Role of alad in lead toxicology

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The enzyme delta-aminolevulinate Dehydratase (ALAD) is a part of the heme synthesis that converts its substrate, Aminolevulinic Acid into porphobilinogen. Porphobilinogen moves on through various reactions to finally synthesize heme that is crucial in forming various physiological functions. Key among these functions is the transport of oxygen that enables the body to optimally metabolize its nutrients via aerobic metabolism. The regulation of the oxidation states of compounds and radicals that are harmful to the body are also controlled by the heme cycle indirectly (Kelada, et al, 2001). Lead toxicity that influences the ALAD not only depends on the extent of exposure, but also on certain genetic factors.

Lead inhibits the action of ALAD in the heme cycle resulting in a low red cell count due to decrease of hemoglobin production. There are two variants of the gene that codes for ALAD that vary in affinity of lead; ALAD1 and ALAD2. These two variants of the enzyme differ in their affinity for lead. ALAD2 binds lead more than ALAD2. The ramification of this is that persons with ALAD2 will have the lead in their system bound, and thus stalling its physiological effects as its content in blood in is low. The symptoms of lead poisoning in this case also vary compared to those of persons with ALAD1 that will have high levels of lead in blood in case of poisoning (Kelada, et al, 2001).

In case of lead poisoning, the inhibition of the enzyme leads to an interruption of the heme cycle leading to the accumulation of substrate of delta-aminolevulinic acid(ALA) in urine and blood. This accumulation of ALA in the liver increases the propensity of getting liver cancer due to the acute intermittent porphyria that results from ALAD deficiency. Furthermore, heme production in the body declines with lead poisoning. The production of

harmful reactive oxygen species (ROS) also occurs with the inhibition of ALAD.