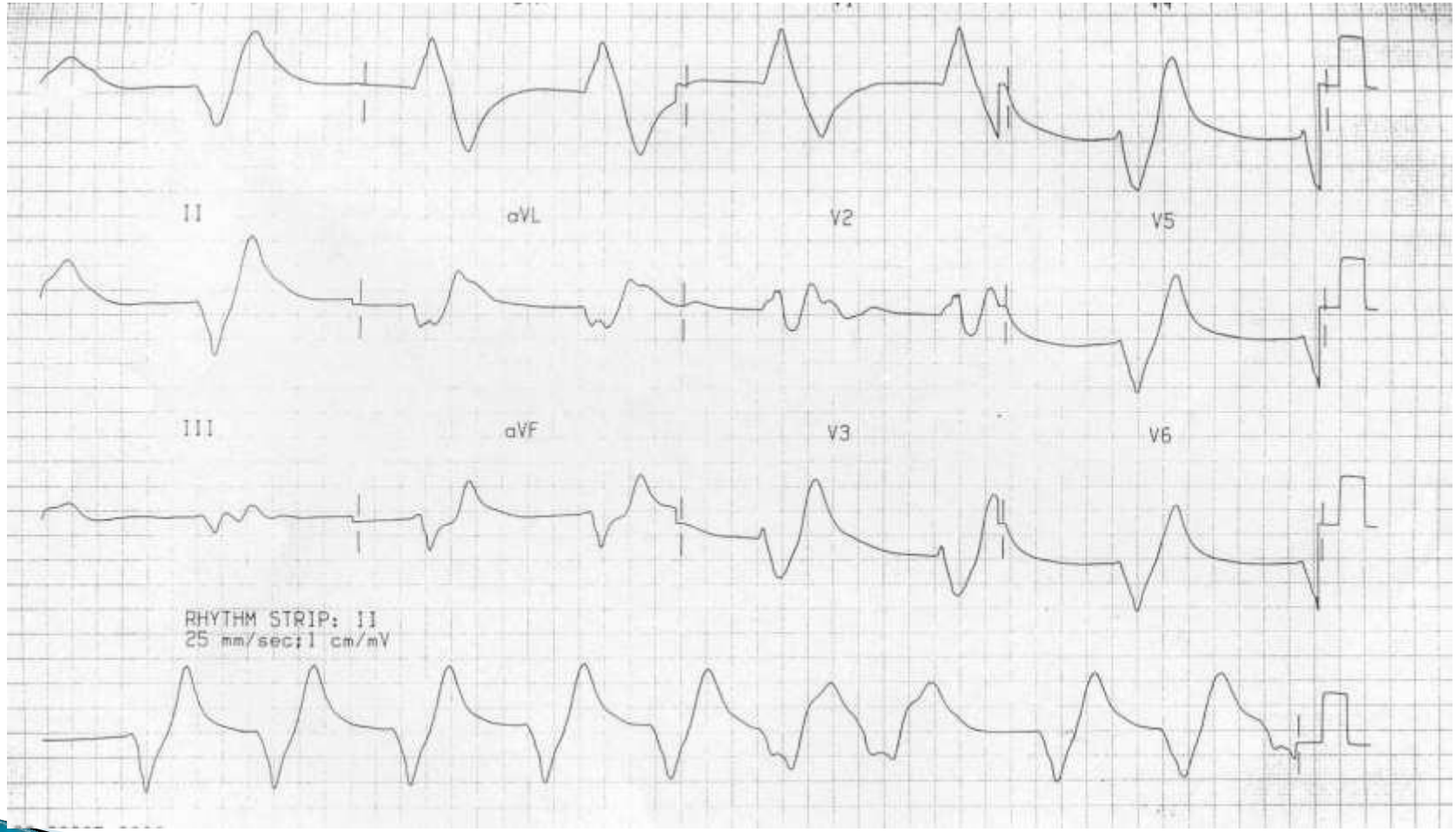
Hyperkalemia

- ECG changes-

Serum potassium	Typical ECG appearance	Possible ECG abnormalities
Mild (5.5-6.5 mEq/L)		Peaked T waves Prolonged PR segment
Moderate (6.5-8.0 mEq/L)		Loss of P wave Prolonged QRS complex ST-segment elevation Ectopic beats and escape rhythms
Severe (>8.0 mEq/L)		Progressive widening of QRS complex Sine wave Ventricular fibrillation Asystole Axis deviations Bundle branch blocks Fascicular blocks



- Tall, symmetrically tented T waves. *This patient had a serum K+ of 7.0.*



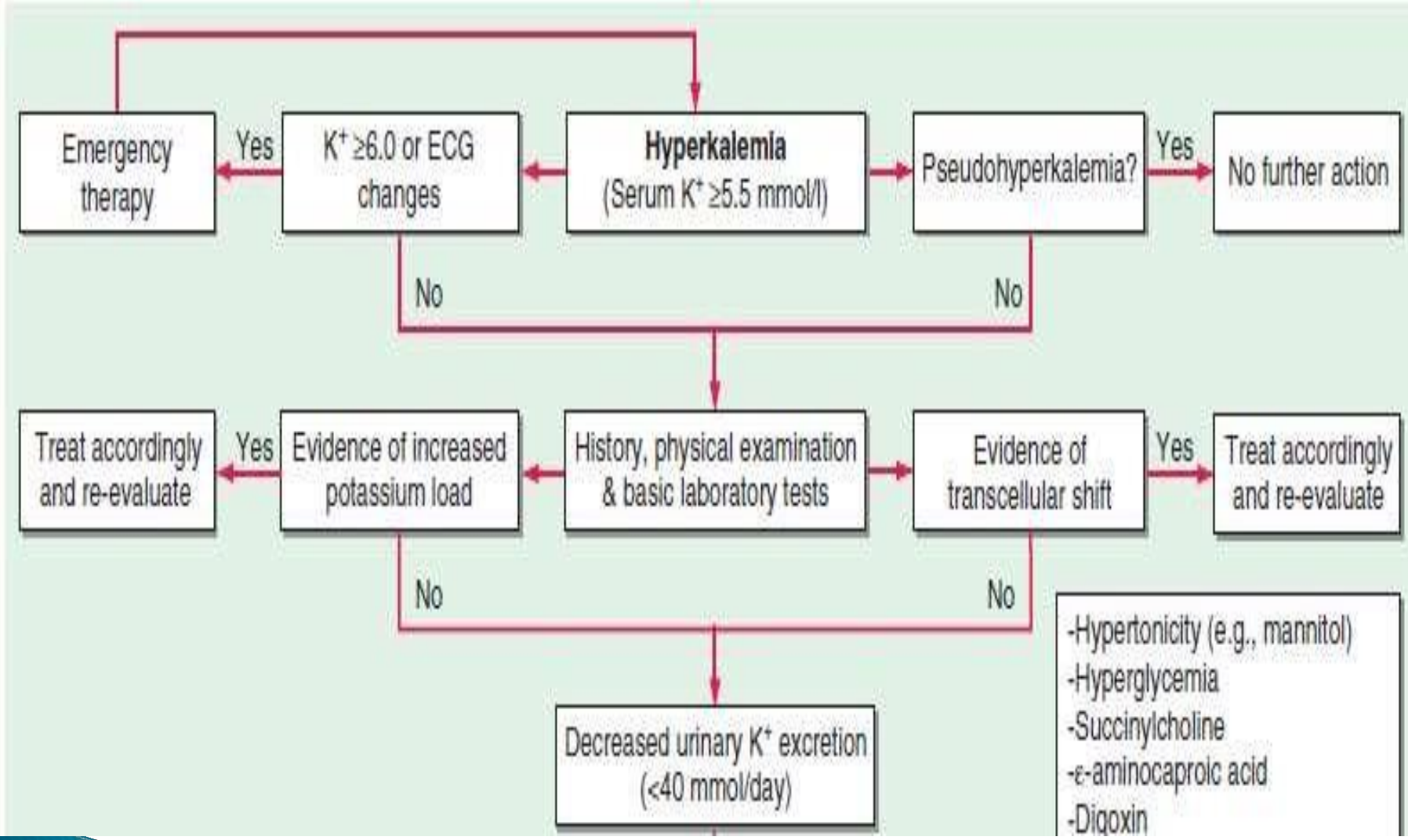
Sine wave appearance with severe hyperkalaemia (K+ 9.9 mEq/L).

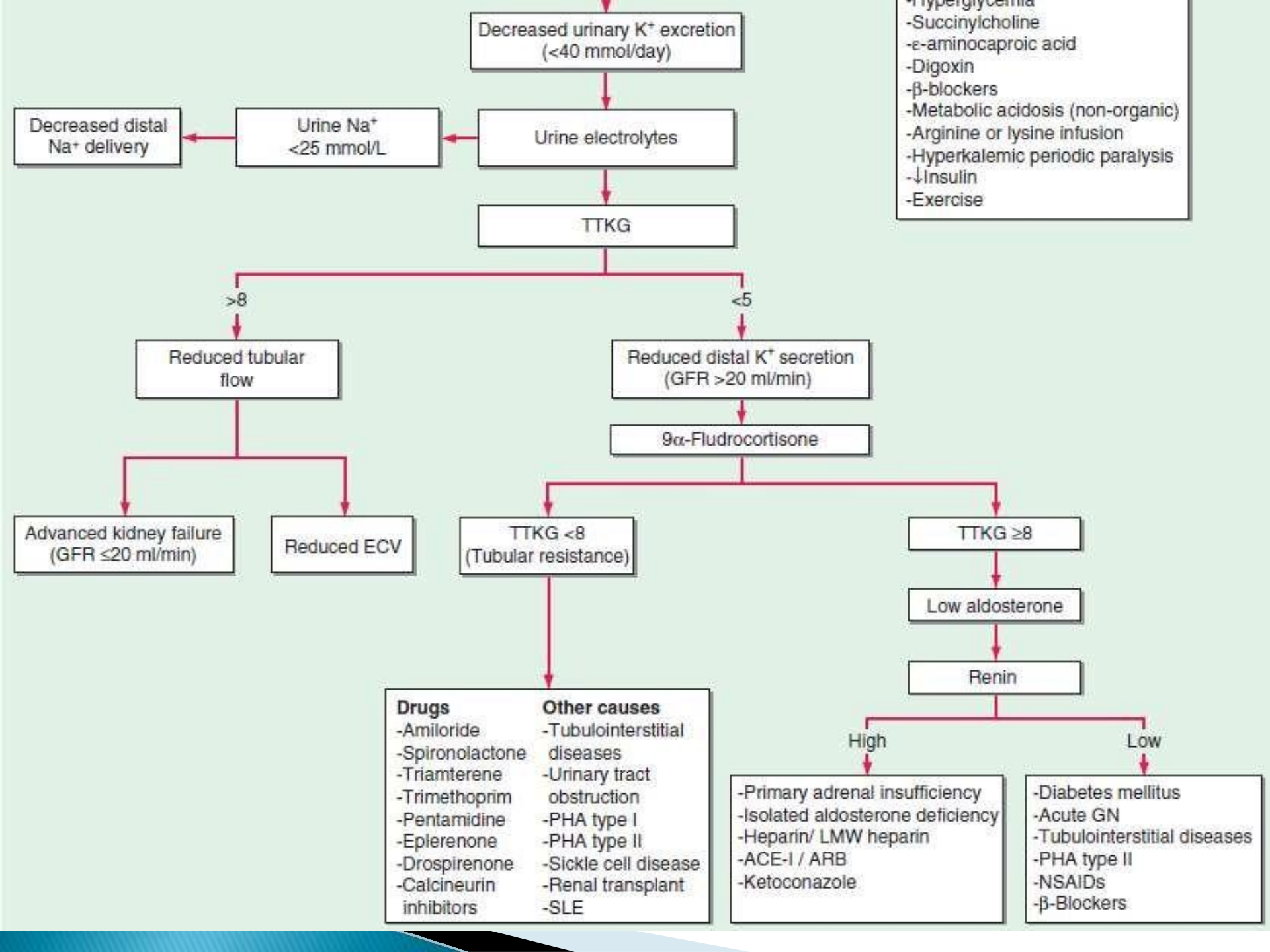
DIAGNOSTIC APPROACH TO HYPERKALEMIA

- Tests In Evaluation of Hyperkalemia
- History on medications,diet,risk factors for kidney failure,reduction in urine output,blood pressure,volume status.
- BUN,creatinine,serum osmolarity,
- Serum Electrolytes- including Mg, Ca
- Urine potassium, sodium, and osmolality
- Complete blood count (CBC)
- ECG

Trans-tubular potassium gradient (TTKG)

- TTKG is an index reflecting the conservation of potassium in the cortical collecting ducts (CCD) of the kidneys.
- It is useful in diagnosing the causes of hyperkalemia or hypokalemia.
- TTKG estimates the ratio of potassium in the lumen of the CCD to that in the peritubular capillaries.
- TTKG= Urine K/ Serum K x serum Osm/Urine osm


Hyperkalemia
(Serum K+ ≥5.5 mmol/l)
Pseudohyperkalemia?
Yes
No further action
No
K+ ≥6.0 or ECG changes
Yes
Emergency therapy
History, physical examination & basic laboratory tests
Evidence of transcellular shift
Yes
Treat accordingly and re-evaluate
No
Evidence of increased potassium load
Yes
Treat accordingly and re-evaluate
No
Decreased urinary K+ excretion
(<40 mmol/day)
-Hypertonicity (e.g., mannitol)
-Hyperglycemia
-Succinylcholine
-ε-aminocaproic acid
-Digoxin


-Hyperglycemia
-Succinylcholine
-ε-aminocaproic acid
-Digoxin
-β-blockers
-Metabolic acidosis (non-organic)
-Arginine or lysine infusion
-Hyperkalemic periodic paralysis
-↓Insulin
-Exercise
Decreased urinary K+ excretion (<40 mmol/day)
Urine electrolytes
Urine Na+ <25 mmol/L
Decreased distal Na+ delivery
TTKG
>8
<5
Reduced tubular flow
Reduced distal K+ secretion (GFR >20 ml/min)
9α-Fludrocortisone
Advanced kidney failure (GFR ≤20 ml/min)
Reduced ECV
TTKG <8 (Tubular resistance)
TTKG ≥8
Low aldosterone
Renin
High
Low
Drugs
-Amiloride
-Spironolactone
-Triamterene
-Trimethoprim
-Pentamidine
-Eplerenone
-Drospirenone
-Calcineurin inhibitors
Other causes
-Tubulointerstitial diseases
-Urinary tract obstruction
-PHA type I
-PHA type II
-Sickle cell disease
-Renal transplant
-SLE
-Primary adrenal insufficiency
-Isolated aldosterone deficiency
-Heparin/ LMW heparin
-ACE-I / ARB
-Ketoconazole
-Diabetes mellitus
-Acute GN
-Tubulointerstitial diseases
-PHA type II
-NSAIDs
-β-Blockers

TREATMENT

- **3 main approaches to the treatment of hyperkalemia** :

- ●Antagonizing the membrane effects of potassium with calcium

- ●Driving extracellular potassium into the cells

- ●Removing excess potassium from the body

- ECG manifestations of hyperkalemia- a medical emergency and treated urgently.
- Patients with significant hyperkalemia ($K^+ \geq 6.5$ m*M) in the absence of ECG changes should also be aggressively* managed
- ***Immediate antagonism of the cardiac effects of hyperkalemia***
- IV calcium raises the action potential threshold and reduces the excitability without change in resting membrane potential
- recommended dose is 10 mL of 10% calcium gluconate, infused intravenously over 2–3 min with cardiac monitoring.

- The effect of infusion strats after 1to 3 min and lasts for 30 to 60 min
- Dose should be repeated if there is no change in ECG findings and they recur after intial improvement

- ***Rapid reduction in plasma K+ concentration by redistribution into cells.***
- ***Insulin*** *lowers plasma K+ concentration by shifting K+in to cells*
- *Can be given as constant infusion or bolus regimen*
- *Infusion regimen:10 units of regular insulin in 500ml of 10%dextroseover 60 min*
- *Bolous regimen: used in emergency conditons recommended dose is 10 units of regular insulin iv followed by 50 ml of 50%dextrose*

- Effect begin 10 to 20 min,peaks at 30 to 60 min and lasts for 4 to 6 hours
- In hyperkalemic patients with **glucose concentrations>200mg/dl** insulin should be given without glucose with blood glucose monitering
- In almost all the patients plasma potassium drops by0.5 to 1.2mmol/L after treatment
- Combined treatment with Beta 2 agonists in addition to providing a synergistic effect with insulin in lowering plasma potassium,may reduce incidence of hypoglycemia

- **β2-agonists**, most commonly albuterol, are effective but underused agents for the acute management of hyperkalemia.
- However 20% of patients with end stage renal disease(ESRD) are resistant to B2 agonists
- **reaches peak at about 90 min lasts for 2-6 hoursThe recommended dose for inhaled albuterol is 10 to 20 mg in 4 ml of normal saline inhaled over 10 min**
- **Effect starts at 30 min**
- Hyperglycemia is a side effect along with tachycardia
- Should be used with caution in hyperkalemia with cardiac disease

- ***Removal of potassium.***
- *use of* ***cation*** **exchange resins, Diuretics, and/or Hemodialysis.**

- **Cation Exchange Resins**
- sodium polystyrene sulfonate (SPS) exchanges Na^+ for K^+ in the gastrointestinal tract and increases the fecal excretion of K^+

- Dose of SPS is 15–30 g of powder, almost always given in a premade suspension with 33% sorbitol.

- **The effect of SPS on plasma K^+ concentration is slow; the full effect may take up to 24 h and usually requires repeated doses every 4–6 h.**

- **Sodium Bicarbonate** administration as a single agent has no role in treatment of hyperkalemia
- Prolonged infusion of isotonic sodabicarbonate in ESRD patients does reduce potassium at 5 to 6 hours by 0.7 mmo/L, half of this effect is due to volume expansion
- Can be used in severely acidemic patient

- **Reversible causes** of impaired renal function asso with hyperkalemia.

- Includes hypovolemia, NSAIDs, urinary tract obstruction, and inhibitors of the renin-angiotensin-aldosterone system (RAAS), which can also directly cause hyperkalemia

- **RX**- Removal of offending agent & Hydration

- Therapy with intravenous saline may be beneficial in hypovolemic patients with oliguria with decresed delivery of Na to disital collecting ducts

- **Loop and Thiazide diuretics** can be used to reduce plasma K+ concentration in volume-replete or hypervolemic patients with sufficient renal function for diuretic response

- usually combined with iv saline or isotonic bicarbonate to achieve or maintain euvolemia

- **Hemodialysis** is the most effective and reliable method to reduce plasma K+ .

- The amount of K+ removed during hemodialysis depends on
- The relative distribution of K+ between ICF and ECF

- The type and surface area of the dialyzer used,
- dialysate and blood flow rates,

- dialysate flow rate, dialysis duration, and the plasma-to- dialysate K+ gradient.

THANK YOU