ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Parenteral Nutrition Primer:
Balancing Acid-Base, Fluids and Electrolytes

Phil Ayers, PharmD, BCNSP, FASHP
Todd W. Canada, PharmD, BCNSP, FASHP, FTSHP
Michael Kraft, PharmD, BCNSP
Gordon S. Sacks, Pharm.D., BCNSP, FCCP

Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:

- **Phil Ayers -** ASPEN: Board Member/Advisory Panel; B Braun: Consultant; Baxter: Consultant; Fresenius Kabi: Consultant; Janssen: Consultant; Mallinckrodt: Consultant
- **Todd Canada -** Fresenius Kabi: Board Member/Advisory Panel, Consultant, Speaker's Bureau
- **Michael Kraft -** Rockwell Medical: Consultant; Fresenius Kabi: Advisory Board; B. Braun: Advisory Board; Takeda Pharmaceuticals: Speaker’s Bureau (spouse)
- **Gordon Sacks** - Grant Support: Fresenius Kabi

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Sodium Disorders and Fluid Balance

Gordon S. Sacks, Pharm.D., BCNSP

Professor and Department Head
Department of Pharmacy Practice
Harrison School of Pharmacy
Auburn University

Learning Objectives

Upon completion of this session, the learner will be able to:

1. Differentiate between hypovolemic, euvolemic, and hypervolemic hyponatremia
2. Recommend appropriate changes in nutrition support formulations when hyponatremia occurs
3. Identify drug-induced causes of hypo- and hypernatremia


No sodium for you!

Presentation Outline

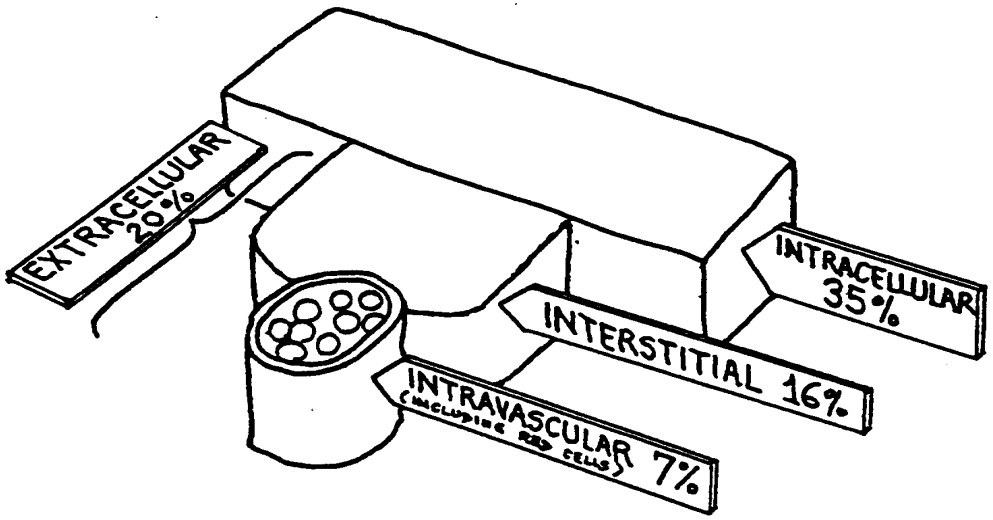
- Overview of sodium and water
- Dehydration vs. Volume Depletion
- Water requirements & Equations
- Hyponatremia
  - Hypotonic
    - Hypovolemic
    - Euvolemic
    - Hypervolemic
- Hypernatremia
  - Hypovolemic
  - Euvolemic
  - Hypervolemic

Sodium and Fluid Balance

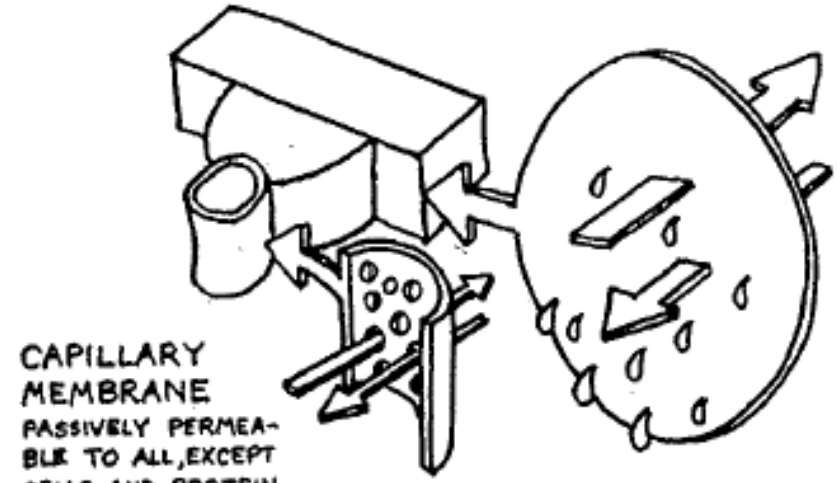
- Helpful hint: total body sodium determines volume status, not sodium status
- Examples of this concept
  - Hypervolemic – too much volume
  - Hypovolemic – too little volume
  - Euvolemic – normal volume

Water Distribution

- Total body water content varies from 50-70% of body weight
  - Dependent on lean body mass: fat ratio
    - Fat water content is ~10% compared to ~75% for muscle mass
- Water is “held” within each compartment primarily by one major solute
  - Sodium & extracellular space
  - Potassium & intracellular space
  - Plasma proteins & intravascular space



FLUID COMPARTMENTS AND THEIR MEMBRANES



CELLULAR MEMBRANE
PASSIVELY PERMEABLE ONLY TO WATER, FOLLOWING OSMOTIC PRESSURE GRADIENTS

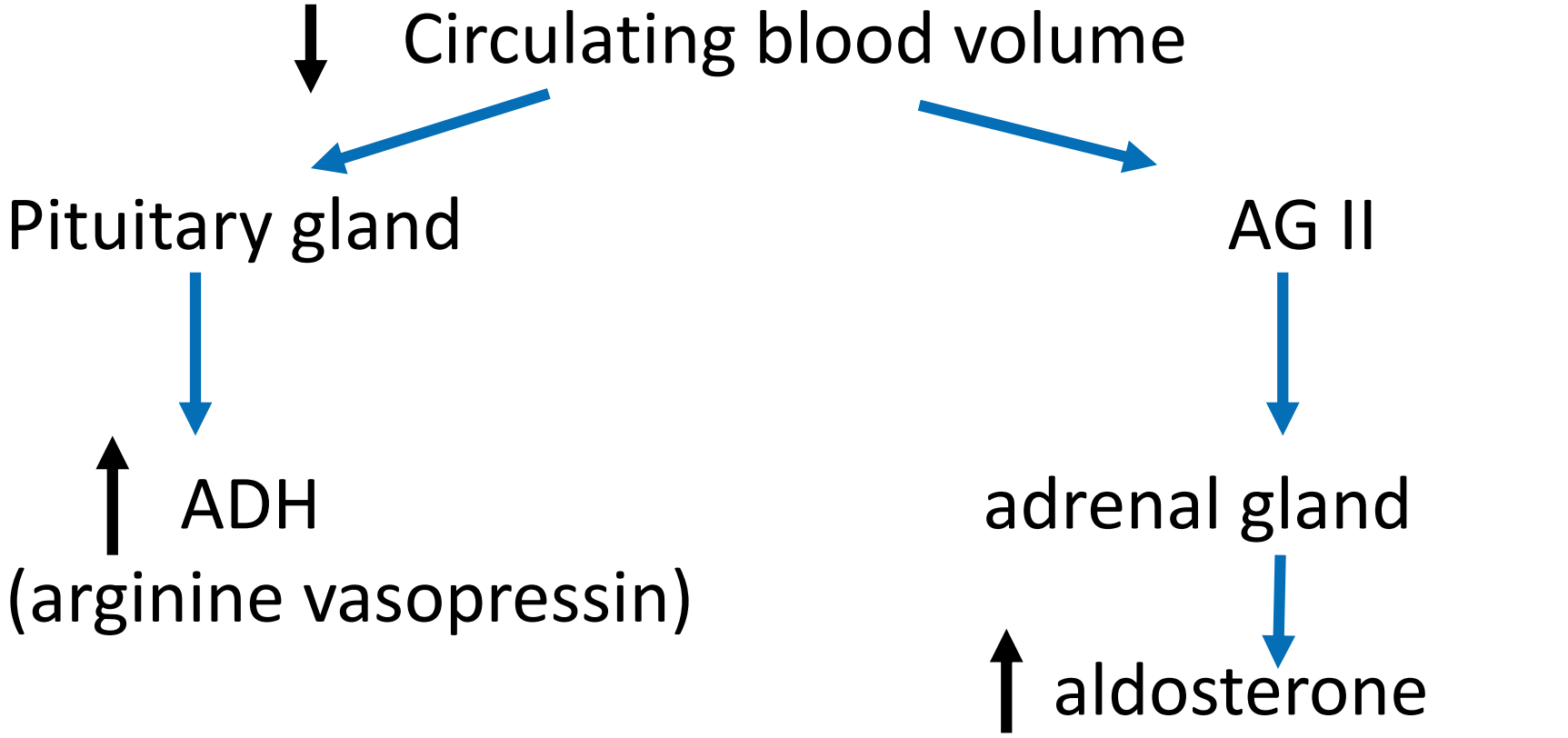
CAPILLARY MEMBRANE
PASSIVELY PERMEABLE TO ALL, EXCEPT CELLS AND PROTEIN, FOLLOWING PRESSURE GRADIENTS

Serum Osmolality

- The number of osmoles (particles) acting to hold fluid within the ECF

- $S_{osm} = (2 \times Na) + \frac{(glucose)}{18} + \frac{(BUN)}{2.8}$

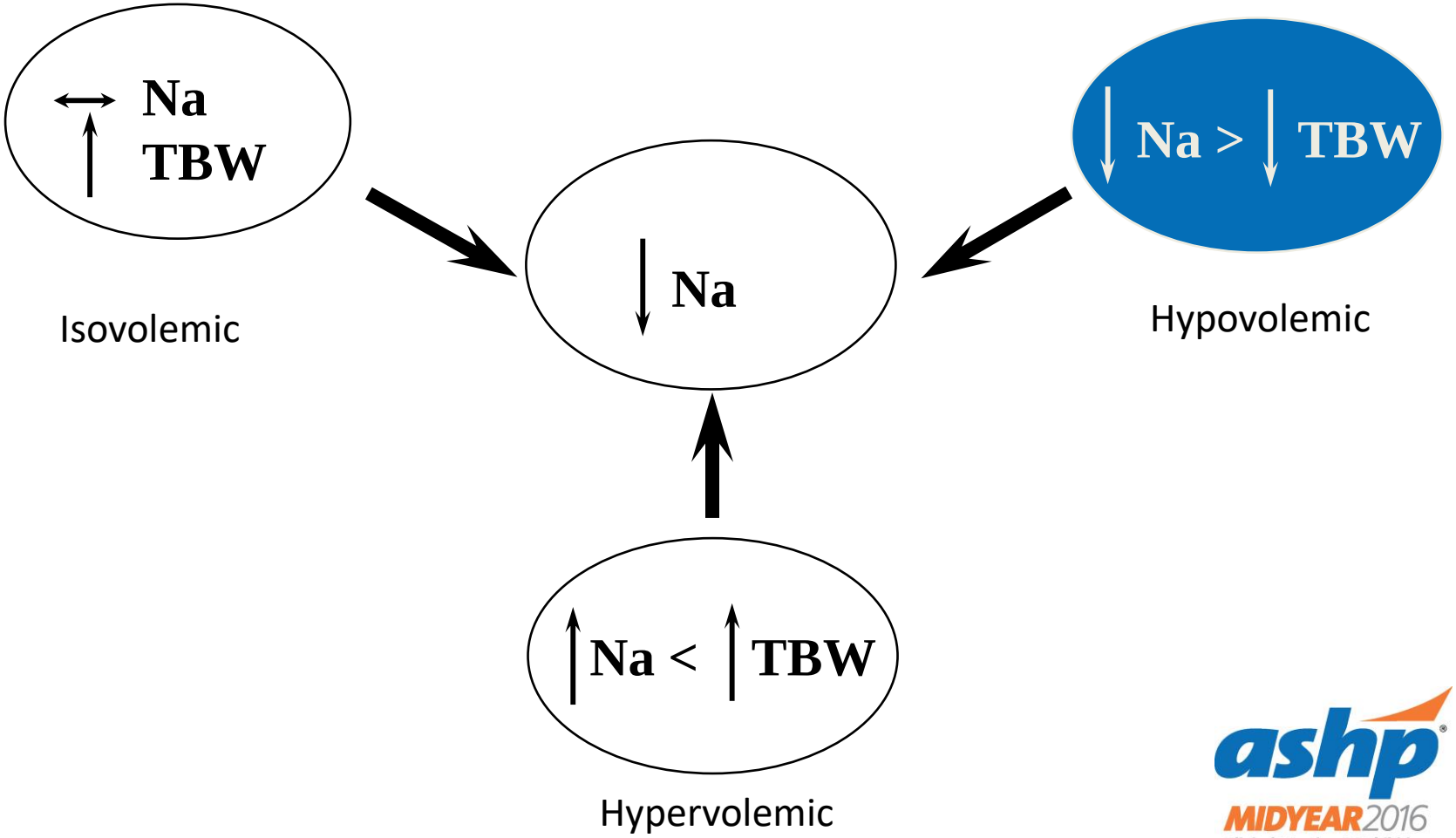
Volume Regulation and Na^+ Metabolism

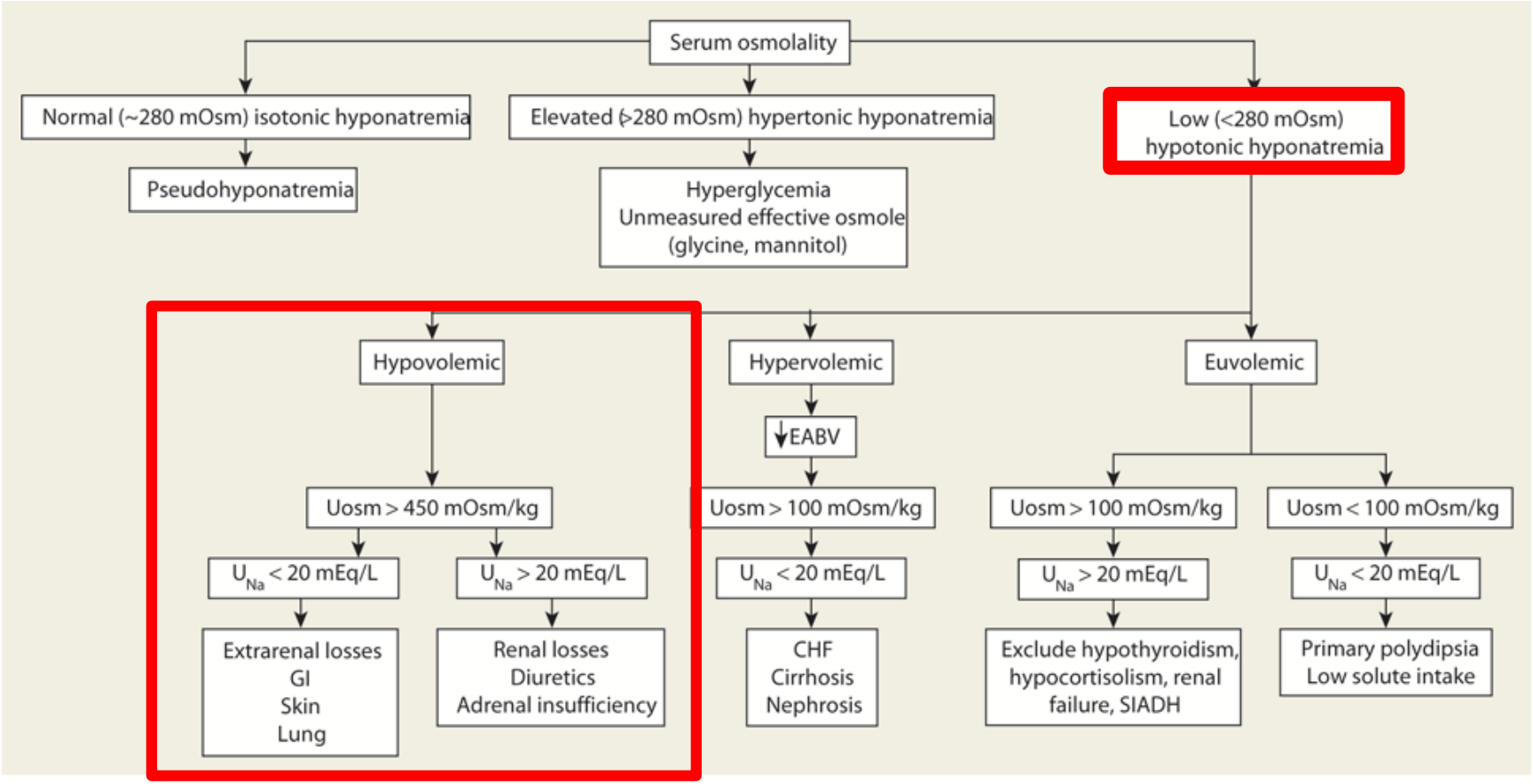


Composition of Gastrointestinal Fluids

	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)
Gastric	60	10	130	--
Small bowel	140	5	100	30
Bile	145	5	100	35
Pancreatic	140	5	75	115
Colon	60	30	40	--

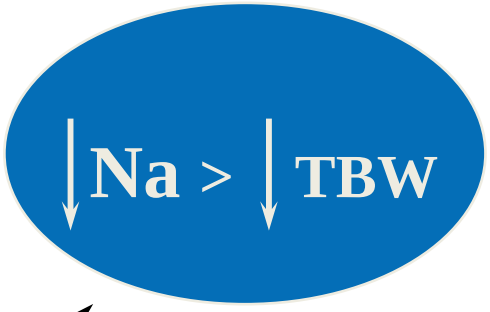
Etiologies of Hypotonic Hyponatremia





Source: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A Pathophysiologic Approach, 8th Edition*: www.accesspharmacy.com

Causes of Hypotonic Hypovolemic Hyponatremia



Extra Renal
GI losses
3rd spacing

Renal
Diuretics
Adrenal ds
Kidney ds

Signs and Symptoms of Hypovolemic Hyponatremia

- Symptoms
  - Lethargy, dizziness, nausea, vomiting
  - Muscle cramps, decreased reflexes
- Signs
  - Flat jugular veins
  - Low blood pressure
  - Tachycardia
  - Poor skin turgor

Management of Volume Depletion

- Volume replacement with 0.9% NaCl in H_2O
  - Hypertonic saline (3% or 5% NaCl) is used for patients having seizures or in a coma due to euvolemic or hypervolemic hyponatremia
    - Severe symptoms: 50-100 mL bolus and/or 1 mL/kg/hr until serum Na has increased by 4-6 mEq/L
    - Mild symptoms: 0.2-0.4 mL/kg/hr
- Stop any diuretics
- Replace water and sodium via PN, EN,IVF, enterostomy, or PO intake to match losses and maintain euvolemia
- Treat underlying cause, such as diarrhea, vomiting

Characteristics of Infusates

Infusate	Na content (mEq/L)
5% NaCl in H_2O	855
3% NaCl in H_2O	513
0.9% NaCl in H_2O	154
Ringer's lactate solution	130
0.45% NaCl in H_2O	77
0.2% NaCl in 5% dextrose	34
5% dextrose	0

Formulas for H_20 & Na Disorders

$$\text{Water Deficit} = \text{Total Body Water (Liters)} \times \left(\frac{\text{Current Serum Sodium (mEq/L)}}{\text{Desired Serum Sodium}} - 1 \right)$$

$$\text{Water Excess} = \text{Total Body Water (Liters)} \times \left(1 - \frac{\text{Current Serum Sodium (mEq/L)}}{\text{Desired Serum Sodium}} \right)$$

$$\text{Sodium Requirement} = \text{Total Body Water} \times (\text{Desired Serum Sodium - Current Serum Sodium (mEq/L)})$$

Change in Serum Na (mEq/L) =

$$\frac{\text{Na (mEq/L) content of infusate} - \text{Current Serum Na (mEq/L)}}{\text{Total Body Water (L)} + 1}$$

Adrogue HJ, et al. **N Engl J Med 2000; 342: 1493-9, 1581-9.**

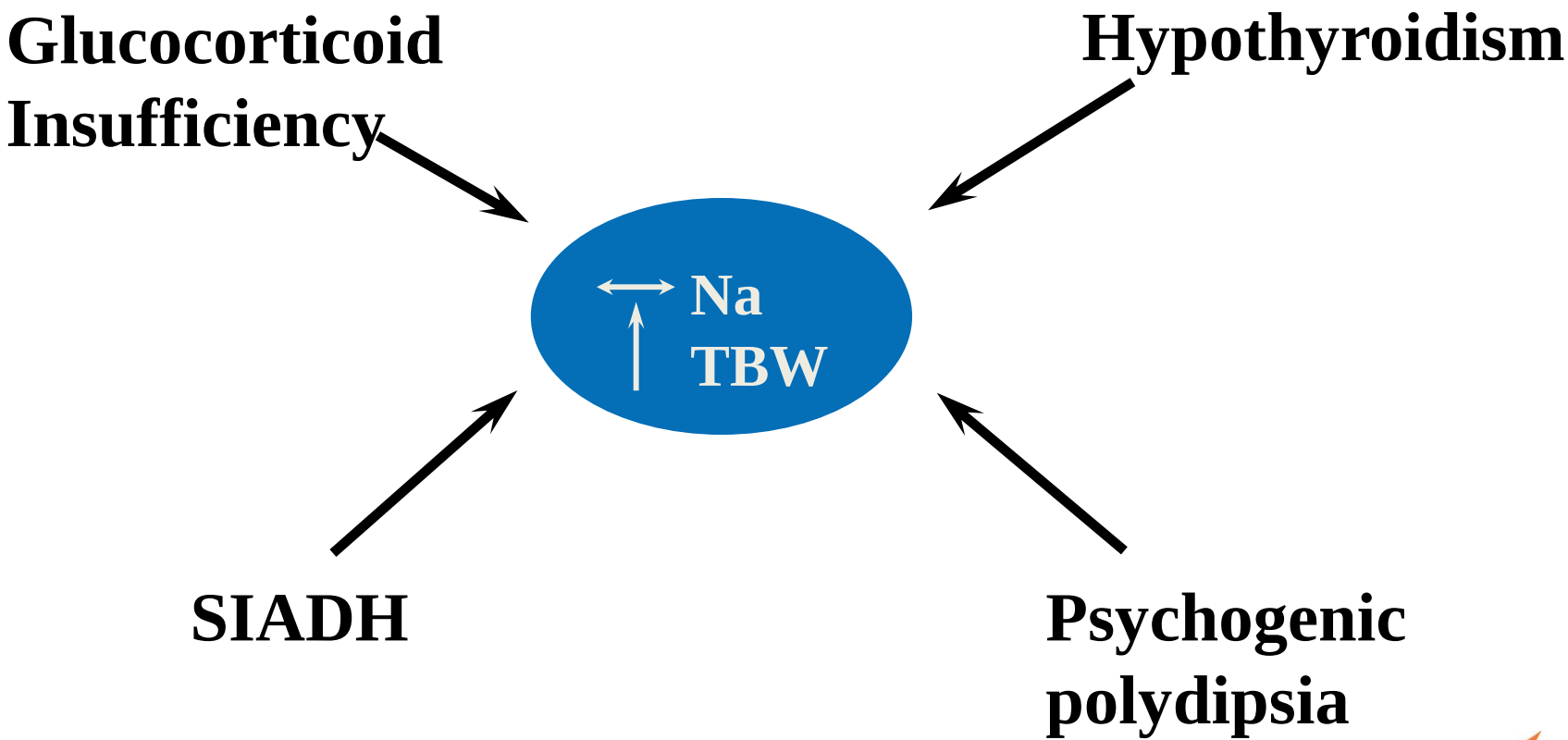
Example Calculation

- 65 yo male (70 kg); Serum Na^+ 128
- Total body water = 0.6 (70 kg) = 42 L
- Change in serum sodium with 0.9% NaCl (NS)
  - (154 mEq/L – 128 mEq/L)/(42L +1) = 0.6 mEq Na^+ per 1L of NS

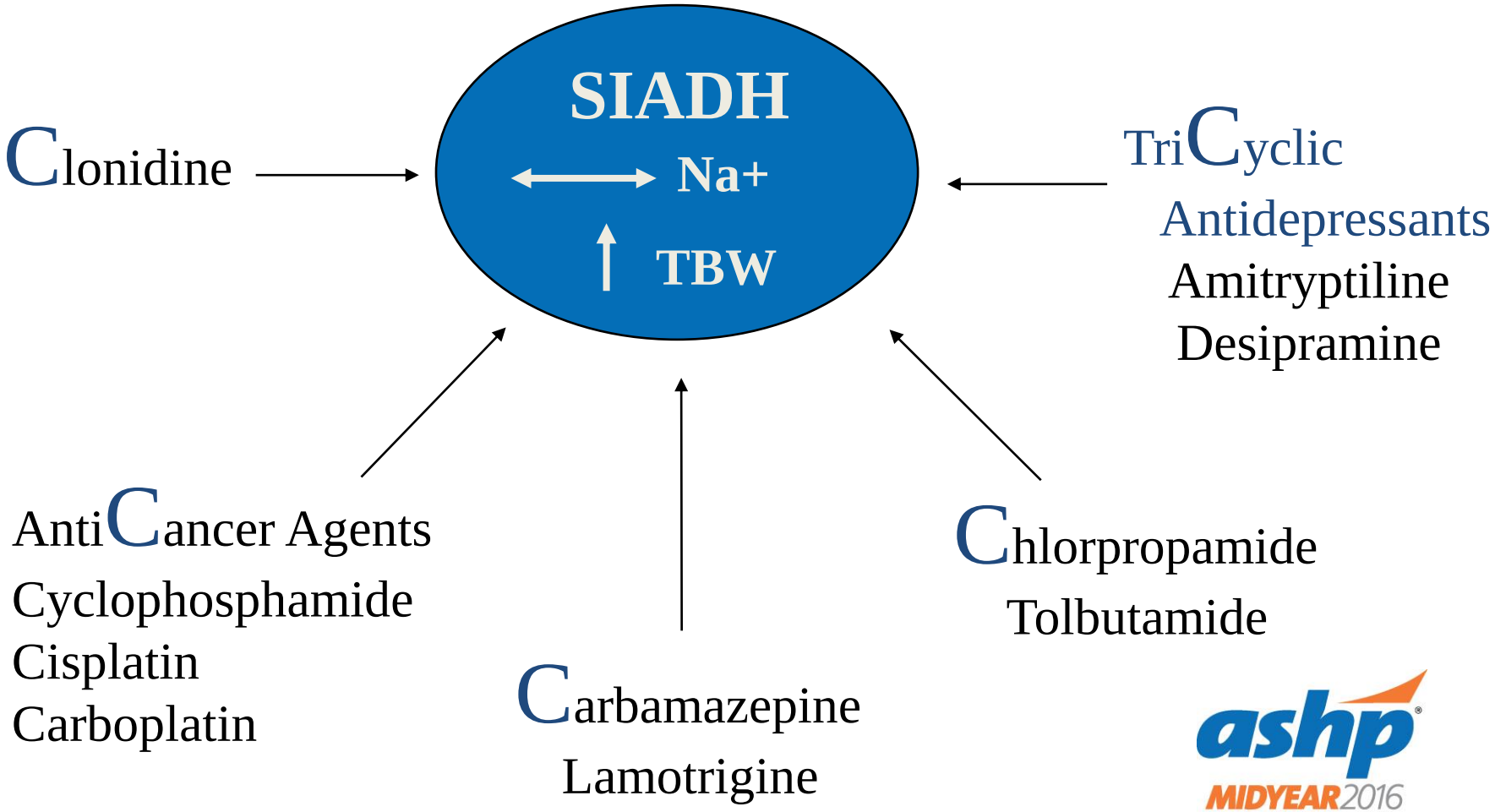
Wesley is an 8-year-old Razorback Musk Turtle from Palatine, IL

Wesley always dreamed of marauding on the high seas, wreaking havoc on unsuspecting boaters...waiting patiently, ready to strike, says Pet Parents Craig and Melanie. Fortunately for us, his dream only comes true once a year on Halloween. The rest of year he is content in fulfilling his role as a peaceful turtle.

Causes of Hypotonic Euvolemic Hyponatremia



Drug-induced Hyponatremia



Signs and Symptoms of SIADH

Signs	Laboratory Indices	
Normal BP	↑	Urine Na
No edema	↑	Urine Osmolality (> 100 mOsm/kg)
No orthostasis	↓	Serum Na
No tachycardia	↓	Serum Osmolality (< 275 mOsm/kg)

Self-Assessment Questions

1. Which of the following medications has been associated with causing SIADH?
   a. Phenytoin
   b. Lithium
   c. Carbamazepine
   d. Amphotericin B

Treatment of Symptomatic Acute Hyponatremia

- Fluid Restriction Strategies
  - Restrict all intake that is consumed by drinking, not just water
  - Aim for a fluid restriction that is 500 mL below the 24-hr urine volume
  - Do not restrict sodium or protein intake
- For severe symptoms
  - 100 mL of 3% NaCl infused over 10 min x 3 as needed
- For mild to moderate symptoms with a low risk of herniation
  - 3% NaCl infused at 0.5 mL/kg/hr
  - avoid correction by more than 12 mEq/L/day
  - Rule of 6's: "6 a day makes sense for safety"

Verbalis et al. Am J Med 2013;126:S1-S42.

Osmotic Demyelination Syndrome (ODS)

- Patients at High Risk for ODS
  - Serum Na ≤ 105 mmol/L
  - Hypokalemia
  - Alcoholism
  - Undernutrition
  - Advance liver disease
- Tips for Avoiding ODS
  - Lower goal of correction for serum Na by 4-6 mmol/L/day with high risk of ODS
  - Do not exceed 8 mmol/L within any 24-hour period

Sterns RH. NEJM 2015;372:55-65.

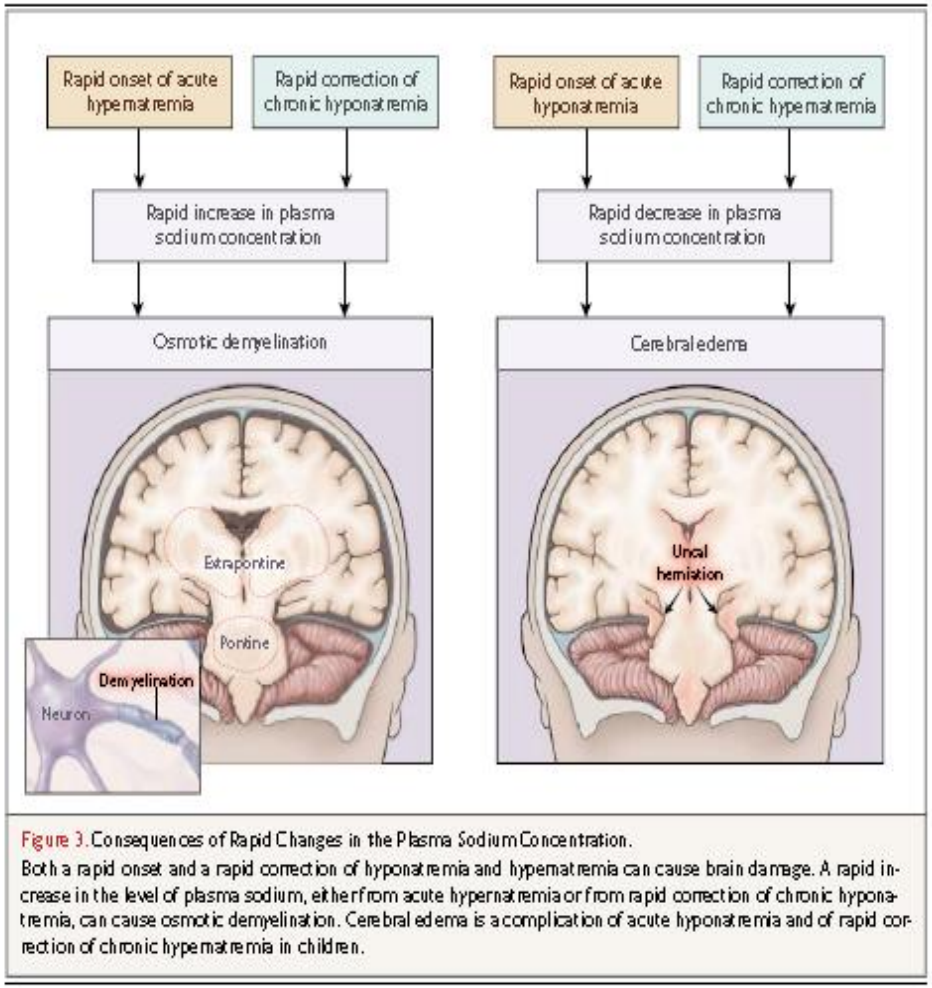
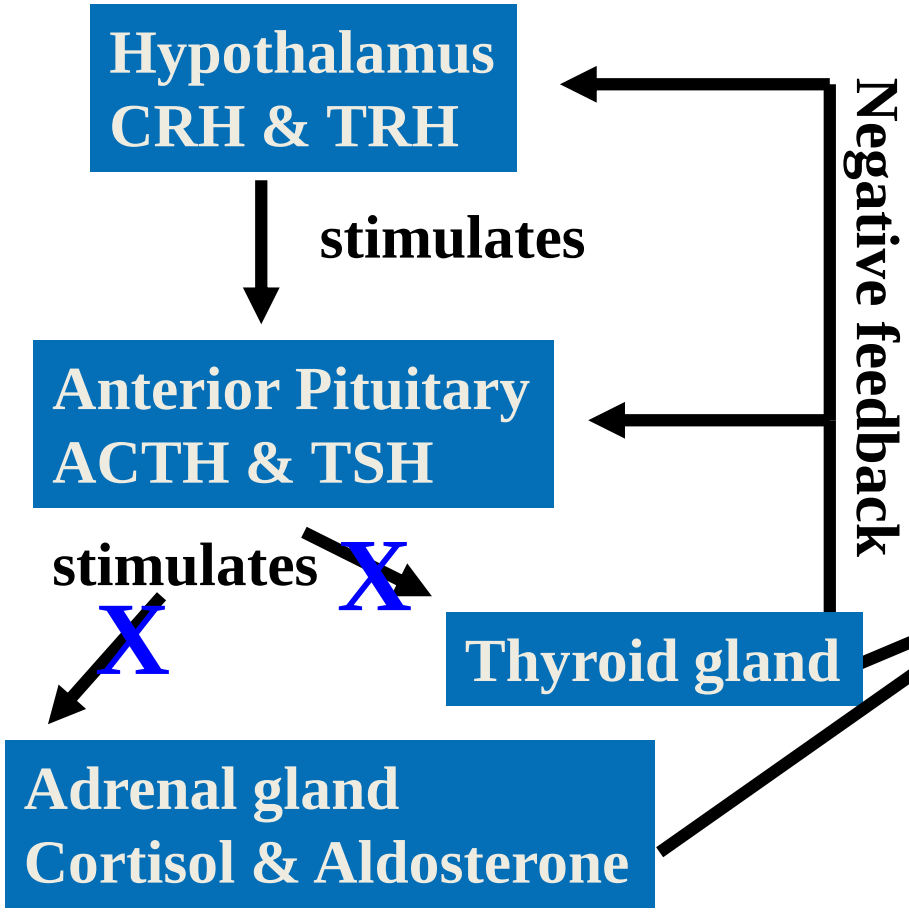


Figure 3. Consequences of Rapid Changes in the Plasma Sodium Concentration.
Both a rapid onset and a rapid correction of hyponatremia and hypernatremia can cause brain damage. A rapid increase in the level of plasma sodium, either from acute hypernatremia or from rapid correction of chronic hyponatremia, can cause osmotic demyelination. Cerebral edema is a complication of acute hyponatremia and of rapid correction of chronic hypernatremia in children.

Verbalis et al. Am J Med 2013;126:S1-S42.

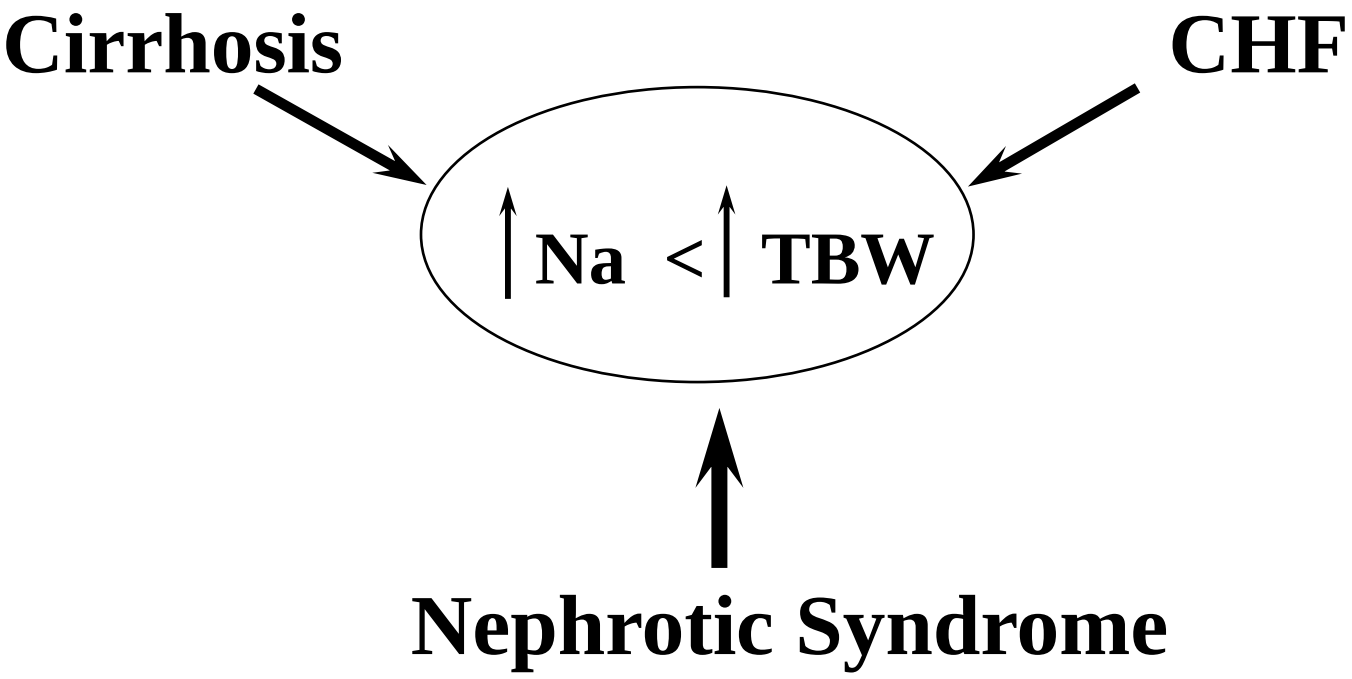
Hyponatremia, Hypothyroidism, & Adrenal Insufficiency

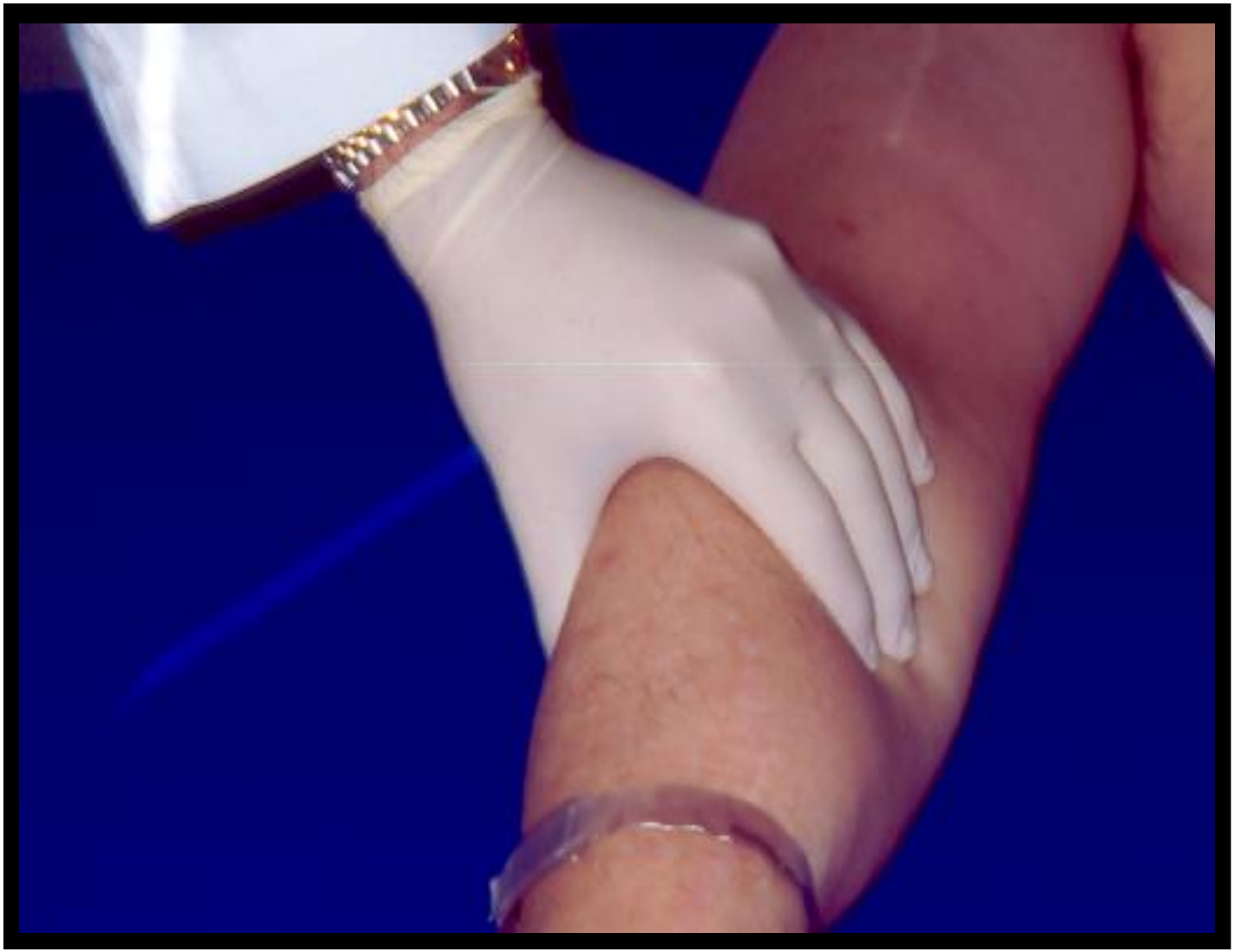


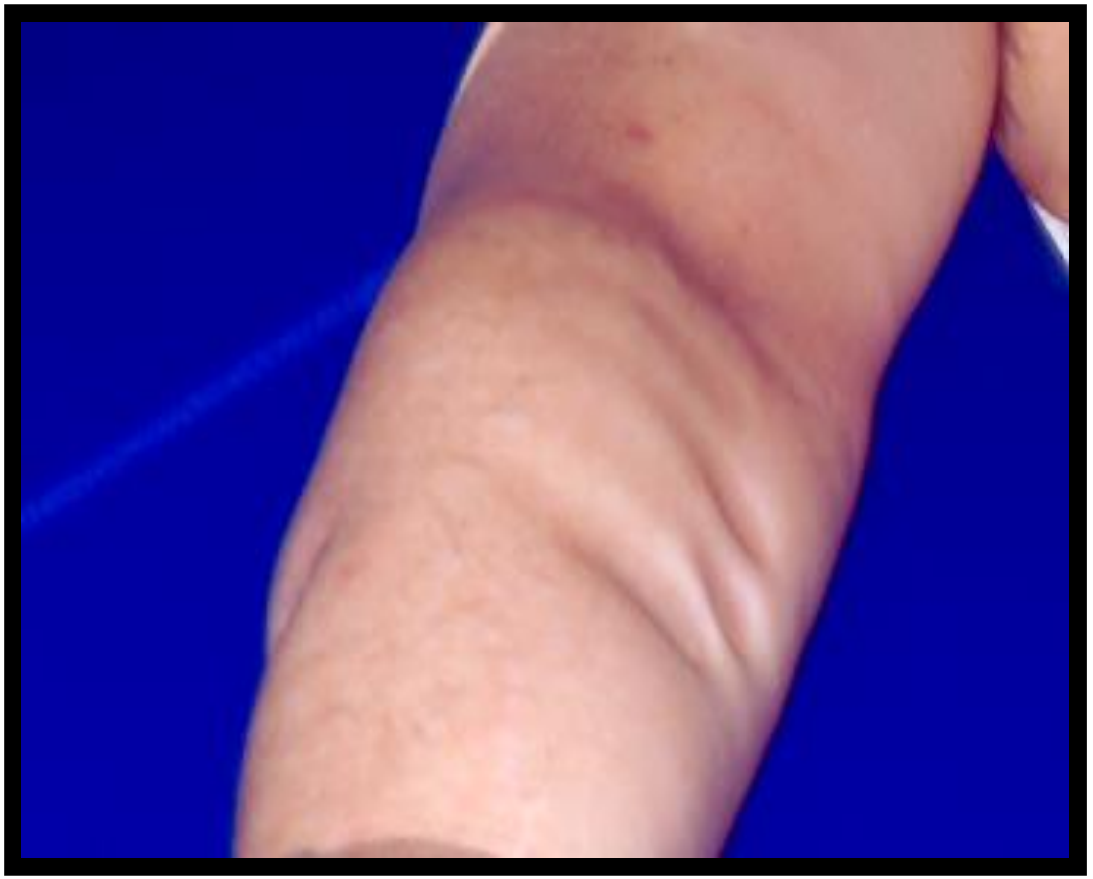
Inability to reabsorb Na/H_2O
Impaired renal free H_2O excretion

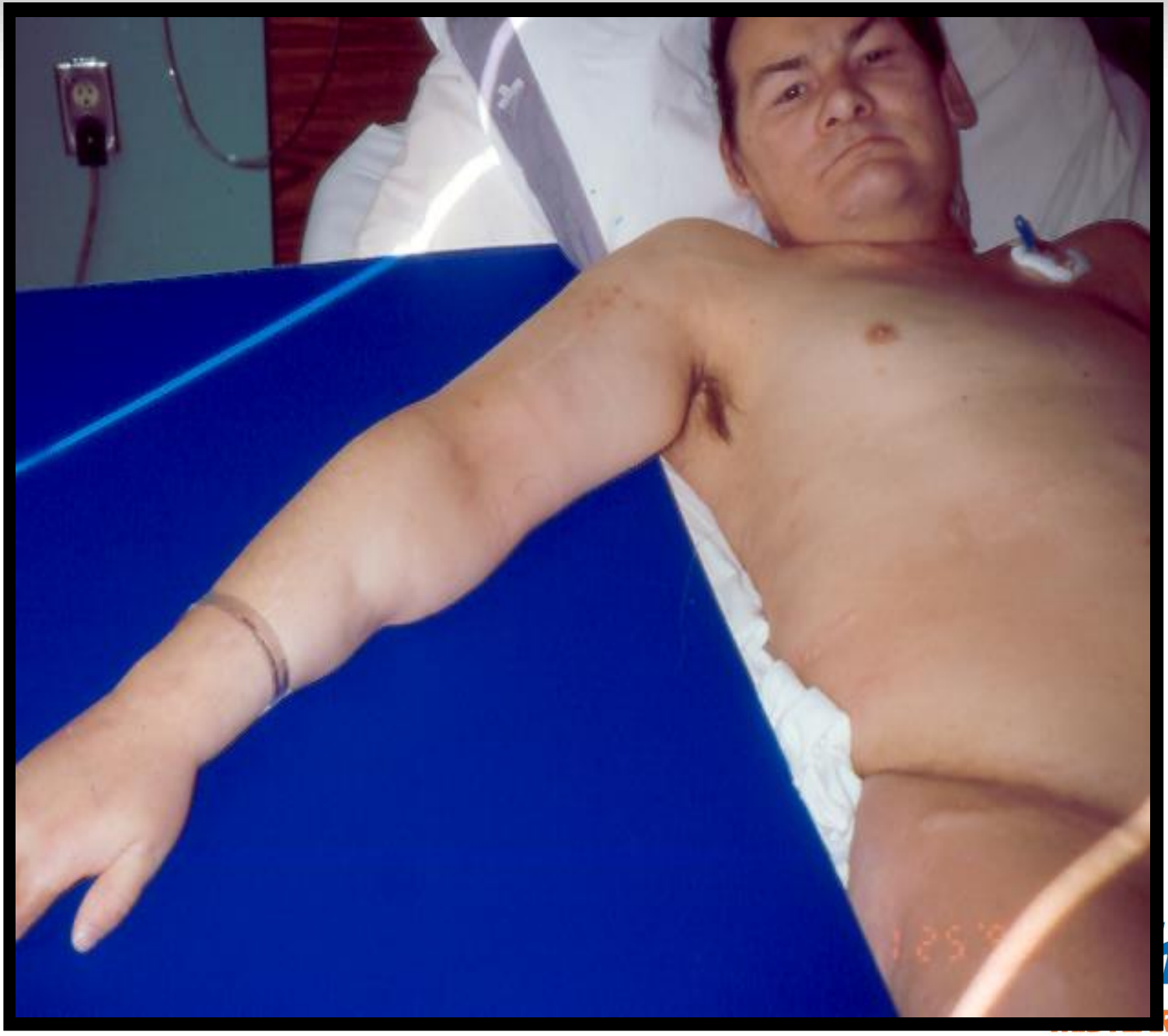
Check Cortisol, ACTH, and TFT's to address low $Na+$

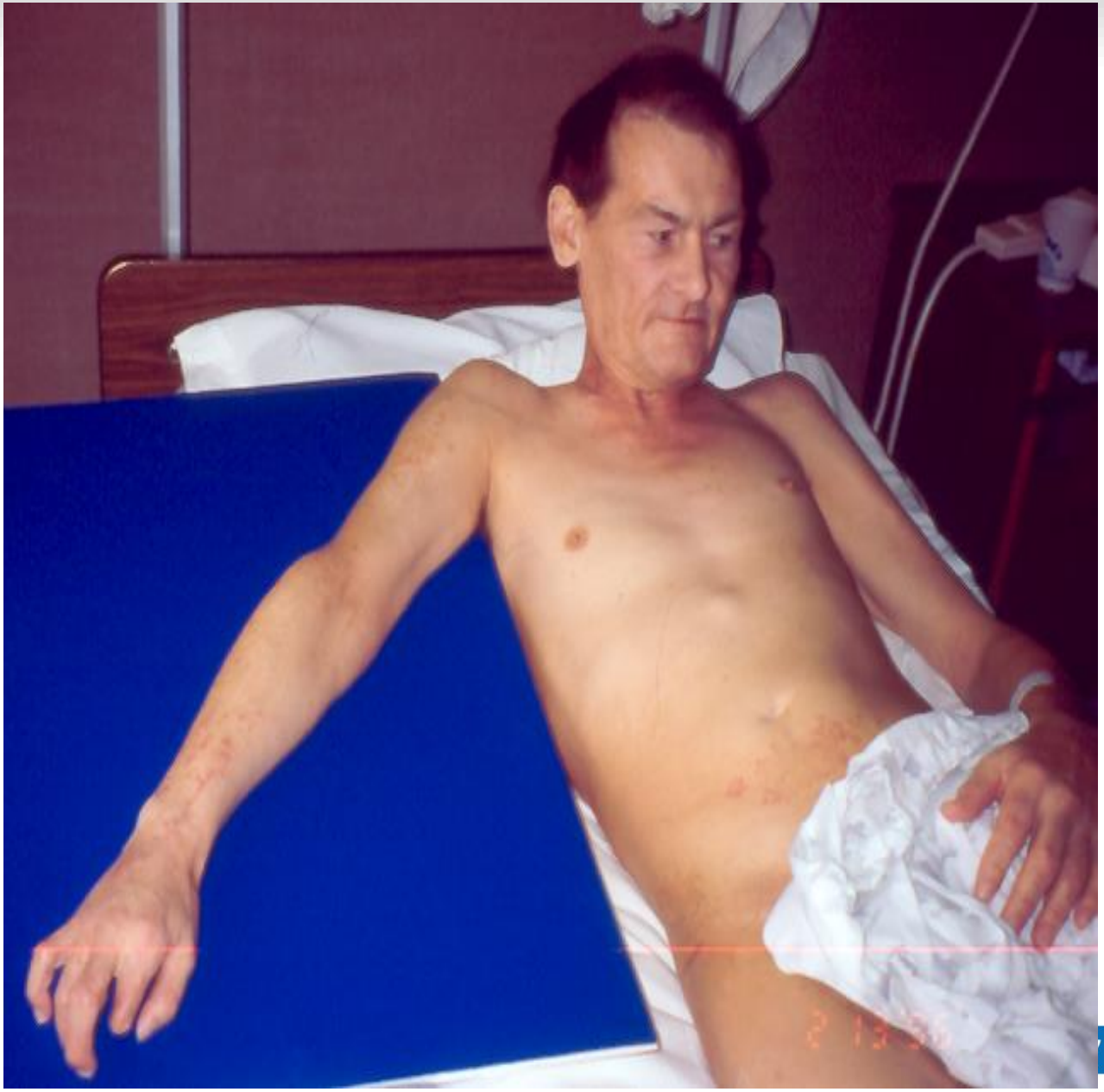
Causes of Hypotonic Hypervolemic Hyponatremia







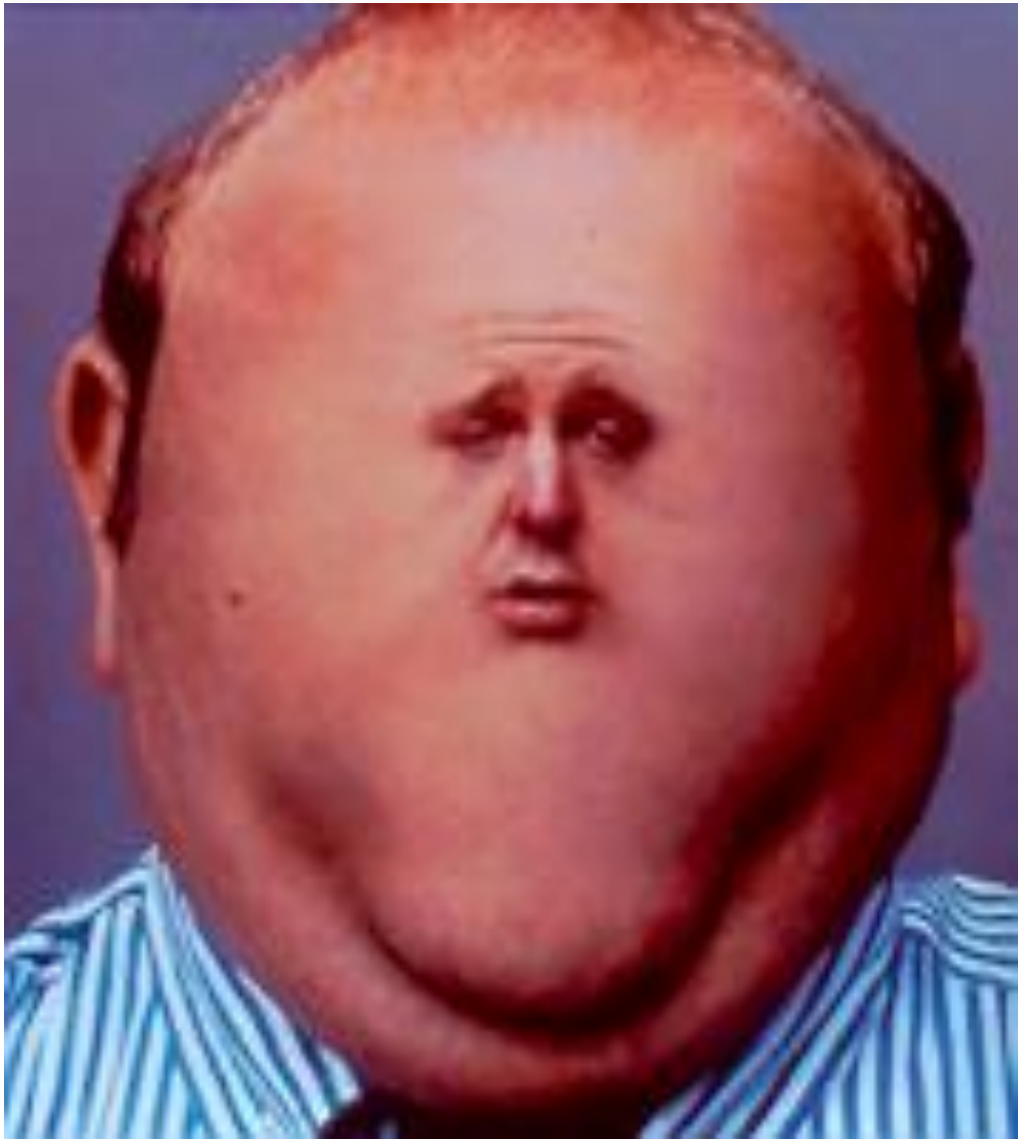




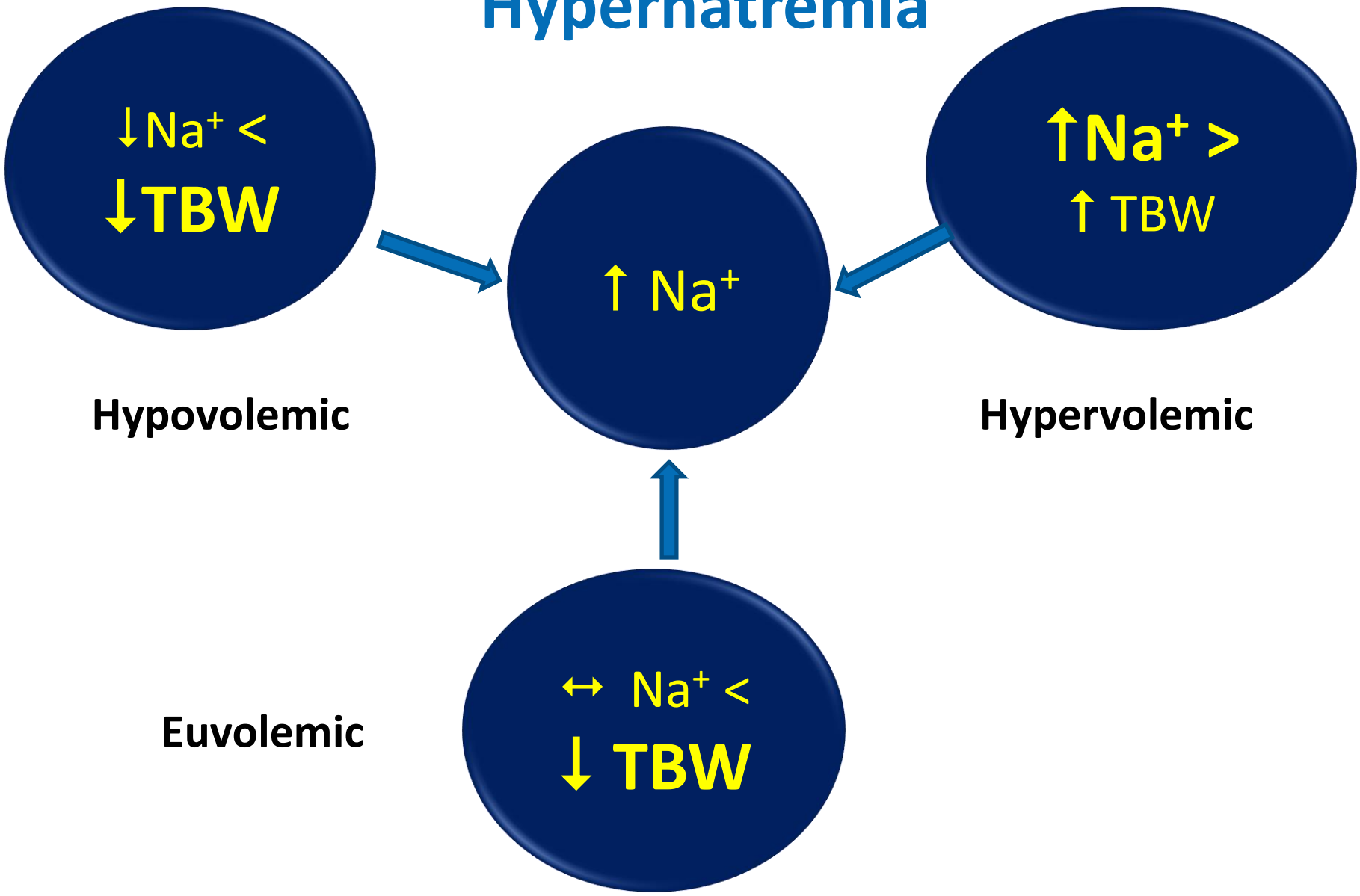
Hypotonic Hypervolemic Hyponatremia - Treatment

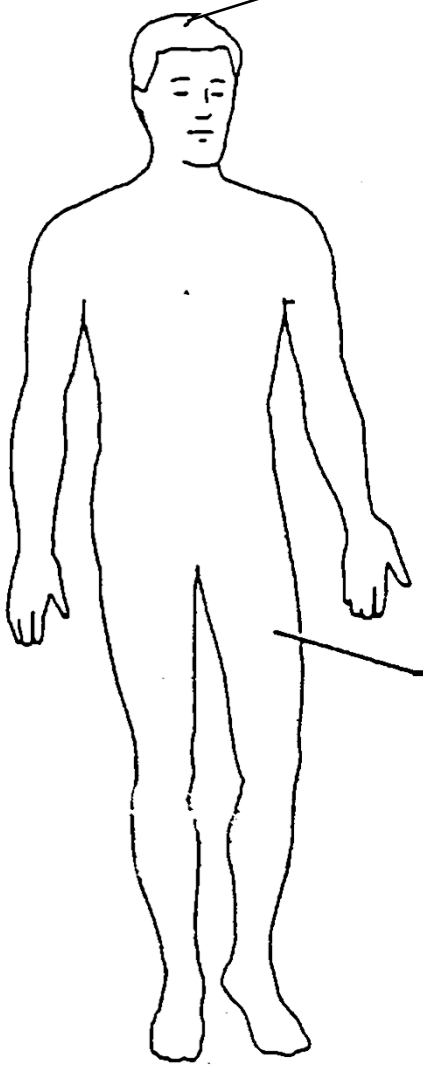
- Reduce fluid intake (begin with restriction of 1 L/day)
- Eliminate sodium intake (PN and IVF)
- May require diuretic therapy (with loop diuretics) combined with 3% NaCl if patient is severely symptomatic
- If fluid restriction unsuccessful, start either conivaptan or tolvaptan and discontinue restriction
- For tolvaptan, it may be titrated up from 15 to 30 to 60 mg/day as necessary to achieve desired Na correction
- Follow serum concentrations of sodium carefully; continue therapy until serum Na has normalized, symptoms improve, or when serum Na is no longer preventing use of diuretic therapy

Verbalis JG et al. Am J Med 2013;126:S1-S42.



Hypernatremia



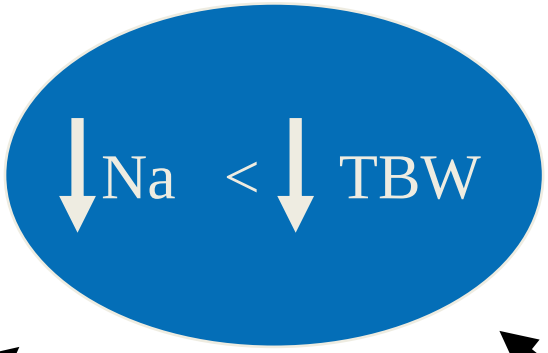


Central Nervous System
Mild: restlessness, lethargy, headache
Moderate: disorientation, confusion
Severe: stupor, coma, seizures

Increased muscle tone
Increased deep tendon reflexes

Signs and symptoms of hypernatremia

Causes of Hypernatremia



Hypovolemic

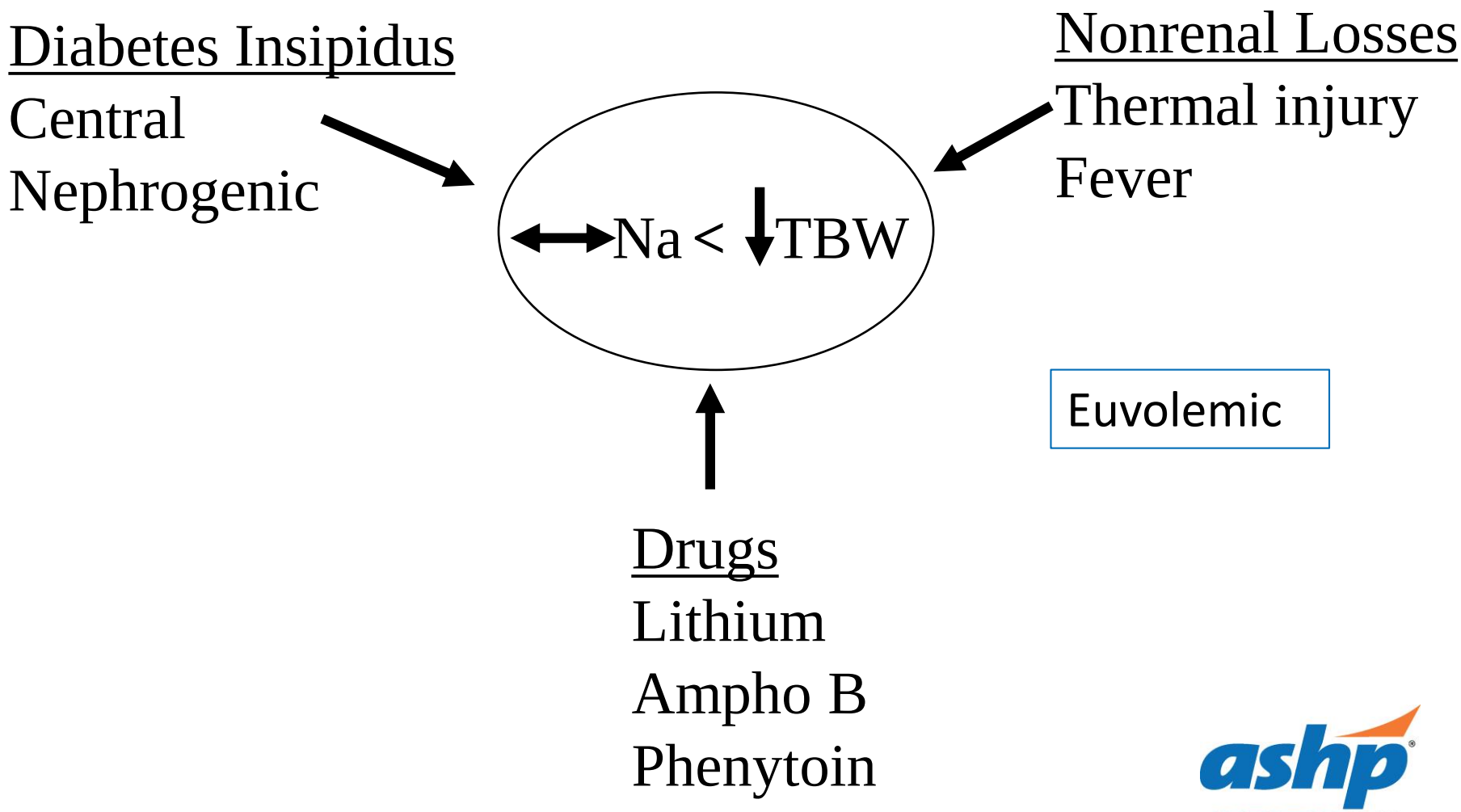
Loss of hypotonic fluids

<u>Drugs</u>
Diuretics
Laxatives

Hypovolemic Hypernatremia Treatment

- Initially, patients need salt and water replacement to perfuse vital organs (NS is usually treatment of choice initially)
- Once volume status has been corrected, hypotonic solutions are appropriate (D5W, ½ NS, ¼ NS)

Causes of Hypernatremia



Euvolemic Hypernatremia

- Caused by loss of primarily free water (thermal injury, fever, diabetes insipidus)
- Hypotonic fluids are the treatment of choice
  - IV – D5W, ½ NS, ¼ NS
  - PO/ Tube – water
- Delete sodium in PN temporarily
- Add water boluses to EN

Euvolemic Hypernatremia – diabetes insipidus

- Central DI
  - Absolute deficiency in ADH
  - Often associated with neurosurgery/ head trauma
  - Replacement is the cornerstone of treatment
- Nephrogenic DI
  - Impaired response to ADH at the nephron/ collecting duct
  - Genetic causes and drug-induced causes
  - Lithium treatment is the #1 cause of acquired nephrogenic DI

Euvolemic Hypernatremia – diabetes insipidus

- Treatment of central DI
  - Nasal or oral desmopressin for chronic care
  - Nasal desmopressin 10 mcg daily (titrate to 10 mcg BID is common)
  - Intravenous desmopressin can be used in acute care (ICU) – 1 mcg IV

Euvolemic Hypernatremia – diabetes insipidus

- Treatment for nephrogenic DI
  - Sodium restriction
  - Thiazide diuretics (paradoxical treatment)
  - Amiloride is effective for lithium-induced nephrogenic DI
  - Induce a mild state of hypovolemia which stimulates proximal tubule reabsorption of water

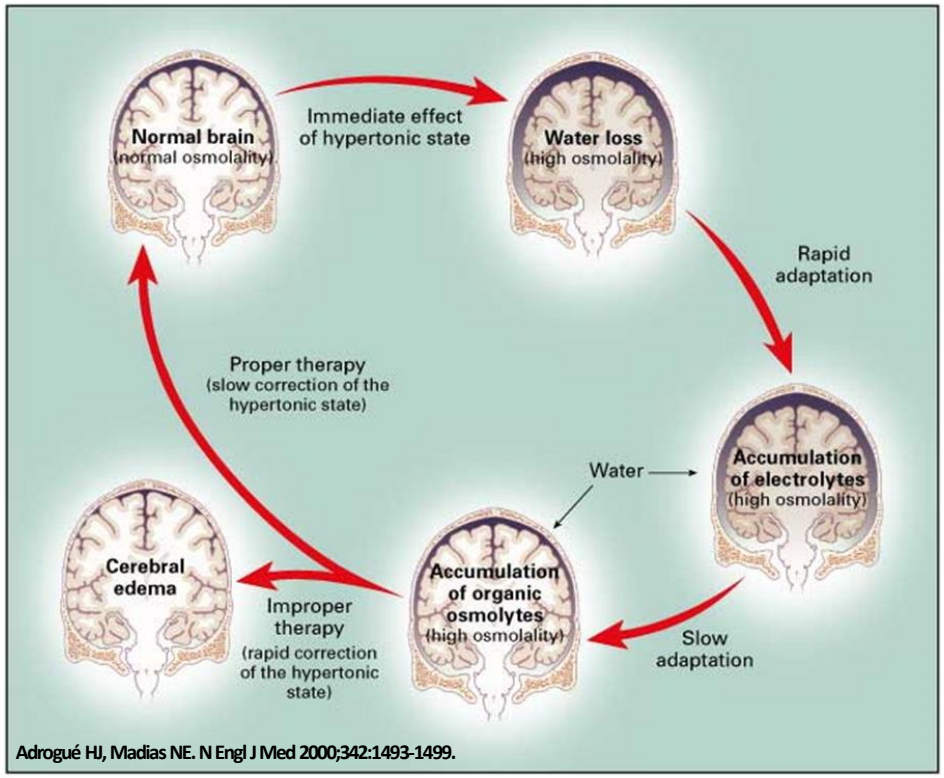
Hypervolemic Hypernatremia

- ↑ Na > ↑ TBW
- Caused by an excess of both water and sodium; however, sodium excesses are greater
- This is usually iatrogenic (i.e., too much NS)
- Minimize fluid/ eliminate sodium/ diuretics
- Concentrate PN formulation – eliminate Na
- Concentrate EN formulation (e.g. 2 kcal/mL formula)

Cautions with Management

- Correction of HYPERnatremia should aim to reduce the serum Na at a maximal rate of 0.5 mEq/liter/hr to prevent cerebral edema and convulsions
- A targeted fall in the serum Na of 6 mmol/liter/day should be the goal, until the Na < 145 mEq/liter
- 0.9% NaCl should only be used in cases of frank circulatory compromise

Cerebral Edema



Adrogué HJ, Madias NE. N Engl J Med 2000;342:1493-1499.

Free H_2O for Hypernatremia

- "Free H_2O" is often ordered for treatment
- "Free H_2O" refers to water not associated with organic or inorganic ions
- H_2O can be replaced orally, however it should NEVER be given IV as "Sterile H_2O for Injection"
- 5% Dextrose in H_2O is appropriate choice for "Free H_2O" given IV

Sodium and Fluid Balance Conclusions

- Disorders of sodium and water balance are common in patients
- The nutrition support formulation is often the major component of fluid intake
- Proper diagnosis of a sodium disorder requires an accurate assessment of volume status
- An effective clinician must be well grounded in disorders of sodium and water

Self-Assessment Questions

2. Which one of the following intravenous fluids would be most appropriate for INITIAL therapy in a patient with hypovolemic hypernatremia and hypotension?
   a. D5W
   b. ¼ NS
   c. D5 ½ NS
   d. NS

Answers to Self-Assessment Questions

1. Answer = c; carbamazepine is associated with inappropriate release of ADH. Phenytoin, lithium, and amphotericin B are associated with diabetes insipidus and hypernatremia
2. Answer = d; The first priority in a dehydrated state is to perfuse the vital organs. This is accomplished most effectively by giving an IVF that will stay in the intravascular space, i.e., NS would be given first in this situation.

References

- Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 2013;126:S1-S42.
- Sterns RH. Disorders of plasma sodium – causes, consequences, and correction. N Engl J Med 2015;372:55-65.
- Palmer BF, Gates JR, Lader M Causes and management of hyponatremia. Ann Pharmacother 2003;37:1694-702.
- Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med 2000;342:1581-9
- Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: Evaluating the correction factor for hyperglycemia. Am J Med 1999;106:399-403.
- Harrigan MR. Cerebral salt wasting syndrome. Crit Care Clin 2001;17:125-38.
- Singh S, Bohn D, Carlotti AP, et al. Cerebral salt wasting: Truths, fallacies, theories, and challenges. Crit Care Med 2002;30:2575-9.

References

- Sterns RH, Hix JK, Silver SM. Management of hyponatremia in the ICU. Chest 2013;144(2):672-679.
- Musch W, Decaux G. Treating the syndrome of inappropriate ADH secretion with isotonic saline. Q J Med 1998;91:749-53.
- Dickerson RN, Brown RO. Long-term enteral nutrition support and the risk of dehydration. Nutr Clin Prac 2005;20:646-53.
- Ghali JK, Koren MJ, Taylor JR, et al. Efficacy and safety of oral conivaptan: A V1a/V2 vasopressin receptor antagonist, assessed in a randomized, placebo-controlled trial in patients with euvolemic or hypervolemic hyponatremia. J Clin Endocrinol Metab 2006;91:2145-52.
- Udelson JE, Smith WB, Hendrix GH, et al. Acute hemodynamic effects of conivaptan, a dual V1a and V2 vasopressin receptor antagnonist, in patients with advanced heart failure. Circulation 2001;104:2417-23.
- Adrogue HJ, Madias NE. Hypernatremia. N Engl J Med 2000;342:1493-9.

References

- Lobo DN, Bjarnason K, Field J, et al. Changes in weight, fluid balance and serum albumin in patients referred for nutritional support. Clin Nutr 1999;18:197-201.
- Xiao H, Barber J, Campbell ES. Econoic burden of dehydration among hospitalized elderly patients. Am J Health-Syst Pharm 2004;61:2534-40.
- Oh H, Seo W. Age differences in fluid balance and serum Na+ and K+ levels after nasogastric tube feeding in stroke patients: Elderly vs Non-elderly. J Parenteral Enteral Nutr 2006;30:321-30.
- Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guidelines on diagnosis and treatment of hyponatremia. Nephol Dial Transplant 2014;29(Suppl 2):ii1-ii39.

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Parenteral Nutrition Management – Focus on Potassium & Magnesium

Todd W. Canada, PharmD, BCNSP, FASHP, FTSHP
University of Texas MD Anderson Cancer Center
Houston, Texas

Disclosure

- **Fresenius Kabi**
  - Advisory Board
  - Consultant
  - Speakers Bureau
- **I hate electrolyte abnormalities**

Objective

- Describe the importance of potassium and magnesium and provide key management strategies in patients receiving nutrition support

Patient Case

- 35-year-old Caucasian male with ulcerative colitis and recurrent seminoma admitted for salvage chemotherapy with paclitaxel, ifosfamide and cisplatin, now with typhilitis on hospital day 8
  - Pale, ill appearing male with distended abdomen, nasogastric tube draining ~ 2 L/day, loose BM x 3
  - Labs

130	100	16	75
3	19	0.38	

	9	
0.1		18
	26.3	

Ion Ca 1.13 / Phos 1.9 / Mg 1.5

Room Air 7.46 / 27 / 97 / 19 / BE -4

TBili: 1.3
Alk Phos: 95
AST / ALT: 26 / 15
Alb: 2.3
Triglycerides: 99

  - Weight 60 kg, Height 66 inches
    - Ideal body weight 63.8 kg (94% of IBW)

Patient Case

- Medications
  - Acyclovir 400 mg IV q12h
  - Caspofungin 50 mg IV q24h
  - Cefepime 2 g IV q8h
  - Hydrocortisone 50 mg IV q8h
  - Pantoprazole 40 mg IV q24h
  - Hydromorphone PCA 0.2 mg q8min
- IV Fluids
  - 0.9% NaCl at 75 mL/hr

1. Which is the most appropriate assessment of hypokalemia prior to initiating PN?

A. Mild with uncompensated respiratory alkalosis

B. Moderate with compensated metabolic acidosis

C. Severe with uncompensated respiratory alkalosis

D. Moderate with uncompensated respiratory acidosis

Answer = A

What Constitutes Serious K^+ & Mg^{++} Abnormalities?

Decreased	Serum Electrolyte	Elevated
< 3.5 mEq / L	Potassium	> 5.5 mEq / L
< 1.2 mg / dL*	Magnesium	> 4.8 mg / dL

* To convert Magnesium to mEq/L, multiply above numbers by 0.833

Decreased	Serum Electrolyte	Elevated
< 3.5 mEq / L	Potassium	> 5.5 mEq / L
< 15 mEq/L	CO_2 Content*	> 40 mEq/L

Definitions of K^+ Abnormalities

Definition	Serum K^+ (mEq/L = mmol/L)	Intensive Care Unit Prevalence in 1st week
Severe Hypokalemia	< 3	3.3 – 4%
Mild Hypokalemia	3 – 3.4	18.2 – 20.2%
Normokalemia	3.5 – 5	
Mild Hyperkalemia	5.1 – 6	16.2 – 17%
Severe Hyperkalemia	> 6	3.6 – 4%

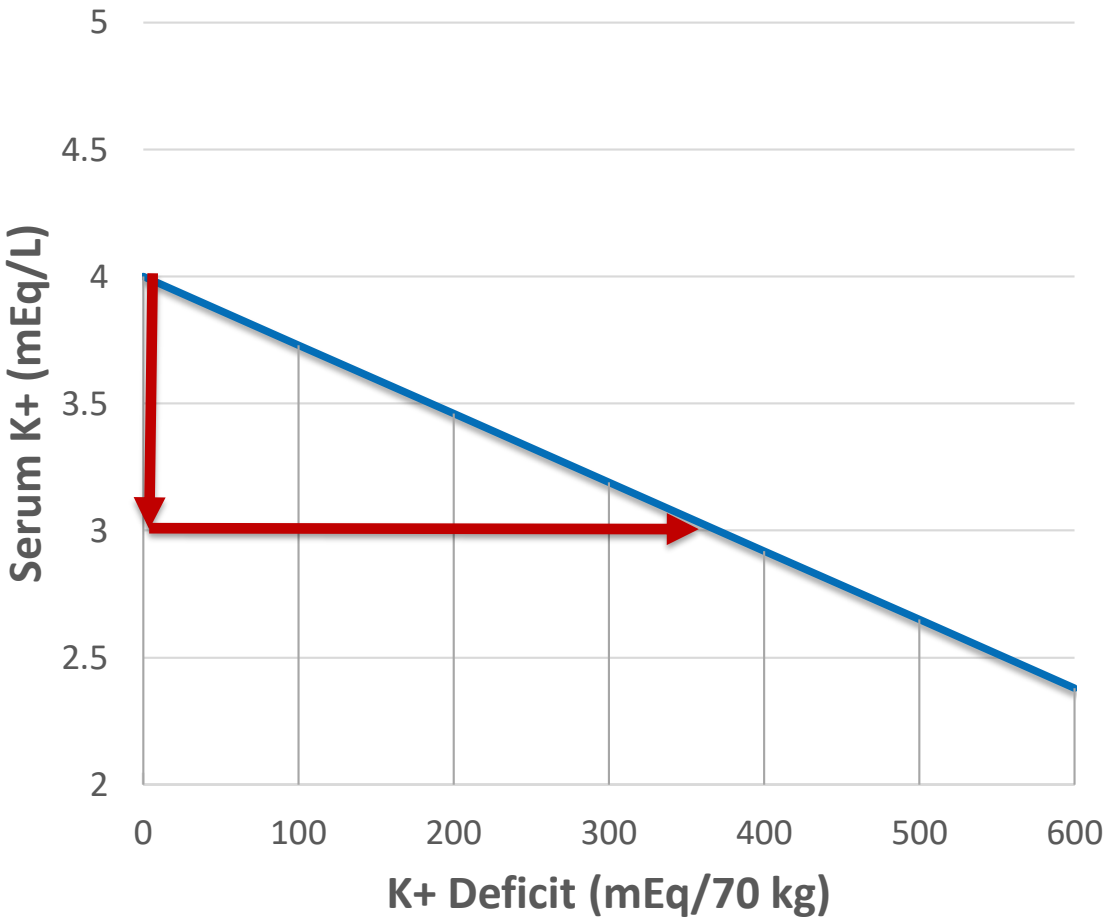
N = 10,451

Mean Age 59.4 yrs, 61% Male

27% Medical / 73% Surgical ICU

Hessels L, et al. *Crit Care* 2015;19:4

Effect of K^+ Depletion on Serum K^+



Data from 7 balance studies (6 were in normal volunteers) of **24** subjects

Each fall in serum K^+ of 0.27 mEq/L corresponded to a 100 mEq deficit

Sterns RH, et al. *Medicine* 1981;60:339-54

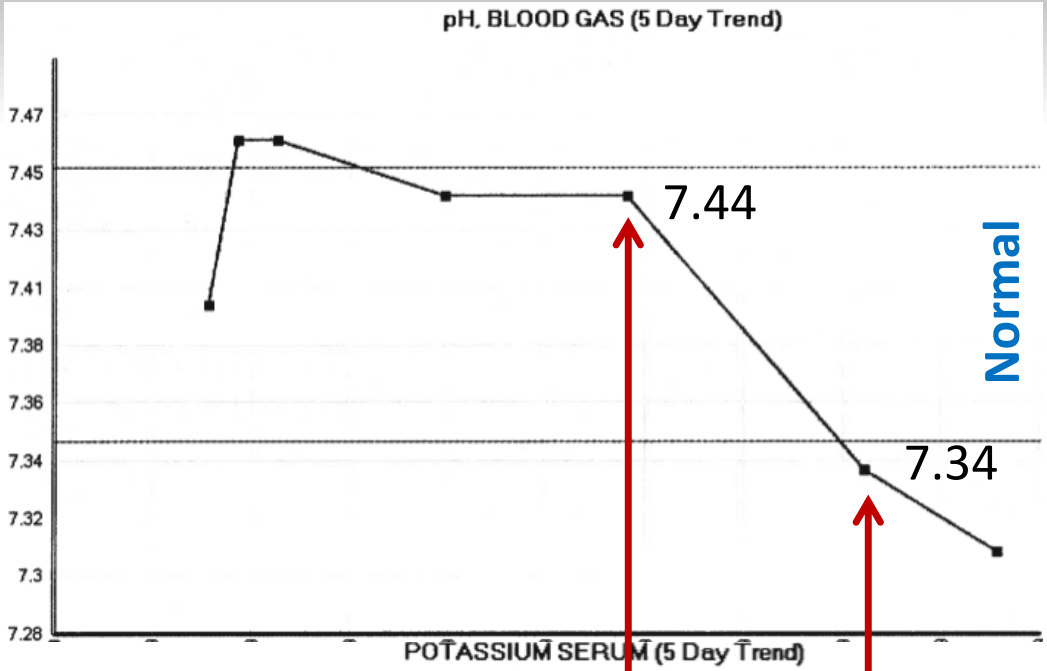
Correlation between Serum K^+ & Arterial pH

pH Range	Serum K^+ (mEq/L) – Mean ± Standard Deviation
7.14 – 7.36	5.1 ± 0.89
7.37 – 7.46	4.66 ± 0.5
7.47 – 7.6	3.58 ± 1.04

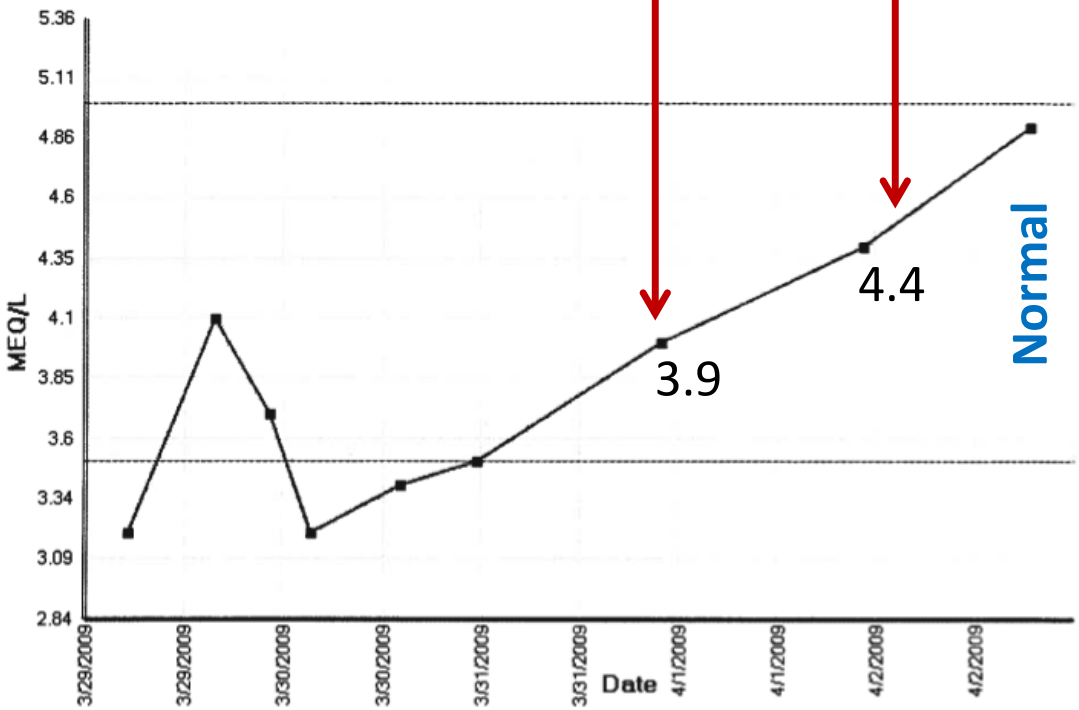
For every 0.1 unit change in pH, the change in serum K^+ is approximately 0.5 mEq/L

Leibman J, et al. *J Clin Invest* 1959;38:2176-88

Serum pH

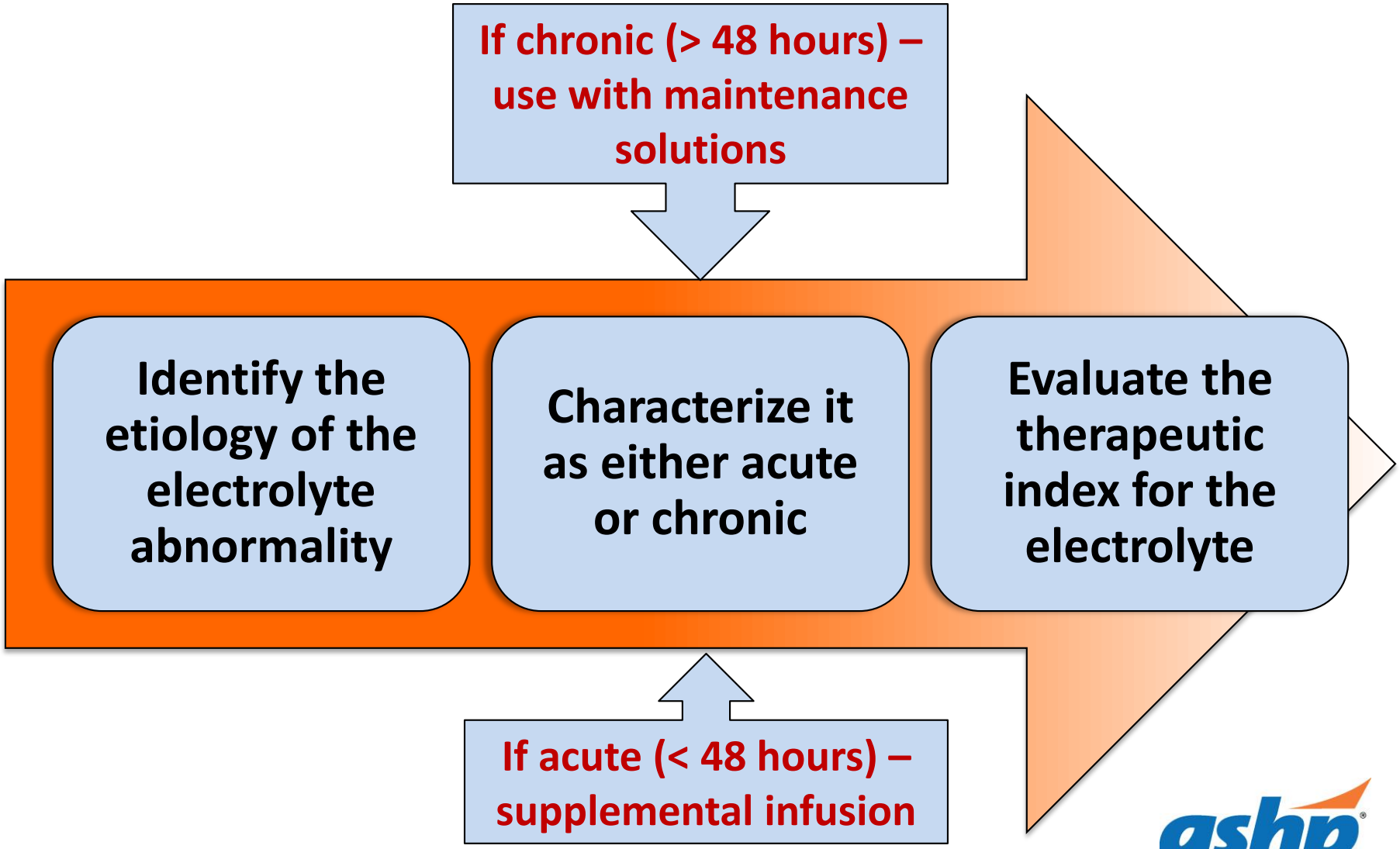


Serum Potassium



For every 0.1 unit change in pH, the change in serum K^+ is approximately 0.5 mEq/L

Correcting Electrolyte Disorders

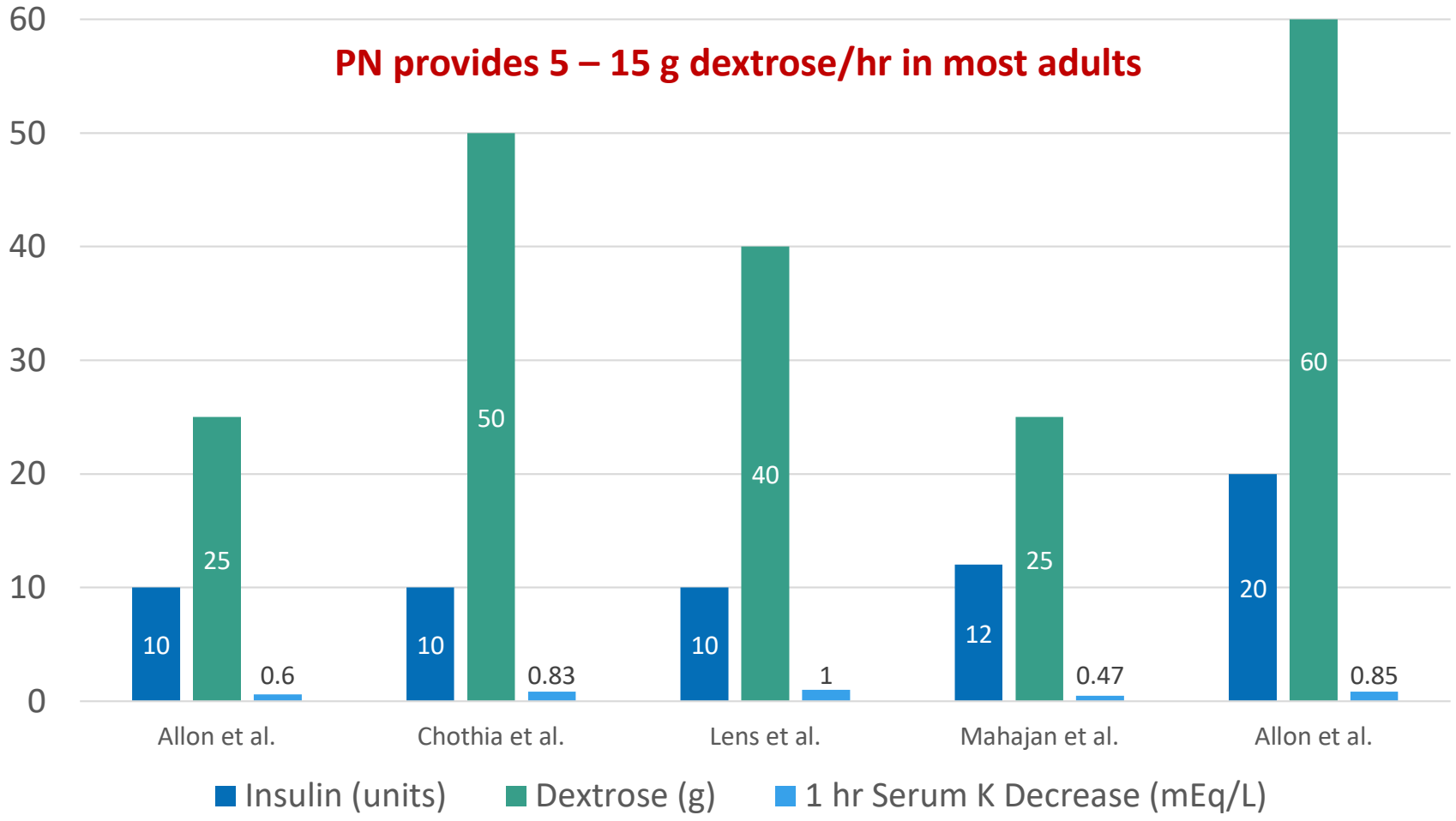


Schmidt GL. *Nutr Clin Pract* 2000;15:94-109

Etiologies of Hypokalemia

- Inadequate dietary K^+ intake
- Hypomagnesemia
  - Cisplatin, Caspofungin
- Diarrhea
  - Typhilitis
- Vomiting or nasogastric losses
  - 2 Liters/day
- High dose corticosteroids
  - Hydrocortisone
- Insulin
- Proximal renal tubular acidosis
  - Ifosfamide

Dextrose & Insulin Effects on Serum K^+



Harel Z, et al. *PLOS One* 2016;11:e0154963

ashp MIDYEAR2016 Clinical Meeting & Exhibition

2. What would be the most appropriate dose of potassium for his PN in mEq/day?

A 60

B 100

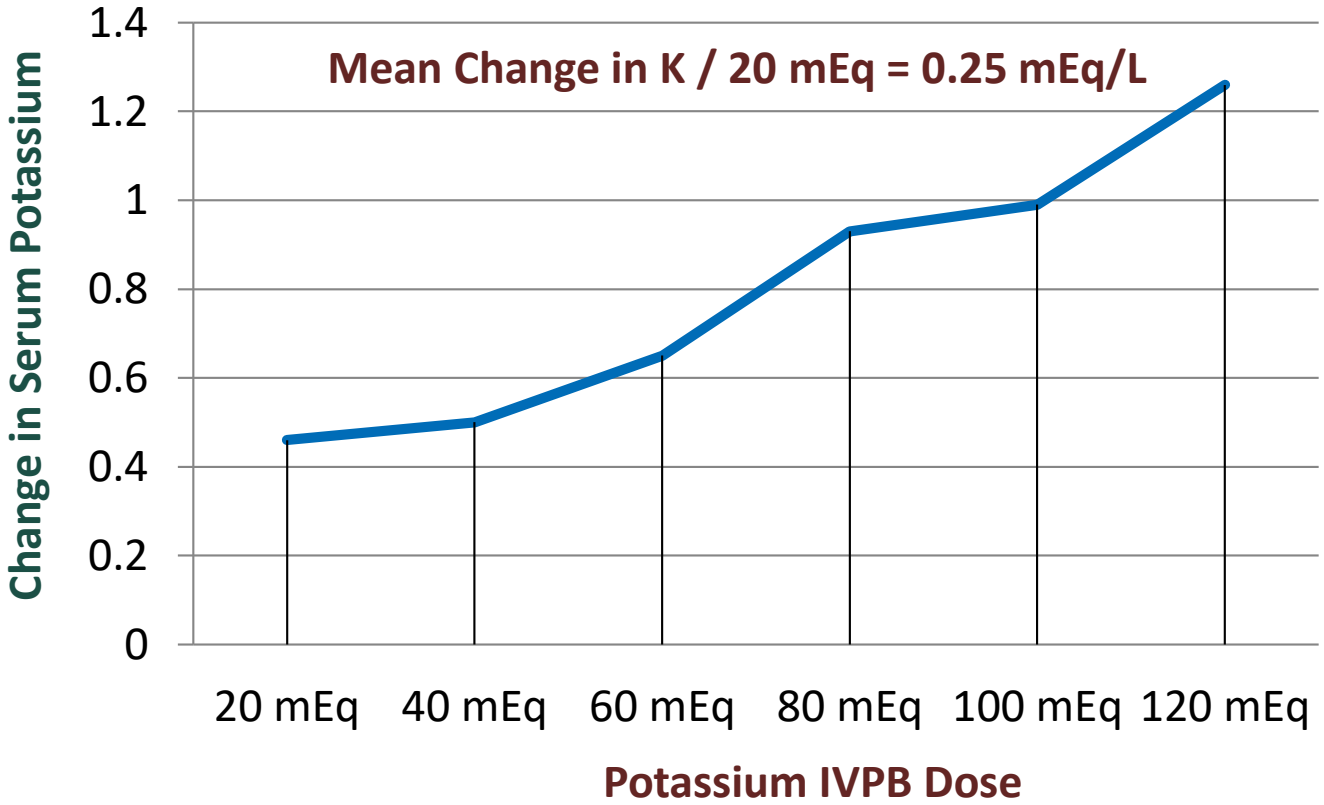
C 150

D 200

Answer = B

Management of Hypokalemia

- K^+ administration is most common cause of hyperkalemia
  - 10 mEq K^+ intravenously increases serum ~0.1 mEq/L

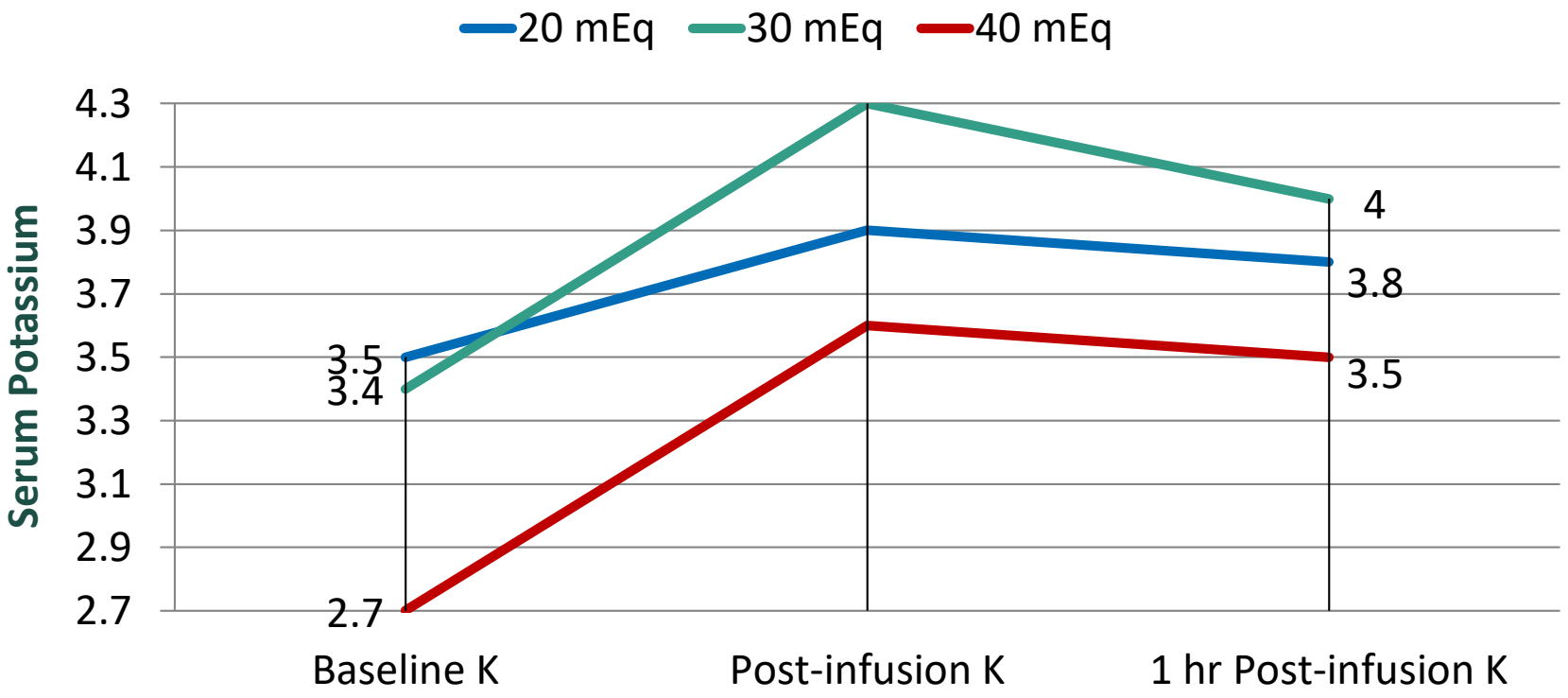


N = 190 (MICU with 32 oliguric)
77% central / 23% peripheral administration

Kruse JA, et al. *Arch Intern Med* 1990;150:613-7

Management of Hypokalemia

- K^+ administration is most common cause of hyperkalemia
  - 10 mEq K^+ intravenously increases serum ~0.1 mEq/L

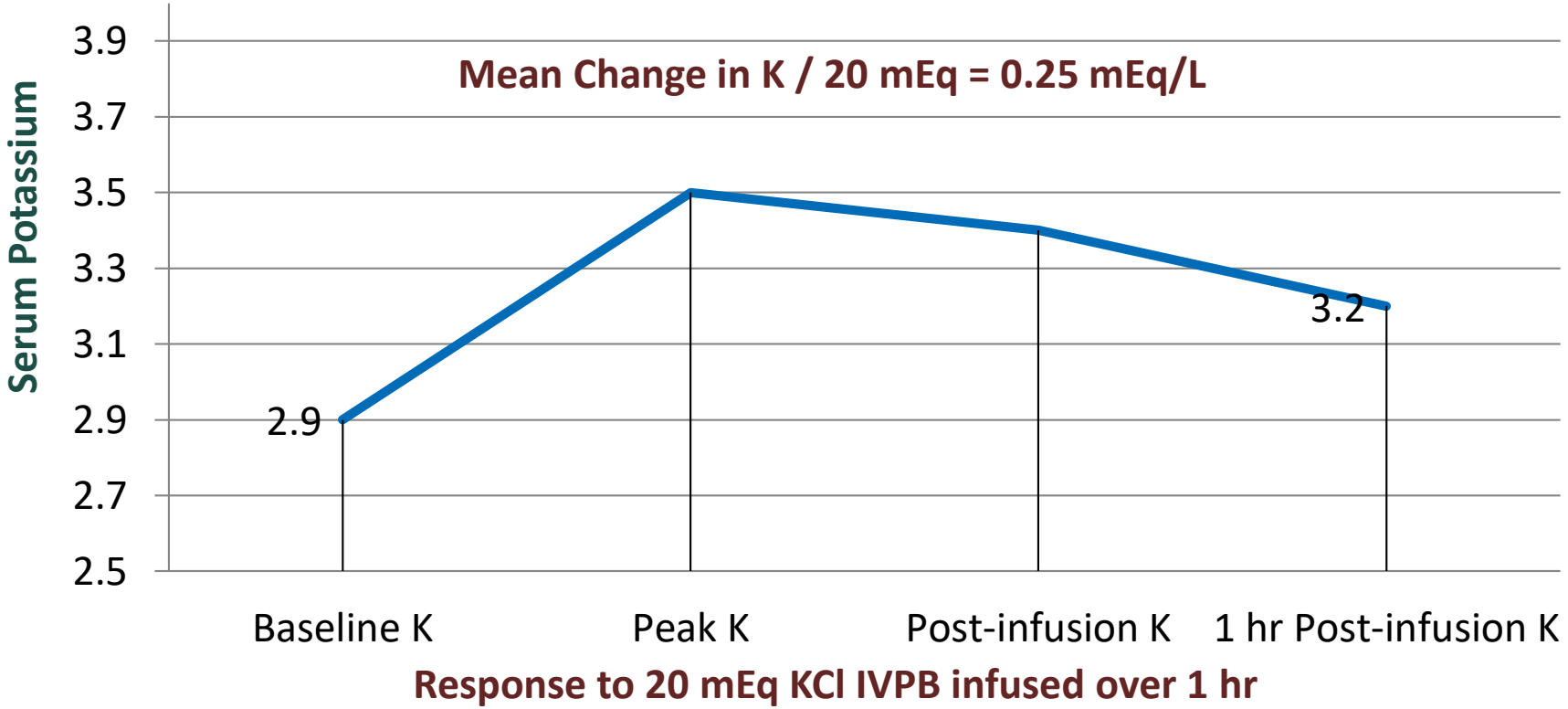


N = 48 (Mixed ICU with Mean Age 59, 62, 41 yrs)
100% central venous catheter administration over 1 hour

Hamill RJ, et al. *Crit Care Med* 1991;19:694-9

Management of Hypokalemia

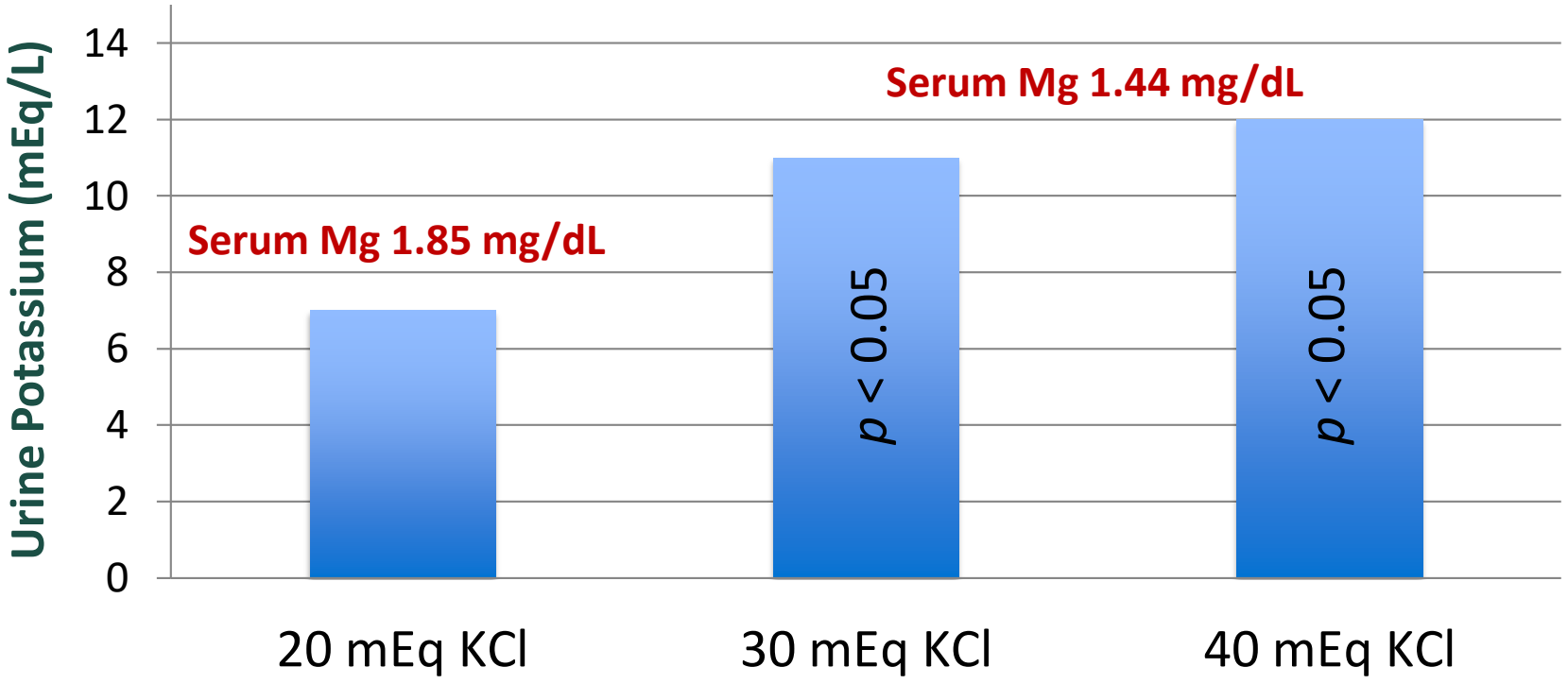
- K^+ administration is most common cause of hyperkalemia
  - 10 mEq K^+ intravenously increases serum ~0.1 mEq/L



N = 40 (MICU with Mean Age 59 yrs)
65% central / 35% peripheral administration

Kruse JA, et al. *J Clin Pharmacol* 1994;34:1077-82

Management of Hypokalemia with Consideration of Hypomagnesemia



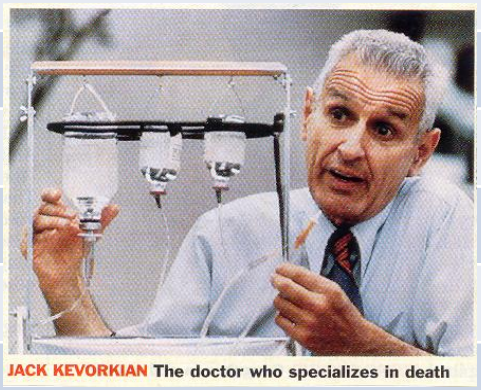
N = 48 (Mixed ICU with Mean Age 59, 62, 41 yrs)
100% central venous catheter administration over 1 hour

Hamill RJ, et al. *Crit Care Med* 1991;19:694-9

Potassium

K^+ = Kevorkian (*It's a Killer*)

< 0.5 mEq/kg/day	1-2 mEq/kg/day	> 2 mEq/kg/day
Anuric Acute Renal Failure	**Normal**	**Metabolic alkalosis**
Chronic Kidney Disease		**K^+ shifters**
K^+ Sparing Drugs		- Catecholamines
- Spironolactone		- Insulin
- Amiloride		**K^+ wasters**
ACE Inhibitors (*Vasotec*)		- Furosemide, Torsemide
Trimethoprim (*Bactrim*)		- Hydrocortisone
		- Amphotericin B
		Severe Diarrhea



Narrow therapeutic index

Clinical judgment and monitoring must be used when determining the most appropriate dose with evaluation of renal function and acid/base status

Mirtallo J, et al. *JPEN J Parenter Enteral Nutr* 2004;28:S39-70

3. What would be the most appropriate dose of magnesium for his PN in mEq/day?

A 16

B 32

C 64

D 96

Answer = C

Prevalence of Hypomagnesemia

Reference	Patient Population	Definition of Hypomagnesemia	Prevalence
Salem (1991)	Emergency Department	< 1 mEq/L	**9%**
Wong (1983)	University Hospital-Medical	< 1.2 mEq/L	11%
Whang (1987)	VA Hospital	< 1.25 mEq/L	6.9%
Whang (1977)	VA Hospital	< 1.25 mEq/L	9%
Rubeiz (1993)	University Hospital-Medical	< 1.25 mEq/L	18%
Whang (1984)	2 University & 1 VA Hospital	< 1.25 mEq/L	26%
England (1992)	Surgical Pre-op	< 1.5 mEq/L	16%
Salem (1991)	Emergency Department	< 1.5 mEq/L	22%
Whang (1990)	Hospitalized	< 1.48 mEq/L	**47%**
Chernow (1989)	Post-op SICU	< 1 mEq/L	**9%**
Desai (1988)	University Hospital-MICU	< 1.2 mEq/L	19%
Rubeiz (1993)	University Hospital-MICU	< 1.25 mEq/L	20%
Fiaccadori (1988)	Pulmonary ICU	≤ 1.4 mEq/L	9.4%
Reinhart (1985)	Community Hospital-MICU	< 1.4 mEq/L	20%
Zaloga (1987)	ICU	< 1.4 mEq/L	33%
Chernow (1989)	Post-op SICU	< 1.5 mEq/L	61%
Ryzen (1985)	University Hospital-MICU	< 1.5 mEq/L	44%
Ryzen (1985)	University Hospital-MICU	< 1.5 mEq/L	65%
England (1992)	Post-op SICU (Mg Treated)	< 1.5 mEq/L	**68%**

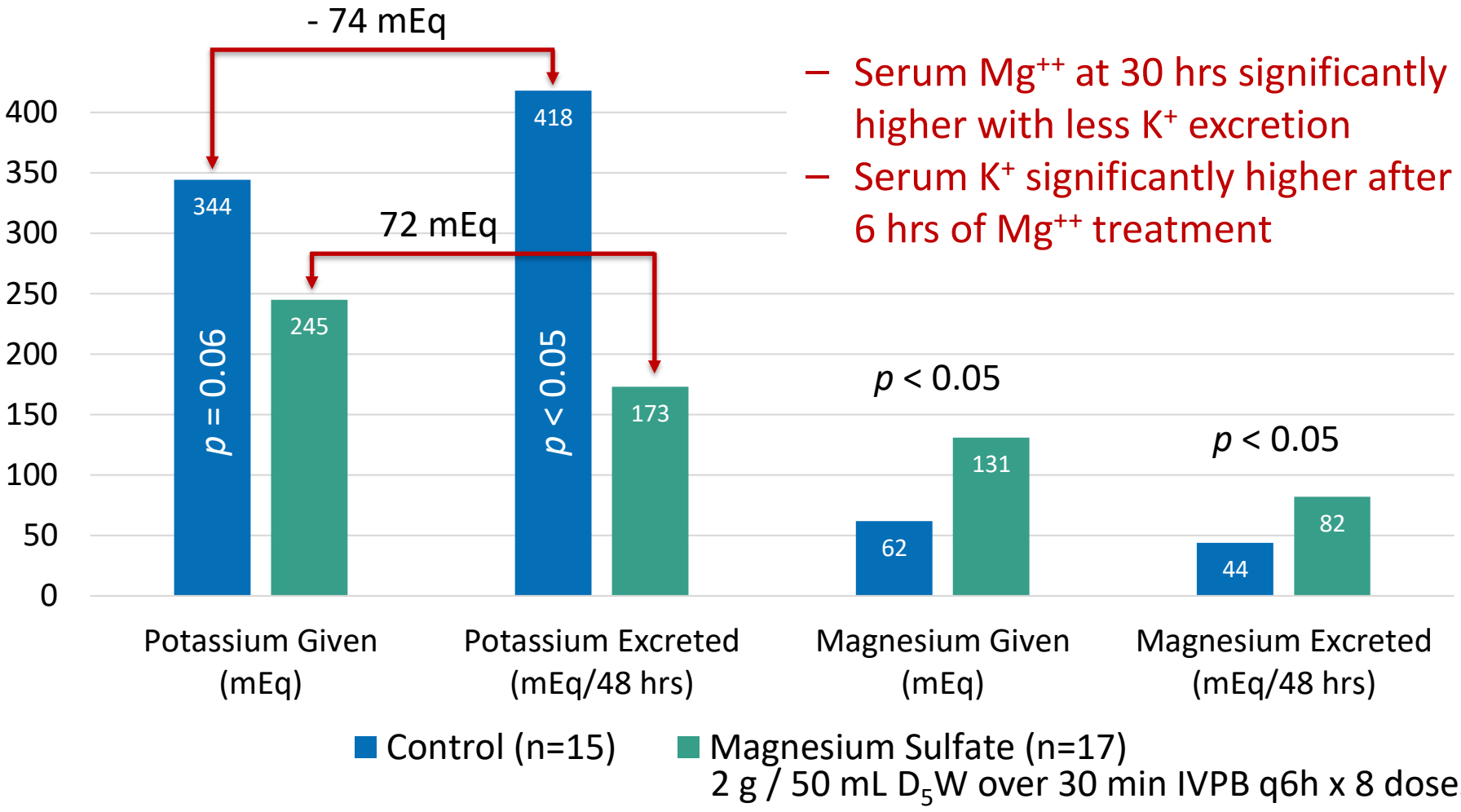
Etiologies & Effects of Hypomagnesemia

- **Inadequate dietary Mg^{++} intake**
- **Medication-related losses**
  - Cisplatin, Ifosfamide
  - Caspofungin
- **Diarrhea**
  - Typhilitis

- **Reduces insulin sensitivity**
  - Decreases autophosphorylation of B-subunit of insulin receptor
- **Reduces glucose cellular uptake**
  - Decreases translocation of glucose transporter protein
- **Impairs insulin secretion**
  - Decreases affinity of insulin binding to its receptor
- **Reduces lipoprotein lipase**

Das UN. *Nutrition* 2016;32:1308-10

Magnesium Replacement Effects on K^+



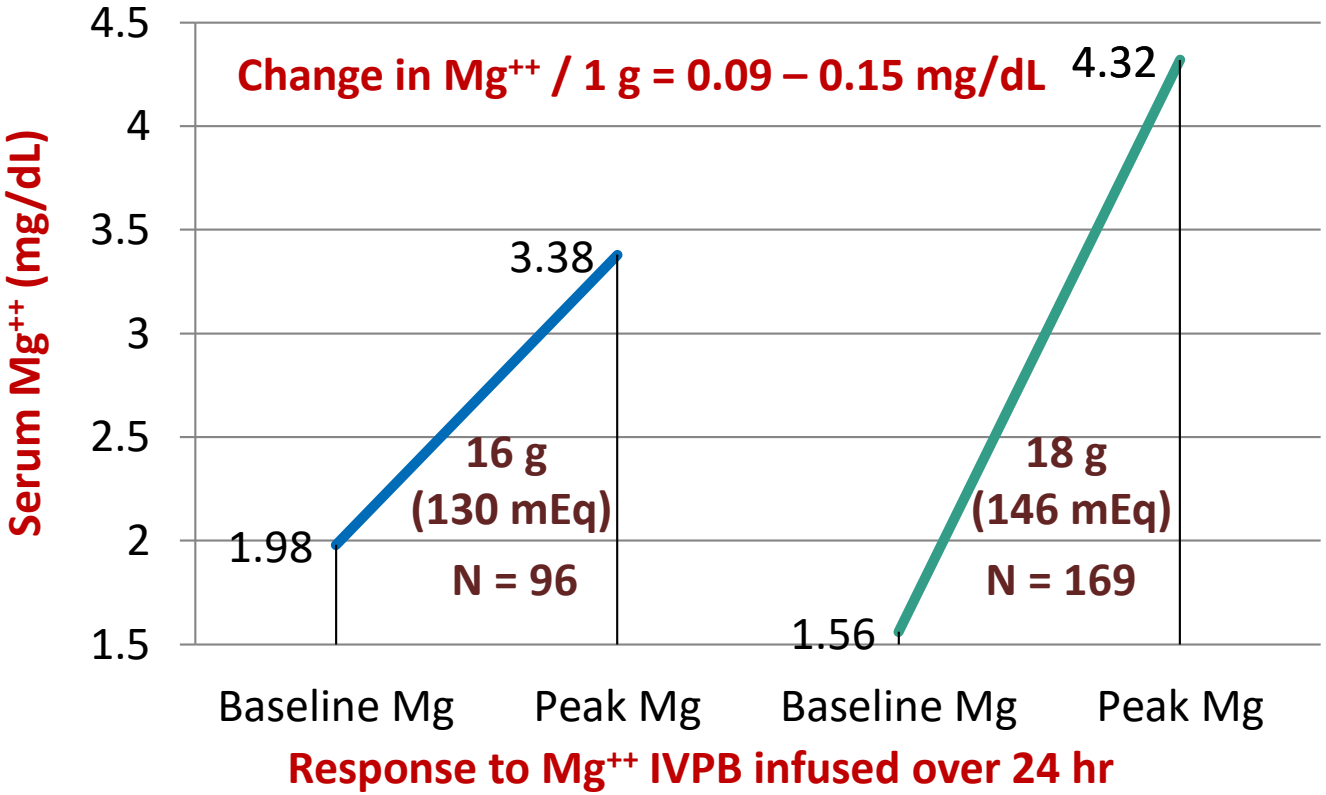
- Serum Mg^{++} at 30 hrs significantly higher with less K^+ excretion
- Serum K^+ significantly higher after 6 hrs of Mg^{++} treatment

N = 32 (SICU with Mean Age 52 vs. 60 yrs) with Serum K^+ < 3.5 mEq/L
Baseline Serum K^+ 3.3 vs. 3.4 mEq/L; Baseline Serum Mg^{++} 2.1 vs. 1.9 mg/dL

Hamill-Ruth RJ, et al. *Crit Care Med* 1996;24:38-45

Management of Hypomagnesemia

- Mg^{++} administration is most common cause of hypermagnesemia
  - 8 mEq (1 g) Mg^{++} IV increases serum ~0.1 mg/dL



Shechter M, et al. *Am J Cardiol* 1995;75:321-23

Raghu C, et al. *Int J Cardiol* 1999;71:209-15

Magnesium in PN
Mg = "May give" more

< 0.25 mEq/kg/day	0.25 – 0.5 mEq/kg/day	> 0.5 mEq/kg/day
Acute Renal Failure	**Normal**	**Alcohol abuse**
- Renal replacement therapy may increase need depending on mode of dialysis	**Wide therapeutic index**	**Magnesium wasters** - Loop diuretics (furosemide, torsemide, bumetanide) - Hydrochlorothiazide > 50 mg/day - Amphotericin B - Aminoglycosides - Cisplatin, carboplatin, oxaliplatin, ifosfamide, cetuximab - Cyclosporine, tacrolimus - Foscarnet - Proton pump inhibitors (e.g., omeprazole)
Chronic Kidney Disease		**Severe diarrhea (any cause)**
Hypermagnesemia		**Renal Replacement Therapy**

K^+ & Mg^{++} Considerations in Compounding PN

- Considerations for adding fat emulsion to PN (3-in-1)
  - Phospholipid emulsifier is anionic
  - Dependent on cations:
    - Trivalent (Iron > 2 mg/L)
    - Divalent (Mg + Ca > 20 mEq/L)
    - Monovalent (Na + K > 150 mEq/L)
  - Emulsion cracking more likely to occur at pH ≤ 5
    - Fat emulsions do not possess pH buffering capacity
      - ➢ Hydrolytic degradation of triglycerides forming free fatty acids can lower the pH over the course of its shelf life
        - ❖ Minimal hydrolysis occurs at a pH of 6.5 – 7

Amino acids 2.5 – 7%
Dextrose 5 – 20%
Fat emulsion 2 – 5%

Driscoll DF, et al. *Am J Health-Syst Pharm* 1995;52:623-34

Electrolyte Dosages in PN

Low Dose†	Electrolyte	High Dose
< 0.5 mEq/kg/day	Potassium	> 2 mEq/kg/day
< 0.5 mEq/kg/day	Acetate*	> 3 mEq/kg/day
< 0.25 mEq/kg/day	Magnesium	> 2 mEq/kg/day

† Although considered a low dose, this may be appropriate given any degree of renal impairment

* Evaluate the blood gas for actual serum pH (*< 7.2 severe acidemia; > 7.6 severe alkalemia*)

Mirtallo J, et al. *JPEN J Parenter Enteral Nutr* 2004;28(Suppl):S39-S70

Key Takeaways

- Key Takeaway #1
  - Magnesium treatment alone augments potassium retention.
- Key Takeaway #2
  - Potassium and magnesium replacement in 3-in-1 PN is limited by their effect on the anionic emulsifier in fat emulsions.
- Key Takeaway #3
  - Safe Practices for Parenteral Nutrition.

Mirtallo J, et al. *JPEN J Parenter Enteral Nutr* 2004;28(Suppl):S39-S70

Importance of Phosphorus and Calcium in Patients Receiving Parenteral Nutrition

Michael D. Kraft, Pharm.D., BCNSP

Clinical Associate Professor – University of Michigan College of Pharmacy

Assistant Director, Education & Reearch – University of Michigan Hospitals and Health Centers

Ann Arbor, MI

ashp MIDYEAR2016 Clinical Meeting & Exhibition

Learning Objectives

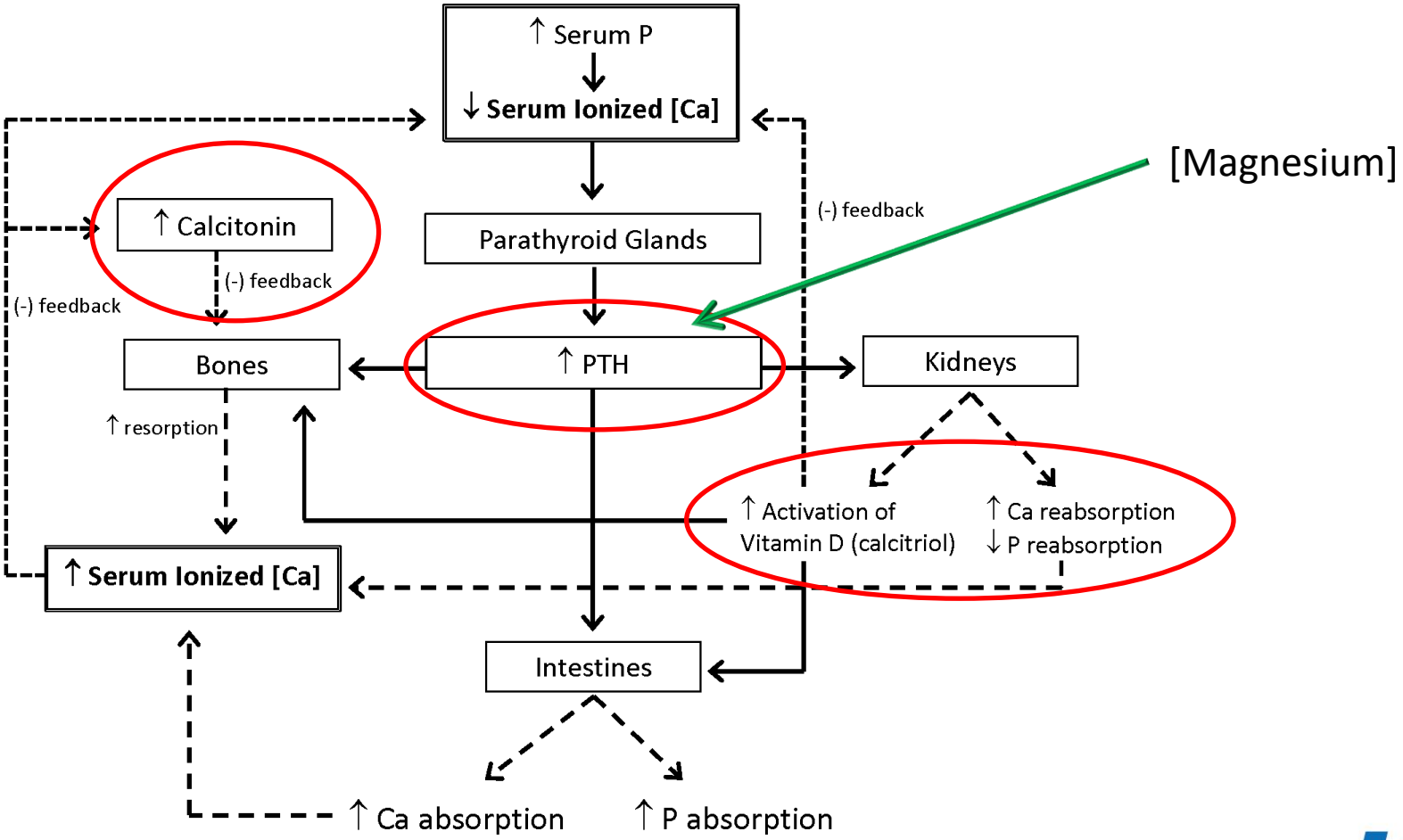
Upon completion of this session, the learner will be able to:

1. List common causes of phosphorus and calcium abnormalities in adult patients receiving nutrition support.
2. Recommend empiric treatment options for phosphorus and calcium abnormalities in adult patients receiving nutrition support.
3. Identify approaches to prevent phosphorus and calcium abnormalities in select adult patients receiving nutrition support.

General Principles

- Mild disorders, asymptomatic: may not require immediate treatment
- Severe disorders: can be urgent/emergent
- Must assess the whole patient, don't just "treat the numbers"
  - Provide appropriate maintenance requirements, anticipate potential abnormalities
  - Dose adjustments in PN ~ 10 – 25% (with some exceptions)
  - Treat the underlying cause
  - Treat and/or prevent symptoms
  - Normalize serum concentrations, avoid overcorrection
  - Avoid/decrease morbidity, mortality
  - Patient safety!

Phosphorus (P) and Calcium (Ca) Homeostasis



Kraft MD. Nutr Clin Pract 2014; Olinger ML. Emerg Med Clin North Am 1989; Bushinsky DA, et. al. Lancet 1998; Khanal RC, et. al. Ann Rev Nutr 2008.

Phosphorus (P)

- Majority in bones and intracellular compartment, ~ 1% in extracellular fluid
- Many essential functions
  - ATP
  - 2,3-Diphosphoglycerate (2,3-DPG)
  - Bone and cell membrane phospholipids
- Adequate stores needed for glucose utilization/glycolysis, protein synthesis, neurologic function, muscle function
- Normal serum [P] ~ 2.7 – 4.5 mg/dL
- Unstressed, well-nourished adults require ~ 20 – 40 mmol/day, or ~ 10 – 15 mmol per 1000 kcals
- Increasing total caloric load → decreased serum [P]
- Inadequate maintenance dosing → severe hypophosphatemia and sequelae

Kraft MD. Nutr Clin Pract 2015; Peppers MP, et. al. Crit Care Clin 1991; Knochel JP. Arch Intern Med 1977; Sheldon GF, et. al. Ann Surg 1975; Mirtallo J, et. al. JPEN J Parenter Enteral Nutr 2004

Phosphorus (P) – Altered Requirements

- Some patients have higher daily P requirements
  - Severely malnourished/risk for refeeding syndrome
  - Critically ill, trauma, traumatic brain injury
  - Thermal injury, liver resection
- Patients with impaired renal function → likely require P restriction (possible exception: renal replacement therapy)
- Typically monitor serum [P] daily in non-stressed, well-nourished adult inpatients receiving nutrition support
- Closer monitoring in special patients listed above, especially when initiating nutrition support (e.g., every 12 hours)

Kraft MD. Nutr Clin Pract 2015; Kraft MD, et. al. Nutr Clin Pract 2005; Loven L, et. al. J Trauma 1986; Gadisseux P, et. al. Neurosurgery 1985; Buell JF, et. al. Arch Surg 1998.

Calcium (Ca)

- Key roles
  - Bone structure, coagulation, platelet adhesion
  - Neuromuscular activity, Endocrine & exocrine secretory functions
- Vast majority (~ 99%) in bones, < 1% in serum
  - ~ 40 – 50% blood Ca bound to proteins (albumin)
  - Ionized [Ca] closely regulated, better indicator of functional Ca status
- Normal serum concentrations
  - Total [Ca] ~ 8.6 – 10.2 mg/dL
  - Ionized [Ca] ~ 1.12 – 1.3 mmol/L
- Adult patients receiving PN (normal renal function) require ~ 10 – 15 mEq/day for maintenance
- Adjusting maintenance doses
  - Depends on daily Ca dose, clinical condition
  - Response to dose changes/supplemental doses

Kraft MD. Nutr Clin Pract 2015; Olinger ML. Emerg Med Clin N Am 1989; Bushinsky DA, et. al. Lancet 1998; Mirtallo J, et. al. JPEN 2004

Phosphorus and Calcium Considerations in Specific Conditions

- Chronic Kidney Disease
  - Hyperphosphatemia, Vitamin D deficiency
  - Renal osteodystrophy, soft-tissue calcification
  - Acid-base abnormalities (e.g., metabolic acidosis)
- Intestinal Failure
  - Malabsorption, Short Bowel Syndrome (SBS), Inflammatory Bowel Disease (IBD)
  - Malabsorption → vitamin D deficiency
  - Chronic corticosteroid therapy → bone demineralization
  - Large GI losses → dehydration, metabolic alkalosis, magnesium deficiency
- Long-term PN/PN-dependence → Metabolic Bone Disease

Kraft MD. Nutr Clin Pract 2015; National Kidney Foundation K/DOQI Clinical Practice Guidelines. Am J Kidney Dis 2003; O'Keefe SJD, et.al. Clin Gastroenterol Hepatol 2006; Seidner DL. JPEN 2002

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Phosphate and Calcium Compatibility in Parenteral Nutrition Admixtures

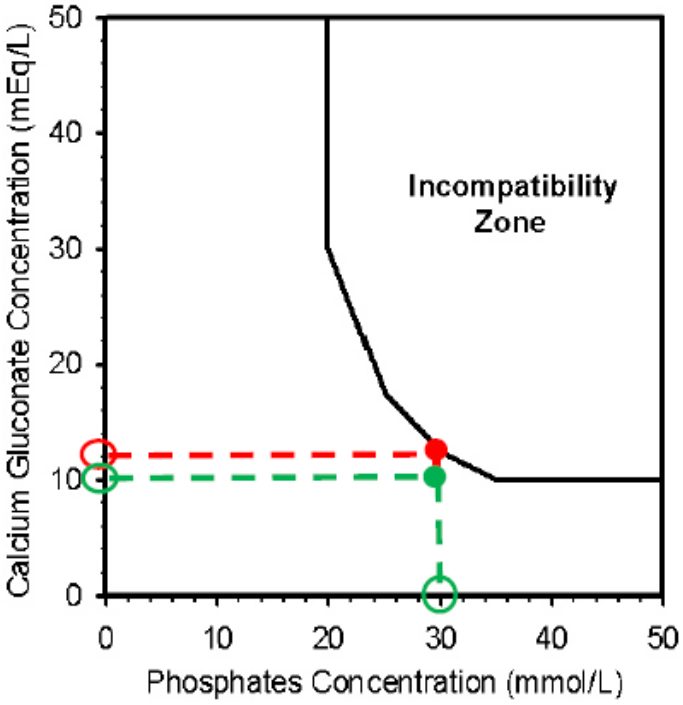
Ca and P Compatibility in PN Admixtures

- $Ca^{2+} + HPO_4^{2-} \rightarrow CaHPO_4$
- Deaths associated with Ca-Phos precipitation in PN admixtures (FDA 1994, JPEN 1996)
- Factors affecting Ca-Phos solubility in PN admixtures:
  - Final pH
  - Amino Acid brand and final concentration
  - Dextrose concentration
  - Ca salt
  - Order of mixing
  - Temperature
  - Time

Kraft MD. Nutr Clin Pract 2015; FDA Safety Alert. Am J Hosp Pharm 1994; Hill SE, et. al. JPEN 1996; Mirtallo J, et. al. JPEN 2004

Ca and P Compatibility in PN Admixtures

- Must follow safe PN practices when compounding PN Admixtures!
  - Use established Ca-Phos solubility curves
  - Consider PO_4 from ALL sources
  - Use Ca Gluconate, avoid Ca Chloride
  - Add PO_4 salts early in sequence, Ca toward end
  - Consider admixture volume at time Ca is added
  - Periodically agitate, check for precipitation
  - Use appropriate in-line filter (0.22-micron or 1.2-micron)
  - Store at appropriate temperature



(Green = current PN order; Red = limit, or the "Range" value)

- Recommended <u>minimum</u> final concentrations: dextrose 10%, amino acids 4%, IV Lipid Emulsion 2% (admixture stability)

Kraft MD. Nutr Clin Pract 2015; Boullata JI, et. al. JPEN 2014; Mirtallo J, et. al. JPEN 2004; FDA Safety Alert. Am J Hosp Pharm 1994

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Hypophosphatemia

Hypophosphatemia

- Serum [P] < 2.7 mg/dL; ~ 2 – 3 % of inpatients, 28 – 80% of critically ill patients
- Associated with higher mortality, longer LOS, longer duration of mechanical ventilation
- Critically ill may be predisposed to hypophosphatemia
- Severe symptoms with serum [P] < 1 mg/dL (~ 0.3 mmol/L)
  - Hypoxia, respiratory failure
  - Weakness, paresthesias, mental status changes
  - Seizures, coma, death
- General causes: inadequate intake/increased demand, altered distribution, altered excretion

Kraft MD. Nutr Clin Pract 2015; Gasbeek A, et. al. Am J Med 2005; Brunelli SM, et. al. Am Soc Nephrol 2007; Kraft MD, et. al. Nutr Clin Pract 2005

Refeeding Syndrome

- Constellation of electrolyte abnormalities and symptoms associated with rapid re-introduction of nutrition (especially carbohydrates) after prolonged starvation
- The Minnesota Experiment: 36 conscientious objectors of war
- Prisoners of War (WWII)
- Hallmark Sign: hypophosphatemia
- Other S/Sx:
  - Hypokalemia, hypomagnesemia
  - Thiamine deficiency, fluid/sodium intolerance, possibly hyperglycemia
- Can lead to severe sequelae: paresthesias, mental status changes, seizures, coma, and death

Keys A, et al. The Biology of Human Starvation, vols I-II. University of Minnesota Press, Minneapolis, MN, 1950. Kalm LM, et al. J Nutr 2005; 135:1347-52; Schnitker MA, et al. Ann Intern Med 1951; 35:69-96; Kraft MD, et. al. Nutr Clin Pract 2005; Stanga Z, et. al. Eur J Clin Nutr 2008; Skipper A. Nutr Clin Pract 2012

Refeeding Syndrome - Pathophysiology

Prolonged Starvation / Severe Malnutrition

Nutrient depletion → glycogen, gluconeogenesis/ protein catabolism, fatty acid catabolism→ ketone production

Electrolyte, vitamin depletion; salt/water intolerance

↓ metabolic rate, ↓ insulin secretion

Re-introduction of CHO → ↑ metabolic rate, ↑ insulin secretion, ↑ glycolysis, anabolism

↑ Glucose uptake, ↑ demand for ATP and O_2, ↑ uptake of Phos, K+, Mg++, ↑ utilization of thiamine

Hypophosphatemia

Hypokalemia

Hypomagnesemia

Thiamine deficiency

Na+/water retention

+/- Hyperglycemia

REFEEDING SYNDROME

Kraft MD, et. al. Nutr Clin Pract 2005; Stanga Z, et. al. Eur J Clin Nutr 2008

Refeeding Syndrome / Refeeding Hypophosphatemia

- Review of 27 patient cases since 2000
  - **Hypophosphatemia = 96%**
  - At least 1 other e-lyte abnormality = 71%
  - Hypomagnesemia = 51%; hypokalemia = 46%
  - Hypocalcemia = 27%; hyponatremia = 8%
  - One documented thiamine deficiency (4%), one with S/Sx of possible thiamine deficiency
  - Paresthesias = 15%, tachycardia/bradycardia = 8% each
  - Edema/excessive wt gain = 22%
  - One pt with heart failure, one with ventricular ectopy
  - Hyperglycemia not reported

Skipper A. Nutr Clin Pract 2012

Refeeding Syndrome/Hypophosphatemia

- Prevention is key!
- "Start low, go slow", AVOID OVERFEEDING
- Correct electrolyte abnormalities *before* initiating nutrition support
- Provide adequate PO_4 (e.g., may require increased maintenance doses by ~ 25 – 50% (or higher) for first several days of PN therapy)
- May require increased monitoring (e.g., serum [P] ~ twice a day)
- Most cases develop in first 3 – 5 days, but some reported > 5 – 7 days

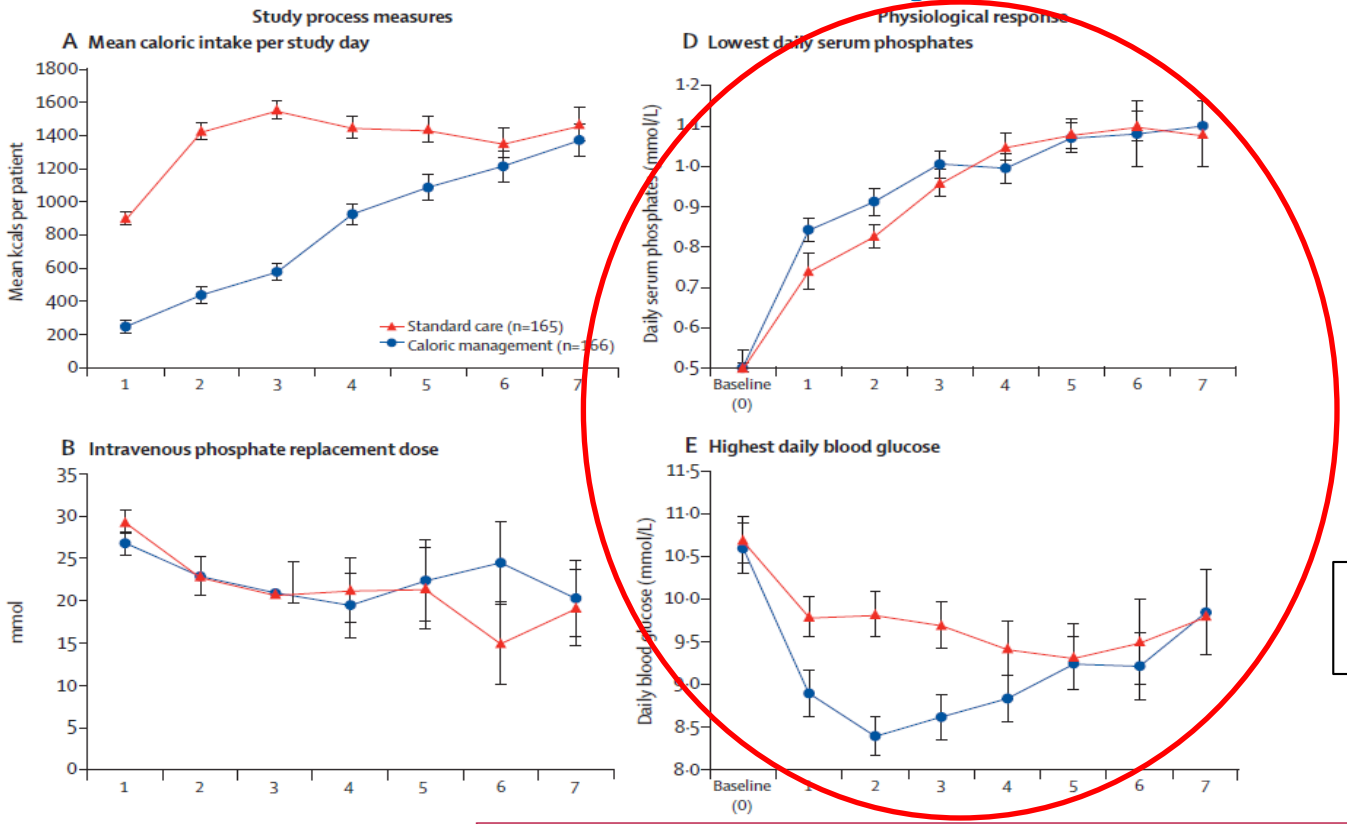
Kraft MD, et. al. Nutr Clin Pract 2005; Stanga Z, et. al. Eur J Clin Nutr 2008; Skipper A. Nutr Clin Pract 2012

Management of Refeeding Syndrome in Critically Ill Adults

- Multicenter, randomized, single-blind, parallel-group study, 339 critically ill adults
- Serum [P] < 0.65 mmol/L (~ 2 mg/dL) (and > 0.16 mmol/L (~ 0.5 mg/dL) decrease) w/in 72-hrs of starting nutrition support
- Randomized to standard vs. caloric restriction (20 kcal/hr x $\geq$ 2 days)
- Gradual return to goal over 2 – 4 days (40 kcal/hr, 60 kcal/hr, 80% goal, 100% goal)
- If serum [P] < 0.71 mmol/L (~ 2.2 mg/dL) → start over

Doig GS, et. al. Lancet Respir Med 2015

Management of Refeeding Syndrome in Critically Ill Adults



Fewer patients required insulin on days 2 – 6

	Standard care (n=165 patients)	Caloric management (n=166 patients)	Risk difference (95% CI)	p value
Vital status (% alive)				
ICU discharge status	150/165 (91%)	157/166 (95%)	3·7% (−5·3 to 12·7)	0·20
Hospital discharge status	135/165 (82%)	151/166 (91%)	9·2% (0·7 to 17·7)	0·017
Day 60 status	128/163 (79%)*	149/164 (91%)*	12·3% (3·9 to 20·7)	0·002
Day 90 status	128/163 (79%)*	143/164 (87%)*	8·7% (0·04 to 17·0)	0·041
Length of stay (days)				
ICU	10·0 (9·2 to 10·9)	11·4 (10·5 to 12·4)	1·4 (−0·42 to 3·5)	0·14
Hospital	21·7 (20·0 to 23·5)	27·9 (25·7 to 30·3)	6·2 (2·0 to 11·2)	0·003

Doig GS, et. al. Lancet Respir Med 2015

Empiric Treatment of Hypophosphatemia

Degree of Hypophosphatemia	Suggested IV phosphate dose*†
2.3 – 2.7 mg/dL (~ 0.75 – 0.9 mmol/L) Mild hypophosphatemia, asymptomatic	0.08 – 0.16 mmol/kg
1.5 – 2.2 mg/dL (~ 0.5 – 0.75 mmol/L) Moderate hypophosphatemia, asymptomatic	0.16 – 0.32 mmol/kg
< 1.5 mg/dL (~ < 0.5 mmol/L) Severe hypophosphatemia, symptoms present, possibly severe	0.32 – 0.64 mmol/kg†

* In patients with normal renal function; patients with renal insufficiency should receive ≤ 50% of the initial empiric dose. Maximum infusion rate = 7.5 mmol phosphate/hour; Suggest using adjusted body weight (AdjBW) in patients who are significantly obese (weight > 130% of IBW or BMI ≥ 30 kg/m^2): AdjBW (males) = ([wt (kg) – IBW(kg)] x 0.3) + IBW; AdjBW (females) = ([wt (kg) – IBW(kg)] x 0.25) + IBW

† Doses up to 1 mmol/kg have been used in adult critically ill trauma patients

Kraft MD, et. al. Am J Health-Syst Pharm 2005; Kraft MD. Nutr Clin Pract 2015; Clark CL, et. al. Crit Care Med 1995; Brown KA, et. al. JPEN 2006; Taylor BE, et. al. J Am Coll Surg 2004; Lentz RD, et. al. Ann Intern Med 1978; Vannatta JB, et. al. Arch Intern Med 1981; Vannatta JB, et. al. South Med J 1983; Rosen GH, et. al. Crit Care Med 1995

IV Phosphate

- Sodium (NaPhos) or Potassium (KPhos) salt
  - 1 mmol NaPhos ~ 1.33 mEq Na^+
  - 1 mmol KPhos ~ 1.47 mEq K^+
- Infuse doses over ~ 4 – 6 hours, max ~ 7 – 7.5 mmol/hour
- Limited data for rates up to 15 mmol/hour, however:
  - No difference in serum [P] vs. 7.5 mmol/hour
  - More patients developed hyperkalemia
  - Trend toward increased fractional PO_4 excretion
- Caution with KPhos, may require central line

Kraft MD. Nutr Clin Pract 2015; Charron T, et. al. Intensive Care Med 2003;
French C, et. al. Crit Care Resusc 2004; Taylor BE, et. al. J Am Coll Surg 2004

Treatment/Prevention of Hypophosphatemia

- Provide adequate maintenance doses in PN, some may require daily supplement or ↑ maintenance dosing in PN
- Deficits typically require several days to fully correct → especially critically ill, malnourished/risk of refeeding
- Consider ALL sources of Na+ and K+ in PN admixtures
- No data/protocols to guide dose adjustments → reasonable to consider adjusting daily doses in PN by ~ 10 – 25%, monitor for response
- Critically ill adults → decrease nutrition to ~ 20 kcal/hr, advance over ~ 4 days
- Further adjustments based on response and clinical condition

Kraft MD. Nutr Clin Pract 2015; Doig GS, et. al. Lancet Respir Med 2015

Monitoring

- Data lacking on optimal time to recheck serum [P] after supplementation
  - Some protocols and guidelines suggest ~ 2 – 6 hours after a dose
  - Several studies have rechecked ~ 12 – 24 hours after supplementation, or on a daily basis
- Reasonable to monitor once-twice daily if actively treating
  - Potentially more frequently in severe/symptomatic cases until resolved

Example Protocol
Empiric Treatment of Hypophosphatemia

Serum Phos Concentration (Goal 2.7 – 4.6 mg/dL)	IV Phosphate Dose	Recommended Serum Phos Monitoring
2 – 2.6 mg/dL	15 mmol over 2 hrs	With next AM labs
1.5 – 1.9 mg/dL	30 mmol over 4 hrs	Within 12 hrs of completing dose or with AM labs
< 1.5 mg/dL	45 mmol over 6 hrs and notify MD	Within 4 – 6 hrs of completing dose

- Only for patients with normal renal function (e.g., est GFR > 60 mL/min)
- Maximum phosphate infusion = 7.5 mmol/hr
- Doses provided as NaPhos; if serum [K+] < 4 mEq/L, contact MD to enter separate order for KPhos replacement

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Hyperphosphatemia

Hyperphosphatemia

- Serum [P] > 4.5 mg/dL (~ 1.45 mmol/L)
- Most common cause → impaired kidney function
  - Tumor lysis, hemolysis, rhabdomyolysis
  - Hypoparathyroidism, vitamin D intoxication
  - Immobility, Acidosis (metabolic, respiratory)
- Severe hyperphosphatemia, acute kidney injury, and dehydration reported after treatment with oral and rectal P-containing laxatives (especially in patients with impaired kidney function)
- Risk of metastatic calcification may increase with serum Ca x P > 55-60 mg^2/dL^2

Kraft MD. Nutr Clin Pract 2015; Peppers MP, et. al. Crit Care Clin 1991; Escalante CP, et. al. South Med J 1997; National Kidney Foundation K/DOQI Clinical Practice Guidelines. Am J Kidney Dis 2003; Block GA, et. al. Am J Kidney Dis 2000

Treatment of Hyperphosphatemia

- Complete assessment of the patient, remove underlying cause(s)
- Adjust/restrict P intake (i.e. reduce phosphate dose in PN), especially patients with impaired kidney function
  - Empirically → reduce maintenance dose ~ 50%?
  - No data, need to use clinical judgment, adjust based on response
- Patients receiving Renal Replacement Therapy → variable requirements depending on form of RRT, native kidney function
- Can consider phosphate binder therapy (e.g., calcium carbonate, sevelamer)

Kraft MD. Nutr Clin Pract 2015; National Kidney Foundation K/DOQI Clinical Practice Guidelines. Am J Kidney Dis 2003; Moe SM, et. al. Kidney Int 2009; Navaneetham SD, et. al. Am J Kidney Dis 2009; Curran MP, et. al. Drugs 2009

Monitoring

- Most therapies have delayed onset → frequent monitoring of serum [P] likely not needed
- Every 24 – 48 hours likely appropriate in most patients
- Critically ill, symptomatic, or receiving CRRT may require more frequent monitoring
- Goal to normalize serum [P], maintain the serum Ca x P < 55 mg^2/dL^2, avoid calcification

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Hypocalcemia

Hypocalcemia

- Serum total [Ca] < 8.6 mg/dL (~2.15 mmol/L), ionized [Ca] < 1.1 mmol/L
- May occur in 15 – 88% of hospitalized patients, ~ 21% of critically ill patients
- Often associated with hypoalbuminemia
  - Sepsis, Pancreatitis, kidney dysfunction, hypoparathyroidism, Vitamin D deficiency
  - Hypomagnesemia, Hyperphosphatemia, Citrated blood
  - Medications: loop diuretics, calcitonin
- Hallmark sign → tetany
  - Muscle cramps, paresthesias, seizures
  - Prolonged QT, heart block, ventricular fibrillation

Kraft MD. Nutr Clin Pract 2015; Bushinsky DA, et. al. Lancet 1998; Zaloga GP. Crit Care Clin 1991; Olinger ML. Emerg Med Clin N Am 1989

"Corrected" Calcium

- Poor correlation between total serum [Ca] & free/ionized [Ca] in:
  - Critically ill
  - Hypoalbuminemia, acid-base disorders
- Monitor ionized [Ca], especially critically ill
- "Corrected" [Ca]: Modified Orrell equation (Developed in non-critically ill patients)

Corrected serum [Ca] (mg/dL) = Serum [Ca] (mg/dL) + [0.8 x (4 – albumin (g/dL))]

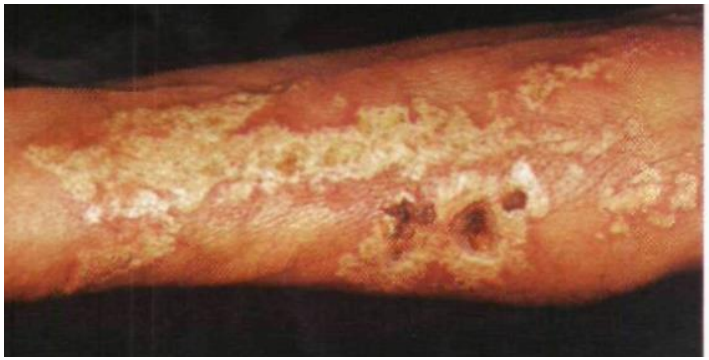
- Dickerson, et. al., 22 methods for correcting [Ca]
  - Sensitivity = 25%, FN = 75%; Specificity = 90%, FP = 10%
  - 85% of crit ill trauma patients with total [Ca] < 7 mg/dL had ionized hypocalcemia (ionized [Ca] < 1.12 mmol/L)
  - Other high-risk: albumin $\leq$ 2 g/dL, pH > 7.45

Kraft MD. Nutr Clin Pract 2015; Dickerson RN, et. al. JPEN 2004; Dickerson RN, et. al. Nutr Clin Pract 2007; Byrnes MC, et. al. Am J Surg 2005; Orrell DH. Clin Chimica Acta 1971; Olinger ML. Emerg Med Clin N Am 1989; Bushinsky DA, et. al. Lancet 1998

Treatment of Hypocalcemia

- Remove underlying cause(s), correct hypomagnesemia
- Critically ill, severe cases → IV treatment
  - 1000 mg Ca Chloride ~ 13.6 mEq Ca^{++}
  - 1 g Ca Gluconate ~ 4.65 mEq Ca^{++}
  - Watch for dosing errors, do not use term “amp”
- DO NOT infuse via the same IV line as PO_4-containing products
- Ca Gluconate for routine supplementation
- Calcium Chloride via central line only!

Risk of extravasation → soft-tissue calcification, ulceration, necrosis (calcinosis cutis)



Kraft MD. Nutr Clin Pract 2015; ISMP Medication Safety Alert! 1997, 1998, 2000, 2001, 2002; Jucgla A, et. al. Br J Dermatol 1995; Semple P, et. al. Anaesthesia 1996.

Empiric Treatment of Hypocalcemia

Degree of Hypocalcemia	Preferred Calcium Salt*	Suggested IV Dose+
Serum ionized [Ca] ~ 1 – 1.12 mmol/L Mild – moderate, asymptomatic	Gluconate	1 – 2 g calcium gluconate, infused over 1 – 2 hrs
Serum ionized [Ca] < 1 mmol/L Severe	Gluconate	3 – 4 g calcium gluconate, infused over 3 – 4 hours
Severe, symptomatic hypocalcemia (with serum ionized [Ca] < 1 mmol/L)	Gluconate or chloride	1 – 3 g calcium gluconate, or 500 – 1000 mg calcium chloride, infused over 10 min, may repeat ~ every 60 min as needed until stabilized, then supplement as suggested above based on serum ionized [Ca] and patient symptoms/ clinical status

* Calcium chloride should be administered via a central venous catheter to avoid extravasation and tissue necrosis; 1,000 mg calcium chloride = 13.6 mEq Ca, 1 g calcium gluconate = 4.65 mEq Ca

+ Typically a calcium gluconate dose of 1 – 2 g (4.65 – 9.3 mEq Ca) is mixed in 100 mL of D5W or NS and infused at a maximum rate of 1 g/hour for routine supplementation (non-emergent situations).

Kraft MD. Nutr Clin Pract 2015; Dickerson RN, et. al. Nutr Clin Pract 2007; Dickerson RN, et. al. Nutrition 2007; Dickerson RN, et. al. JPEN 2005; Dickerson RN, et. al. JPEN 2007

Empiric Treatment of Hypocalcemia

- Serum [Ca] < 7 mg/dL → Measure ionized [Ca] (could empirically treat (1 – 2 g Ca Gluconate) if ionized [Ca] not available)
- No apparent correlation between weight-based dose and change in serum [Ca]
- Reasonable to check serum ionized [Ca] ~ 10 – 12 hours after a dose, possibly more frequent if symptomatic/severe

Kraft MD. Nutr Clin Pract 2015; Dickerson RN, et. al. Nutr Clin Pract 2007; Dickerson RN, et. al. Nutrition 2007; Dickerson RN, et. al. JPEN 2005; Dickerson RN, et. al. JPEN 2007

Example Protocol – Treatment of Hypocalcemia

Serum Ionized [Ca]	IV Calcium Gluconate Dose	Recommended Serum [Ca] Monitoring
1.05 – 1.11 mmol/L	1 g IV over 60 minutes	With next AM labs
0.99 – 1.04 mmol/L	2 g IV over 120 minutes	~ 12-hrs after completing dose
0.93 – 0.98 mmol/L	3 g IV over 180 minutes	~ 12-hrs after completing dose
< 0.93 mmol/L	4 g IV over 120 – 240 minutes and notify MD	~ 12-hrs after completing dose, within 4 – 6-hrs after dose if symptomatic

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Hypercalcemia

Hypercalcemia

- Total serum [Ca] > 10.2 mg/dL (~2.55 mmol/L), ionized [Ca] > 1.3 mmol/L
  - Mild-moderate: total [Ca] 10.3-12.9 mg/dL, ionized [Ca] 1.3-1.6 mmol/L
  - Severe: total [Ca] $\geq$ 13 mg/dL, ionized [Ca] $\geq$ 1.6 mmol/L
- Most common causes: malignancy and primary hyperparathyroidism
  - Adrenal insufficiency, Paget's disease, Immobilization, rhabdomyolysis, Vitamin A or Vitamin D toxicity
  - Medications: thiazide diuretics, lithium
- Can lead to Ca-Phos precipitation, metastatic calcification, renal failure
- Mild hypercalcemia: Remove underlying cause(s), reduce dose in PN, hydration and ambulation

Bushinsky DA, et. al. Lancet 1998; French S, et. al. South Med J 2012; Davis KD, et. al. Crit Care Clin 1991; Mundy GR, et. al. Am J Med 1997

Treatment of Severe Hypercalcemia

- Hypercalcemic crisis: emergency requiring immediate treatment, can lead to acute kidney injury, ventricular arrhythmias, coma, death
- Aggressive hydration → IV normal saline ~200 – 300 mL/hr
- +/- IV loop diuretic (furosemide) → rigorous data lacking, consider if not responding to fluid (ensure adequate resuscitation first
- Consider calcitonin 4 units/kg q 12 hrs if inadequate response → usually limited to a few days (tachyphylaxis)
- Bisphosphonates:
  - Pamidronate 60 – 90 mg IV over 2 – 24 hrs
  - Chronic critical illness: 30 mg IV daily x 3 days (with calcitriol)
  - Zoledronic acid 4 – 8 mg IV over 15 minutes
  - Assess renal function/dosing

Kraft MD. Nutr Clin Pract 2015; Davidson TG. Am J Health-Syst Pharm 2001; Nierman DM, et. al. Chest 2000; Bushinsky DA, et. al. Lancet 1998; French S, et. al. South Med J 2012; Davis KD, et. al. Crit Care Clin 1991; Mundy GR, et. al. Am J Med 1997

Summary

- Phosphorus and Calcium are vital components of nutrition support therapy
- Influenced by several factors, including clinical condition and medications
- Provide appropriate maintenance doses, be pro-active in preventing abnormalities
- Important safety considerations when prescribing and compounding PN admixtures, and when treating abnormalities

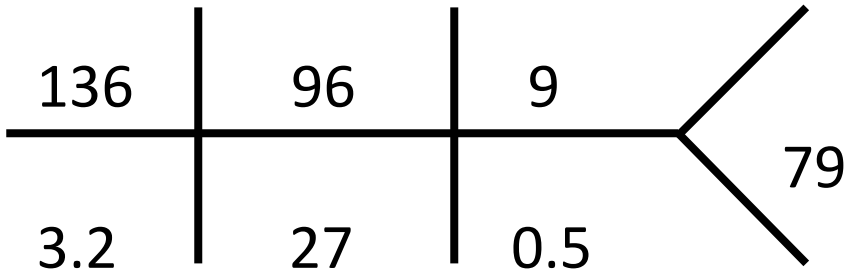
Patient Case

WS, 36-year-old woman, CC of constipation, abdominal pain, distention, nausea, vomiting, decreased appetite and decreased PO intake x 4 days.

- Gradual unintentional weight loss of ~10 pounds (4.5 kg) over the past month
- PMHx: chronic constipation, chronic abdominal pain, recurrent bowel obstructions, severe malnutrition
- PSHx: Multiple abdominal surgeries, including colon resection with colostomy and mucus fistula s/p takedown, SBR x 2 with LOA
- FH/SH: N/C, non-smoker, occ EtOH, endorses chronic prescription opioid Rx for chronic abd pain
- NKDA
- Medications: Hydrocodone/APAP 5mg/325mg 1 tab q 4 – 6 hrs (states taking 1 tab q 4 – 5 hrs ATC); Docusate 100 mg PO twice daily; Polyethylene glycol 3350, 17 g PO daily

PE: 162 cm (~ 5’ 4”), 41 kg, IBW 54.5 kg

Patient Case

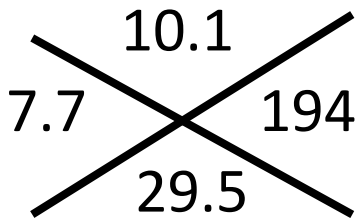


Ca = 7.9 mg/dL

Mg = 1.2 mg/dL

Phos = 2 mg/dL

Alb = 2.7 g/dL



25-OH vitamin D = 9 ng/mL (20-50)

Placed NG, conservative management

Failed several attempts at PO and enteral nutrition, NG replaced, PICC placed, plan to initiate PN

Learning Assessment

Which of the following is a potential cause of hypophosphatemia in this patient?

A. Hypervitaminosis D
B. Severe Malnutrition
C. Respiratory alkalosis
D. Constipation

Learning Assessment

Which of the following treatments for hypophosphatemia would you recommend at this time for this patient (PN therapy has not started)?

A. Initiate PN at goal, increase maintenance dose of phosphate by ~ 25%
B. Administer IV sodium phosphate 30 mmol x 1 over 2 hours
C. Administer oral Na-K phosphate 2 packets (16 mmol) dissolved in water x 1
D. Administer IV potassium phosphate 12 mmol IV x 1 over 2 hours

Learning Assessment

What would you recommend regarding this patient's serum calcium concentration?

A. Check serum ionized calcium concentration

B. Administer IV calcium gluconate 2 g x 1 dose over 1 hour

C. Administer IV calcium chloride 1 g x 1 dose over 1 hour

D. Administer PO calcium carbonate 1,000 mg (20 mEq) x 1 dose

ashp® MIDYEAR 2016
Clinical Meeting & Exhibition

Acid Base Disorders

Phil Ayers, Pharm.D., BCNSP, FASHP
Baptist Health Systems, Jackson, MS
Associate Clinical Professor
School of Pharmacy
University of Mississipp[i]

Objectives

1. Review the role of the kidneys and lungs in acid-base balance.
2. Describe the various acid-base disorders and discuss common causes.
3. Review acid-base disorders that may be seen with the use of parenteral nutrition.

Acid-Base Definitions

- Within cells, the major buffers are
  - Carbonic acid/Bicarbonate
  - Proteins
  - Phosphate
- Within erythrocytes, hemoglobin is major buffer
- Importance of carbonic anhydrase

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

  - Carbohydrate & fat metabolism generate ~15,000 mmol of CO_2 daily
    - ➢ Respiration prevents the accumulation of endogenously produced CO_2

Acid-Base Definitions

- Henderson-Hasselbalch equation (*37°C plasma*)

$$pH = 6.10 + \log \frac{[HCO_3^-]}{[0.03 \times PaCO_2]}$$

- 2 types of HCO_3^-
  - Calculated from arterial pH & $PaCO_2$
    - arterial blood gas
  - Measured as total CO_2 content
    - serum determination

5 Basic Acid Base Disorders

- Metabolic Acidosis
- Metabolic Alkalosis
- Respiratory Acidosis
- Respiratory Alkalosis
- Mixed Disorders

ABG Analysis

pH

- 7.35-7.45
- Normal, compensated or mixed

<7.35

- Acidemia
- Respiratory Acidosis ↑PCO_2
- Metabolic Acidosis ↓HCO_3

>7.45

- Alkalemia
- Respiratory Alkalosis ↓PCO_2
- Metabolic Alkalosis ↑HCO_3

Kidneys

- Regulate the concentration of bicarbonate in the blood
- 90% of reabsorption of bicarbonate occurs in the proximal tubules and is catalyzed by carbonic anhydrase
- Excrete 50-100 mEq/day of nonvolatile acids

Metabolic Acidosis

- Arterial pH less than 7.35 (7.35-7.45)
- Low bicarbonate (22-31mEq/L)
- Compensates by hyperventilating to increase carbon dioxide excretion (low PCO_2)
- **Calculate the Anion Gap**

Metabolic Acidosis

- Anion Gap = Na^+ - (Cl^- + HCO_3^-)
  - 3-11 mEq/L or 12 $\pm$ 4 mEq/L
- Normal Anion Gap (Hyperchloremic Acidosis)
- Elevated Anion Gap

Normal Anion Gap

- Hypokalemic
  - Diarrhea
  - Fistulous Disease
  - RTA-Type 1 (Distal)
  - RTA-Type 2 (Proximal)
  - Carbonic Anhydrase Inhibitors
- Hyperkalemic
  - Hypoaldosteronism
  - HCl
  - RTA-Type 4
  - K^+ Sparing Diuretics

Elevated Anion Gap

- Severe Renal Failure
- Lactic Acidosis
- Ketoacidosis
  - Starvation, Ethanol, DM
- Drug Intoxications
  - Ethylene Glycol, Methanol, Salicylates

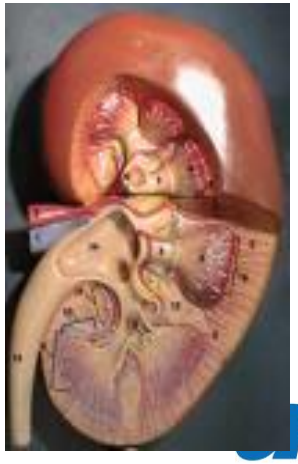
Mnemonics for Metabolic Acidosis

- Elevated Anion Gap
  - M-Methanol
  - U- Uremia
  - D- DKA
  - P- Paraldehyde
  - I- Isoniazid
  - L- Lactic Acidosis
  - E- Ethylene Glycol
  - S- Salicylates

- Normal Anion Gap
  - U- Ureteral diversion
  - S- Saline infusion
  - E- Exogenous Acid
  - D- Diarrhea
  - C- CA inhibitors
  - A- Adrenal insufficiency
  - R- RTA

Metabolic Alkalosis

- Elevated pH greater than 7.45 (7.35-7.45)
- Elevated bicarbonate (22-31mEq/L)
- Some respiratory compensation as a result of hypoventilation (minor)



Metabolic Alkalosis

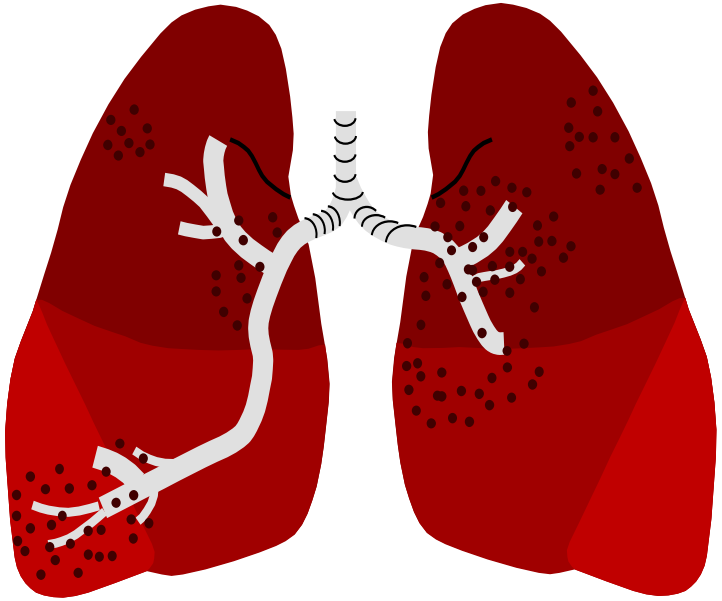
- Saline Responsive
  - Urine Chloride < 10mEq/L
- Diuretics
- Gastric Loss (vomiting, NG suction)
- Exogenous alkali administration (PN salts, bicarbonate, lactated ringers)
- Alkalosis associated with hypokalemia

Metabolic Alkalosis

- Saline-Resistant
  - Urine Chloride > 10mEq/L
  - Normotensive (K^+ depletion, hypercalcemia)
  - Hypertensive (Mineralcorticoids)

Lungs

- Regulate $paCO_2$
- Resting RR 14-18 BPM
- TV apx 500ml
- Oxygenation of blood
- Chemoreceptors
- 90% arterial O_2 is oxy-Hgb

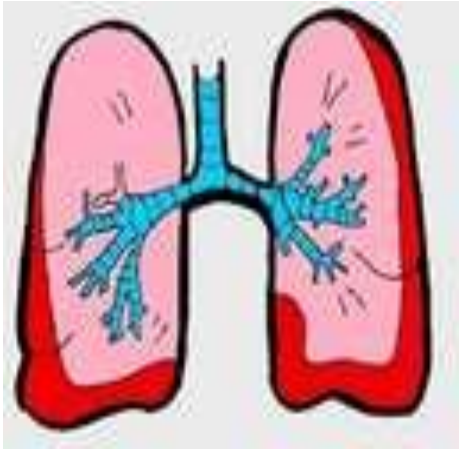


Normal Blood Gas Values

	Arterial Blood	Venous Blood
pH	7.40 (*7.35-7.45*)	7.36 (*7.31-7.41*)
PCO_2	35-45 mm Hg	42-55 mm Hg
PO_2	80-100 mm Hg	30-50 mm Hg
HCO_3^-	22-26 mEq/L	24-28 mEq/L
Base Excess	-2.4 to +2.3 mEq/L	-2.4 to 2.3 mEq/L
O_2 Saturation	> 90%	60-85%

Respiratory Acidosis

- pH less than 7.35 (7.35-7.45)
- Elevated PCO_2 (35-45mmHg)
- Hypoventilation
- Compensation via kidney



Respiratory Acidosis-Acute

- Acute CNS depression
  - Drug overdose (BDZ's, narcotics, propofol)
  - Head trauma
  - CVA
  - CNS infection (encephalitis)

Respiratory Acidosis-Acute

- Acute NM disease
  - Guillain-Barre syndrome
  - Spinal cord injury
  - Botulism
  - Organophosphate poisoning

Respiratory Acidosis-Acute

- Acute airways disease
  - Status asthmaticus
  - Upper airway obstruction
  - Exacerbation of COPD

Respiratory Acidosis-Acute

- Acute parenchymal and vascular disease
- Massive PE
- Acute pleural or chest wall disease
  - Pneumothorax
  - Hemothorax
  - Flail chest

Respiratory Acidosis-Chronic

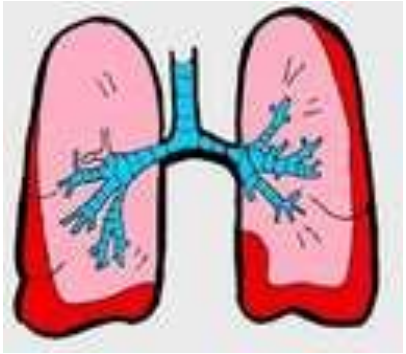
- Central sleep apnea
- Primary alveolar hypoventilation
- Obesity hypoventilation syndrome
- Spinal Cord Injury
- Diaphragmatic paralysis
- Amyotropic lateral sclerosis
- Myasthania gravis

Respiratory Acidosis-Chronic

- Muscular dystrophy
- Multiple sclerosis
- Poliomyelitis
- Hypothyroidism
- Kyphoscoliosis
- COPD
- Severe chronic interstitial lung disease

Respiratory Alkalosis

- Elevated pH greater that 7.45
- Low PCO_2 (35-45mmHg)
- Hyperventilation



Respiratory Alkalosis

- Hypoxia
- Parenchymal lung disease
  - Pneumonia
  - Bronchial asthma
  - Diffuse interstitial fibrosis
  - PE

Respiratory Alkalosis

- Medications and mechanical ventilation
  - Salicylate
  - Nicotine
  - Xanthine
  - Catecholamines
  - Analeptics

Respiratory Alkalosis

- CNS disorders
  - Meningitis, encephalitis
  - Cerebrovascular disease
  - Head trauma
  - Anxiety

Compensation

Disorder	pH	Primary alt.	Compensatory alt.
Met. Acidosis	↓	⇓HCO_3^-	↓$PaCO_2$
Met. Alkalosis	↑	⇑HCO_3^-	↑$PaCO_2$
Resp. Acidosis Acute	↓	⇑$PaCO_2$	↑HCO_3^-
Resp Acidosis Chronic	↓	⇑ $PaCO_2$	⇑ HCO_3^-
Resp Alkalosis Acute	↑	⇓$PaCO_2$	↓HCO_3^-
Resp Alkalosis Chronic	↑	⇓$PaCO_2$	⇓HCO_3^-

Compensation

Disorder	pH	Normal Level of Compensation
Met. Acidosis	↓	↓$PaCO_2$ = 1.2 x ↓ HCO_3^-
Met. Alkalosis	↑	↑ $PaCO_2$ = 0.6 x ↑ HCO_3^-
Resp. Acidosis Acute	↓	↑ HCO_3^- = 0.1 x ↑ $PaCO_2$
Resp. Acidosis Chronic	↓	↑ HCO_3^- = 0.4 x ↑$PaCO_2$
Resp. Alkalosis Acute	↑	↓ HCO_3^- = 0.2 x ↓$PaCO_2$
Resp. Alkalosis Chronic	↑	↓HCO_3^- = 0.4 x ↓ $PaCO_2$

Case Study

77 yo female with PMH significant for COPD. Pt is admitted to ICU with SOB. ABG's and Lab on arrival:

Sodium	146	(135-145mEq/l)	pH	7.38	(7.35-7.45)
Potassium	4	(3.5-5mEq/l)	pCO2	62.9	(35-45mmHg)
Chloride	104	(98-107mEq/L)	PO2	72	(80-100mmHg)
CO_2	34	(22-31mEq/L)	HCO_3	36.5	(24-30 mEq/L)
BUN	27	(7-20mg/dl)	BE	10.0	
Cr	1.2	(0.7-1.5mg/dl)			

What disorder is present

Case Study

77 yo female with PMH significant for COPD. Pt is admitted to ICU with SOB. ABG's and Lab on arrival:

Sodium	146	(135-145mEq/l)	pH	7.38	(7.35-7.45)
Potassium	4	(3.5-5mEq/l)	pCO2	62.9	(35-45mmHg)
Chloride	104	(98-107mEq/L)	PO2	72	(80-100mmHg)
CO_2	34	(22-31mEq/L)	HCO_3	36.5	(24-30 mEq/L)
BUN	27	(7-20mg/dl)	BE	10.0	
Cr	1.2	(0.7-1.5mg/dl)			

Level of Compensation

$HCO_3 = 0.4 \times \uparrow pCO_2 = \uparrow HCO_3 = 0.4 \times (62.9-40)$

$= 0.4 \times 22.9 = 9.16 \; (27 + 9.16 = 36.2)$

Compensated Respiratory Acidosis

Compensation

- Higher 10% predicted
  - Met Alk + Resp Acid
  - Met Acid + Resp Alk
- Lower 10% predicted
  - Met + Resp Acidosis
  - Met + Resp Alkalosis

Mixed Acid-Base Disorders

- Metabolic Acidosis and Respiratory Acidosis
  - Cardiopulmonary arrest
  - Respiratory failure with anoxia
- Metabolic Alkalosis and Respiratory Alkalosis
  - Congestive heart failure and vomiting
  - Diuretic therapy and hepatic failure
  - Diuretic therapy and pneumonia

Mixed Acid-Base Disorders

- Metabolic Alkalosis and Respiratory Acidosis
  - Diuretic Therapy and COPD
  - Vomiting and COPD
- Metabolic Acidosis and Respiratory Alkalosis
  - Salicylate overdose
  - Septic Shock
  - Sepsis and renal failure

Mixed Acid-Base Disorders

- Metabolic Alkalosis and Metabolic Acidosis
  - Diuretic Therapy and ketoacidosis
  - Vomiting and renal failure
  - Vomiting and lactic acidosis/ketoacidosis
- Mixed Hyperchloremic and High AG Metabolic Acidosis
  - Diarrhea and Lactic/ketoacidosis
  - RTA and chronic renal failure

Parenteral Nutrition

- Metabolic acidosis-excessive chloride in PN
- Metabolic alkalosis-excessive acetate in PN
- Respiratory Acidosis-overfeeding (uncommon)

Parenteral Nutrition/IV Therapy

- Know your IV nutritional therapy (Amino Acids)
- Primary IV
- Medication profile
- Determine loss from tubes, drains, ostomy, renal

Parenteral Nutrition

- HPN Study
  - Retrospective observational cohort
  - 39 patients (1989-2006)
  - 10/39 (25.6%) patients showed evidence of acid-base disturbance (4 severe)
  - 8 patients-metabolic acidosis

- PN Error
  - 69yoF (44kg)-bowel resection-short gut syndrome
  - Accidental bolus of PN and IVFE (lipids)
  - 1200mL of 1800mL PN and 200mL of IVFE <1 hour
  - 6.99/64/78/15, lactate 11.8 mmol/L, Glucose 775mg/dl
  - Combined metabolic and respiratory acidosis
  - Hyperviscosity syndrome
  - Plasma exchange

- e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 6 (2011) e31ee35
  J Parenter Enteral Nutr.2016;40:883-885

Case Study 1

A.A. 44-year-old with past medical history significant for lupus is admitted via the ED. The patient has a two-day history of acute severe diarrhea. Patient is dx with RTA-Type 1 by nephrology. Day 8 of hospital stay, patient develops respiratory failure is intubated and transferred to ICU. Pt is placed on MV and sedated with lorazepam.

Current Medication Regimen:

½ NS	50ml/h
TPN	75ml/h
Lorazepam	2mg/h
Enoxaparin	30mg SubQ Daily
Famotidine	20mg IV Daily
Levofloxacin	250mg IVPB Daily

Case Study 1

Electrolytes:		ABG		
Sodium	134 (135-145mEq/l)	pH	7.31	(7.35-7.45)
Potassium	2.9 (3.5-5mEq/l)	pCO2	33	(35-45mmHg)
Chloride	112 (98-107mEq/L)	PO2	93	(80-100mmHg)
CO_2	16 (22-31mEq/L)	HCO_3	16	
BUN	62 (7-20mg/dl)	BD	-9	($\pm$2)
Cr	4.5 (0.7-1.5mg/dl)			

Case Study 1

Electrolytes:			ABG		
Sodium	134	(135-145mEq/l)	pH	7.31	(7.35-7.45)
Potassium	2.9	(3.5-5mEq/l)	pCO2	33	(35-45mmHg)
Chloride	112	(98-107mEq/L)	PO2	93	(80-100mmHg)
CO_2	16	(22-31mEq/L)	HCO_3	16	
BUN	62	(7-20mg/dl)	BD	-9	($\pm$ 2)
Cr	4.5	(0.7-1.5mg/dl)			

Metabolic Acidosis:

1. RTA-1
2. Diarrhea
3. PN
4. Lorazepam

Case Study 1

P.T. 65 yo male admitted to SICU s/p MVC. Currently on mechanical ventilation, sedation with midazolam infusion. Patient's abdomen is distended with no bowel sounds c/w ileus. Nasogastric tube to suction with 300-400cc out per 8 hour shift.

Current Medication Regimen:

Piperacillin/Tazobactam	3.375 IV q 8h
Esomeprazole	40mg IV daily
A.A.5/15 multi-chamber	60ml/h
LR	30ml/h (KVO)
Furosemide/Albumin/Chlorothiazide	10ml/h

240mg 5% 240mg

Case Study 1

Electrolytes:			ABG		
Sodium	144	(135-145mEq/l)	pH	7.52	(7.35-7.45)
Potassium	3.1	(3.5-5mEq/l)	pCO2	48	(35-45mmHg)
Chloride	94	(98-107mEq/L)	PO2	70	(80-100mmHg)
CO_2	40	(22-31mEq/L)	HCO_3	39	
BUN	45	(7-20mg/dl)	BE	14.1	($\pm$ 2)
Cr	2.5	(0.7-1.5mg/dl)			

Case Study 1

Electrolytes:		ABG	
Sodium	144 (135-145mEq/l)	pH	7.52 (7.35-7.45)
Potassium	3.1 (3.5-5mEq/l)	pCO2	48 (35-45mmHg)
Chloride	94 (98-107mEq/L)	PO2	90 (80-100mmHg)
CO_2	40 (22-31mEq/L)	HCO_3	39
BUN	45 (7-20mg/dl)	BE	14.1 ($\pm$ 2)
Cr	2.5 (0.7-1.5mg/dl)		

Metabolic Alkalosis

1. Acetate in PN
2. LR
3. NG to suction
4. Diuretic/Albumin infusion

The commercially available (multi chamber) parenteral nutrition products are balanced equally with chloride/acetate:

A TRUE

B FALSE

The commercially available (multi chamber) parenteral nutrition products are balanced equally with chloride/acetate:

B FALSE

Parenteral nutrition is a common cause of respiratory acidosis:

A TRUE

B FALSE

Parenteral nutrition is a common cause of respiratory acidosis:

B FALSE

Key Takeaways

- Key Takeaway #1
  - Acid-base balance involves kidneys, lungs and other buffers.
- Key Takeaway #2
  - Parenteral nutrition (PN) does play a role in acid-base balance and patients should be stable before initiating PN.
- Key Takeaway #3
  - Determination of acid-base abnormalities requires a review and understanding of disease states and/or medications that may influence acid-base disorders.

References:

1. Roberts AL: Arterial blood gases and acid-base balance. IN: Lee M (ed). Interpreting Laboratory Data, 5th ed. Bethesda, MD: ASHP, 2013: 193-205.
2. DuBose TD, Jr.. Chapter 47. Acidosis and Alkalosis. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson J, Loscalzo J. eds. *Harrison's Principles of Internal Medicine, 18e.* New York, NY: McGraw-Hill; 2012. http://accesspharmacy.mhmedical.com/content.aspx?bookid=331&Sectionid=40726770. Accessed December 29, 2014.
3. Horne C, Derrico D: Mastering ABGs, the art of arterial blood gas measurement. AJN 99 (8):26-32, 1999.
4. Effros RM, Widell JL: Acid-base balance. IN: Murry J, Nadel J (eds). Textbook of Respiratory Medicine, 2nd ed. Philadelphia, PA: W.B. Saunders, 1994: 175-98.
5. Bernards WC, Kirby R: Acid-base chemistry and physiology. IN: Civetta J, Taylor R, Kirby R (eds). Critical Care, 2nd ed. Philadelphia PA: Lippincott, 1992: 343-52.
6. Langley G, Canada T, Day L: Acid-base disorders and nutrition treatment. Nutrition in Clinical Practice, Jun. 2003, vol.18, pp 259-261.
7. Ayers P, Warrington L: Diagnosis and treatment of simple acid-base disorders. Nutrition in Clinical Practice, Vol.23, pp122-127.
8. Ayers P, Dixon C, Mays A: Acid-base disorders: learning the basics. Nutrition in Clinical Practice, published online December 2014.