LE DISIONEMIE: POTASSIO

Ferrara 01/10/18

U.O. Clinica Medica.
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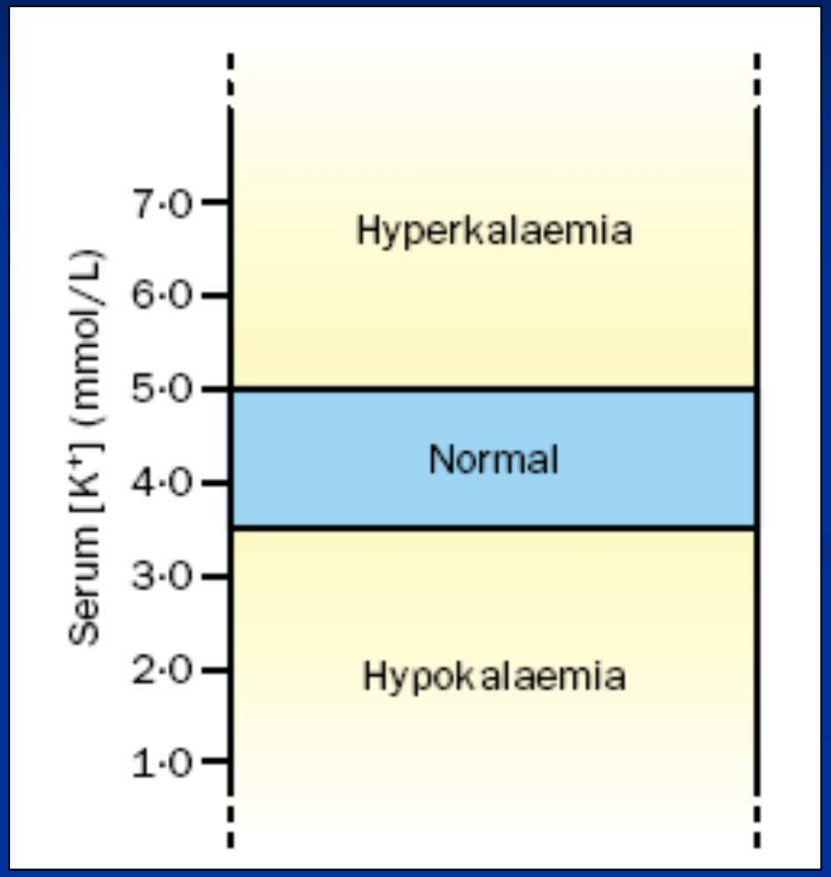
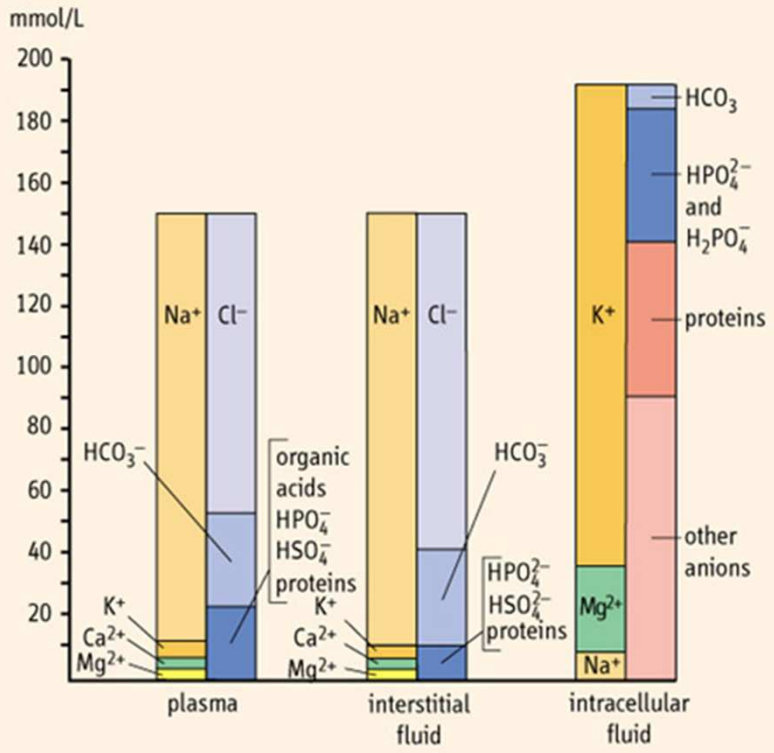
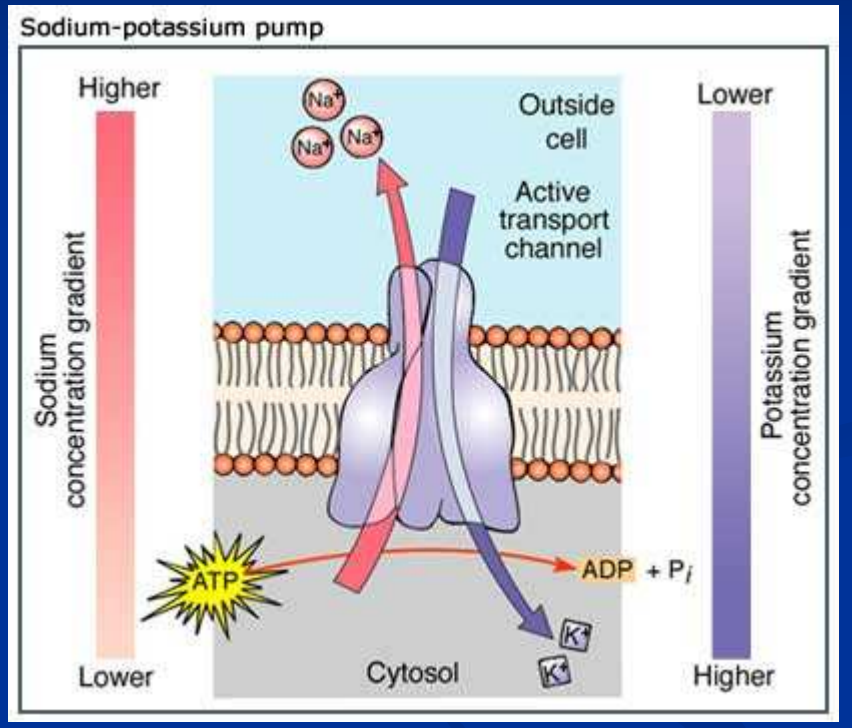
Dott. Christian Molino

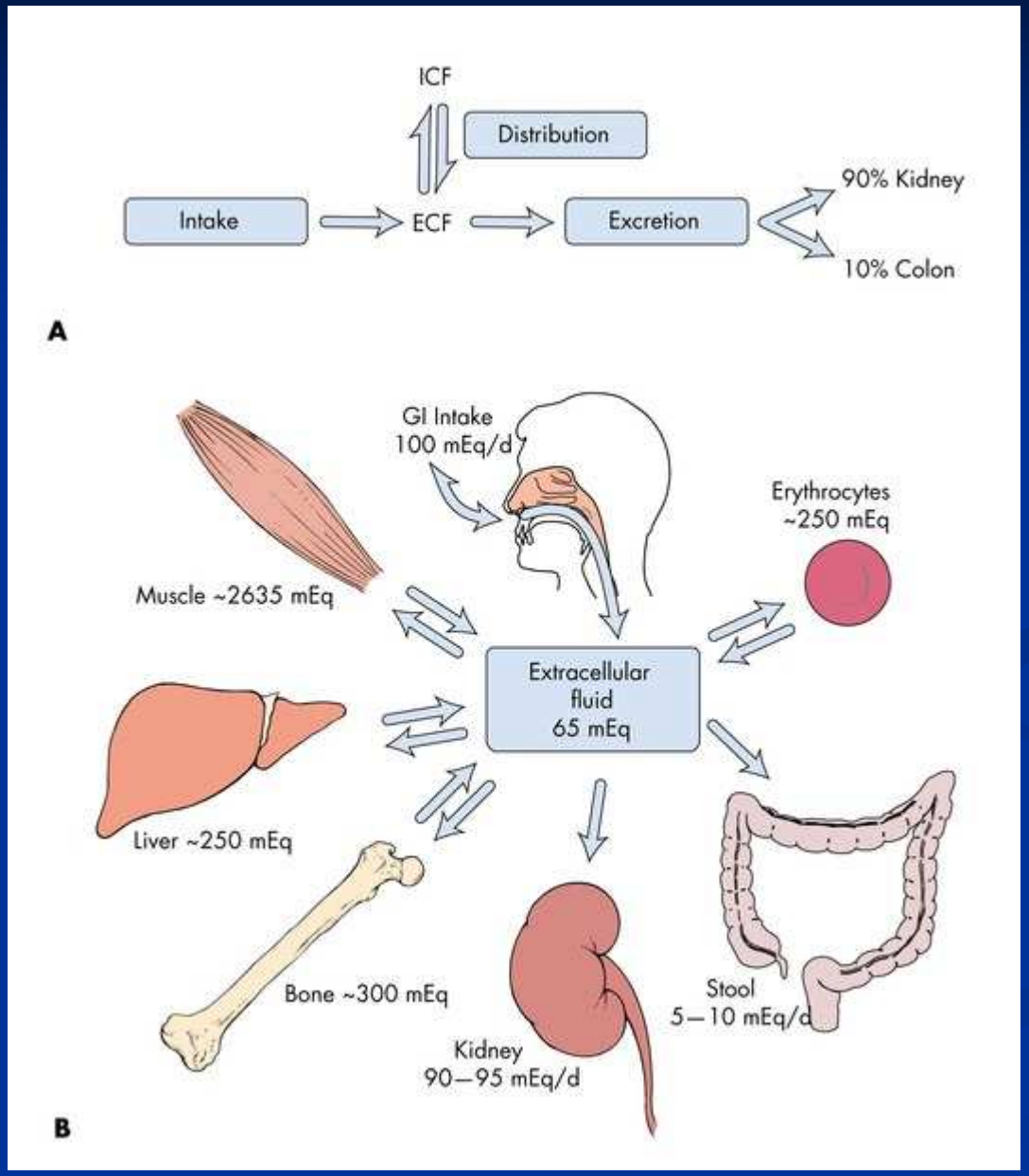

Serum [K+] (mmol/L)
7·0
6·0
5·0
4·0
3·0
2·0
1·0
Hyperkalaemia
Normal
Hypokalaemia

Ionic composition of body fluid





Total body potassium

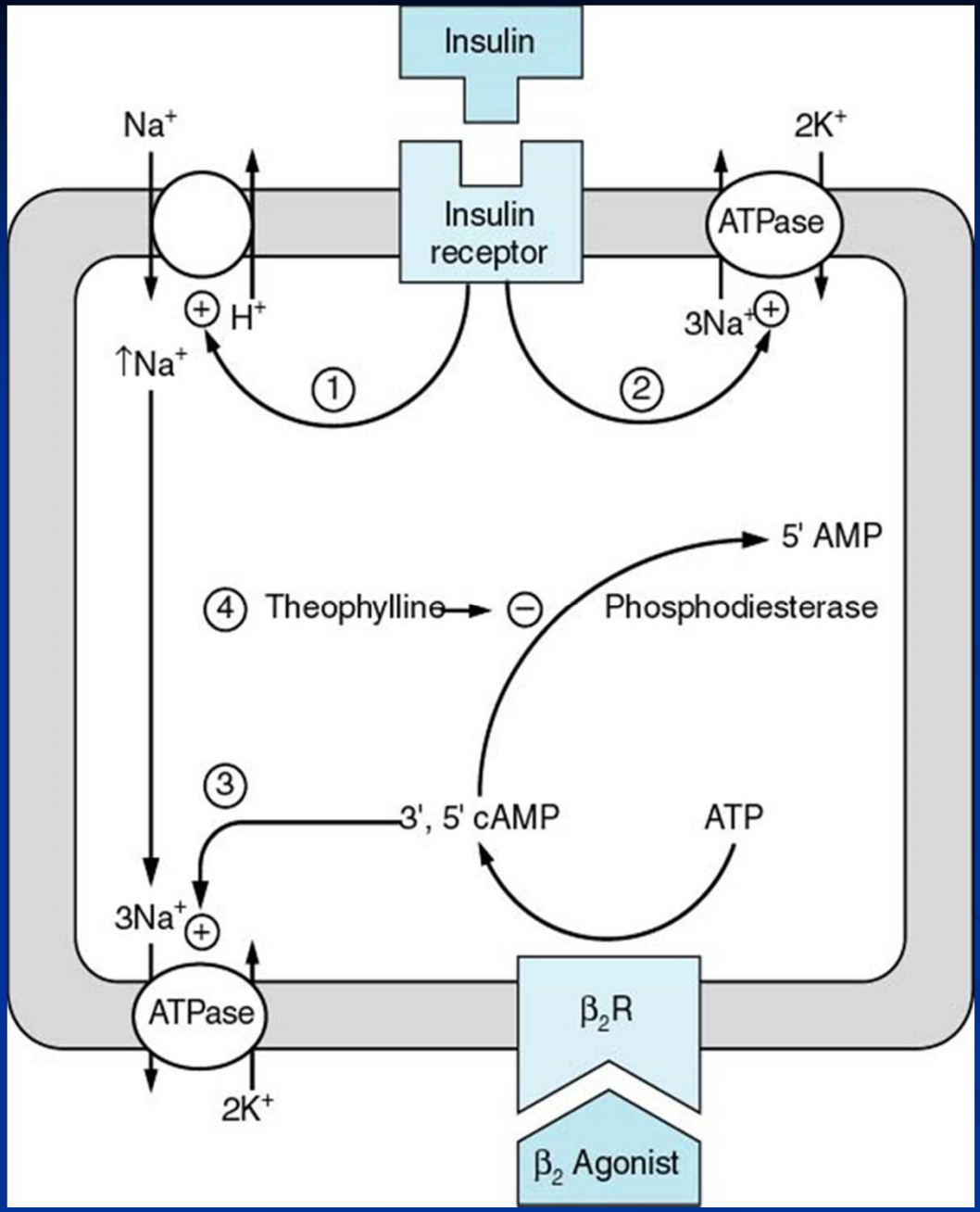


PHYSIOLOGY OF POTASSIUM BALANCE: DISTRIBUTION OF POTASSIUM

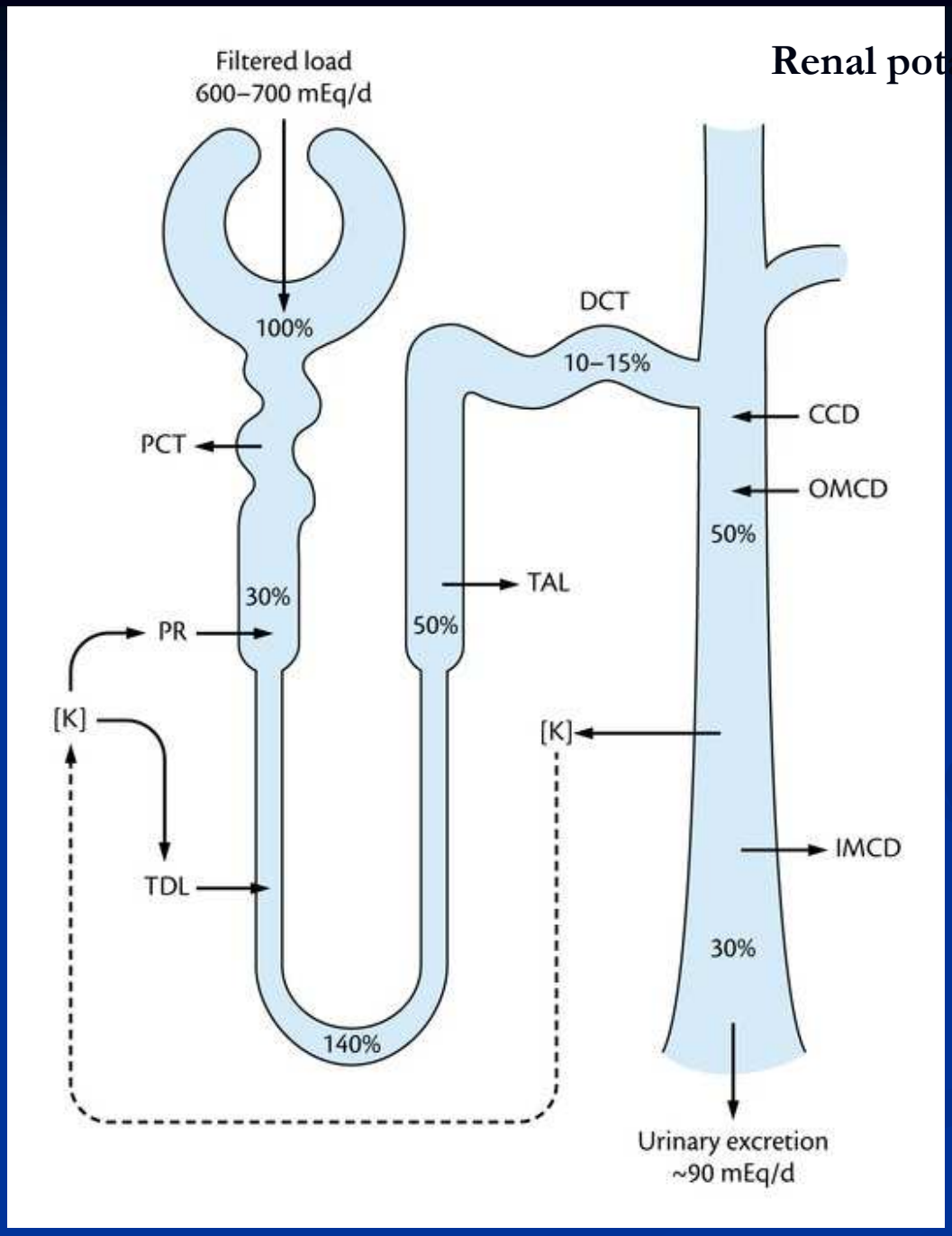
ECF 350 mEq (10%)	ICF 3150 mEq (90%)
Plasma 15 mEq (0.4%)	Muscle 2650 mEq (76%)
Interstitial fluid 35 mEq (1%)	Liver 250 mEq (7%)
Bone 300 mEq (8.6%)	Erythrocytes 250 mEq (7%)
$[K^+]$ = 3.5–5.0 mEq/L	$[K^+]$ = 140–150 mEq/L
Urine 90–95 mEq/d	Urine 90–95 mEq/d
Stool 5–10mEq/d	Stool 5–10mEq/d
Sweat < 5 mEq/d	Sweat < 5 mEq/d

POTASSIO CONTENUTO NEGLI ALIMENTI

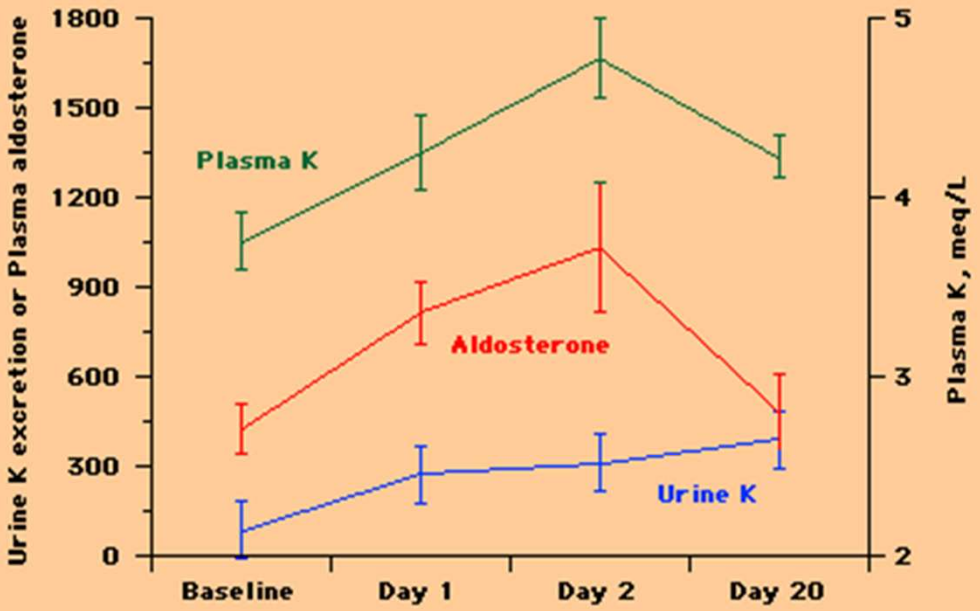
contenuto altissimo	*mg/100 g*	*contenuto alto*	*mg/100 g*	*contenuto medio*	*mg/100 g*	*contenuto basso*	*mg/100 g*
funghi secchi	2000	cacao & cioccolato	300-400	sedano	300	fragole	150
albicocche secche	1560	carciofi	370	carote	280	cetrioli	140
legumi secchi	960	broccoli	370	ravanelli	270	cipolle	140
castagne	890	indivia	360	pomodori	265	pere	128
prugne secche	810	zucchine	340	lattuga	260	mele	125
arachidi	680	finocchi	340	porri	250		
pinoli	630	cavolfiori	330	fagiolini	240		
patate	570	barbabietole	320	ciliege	246		
spinaci	560	melone	320	uva	220		
banane	380	kiwi	310	peperoni	210		
		albicocche fresche	300	ananas	200		
		anguria	280	asparagi	200		
		fichi	260	melanzane	185		
		pesche	260	cachi	180		
		melograno	260	agrumi	170-190		


Insulin
Na+
2K+
Insulin receptor
ATPase
H+
3Na+
↑Na+
1
2
5' AMP
4 Theophylline
Phosphodiesterase
3
3', 5' cAMP
ATP
3Na+
ATPase
2K+
β2R
β2 Agonist

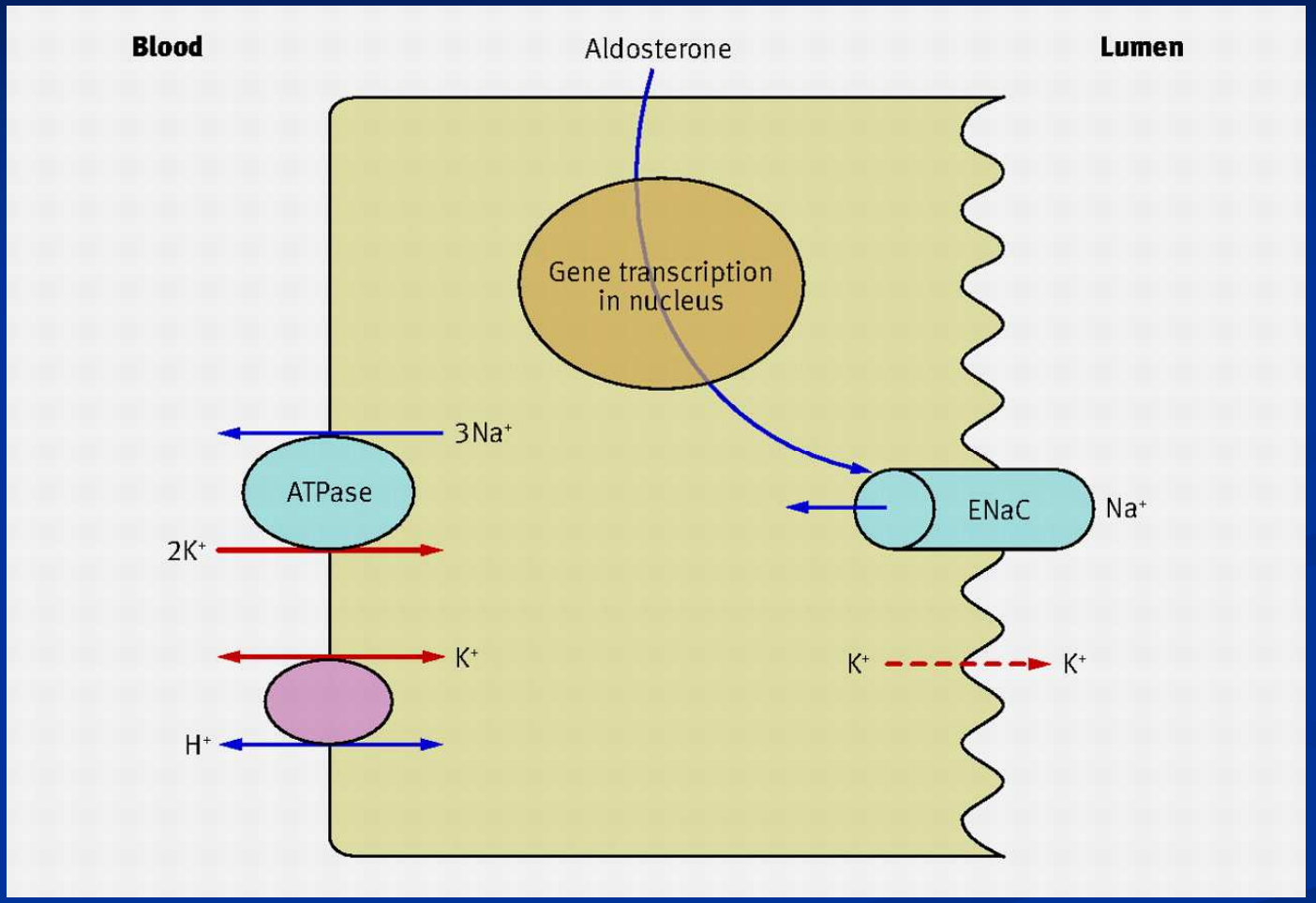
Renal potassium handling



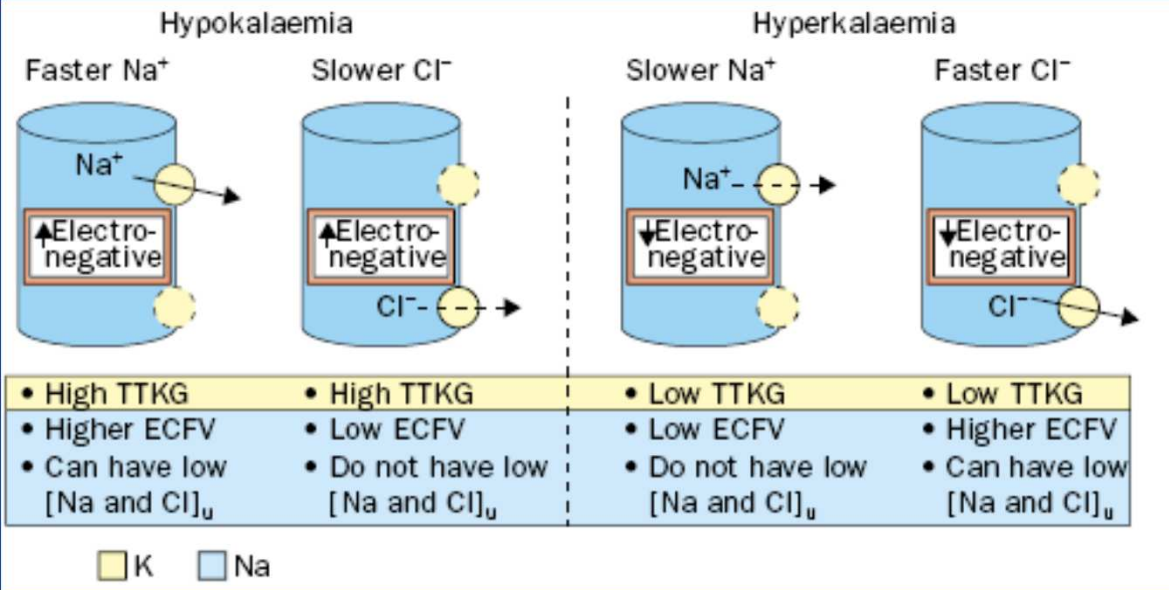
1) ALDOSTERONE
2) POTASSIO
3) FLUSSO TUBOLARE
4) ANIONI NON RIASSORBIBILI TUBULO



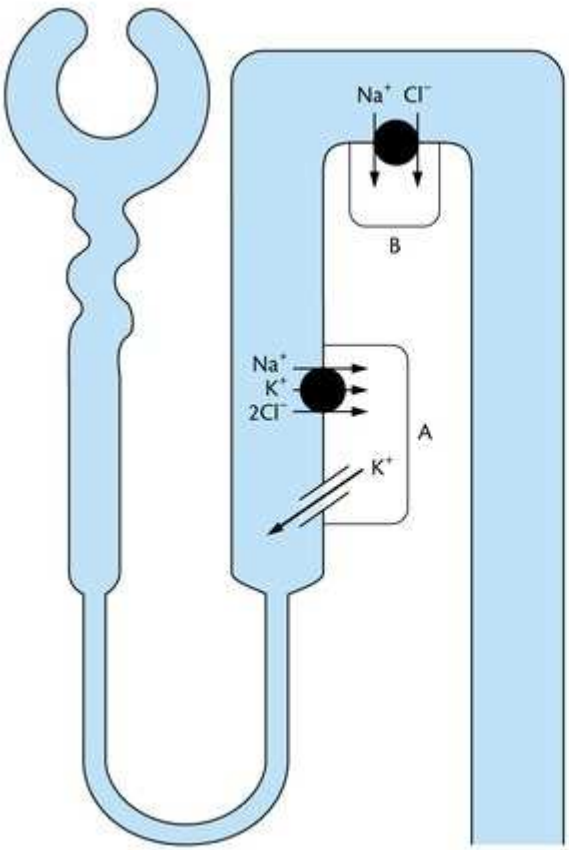
Response to potassium load Response to increasing potassium intake from 100 to 400 meq/day in normal subjects. Urinary potassium excretion rises to over 300 meq/day within two days, a response that is driven by increases in both aldosterone release and the plasma potassium concentration. By day 20, potassium excretion is almost 400 meq/day, the plasma aldosterone level is near normal, and there is only a small rise in the plasma potassium concentration to 4.2 meq/L. (Data from Rabelink, TJ, Koomans, HA, Hené, RJ, Dorhout Mees, EJ, Kidney Int 1990; 38:942.)


Blood
Aldosterone
Lumen
Gene transcription
in nucleus
3Na+
ATPase
2K+
ENaC
Na+
K+
K+
K+
H+

Components of K+ excretion in CCD



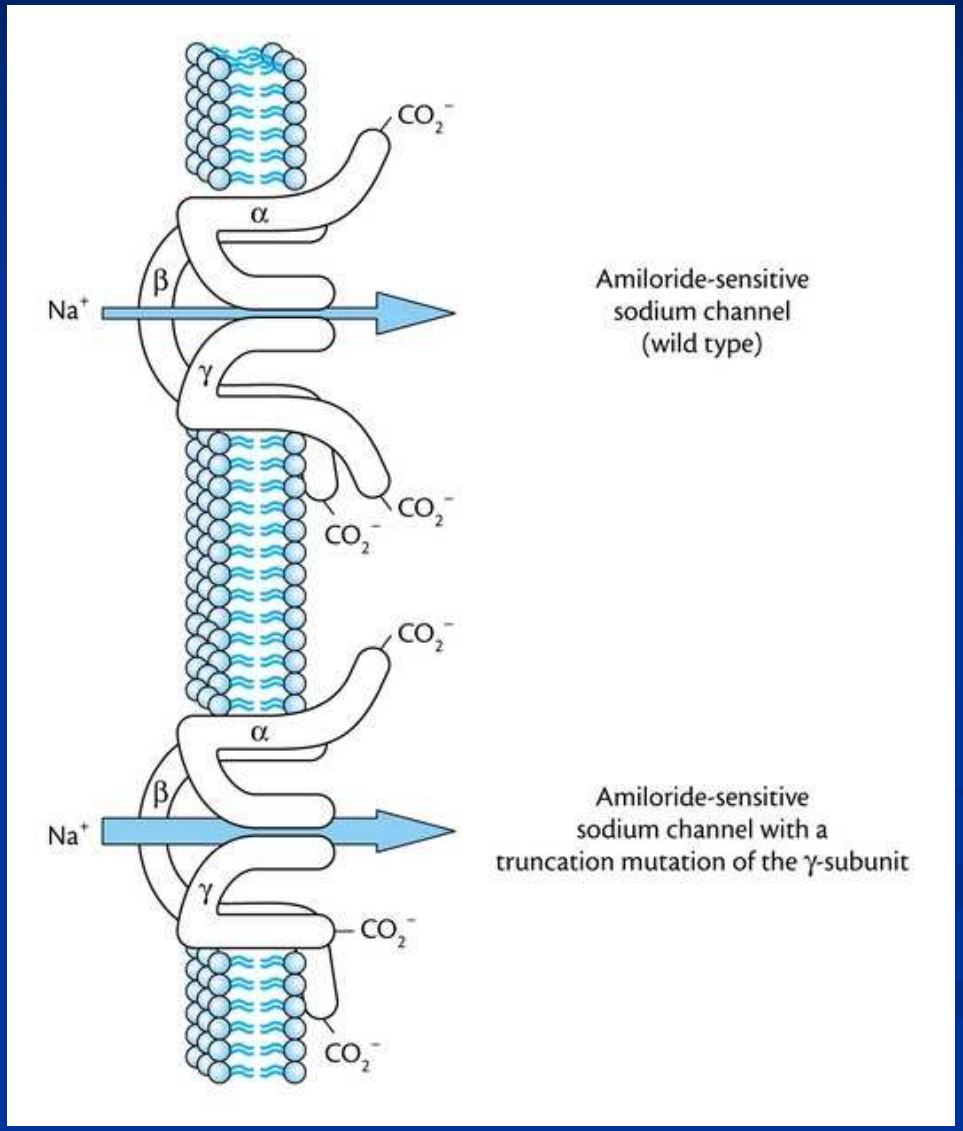
Mechanisms of hypokalemia in Bartter's and Gitelman's syndromes



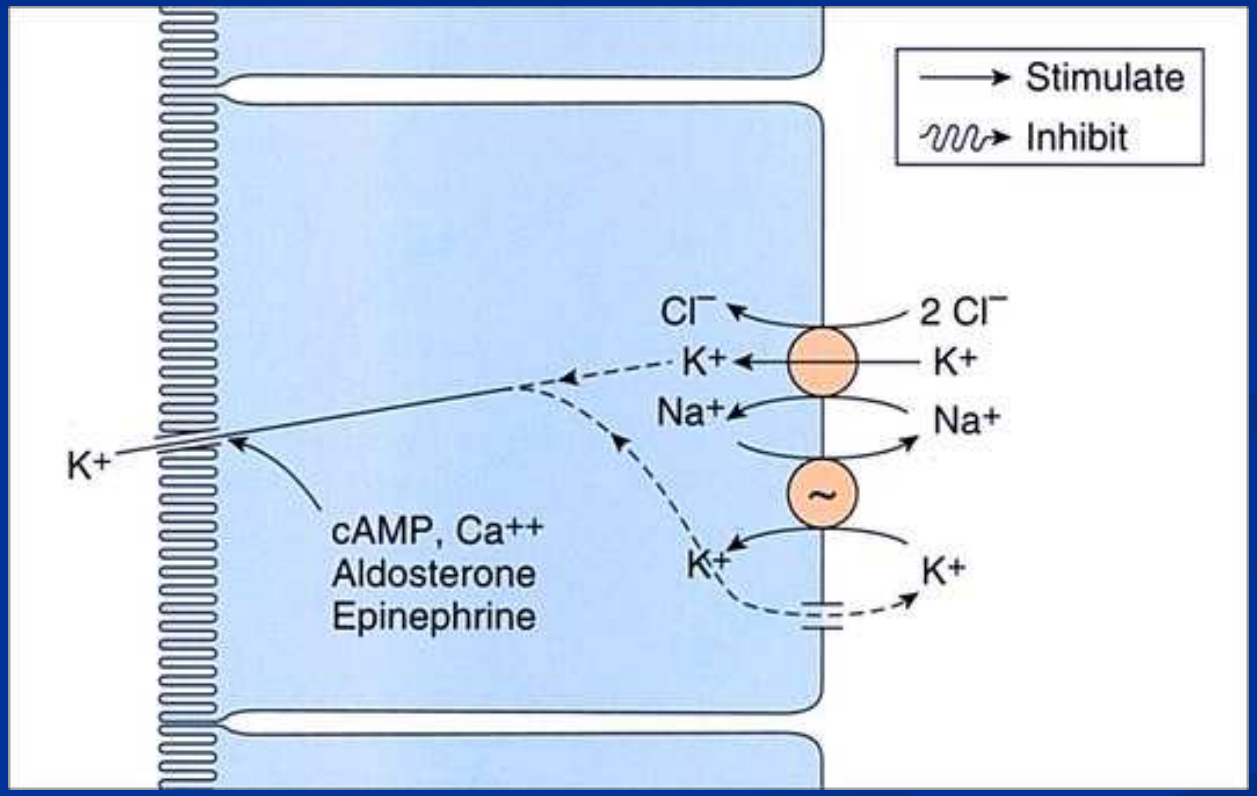
Gitelman's Syndrome
Hypokalemia
Metabolic alkalosis
↑Renin/aldosterone
Hypocalciuria
Normotension
Hypomagnessemia
Age at diagnosis >6 yr
Mild growth retardation

Bartter's Syndrome
Hypokalemia
Metabolic alkalosis
↑Urinary PGE
↑Renin/aldosterone
Normotension
Hypercalciuria
Nephrocalcinosis
Age at diagnosis: infancy
Premature birth/growth retardation

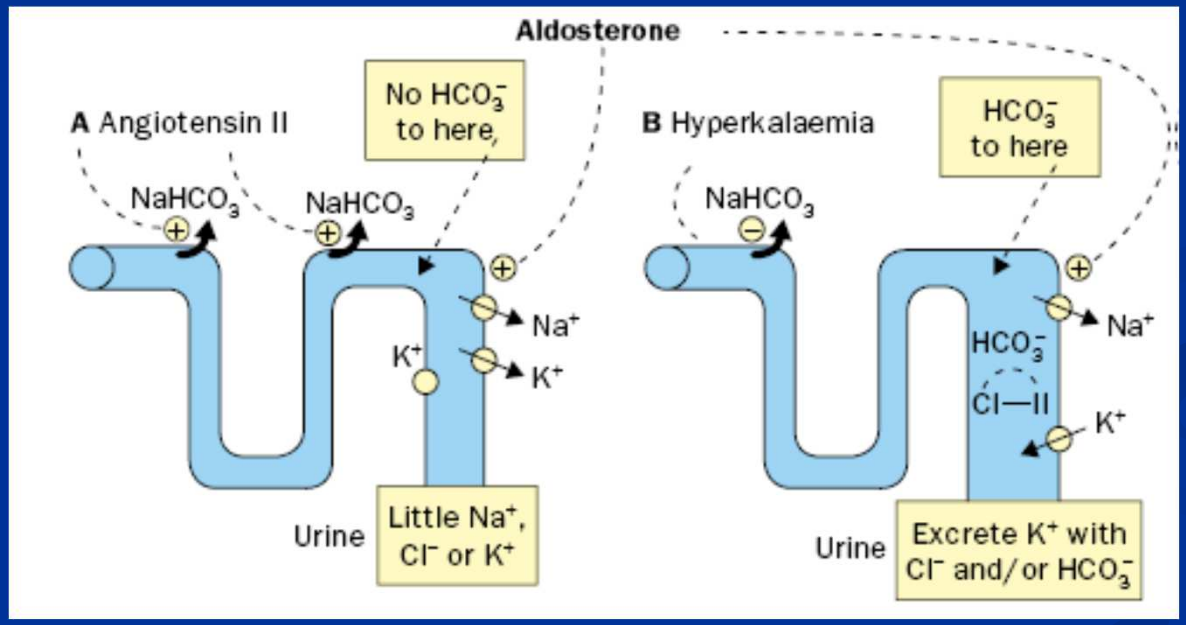
Mechanism of hypokalemia in Liddle's syndrome



Net secretion of potassium from the colon



Role of bicarbonate in modulating effects of aldosterone in CCD

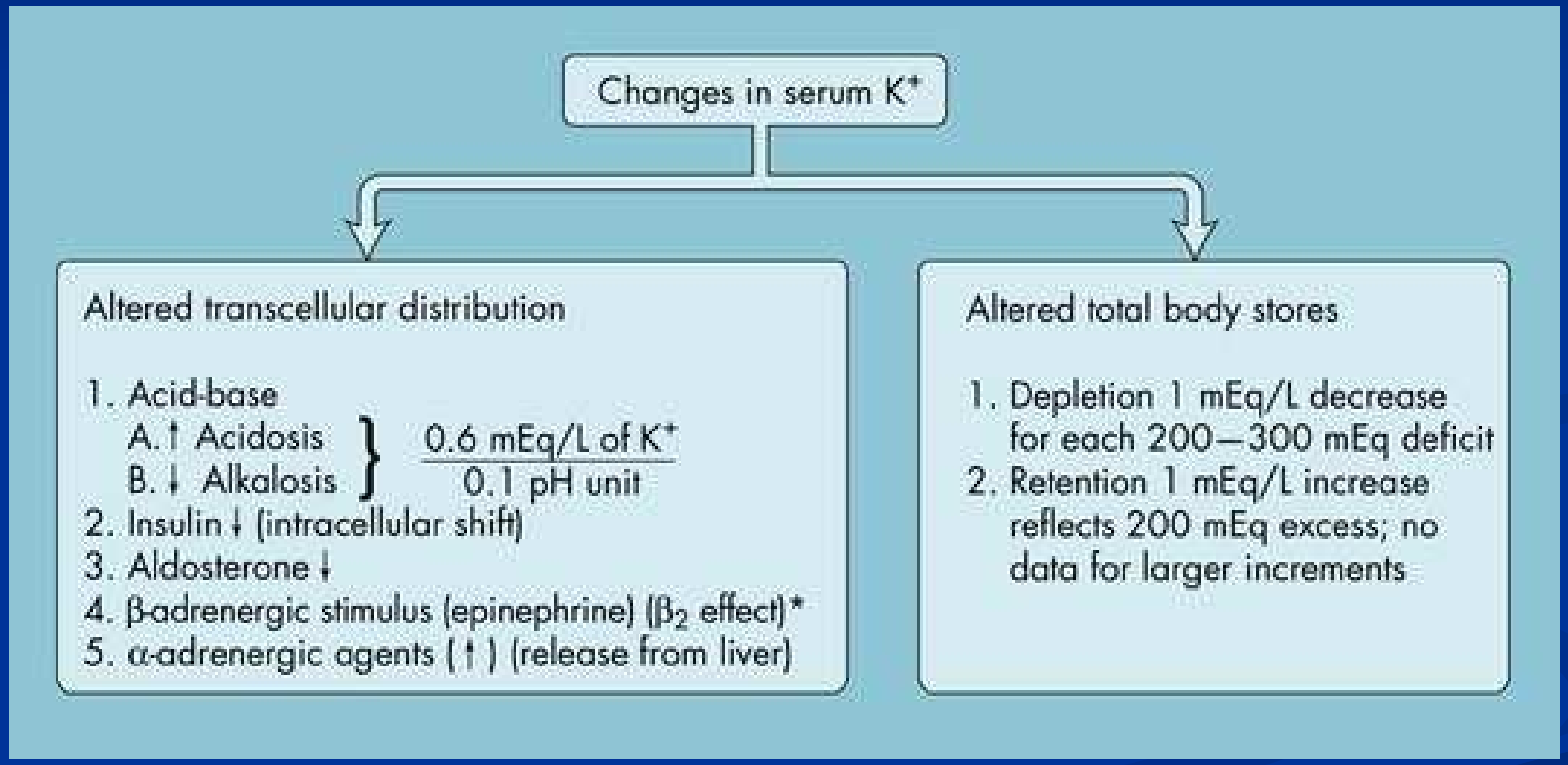


Factors that cause transcellular potassium shifts.

FACTORS CAUSING TRANSCELLULAR POTASSIUM SHIFTS

Factor	Δ Plasma K^+
Acid-base status	
Metabolic acidosis	
Hyperchloremic acidosis	↑↑
Organic acidosis	↔
Respiratory acidosis	↑
Metabolic alkalosis	↓
Respiratory alkalosis	↓
Pancreatic hormones	
Insulin	↓↓
Glucagon	↑
Catecholamines	
β-Adrenergic	↓
α-Adrenergic	↑
Hyperosmolarity	↑
Aldosterone	↓, ↔
Exercise	↑

Changes in serum potassium

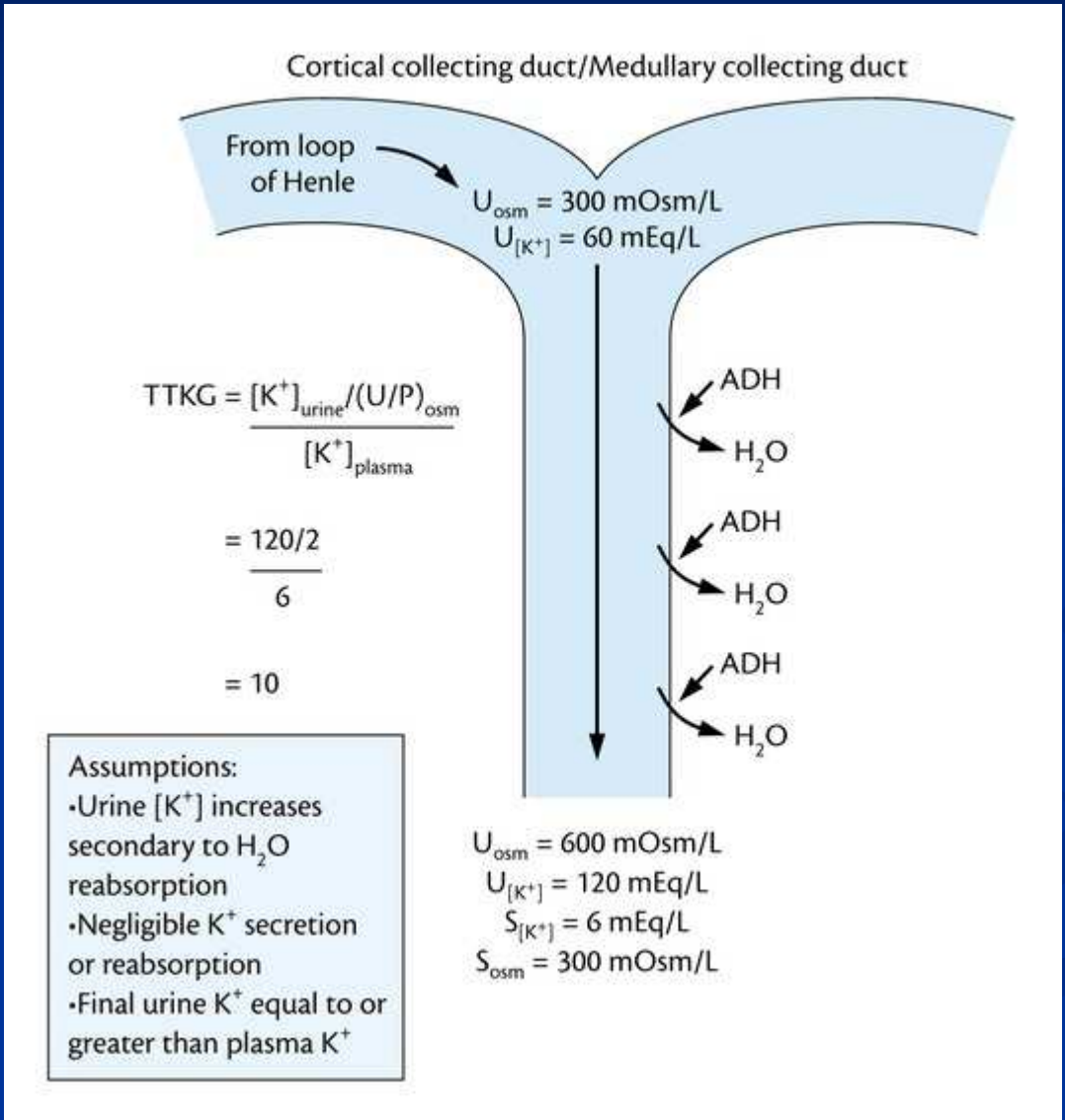


Tests to examine K+ excretion in patients with hypokalaemia or hyperkalaemia

Test	Advantages	Disadvantages	Expected values
24-h K^+ excretion rate or K^+ per creatinine	Indicates overall renal response in patients with hypokalaemia or hyperkalaemia	Does not indicate mechanism responsible for defect; takes 24 h or measurement of creatinine in urine; collections not always accurate	Normal 60–80 mmol/day (or 6–8 mmol/mmol creatinine); hypokalaemia <10 (or 1–1·5); hyperkalaemia >150 (or 10–15)
Spot urine [K^+]	Convenience	Influenced by two independent factors (K^+ secretion and water reabsorption in medulla) so there is a wide gray zone	Hypokalaemia <20 mmol/L if due to renal cause and >20 if due to a renal cause; hyperkalaemia (no "expected" value reported)
TTKG	Corrects for water reabsorption in medullary collecting duct; provides semiquantitative reflection	Assumptions made in calculation of K^+ secretion in CCD	Hypokalaemia due to a non-renal cause <2; hyperkalaemia due to a non-renal cause >10

*Reproduced, with permission, from ref 28.

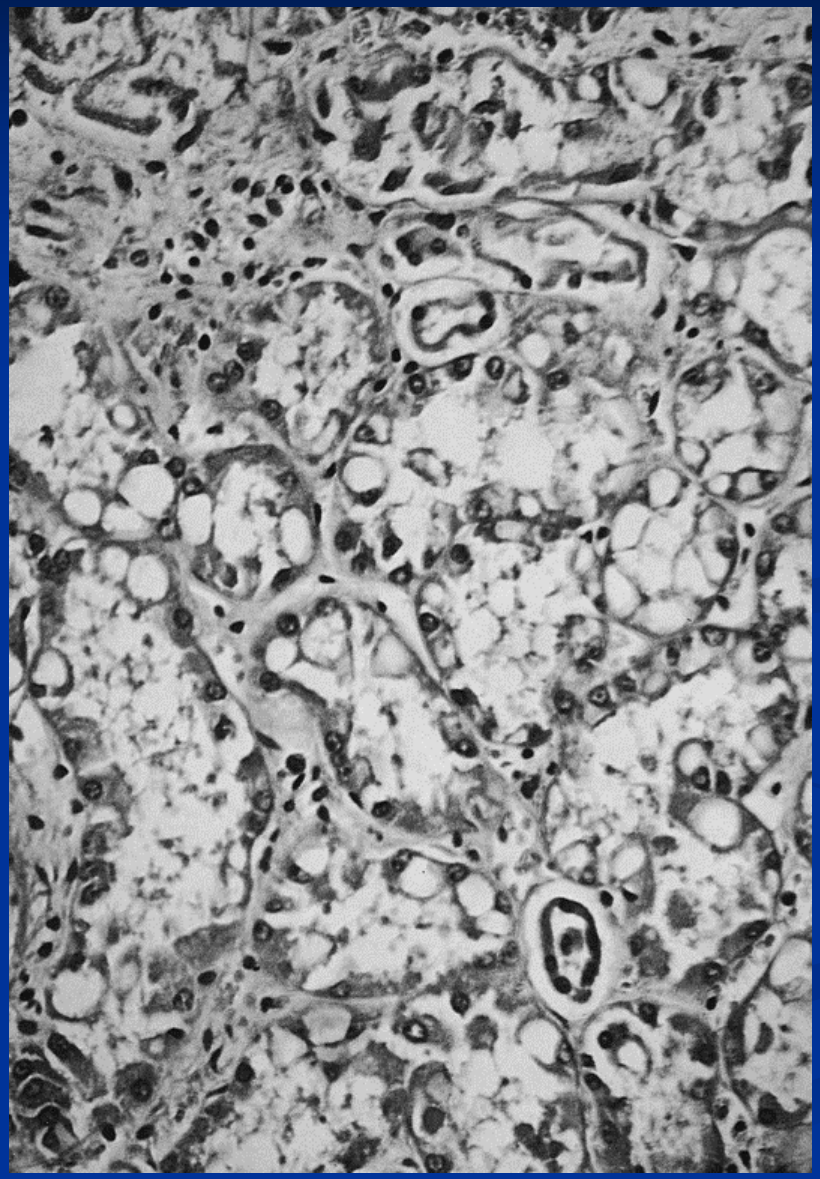
Physiologic basis of the transtubular potassium concentration gradient



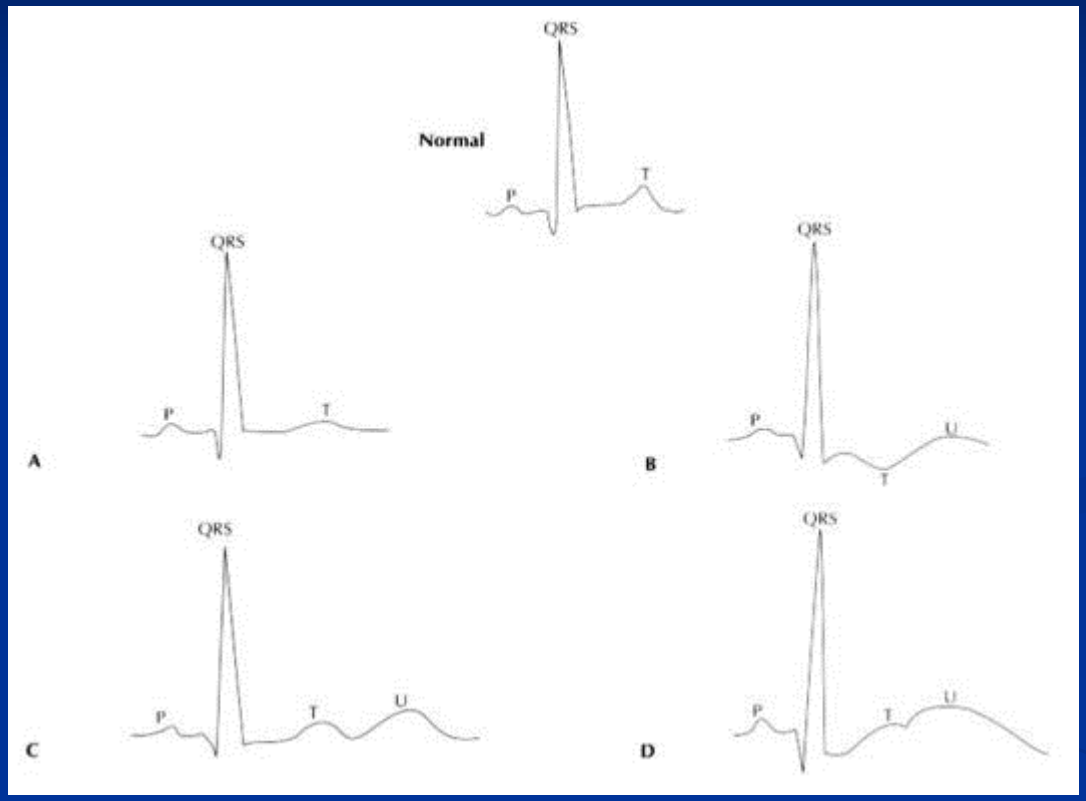
Clinical manifestations of hypokalemia

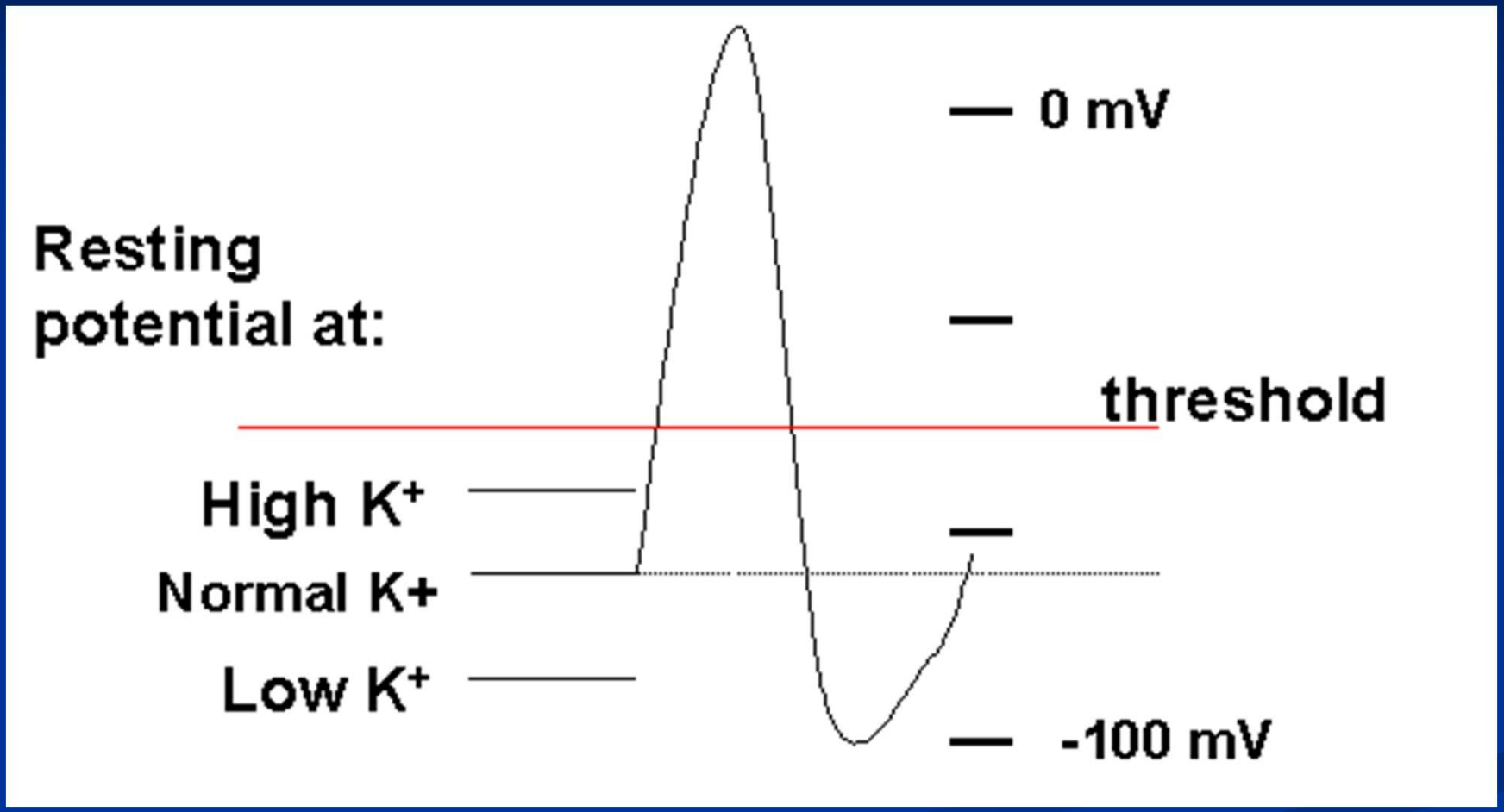
- **CARDIOVASCULAR**
  - Abnormal electrocardiogram
  - Predisposition for digitals toxicity
  - Arrhythmias
  - Hypertension
- **NEUROMUSCOLAR**
  - Constipation/ileus
  - Bladder dysfunction
  - Weakness/cramps
  - Tetany/paralisis
  - Myalgias/Rabdomyolysis
- **RENAL/ELECTROLYTE**
  - Decreased GFR and renal blood flow
  - Renal concentrating defect
  - Incresed renal ammonia production
  - Chloride wasting
  - Metabolik alcalosis
  - Hypercalcuria
  - Phosphaturia
  - Dilation and vacuolization of proximal ubules
  - Medullary cist formation
  - Interstitial nephritis
- **ENDOCRINE/METABOLIC**
  - Decresed insulin secretion
  - Increased renin
  - Decreased aldosterone
  - Alterated prostaglandin sinthesys
  - Growth retardation

Renal lesions in hypokalemia

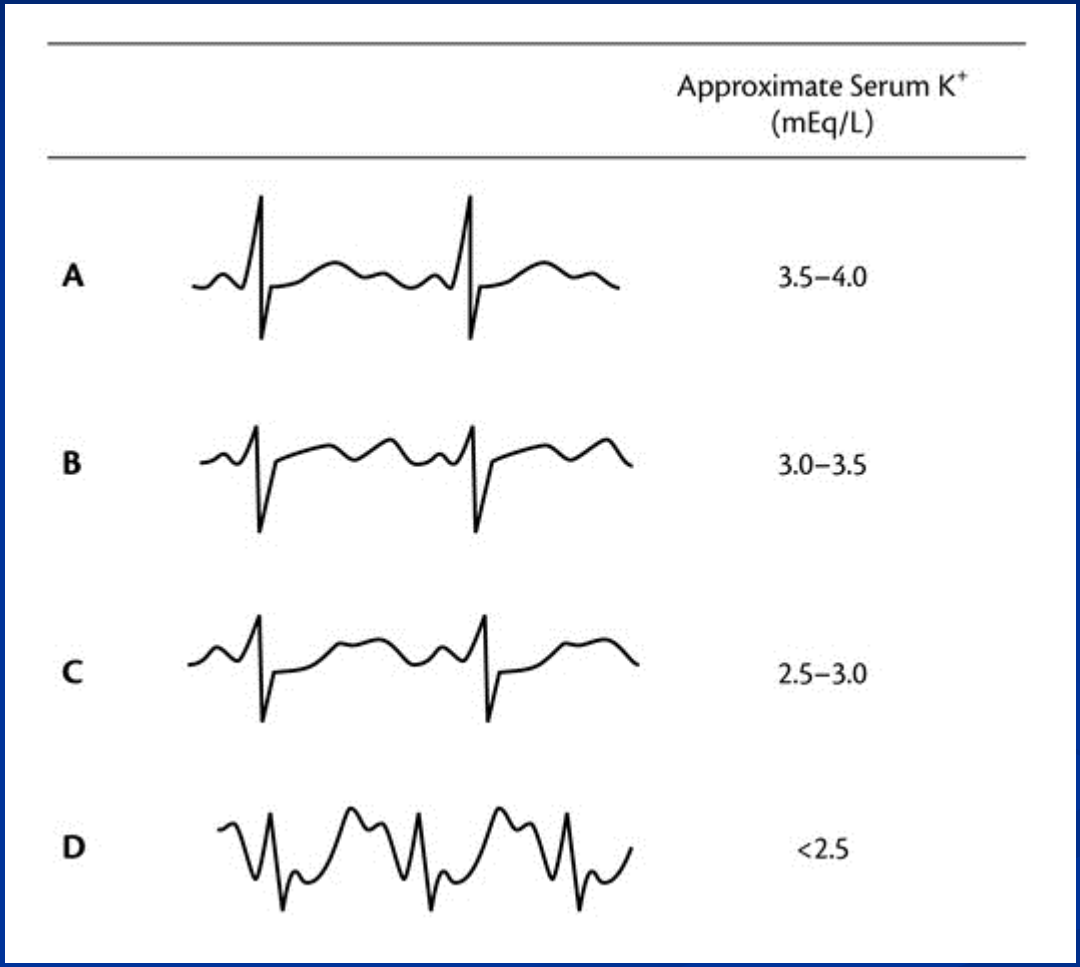


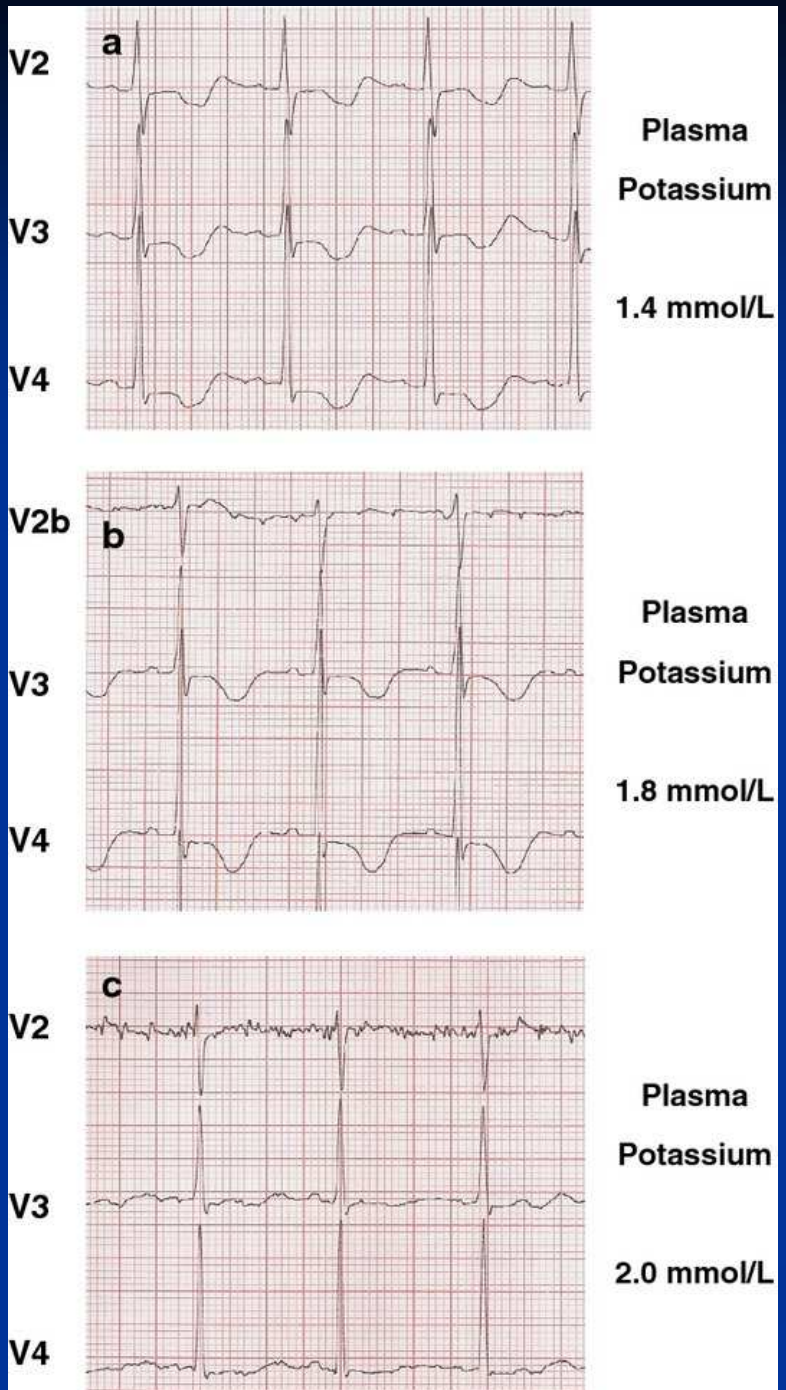
Electrocardiographic changes associated with hypokalemia

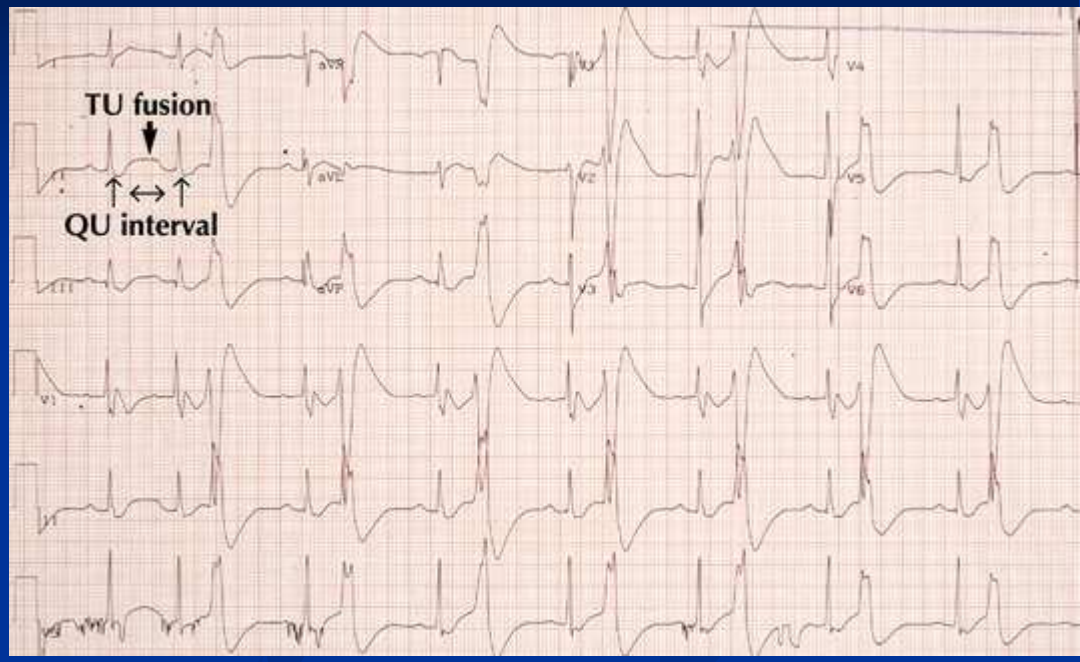


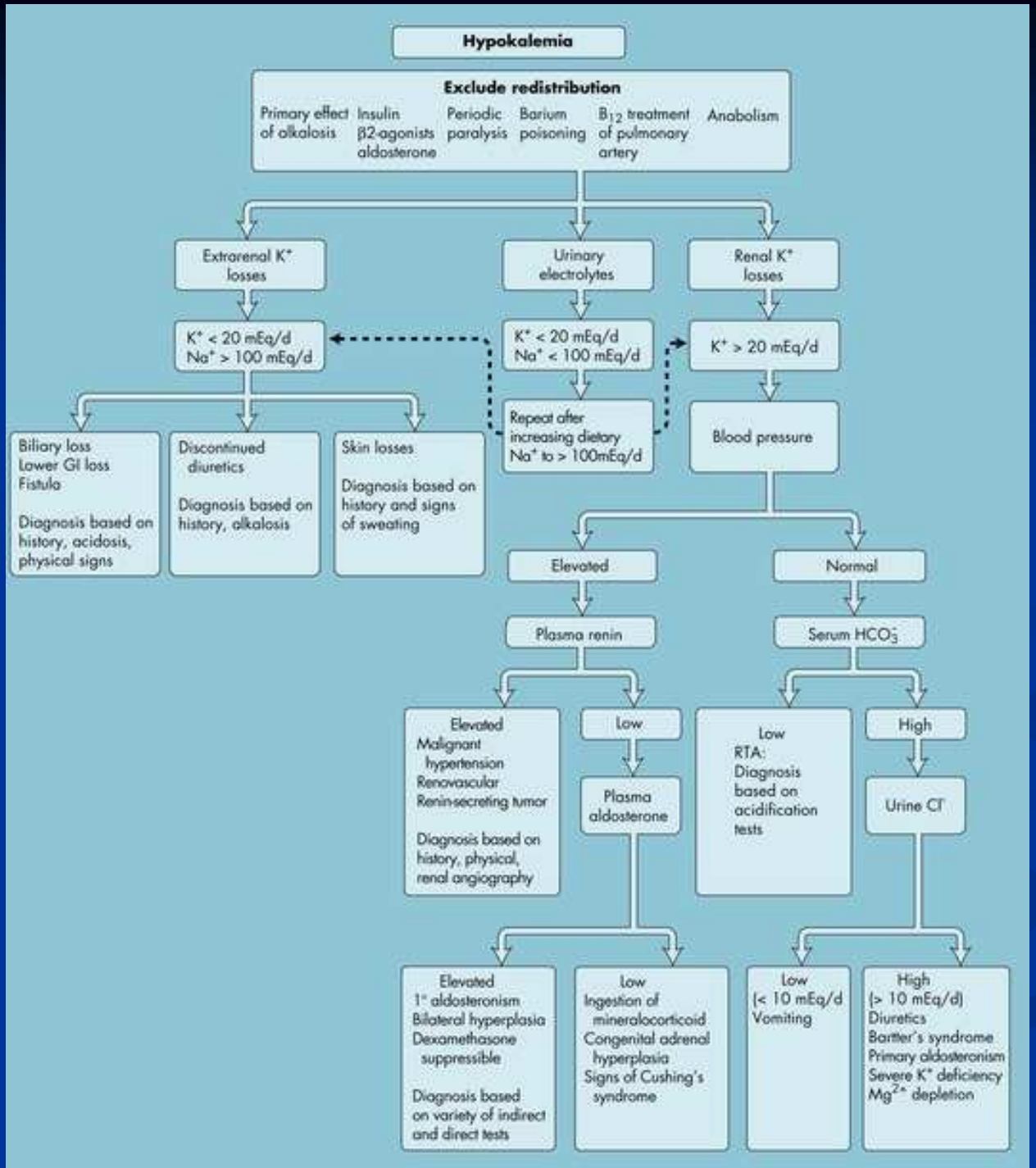

0 mV
Resting
potential at:
threshold
High K+
Normal K+
Low K+
-100 mV

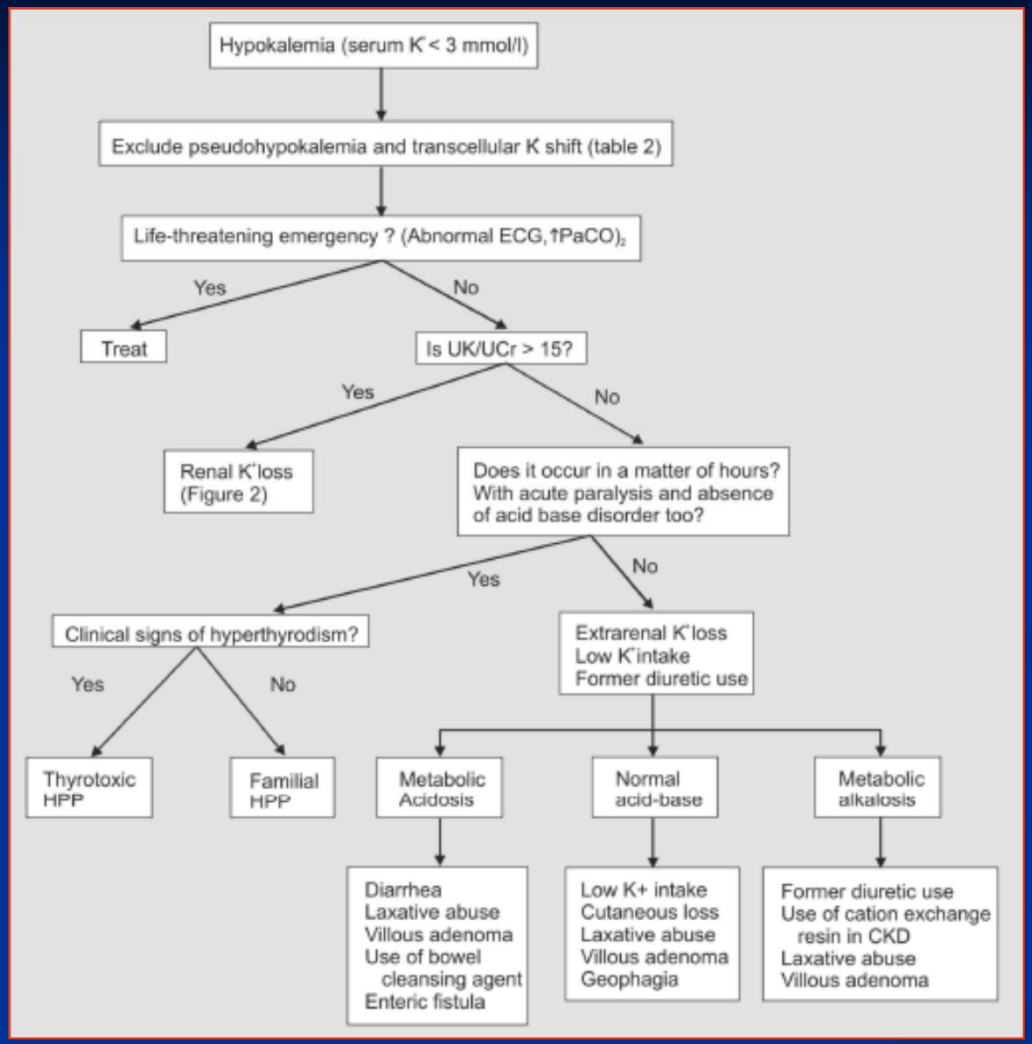
Electrocardiographic changes in hypokalemia

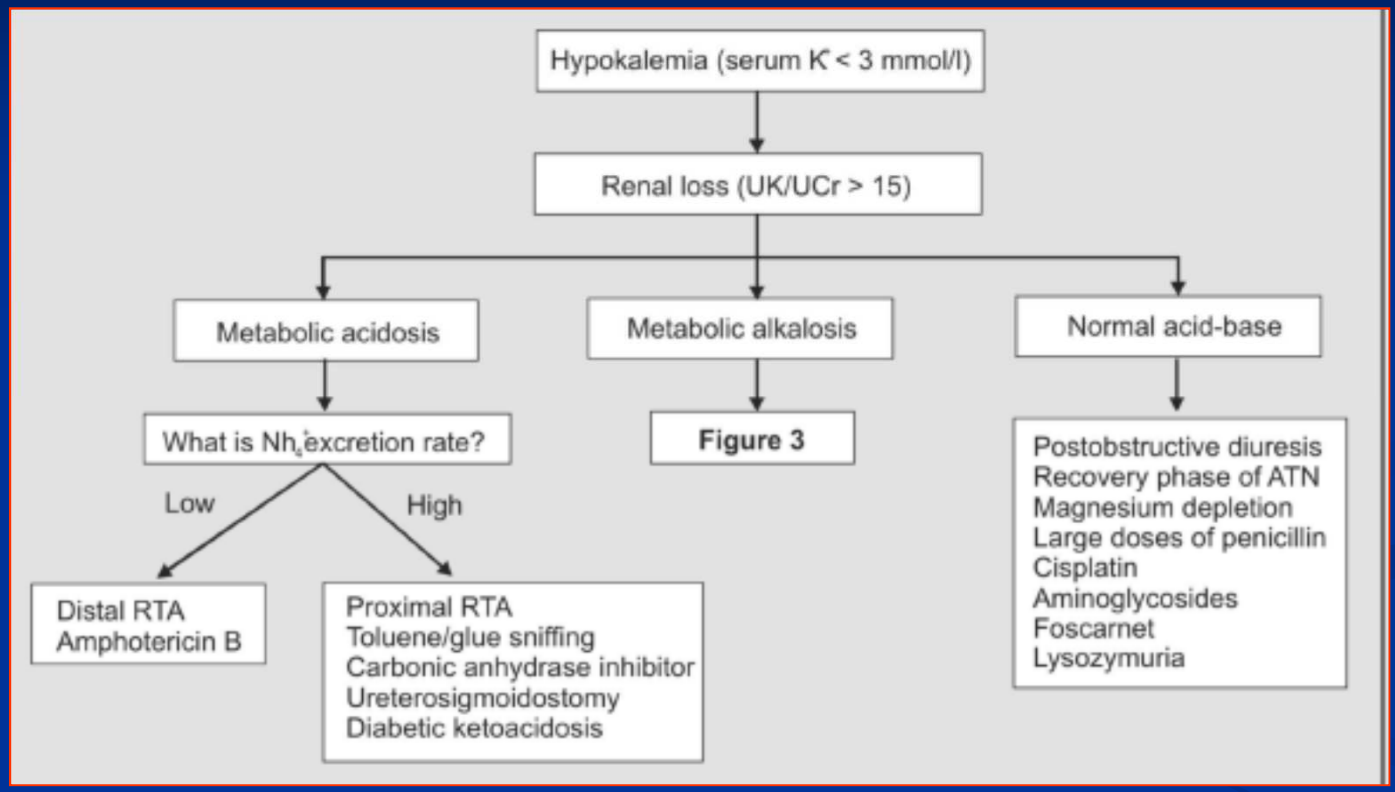


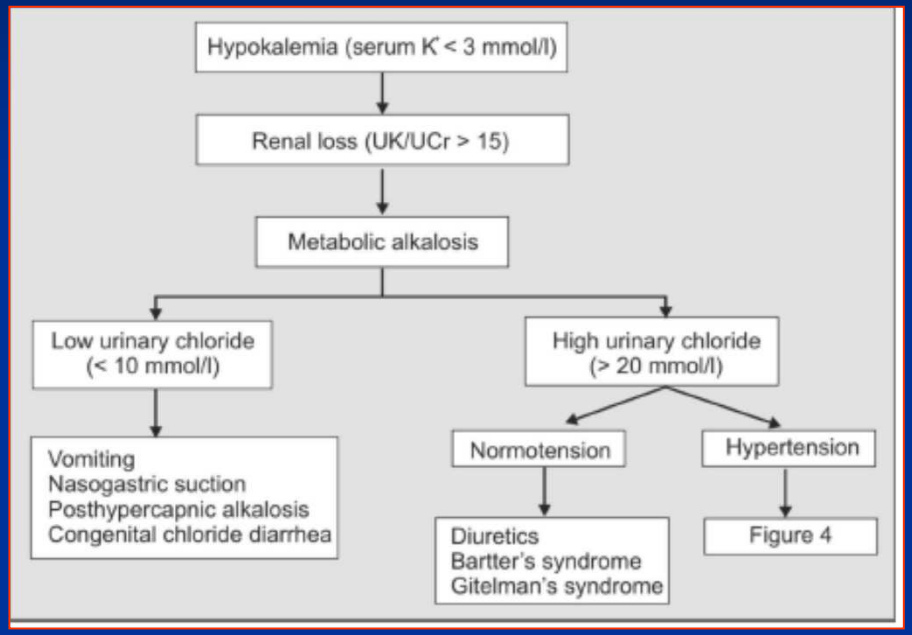

a
V2
V3
V4
Plasma
Potassium
1.4 mmol/L
V2b
b
V3
V4
Plasma
Potassium
1.8 mmol/L
c
V2
V3
V4
Plasma
Potassium
2.0 mmol/L

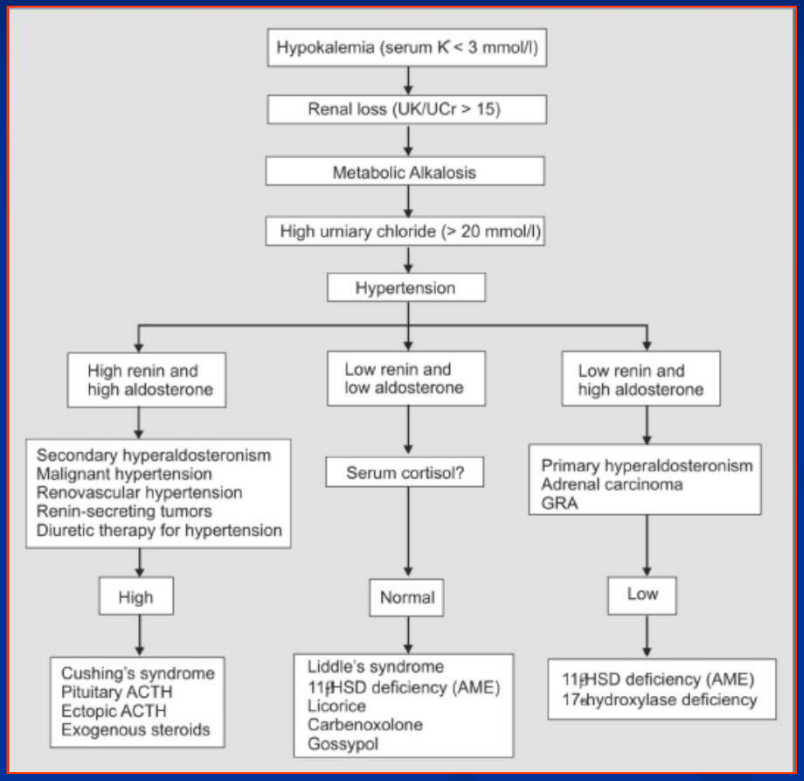

TU fusion
QU interval

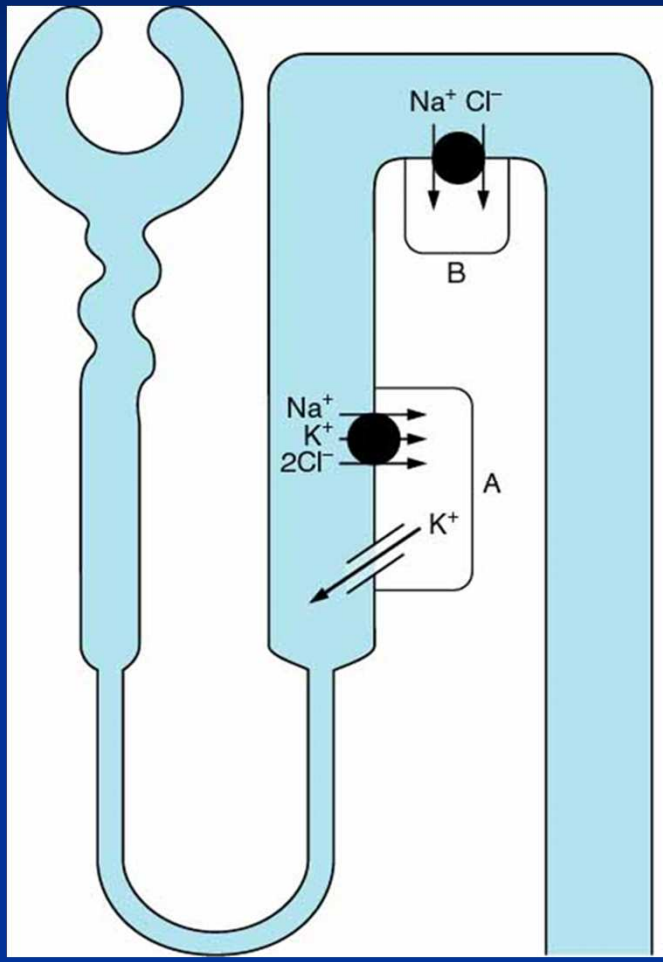

Hypokalemia
Exclude redistribution
Primary effect of alkalosis
Insulin β2-agonists aldosterone
Periodic paralysis
Barium poisoning
B_{12} treatment of pulmonary artery
Anabolism
Extrarenal K^+ losses
Urinary electrolytes
Renal K^+ losses
K^+ < 20 mEq/d
Na^+ > 100 mEq/d
K^+ < 20 mEq/d
Na^+ < 100 mEq/d
K^+ > 20 mEq/d
Repeat after increasing dietary Na^+ to > 100mEq/d
Biliary loss
Lower GI loss
Fistula
Diagnosis based on history, acidosis, physical signs
Discontinued diuretics
Diagnosis based on history, alkalosis
Skin losses
Diagnosis based on history and signs of sweating
Blood pressure
Elevated
Normal
Plasma renin
Serum HCO_3^-
Elevated
Malignant hypertension
Renovascular
Renin-secreting tumor
Diagnosis based on history, physical, renal angiography
Low
Plasma aldosterone
Low
RTA:
Diagnosis based on acidification tests
High
Urine Cl
Elevated
1° aldosteronism
Bilateral hyperplasia
Dexamethasone suppressible
Diagnosis based on variety of indirect and direct tests
Low
Ingestion of mineralocorticoid
Congenital adrenal hyperplasia
Signs of Cushing's syndrome
Low
(< 10 mEq/d
Vomiting
High
(> 10 mEq/d)
Diuretics
Bartter's syndrome
Primary aldosteronism
Severe K^+ deficiency
Mg^{2+} depletion


Hypokalemia (serum K+ < 3 mmol/l)
Exclude pseudohypokalemia and transcellular K shift (table 2)
Life-threatening emergency ? (Abnormal ECG, ↑PaCO2)
Yes
No
Treat
Is UK/UCr > 15?
Yes
No
Renal K+loss (Figure 2)
Does it occur in a matter of hours? With acute paralysis and absence of acid base disorder too?
Yes
No
Clinical signs of hyperthyrodism?
Extrarenal K+loss
Low K+intake
Former diuretic use
Yes
No
Thyrotoxic HPP
Familial HPP
Metabolic Acidosis
Normal acid-base
Metabolic alkalosis
Diarrhea
Laxative abuse
Villous adenoma
Use of bowel cleansing agent
Enteric fistula
Low K+ intake
Cutaneous loss
Laxative abuse
Villous adenoma
Geophagia
Former diuretic use
Use of cation exchange resin in CKD
Laxative abuse
Villous adenoma


Hypokalemia (serum K+ < 3 mmol/l)
Renal loss (UK/UCr > 15)
Metabolic acidosis
Metabolic alkalosis
Normal acid-base
What is NH4+ excretion rate?
Figure 3
Low
High
Distal RTA
Amphotericin B
Proximal RTA
Toluene/glue sniffing
Carbonic anhydrase inhibitor
Ureterosigmoidostomy
Diabetic ketoacidosis
Postobstructive diuresis
Recovery phase of ATN
Magnesium depletion
Large doses of penicillin
Cisplatin
Aminoglycosides
Foscarnet
Lysozymuria


Hypokalemia (serum K < 3 mmol/l)
Renal loss (UK/UCr > 15)
Metabolic alkalosis
Low urinary chloride (< 10 mmol/l)
High urinary chloride (> 20 mmol/l)
Vomiting
Nasogastric suction
Posthypercapnic alkalosis
Congenital chloride diarrhea
Normotension
Hypertension
Diuretics
Bartter's syndrome
Gitelman's syndrome
Figure 4


Hypokalemia (serum K < 3 mmol/l)
Renal loss (UK/UCr > 15)
Metabolic Alkalosis
High urniary chloride (> 20 mmol/l)
Hypertension
High renin and high aldosterone
Low renin and low aldosterone
Low renin and high aldosterone
Secondary hyperaldosteronism
Malignant hypertension
Renovascular hypertension
Renin-secreting tumors
Diuretic therapy for hypertension
Serum cortisol?
Primary hyperaldosteronism
Adrenal carcinoma
GRA
High
Normal
Low
Cushing's syndrome
Pituitary ACTH
Ectopic ACTH
Exogenous steroids
Liddle's syndrome
11βHSD deficiency (AME)
Licorice
Carbenoxolone
Gossypol
11βHSD deficiency (AME)
17αhydroxylase deficiency



Gitelman's Syndrome
- Hypokalemia
- Metabolic alkalosis
- ↑Renin/aldosterone
- Hypocalciuria
- Normotension
- Hypomagnessemia
- Age at diagnosis >6 yr
- Mild growth retardation

Bartter's Syndrome
- Hypokalemia
- Metabolic alkalosis
- ↑Urinary PGE
- ↑Renin/aldosterone
- Normotension
- Hypercalciuria
- Nephrocalcinosis
- Age at diagnosis: infancy
- Premature birth/growth retardation

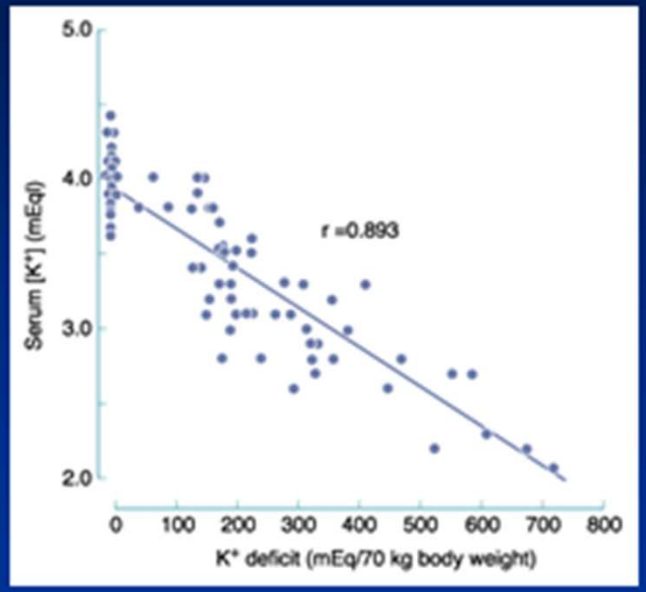
Table 1. Condition or Drugs Causing Hypokalemia due to Transcellular Potassium Shift

Catecholamines: Epinephrine, Dopamine, Dobutamine
Stress-induced catecholamines release (e.g. coronary ischemia, delirium tremens, sepsis)
Bronchodilators : Albutero l, Salbutamol, Terbutaline
Exogenous Insulin
Phosphodiesterase inhibitors: Theophylline, Caffeine
Chloroquine intoxication
Verapamil intoxication
Barium poisoning
Cesium salts
Risperidone, Quetiapine
Hypothermia
Therapy of megaloblastic a nemia
Transfusion of frozen red blood cells
Alkalosis
Familial and thyrotoxic hypokalemic periodic paralysis

K Supplementation

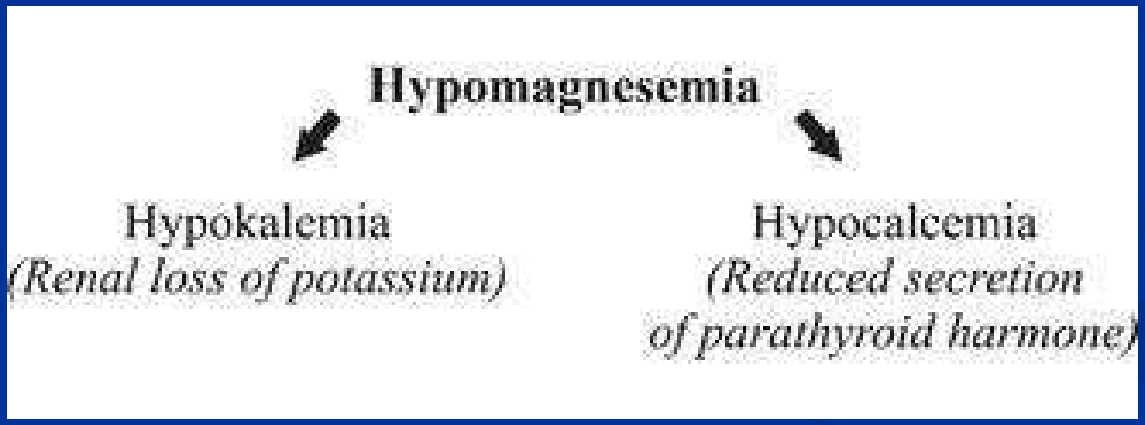
- Magnesium deficit
- Orally-Intravenously
- Potassium chloride
- Potassium phosphate
- Potassium bicarbonate
- Potassium citrate

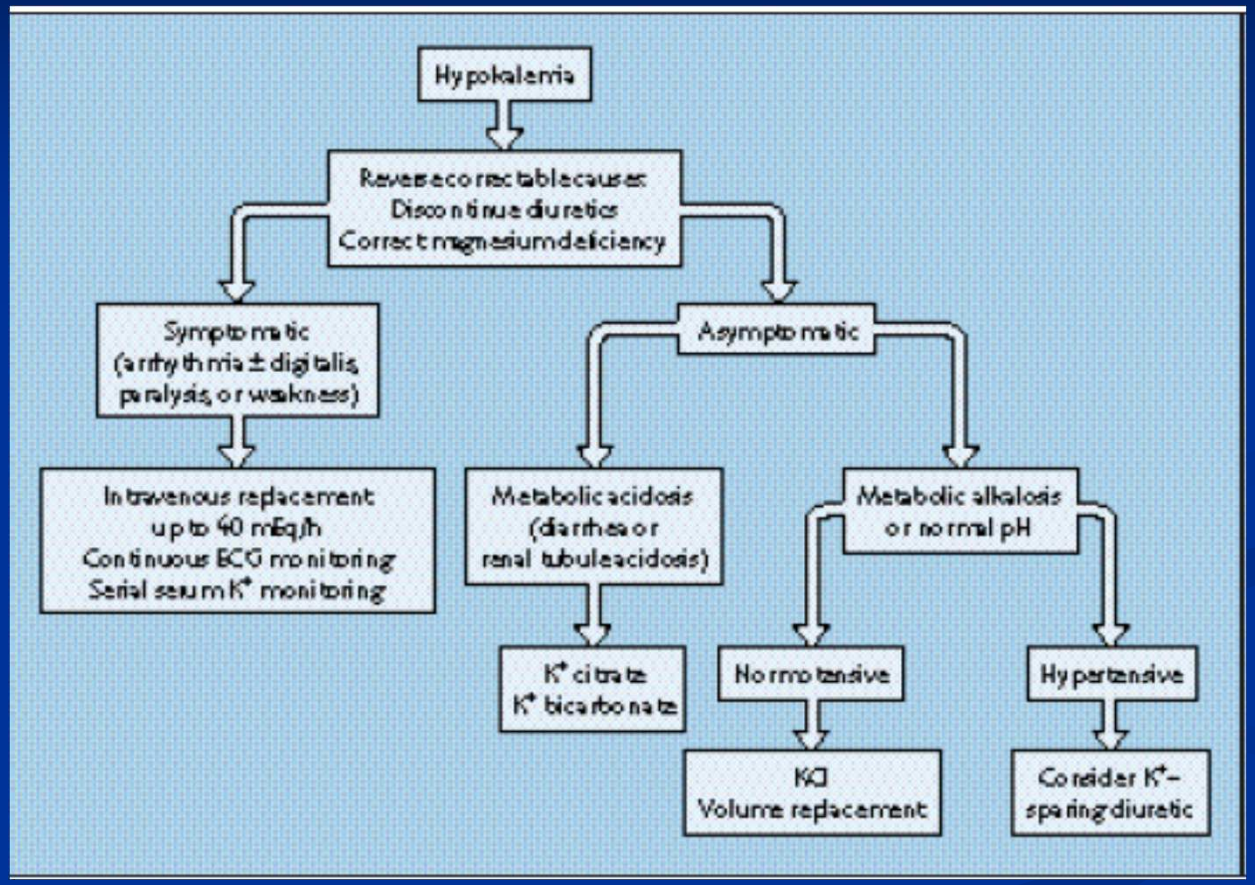
Rapporti tra potassiemia e pool potassico



Per ogni riduzione della potassiemia di 0.3 mEq/L, il deficit prevedibile è circa di 100 mEq (quantità indicativa)

Relation between hypomagnesemia, hypokalemia, and hypocalcemia.




Hypokalemia
Reverse correctable causes:
Discontinue diuretics
Correct magnesium deficiency
Symptomatic
(arrhythmia ± digitalis,
paralysis, or weakness)
Asymptomatic
Intravenous replacement
up to 40 mEq/h
Continuous ECG monitoring
Serial serum K+ monitoring
Metabolic acidosis
(diarrhea or
renal tubule acidosis)
Metabolic alkalosis
or normal pH
K+ citrate
K+ bicarbonate
Normotensive
Hypertensive
KCl
Volume replacement
Consider K+–
sparing diuretic

DEFICIT K

K>3,0 mmol→100-200 mmol

K<3,0 mmol→200-400 mmol

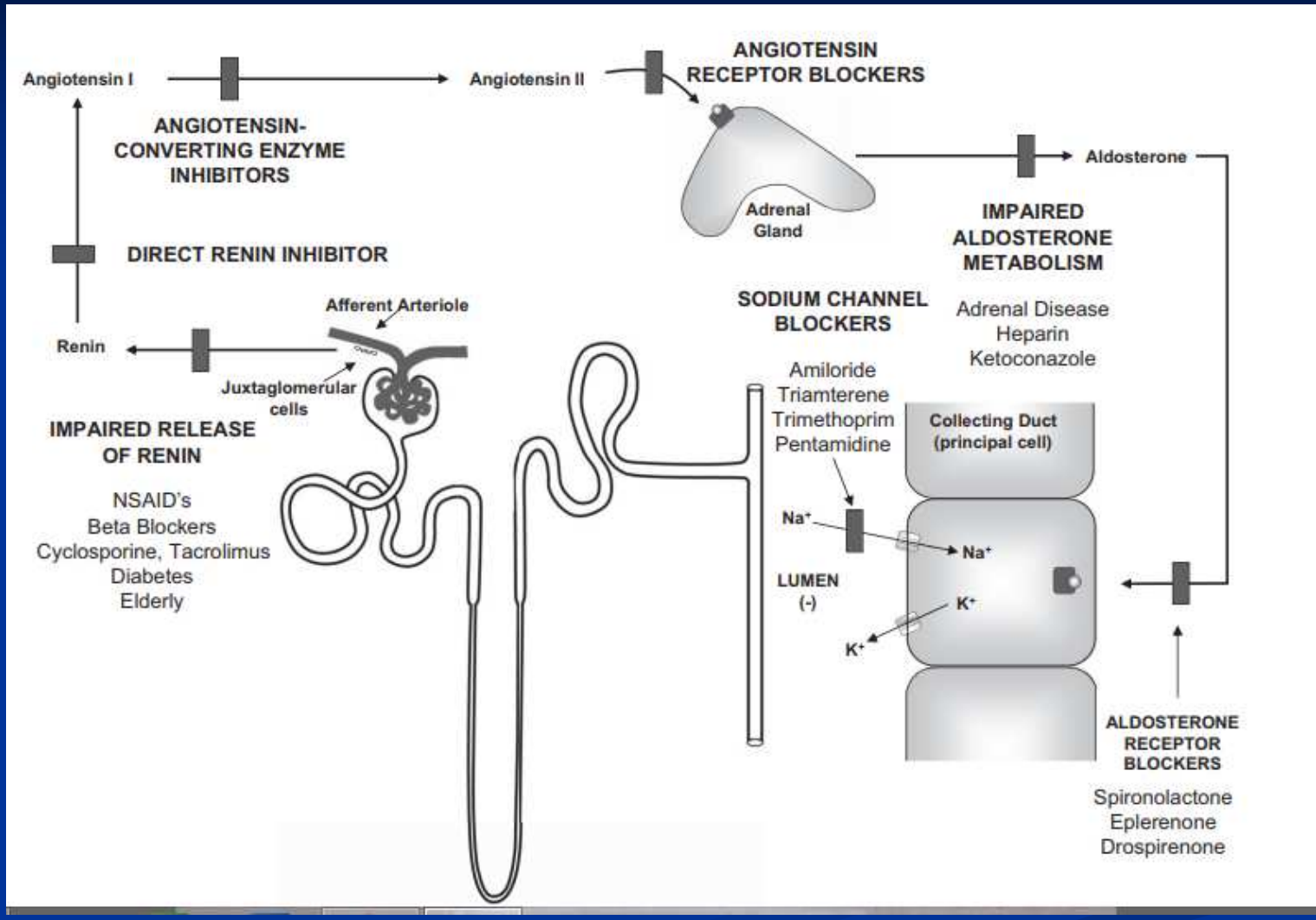
- CONCENTRZIONE MAX: 20 mmol/100 cc
- VELOCITA' MAX: 20 mmol/h

TABLE 1. **Causes of Hyperkalemia***

- **Factitious hyperkalemia**
- **Increased intake**
  - Potassium supplements
  - Penicillin G potassium
  - Nutritional supplements
- **Increased shift from intracellular space**
  - Cell destruction
    - Massive hemolysis
    - Tumor lysis syndrome
    - Rhabdomyolysis
    - Burns
    - Trauma
  - Normal anion gap acidosis
  - Lack of insulin
    - Diabetic ketoacidosis
    - Starvation
    - Somatostatin
  - Hyperosmolality
  - Hyperkalemic periodic paralysis
  - Succinyl choline
  - β-Blockers
  - Digoxin intoxication
  - Dried toad skin (Chan Su/Senso)
  - Intravenous amino acids
- **Impaired renal excretion**
  - Decreased distal flow
    - Decreased effective circulating volume
    - Chronic or acute renal failure
    - Nonsteroidal anti-inflammatory drugs
  - Hypoaldosteronism
    - Primary adrenal insufficiency
    - Medications and herbals
      - Spironolactone
      - Triamterene
      - Amiloride
      - ACE inhibitors/ARBs
      - Trimethoprim/pentamidine
      - Cyclosporine/tacrolimus
      - Heparin
    - Primary renin insufficiency
    - Pseudohypoaldosteronism
    - Distal renal tubular acidosis
    - Congenital adrenal hyperplasia
    - Interstitial renal disease
- **Unknown mechanism**
  - Alfalfa
  - Dandelion
  - Noni juice

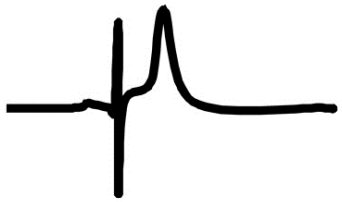
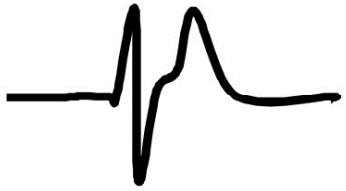
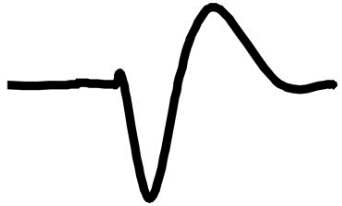
*ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

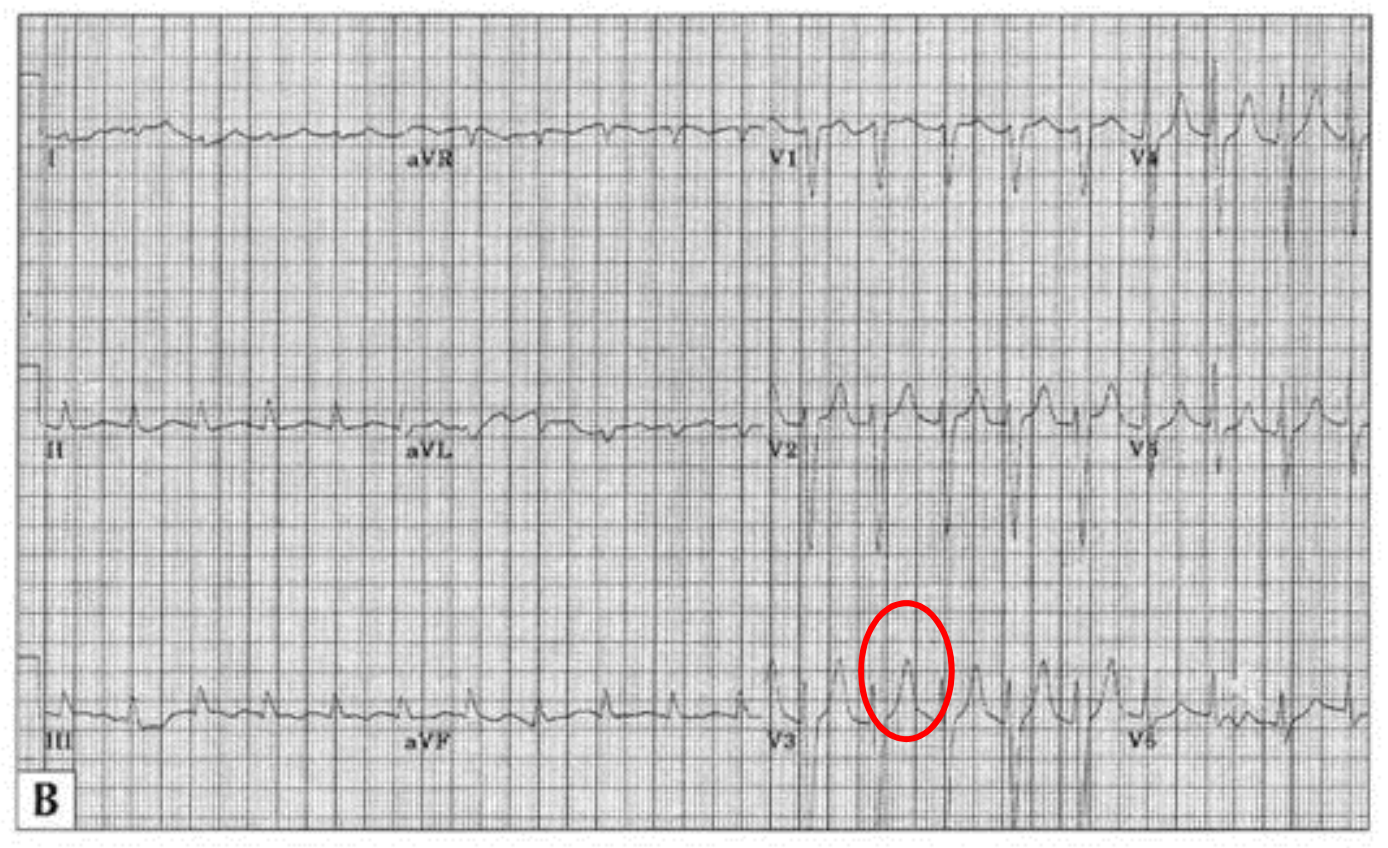
Data from reference 23.


Angiotensin I
ANGIOTENSIN-
CONVERTING ENZYME
INHIBITORS
Angiotensin II
ANGIOTENSIN
RECEPTOR BLOCKERS
Adrenal
Gland
Aldosterone
IMPAIRED
ALDOSTERONE
METABOLISM
Adrenal Disease
Heparin
Ketoconazole
DIRECT RENIN INHIBITOR
Renin
Afferent Arteriole
Juxtaglomerular
cells
IMPAIRED RELEASE
OF RENIN
NSAID's
Beta Blockers
Cyclosporine, Tacrolimus
Diabetes
Elderly
SODIUM CHANNEL
BLOCKERS
Amiloride
Triamterene
Trimethoprim
Pentamidine
Collecting Duct
(principal cell)
Na+
Na+
LUMEN
(-)
K+
K+
ALDOSTERONE
RECEPTOR
BLOCKERS
Spironolactone
Eplerenone
Drospirenone

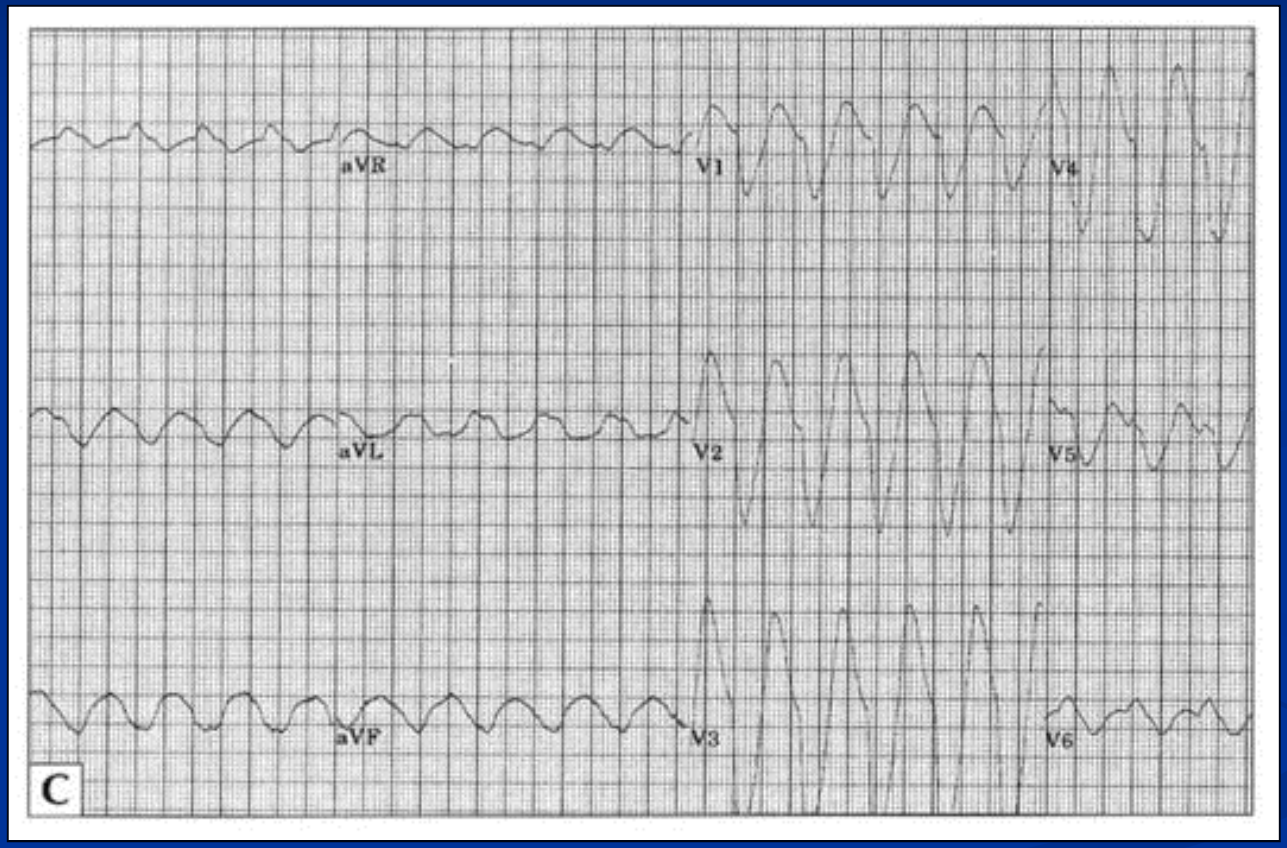
Clinical manifestations of hyperkalemia

- **CARDIOVASCULAR**
  - Arrhythmias
- **NEUROMUSCOLAR**
  - Parhestesias/Respiratory insufficiency
  - Flaccid paralysis
  - Mental confusion

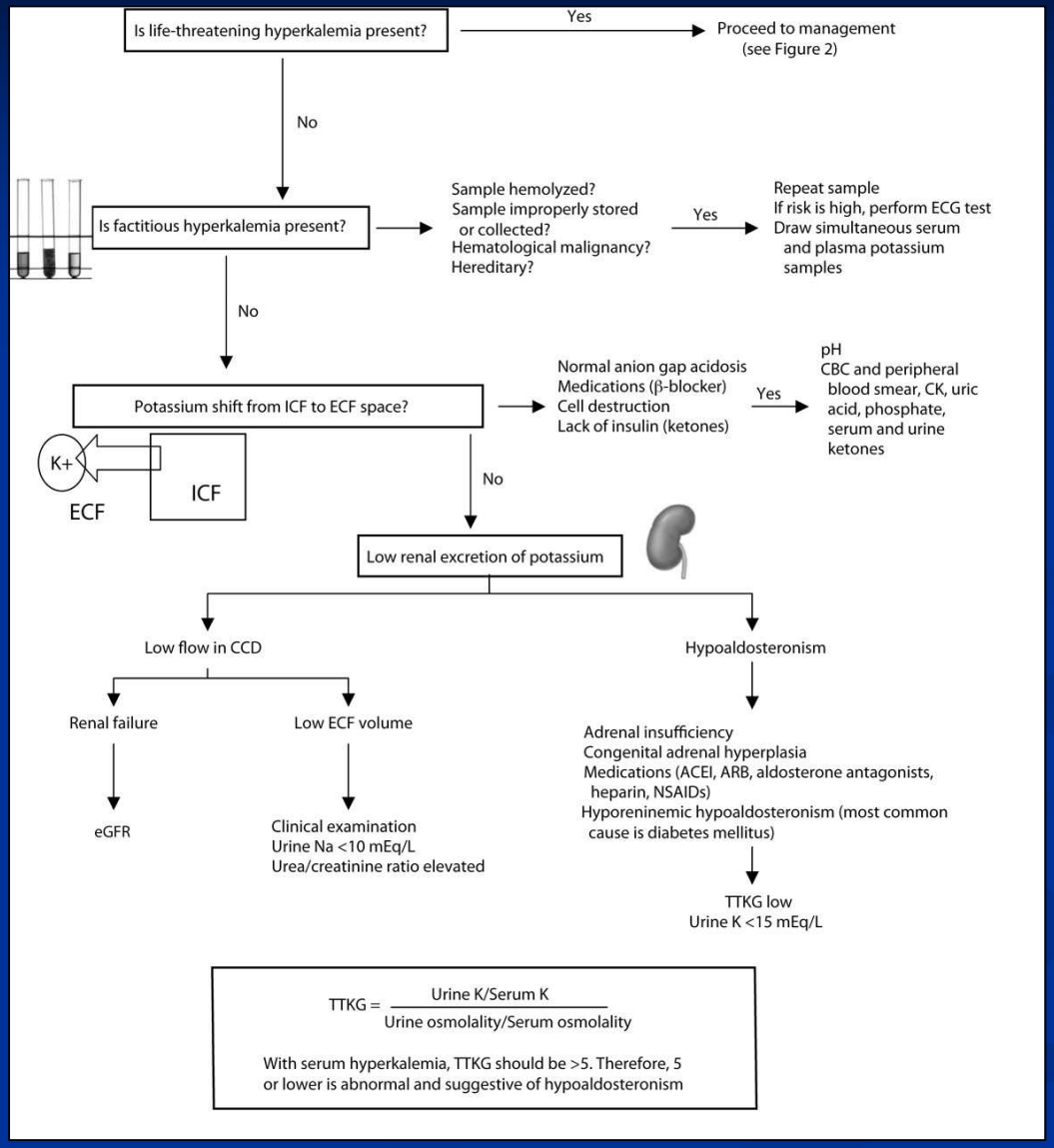
Serum potassium	Typical ECG appearance	Possible ECG abnormalities
Mild (5.5-6.5 mEq/L)		Peaked T waves Prolonged PR segment
Moderate (6.5-8.0 mEq/L)		Loss of P wave Prolonged QRS complex ST-segment elevation Ectopic beats and escape rhythms
Severe (>8.0 mEq/L)		Progressive widening of QRS complex Sine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


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
B

K 9,2 mmol/l



Algorithmic approach to the diagnosis of hyperkalemia



Algorithmic management of hyperkalemia.