Metabolic Nutrition Problem Set Contributions

1. Consider a child born with a SLC39A4 gene mutation. How might a doctor and/or dietitian counsel the parents and treat this child? **(0.5 points)** What other vitamin and/or mineral deficiencies or toxicities might be detected in this child, if the supplement level is too high **(2 points)** or too low **(2 points)?** Hint—stick to issues with other vitamin and/or mineral absorption and tissue distribution issues only as a result of the mutation and its consequences, or problems with supplementation levels. Show at least one peer-reviewed journal article that you used for these answers **(0.5 points).**

A child born with SLC39A4 gene mutation possesses acrodermatitis enteropathica. This is an autosomal recessive disease where the effects are visually noticeable on the skin, including small blisters in various areas, erosions, and lesions. The main source for these skin defects is a zinc deficiency due to the mutation of the SLC394 gene which encodes the zinc transporter Zip4. A health professional such as a doctor or dietitian should counsel the affected child to supplement with zinc in order to alleviate and ease some of these symptoms which can be quite severe. Zinc sulfate is a common supplement, often prescribed for children with the SLC39A4 gene mutation. The results have shown to bring about complete alleviation of symptoms, including the clearing of lesions and arrest of diarrhea. Risks of excess zinc supplementation can severely impact the absorption of copper. This is notably evidenced from patients suffering from “Wilson’s disease,” where the therapeutic effect of zinc will result in reduced copper absorption. All this copper excess begins to accumulate in the liver, resulting in damages to the organ. Additionally, this leads to copper being released, causing more harm to other tissues. High zinc supplementation has also been shown to exhibit negative effects on iron absorption. This was demonstrated through experiments resulting in increased small intestine retention of iron and decreased hephaestin (iron transporter), with zinc supplementation. On the other hand, acrodermatitis enteropathica, in conjunction with symptoms of zinc deficiency, can affect several major function pertaining to Vitamin A (i.e. vision, immunity). Deficiency can also reduce the liver’s ability to release zinc.

References:
2. Bone Metabolism:
   a. Warfarin is usually taken as a blood thinner. What effects might it have on bone metabolism? (2 points). Provide at least one article to support your claim (this cannot be a review article, although you can provide additional citations that are review articles) (0.5 points)

   Warfarin is a well-known and commonly used anticoagulant originally developed as a rodenticide. This medication is also referred to as a blood thinner, used in patients with heart problems that increase the risk for developing blood clots. It affects the reaction of reducing quinone to dihydroquinone through the enzymes quinone reductase and epoxide reductase by inhibiting them. Affecting these enzymes ultimately results in Warfarin disturbing Vitamin K-dependent clotting factors. The conversion of Vitamin K to KH2 (the active form of the vitamin), is essential for bone health. Vitamin K has an effect on calcium by positively regulating its balance and this mineral is an obvious a key player in bone metabolism. With an impairment on the Vitamin K cycle, there are going to be very obvious changes in bone health and metabolism. A relationship was discovered between Warfarin use and an increased likelihood of osteoporotic fractures in older men. There was a 25% overall higher risk for these fractures when the medication was taken for a duration longer than a year.

   References:

   b. Some individuals carry a mutation (termed the 2C9 polymorphism) in their cytochrome P450 protein. Describe how carriers of this polymorphism respond to Warfarin treatment, specifically relating the symptoms, and vitamin interactions (2 points). Include one peer-reviewed (not review paper) reference to support your answer. (0.5 points)

   Those who experience 2C9 polymorphism have an association with Warfarin sensitivity. This mutation is genetic and is due to a single amino acid substitution, similar to how diseases such as sickle-cell anemia and cystic fibrosis come about. With a heightened Warfarin sensitivity, the result is an increased inhibition in the Vitamin K cycle, which inadvertently has an affect on one’s bone health. While Warfarin has been shown to be beneficial when it comes to patients at risk for blood clots, too much sensitivity can lead to severe health problems like excessive bleeding, one of the major effects when using
Warfarin as a treatment; it has been shown that there is an increased bleeding risk in patients with variant 2C9 alleles.²

References: