

Electrolyte Abnormalities in the Hospital: Diagnosis and Management

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A collaboration between
Northwest Kidney Centers and UW Medicine



Objectives

Use a case-based approach to discuss workup and management of...

1. Sodium and water disorders in hospitalized patients
 - Focus on hyponatremia
2. Potassium disorders in hospitalized patients
 - Focus on hypokalemia

Outline

Case 1:
body fluid
compartments

Hyponatremia/Hypernatremia
Case 2: Rave reviews
Case 3: A case of iatrogenesis?
Case 4: How much can you drink?
Case 5: The “un-watered” patient

Hypokalemia
Case 6 – A young woman with heart
failure

Summary &
Take home
points

Case 1: Body fluid compartments

A 20 year old man presents to the hospital after experiencing a grand mal seizure. Exam and vitals on day of admission are normal (PNa was 140mEq/L).

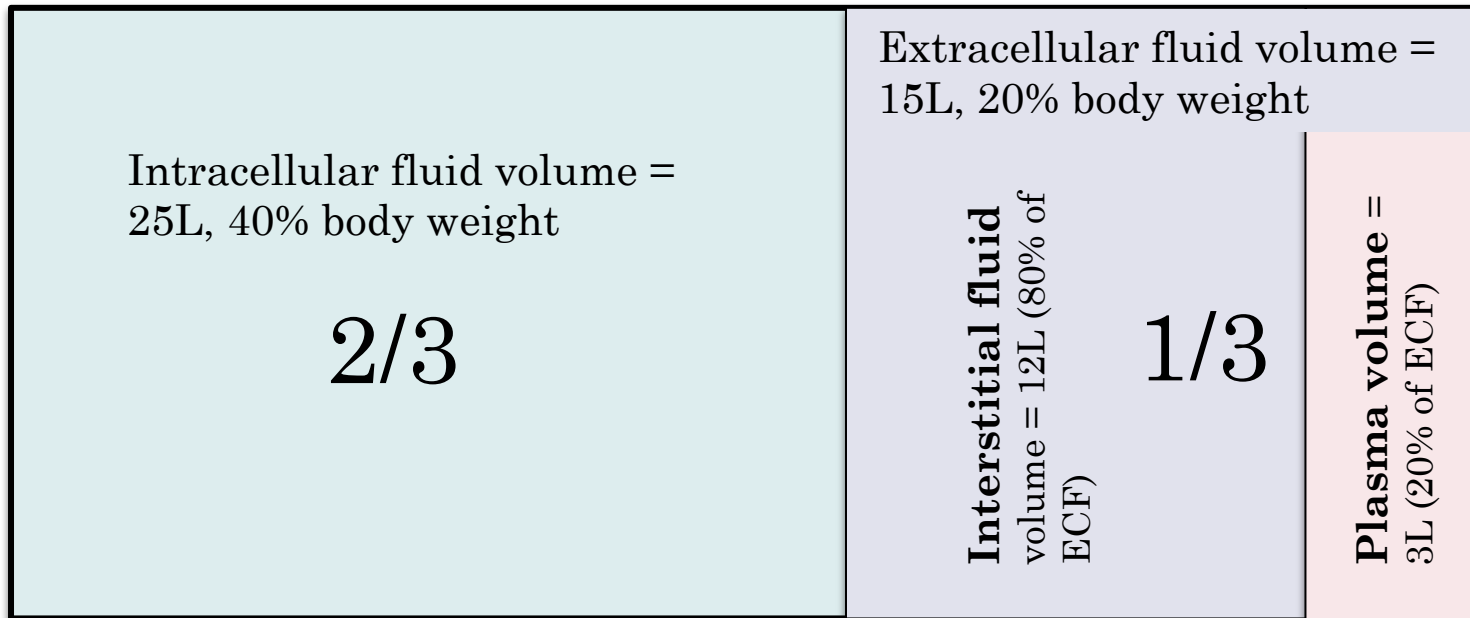
- Experiences a recurrent witnessed seizure x 3 minutes
- Blood drawn immediately → + anion gap metabolic acidosis, returned to normal in less than 1 hour.
- **PNa was 154mEq/L**, but fell back down to 140mEq/L over a short period of time.
- No increase in urine output, or free water administration during this time

Question: What is the basis of the acute rise in PNa?

Body fluid compartments

- Total body water \approx 50-60% of total body mass
 - $2/3$ in ICF and $1/3$ in ECF
 - ECF: 75% interstitial, 25% plasma volume

TBW = 40L (60% body weight of 70 kg person)



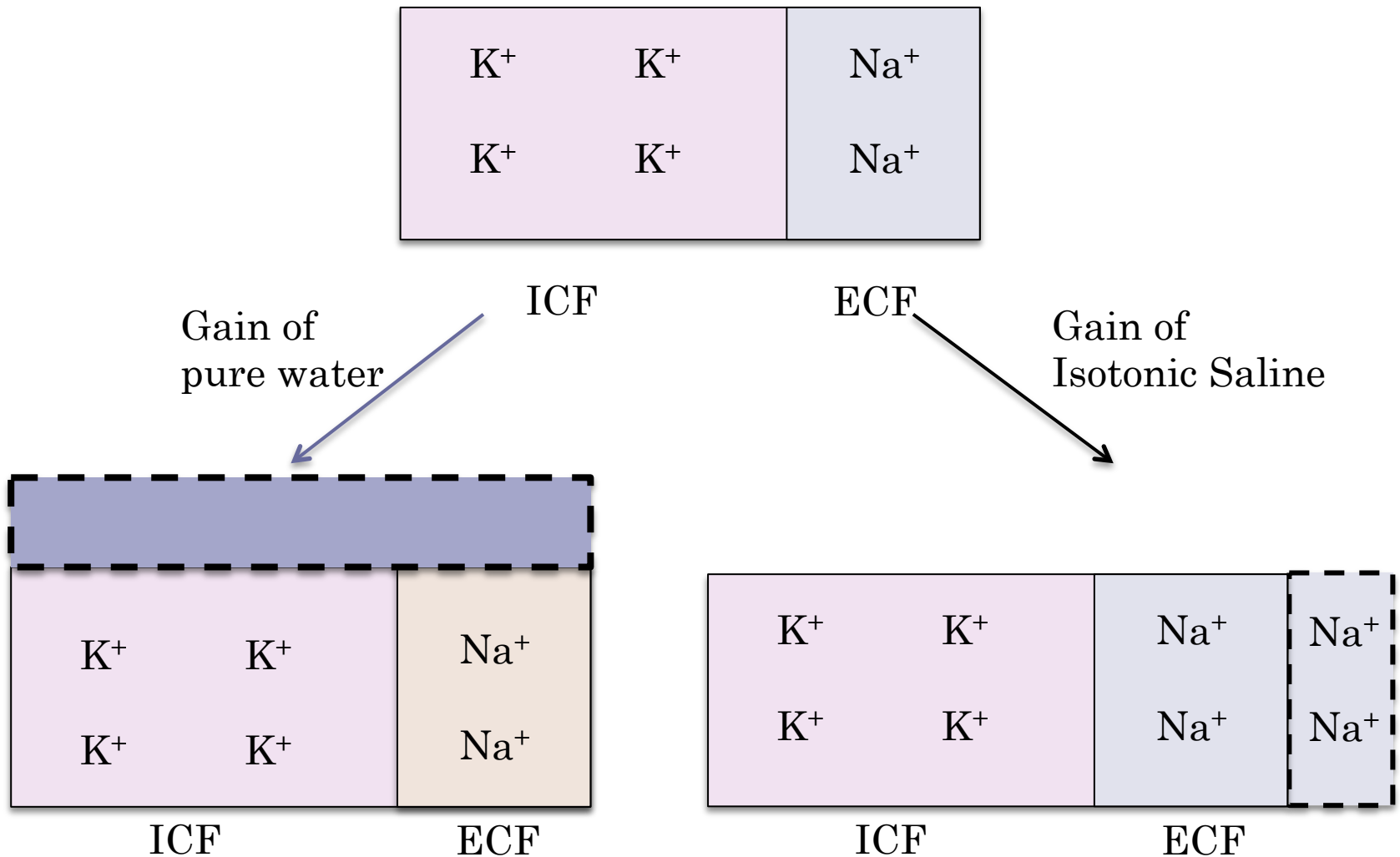
Determinants of volume of cells

- Content of Na in the ECF is the major determinant of its volume.

K ⁺	K ⁺	Na ⁺
K ⁺	K ⁺	Na ⁺
K ⁺	K ⁺	Na ⁺
ICF		ECF

- Concentration of Na in the ECF compartment is the most important factor in ICF volume (*except when cells have other effective osmoles*).
- Major intracellular factor responsible for accumulation of water in cells is retention of K

Changes in volumes of body fluids with IV fluids

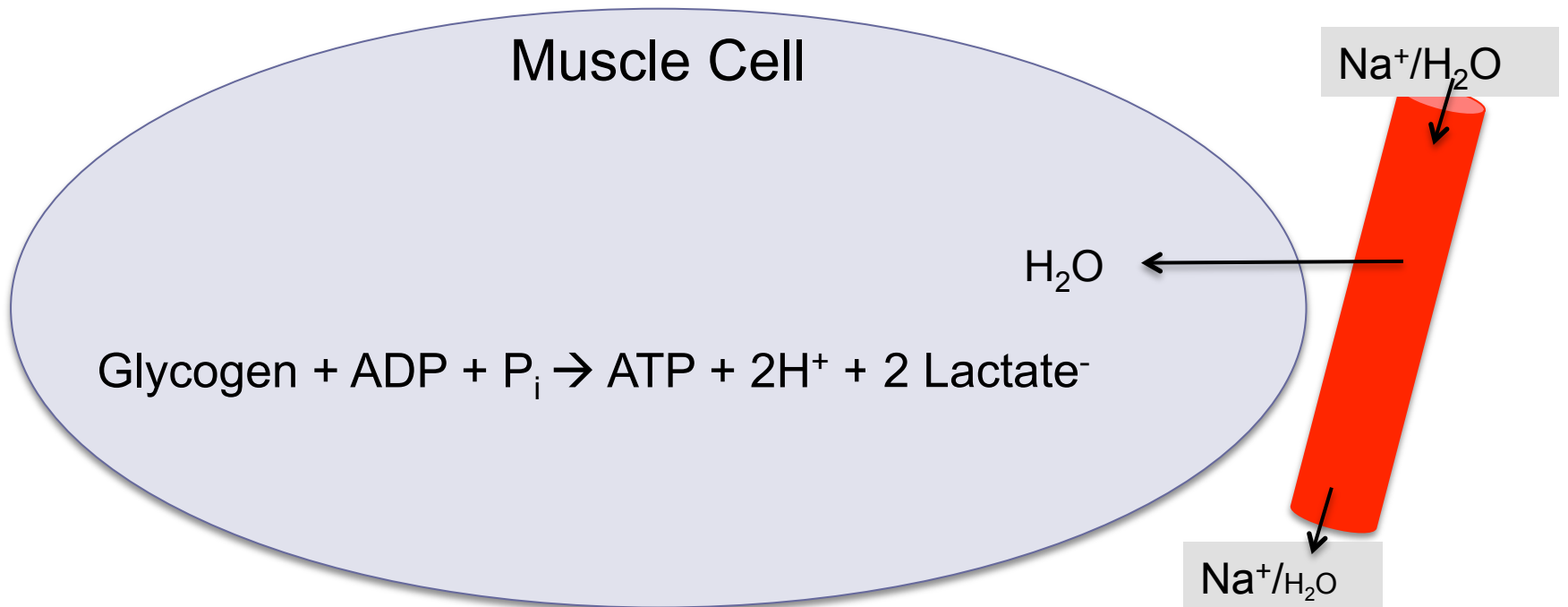


Back to Case 1...

- Case: A 20 year old man presents to the hospital after experiencing a grand mal seizure. Exam and vitals on day of admission are normal (SNa was 140mEq/L). Several hours later he experiences a witnessed grand mal seizure. Surprisingly however his SNa was 154mEq/L, but fell back down to 140mEq/L over a short period of time
- **Question: What is the basis of the acute rise in his SNa?**

Answer

- Transient transcellular shift in water due to sudden and massive increase in effective osmoles in skeletal muscle cells (pulls H₂O in)



Case 2: Rave reviews



- A 19 y/o man with history of anorexia nervosa presents to the ER with complaint of weakness and lethargy. Prior to admission was at a rave where he took MDMA (Ecstasy/Molly) and drank a large amount of water to avoid dehydration from sweating.
- In the ED, he had a grand mal seizure x 3 minutes. Blood was drawn immediately after the seizure and SNa was 130mEq/L. Uosm 700mOsm/kg.
- Admitted to Medicine → next AM, SNa was 120 meq/L

Questions



- Is this acute hyponatremia?
- Why did he have a seizure if the SNa was 130mEq/L?
And why was SNa the next morning lower?
- What role may anorexia nervosa play in the clinical picture?
- How do you manage?



Initial evaluation of Hyponatremia

- True (hypotonic) hyponatremia vs non-hypotonic hyponatremia (including pseudohyponatremia)?
 - Is this true hypotonic hyponatremia?
- Acuity/Severity
 - Is this acute (<48hr) or chronic?
 - Is the patient symptomatic?
- Etiology
 - Is ADH acting or not? Why?
 - What is the volume status of the patient?
 - Where did the excess free water come from?
 - Why can the kidneys not excrete excess water?

Non-hypotonic hyponatremia

- Hypertonic or isotonic hyponatremia
 - Hyperglycemia
 - Dilutional hyponatremia, no risk of cerebral edema
 - Can calculate “corrected” serum sodium (predicted serum sodium w/ correction of hyperglycemia)
 - **2 mEq/L for each 100 mg/dL increase in glucose**
 - Rare other causes
 - IVIG or surgical irrigant solutions (glycine or sorbitol)
- Pseudohyponatremia (laboratory artifact)
 - Hypertriglyceridemia (less relevant in modern era)
 - Monoclonal gammopathy

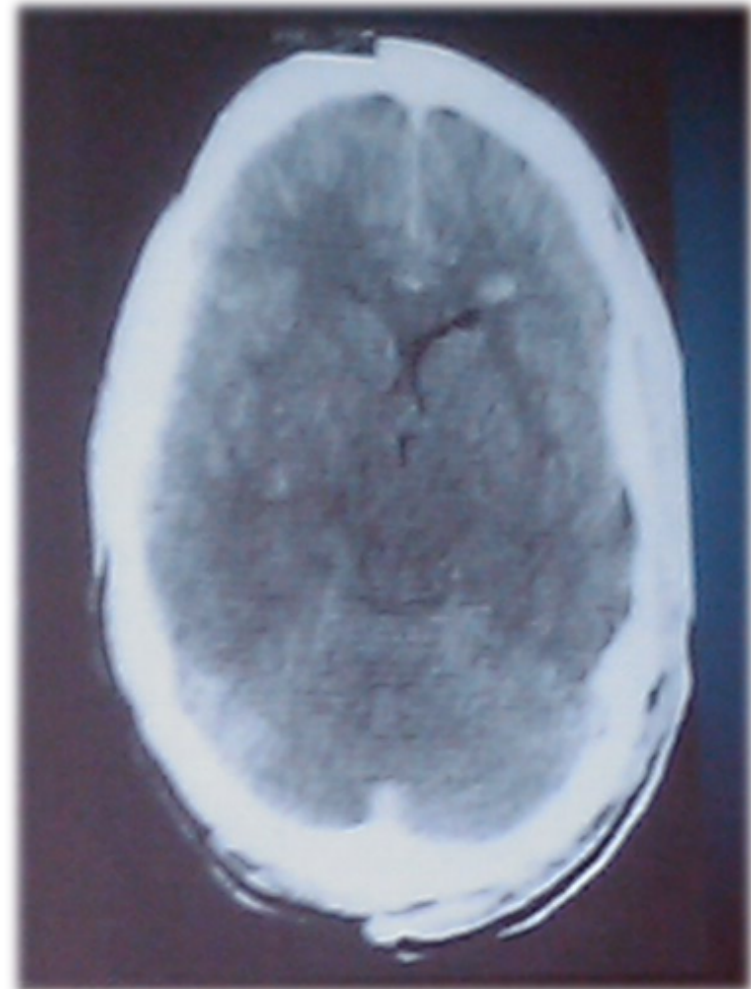
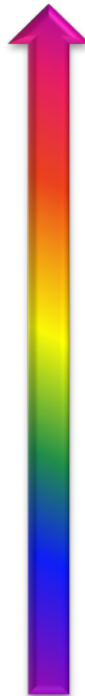
Initial evaluation of Hyponatremia

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 - Not necessary to test for in every case, but to r/o, check serum osm
- Acuity/Severity
 - Is this acute (<48hr) or chronic?
 - Is the patient symptomatic?
- Etiology
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Symptoms of Hyponatremia

Symptom
Respiratory arrest
Coma
Seizures
Delirium
Restlessness
Lethargy
Headache
Fatigue
Confusion
Nausea & vomiting
Asymptomatic

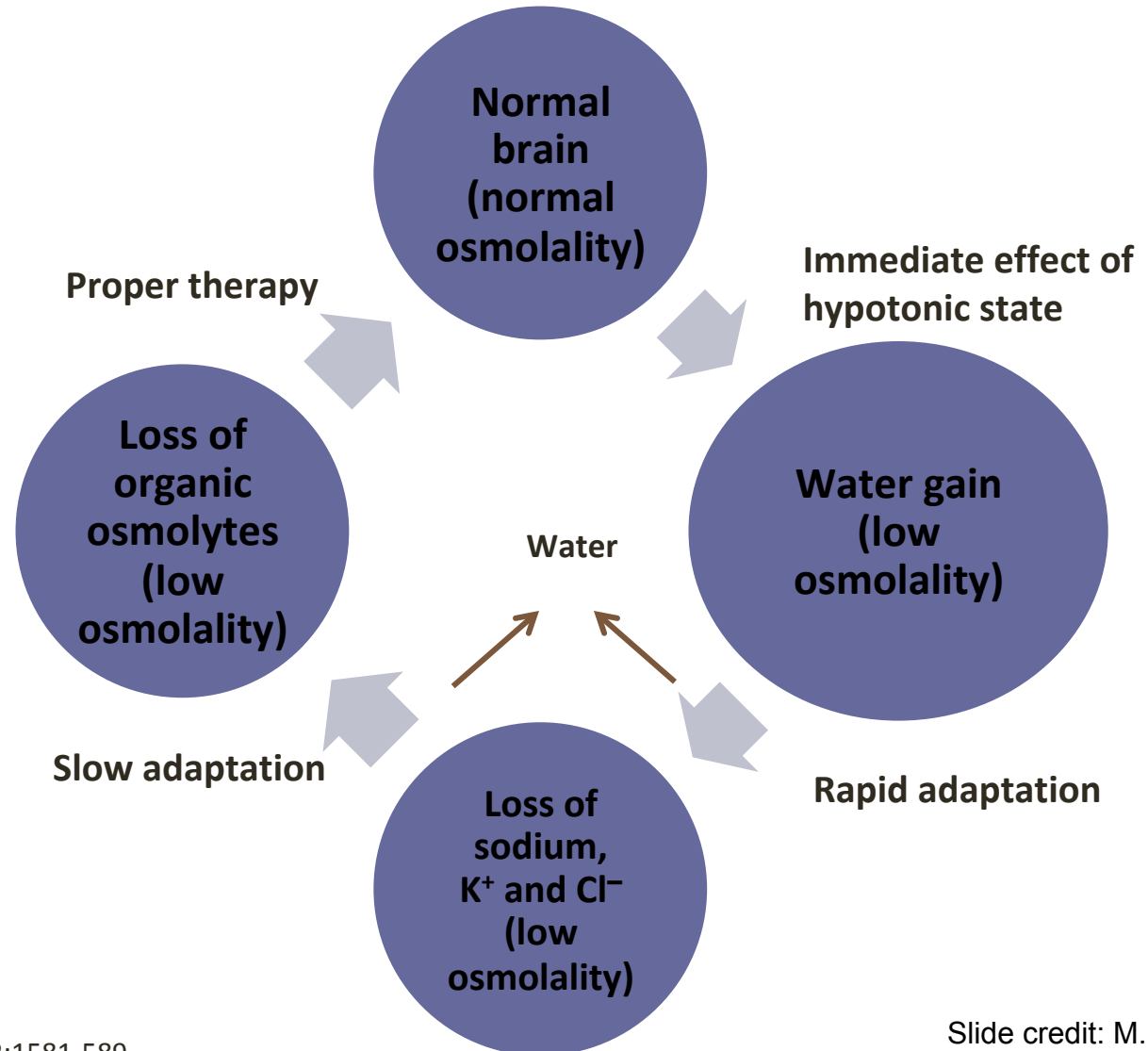
Increasing severity of hyponatremia and rate of $[Na^+]$ decline



Hyponatremic brain

Rate of Hyponatremia: Effects on Cellular Volume

Understanding the cellular adaptations is critical in the proper treatment of acute v. chronic hyponatremia

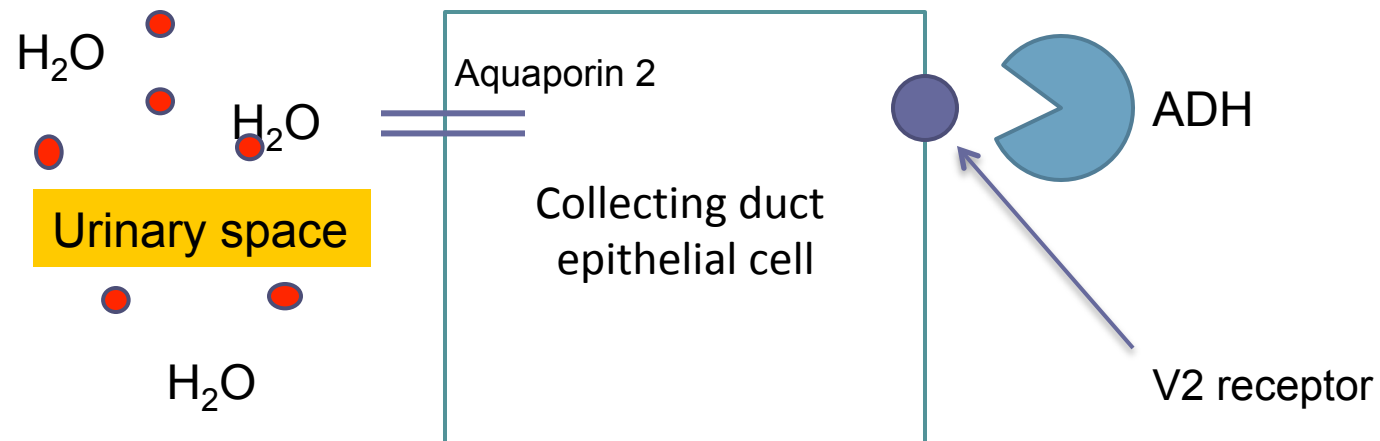
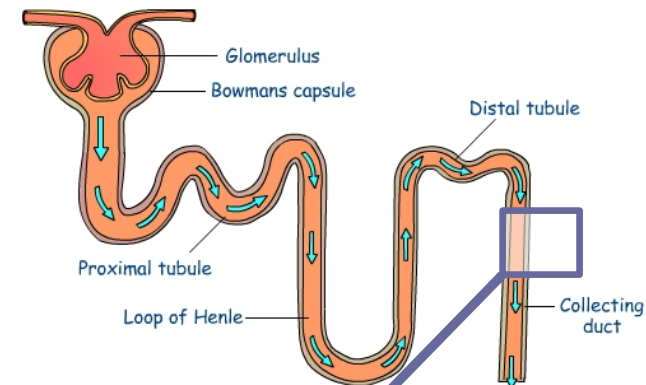


Initial evaluation of Hyponatremia

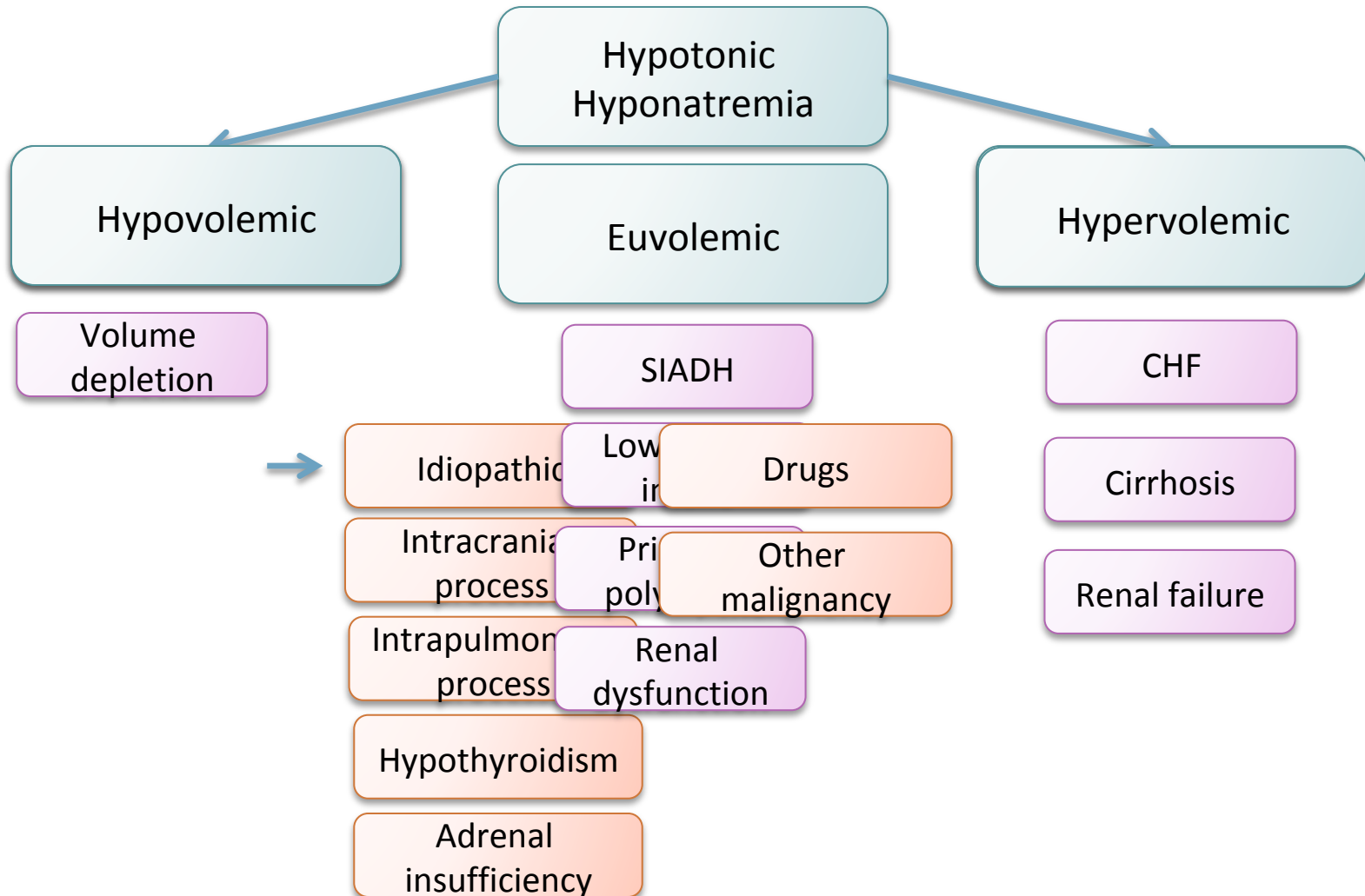
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 - What is the volume status of the patient?
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Interpreting Urine Osmolarity

- ADH “on” or “off” ?
 - ~~[Test serum ADH levels]~~
 - Urine osmolarity?
 - ADH “on” → Uosms >300
 - ADH appropriately “off” → Uosms 50-150

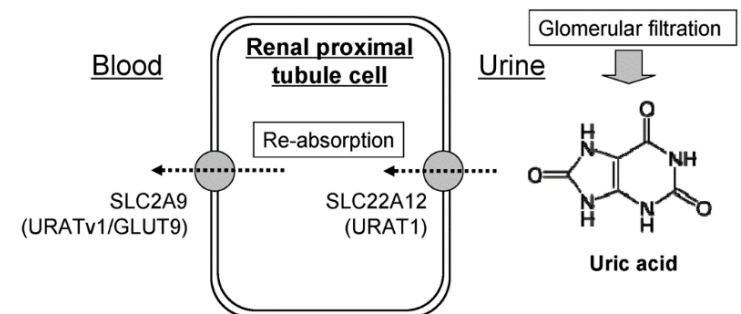


Causes of hypotonic hyponatremia?

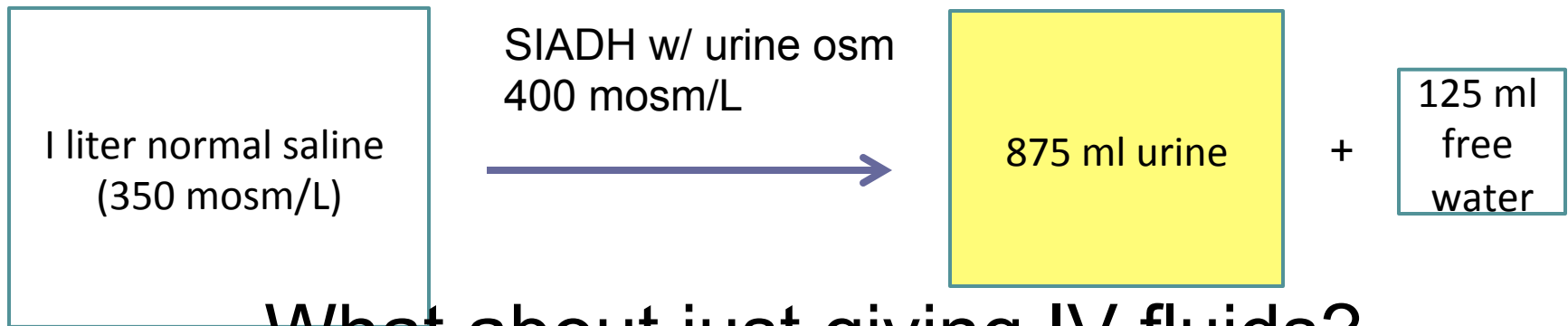


SIADH versus low EABV?

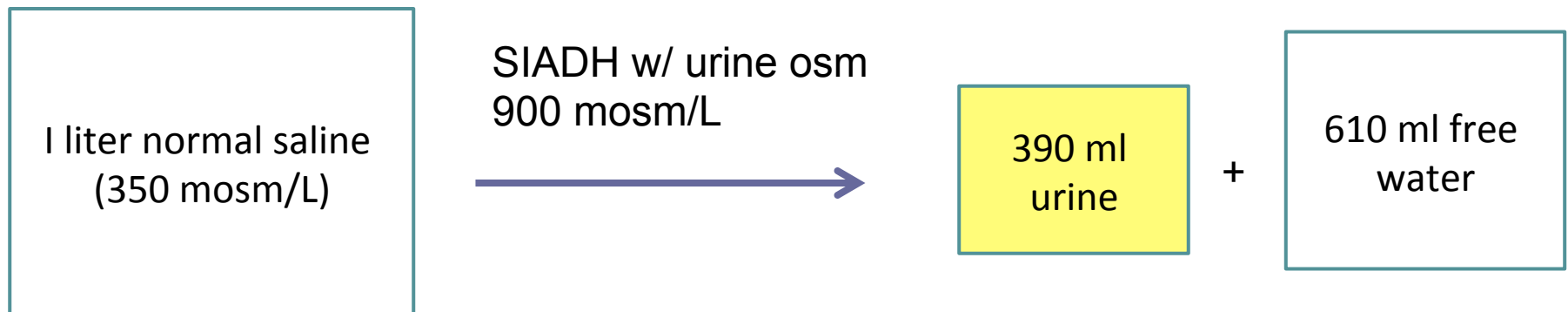
- History?
- Physical examination?
 - Vitals, orthostatics, JVP, etc
 - Advanced exam: IVC collapsibility, bedside TTE
- Lab Tests?
 - Urine sodium
 - Low (<20meq/L) → volume depletion
 - Not low (>40 meq/L) → SIADH
 - Serum uric acid
 - < 4 mg/dl → consistent with SIADH



Other diagnostic maneuvers for SIADH versus low EABV?



What about just giving IV fluids?



Case 2 again



- A 19 y/o man with history of **anorexia nervosa** presents with weakness, lethargy, and inability to concentrate. Prior to admission was at a rave where he took **MDMA and drank lots of water**.
- In the ED, he had a grand mal seizure. Afterward, **SNa was 130mEq/L** and **Uosm was 700mOsm/kg**.
- Vitals: Ht 5'7" and wt 105Lbs (45kg). Afebrile. **HR 80 BP 110/70**
- Exam: **Post-ictal, diaphoretic**. Rales on chest exam

Answers to case 2

- Is this acute hyponatremia?
 - **YES! Why?**
 - Ingestion of large volume of water
 - Ingestion of Ecstasy, a drug that leads to secretion/release of vasopressin, and thus **SIADH**
- Why did he have Sz?
 - **Acute hyponatremia**
 - **SNa from venous sample after Sz overestimates prior SNa.**
Number of osmoles increased in muscle cell during Sz
- What's the role of anorexia nervosa?
 - **Low muscle mass (50% of TBW).**
 - **Smaller positive water balance causes greater fall in his SNa.**

Case 2, continued

- Treatment?
 - Symptomatic and acute: Draw out water from skull by raising the SNa acutely/ASAP
 - Give hypertonic saline rapidly: 1-2 cc/kg bolus of 3% NS over 10 min (maximum of 100cc). May repeat 1-2 more times as needed until symptoms improve.
 - Goal is 4-6 mEq/L increase in SNa over 1-2hr.
 - Closely follow SNa and watch for reabsorption of water from reservoir in intestine or muscle cells.
 - Do not exceed 15 mEq/L in first 48hrs.

Case 3 – A case of iatrogenesis?

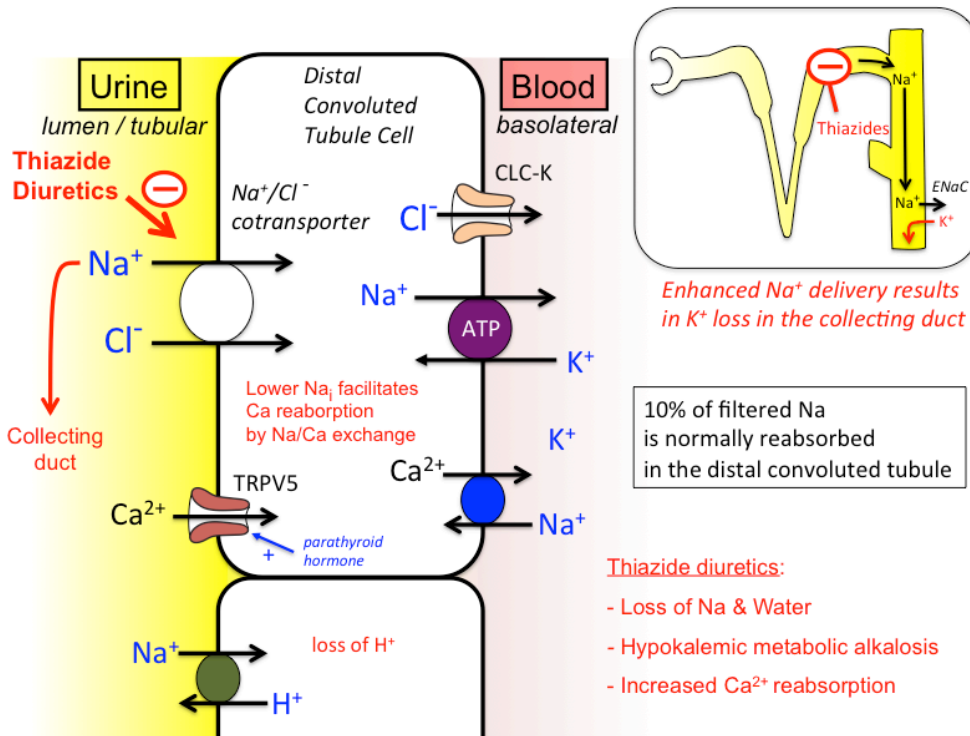
- 80 year old woman is hospitalized for 1 wk history of progressive weakness, nausea and anorexia. Has become bedridden and confused during past 3 days. She has hypertension managed with enalapril and chlorthalidone initiated 3 weeks ago. On admission **SNa was 110mEq/L, K of 3**
- Physical Exam: T 37.3C, BP 110/65, HR 95 and RR 14. Wt 47kg. BMI 20. Cardiac and pulmonary exams normal. No focal deficits on neuro exam. No edema, ascites.

Lab studies

Parameter	Admission Plasma	Admission Urine
Na (mEq/L)	110	30
K (mEq/L)	3	
Cl (mEq/L)	72	30
HCO ₃ (mEq/L)	30	
Cr	1	
BUN	9	
Glucose	90	
Osmolality	231	500

What is the cause of this patient's hyponatremia?

Thiazide-induced hyponatremia



- Increased incidence in women and elderly patients
- Pathogenesis unclear, but potential causes:
 - Volume loss \rightarrow ADH-induced water retention
 - ? Increased thirst due to xerostomia
 - ? Increased ADH release

Returning to the labs...

In ED given 80cc of 3% saline and mentation rapidly improves. After admission, some additional isotonic fluid is given. 10 hours later...

Parameter	Admission Plasma	Admission Urine	10hr Plasma	10hr Urine
Na (mEq/L)	110	30	121	25
K (mEq/L)	3		2.7	
Cl (mEq/L)	72	30		
HCO ₃ (mEq/L)	30			
Cr	1			
BUN	9			
Osmolality	231	500	252	180
Urine Output				400cc/hr

So now what?

- Which of the following is the most appropriate treatment for this patient?

(A) 0.9% Saline

(B) 5% Dextrose in water + KCl

(C) Fluid restriction + KCl

(D) Tolvaptan

Answer

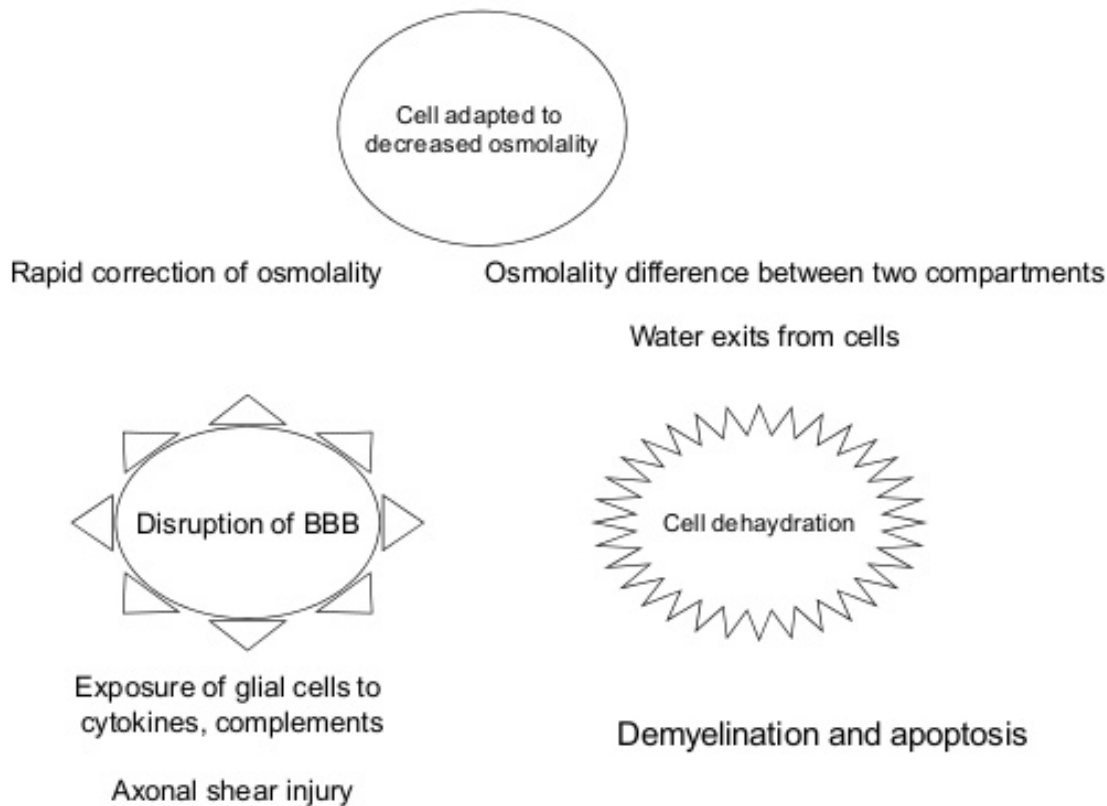
- 5% Dextrose in water + KCl to drop SNa back to goal rate of rise
- What is the goal rate to avoid avoid osmotic demyelination (ODS)?
 - Chronic (>48hr): 0.5mEq/L per hour, ≤10 mEq in first 24 hr (6-8 in those with RF for ODS) and ≤18 in first 48hr.
 - Acute (<48hr) symptomatic: 1-2mEq/L per hour, correcting by 4-6mEq/L and/or correction of symptoms.



Osmotic Demyelination Syndrome (ODS)

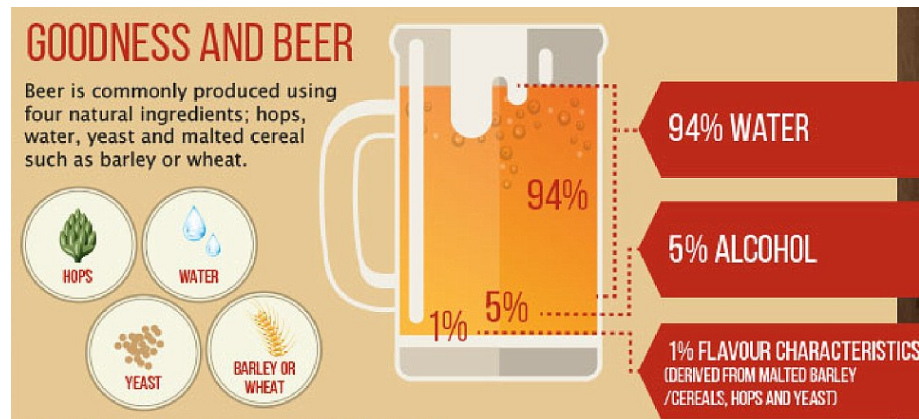
Symptoms seen 2-6 days after correction:

- Dysarthria (CPM)
- Dysphagia (CPM)
- Ataxia, dystonia
- “Locked in” state
- Acute flaccid paralysis
- Coma



Case 4: How much can you drink?

- 45 year old man with schizophrenia, well managed on anti-psychotics, intermittently unhoused, also with alcohol use disorder, presents to the HMC emergency department with right leg swelling, erythema, pain. Diagnosed clinically with cellulitis.
- On arrival, vital signs are stable. Not orthostatic.



Parameter	Value
Plasma values	
Na (mEq/L)	116
K (mEq/L)	3.5
Cl (mEq/L)	88
Bicarb (mEq/L)	26
Creatinine (mEq/dL)	0.8
BUN (mEq/dL)	9
Glucose (mEq/dL)	119
Osmolality (mOsm/kg)	246
Blood alcohol	Undetectable
Urine	
Osmolality (mOsm/kg)	75
Na (mEq/L)	7

Questions

- Is this acute hyponatremia?
- What are the possible etiologies for his hyponatremia?
- How do you manage?



Initial evaluation of Hyponatremia

- True hyponatremia vs non-hypotonic hyponatremia?
 - **True hyponatremia** (low serum osms)
- Severity/chronicity?
 - **Moderate to severe, likely chronic** given asymptomatic
- Etiology
 - Is ADH acting or not?
 - **No! (How do you know)**
 - What is the volume status of the patient?
 - **Euvolemic**
 - Where did the excess free water come from?
 - **Beer + water**
 - Why can the kidneys not excrete the excess water?
 - **Low solute intake w/ high water intake likely**

Primary polydipsia vs. Low solute intake

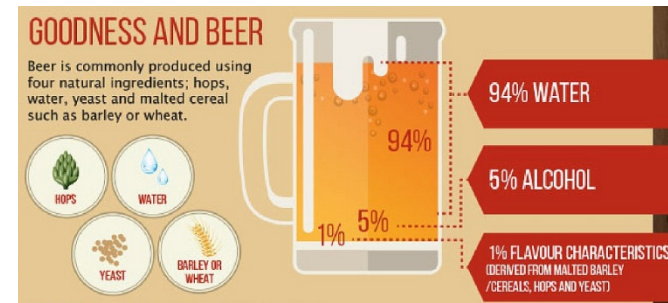
- Key: Hyponatremia ensues when water intake exceeds maximum urine output
- Normal American diet (per day):

600-900
mosms

÷

75
mOsm
per liter

= 8 to 12 liters urine /day



- Low solute intake (“tea-and-toast” or “beer potomania”)

200
mosms

÷

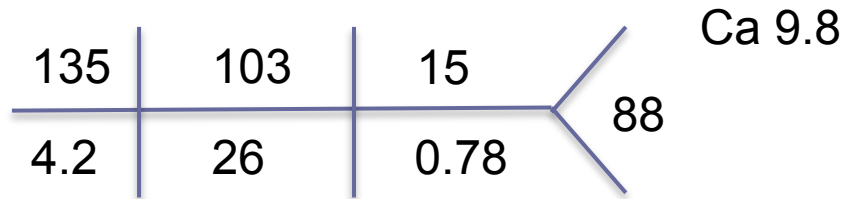
75
mOsm
per liter

= 2.6 liters urine /day

Case 5: The “un-watered” patient

- 61 y/o female with h/o bipolar disorder and past h/o lithium use transferred from Alaska with intractable seizures. Workup demonstrated neuronal K⁺ channel Ab. Patient admitted to ICU, started on pulse steroids, was NPO due to AMS. Also on keppra and depakote.
- Vitals: T 36.1 HR 65 BP 110/68 RR 12 96% RA. Wt 50kg
- Exam:
 - GEN: Somnolent.
 - Neuro: Following simple commands. Intact gag. Face symmetric.
 - Ext: No edema

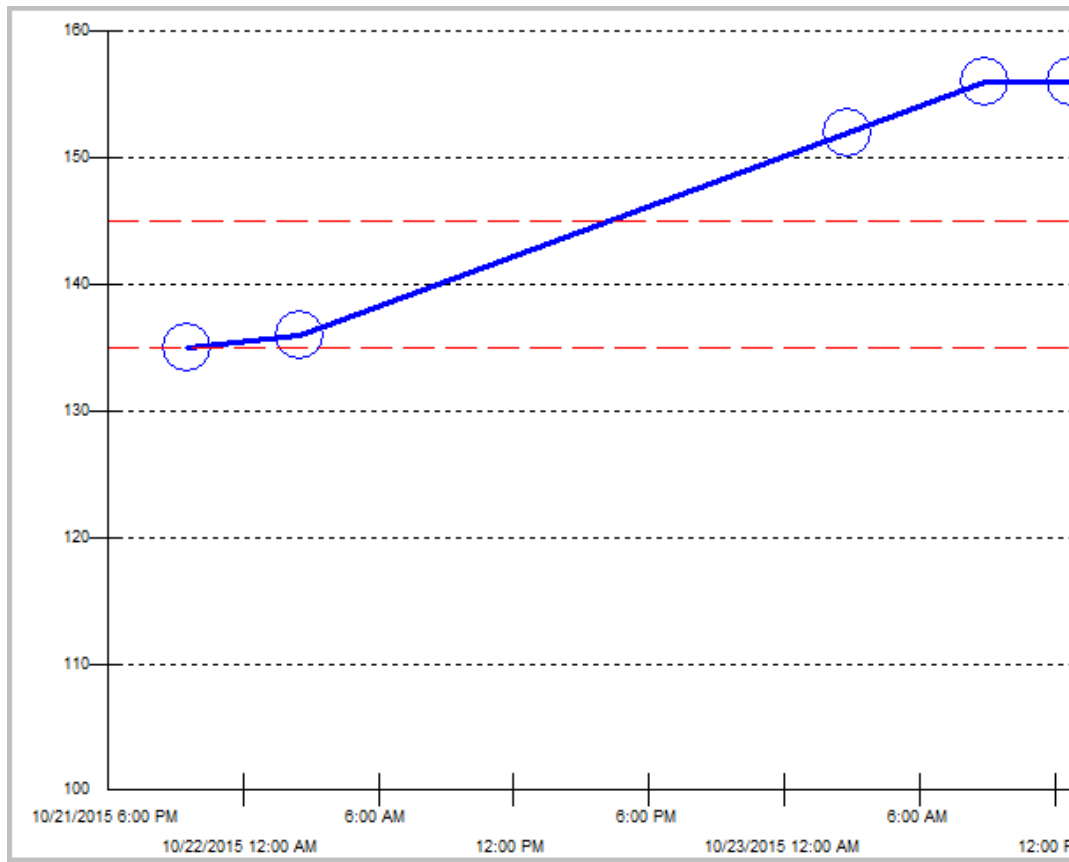
First 36 hours of admission...



SNa 156 (36hrs
after admit)

Outs: Incontinent

Ins: NS 75cc/hr
TF at 45cc/hr



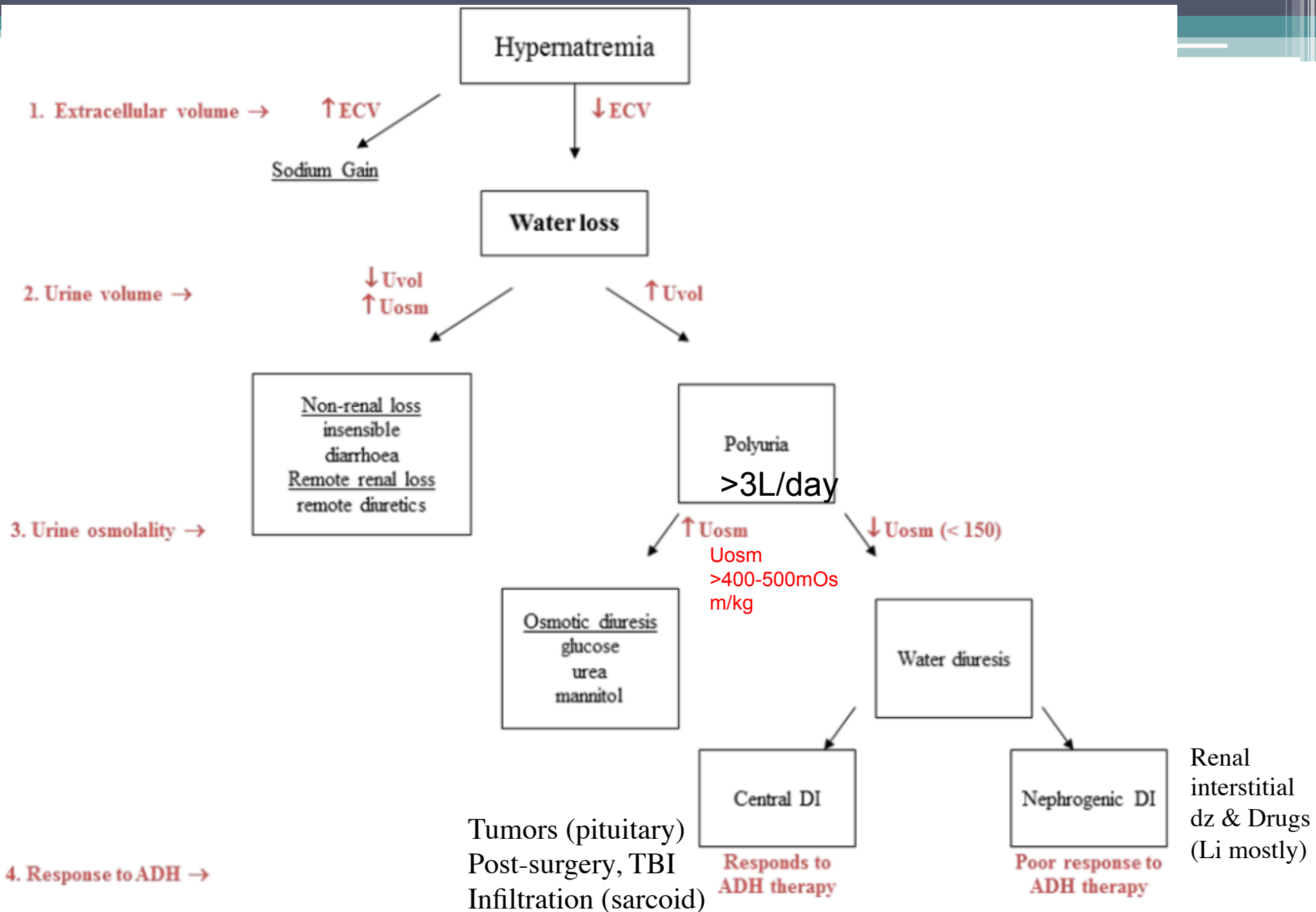
Hypernatremia

Question: What are the major causes of hypernatremia in hospitalized patients?

- Primary water deficit
 - Reduced water intake or defective thirst mechanism
 - Increased water loss
 - Renal loss: Central/nephrogenic DI, osmotic diuresis
 - GI loss: Vomiting, Nasogastric suction, osmotic diarrhea
 - Insensible losses: Respiratory, skin
 - Shift of water into cells: Seizures
- Primary gain of Na⁺
 - Infusion of hypertonic fluid in oliguric patients

Factors to assess the patient with hypernatremia

- Thirst (History): Why is patient not compensating?
- **What is source of water loss? (urine volume?)**
 - High insensible water loss or GI loss (NGT suction, diarrhea)
 - **Polyuria? Urine flow rate and effective osmolality:**
 - **Osmotic diuresis: $U_{osm} 400-500\text{mOsm/kg}$**
 - **Water diuresis: $U_{osm} < 150\text{mOsm/kg}$ (Low ADH)**

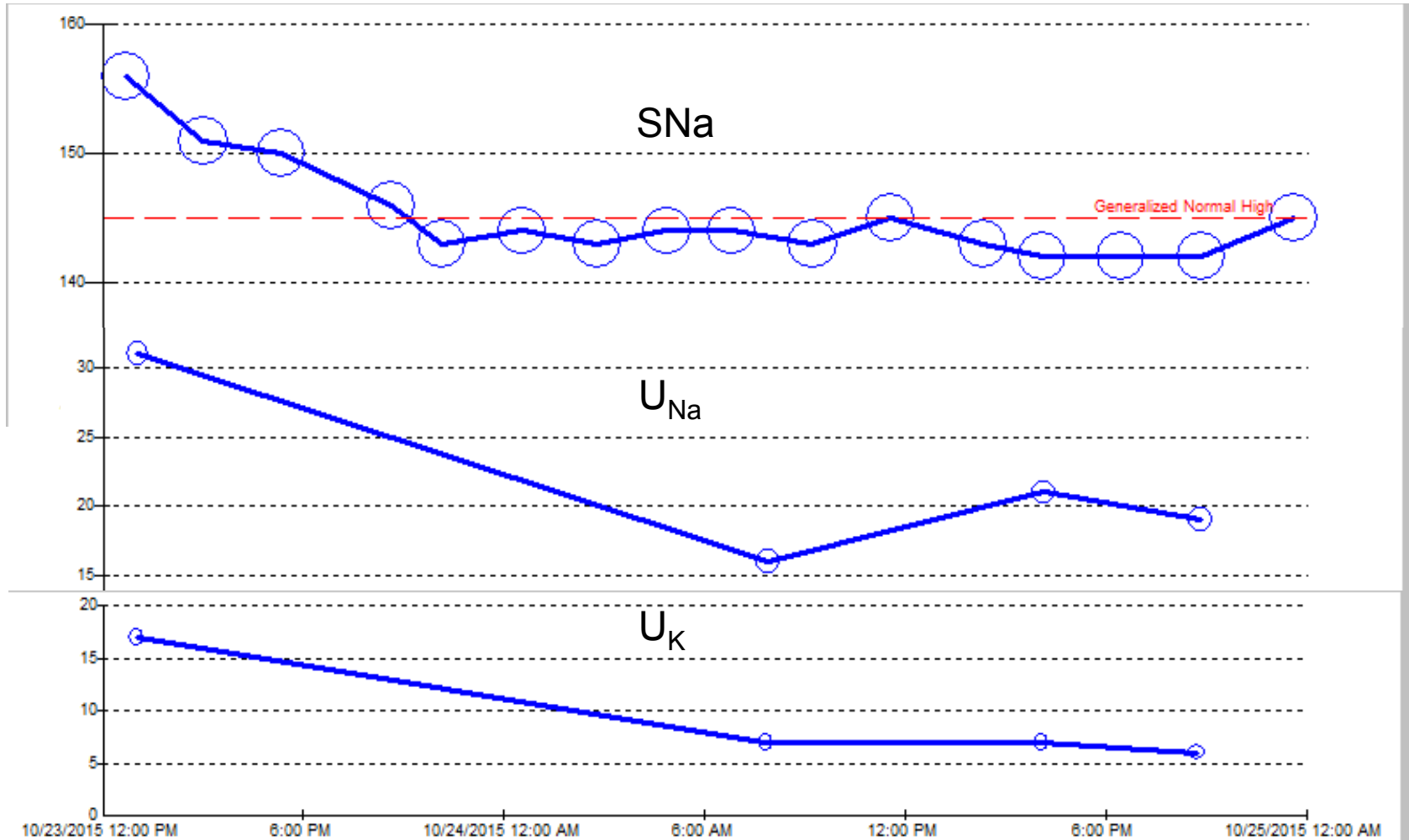


Case 5 - Subsequent management

- Foley catheter placed with UOP 175cc/hr
- SNa = 156
- Urine osm: 140mosm/kg
- Total body free water deficit: $TBW \times ([SNa / 140] - 1)$
 - $25L \times ([156/140] - 1) = 2.9L$
- Treatment: D5W at 250cc/hr and FWB 300Q6hr.

Changes in SNa and UNa

Mentation improve, but UOP now increased to 250-300cc/hr



Questions

- Is this partial or complete nephrogenic DI? What do you do?

Response to DDAVP?

4mcg IV DDAVP: Uosm 100->125 2hr after DDAVP.

- What are treatments for Lithium induced Nephrogenic DI?

A. Stop lithium (if possible, but with caution)

B. Amiloride

C. NSAIDs

- Started on indomethacin with drop in urine output from 250-350cc/hr to 60-125cc/hr

Case 6: A young woman with heart failure

- A 32 year old woman with no PMH presents to urgent care with abdominal pain x 4 months, found to have **BP of 240/180**.
- Denies headaches, visual changes, chest pain
- On ROS, endorses 2 weeks of leg swelling
- Physical Exam: T 37.3C, BP 240/183, HR 87. Cardiac exam with +S3, displaced PMI laterally, 1+ LE edema, lungs with crackles at bases

Case 6, continued

- Initial labs in the ED → **K 2.4, HCO₃ 36, Cr 1.2**, and BNP 3000. EKG concerning for LVH.
- She was given IV Labetolol 30mg, PO Amlodipine 10mg, and PO Lisinopril 10mg with improvement in her BPs to 188/140.
- TTE: Normal LV size, with concentric LVH and moderately reduced systolic function and global hypokinesia (LVEF 30%).

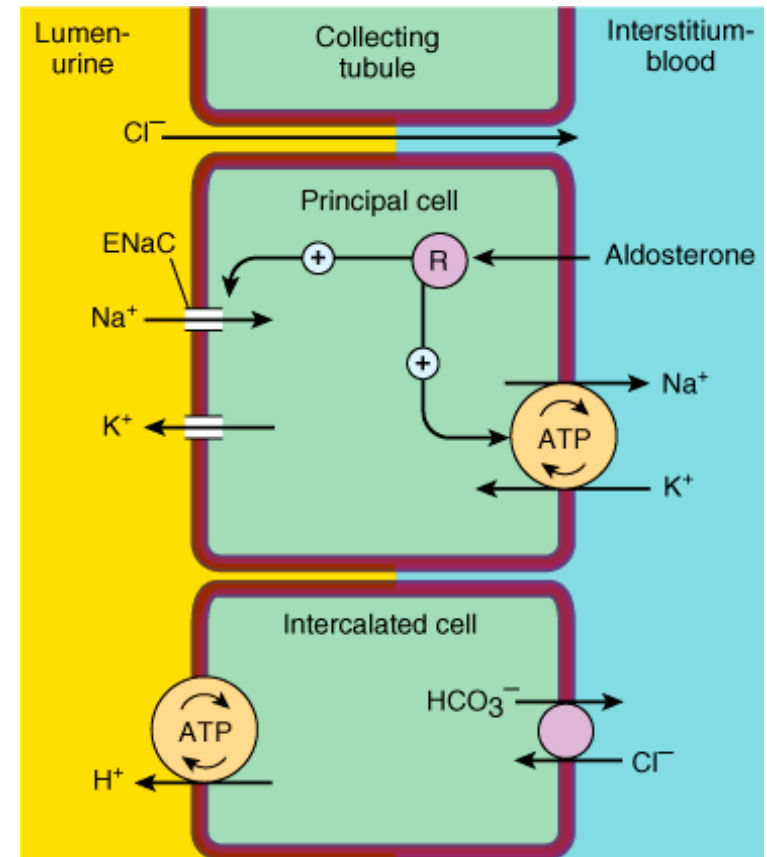
Case 6 questions

What is the differential diagnosis for this patient's hypokalemia with metabolic alkalosis in the setting of severe hypertension?

1. Primary hyperaldosteronism
2. Renal artery stenosis leading to secondary hyperaldosteronism
3. Other rare conditions
 - a) Inherited monogenic disorders
 - b) Apparent mineralocorticoid excess

Hyperaldosteronism

- Estimated to be responsible for 20% of severe/resistant HTN in adults
- Includes both
 - Bilateral adrenal hyperplasia (60%)
 - Aldo-producing adenomas (40%)
- Clinical features
 - HTN
 - Hypokalemia (only ~30%)
 - Metabolic alkalosis (only 10-35%)



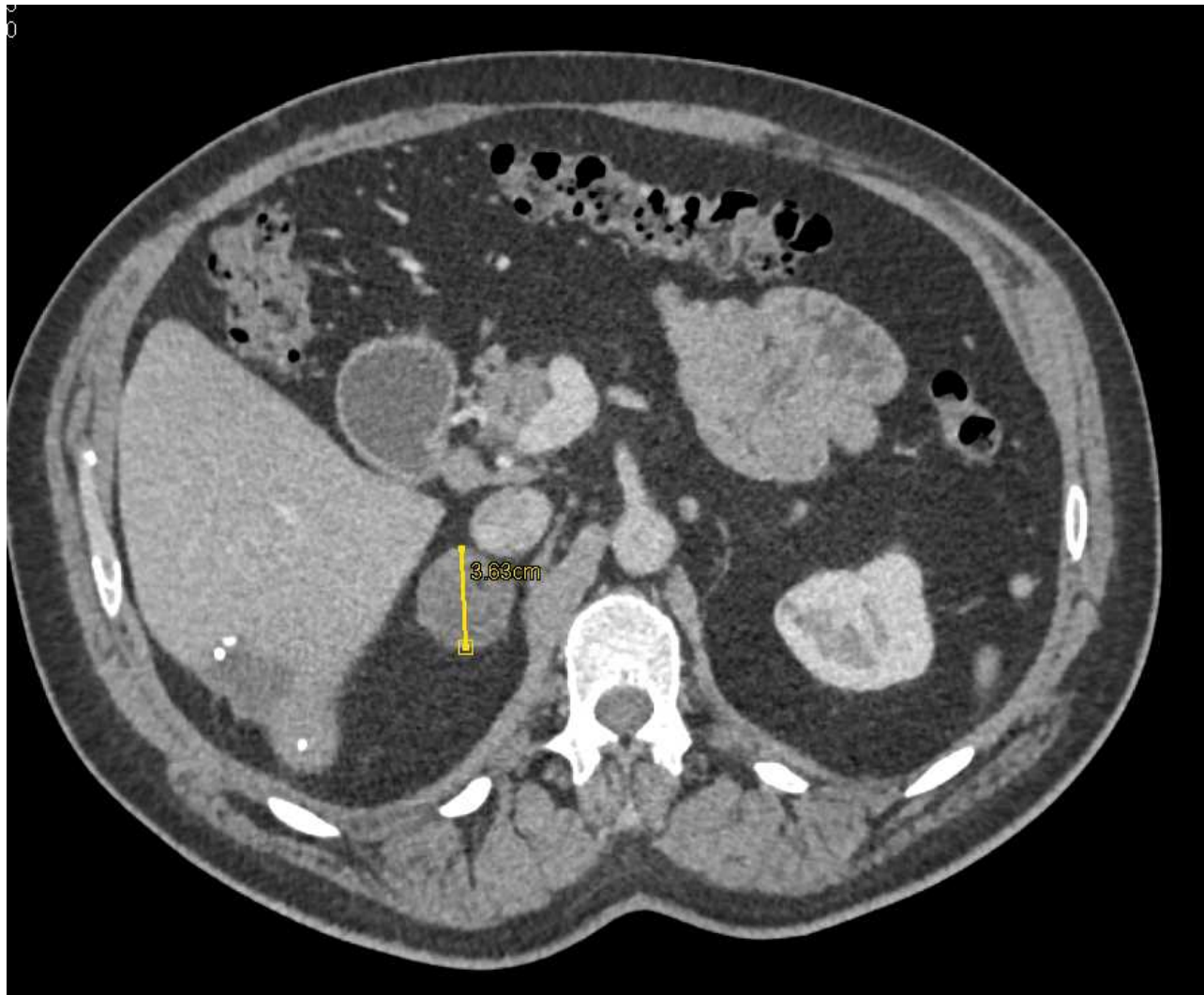
Screening for Hyperaldosteronism

- Lab test: Serum aldosterone and plasma renin activity (PRA)
 - Ideally 8am, OFF MRAs, Ok to be on other drugs
 - Though ACEI/ARB can raise PRA, B-blockers decrease PRA
 - Definition:
 - Aldosterone/PRA > 20, **AND**
 - Serum aldosterone > 15 ng/dL
- I screen everyone with resistant HTN or with HTN + spontaneous (or minimally provoked) hypokalemia or metabolic alkalosis

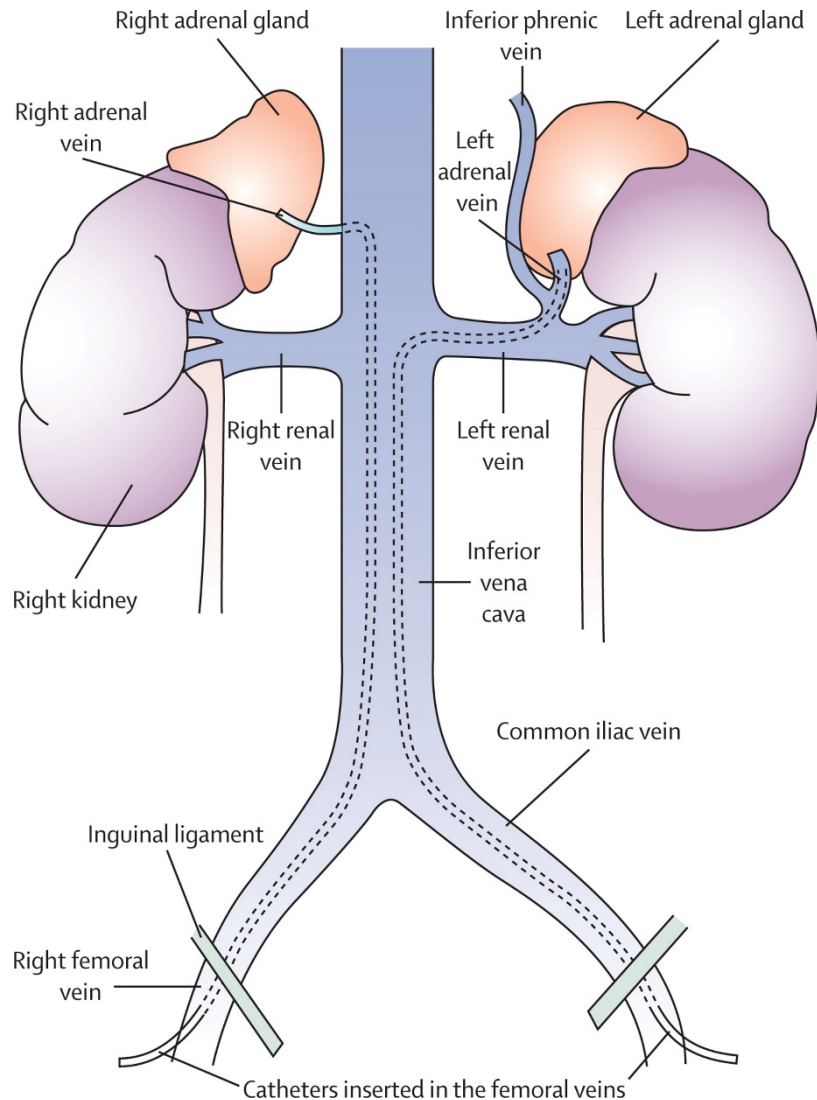
“Case Confirmation” for hyperaldo

- Needed in most cases
 - Exception: HTN, spontaneous hypokalemia, undetectable PRA, PAC >20 ng/dL
- Best choice for inpatients:
 - Saline infusion test: 2L NS over 4 hours, then check serum aldosterone → + test is >12 ng/dL
- Need to control serum potassium and BP **prior**

Hyperaldosteronism confirmed – Next step?

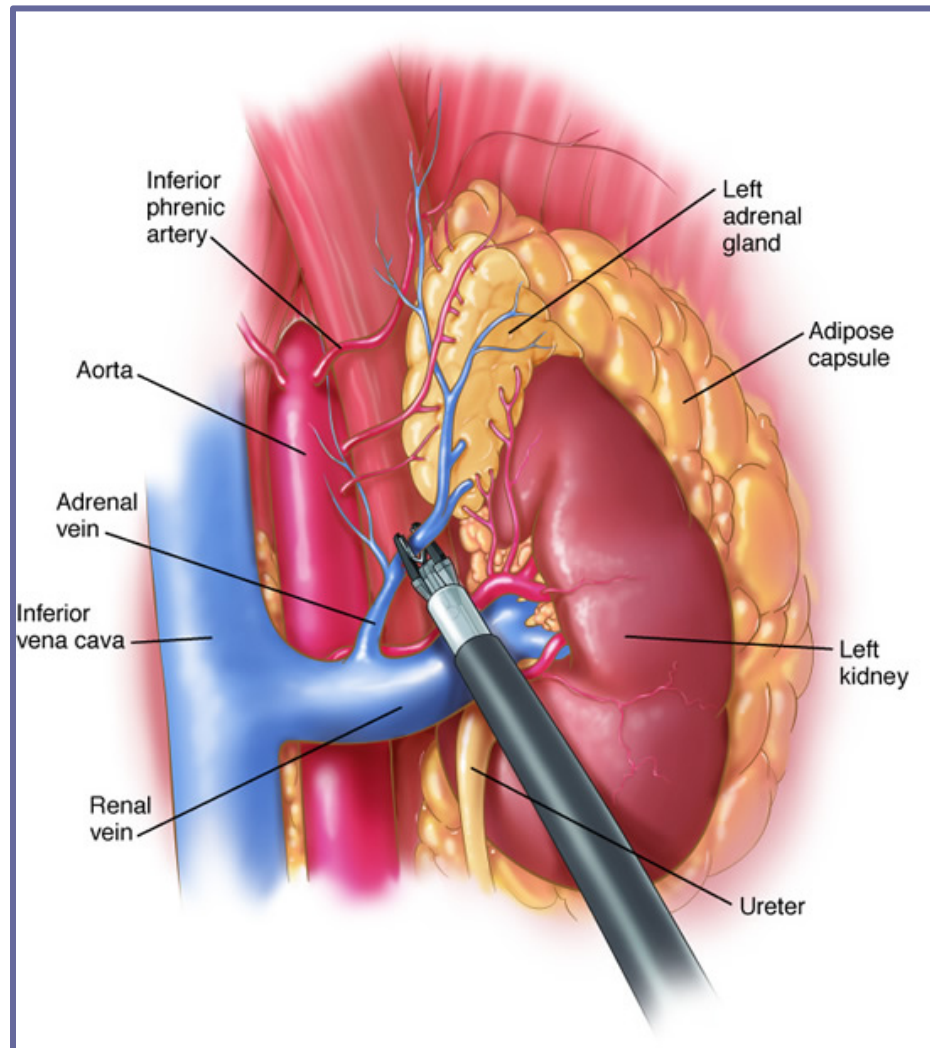


Hyperaldo – Next step?



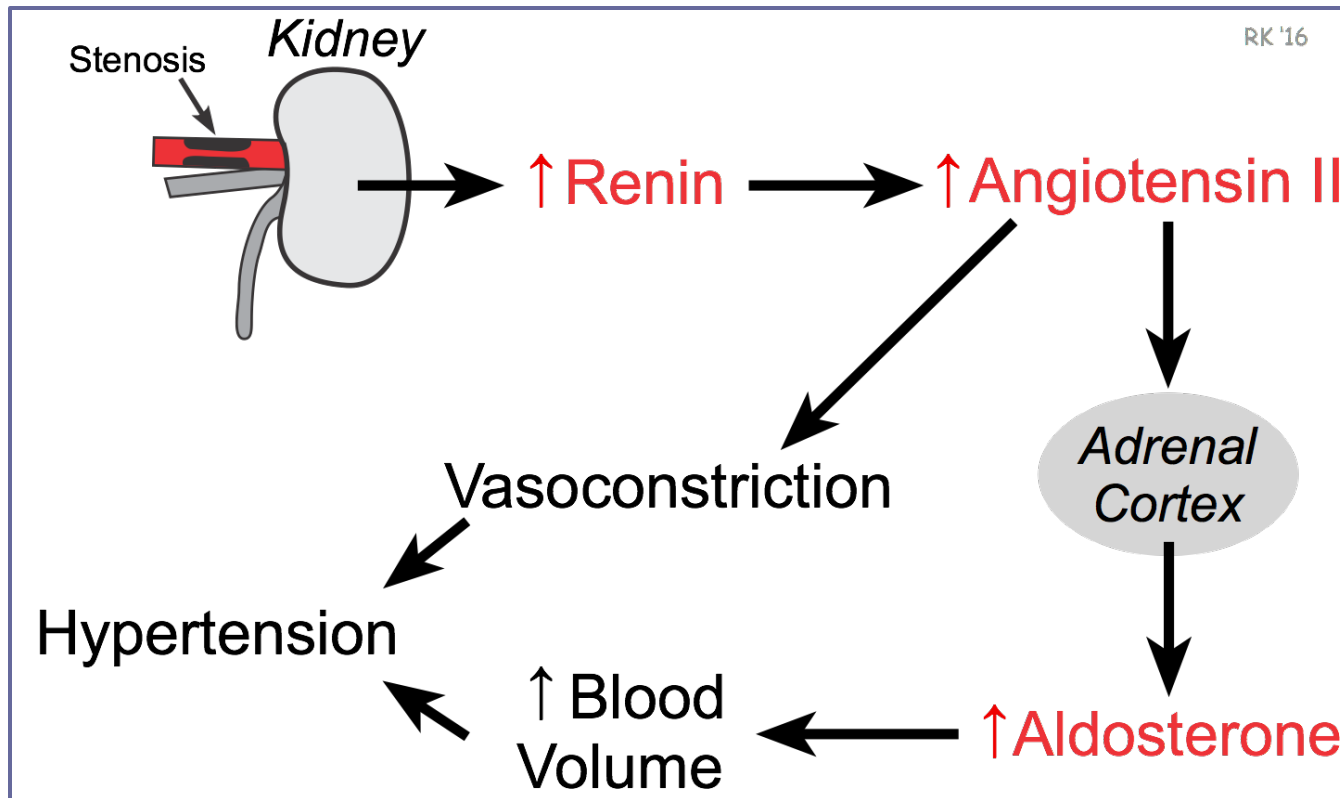
- Adrenal venous sampling by high volume interventional radiologist or vascular surgeon
- Exception: Patients <35 years of age with completely suppressed PRA and PAC >20 ng/dL

Hyperaldo – Next Step?



Renal artery stenosis

- Prevalence 10%-30% in severe or refractory HTN



Renal artery stenosis

- Clinical clues:
 - Diffuse vasculopathy (CAD, CVD, PVD)
 - Young women (FMD)
 - Systolic + diastolic abdominal bruit (specific, not sensitive)
 - Isolated systolic bruit (sensitive, less specific)
 - Headaches, tinnitus, neck pain (FMD)
 - Rise in creatinine with ACEI/ARB (or any anti-HTN therapy)
- Key: know what you will do with results of testing before you proceed

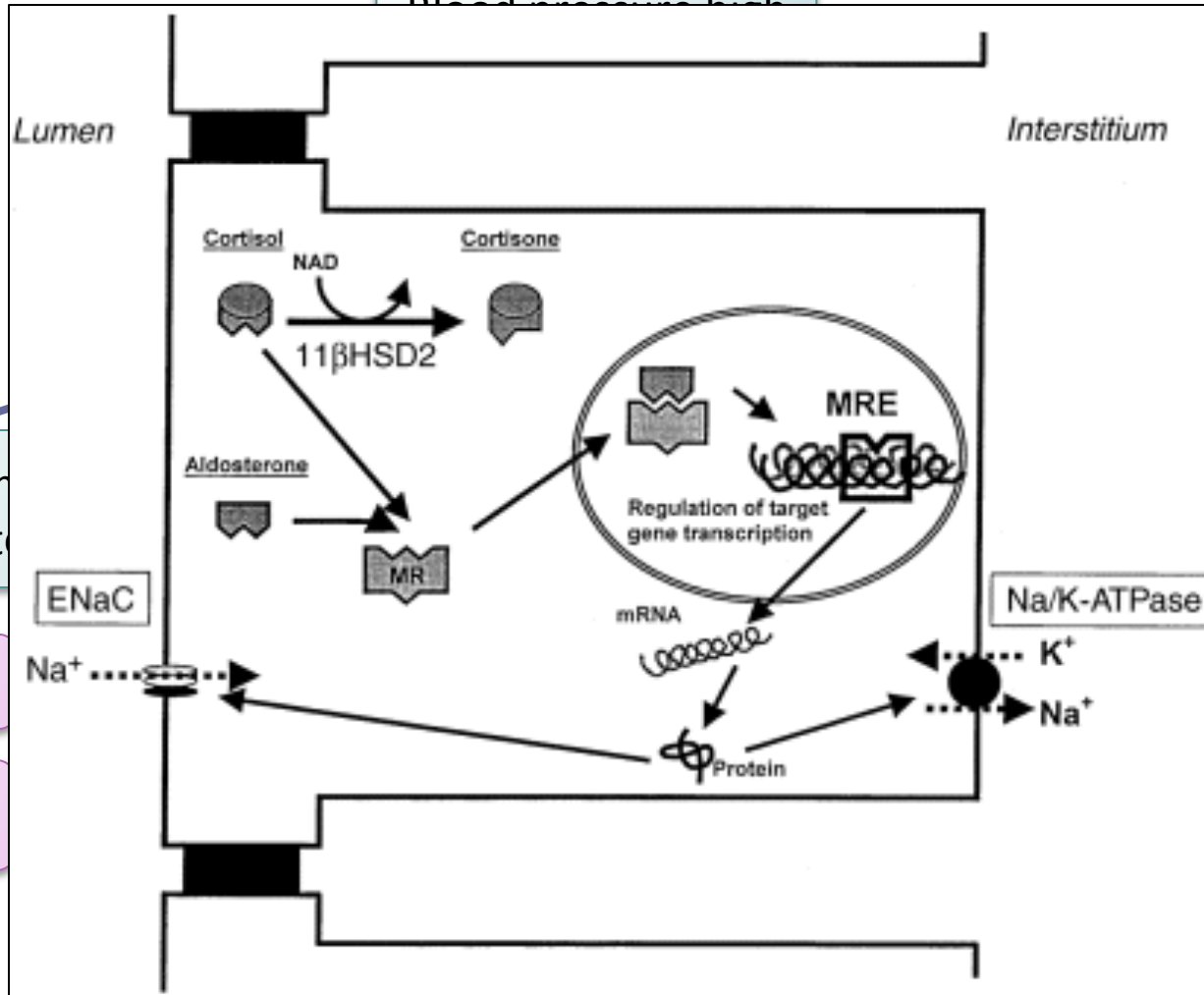
Renal artery stenosis – cont.

- Diagnosis: center dependent
 - Renal artery duplex – only if you have good vascular lab, but gives you some functional results
 - CTA or MRA of the abdomen
- Therapy:
 - FMD - renal artery angioplasty (without stenting)
 - Disease can recur, but typically >5-10 years later
 - Recommended to screen other vascular beds
 - All patients need ASA
 - Atherosclerosis – medical management (CORAL and ASTRAL trials)

Monogenic causes

- Rare, but interesting and demonstrate pathophysiology
- Diseases of distal tubule or collecting duct
- These are often associated with hypokalemia and metabolic alkalosis (mimic primary hyperaldo)
- 3 most common (still rare):
 - Liddle syndrome
 - Apparent mineralocorticoid excess (AME)
 - Glucocorticoid remedial hyperaldosteronism

Evaluation of hypokalemia + metabolic alkalosis...



Blood pressure high

High renin
High aldosterone

Reninoma

Renal artery stenosis

Low renin
High aldosterone

Licorice ingestion

AME

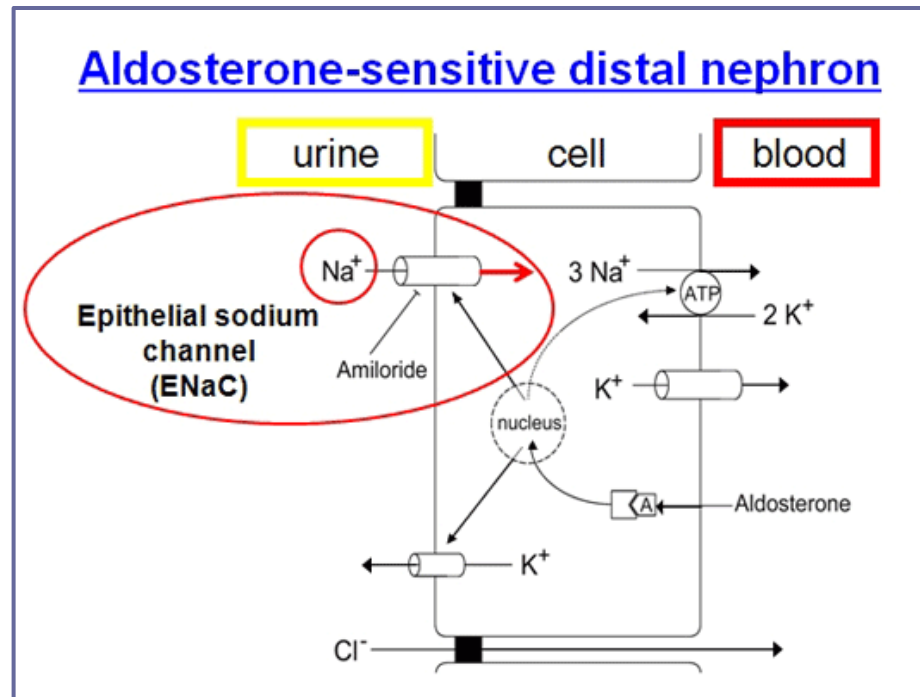
Liddle's syndrome

Back to our patient...

- Aldosterone and renin testing showed:
 - Aldosterone: 4 ng/dL
 - PRA <0.1 ng/mL/hr
- CTA abdomen showed no renal artery stenosis
- Started on HF treatment → carvedilol, Lisinopril, loop diuretic
- Persistent BP >180/100

Liddle syndrome

- Autosomal dominant mutation of the epithelial sodium channel (eNAC)
- Deletions or substitutions cause an inability of these subunits to undergo degradation
- Diagnosis:
 - Aldo and renin are LOW
 - Genetic testing/sequencing
- Treatment: amiloride, start at 5mg daily, up to 15mg daily



Summary & Take home points

1. Hyponatremia and hyponatremia are really disorders of WATER imbalance between fluid compartments
2. Critical challenge in evaluation of hyponatremia is distinguishing low EABV versus SIADH
3. Hypernatremia in a hospitalized patient is nearly always due to inadequate free water administration
4. In inpatients with hypokalemia and hypertension, think about aldosterone

- Acknowledgements:
 - Yoshio Hall, MD, MS
 - Bob Roshanravan, MD, MS

Questions?



A collaboration between
Northwest Kidney Centers and UW Medicine

