Critical issues in electrolyte and acid-base disturbance

Atiporn Ingsathit MD. PhD.

Topics

- Hyponatremia
- Hypernatemia
- Hypokalemia
- Hyperkalemia
- Metabolic acidosis

Hyponatremic patient

Find truly hypo-osmotic hyponatremia

Exclude

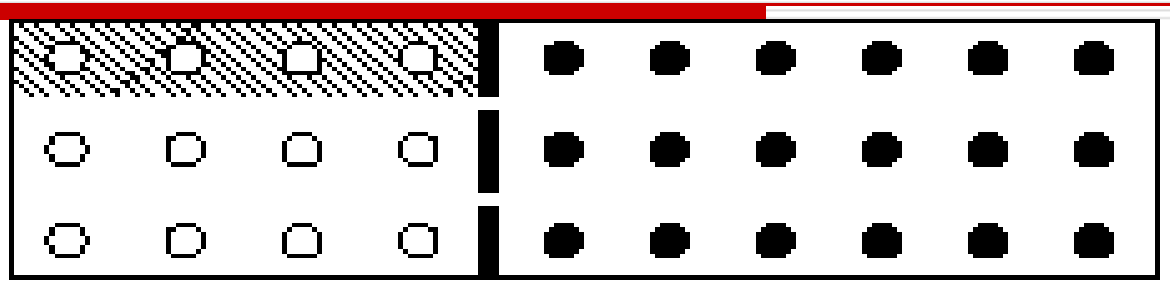
Translocational hyponatremia

Pseudohyponatremia

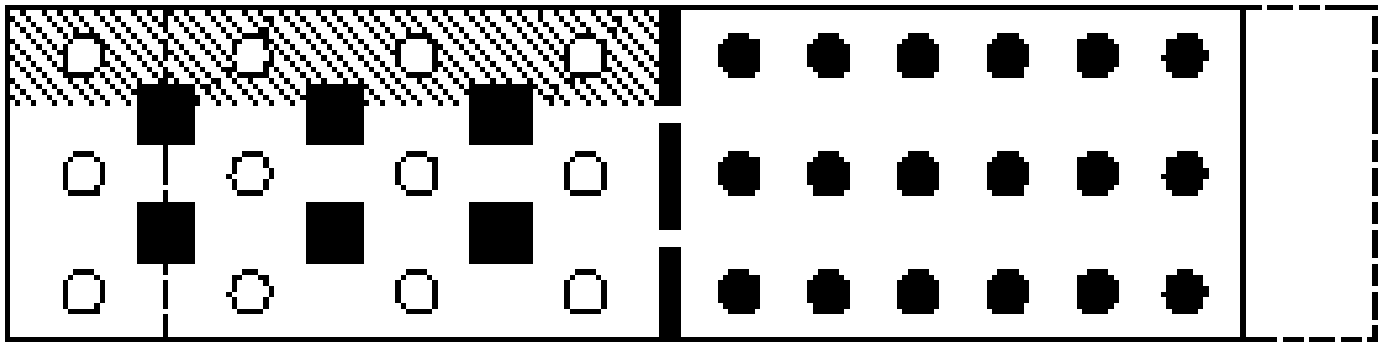
Translocational hyponatremia

- Hypertonic hyponatremia
- High plasma osmolality
- Increase in effective osmolality
  - glucose in insulinopenic state
  - manitol, maltose, glycine

Extracellular fluid Intracellular fluid



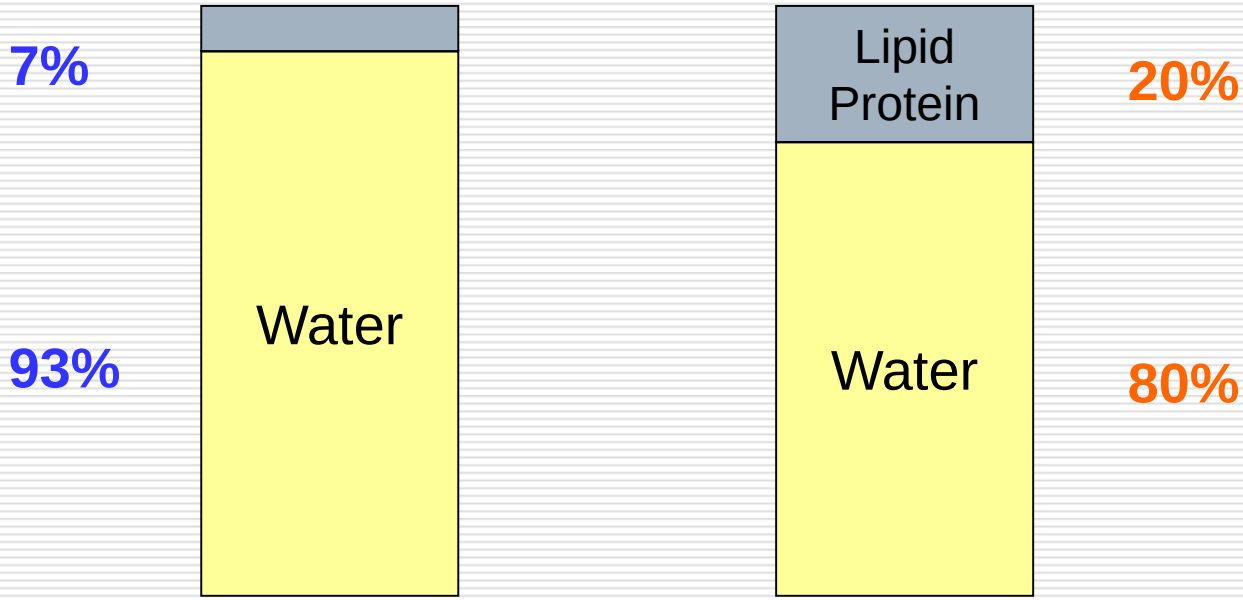
Normal



Hypertonic hyponatremia

Psudohyponatremia

Normal plasma osmolality

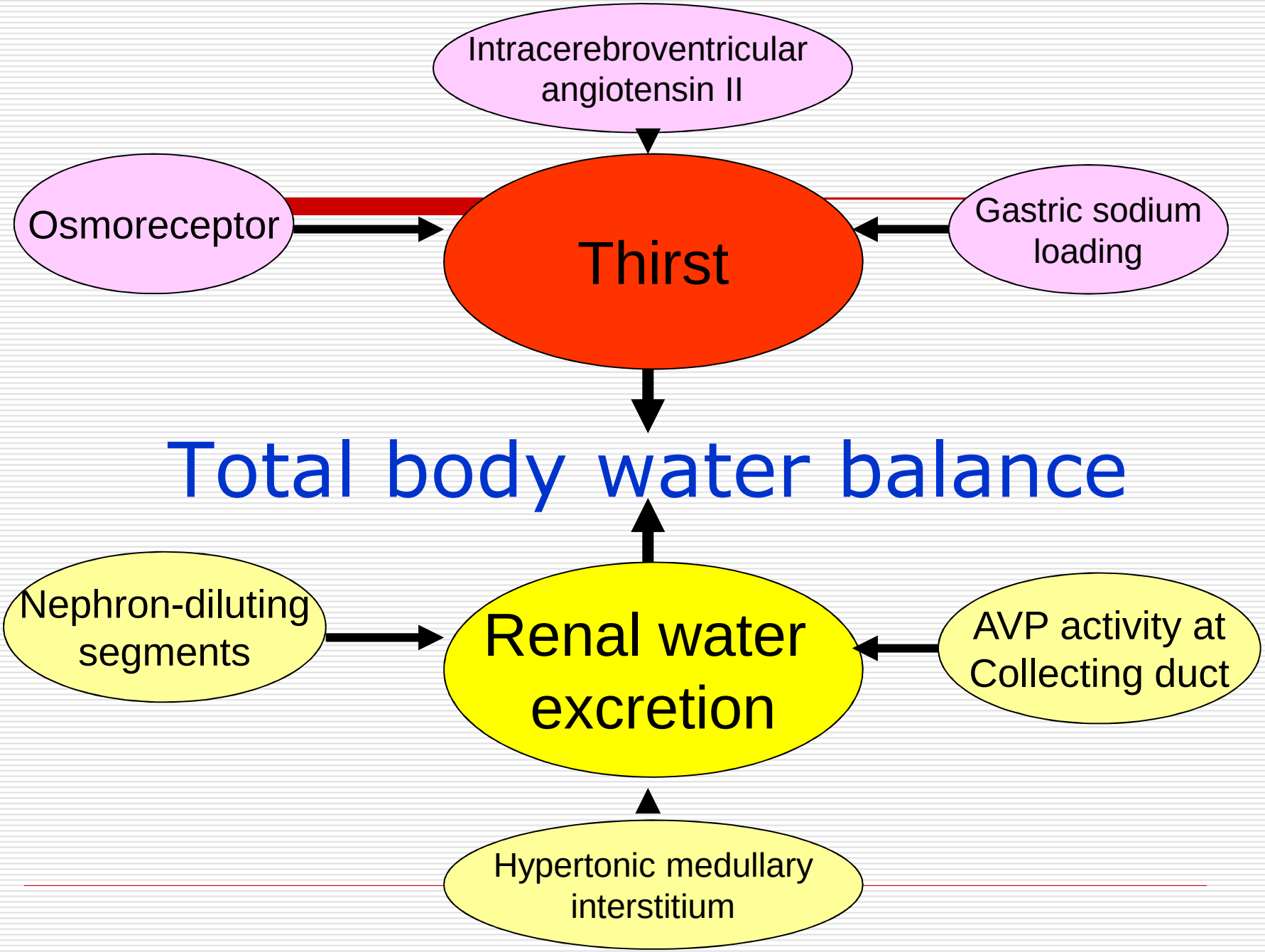


Measured serum [Na+] 142 meq/L

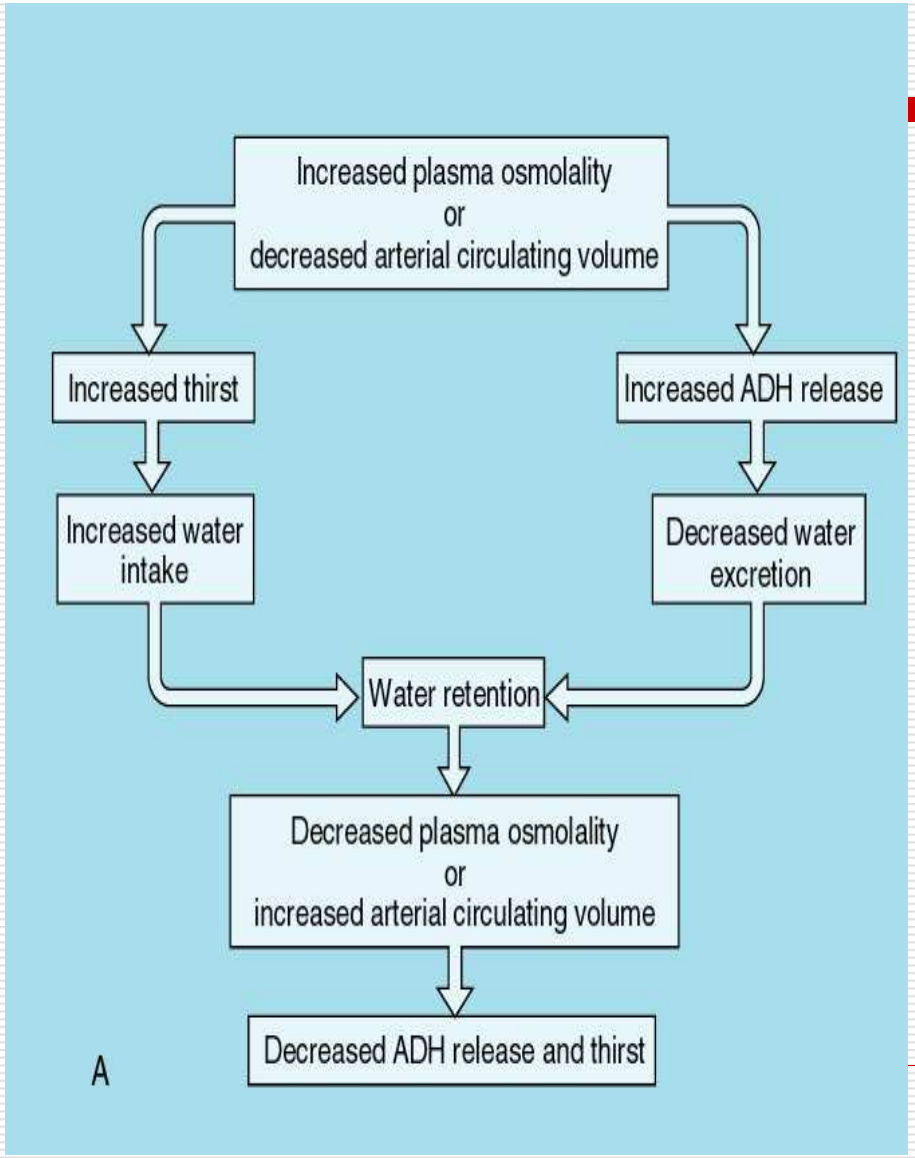
Actual serum [Na+] 153 meq/L

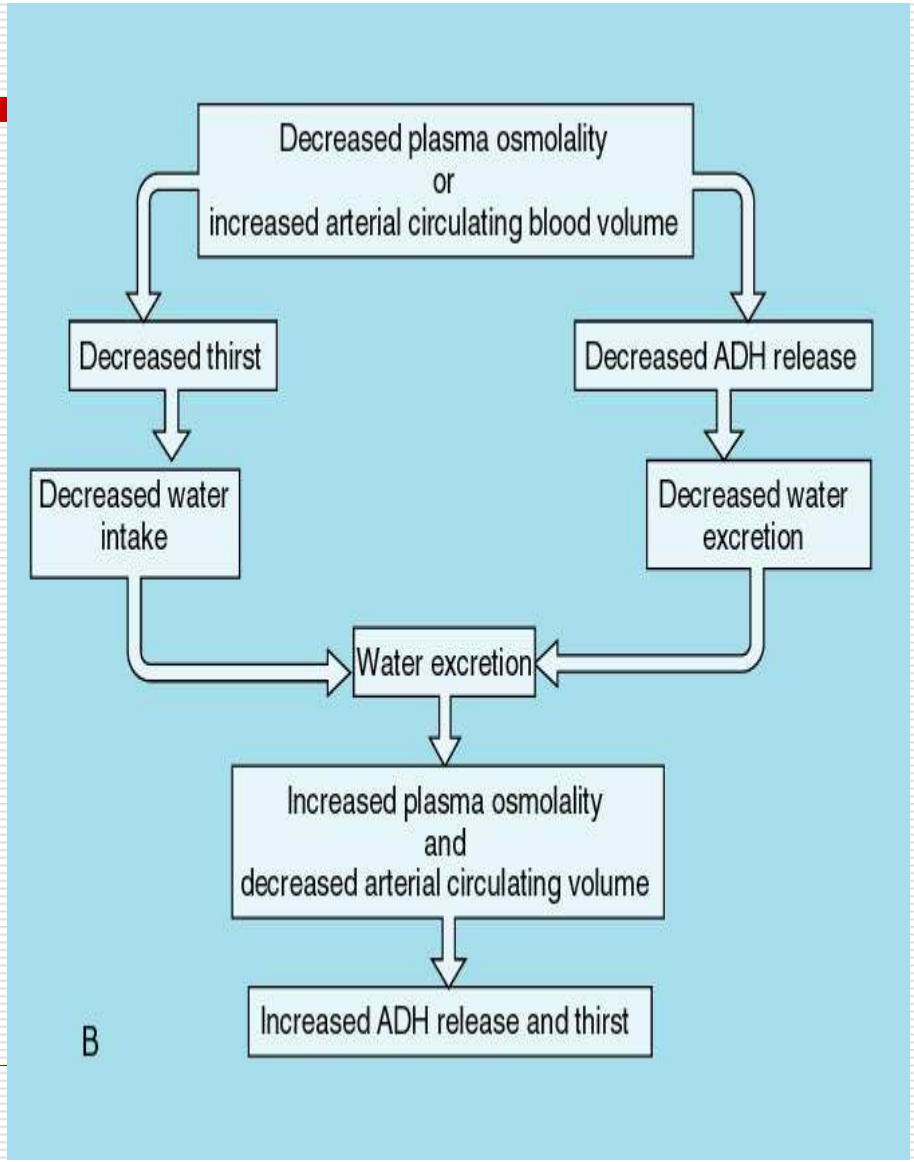
Measured serum [Na+] 122 meq/L

Actual serum [Na+] 153 meq/L


Intracerebroventricular angiotensin II
Osmoreceptor
Thirst
Gastric sodium loading
Total body water balance
Nephron-diluting segments
Renal water excretion
AVP activity at Collecting duct
Hypertonic medullary interstitium

Pathway of water balance



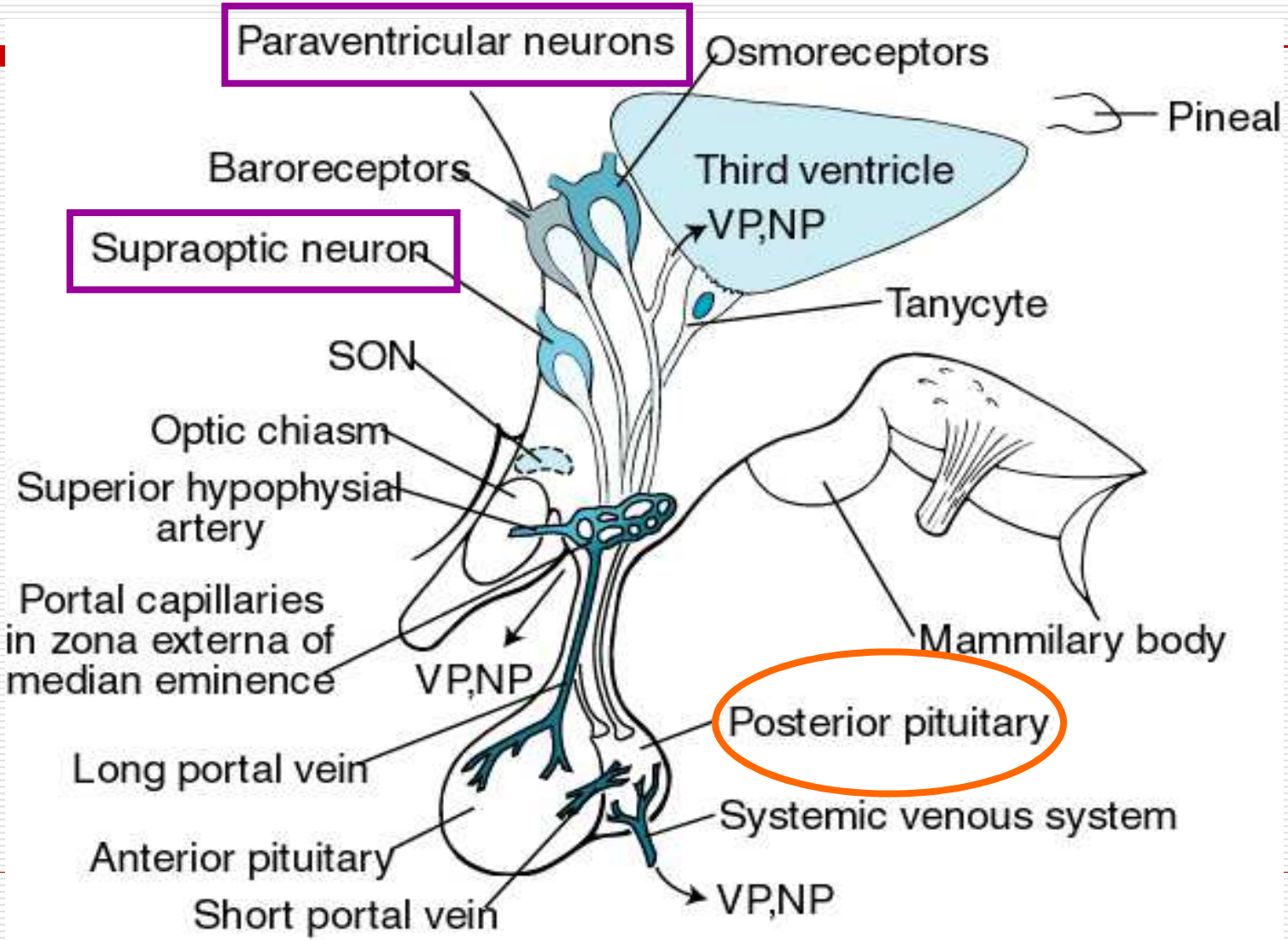


Hypo-osmotic hyponatremia

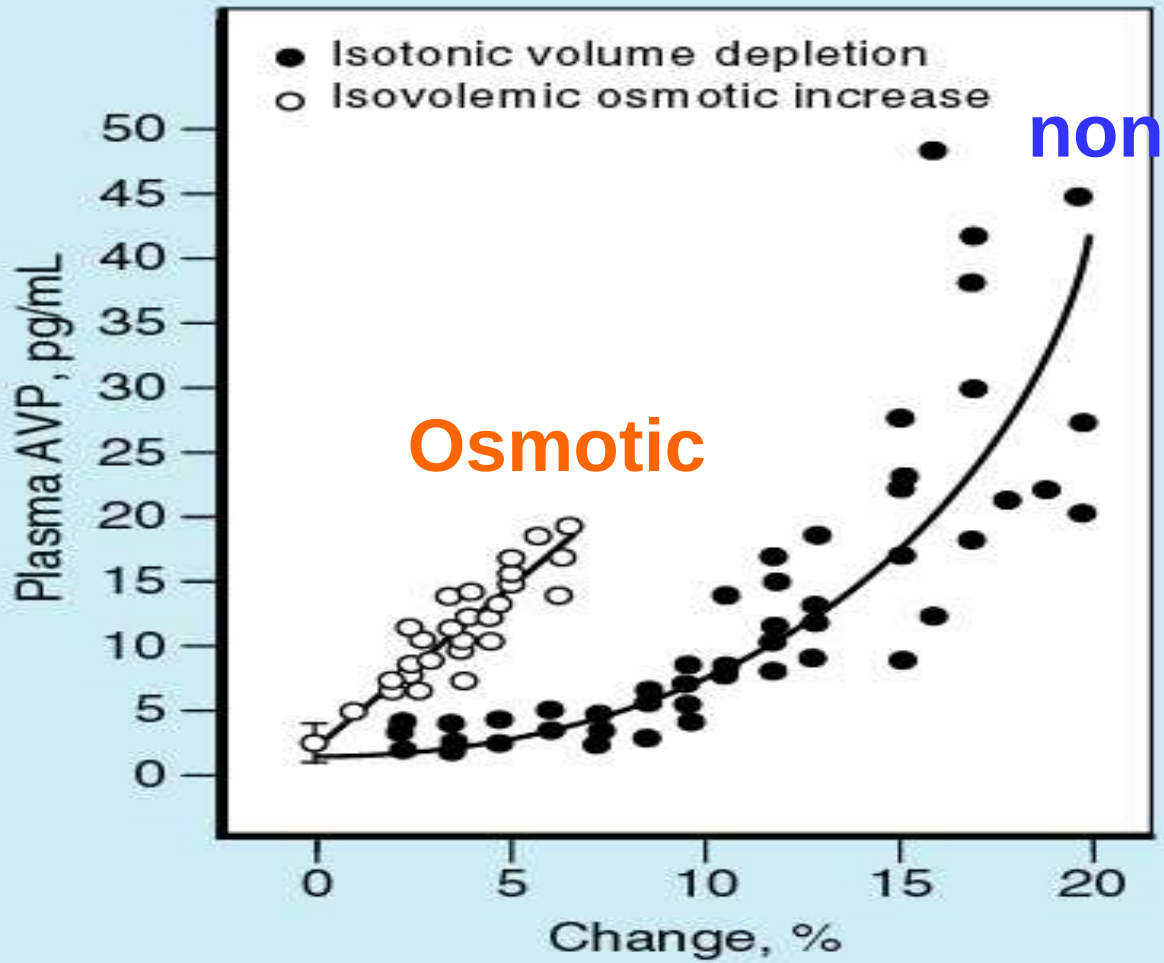
Impaired capacity of renal **water excretion**

Water intake

Pathways of AVP release



Regulation of AVP secretion



non-osmotic

Osmotic

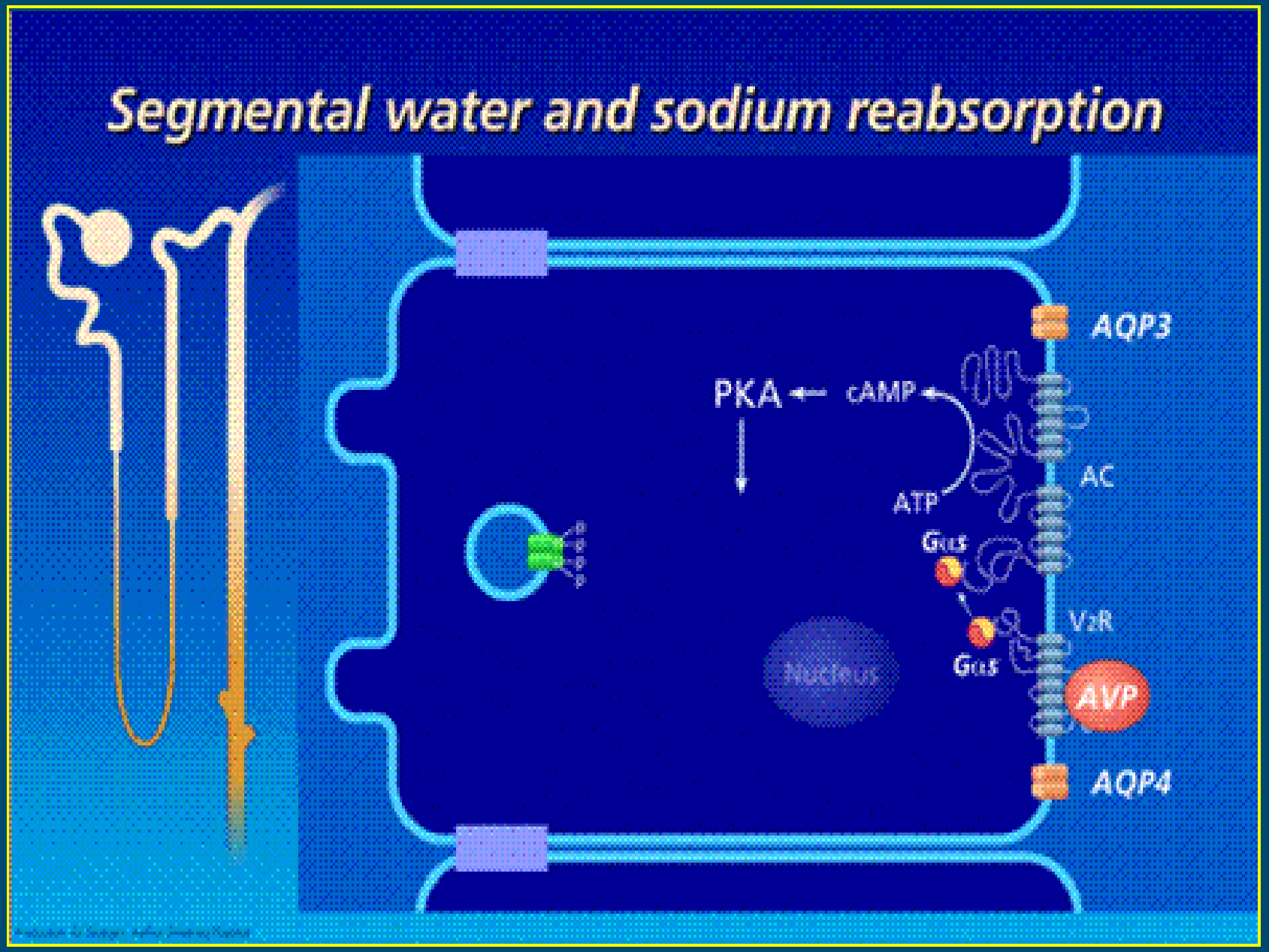
Aquaporins (AQP)
Water channel

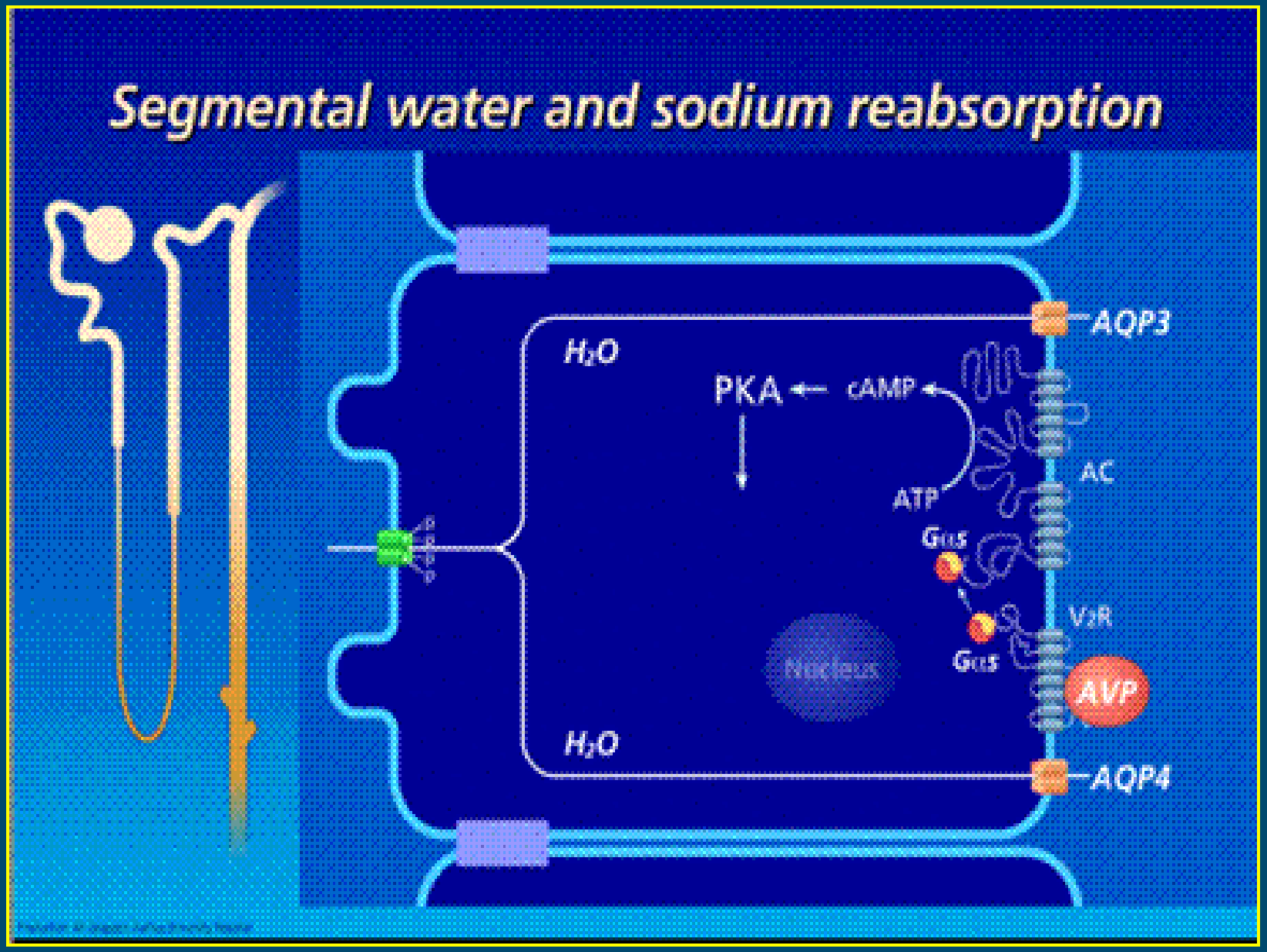
AQP1

Noble Prize in 2003

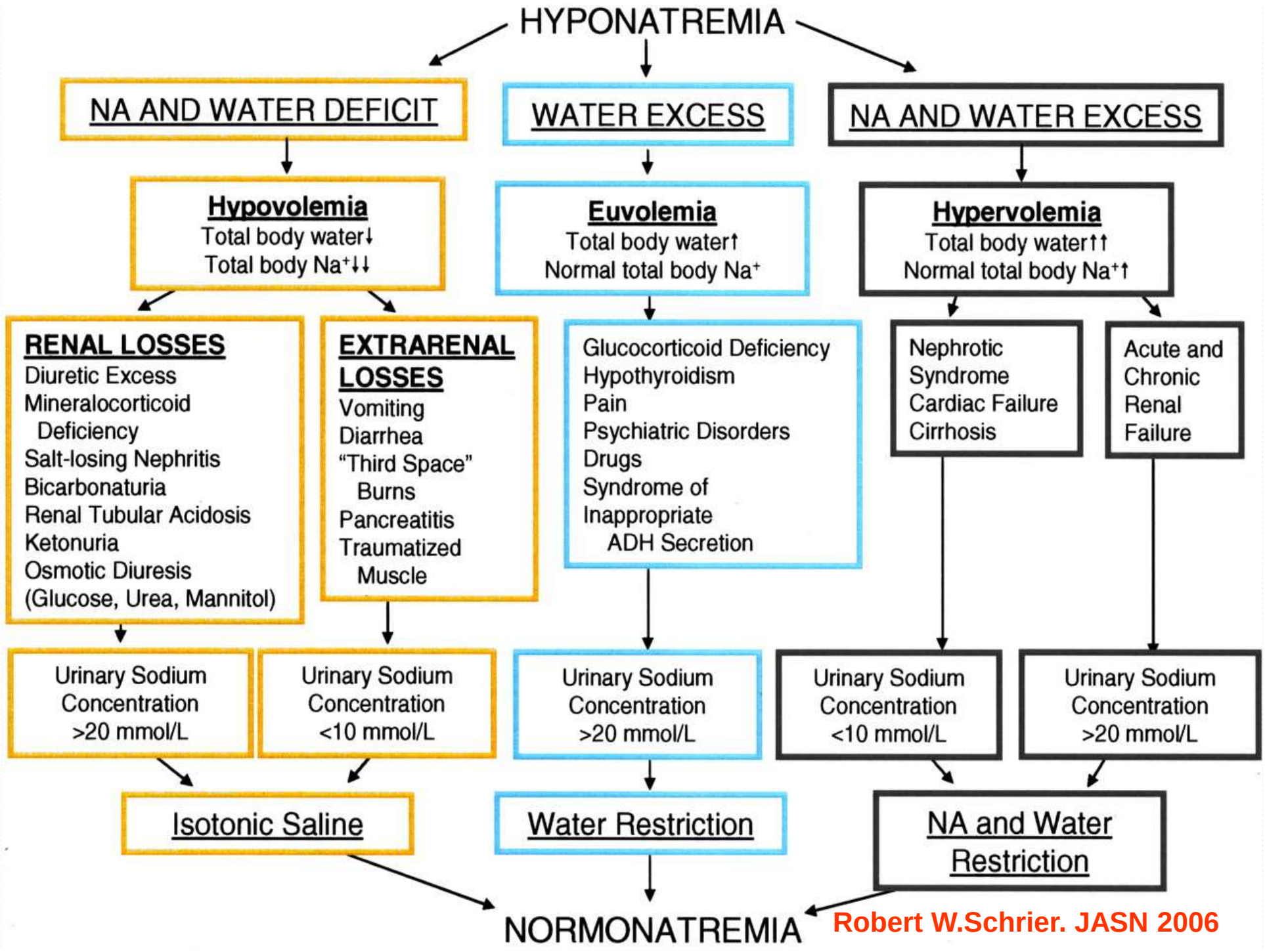
Agre and colleaques

	AQP-1	AQP-2	AQP-3	AQP-4
Size Amino acid	269	271	285	301
Permeability to small solute	No	No	Urea glycol	No
Regulation by **AVP**	No	Yes	No	No
Site	Descending thin limb	Collecting duct; principal cells	-Medullary collecting duct -colon	-Hypothalamus -Collecting duct
Cellular localization	Apical & basolateral membrane	Apical mb & intracellular vesicles	Basolateral mb	Basolateral mb of principal cells
Function	Water channels	Water channels	water exit from cell	-water exit from cell -osmoreceptor


Segmental water and sodium reabsorption
AQP3
PKA
cAMP
AC
ATP
Gαs
Gαs
V2R
Nucleus
AVP
AQP4


Segmental water and sodium reabsorption
H2O
PKA
cAMP
ATP
AC
AQP3
Gαs
Gαs
V2R
Nucleus
AVP
H2O
AQP4

Diagnosis of hyponatremia



Robert W.Schrier. JASN 2006

Assessment of volume status

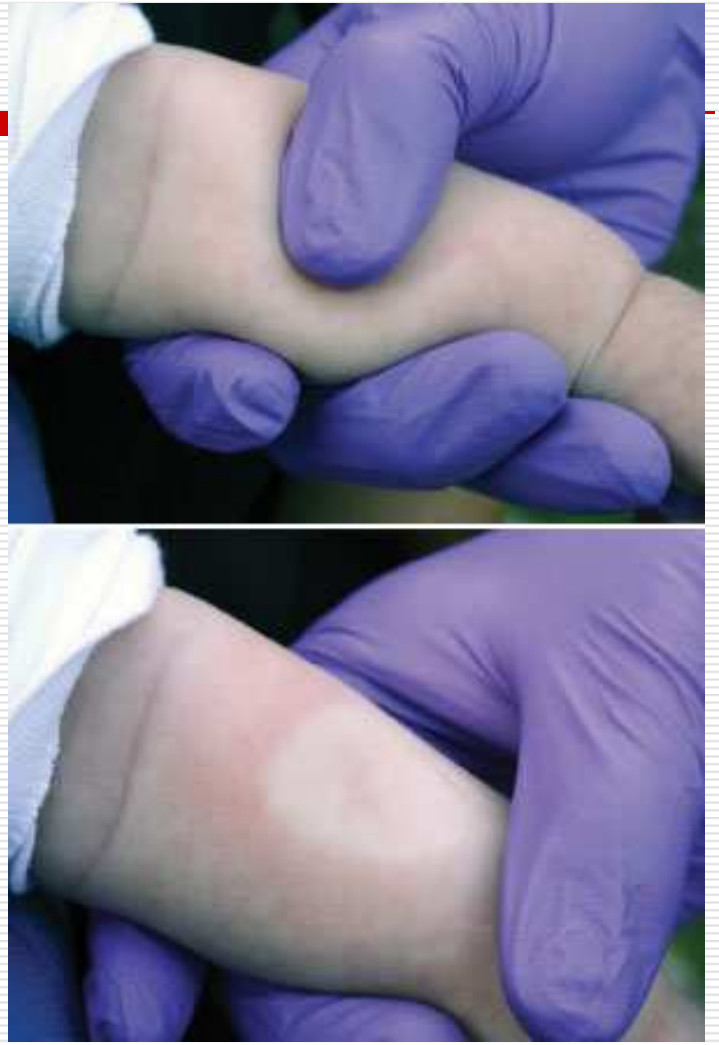
- Clinical examination
- Biochemical markers
- IVC diameter

Clinical assessment
Intravascular volume depletion

- Signs:
  - A fast pulse
  - Infrequent and low volume urination
  - Dry mucous membranes (e.g. a dry tongue)
  - Poor capillary refill (e.g. when the patient's fingertip is pressed, the skin turns white, but upon release, the skin does not return to pink as fast as it should)
  - Decreased skin turgor
  - A weak pulse
  - Orthostatic hypotension (dizziness upon standing up from a seated or reclining position, due to a drop in cerebral blood pressure)
  - Cool extremities (e.g. cool fingers)

Poor capillary refill

Adult



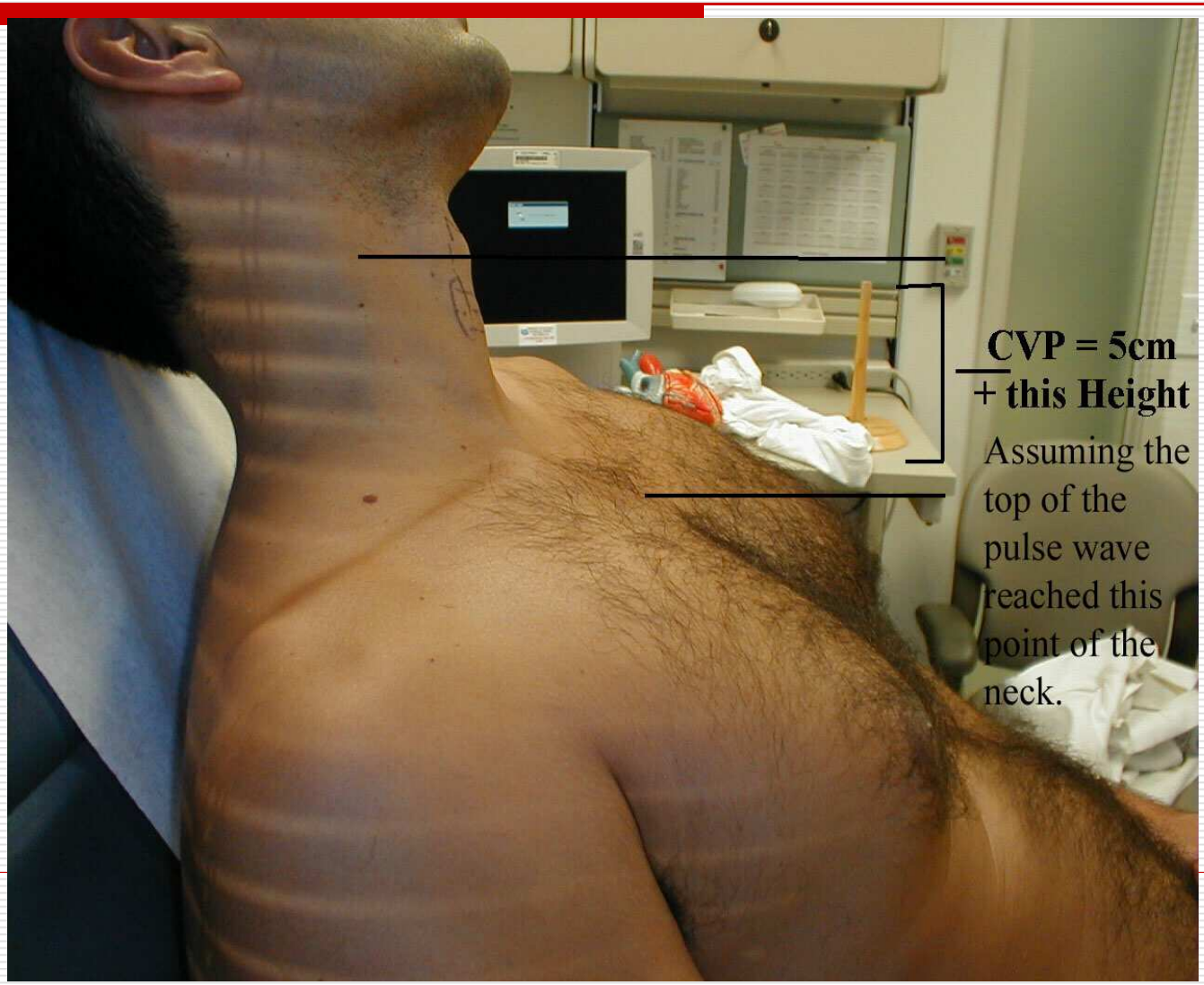
Children

Decreased skin turgor

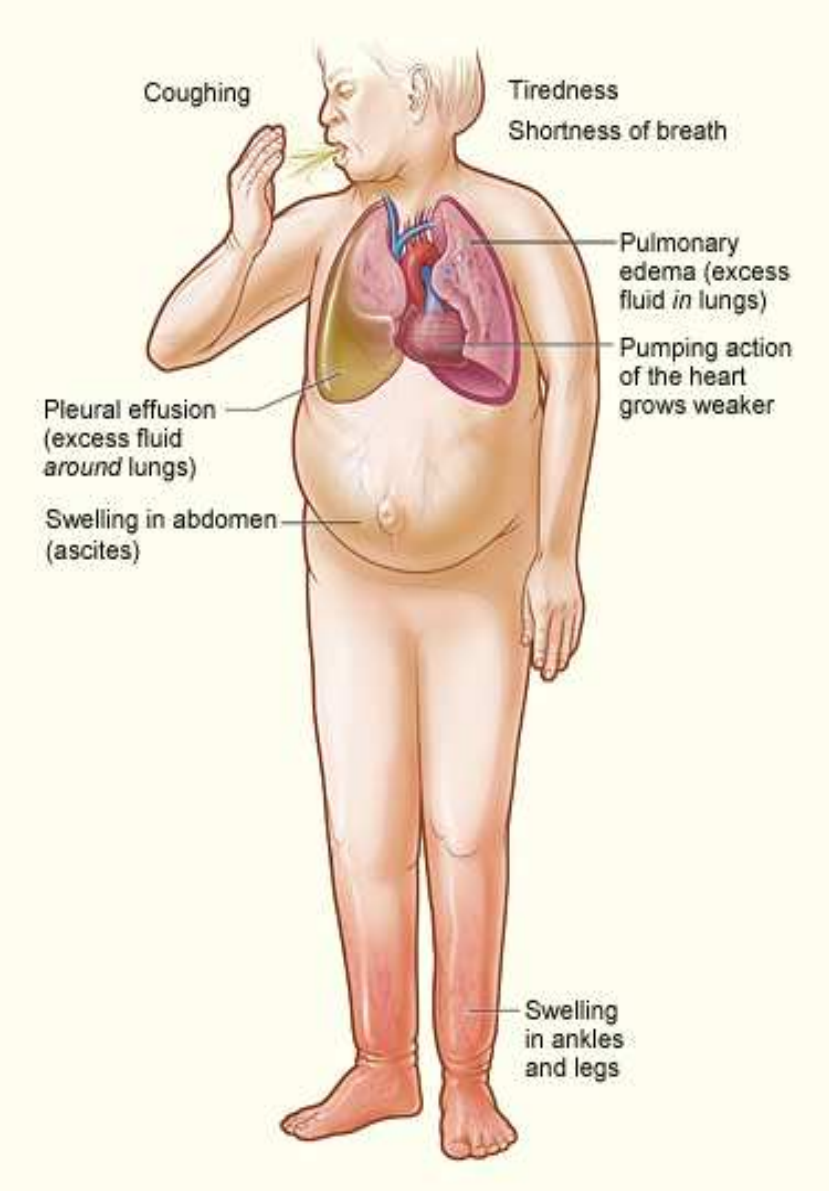
Clinical assessment
Intravascular volume overload

- Signs:
  - An elevated Jugular venous pressure (JVP)
  - Generalize edema
  - Pulmonary edema, rales or crepitation, heard initially in the lung bases
  - Pleural effusion
  - Ascites

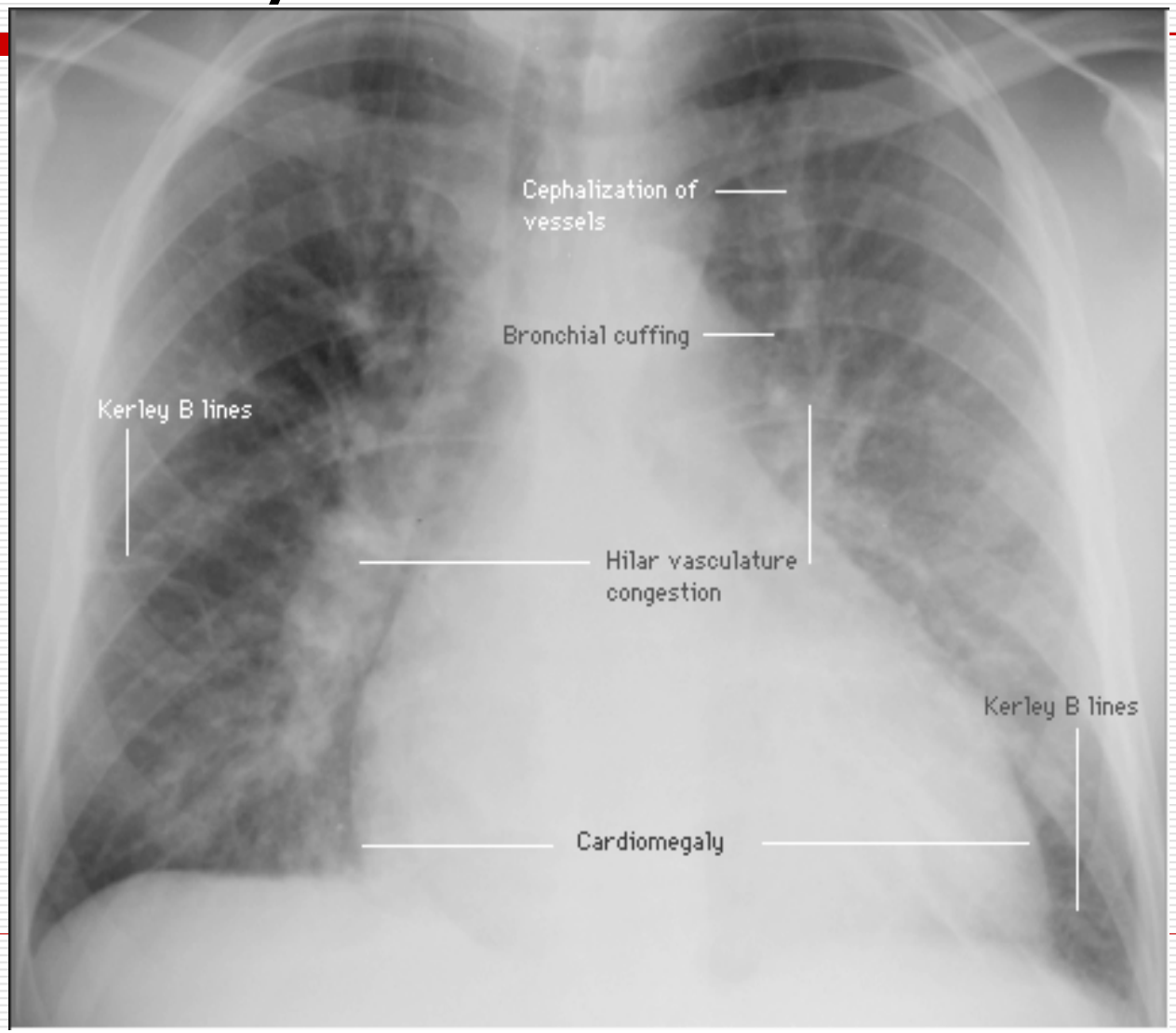
Jugular venous pressure (JVP)



Volume overload



Pulmonary edema

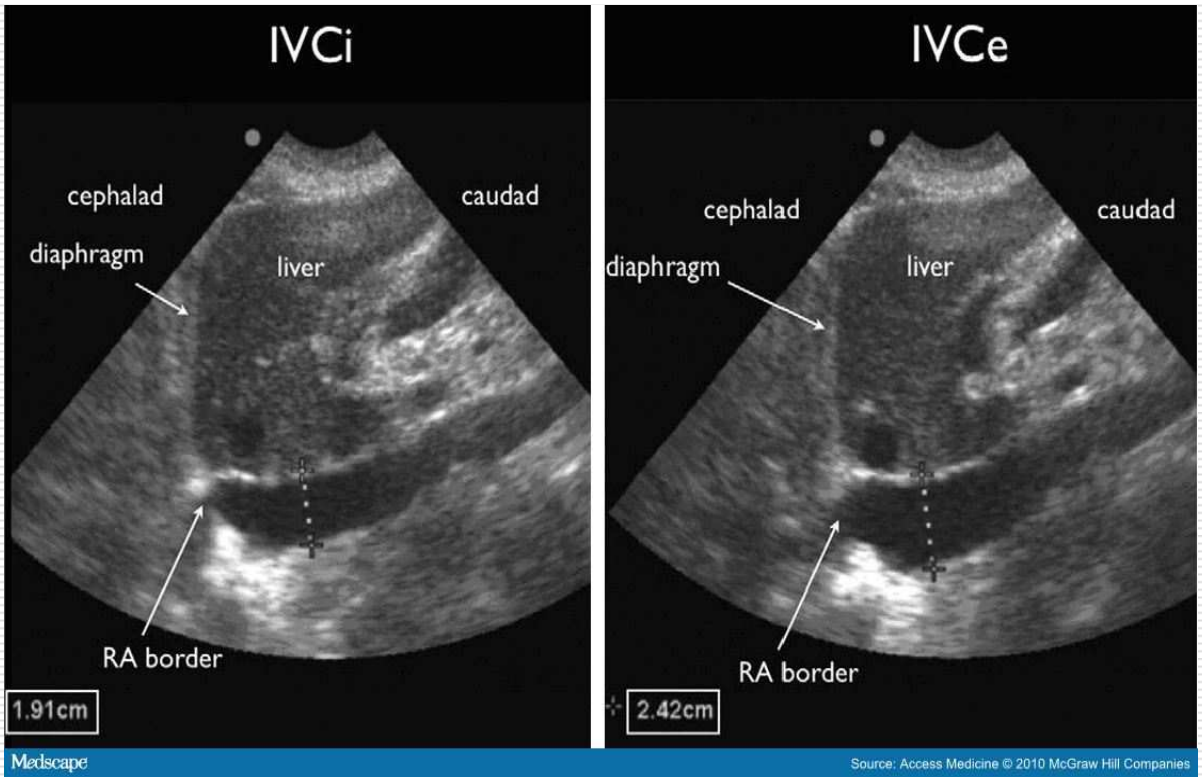


Biochemical markers

- Atrial natriuretic peptide (ANP)
- Brain natriuretic peptide (BNP)
  - Increased levels → marker of volume overload
  - Normalization → the achievement of dry weight

IVC diameter

- Collapse index (CI)



Minimum diameter – inspiration Maximum diameter - expiration

Collapse Index (CI)

$$CI = \frac{\text{Max diameter} - \text{Min diameter}}{\text{Max diameter}} \times 100\%$$

- CI > 50% = RA pressure < 10mmHg
- CI < 50% = RA pressure > 10mmHg

Kircher BJ et al Am J Cardiol 1990 Aug 15;66(4):493-6

Diagnosis of Hyponatremia

- History
  - Fluid loss
  - One of the causes of SIADH
  - Cancer, CNS disorders, Drugs, pulmonary conditions, pain/nausea
  - Symptoms of adrenal insufficiency or hypothyroidism
- Signs
  - Volume depletion
  - Edema/Ascites
  - Adrenal insufficiency or hypothyroidism

Plasma AVP ?

Case I

- 60-year-old man with a history of schizophrenia, who presents with severe right lower quadrant pain is admitted for appendectomy. He did not take any medication for 2 years.
- Lab

Na 116 mmol/l

K 4.0 mmol/l

Cl 106 mmol/l

HCO_3 24 mmol/l

Evaluation :

Hydration status : no hypovolemia

no edema

euvolemia

Urine Na 60, K 10 mmol/l

Serum Osmolarity = 245 mOsm/Kg

Urine Osmolarity = 450 mOsm/Kg

Diagnosis: SIADH

Criteria

1. Hypoosmolarity
2. Euvolemia (mild degree overhydration)
3. Urine osmolarity not maximally diluted
4. Normal renal function
5. No evidence of drug induced hyponatremia
6. Normal cortisol and TFT

Management

1. Fluid restriction VERSUS hypertonic solution

2. Rate of correction

   Osmotic demyelination syndrome

Calculation of sodium deficit

- A mildly symptomatic 60 kg women has a plasma sodium concentration of 116 meq/L. The goal is to raise the plasma sodium concentration by 8 meq/L in the first 24 hours.
- The sodium deficit (in meq) for initial therapy is estimated to be:

$$= 0.5 \times 60 \times (124 - 116)$$
$$= 240 \text{ meq}$$

Rate of correction

- Use 3% NaCl
  - 0.5 mEq of Na = 1 ml
  - 240 mEq of Na = 480 ml

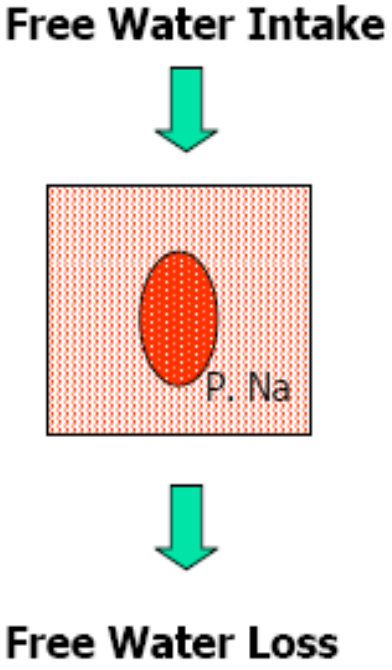
- Rate of correction = 480 ml/24 hr
  - An initial rate = 20 ml/hr

  which would be expected to raise the plasma sodium concentration at the desired rate of 8 meq/L during the first day

Hypernatremia

- 60 year old male with ARDS/intubated//TPN
- Dehydrate, BP = 110/70 mmHg, HR 85/min.
  - Lab
    - Plasma Na 150 mmol/l, glucose 400 mg/dl
    - Urine output 150 ml/hr
    - Urine osmolarity = 504
    - Urine Na = 40 mmol/l
    - Urine dip stick = 2+ glucose

Hypernatremia



- Decreased free water supply
- Water loss
  - Osmotic diuresis, D.I.
  - Osmotic diarrhea
  - Insensible
- Solute load

Major causes of hypernatremia

- Unreplaced water loss (which requires an impairment in thirst or access to water)
  - Insensible and sweat losses
  - Gastrointestinal losses
  - Central or nephrogenic diabetes insipidus
  - Osmotic diuresis
  - Hypothalamic lesions impairing thirst or osmoreceptor function
  - Primary hypodipsia
- Water loss into cells
  - Severe exercise or seizures
- Sodium overload
  - Intake or administration of hypertonic sodium solutions

Approach for hypernatremic patients

- Why is the patient not drinking??
- Is there increased free water loss:
  - ?Polyuria
    - Uosm: if <250 – D.I.
    - Uosm: if >300 – solute diuresis
  - ? GI (osmotic diarrhea)
- Is the patient getting too much solute?

Therapeutic principles

- How can the water deficit be estimated?
  - Water deficit formula
- At what rate can the plasma sodium concentration safely be normalized?
  - The maximum safe rate at which the plasma sodium concentration should be lowered is by ≤0.5 meq/L per hour and no more than by 12 meq/L per day
  - Cerebral edema

Derivation of the water deficit formula

- Total body osmoles = TBW x 2 x plasma [Na+]
- Current body osmoles = Normal body osmoles
  - If current body water(CBW), normal body water(NBW)
- CBW x plasma [Na+] = NBW x 140
- NEW = CEW x plasma [Na+] / 140

- **Water deficit = NBW - CBW**
  = (CEW x plasma [Na+] / 140) – CBW
  = CBW ($\frac{\text{plasma [Na+]}}{140}$ – 1)

Treatment

- **Calculate Amount of Water**
  - 0.4 x body weight x (PNa/140 – 1)
    0.4 x 50 x (150/140 – 1) = 1.4 liters
  - Insensible losses= + 1 liter/24h
  - Total volume=2.4 liters
- **Rate** (0.5meq/hour)
  - For Na to go from 150->140=20 hours
- **Prescription**: Rate of water repletion
  = 2400/20=120ml/hr.

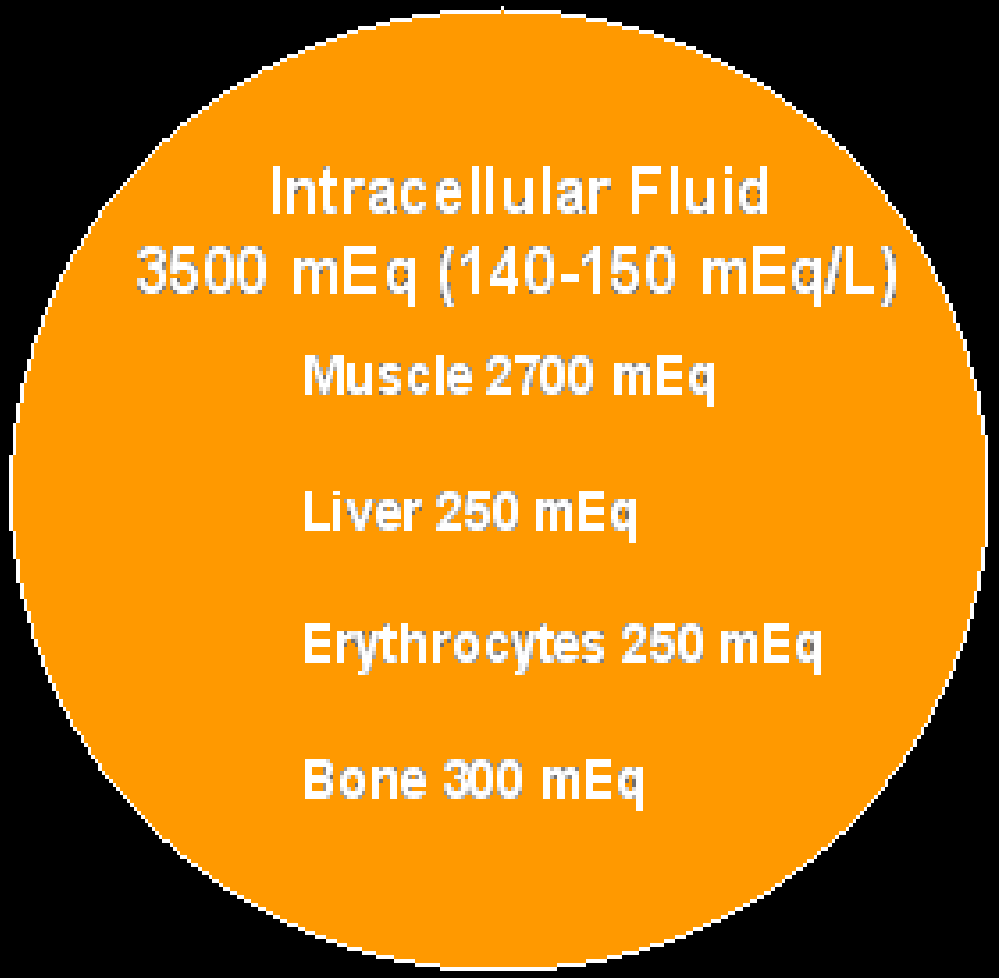
Hypokalemia

- Definition

- Serum K^+ < 3.5 mEq/L

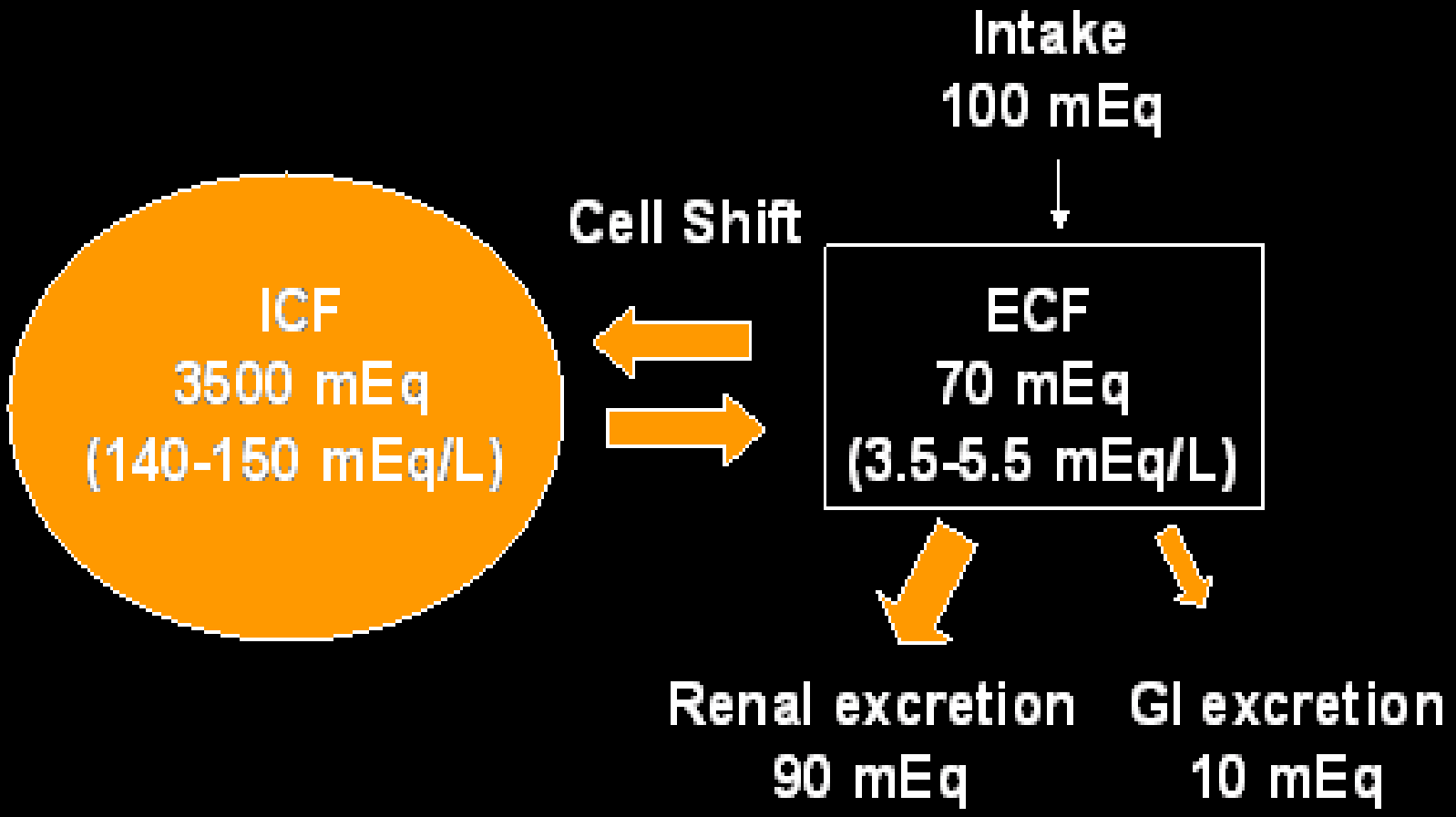
Distribution of Total Body K^+

K^+ Gradient Sets Cell Voltage

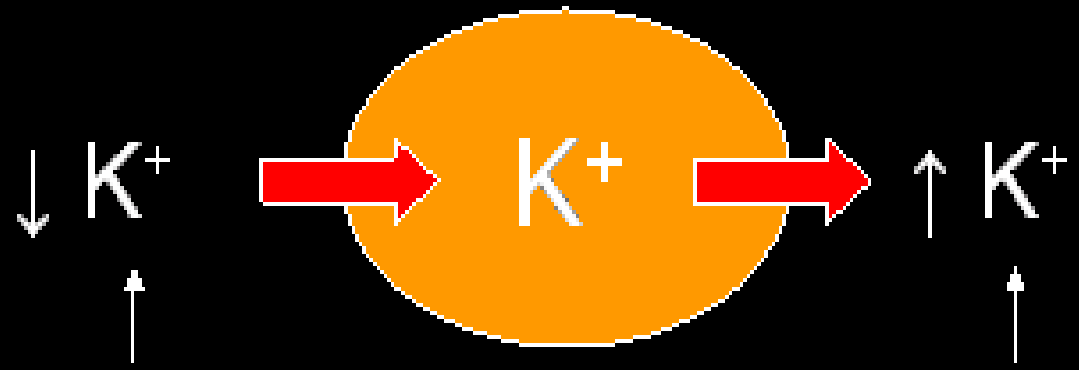


Extracellular fluid
70 mEq (3.5-5.5 mEq/L)

Regulation of K^+ Homeostasis



Factors that Influence the Internal Distribution of K^+

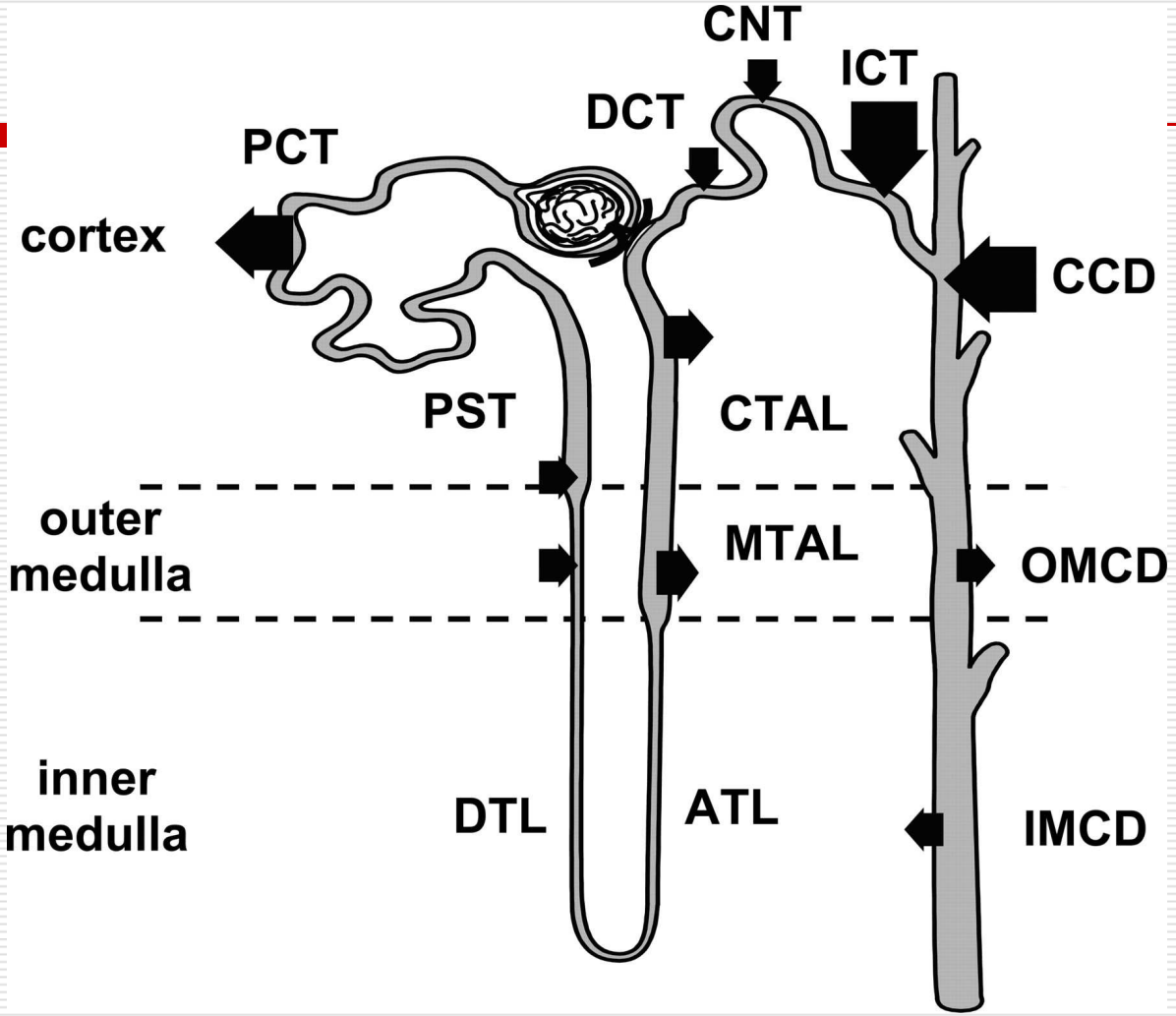


- Insulin*
- B_2-stimulation*
- Alkalosis
- Anabolism

- Mineral acidosis
- ↑ tonicity
- β blockade
- α stimulation

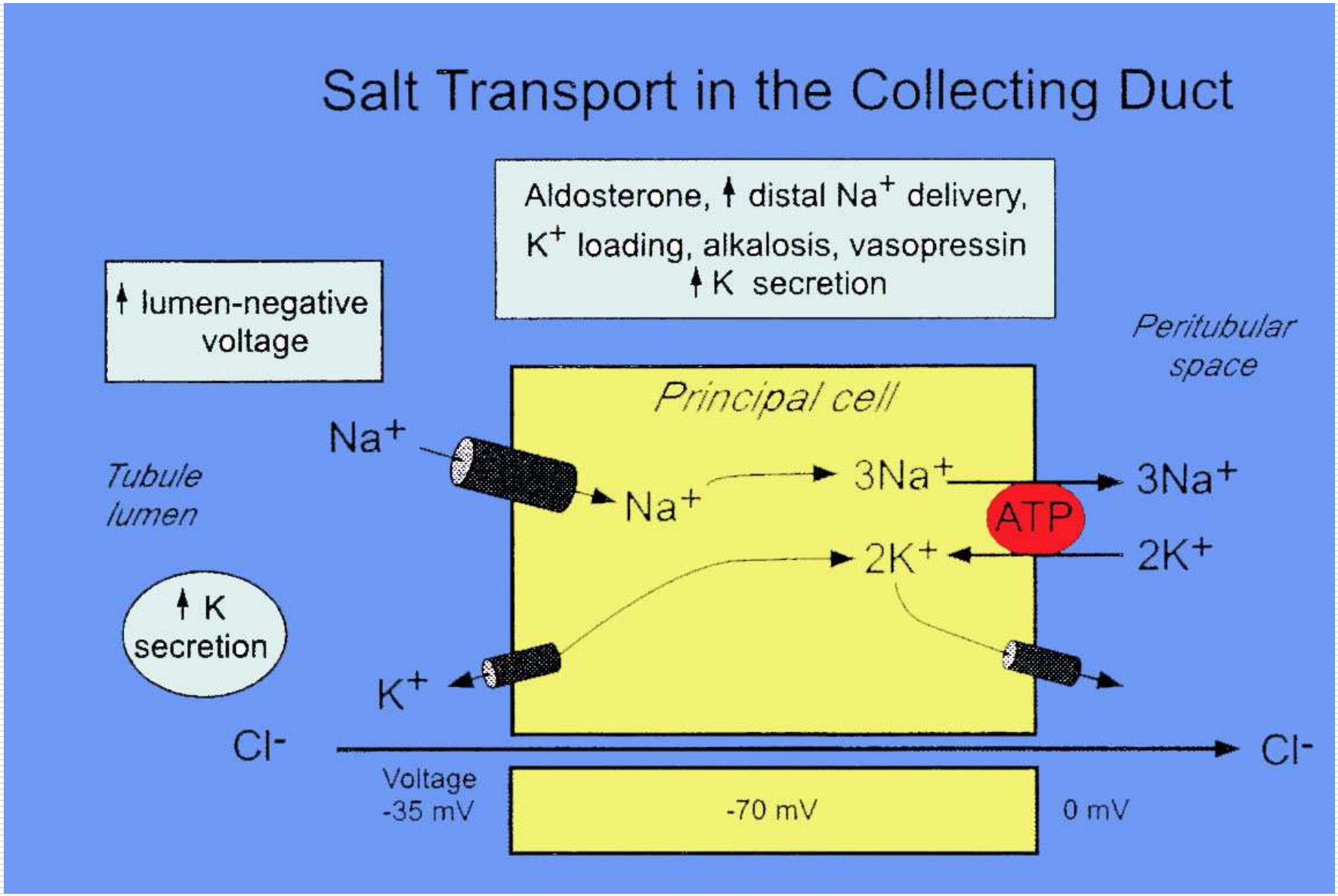
* Important in normal potassium homeostasis

Potassium transport along a simplified nephron

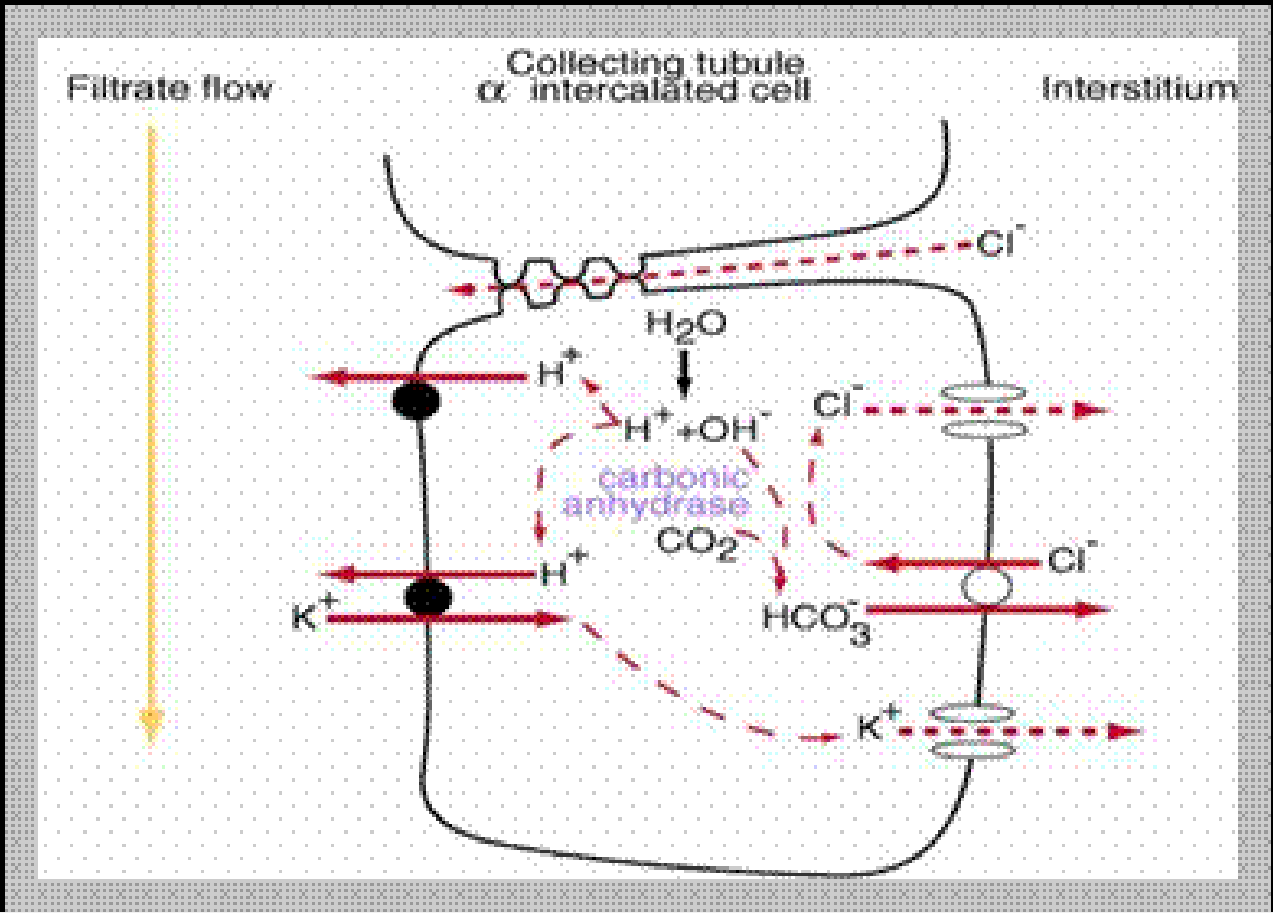


Hebert, S. C. et al. Physiol. Rev. 85: 319-371 2005;

Physiological Reviews


Salt Transport in the Collecting Duct
Aldosterone, ↑ distal Na+ delivery,
K+ loading, alkalosis, vasopressin
↑ K secretion
↑ lumen-negative voltage
Peritubular space
Principal cell
Tubule lumen
Na+
Na+
3Na+
3Na+
ATP
2K+
2K+
↑ K secretion
K+
Cl-
Cl-
Voltage
-35 mV
-70 mV
0 mV

α Intercalated Cell



Physiology of K^+ balance

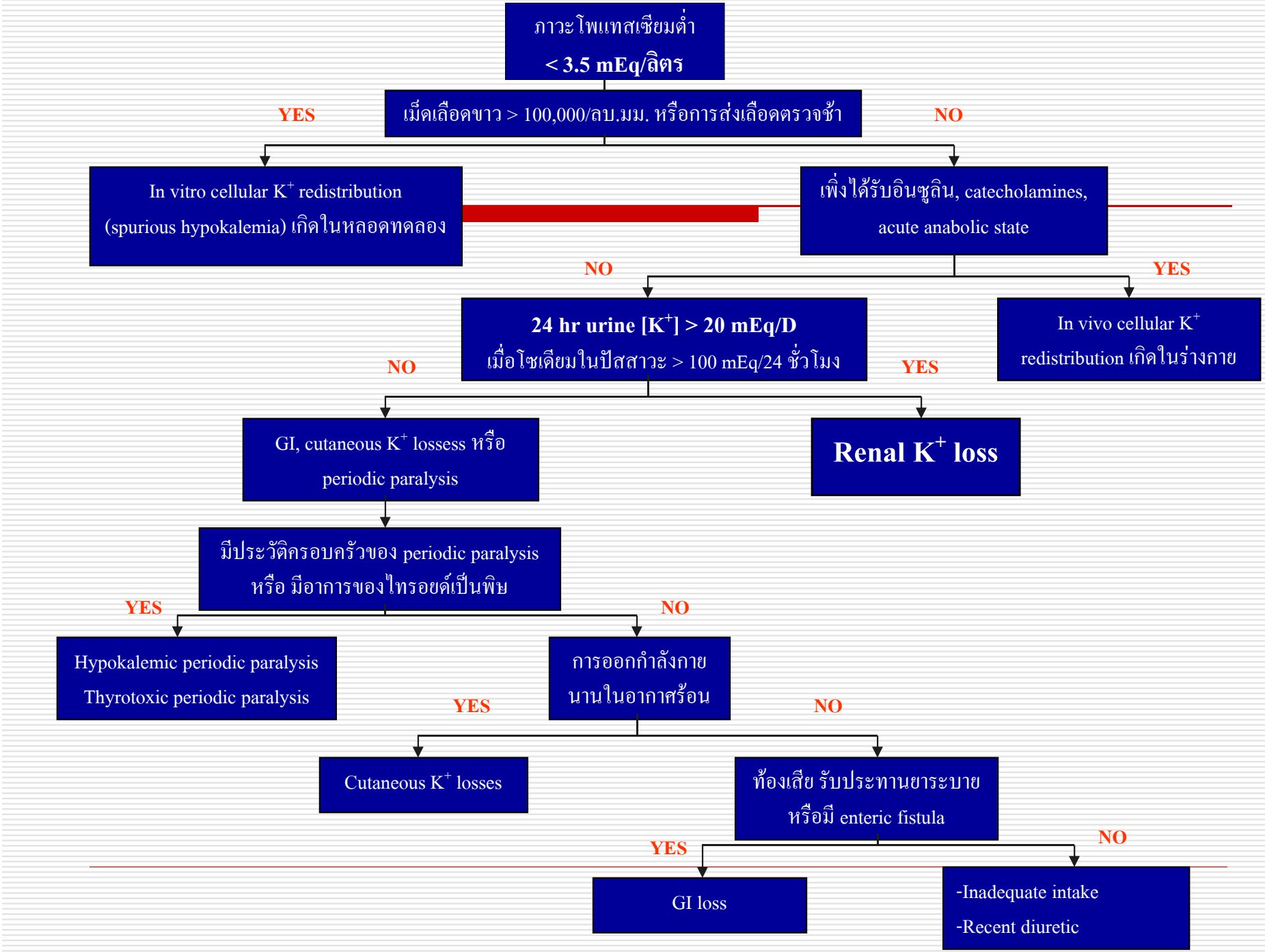
- Small decrements in serum K+ concentration may reflect large deficits in intracellular K+ content.

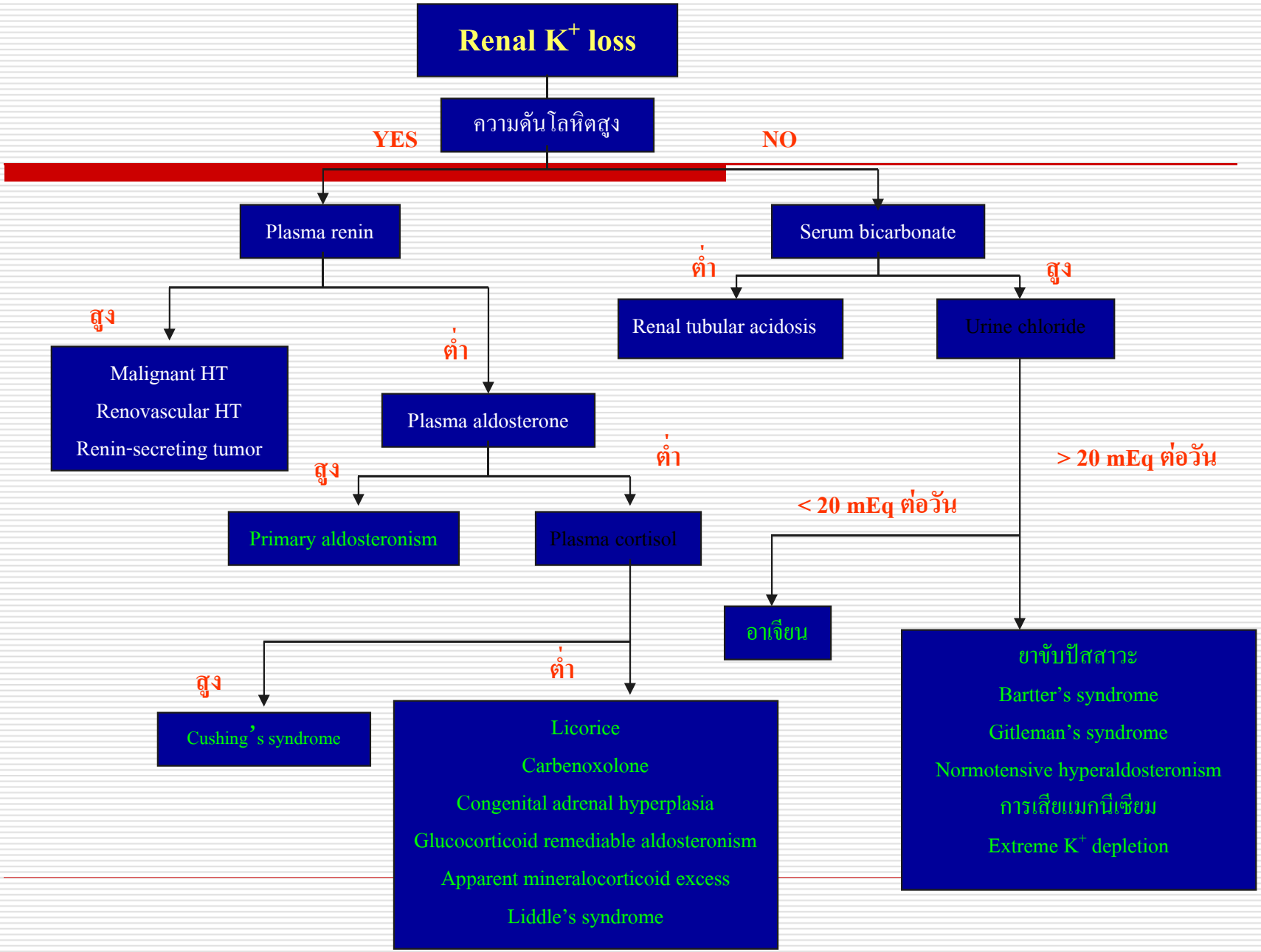
- In general

  ↓ 0.3 mEq/L for each 100 mEq decrement in total body K^+ ($K^+ < 3.5$/L)

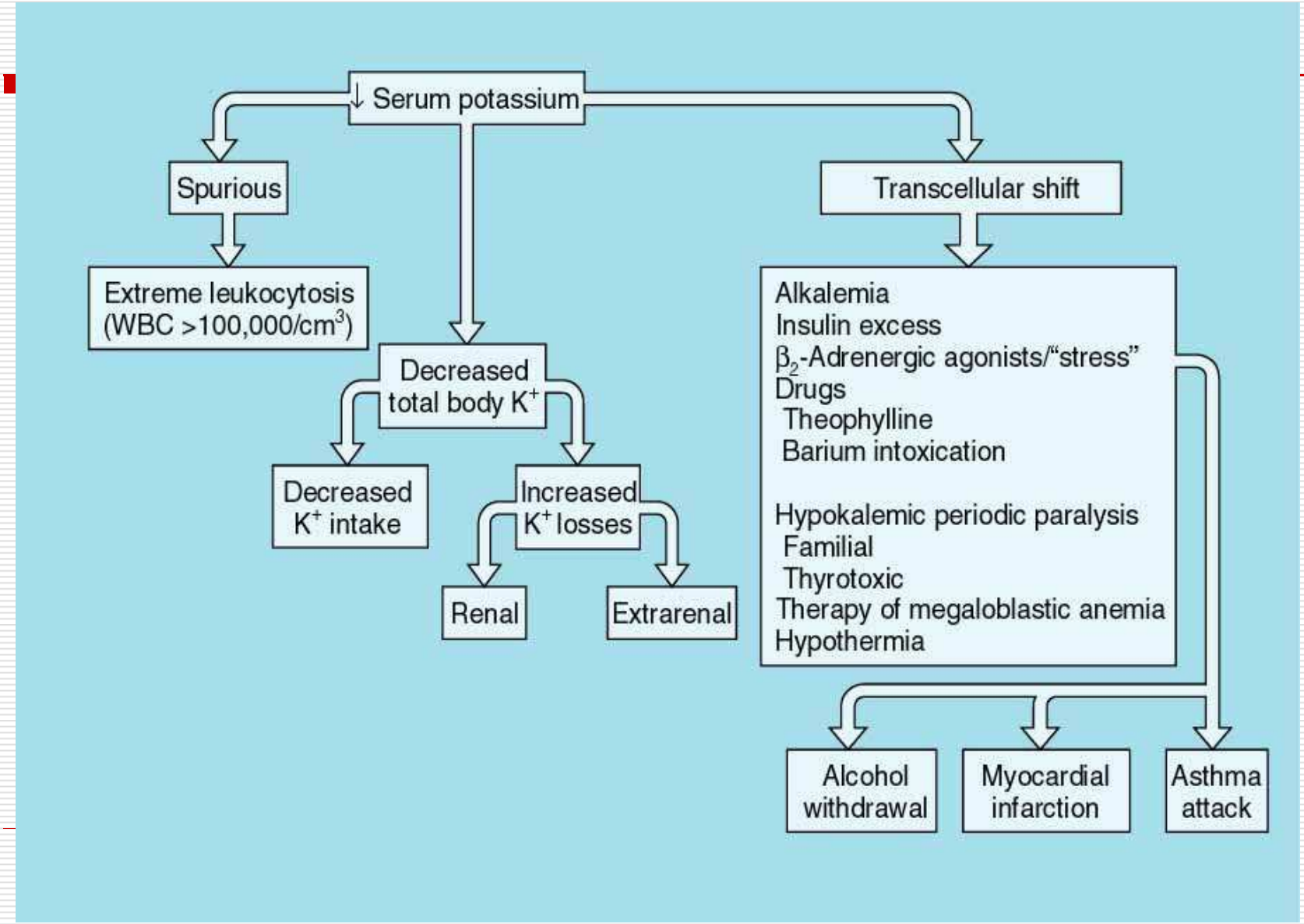
Thus, $K^+ < 3$ mEq/L → 100-300 total body K^+

$K^+ < 2$ mEq/L → 500-700 total body K^+


ภาวะโพแทสเซียมต่ำ
< 3.5 mEq/ลิตร
เม็ดเลือดขาว > 100,000/ลบ.มม. หรือการส่งเลือดตรวจช้า
YES
NO
In vitro cellular K+ redistribution
(spurious hypokalemia) เกิดในหลอดทดลอง
เพิ่งได้รับอินซูลิน, catecholamines,
acute anabolic state
NO
YES
24 hr urine [K+] > 20 mEq/D
เมื่อโซเดียมในปัสสาวะ > 100 mEq/24 ชั่วโมง
In vivo cellular K+
redistribution เกิดในร่างกาย
NO
YES
GI, cutaneous K+ lossess หรือ
periodic paralysis
Renal K+ loss
มีประวัติครอบครัวของ periodic paralysis
หรือ มีอาการของไทรอยด์เป็นพิษ
YES
NO
Hypokalemic periodic paralysis
Thyrotoxic periodic paralysis
การออกกำลังกาย
นานในอากาศร้อน
YES
NO
Cutaneous K+ losses
ท้องเสีย รับประทานยาระบาย
หรือมี enteric fistula
YES
NO
GI loss
-Inadequate intake
-Recent diuretic

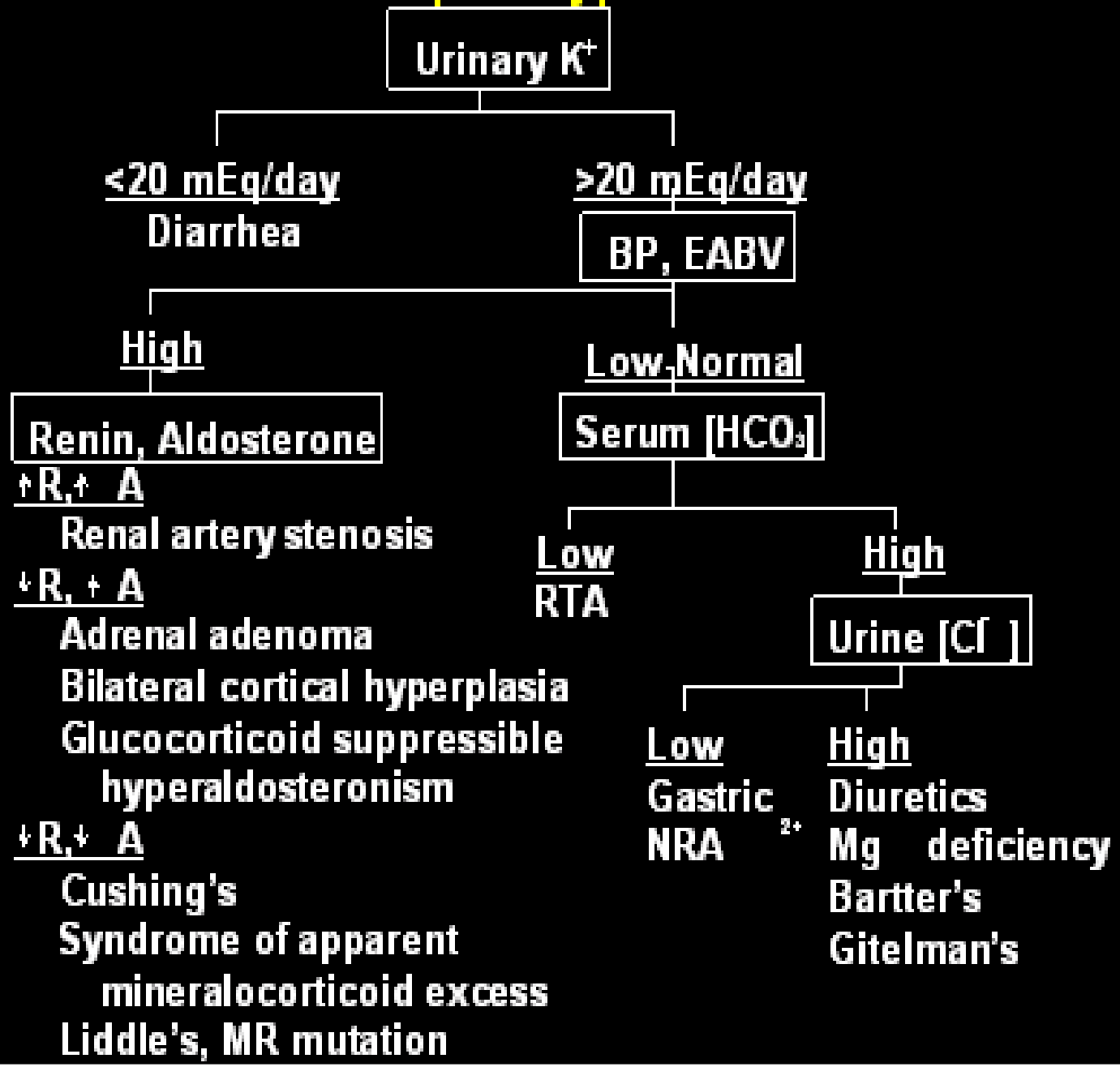

Renal K+ loss
ความดันโลหิตสูง
YES
NO
Plasma renin
Serum bicarbonate
สูง
ต่ำ
ต่ำ
สูง
Malignant HT
Renovascular HT
Renin-secreting tumor
Plasma aldosterone
Renal tubular acidosis
Urine chloride
สูง
ต่ำ
> 20 mEq ต่อวัน
Primary aldosteronism
Plasma cortisol
< 20 mEq ต่อวัน
อาเจียน
สูง
ต่ำ
Cushing's syndrome
Licorice
Carbenoxolone
Congenital adrenal hyperplasia
Glucocorticoid remediable aldosteronism
Apparent mineralocorticoid excess
Liddle's syndrome
ยาขับปัสสาวะ
Bartter's syndrome
Gitleman's syndrome
Normotensive hyperaldosteronism
การเสียแมกนีเซียม
Extreme K+ depletion

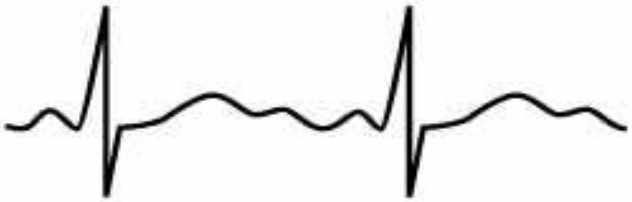
Work up of hypokalemia



Linus

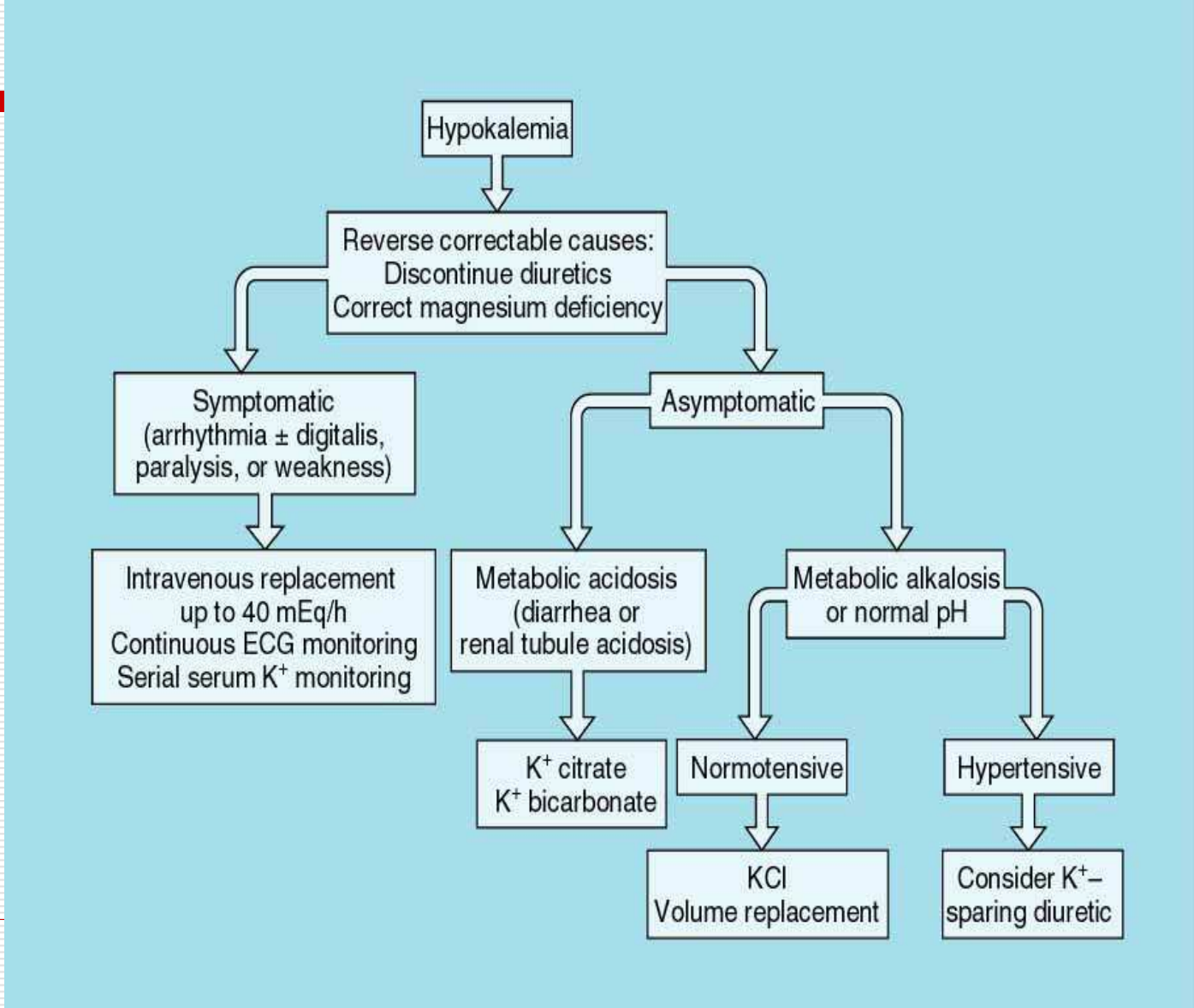
Work up of Hypokalemia



		Approximate Serum K^+ (mEq/L)
A		3.5–4.0
B		3.0–3.5
C		2.5–3.0
D		<2.5

Fredrick V. Osorio and Stuart L. Linus

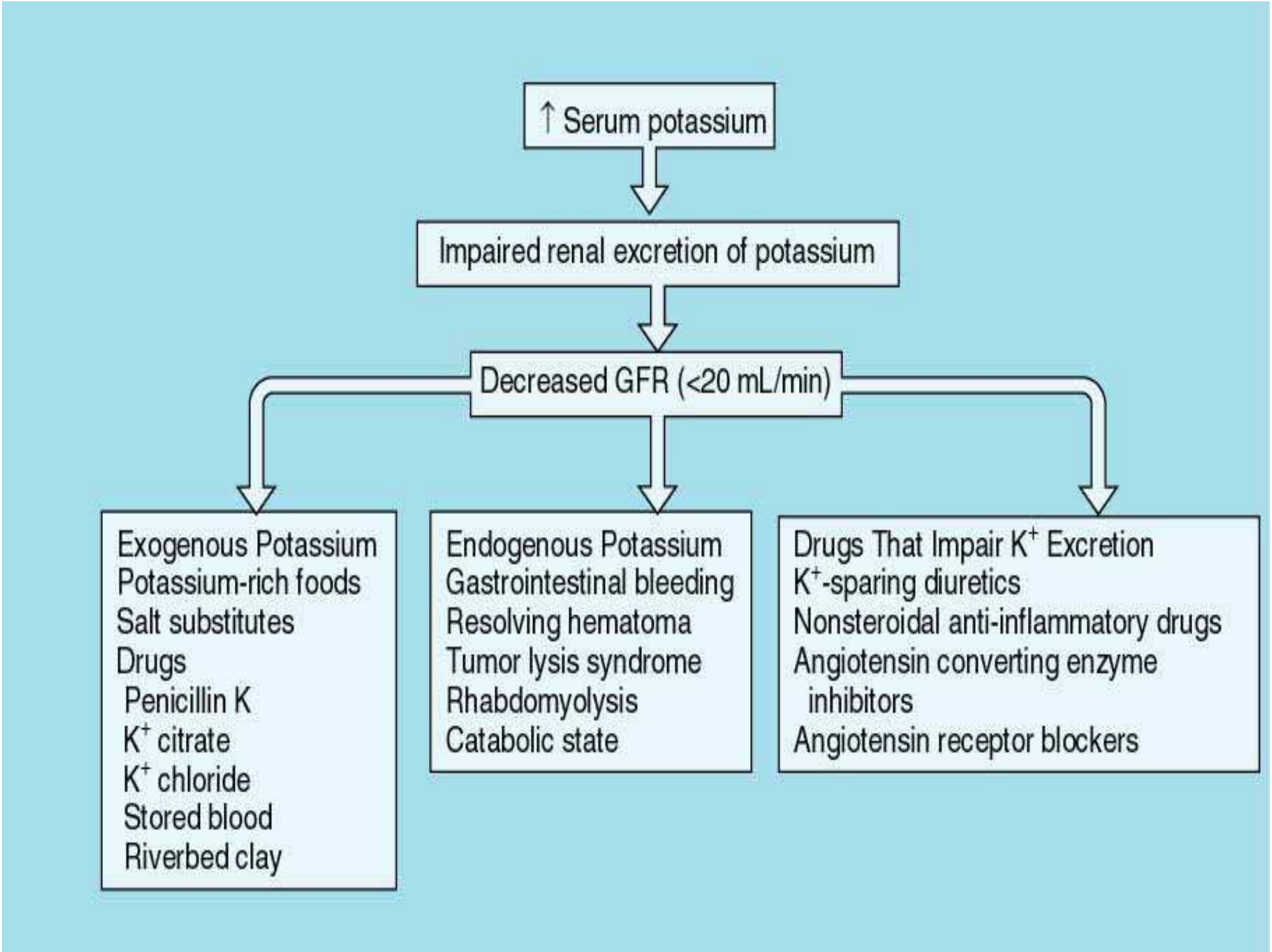
Hypokalemia: Treatment



Hyperkalemia

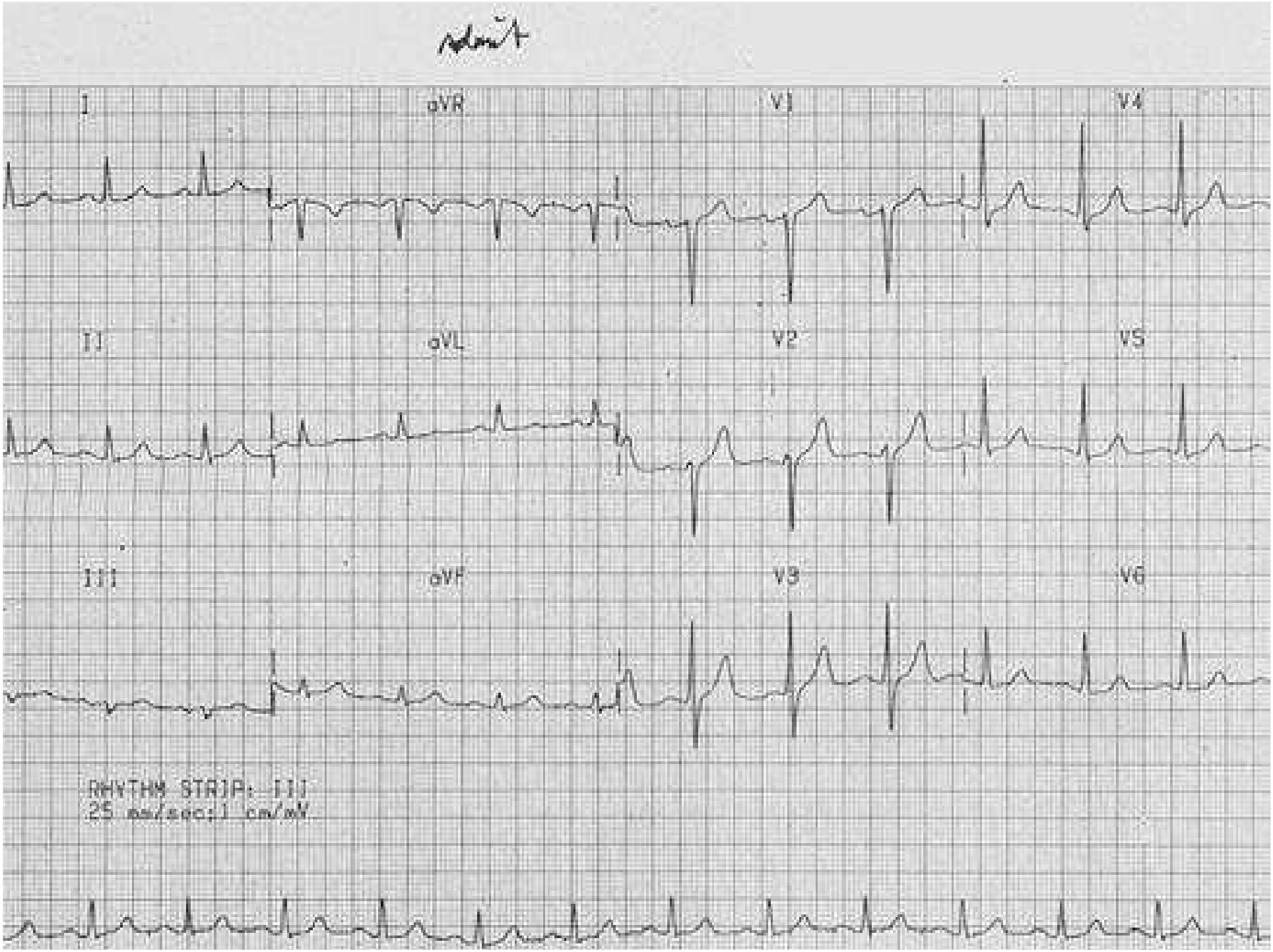
Clinical Approach to Hyperkalemia

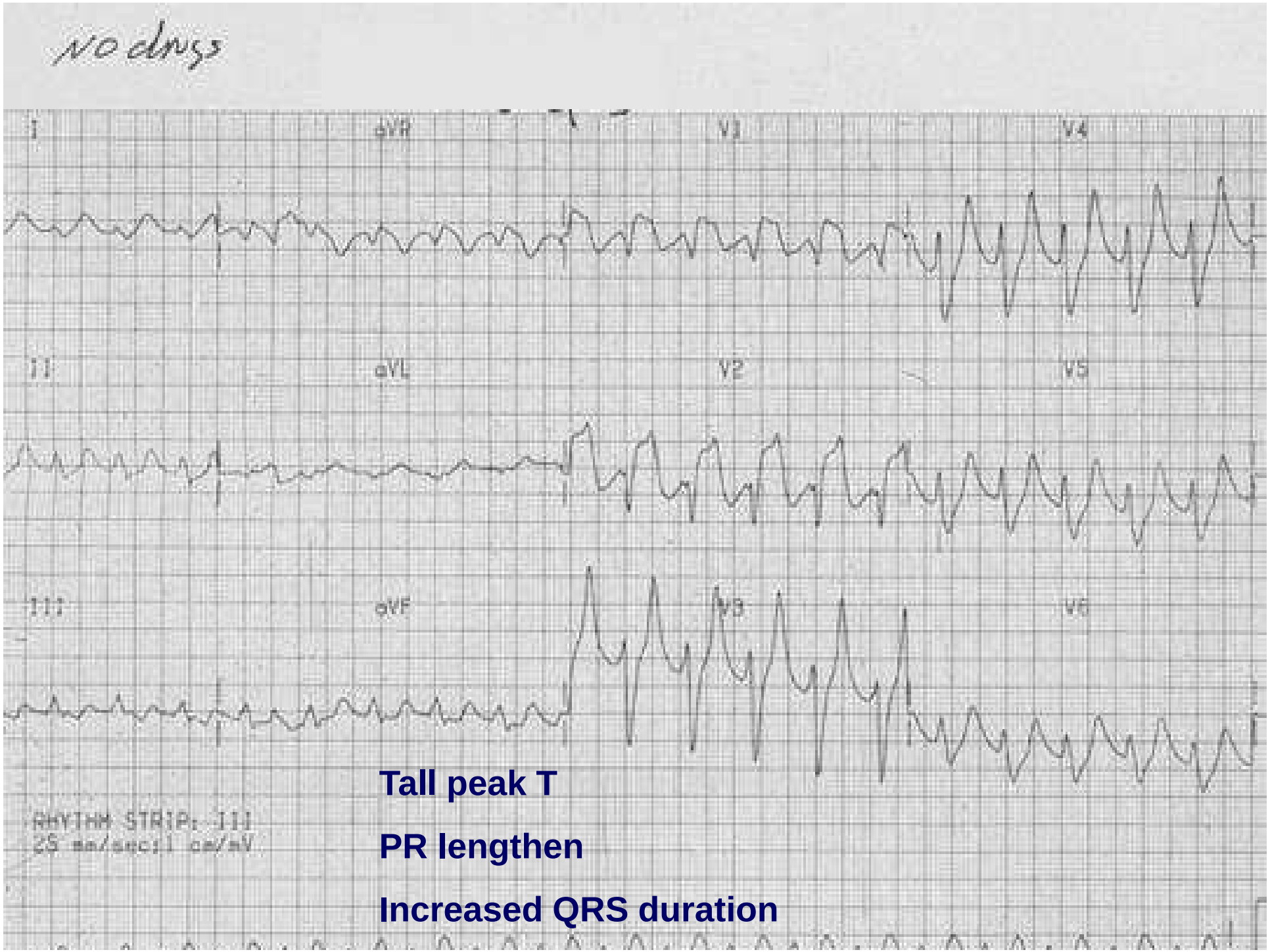
- ICU hyperkalemia
  - Cell shifts
  - Acute renal failure
- Office hyperkalemia
  - Primary decrease in mineralocorticoid activity
  - Abnormal CCD


↑ Serum potassium
Impaired renal excretion of potassium
Decreased GFR (<20 mL/min)
Exogenous Potassium
Potassium-rich foods
Salt substitutes
Drugs
Penicillin K
K+ citrate
K+ chloride
Stored blood
Riverbed clay
Endogenous Potassium
Gastrointestinal bleeding
Resolving hematoma
Tumor lysis syndrome
Rhabdomyolysis
Catabolic state
Drugs That Impair K+ Excretion
K+-sparing diuretics
Nonsteroidal anti-inflammatory drugs
Angiotensin converting enzyme inhibitors
Angiotensin receptor blockers

Clinical Features of Hypo- and Hyperkalemia

	Hypokalemia	Hyperkalemia
Neuromuscular	Weakness, +/- respiratory failure rhabdomyolysis,	Weakness
Cardiac	Arrhythmias	Cardiac standstill
Endocrine	↑ Glucose, Nephrogenic DI	

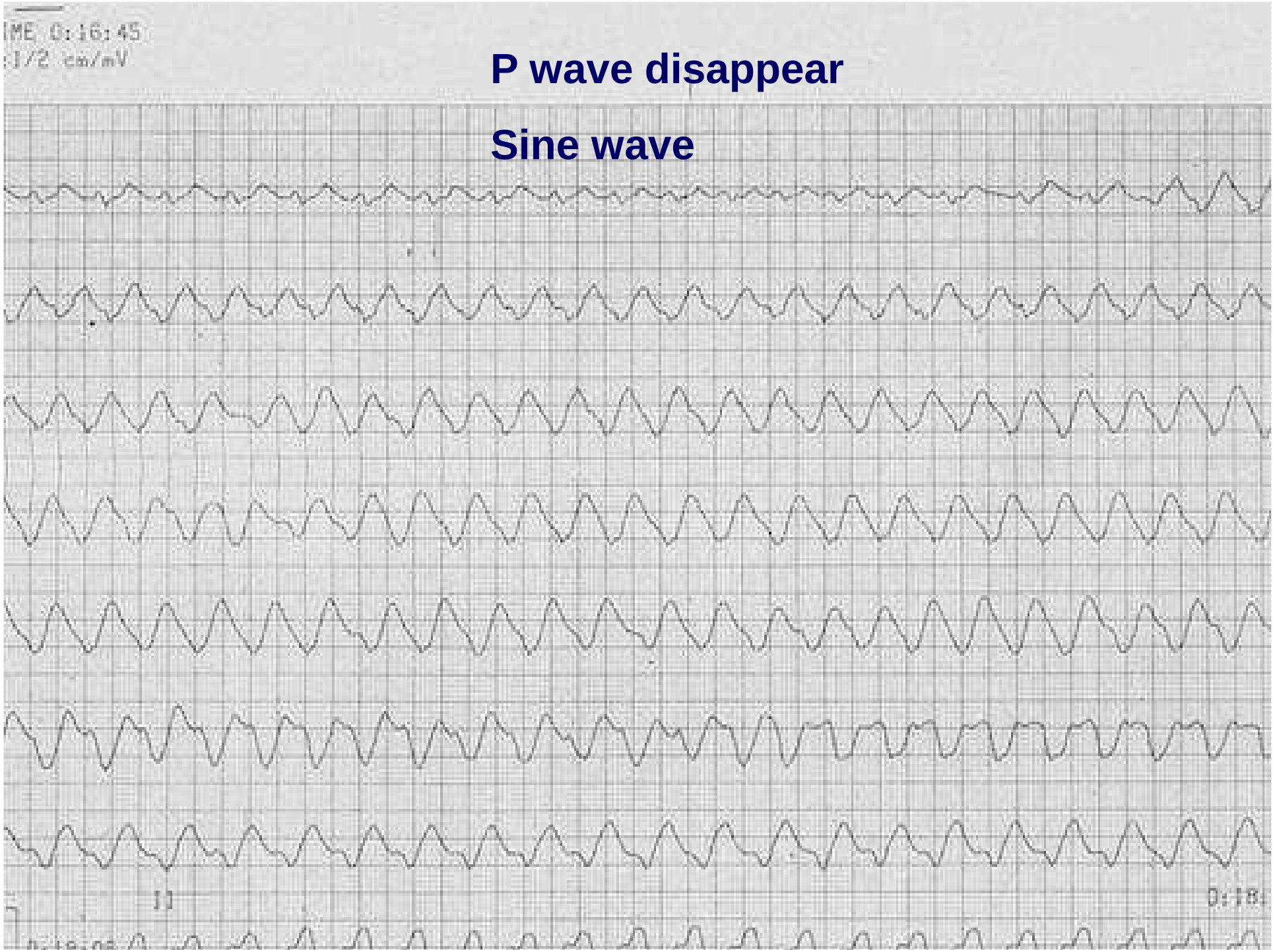

admit
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
RHYTHM STRIP: II
25 mm/sec; 1 cm/mV



Tall peak T

PR lengthen

Increased QRS duration


P wave disappear
Sine wave

Acute Treatment of Hyperkalemia

- CaCl
  - blocks effect of ↑ K^+ on heart
- $NaHCO_3$, Glucose and Insulin, β_2 Agonists
  - shifts K into cells
- Kayexalate, Dialysis
  - removes K^+ from body

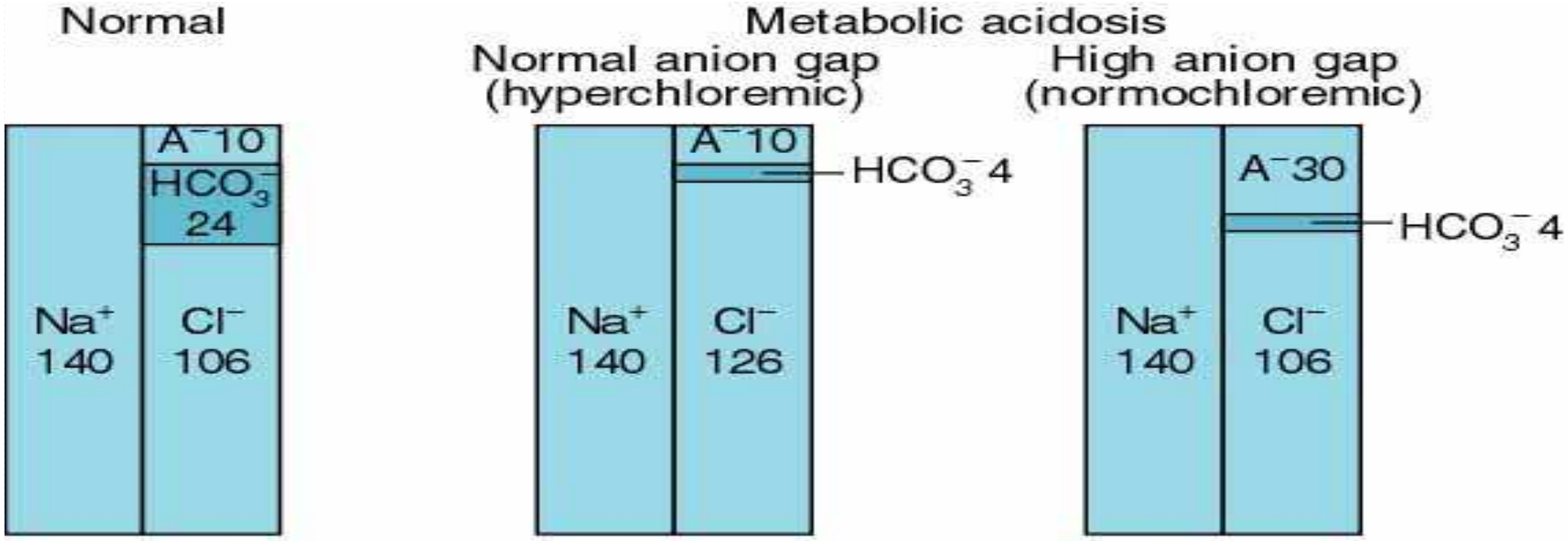
Dosage and action

Drugs	Dosage	Action
Antagonism of membrane action	10% Calcium gluconate 10 cc Infuse over 2-3 min.	Minutes Repeat after 5 min.
Drive extracellular potassium into the cell	50% glucose 50 cc + insulin 10 U	15-60 min.
	7.5% $NaHCO_3$ 50 cc (45 mEq) infuse over 5 min.	30-60 min.
	Albuterol 0.5 mg Epinephrine 0.05 microgram/kg/min	30 min.
Removal of potassium from the body	Cation exchange rasin; Kayexate 20 gm + 100 cc of 20% sorbitol oral or retention enema	4-6 hr.

Chronic Management of Hyperkalemia

- D/C other meds that interfere in K excretion
- Low K diet (70 mEq/d)
- Assess volume and blood pressure
  - ↓ volume, Nl BP: consider fluorinef
  - ↑ volume, ↑ BP
    - Loop diuretics (use furosemide bid)
    - $NaHCO_3$ (650 mg tablet, 8 mEq)
- +/- Kayexalate

Metabolic acidosis



Causes

- Renal acidification defects
  - Proximal renal tubular acidosis
  - Classic distal tubular acidosis
  - Hyperkalemic distal tubular acidosis
  - Early renal failure
- Gastrointestinal loss of bicarbonate
  - Diarrhea
  - Small bowel losses
  - Ureteral diversions
  - Anion exchange resins
  - Ingestion of $CaCl_2$
- Acid infusion
  - HCl
  - Arginine HCl
  - Lysine HCl

Causes

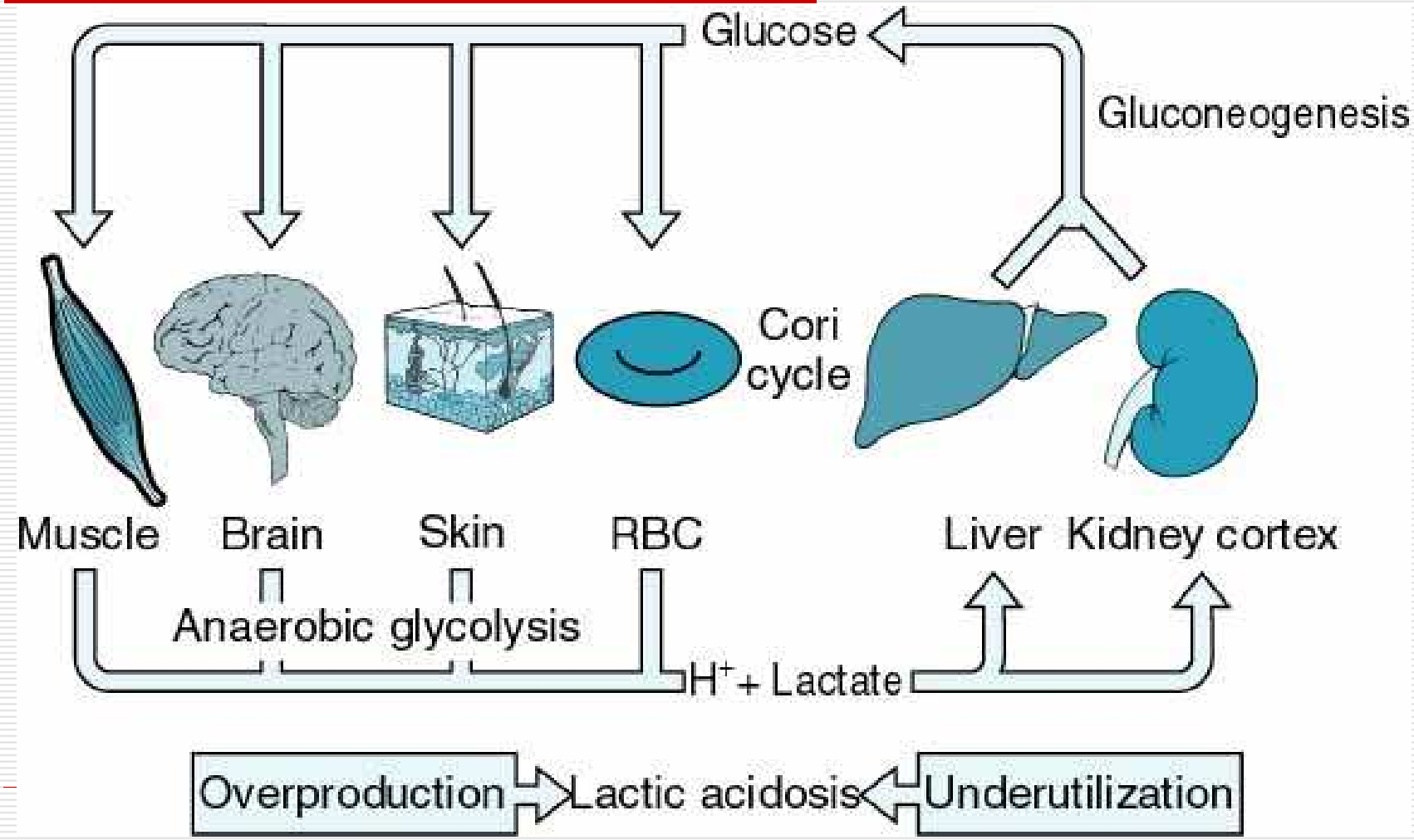
- Endogenous acid load
  - Ketoacidosis
    - Diabetes mellitus
    - Alcoholism
    - Starvation
  - Uremia
  - Lactic acidosis
- Exogenous toxins
  - Osmolar gap present
    - Methanol
    - Ethylene glycol
  - Osmolar gap absent
    - Salicylates
    - Paraldehyde

Critically ill patients

- Acute renal failure

  renal acidification defect
- Lactic acidosis

Lactic acidosis



Lactic acidosis

- Type A : poor tissue perfusion
  - **Shock**
  - **Hypoxia**
  - **Severe anemia**
  - **CO poisoning**
  - **Severe asthma**
- Type B : no evidence of poor tissue perfusion

Associated with common disorder

- **Liver failure**
- **Leukemia**
- **Thaiamine def.**

Drug

- **metformin, phenformin, buformin, NRTI (Zidovudine, stavudine)**

Enzyme defect

- **Fructose1,6-diphosphatase def.**
- **Glucose6phosphatase def.**

- D-lactic acidosis

Is acidosis a problem?

- Relationship of extra cellular and intracellular pH
- Cardiovascular effects
  - -Decreased contractility
  - -Decrease response to CA
- Respiratory
  - -Increased minute ventilation

Management

- Goal: raised ECF pH with parallel raising ICF pH

- Removing the stimulus to acid production
- Increasing ventilation
- Bicarbonate therapy

Bicarbonate therapy

- pH <7.1

  decreased cardiac contractility

  continued tissue hypoperfusion

Bicarbonate therapy

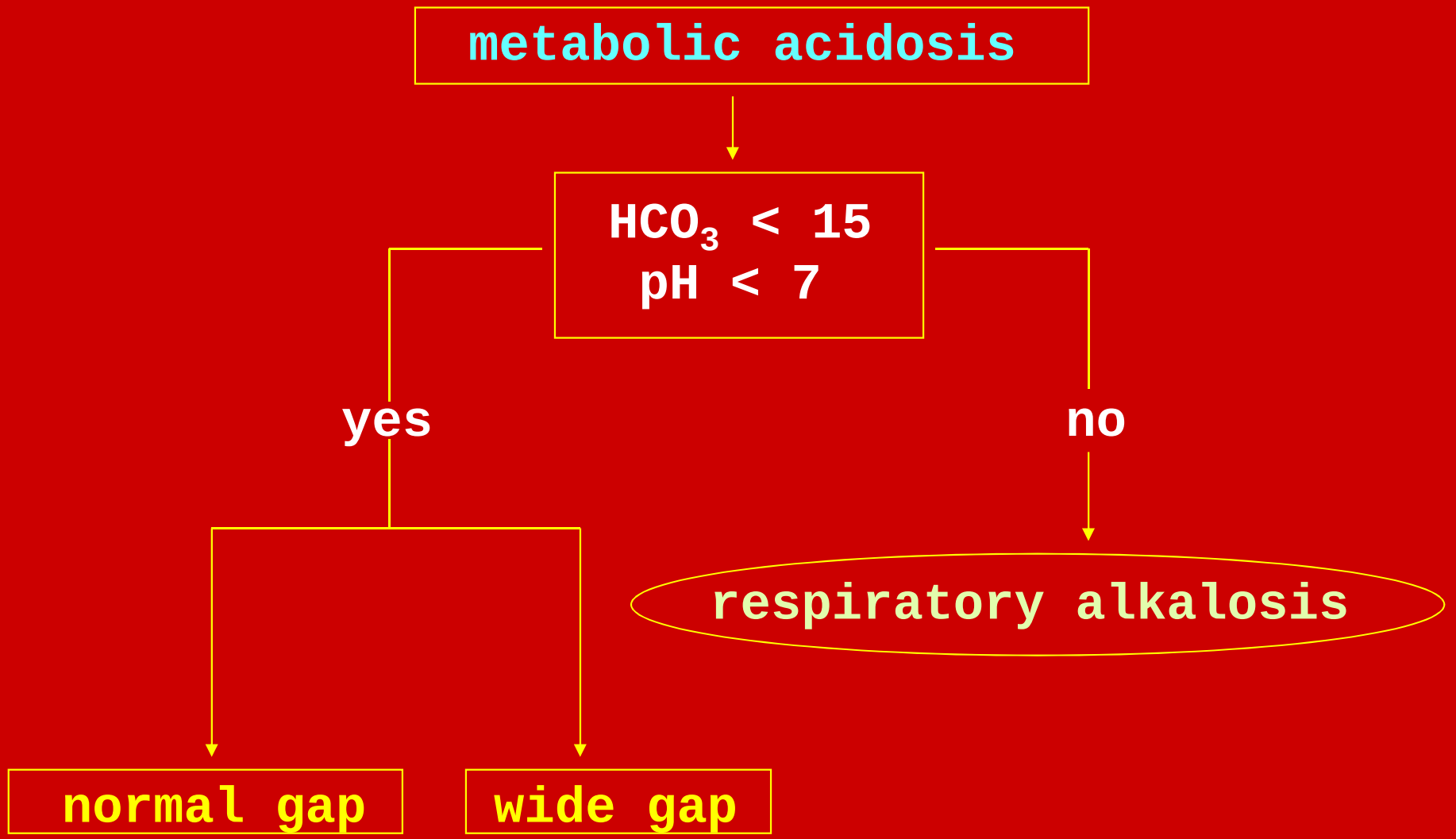
- Problem
- Fluid overload
- Postrecovery metabolic alkalosis
- Hypernatremia
- Raise CO2 generation in venous blood may exacerbate ICF acidosis
- Impaired hepatic lactate utilization and cardiac contractility

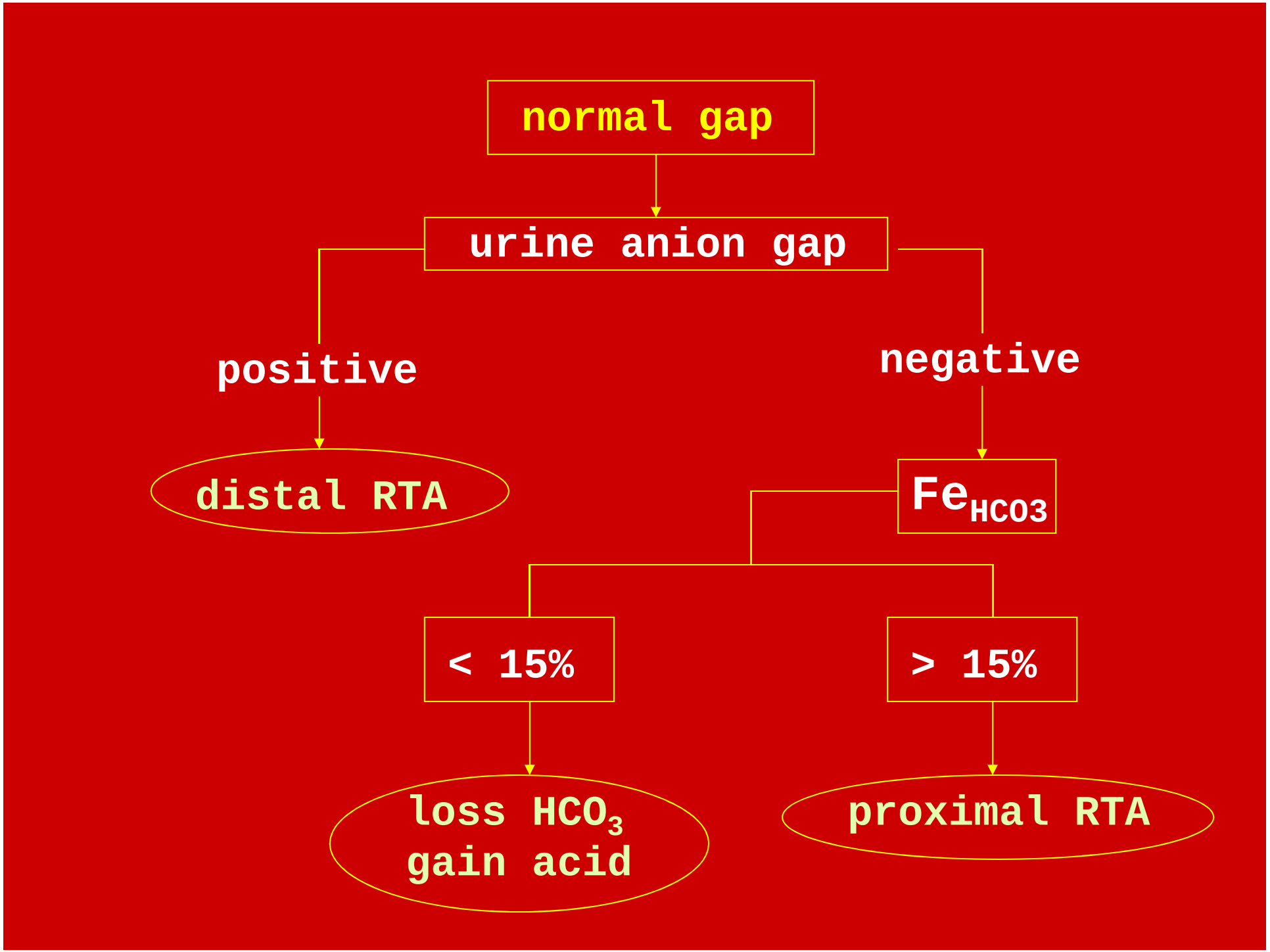
Bicarbonate therapy

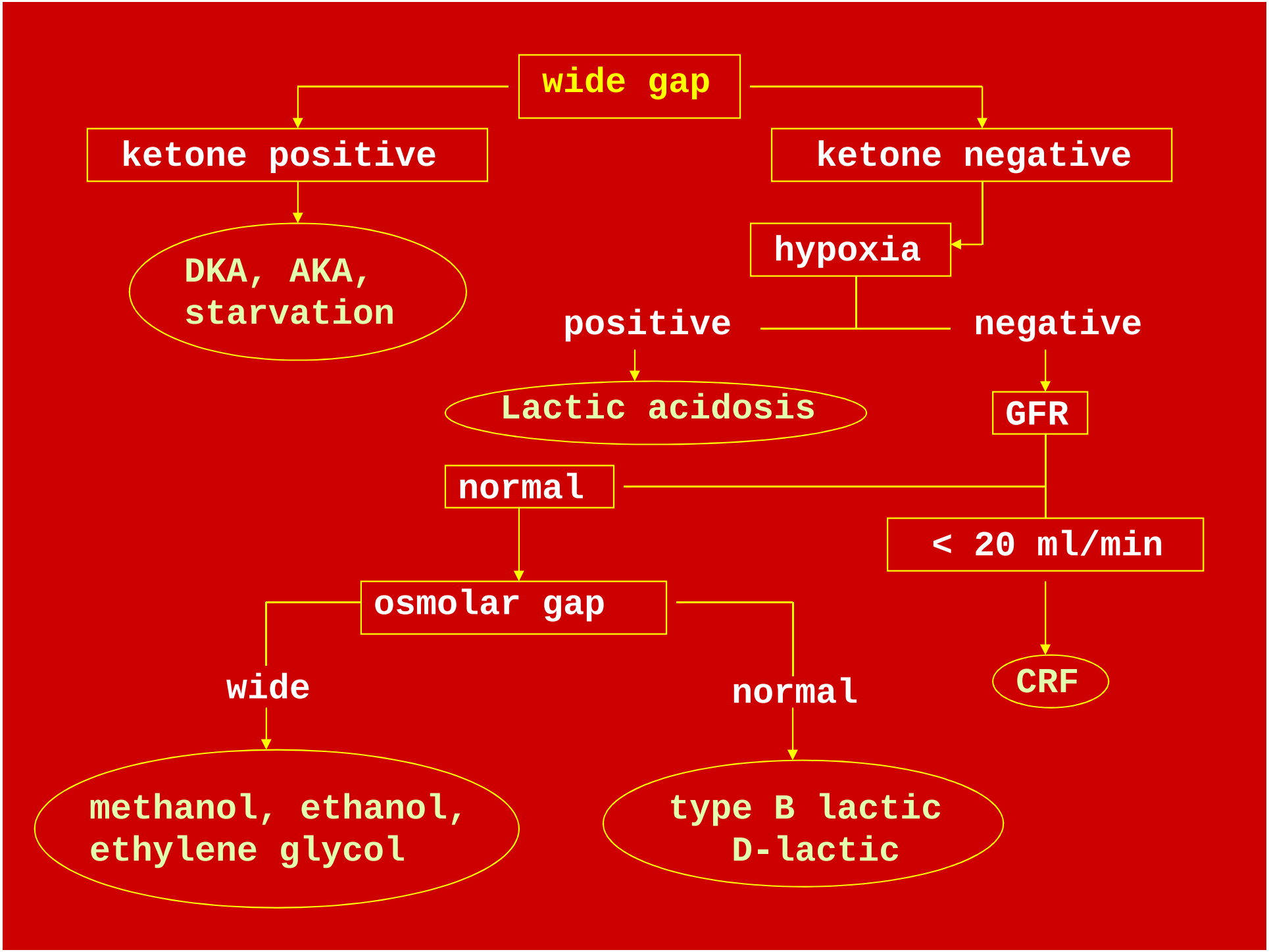
- Study in patients with shock-induced lactic acidosis have not demonstrated any improvement in CO or SBP

Cooper et al. Ann Intern Med 1990;112:492

Approach to Metabolic Acidosis




normal gap
urine anion gap
positive
negative
distal RTA
Fe_{HCO3}
< 15%
> 15%
loss HCO_3
gain acid
proximal RTA


wide gap
ketone positive
ketone negative
DKA, AKA, starvation
hypoxia
positive
negative
Lactic acidosis
GFR
normal
< 20 ml/min
osmolar gap
wide
normal
CRF
methanol, ethanol, ethylene glycol
type B lactic D-lactic

Thank you