

# CARPHOLOGY by A Fo Ben



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## MS: the old...

Sometimes the most acute observation is possible when you encounter it fresh—as an outsider. When Geoffrey Dean (1918–2009) arrived in South Africa in 1947, he noticed the marked variation in multiple sclerosis prevalence among the different ethnic groups. With John Kurtzke, he established that immigration before aged 15 years old was associated with a lower risk of multiple sclerosis in immigrants from Northern Europe. He was also a vocal antiapartheid critic—he was arrested for this—and published his last paper in *Neurology* when aged 89; he died aged 90.

*BMJ* 2009;**339**:b5100.

## ...and the new

*New England Journal of Medicine* has treated us to three quality trials of novel MS agents. Oral fingolimod (preventing lymphocyte egress from lymph nodes) reduced both relapses and progression in a 2 year randomised trial. A second trial (1 year, double blind) compared fingolimod (oral) with interferon (intramuscular): relapse rate and MRI findings with fingolimod were significantly better but the fingolimod group had two fatal infections. Finally, cladribine (for hairy cell leukaemia) reduced MS relapse rate versus placebo over 96 weeks, again with MRI benefits and predictable infection related adverse effects. How and when to use these promising agents is currently not clear.

<http://content.nejm.org/cgi/content/short/362/5/387?query=TOC>

<http://content.nejm.org/cgi/content/short/362/5/402?query=TOC>

<http://content.nejm.org/cgi/content/short/362/5/416?query=TOC>

## Stammering genes

People who stammer are often teased, but rather than a 'psychological weakness', a mis-sense mutation in the *N*-acetylglucosamine-1-phosphate transferase gene (*GNPTAB*) appears to be to blame. The first of these genes has been identified in 10% of non-syndromal Pakistani stammering families. This and related mutations affect the

mucopolysaccharide system. Thus stammering becomes associated with rare lysosomal storage disorders, more commonly causing bone, connective tissue and neurological symptoms.

<http://content.nejm.org/cgi/content/full/NEJMoa0902630>.

## Don't panic

To keep calm and carry on, we need adequate central  $\gamma$ -aminobutyric acid levels: deficiency is associated with panic disorders. This is perhaps one reason why benzodiazepines are effective in affective disorders. This study showed that stimulating orexin synthesising neurons in rats increased anxiety levels. We may be familiar with low CSF orexin (or hypocretin) levels in narcolepsy: people with panic disorder have higher CSF orexin levels than controls. This suggests orexin blocking drugs may prove an alternative to benzodiazepines for anxiety disorders.

*Nat Med* 2009;**16**:111–15.

## Our second favourite organ

For neurologists, it's surely the heart (*pace* Woody Allen). Large thrombolysis trials in myocardial infarction (MI) heralded acute stroke thrombolysis, and now offer something more. Preventing cardiac reperfusion injury (irreversible damage of previously ischaemic myocardium on reperfusion) remains cardiology's holy grail. In animals, repeated brief ischaemia of remote organs before cardiac reperfusion limits lethal reperfusion injury. Thus when half of 333 patients with a first MI were randomly assigned to blood pressure cuff inflation and deflation at 5 min intervals in the ambulance, myocardial salvage significantly increased (0.75 vs 0.55,  $p=0.033$ ). As this becomes standard practice for acute MI, its trial in acute stroke is already overdue.

*Lancet* 2010;**375**:727–34.

## What's wrong with mummy?

A good neurological history always includes a family history but only a brave clinician charts a pedigree to late 18th century BCE.

Genetic fingerprinting (microsatellite based haplotype segregation) recently confirmed Tutankhamun's father as Akhenaten in a neighbouring sarcophagus. Despite both Pharaohs' feminised appearances, there was no gynaecomastia, no Marfan's or Antley-Bixler syndrome: probably it was just the Amarna artistic style. Unsurprisingly, four of the 16 mummies studied showed malaria tropica. Tutankhamun himself had metatarsal aseptic necrosis and also a cleft palate and clubfoot, but then again his parents were brother and sister.

*JAMA* 2010;**303**:638–47.



Akhenaten (CT reconstruction) confirmed as Tutankhamun's father. Reproduced with permission from *JAMA* 2010;**303**:638–47. Copyright © 2010 American Medical Association. All rights reserved.