Water & Sodium Disorders
(H_2O/Na^+)

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Intended Learning Outcomes:

- By the end of this lecture the student should be able to:
  1. Recognize the systems that control body sodium and water contents
  2. Differentiate between total body sodium content (volume status) and serum sodium concentration (Hypo- and Hypernatremia)
  3. Use the different types of IV fluids in clinical practice
  4. Calculate the water deficit in Hypernatremia
  5. Explain the workup of Hyponatremia

Structure

1) Composition of the fluid compartments

2) Mechanisms which regulate fluid and Sodium balance

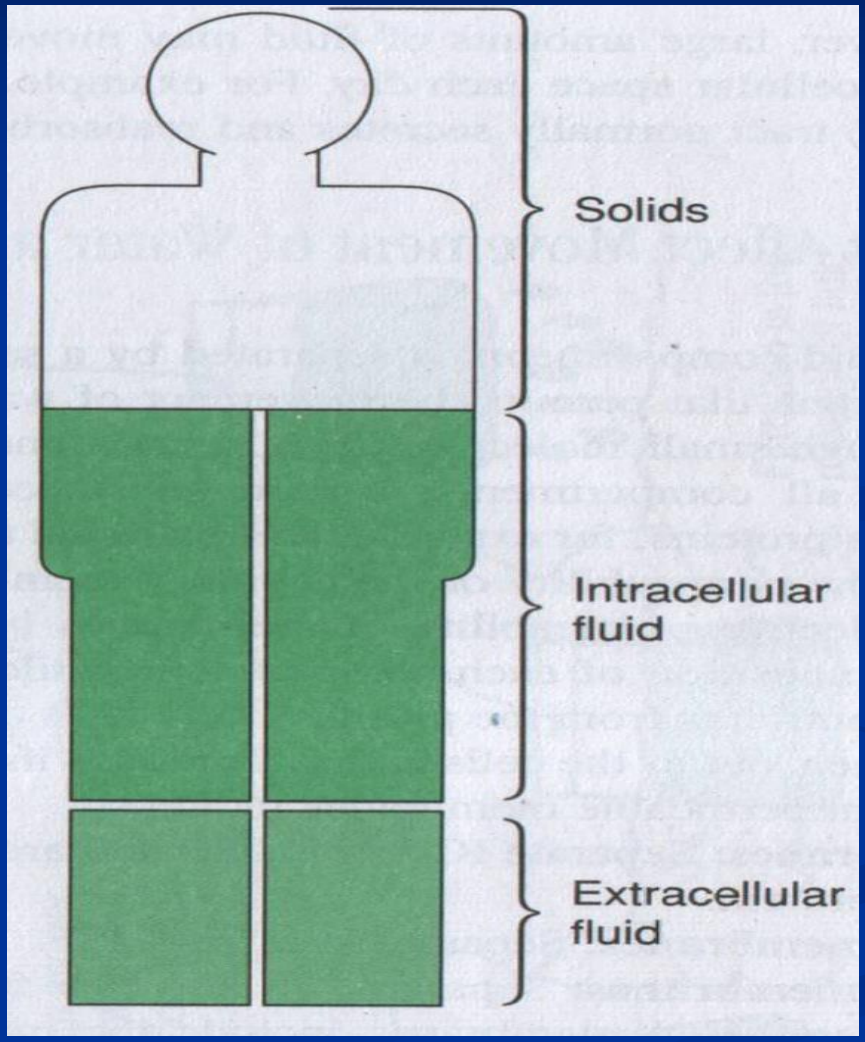
3) Disorders of water balance

4) Disorders of Sodium balance

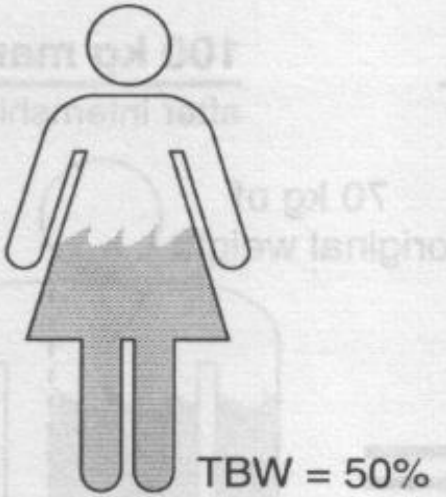
Homeostasis

A relative constancy in the internal environment of the body, naturally maintained by adaptive responses that promote cell function and survival

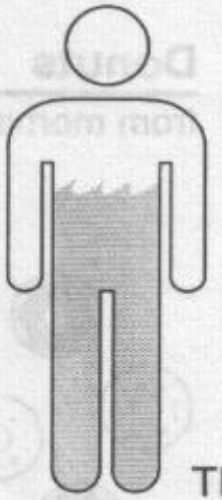
Total Body Fluid:



Total body water ▸ TBW is affected by gender and age.



TBW = 50%

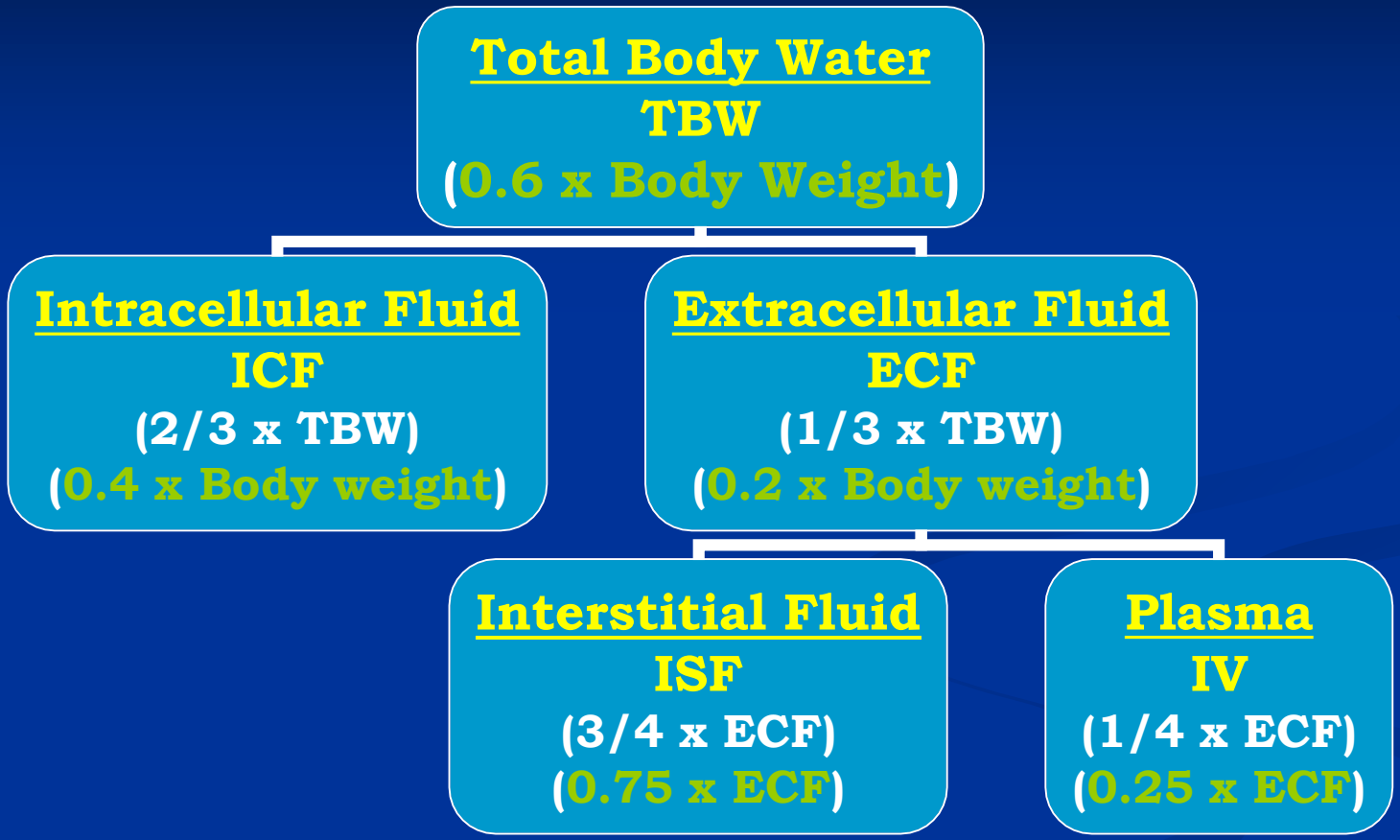


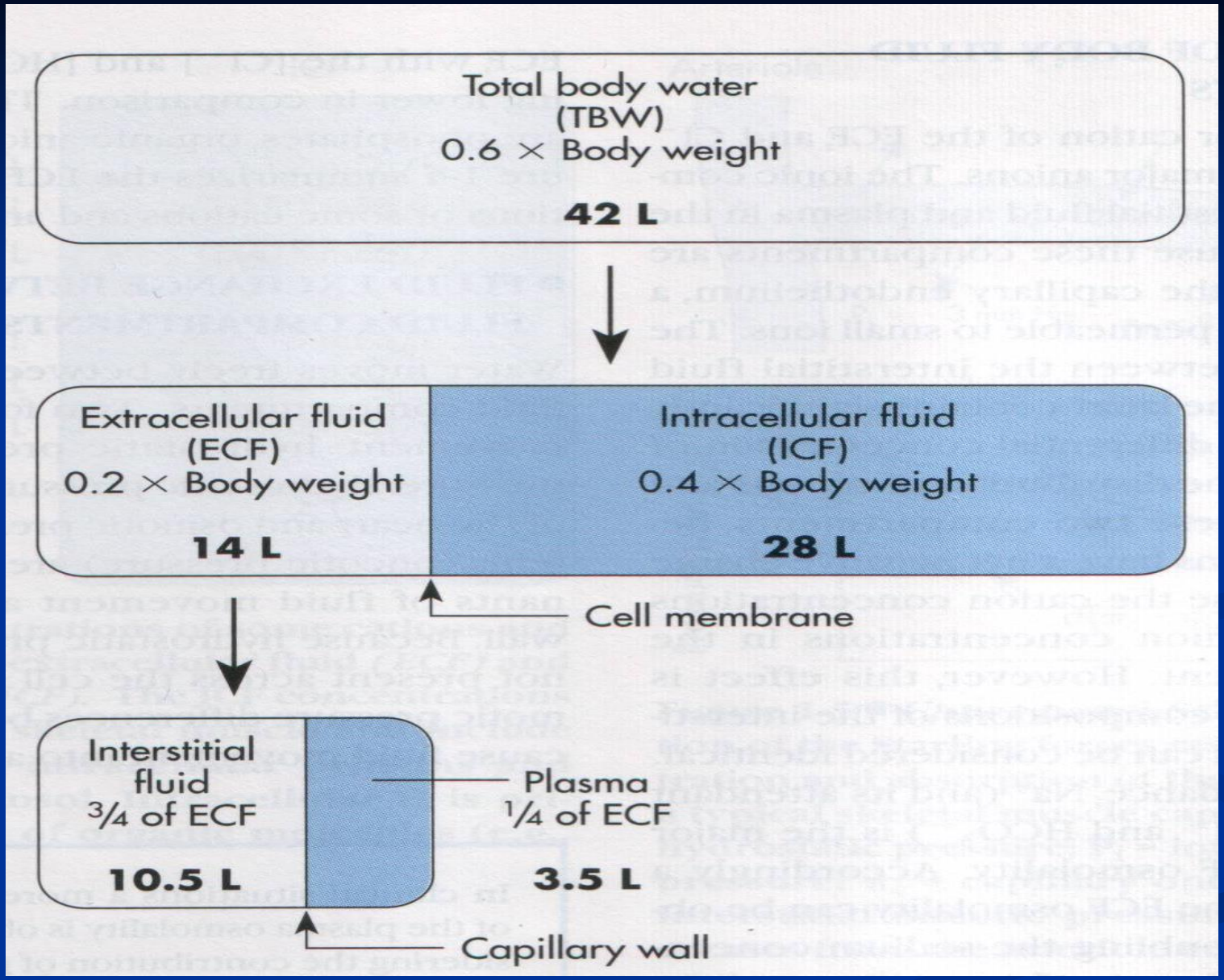
TBW = 60%

TBW = 70%

TBW = 50%

Body Fluid Compartments




Total body water
(TBW)
0.6 × Body weight
42 L
Extracellular fluid
(ECF)
0.2 × Body weight
14 L
Intracellular fluid
(ICF)
0.4 × Body weight
28 L
Cell membrane
Interstitial
fluid
¾ of ECF
10.5 L
Plasma
¼ of ECF
3.5 L
Capillary wall

Body Fluid Compartments

- Fluid compartments are separated by thin semi-permeable membranes with pores to allow fluid movement and molecules of a specific size to pass while preventing larger heavier molecules from passing
- The bodies fluid is composed of water and dissolved substances known as *solutes* (electrolytes or non-electrolytes)
- Electrolytes are substances dissolved in solutions and dissociated into particles called ions
  - *Cations:* Positively charged ions
  - *Anions:* Negatively charged ions

Definitions:

- *Osmosis:* movement of water
- *Diffusion:* movement of solutes
- *Filtration:* movement of both solutes and water
- *Osmolality:*
  - Osmoles in solution: mOsm/kg water
  - Calc Posm = (2 x serum Na^+) + blood urea + glucose
  - For Na+, K+ and Cl-: 1 mEq = 1 mOsm
  - Normal osmolality of body fluids: 283-292 mOsm/kg water

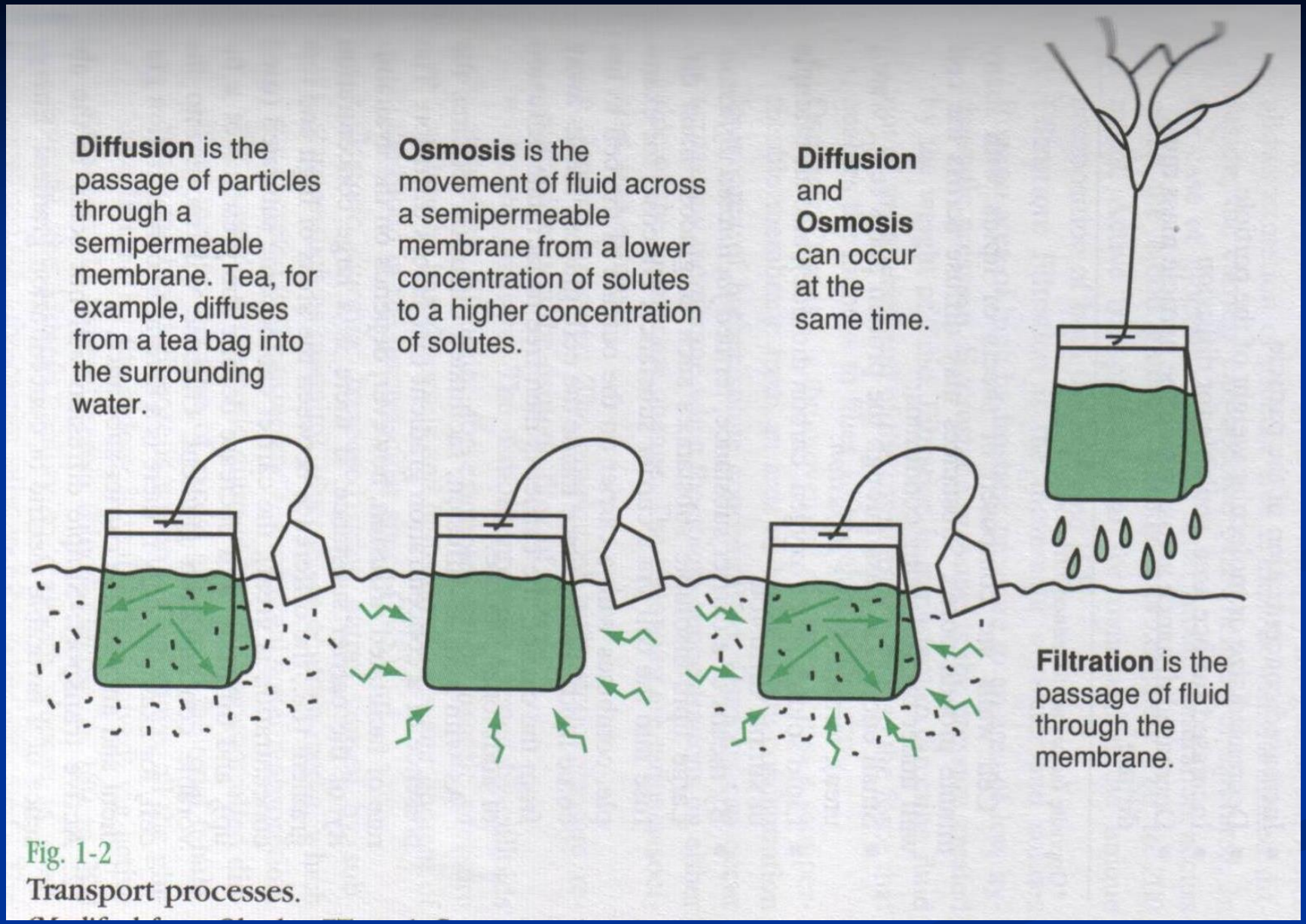


Fig. 1-2
Transport processes.

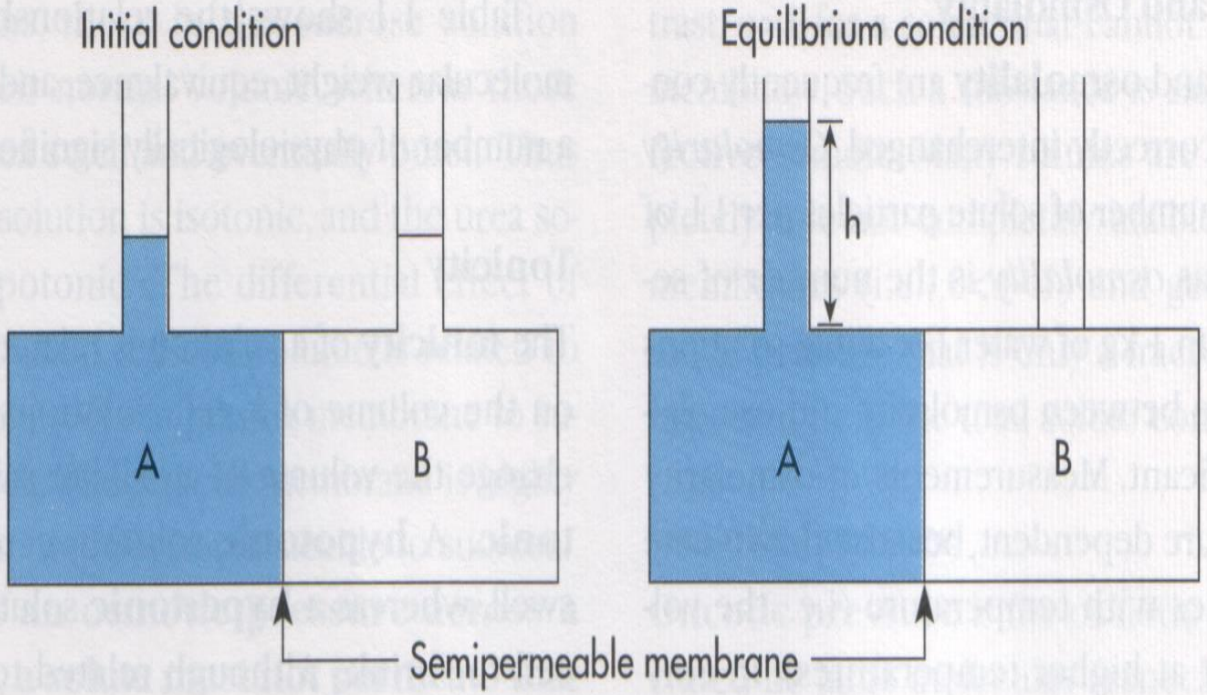
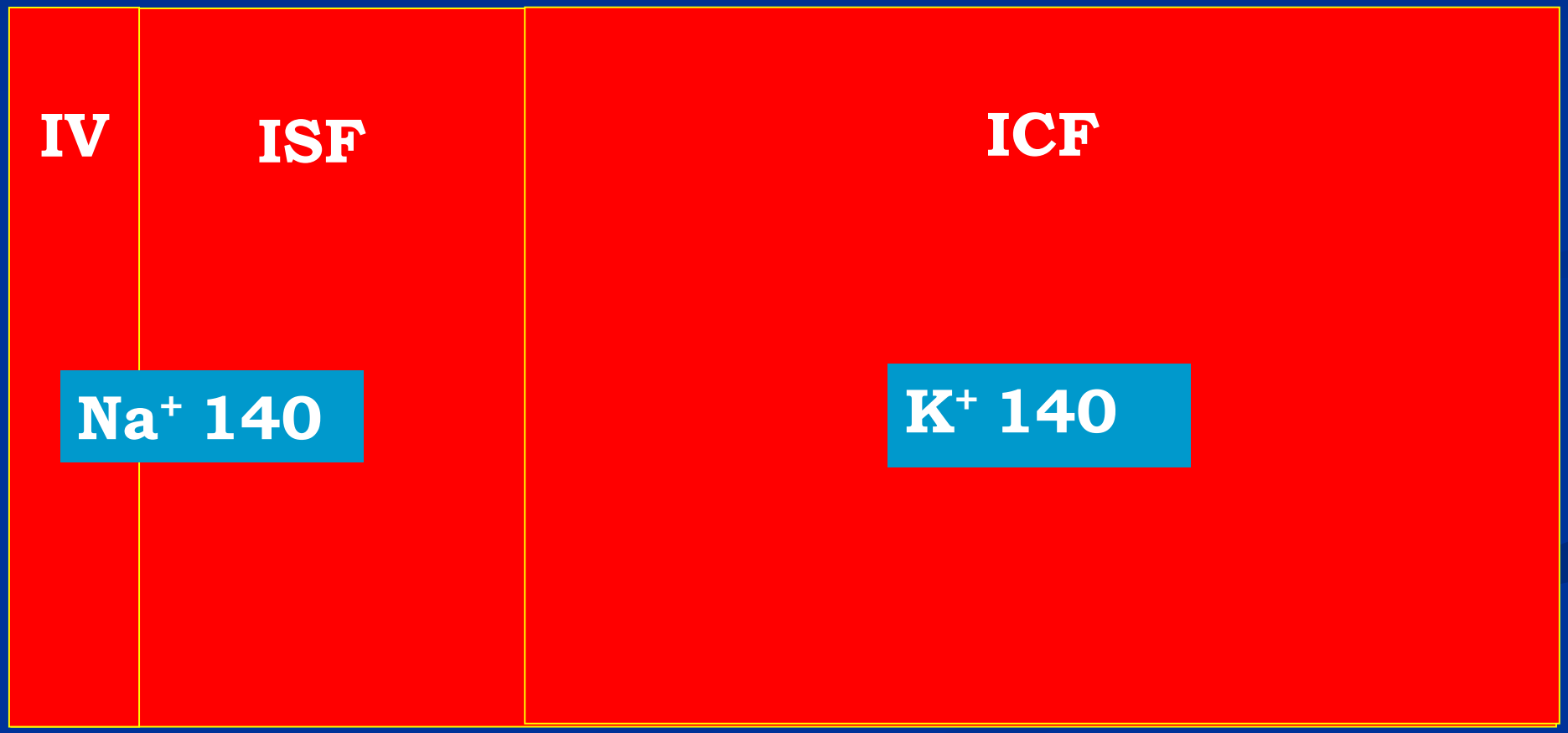


Figure 1-1 ■ Schematic representation of osmotic water movement and the generation of an osmotic pressure. The solute particles in compartment *A* cause water to move by osmosis from compartment *B* across the semipermeable membrane into compartment *A*. The water column in compartment A will rise until the hydrostatic pressure generated by the water column *(h)* stops the flow of water from compartment *B* into compartment *A*. This hydrostatic pressure is equal to the osmotic pressure generated by the solution in compartment *A*.

Body Fluid Compartments

- ECF and ICF are in ***osmotic equilibrium***
- **ICFosm = ECFosm = Posm**



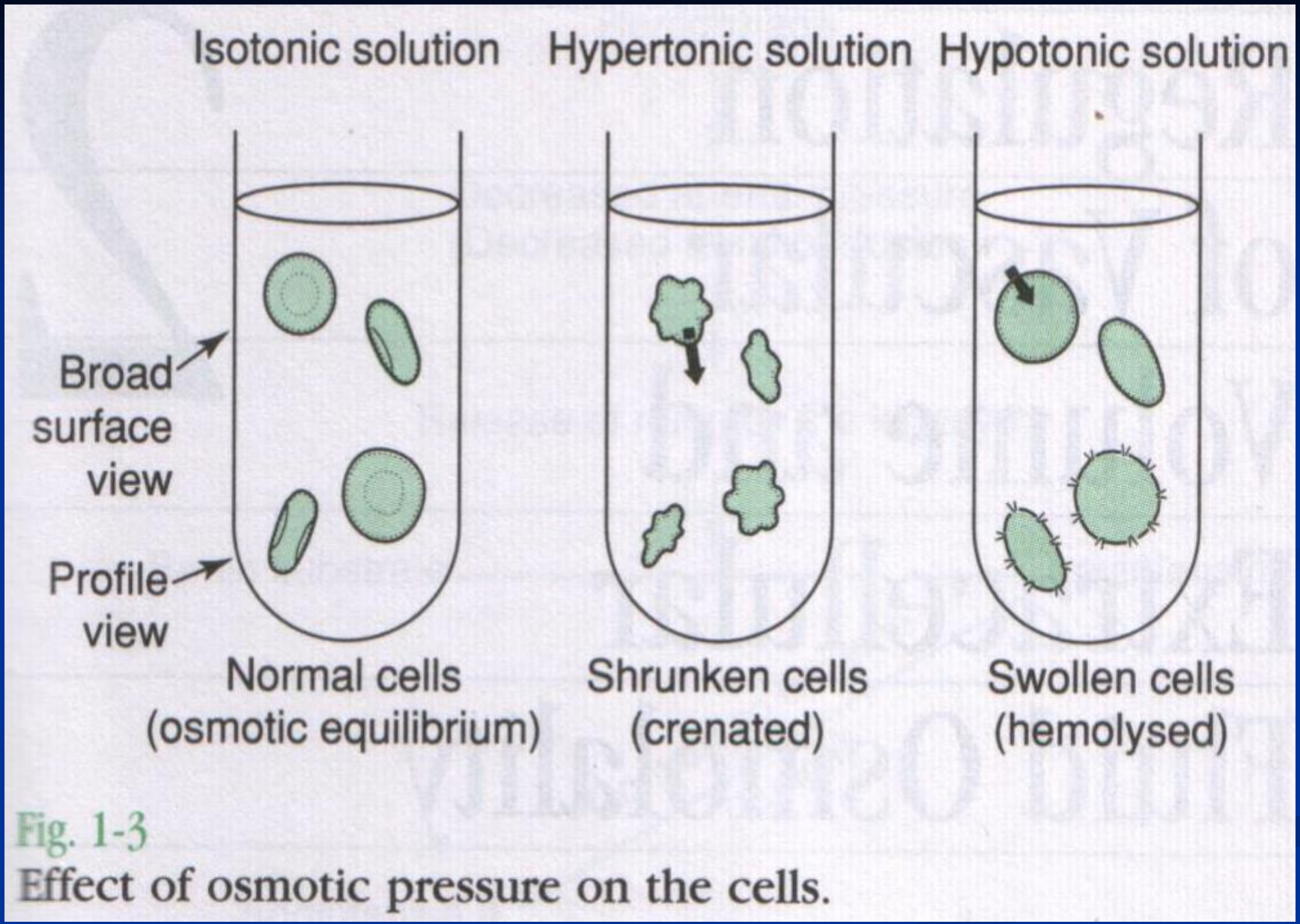
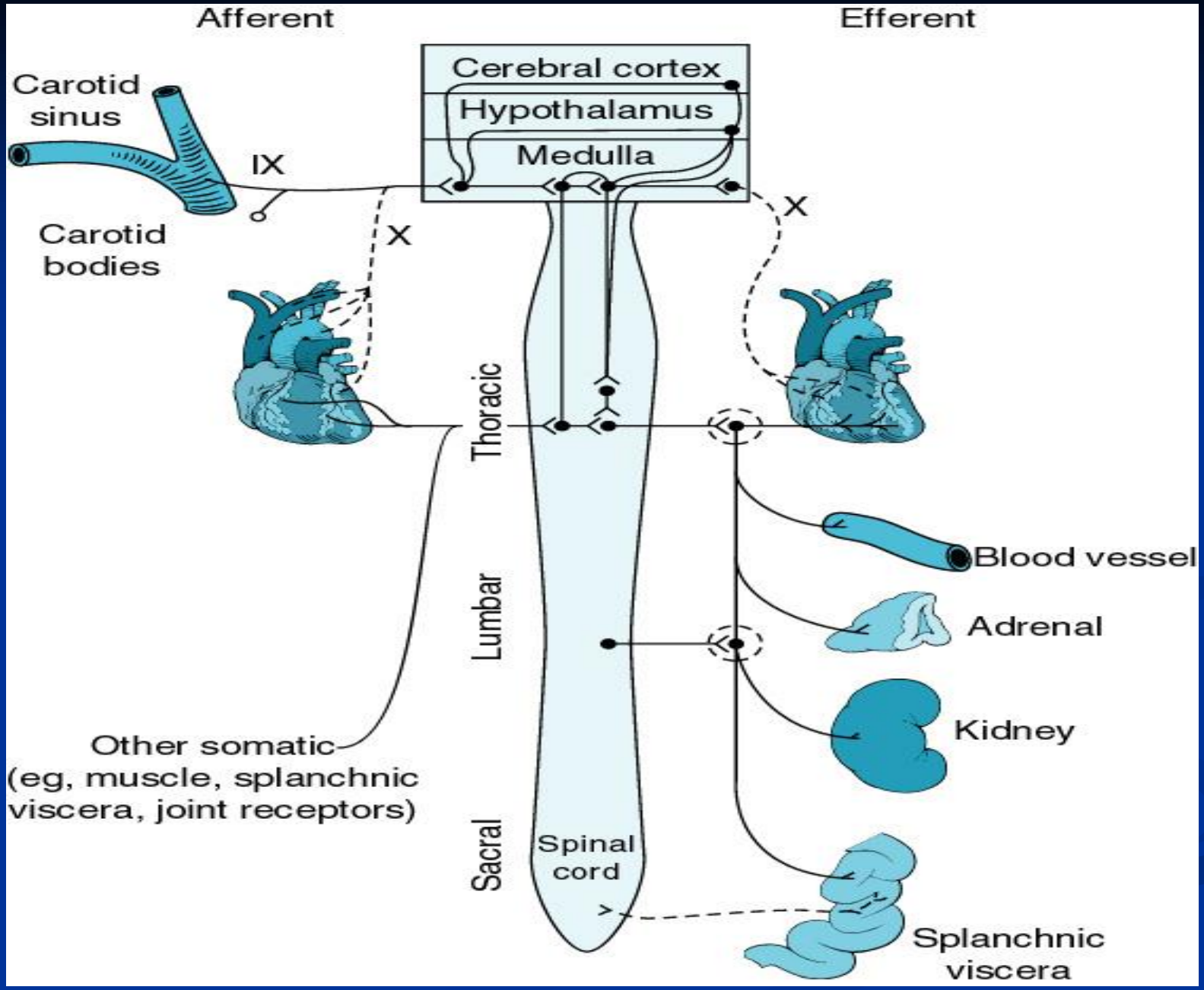


Fig. 1-3
Effect of osmotic pressure on the cells.

Regulation Mechanisms of Fluid and Electrolytes:

- Regulation of osmolality and volume is achieved through thirst and the osmoreceptor-antidiuretic hormone system (vasopressin)
  - Volume is more important than osmolality

- The regulation of volume also occurs through neurological and renal mechanisms
  - The stretch receptors (baroreceptors)
  - The Renin-Angiotension-Aldosterone System
  - The Natriuretic peptides
  - Kinins & Prostaglandins


Afferent
Efferent
Cerebral cortex
Hypothalamus
Medulla
Carotid sinus
IX
Carotid bodies
X
X
Thoracic
Lumbar
Sacral
Spinal cord
Blood vessel
Adrenal
Kidney
Other somatic (eg, muscle, splanchnic viscera, joint receptors)
Splanchnic viscera

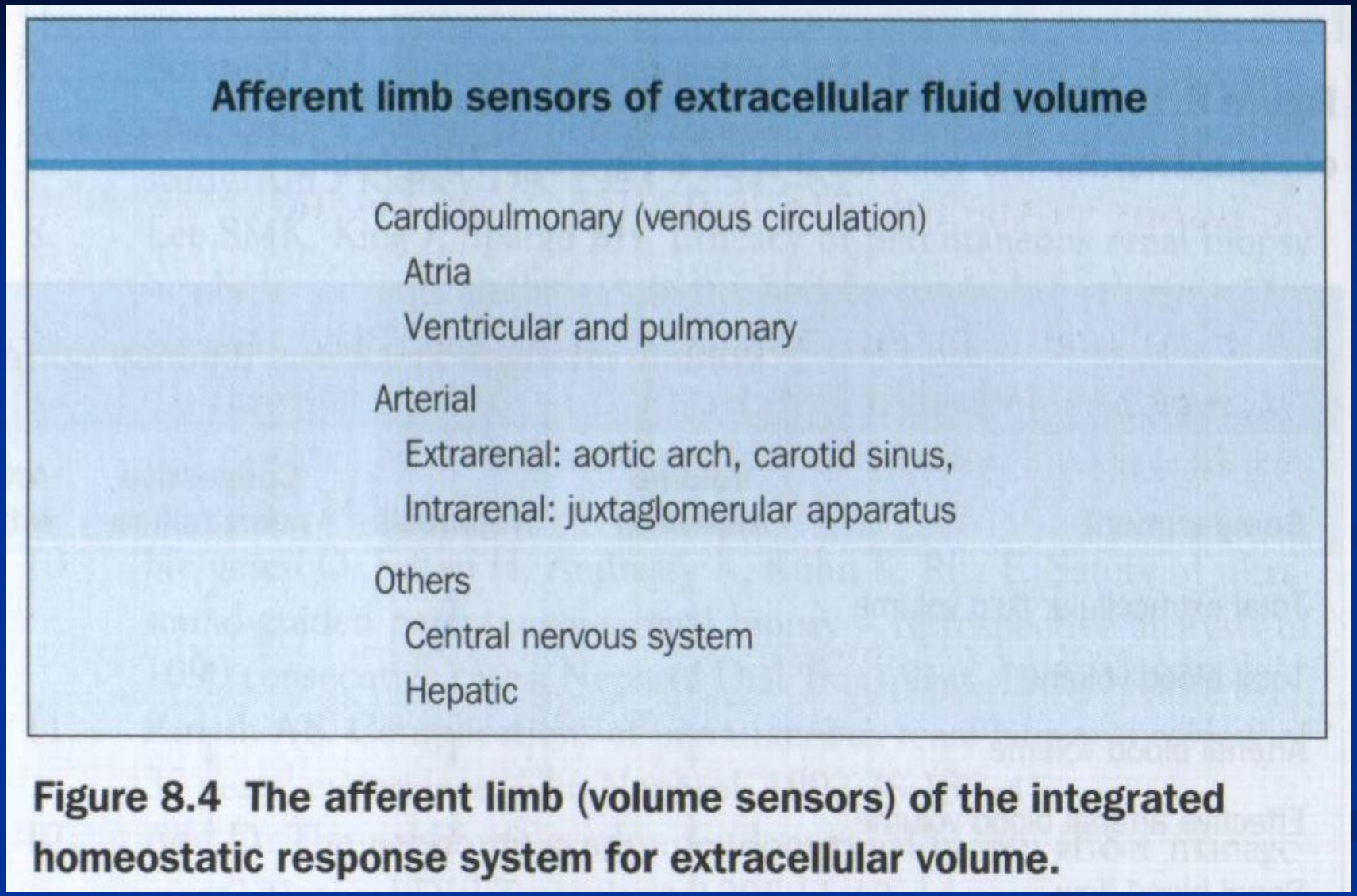


Figure 8.4 The afferent limb (volume sensors) of the integrated homeostatic response system for extracellular volume.

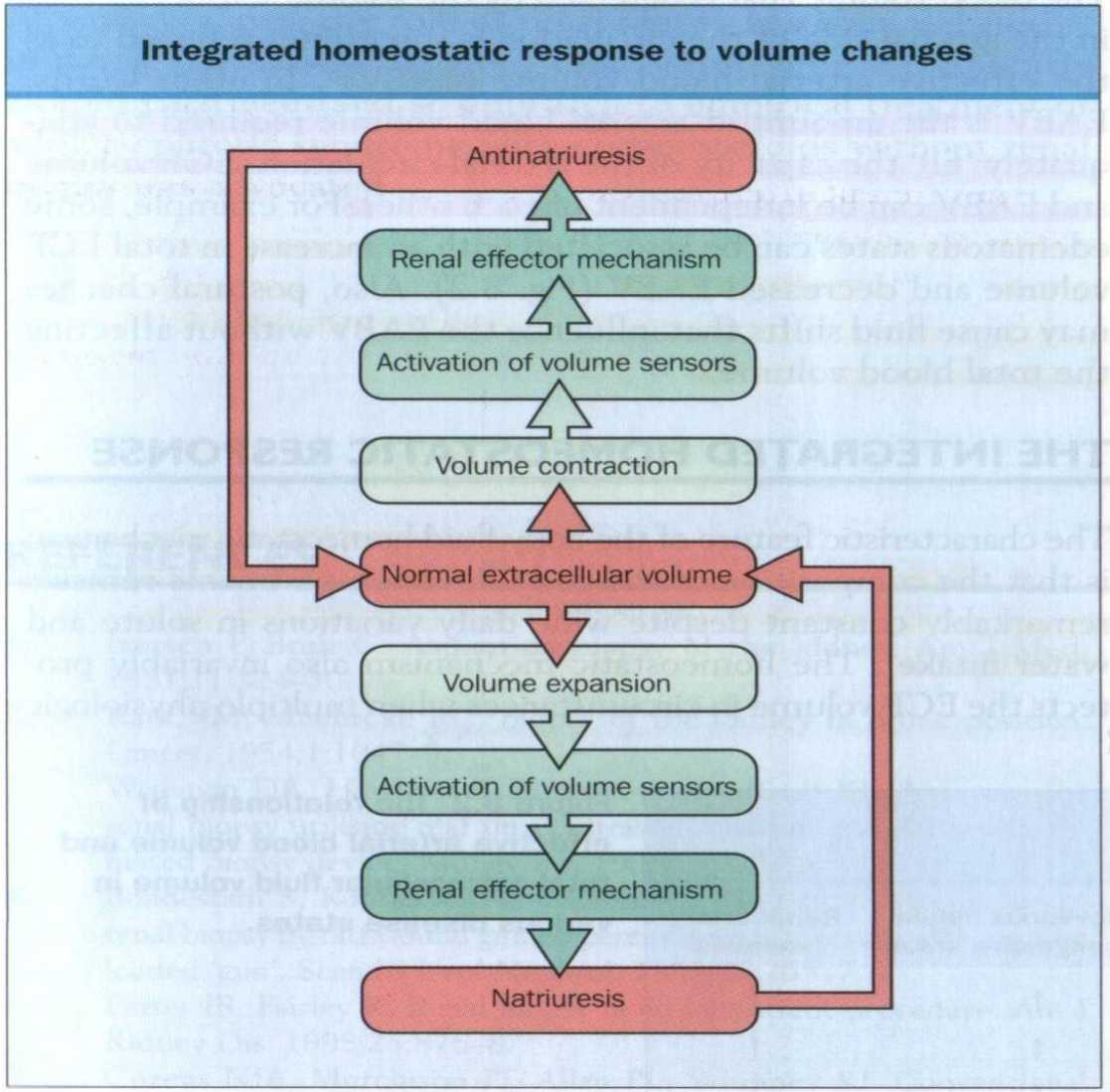
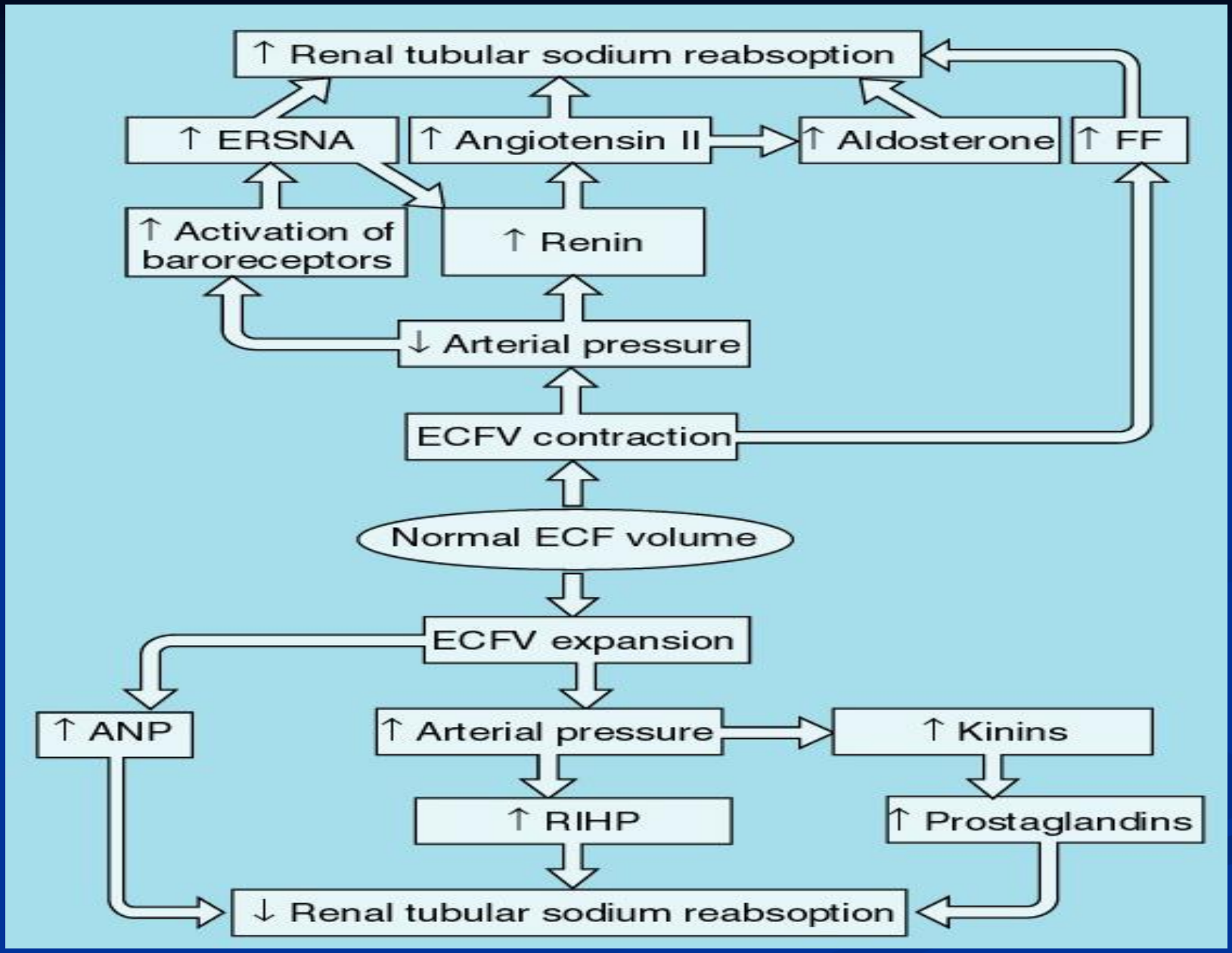
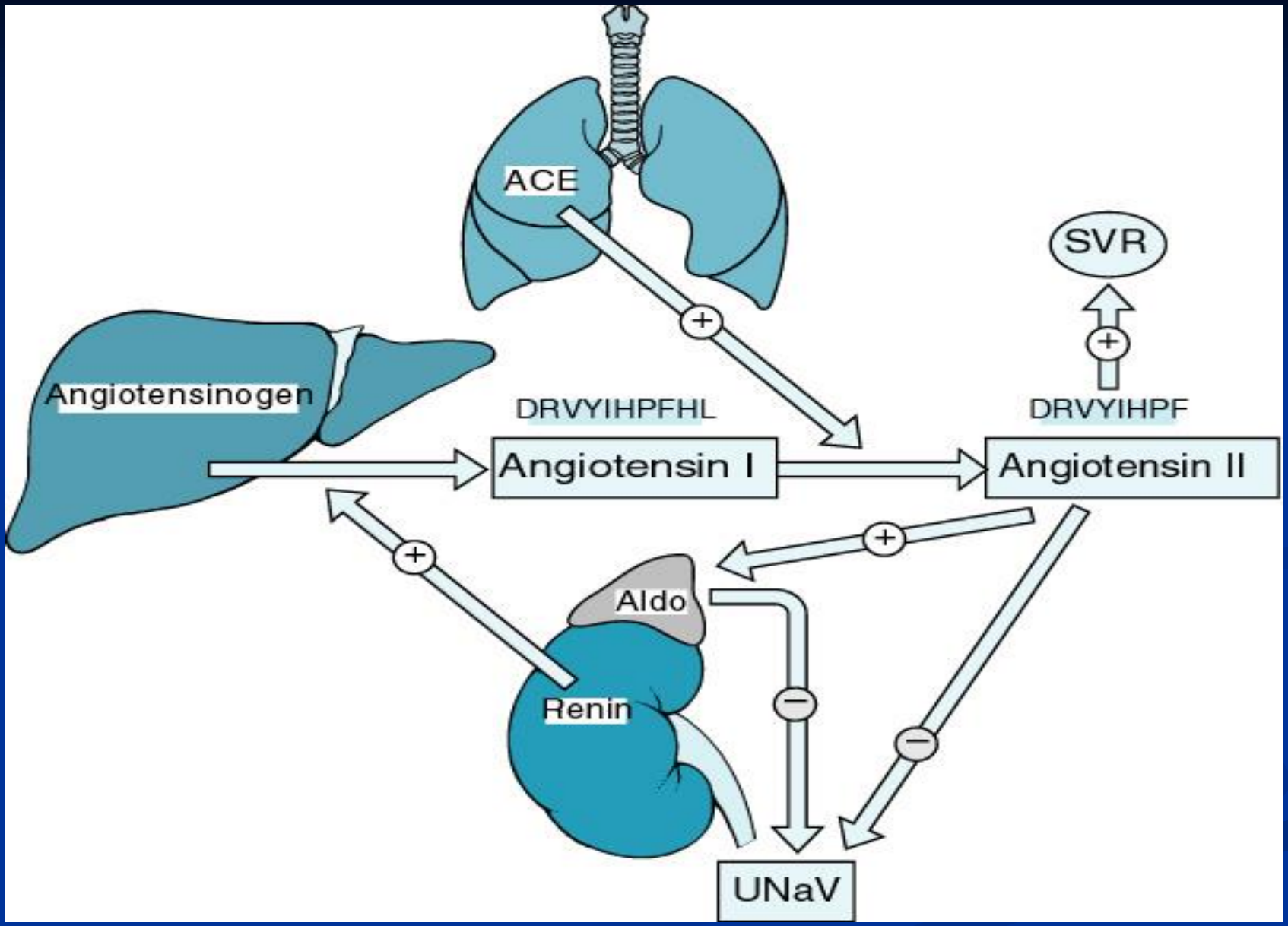
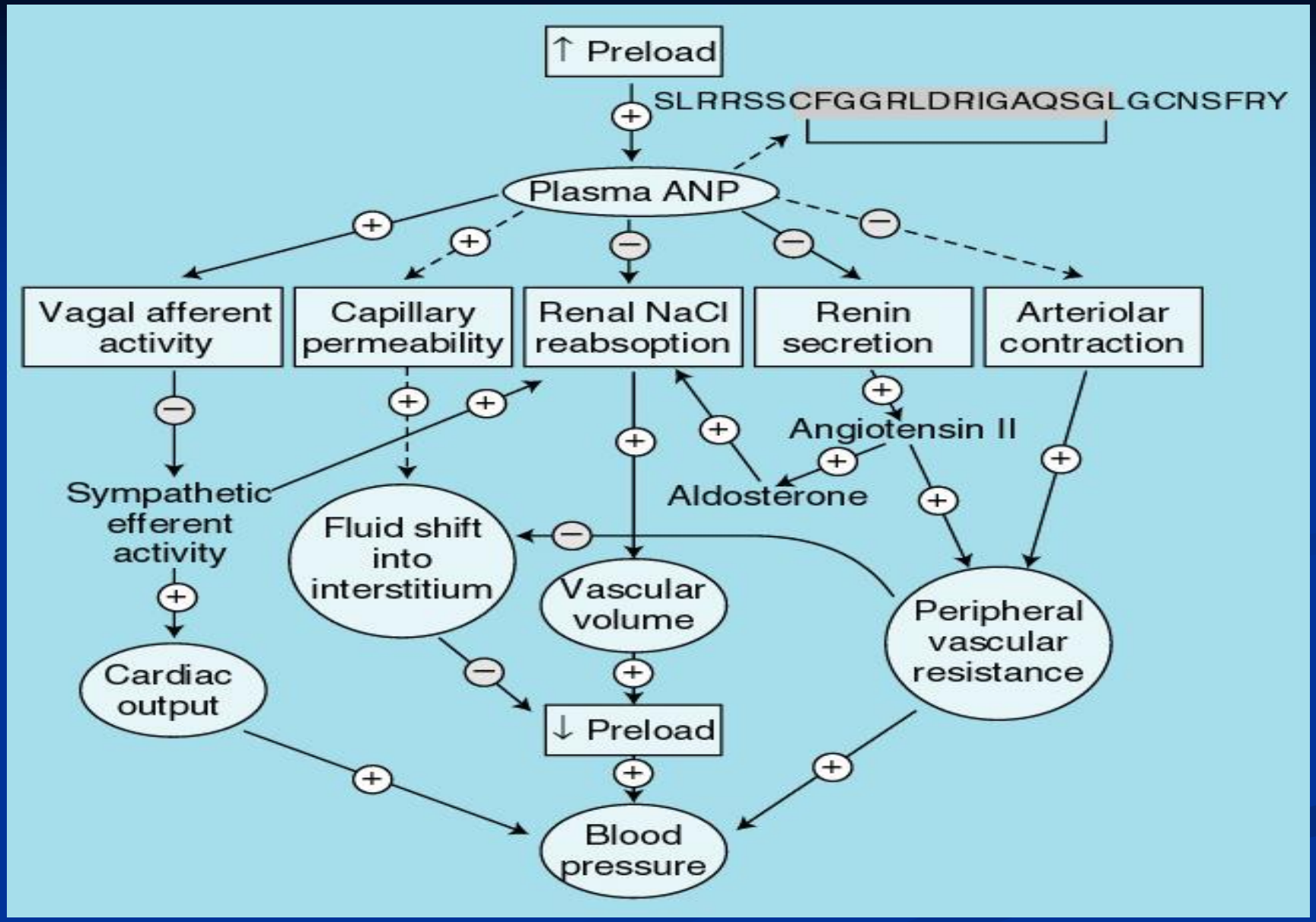
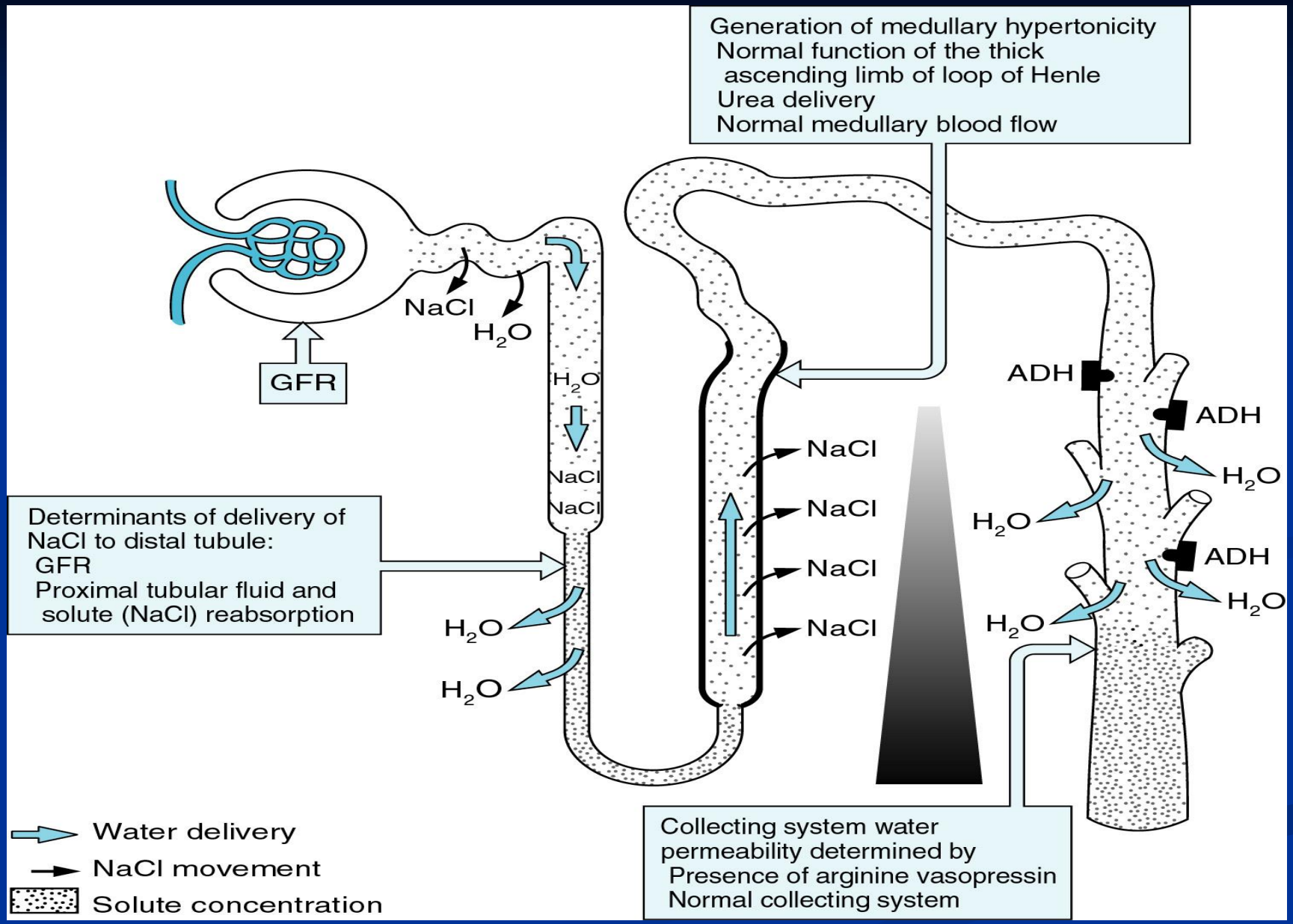


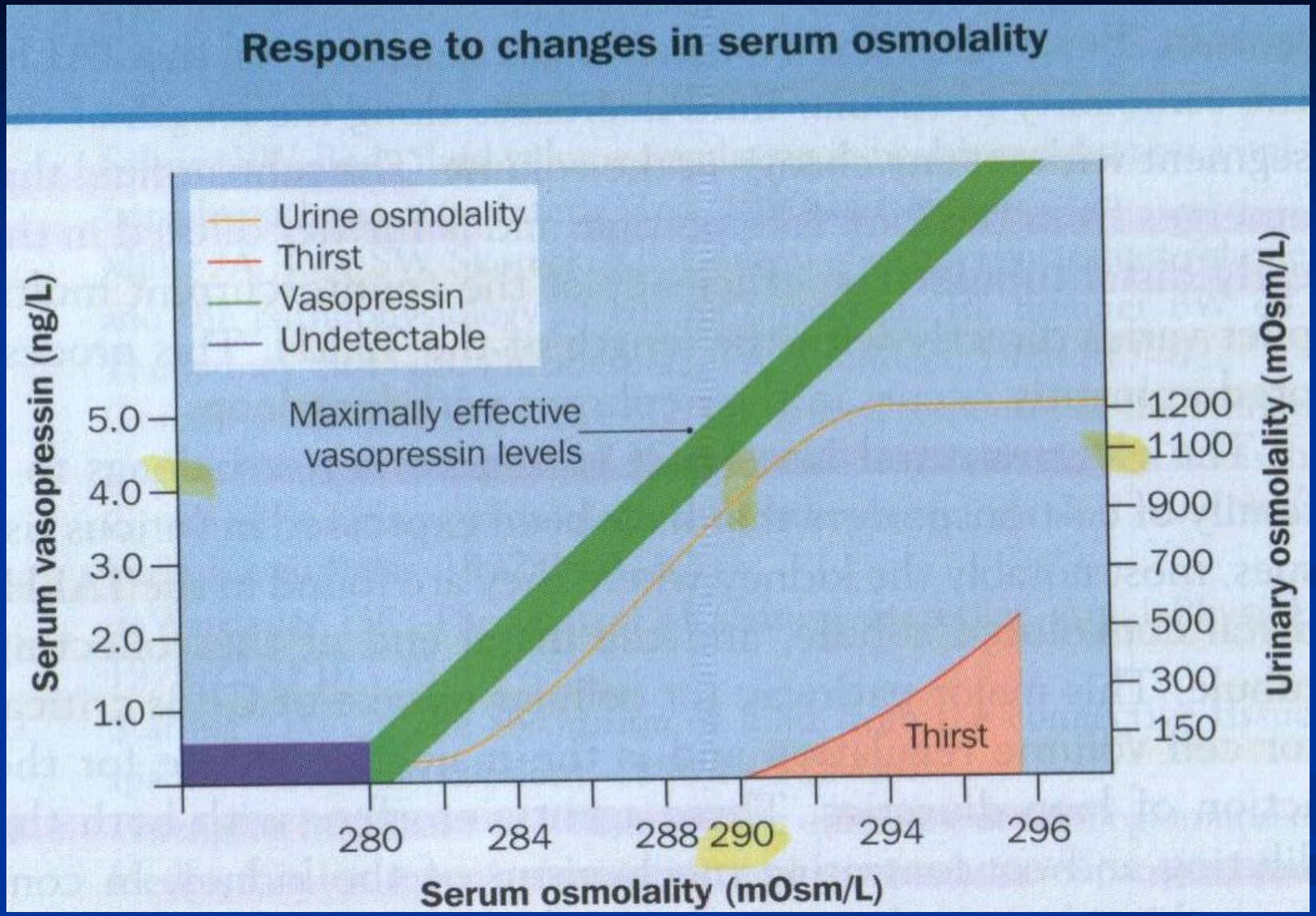
Figure 8.3 A general overview of the integrated homeostatic response system regulating extracellular fluid volume during volume contraction and expansion.


↑ Renal tubular sodium reabsoption
↑ ERSNA
↑ Angiotensin II
↑ Aldosterone
↑ FF
↑ Activation of baroreceptors
↑ Renin
↓ Arterial pressure
ECFV contraction
Normal ECF volume
ECFV expansion
↑ ANP
↑ Arterial pressure
↑ Kinins
↑ RIHP
↑ Prostaglandins
↓ Renal tubular sodium reabsoption

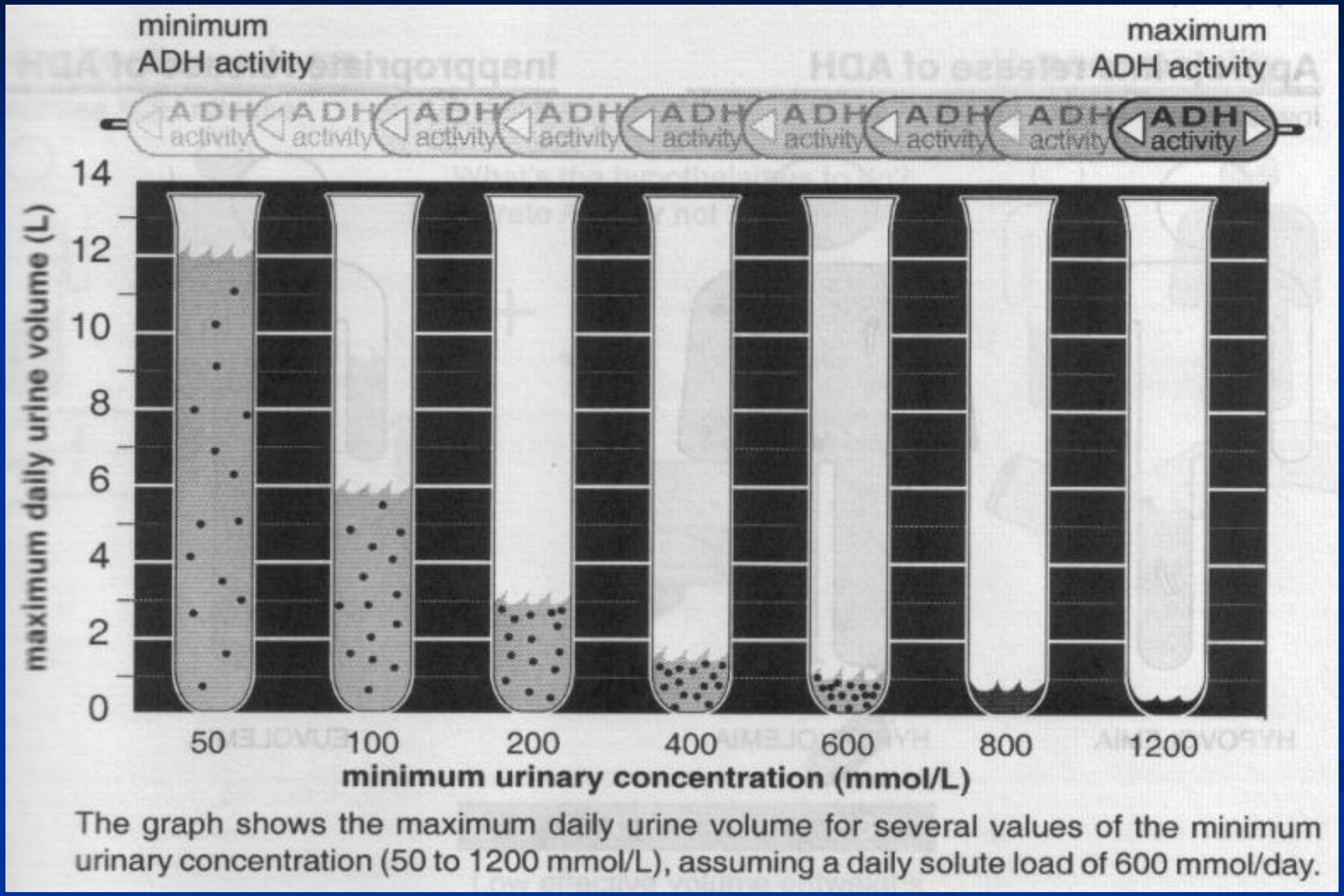

ACE
SVR
Angiotensinogen
DRVYIHPFHL
DRVYIHPF
Angiotensin I
Angiotensin II
Aldo
Renin
UNaV


↑ Preload
SLRRSSCFGGRLDRIGAQSGLGCNSFRY
Plasma ANP
Vagal afferent activity
Capillary permeability
Renal NaCl reabsoption
Renin secretion
Arteriolar contraction
Angiotensin II
Aldosterone
Sympathetic efferent activity
Fluid shift into interstitium
Vascular volume
Peripheral vascular resistance
Cardiac output
↓ Preload
Blood pressure


Generation of medullary hypertonicity
Normal function of the thick ascending limb of loop of Henle
Urea delivery
Normal medullary blood flow
GFR
NaCl
H_2O
H_2O
NaCl
NaCl
Determinants of delivery of NaCl to distal tubule:
GFR
Proximal tubular fluid and solute (NaCl) reabsorption
H_2O
H_2O
NaCl
NaCl
NaCl
NaCl
ADH
ADH
H_2O
H_2O
ADH
H_2O
H_2O
Collecting system water permeability determined by
Presence of arginine vasopressin
Normal collecting system
Water delivery
NaCl movement
Solute concentration


Response to changes in serum osmolality
Urine osmolality
Thirst
Vasopressin
Undetectable
Maximally effective vasopressin levels
Thirst
Serum vasopressin (ng/L)
5.0
4.0
3.0
2.0
1.0
Urinary osmolality (mOsm/L)
1200
1100
900
700
500
300
150
280
284
288
290
294
296
Serum osmolality (mOsm/L)

Urine Output & Daily Solute Load



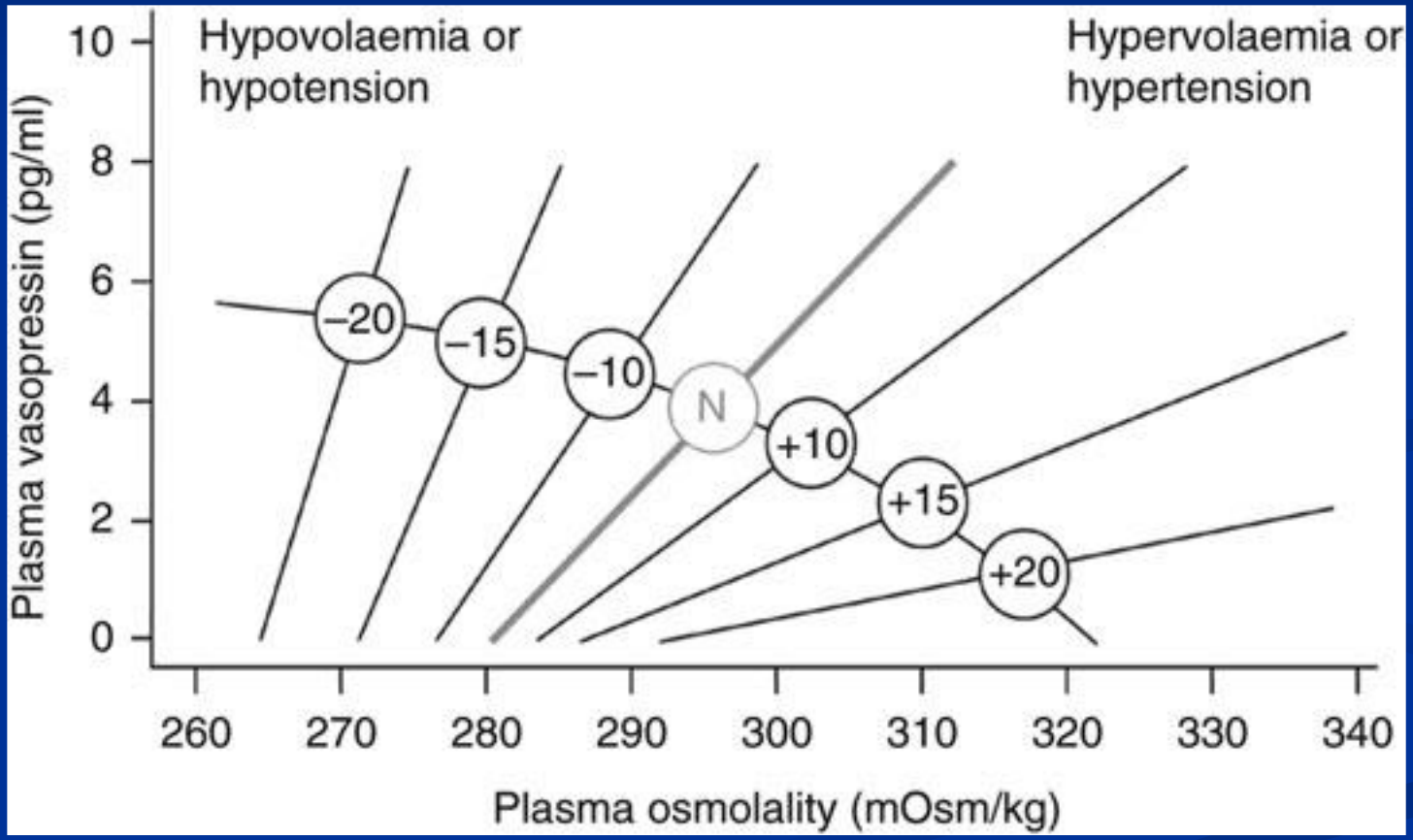
The graph shows the maximum daily urine volume for several values of the minimum urinary concentration (50 to 1200 mmol/L), assuming a daily solute load of 600 mmol/day.

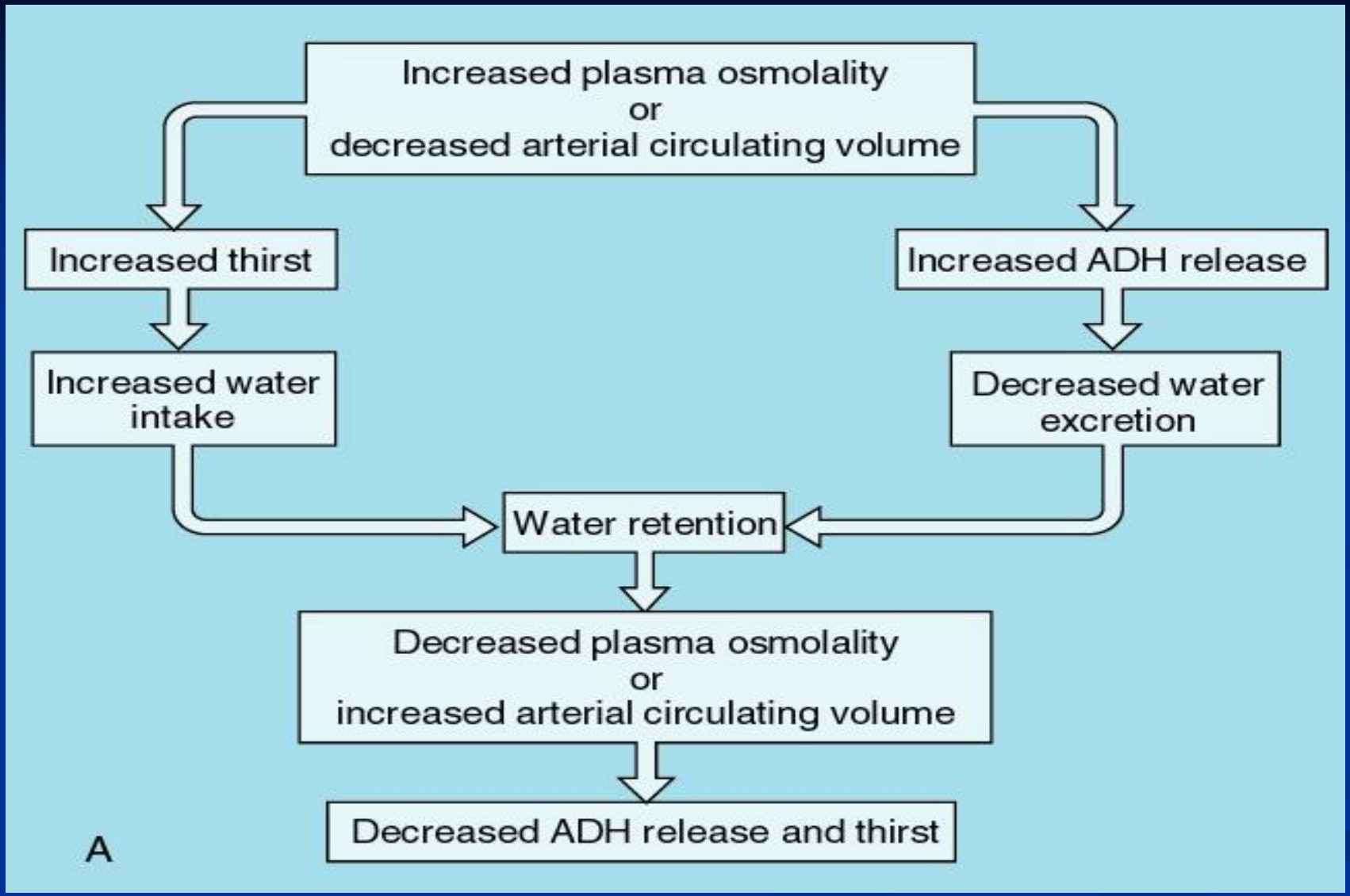
The Linear Relationship Between Urine Specific Gravity and Uosm

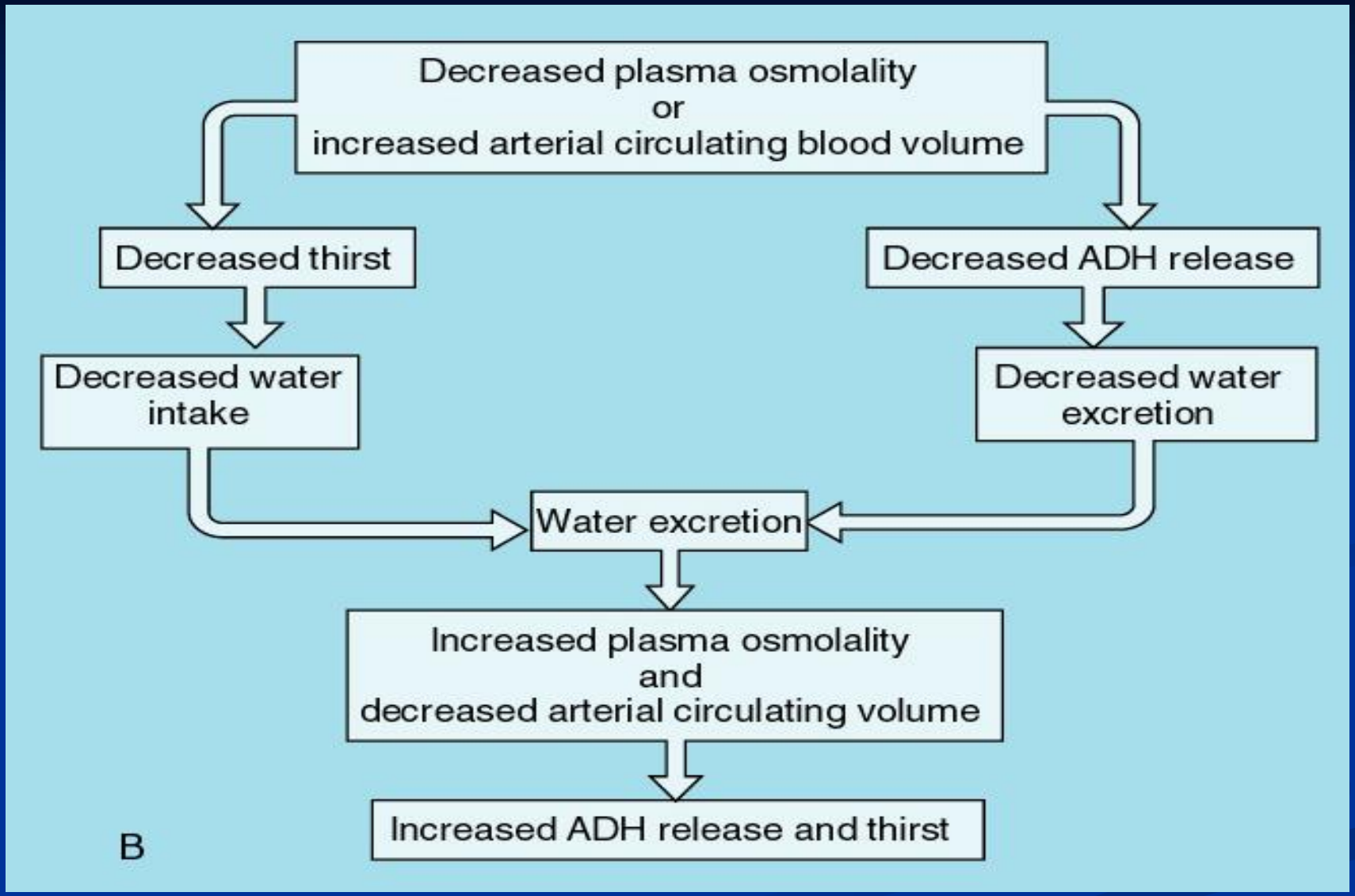
SG	Osmolality (mOsm/Kg H_2O)
1.010	300 – 400
1.020	700 – 800
1.030	1000 – 1200

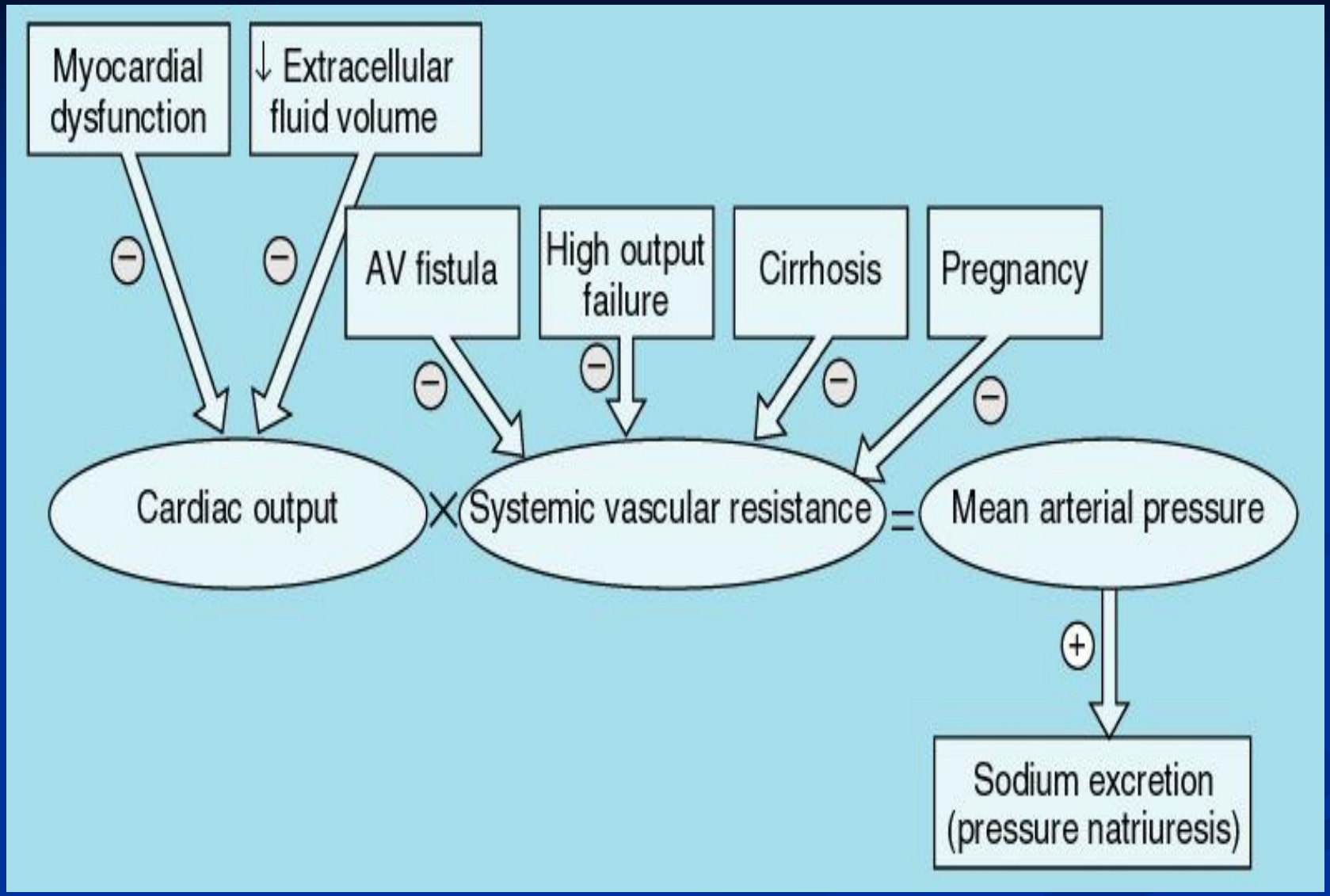
Plasma SG ~ 1.008

Effect of Hypovolemia on Osmoreceptor Gain




Increased plasma osmolality
or
decreased arterial circulating volume
Increased thirst
Increased ADH release
Increased water intake
Decreased water excretion
Water retention
Decreased plasma osmolality
or
increased arterial circulating volume
Decreased ADH release and thirst
A


Decreased plasma osmolality
or
increased arterial circulating blood volume
Decreased thirst
Decreased ADH release
Decreased water intake
Decreased water excretion
Water excretion
Increased plasma osmolality
and
decreased arterial circulating volume
Increased ADH release and thirst
B


Myocardial dysfunction
↓ Extracellular fluid volume
AV fistula
High output failure
Cirrhosis
Pregnancy
Cardiac output
Systemic vascular resistance
Mean arterial pressure
Sodium excretion (pressure natriuresis)

Effective Arterial Blood Volume (EABV):

- Although the absolute volume of the intravascular space is an important component of circulatory "fullness", ***the adequacy of the circulation*** (more commonly called **the effective arterial blood volume or EABV**) also is determined by cardiac output and systemic vascular resistance

Effective Arterial Blood Volume (EABV):

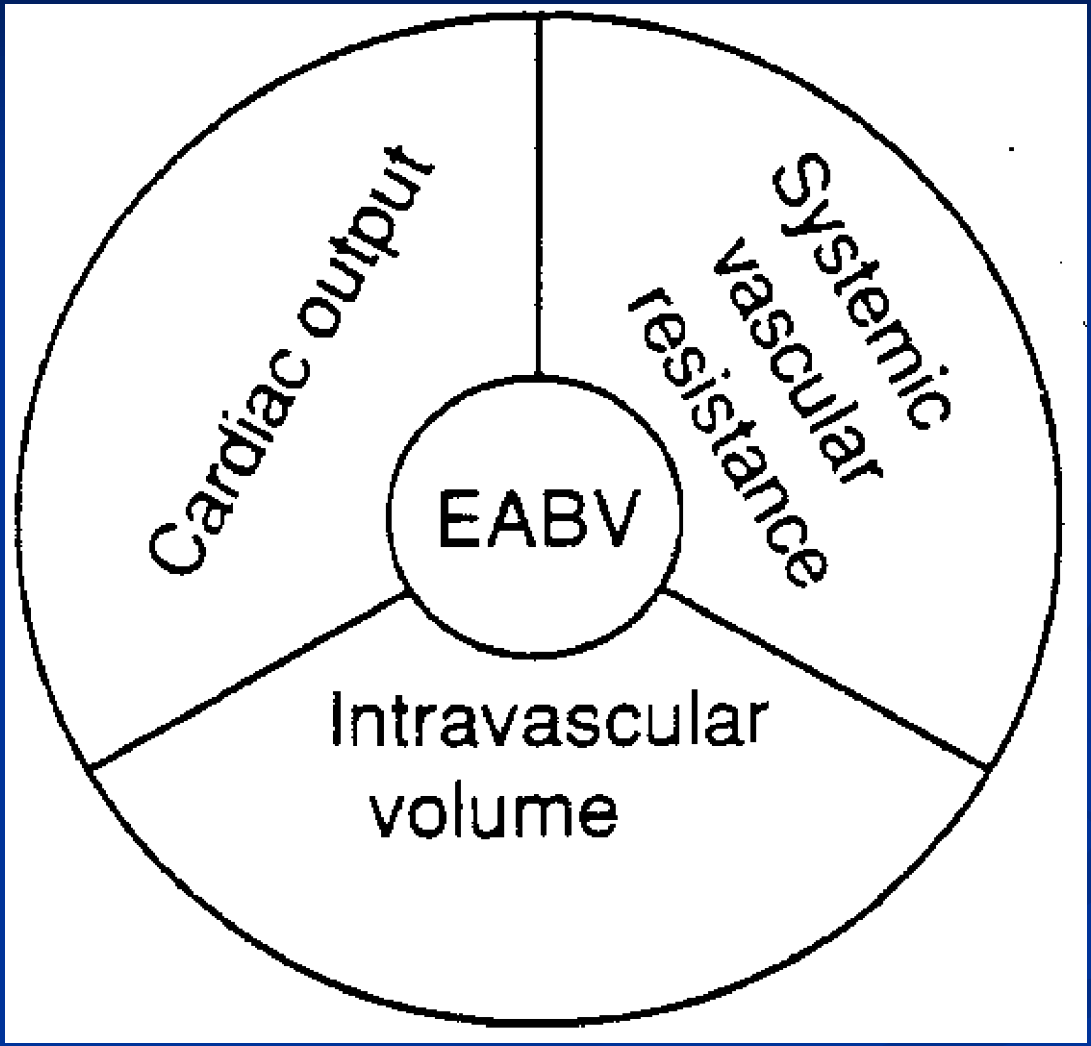
- **↓ EABV:**
  - ↑ CO
  - ↑ SVR
  - ↑ Renal Na retention
- **↑ EABV:**
  - ↓ CO
  - ↓ SVR
  - ↓ Renal Na retention

Effective Arterial Blood Volume (EABV):

- **EABV is the amount of arterial blood volume required to adequately 'fill' the capacity of the arterial circulation**

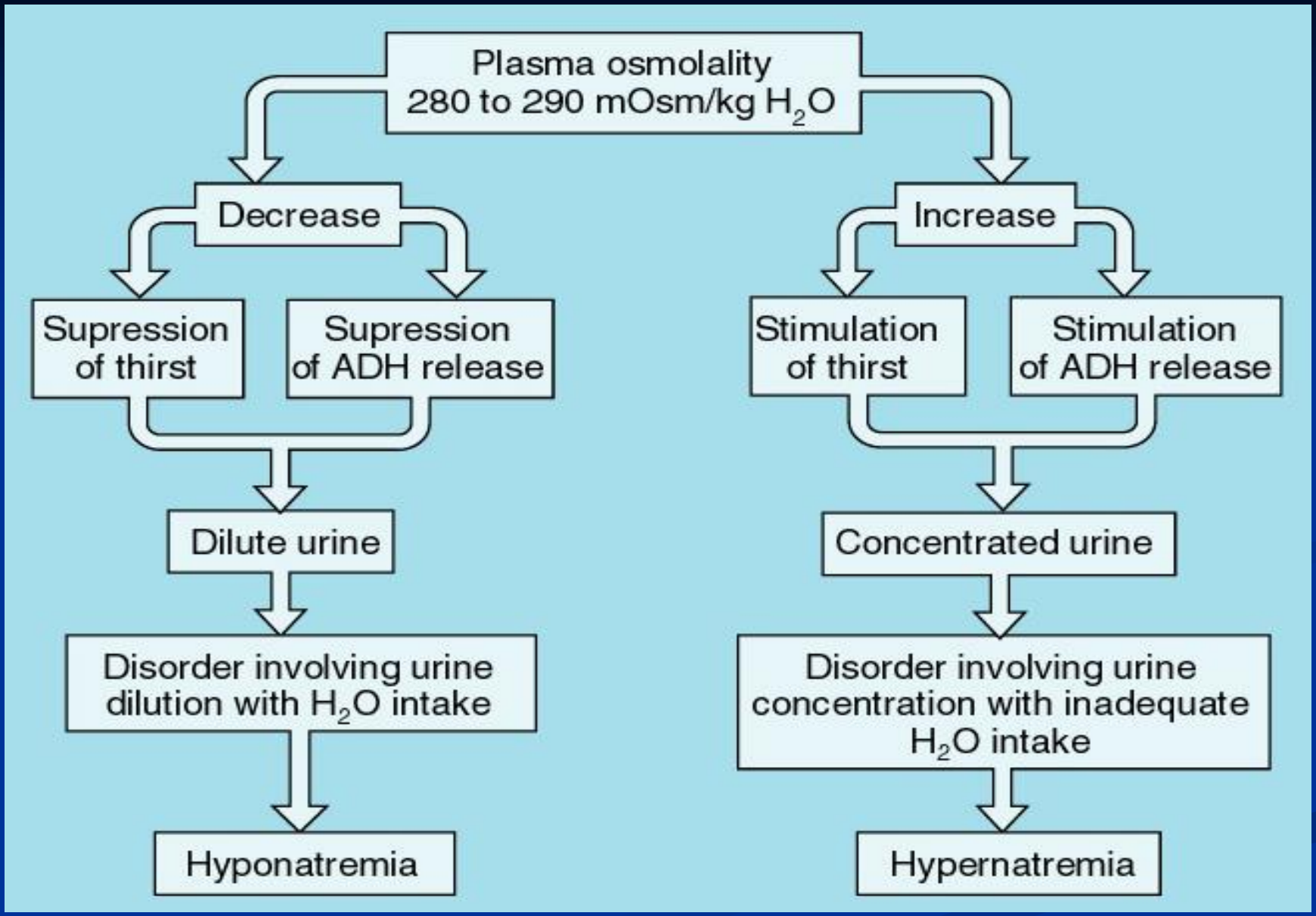
- ECF volume and EABV can be independent of each other
  - Edematous states: increase in total ECF volume and decreased EABV
  - Postural changes may cause shifts that influence the EABV without affecting the total blood volume

Effective Arterial Blood Volume (EABV):



Clinical features of Hypovolemia & Hypervolemia

	Hypovolemia	Hypervolemia
Symptoms	Thirst	Ankle swelling
	Dizziness on standing	Abdominal swelling
	Weakness	Breathlessness
Signs	Low JVP	Raised JVP
	Postural hypotension	Peripheral edema
	Tachycardia	Pulmonary crepitations
	Dry mouth	Pleural effusion
	Reduced skin turgor	Ascites
	Reduced urine output	Hypertension (sometimes)
	Weight loss	Weight gain
	Confusion, stupor	


Plasma osmolality
280 to 290 mOsm/kg H_2O
Decrease
Increase
Supression of thirst
Supression of ADH release
Stimulation of thirst
Stimulation of ADH release
Dilute urine
Concentrated urine
Disorder involving urine dilution with H_2O intake
Disorder involving urine concentration with inadequate H_2O intake
Hyponatremia
Hypernatremia

Sodium and Water:

- ECF volume= ***absolute*** amounts of Sodium and water
- Plasma [Na^+] = ***ratio*** between the amounts of Sodium and water (Concentration)

- Hyponatremia = Water Excess
- Hypernatremia = Water Deficit

- Hypervolemia = Sodium Excess ("Edema")
- Hypovolemia = Sodium Deficit ("Dehydration")

Sodium and Water:

	Hyponatremia (Water Excess)	Hypernatremia (Water Deficit)
Hypovolemia (Dehydration) (Sodium Deficit)	Hemorrhagic Shock with good oral water intake	Diarrhea in Children and Seniors
Hypervolemia (Edema) (Sodium Excess)	Advanced Congestive Heart Failure	Hemodialysis Patient after 3% Saline infusion

Tonicity

- To compare the osmolality of a solution to that of another solution (body fluid compartments)

- Used to compare the osmolality of intravenous solutions to that of the serum:
  - *ISOTONIC*
  - *HYPOTONIC*
  - *HYPERTONIC*

Hypotonic	*Isotonic*	*Hypertonic*
Solutions have more water than solutes comparing to ECF	Solutions have the same solute concentration as the ECF	Solutions have more solutes than water comparing to ECF
Water will move from ECF into ICF	It will remain in the ECF	Water will move from ICF to ECF
Distilled Water 0.45% NaCl (1/2) 0.33% NaCl (1/3)	NS (0.9% NaCl) Ringers Lactate 2/3 DW-1/3 NS 5% Dextrose in Water (D5W)	3% NaCl 10%-50% Dextrose D5W-1/2 NS D5NS Amino acid solution

Intravenous Solutions

- *Crystalloids* vs *Colloids*
- *Crystalloids* are intravenous solutions that contain solutes that readily cross the capillary membrane
  - Dextrose and electrolyte solutions
- *Colloids* are intravenous solutions that DO NOT readily cross the capillary membrane
  - Blood, albumin, plasma

Solution	*Gluc*	*Na^+*	*K^+*	*Ca^{+2}*	*Cl^-*	*Lact*	*mOsm/L*
D_5W	50	0	0	0	0	0	253
$D_{10}W$	100	0	0	0	0	0	506
NS	0	154	0	0	154	0	308
½ NS	0	77	0	0	77	0	154
D_5 NS	50	154	0	0	154	0	561
D_5 ½ NS	50	77	0	0	77	0	407
2/3-1/3	33	50	0	0	50	0	285
Ringer's Lactate	0	130	4	3	109	28	274

D5W: 5 g dextrose/100 mL (50 g/L)

D10W: 10 g dextrose/100 mL (100 g/L)

NS (0.9% NS): 0.9 g NaCl/100 mL (9 g/L)

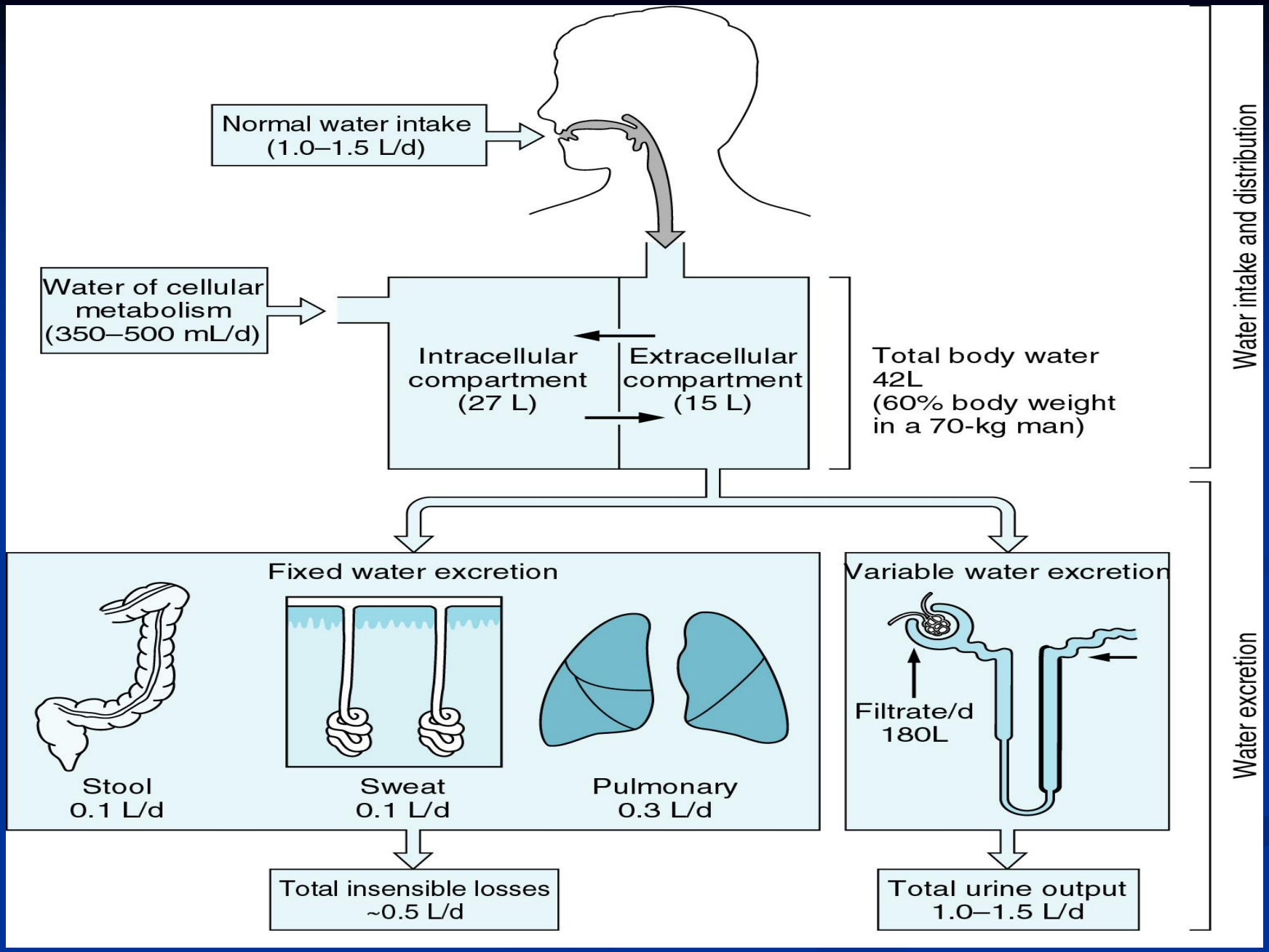
½ NS (0.45% NS): 0.45 g NaCl/100 mL (4.5 g/L)

2/3-1/3: 2/3 D5W (33 g/L) + 1/3 NS (0.33 g NaCl/100mL or 3.3 g NaCl/L)

Lytes: mEq/L

Gluc: g/L

Parental Fluid	ECF (1/3 TBW)		ICF (2/3 TBW)
	IV (1/4 ECF)	ISF (3/4 ECF)	
1000 ml D_5W	80 ml	250 ml	670 ml
1000 ml NS	250 ml	750 ml	---
Colloids (PRBC)	300 ml	---	---
1000 ml ½ NS:			
(500 ml NS)	125 ml	375 ml	---
(500ml water)	40 ml	125 ml	335 ml
Total	165 ml	500 ml	335 ml
1000 ml D_5½NS	165 ml	500 ml	335 ml
1000 ml $D_{10}W$	80 ml	250 ml	670 ml
1000 ml D_5NS	250 ml	750 ml	---


Normal water intake
(1.0–1.5 L/d)
Water of cellular metabolism
(350–500 mL/d)
Intracellular compartment
(27 L)
Extracellular compartment
(15 L)
Total body water
42L
(60% body weight
in a 70-kg man)
Water intake and distribution
Fixed water excretion
Variable water excretion
Stool
0.1 L/d
Sweat
0.1 L/d
Pulmonary
0.3 L/d
Filtrate/d
180L
Water excretion
Total insensible losses
~0.5 L/d
Total urine output
1.0–1.5 L/d

Basal Requirements:

- Basal Water:
  - 1st 10 kg: 4 ml/kg/h +
  - 2nd 10 kg: 2 ml/kg/h +
  - > 20 kg: 1 ml/kg/h

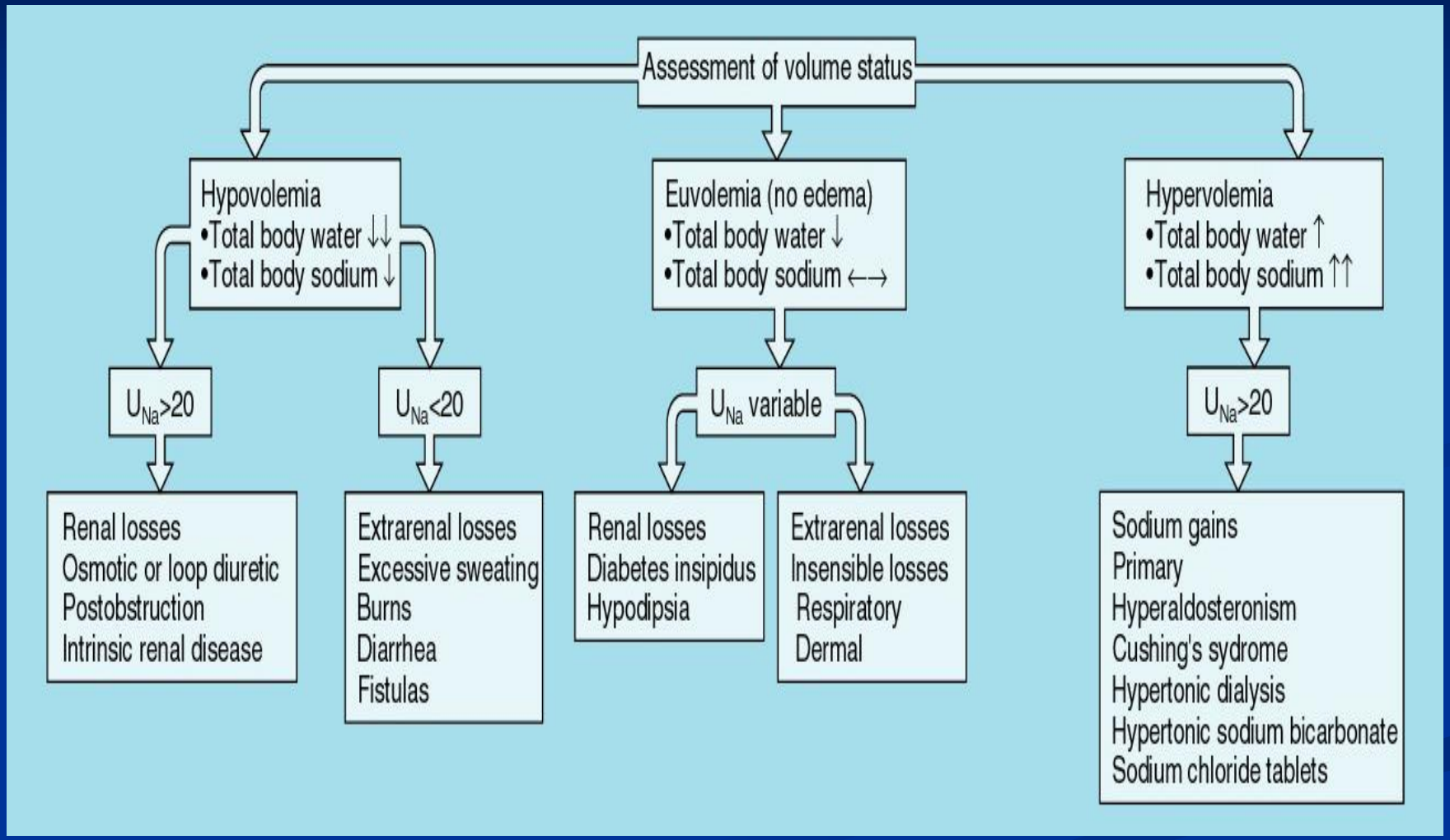
- Insensible water loss:
  - Stool, breath, sweat: 800 ml/d
  - Increases by 100-150 ml/d for each degree above 37 C

Basal Requirements:

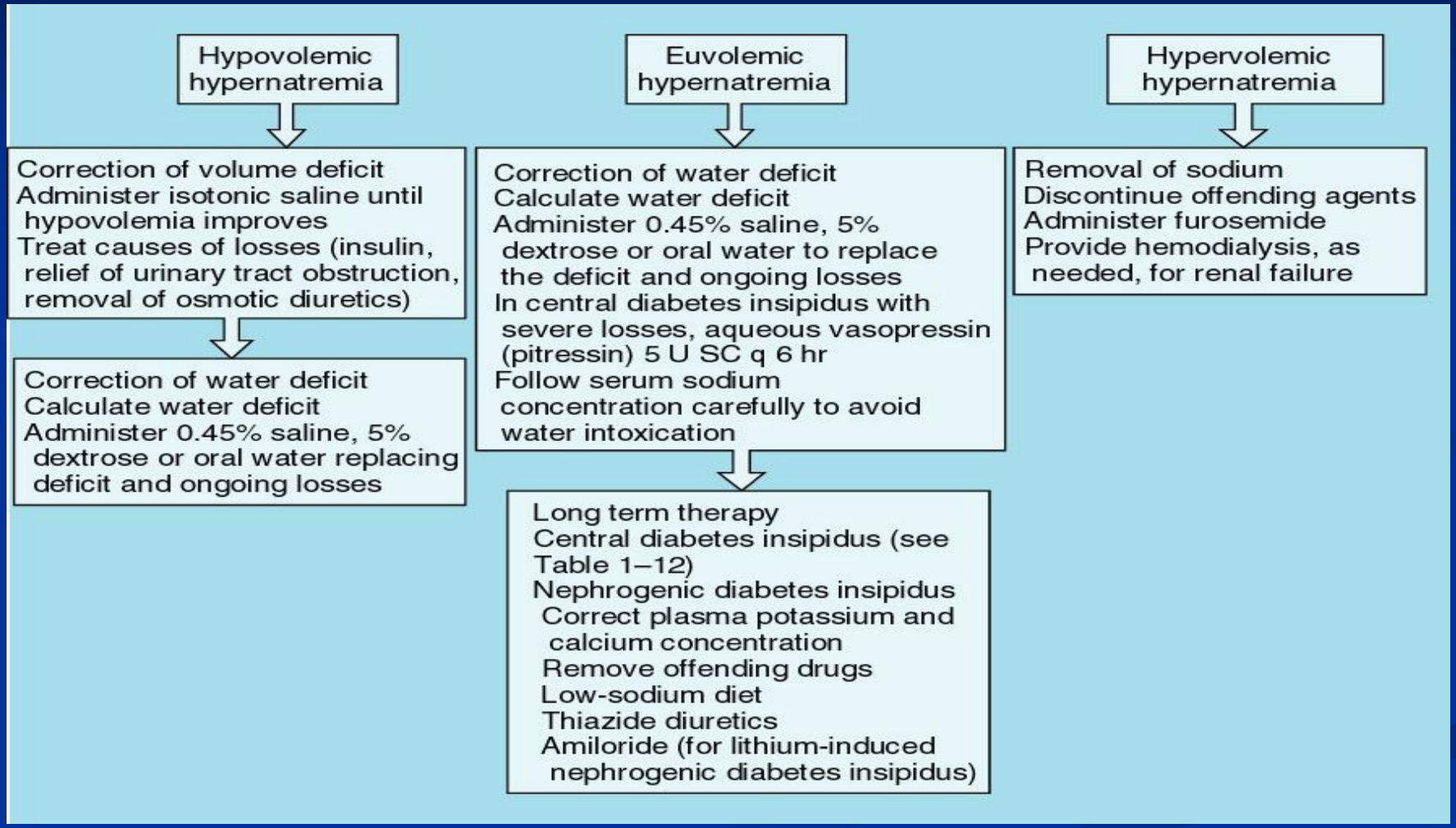
- Electrolytes:
  - Na: 50-150 mmol/d (NaCl)
  - Cl: 50-150 mmol/d (NaCl)
  - K: 20-60 mmol/d (KCl)
- Carbohydrates:
  - Dextrose: 100-150 g/d
  - IV Dextrose minimizes protein catabolism and prevents ketoacidosis

Hypernatremia

Hypernatremia: Causes



Hypernatremia: Treatment



Water Deficit Calculation:

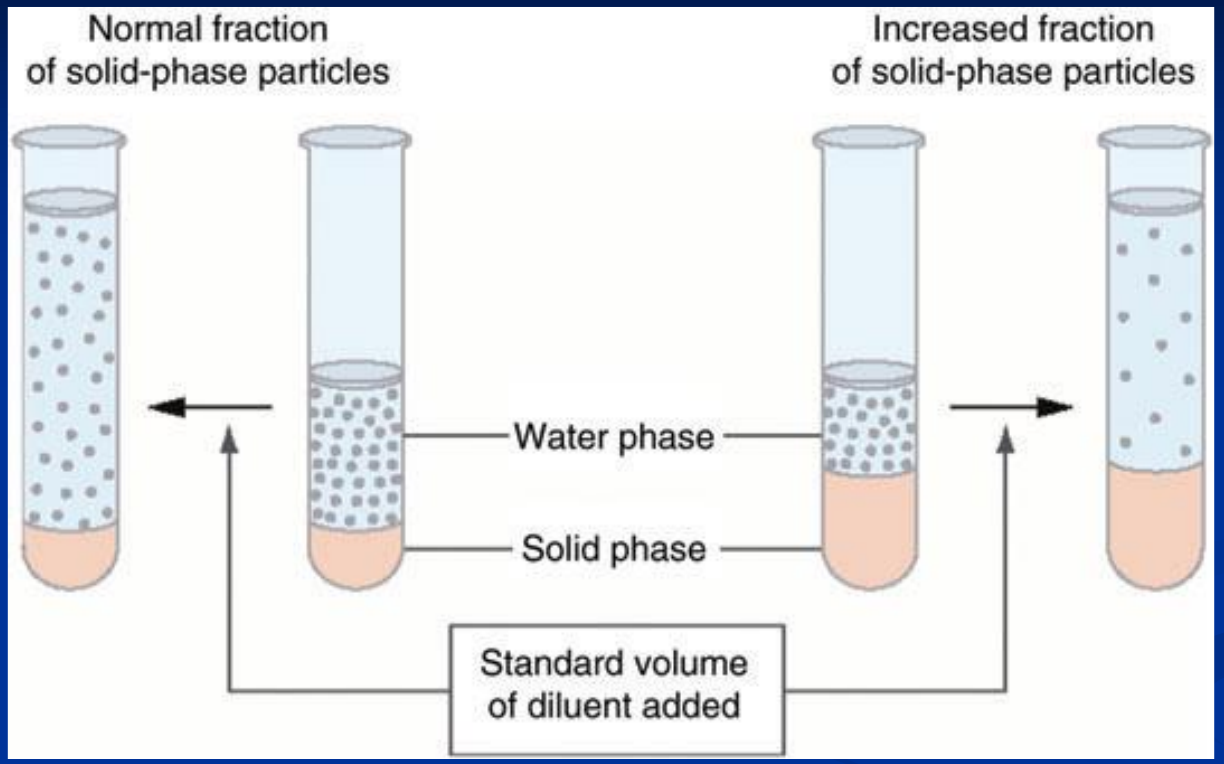
- Current Total Body Water = 0.6 x Current Body Weight
- Current TBW x Current [Na^+] = Target TBW x Target [Na^+]
- Target TBW – Current TBW = Water Deficit
- Ongoing loss
- IVF: type and rate
- Reassessment

Hyponatremia

Hyponatremia

1. *Normotonic or Isotonic Hyponatremia*
    1. *Factitious Hyponatremia*
    2. *Pseudohyponatremia*
    3. Results from laboratory artifact due to high concentrations of proteins or lipids

Pseudohyponatremia:



- Flame photometric or Indirect potentiometry measurement of PNa^+
- Normal Measured PNa^+ = 153 mmol/L of **Plasma Water**
- Normal Plasma Water Phase = 93% of One liter of Plasma
- Reported Plasma Na^+ = 153 x 0.93 = 142 mmol/L of Plasma

Hyponatremia

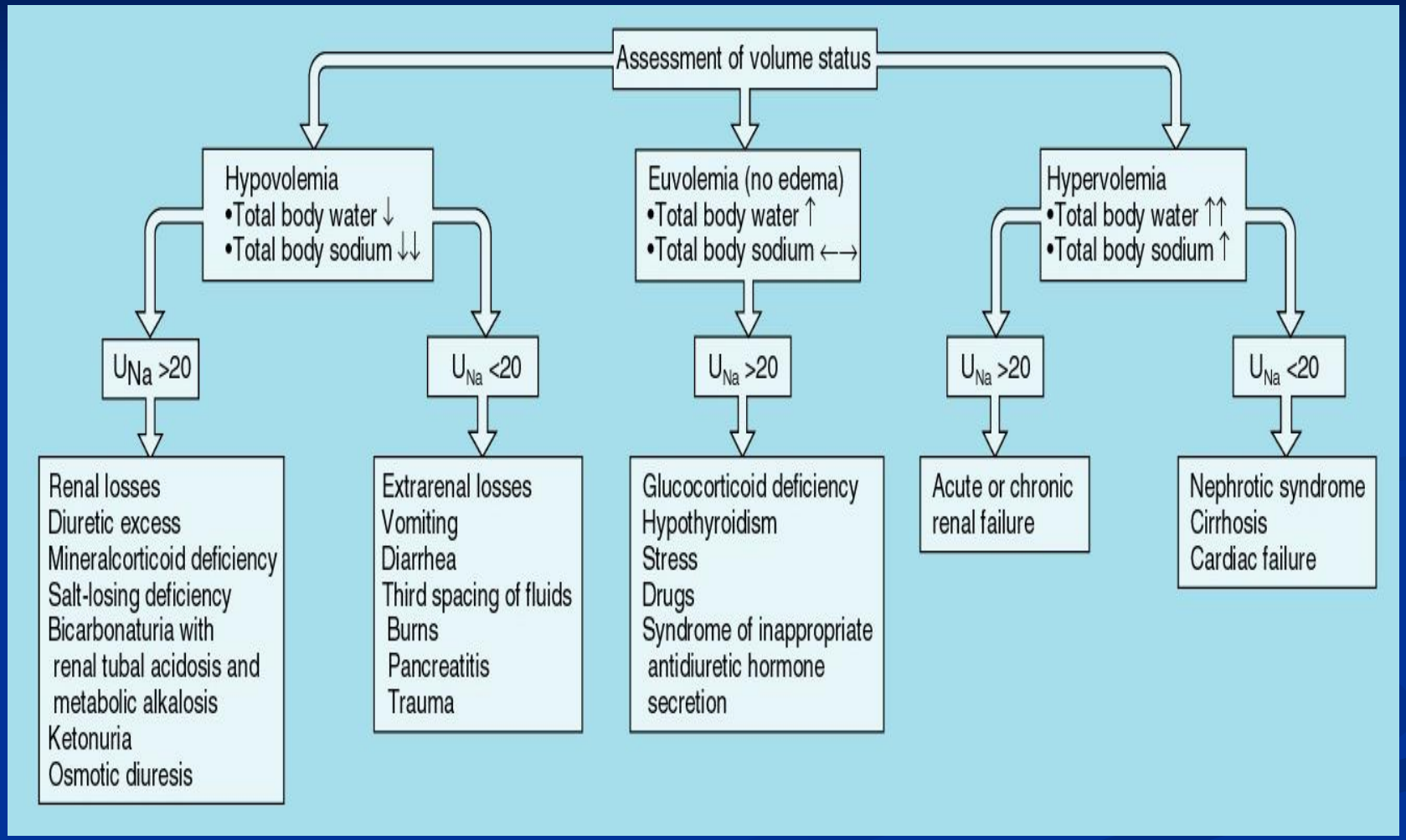
2. Hypertonic Hyponatremia
    1. Translocational Hyponatremia

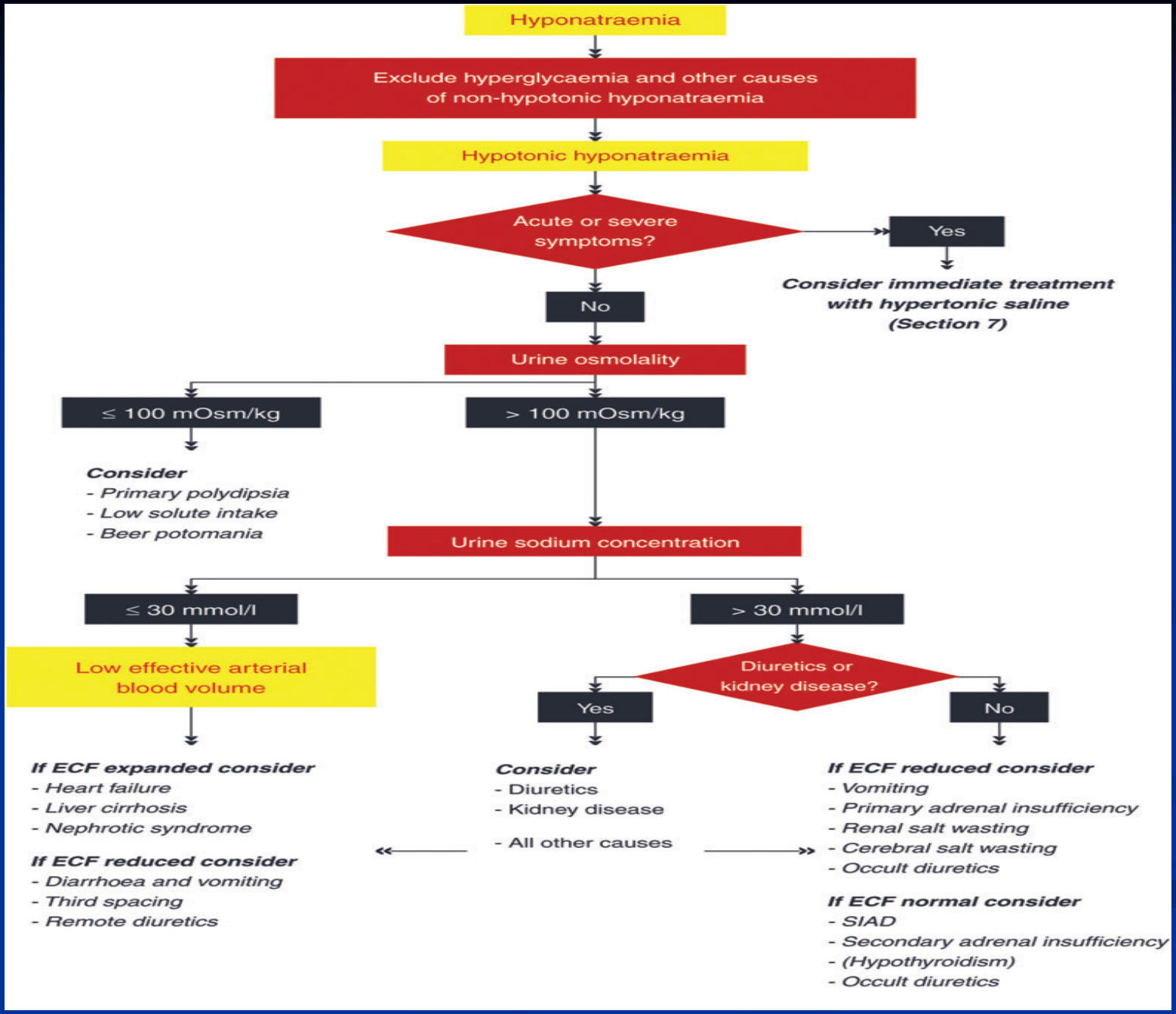
    2. Results from non-Na osmoles in serum (often glucose or mannitol) drawing Na-free H_2O from cells

    3. $[Na^+]$ declines by ~2.4 mEq/L for each 100 mg/dL [5.5 mmol/L] increase in serum glucose

Spasovski et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Nephrol Dial Transplant (2014) 0: 1–39

Hypotonic Hyponatremia: Causes




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

Classification of Symptoms of Hyponatremia

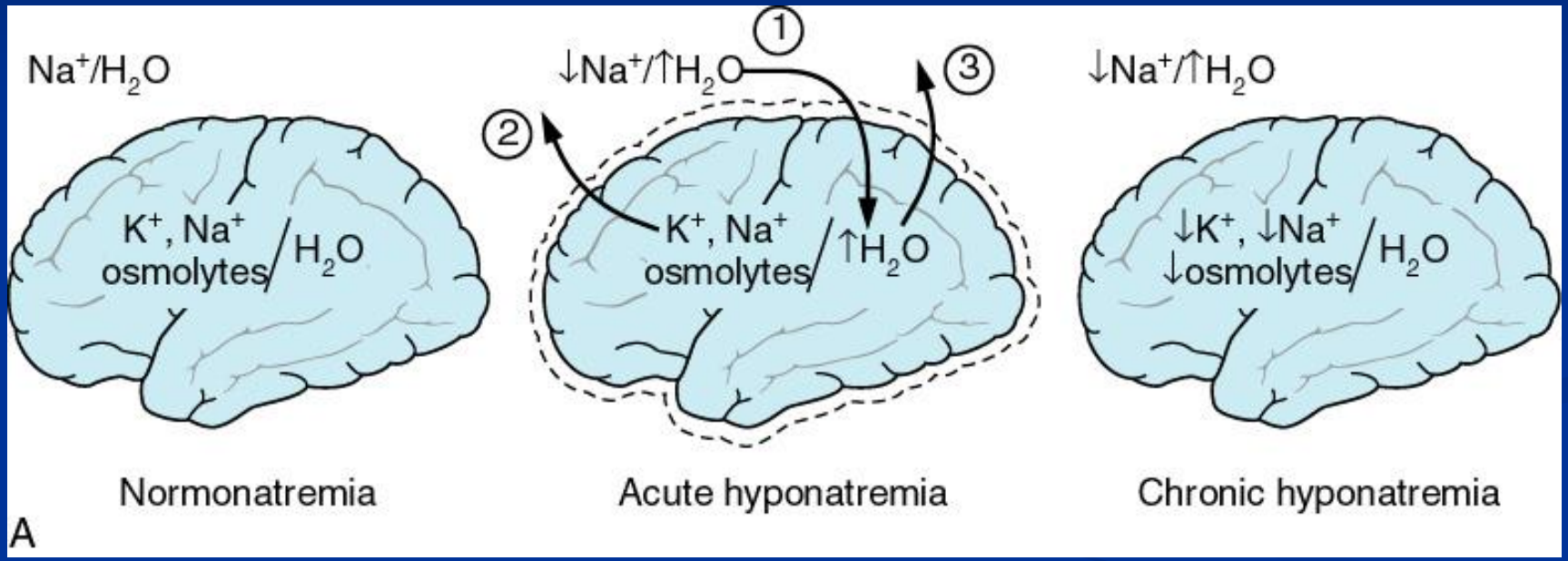
- All symptoms that can be signs of cerebral edema should be considered as severe or moderate symptoms that can be caused by hyponatremia

- **Moderately Severe**
  - Nausea without vomiting
  - Confusion
  - Headache

- **Severe**
  - Vomiting
  - Cardiorespiratory distress
  - Abnormal and deep somnolence
  - Seizures
  - Coma (Glasgow Coma Scale ≤8)

Management of Hyponatremia:

- Symptoms & Signs
  - Volume Status
- Serum:
  - Osmolality
  - TSH, FT4, Cortisol
  - Albumin, Total Proteins
  - Uric Acid
- Urine:
  - Electrolytes (Na/K/Cl/Urea/Creatinine)
  - Osmolality
  - Urinalysis
- Rate of correction:
  - 0.5 mmol/L/h ~ 10-12 mmol/L/d


Na+/H2O
↓Na+/↑H2O
1
2
3
↓Na+/↑H2O
K+, Na+ osmolytes / H2O
K+, Na+ osmolytes / ↑H2O
↓K+, ↓Na+ ↓osmolytes / H2O
Normonatremia
Acute hyponatremia
Chronic hyponatremia
A

Diagnostic Criteria for SIADH

- **Essential criteria**
  1. Effective serum osmolality <275 mOsm/kg
  2. Urine osmolality >100 mOsm/kg
  3. Clinical euvolemia
  4. Urine sodium concentration >30 mmol/l with normal dietary salt and water intake
  5. Absence of adrenal, thyroid, pituitary or renal insufficiency
  6. No recent use of diuretic agents

Diagnostic Criteria for SIADH

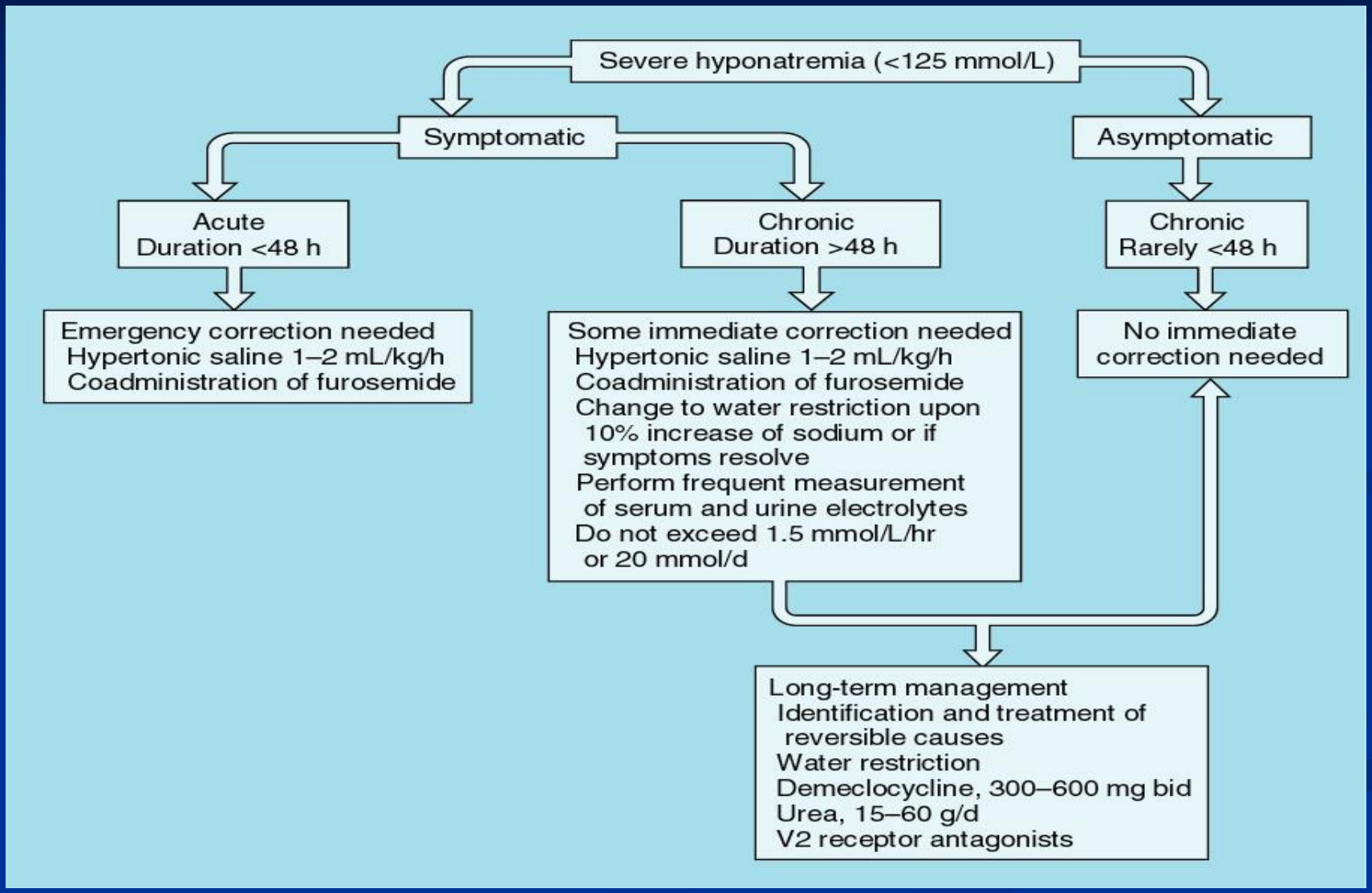
- **Supplemental criteria**
  1. Serum uric acid <0.24 mmol/l (<4 mg/dl)
  2. Serum urea <3.6 mmol/l (<21.6 mg/dl)
  3. Failure to correct hyponatremia after 0.9% saline infusion
  4. Fractional sodium excretion >0.5%
  5. Fractional urea excretion >55%
  6. Fractional uric acid excretion >12%
  7. Correction of hyponatremia through fluid restriction

SIADH: "HIVE"

- H: Hypoosmolar Hyponatremia (Posm <275 mOsm/Kg H_2O)
- I: Inappropriate urine concentration (Uosm >100 mOsm/Kg H_2O)
- V: Euvolemia, No diuretic use
- E: Endocrine = normal Thyroid, adrenal and renal function

- Hypouricemia (<238 mcmol/L) and low Urea (<3.5 mmol/L)

Hyponatremia: Treatment



Questions????