A Quick Reference on Phosphorus

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KEYWORDS

• Phosphorus • Phosphate • Anion • Hypophosphatemia • Hyperphosphatemia

KEY POINTS

- Phosphorus, or phosphate, is the body's major intracellular anion involved in cellular energy, membrane integrity, and metabolism.
- Technically, phosphorus is an element and phosphate is a molecular anion; however, the terms are often used interchangeably. For simplicity, phosphate will be used throughout the text to refer to either.
- Phosphate is vital to normal dentition and osseous matrix, tissue oxygenation, and enzymatic processes.
- Distribution of phosphate is primarily intracellular; thus, measuring serum phosphate is not necessarily reflective of total body stores.
- Numerous causes of hypophosphatemia and hyperphosphatemia exist in dogs and cats, and the underlying cause should be treated in addition to managing the phosphate derangement.

- Phosphorus, or phosphate, is the body's major intracellular anion and is required to produce ATP, guanosine triphosphate, cyclic adenosine monophosphate, and phosphocreatine, which function to maintain cellular membrane integrity, energy stores, metabolic processes (muscle contraction, nerve impulse conduction, cell transport), and biochemical messenger systems.[1–3] In addition, phosphorus is vital in maintaining normal bone and dental matrix, regulating tissue oxygenation (2,3-diphosphoglycerate [2,3-DPG]), buffering acidotic conditions in the body, and regulating many enzymes (eg, 1α-hydroxylase and glutaminase).
- Phosphate distribution
  - 80% to 85% stored as hydroxyapatite in bone matrix
  - 14% to 15% stored in soft tissues, such as muscle
  - Less than 1% stored in the extracellular space

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- Phosphate regulation
  - Parathyroid hormone (↑ release of phosphate from bone, ↑ renal phosphate excretion), calcitriol (↑ intestinal phosphate absorption), and calcitonin (↑ renal phosphate excretion) regulate phosphate.
  - Phosphatonins, such as fibroblast growth factor-23 (FGF-23), are phosphate regulatory substances with autocrine, paracrine, or endocrine mechanisms of action. FGF-23 has primarily a phosphaturic action.
  - Gastrointestinal absorption of phosphorus is linearly related to intake and 60% to 70% of ingested phosphorus is absorbed in the small intestine.
  - In the kidneys, 60% to 100% (depending on bodily needs) of filtered phosphate is reabsorbed in the proximal convoluted tubule. Growth hormone, insulin, insulin-like growth factor 1, and thyroxine increase renal tubular phosphate reabsorption.

ANALYSIS

- Indications
  - Serum phosphate is commonly measured during systemic disease and is included in many chemistry panels. It should be measured and monitored regularly in patients with acute kidney injury or chronic kidney disease, in those taking oral phosphate binders, in those undergoing chemotherapy with a high tumor burden, after refeeding if severely malnourished, in those being treated for diabetes mellitus or hyperosmolar conditions, in patients with concurrent hypercalcemic conditions, and in those with acute or chronic anorexia, vomiting, or diarrhea.
- Reference range
  - Serum concentrations of phosphate measured by blood chemistry analyzers do not necessarily reflect whole-body phosphate balance because it is the predominant intracellular anion and rapid transcellular shifts can occur.
  - Phosphate concentration is typically expressed as phosphate mass (mg/dL). Normal range of serum phosphate concentration in dogs and cats is 2.5 mg/dL to 6 mg/dL (0.8–1.9 mmol/L), with variation expected based on patient age and chemistry analyzer used. Serum phosphate concentrations up to 10 mg/dL have been reported in normal healthy puppies.
  - Conversion: normal serum phosphate concentration of 3.1 mg/dL = 1 mmol/L phosphate = 1.8 mEq/L phosphate
  - Transient peaks in serum phosphate occur 6 to 8 hours after a meal; therefore, ideally collect blood samples after a 12-hour fast.
- Danger values
  - Severe hypophosphatemia (below 1 mg/dL or 0.31 mmol/L) is generally associated with whole-body phosphate depletion and can result in hemolysis or rhabdomyolysis.
  - Severe hyperphosphatemia can result in tetany (due to hypocalcemia), soft tissue mineralization (especially if calcium × phosphate product is >60–70), and metabolic acidosis (for each 1-mg/dL increase in phosphate expect a 0.55-mEq/L decrease in bicarbonate). Severe acute hyperphosphatemia without coexisting hypercalcemia (eg, phosphate enema toxicity) can result in acute kidney injury.
- Artifacts
  - Mannitol (≥25 mmol/L) can interfere with DuPont Automatic Clinical Analyzer colorimetric tests, leading to spurious hypophosphatemia.
  - Hemolysis, hypertriglyceridemia, hyperbilirubinemia, and presence of a monoclonal gammopathy can lead to spurious hyperphosphatemia.