department.¹ An investigation of reported clinical incidents undertaken by the NSW Clinical Excellence Commission in 2012 revealed that 11% (3/27) of incidents resulting in serious harm (e.g., patient death) and 32% (24/75) of incidents with major consequences for patients were related to poor test result follow-up. Health information technology (IT) has a key role to play in the communication and follow-up of test results.¹ Effective solutions must engage all stakeholders to arrive at decisions about who needs to receive the test results, how and when the results are communicated, and how they are acknowledged and acted upon.

Reference

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TODDLER WITH A TIME BOMB: THE CHALLENGES OF HOMOZYGOUS FAMILIAL HYPERCHOLESTERO LAEMIA

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Homozygous familial hypercholesterolaemia (HoFH) is rare, affecting 1:1,000,000 individuals worldwide. Patients usually have a mutation on each LDL receptor allele resulting in markedly impaired LDL clearance by the liver and very high LDL levels (>13 mmol/L). Untreated, the mean age for first major cardiac event is 12.8±5.9 years, and mean age of death 18.4±10.1 years. Treatment with statin therapy only provides mild improvement in LDL levels. We present a boy who, at age 2.5 years, was found to have cutaneous xanthomas and a cholesterol level of 23.8 mmol/L with LDL of 21.7 mmol/L. Genetic testing was confirmatory for homozygous LDL receptor C660X mutation. Treatment with statins was challenging and as expected only mildly effective. Plasmapheresis was successful in reducing LDL levels but technically challenging and could not be sustained long term. Newer medications currently in clinical trials were considered. He proceeded to a liver transplant age 4 years with good outcome.

INBORN ERROR OF MANGANESE METABOLISM – THE 'NEW' WILSON'S DISEASE

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The first inherited disorder of manganese metabolism was described in 2012. Dystonia with brain manganese accumulation was described in 10 families due to mutations in the SLC30A10 gene (solute carrier family 30, member 10). SLC30A10 encodes a manganese transporter and a defective protein results in accumulation of manganese in the basal ganglia and cerebellum causing chronic neurological impairment and early death. In 2014 three children from a family of Middle Eastern origin were identified and diagnosed with this manganese disorder through

the Children's Hospital Westmead. The three children (consanguineously related parents) suffered chronic dystonia of unknown origin. Laboratory tests displayed the unique 'metabolic signature' of manganese accumulation (extreme hyper-manganaemia, polycythaemia and depleted iron stores). Paediatric neurologists implemented chelation therapy, a low manganese diet and monitoring by 24 h urinary manganese excretion. All had marked improvement in movement control and they remain carefully monitored. The discovery of a new manganese disorder is a 'game-changer' in the area of dystonic disorders and an exciting advance in clinical chemistry. Along with Wilson's disease these 'inherited metal transporter disorders' will yield important new information on trace element metabolism and the critical role of regulators to limit toxic accumulation.

Reference

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CHALLENGES IN THE MANAGEMENT OF PYRIDOXAMINE 5'-PHOSPHATE OXIDASE (PNPO) DEFICIENCY

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Pyridoxamine 5'-phosphate oxidase (PNPO) deficiency is a recently described metabolic cause of neonatal epilepsy. This 11-year-old boy presented at 24 h of age with seizures refractory to standard anticonvulsant therapy and pyridoxine. At 28 days his seizures resolved after commencement of pyridoxal phosphate (PLP). Genetic testing confirmed heterozygous mutations in the PNPO gene. By 2 years of age his dose of PLP was titrated to 100 mg/kg/day to prevent encephalopathic episodes. Blood tests showed significantly deranged liver function tests (LFTs). A liver biopsy showed early cirrhosis with marked elevation of hepatic pyridoxal and pyridoxic acid levels. No cause other than the PLP therapy could be identified for cirrhosis. His PLP dose was weaned to 50 mg/kg/day before episodes of encephalopathy recurred with concurrent improvement in LFTs; however, hepatic fibrosis and portal hypertension persisted. The possibility of hepatotoxicity due to PLP degradation products was considered but changes in formulation/mode of administration of PLP have not influenced the hepatic abnormalities. He continues to have episodes of seizure/encephalopathy if doses of PLP are missed or delayed. He has had an excellent developmental outcome despite early onset refractory seizures. The challenges of managing a newly described metabolic disease are discussed.

BREAKTHROUGH TREATMENT IN CYSTIC FIBROSIS – IVACAFTOR AND SWEAT CHLORIDE

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Cystic fibrosis (CF) is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Over 2000