Hyponatremia

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Trivia

Who is the person who created?

UpToDate®

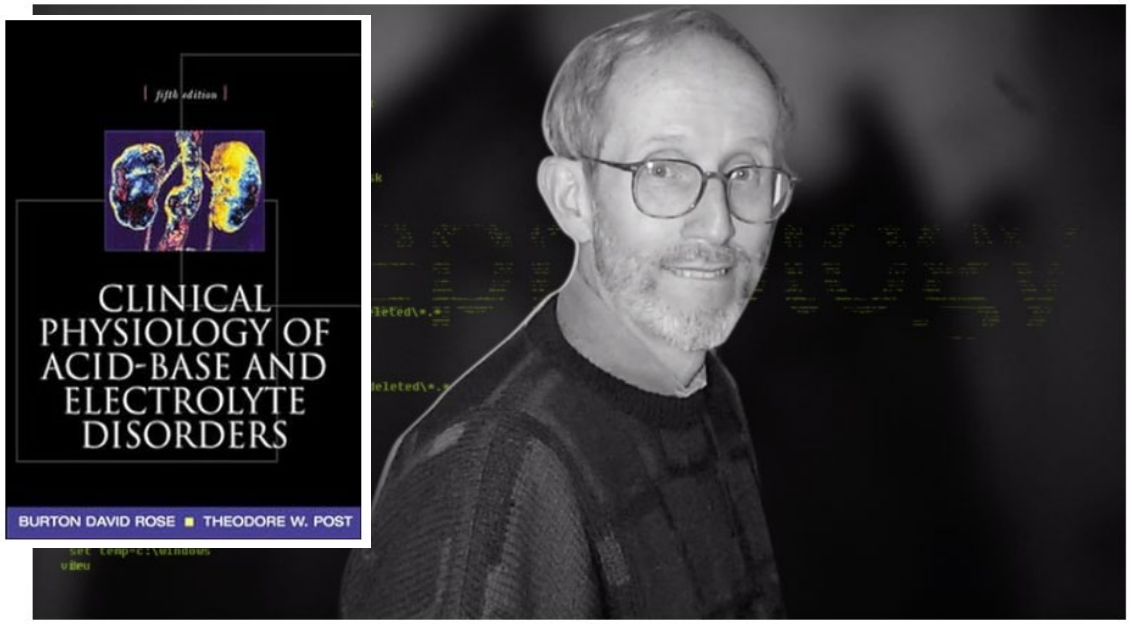
Who created UpToDate®?

- Dr. Burton "Bud" Rose, a brilliant kidney specialist; clinical professor of medicine at Harvard University.
- UpToDate first focused on nephrology, then gradually opened the lens to include virtually all of medicine.
- Rose created the **first version** of **UpToDate**, in his house in **1992**.
  - It was released on floppy disks

FIRST OPINION

Remembering UpToDate creator Burton (Bud) Rose, the 'Steve Jobs of medicine'

By Martin Pollak, Mark Zeidel, and Theodore Steinman April 25, 2020 Reprints



Burton "Bud" Rose started UpToDate in 1992

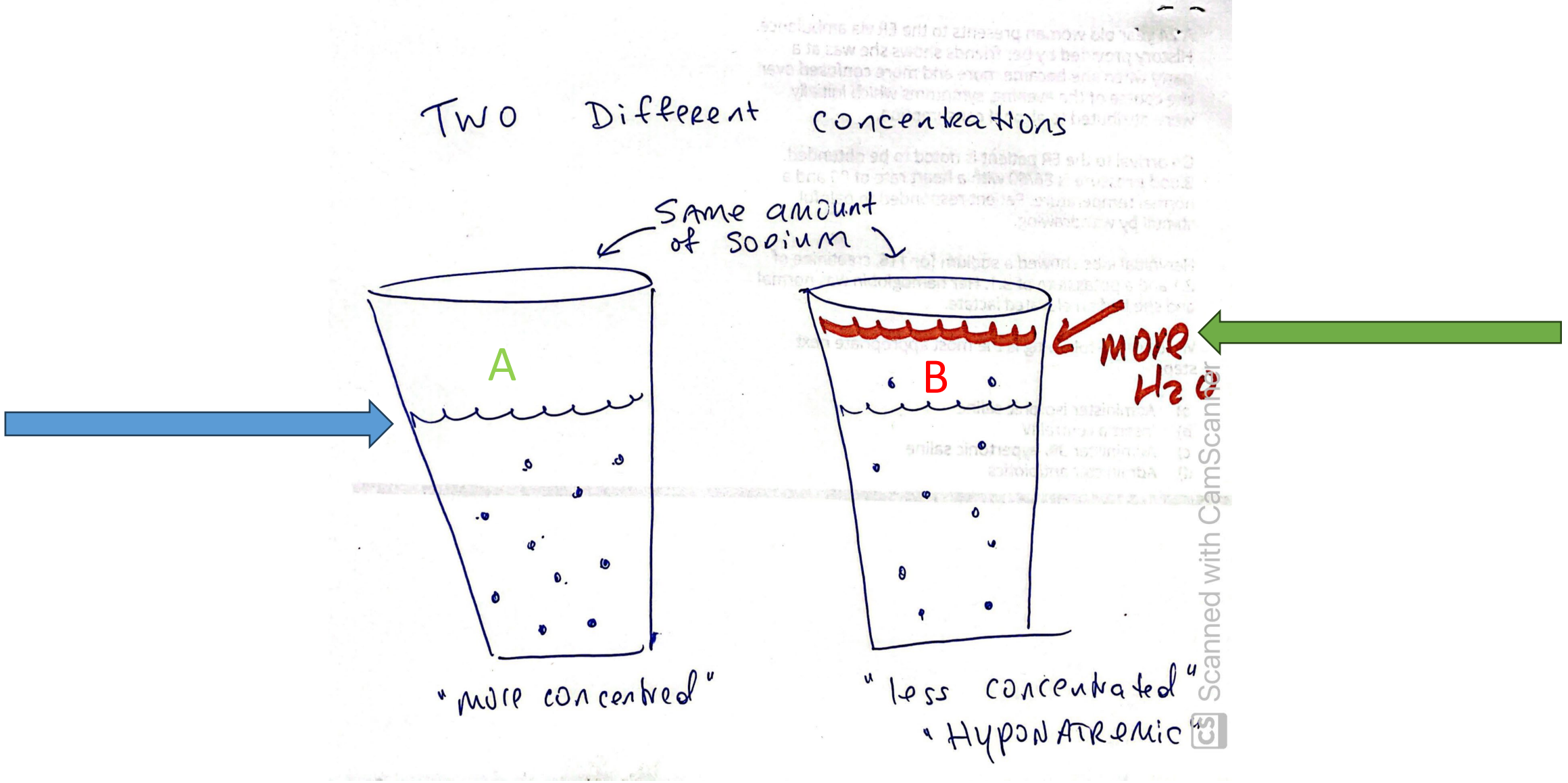
COURTESY WOLTERS KLUWER

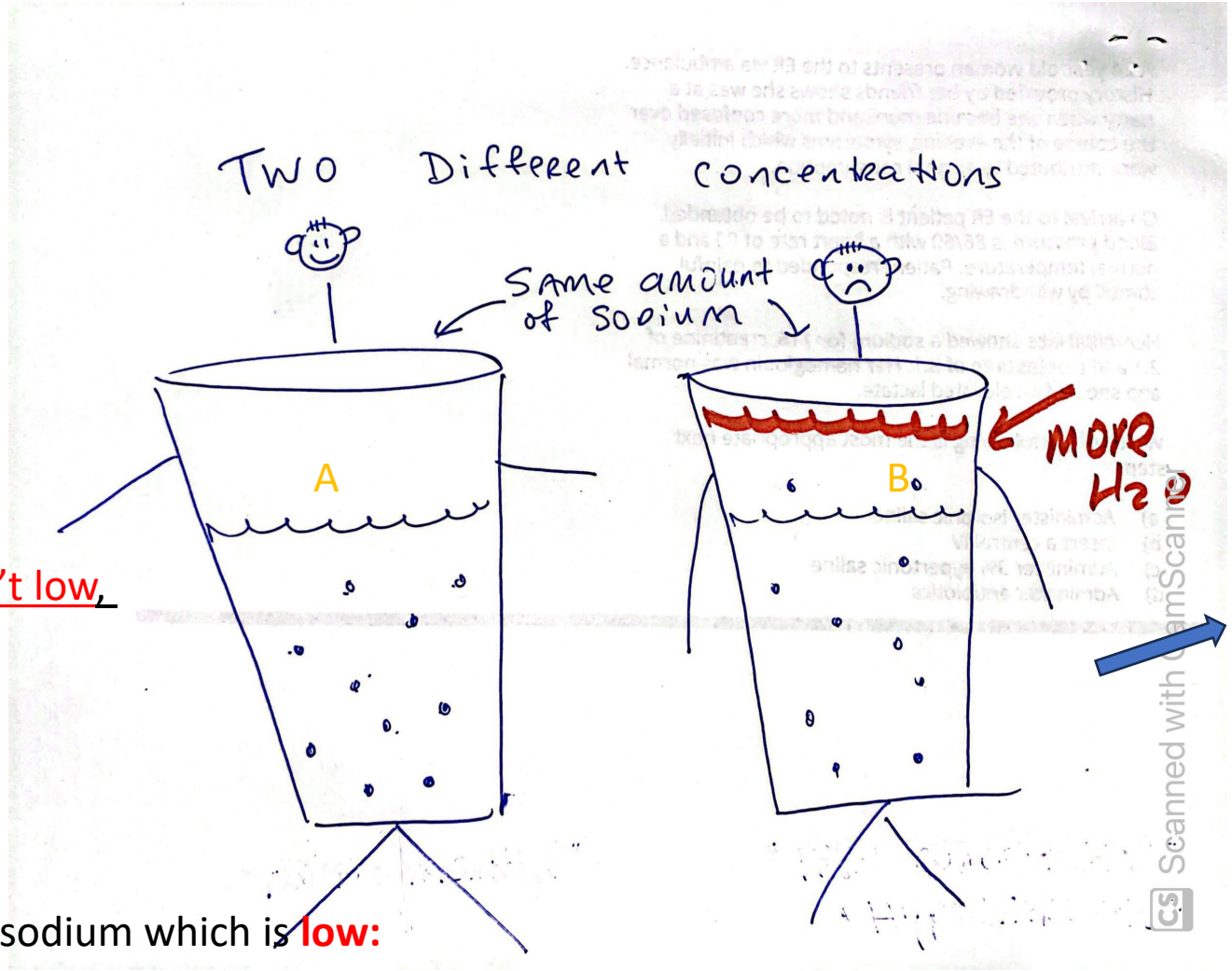
Objectives

- ❑ Review sodium and water physiology
- ❑ Review medication side effect sodium excretion
- ❑ Discuss symptoms of hyponatremia
- ❑ Discuss differential for hyponatremia
- ❑ Review management of hyponatremia
- ❑ Review clinical questions/cases

- What does it mean to have hyponatremia?
  - Does it mean you have “low sodium”?
  - Does it mean you have “too much water”?
  - Is it both a problem of too much water and too little salt?
- Understanding what it means helps treat the problem …

Basics of sodium concentration





Dear Mr B- Your sodium isn't low,

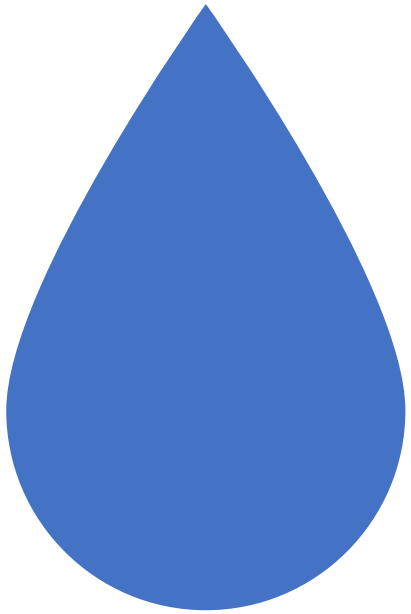
It is your concentration of sodium which is **low:**

- Because you **retained water**
  - Because of ADH that was released when …
    1. Sensed low volume (hypovolemic)
    2. Inappropriately released ADH (SIADH)
    3. Sensed low perfusion pressure (e.g heart failure) (hypervolemic)

More H2O:

1. Water intake is too large
2. Water excretion is too low
3. Combination of both

Disorders of sodium concentration typically reflect disorders of water imbalance



What retains water?

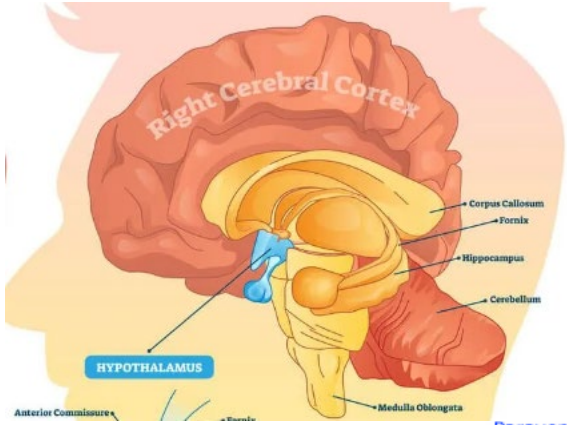
- ADH

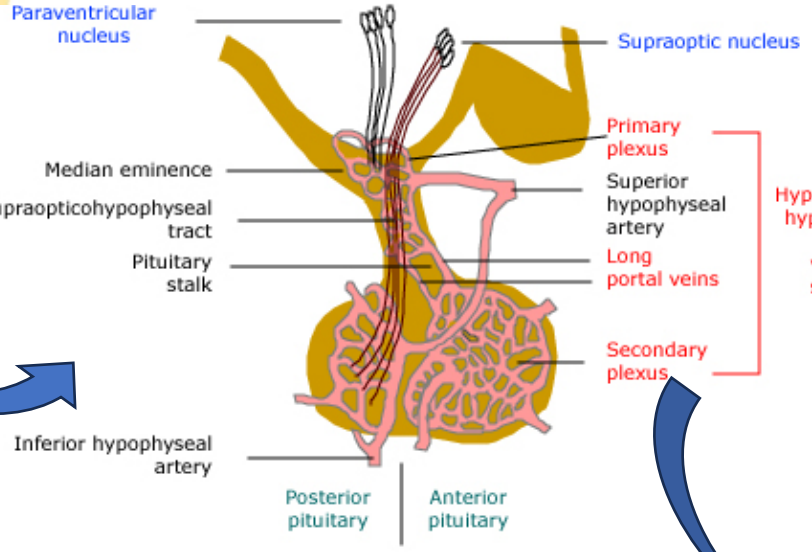
Anti-Diuretic Hormone (ADH) aka arginine vasopressin (AVP)

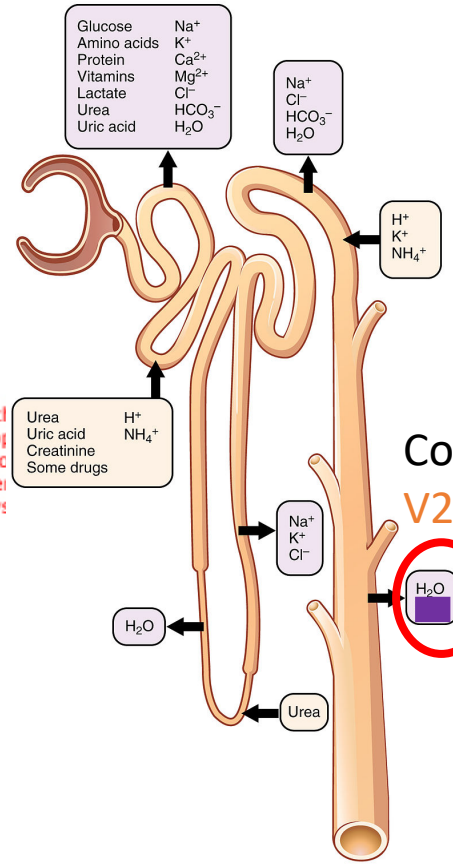
1. **Hypothalamus** makes ADH
    1. paraventricular neurons
2. **Posterior pituitary** stores ADH
3. ADH is released in response to stimulation of osmoreceptors of anterior hypothalamus, the circumventricular organs:
    1. the organum vasculosum laminae terminalis (OVLT)
    2. subfornical organ (SFO)
4. ADH binds to **V2 receptors** in the **collecting ducts** of the nephron
5. Upregulation of **Aquaporin-2 (AQP2**) channels on the apical membrane allows for water re-absorption provided there is **an osmotic gradient**

https://youtu.be/MR8BABoFTP8

Koshy et al In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-







Collecting tubule

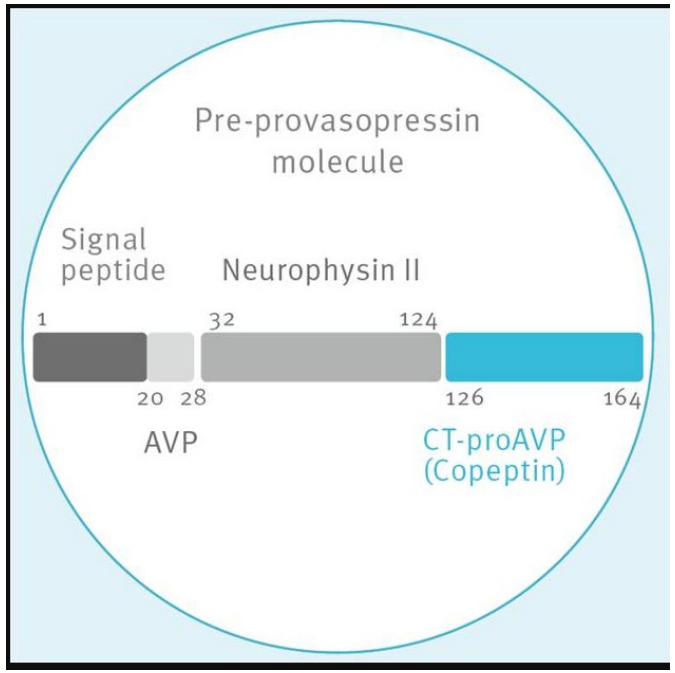
V2 receptors

Water reabsorption via AQP channels down the **gradient**

https://commons.wikimedia.org/wiki/File:2618_Nephron_Secretion_Reabsorption.jpg#/media/File:2618_Nephron_Secretion_Reabsorption.jpg

Arginine vasopressin (AVP):

- **Made** in hypothalamus as *pre-pro-AVP*
  - This is then cleaved into:
    1. **Vasopressin (ADH)**
       - **Cannot measure**
    2. **Neurophysin II**
       - **Cannot measure**
    3. **Copeptin** (serves as surrogate for ADH)
       - **Measurable** (in research)
- **Stored** in the granules of **posterior pituitary**
- **Released** (or release is shut off) upon
  - **1**) OSMOTIC ***or***
  - ***2)*** NON-OSMOTIC stimuli:

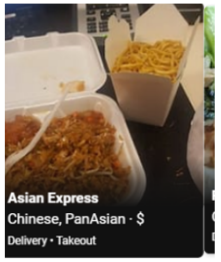


Osmotic stimulus for ADH release

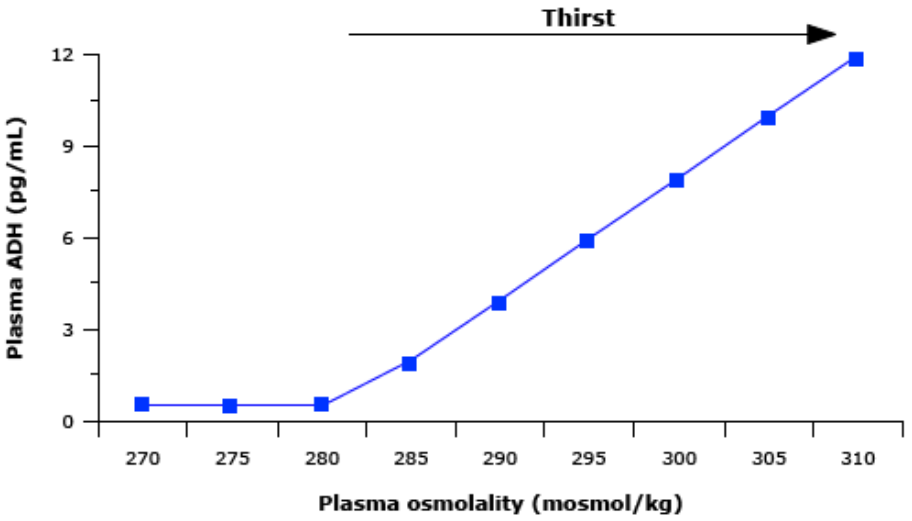
Salt Loading

Condensed soup 1600mg per can

Asian take out: chow main- **980**, kang pau chicken – **800**, egg roll **390**, hot and saur soup **– 930** , soy sauce table spoon - **1,000** mg per tablespoon

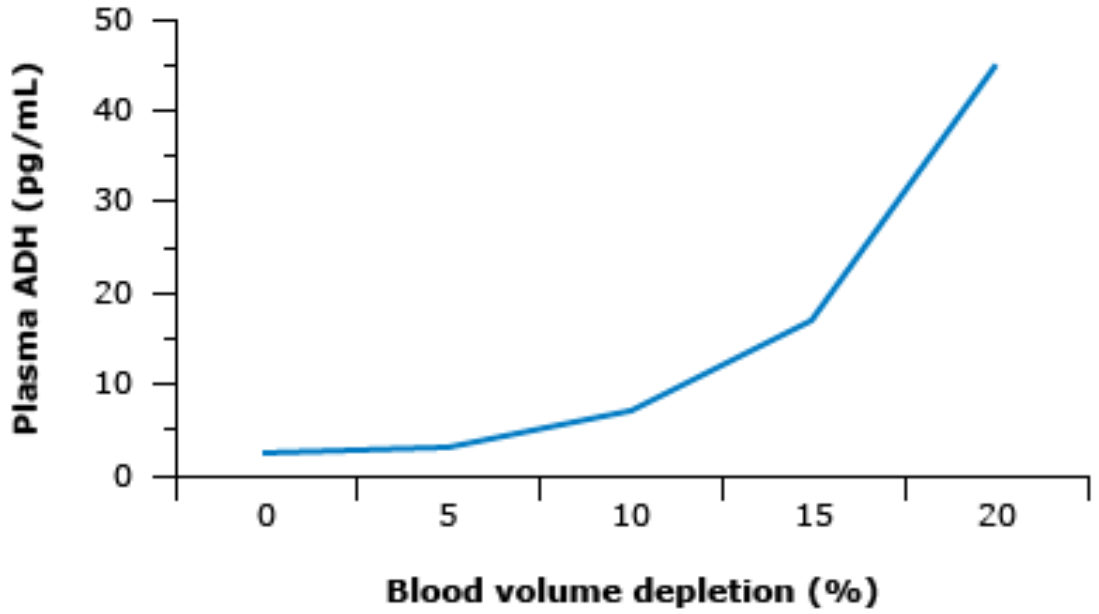


total daily sodium= 6000 – 7000 or more ….



Remember: major component of plasma osmolality is sodium

Nonosmotic stimulus for ADH release



Nonosmotic stimuli:

1. Volume depletion
2. Low effective circulating volume (CHF, HRS)
3. Nausea
4. Drugs (SSRIs)
5. Others … (e. g. pain)

- Why is hyponatremia a problem?
    - Mainly a problem for the brain

Hyponatremia: Physiology review

- Brain cell :

More particles, more concentrated

- Interstitial space:

More water= hyponatremia; “less concentrated, less particles”

H_2O

Acute Hyponatremia =bad for the brain

- Brain cell :

More particles, more concentrated

- Interstitial space:

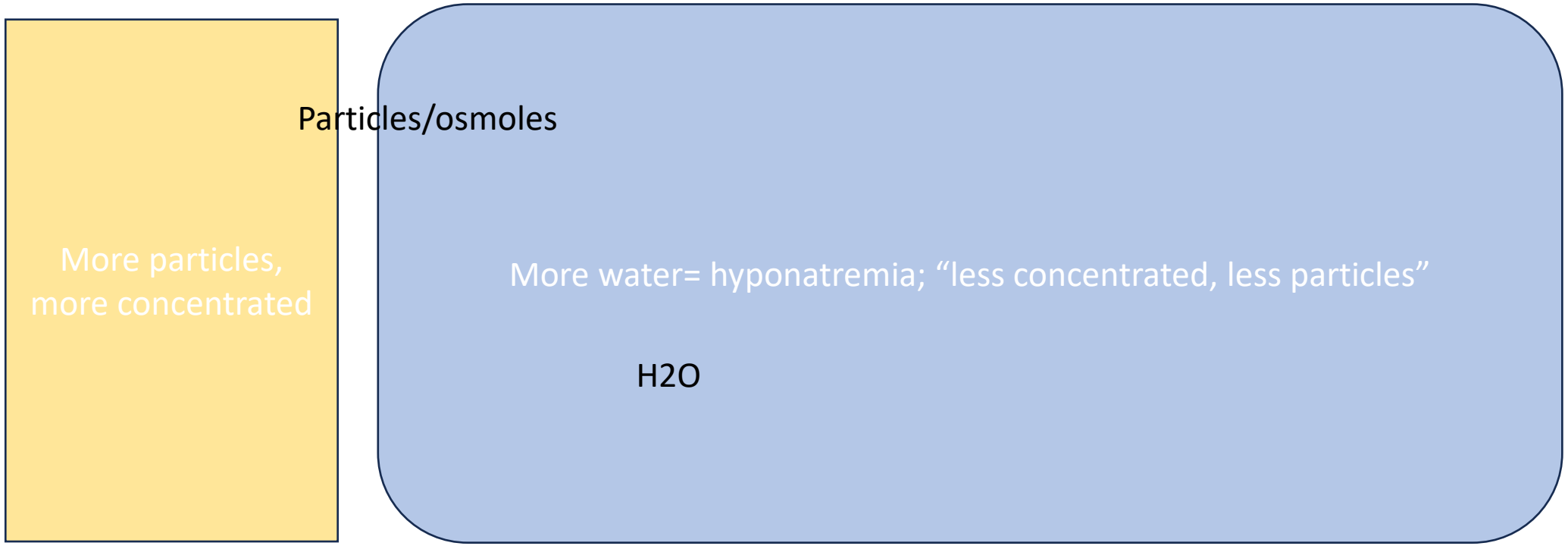
More water= hyponatremia; “less concentrated, less particles”

H2O

BUT the brain won’t allow the cells to expand easily – because the brain is inside a **solid/bony calvarium**, so as the brain edema ensues there is increasingly higher and higher pressure inside the brain- **seizures, AMS, herniation** 😳

Chronic hyponatremia (> 48hrs): brain compensation

- Brain cell :
- Interstitial space:



We don’t know what those osmoles are. Maybe glutamine, potassium, inositol, taurine

Summary

- ✓ADH release
- ✓Retention of water retention
- ✓Why it’s bad for brain to be hyponatremic
- Now … clinical presentations and treatment

Hyponatremia Definitions

- Severe hyponatremia : serum sodium concentration of <120 mEq/L
- Moderate hyponatremia : serum sodium concentration of 120 to 129 mEq/L
- Mild hyponatremia : serum sodium concentration of 130 to 134 mEq/L is "mild hyponatremia."
- acute vs chronic 48 hours

HYPONATREMIA , SNA < 135 meq/L

Hypovolemic

ADH release d/t low volume

UNA < 10
UCl < 10
Urine Osm > 100

Euvolemic (SIADH)

Constant ADH release without osm or volume stimulus

UNA>20
UCl > 20
Urine Osm > 100

Hypervolemic

ADH release due to low “effective” circulating volume

UNA < 10
UCl < 10
Urine Osm > 100

* Because water is removed from the urine, urine is more concentrated; w/ presence of ADH urine is very concentrated, urine osm >> 100 (600-1200); unless … it is psychogenic polydipsia – urine osm can be low; urine can also be low in tea and toast diet (not enough osmoles).

You rely on history and physical exam to determine cause of hyponatremia NOT just urine sodium; urine sodium is helpful in putting together the entire clinical picture

HYPONATREMIA

Hypovolemic

ADH release d/t low volume

1. Vomiting
2. Diarrhea

Euvolemic (SIADH)

Constant ADH release without osm or volume stimulus

Hypervolemic

ADH release due to low “effective” circulating volume

A 61-year-old woman is hospitalized for a 5-day history of nausea and vomiting and decreased oral intake and a 2-day history of postural lightheadedness. Her creatinine level is 7 mg/dL (creatinine level 1 month ago was 1 mg/dL). She has a history of hypertension and type 2 diabetes mellitus. Medications are aspirin, glipizide, enalapril, and chlorthalidone.

On physical examination, heart rate is 98/min and blood pressure is 85/60 mm Hg. Skin turgor is decreased. Cardiac and pulmonary examinations are normal. There is no peripheral edema. On neurologic examination, she is alert and oriented and there are no focal neurologic signs.

Laboratory studies:
Blood urea nitrogen 85 mg/dL
Creatinine 8 mg/dL
Sodium 120 meq/L
Potassium 3.7 meq/L
Chloride 86 meq/L
Bicarbonate 26 meq/L
Urinalysis Several hyaline casts/hpf
Urine sodium 4 meq/L (low is < 20 usually)

A 61-year-old woman is hospitalized for a 5-day history of **nausea and vomiting and decreased oral intake** and a 2-day history of **postural lightheadedness**. Her creatinine level is 7 mg/dL (creatinine level 1 month ago was 1 mg/dL). She has a history of hypertension and type 2 diabetes mellitus. Medications are aspirin, glipizide, enalapril, and chlorthalidone.

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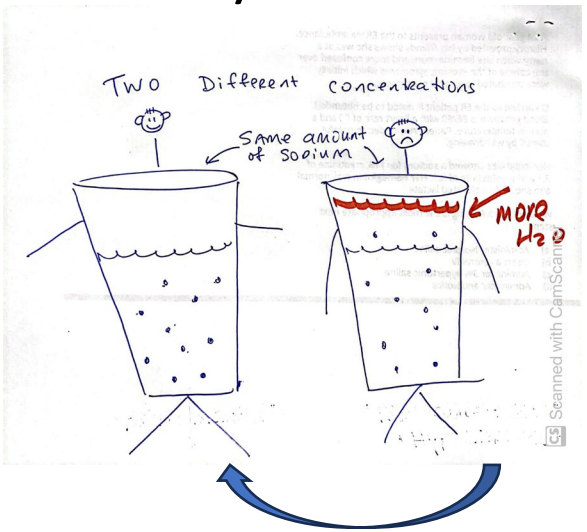
Chloride 86 meq/L
Bicarbonate 26 meq/L
Urinalysis Several **hyaline casts**/hpf
Urine sodium 4 meq/L (low is < 20 usually) * low urine sodium is telling that kidney are working hard to reabsorb sodium, **note FENA not necessary**

Which of the following is the next best step in this patient's management?

(A) Dialysis
(B) Fluid restriction
(C) Intravenous normal (0.9%) saline
(D) Intravenous 3% sodium chloride

- Why did hyponatremia correct with 0.9NS admin?
  A. Is it because we gave saline and hence salt to replace the losses
  B. Is it because we turned off nonosmotic stimulus for ADH and no longer reabsorbing the water
  C. Is it because we turned off nonosmotic stimulus for ADH and now you are peeing out the water to improve sodium concentration



HYPONATREMIA

Hypovolemic

ADH release d/t low volume

Euvolemic (SIADH)

Constant ADH release without osm or volume stimulus

1. Drugs: SSRI
2. diuretic: thiazide (HCTZ)
3. Pain
4. Nausea
5. Cancer
6. Hypothyroid
7. Adrenal insufficiency

Hypervolemic

ADH release due to low “effective” circulating volume

HYPONATREMIA

Hypovolemic

ADH release d/t low volume

Euvolemic (SIADH)

Constant ADH release without osm or volume stimulus

Hypervolemic

ADH release due to low “effective” circulating volume

1. CHF
2. Cirrhosis
3. Nephrotic syndrome

HYPONATREMIA TREATMENT

Hypovolemic

ADH release d/t low volume

Vomiting

Isotonic saline

Euvolemic (SIADH)

ADH release for reason other than volume or osmolality

Drugs: SSRI, HCTZ

- ❑ Stop meds
- ❑ <u>Fluid restriction</u>

- ❑ Loop diuretic
- ❑ Salt tabs
- ❑ Urea
- ❑ Tolvaptan

Hypervolemic

ADH release due to low "effective" circulating volume

1. CHF, cirrhosis

<u>Fluid restriction</u>
<u>Loop diuretic</u>
Underlying condition management- inotropes, liver transplant, heart transplant , etc

Euvolemic (SIADH) Treatment

- <u>Fluid restriction</u> 800ml to 1000ml *(4 glasses of water/liquids)*
    - *Not 2000ml . 2000 ml is 8 -10 glasses of water/liquids – unless liquid tastes like salt it's made of water, so restriction is in all liquids.*

❖ *most important*

Euvolemic (SIADH) Treatment

- Other treatments:

1. **Loop diuretic** can ALSO be used to **treat** hyponatremia of SIADH
   * Abolish the gradient

2. **Oral NaCL (salt tab),** dose ~ equivalent to American diet of salt intake or that of 0.9NS isotonic saline
   3gm TID or 9 gm a day of NACL
   - Oral salt tablets should *not be given to edematous patients*
   - osmotic diuresis -> peeing out more water
   - may need to admin along with loop diuretic

1. **V2 receptor blockers** (Vasopressin receptor *antagonists*, e.g. Tolvaptan) prevents ADH from binding to its target in the collecting tubule thus blocking water reabsorption

   1. tolvaptan should not be used in any patient for longer than 30 days and should not be given to patients with **liver disease (including cirrhosis)**

2. **Urea** : creates osmotic diuresis, poor taste, patients don't stay compliant easily with this

A 35 year old woman is seen in the office eight days after being admitted for pyelonephritis. Her urine culture grew sensitive E.Coli and she was discharged home on trimethoprim-sulfamethoxazole and acetaminophen. She takes no other medications except for an oral contraceptive that she has been on for three years.

On physical examination, temperature is 36.6 °C (97.8 °F), heart rate is 84/min, respiration rate is 12/min, and blood pressure is 110/60 mm Hg without orthostatic changes. She appears thin and in no apparent distress, Cardiac examination is normal. The lungs are clear. There is no peripheral edema. Neurologic examination, including mental status, is normal.

Laboratory studies:

Glucose 122 mg/dL
Blood urea nitrogen 12 mg/dL
Creatinine 0.7 mg/dL
Sodium 124 mEq/L
Potassium 3.6 mcq/L
Serum osmolality: 266 mosm/kg H_2O

Urine sodium 110 meq/L
Urine osmolality 407 mosm/kg H_2O

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Laboratory studies:

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Potassium 3.6 mcq/L
Chloride 22 meq/L
Serum osmolality: 266 mosm/kg H_2O

Urine sodium 110 meq/L
Urine osmolality 407 mosm/kg H_2O

Which of the following is the most likely cause of her hyponatremia?

A) Adrenal insufficiency
B) Polydipsia
C) Oral Contraceptives
D) SIADH
E) Volume depletion

A 60-year-old male presents to the clinic to review labs. He has a history of hypertension, diabetes, and lung cancer for which he is undergoing treatment. He voices no complaints at this time. He underwent a colonoscopy two years ago that did not identify any lesions or polyps. He is up to date with his eye exams. He says his appetite has been great and denies any weight loss. He also denies vomiting or diarrhea. His only medications are metformin and lisinopril.

His blood pressure is 124/82mmHg Standing and 120/80mmHg sitting. His physical exam does not reveal any jugular venous distention (JVD) or lower extremity edema.

Labs show:
HgbA1c 6.4%
CBC normal
LDL 58mg/dL
CMP is normal except for a sodium level of 123mg/dL
Serum osmolarity 250mOsm/L

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His blood pressure is **124/82mm**Hg Standing and **120/80mmHg sitting**. His physical exam does **not reveal any jugular venous distention (JVD) nor lower extremity edema.**

Labs show:
HgbA1c 6.4%
CBC normal
LDL 58mg/dL
CMP is normal except for a sodium level **of 123mg/dL**
Serum osmolarity **250mOsm/L**

Which of the following is the best solution for his hyponatremia at this time?

A. Furosemide

B. 3% normal saline

C. 0.9% normal saline

D. Fluid restriction

E. 5% dextrose in water (D5W solution)

Unusual causes of hyponatremia

- Focus on (in the middle section , SIADH category) :
  - Adrenal insufficiency
  - Hypothyroid
  - Thiazides
  - Renal failure , aka ‘ESRD’ or ‘ESKD’

Adrenal Insufficiency Hyponatremia

Primary Adrenal Insufficiency

- deficiencies are at the level of adrenal gland
- Not seen w/ secondary (at level of brain/pituitary)

Deficiency of aldosterone **AND** cortisol

Main causes:

- TB
- autoimmune adrenalitis (addison's disease)
- meningococcal septicemia
- acute adrenal hemorrhage
- surgical resection

RARE

- 144 per million

Adrenal Insufficiency

- Mechanisms for increase in ADH release (multifactorial) :

1. Hypovolemia (low cardiac output, low volume)
2. ↑ in ADH b/c normally cortisol provides negative feedback on ADH- *main reason;* Normally cortisol causes (-) feedback on CRH and ACTH; Inhibitory effect that is removed with adrenal insufficiency

↑ hypothalamic secretion of corticotropin-releasing hormone (CRH)- *

↑ in CRH causes a nonosmotic stimulus for ADH release

- **primary adrenal** insufficiency: **BOTH** aldosterone and cortisol are low, low aldosterone is what leads to **hyperkalemia**

Treatment for Adrenal Insufficiency

- ✓Cortisol administration (hydrocortisone)
- ✓Volume repletion (Isotonic saline)

A 22-year-old woman is evaluated in the emergency department because of severe dizziness, weakness, nausea, and vomiting of 1 week's duration. She has noted fatigue and moderate weight loss over the preceding 2 months. She has a history of hypothyroidism and takes levothyroxine, 100 mcg daily.

On physical examination, the patient is 168 cm (66 in) tall and weighs 53 kg (116 lb). Blood pressure is 90/60 mm Hg supine and 80/50 mm Hg standing, and pulse rate is 84/min supine and 96/min standing. Her skin is tanned, and there is markedly increased pigmentation of the gums and palmar creases.

Labs reveal:

Serum creatinine 1.2 mg/dL
Blood urea nitrogen 39 mg/dl.
Serum sodium 124 meq/L
Serum potassium 5.8 meq/L.
Plasma glucose 61 mg/dl.

A 22-year-old woman is evaluated in the emergency department because of severe **dizziness**, **weakness**, **nausea**, and **vomiting** of **1 week's** duration. She has noted **fatigue** and moderate **weight loss** over the preceding 2 months. She has a history of **hypothyroidism** and takes levothyroxine, 100 mcg daily.

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Labs reveal:

Serum creatinine 1.2 mg/dL
Blood urea nitrogen 39 mg/dl.
Serum sodium 124 meq/L
Serum potassium 5.8 meq/L.
Plasma glucose 61 mg/dl.

What is the most likely underlying cause of the hyponatremia?

(A) Acute adrenal hemorrhage

(B) Autoimmune adrenalitis (Addison's disease)

(C) Fulminant meningococcemia

(D) Pituitary apoplexy

(E) Tuberculosis

- Focus on :
  - Adrenal insufficiency
  - **Hypothyroid**
  - Thiazides
  - Renal failure , aka ‘ESRD’ or ‘ESKD’

Hyponatremia of Hypothyroid (hypothyroidism is severe)

- Proposed mechanisms (multifactorial):

1. ↓ cardiac output → ↑ ADH via the carotid sinus baroreceptors

2. ↓ GFR may also be a contributing cause of hyponatremia

    - Not filtering out the water drunk

3. SIADH
    - Urinary sodium is *not* typically low in hypothyroid
        - as would be expected if a reduced cardiac output or kidney function impairment were responsible

Transition slide

- Focus on :
  - Adrenal insufficiency
  - Hypothyroid
  - **Thiazides**
  - Renal failure , aka ‘ESRD’ or ‘ESKD’

Thiazide induced hyponatremia

- Within the first **one to two** weeks
  - Occasionally, may occur **months or years** after initiation of thiazide therapy
    - usually during an illness that results in inappropriate ADH secretion (two hit)
- Can **recur** after rechallenge with the thiazide
- **Clinically euvolemic (SIADH)**

Thiazide induced hyponatremia

Risk factors:

- Older women with low body weight are most susceptible
- low dietary solute intake

Thiazide Hyponatremia: Mechanisms (complicated!)

- An underlying tendency to *increased water intake ,* 2543 versus 1828 mL/day

- *Volume depletion* stimulates the release of ADH

Thiazide Hyponatremia: Mechanisms (complicated!)

- Increased **water permeability** leading to more water reabsorption in the inner medullary collecting duct (in vitro data)
    - an effect that is *independent* of ADH
- Increased **sodium and potassium excretion** (due to the diuretic) and enhanced water reabsorption (due to ADH)

Thiazide Hyponatremia: Mechanisms (complicated!)

- ~ 50 % who develop thiazide-induced hyponatremia carry a *single-nucleotide* ***polymorphism*** in the gene encoding the **prostaglandin transporter**, expressed in the renal collecting duct.
    - The variant transporter allows higher levels of luminal prostaglandin E2, which activate the luminal prostaglandin E2 receptor 4, activating water reabsorption in the collecting duct, despite suppression of ADH

A 73-year-old woman is brought to the emergency department after falling at home. Her family states that she has been very confused and disoriented over the past 2 days and that she began a new medication 4 days ago. She has type 2 diabetes mellitus, hypertension, and glaucoma. A bag containing the patient's medications includes glyburide, metformin, hydrochlorothiazide, acetazolamide, and enalapril.

On physical examination, temperature is 37 °C (98.6 °F), heart rate is 68/min, respiration rate is 12/min, and blood pressure is 115/65 mm Hg. She is confused and unable to
answer questions appropriately. Cardiac examination is nor
mal. The lungs are clear. There is no edema.

Laboratory studies:

Blood urea nitrogen 17 mg/dL
Creatinine 1.1 mg/dL.
Sodium 107 meq/L
Potassium 2.9 meq/L
Chloride 76 meq/L
Bicarbonate 24 meq/L

A **73-year-old woman** is brought to the emergency department after **falling** at home. Her family states that she has been very **confused and disoriented** over the **past 2 days** and that she began a new medication **4 days ago.** She has type 2 diabetes mellitus, hypertension, and glaucoma. A bag containing the patient's medications includes glyburide, metformin, **hydrochlorothiazide**, acetazolamide, and enalapril.

On physical examination, temperature is 37 °C (98.6 °F), heart rate is 68/min, respiration rate is 12/min, and blood pressure is **115/65 m**m Hg. She **is confused** and unable to answer questions appropriately. Cardiac examination is nor mal. The lungs are clear. There is **no edema**.

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Bicarbonate 24 meq/L

Which of the following drugs was most likely recently started in this patient?

(A) Acetazolamide

(B) Enalapril

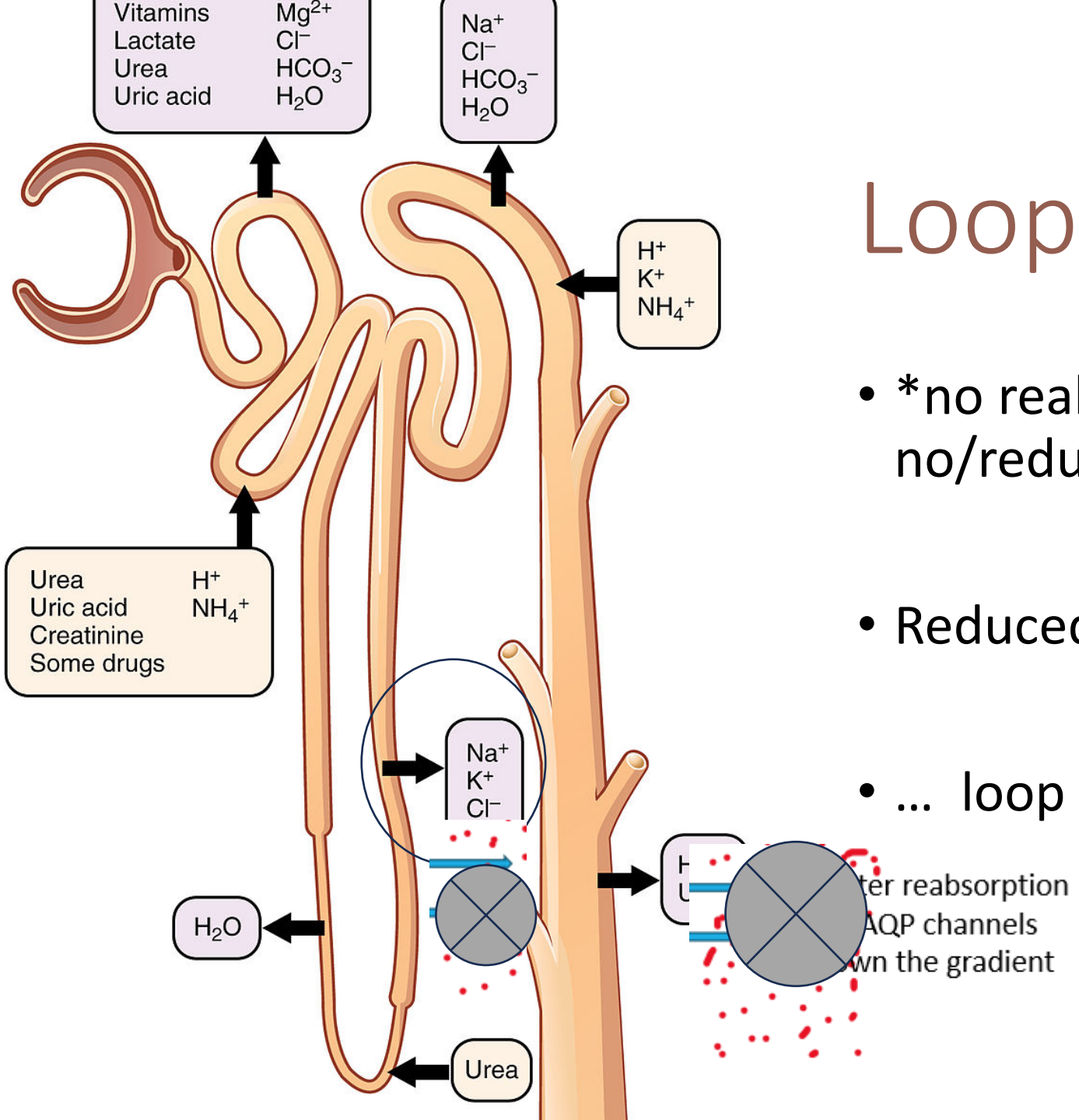
(C) Glyburide

(D) Hydrochlorothiazide

(E) Metformin

Loop diuretics

- Do loop diuretics cause hyponatremia?
  - No
  - Loop diuretics interfere with the generation of high osmotic gradient in the medullary interstitium



Loop diuretics

- *no reabsorbing Na/CL/K - > no/reduced medullary osmotic gradient
- Reduced response to ADH
- … loop diuretic can fix hyponatremia!

Severe, Symptomatic hyponatremia when to use 3% saline

- Sna < 120

  - **With symptoms (**symptoms are due to brain swelling/increased brain volume)

    - * AMS, seizures, tremors, brainstem herniation, coma, death
    - * * more common in “acute” (less than 48 hours) hyponatremia, because brain has not had time to adapt to hyponatremia

Severe, Symptomatic hyponatremia when to use 3% saline

- * 3% saline (554 meq of NA)
    - 100ml bolus over 10 “ to raise (about 50 meq) to raise serum sodium concentration 4 -6 meq to decrease brain edema

Without symptoms:

- * majority of hyponatremia is without symptoms
- * 3% not indicated

Severe Hyponatremia Treatment

Correct serum sodium by **less than** 6-8 meq/day (‘chronic’ 48-56hours)

- **LIMIT** (not a goal) rate of correction of approximately 6-8 mEq/L per day
  - No matter how low the initial sodium is

A 24 year old woman presents to the ER via ambulance. History provided by her friends shows she was at a party when she became more and more confused over the course of the evening, symptoms which initially were attributed to alcohol consumption.

On arrival to the ER patient is noted to be obtunded. Blood pressure is 86/60 with a heart rate of 80 and a normal temperature. Patient responded to painful stimuli by withdrawing.

Her initial labs showed a sodium for 116, creatinine of 2.1 and a potassium of 3.1. Her hemoglobin was normal and she had an elevated lactate.

A 24 year old woman presents to the ER via ambulance. History provided by her friends shows she was **at a party** when she became **more and more confused** over the course of the **evening**, symptoms which initially were attributed to alcohol consumption.

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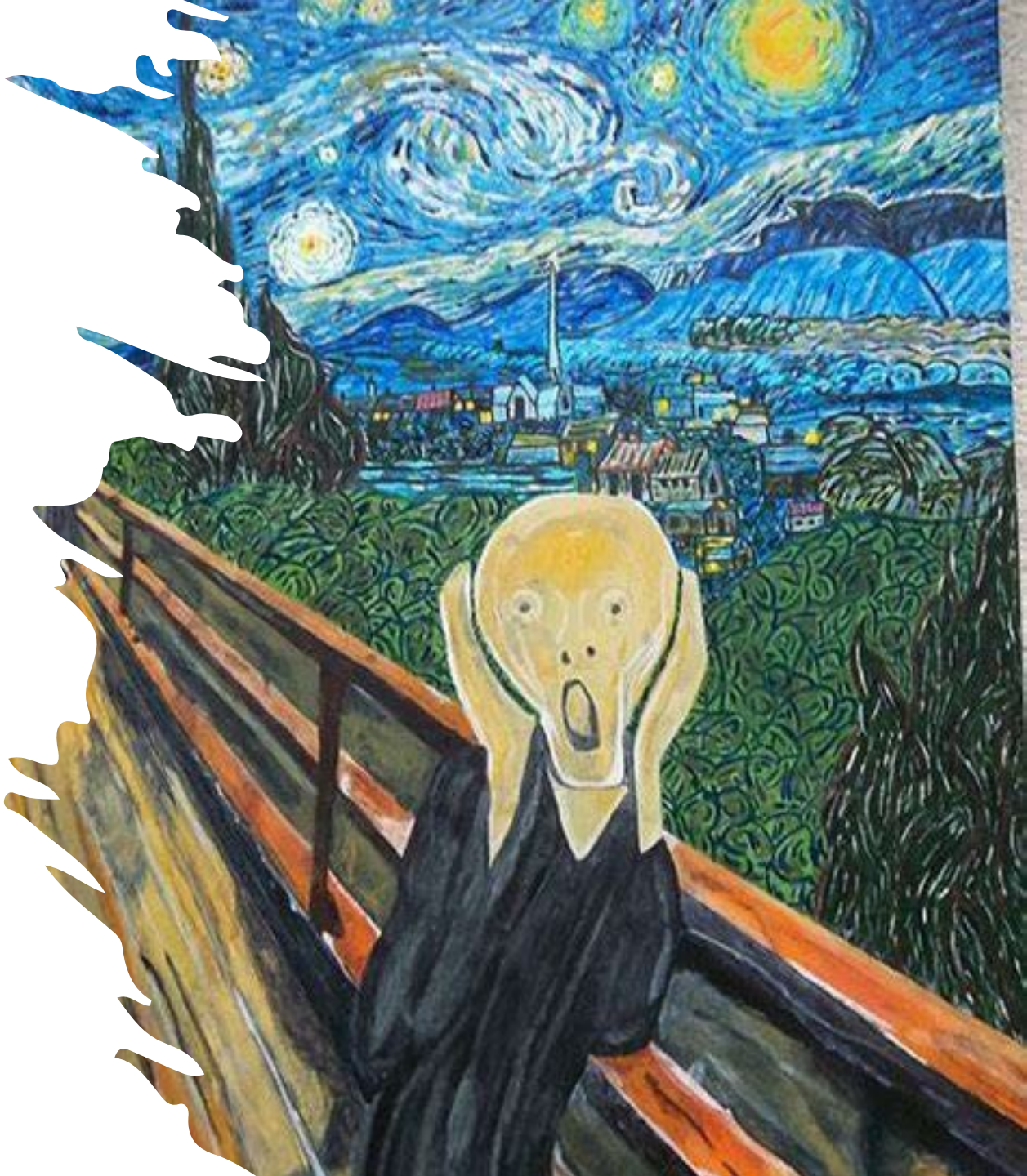
Which of the following is the most appropriate next step:

a) Administer isotonic saline
b) Insert a central IV
c) Administer 3% hypertonic saline
d) Administer antibiotics

Why slow is better?

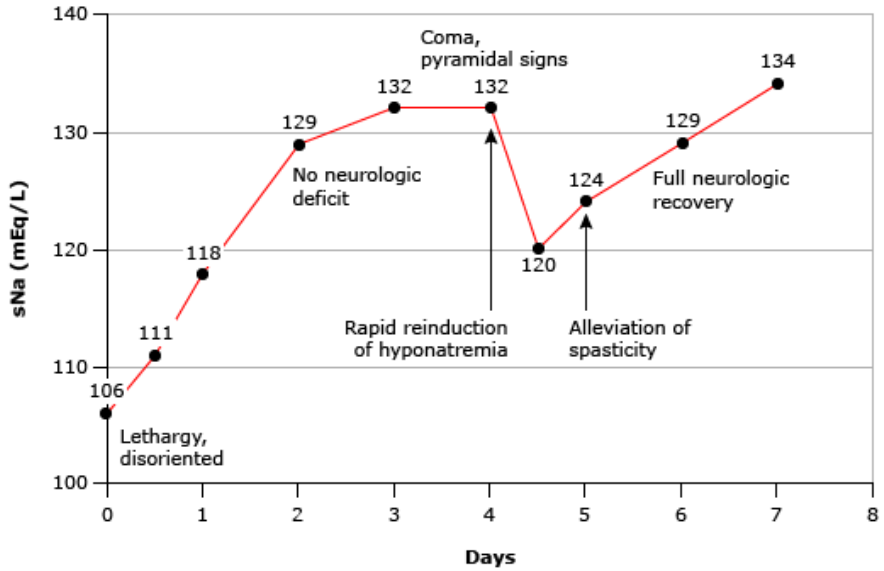
- **Osmotic Demyelination Syndrome:**
  - The majority of ODS cases occur in patients whose sodium concentrations at presentation are ≤110 mEq with correction rates > 6-8 meq /l per day
  - How the ODS occurs is not completely understood
  - **Risk factors:**
    - liver disease, malnourished, risk of rapid over correction after stimulus for ADH has been removed



ODS Symptoms

- Dysarthria
- Dysphagia
- paraparesis
- **Quadriparesis**
- behavioral disturbances
- movement disorders
- **Seizures**
- Lethargy
- Confusion
- Disorientation
- Obtundation
- Coma
- **"locked in“**
- **Mute**
- Corticospinal signs

Delayed appearance of osmotic demyelination and relowering of the serum sodium

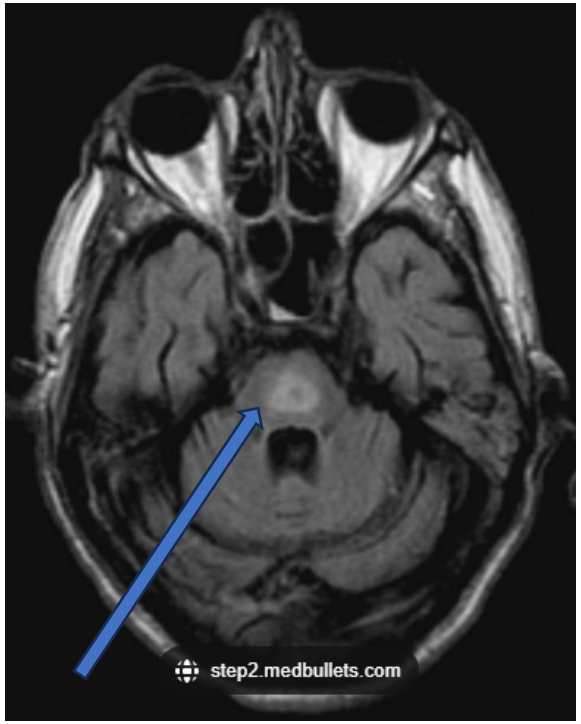


Neurologic symptoms of osmotic demyelination syndrome (ODS) typically occur 2 to 6 days after correction of the hyponatremia. In this patient, severe hyponatremia was corrected too quickly (23 mEq/L in 48 hours), and coma developed 2 days later. The serum sodium was quickly relowered and then slowly corrected. Neurologic symptoms improved, which may have been due to relowering of the serum sodium or may have represented spontaneous resolution.

sNa: serum sodium.

ODS Diagnosis: Clinical

- Imaging: brain MRI
  - Bright spot in pons



- central pontine demyelination **only**
- **both** central pontine and extrapontine demyelination
- **extrapontine** demyelination only

Other hyponatremias

Pseudohyponatremia

- Due to indirect potentiometry measurement
- Order “whole blood sodium” for direct potentiometry
  - Check
    - Lipids
    - total protein (r/o MM)

Use serum osm to confirm it is true hyponatremia

- Remember normal serum osm 285-295, and sodium is biggest contributed

- Hyperglycemia hyponatremia
  - Calculate corrected serum sodium:
    - Add 2 mEq/L to the serum sodium for every 100 mg/dL of serum glucose above the normal value

Hyponatremias that don’t fit into categories

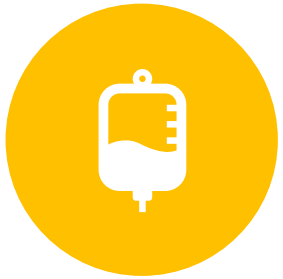
Renal failure … esrd … eskd … no urine … anephric

- ❑nothing for ADH to act on – no AVP2, kidneys aren’t working
- ❑d/t Impaired water excretion in renal failure (no GFR)
  - ❑occurs if there is severe impairment in glomerular filtration rate
  - ❑prob NOT ADH mediated
  - ❑Treatment: water restriction , loop diuretics, dialysis
  - ❑? Does it fit into any of the categories discussed earlier … kind of , not really, treatment same , mechanism is different (not ADH mediated)

When hyponatremia and urine osm is dilute (Osm < 100)

Massive water intake, thereby overwhelming a normal ability to excrete water?

Was the diet deficient in protein, severely limiting urine solute secretion? ‘tea and toast’



Was urine osmolality measured after the cause of increased ADH release had already resolved? ‘correction of volume status w/ saline’

Does the patient have a reset osmostat? - we can talk about this off lecture

Review questions

1. What is the main reason for ADH release in primary adrenal insufficiency?
2. What medications can be used to bind to V2 receptor that usually binds ADH?
3. What makes ADH ? – paraventricular neurons of hypothalamus as pre-pro-AVP
4. What stores ADH ? – posterior pituitary
5. What must be present in order for water reabsorption to occur once ADH binds to its receptor and increases number of AQP channels? – osmotic gradient
6. Which diuretic is likely to cause hyponatremia, loop or distal?
7. Which diuretic can be used to treat hyponatremia, loop or distal?
8. Hyperkalemia occurs w/ primary adrenal insufficiency or secondary and why?
9. Be able to interpret urine sodium without doing FENA
10. How much “salt” or NaCL is in 1 liter 0.9NS? 9 gm
11. How much “sodium” or Na is in 1 liter 0.9NS? ~ 3.5 gm
12. **to ponder on … do esrd or anephric patients have nephrons, how do they get hyponatremic**

- - thiazide mediated hyponatremia is purely d/t development of hypovolemia T/F?
- Name some non-osmotic stimuli for ADH release
- What is the most important treatment for SIADH? Fluid restriction 800ml to 1000ml ,
- Why do we have to rely on physical exam and history for assessment rather than just measure ADH? ADH is not measurable
- Which molecule serves as a surrogate for ADH? – copeptin
- What is the major determinant of plasma osmolality? Potassium, sodium, urea, glucose ?? .. Sodium ; when you have hyponatremia serum osm should be also low
- T or F, Patients with thiazide induced hyponatremia are usually hypovolemic
- How does tolvaptan treat hyponatremia?
- In which case you cannot administer tolvaptan?
- T or F, it safe to administer oral salt tab to patients with peripheral, pulmonary, or both edema
- T or F , a single cause can explain why hyponatremia may develop in primary adrenal insufficiency

- If there is time

From the perspective of salt: the lay of the land

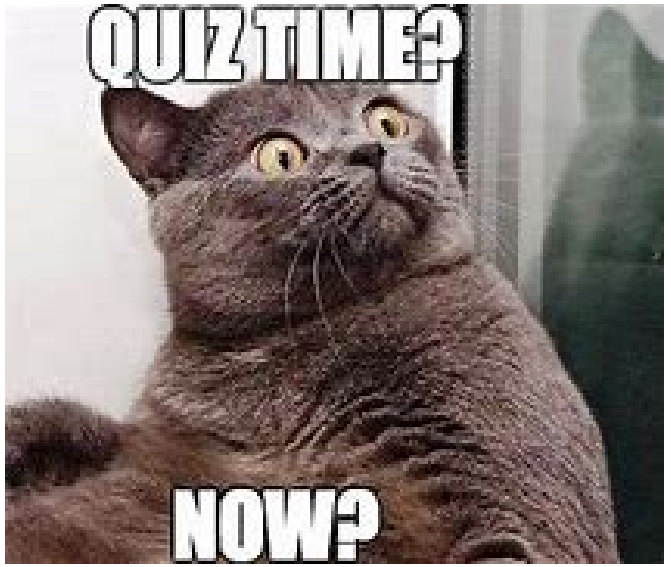
- Teaspoon of salt -> 2300mg of Na+ (NA+ vs NACL)
- 2000mg is typical total **daily** sodium restriction for patients with congestive heart failure, chronic kidney disease, hypertension, and cirrhosis

Type	Approximate amount of sodium in 1 teaspoon
Iodized table salt, fine	2,300 mg
Kosher salt, coarse	1,920 mg
Kosher salt, fine, Diamond Crystal®†	1,120 mg
Sea salt, fine	2,120 mg
Sea salt, coarse	1,560 mg
Pink (Himalayan) salt	2,200 mg
Black salt	1,150–2,200 mg
Fleur de sel	1,560–2,320 mg
Potassium salt (salt substitute)	0 mg (contains 2,760–3,180 mg potassium)

Salt and Sodium | The Nutrition Source | Harvard T.H. Chan School of Public Health

Trivia

- How much sodium is in sea water?
  - **Seawater** has a salinity of about 3.5% (35 g/L, 35 ppt, 600 mM)
  - * this is **equivalent** to **3% saline (IV)**
- How much sodium is in tablespoon soy sauce?
  - **1 tablespoon** of table salt contains ~ **1000 milligram**s of sodium.



Salt Comparisons

- Condensed soup 1600mg per

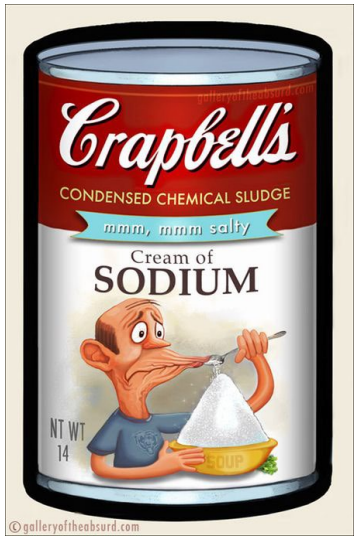
- 0.9% Saline (1L) 3500mg of Na

- 3% Saline (1L) (12,000mg)

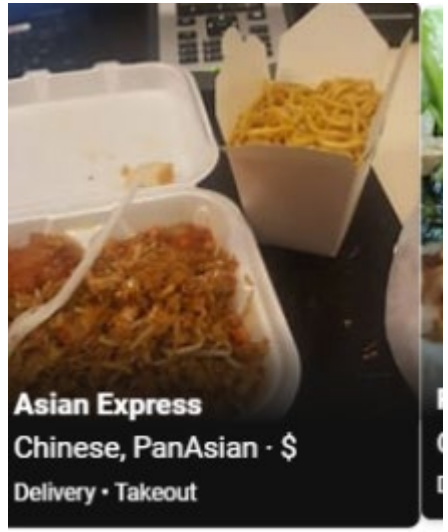
Salt Loading

1260

Condensed soup 1600mg per can



Asian take out: chow main- **980**, kang pau chicken – **800**, egg roll **390**, hot and saur soup **– 930** , soy sauce tablespoon - **1,000** mg per tablespoon



Average American total daily sodium intake = 6000 – 7000 or more ….

Should we advise someone with hyponatremia to drink Gatorade – an electrolyte rich fluid ?

How many teaspoons of sodium are in a liter of Gatorade?

Gatorade

Nutrition Facts

Serving Size 8 fl oz (240 mL)
Servings Per Container 4

Amount Per Serving	
Calories 50	
	% Daily Value*
Total Fat 0g	**0%**
Sodium 110mg	**5%**
Potassium 30mg	**1%**
Total Carbohydrate 14g	**5%**
Sugars 14g	
Protein 0g	

Not a significant source of Calories from Fat, Saturated Fat, Cholesterol, Dietary Fiber, Vitamin A, Vitamin C, Calcium, Iron.

* Percent Daily Values are based on a 2,000 calorie diet.

- One bottle 1 liter of Gatorade
  - 110mg of sodium per serving x 4 servings => 440mg per liter
  - 1/5th of teaspoon! (19meQ of NA)

Can you replace salt (rehydrate with electrolytes (AKA sodium) with Gatorade? NO

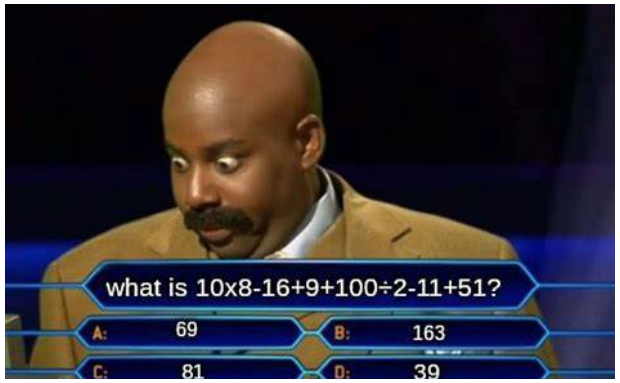
Can you replace salt (rehydrate with electrolytes (AKA sodium) with soy sauce? – YES
1.5 tablespoons and four cups of water

Thus you are adding 960ml of ‘free ‘ water (almost same as a liter of D5W) to your ECF and ICF (2/3, 1/3)

Gatorade Trivia

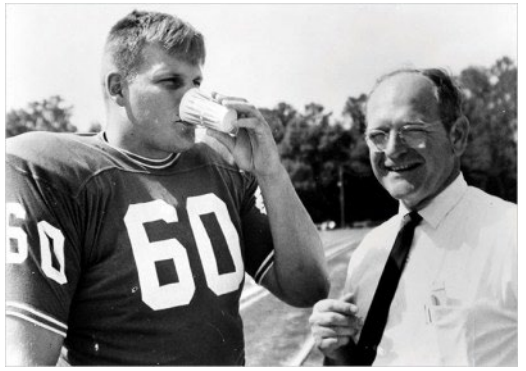
- Who is the lead inventor for Gatorade and it’s billion $$$ business?

“The test won’t even be that hard. It’s multiple choice.”



The University of Florida **Nephrologist**

- Dr. J Robert Cade (1927-2007)



•Sodium 45 mEq (45x23=**1035mg**) in 1 liter

Oral Rehydration Therapy

PEDIALYTE (1 liter)

½ teaspoon of salt (same is in McD’s breakfast sandwich and less than in a can of soup)

Osmolality 250 mOsm/kg

Sodium 45 mEq (45x23=**1035mg**)

Potassium 20 mEq

Chloride 35 mEq