

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Ornithine Transcarbamylase Deficiency

Ornithine Transcarbamylase (OTC) Deficiency is the most common of six disorders relating to the urea cycle. It results from a defect in the OTC gene leading to inactivation of this enzyme. OTC is involved in the conversion of ornithine and carbamoyl phosphate to citrulline, which is an essential process in the overall conversion of ammonia and urea. Patients with genetic defects in any of the enzymes involved in this pathway are subject to problems associated with hyperammonaemia, which commonly manifest as neurological symptoms.

OTC deficiency is an X-linked disorder, with an incidence of approximately one in 14 000 births. Many affected males will die in infancy following acute hyperammonaemia. Heterozygous females often remain asymptomatic until they undergo a particular physiological stress later in life. The presentation of OTC, however, varies greatly between individuals due to random inactivation of the OTC gene by the liver.

The triggers most commonly involved with late onset OTC include sudden increases in protein content intake, rapid weight loss, illness, childbirth, trauma, surgery and anaesthesia. Symptoms include headache, vomiting, seizures, disorientation, confusion and hyperventilation. Voluntary exclusion of protein from the diet is also commonly noted in affected individuals.

OTC deficiency should be considered as a differential diagnosis for patients who have unexplained neurological and behavioural disturbances, in conjunction with selective anorexia, unexplained coma with cerebral oedema, and respiratory alkalosis. The diagnosis is confirmed with raised plasma ammonia levels, and specific amino acid levels. Due to the defect in the urea cycle, arginine and citrulline levels are decreased, and glutamine levels are increased. Urine tests for orotic acid and uridine are also diagnostic. DNA mutation testing should be performed for patients where the diagnosis of OTC is suspected. Alternatively, enzyme activity may be measured by performing a liver biopsy. Further tests are available but they are usually not used in the clinical setting. These include the allopurinol test and the Protein Loading test. Allopurinol loading leads to an increase in the excretion of orotic acid in the urine. Protein loading results in worsening of symptoms in affected individuals.

Acute treatment for hyperammonaemia involves fluid replacement, which helps to decrease protein catabolism, and haemodialysis to remove excess ammonia. Maintenance treatment consists of replacement of depleted amino acids, such as arginine and citrulline. This is usually used in conjunction with benzoic acid or phenylbutyrate. These agents scavenge ammonia to form a water soluble compound that can be excreted in the urine. Patients are also encouraged to ensure intake of adequate calories, while minimising protein load. Liver transplants are considered for some patients, but usually only for those who have life threatening symptoms at the time of diagnosis.

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**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@rgh.sa.gov.au](mailto:chris.alderman@rgh.sa.gov.au)**  
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