Carphology by A Fo Ben

doi:10.1136/practneurol-2019-002452

CHAPEAU TO THE ASO!

What is more important than identifying a rare disease promptly? Initiating targeted treatment promptly. Buckle up—this is quite a story. A 6-year-old girl presented with the insidious onset (2 years) of blindness, ataxia, seizures and developmental regression. Standard and extended investigations suggested Batten's disease but only one mutation was identified in *CLN7* (it is a recessive disorder). Diligent inspection identified first chimeric reads deep in intron 6 of *MFSD8* which led a hypothesis that there may be an insertion of an SVA retrotransposon. This was confirmed in mother and child, which effectively modified the splicing of nearby *CLN7*. The team extrapolated that modifying the antisense oligonucleotide (ASO), nusinersen (which changes the splicing pattern of *SMN2* RNA) could restore *NFSD8* expression. They designed the ASO, tested it in patient fibroblasts and initiated a clinical study of the ASO in the patient a month after starting toxicology studies in animals. Treatment began at 7 years of age and seizures reduced by more than 50% and tests of neurodevelopment remained stable. This is not a new drug for Batten's but instead a landmark designer drug produced at great cost, but also at great speed, which appears to have stabilised a progressive and fatal disorder. This is how you get a 'case report' into the New England Journal of Medicine (and Carphology!)

N Engl J Med 2019. doi: 10.1056/NEJMoa1813279.

DON'T DO THAT OR YOU'LL GO BLIND!

Our sympathies go out to the junk-food-obsessed 14 year old who is central to a case report from Bristol. Described as a fussy eater, his general practitioner identified that he was anaemic and had low B_{12} levels; a course of B_{12} jabs naturally followed to treat his fatigue. However, by the age of 15, he developed hearing loss and visual difficulties, with a blameless brain MRI and eye examination. The situation deteriorated over the next 2 years to the stage where he was legally blind. He was now vitamin B_{12} deficient and had very low levels of copper, selenium and vitamin D. Quizzed directly on what constituted being a 'fussy eater'—he responded that he exclusively ate Pringles, white bread, processed ham slices and sausages. Nutritional optic neuropathy is rare in western countries and is potentially reversible, be alert to the selective eating disorder.

Ann Intern Med 2019. doi: 10.7326/L19-0361.

SCRAMBLED EEGS

A Fo Ben is always worried when 'maverick scientists' use EEG to identify extrasensory perception in geese, or a sense of humour in elk—as we struggle to use EEG to spot spike and wave discharges in perfect conditions in people we think have had a seizure. Two papers to ponder therefore—the first is the more heavyweight; of 104 prospective unresponsive ITU patients, EEG could detect 'brain activation' in response to spoken commands in 16 (15%). It really shows how crude our tests of 'unresponsivity' are and how variable patients are following brain injury. In the second paper, EEG was used to see if humans, like many animals, are responsive to a change in alignment with respect to the Earth's natural magnetic field. A reduction in the amplitude of alpha frequency rhythms was seen following geomagnetic stimulation. This was repeatable, but it is still a stretch to presume we can truly sense mother Earth's natural magnetism.

eNeuro. 2019;6 (2):483-18.

N Engl J Med 2019;380:2497–2505.

CRASH! BANG! WALLOP!

Can tranexaminc acid, which reduces surgical bleeding, help halt intracranial bleeding following a traumatic brain injury (TBI)? Yes. Yes, it can. A large randomised, placebo-controlled trial was performed in 175 hospitals in 29 countries. Adults with TBI were recruited within 3 hours of injury, with a Glasgow Coma Scale score of 12 or lower (or any intracranial bleeding on CT scan), and no major extracranial bleeding. Patients were randomised to tranexamic acid versus placebo; the drugs were given as a loading dose and then 8 hours of infusion. Twelve thousand seven hundered and thirty-seven people were randomised and 9202 were treated within 3 hours of injury. Treatment was better than placebo for the primary endpoint (head-injury-related death) 18·5% versus 19·8% risk ratio (RR) 0·94 (95% CI 0·86 to 1·02). The subgroups that benefited from tranexamic acid most were mild-to-moderate head injury (RR 0·78 (95% CI 0·64 to 0·95)) and those that received earlier treatment. The risk of seizures was similar in both groups. That this drug is common, low cost and readily available may mean that these findings could have a global impact on the management of TBI.

Lancet 2019 Oct 14. pii: S0140-6736(19)32233-0.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.