Thrombolysis for ischaemic stroke

In their article dealing with thrombolysis treatment for acute ischaemic stroke, Jenkins et al (Clin Med June 2008 pp 253–8) omitted mentioning two other important flaws in the National Institute of Neurological Disorders and Stroke (NINDS) trial.

Firstly, the relevant part of the trial (part 2), that provided the main impetus for this form of treatment, relied on a global test statistic as the primary measure of outcome, and not on incontrovertible hard end-points. The global statistic was itself a composite function of four inter-related neurological scores (the Barthel Index, the Modified Rankin Scale, the National Institutes of Health Stroke Scale, and the Glasgow Outcome Scale). Clinically and statistically significant differences depending on any such composite of inter-related scores must be inherently suspect.

Secondly, part 2 of the trial also required that patients in the control and active treatment groups not receive aspirin in the first 24 hours. Thus, patients treated with recombinant tissue plasminogen activator (tPA) were compared to controls in receipt of suboptimal standard therapy. To overcome the risk of serious intracranial bleeding due to combined therapy with tPA and aspirin, the investigators should have administered dummy aspirin to the active treatment group and genuine aspirin to the controls.

CR KUMANA
Professor Emeritus
Queen Mary Hospital, Hong Kong

BERNARD MY CHEUNG
Professor of Clinical Pharmacology and Therapeutics
University of Birmingham

Reference

In response

We thank Kumana and Cheung for their comments and accept that there are often inherent weaknesses and limitations in neurological scoring systems, although the degree of potential statistical error in this case is debatable in our view. We believe the core aim of the NINDS study was to demonstrate improvement in disability following thrombolysis and, in this respect, we consider that the end-points chosen by the investigators were reasonable. We agree with Kumana and Cheung that the omission of aspirin was not ideal.

PAUL JENKINS
Professor of Medicine
University of Western Australia, Perth

MARTIN TURNER
Specialist Registrar in Neurology
John Radcliffe Hospital, Oxford

PETER JENKINS
Foundation Year 1
Guys and St Thomas’ Hospital, London

Post-infective irritable bowel syndrome and dyspepsia

Spiller, in his interesting review (Clin Med August 2008 pp 417–9), tabulated nine outbreaks of gastroenteritis followed by irritable bowel syndrome (IBS). However, just as IBS is merely one component of the functional irritable gut syndrome, so some after enteritis had dyspepsia as well as IBS, a phenomenon not detectable using Rome I questionnaires.

The early two Sheffield and three Nottingham studies were uncontrolled. A general practitioner database found that 12 of 318 patients with documented bacterial enteritis developed new IBS, 11 times uninfected controls.1 In Beijing, 329 of 450 with Shigella gastroenteritis were followed for one to two years as were 243 unaffected siblings or spouses.2 Functional bowel disorders developed in 10% who had dysentery <1 week, 31% for 1–2 weeks, and 33% >2 weeks, significantly higher than in controls. A year after a Shigella outbreak in Seoul, incidence of IBS was 17%, but 6% in age- and sex-matched healthy volunteers.3 Two years after a Canadian Escherichia coli/Campylobacter jejuni outbreak, IBS incidence was 24% but 10% in controls.4 Dyspepsia was investigated in two studies. Three months after the Nottingham C. jejuni infections 30 with IBS scored 9 for indigestion and 8 for diarrhoea – significantly higher than 28 ‘controls’ (6 and 3) or 40 healthy volunteers (3 and 3).5 A one-year follow-up study of a salmonella outbreak in 1,243 Catalan villagers gave a cumulative risk of IBS of 11.6% v 1.5% in controls; the risk of dyspepsia (pain, discomfort, fullness, nausea) was 17.2% v 3.3% in controls.6 At 12 months there were 18 villagers who had developed only dyspepsia, 9 with only IBS and 15 with both.

Dr PAUL GRANT
Specialist Registrar in Diabetes and Endocrinology
Eastbourne District General Hospital

So, is this text likely to help one succeed as a hospital doctor? Well it is certainly not a ‘how to’ guide, but for those who are determined to succeed and have palpably considered taking action in such a direction, it will act as a useful guide along the way.