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Introduction to Maple Syrup Urine DiseaseMaple syrup urine disease (MSUD) isa genetic metabolic disorder of branched chain amino acids (BCAA) catabolism (Levy, et al.

, 2013). This causesdeficiency in BCKD resulting in a metabolic error (Strauss, et al., 2006).

The symptoms include maple syrupodour of urine and ear wax, poor feeding, nausea, vomiting, irritability, lethargy, seizures, and ataxia (Levy, et al., 2013). It can lead to encephalopathy, coma, mental disorders and death (Strauss, et al.

, 2006). Blood test will reveal increasedplasma concentration of BCAA, especially leucine (Strauss, et al., 2006). Urine testing can identify ketonuria and other organic acids (Levy, et al.

, 2013). Genetic testing to reveal mutations isalso performed (Strauss, et al., 2006). The first step in intervention willbe to discontinue all protein intake (Levy, et al.

, 2013). Haemodialysis can be useful inmanaging brain oedema (Strauss, et al., 2006).

Another possibletherapy is also a liver transplant (Burrage, et al., 2014). BCAA Catabolism and MSUDBCAAs are leucine, isoleucine andvaline (Figure 1.) and they classify as essential amino acids (Cole, 2015). Valine is purelyglucogenic, leucine is ketogenic and isoleucine has both ketogenic andglucogenic nature (Brosnan & Brosnan, 2006).

Out of total aminoacid requirement of the body, BCAAs represent approximately 35% (Brosnan & Brosnan, 2006). The BCAA catabolism is unique asthe primary catabolic steps proceed in skeletal muscle mitochondria not in theliver (Brosnan & Brosnan, 2006) and the first twosteps share enzymes (Burrage, et al., 2014). The first step(Figure 2.

) is a transamination reaction catalysed by branched chainaminotransferase (BCAT) (Burrage, et al., 2014). There are two formsof BCAT, cytosolic and mitochondrial (Cole, 2015). During transamination, ?-oxoglutarate accepts the ?-amino group from thespecific BCAA and will form glutamate, the BCAA will form their derivativebranched chain keto acid (BCKA) (Cole, 2015).

The cofactor for this reaction is vitamin B6 (Cole, 2015). The second step (Figure 3.) is rateregulating and irreversible (Cole, 2015)oxidative decarboxylation of BCKA (Burrage, et al., 2014). The enzyme in thisreaction is BCKD complex requiring these cofactors: thiamine pyrophosphate(vitamin B1), coenzyme A, Flavin and nicotinamide adenine dinucleotides (FADand NAD) and lipoamide (Burrage, et al., 2014).

After the secondstep, each BCAA will follow different pathway (Figure 4.) according to theirglucogenic or ketogenic nature (Cole, 2015). In MSUD, the deficiency of BCKDprevents the second step from proceeding (Cole, 2015) (Figure 5.), therefore the BCAAs and their derivative BCKAs will accumulate inthe plasma causing the previously mentioned symptoms. Their neurotoxicitymechanism is to be yet completely understood, however leucine is the mostneurotoxic (Burrage, et al.

, 2014). It is possible thatleucine prevents the precursors of neurotransmitters from transporting acrossthe blood-brain barrier and also disturbing the energy metabolism in the brain (Burrage, et al., 2014). The accumulation ofBCKAs in plasma can lead to metabolic acidosis which can be fatal (Levy, et al., 2013).