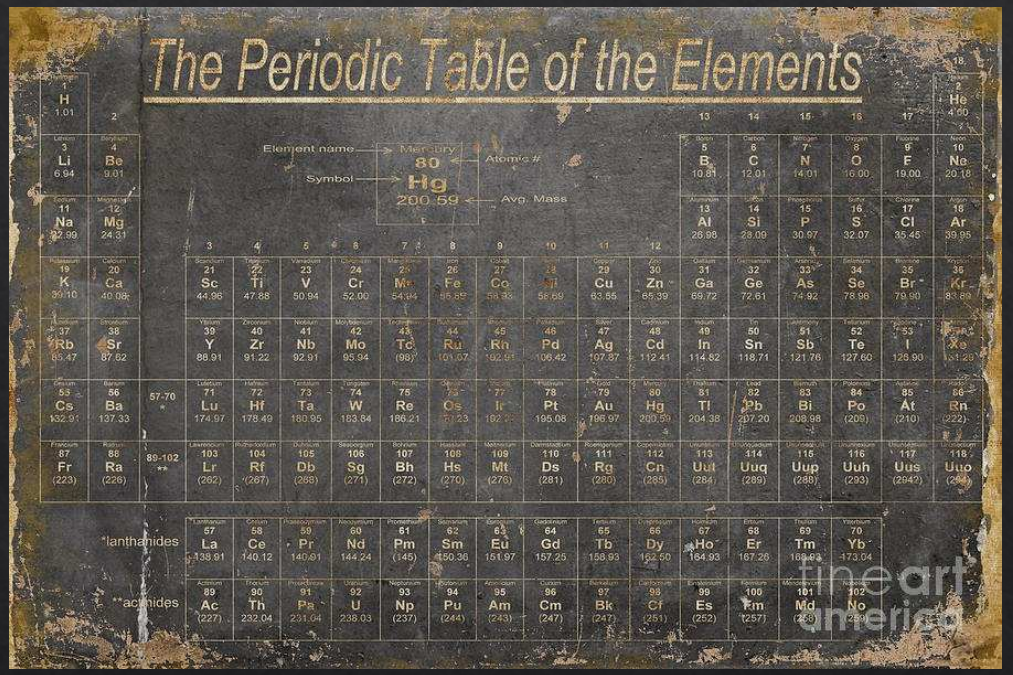
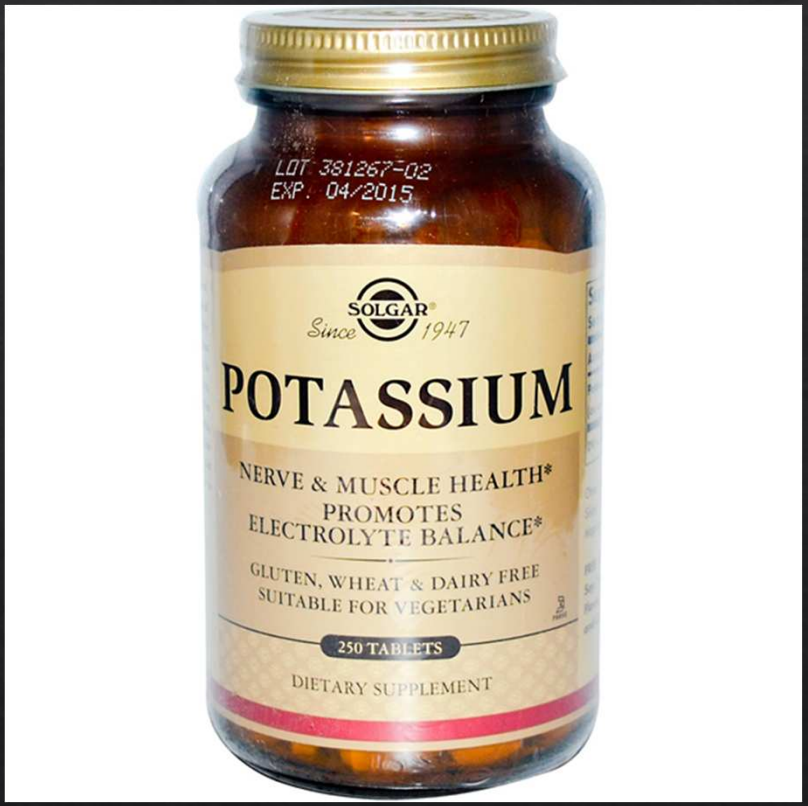
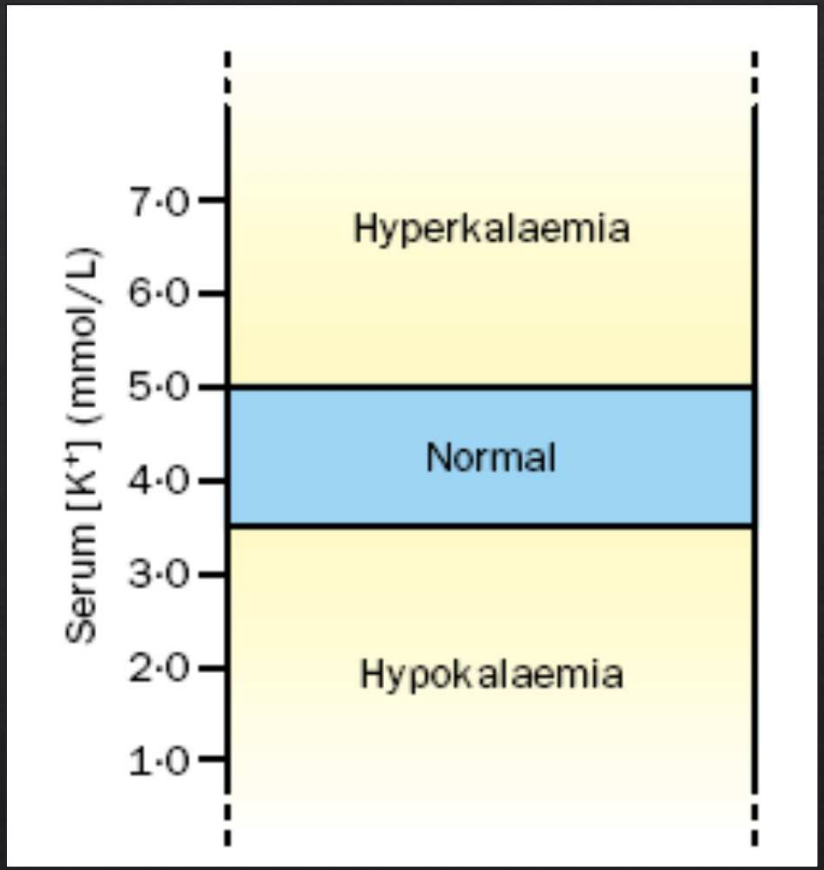
LE PRINCIPALI DISIONEMIE

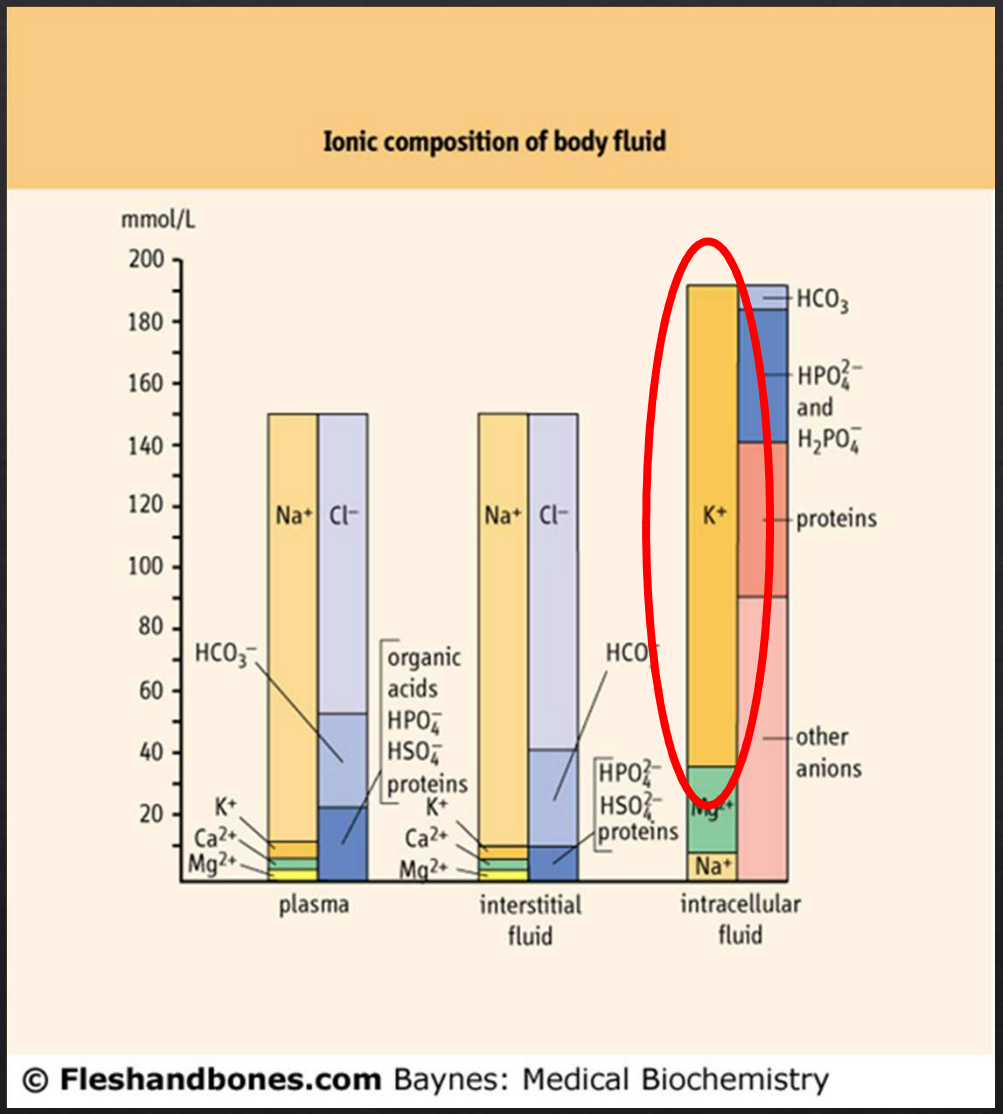


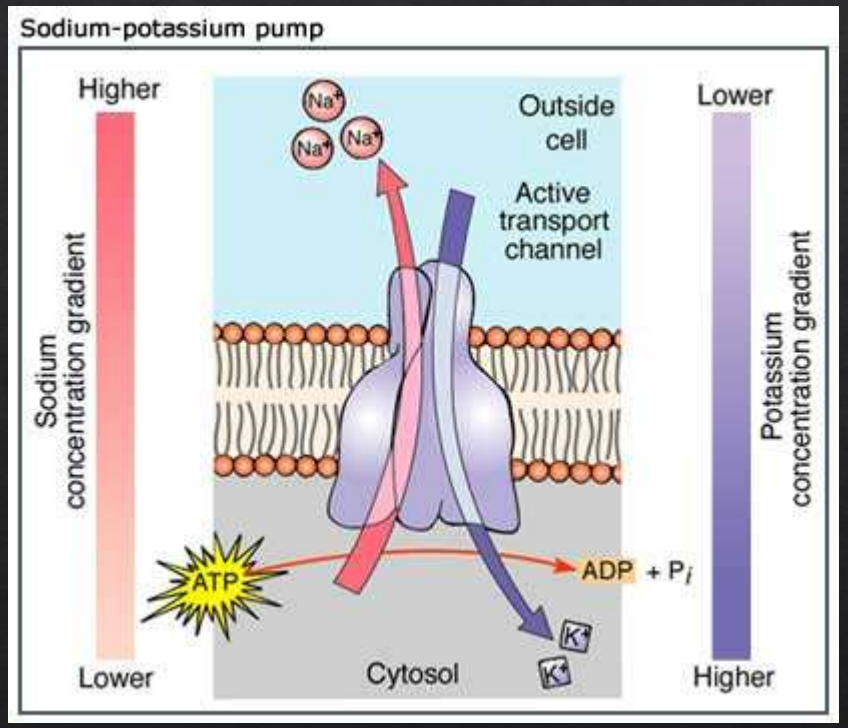
LEZIONE MEDICINA INTERNA
Ferrara 24/10/18
Dott. C. Molino

POTASSIO

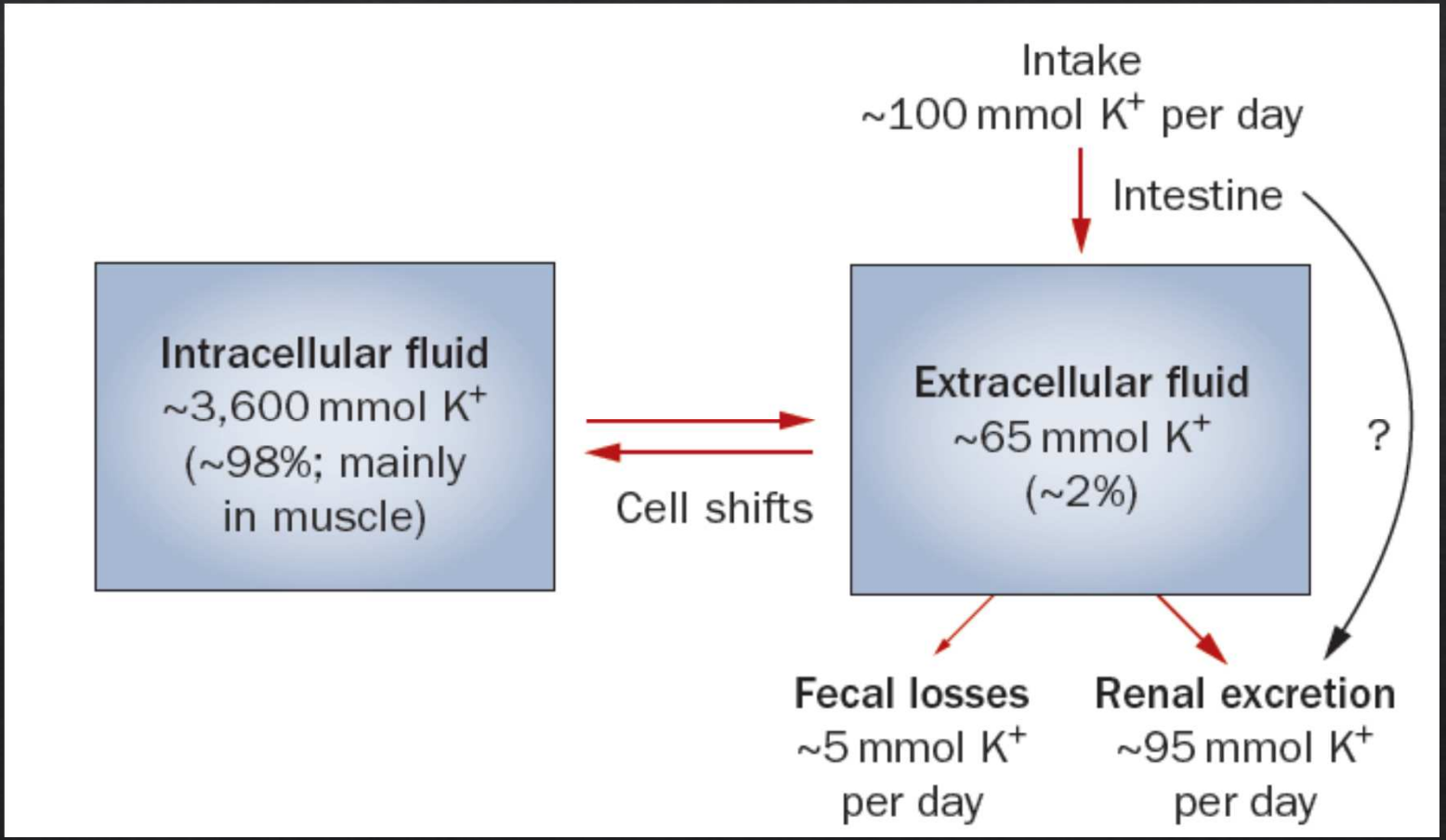

LOT 381267-02
EXP. 04/2015
SOLGAR
Since 1947
POTASSIUM
NERVE & MUSCLE HEALTH*
PROMOTES
ELECTROLYTE BALANCE*
GLUTEN, WHEAT & DAIRY FREE
SUITABLE FOR VEGETARIANS
250 TABLETS
DIETARY SUPPLEMENT


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
mmol/L
200
180
160
140
120
100
80
60
40
20
Na+
Cl−
HCO3−
organic acids
HPO4−
HSO4−
proteins
K+
Ca2+
Mg2+
plasma
interstitial fluid
intracellular fluid
HCO3
HPO4 2−
and
H2PO4−
proteins
other anions
HSO4 2−
© Fleshandbones.com Baynes: Medical Biochemistry


Sodium-potassium pump
Higher
Lower
Sodium concentration gradient
Outside cell
Active transport channel
Na+
Na+
Na+
ATP
ADP + Pi
K+
K+
Cytosol
Lower
Higher
Potassium concentration gradient

Total body potassium

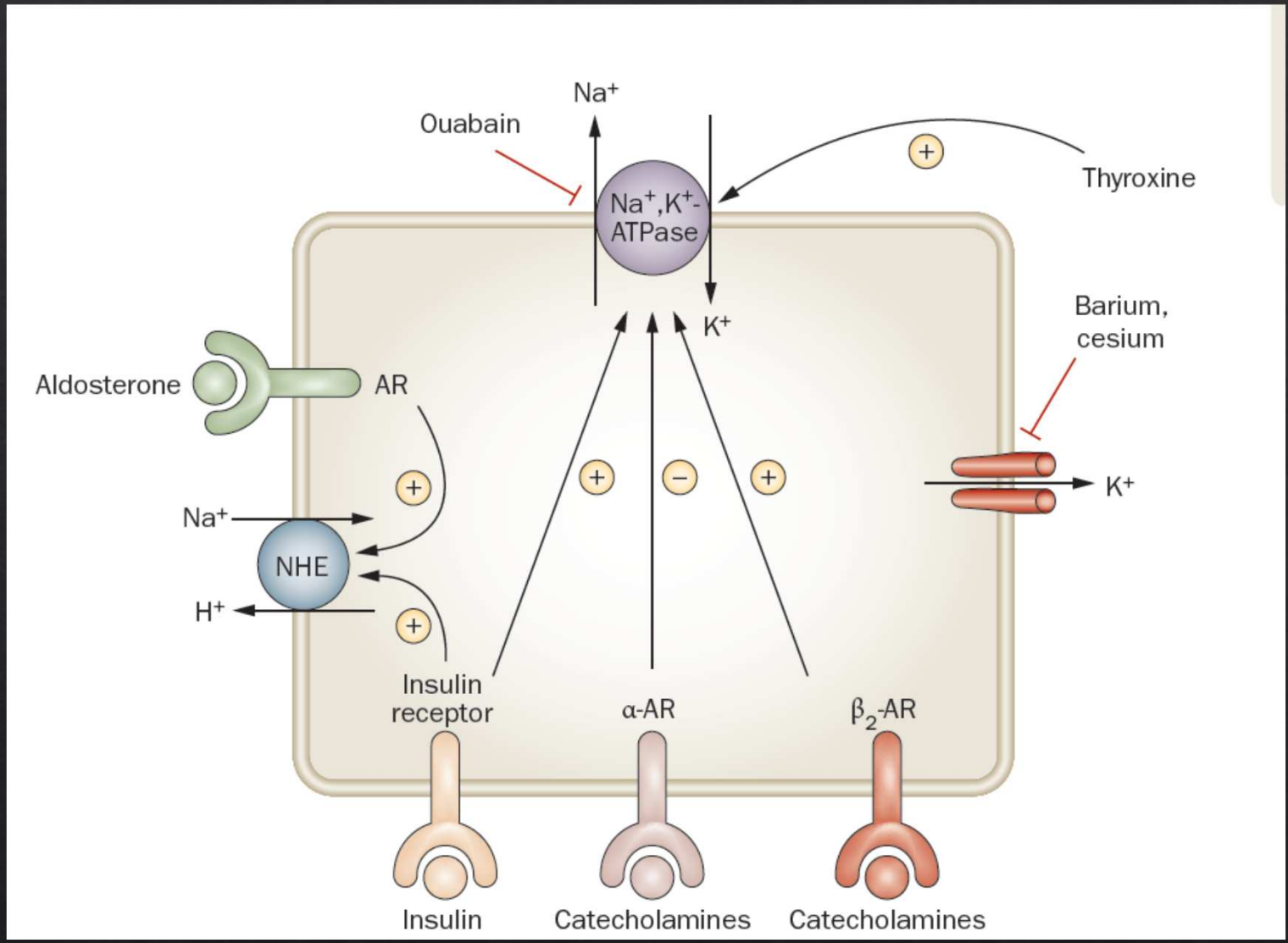


POTASSIO CONTENUTO NEGLI ALIMENTI

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		

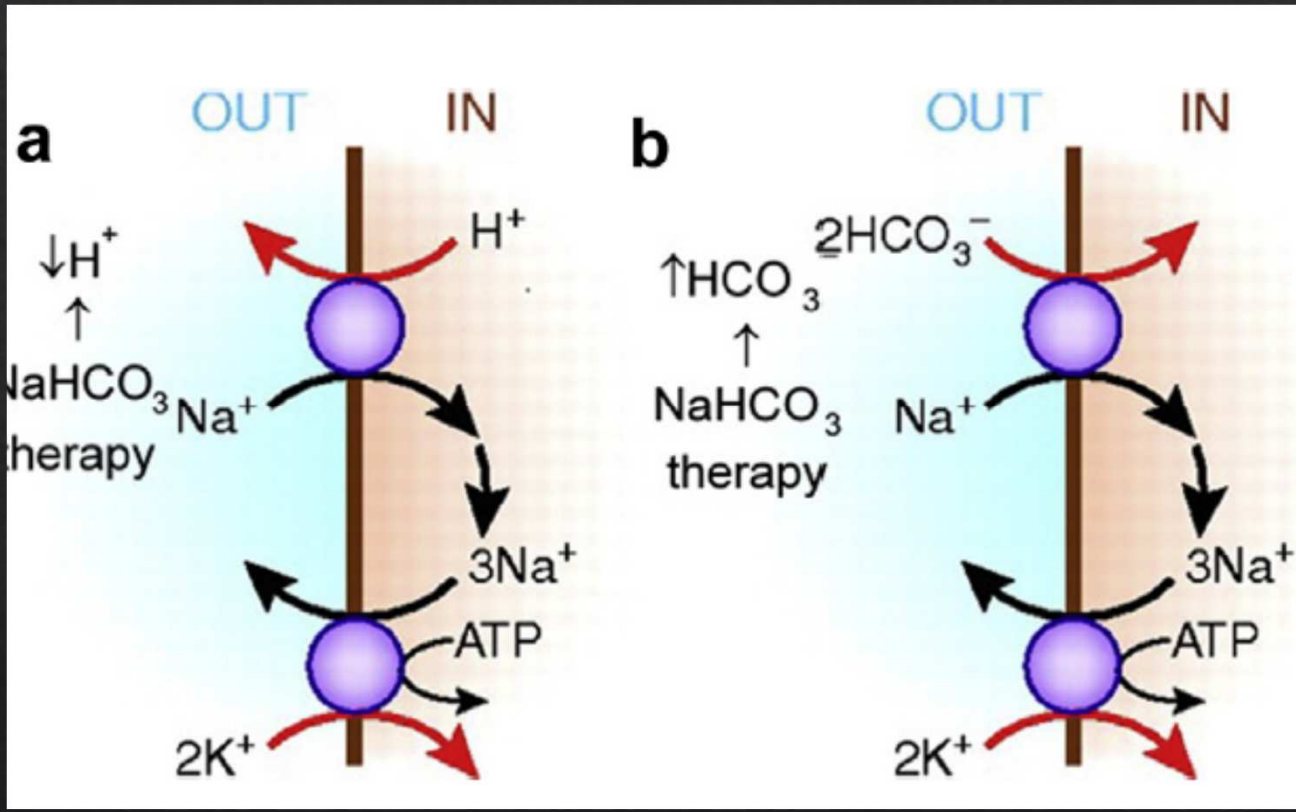
Changes in serum potassium

Regulators	*Mechanism of action*	*Potassium shift into cells*
Insulin	Activation of sodium-potassium ATPase	Increase
Catecholamines	Activation of β_2 receptors	Increase
	Activation of α receptors	Decrease
Mineralocorticoids	Unknown	Mild increase
Parathormone	Unknown	Mild decrease
Acid-base changes	Exchange of H+ for K+	See table 2
Hyperosmolality	Solvent drags	Shifts potassium extracellularly

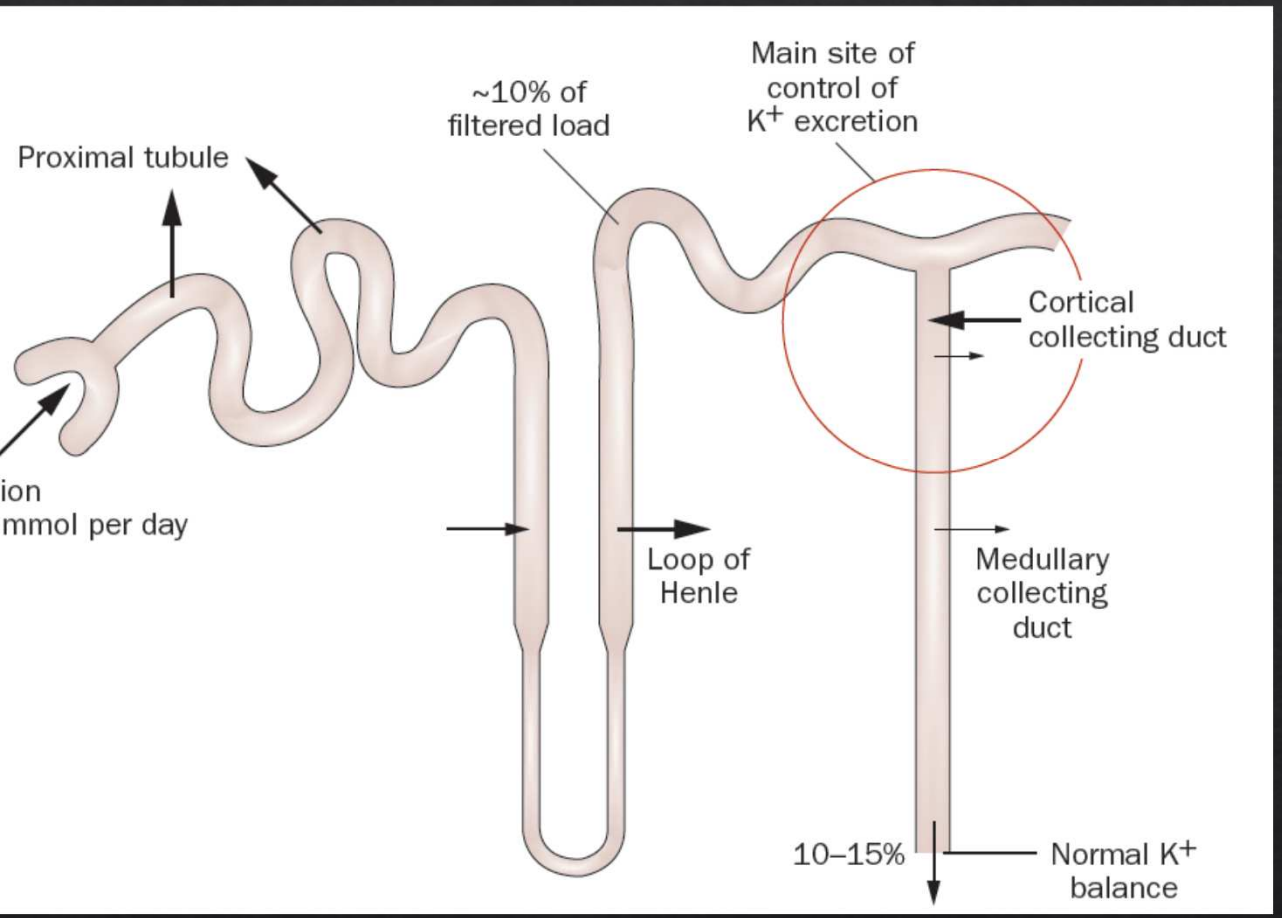

Na+
Ouabain
Na+,K+-
ATPase
Thyroxine
K+
Barium,
cesium
Aldosterone
AR
Na+
NHE
H+
K+
Insulin
receptor
α-AR
β2-AR
Insulin
Catecholamines
Catecholamines

1: Effect of acid-base disorders on
m potassium

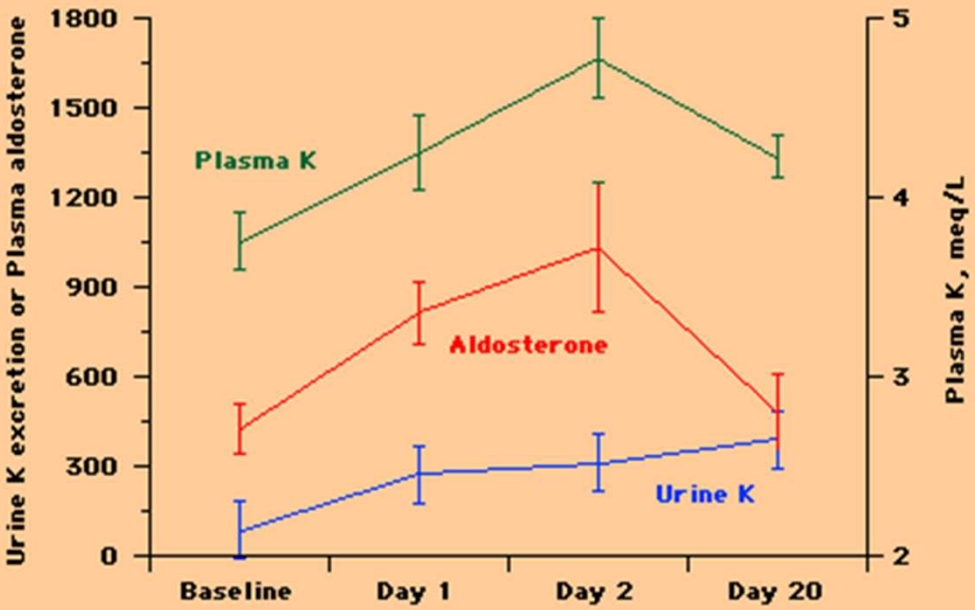
r any pH change the effect of acidae-
a is greater than alkalaemia.
on-organic (mineral acidosis) results in
hift of 0.24–1.7 mmol/l per 0.1 unit pH
ange.
rganic acidosis has little to no effect on
tassium shift.
espiratory and metabolic alkalosis and
spiratory acidosis result in similar small
ift of potassium into and out of cell
spectively (0.1–0.4 mmol/l on average).
chronic acid-base disorders the final
tassium reflects primarily the effect on
nal handling of potassium and to lesser
tent of transcellular shift.



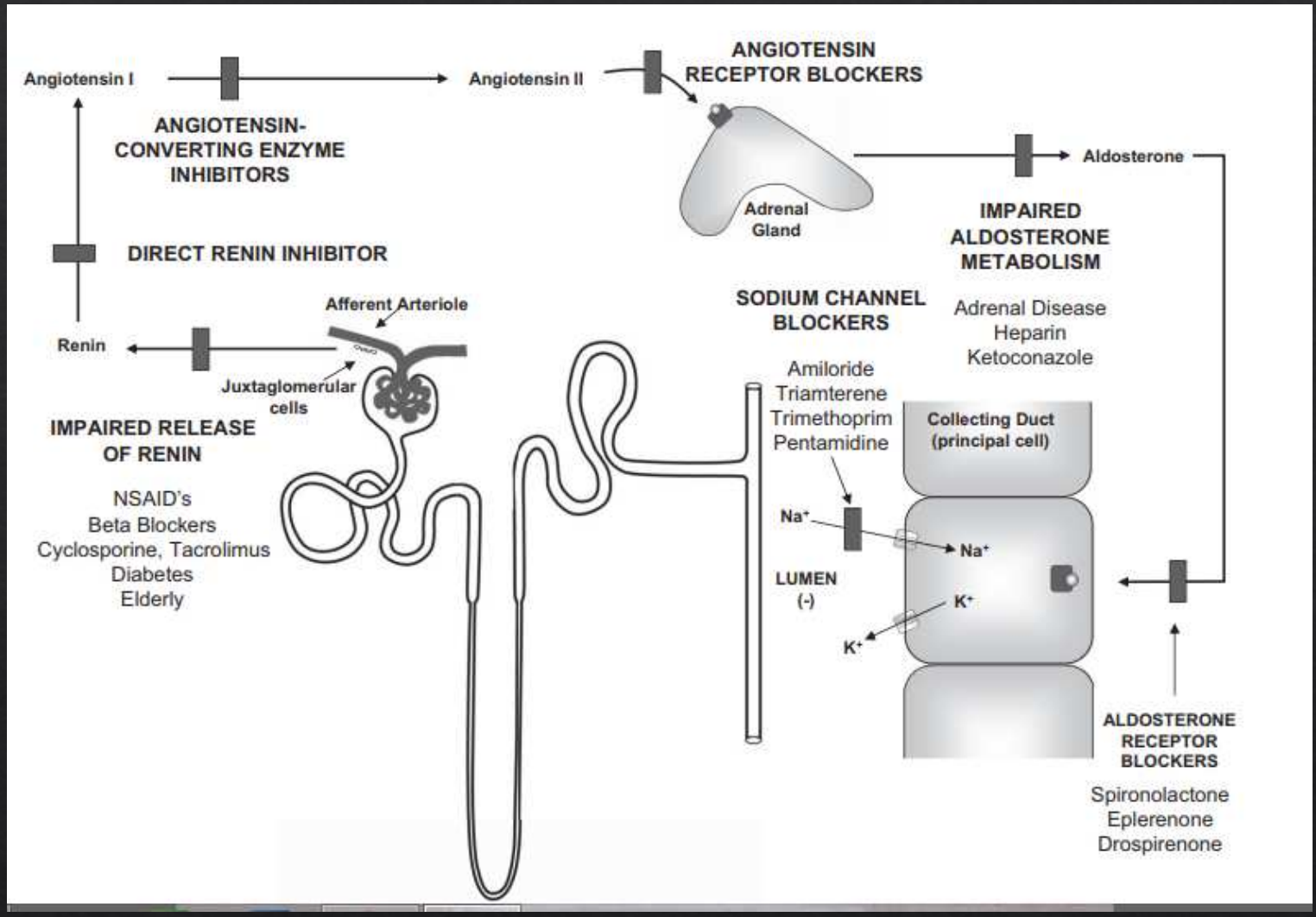
Renal potassium handling



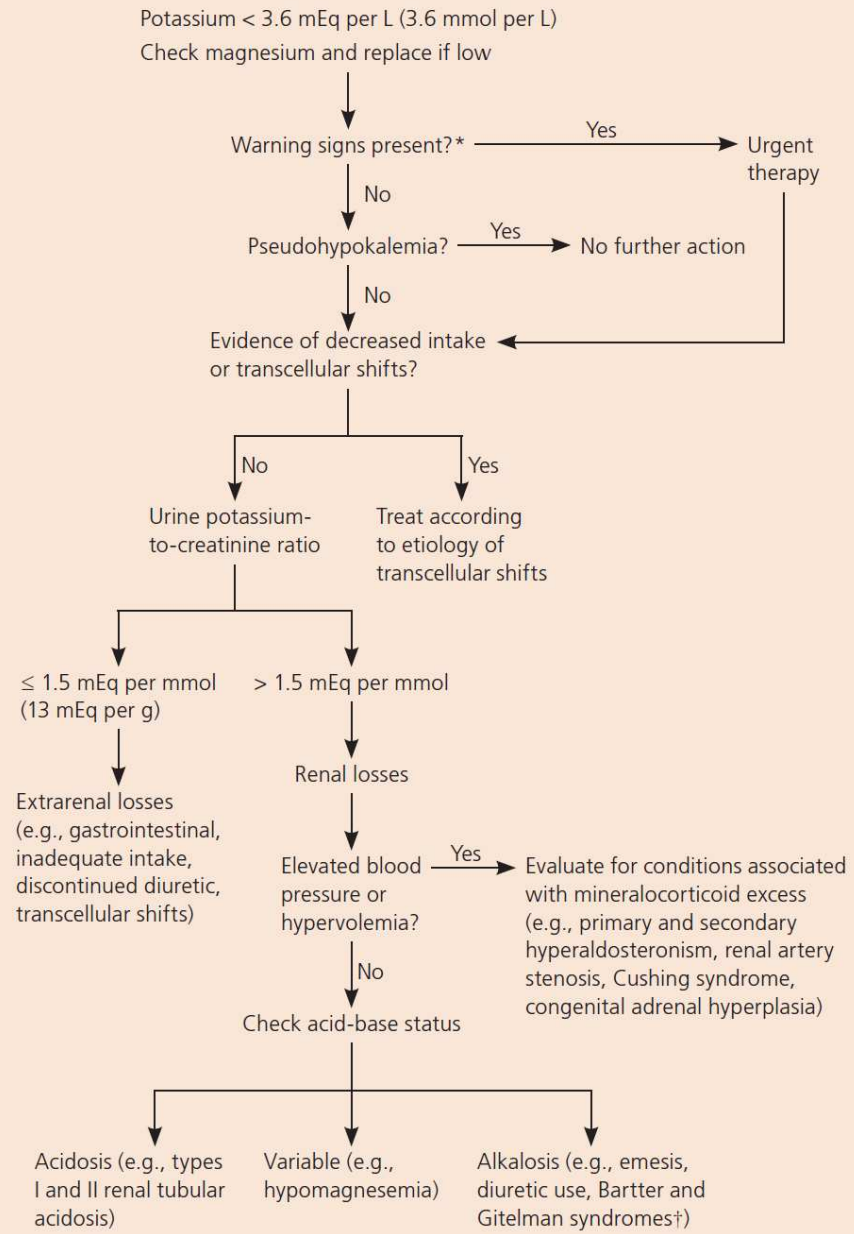
1) **ALDOSTERONE**
2) **POTASSIO**
3) **FLUSSO TUBOLARE**
4) **ANIONI NON RIASSORBIBILI TUBULO**

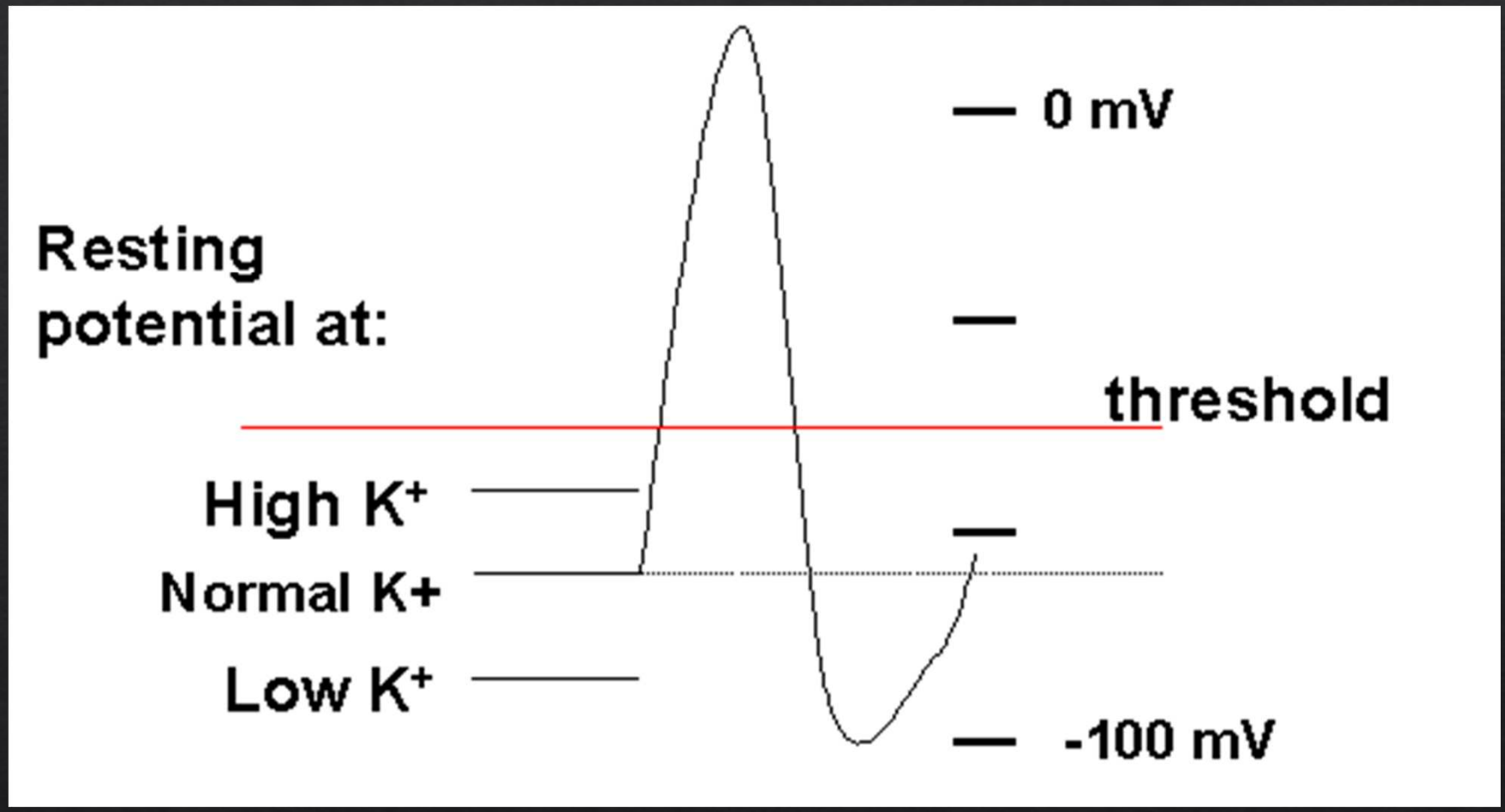


Response to potassium load Response to increasing potassium intake from 100 to 400 meq/day in normal subjects. Urinary potassium excretion rises to over 300 meq/day within two days, a response that is driven by increases in both aldosterone release and the plasma potassium concentration. By day 20, potassium 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.)


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

Evaluation of Hypokalemia

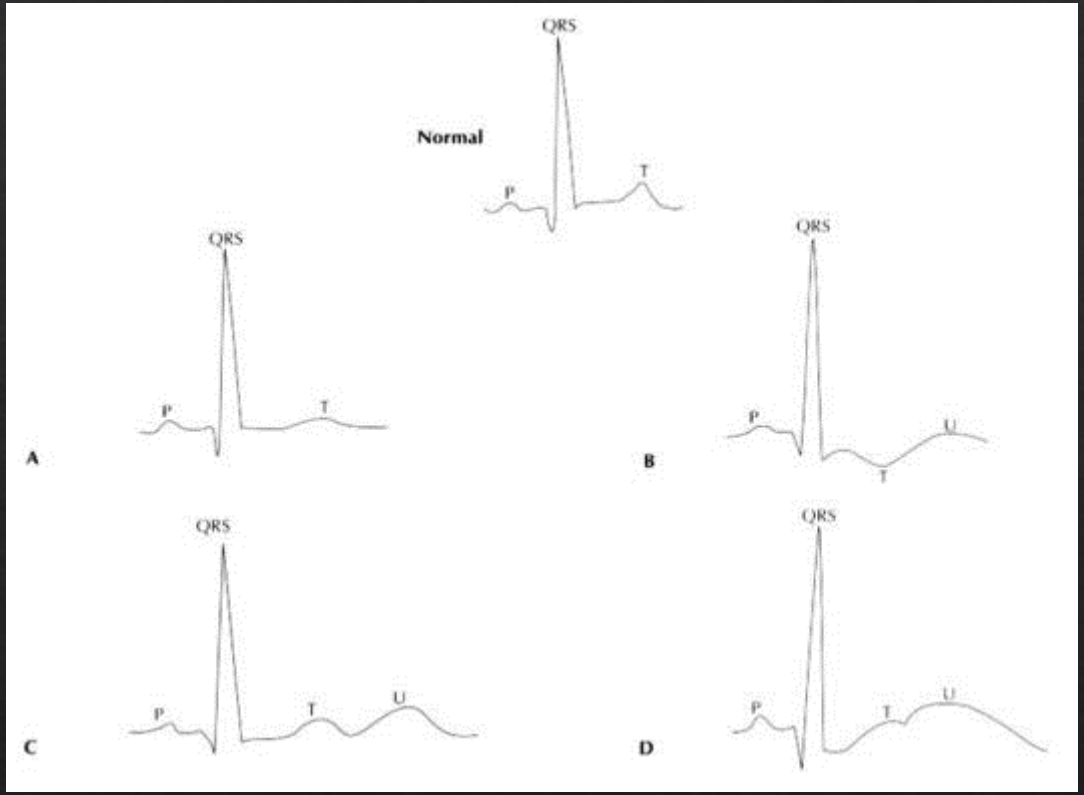



0 mV
Resting
potential at:
threshold
High K+
Normal K+
Low K+
-100 mV

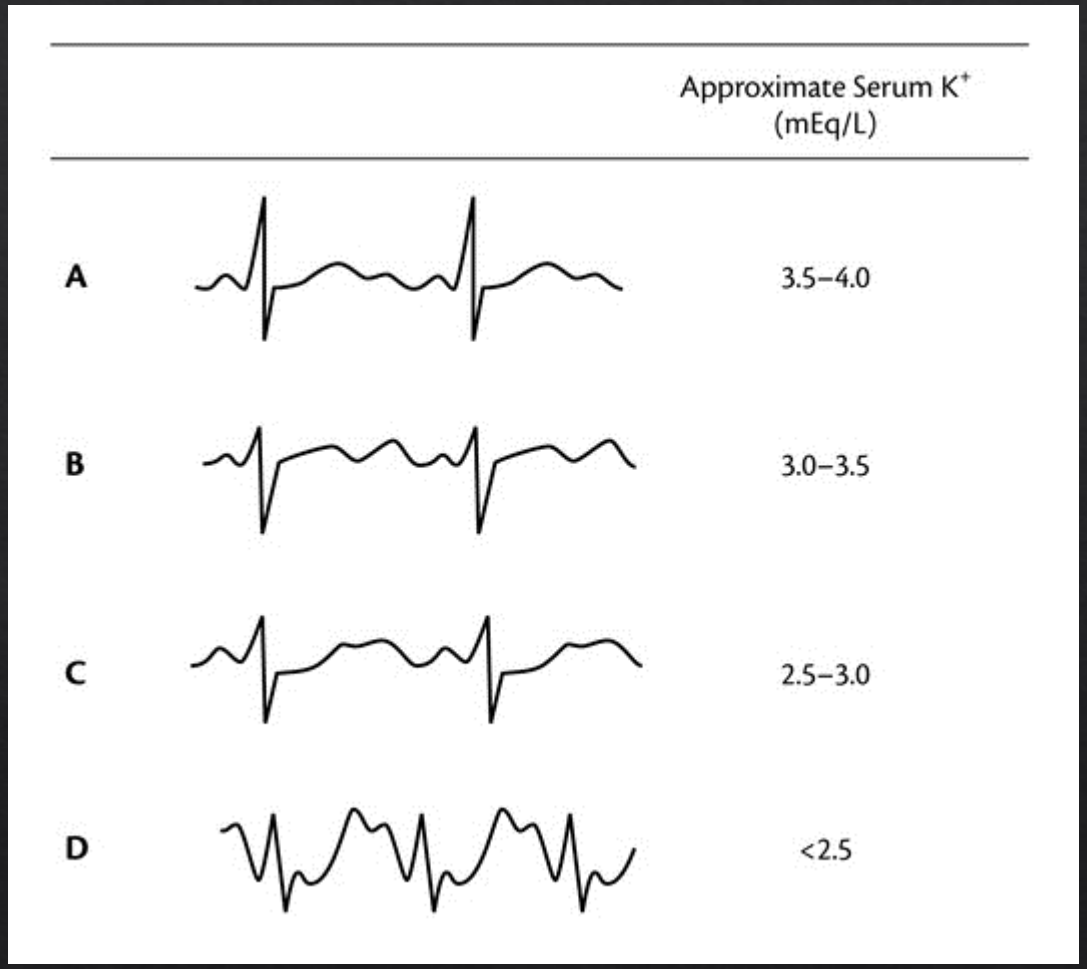
Clinical manifestations of hypokalemia

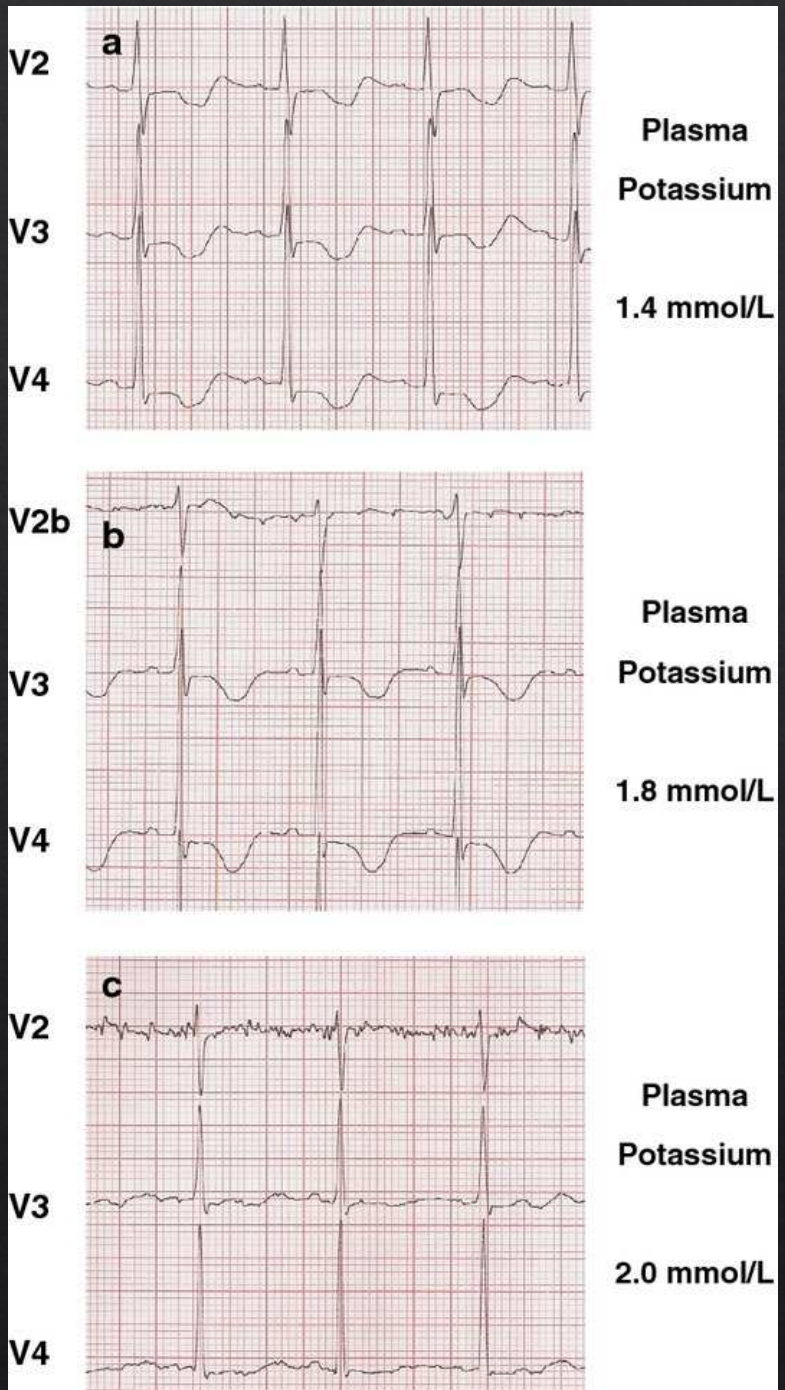
- **CARDIOVASCULAR**
  - Abnormal electrocardiogram
  - Predisposition for digitals toxicity
  - Arrhythmias
  - Hypertension
- **NEUROMUSCOLAR**
  - Constipation/ileus
  - Bladder dysfunction
  - Weakness/cramps
  - Tetany/paralisis
  - Myalgias/Rabdomyolysis
- **RENAL/ELECTROLYTE**
  - Decreased GFR 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

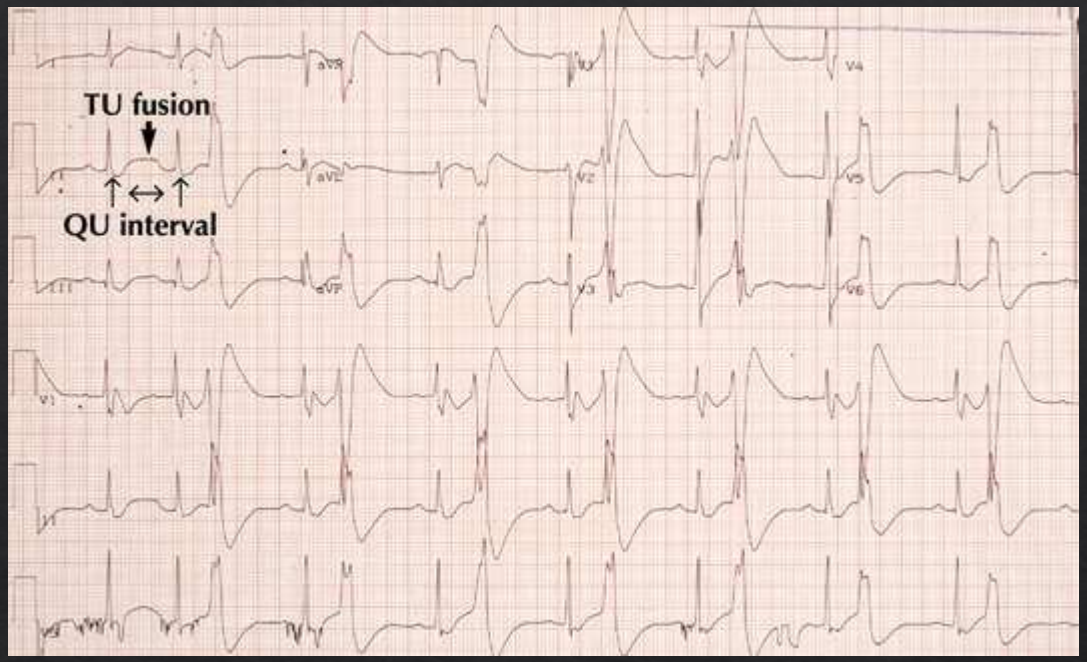
Electrocardiographic changes associated with hypokalemia



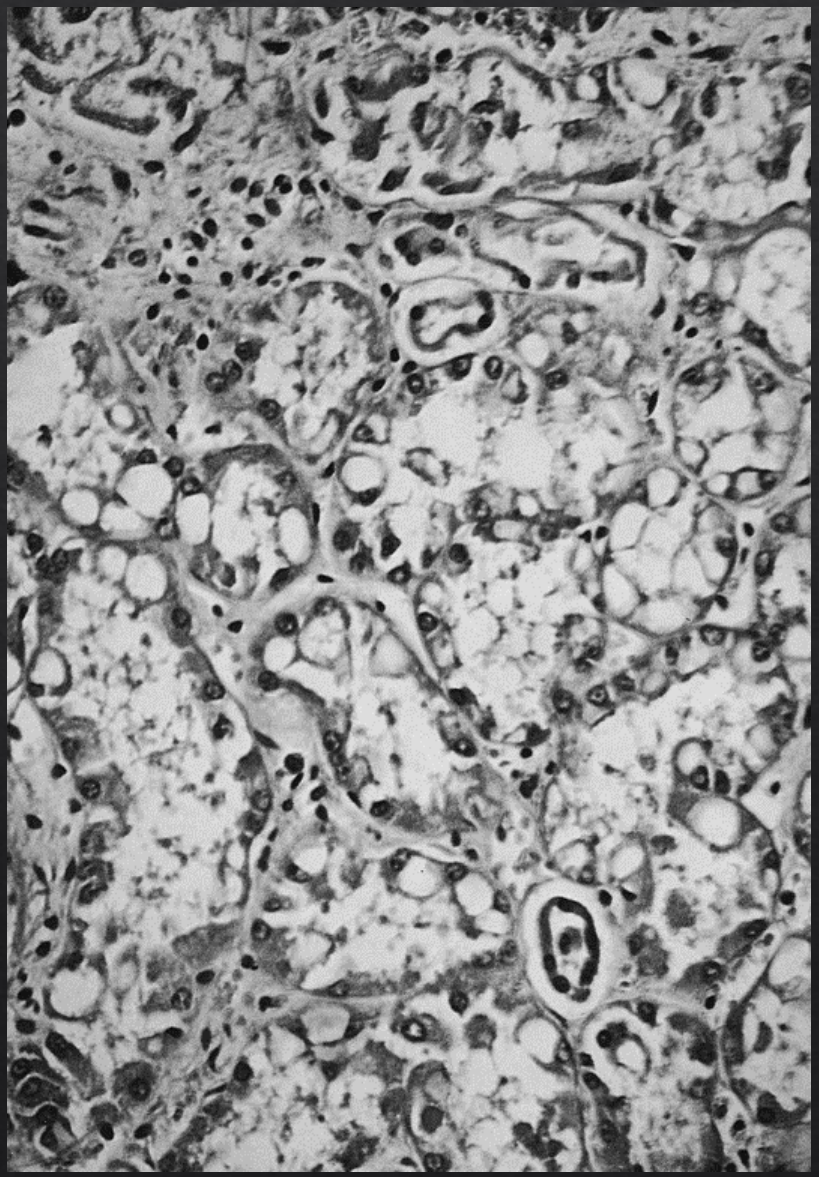
Electrocardiographic changes in hypokalemia




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


TU fusion
QU interval

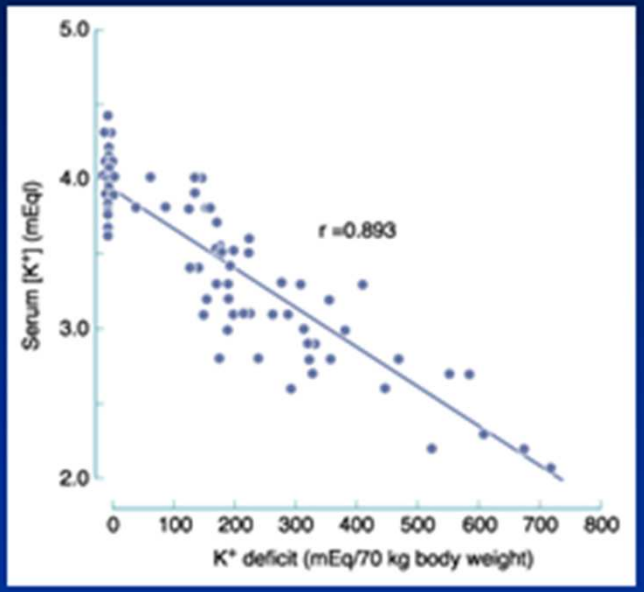
Renal lesions in hypokalemia



K Supplementation

- 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)

Box 4: Treatment of hypokalaemia

(1) Intravenous potassium (as potassium chloride)

- Usually reserved for severe hypokalaemia (serum potassium of <2.6 mmol/l).
- The rate of should not exceed 20 mmol/hour.

(2) Oral potassium

- Potassium chloride: 40–100 mmol/day in divided doses.
- Potassium phosphate (in patients with hypokalaemia and hypophsphataemia).
- Potassium bicarbonate (in patients with acidosis).

DEFICIT K

K>3,0 mmol→100-200 mmol

K<3,0 mmol→200-400 mmol

REINTEGRO K

10 mmol ev→0.1 mmol

- CONCENTRZIONE MAX: 20 mmol/100 cc
- VELOCITA' MAX: 20 mmol/h
- PERICOLO MORTE (20 mmol in 5.10 min)

Relation between hypomagnesemia, hypokalemia, and hypocalcemia.

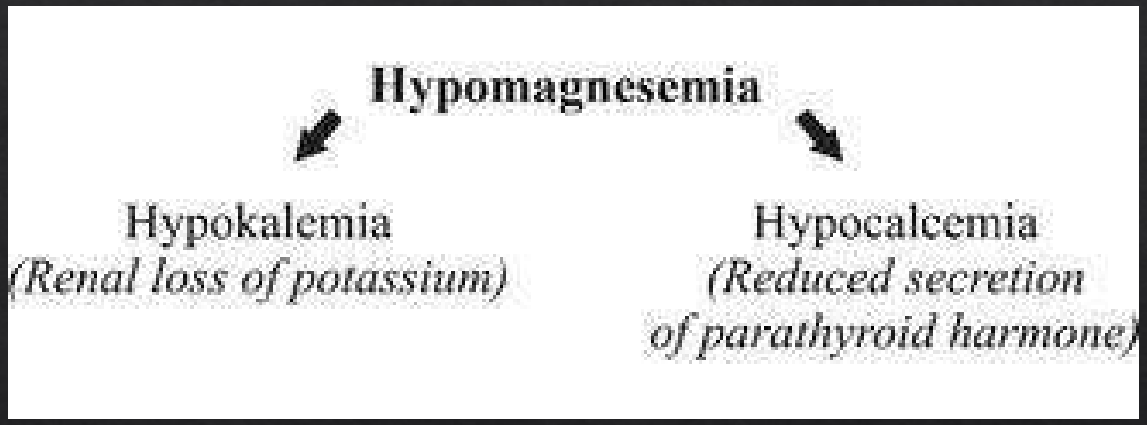


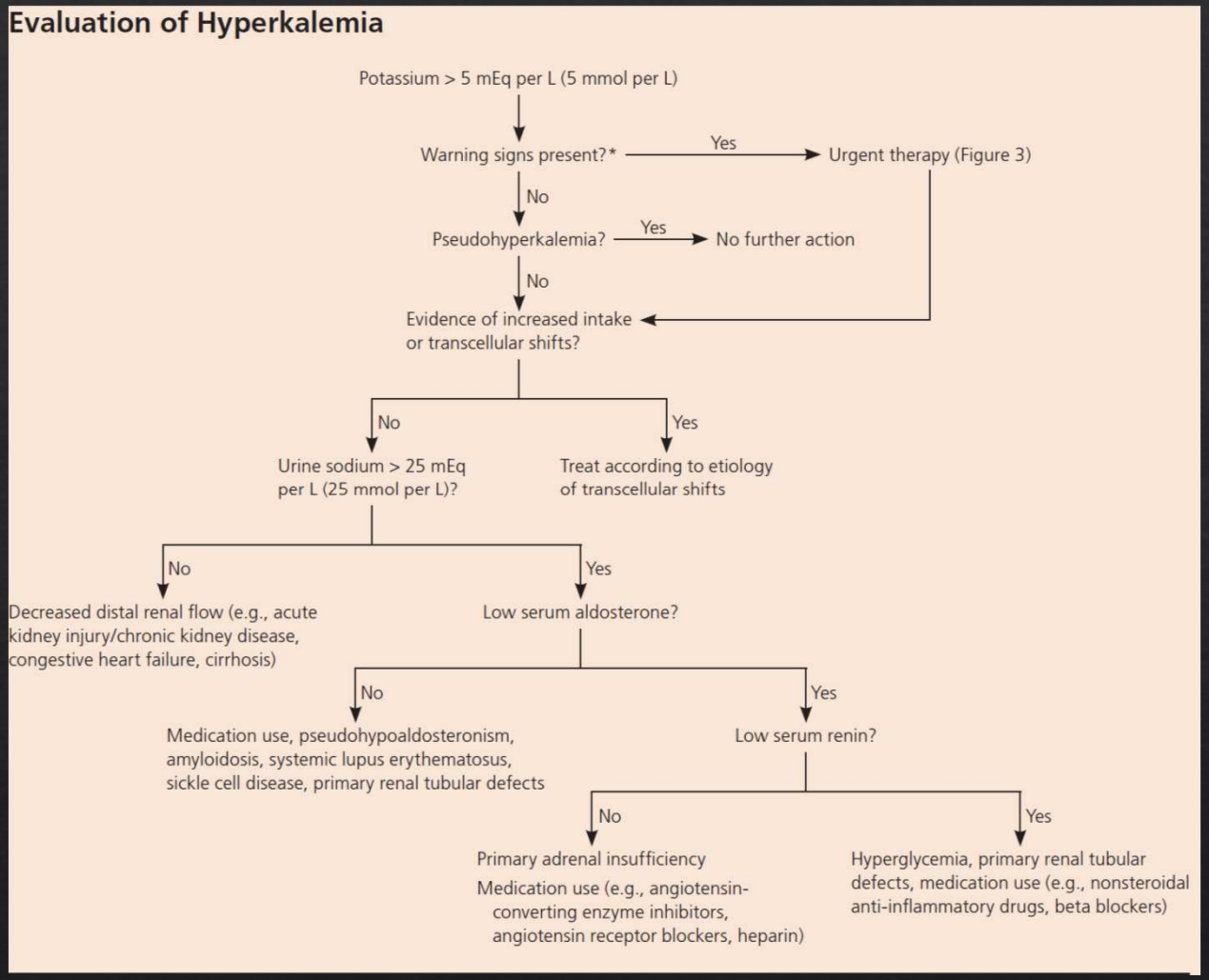
TABLE 1. **Causes of Hyperkalemia***

- **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.

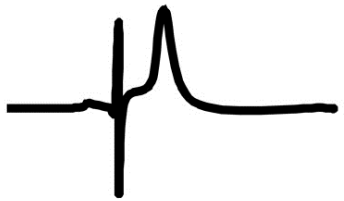
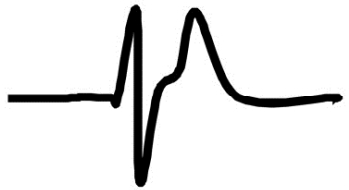
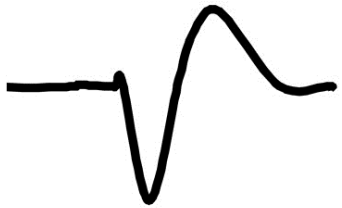
Evaluation of Hyperkalemia



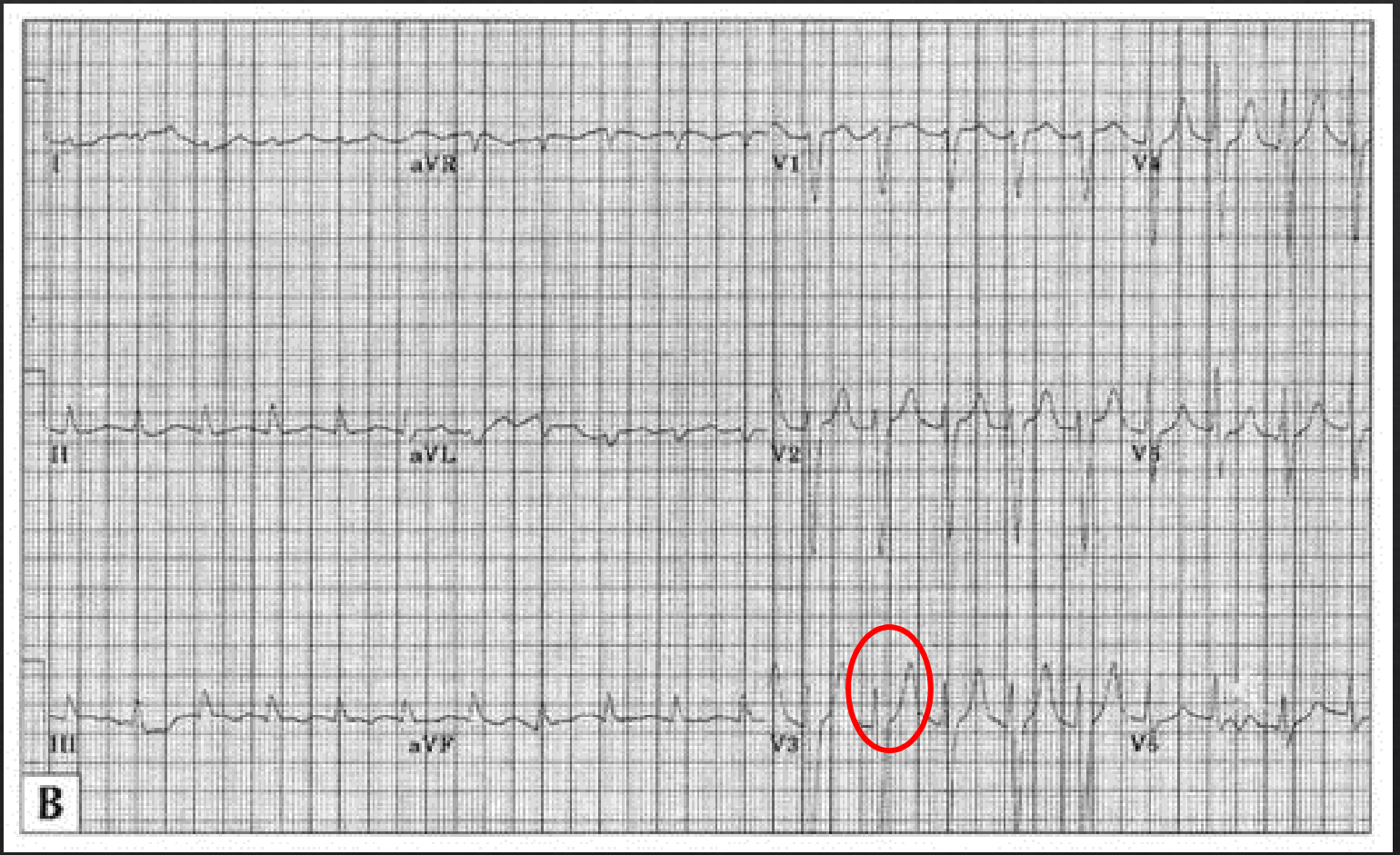
Clinical manifestations of hyperkalemia

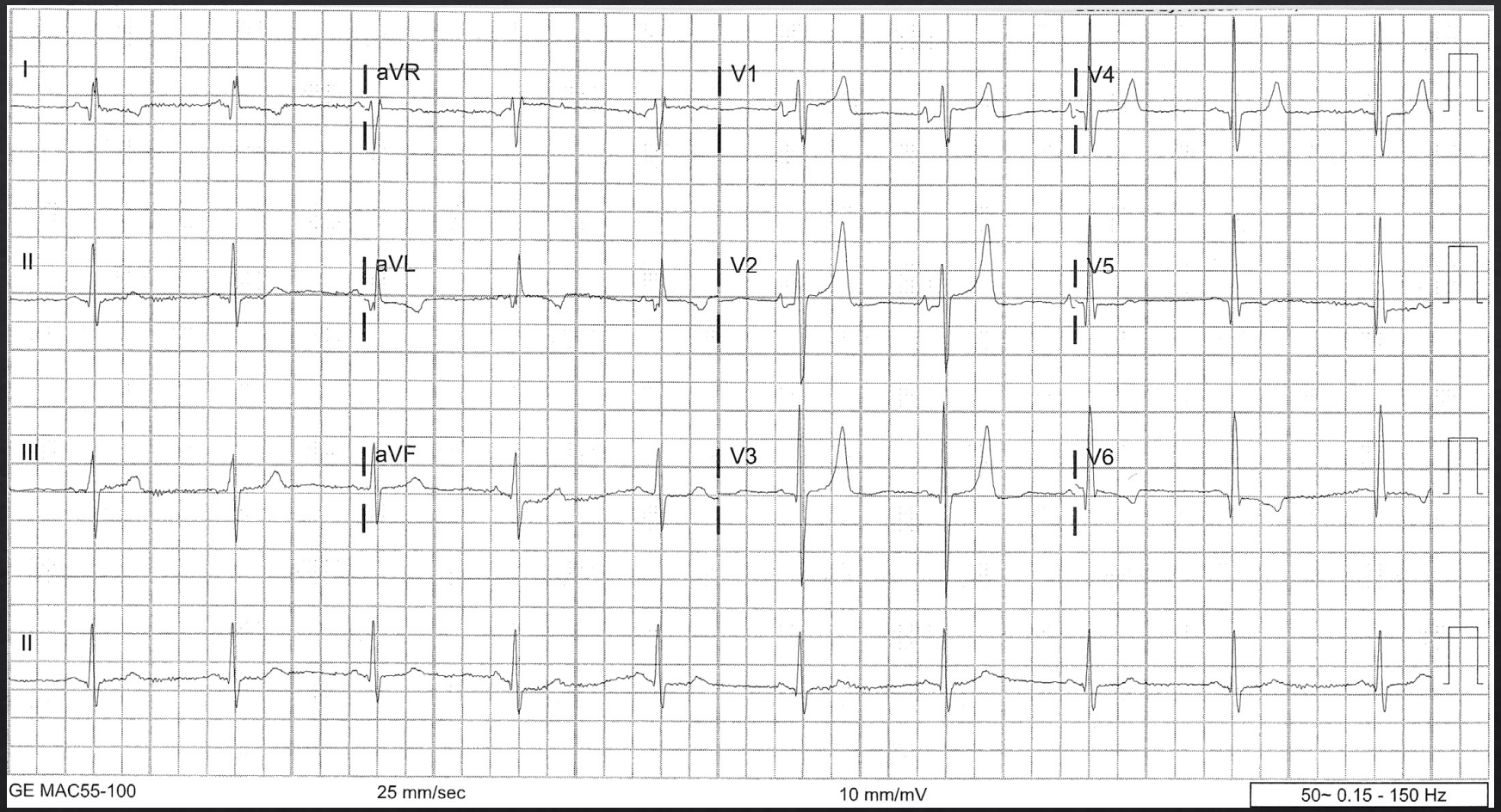
- **CARDIOVASCULAR**
  - Arrhythmias

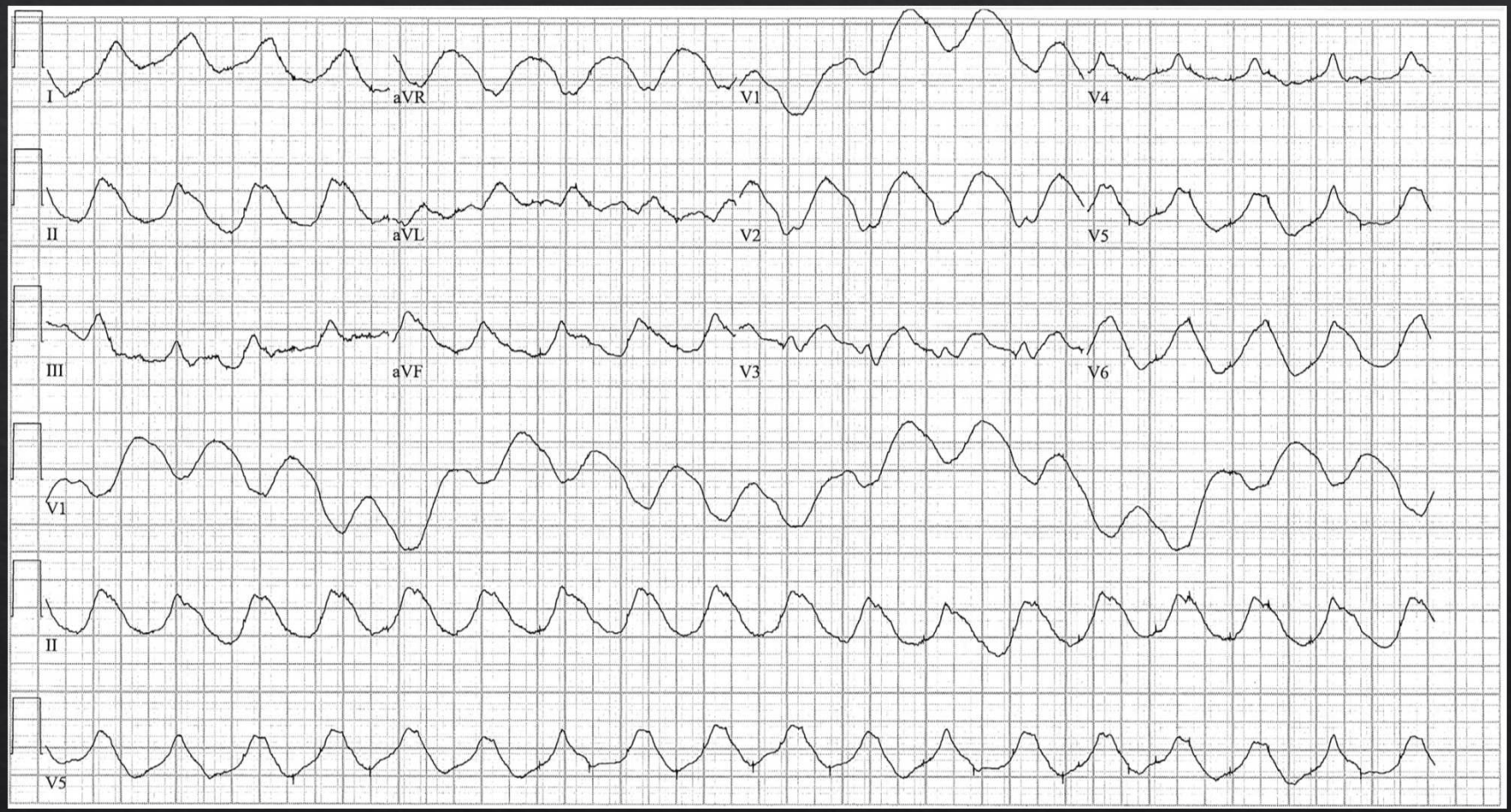
- **NEUROMUSCOLAR**
  - Parhestesias/Respiratory insufficiency
  - Flaccid paralysis
  - Mental confusion

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

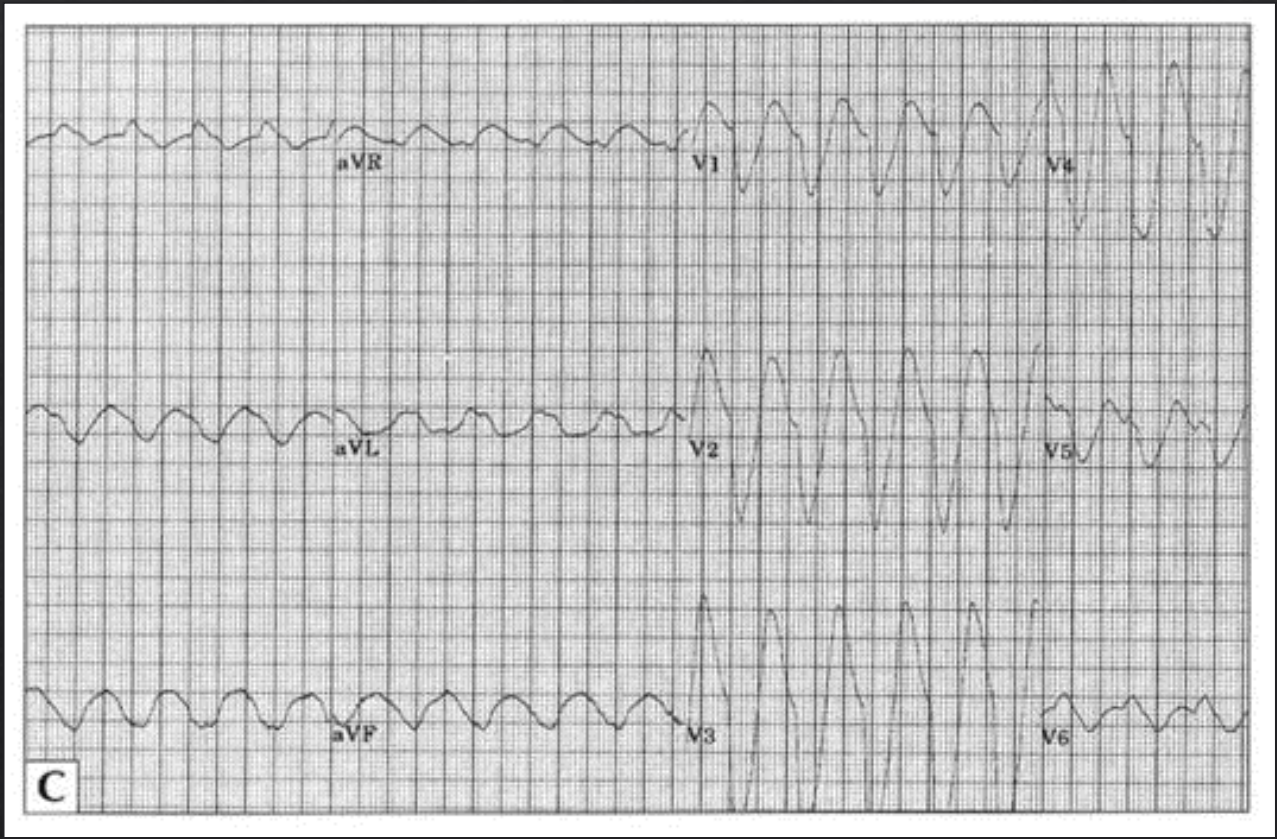
Potassium (mmol/l)	MAJOR ECG CHANGES	
5.5	**Tall, peaked (tented) T waves [T wave larger than R wave in more than 1 lead]**	
6.5		
7.0	**Prolonged PR interval**	
7.5	**Flattened or absent P waves**	
8.0		
8.5	**Widened QRS [greater than 0.12 seconds]**	**High risk of Cardiac arrest**
>9.0	Sine wave pattern (S and T waves merging)	
	Bradycardia	
	Ventricular tachycardia	


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

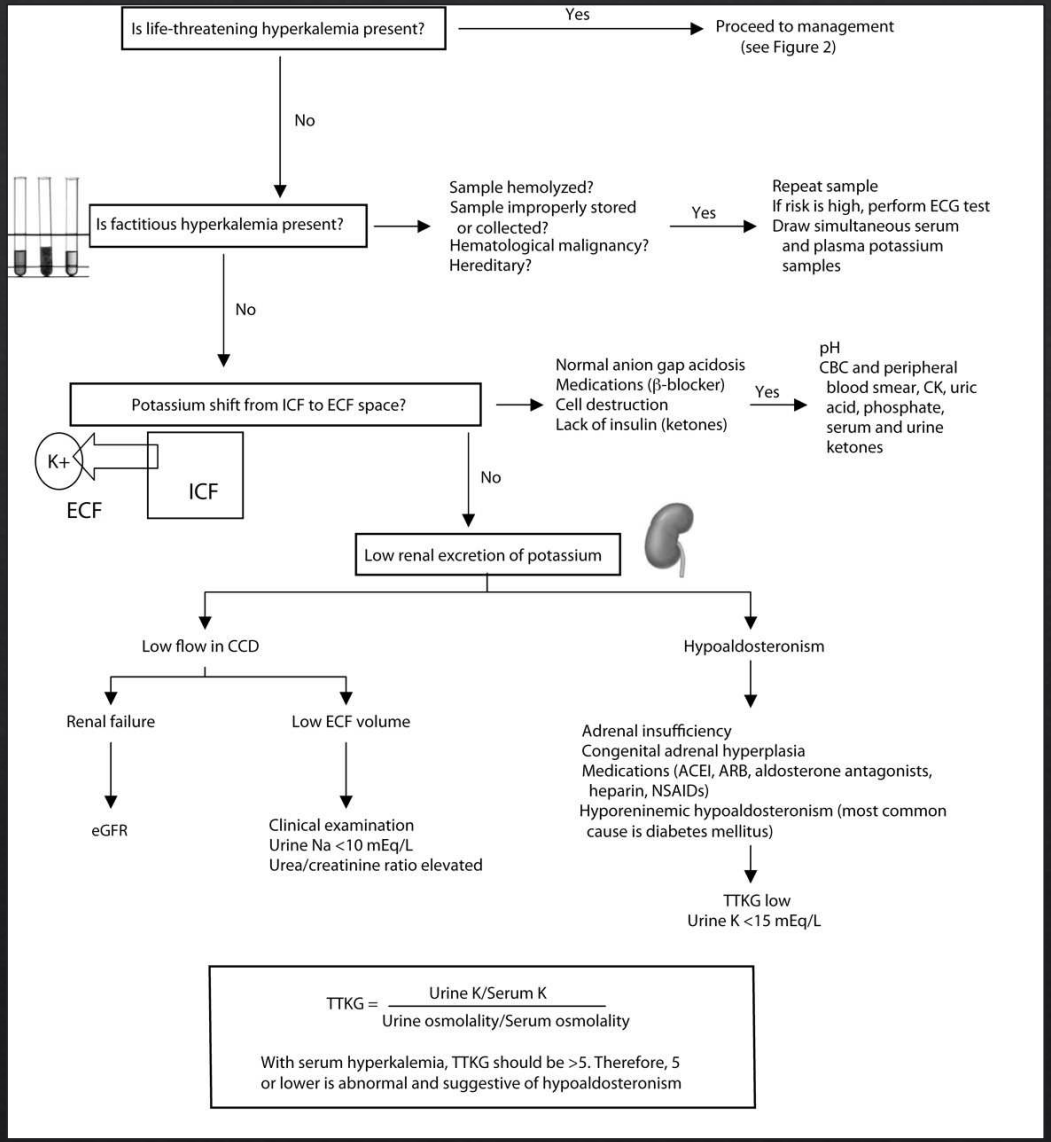

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
GE MAC55-100
25 mm/sec
10 mm/mV
50~ 0.15 - 150 Hz


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

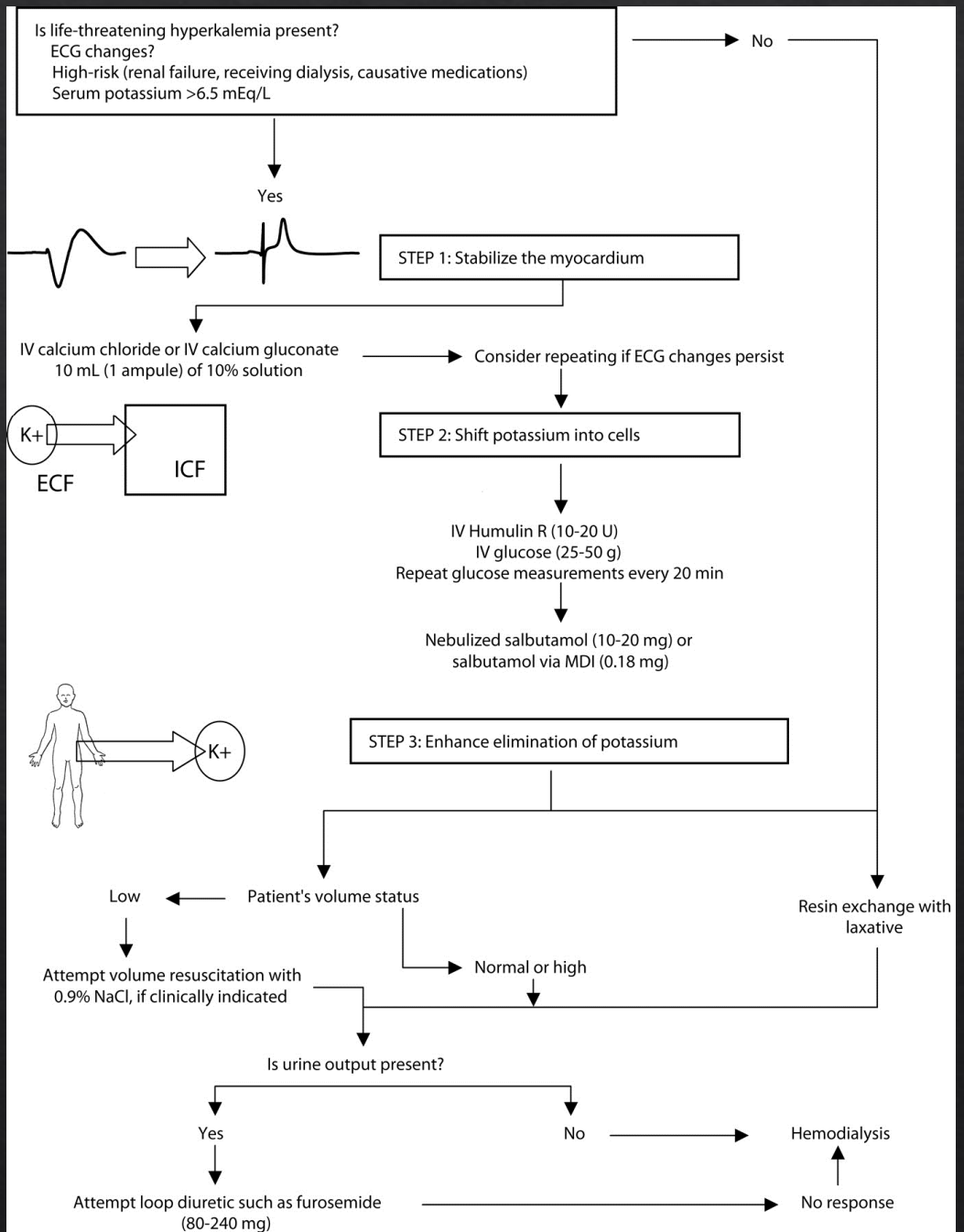
K 9,2 mmol/l



Algorithmic approach to the diagnosis of hyperkalemia

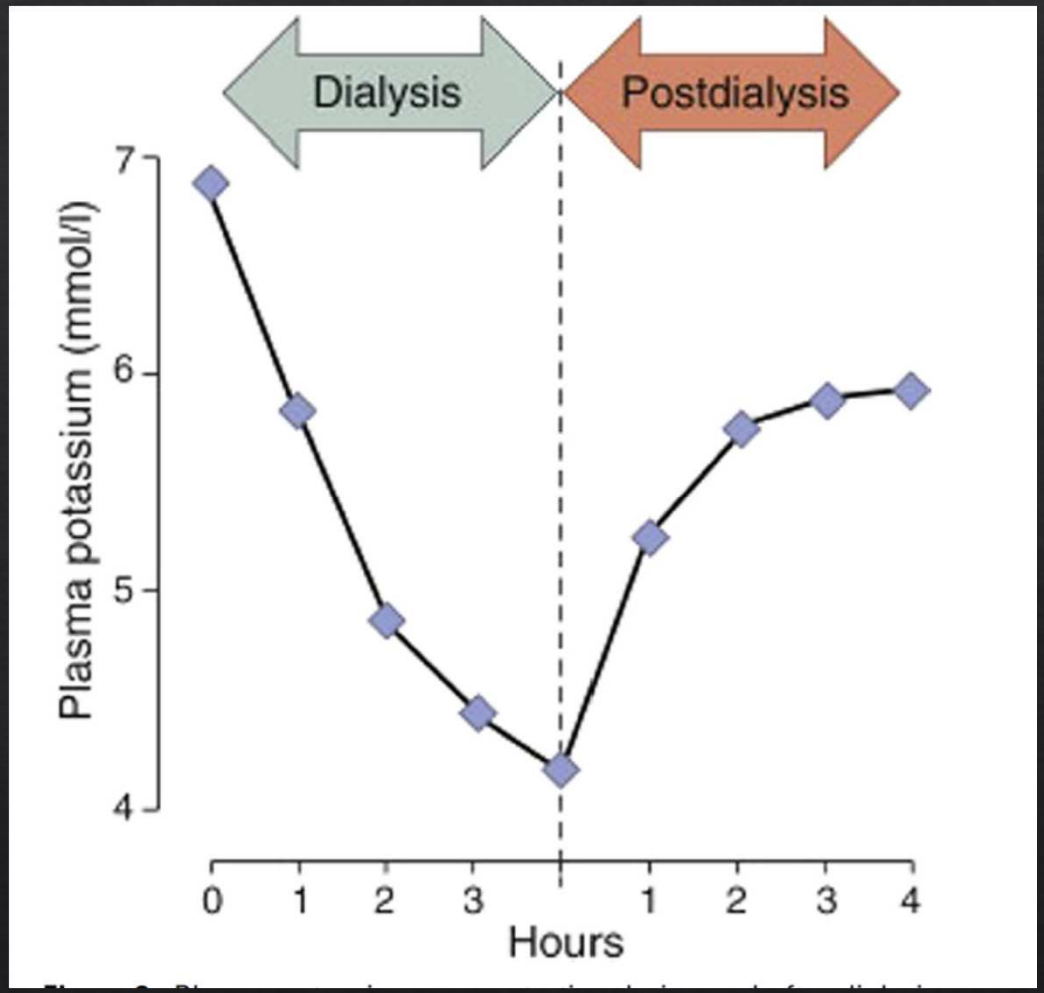


Algorithmic management of hyperkalemia.



Medications for the Treatment of Hyperkalemia

Medication	*Dosage*	*Onset*	*Duration*	*potassium-lowering effect*	*Mechanism*	*Cautions*
Acute treatment						
Calcium	Calcium chloride, 10 mL of 10% solution IV over 5 to 10 minutes, or calcium gluconate, 30 mL of 10% solution IV over 5 to 10 minutes	Immediate	30 to 60 minutes	—	Stabilizes cardiac muscle cell membrane; no effect on serum potassium or total body potassium	May potentiate digoxin toxicity; calcium chloride can cause phlebitis and tissue necrosis
Insulin	Regular insulin, 10 units IV followed immediately by 50 mL of 50% glucose (25 g) IV	15 minutes	≥ 2 hours	0.7 to 1 mEq per L (0.7 to 1 mmol per L)	Shifts potassium into cells; no effect on total body potassium	May cause hypoglycemia; glucose is unnecessary if serum glucose level is > 250 mg per dL (13.9 mmol per L); additive effect when combined with albuterol
Albuterol	10 to 20 mg nebulized	30 minutes	≥ 2 hours	0.5 to 1 mEq per L (0.5 to 1 mmol per L)	Shifts potassium into cells; no effect on total body potassium	Can cause tachycardia and thus should be used with caution in patients with underlying heart disease; potassium-lowering effect not reliable in all patients; additive effect when combined with insulin
Subacute treatment						
Sodium polystyrene sulfonate (Kayexalate)	Oral: 15 g, 1 to 4 times daily Rectal: 30 to 50 g every 6 hours in a retention enema	2 to 24 hours	Variable	Variable	Binds potassium in exchange for sodium; lowers total body potassium	Association with gastrointestinal complications, particularly when combined with sorbitol; should be avoided in patients at risk of abnormal bowel function


Dialysis
Postdialysis
Plasma potassium (mmol/l)
7
6
5
4
0
1
2
3
1
2
3
4
Hours

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Patients with a history of congestive heart failure or myocardial infarction should maintain a serum potassium concentration of at least 4 mEq per L (4 mmol per L).	C	15
Intravenous potassium should be reserved for patients with severe hypokalemia (serum potassium < 2.5 mEq per L [2.5 mmol per L]), hypokalemic ECG changes, or physical signs or symptoms of hypokalemia, or for those unable to tolerate the oral form.	C	22
Prompt intervention and possible ECG monitoring are indicated for patients with severe hypokalemia (serum potassium < 2.5 mEq per L) or severe hyperkalemia (serum potassium > 6.5 mEq per L [6.5 mmol per L]); ECG changes; physical signs or symptoms; possible rapid-onset hyperkalemia; or underlying kidney disease, heart disease, or cirrhosis.	C	7, 15, 24, 30, 33-35
Intravenous calcium should be administered if hyperkalemic ECG changes are present.	C	24, 25, 35
Intravenous insulin and glucose, inhaled beta agonists, and dialysis are effective in the acute treatment of hyperkalemia.	B	39
Sodium polystyrene sulfonate (Kayexalate) may be effective in lowering total body potassium in the subacute setting.	C	25

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.

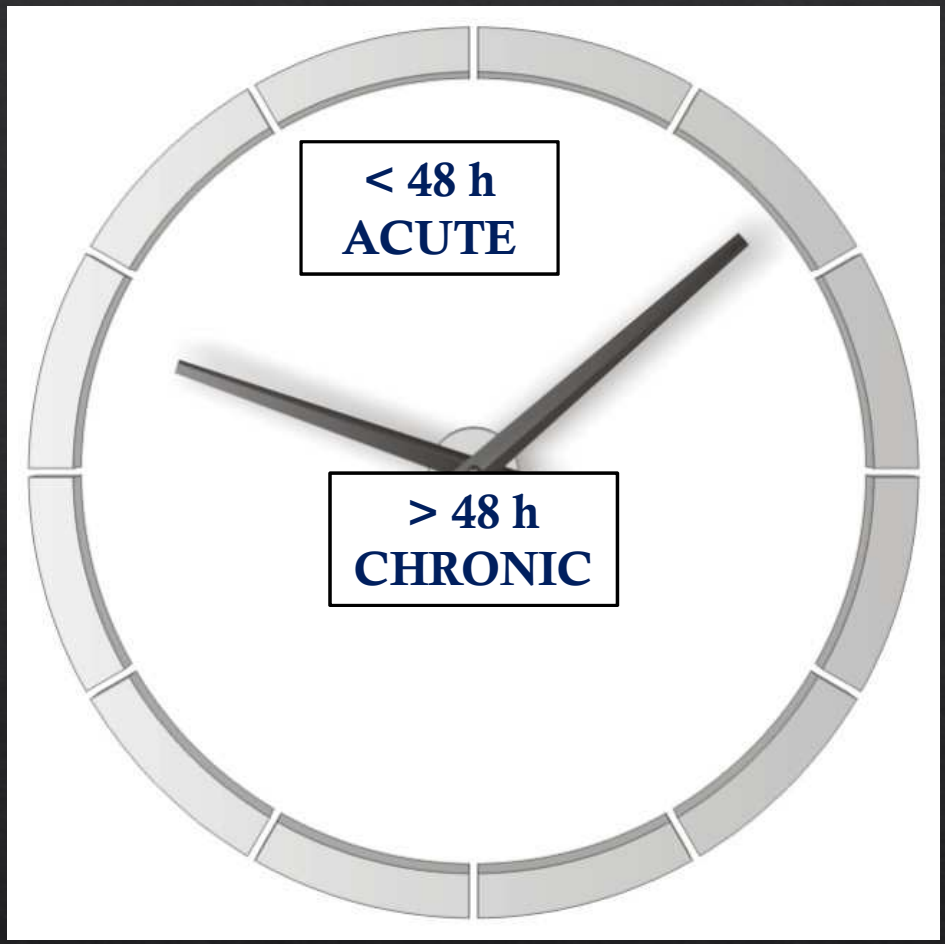
IPONATREMIA

DEFINITION HYOPONATRAEMIA (Sodium < 135 mmol)

MILD 130-135 mmol

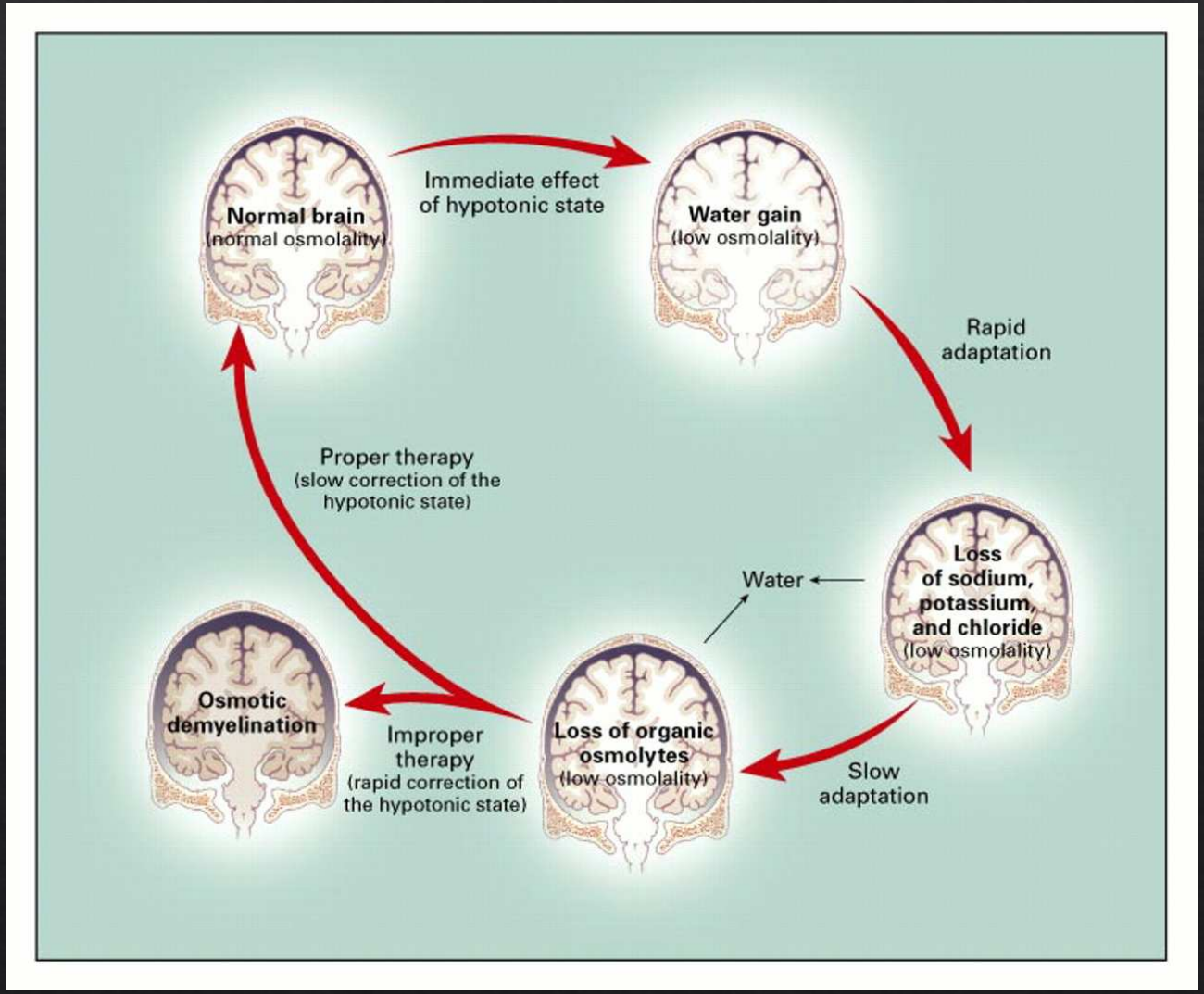
MODERATE 125-129 mmol

SEVERE < 125 mmol



If hyponatraemia cannot be classified, we consider it being chronic, unless there is clinical or anamnestic evidence of the contrary (Table 8).

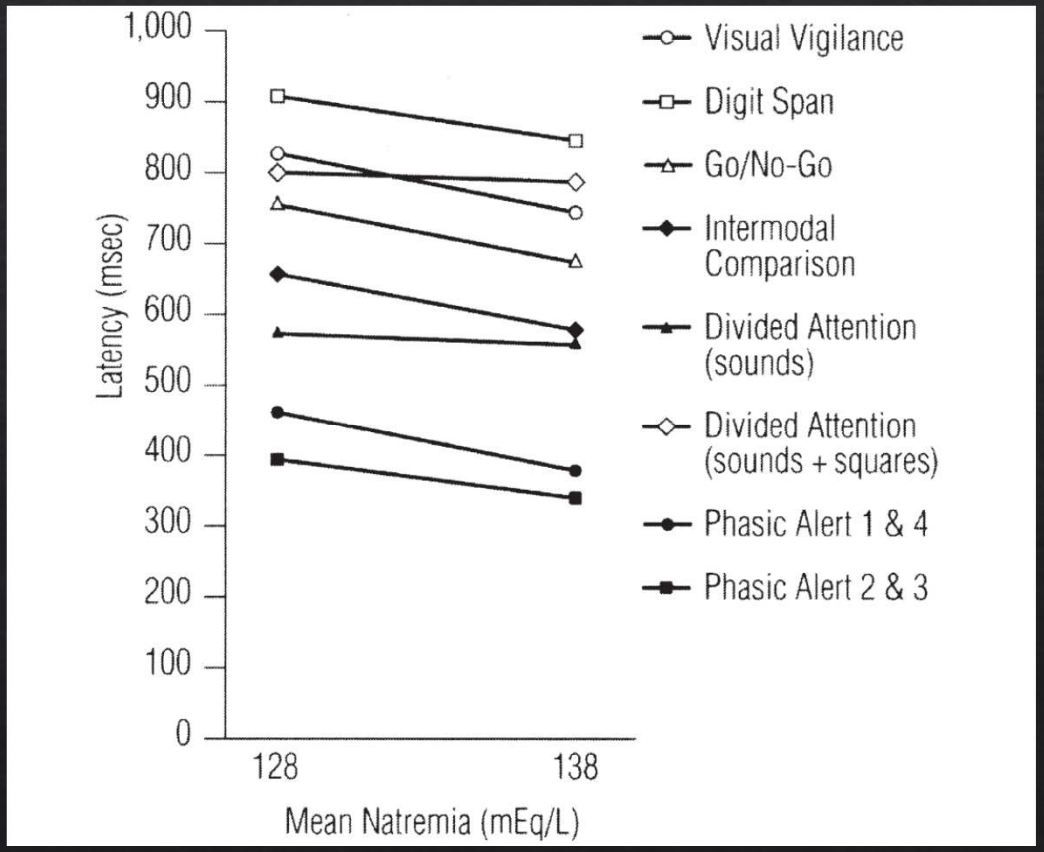
Brain Damage



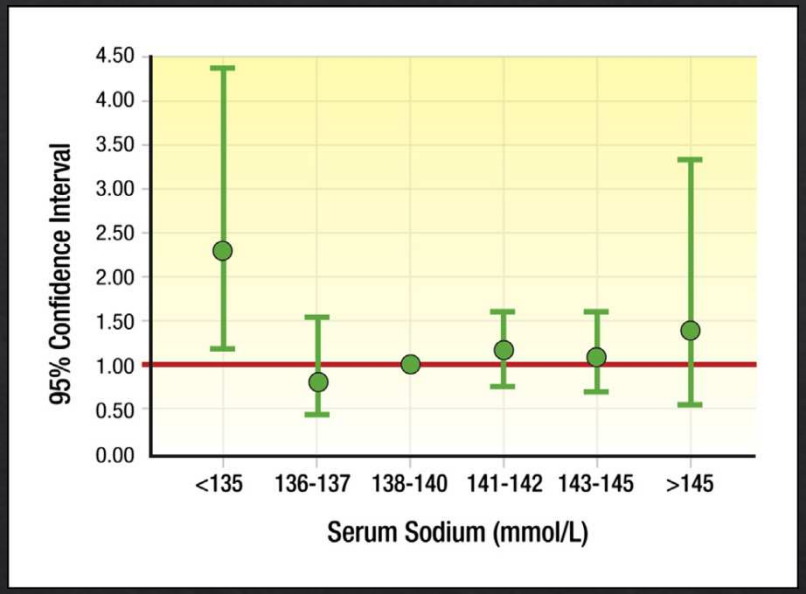
Severity	Symptom
Moderately severe	Nausea without vomiting
	Confusion
	Headache
Severe	Vomiting
	Cardiorespiratory distress
	Abnormal and deep somnolence
	Seizures
	Coma (Glasgow Coma Scale ≤ 8)

Is Asymptomatic Hyponatremia Really Asymptomatic?

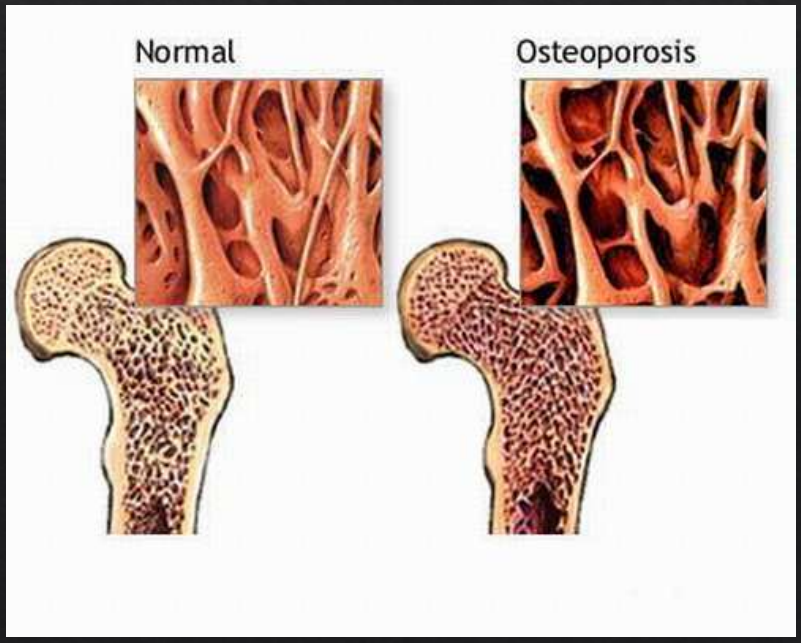
- Evolution of median response latencies in 8 attention tests performed in 16 patients with mild chronic hyponatremia



Risk of bone fracture in relation to serum [Na]

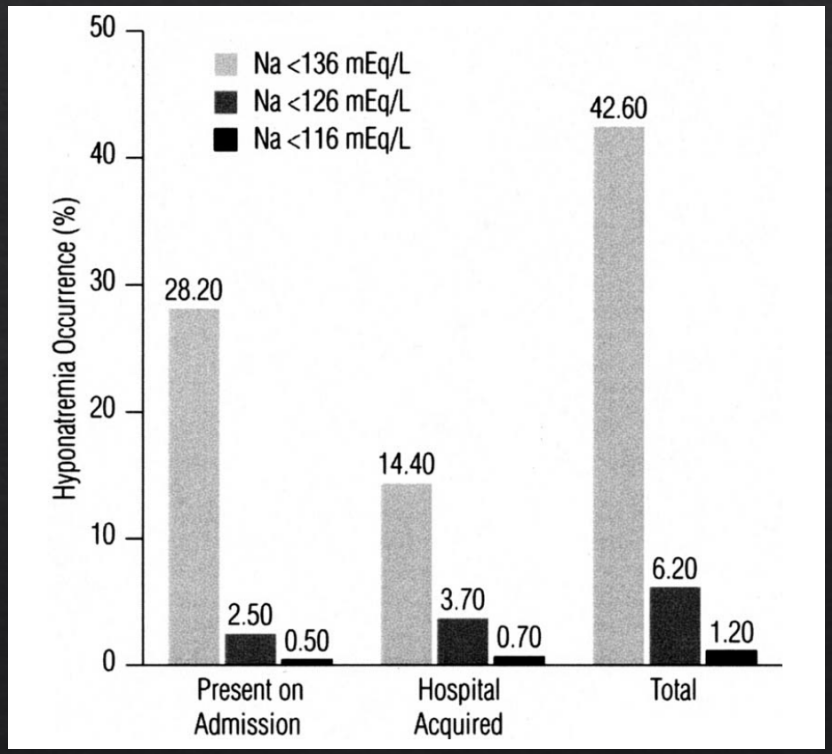


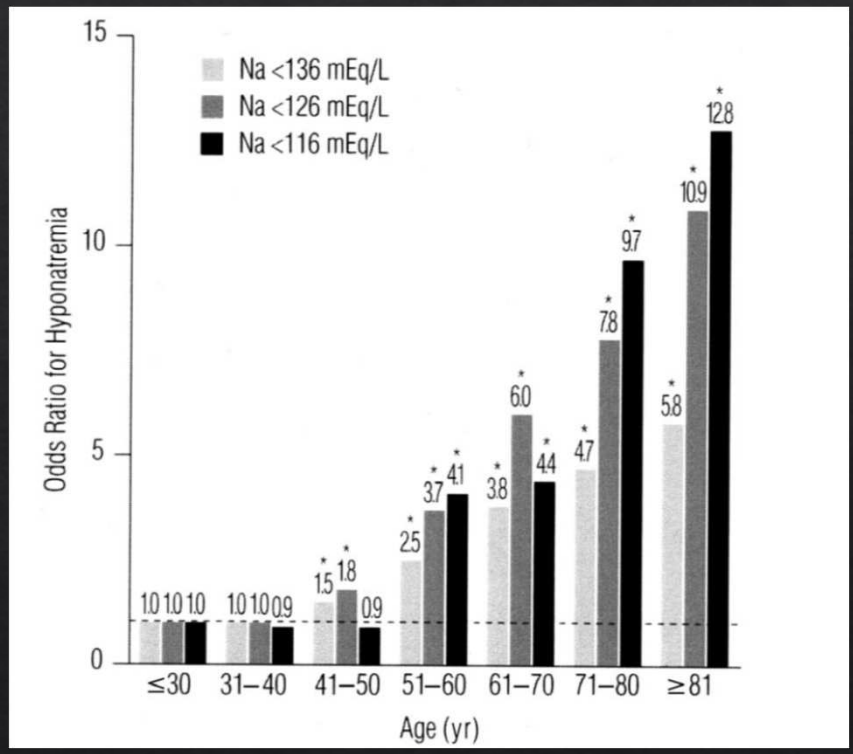
Clin J Am Soc Nephrol. 2010



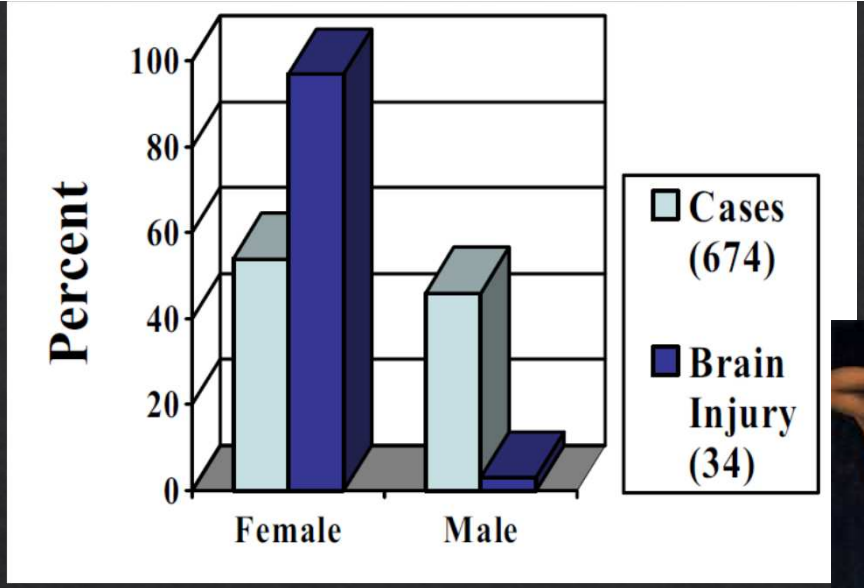
EPIDEMIOLOGY

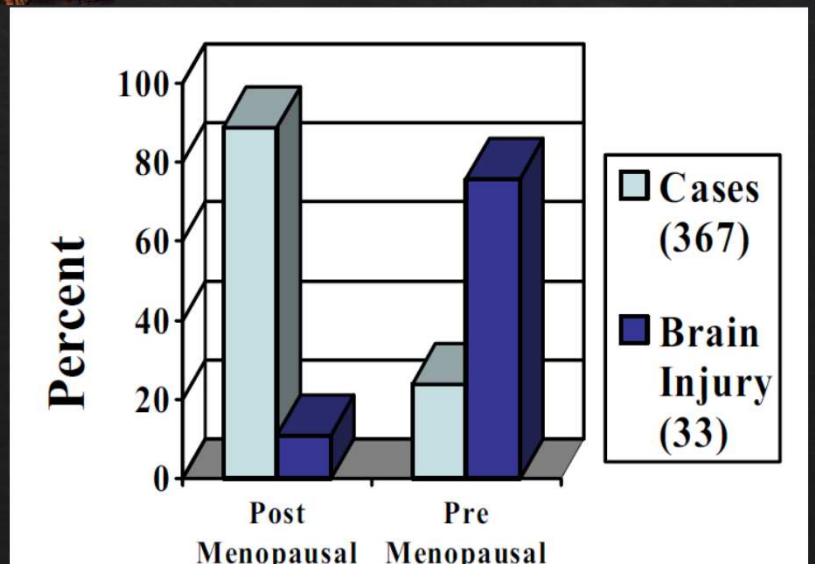
- **Hyponatremia is the most common electrolyte abnormality encountered in clinical practice**





Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. *Clin Chim Acta*. 2003;337:169–172.





Arieff NEJM 1986

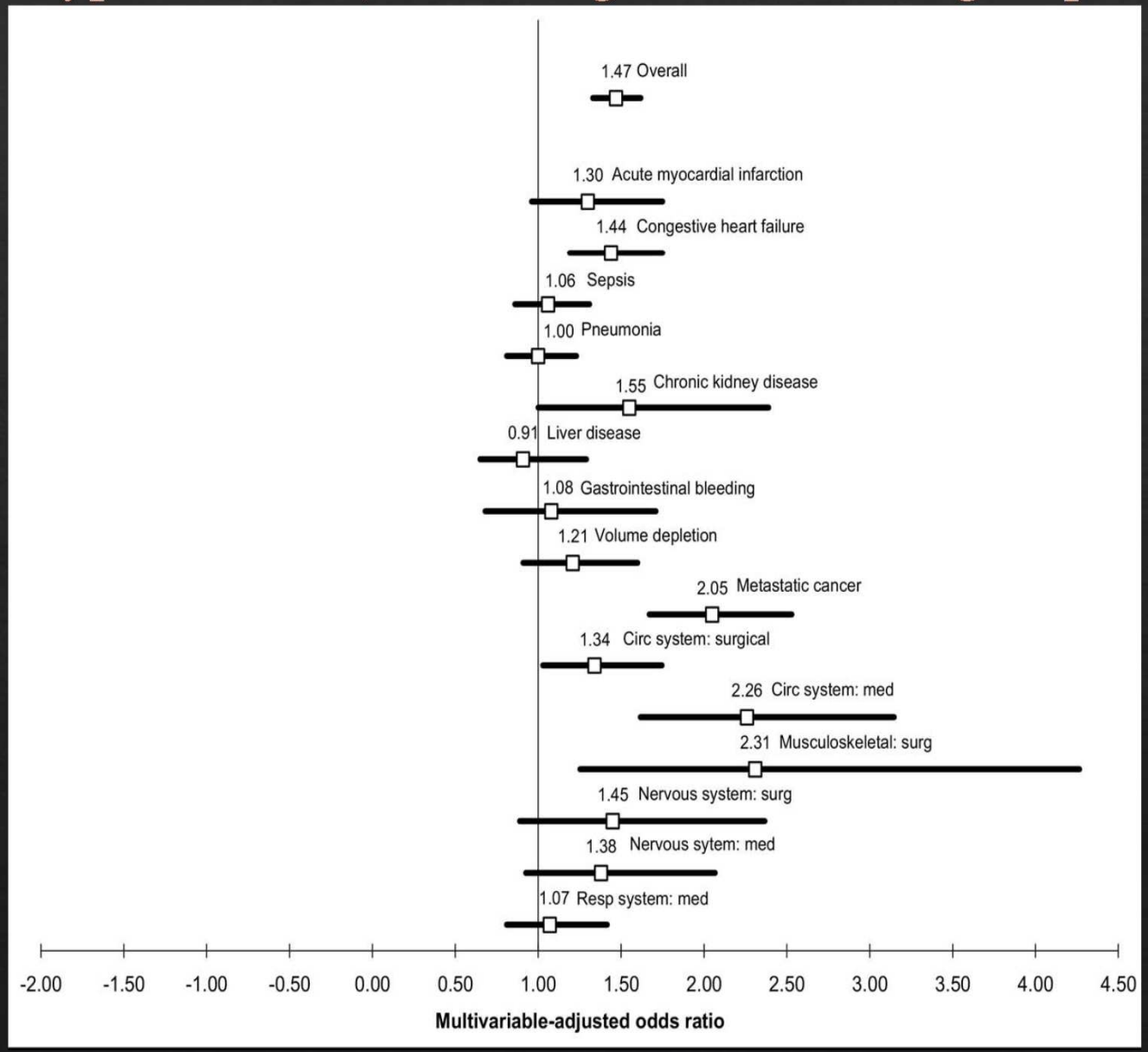
Arch Intern Med. 2010;170(3):294-302. doi:10.1001/archinternmed.2009.513

Table 2. Unadjusted and Adjusted Relationships Between Hospital Admission Serum [Na^+] and In-Hospital Mortality, Discharge to a Facility, and Length of Stay[a]

Admission [Na^+], mEq/L	Admissions, No.	Deaths, No.	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
In-hospital mortality				
138-142	33 055	671	1 [Reference]	1 [Reference]
<138	20 181	686	1.70 (1.53-1.89)	1.52 (1.36-1.69)
133-137	16 023	466	1.45 (1.28-1.63)	1.34 (1.18-1.51)
128-132	3075	151	2.49 (2.08-2.99)	1.99 (1.65-2.40)
123-127	759	49	3.33 (2.46-4.50)	2.54 (1.87-3.45)
118-122	211	13	3.17 (1.79-5.59)	2.46 (1.38-4.39)
<118	113	7	3.18 (1.51-6.68)	2.46 (1.19-5.10)
Discharge to a short- or long-term care facility				
138-142	32 384	10 900[b]	1 [Reference]	1 [Reference]
<138	19 495	7313[b]	1.15 (1.11-1.19)	1.12 (1.08-1.17)
133-137	15 557	5633[b]	1.11 (1.06-1.15)	1.09 (1.05-1.14)
128-132	2924	1233[b]	1.35 (1.24-1.46)	1.23 (1.13-1.34)
123-127	710	303[b]	1.53 (1.32-1.78)	1.34 (1.14-1.58)
118-122	198	95[b]	1.94 (1.43-2.63)	1.77 (1.27-2.47)
<118	106	49[b]	1.78 (1.19-2.68)	1.80 (1.14-2.83)
Hospital length of stay				
138-142	32 384	NA	1 [Reference][c]	1 [Reference][d]
<138	19 495	NA	1.13 (1.10-1.15)[c]	1.14 (1.11-1.16)[d]
133-137	15 557	NA	1.10 (1.07-1.12)[c]	1.11 (1.09-1.13)[d]
128-132	2924	NA	1.27 (1.20-1.34)[c]	1.27 (1.20-1.36)[d]
123-127	710	NA	1.22 (1.14-1.30)[c]	1.20 (1.12-1.29)[d]
118-122	198	NA	1.17 (1.03-1.33)[c]	1.20 (1.05-1.36)[d]
<118	106	NA	1.37 (1.12-1.67)[c]	1.47 (1.21-1.78)[d]

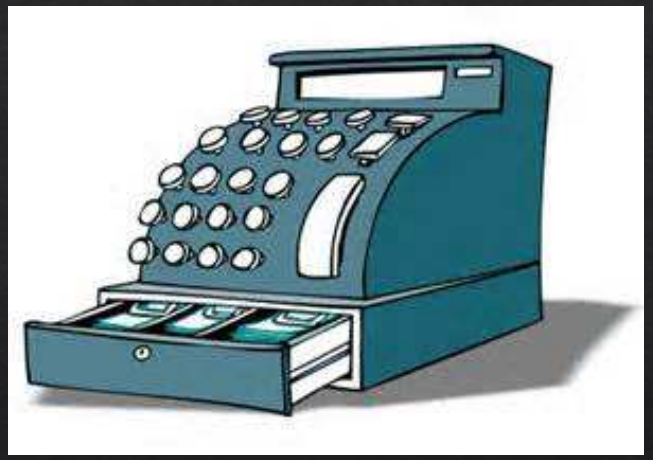
Abbreviations: CI, confidence interval; NA, not applicable; [Na^+], sodium concentration.
SI conversion factor: To convert [Na^+] to millimoles per liter, multiply by 1.0.
[a] All the models are adjusted for age, sex, race, admission service, and Deyo-Charlson Comorbidity Index[21,22] score (0 to ≥3). Hospitalizations in which patients died were excluded from the analyses of discharge to a facility and hospital length of stay.
[b] Number of patients discharged to a facility.
[c] Unadjusted relative prolongation (95% CI).
[d] Adjusted relative prolongation (95% CI).

Odds ratios for death in patients with versus without hyponatremia, according to clinical subgroups



Wiaker AJM 2006

Economic Burden



1,6 - 3,6 Bilion annualy

2000

2007

Hyponatremia Treatment Guidelines 2007: Expert Panel Recommendations. Joseph G. Verbalis et al.

2013

2014

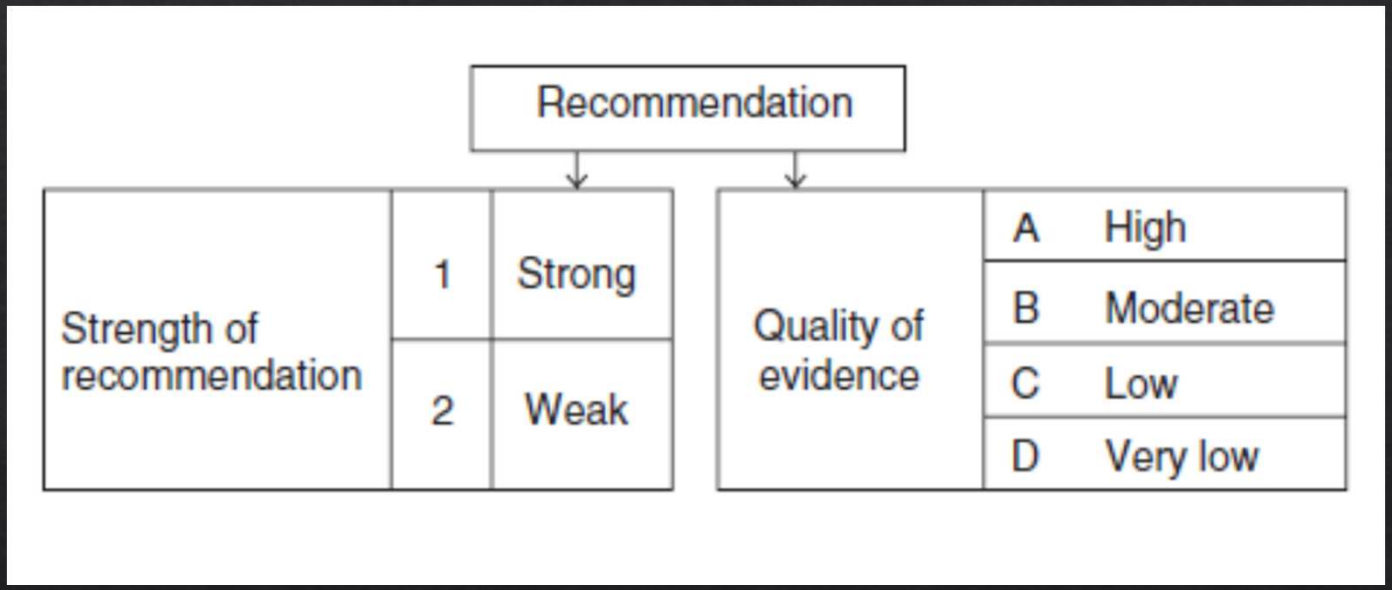
European Society of Intensive Care Medicine (ESICM),

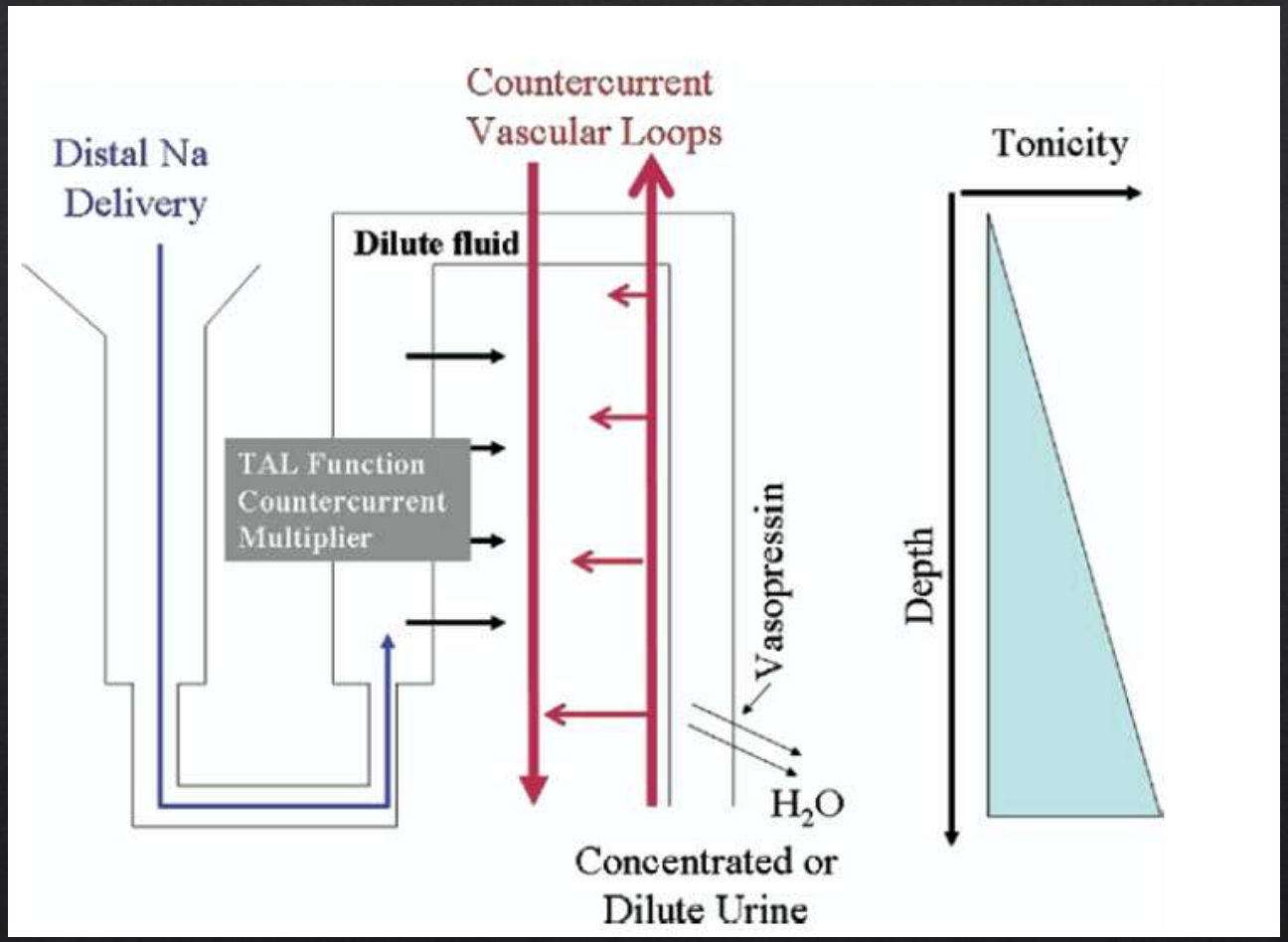
European Society of Endocrinology

European Renal Association – European Dialysis and Transplant Association (ERA–EDTA)

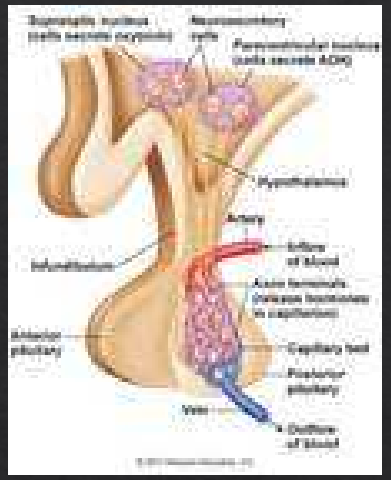
Clinical practice guideline on diagnosis and treatment of hyponatraemia

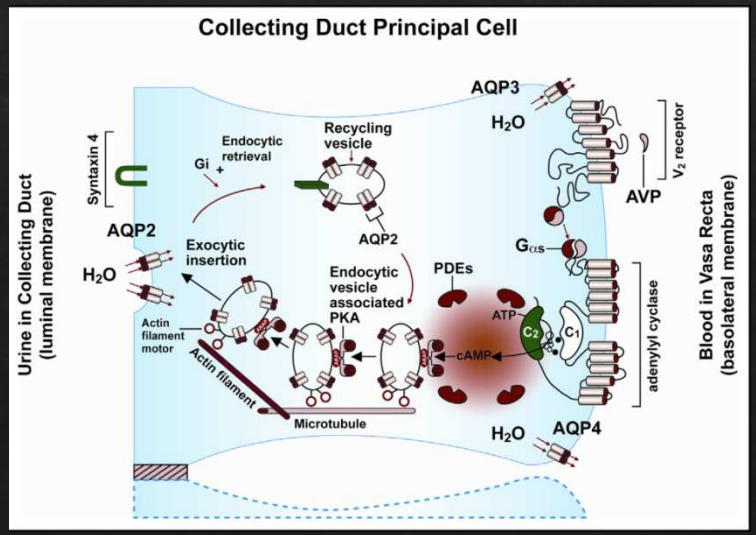
European Journal of Endocrinology
(2014) 170, G1–G47

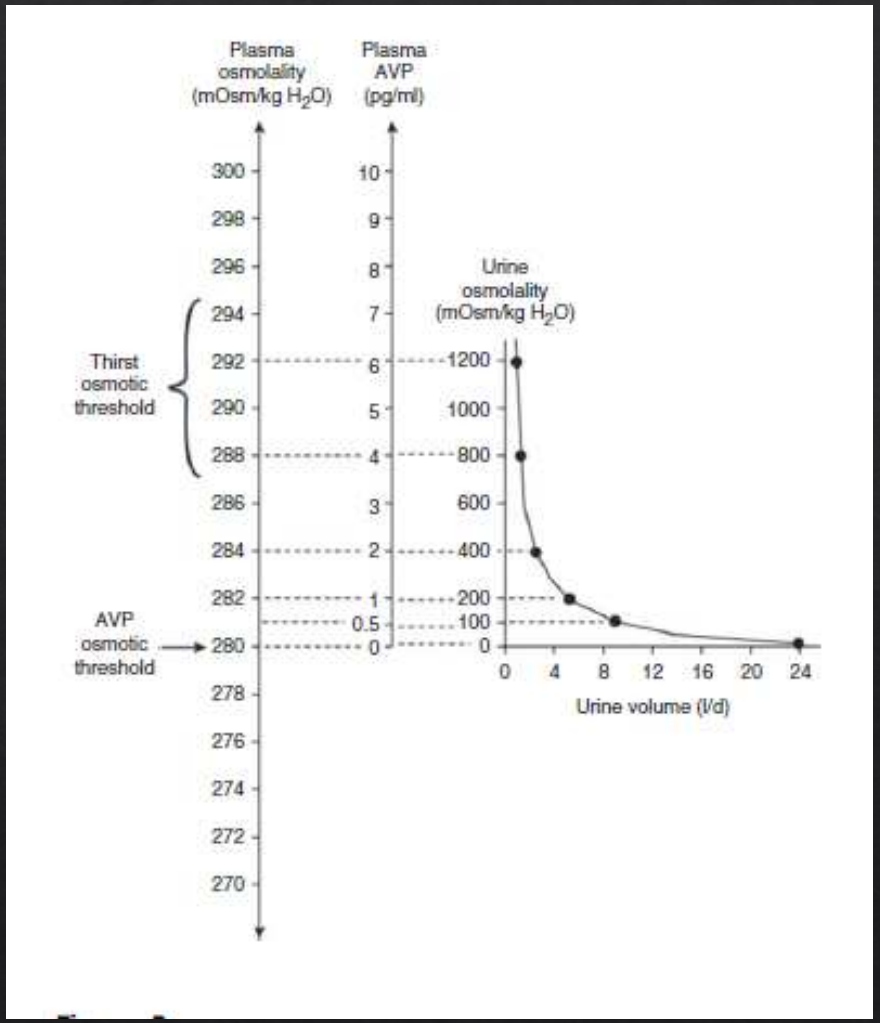

Recommendation
Strength of recommendation
1
Strong
2
Weak
Quality of evidence
A
High
B
Moderate
C
Low
D
Very low

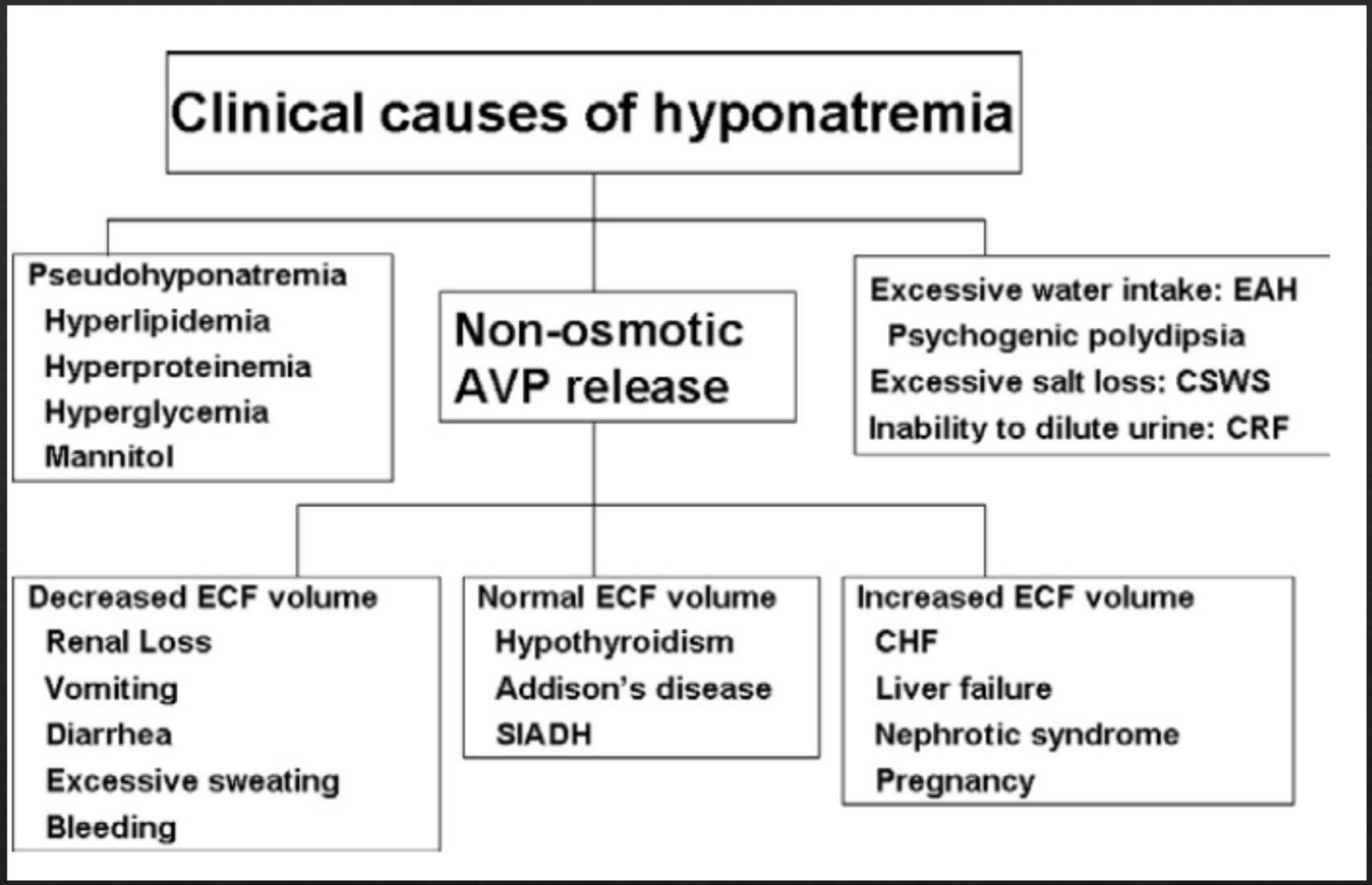

Countercurrent
Vascular Loops
Distal Na
Delivery
Dilute fluid
TAL Function
Countercurrent
Multiplier
Vasopressin
H_2O
Concentrated or
Dilute Urine
Tonicity
Depth

Osmotic regulation of vasopressin release



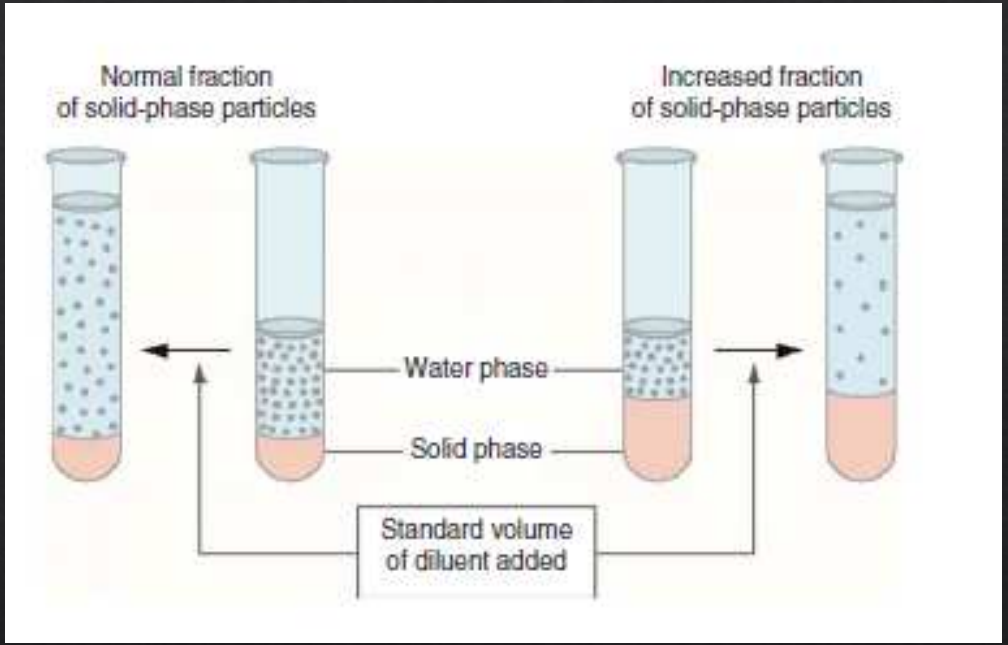





Clinical causes of hyponatremia
Pseudohyponatremia
Hyperlipidemia
Hyperproteinemia
Hyperglycemia
Mannitol
Non-osmotic AVP release
Excessive water intake: EAH
Psychogenic polydipsia
Excessive salt loss: CSWS
Inability to dilute urine: CRF
Decreased ECF volume
Renal Loss
Vomiting
Diarrhea
Excessive sweating
Bleeding
Normal ECF volume
Hypothyroidism
Addison's disease
SIADH
Increased ECF volume
CHF
Liver failure
Nephrotic syndrome
Pregnancy

SEMPRE TROPPA ACQUA

Pseudohyponatremia



SIADH

Essential criteria

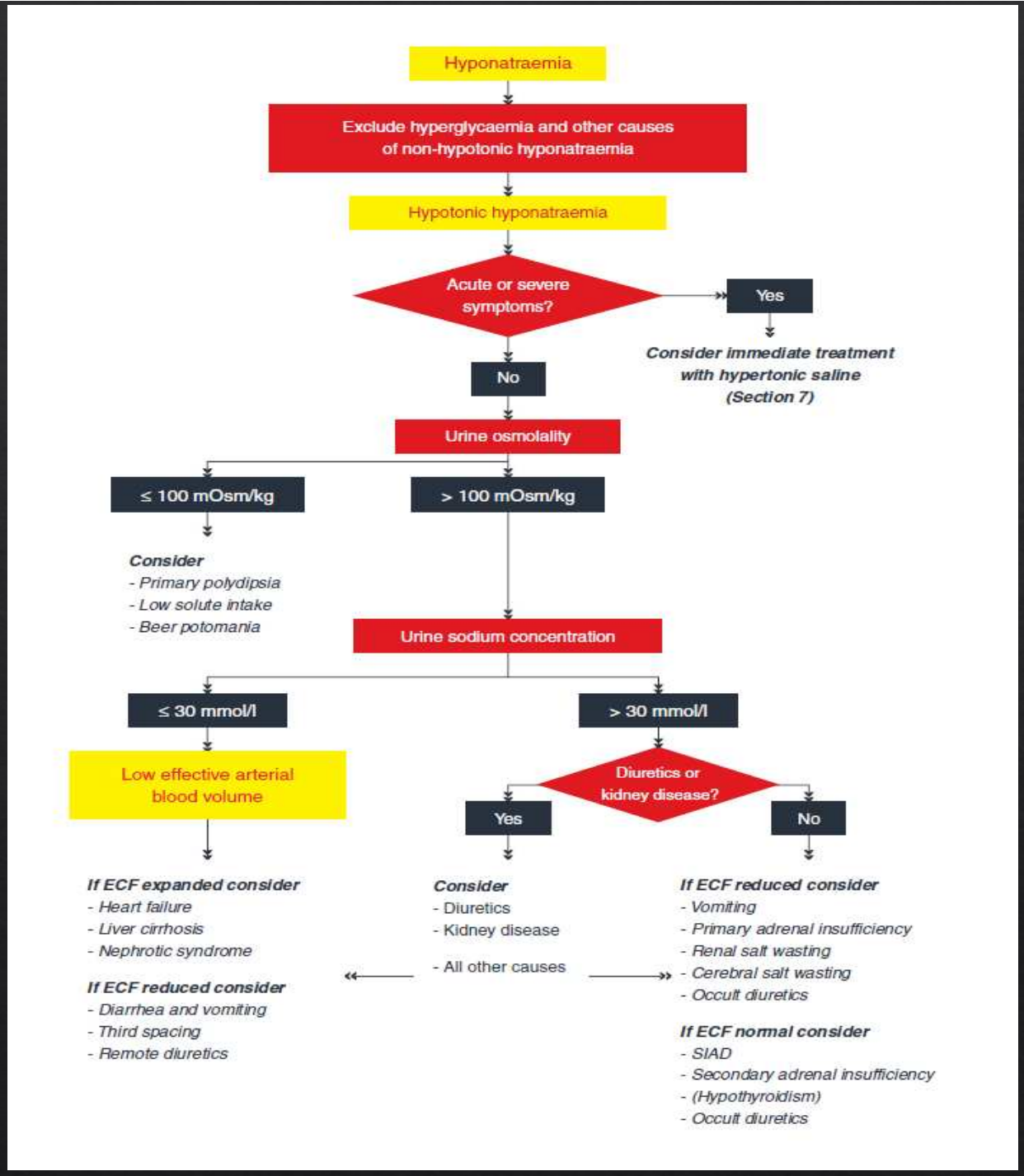
- Effective serum osmolality <275 mOsm/kg
- Urine osmolality > 100 mOsm/kg at some level of decreased effective osmolality
- Clinical euvolaemia
- Urine sodium concentration > 30 mmol/l with normal dietary salt and water intake
- Absence of adrenal, thyroid, pituitary or renal insufficiency
- No recent use of diuretic agents

Supplemental criteria

- Serum uric acid <0.24 mmol/l (<4 mg/dl)
- Serum urea <3.6 mmol/l (<21.6 mg/dl)
- Failure to correct hyponatraemia after 0.9% saline infusion
- Fractional sodium excretion >0.5%
- Fractional urea excretion >55%
- Fractional uric acid excretion > 12%
- Correction of hyponatraemia through fluid restriction

Table 7 Causes of the syndrome of inappropriate antidiuresis. Adapted from Liamis G, Milionis H and Elisaf M. A review of drug-induces hyponatraemia. *American Journal of Kidney Diseases* 2008 52 144–153. (247)

Malignant diseases	Pulmonary disorders	Disorders of the nervous system	Drugs	Other causes
Carcinoma	Infections	Infection	Vasopressin release or action stimulants	Hereditary
Lung	Bacterial pneumonia	Encephalitis	Antidepressants	Gain-of-function mutation of the vasopressin V2 receptor
Oropharynx	Viral pneumonia	Meningitis	SSRIs	Idiopathic
Gastrointestinal tract	Pulmonary abscess	Brain abscess	Tricyclic	Transient
Stomach	Tuberculosis	Rocky Mountain spotted fever	MAOI	Exercise-associated hyponatraemia
Duodenum	Aspergillosis	AIDS	Venlafaxine	General anaesthesia
Pancreas	Asthma	Malaria	Anticonvulsants	Nausea
Genitourinary tract	Cystic fibrosis	Vascular and masses	Carbamazepine	Pain
Ureter	Respiratory failure associated with positive-pressure breeding	Subdural hematoma	Oxcarbazepine	Stress
Bladder		Subarachnoid haemorrhage	Sodium valproate	
Prostate		Stroke	Lamotrigine	
Endometrium		Brain tumours	Antipsychotics	
Endocrine thymoma		Head trauma	Phenothiazides	
Lymphomas		Other	Butyrophenones	
Sarcomas		Hydrocephalus	Anticancer drugs	
Ewing's sarcoma		Cavernous sinus thrombosis	Vinca alkaloids	
Olfactory neuroblastoma		Multiple sclerosis	Platinum compounds	
		Guillain–Barré syndrome	Ifosfamide	
		Shy–Drager syndrome	Melphalan	
		Delirium tremens	Cyclophosphamide	
		Acute intermittent porphyria	Methotrexate	
			Pentostatin	
			Antidiabetic drugs	
			Chlorpropamide	
			Tolbutamine	
			Miscellaneous	
			Opiates	
			MDMA (XTC)	
			Levamisole	
			Interferon	
			NSAIDs	
			Clofibrate	
			Nicotine	
			Amiodarone	
			Proton pump inhibitors	
			MABs	
			Vasopressin analogues	
			Desmopressin	
			Oxytocin	
			Terlipressin	
			Vasopressin	


Hyponatraemia
Exclude hyperglycaemia and other causes of non-hypotonic hyponatraemia
Hypotonic hyponatraemia
Acute or severe symptoms?
Yes
Consider immediate treatment with hypertonic saline (Section 7)
No
Urine osmolality
≤ 100 mOsm/kg
> 100 mOsm/kg
Consider
- Primary polydipsia
- Low solute intake
- Beer potomania
Urine sodium concentration
≤ 30 mmol/l
> 30 mmol/l
Low effective arterial blood volume
Diuretics or kidney disease?
Yes
No
If ECF expanded consider
- Heart failure
- Liver cirrhosis
- Nephrotic syndrome
If ECF reduced consider
- Diarrhea and vomiting
- Third spacing
- Remote diuretics
Consider
- Diuretics
- Kidney disease
- All other causes
If ECF reduced consider
- Vomiting
- Primary adrenal insufficiency
- Renal salt wasting
- Cerebral salt wasting
- Occult diuretics
If ECF normal consider
- SIAD
- Secondary adrenal insufficiency
- (Hypothyroidism)
- Occult diuretics

EVITARE MANOVRE PERICOLOSE

Formulas for Use in Managing Hyponatremia and Characteristics of Infusates.

TABLE 2. FORMULAS FOR USE IN MANAGING HYPONATREMIA AND CHARACTERISTICS OF INFUSATES.

FORMULA*	CLINICAL USE
1. Change in serum $Na^+ = \frac{\text{infusate } Na^+ - \text{serum } Na^+}{\text{total body water} + 1}$	Estimate the effect of 1 liter of any infusate on serum Na^+
2. Change in serum $Na^+ = \frac{(\text{infusate } Na^+ + \text{infusate } K^+) - \text{serum } Na^+}{\text{total body water} + 1}$	Estimate the effect of 1 liter of any infusate containing Na^+ and K^+ on serum Na^+

INFUSATE	INFUSATE Na^+	EXTRACELLULAR-FLUID DISTRIBUTION
	mmol per liter	%
5% Sodium chloride in water	855	100†
3% Sodium chloride in water	513	100†
0.9% Sodium chloride in water	154	100
Ringer's lactate solution	130	97
0.45% Sodium chloride in water	77	73
0.2% Sodium chloride in 5% dextrose in water	34	55
5% Dextrose in water	0	40

*The numerator in formula 1 is a simplification of the expression (infusate Na^+ − serum Na^+) × 1 liter, with the value yielded by the equation in millimoles per liter.[38] The estimated total body water (in liters) is calculated as a fraction of body weight. The fraction is 0.6 in children; 0.6 and 0.5 in nonelderly men and women, respectively; and 0.5 and 0.45 in elderly men and women, respectively.[39] Normally, extracellular and intracellular fluids account for 40 and 60 percent of total body water, respectively.[39]

†In addition to its complete distribution in the extracellular compartment, this infusate induces osmotic removal of water from the intracellular compartment.

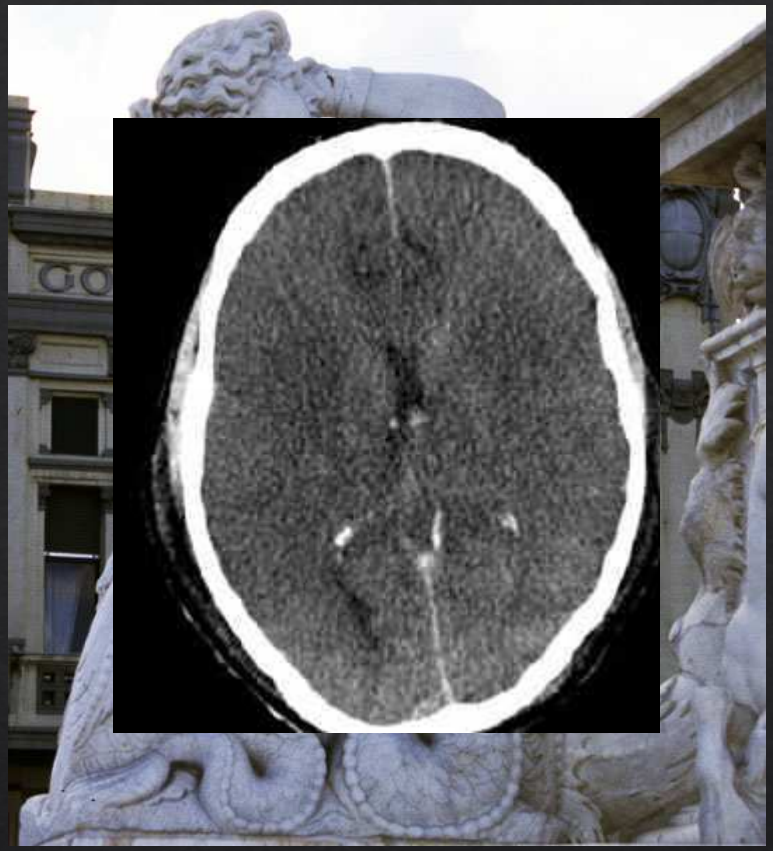
Adrogué HJ, Madias NE. N Engl J Med 2000;342:1581-1589.

The NEW ENGLAND JOURNAL of MEDICINE

Table 8 Drugs and conditions associated with acute hyponatraemia (<48 h).

Postoperative phase
Post-resection of the prostate, post-resection of endoscopic uterine surgery
Polydipsia
Exercise
Recent thiazides prescription
3,4-Methylenedioxymethamfetamine (MDMA, XTC)
Colonoscopy preparation
Cyclophosphamide (i.v.)
Oxytocin
Recently started desmopressin therapy
Recently started terlipressin, vasopressin

ACUTE



CEREBRAL EDEMA

Iponatremia con sintomatologia grave

Gestione del trattamento nella prima ora, indipendentemente dalla classificazione dell'iponatremia in acuta o cronica

Si raccomanda una pronta infusione di 150 ml di salina ipertonica al 3% o equivalente in 20 minuti. (1D).

Si suggerisce di controllare la concentrazione di sodio nel siero dopo 20 minuti, ripetendo un'infusione di 150 ml di salina ipertonica al 3% o equivalente nei successivi 20 minuti. (2D).

Si suggerisce di ripetere le due raccomandazioni terapeutiche sopra menzionate per due volte o fino al raggiungimento di un target di 5 mmol/L di aumento della concentrazione sierica di sodio. (2D).

Si suggerisce di gestire il paziente con iponatremia gravemente sintomatica in un ambiente nel quale è possibile provvedere ad uno stretto monitoraggio biochimico e clinico. (Non graduata)

Gestione del follow up in caso ora, ndipendentemente dadi miglioramento dei sintomi dopo un aumento della concentrazione di sodio nel siero pari a 5 mmol/L nella prima lla classificazione dell'iponatremia in acuta o cronica

- Si raccomanda di sospendere l'infusione di salina ipertonica (1D)
- Si raccomanda di mantenere pervia la linea di infusione endovenosa, del più piccolo volume possibile di salina allo 0.9% fino a che sia iniziato il trattamento specifico della causa. (1D)
- Si raccomanda di iniziare un trattamento specifico per la diagnosi, se conosciuta,con l'obiettivo almeno di stabilizzare la concentrazione di sodio nel siero.
- Si raccomanda di limitare l'aumento della concentrazione di sodio nel siero ad un totale di 10 mmol/L durante le prime 24 ore, e ad ulteriori 8 mmol/L per ciascun periodo successivo di 24 ore, fino a che la concentrazione di sodio nel siero non raggiunga 130 mmol/L. (1D)
- Si suggerisce di controllare la concentrazione di sodio nel siero dopo 6 e 12
- ore, e poi quotidianamente, fino a che la concentrazione sierica di sodio si
- sia stabilizzata in corso di regolare trattamento. (2D)

Gestione del follow-up in caso di mancato miglioramento dei sintomi dopo aumento della concentrazione sierica disodio di 5 mmol/L nella prima ora, indipendentemente dalla classificazione dell'iponatremia in acuta o cronica

- Si raccomanda di proseguire l'infusione endovenosa di salina ipertonica al 3% o equivalente con l'obiettivo di un ulteriore aumento di 1 mmol/L/h della concentrazione di sodio nel siero. (1D).
- Si raccomanda di sospendere l'infusione di salina ipertonica al 3% o equivalente, quando i sintomi migliorano, quando la concentrazione di sodio nel siero aumenta complessivamente di 10 mmol/L, o quando la concentrazione sierica di sodio raggiunga i 130 mmol/L, qualunque di questi si verifichi per primo. (1D).
- Si raccomanda un'ulteriore ricerca di altre cause che possano determinare la sintomatologia invece dell'iponatremia. (1D).
- Si suggerisce di controllare la concentrazione di sodio nel siero ogni 4 ore, fino quando l'infusione endovenosa di salina ipertonica al 3% o equivalente venga proseguita. (2D)

Iponatremia con sintomatologia moderatamente grave

Sospendere, se possibile, i farmaci ed altri fattori che possono contribuire o provocare l'iponatremia. (Non graduata).

Si raccomanda un trattamento specifico per la causa.Si suggerisce l'immediato trattamento con una singola infusione endovenosa di 150 ml di soluzione salina ipertonica al 3%, o equivalente, in 20 minuti.
(2D)
Si suggerisce di ottenere un aumento di 5 mmol/L/24 h della concentrazione di sodio nel siero. (2D).

Si suggerisce di limitare l'aumento della concentrazione di sodio nel siero a 10 mmol/L nelle prime 24 ore, e a 8 mmol/L in ciascun giorno successivo, fino a che non venga raggiunta una concentrazione di sodio nel siero di 130 mmol/L. (2D).

Si suggerisce di controllare la concentrazione sierica di sodio a 1-6-12 ore (2D) Si suggeriscono ulteriori indagini diagnostiche rivolte ad individuare altre possibili cause che possano spiegare la sintomatologia se i sintomi non migliorano in parallelo all'aumento della concentrazione di sodio nel siero. (2D).

Si suggerisce di considerare di gestire un paziente come gravemente sintomatico se la concentrazione di sodio nel siero si riduce ulteriormente nonostante il trattamento della diagnosi di fondo. (2D).

Iponatremia acuta in assenza di sintomatologia grave o moderatamente grave

Assicurarsi che la concentrazione di sodio nel siero sia stata misurata utilizzando le stesse tecniche utilizzate per le misure precedenti, e che non sianostati commessi errori nella gestione del campione. (Non graduata).

Se possibile, sospendere i fluidi, i farmaci ed altri fattori che possono contribuire o provocare l'iponatremia. (Non graduata).

Si raccomanda di iniziare una rapida valutazione diagnostica. (1D).

Si raccomanda un trattamento specifico per la causa. (1D).

Se la riduzione acuta della concentrazione di sodio nel siero supera 10 mmol/L, si suggerisce una singola infusione endovenosa di 150 ml di salina ipertonica al 3% o equivalente in 20 minuti. (2D).

Si suggerisce di controllare la concentrazione di sodio nel siero dopo 4 ore, usando la stessa tecnica utilizzata per le misure precedenti. (2D) 3.4. Iponatremia cronica in assenza di sintomatologia.

Cosa fare in caso di correzione troppo rapida dell'iponatremia?

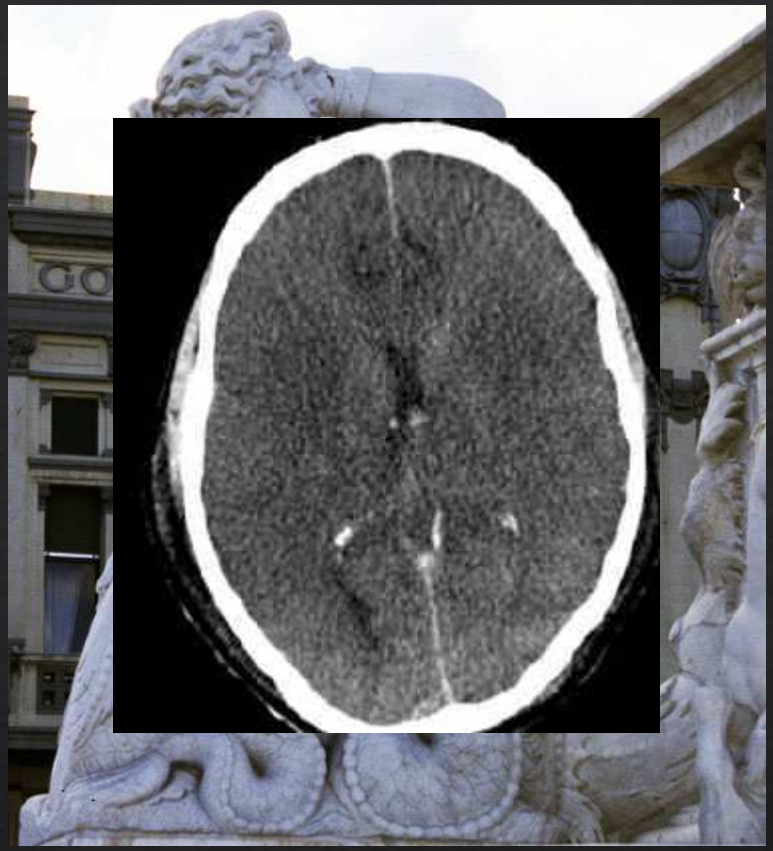
Si raccomanda un pronto intervento per riabbassare la concentrazione sierica di sodio se l'aumento è stato maggiore di 10 mmol/L durante le prime 24 ore o maggiore di 8 mmol/L durante ciascun periodo di 24 ore nei giorni successivi. (1D).

Si raccomanda di interrompere il trattamento attivo in corso. (1D).

Si raccomanda di consultare un esperto per discutere se sia appropriato iniziare un'infusione di 10 mL/kg di peso corporeo di acqua senza elettroliti (ad esempio soluzione glucosata) in un'ora, con stretto monitoraggio dell'output urinario e del bilancio dei fluidi. (1D).

Si raccomanda di consultare un esperto per discutere se sia appropriato aggiungere desmopressina alla dose di 2 microgrammi per via endovenosa, sapendo che non può essere ripetuta più spesso di ogni 8 ore. (1D)

ACUTE



CEREBRAL EDEMA

Factors That Place Patients at High Risk of Developing the Osmotic Demyelination Syndrome with Correction of ChronicHyponatremia

- Serum sodium concentration 105 mmol/L
- Hypokalemia
- Alcoholism
- Malnutrition
- Advanced liver disease

Iponatremia cronica in assenza di sintomatologia grave o moderatamente grave

Sospendere i fluidi non essenziali, le terapie ed altri fattori che possono contribuireo provocare l'iponatremia. (Non graduata).

Si raccomanda un trattamento specifico per la causa. (1D).

In caso di iponatremia lieve, si suggerisce di non trattare lo squilibrio con il solo scopo di aumentare la concentrazione di sodio nel siero. (2C).

In caso di iponatremia moderata o grave, si raccomanda di evitare un aumento della concentrazione di sodio nel siero maggiore di 10 mmol/L durante le prime 24 ore, e maggiore di 8 mmol/L in ciascuna delle 24 ore successive. (1D).

In caso di iponatremia moderata o grave, si suggerisce di controllare la concentrazione di sodio nel siero ogni 6 ore, fino a che la concentrazione di sodio nel siero si sia stabilizzata in corso di regolare trattamento. (2D)
In caso di iponatremia non risolta, riconsiderare l'algoritmo diagnostico e richiedere il consiglio di un esperto. (Non graduata)

Pazienti con sindrome da inappropriata antidiuresi

In caso di iponatremia moderata o grave, si suggerisce di restringere l'apporto di fluidi come prima linea di trattamento. (2D).

In caso di iponatremia moderata o grave, si suggerisce come seconda linea di trattamento di aumentare l'apporto di soluti con somministrazione di urea per os da 0.25 fino a 0.50 g/kg/die, o una combinazione di diuretico dell'ansa a basso dosaggio e cloruro di sodio per os. (2D).

In caso di iponatremia di grado moderato o grave, si raccomanda di non utilizzare litio o demeclociclina. (1D).

In caso di iponatremia di grado moderato, si raccomanda di non usareantagonisti del recettore della vasopressina. (1C).

In caso di iponatremia grave, si raccomanda di non usare antagonisti delrecettore della vasopressina. (1C).

OLIMEL n 7 2 lit: 70 mmol

CLINIMIX n 9 2 lit: 70 mmol

CLINIMIX n 12 2 lit: 70 mmol

NUTRIPERILIPID 1875 : 75 mmol

ISOLYTE 2 lit: 100 mmol

HCO3Na 0,5 lit: 167 mmol