Carol Rees Parrish, M.S., R.D., Series Editor

# Low Serum Phosphorus Got You Down?



Kendra Glassman

Phosphorus is an essential mineral utilized by every cell in the body. Alterations in serum values can have significant clinical ramifications especially in the critically ill patient with low phosphorus levels. Until recently, repleting low phosphorus levels was a routine process and supply issues were not a concern. However, phosphorus was not spared with the numerous other drug and nutrient shortages. Clinicians must now become creative and judicial with phosphorus repletion in the critical care setting. This article will outline the importance of phosphorus, clinical sequelae for high and low phosphorus levels, as well as alternative suggestions for supplementing low levels.

#### INTRODUCTION

The recent medication and nutrient shortages have left clinicians with no other choice but to be resourceful in devising alternative solutions to provide optimal patient care. Phosphorus, a critical component of all living cells, has unfortunately not been spared from these shortages. This article will give you the background on the importance of phosphorus as well as creative ways to manage the shortages.

Phosphorus is the second most abundant mineral in the body and is an essential element for all cells. It is found mainly in the bones and soft tissues with only 1% of the body's phosphorus stores reflected in serum levels. It mainly exists as phosphate in the serum and is the main intracellular anion. Phosphorus serves

Kendra Glassman MS, RD, CNSC, Nutrition Support Specialist, University of Virginia Health System, Digestive Health Center, Charlottesville, VA Rocky Mountain Hospital for Children, Denver, CO. a variety of important functions including: bone and cell membrane composition, maintenance of serum pH, glucose utilization, glycolysis, tissue oxygenation, neurological function, and muscular function (especially the myocardium and diaphragm). It is also required in all cellular functions that require energy by providing energy rich bonds in the form of adenosine triphosphate (ATP).<sup>1</sup>

Serum phosphorus levels are regulated by interplay between phosphorus uptake and excretion as well as intestinal absorption, redistribution between intracellular and extracellular fluids, and hormone regulated bone metabolism to maintain a serum phosphorus level of 2.7 to 4.5 mg/dL. The typical diet provides ~800-1500 mg (26-48 mMol) phosphorus daily. The Reference Daily Intake (RDI) for phosphorus is 700 mg (22.6 mMol) per day.<sup>2,3</sup>

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#### Hyperphosphatemia

Hyperphosphatemia most often occurs in the setting of renal insufficiency. It can also occur as a result of cellular destruction as phosphorus is released into the ECF. This often occurs with massive trauma, cytotoxic agents, hypercatabolism, hemolysis, rhabdomyolysis, and malignant hyperthermia. Respiratory or metabolic acidosis and provision of large quantities of phosphatecontaining laxatives or enemas (Fleet<sup>®</sup>, Fleet<sup>®</sup> Neutra-Phos<sup>®</sup>), especially in the elderly can also cause phosphorus to shift. Use enemas with caution as risks may include:

- Significant fluid shifts within the colon resulting in intravascular volume depletion.
- A phosphate nephropathy has been documented due to transient, and sometimes severe increases in serum phosphate, in conjunction with volume depletion from fluid shifts.

#### Table 1. Causes of Hyperphosphatemia<sup>1,2</sup>

- Cellular Breakdown
  - o Trauma
  - o Burns
  - o Tumor lysis syndrome
  - o Rhabdomyolysis
  - o Chemotherapy
  - o Radiation
  - o Hemolysis
- Excessive intake
  - o Fleets enema
  - o NaPhos bowel prep in renal failure
- Intracellular—extracellular transfer
- Renal insufficiency

#### Table 2. Symptoms of Hypophosphatemia<sup>7</sup>

#### Respiratory

- Respiratory muscle dysfunction Acute respiratory failure
  - Failure to wean from mechanical ventilation

Decreased peripheral oxygen delivery

#### Cardiovascular

- Decreased myocardial contractility Acute heart failure Increased inotropic requirement
- Arrhythmia

Ventricular tachycardia Supraventricular tachycardia Premature beats

#### Hematologic

Hemolysis

Leukocyte dysfunction

#### Endocrine

Insulin resistance

#### Neuromuscular

Skeletal muscle weakness

Rhabdomyolysis

Polyneuropathy

Altered mental status

Seizures

Encephalopathy

Central pontine myelinolysis

- Electrolyte disturbances such as hyperphosphatemia, hypocalcemia, and hypokalemia.
- Rise in serum phosphate even in those patients with normal renal function.<sup>4</sup>

The most serious complication of hyperphosphatemia is metastatic and vascular calcification of non-skeletal tissues.<sup>2</sup> Additional consequences of hyperphosphatemia include secondary hyperparathyroidism and renal osteodystrophy. Other signs and symptoms of hyperphosphatemia are due to the development of hypocalcemia and manifest as anorexia, nausea, vomiting, dehydration, and neuromuscular irritability. Although hyperphosphatemia can cause long-term complications, an elevated phosphorus level is not an acute, critical concern.<sup>5</sup> There are no concrete guidelines regarding when to treat elevated phosphorus levels, however, our nephrologists at UVA typically monitor and only add phosphorus binders if phosphorus levels remain high for a prolonged period of time (i.e., treat a phosphorus of 9 immediately, while a phosphorus of 6 can wait for many weeks). Given concerns for metastatic calcification (as it is microscopic and affects the vasculature), when the calcium-phosphorus product remains elevated, it is prudent to try to keep this value below 55-65 with the use of phosphorus binders. See Table 1 for causes of hyperphosphatemia.

#### Hypophosphatemia

Hypophosphatemia on the other hand, can have more serious acute clinical ramifications such as in refeeding syndrome.<sup>6</sup> Symptoms do not occur in all cases of hypophosphatemia, but they can be fatal when they do. Symptoms of hypophosphatemia include: respiratory, cardiovascular, hematologic, endocrine and



Figure 1. Phosphate Metabolism and Causes of Hypophosphatemia<sup>7</sup>

#### Table 3. Medications that lower Phosphorus<sup>9</sup>

#### Antacids

(containing aluminum, calcium or magnesium bind phosphate in the gut)

• Mylanta, Maalox, Tums

#### **Anticonvulsants**

• Phenobarbital, carbamazepine

#### Bile Acid Sequestrants (can decrease oral absorption of phosphate)

- Cholestyramine (Questran)
- Colestipol (Colestid)

# Corticosteroids

#### (may increase urine Phosphorus levels)

• Prednisone, methylprednisolone

#### Anti-ulcer (binds Phosphorus)

Carafate

#### **Phosphorus Binders**

 Calcium Acetate (Phos-Lo®), Sevelamer (Renagel®) and Sevelamer Carbonate (Renvela®)

neuromuscular (see Table 2).<sup>7</sup> Respiratory and cardiac effects are the most serious symptoms. Low phosphorus levels are associated with respiratory muscle weakness, which can result in acute respiratory problems and difficulty weaning from the ventilator. Phosphate is also contained in 2,3 DPG (diphosphoglycerate), an important component of functioning hemoglobin. Depletion of 2,3-DPG decreases oxygen delivery to peripheral tissues by creating a local "hypoxia" if you will—2,3 DPG will not release oxygen in the periphery in the setting of hypophosphatemia. Hypophosphatemia can also cause myocardial dysfunction and arrhythmias

#### Table 4. Concentrated Phosphate Shortage Guidelines<sup>8</sup>

- 1. Consider using the alternate salt IV phosphate as available and balance the sodium and potassium accordingly.
- 2. Consider oral or enteral phosphate products/ supplements to replete or maintain serum phosphorus concentrations.
- 3. Consider commercially available standardized, commercial PN products that contain phosphate.
- 4. Decrease the daily amount/dose of phosphate added to PN formulations.
- 5. Reserve phosphates for pediatric and neonatal patients requiring PN.
- 6. Reserve phosphates for those patients with a therapeutic medical need for phosphorus.
- 7. Consider provision of daily IV fat emulsion to all PN patients as clinically appropriate.

# Note: IV fat emulsions contain 15 mmol/liter of phosphate as egg phospholipids.

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due to decreased levels of ATP in the myocardium, leading to decreased contractility.<sup>7</sup> See Figure 1 for a detailed view of phosphate metabolism and causes of hypophosphatemia.

The growing and critical shortage of phosphorus

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#### Table 5. Phosphorus Content of Select Medications<sup>9,10</sup>

Oral Phosphorus Supplementation	Other Medications		
Phos-Nak ® powder per packet:	Fleet® Phospho-Soda*: Dose = 30mL		
<b>8 mmol Phos;</b> 7.1 mEq K; 6.9 mEq Na	125 mmol Phos (4.16 mmol/mL);		
K-Phos Neutral® tablet:	145 mEq Na		
<b>8 mmol Phos;</b> 1.1 mEq K; 13 mEq Na	Intravenous Fat Emulsions		
	15 mmol/liter Phos (as egg phospholipids)		
Neutra-Phos® per packet:	Not to be given via feeding tube or PEG:		
<b>8 mmol Phos;</b> 7.1 mEq K; 7.1 mEq Na	Fleet® Enema: Dose = 114mL		
Neutra-Phos K® per packet:	163 mmol Phos (1.43mmol/mL);		
<b>8 mmol Phos;</b> 14.25 mEq K; 0 mEq Na	184 mEq Na per enema		
	Fleet® Enema EXTRA®: Dose = 197mL		
	184 mmol Phos (0.93 mmol/mL);		
	189 mEq Na per enema		

\* Caution when used as an over the counter bowel cleansing regimen as it could cause acute kidney injury in those at risk. http://www.fda.gov/ Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126084.htm

makes intravenous replacement near impossible, let alone provision of baseline needs for those patients requiring parenteral nutrition (PN). One of the first steps is to review medications that may bind phosphorus aggravating low serum levels (see Table 3). Oral/enteral supplementation is preferred if hypophosphatemia is mild and the patient has a functional GI tract. Supplementing intravenously is often indicated if symptoms are moderate to severe, if oral phosphorus supplementation is not tolerated, and/or in those patients without a functional gut (although these shortages has made many a clinician reevaluate when a GI tract is

functional or not). The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) has developed conservation recommendations and alternate therapy measures in order to cope with the shortages (see Table 4).<sup>8</sup>

Using alternative phosphorus salts (i.e. potassium or sodium), depending on availability, is the easiest route, as well as using pre-mixed PN solutions, which contain phosphorus. The clinician should also seriously consider oral/enteral phosphorus supplementation. If any medications are given orally/enterally, a trial of oral

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## Table 6. Sources of Phosphorus in Food Items <sup>11</sup>

Food Item (1/2 cup = 120 mL)	Ph	Phosphorus Content		
(	Mg	mMol	mEq	
Milk (lactose free or regular)				
Whole Milk	103	3.3	6.6	75
• Low Fat (2%)	137	4.4	8.8	70
• Skim	128	4.1	8.3	45
Chocolate (low-fat)	128	4.1	8.3	90
Buttermilk (reduced fat)	101	3.2	6.5	70
Condensed milk	387	12.5	25.0	490
Evaporated milk	256	8.3	16.5	169
<ul> <li>Fortified milk (1/2 cup skim with 2 Tb skim milk solids added)</li> </ul>	328	10.6	21.2	80
Yogurt				
• Fat Free	135	4.3	8.7	55
Greek (plain, nonfat)	153	4.9	9.9	65
Whole	108	3.5	7.0	70
• Fruit, low fat	123	4.0	8.0	110
Kefir/liquid yogurt	113	3.6	7.3	70
<ul> <li>Danimals Smoothie ™</li> </ul>	56	1.8	3.6	70
Pudding, instant (prepared with 2% milk)				
Chocolate	338	11.2	21.8	150
• Vanilla	106	3.4	6.8	130
Other Food Items				
Chocolate Milkshake	96	3.1	6.2	120
Vanilla Milkshake	82	2.6	5.3	125
• Eggnog	139	4.5	9.0	110
Ensure®/Ensure® Plus	88/105	2.8/3.4	5.6/6.8	125/175
Boost®/Boost® Plus	105/105	3.4/3.4	6.8/6.8	120/180
<ul> <li>Carnation Instant Breakfast™ (made with nonfat milk)</li> </ul>	350	11.3	22.6	110

## Note: (DRI = 700mg/ 22.6mMol/ 45.2mEq)

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phosphorus supplementation is warranted. Encouraging the patient to eat high phosphorus containing foods or administering liquid food items high in phosphorus through a feeding tube is another tool one can use to help with repletion. Administering medications high in phosphorus such as Fleet® enemas or NaPhos® bowel preps may work to your advantage in those that need phosphorus AND a bowel regimen. See Table 5 and 6 for a list of oral phosphorus replacements and foods high in phosphorus, respectively.

#### CONCLUSION

Phosphorus is a key nutrient in the human body, involved in many critical functions, not the least of which is nutrient utilization. The recent PN shortages have made supplementing low phosphorus levels difficult, but not impossible. Sometimes these challenges force us to rethink our practices, and make it even better. There is more than one way to treat hypophosphatemia; utilizing oral/enteral medications or food/beverages should be considered in lieu of intravenous supplementation when the GI tract is available; we have found it is even more available than we realized before.

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