was suspected. Magnetic resonance imaging of the brain was normal and he made a good neurological recovery.

Conclusion: Hyponatraemia due to a low solute diet and impaired free water excretion is uncommon. Treatment of this type of hyponatraemia with a solute load can result in a rapid correction of plasma sodium concentration, placing patients at risk of the osmotic demyelination syndrome.

A TALE OF LOCUST SWARMS, CANNIBALS, AGEING AND HUMAN OBESITY

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There can be few more important challenges in modern biology than explaining how the phenotypic features of organisms contribute to the populations, communities and ecosystems within which they exist, and how these in turn respond to changing environmental conditions. The phenotype sits at the confluence of influences arising from the genes and the environment and it is the phenotype which is subject to natural selection. I will begin with my group's work on locusts and other insects to show how spanning individuals to ecosystems can be achieved by combining theory, laboratory and field experiments and by using techniques from a range of disciplines, including molecular biology, neurophysiology, biochemistry, behaviour, mathematics, statistical physics, computer science, engineering, evolutionary theory and landscape ecology. Locust plagues are one of the most infamous insect scourges, affecting the lives of 1 in 10 people on the planet. While of interest in their own right, locusts have also provided important new clues into the causes of human obesity and metabolic disease, how we age, and the complex behaviour of crowds. Many of these insights have arisen through a new understanding of the role of nutrition in shaping phenotypic plasticity. I will introduce the principles of nutritional geometry, which arose initially from studies on locusts, and show how using this powerful conceptual framework has yielded fundamental new understanding about the human obesity epidemic and the nutritional determinants of reproduction, aging and lifespan.

THE ABORIGINAL HUNTER-GATHERER LIFESTYLE: LESSONS FOR CHRONIC DISEASE PREVENTION

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In 1982 when a group of middle-aged Aboriginal people with type 2 diabetes reverted to their traditional hunter-gatherer lifestyle for just 7 weeks, all of the metabolic abnormalities of diabetes were greatly ameliorated or reversed, as were the major risk factors for cardiovascular disease. Three factors were likely responsible for these striking improvements: low energy intake; high protein, low fat diet; and elevated physical activity. Low energy intake (estimated 1200 kcal/day) was probably the most important.

The most important lesson that can be drawn from this study is that metabolic control in type 2 diabetes can be greatly improved with healthy lifestyle interventions. The diet in the 1982 study

was rich in very lean meat from wild animals: its high protein content aided satiety despite low energy intake. The carbohydrate was mostly high fibre and slowly digested. The fat content was low, but relatively rich in long chain highly polyunsaturated fats (omega-3 and omega-6). Recent research has demonstrated that ectopic fat is a driver of both defects of type 2 diabetes: insulin resistance when in the liver, and impaired insulin secretion when in the pancreas. Both are potentially reversible by healthy diets instituted early in the disease process. However, current population trends to increased obesity are driven by the powerful transnational food industry. Preventive interventions will therefore be very challenging.

HUNTING FOR THE SIGNATURES OF CANCER BY PLASMA DNA SEQUENCING

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Liquid biopsy refers to the analysis of DNA released by tumours into the circulation of patients for the detection, prognostication, selection of therapeutic targets or monitoring of malignancies. For example, regulatory approval has been granted for the detection of epidermal growth factor receptor mutations in plasma of patients with non-small cell lung cancers as a means to stratify therapy. However, the key challenge in the diagnostics of cancer is about its early detection. Given that cancers are highly heterogeneous, our group has been developing whole genome approaches to detect the signatures of cancer via a liquid biopsy. The rationale is to extract as much of the molecular information as possible from a plasma sample to catch a glimpse of the possible presence of cancer. Genome-wide approaches to detect tumour-associated copy number aberrations, molecular size profile, DNA methylation signatures and transcriptomic features from circulating nucleic acids have been developed. We have further developed an approach to pinpoint the anatomical location of malignancy, naming to determine a tissue map non-invasively. In summary, many facets of molecular information could be extracted from a liquid biopsy.

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HOW SHOULD WE DEAL WITH MISSED TEST RESULTS AND PENDING RESULTS AT DISCHARGE?

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The failure to follow-up test results is an area of patient safety risk which can have major consequences for the quality of care, potentially leading to missed diagnoses and sub-optimal patient outcomes. Previous research has shown that pathology and imaging test results fail to be followed up in 20–62% of inpatients, and in up to 75% of patients treated in an emergency

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

1. Georgiou A, Lymer S, Forster M, *et al.* Lessons learned from the introduction of an electronic safety net to enhance test result management in an Australian mothers' hospital. *J Am Med Inform Assoc* 2014; 21: 1104–8.

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

1. Stamelou M, Tuschl K, Chong WK, *et al.* Dystonia with brain manganese accumulation resulting from SLC30A10 mutations: a new treatable disorder. *Mov Disord* 2012; 27: 1317–22.

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