



SUCH A TEASE

Medical history is literally strewn with moments of deserved elation. Few triumphs, though, are impermeable to subsequent challenge. Even world changers like the discovery of penicillin aren't immutable, antimicrobial resistance, now a perennial feature in the WHO top ten global health threat compilations, the spanner in the works.

The (infinitely more poignant) corollary is the scenario in which a 'new intervention' clearly works, but persuading the (for want of a better word) 'community' to engage becomes an even larger hurdle than the evidence accumulated. Think of the Wright brothers and their early attempts in Kitty Hawk to launch; the arrival, stage left of the lover seconds after the star-crossed partner ruffles the blue velvet curtain and leaves to the right; the banked on favourite for the quarter mile title slipping in the final straight to be usurped at the tape.

This, though, is how events so often play out.

FOLIC ACID

Archives has detailed the chronology of the folic acid-neural tube defect saga closely over many years: the inertia after Smithells' seminal 1991 MRC RCT; the subsequent hesitancy over generalisability and periconceptual advice; the circular debate about alternative (food-based fortification) approaches and, now, after multiple iterations a (many would argue overdue, but let's not be churlish) a change

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in policy regarding non-wholemeal bread supplementation.

Moving seamlessly from the prologue to the present, Jenniger Brougham at the National Disease Registration Service and perinatal epidemiology colleagues from around England, present baseline data from a 20 year period (2000–2019) on which to base future assessments of change in NCD incidence. In the first 15 years, the legacy database provided the source, in the most recent 5 year period the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS). Though one could try to mitigate the trends on the basis of registration bias, the unwelcome reality is that NCDs (anencephaly particularly) became more common over this era (incidence rate ratio (IRR) 1.01, 1.00 to 1.02) rather than less so. Worse still, the mean maternal folic acid levels are falling despite advice on periconceptual pharmacological supplementation. *See page 106*

SWEET TOOTH

The properties of xylitol, a naturally occurring sugar, in older children are reasonably well established in the prevention of caries. Though it has attractive antibacterial properties, data on benefits in young children are scarce. In an elegant RCT, Navindra Persaud and colleagues at the University of Toronto, Canada tested whether xylitol syrup (given orally twice a day for 6 months) has a role in the prevention of physician diagnosed acute otitis media (AOM) in 1–5 year old children. Though the numbers were smaller than expected (a pandemic didn't help recruitment.) there was no difference in rates of AOM or (as a secondary outcome) caries. An intriguing, important negative – and the search goes on. *See page 121*

SICKLE CELL CRISES

It's rare to be able to single out centres as (genuinely) world leading in any specific area. One exception is the Medical

Research Council Sickle Cell Disease centre in Kingston, Jamaica. Graham Serjaent and colleagues describe the course of a cohort of neonatal-screen identified children born between 1973 and 1981 in terms of outcome after acute splenic sequestration. ASS is one of several SCD crises and, justifiably, deserving its reputation. In these days of MR imaging, whole exome sequencing... this beautiful paper is a reminder that so much is possible with that often (criminally) overlooked commodity, observation. *See page 100*

VALPROATE

In its heyday, valproate (VLP to its prescribing friends) was the go-to anti-convulsant. For, almost, everything. It was versatile across a wide range of epilepsy phenotypes, effective as monotherapy or in combination, reasonably predictable in terms of side effects, easy and quick to initiate – and cheap. But, then some other numbers became impossible to ignore: the staggeringly high incidence of learning difficulties in children of VLP-treated mothers (at least 30%) and a congenital malformation rate of 10%. Confounding by genetic susceptibility couldn't be blamed and the drug immediately fell out of favour in girls of childbearing age, the deal sealed by the Medicines and Healthcare products Regulatory Agency in 2018 recommending against its use in this group unless all alternatives had been explored and that a pregnancy prevention plan was in place for all prescribed the drug.

The audit by Lilly Lang and colleagues at the Alder Hey hospital, Liverpool makes reassuring reading in terms of adherence. Only 7 girls over 12 years of 750 children treated had been prescribed VLP since the MRHA edict- and these all fulfilled the criteria. Practice has, rightly, changed. *See page 174*

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