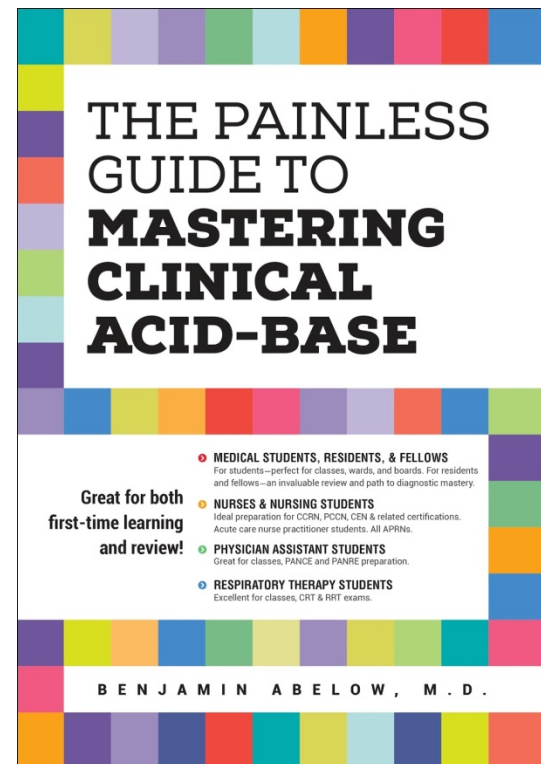
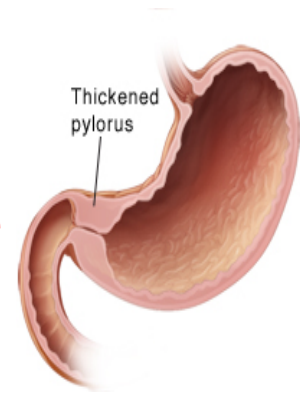


Fluid, Electrolytes, Acid Base Balance



45 yrs old adult male with severe vomiting due to pyloric obstruction

- ER visit
- Clinical finding
 - : physical examination
 - **BP 80 / 50 mmHg, PR 90 / min, dehydrated skin/tongue**
 - : lab check (serum Na/Cl/K/ABGA)
 - **Na 129 mEq/L**
 - Cl 115 mEq/L**
 - K 3.1 mEq/L**
 - ABGA pH 7.5 / HCO₃ 29 mEq/L / PaCO₂ 44mEq/L**



Normal value →

BP	120 / 80 mmHg
PR	70 /min
S.Na	135 – 145 mEq/L(140)
S.K	3.5 – 5 mEq/L(4.5)
S.Cl	95 – 105 mEq/L(102)
ABGA :	
pH	7.35 – 7.45(7.4)
PaCO ₂	35 – 45 mmHg(40)
HCO ₃	22 – 26 mEq/L(24)

45 yrs old adult male with severe vomiting due to pyloric obstruction

BP 80 / 50 mmHg
PR 90 / min
Dehydrated skin,tongue



Volume Depletion

- fluid disturbance
- **Na content** disturbance

K 3.1 mEq/L



Hypokalemia

- electrolyte disturbance
- **K** concentration disturbance

Na 129 mEq/L



Hyponatremia

- osmolality disturbance
- **Na concentration** disturbance
(→ **water** control disturbance)

ABGA pH 7.5
HCO₃ 29 mEq/L
PaCO₂ 44 mEq/L



Metabolic Alkalosis

- acid-base disturbance
- **H⁺** concentration disturbance

INTRODUCTION

Role of kidney

Body fluid : compartment and composition

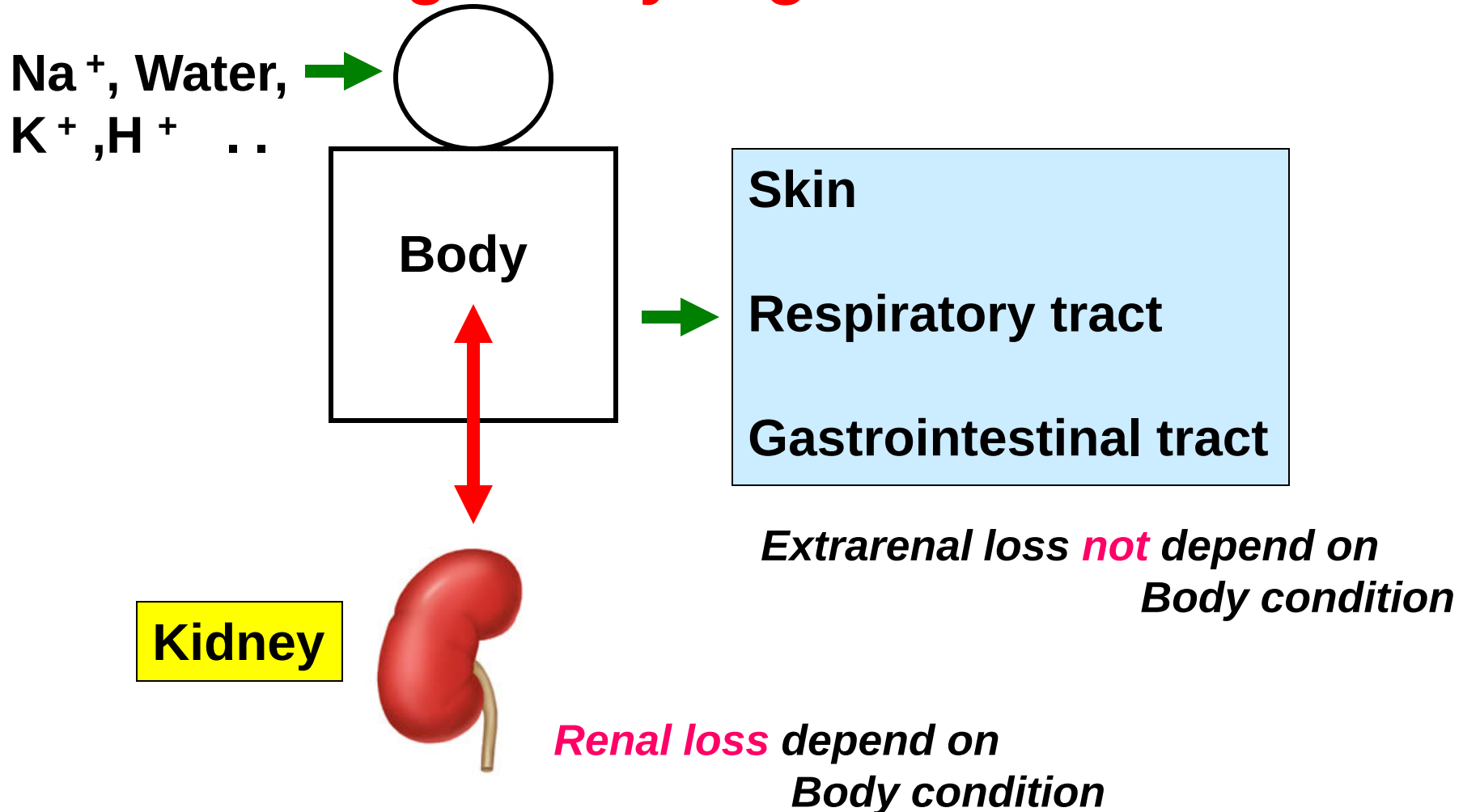
**Regulation of fluid transfer among compartments
(ICF, ECF, IVS)**

Major types of imbalance

Role of kidney

KIDNEY in fluid, electrolyte, acid-base balance ?

→ **Regulatory organ**



BODY FLUID

: Compartment and Composition

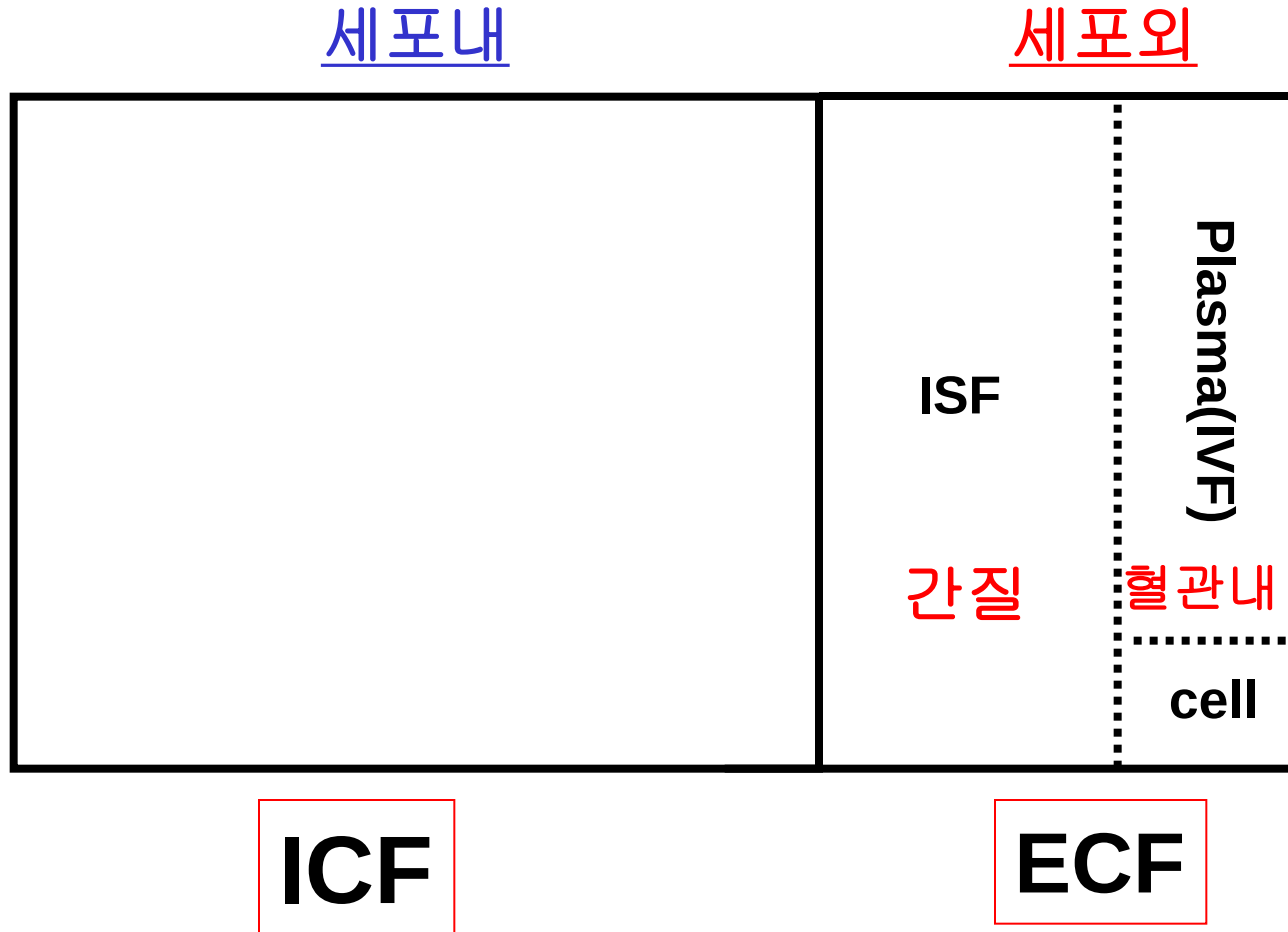
Two major compartment (ICF and ECF)

Body water distribution

Electrolyte distribution

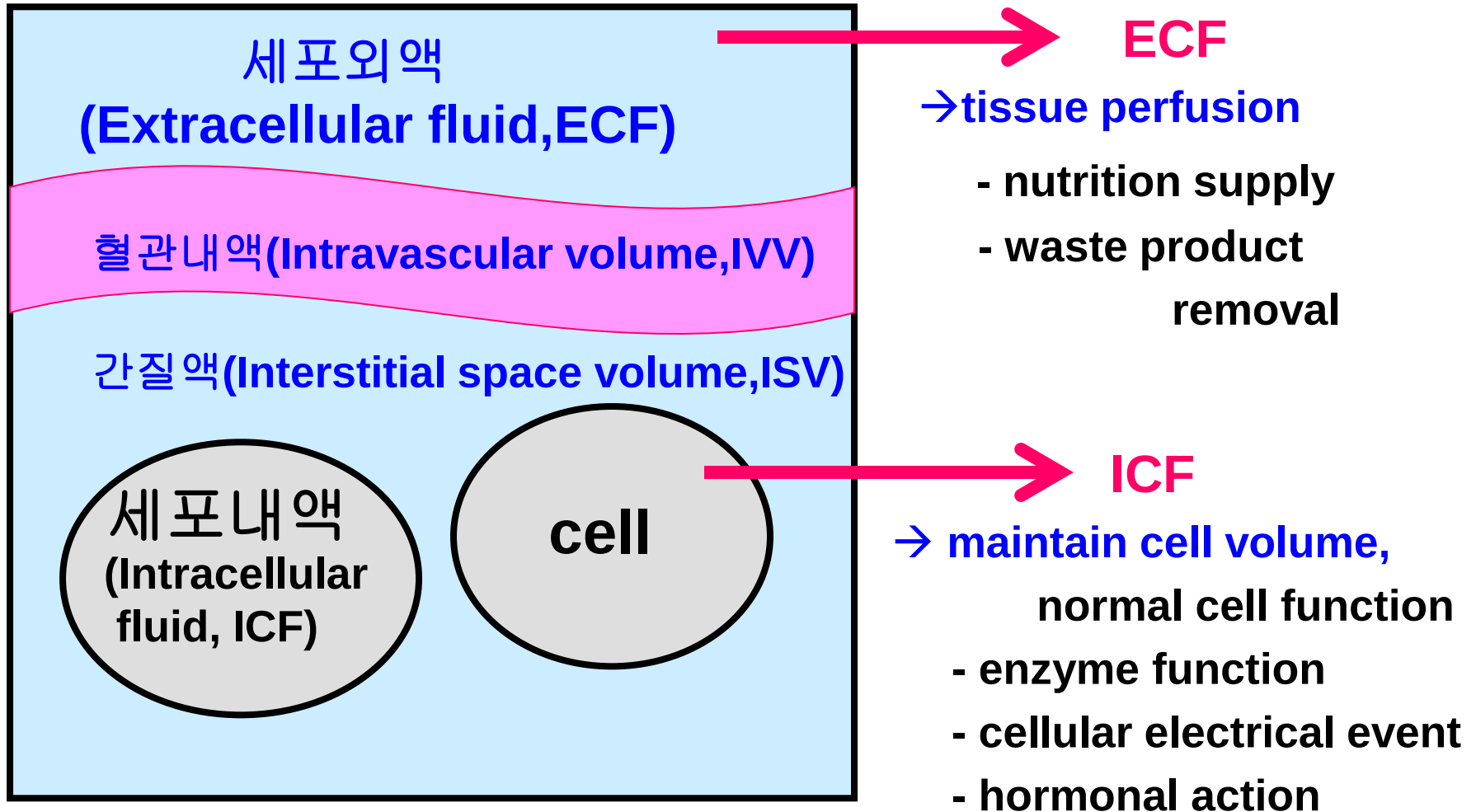
Two major compartment

2 compartments : ICF and ECF (ISF and IVF)



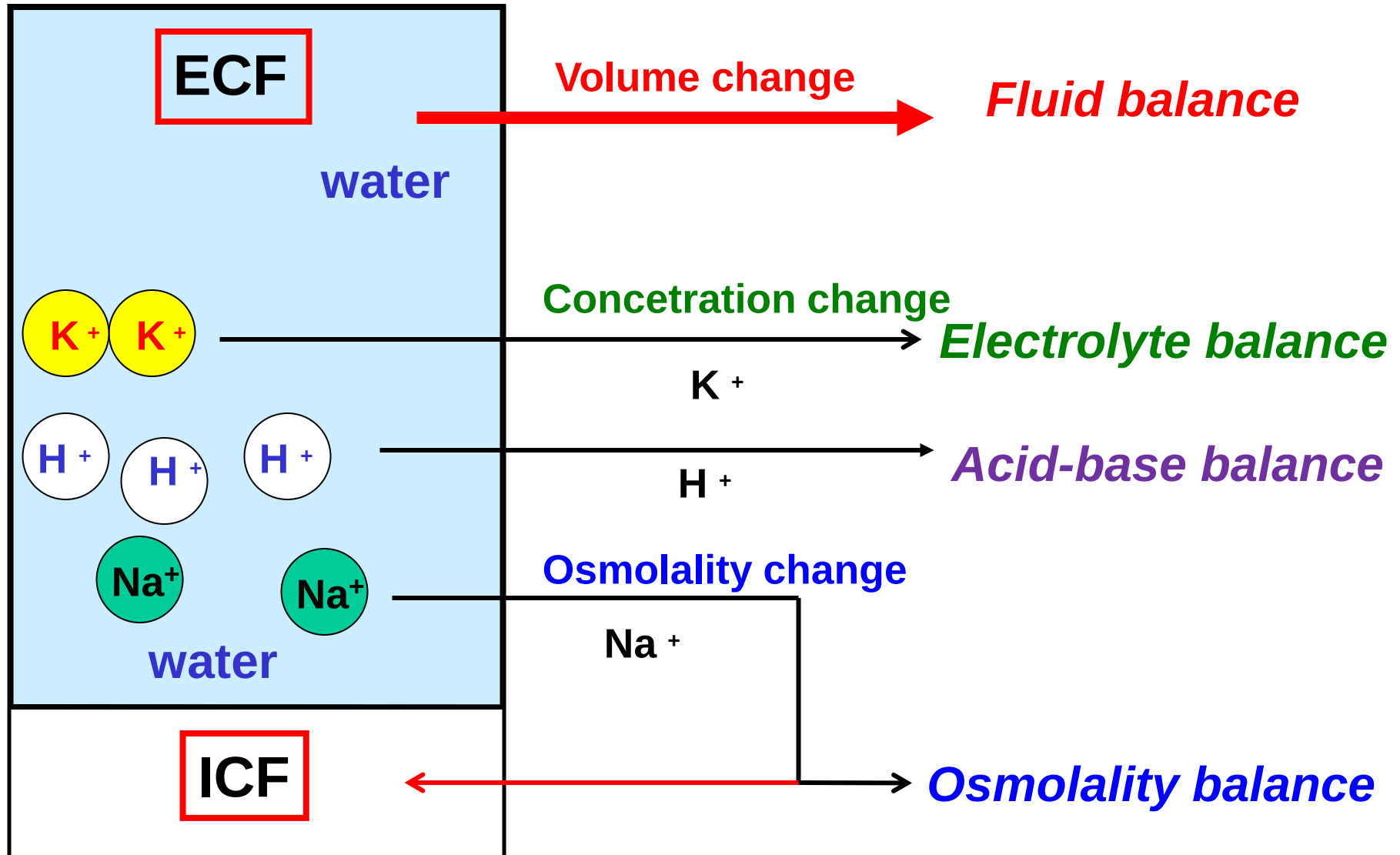
Two major compartment

Function of ICF and ECF



Two major compartment

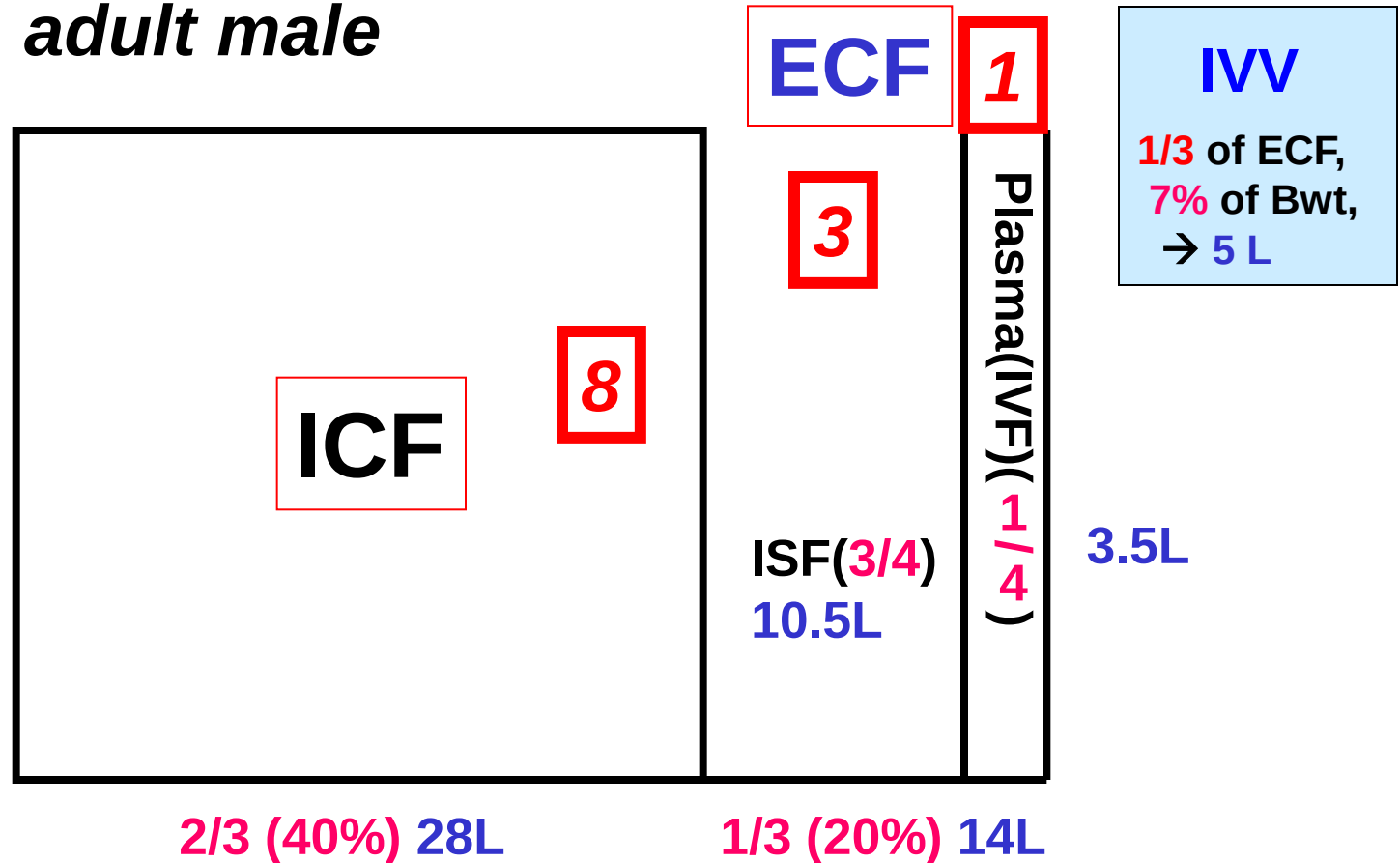
Alteration in **ECF** is important for normal balance



Body Water Distribution

Distribution of water between ECF and ICF

In 70 kg adult male



Total Body Water(60%) 42L

Electrolytes Distribution

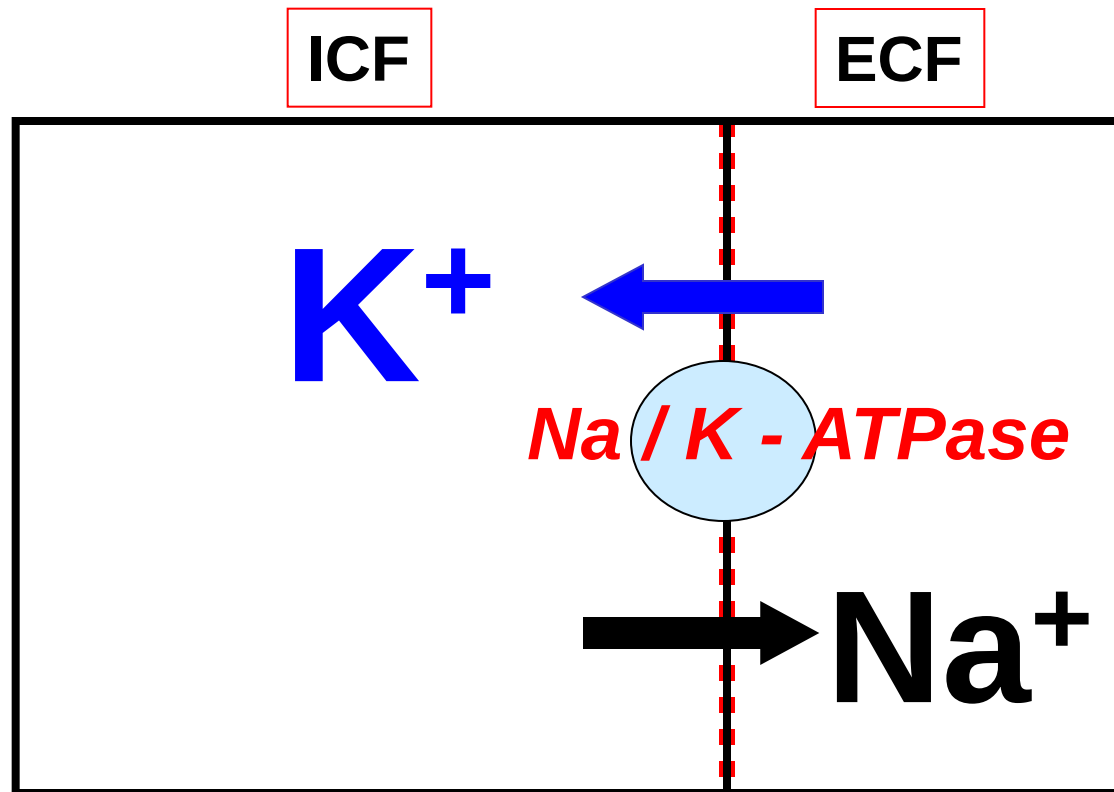
	ICF	ECF	
Cation	K^{+}	Na^{+}	Normal value in ECF
Anion	Organic Phosphate ester (ATP, CrP, Phospholipid)	Cl^{-} HCO_3^{-}	Na : 135 - 145 K : 3.5 - 5.0 Cl : 95 - 105 HCO_3 : 22 - 26 → mEq/L or mmol/L

Sum of total cation = sum of total anion

Electrolytes Distribution

Na / K between ICF and ECF

Na / K - ATPase



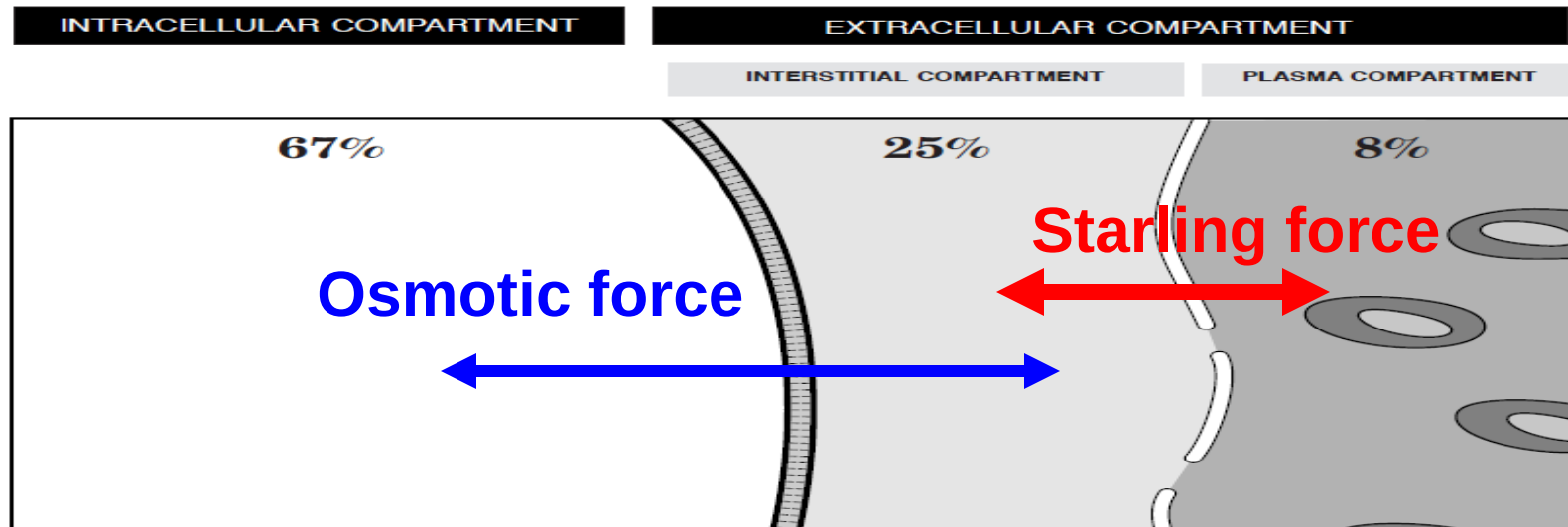
REGULATION OF FLUID TRANSFER AMONG COMPARTMENTS (ICF, ECF, IVS)

1. Water movement between

ISS and IVS compartment

2. Water movement between

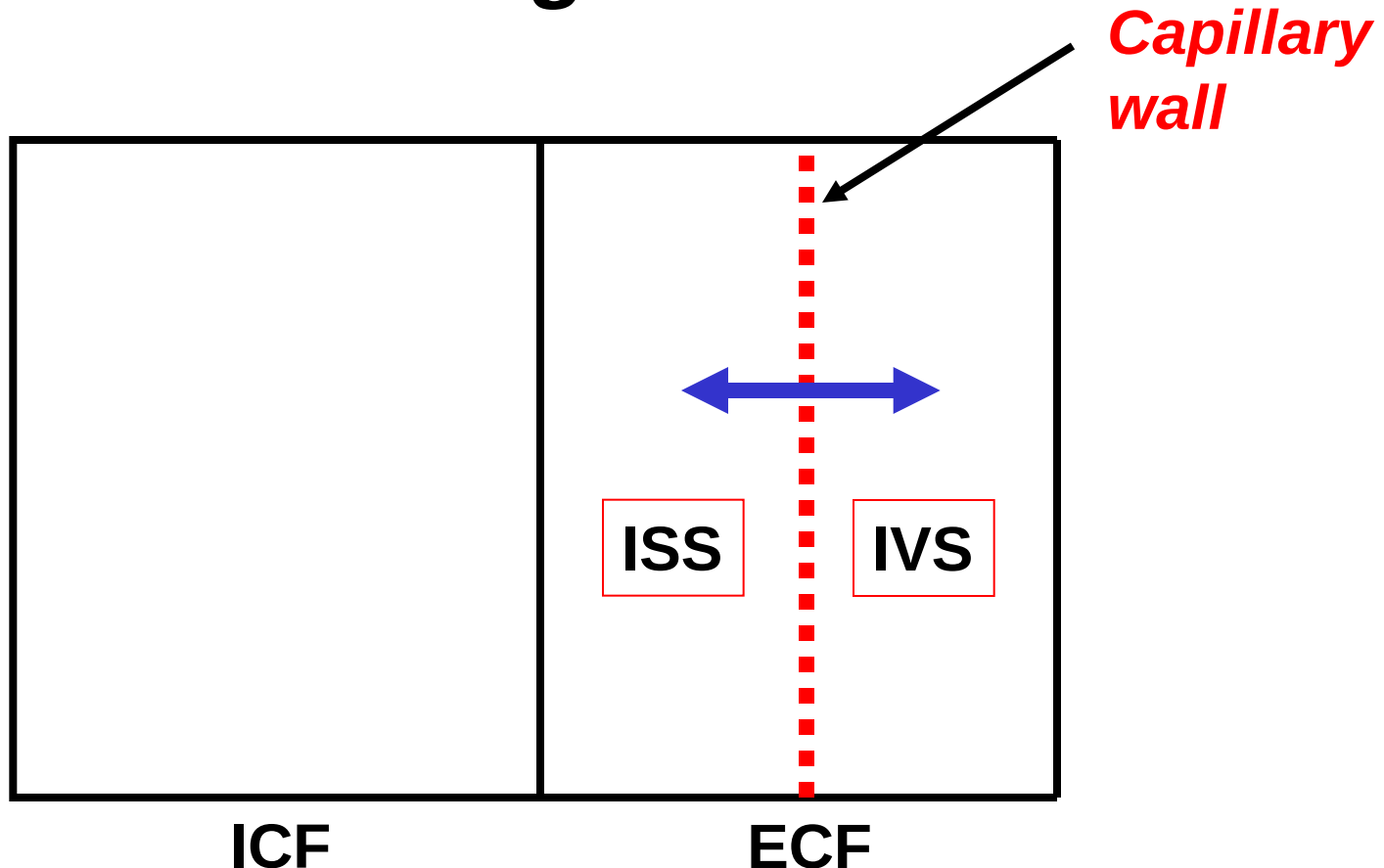
ICF and ECF compartment



Water movement between ISS and IVV

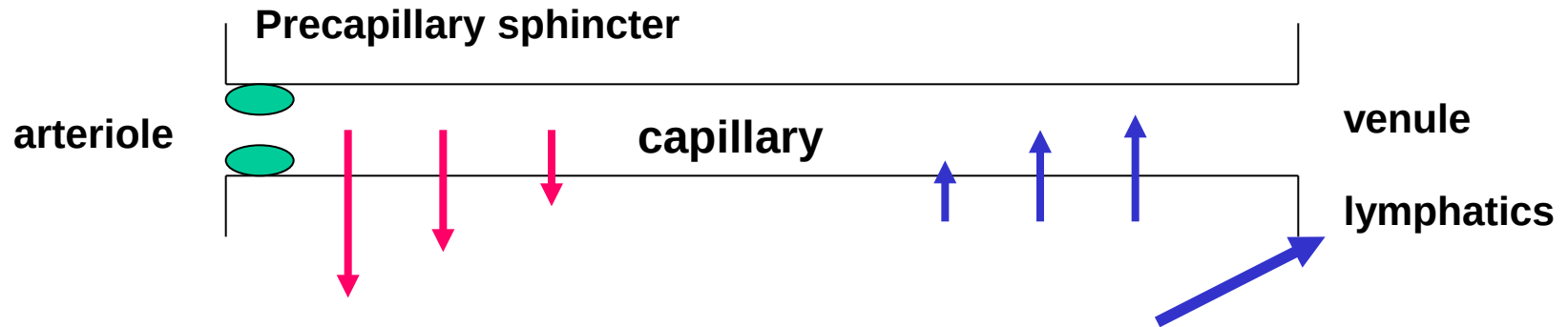
Main force for water movement (ISS/IVV)

Starling forces



Water movement between ISS and IVV

Starling forces



$$J_v = K_f (\Delta P - \Delta \pi)$$

J_v : rate of fluid transfer

K_f : water transfer permeability

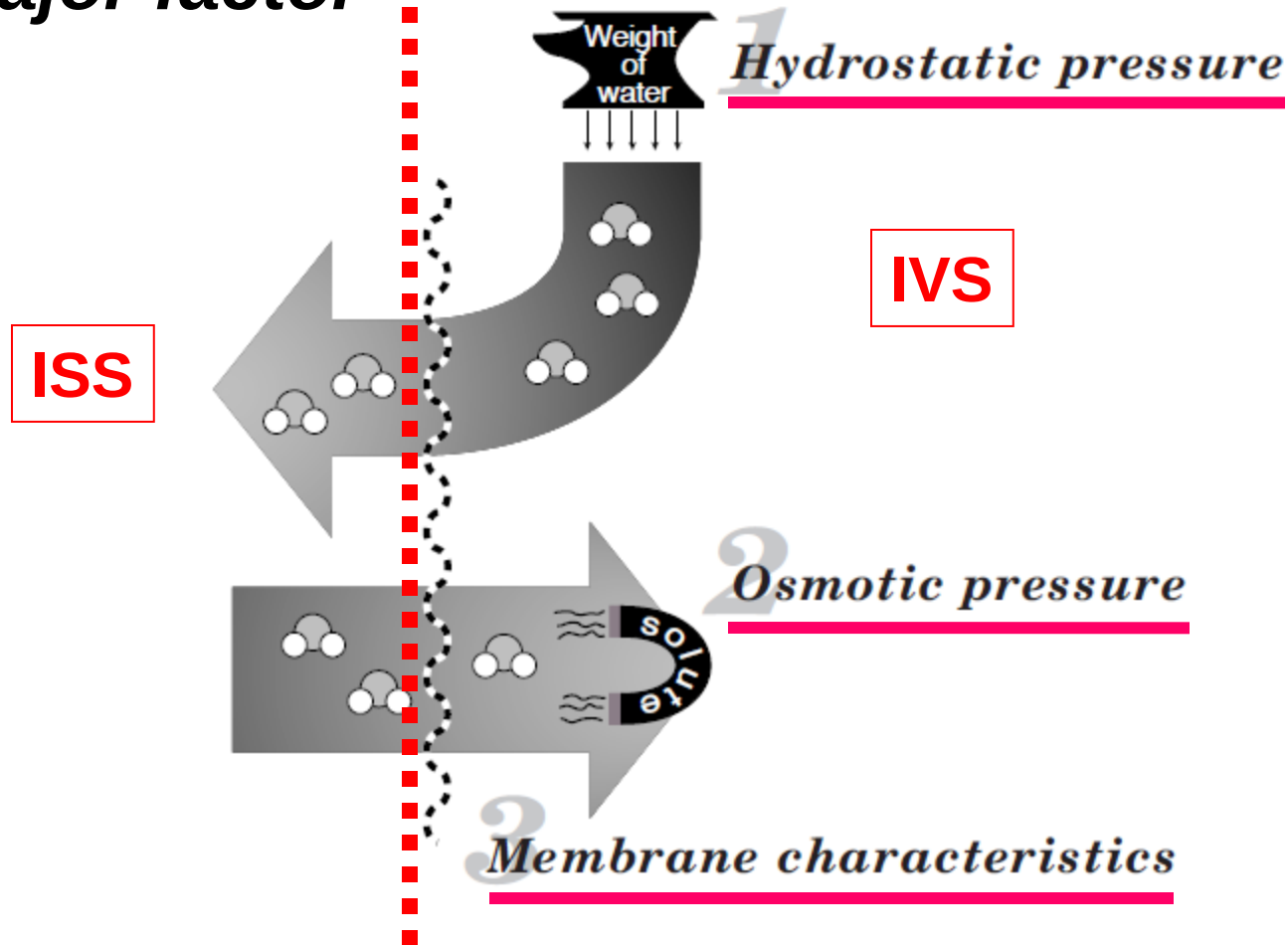
ΔP : hydrostatic Pr difference

$\Delta \pi$: oncotic Pr difference

Water movement between ISS and IVV

Starling forces

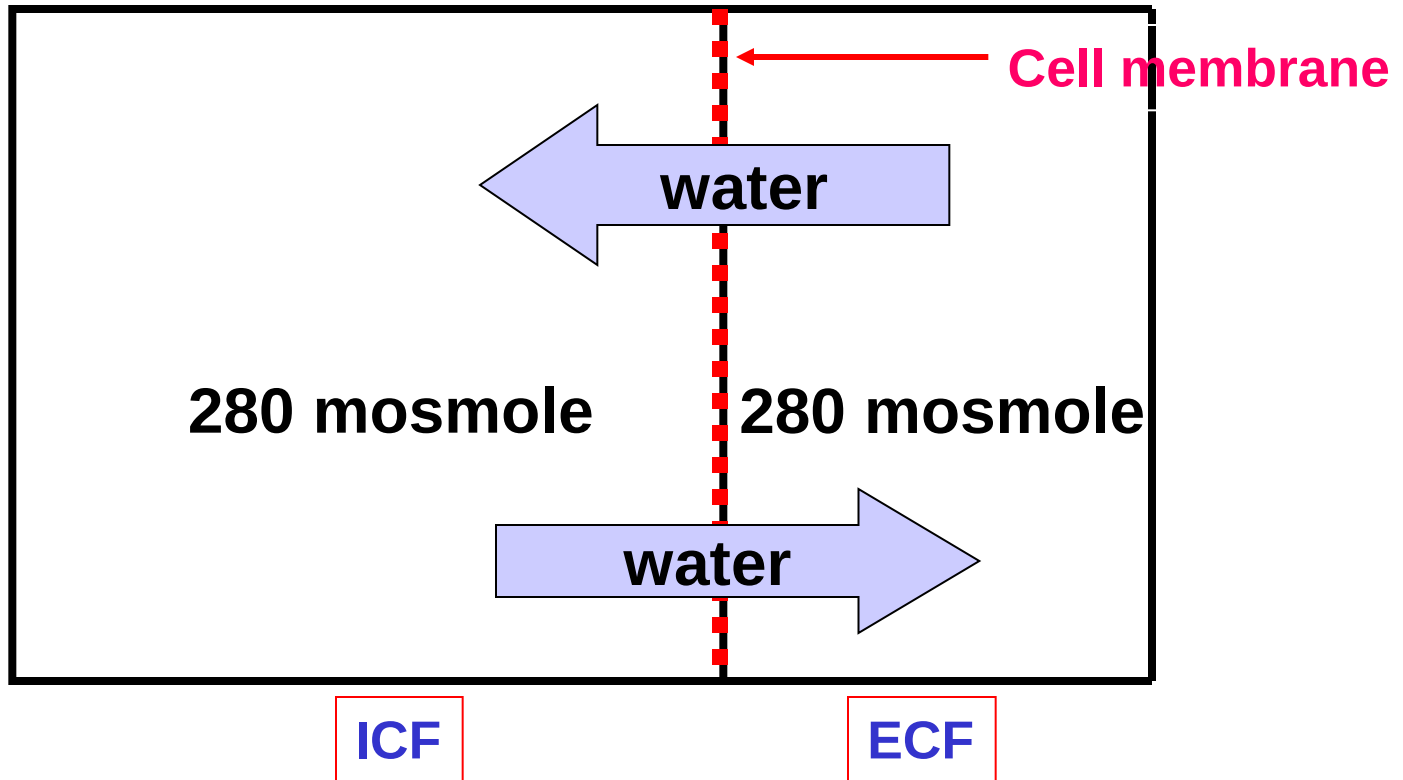
Major factor



Water movement between ICF and ECF

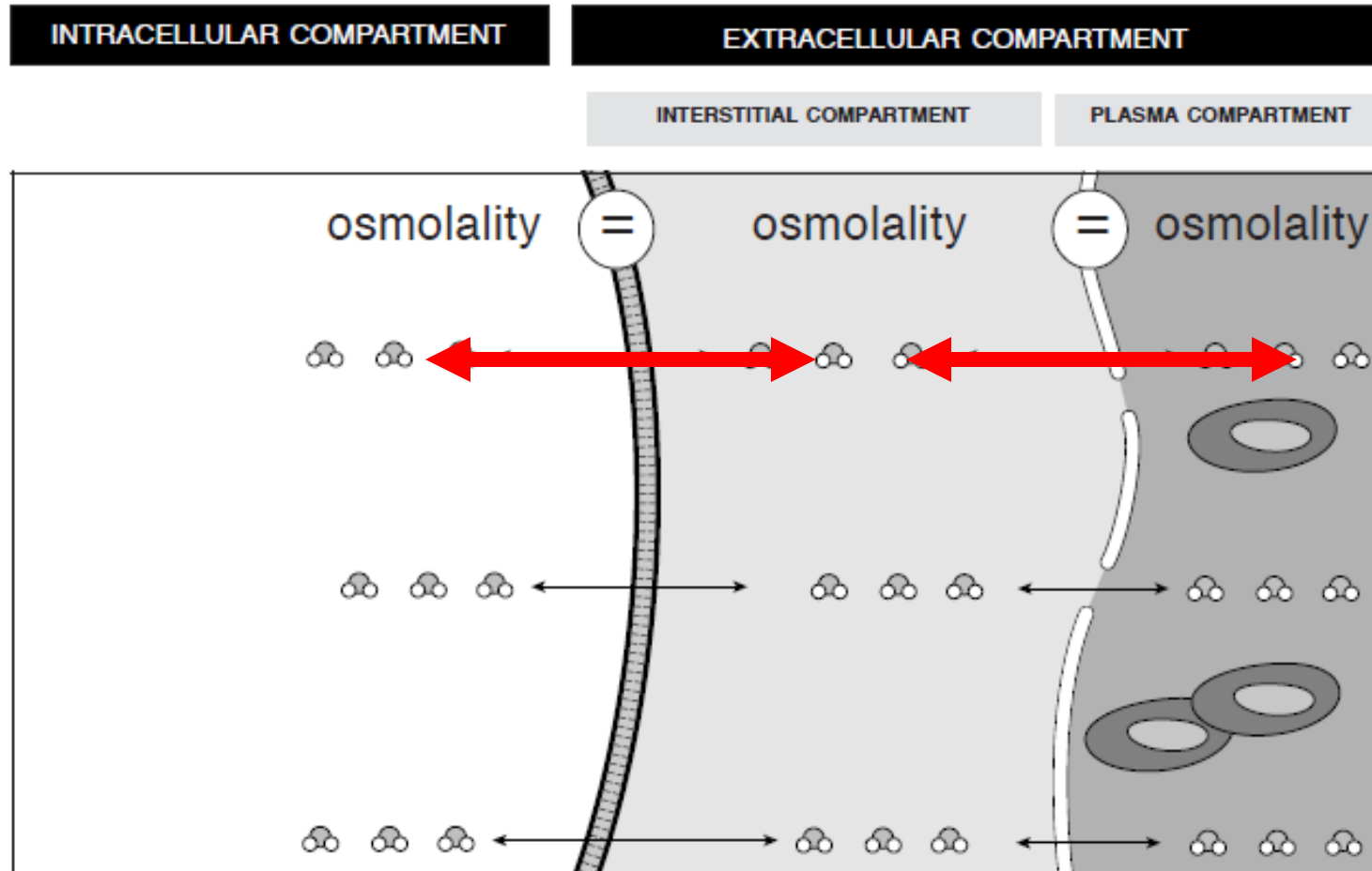
Main force for water movement (ICF/ECF)

Osmotic forces



Water movement between ICF and ECF

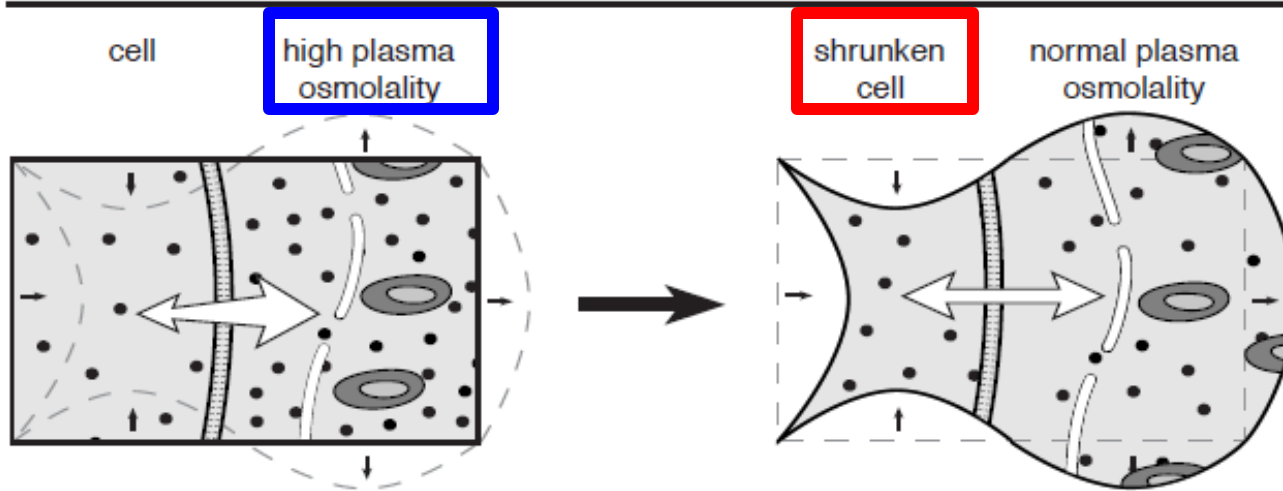
Osmolality of all three compartment is same



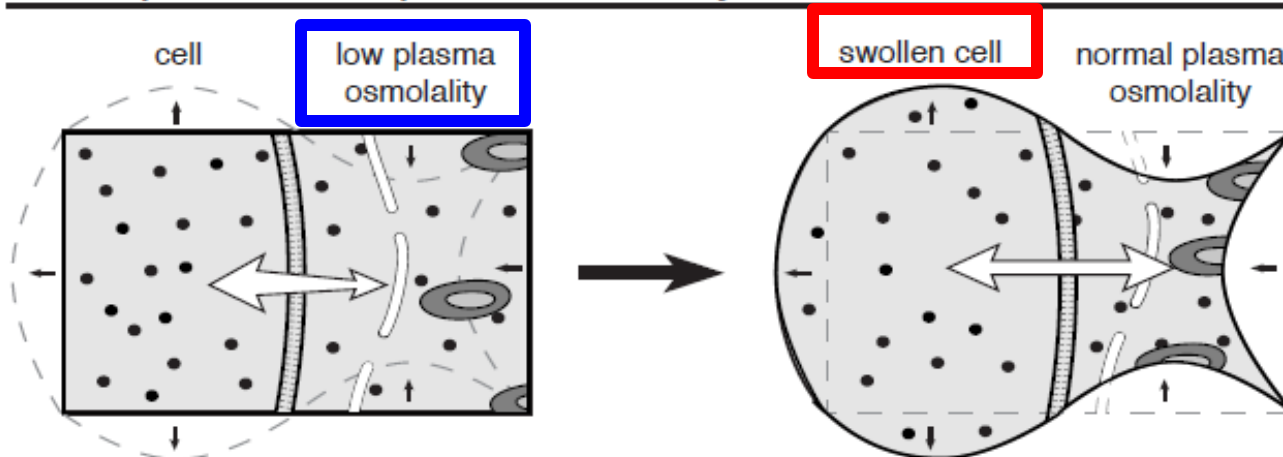
Water movement between ICF and ECF

ECF osmolality change → ICF volume change

Consequence of high plasma osmolality

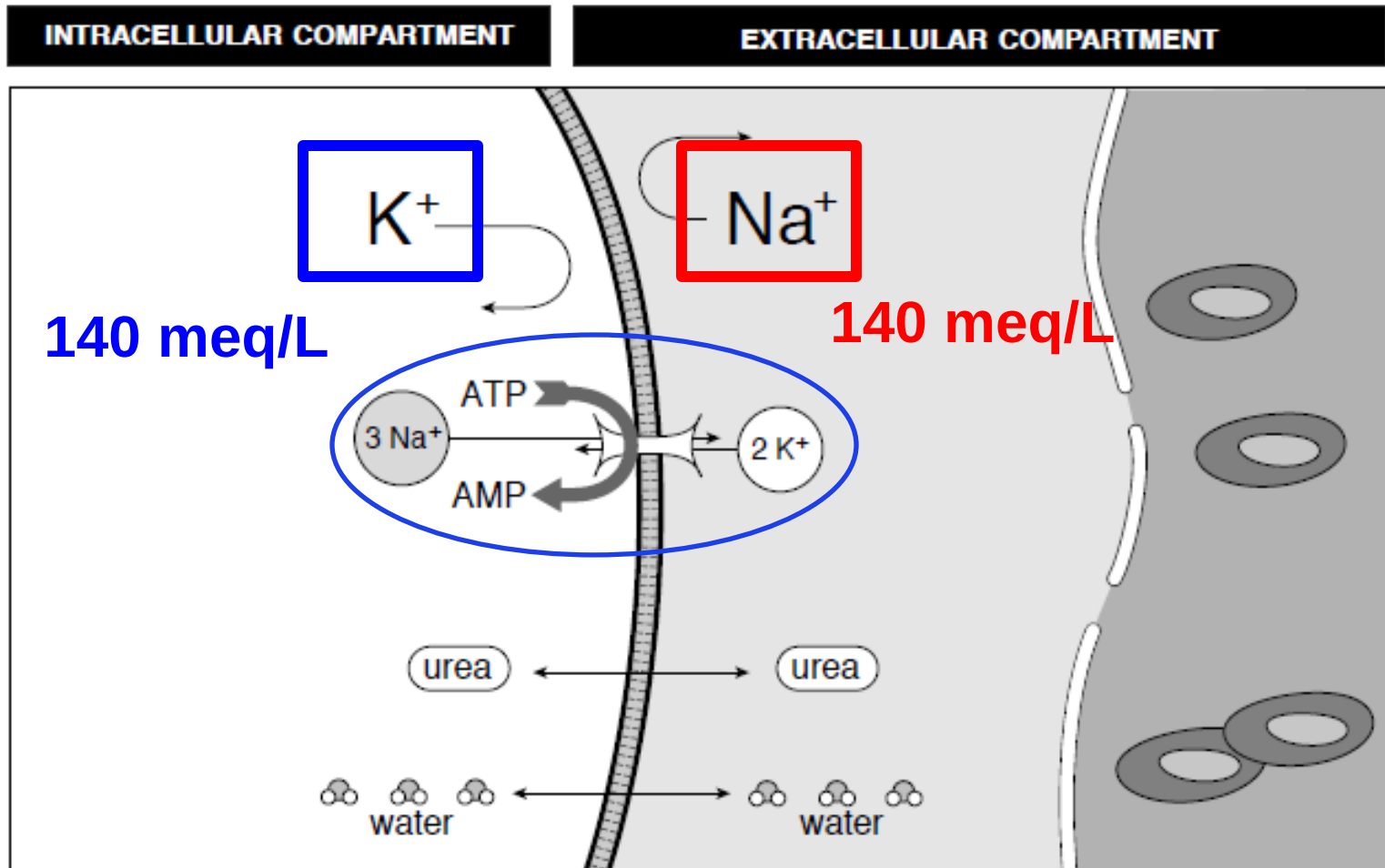


Consequence of low plasma osmolality



Water movement between ICF and ECF

Principal osmoles in ECF and ICF for osmotic pr



MAJOR TYPE OF IMBALANCE

Fluid(volume) imbalance

: Na^+ content change

Electrolyte imbalance

: K^+ concentration change

Osmolality imbalance

: Na^+ concentration change

Acid base imbalance

: H^+ concentration change

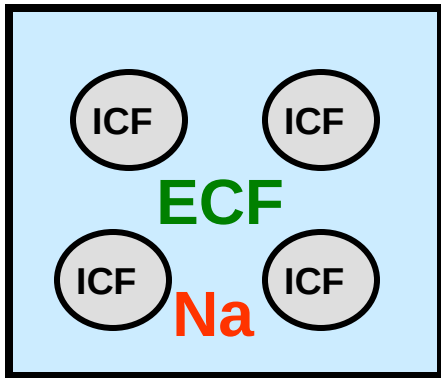
* If multiple disorder were existed,

*The most important disorder is volume disorder
especially volume depletion*

Fluid Imbalance

Volume(Na content) change in **ECF**, not in ICF

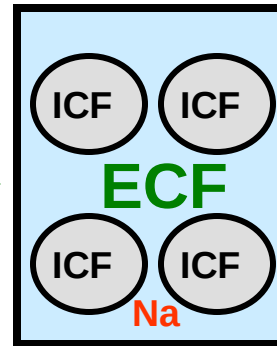
Normal



Diarrhea, vomiting,
hemorrhage

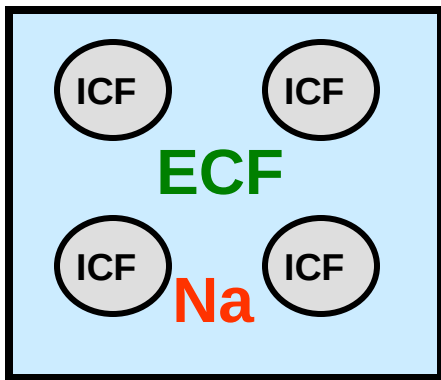


ECF volume loss



**Volume
depletion**

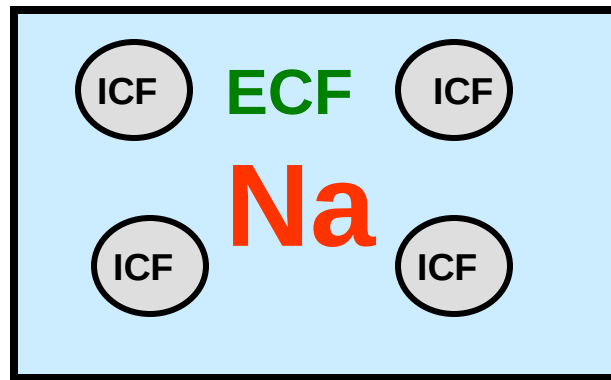
- Hypotension
- Decreased tissue perfusion



CHF, LC, NS



ECF volume
expansion

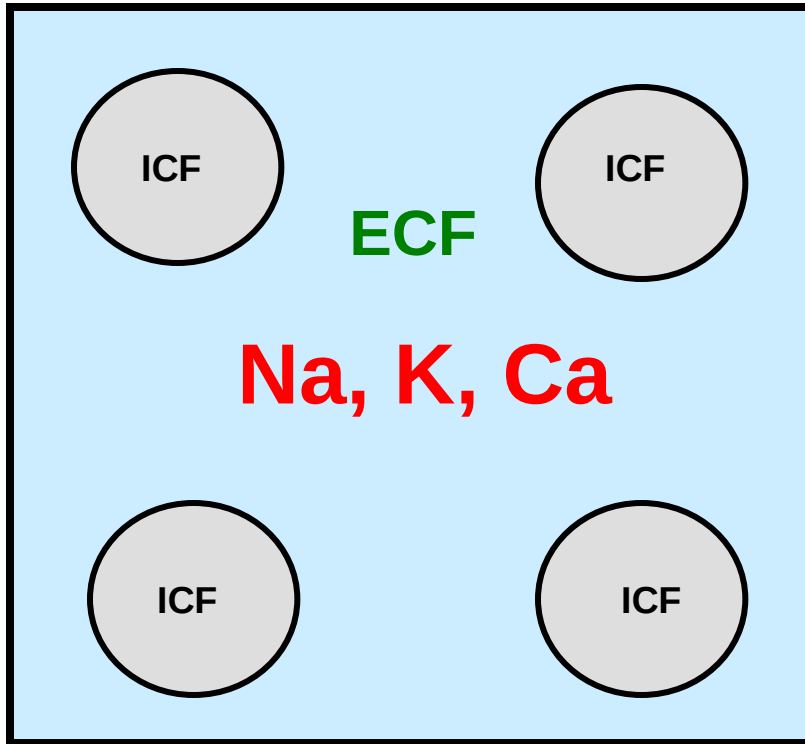


**Volume
expansion**

- Edema
- Hypertension

Electrolytes Imbalance

Change in electrolyte concentration in **ECF**



Change in **Na, K, Ca** ..
Concentration in ECF



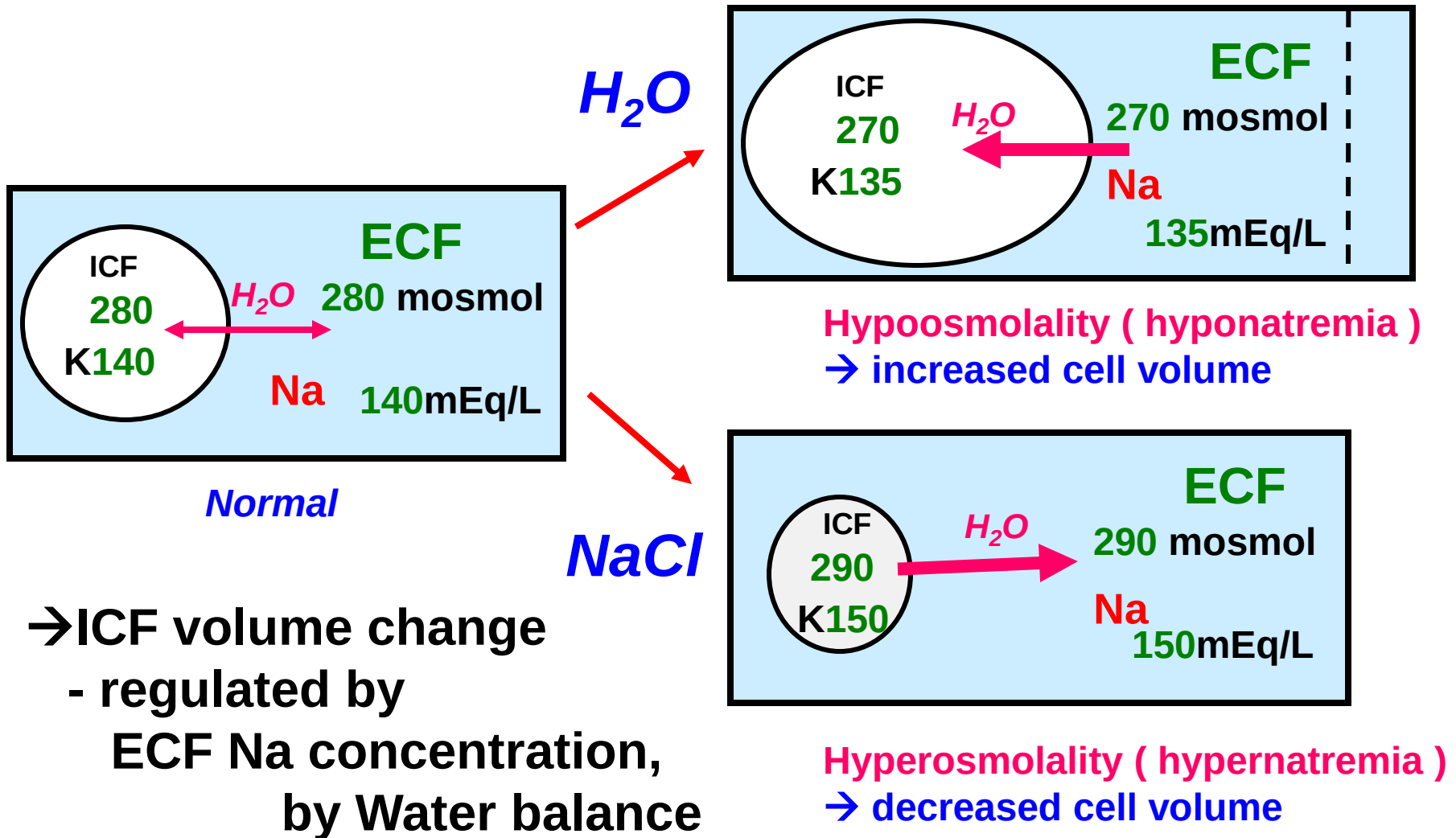
Hypo, perkalemia
Hypo, percalcemia
Hypo, pernatremia



change in cell volume,
disturbance in
neuromuscular system..

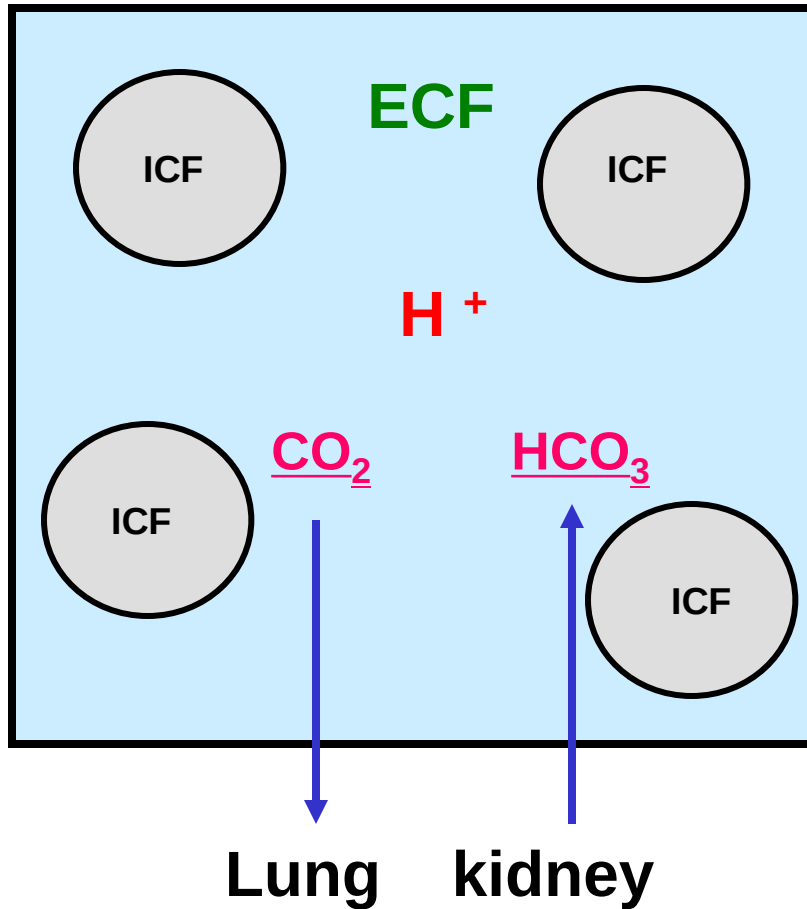
Osmolality Imbalance

Hypo,pernatremia → Osmolality imbalance



Acid-base Imbalance

Change in Hydrogen ion (H^+) in ECF



H^+ concentration change
→ by CO_2 , HCO_3
concentration in ECF

Metabolic acidosis, alkalosis
Respiratory acidosis, alkalosis

Change in all organ function

VOLUME DISTURBANCE

Normal volume regulation

Volume disorder

- 1. Volume depletion**
- 2. Volume expansion**

NORMAL VOLUME REGULATION

Volume regulation



for **ECF Volume** regulation
- *Tissue perfusion*

by **Na Content** in ECF

most important in multiple imbalance

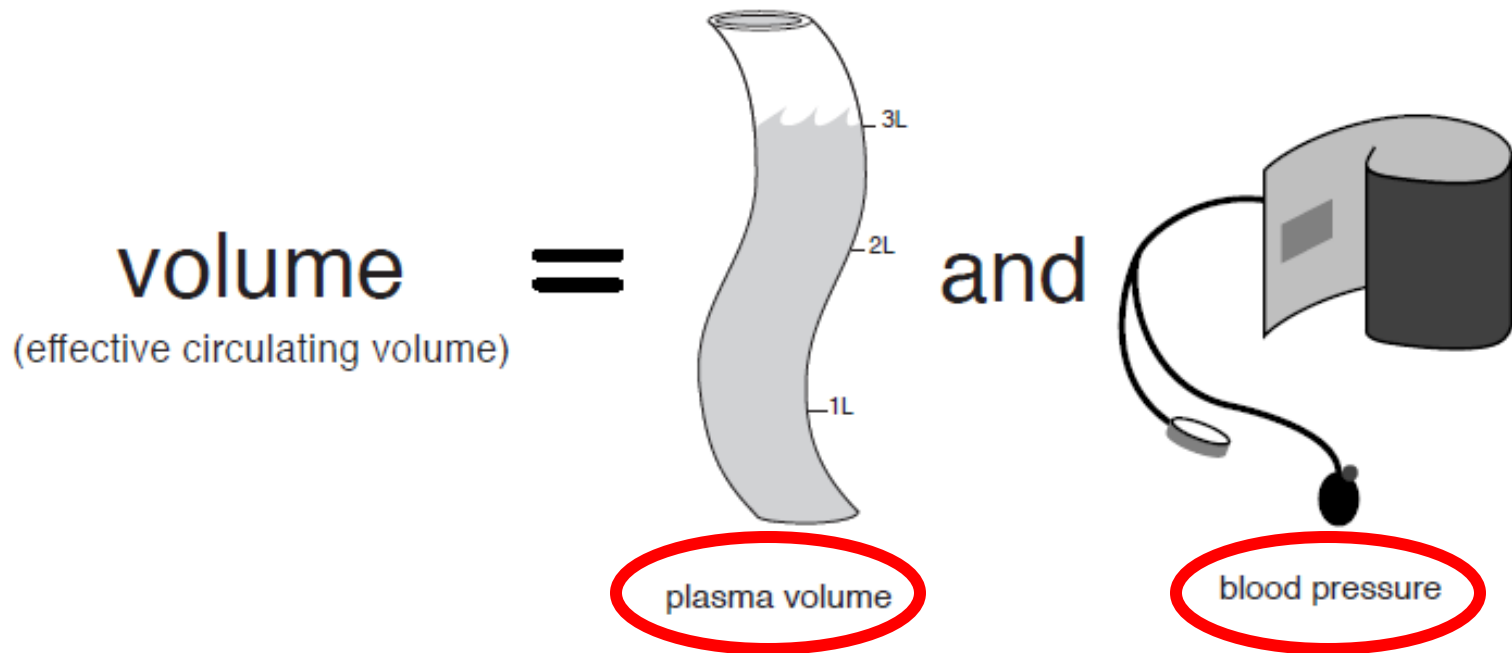
Factors for Volume control

Volume control (effective circulating volume)

→ adequate **plasma volume**

+

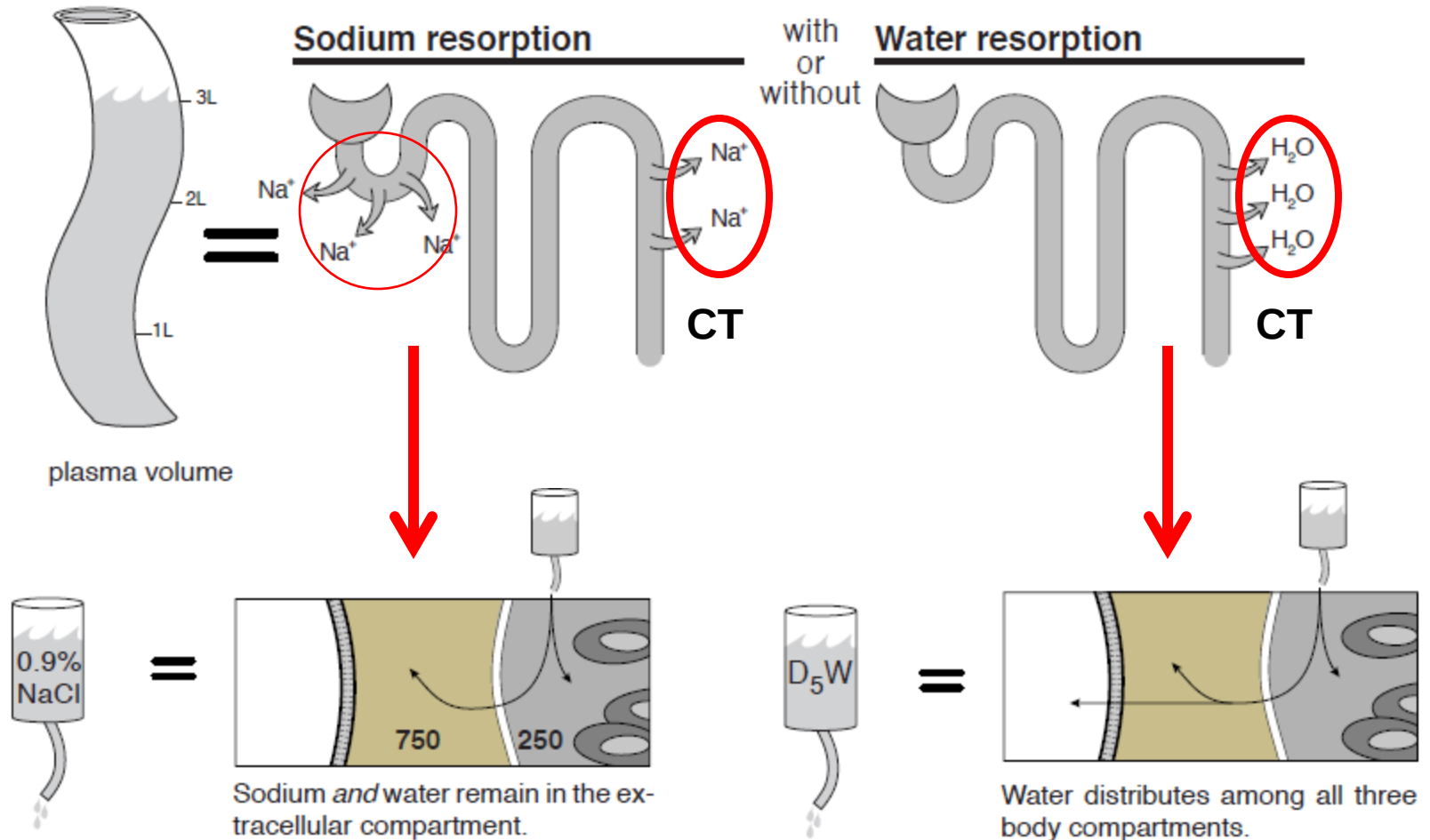
adequate tissue perfusion that plasma moves (**BP**)



Factors for Volume control

I. Plasma volume

Na and Water

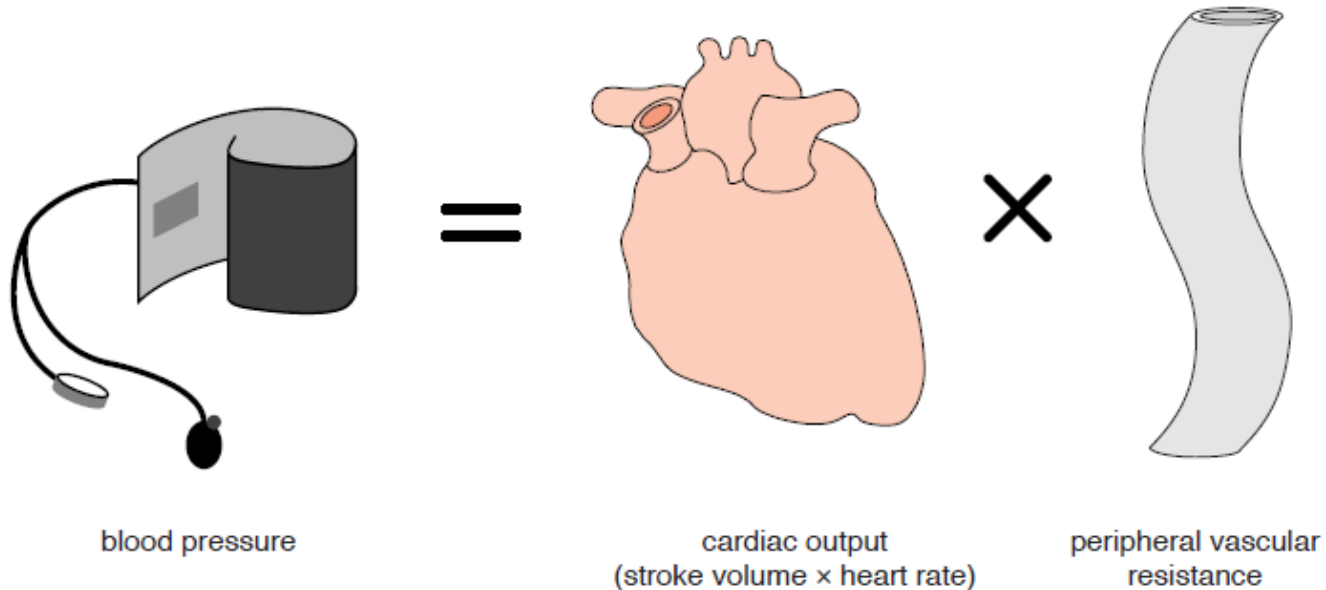


first line defence in volume loss

Second line defence

Factors for Volume control

2. Blood pressure = CO x PVR



CO = stroke volume x heart rate

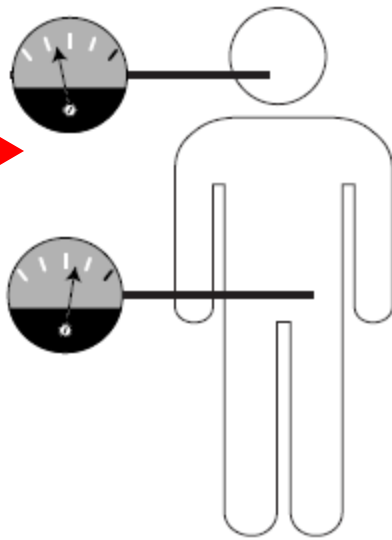
PVR = dilatation or constriction of Vasculature

Mechanism of volume regulation

Overview of volume regulation

Stimulus (ECBV, EAV,ECV)

Monitoring



baroreceptor

Signaling

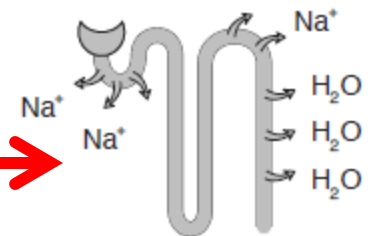
renin
angiotensin II
aldosterone



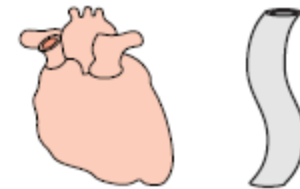
RAAS
SNS
ADH

sympathetic activation

Action at targets



plasma volume



blood pressure

Kidney
Heart
Vasculature

Mechanism of volume regulation

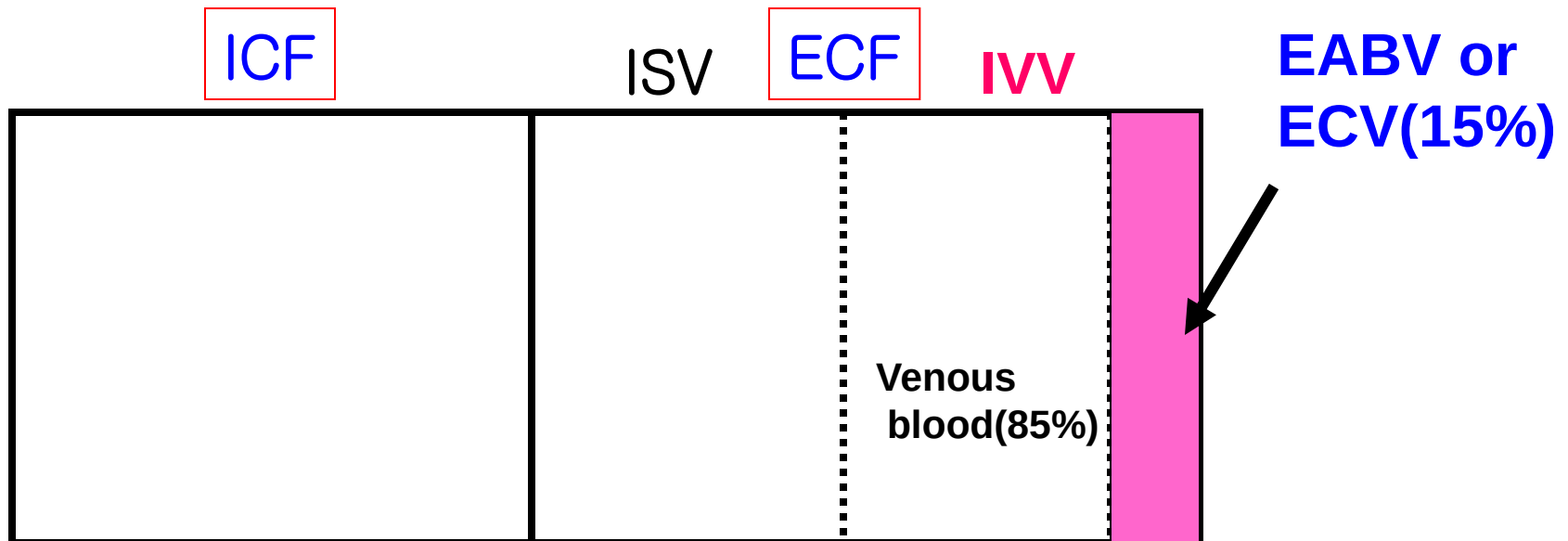
Stimulus

ECV

is a stimulus for volume regulation

is a blood flowing to volume sensitive organ
(brain and kidney)

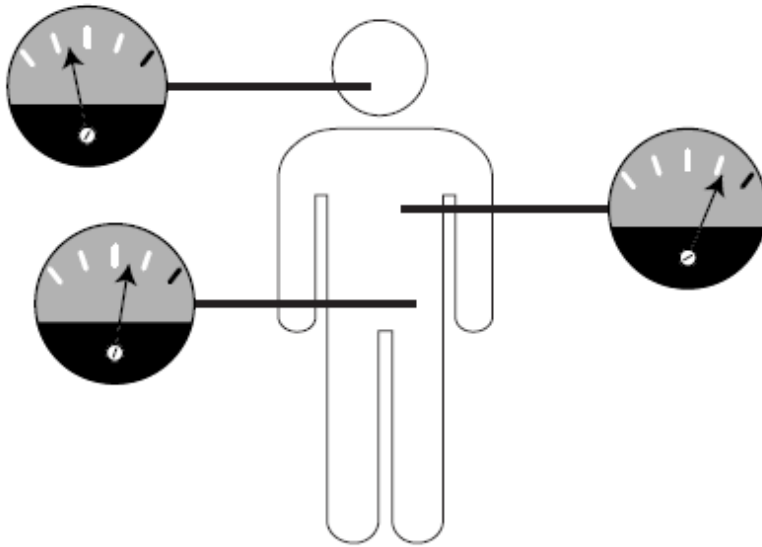
is a blood flow for tissue perfusion



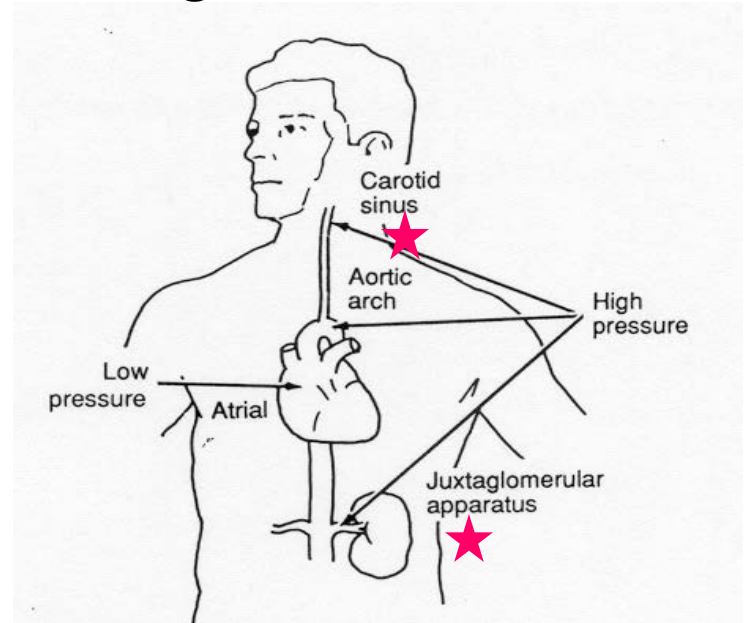
Mechanism of volume regulation

Sensor(monitoring)

Baroreceptor : respond to BP change



Baroreceptors monitor blood pressure and affect
blood pressure and plasma volume.



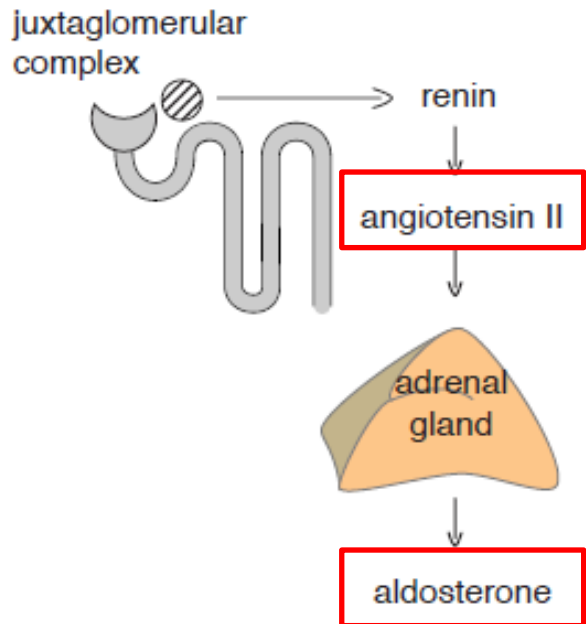
**Baroreceptor in carotid sinus and
afferent arteriole of glomerulus**

Mechanism of volume regulation

Signaling(mediator)

Signal : act to increase P.volume and BP

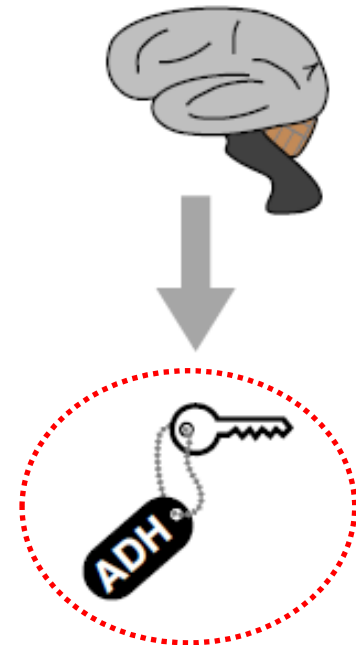
Renin-angiotensin II-aldosterone



Sympathetic stimulation



ADH



RAAS and SNS: primary signal

ADH: only when volume is extremely low

Mechanism of volume regulation

Signaling(mediator)

Signal : 3 hormone system (“ hypovolemic hormone”)

1.RAAS

- angiotensin II, aldosterone

2.Sympathetic nervous system

- epinephrine, norepinephrine

3.Antidiuretic hormone

- ADH (final signal, released in 10-15 mmHg BP down)



effect on renal Na absorption,
(GFR and tubular Na reabsorption)
also on systemic hemodynamic action
(Heart rate, vasoconstriction)

Mechanism of volume regulation

Effect(action at target)

Effect : for volume regulation (ex,volume depletion)

Renal response

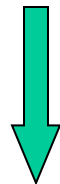
PLASMA VOLUME

SODIUM RESORPTION

WATER RESORPTION



angiotensin II
aldosterone
sympathetic activity



Urinary Na excretion

= external salt and water balance =



anti-diuretic hormone

Cardiovascular response

BLOOD PRESSURE

CARDIAC OUTPUT

VASCULAR RESISTANCE



sympathetic activity



Protect hemodynamic change

= Systemic Hemodynamic change =



angiotensin II
sympathetic activity

VOLUME DISORDER

Volume depletion(Hypovolemia)

→ by decreased Na content

→ cause hypoperfusion, shock

Volume expansion(Hypervolemia)

→ by increased Na content

→ cause edema

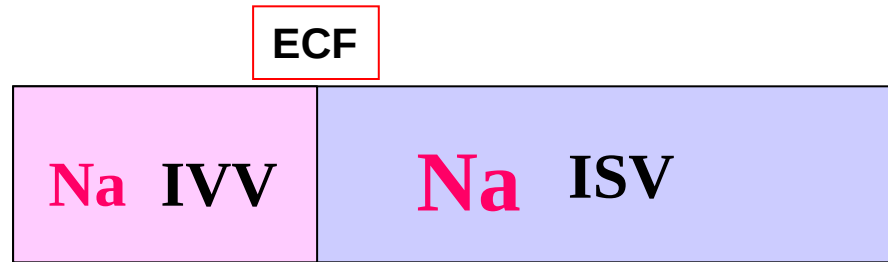
VOLUME DEPLETION

Hypovolemia

→ reduction in the volume of **ECF compartment** in relation to its capacitance

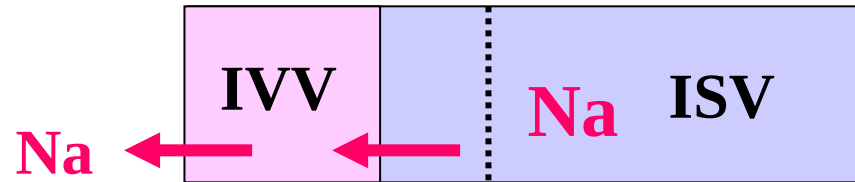
State of volume depletion

Normal



1. Renal, extrarenal loss (hypovolemia with **decreased Na**)

*Ex, Hemorrhage,
vomiting,
diuretics*

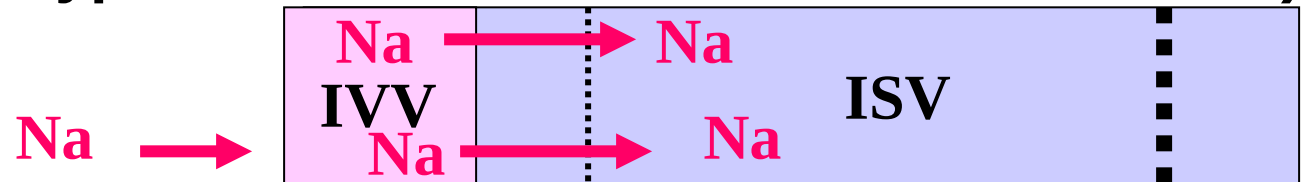


→ **Absolute hypovolemia**  **ECV** ↓

2. Circulatory compromise without fluid loss (hypovolemia with **normal** or **increased Na**)

Ex, Sepsis,

NS



→ **Relative hypovolemia**: state of vasodilation, generalized edema
 **ECV** ↓

State of volume depletion

Relative hypovolemia

- ECF volume is not reduced (but reduced EABV)
→ clinical manifestation mimic absolute hypovolemia

Two categories

1. State of vasodilation

- drug causing arteriolar vasodilation
: hydralazine, minoxidil
- **sepsis** with peripheral vasodilation and low SVR

2. State of positive Na/Water balance and generalized edema with decreased IVV

- heart failure, decompensated cirrhosis with ascites, **NS**

Cause of volume depletion

Volume loss

```
graph TD; A[Volume loss] --> B[Renal Cause]; A --> C[Extrarenal Cause];
```

Renal Cause

Absolute

- diuretics
- inherited sodium wasting tubulopathies
- TI Ds
- endocrine disorder
(hypoaldosteronism,
adrenal insufficiency)

Relative

- Nephrotic syndrome

Extrarenal Cause

Absolute

- Bleeding : M/C
- Cutaneous : burn, sweat
- GIT loss : vomiting
diarrhea
- Respiratory loss

Relative

- third-space loss
- sepsis
- edema state(CHF, LC)

Clinical manifestation

Clinical finding

→ due to underfilling of arterial tree,
to the subsequent *renal and*
hemodynamic response

Clinical manifestation

Clinical finding

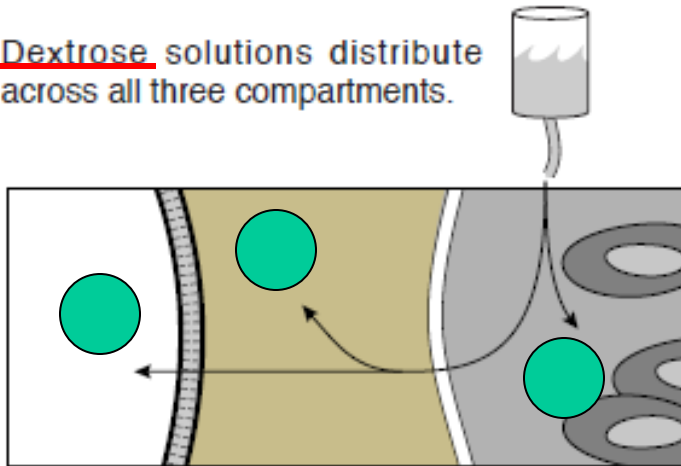
- Nonspecific : fatigue, weakness, thirst, postural dizziness
- More severe state: oliguria, cyanosis, abd/chest pain, confusion or obtundation
- **Symptoms by blood volume loss**
 - : IVV loss < 5% → no sx
 - > 5 – 15 % → sx begin to appear
 - : Severe degree hypovolemia(IVV loss > 10 – 20%)
 - hypotension(even in supine position)
 - peripheral cyanosis
 - cold extremity
 - reduced level of consciousness

Clinical manifestation

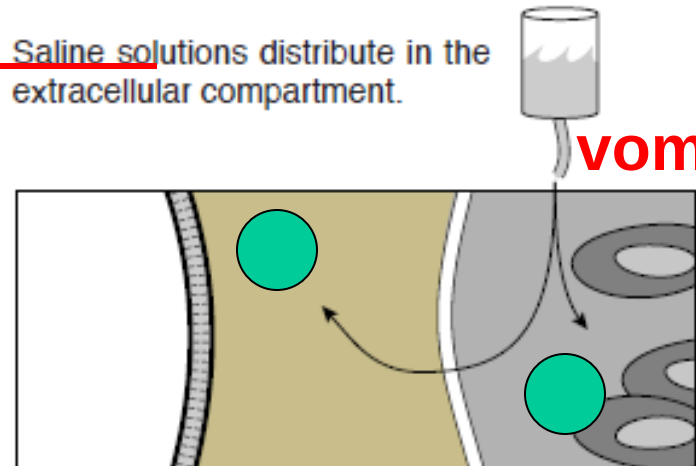
Clinical finding : Nature of fluid loss

DI

Dextrose solutions distribute across all three compartments.

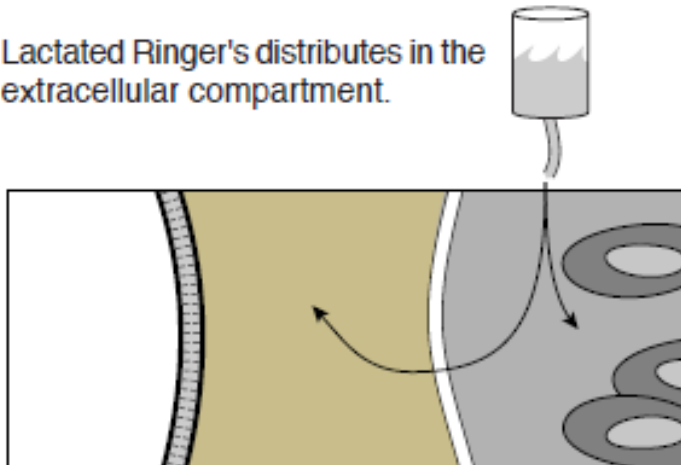


Saline solutions distribute in the extracellular compartment.

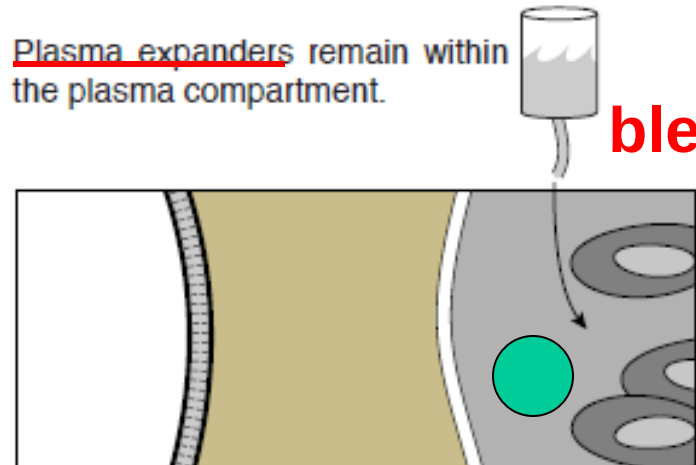


vomiting

Lactated Ringer's distributes in the extracellular compartment.



Plasma expanders remain within the plasma compartment.



bleeding

Clinical manifestation

Physical examination

- orthostatic tachycardia($> 15-20$ beat/min),
orthostatic hypotension(drop 10-20 mmHg),
reduced JVP
→ reliable sign of hypovolemia
- 1. decrease in the **interstitial volume**
 - decreased **skin turgo and moistness of MM**
- 2. decrease in **the plasma volume**
 - decreased systemic **blood pressure**,
venous pressure in the jugular veins.

Clinical manifestation

Physical examination

- in septic circulatory collapse
 - : **warm extremity** due to vasodilation

in true hypovolemia

- : **cool, cyanotic extremity**
due to vasoconstriction

Clinical manifestation

Physical finding in volume disorder

	ECFV expansion	ECFV depletion
<i>Intravascular</i>	Hypertension S3 gallop elevated JVP HJR Hepatic congestion	Mild - orthostatic change in BP, PR - decreased JVP Severe - Hypotension - Shock
<i>Interstitial</i>	pitting edema pulmonary rale	diminished skin turgor
<i>Transcellular</i>		dry mouth
<i>Others</i>	pleural effusion ascites	diminished IOP

Diagnosis

1. Initial assessment of circulatory dynamics

- pulse(> 15 -20/min) and BP(<10 -20mmHg) **change with position change**
 - : orthostatic decrease in D pressure > 10 mmHg is reliable indicator of significant volume depletion
- venous pressure, skin temperature, skin turgo

2. Laboratory finding

3. Fluid challenge

- : 500 ml N/S infusion over 1- 3 hrs

4. Invasive hemodynamic monitoring

- : PCWP,CVP

Diagnosis

Laboratory finding

1. Urine sodium concentration : **U na < 20 mEq/L**
 - * in hypovolemia with hypochloremic **M. alkalosis**
 - **U.Cl** is more accurate than U.Na for volume state
2. Fractional excretion of **Na < 1%**
 - Fractional excretion of **urea < 30- 35%**
3. Urine osmolality **> 400- 450 mosmol/kg**
4. Urine specific gravity **> 1.020**
5. Urinalysis finding
 - relatively normal

Diagnosis

Laboratory finding

6. BUN and plasma creatinine concentration

- In normal subjects → BUN/P Cr is 10 : 1

In hypovolemic state

→ increased proximal Na reabsorption
with urea reabsorption

→ **BUN/ P cr > 20 : 1**

7. acid-base change

- hypokalemia with **M.alkalosis**: **vomiting**, diuretics
- hypokalemia with **M.acidosis** : **diarrhea**

8. Hgb, Na, K

Treatment

Treatment goal

- expand the circulating blood volume,
tissue perfusion
by control of fluid volume, rate, composition
- Fluid selection
 - depend on nature of lost fluid
 - but usually **N/S**
is first choice of fluid resuscitation

Treatment

Treatment of relative hypovolemia

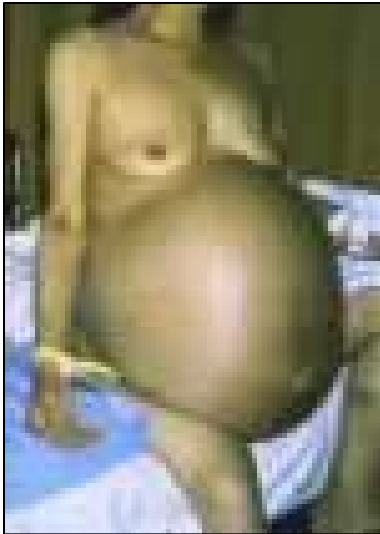
I. In peripheral vasodilation

- reversal of underlying cause and restoration of normal vascular reactivity
- 1) isotonic crystalloid solution (N/S)
 - : caution in volume and rate because of no absolute deficit
- 2) vasoconstrictor agent

II. In state of edema

- underlying disease control

VOLUME EXPANSION (EXCESS)



Volume expanded state

characterized

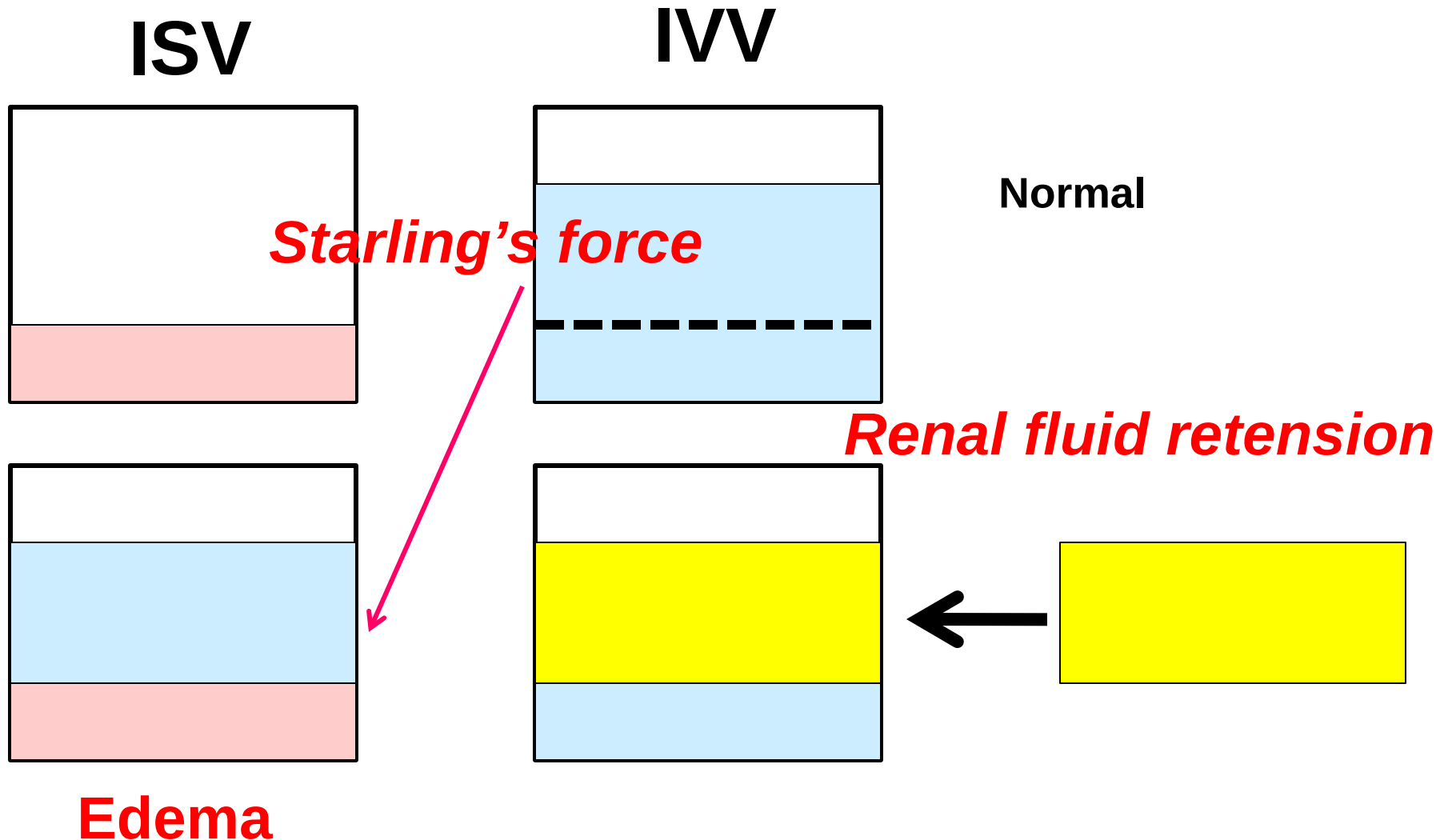
by increase in total body water

**by increase in total body Na
(especially in ECF)**

but also may associated with decreased CBV

Pathophysiology of Volume expanded state

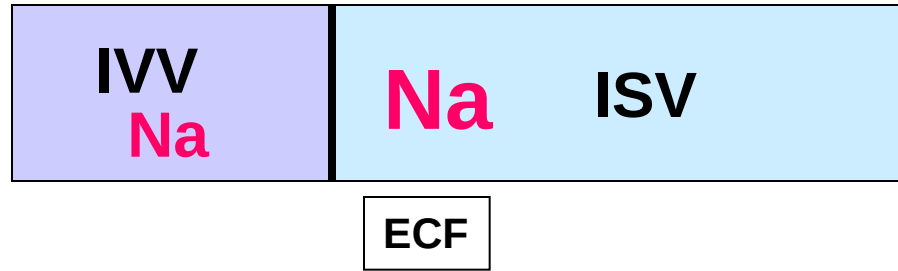
Peripheral edema is maintained by Na retention



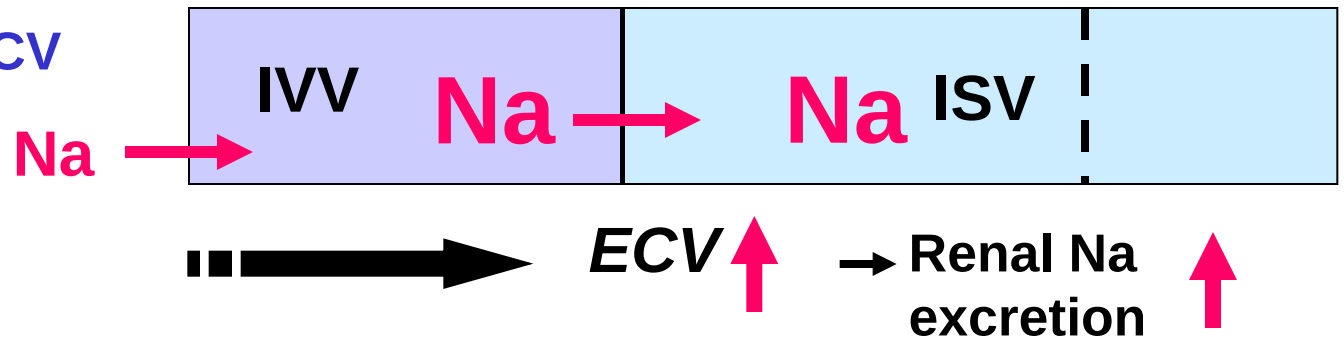
Pathophysiology of Volume expanded state

2 state

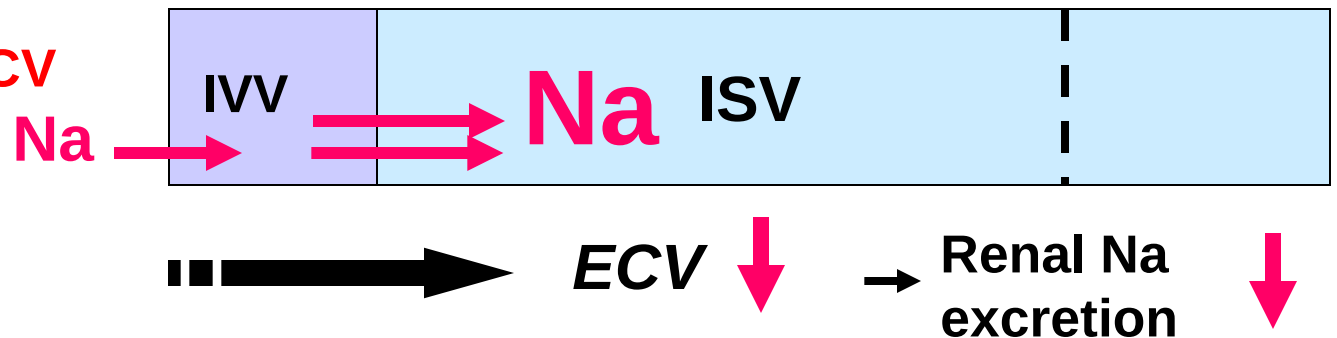
Normal



Hypervolemia
with **increased ECV**
(AGN)



Hypervolemia
with **decreased ECV**
(CHF, LC, NS)



Cause of volume expansion

Volume expansion

Secondary renal Na retention
(Disturbance in Starling forces)
(**reduced** ECBV)

1. increased systemic venous Pr
: **RHF**, *constrictive pericarditis*
2. local elevation in pulmonary Pr
or SVPr
: **LHF**, *vena cava and P vein obst*
3. reduced plasma oncotic Pr
: **NS**
4. combination
: **LC** *with ascites*
(*hypoalbuminemia,*
portal hypertension)

Primary renal sodium retention
(**increased** ECBV)

1. renal disease
: **acute GN**, *renal failure*
2. endocrine disorder
 - 1) **mineralocorticoid excess**
: *primary*
hyperaldosteronism
 - 2) excess ADH
: **SIADH**

Clinical manifestation

- **Edema**
- **Shortness of breath**
- **Paroxysmal nocturnal dyspnea**
- **Orthopnea**
- **Hypertension**

Clinical manifestation

Physical finding

ECFV expansion

ECFV depletion

Intravascular

Hypertension
S3 gallop
elevated JVP
HJR
Hepatic congestion

Mild

-orthostatic change
in BP,PR

- decreased JVP

Severe

- Hypotension

- Shock

diminished skin turgor

Interstitial

pitting edema
pulmonary rale

Transcellular

Others

pleural effusion
ascites

dry mouth

diminished IOP

Diagnosis

Underlying disease

Clinical manifestation

: edema,
elevated jugular venous Pr,
inspiratory pulmonary crepitations,
pleural effusion,
hypertension

Lab

: **Elevated BNP** in cardiac failure and renal disease
→ support the diagnosis of hypervolemia

Treatment

I. underlying disease treatment

II. reduce ECF volume by negative sodium balance

- 1) dietary sodium restriction**
- 2) diuretics**
- 3) extracorporeal fluid removal by ultrafiltration**

Intensity of treatment depend on clinical situation

- manifestation of hypervolemia that may be harmful**
 - : hypertension**
 - : pulmonary edema or pleural effusion with compromised respiratory function**
 - : hepatic congestion and ascites**
 - : peripheral edema that compromise skin integrity and predispose the patient to cellulitis**
- diuretic IV infusion and ultrafiltration**

Treatment

Diuretics : increase urine excretion of Na

1. Proximal tubule diuretics

- acetazolamide, metolazone

2. Loop diuretics

- furosemide(**lasix**), ethacrynic acid, bumetanide, torsemide
- **most potent diuretics**
- effective in CKD

3. Distal tubule diuretics(early distal diuretics)

- hydrochlorothiazide(**dichlozid**), chlorthalidone, metolazone
- **ineffective in CKD**

4. Collecting duct diuretics(late distal diuretics)

- spironolactone(**aldactone**), eplerenone : aldosterone antagonist
- trimaterene, amiloride : non aldosterone antagonist

* **Nesiritide** : recombinant form of natural BNP

OSMOLALITY DISTURBANCE

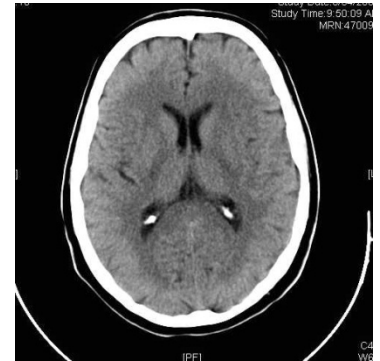
Normal osmolality regulation

Osmolality disorder

: Hypotonic disorder (Hyponatremia)

: Hypertonic disorder (Hypernatremia)

Polyuria and polydipsia



OSMOLALITY REGULATION

Osmoregulation

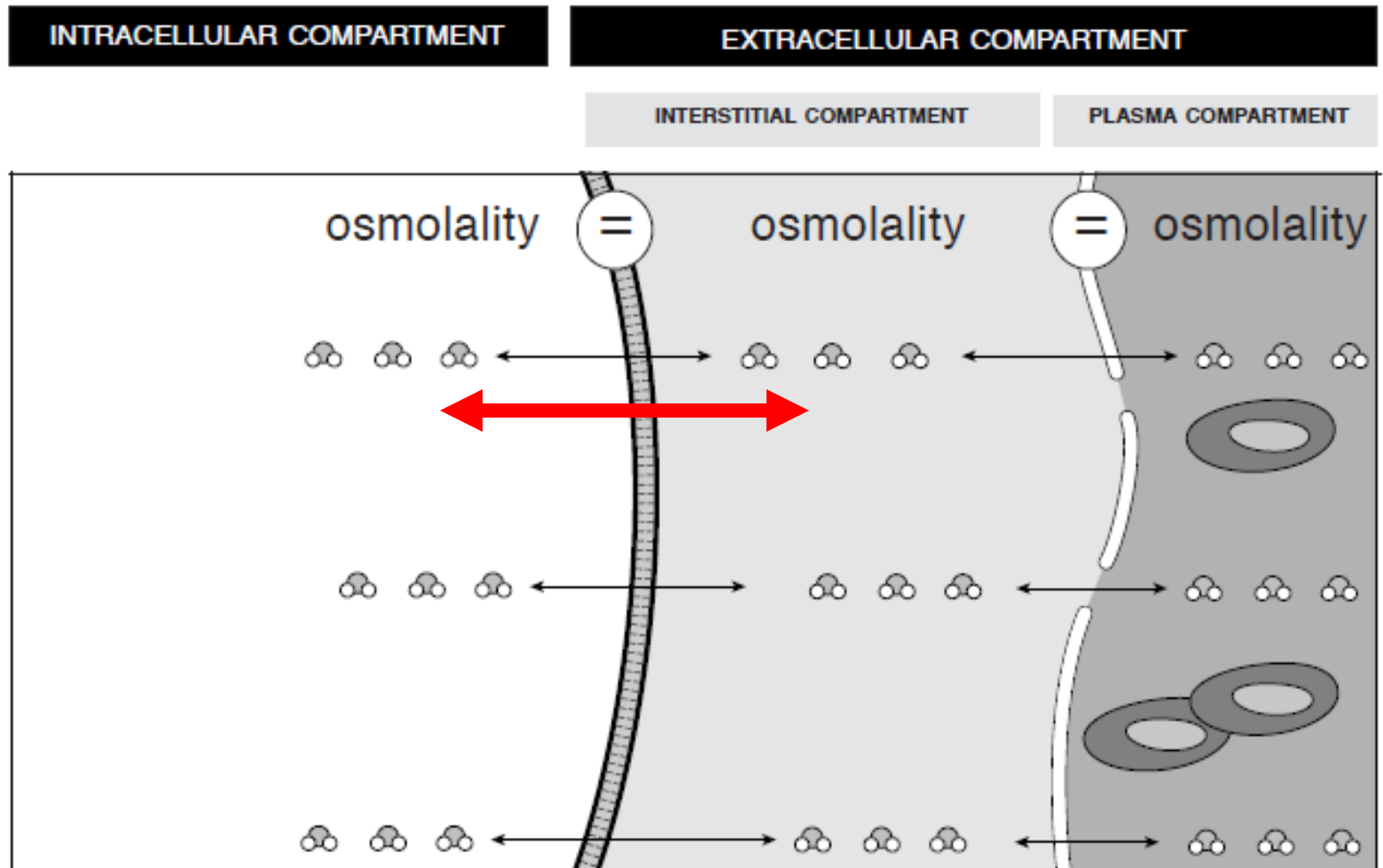


*for **ICF volume** regulation
(cell volume)*



*by ECF **osmolality**
→ by ECF **Na concentration**
(= ECF Na content / **Water**)*

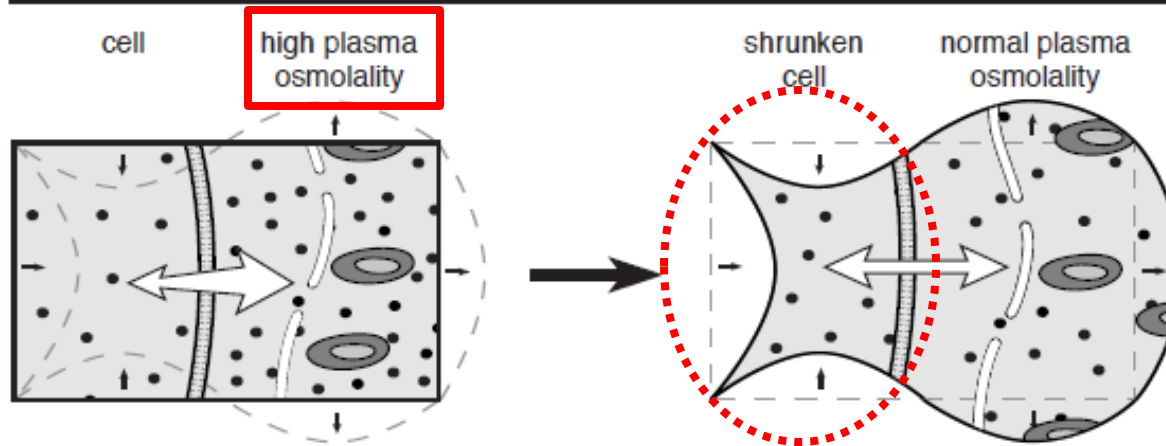
Water distribution between ICF and ECF by osmotic pressure



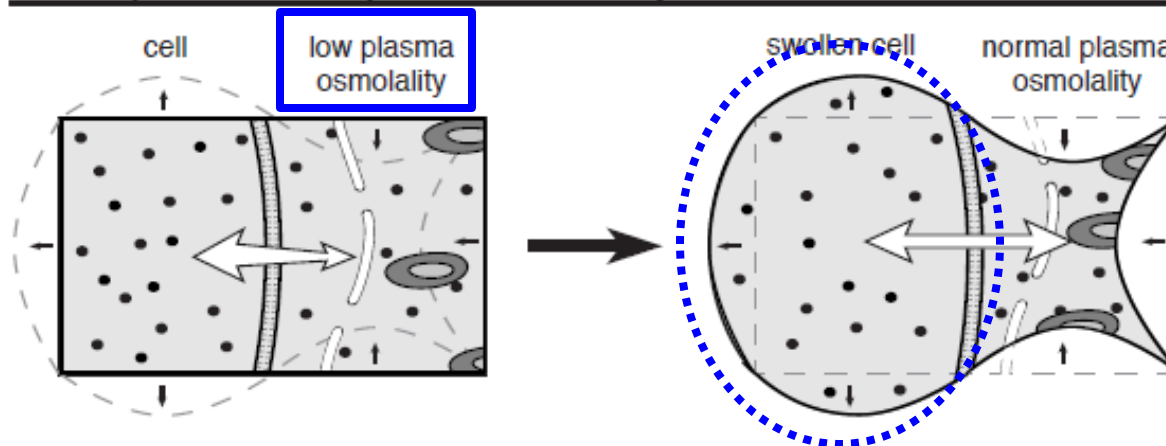
Water distribution between ICF and ECF

ECF Osmolality change → change cell volume

Consequence of high plasma osmolality

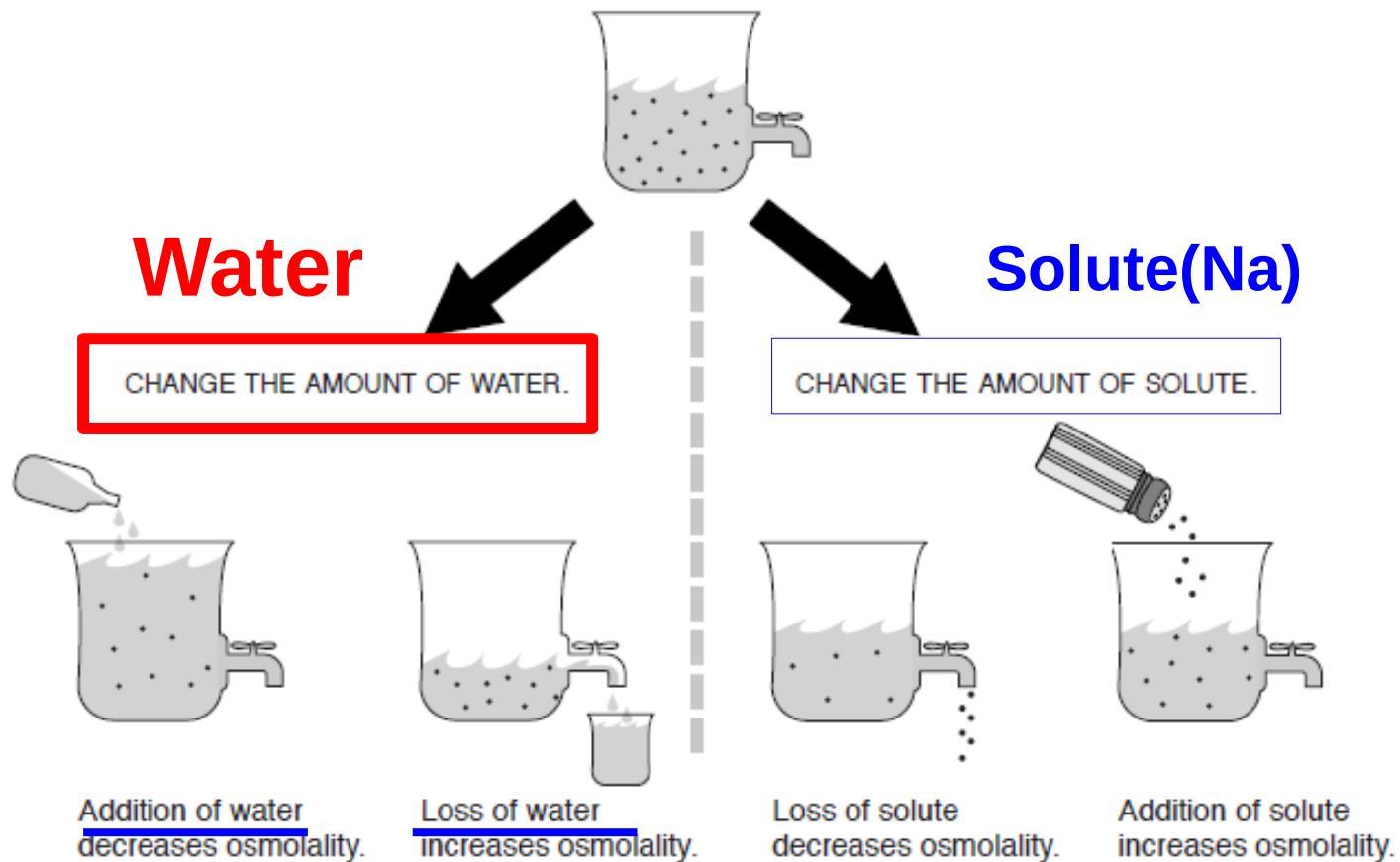


Consequence of low plasma osmolality



Physiology of Osmoregulation

Two ways to change osmolality



Physiology of Osmoregulation

Water regulation

Water ingestion

→ Primary stimulus is **thirst**

Renal Water excretion

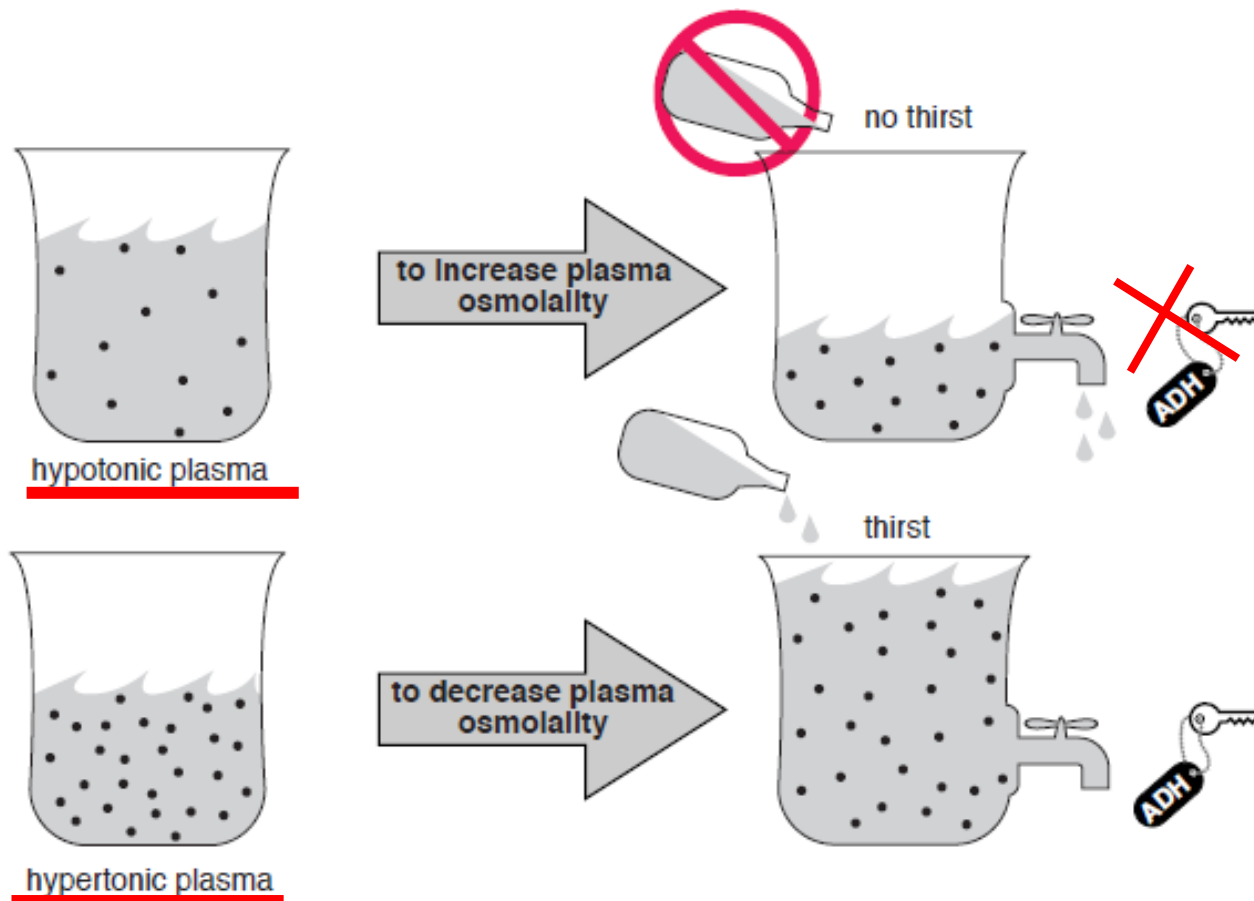
→ Principal determinant is **vasopressin(AVP,ADH)**

AVP (Arginine vasopressin)

- bind **V2R** and stimulate insertion of **aquaporine 2**,
Water channel protein into luminal membrane
→ increase water permeability
- act at principal cell in collecting duct

Physiology of Osmoregulation

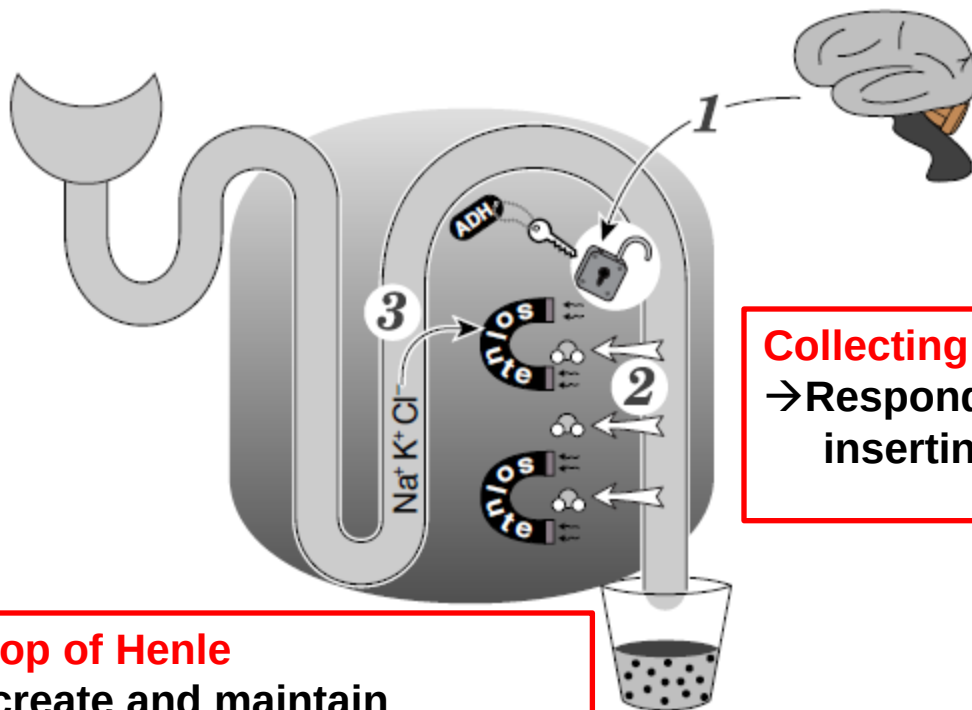
Body water change to control P.osmolality
→ through **thirst** and **ADH**



Physiology of Osmoregulation

Body water change to control P.osmolality

*Three step process of
concentrated Urine formation by **ADH***



Hypothalamus

- Detect increased osmolality
- Trigger release of ADH

Collecting tubule

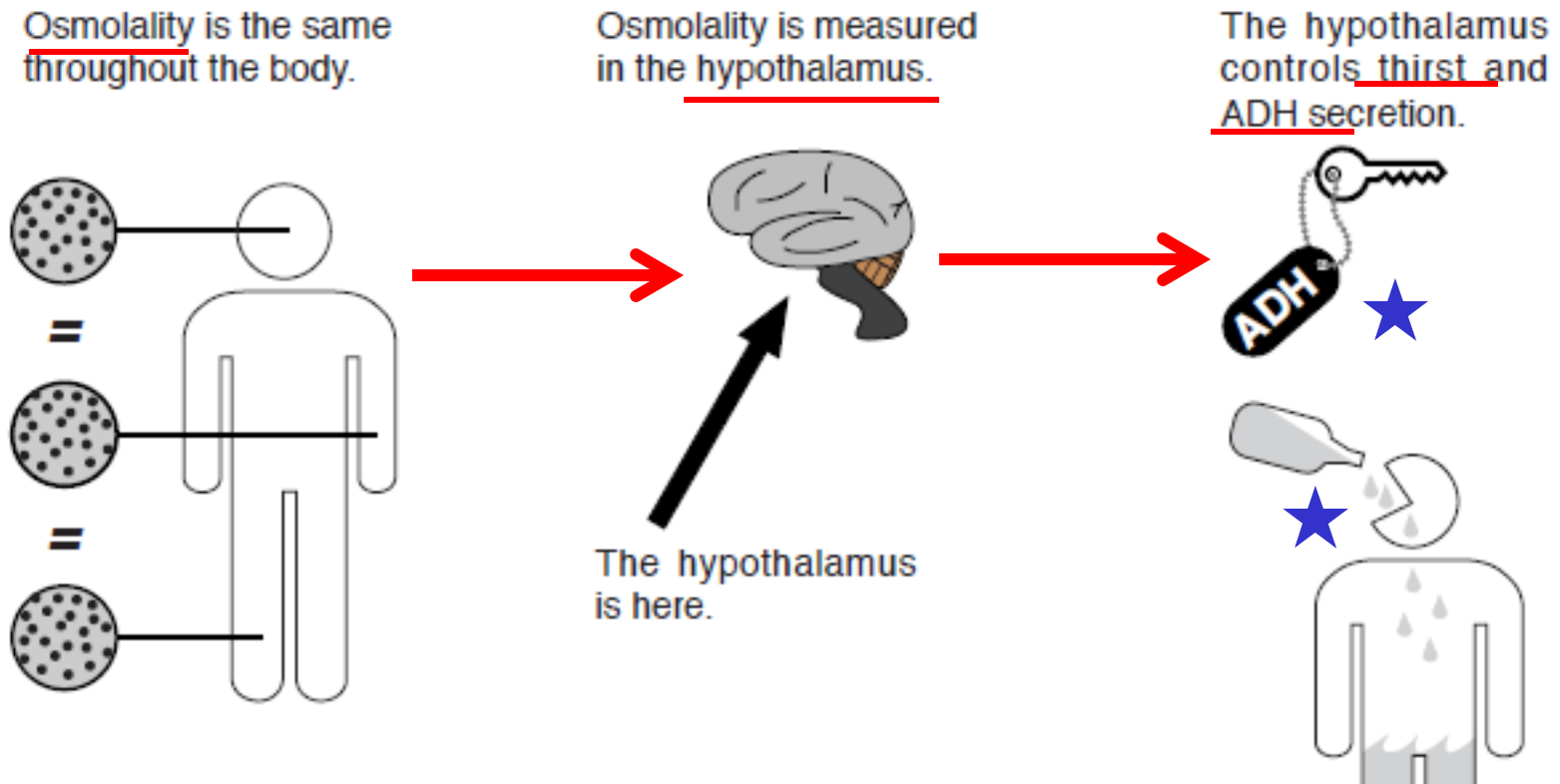
- Respond to ADH by inserting water channel

Loop of Henle

- create and maintain concentrated medullary interstitium

Control of osmoregulation

Overview of osmolality control



stimuli

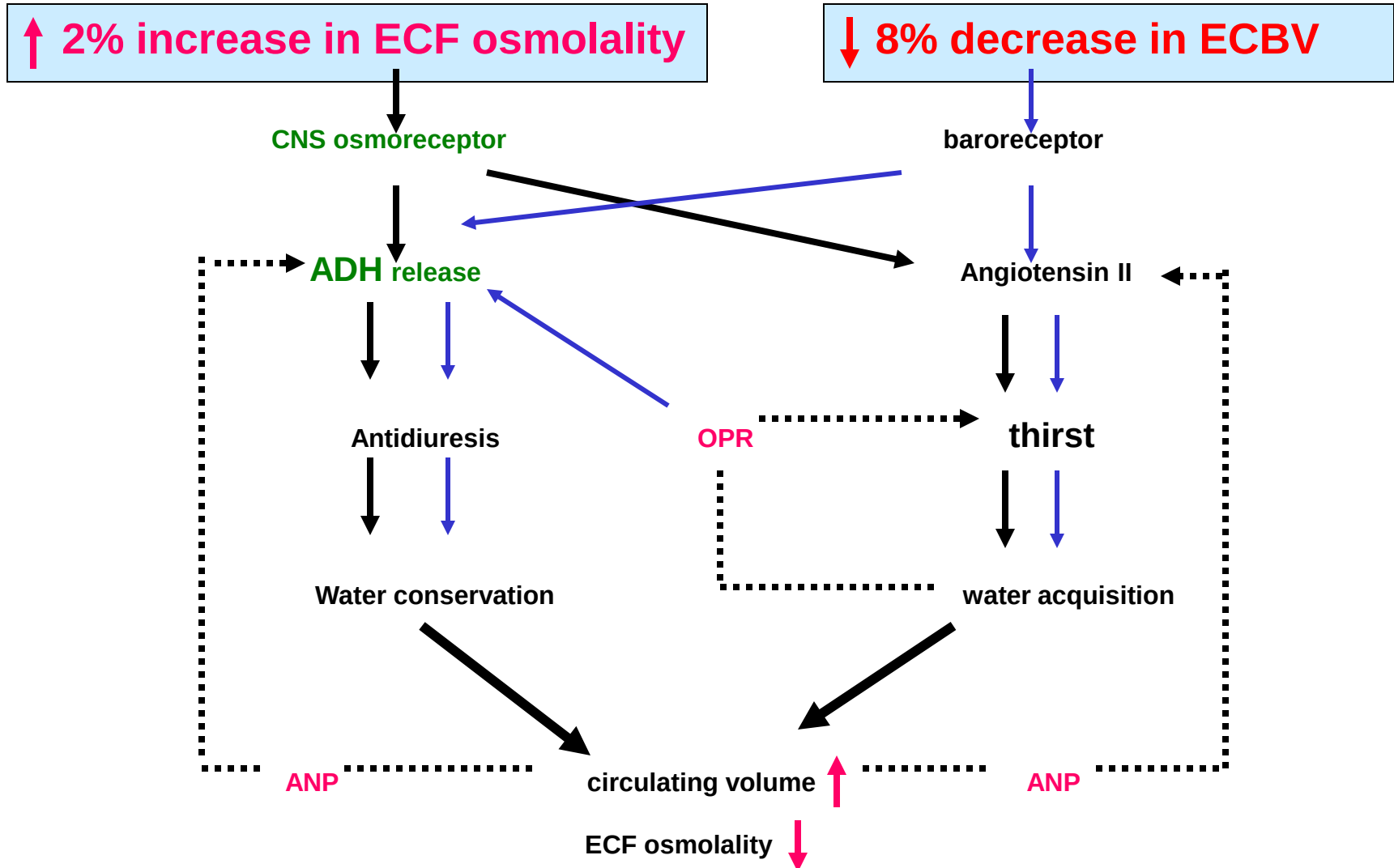
sensor

mediator

→ **Effect on renal water excretion**

Control of osmoregulation

Overview of osmolality control

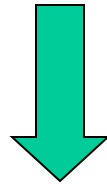


Control of osmoregulation

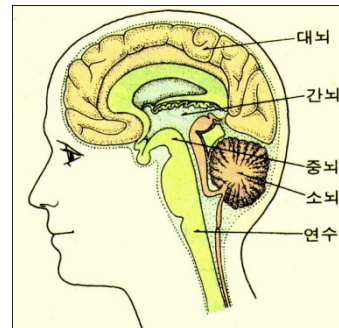
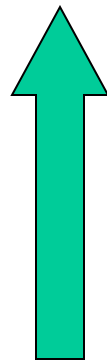
Volume regulation and Osmoregulation

	<i>Osmoregulation</i>	<i>Volume regulation</i>
What is being sensed	Plasma osmolality	ECBV
Sensor	Hypothalamic osmoreceptor	Carotid sinus Afferent arteriole Atria
Effector	ADH	RAAS SNS ADH Pressure natriuresis ANP
what is affected	water excretion and via thirst, water intake	urine Na excretion

OSMOLALITY DISORDER



**Hypotonic and Hypertonic disorder
(Hypo- and Hypernatremia)**



Disturbance of water balance

HYPONATREMIA

Definition

- serum Na < 135 meq/L
(osmolality < 285 mosm/kg)
- always result of
increased circulating **AVP** or
increased AVP sensitivity
with free **water intake**

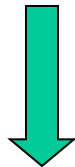
INTRODUCTION

Plasma osmolality

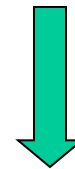
Total osmolality

= **effective osmolality** + ineffective osmolality
(tonicity)

= 2x **Na** + **glucose** / 18 + BUN / 2.8 + ethanol / 4.6



Influence ECF- ICF
Water distribution

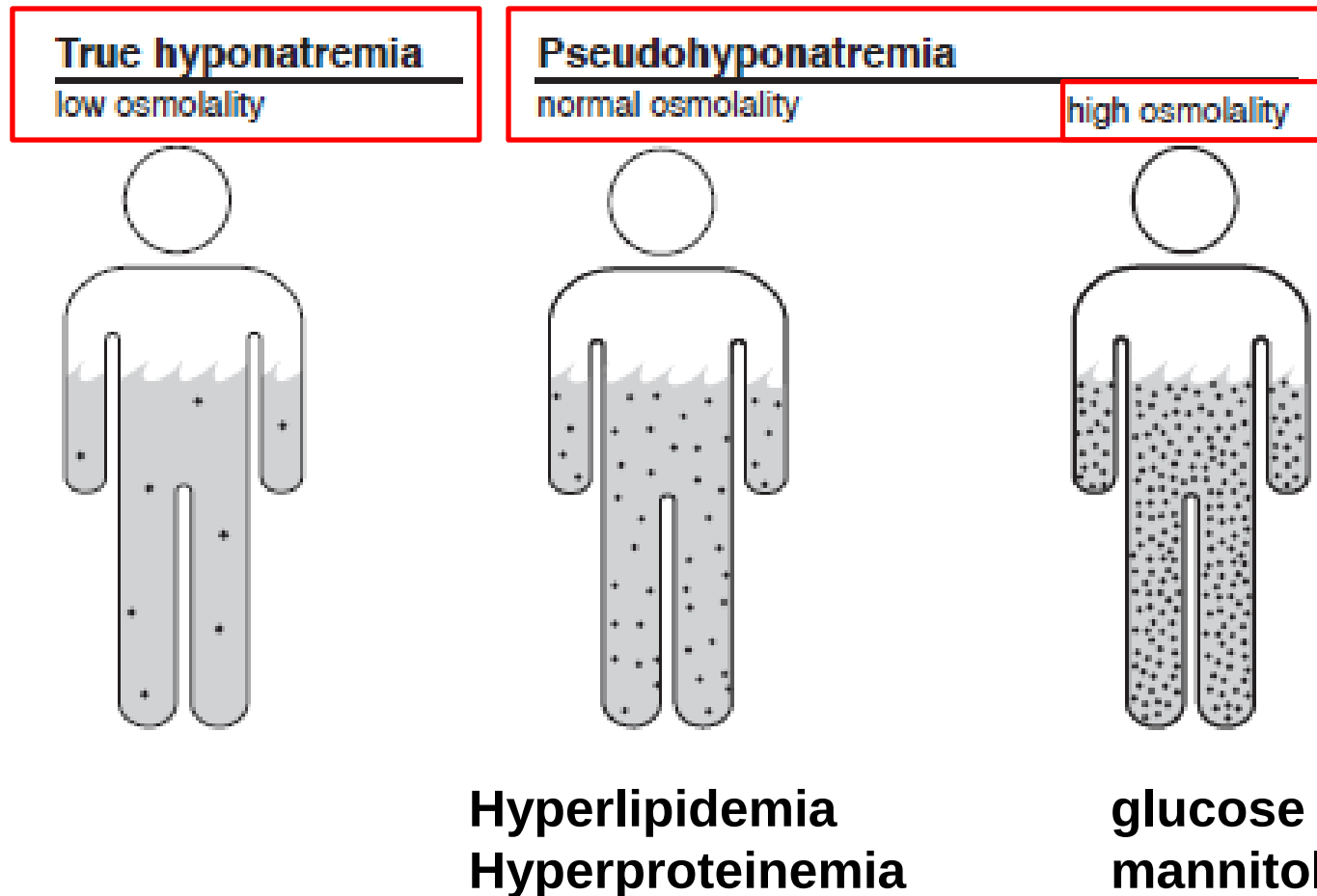


Does not alter
ECF-ICF waer
distribution

Introduction

Three osmolality state in Hyponatremia

True hyponatremia and Pseudohyponatremia

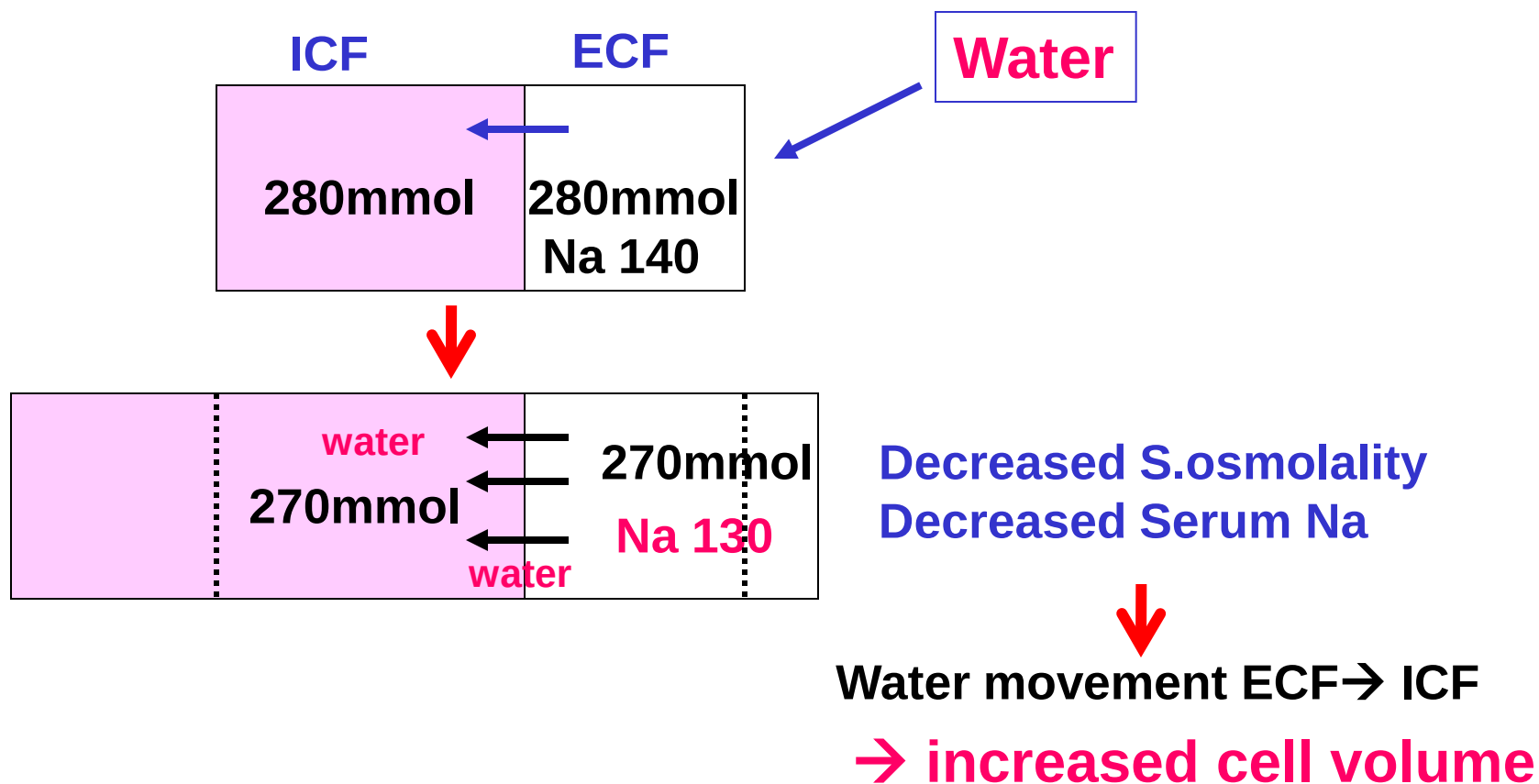


Introduction

Three osmolality state in Hyponatremia

1. Hyponatremia with low p.osmolality

(True hyponatremia, hypotonic hyponatremia)

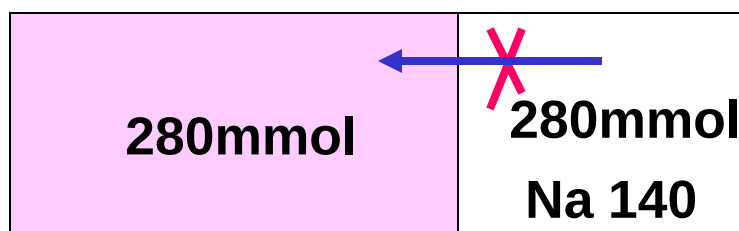


Introduction

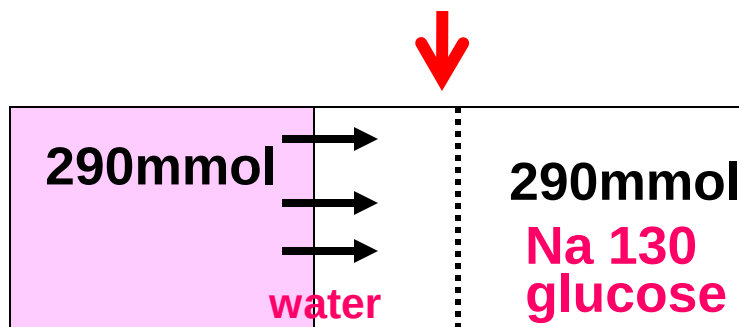
Three osmolality state in Hyponatremia

2. Hyponatremia with high p. osmolality (Hypertonic hyponatremia)

due to Impermeable solute (Increased non Na ECF solute)



glucose



Increased S.osmolality
Decreased Serum Na

Water movement ICF → ECF
→ decreased cell volume

Introduction

Three osmolality state in Hyponatremia

3. Hyponatremia with Normal p.osmolality (isotonic hyponatremia = Pseudohyponatremia)

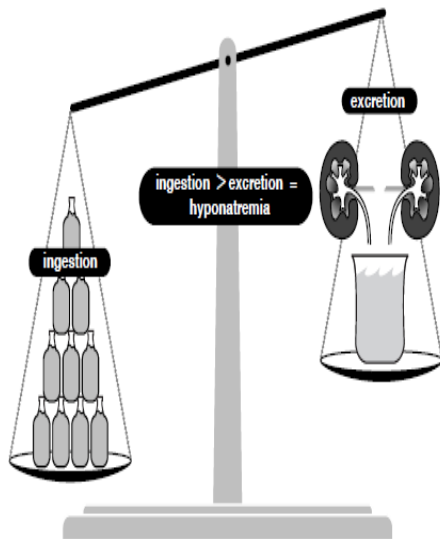
laboratory artifact :
hyperlipidemia,
hyperproteinemia

PATHOGENESIS

True Hyponatremia

: relative excess of water

→ due to water ingestion that exceed renal excretion



3 state in relative water excess

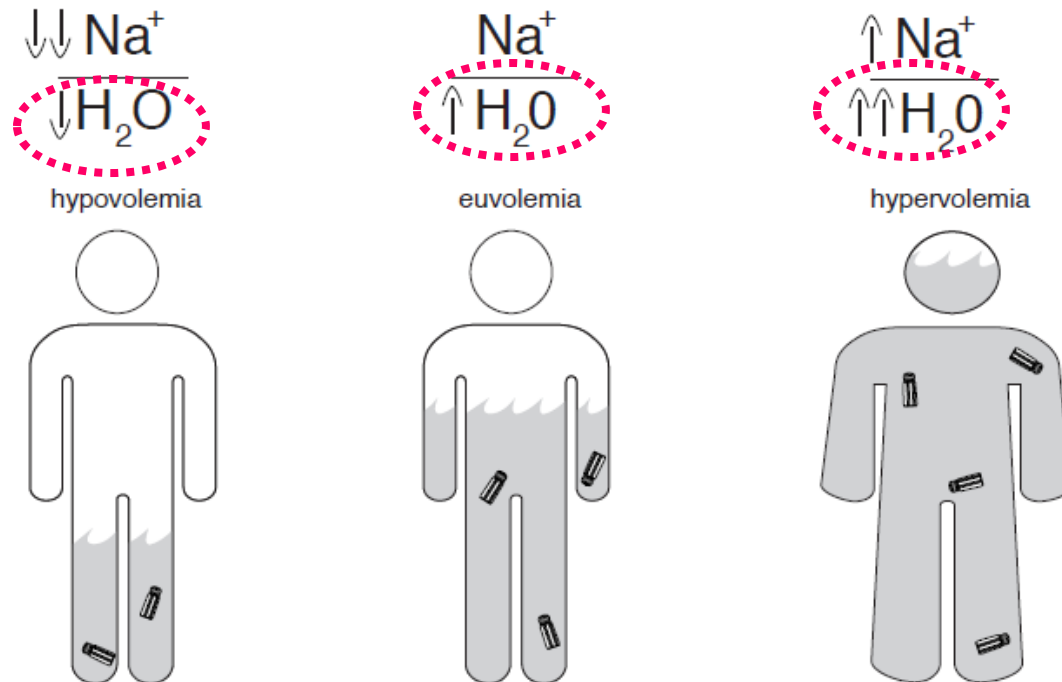
1. ingestion of **too much water** which overwhelms **normal kidney**
ex, **psychogenic polydipsia**
2. ingestion of **normal amount** of water in **renal failure**
ex, **CKD**
3. ingestion of **normal amount** of water in presence of **ADH**
ex, **SIADH, Hypovolemia**

Pathogenesis of True Hyponatremia

3 volume state in hyponatremia

: hypovolemia, euvoolemia, hypervolemia

: useful in D/D of hyponatremia



ETIOLOGY

Hyponatremia

Hyperlipidemia
Hyperproteinemia
Hyperglycemia

Hypotonic Hyponatremia

ECF Volume

Hypovolemic

Vomiting
Diarrhea
Diuretics excess
Mineralocorticoid
deficiency
CSW

Hypervolemic

CHF
LC
NS
RF

Euvoletic

SIADH (M/C)
Hypothyroidism
Glucocorticoid
deficiency
Primary polydipsia

Etiology

Clinical etiology of hyponatremia

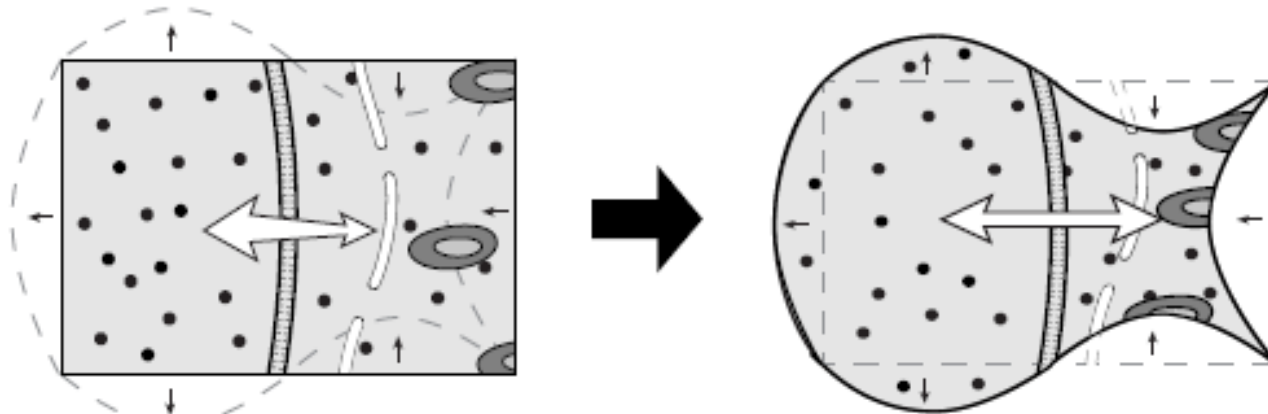
- mostly chronic cause

Acute hyponatremia

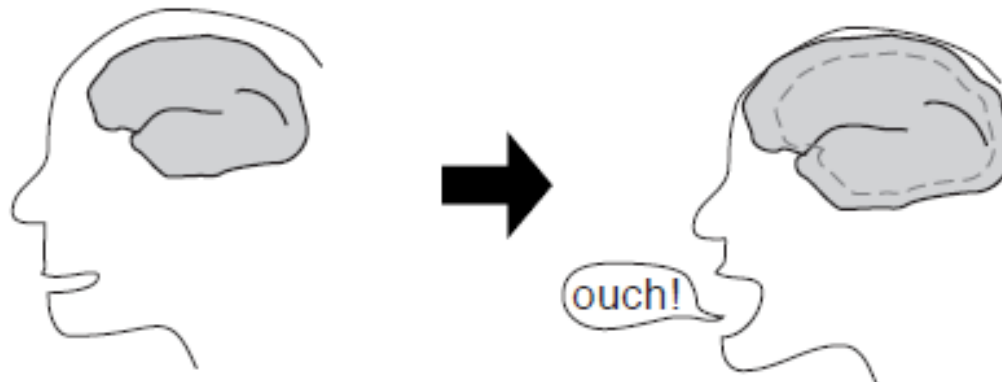
- much more common in premenopausal women
- cause
 - : iatrogenic components, such as
 - hypotonic fluid in postoperative patient
 - with cause of increased ADH,
 - colonoscopy preparation,
 - : recent institution of thiazide
 - : exercise-induced (marathon)

Clinical manifestation

Brain edema



In hyponatremia, water is osmotically drawn into the intracellular compartment which causes cells to swell.



Cellular swelling is particularly problematic in the brain.

Clinical manifestation

1. Acute hyponatremia (< 48 hrs)

- due to brain edema, cerebral encephalopathy
- early symptoms
 - nausea, headache, vomiting, lethargy, weakness, somnolence
- progression rapidly
 - seizure, coma, death
- respiratory failure(noncardiogenic pulmonary edema)
- untreated acute water intoxication
 - nearly uniformly fatal and represent a medical emergency

Clinical manifestation

2. Chronic hyponatremia(> 48 hrs)

- CNS manifestation are far less common,
even when serum Na is as low as 100 mEq/L
- chronic hyponatremia
 - cause **impaired cognitive function** and **decreased bone density(BMD)**
 - increase fall and bone fracture

Diagnosis

Hyponatremia

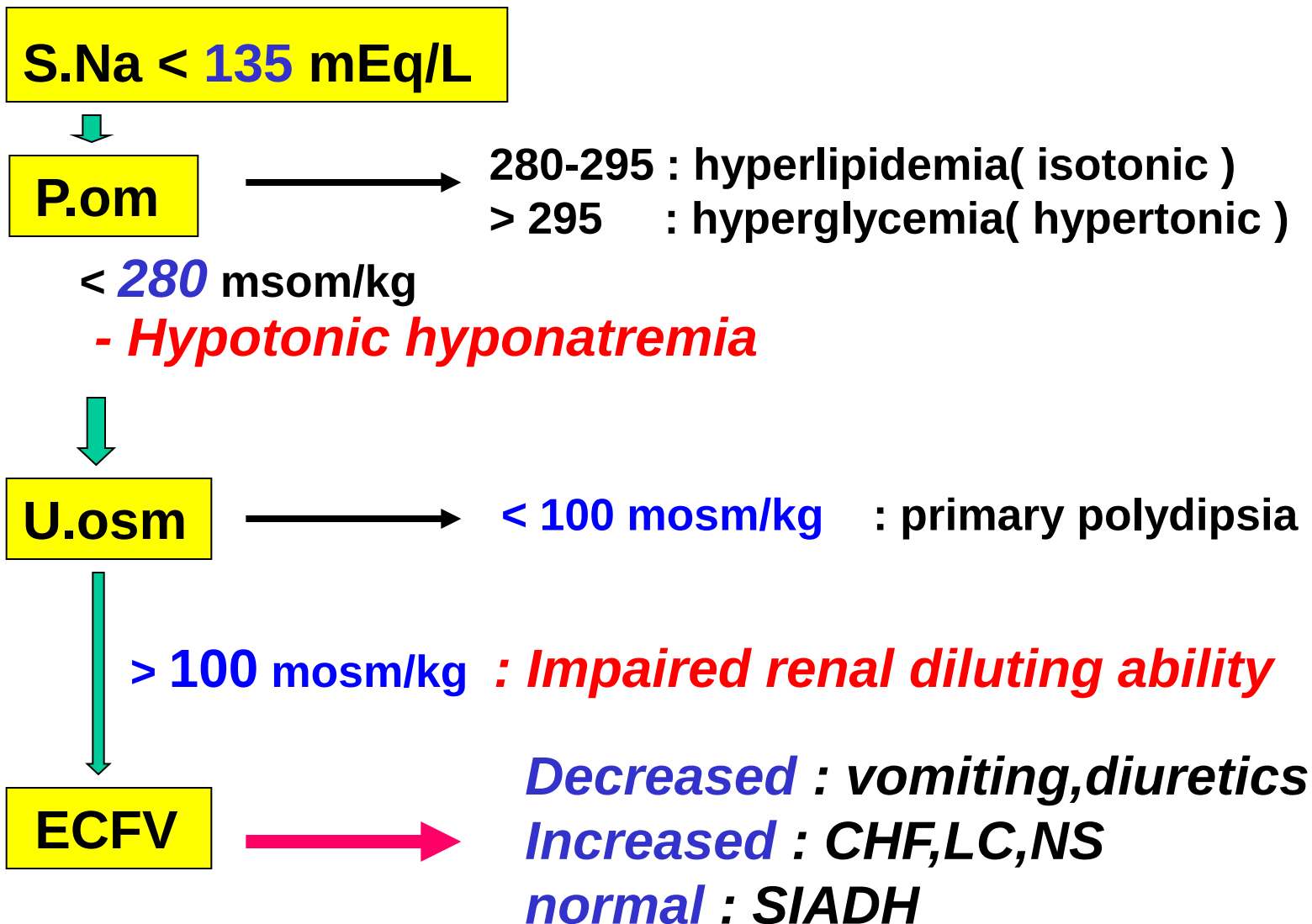
→ should be considered in sudden deterioration
in CNS function
such as in **intractable heart failure,**
hepatic cirrhosis with ascites,
administration of large volume of IV fluid

4 lab finding for D/D

- 1) plasma osmolality
- 2) urine osmolality
- 3) urine Na concentration
- 4) urine K concentration

Approach

Simple approach



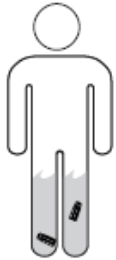
Treatment

Three consideration for guiding therapy

1. presence and severity of symptoms
 - determine urgency and goal of therapy
 - acute (< 48 hrs)
 - chronic (> 48 hrs)
2. ODS risk in chronic patient
 - increased risk in chronic patient with rapid correction
($> 8 - 10$ mM in 24hrs, > 18 mM in 48 hrs)
3. F/U plasma Na because of unpredictable response to intervention(hypertonic saline, saline...)

Treatment

4 general strategies in tx of hyponatremia



HYPOVOLEMIC
HYPONATREMIA

Restoration of
normal plasma volume
: **volume replacement**
→ N/S



HYPERVOLEMIC
HYPONATREMIA

Treatment of
underlying disease,
water restriction,
VRA



EUVOLEMIC, ACUTE
SYMPTOMATIC

Quickly Restoration
of S.Na
: rapid removal of
water (**hypertonic
saline**),
water restriction



EUVOLEMIC, CHRONIC
ASYMPTOMATIC

Slow Restoration of
S.Na
: slow removal of
excess water,
water restriction,
VRA

Treatment

Treatment of chronic hyponatremia

- slow correction rate

- : S Na < 8-10 mM in first 24 hrs, < 18 mM in first 48 hrs

Vasopressin antagonist (vaptans: tolvaptan)

- : highly effective in treating SIADH and

- hypervolemic hyponatremia d/t heart failure or cirrhosis

- : no role in acute hyponatremia

Treatment complication

Osmotic demyelination syndrome (ODS)

- by **rapid correction of serum Na level**
(> 8-10mM in 24 hrs or 18 mM in 48 hrs)
- demyelinating lesion of brain, **pons**
- most have debilitating disease
such as *malnutrition, alcoholism*
- 3 risk factor
 - : S Na at presentation(**S Na < 120 meq/L**),
duration(**more than 2-3 days**),
rate of correction (**S Na 8-10 meq/L or more in 24 hrs**)

Treatment complication

Osmotic demyelination syndrome (ODS)

Clinical characteristics

- occur **several day**(after 2 – 6 days)
after too rapid hyponatremia correction
- para-quadruparesis, dysphagia,dysarthria,diplopia,
locked in syndrome,LOC
- poor prognosis, Prevention is important

SIADH(Syndrome of Inappropriate ADH, SIAD)

- Is a disorder of impaired water excretion caused by inability to suppress secretion of ADH
- Is the **most common cause of euvolemic hyponatremia**

Pathophysiology

Persistent **ADH** activity

+

H_2O



Water retention
Increased TBW



P osmolality
Plasma Na



ECFV expansion ?



Urine Na excretion
with **U Na > 40 meq/L**

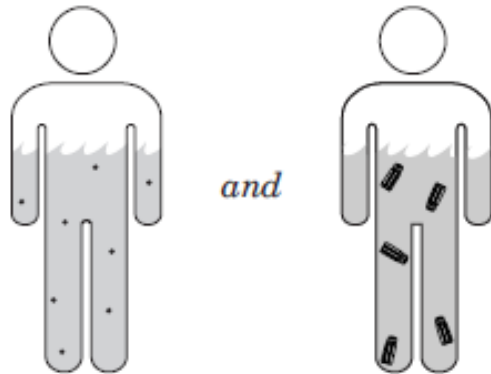


combination of water retention and
secondary solute (sodium plus potassium) loss

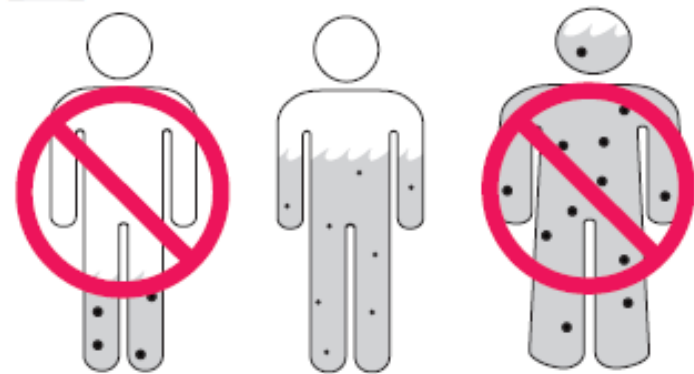
SIADH

4 characteristics of SIADH

1 HYPOTONIC HYPONATREMIA



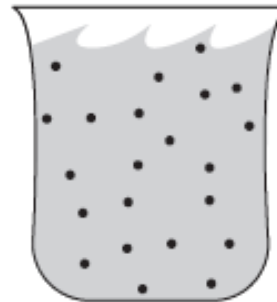
2 EUVOLEMIA



3 HIGH URINE SODIUM CONCENTRATION



4 HIGH URINE OSMOLALITY



Common etiologies of SIADH

1. Malignant neoplasia

- **SCLC(75% in SIAD of cancer)**
- lymphoma, leukemia

2. CNS disorder

- tumor, infection, trauma, porphyria

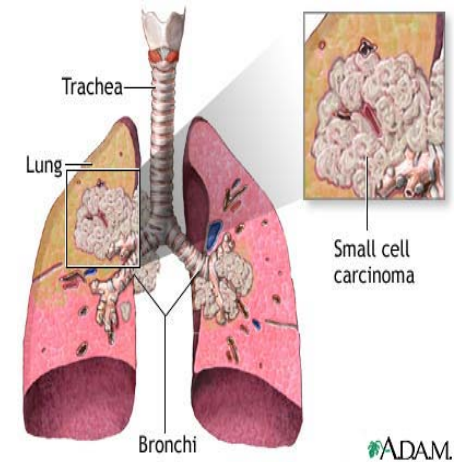
3. Drug

- SSRI
- chlorpropamide, vincristine, carbamazepine, clofibrate
- CPM, desmopressin, oxytocin

4. Pulmonary disease

- tuberculosis, pneumonia, lung abscess
- ventilator with positive pressure

5. Others (Idiopathic)



Criteria for the diagnosis of SIADH

1. decreased plasma osmolality (< 275 mosm)
2. inappropriate urinary concentration
 - **U osm > 100 mosm** with normal renal function
3. elevated **urinary sodium excretion**(**U Na > 40**)
4. clinical **euvolemia**
 - absence of sign of hypovolemia
5. absence of other potential cause of euvolemic hypoosmolality
 - **hypothyroidism, hypocortisolism**, diuretic use
6. others finding : hypouricemia(< 4 mg/dl)

Treatment

- Three treatment
 1. tx of underlying disease
 2. initial therapy to raise S. Na
 3. prolonged therapy
- **Fluid restriction** : mainstay of therapy (< 800 ml/day)
- **Vasopressin receptor antagonist** (V2 R antagonist)
: IV conivaptan and oral tolvaptan
- NaCl (oral or IV saline)
- Demeclocycline or lithium

HYPERNATREMIA

Definition

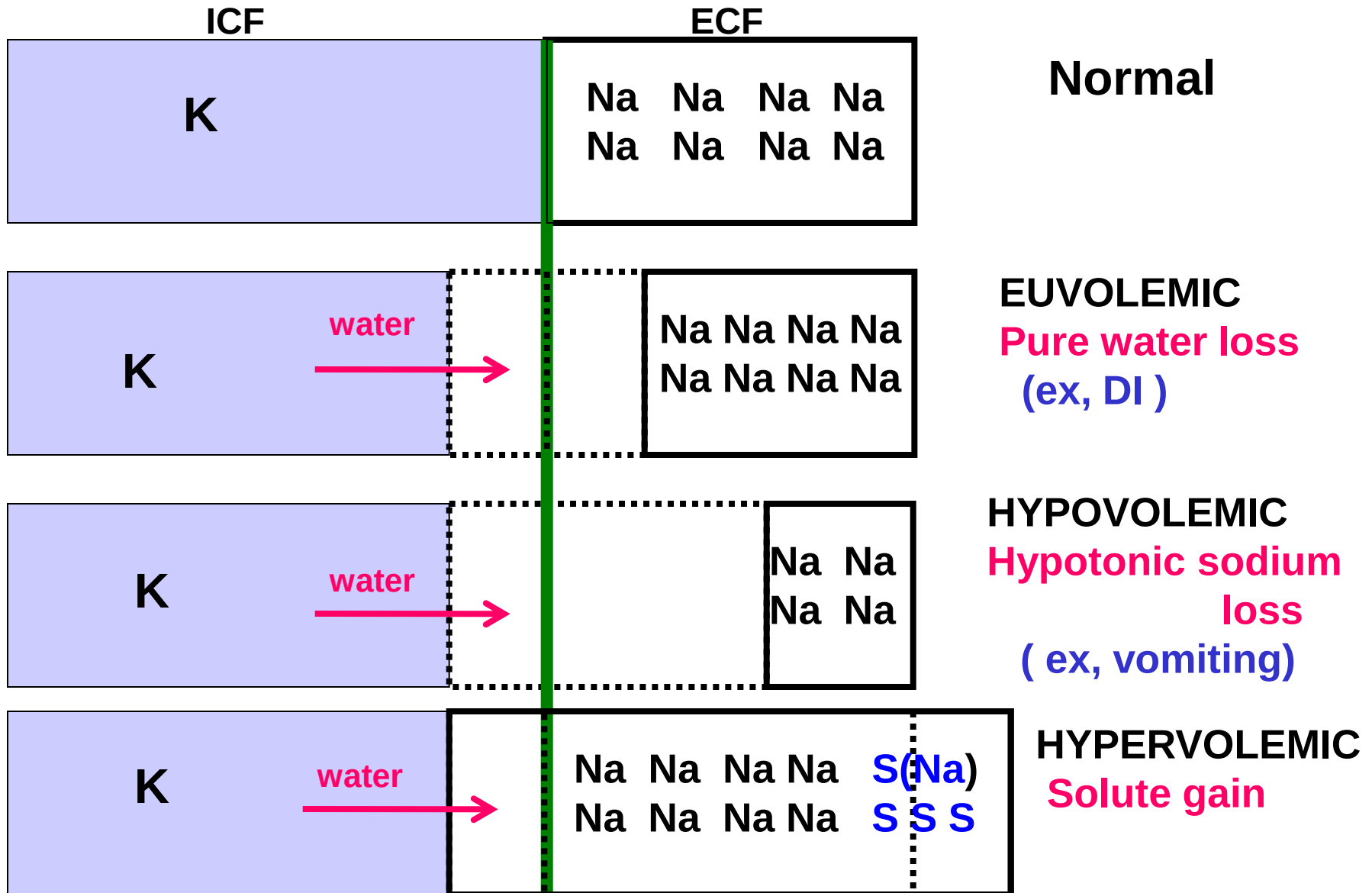
S. Na > 145 mEq/L

→ always hypertonic state

**Hypernatremia is a less common
than Hyponatremia**

Pathogenesis

State of hypernatremia



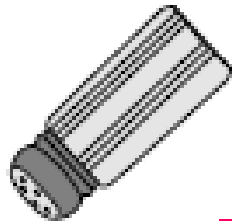
Development of hypernatremia

2 step process

1 *Generation*

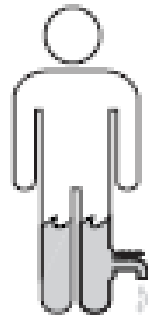
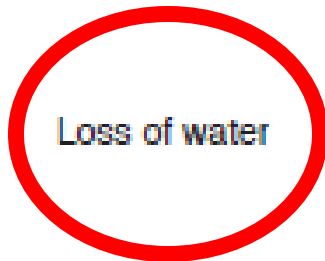
Factors which
predispose to hypernatremia

Gain of sodium



or

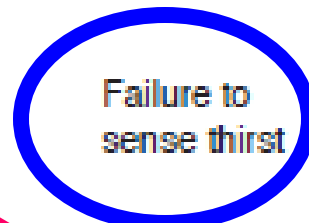
Loss of water



2 *Maintenance*

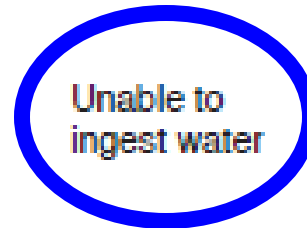
Factors which
interfere with thirst

Failure to
sense thirst



or

Unable to
ingest water



Causes

1. euvolemic hypernatremia (pure water loss)

- extrarenal loss
 - : **fever**
- renal loss
 - : central DI, nephrogenic DI
- others
 - : inability to gain access to fluid



2. hypovolemic hypernatremia (water deficit > Na deficit)

- extrarenal loss
 - : **diarrhea, vomiting**
- renal loss
 - : **osmotic diuresis, loop diuretics**

3. hypervolemic hypernatremia (Na gain > water gain)

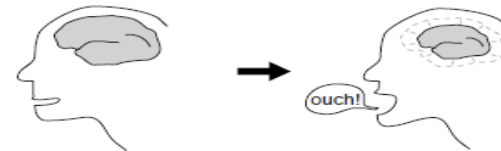
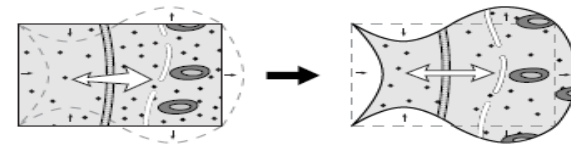
- : hypertonic saline, mineralocorticoid excess

Clinical manifestation

*Elderly patient with reduced thirst and
diminished access to fluid
→ highest risk of developing hypernatremia*

Symptoms of hypertonicity

→ are referral to CNS
(**contracted ICF volume**)



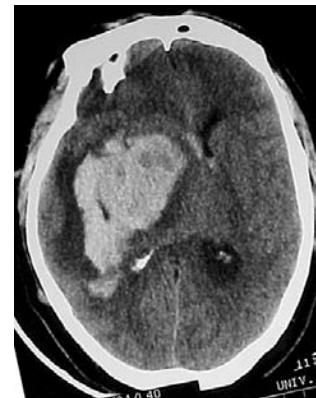
major symptoms are **neurologic symptoms**

: somnolence, confusion, coma

: respiratory paralysis, death

brain cell shrinkage

is associated with risk of **SAH or ICH**



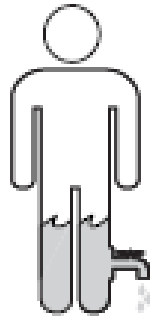
Diagnosis

Question 1

What predisposed to hypernatremia?



addition of sodium



loss of water

Water loss

Question 2

Why isn't the patient drinking water?



- infant who cannot ask for water
- older patient with mental status changes
- no access to water

Treatment

Main component of treatment

- 1. Treat underlying disorder**
- 2. Correct the abnormality in ECF volume**
- 3. Replace the water deficit**
- 4. Provide maintenance fluid**

Treatment

Main component of treatment

1. Volume replacement

- N/S initially IV

2. Replacement of water deficit(half N/S, 5%D/W)

- rapid correction of hypertonicity to normal S.osmolality
is hazardous and may cause brain edema
- slowly correction over 48 – 72 hrs
in severe hypernatremia(S.Na > 160 mM)
: correction rate < 10 mM/day

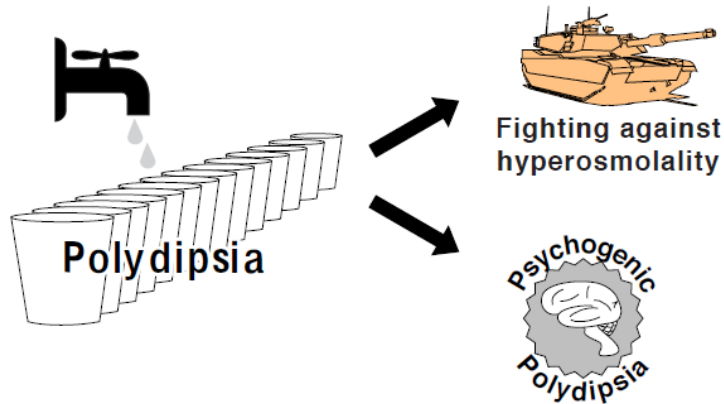
3.Underlying disease control(AVP, thiazide in DI)

POLYDIPSIA, POLYURIA

Definition

Polydipsia

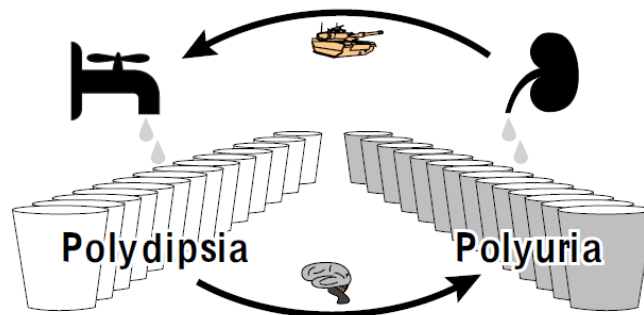
: is defined as increased thirst, intake



Polyuria

: increased UO (**3.0L/day**)

: can cause or result from polydipsia

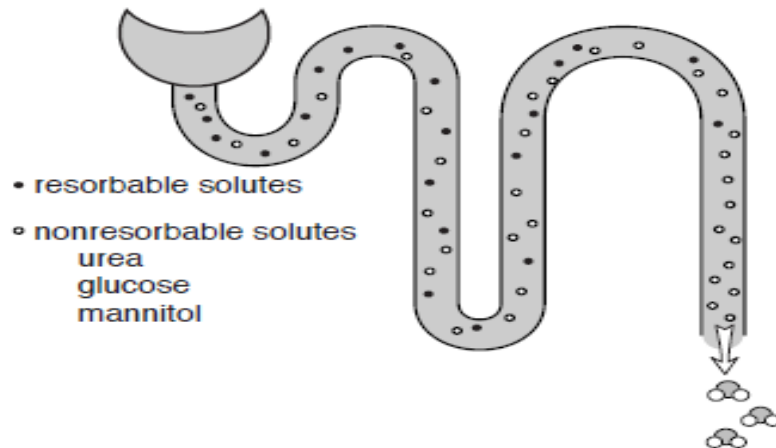


Polyuria

- U/O > 3 L/day

Two pathogenetic mechanism

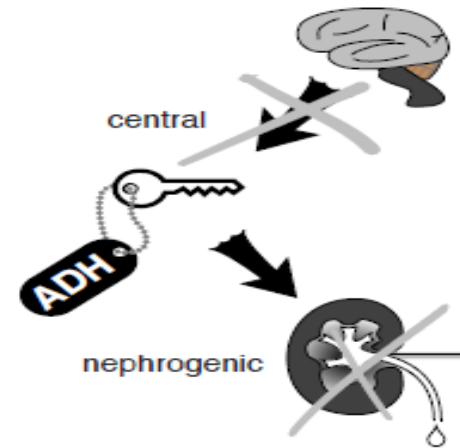
Osmotic diuresis



excessive urine solute excretion
(solute diuresis)

U.osmolality > 300 mosmol/L

Diabetes insipidus



abnormal urine concentration
mechanism (water diuresis)

U. osmolality < 250 mosmol/L

Cause

Solute diuresis

- excretion of nonabsorbable solute
 - electrolyte
 - : loop diuretics(sodium), DK(ketoanion)
 - non-electrolyte
 - : DK(glucose), renal glycosuria
 - : protein or amino acid loading, mannitol

Water diureis

- excretion of water
 - (usually defect in ADH production or renal responsiveness)
- DI
- polydipsia

Cause

Diabetes insipidus : central, nephrogenic

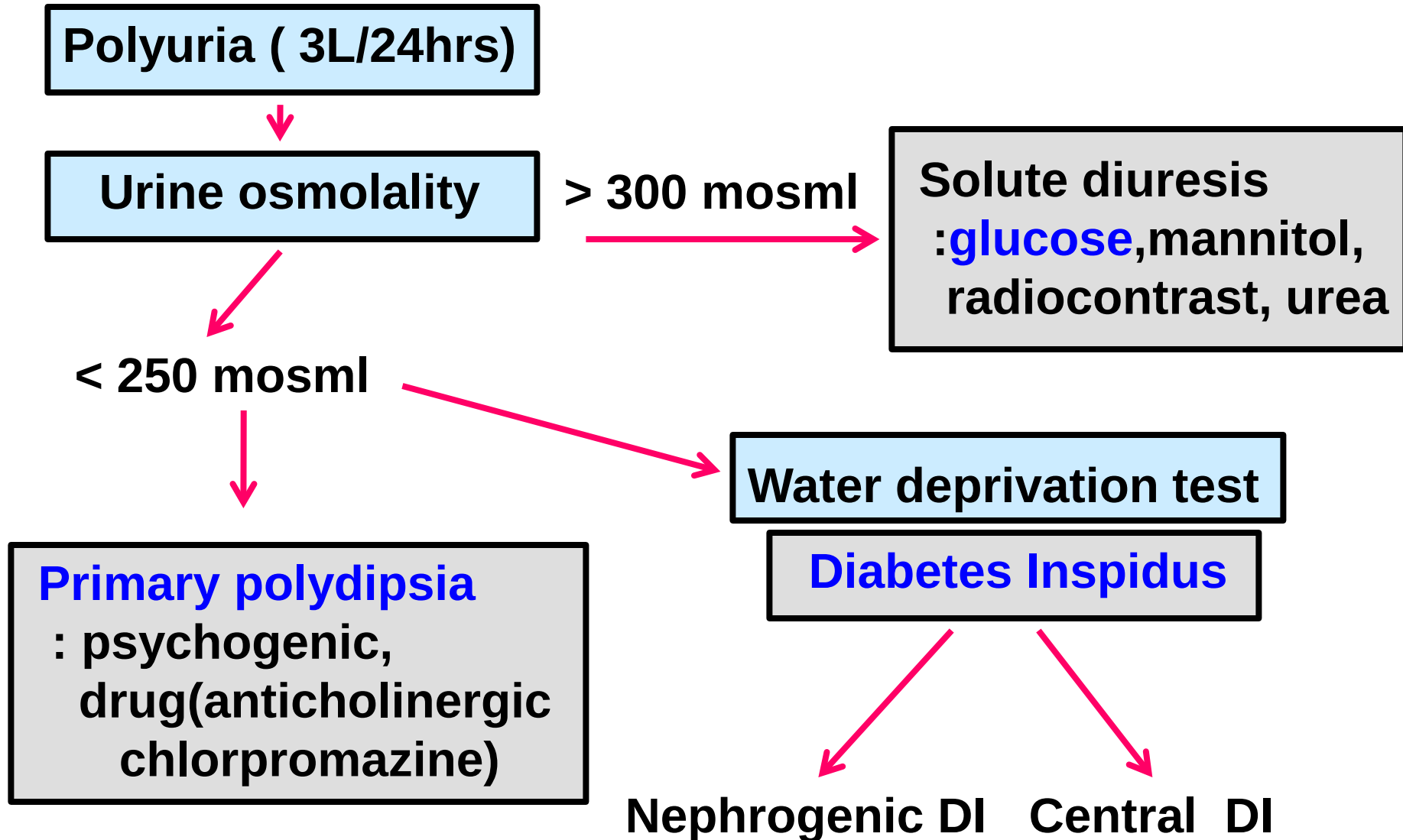


2. **nephrogenic**: no ADH response in renal tubule

- CT : lithium, demeclocycline, congenital
- HL : hypercalcemia, hypokalemia, loop diuretics

Polyuria

Evaluation



POTASSIUM DISTURBANCE

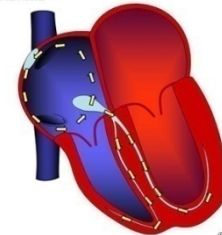
Potassium regulation

Potassium disorder

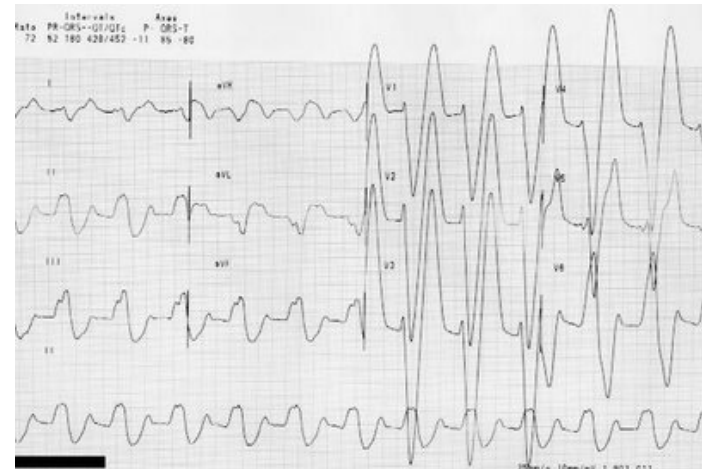
: Hypokalemia

: Hyperkalemia

Typical Atrial Flutter



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POTASSIUM REGULATION

INTRODUCTION

Major difference between Na and K

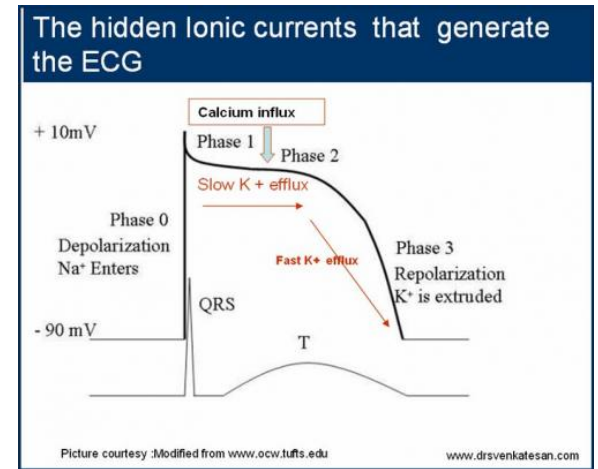
Na	K
- primary EC cation	- primary IC cation
- alteration in Na ⁺ con → osmotic movement of water	- alteration in K ⁺ con → electrical signal change
→ clinical sx is cerebral edema or dehydration	→ clinical sx is abnormal cardiac rhythm, muscle activity, nerve conduction

Introduction

Physiologic functions of K

1.electrical effect

- by ICF / ECF K concentration
- in cardiac myocyte
 - : K imbalance cause arrhythmia
- in skeletal muscle
 - : K imbalance cause muscle paralysis



2.enzymatic reaction(protein synthesis)

3.cell volume regulation

4.local mediator of vascular tone

in muscle beds

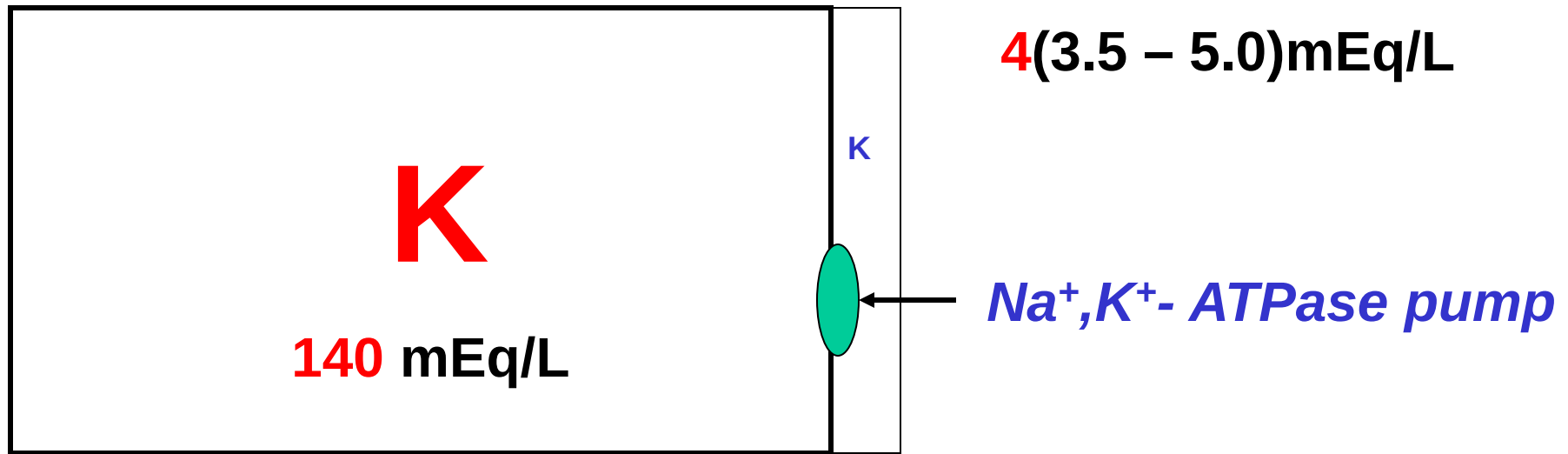
Body K distribution

Total 3500mEq in 70 kg Bwt(2500 - 4000)

→ 2% in ECF, 98 % in ICF (primarily in skeletal muscle)

ICF (98%)

ECF (2%, 56 (50-60) mmol)



**** Ratio of ICF to ECF K concentration**

→ crucial for normal neuromuscular function

**** Small change in plasma K**

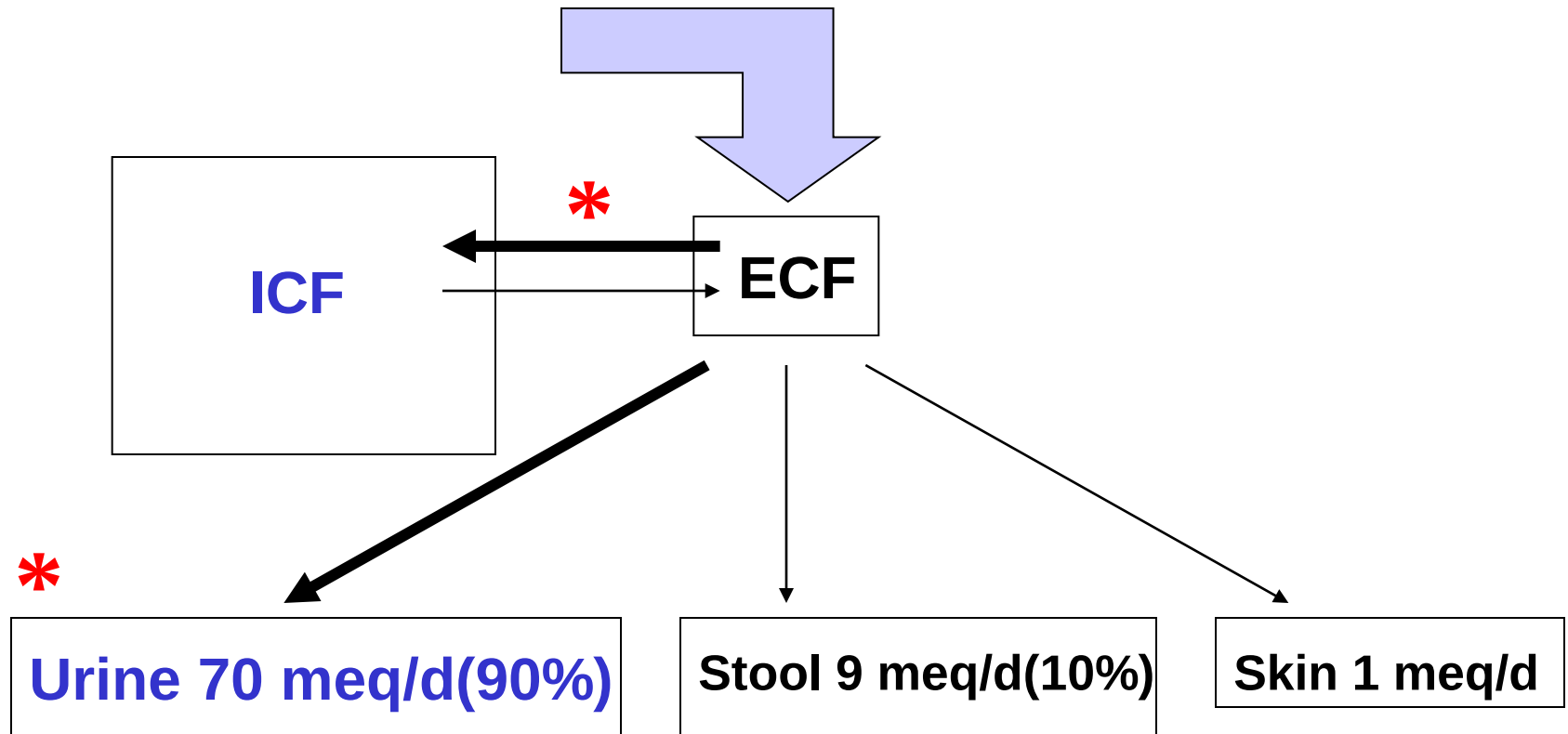
→ dramatic clinical problem

1% of ICF K movement to ECF → can **stop heart**

Regulation of serum K balance

Uptake and excretion of K

Diet K 80(50-100) meq/d

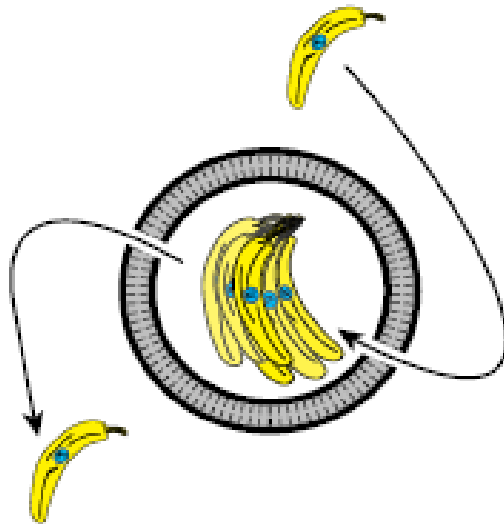


Regulation of serum K balance

K : maintained by cell and kidney

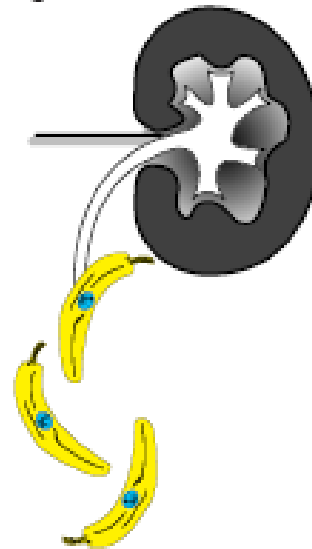
Intracellular buffering

immediate response



Renal regulation

long-term control



Cellular control of potassium movement is influenced by:

- catecholamines
- insulin
- plasma pH
- cellular synthesis
- cellular destruction
- plasma potassium

Renal potassium regulation is governed by:

- plasma potassium
- aldosterone
- flow in the distal nephron

Regulation of serum K balance

Internal and external balance

1. Internal balance

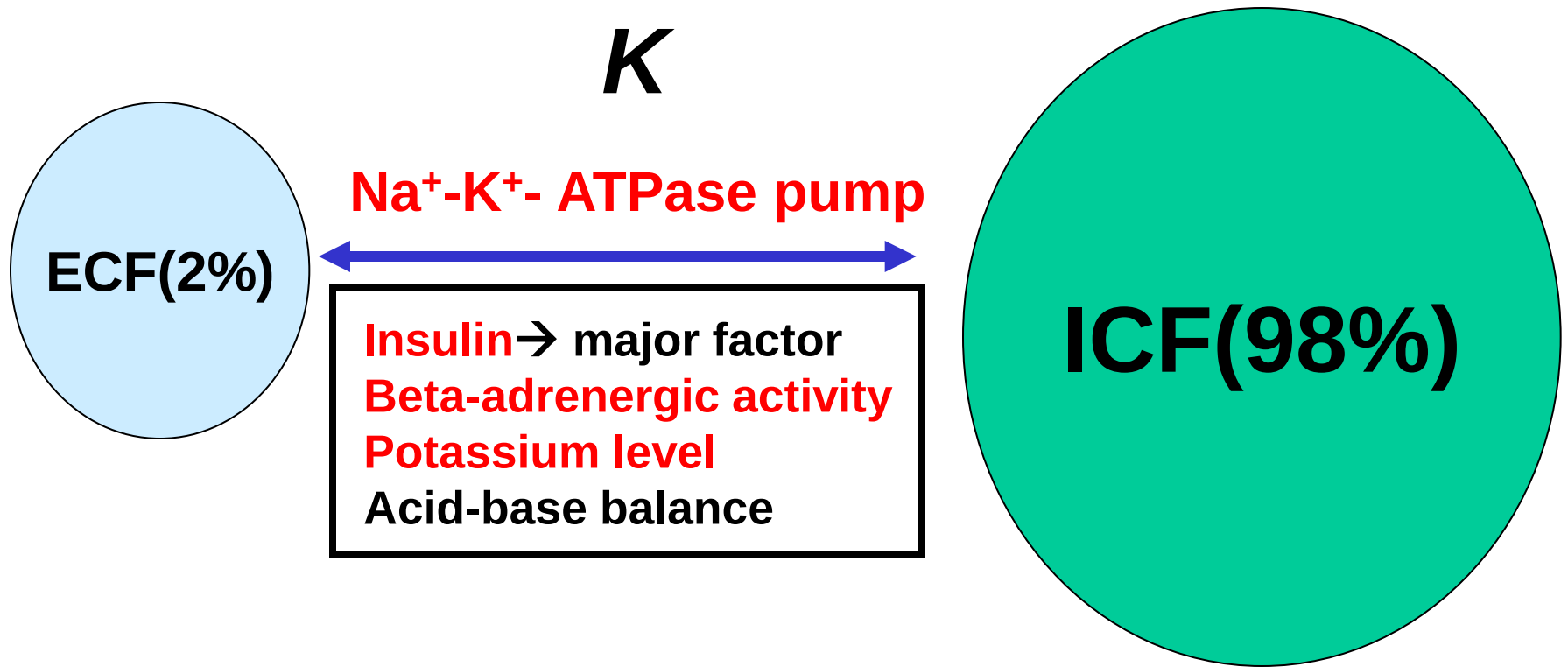
- : K exchange between intracellular and extracellular compartment
 - *important determinant of plasma K concentration*
- : serum K 1 mEq/L decrease → 300 mEq K loss
- : acutely increased serum K
 - prevented by cellular uptake

2. External balance

- : depend on dietary K intake and renal K excretion

Regulation of serum K balance

Internal K balance(cell)

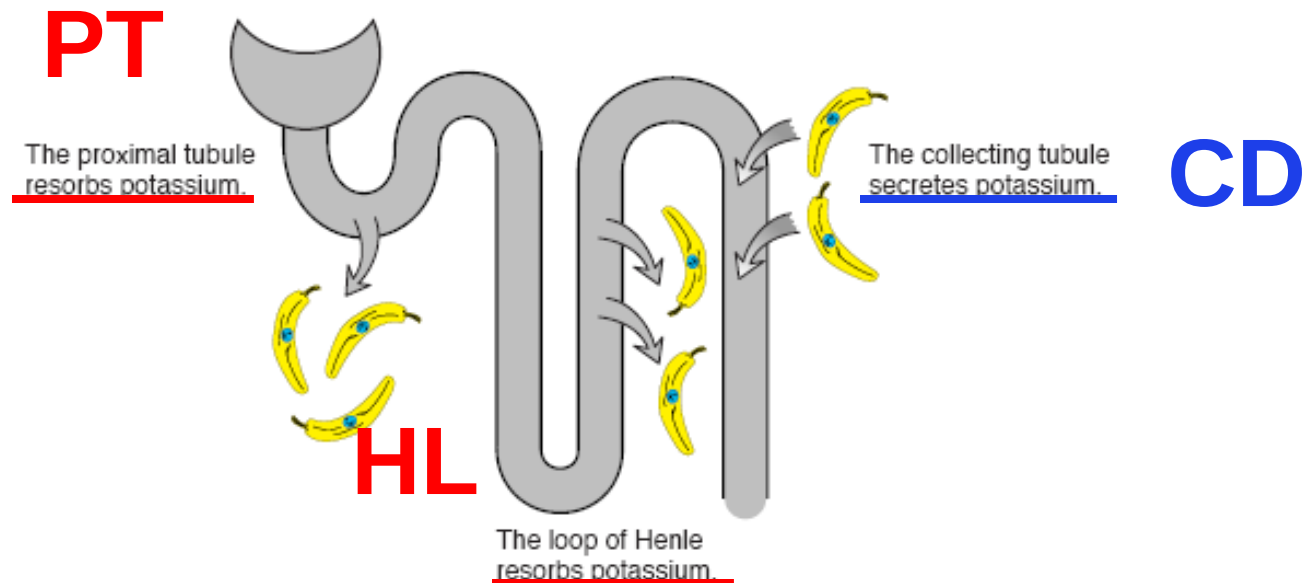


factor regulating internal K balance

Regulation of serum K balance

External balance(kidney)

longterm K control by **resorption** and
selective **secretion** of K



In PT : **K resorption** without regard for body K status

In HL : **K resorption** by Na-K-2Cl pump

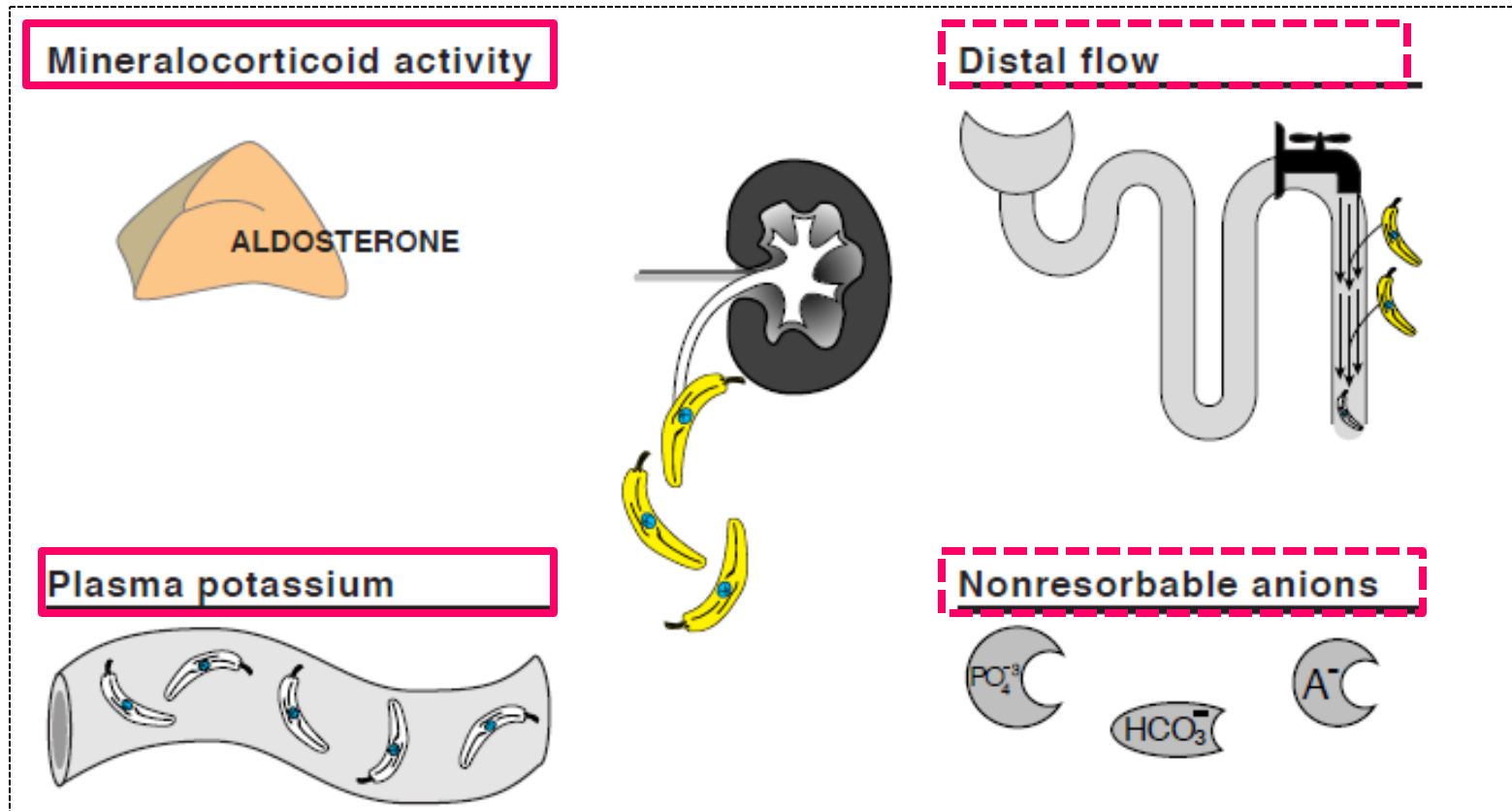
→90% resorption

In cortical CD : primary site of K regulation(**K secretion**)

Regulation of serum K balance

External K balance(Kidney)

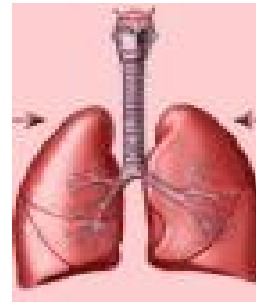
4 factors for K handling in **DN(CD)**



POTASSIUM DISORDER

Hypokalemia ($K < 3.5 \text{ mEq/L}$)

Hyperkalemia ($K > 5.0\text{-}5.5 \text{ mEq/L}$)



HYPOKALEMIA

Serum Potassium : < 3.5 mEq/L

Common clinical problem

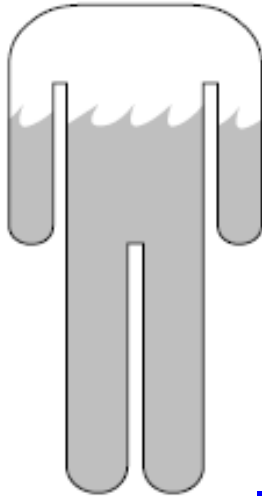
ETIOLOGY

DECREASED INTAKE



Uncommon

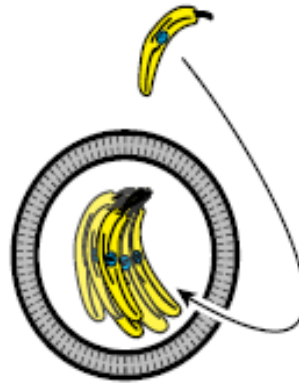
- alcoholic
- elderly



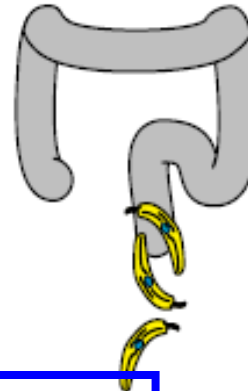
INCREASED LOSS

EXTRA-RENAL

RENAL



GI loss
- diarrhea



Renal loss
- diuretics
- primary hyperaldosteronism
- vomiting
- Bartter/Gitel syndrome

Movement into Cell
- insulin
- catecholamine
- alkalemia
- thyroid H

Etiology

I. Inadequate K intake

- Uncommon cause
- Most diet are rich in potassium
- Good renal response
 - : $U K < 5 \text{ mEq/day}$ in low K diet
- Uncommon hypokalemia in just low diet

II. K redistribution

- insulin
- catecholamine
- alkalemia
- **periodic paralysis**(familial, thyrotoxic)

II. K redistribution

Hypokalemic periodic paralysis

- movement of ECF K into cell cause paralysis
- rare disease, due to defect in voltage gated **Ca channel**
- autosomal dominant channelopathy

- Painless muscle weakness or paralysis
- Sx : begin in **rest after strenuous exercise**,
high carbohydrate meal,
meal with high sodium content, stress

- Tx: prevention of further attack
potassium oral or IV
in chronic disabling attack : acetazolamide

III. K loss

1. GI loss of K

- **Diarrhea** : M/C cause of GI K loss

2. Renal loss of K

1) increased distal flow

: **diuretics**, bartters/ gitelman's syndrome

2) increased secretion of potassium

: Increased mineralocorticoid activity

→ **primary hyperaldosteronism**, cushing's syndrome

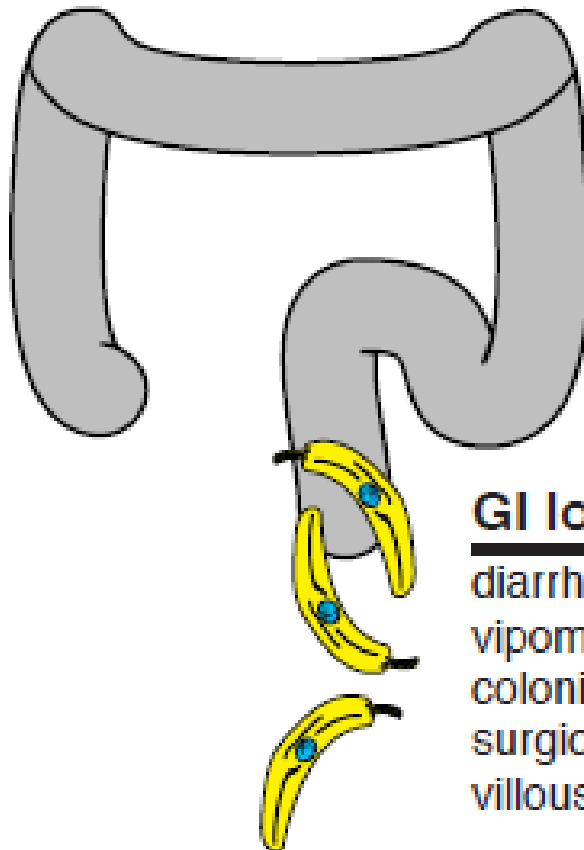
: Nonresorbable anion in distal tubule

→ **vomiting**, RTA

III.K loss

1. Gastrointestinal loss

Lower GI loss → Diarrhea : M/C cause of GI K loss



GI loss of potassium

diarrhea

vipoma

colonic fistulas

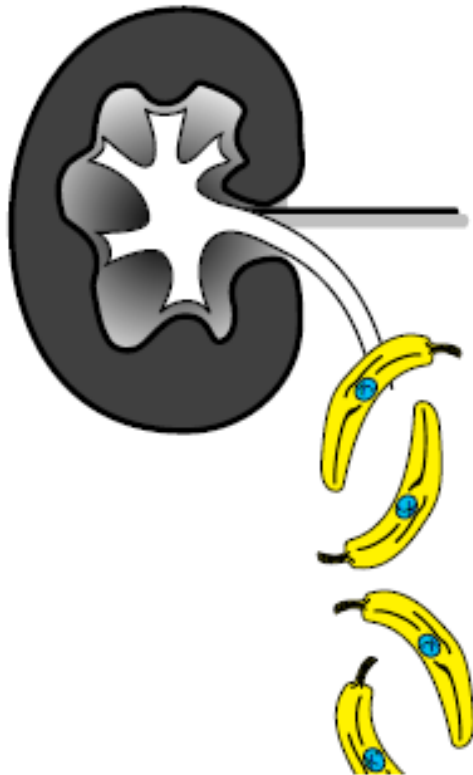
surgical drains

villous adenoma

III. K loss

2. Renal K loss

→ is M/C cause of clinically significant hypokalemia



Renal loss of potassium

Increased distal flow

diuretics

Bartter's syndrome

Gitelman's syndrome

Increased mineralocorticoid activity

primary hyperaldosteronism

Cushing's syndrome

congenital adrenal hyperplasia

hyperreninism

pseudohyperaldosteronism

Nonresorbable anions in the distal tubule

diabetic ketoacidosis

vomiting

renal tubular acidosis

penicillin derivatives

toluene

III. K loss

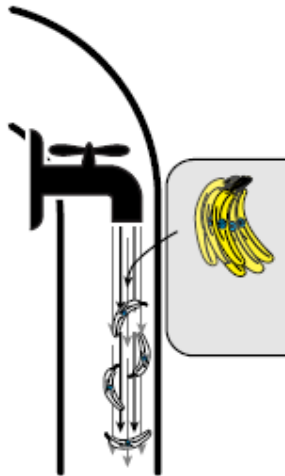
2. Renal K loss

: increased distal flow

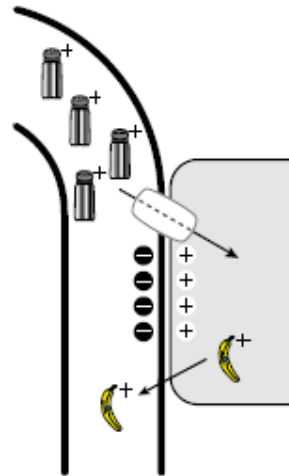
loop and thiazide diuretics

→ Increased distal flow

→ increase renal K excretion



Increased flow of fluid quickly washes away secreted potassium to maintain the concentration gradient.



Increased delivery of sodium increases sodium resorption and enhances the electrical gradient.

Etiology

III. K loss

2. Renal K loss

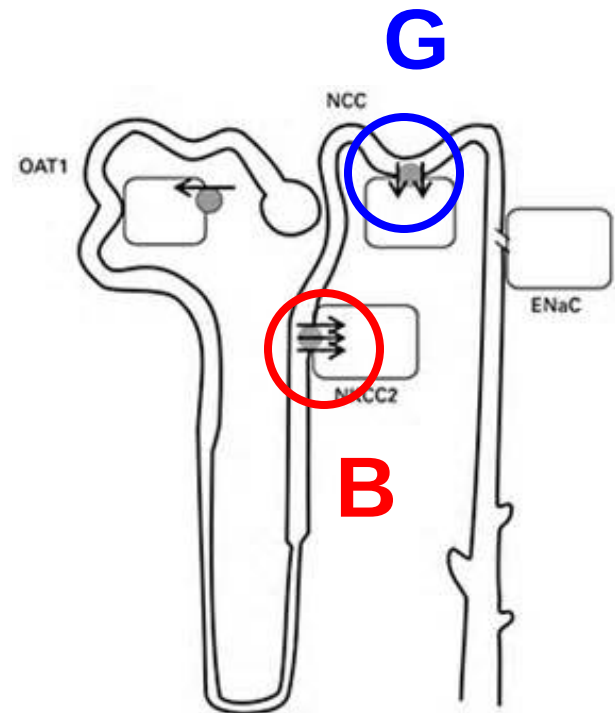
: increased distal flow

Bartter's syndrome

: incomplete reabsorption of NaCl
in thick ascending Limb
(lasix ?)

Gitelman's syndrome

: incomplete reabsorption of NaCl
in distal CT
(thiazide ?)

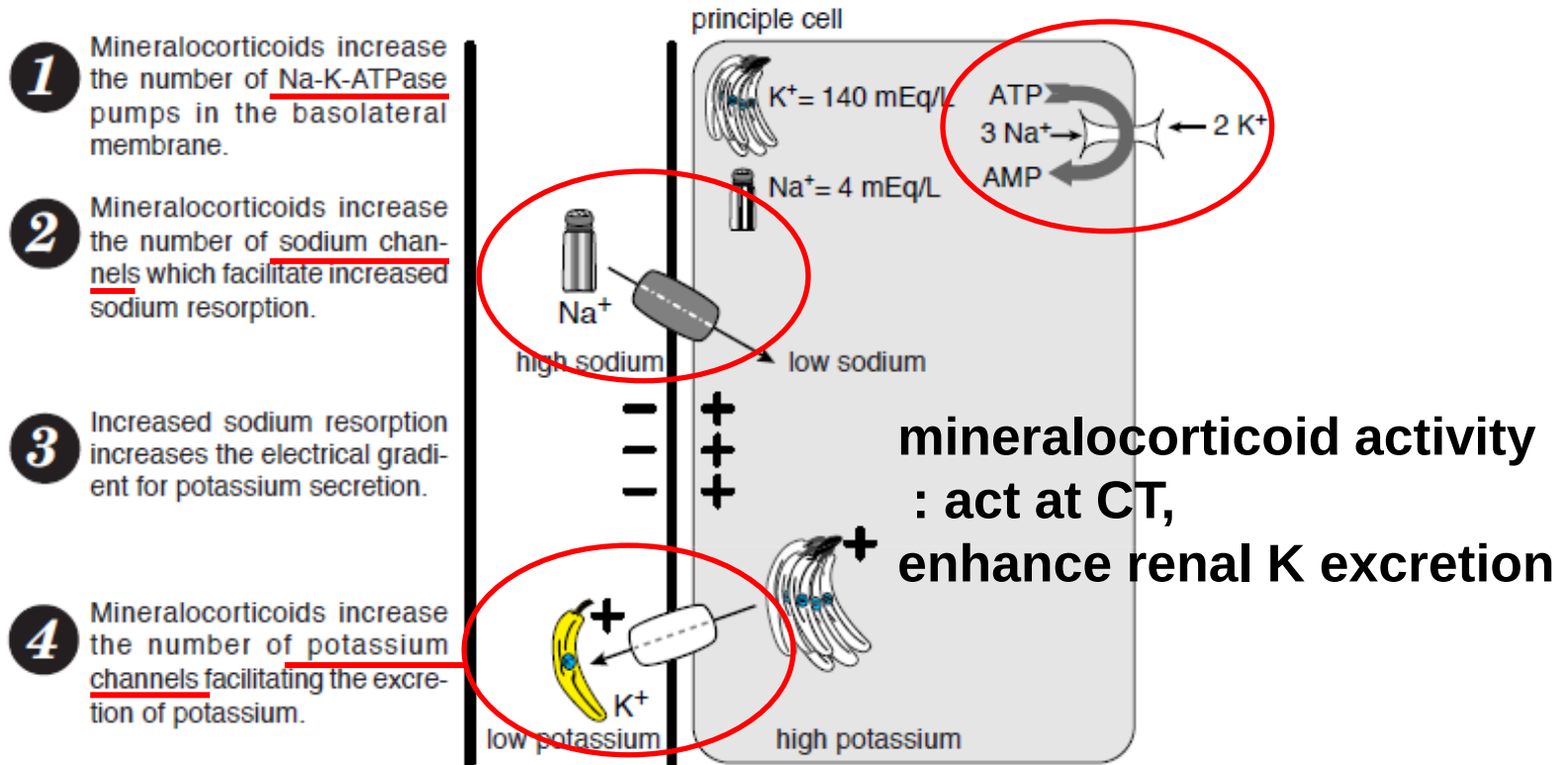


III. K loss

2. Renal K loss

:Increased mineralocorticoid

Primary hyperaldosteronism



Etiology

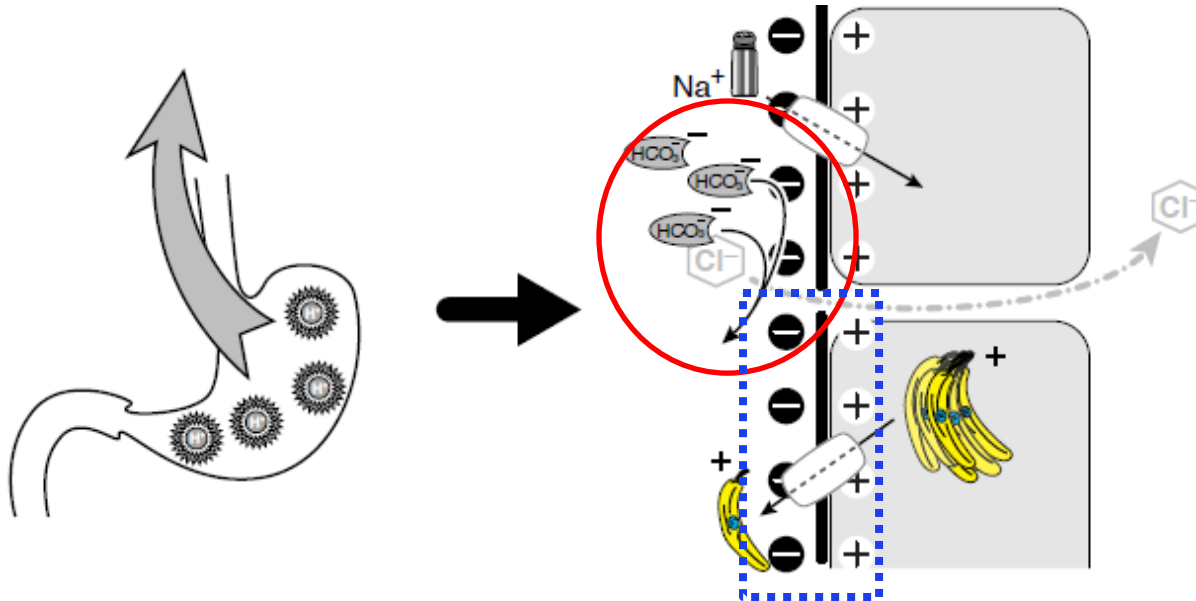
III. K loss

2. Renal K loss

:Increased anion in tubule

Vomiting

: Hypokalemia due to renal K loss



Hypokalemia in vomiting

: due to increased bicarbonate in DN from M.alkalemia

Clinical manifestation

The **most serious disturbance** is

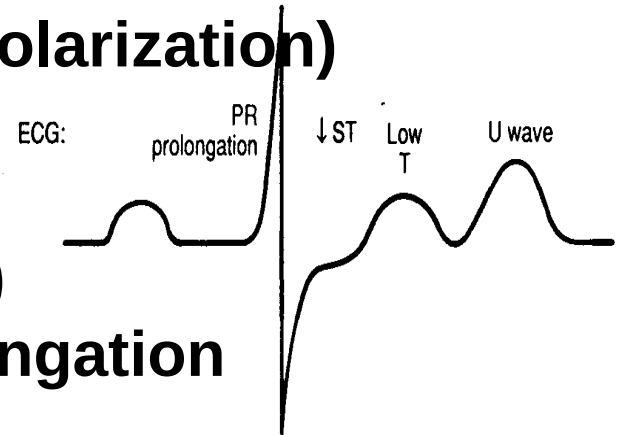
→ neuromuscular system disturbance
(cardiac, skeletal, intestinal muscle)

Symptoms occur < 3.0 mmol/L

Fatigue, myalgia, M weakness of lower extremity
Progressive weakness, hypoventilation, paralysis

Cardiac arrhythmia (delay in repolarization)

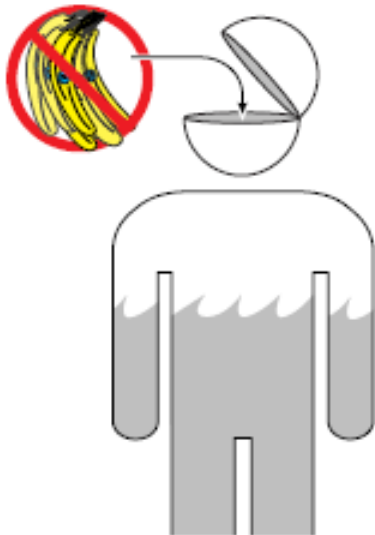
- : usually in serum K < 3.0 mmol/L
- : EKG abnormality (K < 2.7 mmol)
 - flat T, ST depression, QT prolongation
- : prone to tachyarrhythmia



Diagnosis

Good history

DECREASED INTAKE

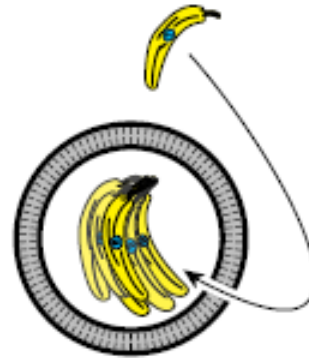


History of malnutrition:
anorexia
alcoholism
quick weight loss
liquid diets

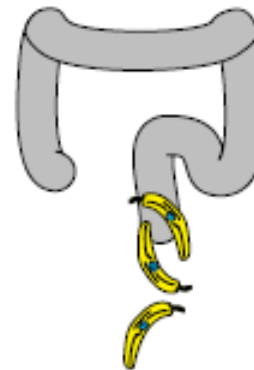
INCREASED LOSS

EXTRA-RENAL

24-hour urine potassium < 30 mEq



History of:
alkalemia
insulin use
beta agonists
periodic paralysis
delirium tremens



History of:
diarrhea
colonic fistulas
vipoma

RENAL



History of:
hypertension
weight gain
muscle weakness
striae

If unknown cause,
diuretic and laxative abuse should be considered

Diagnosis

Approach

Hypokalemia < 3.5 mEq/L

Potassium depletion

Redistribution
Inadequate intake

Urinary K excretion

Renal K loss

> 15 mEq/day or 15 mmol/gCr

< 15 mEq/day or mmol/gCr

Extrarenal K loss/
remote renal loss

lower GI K loss
(diarrhea, laxative)
remote diuretics
remote vomiting

assess K secretion (TTKG)

TTKG > 4

Increased distal
K secretion

Blood Pressure

Low or Normal BP

RTA
Diuretics
(loop/thiazide)
vomiting
G/B syndrome

TTKG < 2

Tubular flow
increase

Osmotic
diuresis

High BP

High aldosterone
- PA
- RAS
Low aldosterone
- Cushing's syndrome

TTKG → TransTubular K concentration Gradient

- rapid and simple test designed to evaluate the driving force for **net K secretion**
- $TTKG = \frac{K \text{ in CCD}}{K \text{ in plasma}} = \frac{\text{Urine K}}{\text{plasma K}} / (U \text{ osmolality} / P \text{ osmolality})$
- normal value in regular diet → 8 - 9
- in Hyperkalemia
 - : normal response → $TTKG > 7 - 8$
 - : $TTKG < 7$ → indicate mineralocorticoid deficiency
- in Hypokalemia
 - : **normal response** → $TTKG < 3$
 - : $TTKG > 4$ → indicate **increased distal K secretion**

Treatment

Goal of therapy

- prevent life threatening and / or chronic consequence
- replace associated K deficit
- correct underlying cause and or mitigate future hypokalemia

Degree of K depletion

: decrement of 0.27 mmol/L in plasma K
→ total body K deficit is 100 mmol mmol

K replacement

1. Oral K replacement

- is safe
- KCl capsule

2. IV therapy($K < 3.0$)

- K preparation
 - KCl is the salt of choice for IV K replacement
- **protocol of IV K replacement(mixed in N/S)**
 - 1) concentration : K **20 - 40 in PV,**
– 60 in CV (mEq/in N/S L)
 - 2) rate : IV no more than **10 - 20 mEq /hr**
 - 3) total K not exceed **200 - 250 mEq/day**

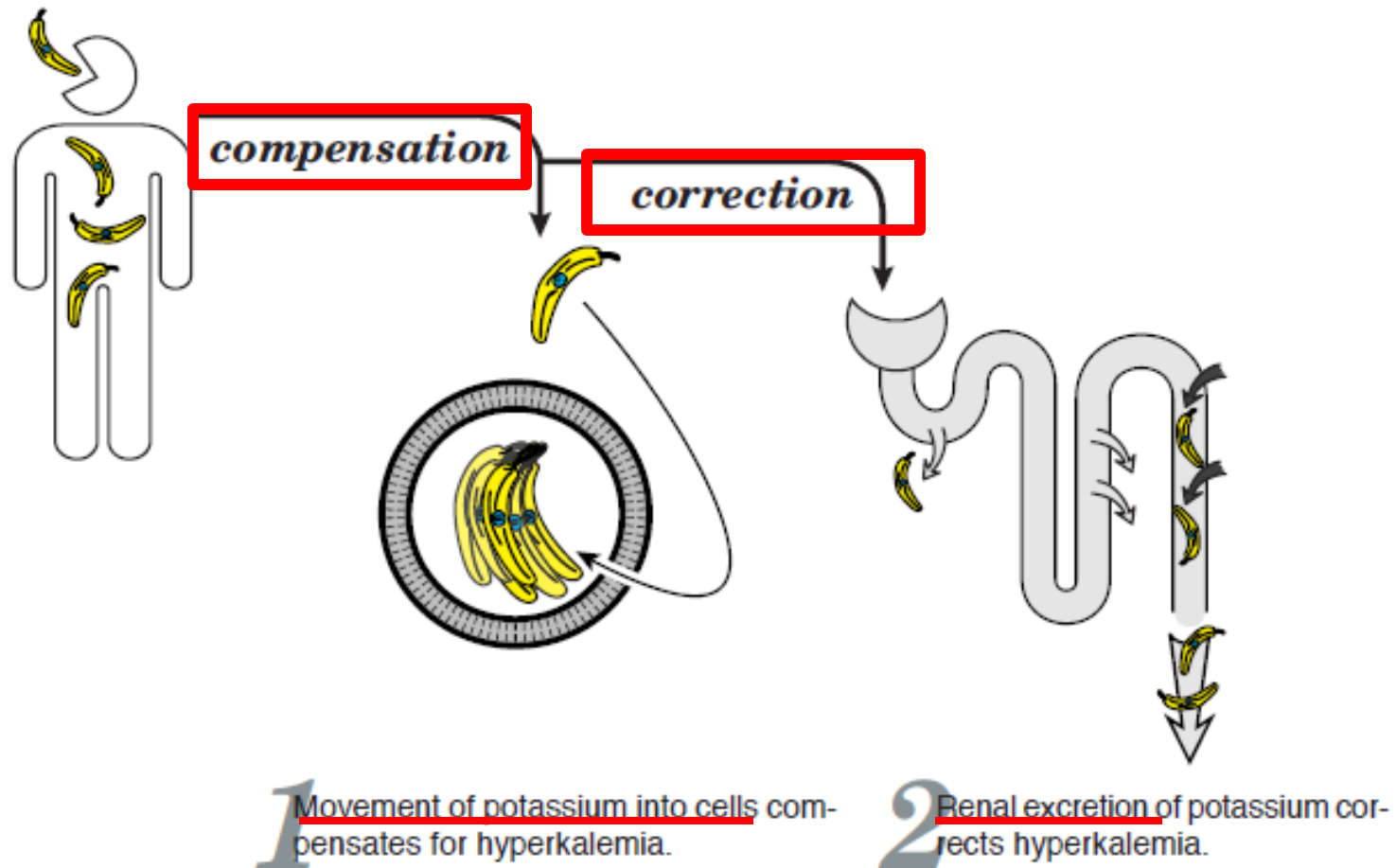
HYPERKALEMIA

Serum Potassium > 5.0 - 5.5 meq/L

- common complication of renal failure
- in absence of renal failure
→ hyperkalemia is uncommon
and check systemic Ds

Introduction

Two step defence against hyperkalemia

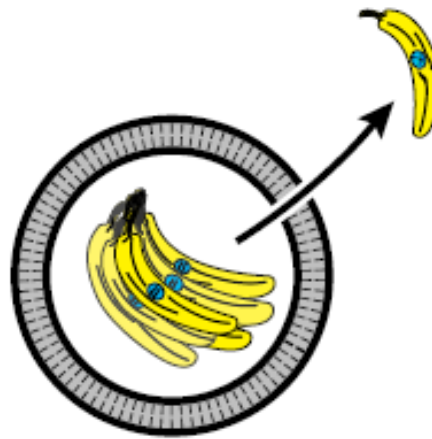


ETIOLOGY



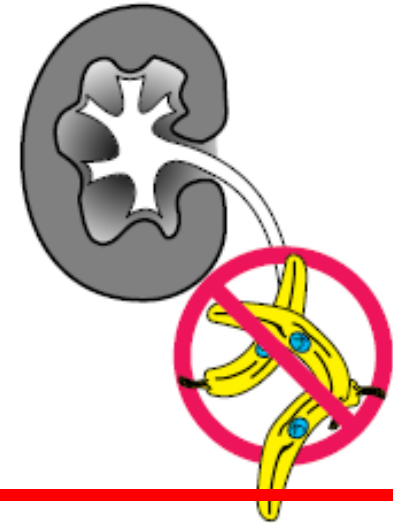
increased intake

- Blood transfusion
 - Penicillin G
 - Maintenance fluid
- * Uncommon
but significant
in renal insufficiency



movement out of cells

- Cell death
(trauma, hypothermia)
- Metabolic acidosis
- Lack of insulin
- Med
(beta-blocker, digoxin)
- severe exercise



impaired renal excretion

- Renal failure
- hypoadosteronism

Etiology

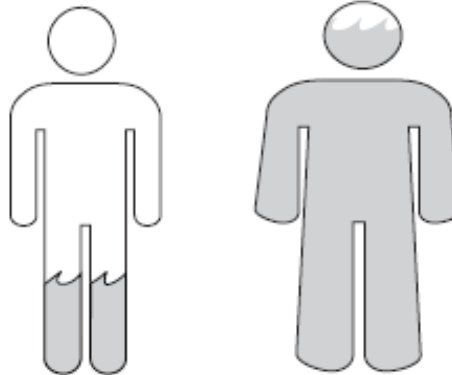
Decreased renal excretion

3 causes

Renal failure



Effective volume depletion



Hypoaldosteronism



ECV depletion alone dose not cause hyperkalemia,
but can be contributing factor

Decreased renal excretion

Acute and chronic kidney disease

1. Acute kidney injury

: most prevalent in oliguric patients

2. Chronic kidney disease

**: ability to excrete potassium at near-normal levels
until severe impaired GFR(**GFR < 10ml/min**)**

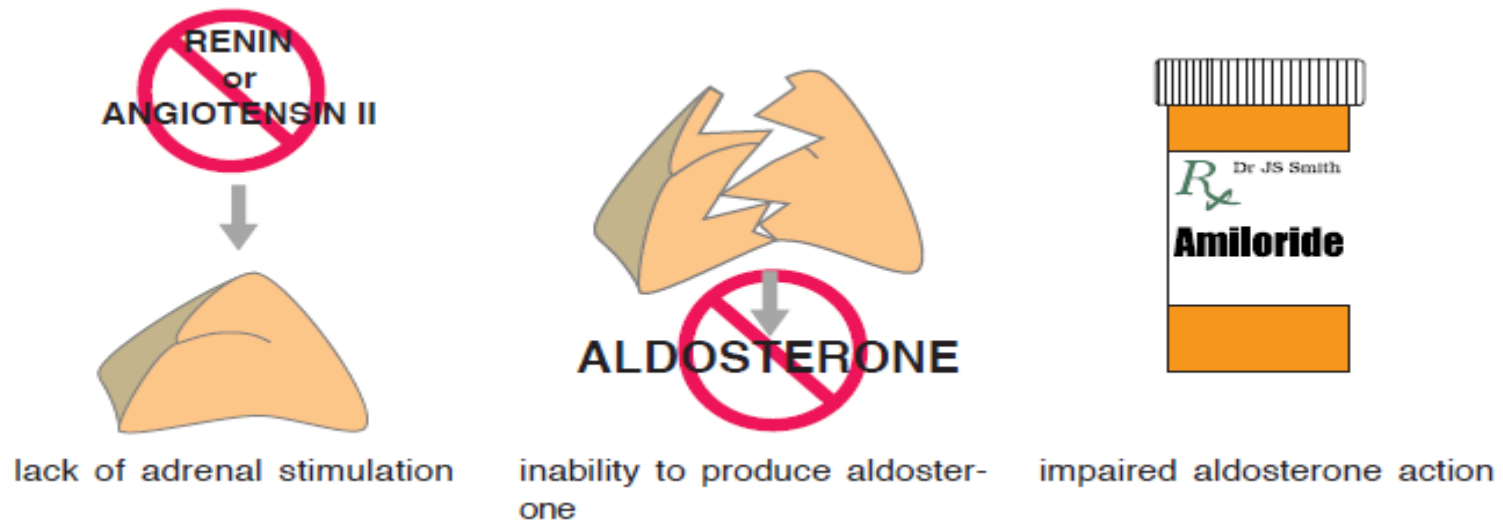
**: Hyperkalemia is most commonly seen
in patients who are oliguric or
in high K diet, increased tissue breakdown,
reduced aldosterone secretion or responsiveness**

Etiology

Decreased renal excretion

Hypoaldosteronism

- 3 type



Hyporeninemic hypoaldosteronism

- **DM**, renal failure

Medication that **block release of aldosterone** from adrenal gland

- **NSAID, ACEI, ARB**, cyclosporine

Primary
adrenal insufficiency

K sparing diuretics
(**spironolactone**,
amiloride,
triamterene)

Etiology

Drug associated with Hyperkalemia

Med that interfere with urinary K excretion

- **ACEI, ARB**
- **K sparing diuretics (amiloride, spironolactone)**
- **NSAIDs**
- **calcineurin inhibitor(cyclosporin, tacrolimus)**
- **trimethoprim**
- **pentamide**

Excessive release from cell

- **beta blocker, digoxin overdose, succinylcholine**

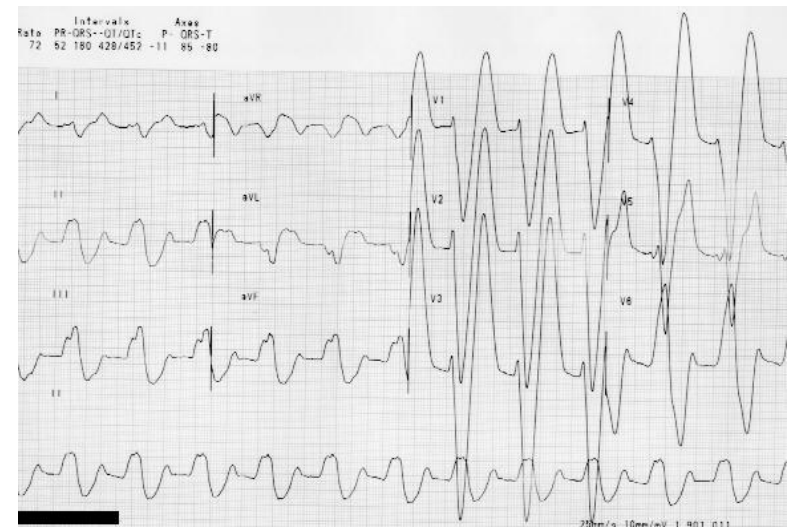
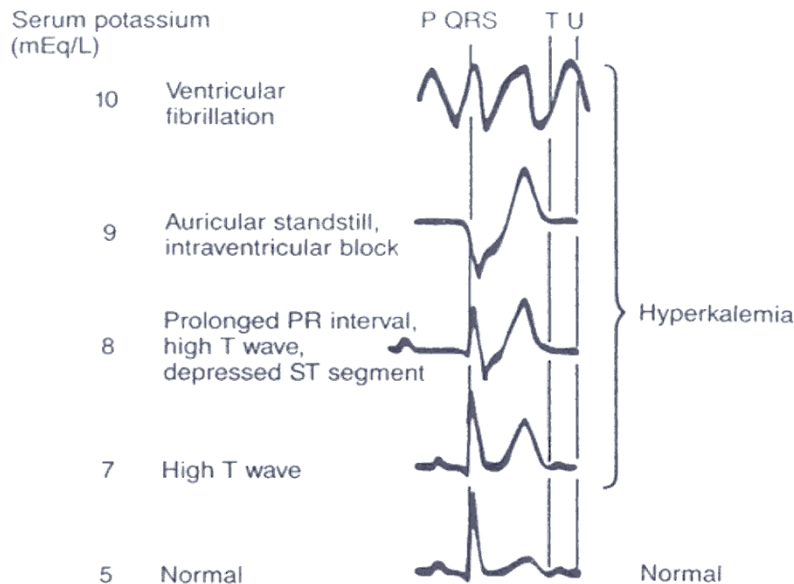
Others

- **heparin**

Clinical manifestation

Cardiac excitability alteration(cardiac arrhythmia) (rapid repolarization)

- is the most important clinical manifestation
- usually in serum K > 6 mmol/L
- **EKG** is the single most important guide
in appraising the threat,therapeutic approach



Diagnosis

Exclude pseudohyperkalemia,
transcellular K shift,
renal failure
Stop NSAIDs and ACE inhibitors

Assess K secretion(TTKG)

TTKG < 5

Reduced distal K
secretion(GFR> 20ml/min)

Response to fludrocortisone

TTKG > 8

Low aldosterone

DM, T1Ds
primary adrenal insufficiency
ACEI/ARB,b-blocker,NSAIDs

TTKG > 8

Reduced tubular fluid

Decreased ECBV
Advanced kidney
failure(GFR< 20ml/min)

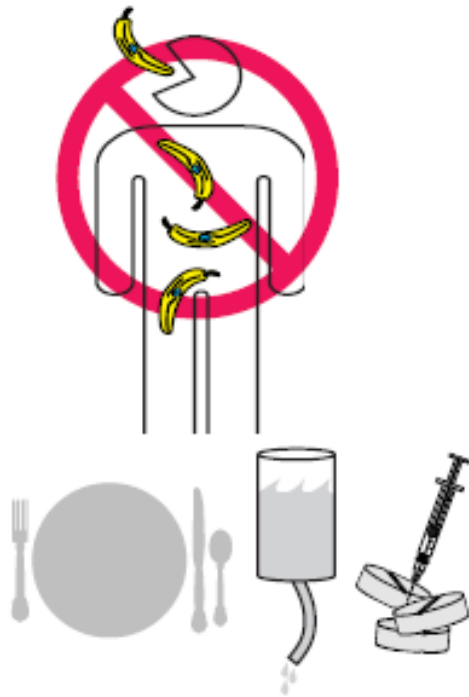
TTKG < 8

Tubular resistance

amiloride, triamterene,spironolactone
T1Ds, UTO,SLE, PHA

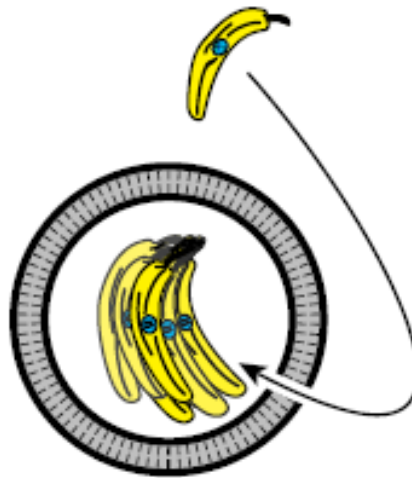
Treatment

1 Stop all potassium intake.



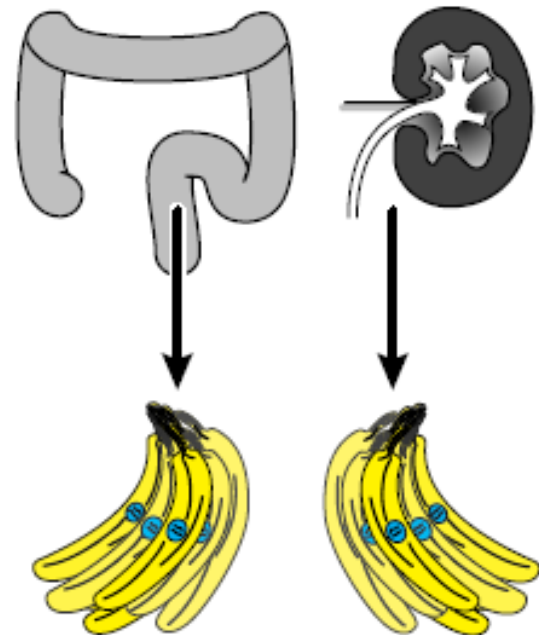
+ calcium

2 Compensation: promote the shift of plasma potassium into cells.



Insulin and glucose
Sodium bicarbonate
Beta 2 agonist

3 Correction: Remove potassium from the body via the kidney, colon and/or dialysis.



Cation exchange resin
Dilaysis
Loop diuretics in In normal renal function

Maneuver for K removal

1.Promote transfer of K from ECF to ICF

: insulin

beta 2 agonist (albuterol)

sodium bicarbonate

- no role in routine Tx

- may use in metabolic acidosis

2.Potassium elimination from the body

: diuretics

cation exchange resin(sodium polystyrene sulfonate)

dialysis

Treatment

Three stage in urgent treatment of hyperkalemia

1. Immediate antagonism of cardiac effect of hyperkalemia

: in severe hyperkalemia(EKG change, $K > 7 \text{ mEq/L}$),

calcium raise the action potential threshold and
reduce excitability

- 10% calcium gluconate
10ml IV over 2-3 min



2. Rapid reduction in plasma K by redistribution into cell

: **insulin** RI 10 U and 50% D/W 50 ml IV

3. Beta 2 agonist (albuterol) inhalation

: **albuterol** 10-20 mg in N/S 4ml over 10 min

: use with insulin therapy

ACID – BASE BALANCE

I. Acid base regulation

II. Acid base disorders

- Metabolic acidosis**
- Metabolic alkalosis**
- Respiratory acidosis**
- Respiratory alkalosis**

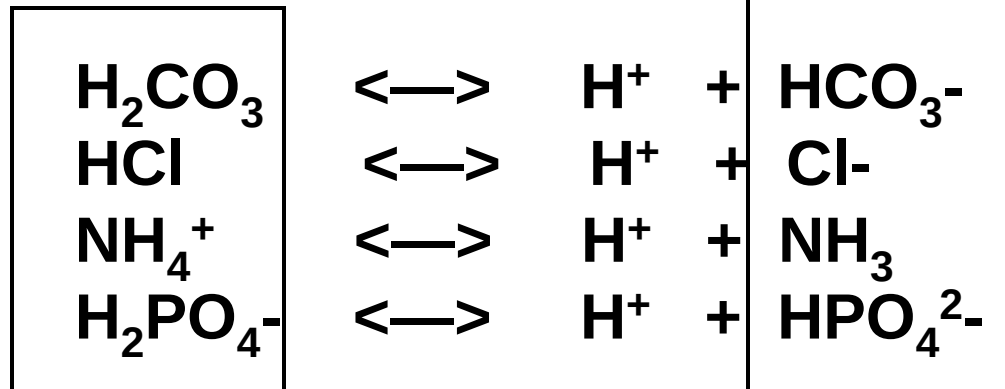
Introduction

Acid and Base ?

Acid is a substance that can donate **H⁺ ions**

Base is a substance that can **accept H⁺ ions**

→ H₂CO₃, HCl, NH₄⁺, and H₂PO₄⁻ all can act as acids



Acid

Base

Introduction

What is acid base balance ?

→ Hydrogen ion (H^+) control

Normal ECF H^+ concentration at pH 7.40 : 40 nEq/L

$$\text{pH} = -\log [H^+]$$

$$H^+ = 24 \times P\text{co}_2 / \text{HCO}_3$$

$$\text{pH} \rightarrow 6.1 + \log [\text{HCO}_3] / 0.03 P\text{co}_2$$

(Henderson-Hasselbalch Equation)

Introduction

What is acid base balance ?

Blood pH control(normal : 7.35 - 7.45)

→ by regulation of **hydrogen ion** balance

$$\text{pH} \rightarrow 6.1 + \frac{\log [\text{HCO}_3]}{0.03 \text{ Pco}_2} : \text{regulated by kidney}$$

regulated by lung

* Normal value

pH : 7.35 - 7.45

PCO₂ : 35 - 45 mmHg

HCO₃ : 22 - 28 mmol

Significance of acid base balance ?

→ essential for Normal metabolic function,
especially activity of **protein** molecule

- activity of enzyme
- activity of element for blood clotting
- muscle contraction
- excitability of nerve
- influence K level in body

Production of Acid

Two source of acid

1. Metabolism of carbohydrate and fat

→ carbonic acid formation(volatile acid)

: production of CO_2 , 15,000-20,000 mmol /day

→ CO_2 Excreted by lung

2. Metabolism of protein

→ acid other than carbonic acid(nonvolatile acid)

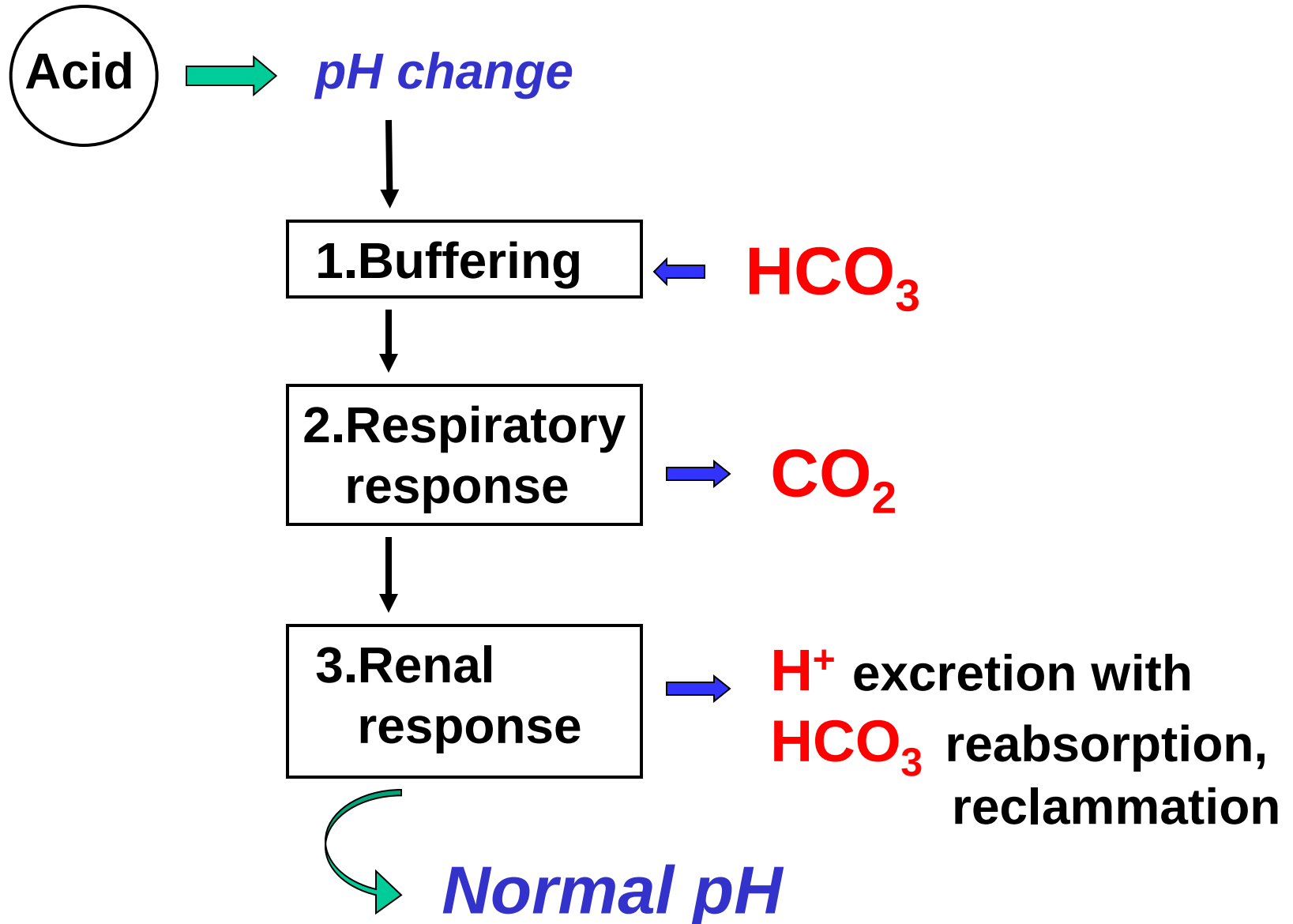
: sulfur containing AA acid(cysteine, methion),
phosphate (P-protein, P-lipid, P-nucleotide),

→ production of noncarbonic acid (H^+),

(50 to 100 meq, 1-2 meq/Bwt /day)

→ these H^+ ions are then excreted in the urine.

Homeostatic response



ACID BASE DISORDER

- Diagnostic approach
- 4 disturbance
 1. Metabolic acidosis
 - * Renal Tubular Acidosis(RTA)
 2. Metabolic alkalosis
 3. Respiratory acidosis
 4. Respiratory alkalosis

Diagnostic approach to acid base imbalance



1.ABGA (pH, HCO₃, PCO₂)
- Type of imbalance

2.Check compensation

3.Serum AG

4.Urine AG

Delta ratio

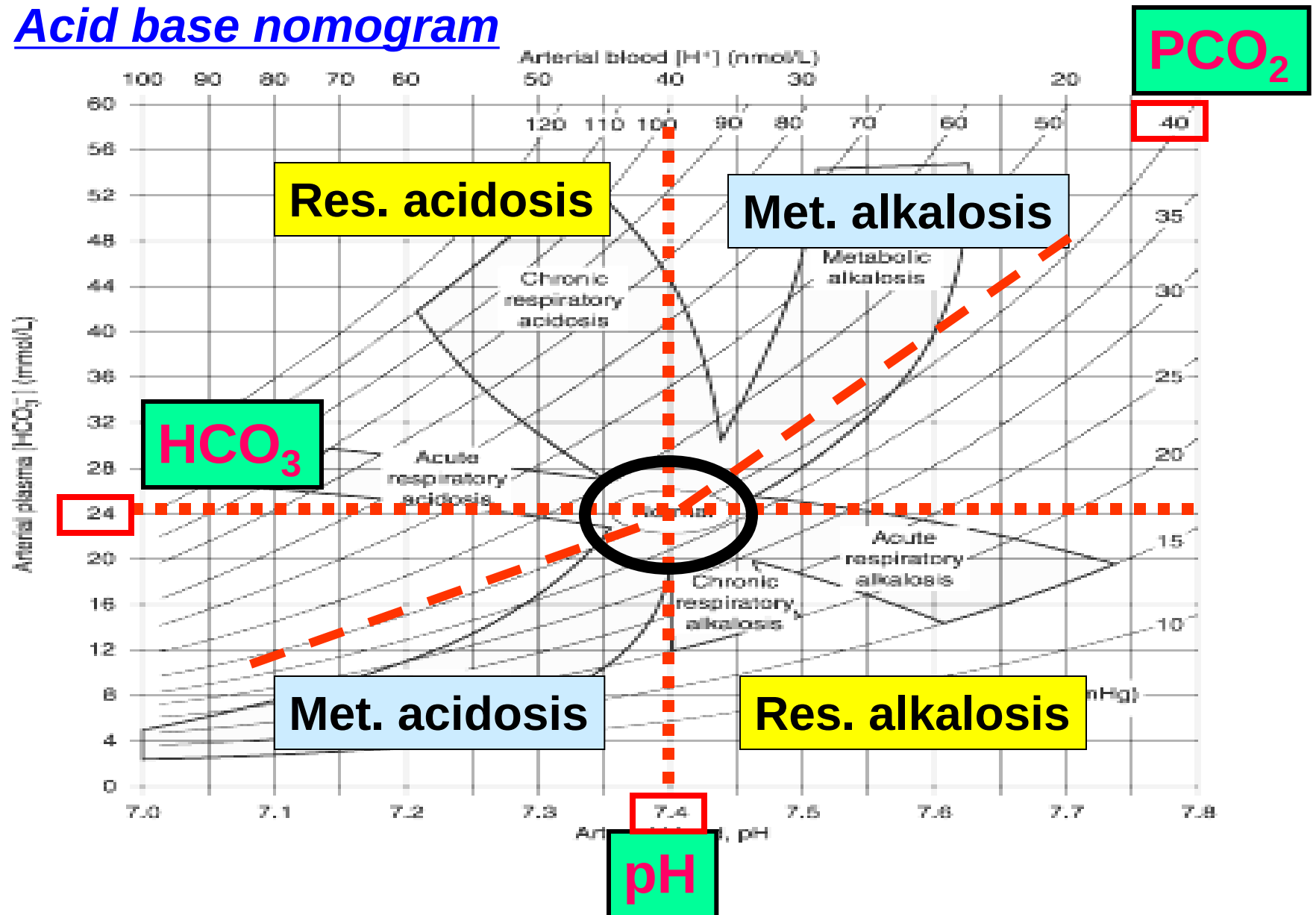
Osmolal gap

Normal Values

pH	7.35-7.45
CO ₂	35-45
pO ₂	80-100
HCO ₃	22-26
O ₂ Sat.	95-100%

1. Type of acid-base abnormalities

Acid base nomogram



1. Type of acid-base abnormalities

begin with **ABGA**

→ Acidosis or Alkalosis and
Metabolic or Respiratory

pH

PCO₂

HCO₃

M acidosis



M alkalosis



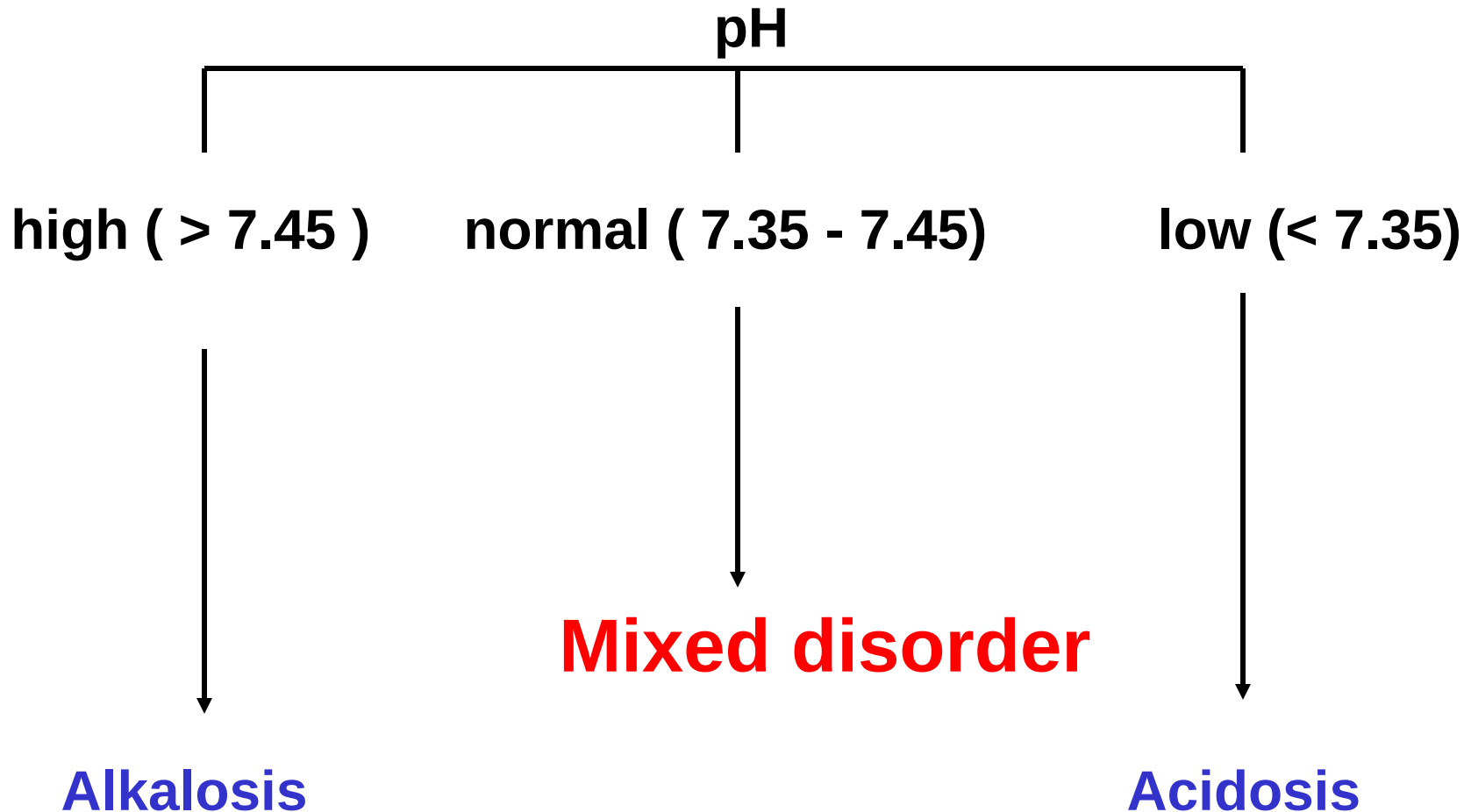
R acidosis



R alkalosis



1. Type of acid-base abnormalities



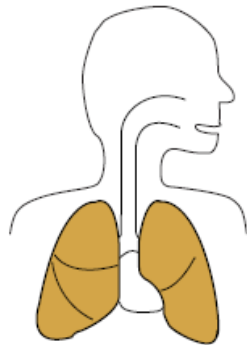
2. Check Compensation

Compensation for normal pH maintenance

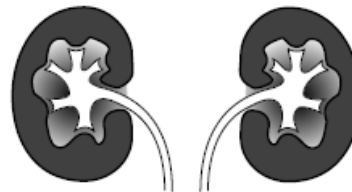
$$\text{pH} \rightarrow 6.1 + \frac{\log [\text{HCO}_3]}{0.03 \text{ Pco}_2} : \text{regulated by kidney}$$

: regulated by lung

By ventilation



Normal PCO_2 : 40 mmHg
The lungs affect the plasma PCO_2 by increasing or decreasing ventilation.

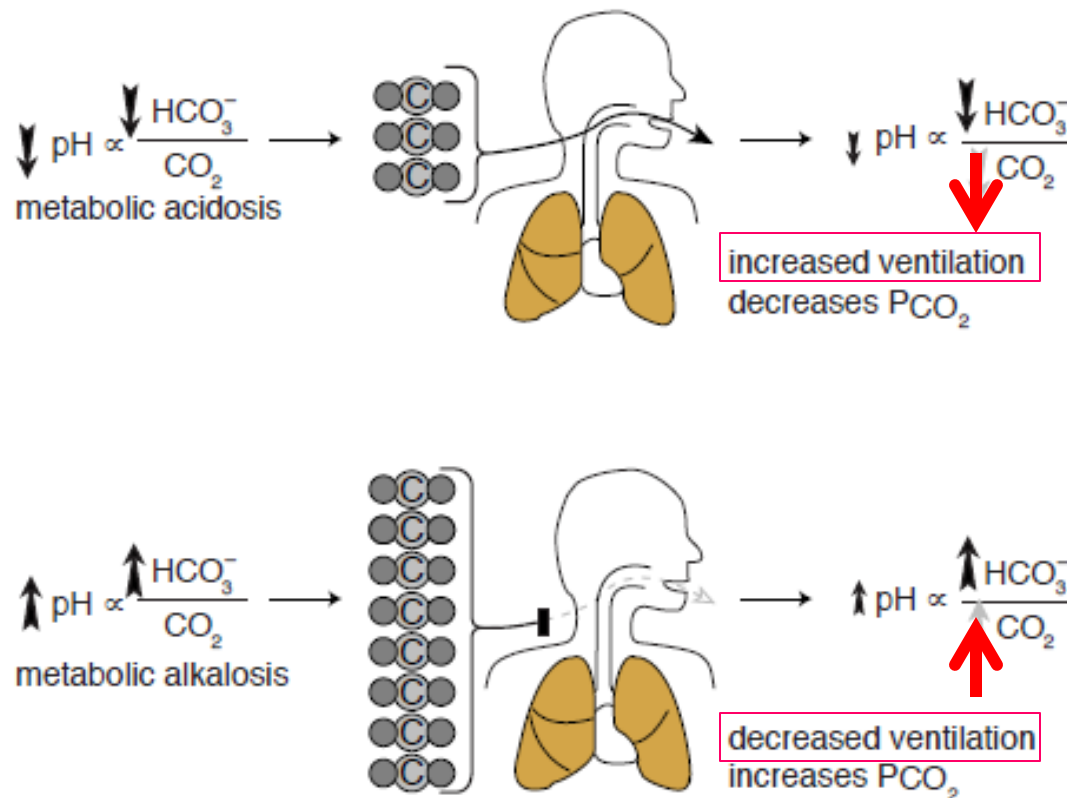


By bicarbonate excretion/production

Normal bicarbonate: 24 mEq/L
The kidney affects the plasma bicarbonate concentration by increasing or decreasing bicarbonate excretion and production.

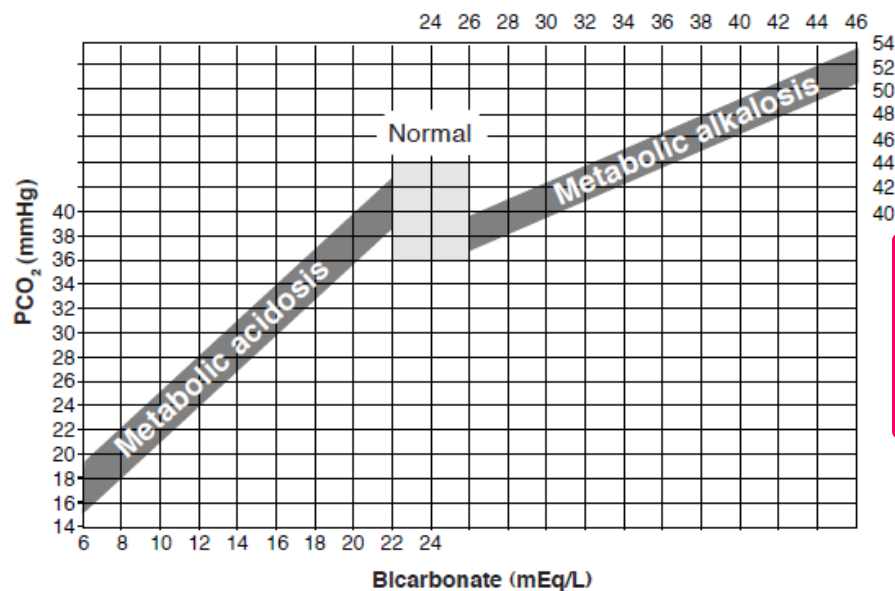
2. Check Compensation

Compensation for metabolic acidosis/alkalosis
→ is a change in PCO_2



2. Check Compensation

Compensation for metabolic acidosis/alkalosis
→ is a change in PCO_2



METABOLIC ALKALOSIS

$$\text{Expected } \text{PCO}_2 = 0.7 \times \text{HCO}_3^- + 20 \pm 1.5$$

$$\Delta \text{PCO}_2 = 0.75 / \Delta \text{HCO}_3^-$$

or

$$\text{PCO}_2 = \text{HCO}_3^- + 15$$

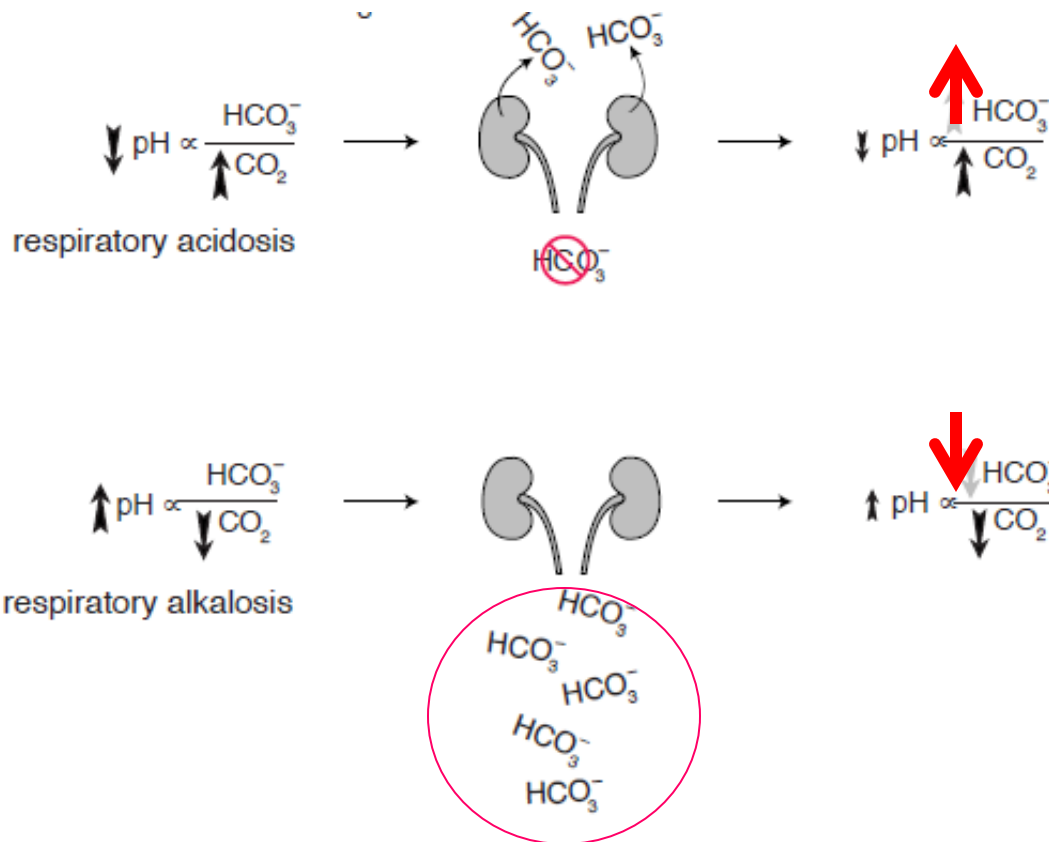
METABOLIC ACIDOSIS

$$\text{Expected } \text{PCO}_2 = (1.5 \times \text{HCO}_3^-) + 8 \pm 2$$

$$\text{or } \text{PCO}_2 = \text{HCO}_3^- + 15$$

2. Check Compensation

Compensation for respiratory acidosis/alkalosis
→ is a change in HCO_3^-



3. Serum anion gap

Anion gap ?

cation	anion
Na 140	Cl 104
	HCO ₃ ⁻ 24
UC 11	AG 12

$$\text{Na} + \text{UC} = \text{Cl} + \text{HCO}_3 + \text{UA}$$

$$\text{UA} - \text{UC} \text{ (AG)} \\ = \text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

Anion Gap

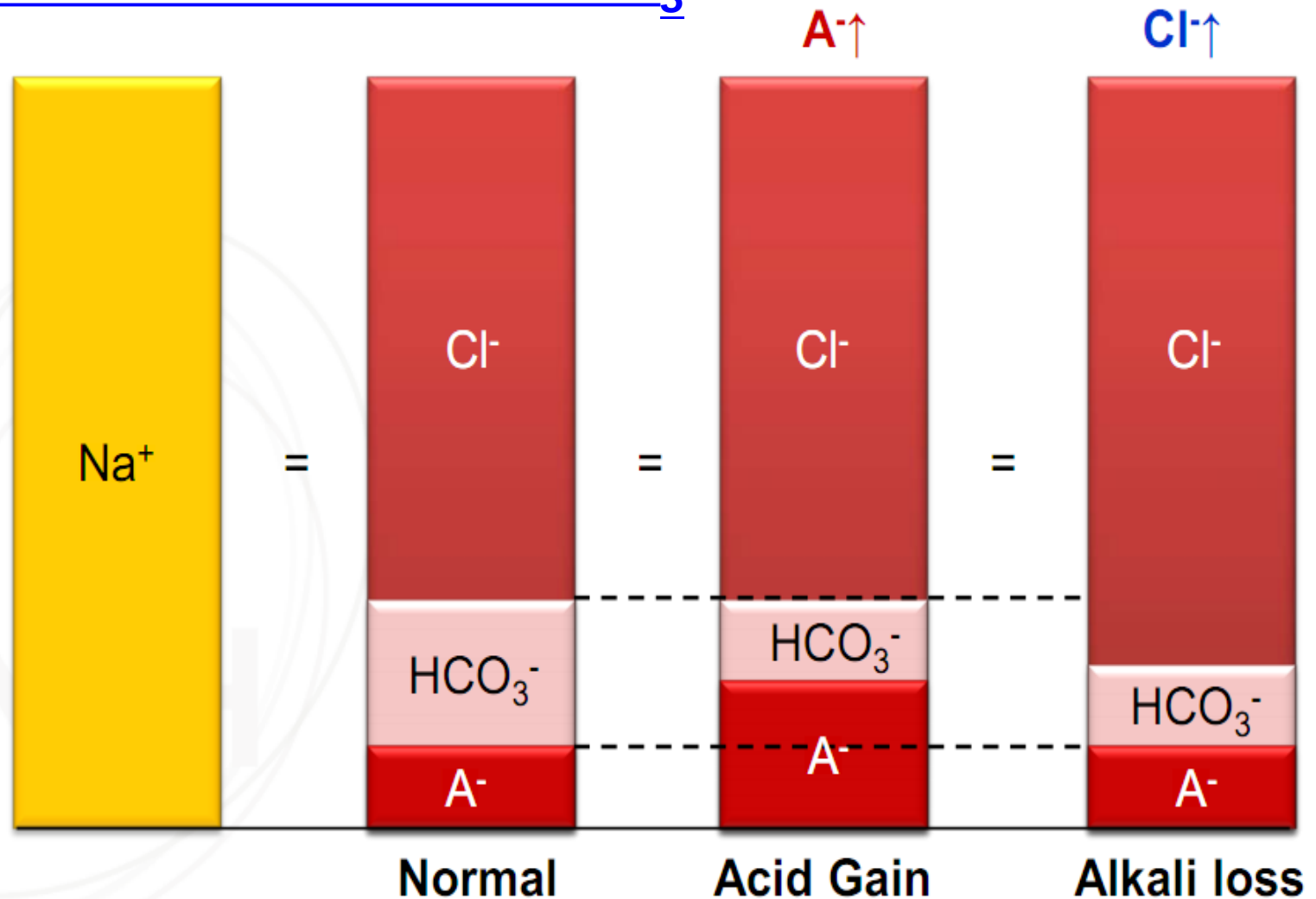
UA 23

AG normal : 8 – 12 mEq/L

AG Correct in hypoalbuminemia : $\text{AG} + (4 - \text{albumin}) \times 2.5$

3. Serum anion gap

Two causes of low HCO_3^-



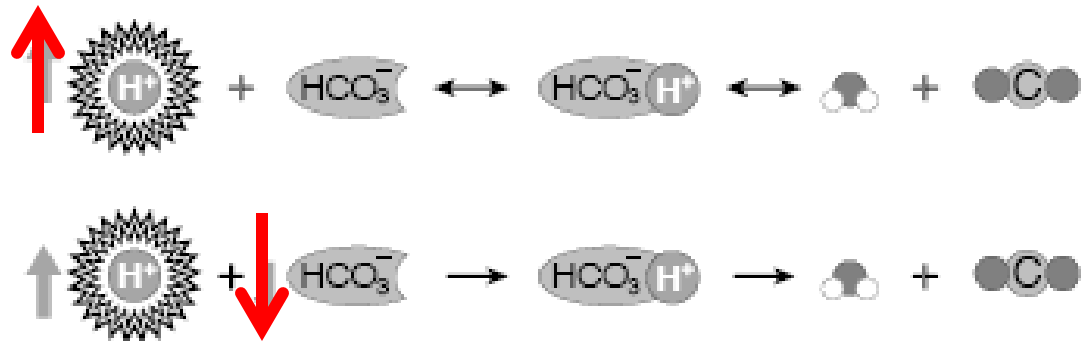
3. Serum anion gap

Two causes of low HCO_3^-

1) Acid addition → High AG metabolic acidosis

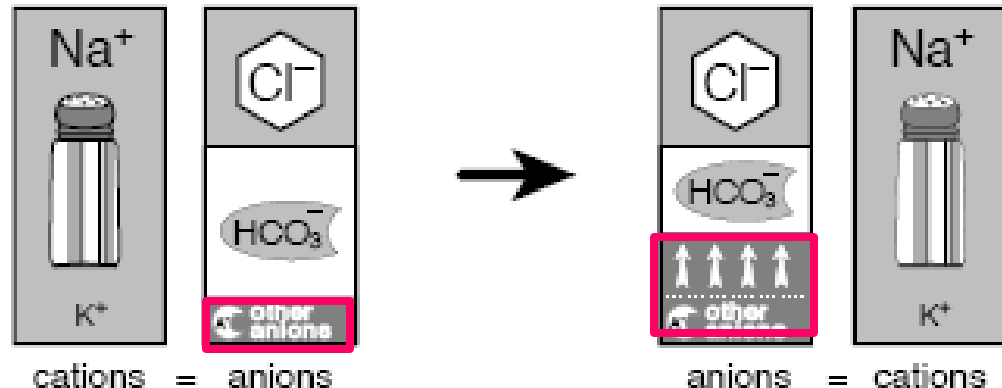


The addition of hydrogen ions lowers pH. Bicarbonate is consumed buffering the added hydrogen.



$\uparrow$ Gap

The anions associated with the acid increase the anion gap. Chloride concentration is unchanged.



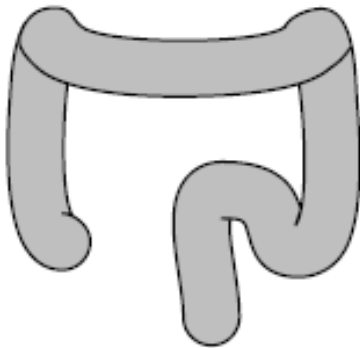
3. Serum anion gap

Two causes of low HCO_3^-

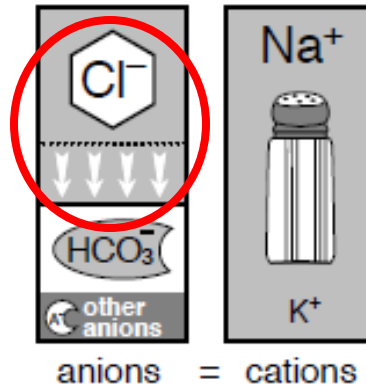
2) loss of bicarbonate

→ *Non-anion gap metabolic acidosis*

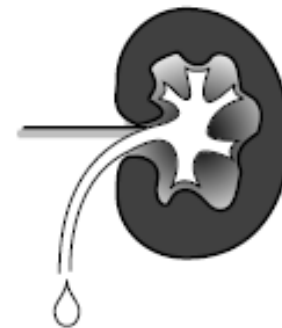
GI LOSS OF HCO_3^-



GI loss
diarrhea
surgical drains
fistulas
ureterosigmoidostomy
obstructed ureteroileostomy
cholestyramine



RENAL LOSS OF HCO_3^-



Renal tubular acidosis (RTA)
proximal (type 2 RTA)
distal (type 1 RTA)
hypoaldosteronism (type 4 RTA)

3. Serum anion gap

$$\text{Anion Gap} = \text{S.Na} - (\text{S.Cl} + \text{S.HCO}_3)$$

- normal level : **8 – 12 meq/L**

4 causes of high AG acidosis

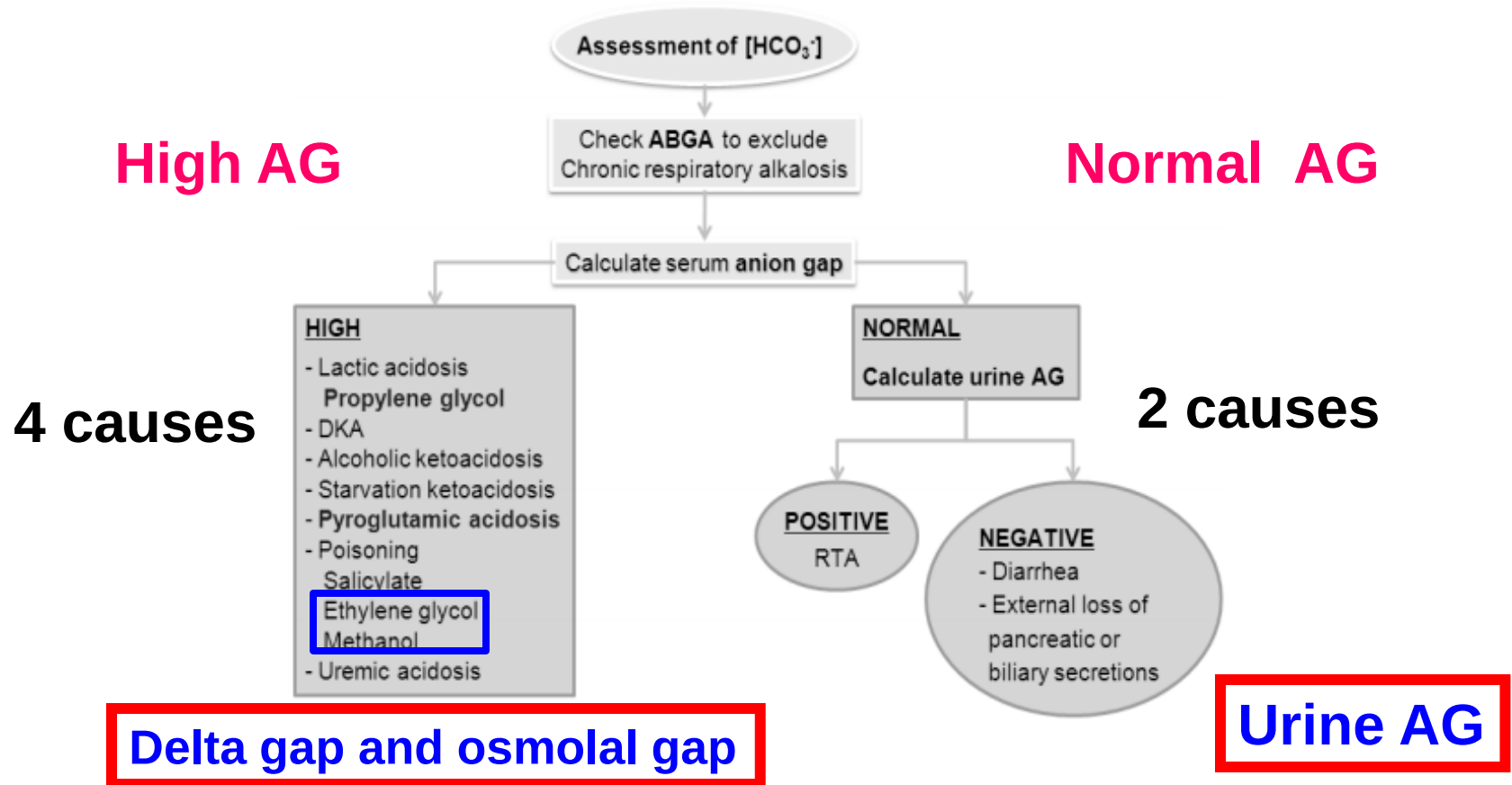
- ketoacidosis
- lactic acidosis
- renal failure(acute/chronic)
- toxin(ingested)

2 causes of nongap acidosis

- bicarbonate loss
(diarrhea) from GIT
- RTA

4. Further Approach to acid base disorders

In Metabolic acidosis



4. Further Approach to acid base disorders

1) Urine AG in normal AG M. acidosis

- $\text{UAG} = (\text{U Na}^+ + \text{U K}^+ + \text{NH}_4^+) - \text{U Cl}^-$
- for urine ammonium ion(NH_4) check
- for D/D between
 - RTA** → zero or positive UAG
 - extrarenal bicarbonate loss(ex,diarrhea)**
→ negative UAG

4. Further Approach to acid base disorders

2) Delta gap or ratio(= $\Delta AG / \Delta HCO_3^-$)

in high AG M acidosis

- for determining if a mixed acid base disorder is present
- Comparing the change in the AG (AG – 12)
to the change in HCO_3^- (24 - HCO_3^-)

DELTA-DELTA

$$\frac{\Delta \text{gap}}{\Delta HCO_3^-} = \frac{\text{measured anion gap} - \text{ideal anion gap}}{\text{ideal } HCO_3^- - \text{measured } HCO_3^-}$$

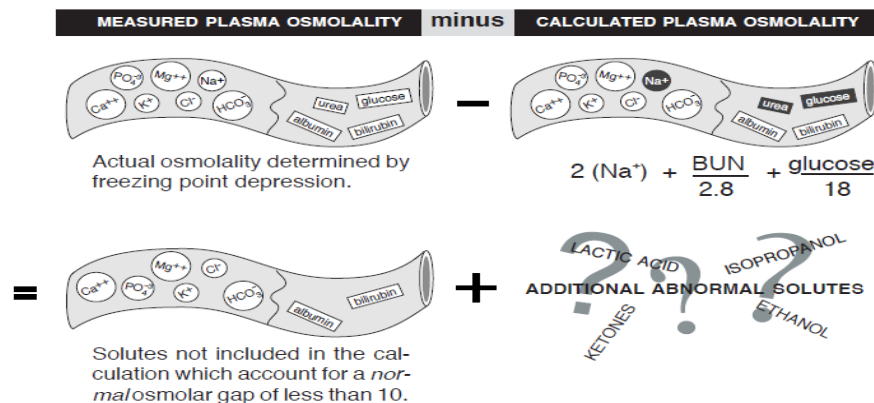
- if > 2 , then a metabolic alkalosis is present
- if < 1 , then a non-anion gap metabolic acidosis is present

4. Further Approach to acid base disorders

3) Osmolal gap in high AG M acidosis

Osmolal Gap

→ measured Osmolality - calculated Osmolality
($2 \times \text{Na} + \text{glucose}/18 + \text{BUN}/2.8$)
: normal < 10-15 mosmo/kg



Common Cause of High OG (> 15-20 mosmol/kg)

- methanol ingestion
- ethylene glycol ingestion

Overview of Diagnostic approach

Interpretation of Handerson Hasselbalch approach

STEP 1	Re-check the data $\rightarrow [H^+] = 24 \times pCO_2 / [HCO_3^-]$ $[H^+] \text{ mEq/L} = (7.80 - pH) \times 100$
STEP 2	Acidemia (pH < 7.37) or alkalemia (pH > 7.42) ?
STEP 3	Determining the primary disorder : <u>metabolic or respiratory</u> ? $\rightarrow$ look any ΔpCO_2 and HCO_3^-
STEP 4	Determining compensatory mechanisms $\rightarrow$ expected or excessive deviation ?
STEP 5 (for metab acidosis)	Anion Gap = $[Na] - ([Cl] + [HCO_3])$ n < 12 Hypoalbuminemia $\rightarrow AG_c = AG + (2.5 \times \Delta \text{albumin})$
STEP 6 (for AG > 12)	Delta/delta = $\Delta AG / \Delta HCO_3 = (AG - 12) / (24 - HCO_3)$ Delta/delta > 1 = metab acidosis + alkalosis Delta/delta < 1 = metab. acidosis gap + non-gap

Simple or mixed



UAG

OG

METABOLIC ACIDOSIS

↓ HCO_3^- (primary event)

↓ pH

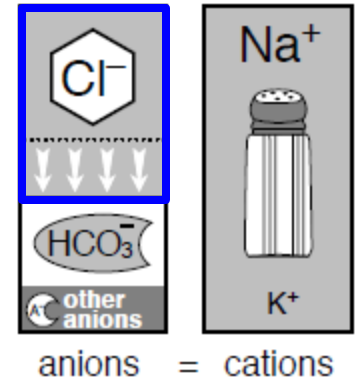
↓ PCO_2 (secondary event)

Pathogenesis

Generation of metabolic acidosis

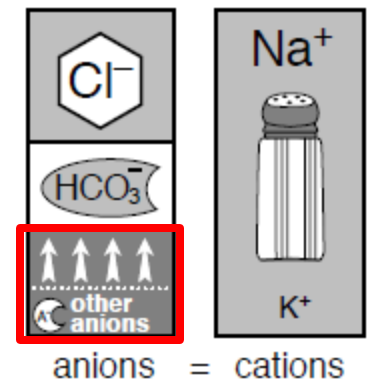
1. Loss of bicarbonate(**normal AG**)

- **Diarrhea**
- **RTA**



2. Increased H^+ (**high AG**)

- endogenous
 - : **lactic acidosis, ketoacidosis, uremia**
- exogenous
 - : **salicylate, methanol, ethylene glycol**

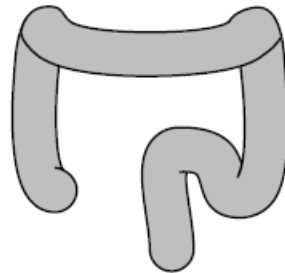


Causes

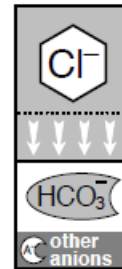
Two form

Normal AG

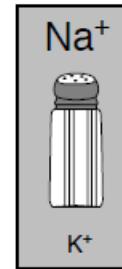
GI LOSS OF HCO_3^-



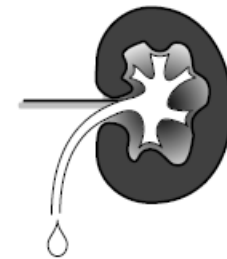
GI loss
 diarrhea
 surgical drains
 fistulas
 ureterosigmoidostomy
 obstructed ureteroileostomy
 cholestyramine



anions = cations

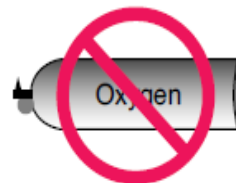


RENAL LOSS OF HCO_3^-



Renal tubular acidosis (RTA)
 proximal (type 2 RTA)
 distal (type 1 RTA)
 hypoaldosteronism (type 4 RTA)

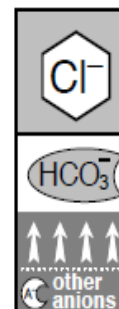
High AG



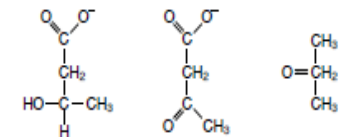
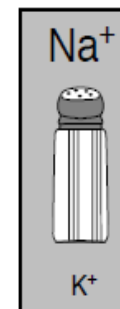
LACTIC ACIDOSIS



RENAL FAILURE



anions = cations



KETOACIDOSIS



INGESTIONS

Causes

Two form of metabolic acidosis

Normal AG

1. Renal cause

- bicarbonate loss
: Proximal **RTA**
- failure of bicarbonate
regeneration
: Distal RTA

2. GI cause

- **diarrhea**

3. Acidifying salt

- ammonia chloride

Increased AG

1. Endogenous cause

- **uremic acidosis**
- **lactic acidosis**
- **ketoacidosis**
(diabetic, alcoholic,
starvation)

2. Exogenous cause

- **salicylate**
- methanol
- ethylene glycol

Causes

Normal anion gap metabolic acidosis

Diarrhea

- **most common cause of non AG M acidosis**
- all GI tract secretion below stomach
are rich in bicarbonate

RTA

- defect in bicarbonate resorption and
regeneration (hydrogen ion excretion)
- PRTA(decreased HCO_3 reabsorption),
DRTA(decreased H secretion),
type IV RTA(decreased H excretion bound to ammonia)

Causes

High anion gap metabolic acidosis

- Due to addition of acid(with anion)

Four causes

1. lactic acidosis

2. ketoacidosis

: diabetic, alcoholic, starvation

3. uremic acidosis

: renal failure

4. toxin ingestion

: salicylate, methanol, ethylene glycol, paraldehyde

Clinical manifestation

- tired, exertional dyspnea, nausea, vomiting are common

Cardiorespiratory Effects

: significant effects particularly affecting the respiratory & cardiovascular systems

1. Respiratory Effects

- hyperventilation(Kussmaul's respiration)

2. Cardiovascular Effects

- depression of myocardial contractility
- sympathetic overactivity
- resistance to the effects of catecholamines

Diagnosis of M acidosis

Underlying disease

ABGA

Serum electrolyte

Step approach

: SAG, compensation,
UAG, Delta ratio, Osmolal gap

Treatment

Four Key Principles in the Treatment of Metabolic Acidosis

1. **Accurate diagnosis** of the cause of the M. acidosis
2. Treat the **underlying disorder** and treatment varies depending upon underlying Ds
3. Provide **supportive treatment**
(fluids, oxygen, treatment for hyperkalaemia)
4. In most cases,
IV **sodium bicarbonate**
→ **is NOT necessary, NOT helpful,**
may even be harmful in the treatment of M. acidosis.

High Anion Gap M. Acidosis

4 common causes

1. Lactic acidosis
2. Ketoacidosis (diabetic, alcoholic, starvation)
3. Uremic acidosis(acute or chronic renal failure)
4. Ingested toxines
 - ethylene glycol, methanol, salicylate

Non Anion Gap Metabolic Acidosis

→ Hyperchloremic metabolic acidosis

1. Nonrenal cause

- diarrhea

- urinary diversion

→ HCO_3 loss from GI tract(below stomach)

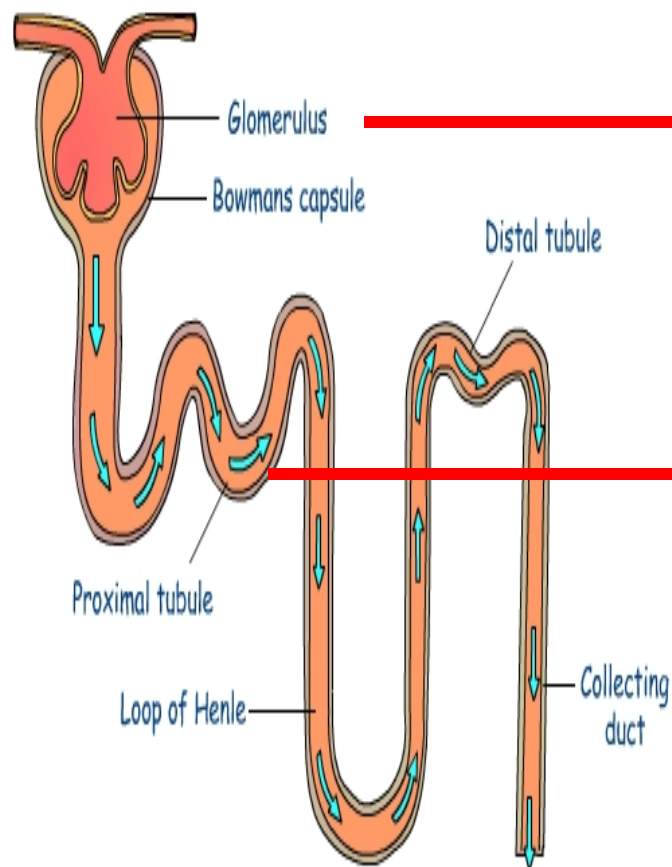
2. Renal cause(RTA)

- proximal RTA

- distal RTA

- type 4 RTA

RENAL TUBULAR ACIDOSIS(RTA)



Predominantly glomerular damage

→ High anion gap acidosis

- Acidosis of acute renal failure
- Uremic acidosis

Predominantly tubular damage

→ Normal anion gap acidosis (**RTA**)

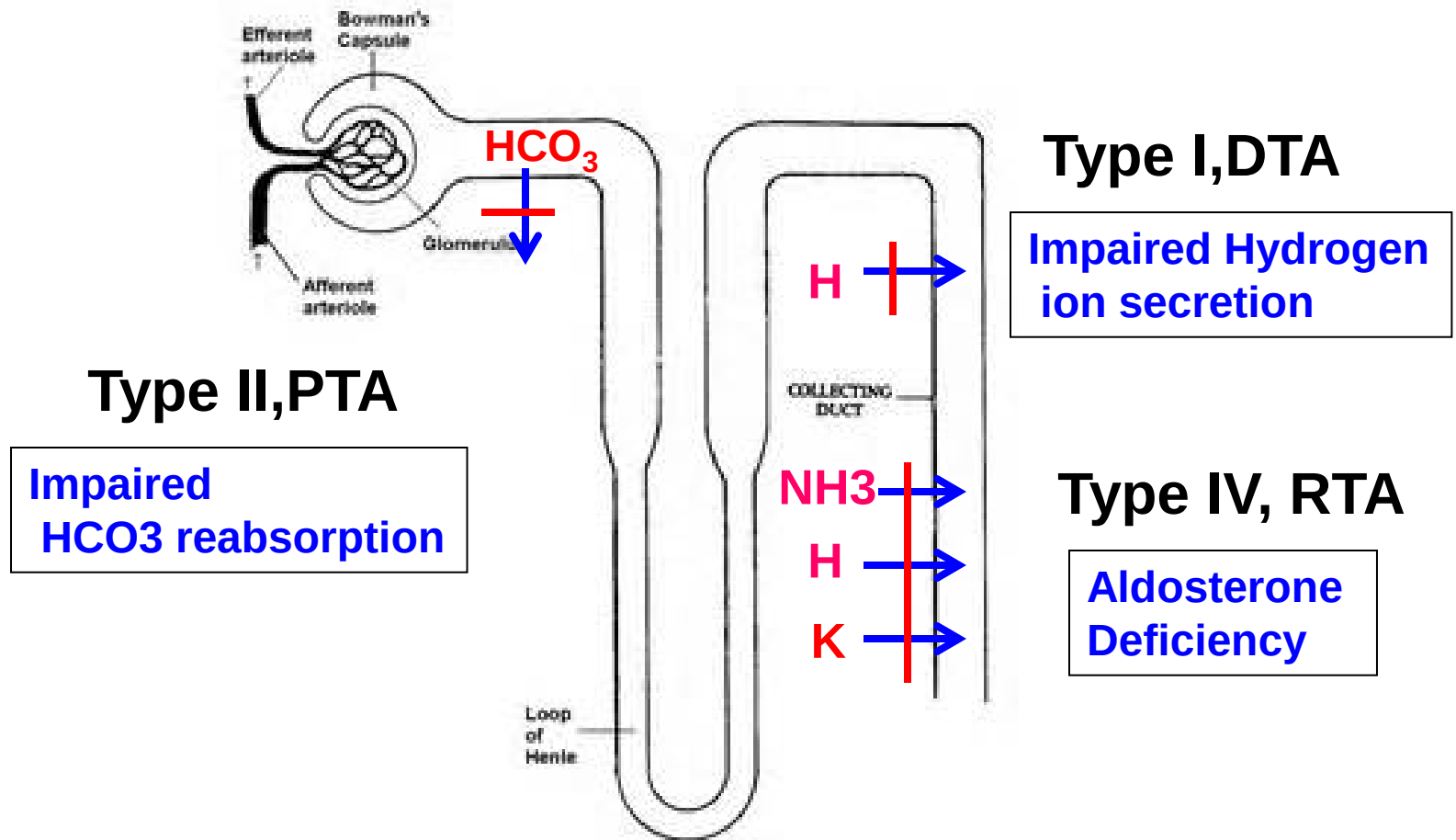
- Distal (or type 1) RTA
- Proximal (or type 2) RTA
- Type 4 RTA

What is Renal tubular acidosis ?

RTA

- is a chronic metabolic acidosis result from
 - 1) diminished HCO_3 reabsorption in PT
 - 2) diminished net tubular H^+ secretion in DT
- three type
 - 1) distal RTA(type 1)
 - 2) proximal RTA (type 2)
 - 3) hyperkalemic RTA(type 4)
- characterized by Normal AG and positive U. AG
- relatively unusual in adult (except type 4 RTA)

Three type of RTA



Three type of RTA

Type II, proximal RTA

- Cause
 - : most commonly associated with **Fanconi's syndrome**
 - : genetic disease
 - : **MM , amyloidosis, PNH in adult,**
- self limited and typically mild state
- hypokelamia,
urine pH less than 5.3(intact DT acidification)
no nephrolithiasis
bone destruction(+)

Three type of RTA

Type I, classic RTA, distal RTA

- due to inability to excrete Hydrogen ion in CD (impaired distal acidification)
- accompanied by hypercalciuria, **nephrocalcinosis**
- more severe acidosis and **urine pH > 5.3, hypokalemia**



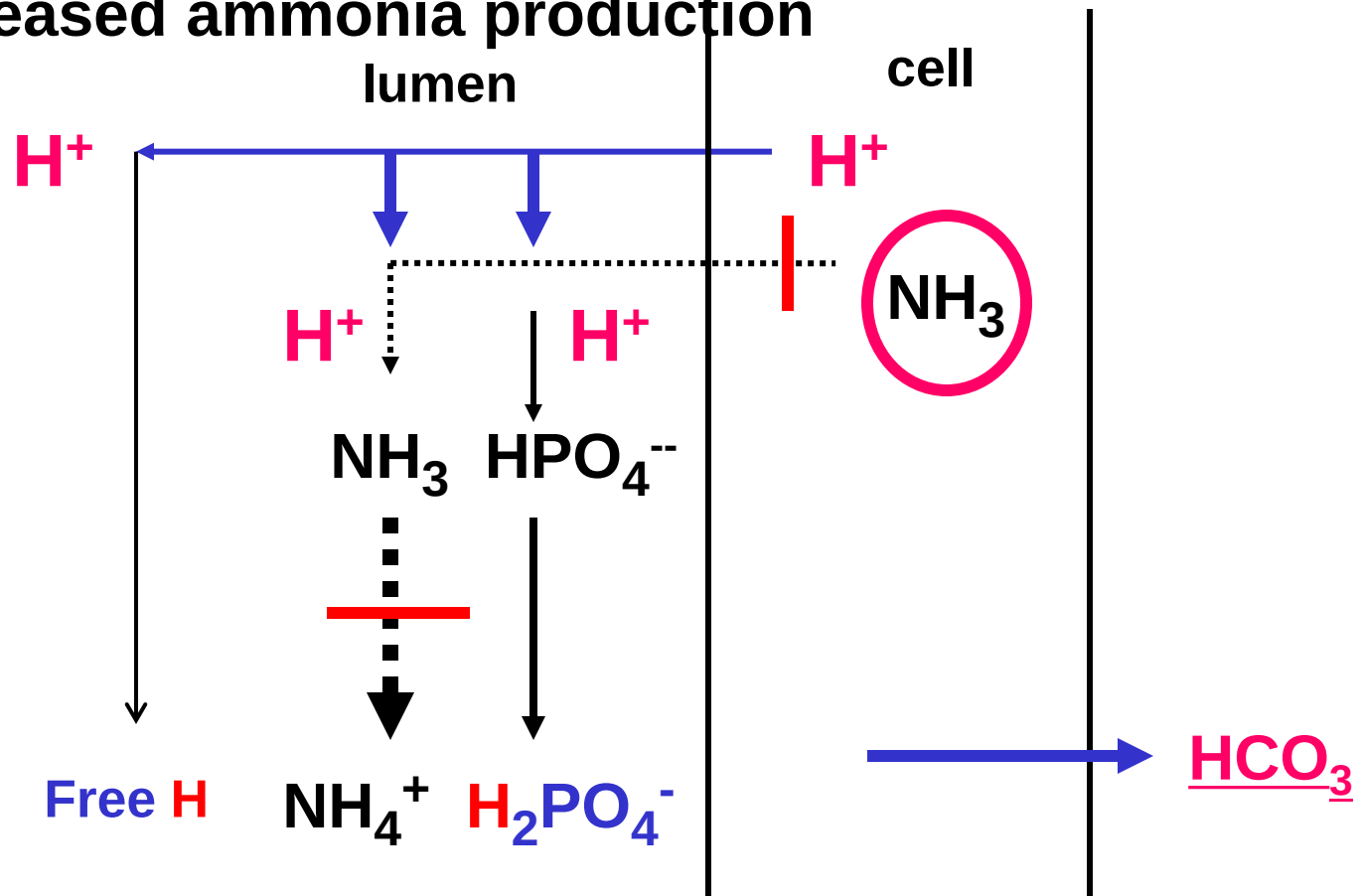
- Cause
: associated with autoimmune disorder
(**sjogren' syndrome, SLE, RA**)

Three type of RTA

Type IV, hyperkalemic RTA

Aldosterone defect → hypokalemia

→ decreased ammonia production



Three type of RTA

Type IV, hyperkalemic RTA

- due to aldosterone deficiency or resistance
- cause
 - : mineralocorticoid deficiency/ resistance
 - : **hyporeninemic-hypoaldosteronism**
 - in **diabetic renal disease**, other TI disease
- **hyperkalemia**, mild-moderate renal dysfunction
(GFR 20 – 50 ml/min)
- Tx
 - : low K diet, loop diuretics, K binding resin

D/D of RTA

Finding	Type 1 RTA	Type 2 RTA	Type 4 RTA
Basic	decreased distal acidification	diminished proximal HCO ₃ reabsorption	aldosterone deficiency
S.AG	N	N	N
U.AG	+	-	+
Minimum U.pH	> 5.5	variable	variable
Serum K	low	low	high
GFR	N	N	low
Stone	+	-	-
Fanconi S	-	+	-

METABOLIC ALKALOSIS

↑ HCO_3 (primary event)

↑ pH

↑ PCO_2 (secondary event)

Pathogenesis

Normal renal response to high HCO_3 load

- Renal excretion of excess HCO
is **rapid and effective**
→ this protective bicarbonaturic response
is extremely effective
- For metabolic alkalosis maintenance
→ require the presence of
defect in HCO_3 excretion

Development of M.alkalosis

Generation (*new HCO_3 add in ECF*)

by **loss of hydrogen ion** or
gain of HCO_3



Maintenance (*sustained new elevated HCO_3*)

by abnormal **renal retention** of HCO_3



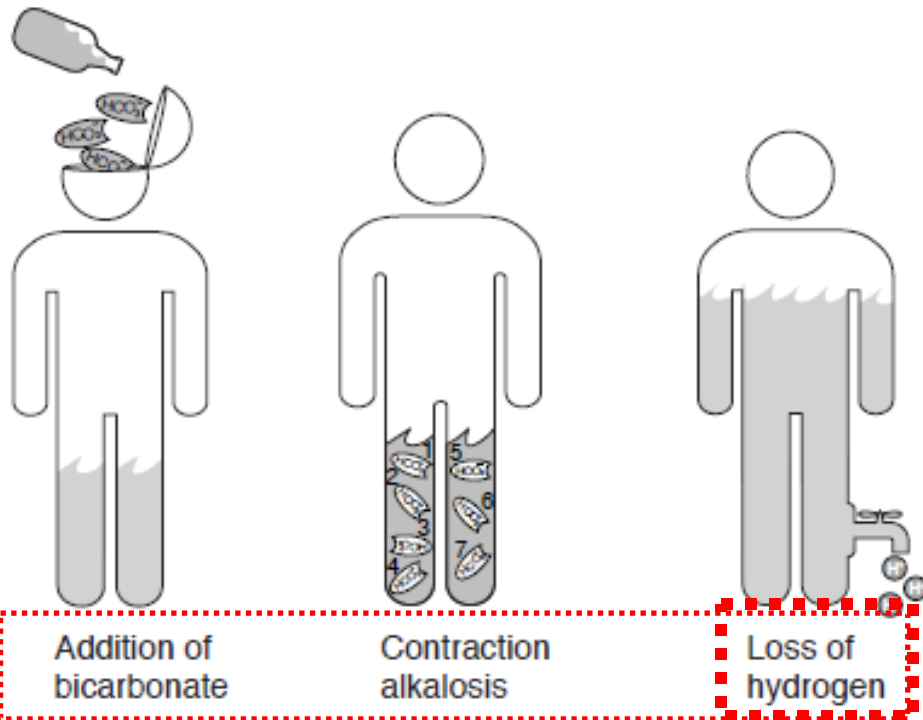
Volume depletion
Reduced GFR
Low K,Cl
Excess mineralo

Metabolic alkalosis

Development of M.alkalosis

Generation and Maintenance

Generation



Increase P.bicarbonate

Maintenance

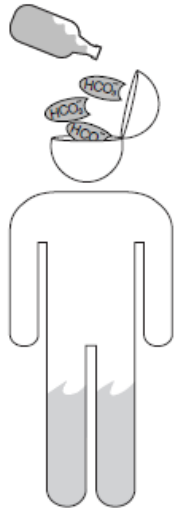


Inability of kidney to excrete excess bicarbonate

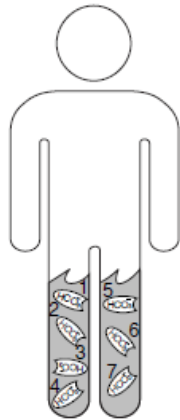
Development of Metabolic Alkalosis

Generation and Maintenance

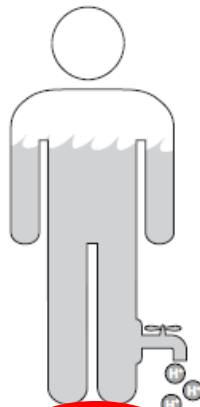
Generation



Addition of bicarbonate



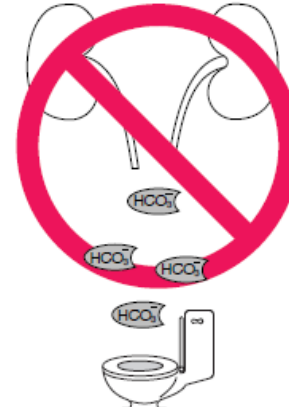
Contraction alkalosis



Loss of hydrogen

vomiting
diuretics

Maintenance



Inability to excrete excess bicarbonate

hypovolemia
excess mineralocorticoid
low chloride
low GFR

Extrarenal

: **vomiting**

Renal

: **excess mineralocorticoid**

: **diuretics**

: **rapid correction**

of chronic Res. acidosis

Causes

I. loss of hydrogen

1) Gastrointestinal loss

- with volume depletion

: Vomiting

2) Renal loss

- with volume depletion

: Diuretics(loop and distal)

: Bartter's syndrome, Gitelman's syndrome

: Posthypercapnic

- with volume expansion and hypertension

: Mineralocorticoid excess

II. Hydrogen movement into cell

- Hypokalemia

III. Contraction alkalosis(loss of fluid that is low in bicarbonate)

- Diuretics

- Gastric loss (vomiting)

IV. Addition of bicarbonate

- lactate, citrate(BT), bicarbonate

**** loss of gastric acid(vomiting) and diuretics use
→ 90% of clinical cause**

Loss of hydrogen

1. GI origin

- M/C cause is due to **gastric alkalosis(vomiting/ NGS)**

Vomiting

- : can result in both generation and maintenance of m.alka
- : generation

due to hydrogen ion loss(bicarbonate gain)
and chloride rich fluid loss

maintenance

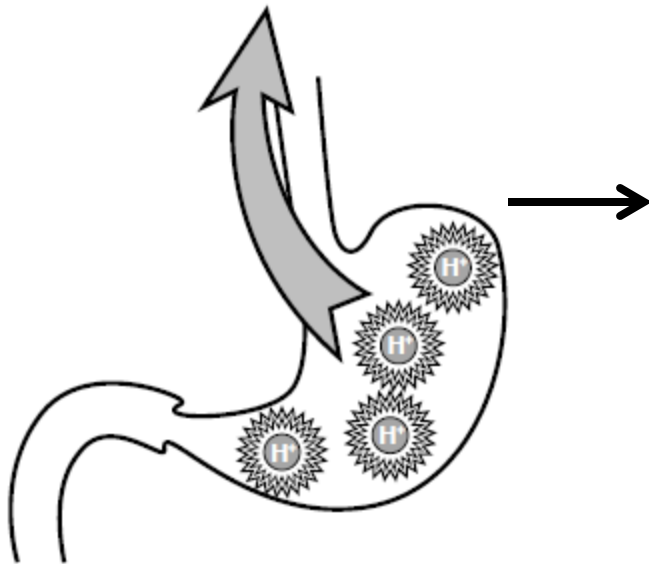
due to hypovolemia, hypochloremia, hypokalemia,
excess mineralocorticoid activity

Causes

Loss of hydrogen

1. GI origin

Vomiting



Generation

: Hydrogen loss, Cl loss

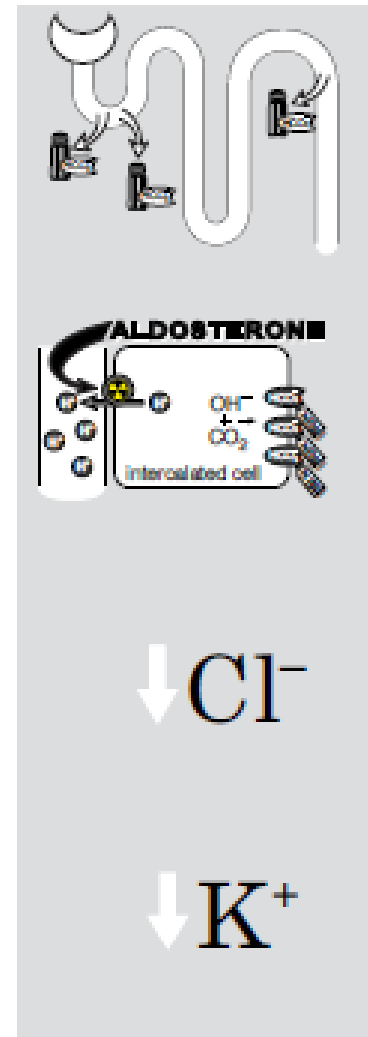
Maintenance

Hypovolemia

Excess
mineralo-
corticoid

Hypochloremia

Hypokalemia



Loss of hydrogen

2. Renal origin

- with volume depletion

Diuretics

: M/C cause

Bartter's syndrome

Gitelman's syndrome

Posthypercapnia

- with volume expansion
(increased Na reabsorption)
increased mineralocorticoid

Clinical manifestation

Effect on CNS

- frequently associated with M.encephalopathy
- confusion, obtundation, delirium, coma
- tetany, paresthesia, muscular cramping
- neurologic finding is seen > pH 7.55

Cardiac arrhythmia, hypotension

Diagnosis

Two categories of Metabolic alkalosis

1. **Chloride responsive** metabolic alkalosis
 - associated with ECF and chloride depletion
 - in **gastric fluid loss and diuretic use**

2. **Chloride unresponsive** metabolic alkalosis
 - associated with ECF expansion
 - in **primary aldosteronism and hypokalemia**

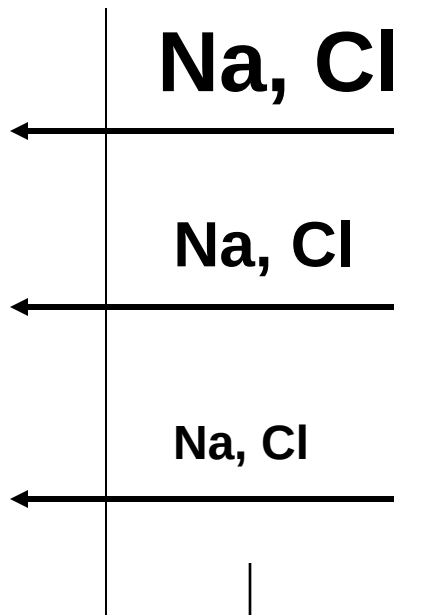
Diagnosis

Urine chloride

for D/D of saline(Cl) responsive and resistance

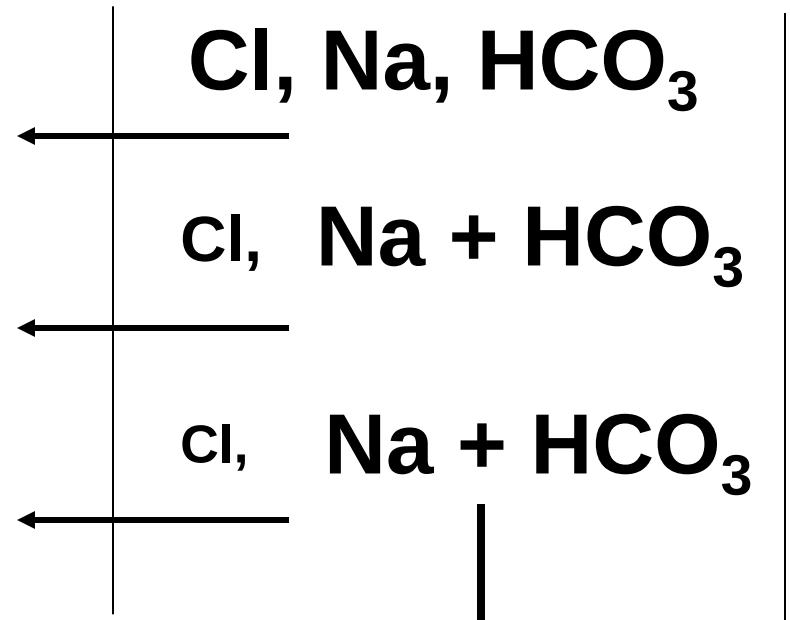
Volume depletion **without M.alkalosis**

Volume depletion **with M.alkalosis**



Na, Cl

Urine : low Na,Cl



Cl, Na + HCO₃

Urine : low Cl,
Na higher than expected level

Diagnosis

D/D of saline(Cl) responsive and resistance

1. Urine chloride < 10- 20 mmol/L(Cl responsive)
 - : associated with volume depletion
 - : respond to saline infusion
 - : causes
 - vomiting, diuretics
 - posthypercapnic state
2. Urine chloride > 10 – 20 mmol/L(Cl resistant)
 - : associated with volume expansion and hypokalemia
 - : resistant to saline infusion
 - : causes
 - mineralocorticoid excess, hypokalemia

Treatment

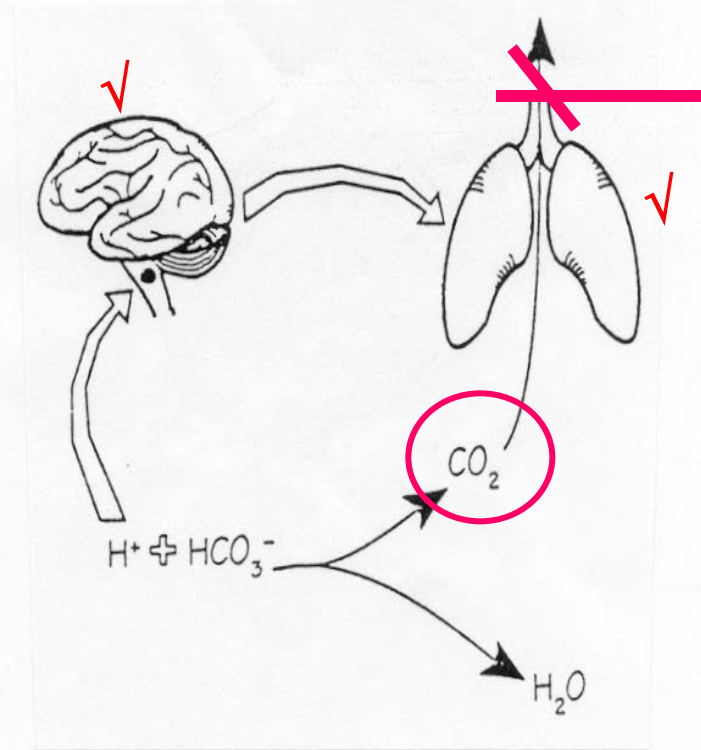
Two group by chloride response

- 1. Chloride responsive patient**
 - NaCl with KCl
- 2. Chloride resistant patient**
 - treatment is underlying disease control
 - K replacement
 - spironolactone and amiloride

RESPIRATORY ACID BASE IMBALANCE

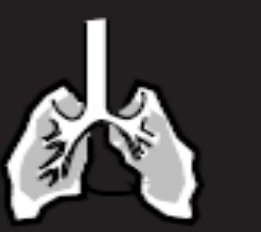
Respiratory acidosis

Respiratory alkalosis



Respiratory alkalosis and acidosis

Clinical correlation: Depending on severity, the same pulmonary diseases can cause respiratory alkalosis or respiratory acidosis.

	 Mild disease	 Moderate disease	 Severe disease
PO_2	normal	low	low
PCO_2	low	low	high
Acid-base disorder	respiratory alkalosis	respiratory alkalosis	respiratory acidosis

Some of the same pulmonary diseases which cause respiratory alkalosis can also cause respiratory acidosis. Pulmonary diseases that affect respiration can be thought of as occurring on a continuum: respiratory alkalosis with mild, early disease and respiratory acidosis with more severe, end-stage disease.

Acute pulmonary conditions such as pneumonia, pulmonary edema, pulmonary embolism and asthma can impair respiration and compromise oxygenation. In response to hypoxia, ventilation increases through increased respiratory effort and rate. If the pulmonary insult is mild, increased ventilation may be sufficient to return PO_2 to normal at the expense of decreased carbon dioxide and respiratory alkalosis.

45 yrs old adult male with severe vomiting due to pyloric obstruction

- visit to ER
- doctor in emergency room
 - : Physical Examination
 - **BP 80 / 50 mmHg, PR 90 / min, dehydrated skin and tongue**
 - : Initial Lab check (serum Na/K/ABGA)
 - **Na 129 mEq/L**
K 3.1 mEq/L
ABGA pH 7.5 / HCO₃ 29 mEq/L / PaCO₂ 44mEq/L

Remember →

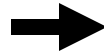
Normal value

BP *120 / 80 mmHg*
PR *70 /min*

Na *135 – 145 mEq/L(140)*
K *3.5 – 5 mEq/L(4.5)*
pH *7.35 – 7.45(7.4)*
PaCO₂ *35 – 45 mmHg(40)*
HCO₃ *22 – 26 mEq/L(24)*

45 yrs old adult male with severe vomiting due to pyloric obstruction

BP 80 / 50 mmHg
PR 90 / min
Dehydrated skin, tongue



Volume depletion

- fluid disturbance
- **Na content** disturbance

Na 129 mEq/L



Hyponatremia

- electrolyte disturbance
- (**osmolality** disturbance)
- **water** control disturbance
- (**Na concentration** disturbance)

K 3.1 mEq/L



Hypokalemia

- electrolyte disturbance
- **K** concentration disturbance

ABGA pH 7.5
HCO₃ 29 mEq/L
PaCO₂ 44mEq/L



Metabolic alkalosis

- acid-base disturbance
- **H⁺** concentration disturbance