Hemolytic Anemia in Dogs and Cats Due to Erythrocyte Enzyme Deficiencies

Jennifer L. Owen, DVM, PhD, John W. Harvey, DVM, PhD*

KEYWORDS

- Hemolytic anemia • Erythrocyte • Pyruvate kinase deficiency
- Phosphofructokinase deficiency • Dogs • Cats

Mature mammalian erythrocytes or red blood cells (RBCs) circulate in the blood for several months despite limited synthetic capacities and repeated exposure to mechanical and metabolic insults. RBCs do not have nuclei, so they cannot synthesize nucleic acids or proteins. In addition, the loss of mitochondria during the maturation of reticulocytes prevents the generation of adenosine triphosphate (ATP) by the Krebs cycle and oxidation phosphorylation. However, erythrocytes still require energy in the form of ATP for maintenance of shape, deformability, active membrane transport, and the synthesis of glutathione.[1] Thus, mature erythrocytes depend solely on anaerobic glycolysis or the Embden-Meyerhof pathway for ATP generation (**Fig. 1**). Consequently, deficiencies of rate-controlling enzymes required for anaerobic glycolysis can have significant effects on erythrocyte function and survival, leading to hemolytic anemia.[1]

DIFFERENTIAL DIAGNOSIS

Congenital deficiencies of rate-controlling enzymes involved in anaerobic glycolysis such as phosphofructokinase (PFK) and pyruvate kinase (PK) result in hemolytic anemia with a regenerative bone marrow response characterized by a reticulocytosis and polychromasia. These enzyme deficiencies must be differentiated from more common causes of hemolytic anemia including primary or idiopathic immune-mediated hemolytic anemia (IMHA) or IMHA secondary to another underlying cause such as hemotrophic parasites (eg, *Mycoplasma haemocanis, Mycoplasma haemofelis, Babesia canis, Babesia gibsoni, Cytauxzoon felis,* or *Bartonella* spp), other infectious agents, neoplasia, or drug/chemical/toxin exposure. Congenital enzyme-deficient animals should be Coombs' test negative,

The authors have nothing to disclose.
Department of Physiological Sciences, University of Florida College of Veterinary Medicine, Gainesville, FL 32610, USA
* Corresponding author. 1600 SW Archer Road, PO Box 100144, Gainesville, FL 32610-0144.
E-mail address: jwharvey@ufl.edu

Vet Clin Small Anim 42 (2012) 73–84
doi:10.1016/j.cvsm.2011.09.006 **vetsmall.theclinics.com**
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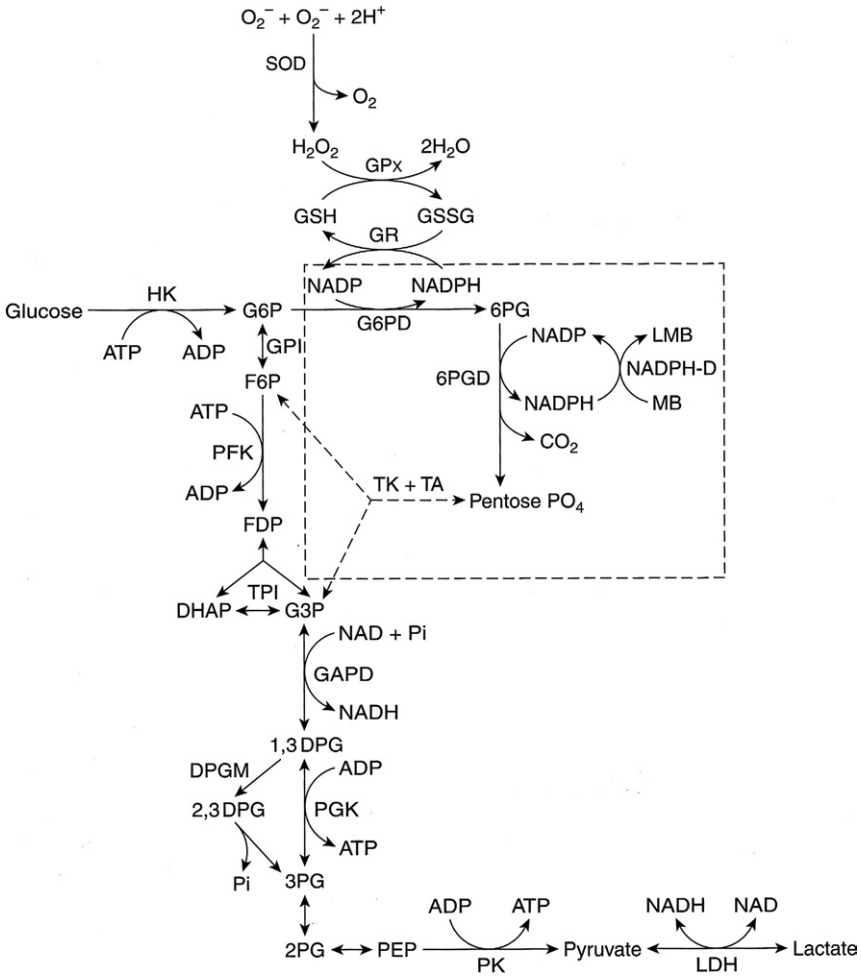

Fig. 1. Major metabolic pathways of the mature erythrocyte (glycolysis, pentose phosphate pathway, and 2,3-bisphosphoglycertate metabolism). The dotted lines surround pentose phosphate pathway reactions shown in abbreviated form. 1,3DPG, 1,3-diphosphoglycerate; 2,3DPG, 2,3-diphosphoglycerate; 2PG, 2-phosphoglycerate; 3PG, 3-phosphoglycerate; 6PGD, 6-phosphogluconate dehydrogenase; ADP, adenosine diphosphate; ATP, adenosine triphosphate; DHAP, dihydroxyacetone phosphate; DPGM, diphosphoglycerate mutase; F6P, fructose-6-phosphate; FDP, fructose-1,6-diphosphate; G3P, glyceraldehyde-3-phosphate; G6P, glucose-6-phosphate; G6PD, glucose-6-phosphate dehydrogenase; GAPD, glyceraldehyde-3-phosphate dehydrogenase; GPI, glucose phosphate isomerase; GPx, glutathione peroxidase; GR, glutathione reductase; GSH, reduced glutathione; GSSG, oxidized glutathione; HK, hexokinase; LDH, lactate dehydrogenase; MPGM, monophosphoglycerate mutase; NAD, nicotinamide adenine dinucleotide; NADH, reduced nicotinamide adenine dinucleotide; NADP, nicotinamide adenine dinucleotide phosphate; NADPH, reduced nicotinamide adenine dinucleotide phosphate; PEP, phosphoenolpyruvate; PFK, phosphofructokinase; PGK, phosphoglycerate kinase; Pi, inorganic phosphate; PK, pyruvate kinase; SOD, superoxide dismutase; TA, transaldolase; TK, transketolase; TPI, triosephosphate isomerase. (*From* Harvey JW. The erythrocyte: physiology, metabolism and biochemical disorders. In: Kaneko JJ, Harvey JW, Bruss ML, editors. Clinical biochemistry of domestic animals. 6th edition. San Diego (CA): Academic Press; 2008. p. 173–240; with permission.)