Report of Metbionet workshop on Oxalate and Inborn errors of dopamine and serotonin metabolism held at UCL Hospitals February 23rd 2006

This meeting covered two quite diverse topics reflecting specialist services offered by UCL Hospitals Clinical Biochemistry (Molecular Urology unit) and the National Hospital for Neurology and Neurosurgery Neurometabolic unit, both of which are associate labs within Metbionet.

A total of 31 delegates attended the meeting .

The morning session was devoted to primary hyperoxaluria. Dr Gill Rumsby (Molecular Urology, UCLH) opened the session with an introduction to oxalate starting off with factors affecting its absorption from the gut and the paradoxical role of calcium in limiting uptake of dietary oxalate. The main precursor of oxalate *in vivo* is glyoxylate and the role of the enzymes alanine:glyoxylate aminotransferase and glyoxylate reductase in removing glyoxylate and thus preventing hyperoxalurias are illustrated by the diseases Primary hyperoxaluria type 1 (PH1) and type 2 (PH2) . The laboratory investigation of hyperoxaluria was reviewed emphasising the dangers of collection artefacts and difficulties with interpretation of results particularly in young children. This talk was concluded by reviewing the diagnosis of PH1 and PH2 by analysis of liver enzyme activity.

Dr Emma Williams (Molecular Urology, UCLH) described the genetics of PH and the work she had done in evaluating a genetic approach to diagnosis of this disease. This approach obviates the need to take a liver biopsy and the problems with shipping such samples around the world. By analysis of more than 300 patients with liver biopsy-proven PH, it had been possible to establish the sensitivity of a limited mutation screen with the result that a diagnosis of PH1 (2 mutations found) was possible in 43% of cases, while a single mutation, and therefore a strong suspicion of PH1 was found in a further 30%. Methods are also available for linkage analysis to diagnose the disease in other family members. The success of these methods is strongly dependent on proper clinical and biochemical evaluation of the patient before hand.

Dr William Van't Hoff (Nephrology, Gt Ormond St) gave an excellent talk on the clinical presentation of the primary hyperoxalurias noting that some 50% of patients will present within the first decade. The younger patients tend to present with systemic effects while the older children and adults have stones or nephrocalcinosis. One important point made was that urine oxalate can be raised in patients in preterms on formula feeds. Treatment of these disorders ranges from high fluid intake and low oxalate diet, to citrate and phosphate as inhibitors of crystallization. The ultimate treatment for PH1 (and possibly PH2) is liver and liver-kidney transplantation.

The afternoon session on inborn errors of dopamine and serotonin was started off by Prof Robert Surtees (Institute of Neurology) who described the clinical presentation of monoamine disorders. Not daunted by the inability of the laptop to play his video clips, he acted out the movements of each of the Dopa responsive dystonias. To those of us who were not medically trained, this was an extremely informative explanation of complex medical terminology. Prof Surtees reviewed the inherited disorders of GTP cycloydrolase, tyrosine monooxygenase deficiency, sepiapterin reductase

deficiency and disorders of pyridoxal phosphate metabolism before moving on to infantile Parkinsonism dystonia and acquired Parkinsons disease.

Dr Simon Heales (Neurometabolic Unit, National Hospital) described the laboratory investigation of monoamine disorders particularly of those caused by deficiency of tetrahydrobiopterin, an essential cofactor for tyrosine (and therefore dopamine) synthesis. The typical patterns of CSF metabolites (HVA, 5HIAA, BH_4 and pterins) seen in GTP cyclohydrolase deficiency, PTP synthase and DHPR deficiencies were reviewed. For the analysis of CSF it was important to note that patients needed to be off L-dopa for a week before the lumber puncture is performed but a phenylalanine loading test could be performed without stopping treatment.

Mr Tony Briddon (Neurometabolic Unit, National Hospital) described the phenylalanine loading test in more detail and advocated the use of the phenylalanine:tyrosine ratio as a better assessment of BH_4 deficiency, BH_4 being an essential cofactor for phenylalanine hydroxylase.

Dr John Land (Neurometabolic Unit, National Hospital) described situations in which secondary perturbations of monamine metabolism occurred. For example, a bloody CSF tap could show apparent reduction of HVA and 5HIAA, although this could be dealt with by rapid centrifugation and separation of the CSF. In addition, Wilson's disease patients were known to have decreased 5HIAA in CSF due to perturbation of the serotonin pathway. A number of drugs are known to have effects on L-dopa and its precursors including MAO inhibitors, dopamine receptor agonists, SSRIs and antiemetics. Finally, it was noted that heroin vapour inhalation could lead to profound Parkinsonism through an unknown mechanism but was associated with decreased HVA, 5HIAA and BH4.

The review of questionnaires collected from delegates was overwhelmingly positive. One delegate noted that photocopies of the talks would have been helpful and maybe this should be considered for future meetings.

Gill Rumsby March 31st 2006