

Rapid-Fire Electrolyte Cases for the Hospitalist: HyperCa, HypoNa

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Hypercalcemia

PTH- high normal or elevated

- 1° hyperparathyroidism
 - parathyroid adenoma
 - parathyroid hyperplasia
 - parathyroid carcinoma
- Lithium, teriparatide
- Familial hypocalciuric hypercalcemia
- 3° hyperparathyroidism
- Tumor (rare)- usually PTHrP

PTH – suppressed (<25)

- PTHrP mediated- e.g., lung, renal neoplasm
- Bony metastasis- neoplastic, myeloma
- ↑ Vitamin D 1,25 –OH
 - granulomatous disease: sarcoid, MTB, GPA(Wegener's), Crohn's, silicosis, histoplasmosis, foreign body granuloma
 - lymphoma- especially Hodgkin's
 - Intoxication (calcitriol)
- ↑ Vitamin D 25-OH (storage) - intoxication
- Milk Alkali Syndrome
- Meds: HCTZ, Vit A, theophylline
- Endo: hyperthyroid, acromegaly, pheochromocytoma, adrenal insufficiency
- Immobilization- + something else
- TPN
- Recovery from rhabdomyolysis

Hypercalcemia

Evaluation

- H&P- meds, HCTZ, immobilization
- Albumin, calcium, phosphorous, alk phos
- PTH
- PTHrP
- vitamin D 1,25 OH
- ANCA, endoscopy, MTB eval (if unexplained vit D 1,25 elevated)
- Vitamin D 25- OH
- ACE level, chest CT
- PET CT- for neoplasm or sarcoid
- SPEP, UPEP, serum free LC, bone marrow
- Blood level- Li, theophylline, Vit A
- TFT, cortisol stim test, IGF-1
- Pheo- plasma metanephrines, MRI adrenal
- Sestimibi scan- for parathyroid adenoma
- 24 h U for calcium- for FHHC

Tx

- acute- NS, bisphosphonate, calcitonin 4 IU/kg SQ bid, furosemide, dialysis
- zolindronate or pamidronate- renal dose.
- denosumab
- Prednisone, ketoconazole, plaquenil for vitamin D mediated
- Sensipar (cinacalcet)
- Parathyroidectomy
- Treat underlying cause

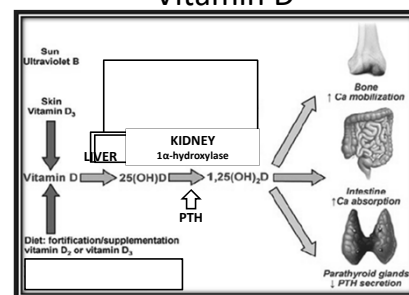
Hormones in Hypercalcemia

- PTH - normal value ~15-65
- PTHrP
- vit D 1,25
- vit D OH-25

PTH vs. PTHrP

- PTHrP has similar but not identical effects as PTH
- PTHrP biologic function:
 - ↑ U Ca reabsorption like PTH (↑ serum Ca)
 - ↑ U phos excretion like PTH (↓ serum phos)
 - but does not increase production of Vit D 1, 25 (however PTH raises this)

Vitamin D



Source: Public domain - Researchgate

Hypercalcemia

55 yo male

- mildly elevated
Ca 10.7 (8.4 - 10.2 mg/dL)
- phos 2.5 (2.5 – 4.5 mg/dL)
- PTH 120 (15-65 pg/mL)

DDx: PTH – nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

↑Ca & ↑ PTH: Classic 1° Hyperparathyroidism

Hypercalcemia

62 M with HTN recently switched from amlodipine to HCTZ. PTH 110

BEFORE HCTZ	AFTER HCTZ
Ca 9.7-9.9	Ca 10.4

Calcium - normal range: (8.4 - 10.2 mg/dL)

DDx: PTH - nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

1° hyperparathyroidism, unmasked from HCTZ

Hypercalcemia

36 female

- Ca 10.4 (8.4 - 10.2 mg/dL)
- PTH 52 (15-65 pg/mL)

DDx: PTH - nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

↑Ca & inappropriately “normal” PTH:
1° Hyperparathyroidism

Hypercalcemia

24 yo male with bipolar disorder. Routine labs:

- Ca 10.9 (8.4 - 10.2 mg/dL)
- PTH 110 (15-65 pg/mL)

DDx: PTH - nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

Lithium mimicking 1° Hyperparathyroidism

Hypercalcemia

82 yo frail, non-ambulatory, female patient with dementia and malnutrition

- Ca 10.1 (8.4 - 10.2 mg/dL)
- PTH 325 (15-65 pg/mL)
- Vitamin D OH 25- undetectable

DDx: PTH - nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

1° Hyperparathyroidism,
masked by Vitamin D deficiency

Hypercalcemia

37 yo male with ESRD, not taking any meds

- Ca 11.2 (8.4 - 10.2 mg/dL)
- PTH 2500 (15-65 pg/mL)

DDx: PTH - nl or ↑

- 1° hyperpara
 - adenoma
 - hyperplasia
 - carcinoma
- Li, teriparatide
- FHCC
- 3° hyperpara
- Tumor- usually PTHrP

3° Hyperparathyroidism

Hypercalcemia

65 yo male smoker with confusion, diffuse bony mets.

- Ca 14 (8.4 - 10.2 mg/dL)
- PTH 5 (15-65 pg/mL)
- PTHrP- zero

DDx: PTH - suppressed (<25)

• PTHrP mediated- e.g., lung, renal neoplasm
 • Bony mets- neoplastic, myeloma
 • ↑ Vitamin D 1,25 -OH
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ Vitamin D 25-OH intoxication
 • Milk Alkali
 • Meds: HCTZ, Vit A, theoph
 • Endo: hyperthyroid, acromegaly, pheo, AI
 • Immobile + something else
 • TPN
 • Recovery from rhabdo

Hypercalcemia from local osteolytic process

Hypercalcemia

72 yo female smoker with confusion. Torso CT is negative for metastatic disease but shows a 3 cm lung mass.

- Ca 14 (8.4 - 10.2 mg/dL)
- PTH 5 (15-65 pg/mL)
- PTHrP- elevated

DDx: PTH - suppressed (<25)

• PTHrP mediated- e.g., lung, renal neoplasm
 • Bony mets- neoplastic, myeloma
 • ↑ Vitamin D 1,25 -OH
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
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 • Meds: HCTZ, Vit A, theoph
 • Endo: hyperthyroid, acromegaly, pheo, AI
 • Immobile + something else
 • TPN
 • Recovery from rhabdo

Humoral hypercalcemia of malignancy

Hypercalcemia

38 yo male with chronic cough. CXR shows hilar adenopathy... Should you suggest sunscreen?

- Ca 10.8 (8.4 - 10.2 mg/dL)
- PTH 12 (15-65 pg/mL)
- Vitamin D 1,25 OH 120 (15-65 pg/mL)

DDx: PTH - suppressed (<25)

• PTHrP mediated- e.g., lung, renal neoplasm
 • Bony mets- neoplastic, myeloma
 • ↑ Vitamin D 1,25 -OH
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ Vitamin D 25-OH intoxication
 • Milk Alkali
 • Meds: HCTZ, Vit A, theoph
 • Endo: hyperthyroid, acromegaly, pheo, AI
 • Immobile + something else
 • TPN
 • Recovery from rhabdo

Sarcoidosis → Sunscreen & move to Boston

Hypercalcemia

69 yo with chronic dyspepsia

- Ca 12.5 (8.4 - 10.2 mg/dL)
- bicarb 34 mg/dL, SCr 2.3 mg/dL.
- PTH 8 (15-65 pg/mL)

DDx: PTH - suppressed (<25)

• PTHrP mediated- e.g., lung, renal neoplasm
 • Bony mets- neoplastic, myeloma
 • ↑ Vitamin D 1,25 -OH
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
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 • Immobile + something else
 • TPN
 • Recovery from rhabdo

What OTC medication is he taking?

CaCO₃: Milk – Alkali Syndrome

Hypercalcemia

24 yo female with weight loss, sweats, tremor and diarrhea.

- TSH undetectable
- Free T4 5.1 ng/dL
- Ca 10.8 (8.4 - 10.2 mg/dL)
- PTH 10 (15-65 pg/mL)

DDx: PTH - suppressed (<25)

• PTHrP mediated- e.g., lung, renal neoplasm
 • Bony mets- neoplastic, myeloma
 • ↑ Vitamin D 1,25 -OH
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ Vitamin D 25-OH intoxication
 • Milk Alkali
 • Meds: HCTZ, Vit A, theoph
 • Endo: hyperthyroid, acromegaly, pheo, AI
 • Immobile + something else
 • TPN
 • Recovery from rhabdo

Hyperthyroidism

Hypercalcemia

63 yo asymptomatic healthy female who has stable, mild hypercalcemia for her entire life.

- Ca 10.1-10.5 (8.4 - 10.2 mg/dL)
- PTH 70 (15-65 pg/mL)
- 24h U Ca of 50 mg is low
- Vitamin D 25-OH is normal at 35 (30-80 ng/dL)

DDx: PTH - nl or ↑

• 1° hyperpara
 • adenoma
 • hyperplasia
 • carcinoma
 • Lj, teriparatide
 • FHCC
 • 3° hyperpara
 • Tumor- usually PTHrP

FHCC: Note, 1° Hyperparathyroidism + vitamin D def also has low 24 h U Ca excretion

Hypercalcemia

30 yo male recovering from rhabdo
(peak CPK of 300K)

- Ca 6 → 14 (8.4 - 10.2 mg/dL)
- PTH 10 (15-65 pg/mL)
- Patient received large amounts of IV calcium during the hospitalization

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histo, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds**: HCTZ, Vit A, theoph
 • **Endo**: hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

Ca sink...

Hypercalcemia

Ca (8.4 - 10.2 mg/dL)	PTH (15-65 pg/mL)	PTHrP (0)	Vitamin D 1,25 OH (15-65)	Dx
11	6	Elevated	18	?
11	6	0	90	?
11	200	0	78	?

Physiologic production of vit D 1,25 OH requires nl kidneys and PTH.

Hypercalcemia

Ca (8.4 - 10.2 mg/dL)	PTH (15-65 pg/mL)	PTHrP (0)	Vitamin D 1,25 OH (15-65)	Dx
11	6	Elevated	18	Humoral
11	6	0	90	?
11	200	0	78	?

Physiologic production of vit D 1,25 OH requires nl kidneys and PTH.

Hypercalcemia

Ca (8.4 - 10.2 mg/dL)	PTH (15-65 pg/mL)	PTHrP (0)	Vitamin D 1,25 OH (15-65)	Dx
11	6	Elevated	18	Humoral
11	6	0	90	Sarcoid
11	200	0	78	?

Physiologic production of vit D 1,25 OH requires nl kidneys and PTH.

Hypercalcemia

Ca (8.4 - 10.2 mg/dL)	PTH (15-65 pg/mL)	PTHrP (0)	Vitamin D 1,25 OH (15-65)	Dx
11	6	Elevated	18	Humoral
11	6	0	90	Sarcoid
11	200	0	78	1° Hyperpara

Physiologic production of vit D 1,25 OH requires nl kidneys and PTH.

Hypercalcemia

42 yo admitted with mild confusion, headache.

- Skin is yellow but sclera is white
- Na 142 , Tbili 1.8 mg/dL, ALT 110 U/L, AST 77 U/L
- Ca 11.4 (8.4 - 10.2 mg/dL)
- PTH 10 (15-65 pg/mL)
- Vitamin D 1,25 OH- 12 (low)

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histo, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds**: HCTZ, Vit A, theoph
 • **Endo**: hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

*She admits to drinking 10 pints of carrot juice daily
(Vitamin A)*

Hypercalcemia

50 yo admitted with confusion. Admits to taking high dose vitamin supplements.

- Calcium 12 (8.4-10.2 mg/dL)
- Albumin 4 g/dL
- PTH 8 (15-65 pg/mL)
- Vit D 1,25-OH = 32 (15-65 pg/mL)
- Vit D 25-OH (storage) = 330 (30-80 ng/mL)

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds:** HCTZ, Vit A, theoph
 • **Endo:** hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

Hypervitaminosis D

Hypercalcemia

77 yo admitted with confusion and bony pain.

- Total protein 12 (8)
- Ca 13 (8.4-10.2 mg/dL)
- Cr 4 mg/dL
- **PTH 12 (15-65 pg/mL)**
- Vit D 1,25 OH = 12 (15-65 pg/mL)
- Vit D 25 OH= 31 (30-80 ng/mL)
- SPEP= IgG kappa- 6 grams

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds:** HCTZ, Vit A, theoph
 • **Endo:** hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

Myeloma – lytic lesions releasing Ca

Hypercalcemia

65 yo healthy male seen in clinic.

Routine labs:

- Ca 10.9 (8.4-10.2)
- PTH 52 (15-65)
- Vit D 25-OH= 28 (30-80)
- Vit D 1,25-OH = 14 (15-65)
- SPEP= IgG kappa 300 mg (low)

DDx: PTH - nl or ↑

• 1° hyperpara
 • adenoma
 • hyperplasia
 • carcinoma
 • Li, teriparatide
 • FHCC
 • 3° hyperpara
 • Tumor- usually PTHrP

*Don't get fooled...1° hyperparathyroidism
 Not myeloma...It's MGUS*

Hypercalcemia

57 yo with leaking silicone calf implants.

- Ca 12.5 (8.4 - 10.2 mg/dL)
- PTH 12 (15-65 pg/mL)
- PTHrP- zero
- Vitamin D 1,25 OH= 114 (15-65)

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds:** HCTZ, Vit A, theoph
 • **Endo:** hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

Silicone implant related granulomatous disease.

Hypercalcemia

33 yo with HIV admitted with febrile syndrome. + U histo Ag, BM bx → histo, Dxd with disseminated histoplasmosis

- Ca 11.8 (8.4 - 10.2 mg/dL)
- PTH 7 (15-65 pg/mL)
- Vit D 1,25 OH _____ (15-65)

DDx: PTH - suppressed (<25)

• **PTHrP mediated**- e.g., lung, renal neoplasm
 • **Bony mets**- neoplastic, myeloma
 • ↑ **Vitamin D 1,25-OH**
 • granulomatous dz: sarcoid, MTB, Wegener's, Crohn's, histio, silicosis, foreign body granuloma
 • lymphoma- esp hodgkin's
 • Intoxication (calcitriol)
 • ↑ **Vitamin D 25-OH** intoxication
 • **Milk Alkali**
 • **Meds:** HCTZ, Vit A, theoph
 • **Endo:** hyperthyroid, acromegaly, pheo, AI
 • **Immobile** + something else
 • **TPN**
 • Recovery from **rhabdo**

Vit D 1,25 = 110...Histo granulomatous dz

Hypercalcemia

PTH- high normal or elevated

- Primary hyperparathyroidism
 - parathyroid adenoma
 - parathyroid hyperplasia
 - parathyroid carcinoma
- Lithium use, teriparatide
- Familial hypocalciuric hypercalcemia
- Tertiary hyperparathyroidism
- Tumor (rare)- usually PTHrP

PTH – suppressed (<25)

- PTHrP mediated- e.g., lung, renal neoplasm
- Bony metastasis- neoplastic, myeloma
- ↑ Vitamin D 1,25-OH
 - granulomatous disease: sarcoid, MTB, GPA (Wegener's), crohn's, silicosis, histoplasmosis, foreign body granuloma
 - lymphoma- especially hodgkin's
 - Intoxication (calcitriol)
- ↑ Vitamin D 25-OH intoxication
- Milk Alkali Syndrome
- **Meds:** HCTZ, Vit A, theophylline
- **Endo:** hyperthyroid, acromegaly, pheochromocytoma, adrenal insufficiency
- Immobilization- + something else
- **TPN**
- Recovery from rhabdomyolysis

Hypercalcemia

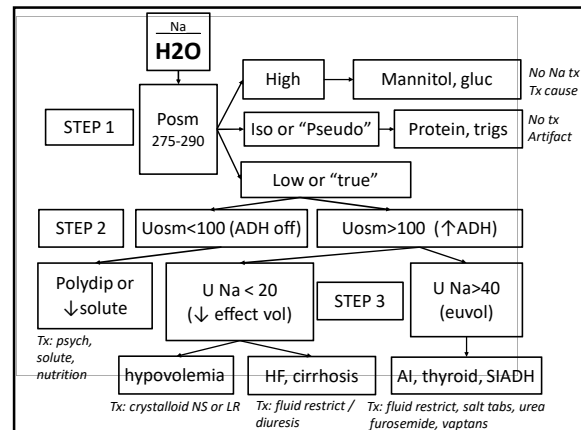
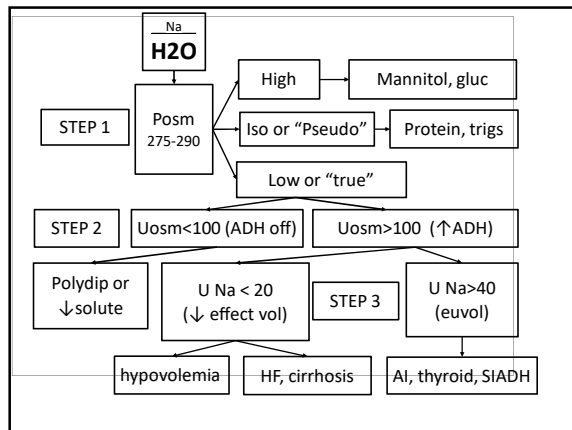
Evaluation

- H&P- meds, hctz, immobilization
- Albumin, calcium, phosphorous, alk phos
- PTH
- PTHrP
- vitamin D 1,25 OH
- ANCA, endoscopy, MTB eval (if unexplained vit D 1,25 elevated)
- Vitamin D 25- OH
- ACE, chest CT
- PET CT- for neoplasm or sarcoid
- SPEP, UPEP, serum free LC, bone marrow
- Blood level- Li, theophylline, Vit A
- TFT, cortisol stim test, IGF-1
- Pheo- plasma metanephrines, MRI adrenal
- Sestimibi scan- for adenoma
- 24 h U for calcium- for FHHC

Tx

- acute- NS, bisphosphonate, calcitonin 4 IU/kg SQ bid, furosemide, dialysis
- zolindronate or pamidronate- renal dose.
- denosumab
- Prednisone, ketoconazole, plaquenil for vitamin D mediated
- Sensipar (cinacalcet)
- Parathyroidectomy
- Treat underlying cause

HypoNa



For simplicity, units will be...

- Serum Na (mmol/L)
- Posm and Uosm (mosm/kg)
- U Na (mEq/L)

RAAS- renin-angiotensin-aldosterone

- EABV- effective arterial blood volume
- Low EABV- causes renin>angiotensin>aldosterone release
- Aldosterone – causes renal reabsorption of Na to increase EABV
- Reabsorption of urinary Na- leads to low urine Na concentration
- Low EABV- is from true hypovolemia or hypervolemia (CHF, Cirrhosis)
- Hypervolemia- by definition there has to be “ intravascular volume depletion”. The kidney senses “ volume depletion”
- H&P determines if true hypovolemia or hypervolemia is present in setting of low urine Na.
- Urine Na <20 means RAAS is activated and aldosterone is elevated.
- Urine Na <20- either true hypovolemia or hypervolemia is present
- Urine Na >40 means RAAS is off. Aldosterone is low. Implies euvolemia.

ADH

- ADH is released from posterior pituitary for hyperosmolarity and low EABV.
- Low EABV is potent stimulus for ADH release regardless of serum osmolarity.
- ADH is released in states of hypovolemia or hypervolemia (similar to RAAS).
- Urine osmolarity can be used as surrogate marker for serum ADH presence.
- A urine osmo < 100 implies no ADH.
- A urine osmo > 100 implies ADH presence
- The 100 cut off is somewhat arbitrary. Levels below 100 reliably indicate there is no ADH present.
- However, urine osmo in the borderline range 100-200 is intermediate.
- Urine osmo >200 indicates ADH is present.

- # HypoNa
- 65 yo male with CHF presents with SOB.
- Na 123
 - Posm 252 (low)
 - U osm 700 (↑ ADH)
 - U Na 13, U Cl 14
 - Edema on exam
-
- ```
graph TD
 S1[STEP 1] --> P1[Posm 275-290]
 P1 --> H[High]
 P1 --> P1_pseudo[pseudo]
 H --> M[Mannitol, gluc]
 P1_pseudo --> PT[Protein, tript]
 M --> L[Low or "true?"]
 PT --> L
 L --> S2[STEP 2]
 S2 --> U1[Uosm < 100]
 U1 --> U100[Uosm > 100 (↑ADH)]
 U100 --> S3[STEP 3]
 S3 --> U2[U Na < 20 (↓ effect vol)]
 U2 --> P2[Polydipsia
↓ solute]
 P2 --> H2[hypovol]
 P2 --> HF[HF, cirrhosis]
 U2 --> U3[U Na > 40 (euvo)]
 U3 --> AT[A1, thyroid, SIADH]
```
- CHF → +RAAS, + ADH
- Tx: Fluid restrict, Furosemide - to dilute urine

# ADH

The diagram illustrates a nephron with its distal tubule and collecting duct. The distal tubule is shown in the cortex, and the collecting duct extends into the medulla. The collecting duct is divided into two sections: the upper section, which is wider and contains fewer water molecules (H<sub>2</sub>O), and the lower section, which is narrower and contains many more water molecules. The lower section is labeled 'Small volume of concentrated urine'. The diagram is labeled 'Cortex' at the top and 'Medulla' at the bottom. The distal tubule is labeled 'Distal tubule' and the collecting duct is labeled 'Collecting duct'. The water molecules are represented by H<sub>2</sub>O. The solutes are represented by small dots. The diagram shows that ADH causes the collecting duct to become narrower and more permeable to water, leading to the reabsorption of water and the formation of a small volume of concentrated urine.

Source: Public domain

# HypoNa

45 yo with CHF, Na 125

- P osm 260 (low)
- U osm 500 ( $\uparrow$ ADH)
- U Na 44, U Cl 41
- Patient on high dose furosemide.
- Has severe edema.

```

graph TD
 S1[STEP 1: P osm 275-290] -- High --> H1[Mannitol, gluc]
 S1 -- Pseudo --> H2[Protein, trig]
 S1 -- "Low or 'true'" --> S2[STEP 2]
 S2 -- "U osm <100" --> S3[STEP 3]
 S2 -- "U osm >100 (*ADH)" --> S4[U Na > 40 euvo]
 S3 -- "U Na < 20 ($\downarrow$ effect vol)" --> S5[hypovol]
 S3 -- "U Na > 40 euvo" --> S6[AI, thyroid, SIADH]
 S5 --> S7[HR, anthesis]

```

Dx: Heart failure, urine lytes confounded by furosemide

With CHF, you expect low U<sub>Na</sub>, but furosemide leads to urinary Na wasting. Looks like euvoalemia by U<sub>Na</sub>. If furosemide were held, then a few days later U<sub>Na</sub> 11 & Cl 12 for example, would be low as expected.

# HypoNa

28 yo man presents with diarrhea

- Na 129
- P osm 262 (low)
- U osm 700 (↑ ADH)
- U Na 15 and U Cl 12
- No edema

```
graph TD
 S1[STEP 1] --> P275[Posm 275-290]
 P275 -- High --> M[mannitol, gluc]
 P275 -- High --> PT[Protein, trigs]
 P275 -- Pseudo --> L[Low or "true"]
 L --> S2[STEP 2]
 S2 --> U100[Uosm < 100]
 S2 --> U100_2[Uosm > 100 (↑ADH)]
 U100 --> PPS[Polydip or ψ-solute]
 U100_2 --> UN20[U Na < 20 (ψ effect vol)]
 U100_2 --> UN40[U Na > 40 (euvol)]
 UN20 --> S3[STEP 3]
 UN40 --> S3
 S3 --> H[hypovol]
 S3 --> HFC[HF, cirrhosis]
 S3 --> AI[AI, thyroid, SIADH]
```

diarrhea → hypovolemic → + RAAS, + ADH

# Hypona

35 yo male presents with n/v

- Na 127
- P osm 259 (low)
- U osm 500 ( $\uparrow$ ADH)
- **U Na 62, U Cl 17**
- ABG - **pH 7.58, HCO<sub>3</sub>=36**, pCO<sub>2</sub>= 46

```

graph TD
 S1[STEP 1] --> P275[Postm 275, 290]
 P275 --> High[High]
 P275 --> Pseudo[Pseudo]
 High --> MGL[Mannitol, gluc]
 High --> PT[Protein, trigls]
 Pseudo --> LowLow[Low or "true?"]
 S2[STEP 2] --> U300[Uosm < 300]
 S2 --> U100[Uosm > 100 (<math>\uparrowADH)]
 U300 --> Polydip[Polydip or <math>\downarrow-solute]
 Polydip --> UCl20[U Cl < 20 (<math>\downarrow-effect vol)]
 UCl20 --> Hypovol[hypovol]
 UCl20 --> HFC[HF, cirrhosis]
 UCl20 --> AlTH[Al, thyroid, SAHn]
 S3[STEP 3] --> X[X]

```

- Normally, U Na and U Cl trend together
- But in metabolic alkalosis, they may not
  - Excess negatively charged HCO<sub>3</sub><sup>-</sup> traps positive Na<sup>+</sup> in urine
  - So urine Na less reabsorbed despite volume depletion.
  - Instead, use U Cl, not U Na to assess volume in metabolic alkalosis

Vomit → met alkalosis + hypovolemia= low urine Cl

Vomit → met alkalosis + hypovolemia = low urine Cl

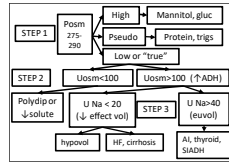
## HypoNa

55 yo with lung cancer

- Na 122
- P osm 250 (low)
- U osm 700 (↑ADH)
- U Na 100, U Cl= 97
- No HTN

Dx: tumor → SIADH

Tx: Fluid restrict +/- furosemide and salt tabs or urea



## Importance of PO solute in HypoNa

- The kidney can't excrete free H<sub>2</sub>O alone.
  - Kidney requires solute to excrete free H<sub>2</sub>O.
  - Urinary solute consist of mostly NaCl and urea.
  - Urea derives from dietary protein
- E.g. How much can a healthy patient drink before developing hypoNa?
- 600-900 mOsm/day in a normal diet. Daily solute intake = daily solute excretion
  - Healthy kidneys can maximally dilute urine to Uosm 50 mOsm/L
  - If patient ingests more than 18L then no more osmoles to excrete water.
  - This patient becomes hyponatremic if ingests more than 18L water.

$$\text{H}_2\text{O} = 900 \text{ mosm} / (50 \text{ mosm/L}) = 18\text{L}$$

## HypoNa

$$\text{H}_2\text{O excreted} = \text{solute ingested} / \text{Uosm}$$

|                                                      | Young and healthy | Elderly, living alone | EtOH | Lung tumor |
|------------------------------------------------------|-------------------|-----------------------|------|------------|
| PO Solute/day                                        | 900               | 100                   | 150  | 600        |
| U osm                                                | 50                | 100                   | 50   | 300        |
| Volume H <sub>2</sub> O that can be excreted per day | 18 L              | 1 L                   | 3 L  | 2 L        |
| Dx                                                   |                   |                       |      |            |

## HypoNa

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| Dx                                                   | Psychogenic polydipsia |                       |      |            |

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| Dx                                                   | Psychogenic polydipsia | Tea and toast         | Beer potomania |            |

## HypoNa

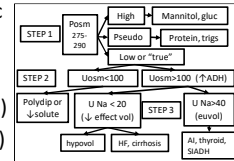
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| U osm                                                | 50                     | 100                   | 50             | 300        |
| Volume H <sub>2</sub> O that can be excreted per day | 18 L                   | 1 L                   | 3 L            | 2 L        |
| Dx                                                   | Psychogenic polydipsia | Tea and toast         | Beer potomania | SIADH      |

## HypoNa

21 yo patient admitted from clinic

- Na 121
- P osm 249 (low)
- U osm 75 (approp low, no ADH)
- U Na 12 (ignore. Stop at step 2)



**DX:** Psychogenic polydipsia or Tea and Toast  
– depends on history

## HypoNa

70 year male with multiple myeloma

- Na 128
- P osm 282 ( normal)
- ABG drawn within 15 minutes of BMP shows **Na 136**
- Total protein 12 g/dL. IgG kappa 7 grams

Isoosmolar or “pseudoHypoNa” = Lab artifact  
Confirm with ABG  
Do not treat the “HypoNa”

## HypoNa

36 yo female admitted with recurrent pancreatitis.

- Na 130
- P osm 282 ( normal)
- ABG shows Na 137
- Triglycerides 30,000.



Source: AAFP

**Dx:** PseudoHypoNa  
Do not treat the “HypoNa”

## HypoNa

65 yo - glucose 700 mg/dL, Na 125, Cl 95, bicarb 20. Alb 4.

Is the pt in DKA?

- Corrected Na =  $2((\text{glucose}-100)/100) + \text{measured Na}$   
=  $2((700-100)/100) + 125 = 137$

|           | Using <del>Corrected</del> Na | Using measured Na    |
|-----------|-------------------------------|----------------------|
| Anion Gap | 137 - (95 + 20) = 22          | 125 - (95 + 20) = 10 |

- 1) Hyperosmolar HypoNa
- 2) Not in DKA. Use the measured Na to calculate AG b/c hyperglycemia also leads to dilution of Cl, HCO<sub>3</sub>

## HypoNa

45 yo with AKI and severe edema

- Na 125, BUN 140, Cr 10, glucose 90
- P osmolality 310 (high)
- Recall BUN is ineffective osmole

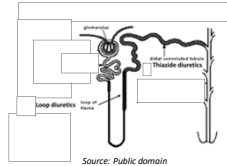
$$\begin{aligned} \text{Calculated osmolality} &= 2\text{Na} + \text{BUN}/2.8 + \text{glucose}/18 = 305 \text{ (high)} \\ \text{VS} \\ \text{Calculated osmolality} &= 2\text{Na} + \text{BUN}/2.8 + \text{glucose}/18 = 255 \text{ (low)} \end{aligned}$$

**Dx:** hypoosmolar HypoNa  
Careful working up hypoNa in renal failure...High BUN is clue...This is not hyperosmolar HypoNa

## HypoNa

52 yo with HTN recently started on HCTZ. Admitted with encephalopathy

- Na 110
- P osm 229
- U osm 250
- U Na 22, U Cl 24

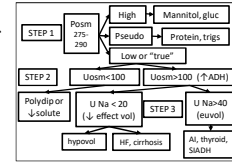


Dx: Hypoosmolar hypovolemic HypoNa  
Thiazides cause HypoNa  
loop diuretics ( furosemide)- generally do not cause HypoNa

## HypoNa

88 yo frail man has chronic hypoNa (128 to 132) for 5 yr

- P osm 262
- U osm 340
- U Na 45

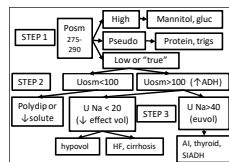


Dx: Probably reset osmostat. Mimics SIADH.  
Reset osmostat- Na remains unchanged if patient given a water load.  
SIADH- Na would decrease with water load.

## HypoNa

40 yo with severe subarachnoid hemorrhage admitted to ICU.

- Na 128
- P osm 263
- U osm 400
- U Na 50
- U output is 7 L per day.
- SIADH vs cerebral salt wasting (CSW)
- Clue: Low urine output in SIADH, not CSW

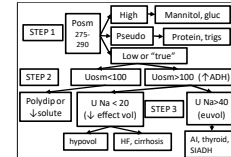


Dx: cerebral salt wasting- note polyuria  
Mimics SIADH  
Give NS, do not fluid restrict

## HypoNa

65 yo presents with malaise. SBP 88 mm Hg.

- Na 128
- P osm 259
- U osm 344
- U Na 80, U Cl 75
- WBC 10,000, 8% eos
- Ca 10.2
- Cosyntropin stim test: peak cortisol is 7 ( normal response is >20)



Dx: Adrenal insufficiency- mimics SIADH  
Tx: volume expand and give steroids.

## HypoNa

35 yo with depression on fluoxetine with diarrhea and Na 121

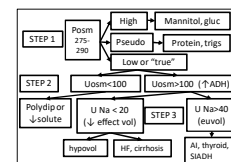
|       | ER  | After 3L NS | After 2 more L NS |
|-------|-----|-------------|-------------------|
| Na    | 121 | 128         | 126               |
| P osm | 248 |             |                   |
| U osm | 450 |             |                   |
| U Na  | 13  | 80          | 95                |
| U Cl  | 12  |             |                   |

Hypovolemia corrected  
Underlying SIADH revealed;  
H2O in IVF retained

## HypoNa

65 yo male admitted with decompensated CHF and severe edema

- Na 125
- P osm 258
- U osm 500
- U Na 18, U Cl 19

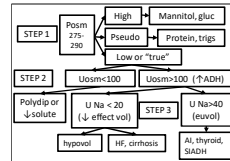


Dx: Hypoosmolar hypervolemic HypoNa  
Tx: Fluid restrict, Furosemide- for edema, and to dilute urine

## HypoNa

65 yo with small cell lung cancer

- asymptomatic hypoNa
- Na 118
- P osm 242
- U osm 300,
- U Na 88, U Cl 82.



Dx: SIADH

Fluid restrict, +/- furosemide+ salt tabs, urea or suggest more dietary protein. Treat cancer.

## Salt tabs and oral urea

- 1 g NaCl= 17 mosm Na
- 15 grams urea = 250 mosm urea
- Usual dose of oral urea is 15 grams QD or BID
- 2 doses of urea ( 500 mosm)= ~30 grams NaCl (30 salt tabs)
- Dietary protein is converted to urea
- High protein diet would have same effect as oral urea supplementation.

## HypoNa- Tx

70 yo male with metastatic lung cancer.

- Na 129
- P osm 241 ( low)
- U osm 500
- U Na 110
- Dx: SIADH
- If his U osm is fixed at 500 and he consumes a diet that produces 500 mosm of U solute per day, what should his fluid restriction have to be to maintain a stable Na?
- 500 mosm / 500 mosm/L= 1 L ( 1.5 L with insensible losses of 0.5 L)

## HypoNa- Tx

- U osm fixed at 500. If U solute increases to 1000 mosm/day, then 2 L fluid restriction would suffice. 1000mosm/day /500 mosm/L = 2 L/day.
- furosemide + salt tabs or urea> furosemide lowers U osm. For example furosemide may decrease U osm from 500mosm/L to 250 mosm/L. Less concentrated urine = more free water excretion.
- If solute intake is 500 mosm/day and urine osmo is lowered to 250 mosm/L =then patient can consume 2L per day before becoming hyponatremic as opposed to 1 L if urine osmo were 500.

## HypoNa- Tx

50 yo male with metastatic lung cancer.

- Na 121
- P osm =248
- U osm 600 mosm/L
- U Na 133

Dx: SIADH

Tx: fluid restrict.

Tx: if ineffective then add furosemide with salt tabs.

Tx: or suggest more dietary protein or add po urea

Tx: if solute intake were 600 mosm/day, then fluid intake > 1 L/day would worsen HypoNa.

Tx: furosemide dilutes U. If U osm 400, then fluid restriction could be 1.5 L

## HypoNa- Tx

60 yo with renal cell cancer

- Na 115.
- P osm 238
- U osm 600
- U Na 66. BP 110/70

Dx SIADH

• Fluid restrict

• Add furosemide and salt tabs or urea if fluid restriction ineffective

• Same patient with BP 180/95. Salt tabs would be relatively contraindicated due to HTN. Use urea.

• Urea more effective than salt tabs but usually more expensive

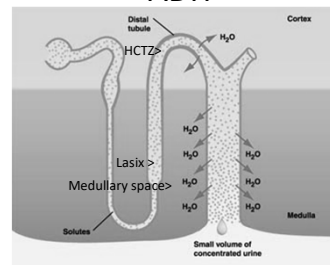
## HypoNa- Tx

60 yo admitted with severe confusion. Started on HCTZ last week. Na 115. Previous Na was 136.

- Hypertonic saline 100 cc IV stat- results in 2-3 meq Na increase.
- Typical hypertonic rate is 15- 30 cc per hr
- Monitor Na q2 h
- Increase Na 3-5 meq over first few hrs
- Target increase of Na 4-6 meq over 24 hrs. Max 8 meq over 24 hrs
- Example: If Na increased from 115 to 120 in first 5 hrs then target Na would be 121 over next 19 hrs with max increase to 123.
- Use IV D5W + desmopressin( DDAVP) if too rapid correction of Na
- Risk is osmotic demyelinating syndrome if Na rises too quickly.

## ADH

Lasix blocks Na from entering medullary space. HCTZ does not.



Source: Public domain

## Hyponatremia

- Thiazides may cause hyponatremia but loop diuretics generally do not (e.g., furosemide).
- Treatment of hypovolemia, adrenal insufficiency or the underlying cause of SIADH can cause a rapid increase in the serum Na because the stimulus for ADH release has resolved.
- Conversely, the underlying cause of CHF or cirrhosis will usually not quickly resolve. Therefore less risk for rapid correction.
- Some examples:
- Patient diagnosed with hyponatremia from severe adrenal insufficiency. Serum Na is 122. Initiating hydrocortisone would remove the stimulus for ADH. The patient may rapidly correct and be at risk for ODS.
- Patient with severe diarrhea and hyponatremia. Correction of the hypovolemia with NS removes the stimulus for ADH release. Rapid Na correction may ensue.
- Patient with psychogenic polydipsia is placed on fluid restriction. At risk for rapid Na correction
- On the other hand, patients with cirrhosis or CHF have ongoing elevated ADH levels due to the underlying pathophysiology that is not quickly reversed. These patients are at a lower risk for rapid hyponatremia correction.
- Use ABG or VBG Na if concern for pseudohyponatremia
- Degree of hyponatremia correlates with prognosis in CHF and Cirrhosis. More severe disease correlates with higher serum ADH. Higher ADH correlates with more severe hyponatremia.