Highlights from this issue

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INVESTIGATING: DEVELOPMENTAL DELAY

This issue is big on investigations, and I would like to kick off with the paper by Hart *et al* in which 699 cases over 6 years were investigated for developmental delay in Sheffield, and the utility of the investigations is reported. In an accompanying letter, Hart *et al* add some information on the costs, which are important because developmental delay is a common non-acute problem. Arnab Seal teases out issues from this paper, as well as two others in this Edition, in his Editorial. The bottom line? First-line investigations should include microarray and thyroid function, but 'screening' investigations are not useful. ***See pages 1004, 1092, 999***

…GENETIC CONDITIONS

In a similar vein to Hart *et al* (previous Atom), Best *et al* report 15 years' experience of genetic investigations in London. They had 749 patients of whom just over half had genetic testing, and in their community clinic in Tower Hamlets 4 out of every 10 tested patients turned out to have a genetic diagnosis. The only problem with a 15 year overview is that the genetic world has changed a good deal over that time, particularly in relation to the introduction of microarray investigation. Another 3 out of 10 investigated patients were considered to 'probably' have a genetic condition, so the introduction of next-generation sequencing may yet enable these patients to be diagnosed. ***See page 1014***

…INBORN ERRORS

So right on cue, after the last two Atoms, we have a paper on next-generation sequencing, discussing both whole exome and whole genome approaches. Admittedly the focus of Ghosh *et al* was inborn errors of metabolism, but you could substitute 'developmental delay' or 'suspected genetic disorder' and probably come out with the same answer; indeed I will be interested to see how long microarray testing will survive when next-generation sequencing becomes very cheap. A caveat is that Ghosh *et al* excluded mitochondrial and glycosylation disorders on the grounds of their genetic heterogeneity. The results suggest not only that biochemical testing and next-generation sequencing are complementary, but that sequencing should be done early in the diagnostic pathway, may avoid other expensive investigations, and can be useful even when negative. ***See page 1019***

AND MITOCHONDRIAL DISEASE

If you were disappointed that Ghosh *et al* threw no light on mitochondrial disease, *ADC* comes to the rescue with a detailed review by Davison & Rahman on recognising, investigating and managing children with mitochondrial disease. As a group of diseases, mitochondrial disorders are not especially rare: Davison & Rahman quote a prevalence of around 1:5000, though not all of them present in childhood. Unless they arise by new mutation, they have the distinction of being inherited only from the mother, because you only get mitochondria from eggs, not sperm. Sadly, most of them do not have specific or effective therapies, though there are a few that respond to pharmacological doses of biotin, riboflavin, thiamine, ubiquinone (Coenzyme Q_{10}) or folinic acid, depending on the precise diagnosis. They give rise to multiorgan disease so patients can be faced with a daunting potential list of specialists and therapists for their various ailments. ***See page 1082***

VITAMIN D AND AUTISM

Vitamin D? Vitamin Disappointment, I'm afraid. Kerley et al randomised 42 children with autism spectrum disorder to vitamin D_3 or placebo for a 20 week trial. The dose was 2000 IU daily, so there was no question of under-dosing, adherence was good, and 38 subjects were analysed on intention-to-treat. The primary pre-specified endpoint was stereotypical behaviour, and there was no difference between the groups. Of the 10 sub-analyses, there was a significant improvement in one, 'self-care'. So therapeutic vitamin D does not work, and shows no promise of working, in ASD. ***See page 1030***

CLINICAL IMPRESSIONS

In an era of NEWS, MEWS, PEWS, MEOWS, NEWTTS, and sundry other animals, clinicians have insisted that something is not captured: the 'gut feeling' that a child, in spite of all reassuring physiological data to the contrary, is ill. Readers may remember that we recently carried a paper about various paediatric scores used in the UK (DOI: 10.1136/archdischild-2016-311088). Zachariasse *et al* studied 11 024 children who visited their emergency department with a medical illness. Of the attenders, 6390 had a nurse's clinical impression recorded, and of these, 1 in 5 was considered to be ill. Nurses' impressions turned out not to be a particularly accurate reflection of the children's objective degree of illness, but not surprisingly, the authors still felt that the additional information they provided was of value. ***See page 1052***

NON-SPECIFIC VACCINE EFFECTS

Vaccines are generally developed with a very narrow focus: the prevention of disease caused by a single organism. But they work by affecting the immune system which is complex and not entirely predictable, so the question of non-specific effects, which may affect many children, is as important as specific though rare unwanted effects, such as vaccine-related poliomyelitis. Pollard *et al* review this complicated subject, drawing together evidence from epidemiology and immunology, to clarify what might be going on. The message that I took away is that there are too many observational studies, not all of great quality, and insufficient randomised trials, to answer the key questions with confidence. This is a tragedy as well as an ethical problem: interventions foisted on large populations have the potential for large scale harm as well as large scale good and are at least as deserving of the most rigorous evaluation as are drugs for much smaller groups of patients. ***See page 1077***

AVE ATQUE VALE

This is my last column of Atoms as interim Editor in Chief. By the time you read this, Nick Brown will have taken over the hot seat as from 1st October, and I wish him every success in the role.