Disorders of Calcium and Phosphate Metabolism in Horses

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KEYWORDS

• Hypocalcemia • Hypercalcemia • Parathyroid • Horse • Foal
• Hyperphosphatemia

CALCIUM

Several cellular processes (intracellular, extracellular, physiologic, and pathologic) depend on calcium as a regulatory ion. Calcium is necessary for blood coagulation, neuromuscular excitability, muscle contraction, enzymatic activation, hormone secretion, cell division, and cell membrane stability.[1] Calcium is also central to cell death by participating in free radical production, cytokine release, protease activation, and apoptosis. Because of its physiologic and pathologic functions, keeping extracellular calcium concentrations within a narrow range is important.[1] Calcium is found in 3 main compartments: *the skeleton, soft tissues*, *and the extracellular fluid* where it has structural and nonstructural functions. Approximately 99% of the total body calcium is in the skeleton as hydroxyapatite crystals, providing support against gravity, protecting internal organs (brain, spinal cord, lungs, heart), acting as a niche for blood-forming elements, and serving as a reservoir for calcium. The rest of the calcium is in the cell membrane, mitochondria, endoplasmic reticulum (0.9%), and in the extracellular fluid (0.1%).[2] Cytosolic free calcium concentrations are low. In equine blood, calcium is found in free or ionized form (50%–58%); bound to proteins (40%–45%); and complexed to anions, such as citrate, bicarbonate, phosphate, and lactate (5%–10%) (**Fig. 1**).[1–6] Free or ionized calcium (Ca^{2+}) is the biologically active form of calcium. Albumin is the main calcium-binding protein and its affinity for Ca^{2+} is pH-dependent. In acidosis there is decreased Ca^{2+} binding to albumin (higher blood Ca^{2+}); whereas, in alkalosis blood Ca^{2+} concentrations are lower. Total calcium concentrations remain unchanged. Hypoalbuminemia results in total hypocalcemia (pseudohypocalcemia) with Ca^{2+} concentrations within the normal range. Plasma and serum calcium concentrations are lower in foals than in adult horses.[7]

1 mg/dL $\times$ 0.25 = mmol/L; 1 mmol/L = 4 mg/dL of calcium.

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Vet Clin Equine 27 (2011) 129–147
doi:10.1016/j.cveq.2010.12.010 **vetequine.theclinics.com**
0749-0739/11/$ – see front matter

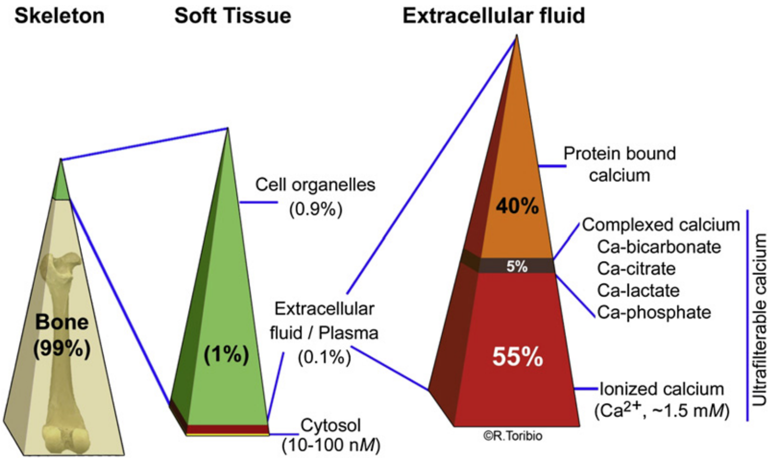

Fig. 1. Calcium distribution in the body. Around 99% of the total calcium in the body is in bone with the remaining 1% present in the extracellular fluid (0.1%) and cellular organelles (0.9%). In the extracellular compartment, calcium exists as a free, ionized or active form (Ca^{2+}), bound to proteins, and complexed to anions, such as bicarbonate, phosphate, citrate, and lactate. In horses, serum ionized calcium represents 50% to 58% of the total extracellular calcium.[4–6] Ionized and complex calcium are filtered through the glomerulus (ultrafilterable) but are rapidly reabsorbed by the nephron. (*Courtesy of* Ramiro E. Toribio, DVM, MS, PhD, Columbus, OH.)

As for calcium, total magnesium in blood is bound to proteins, complexed to anions and free or ionized (Mg^{2+}; active). See the article by Stewart elsewhere in this issue for further exploration of this topic.

PHOSPHORUS

Phosphorus represents approximately 1.0% of the body weight, with most (85%) located in the bone matrix as hydroxyapatite, 15.0% in blood and soft tissues, and less than 0.1% in the extracellular fluid. In blood and soft tissue, phosphorus is the major intracellular anion existing in organic (phospholipids, nucleic acids, phosphoproteins, creatine phosphate, adenosine triphosphate, cyclic adenosine monophosphate, nicotinamide adenine dinucleotide phosphate, 2,3-diphosphoglycerate) and inorganic forms. Similar to free cytosolic calcium, free cytosolic phosphate concentration is low. In blood, phosphorus exists as organic and inorganic phosphates. Organic phosphate consists of phosphate esters (phospholipids) bound to proteins and blood cells, representing most of the phosphorus in circulation (70%); however, only inorganic phosphate (P_i) is measured by routine methods. P_i is found as ionized phosphate (approximately 50%), complexed with cations (Na^+, Ca^{2+}, Mg^{2+}; approximately 35%), and bound to proteins (approximately 15%). Four forms of P_i exist in biologic fluids: H_3PO_4, $H_2PO_4^-$, HPO_4^{2-}, PO_3^{2-}; however, at physiologic pH only divalent (HPO_4^{2-}) and monovalent ($H_2PO_4^-$) are present at significant concentrations. The average valence of serum P_i of –1.8, giving a milliequivalency of 1.8 mEq per 1 mmol of P_i. 1 mmol/L = 3.1 mg/dL; mg/dl $\times$ 0.323 = mmol/L.

Phosphate plays essential roles in muscle contraction; neurologic function; enzyme activity; electrolyte transport; oxygen transport; gene transcription; and in the metabolism of proteins, carbohydrates, and fats.[8] Unlike Ca^{2+}, serum P_i has more fluctuations that are influenced by diet, age, physiologic status, activity, diseases, glycemia,