# Ammonia Intoxication in Portal Systemic Encephalopathy

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Portal systemic encephalopathy (PSE) comprises of five major features, of which ammonia intoxication of the central nervous system is the only specific feature.

Ammonia is a key intermediate in the metabolism of nitrogen. Oxidative deamination of aminoacids is one of the major ammonia producing pathways. It occurs predominantly in the liver, to a lesser extent kidneys and also in the brain. The synthesis of glutamine is metabolically an extremely important ammonia utilizing reaction and is first line of defence against ammonia toxicity (Brown et al., 1957).

The most impressive evidence in favour of ammonia as the cause of PSE is the frequency with which the whole syndrome is precipitated in patients by a variety of ammonium salts and of other simple substances that liberate ammonia (Kirk, 1936; Phillips et al., 1952; White et al., 1955).

The second important line of evidence is the correlation of blood ammonia levels with PSE and the associated decrease in the concentration that accompanies effective therapy. A close positive correlation between blood ammonia levels and the presence and degree of PSE was reported by several investigators (Schwartz et al., 1953; Bessman et al., 1954; White et al., 1955; Fisher and Faloon, 1957; Vanamee and Poppel, 1960; Egense, 1963). Others have reported a poor correlation (Phillips et al., 1952; Alexander et al.j 1955; Reynolds et al., 1958). Clearly the correlation is good but not perfect.

Ammonia toxicity takes place at an intracellular site. At the lower pH of intracellular fluid, the partial pressure of ammonia is lower than that of the extracellular fluid and ammonia diffuses from the extracellular fluid into the intracellular fluid. Anything that increases the pH gradient between the extra cellular and intracellular fluid favours the passage of ammonia into the cells and presumably increases its toxicity. Metabolic or respiratory acidosis decreases the pH of extracellular fluid and thus favours the diffusion of ammonia from the intracellular to the extracellular compartment. Hyperventilation induces extracellular respiratory alkalosis and thus increases the pH gradient causing ammonia to enter the cells. Metabolic alkalosis has the similar effect.

The mechanism by which ammonia exerts its nefarious effect is its interference with brain energy metabolism. The concept that ammonia suppresses cerebral energy metabolism is based primarily on the effect of the biochemical detoxification of ammonia in the brain. Accumulation of ammonia results in the depletion of alpha ketoglutaric acid which may in turn slow the tricarboxylic acid cycle, the primary source of high energy phosphates. Since glutamine synthesis also utilizes energy in the form of ATP, ammonia is not converted to glutamine which serve as non-toxic storage form (Brown et al., 1957). Such defects in energy metabolism would be associated with decreased oxygen consumption by the brain (Fazekas et al., 1956, 1957; Maiolo et al., 1971; James et al., 1969; Posner and Plum, 1960). Since high energy phosphates are required for neuronal repolarization and a variety of other essential central nervous system functions, the combination of decreased synthesis and increased expenditure of ATP can induce profound neurologic and encephalogic and encephalopathic disturbances.

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