Water Balance Made Easier

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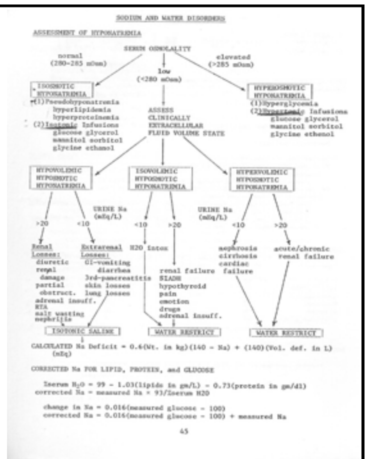
Extracellular fluid (ECF) compartment volume control

- Humans regulate ECF volume mainly by regulating body sodium content.
- Several major systems work together to balance sodium content.

We'll first divide these into the
1. Affector (sensing) systems
2. Effector systems

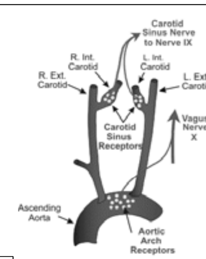
The non-cognitive approach

May lead you astray to the incorrect etiology, incorrect therapy, and poor outcome.

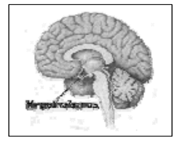


Affector systems

Baroreceptors
- Aortic arch
- Carotid arteries
- Atria
- Brain, liver, kidney



"Osmostat"
Hypothalamus



Effector systems

Renin-Angiotensin-Aldosterone System (RAAS)

Ang II → peripheral arterial vasoconstrictor

Aldosterone → Na and water retention

Vasopressin (VP) = Anti-diuretic hormone (ADH)

Systemic vasoconstrictor

Water retention

VP action at the kidney

- Can produce urine with osmolality ranging from 50 to 1,200 mosm/kg.
- Urine at the end of the DCT is maximally diluted. (Always 50-100 mosm/kg).
- As the urine travels down the collecting duct one of two things can happen:

Vasopressin (VP)

Stimuli for vasopressin release:

- Elevated serum osmolality (via the osmostat)
- Decreased baroreceptor stretch
- Nausea
- Pain

→ If VP is present and all of these "appropriate" stimuli are absent, then the diagnosis of SIADH can be made!

VP action at the kidney

If VP is absent:

→ Large amount of dilute urine produced

(Maximally dilute urine = 50 mosm/kg)

If VP is present:

→ Small amount of concentrated urine produced

(Maximally concentrated = 1,200 mosm/kg)

So, how do we know if VP is being secreted?

<u>Urine osmolality</u>

For a young person with healthy kidneys

> 100 VP is present

≤ 100 VP is absent

For an older patient or patient with kidney dz

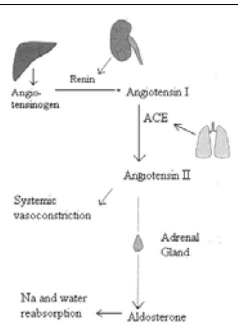
> 300 VP is present

≤ 300 VP is absent

Stimuli for renin release

- **Decreased delivery of Na^+ to the macula densa**
  (*eg* volume depletion)
- **Decreased stretch of the afferent arteriole**
  (*eg* low arterial pressure)
- **Increased sympathetic tone**
  (beta-adrenergic stimulation)

The classical RAS pathway



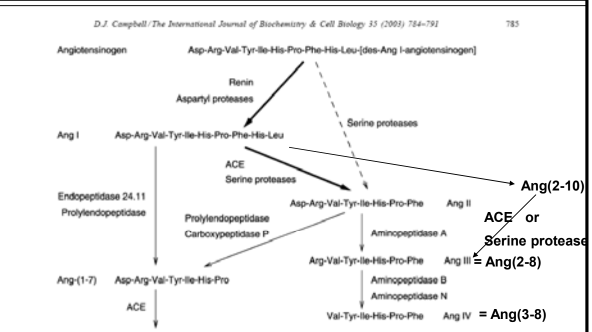


Fig. 1. Outline of the renin–angiotensin system. ACE, angiotensin converting enzyme. Not shown is the metabolism of Ang I by aminopeptidase A to form Ang-(2–10), which may then be metabolised by ACE or serine protease to form Ang III. Renin cleaves between Leu^{10} and Val^{11} of the human angiotensinogen sequence. Of the several alternate pathways of metabolism, the bold, plain and dashed arrows indicate pathways of decreasing contribution, although the minor pathways can assume major importance when the main pathway is inhibited.

Campbell, DJ. The International Journal of Biochemistry & Cell Biology. The renin-angiotensin and the kallikrein-kinin systems. 2003;35:784-791.

How can we determine if the RAAS has been activated?

Urine sodium measurement

< 10 RAAS is active

> 10 RAAS is inactive

What data are we taught to gather in evaluating a patient with an abnormal serum sodium?

- Serum osmolality
- Patient's volume status
- Urine sodium
- Urine osmolality

Interplay of afferent and efferent systems

- Osmostat (↑ serum osm) → VP (ADH) secreted
- Baroreceptors (inadequate stretch) → RAAS activated

Here is what these data are really telling us?

- Serum osmolality →What the osmostat is sensing
- Patient's volume status →What the baroreceptors are sensing
- Urine sodium →Is the RAAS on or off
- Urine osmolality →Is VP being produced *and* having an effect at the kidney

By interpreting these data within the context of the history and physical exam we can better understand why a patient has developed hypo- or hypernatremia.

Let us not be led astray by mindlessly following a flow chart.

For each patient we must ponder:

1. What the afferent systems are sensing
2. What the efferent systems are doing in response

Integration of normal water balance mechanisms

- Starting with a euvolemic "normal" person with normal electrolytes and Posm…

•What happens when the person drinks a water load? (For example 2 Liters over 30 minutes).

Integration of normal water balance mechanisms

- Starting with a euvolemic "normal" person with normal electrolytes and Posm…

NL response to a water load

- Water is absorbed from the gut.
- Serum sodium and serum osm are reduced.
- VP release is suppressed (via osmostat).
- Collecting ducts become impermeable to water.
- Large output of maximally diluted urine occurs.

Integration of normal water balance mechanisms

- What happens when the person is deprived of water for several hours?

NL response to water restriction

- If no water is taken in, eventually serum osmolality will rise to the threshold that causes thirst.
- Thirst prompts person to drink water.
- Serum sodium and serum osm are reduced toward normal.

NL response to water restriction

- Insensible losses are ongoing (breath & sweat).
- Serum sodium and serum osm increase.
- VP is released when a threshold serum osm is reached.
- Collecting ducts become permeable to water.
- Smaller output of more concentrated urine occurs.

Clinical approach to hyponatremia

When hyponatremia is detected:

1. Repeat serum electrolytes
2. Take a directed history
3. Perform a directed physical exam (focus on volume status)
4. Initial labs as discussed previously (Serum osm, urine Na, urine osm)

Hyponatremia case #1

- Young adult
- 3 days of nausea, vomiting, & diarrhea
- Told by nurse to drink plenty of liquids
- Sweaty, pale, dry mucus membranes
- Tachycardic, mildly hypotensive

Your assessment

1. Estimated volume status: Low
2. Status of each effector system:
   Catecholamines? Active
   RAAS? Active
   VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?

Labs

- Serum Na 128 meq/L
- Serum osm 270 mosm/kg
- Urine osm 1100 mosm/kg
- Urine Na < 10 meq/L

Hyponatremia case #2

- 60 y/o male with known ASCAD
- History consistent with MI ~2 weeks earlier
- Sweaty, pale, and nervous
- Neck veins distended
- S3 & S4 present
- Crackles ½ way up on lung exam
- 2+ pitting edema

Your assessment

1. Estimated volume status: High
2. Status of each effector system:

Catecholamines?	Active
RAAS?	Active
VP system?	Active

3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?

Labs

• Serum Na	128	meq/L
• Serum osm	270	mosm/kg
• Urine osm	1100	mosm/kg
• Urine Na	< 10	meq/L

What is the difference between these labs and the first patient's labs?

Labs

• Serum Na	128	meq/L
• Serum osm	270	mosm/kg
• Urine osm	1100	mosm/kg
• Urine Na	< 10	meq/L

Hyponatremia case #3

- 60 y/o male, 80 pack-year smoking history
- Presents with viral gastroenteritis x 2-3 days
  → Anorexia, limited water/food intake
- ROS: Cough, hemoptysis, 20-lb weight loss
- No medications
- Exam: Appears tired and ill, otherwise NL exam
- 2 Liters normal saline given IV in clinic
- CXR: Large perihilar mass c/w lung CA

Labs: before and after 2 Liters IV normal saline

	Before		After 2 Liters
Serum Na	120	→	120 meq/L
Serum osm	250	→	250 mosm/kg
Urine osm	600	→	600 mosm/kg
Urine Na	12	→	40 meq/L

Will this patient's hyponatremia get better or worse with further normal saline infusion?

Your assessment

1. Estimated volume status: Euvolemic, by exam
2. Status of each effector system:
   Catecholamines? Inactive
   RAAS? Active initially, inactive post NS
   VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?

Clinical approach to hypernatremia

- Think of hypernatremia and hyponatremia as disturbances of water balance along a continuum.
- Assess the affector/effector systems the same way we did for hyponatremia.
- You need to ask patients two key questions:

1. Are you thirsty?
2. Are you urinating a little or a lot?

Hypernatremia case #1

- 72 y/o male in nursing home s/p hip fracture
- Confined to bed
- Alert, oriented
- Thin, wasted
- Dry mucous membranes, no edema

Clinical approach to hypernatremia

1. Are you thirsty?
2. Are you urinating a little or a lot?

His answers:

1. Yes, quite thirsty.
2. Urinating a little.

Labs

• Serum Na	150	meq/L
• Serum osm	310	mosm/kg
• Urine osm	850	mosm/kg
• Urine Na	16	meq/L

Your assessment

1. Estimated volume status: Low
2. Status of each effector system:
   Catecholamines? +/-
   RAAS? Active
   VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hypernatremic.
5. What is your treatment strategy?

Some finer points

- Shouldn't the urine osm be 1100 or 1200?
- 850 is likely the maximum concentration that the patient's elderly kidney can achieve.
- Shouldn't the urine sodium be lower (<10)?
- Again, the age of the patient must be taken into account. The elderly kidney may not be able to achieve a lower urine sodium.

Summary

The requirements for maintaining normal water balance are:

1. Functioning baroreceptors and osmostat
2. Normal VP production and release.
3. A kidney that responds normally to VP and the RAAS
4. Normal thirst and water intake

Hypernatremia

- Not thirsty, urinating only a little
  - →Check for damage to thirst center
- Thirsty, urinating a lot
  - →DI, psychogenic polydypsia
  - →Water deprivation test

Summary

- Use the labs to determine what the affector systems are sensing and what the effector systems are doing.
- To reverse the hypo- or hypernatremia, aim your treatment at the underlying problem.
- Don't give every patient with hyponatremia normal saline unless you understand the underlying cause of the hyponatremia.