Atoms

Nick Brown, *Editor in Chief*

IT WAS ONLY AFTER THE TRUNK WAS DISINTERRED…

Swathed in fluorescent peach reflective stripes, the search party had set off, torches aloft, in the penumbral half-light, eager, zestful and optimistic. Their task, the exhumation and recovery of a box of documents from confidential lab work undertaken by M15 during the height of the Kong offensive had seemed straightforward enough at the outset. This initial impression, though, proved naïve. The forest was denser, the tracks fainter, the maps less reliable and the mosquitos more aggressive than the 'initial surveys' had led them to believe. As dawn approached, their spirits sapped even the serendipitous finding of a break in the ubiquitous moss, failed to raise morale or pulse. What did, though, change the mood was the timbre of shovel on oak some three feet into the excavation. There it was. In many ways modest, a small casket shrouded by cobwebs and rust, but none the less clearly the object of their mission. The lock code proved a cakewalk in comparison to the chase, the stiffness of the hinges almost more of a challenge, but the contents…

OVER THE COUNTER: UNDER THE RADAR

Despite the lack of anything resembling concrete evidence of benefits, the over-the-counter market for self-limiting symptoms (most notably cough and diarrhoea) continues to flourish. Does this matter? Emphatically, yes. First, because this is treatment directed purely at symptoms rather than underlying cause. Suppressing a cough or reducing ileal peristalsis might be superficially reassuring, the dearth of hard data (unlike what the brochures claim) but simply masking symptoms of what are largely benign self-limiting illnesses might delay the investigation of those for whom a search for an underlying cause is warranted. Second, there is the potential for harm in the form of addiction (many such preparations are opioid based) or prolonging symptoms even if appearing to attenuate them in the short term, intestinal bacterial overgrowth from stasis a common consequence. Finally, and this is where Paul Turner's and John Warner's insightful commentary hits hard, the risk of anaphylaxis both to the opioid and to seemingly unrelated drugs. The proposed mechanism is of IgE cross-sensitisation between ammonium ions in pholcodine and quaternary ammonium ions in, for example, anaesthetic neuromuscular blocking drugs such as rocuronium. This isn't simply speculative as ORs from case control studies and reports of likely anaphylaxis during anaesthesia testify. And it isn't only NMDAs, an association between pre-operative pholcodine intake and cephalozlin prophylaxis has been noted in Australia. The pathway hasn't yet been completely nailed immunologically, but the suspicion at a notch so high that the European Medicines Agency has now recommended withdrawal of these preparations, advice identical to that of both the US FDA and WHO. *See page 576*

ALTERNATIVES TO IONTOPHORESIS

Many of us are now habituated to the rapid genetic confirmation of cystic fibrosis after successive high blood spot immunoreactive trypsinogen results, delta 508 and younger siblings now rolling off the tongue like old acquaintances. This though is very much the high-income country approach and even here, the gold standard (the phenotypic marker) remains the sweat chloride. In low- and middle-income countries (LMICs), life expectancy for children with CF is in the twenties, while in their North American and European counterparts in the 40+age group, delay likely an explanatory factor. Add to this, the dearth of personnel and laboratory facilities to undertake the time-consuming chloride evaluation test. Renata Bedran and colleagues in Belo Horizonte, Brazil validate the use of the much-easier-to-measure sweat conductivity, a technique not just faster but cheaper against the chloride standard, the tests taken concurrently in children with two positive IRT values. The positive and negative predictive values were both extremely high suggesting this is (almost) comparable as a tool and one transposable to remote and rural settings with earlier intervention the clear implication. *See page 538*

ENERGY TO BURN

How does one gauge that an intervention is 'working'. Blood measures, functional assessment, anthropometry or (scandalously underrated) feelings of well-being. Until now, resting energy expenditure has been used primarily as a research adjunct, the tools a composite of indirect calorimetry and dual energy X-ray absorptiometry, both time consuming. Think, though, of the potential implications of serial measurement as a marker of response to treatment in, for example, endocrine or inflammatory disorders. Laura Watson, Tim Cole and colleagues at the NIHR research facility, Cambridge describe the derivation of centiles for REE adjusted for lean mass vs age using previously tested LMS methodology in a group of children and adults, charts that will likely open doors previously the sole premise of biomedical science hypothesis generation work. *See page 545*

IN THE GENES

Many moons ago, I had the privilege of being one of Victor Dubovitz's SHOs at the Hammersmith neuromuscular unit, then as now a quaternary referral point for children with diagnosed and undiagnosed hypotonia. Whichever category a child fitted before assessment, the prognosis was rarely a positive one, though non-invasive ventilation was beginning to offer a previously unavailable avenue, at least in some of the dystrophy patients. The importance of checking the maternal handshake (myotonia), the tongue (for fasciculation typical of anterior horn cell disease), Gower's sign and reflexes still ring true. Fast forward a generation, a frenzy of molecular research and the options for spinal muscular atrophy now have a lustre unthinkable even a decade ago. There are now three licensed treatments (nusinersen, onasemnogene and risdiplam) all based on augmenting the missing SMN1 gene or enhancing the activity of its genetic neighbour the SMN2. Vasanta Gowda and colleagues at the Evelina hospital in London, describe the gestation and early infancy of these breakthrough treatments. *See page 511*

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