

letters to the editor

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Compliance with NICE guidance on the use of anti-TNF agents in ankylosing spondylitis

Editor – I read with great interest the regional audit on anti-TNF therapy in ankylosing spondylitis patients carried out in the Midlands (*Clin Med* Aug 2012 pp 324–327). We are presently undertaking a similar audit in the north-west, looking at NICE compliance with anti-TNF therapy in patients with psoriatic arthritis. My question was relating to the data on 'reasons for switching anti-TNF agents'. As per NICE guidance, unless one applies for special funding from the PCT, one *cannot* switch anti-TNF therapy if the patient has shown either an inadequate initial response or a secondary loss of effect. Patients can only be switched to another agent if they develop side effects to the first anti-TNF treatment. With this in mind, were the study group able to determine whether PCT funding had been officially requested in the 15 patients who were switched to another anti-TNF agent because of inadequate or secondary loss of effect? If funding had not been applied for in these cases then the team should have highlighted this in their discussion as it would be another recommendation to make for closure of the audit loop in the future.

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Response

Thank you for your interest in our article. The 2008 NICE Technology Appraisal 143 states that prescription of an alternative TNF α inhibitor is not *recommended* in patients who have either not achieved an

adequate initial response to treatment with adalimumab or etanercept, or who experience loss of the initially adequate response to treatment. However, as these are guidelines (rather than strict protocols), PCTs interpret the NICE guidance with varying degrees of rigidity with some strictly allocating funding according to the guidance and others being more liberal in their interpretation.

Of the 15 patients in the Midlands audit who switched due to an inadequate response: one received anti-TNF under the care of the dermatologists for psoriasis before treatment was started for their ankylosing spondylitis; one received their first treatment as part of a clinical trial; three were switched from infliximab (started prior to the 2008 guideline publication) and one received a different anti-TNF after a prolonged period off any biologic treatment. Each of these cases can be seen to require a degree of interpretation when applying the guidelines. Unfortunately, because a question regarding PCT funding was not included in the audit proforma, no further information was available on the remaining nine patients.

We can only speculate, but these remaining patients may have switched prior to publication of the NICE guidance, or the Trusts involved may have interpreted the guidance on an individual basis which may or may not have involved applying for external funding.

We agree that including a question exploring PCT funding streams for patients switching anti-TNF therapy in any future re-audit would provide useful additional information.

FRANCES REES

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Austerity: a failed experiment on the people of Europe

Editor – McKee and his colleagues should be commended for the excellent article of the effects on European citizens of current economic policies in Europe (*Clin Med* August 2012 pp 346–50). Conditions common in the 18th and 19th centuries, such as poor housing, inadequate sanitation, child labour and unsafe work practices, are now far less common and life expectancy has increased enormously in all European countries. Beveridge's 'Five Giants' of want, disease, ignorance, squalor and idleness¹ persist, albeit in ways less immediately obvious. The medical profession has always been concerned with improvements in levels of health and reduction of illness and disability.

The profession must not shy away from advocating political messages. We must continue to criticise and comment on policies that have been shown to do harm as, for

example, Virchow in Silesia² and Sir John Simon in England³ have done in the past.

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References

- 1 Timmins N. *The Five Giants: A Biography of the Welfare State*. London: Harper Collins, 1995.
- 2 Reilly RG, McKee M. 'Decipio': examining Virchow in the context of modern 'democracy'. *Public Health* 2012;126:303–307.
- 3 Royston Lambert. *Sir John Simon 1816–1904*. London: McGibbon and Kee, 1963.

Simultaneous myocardial infarction and ischaemic stroke secondary to paradoxical emboli through a patent foramen ovale

Editor – Grogono *et al* report on an interesting patient but I do not think that they have proven the case for the association that they postulate (*Clin Med* August 2012 pp 391–2).¹ There does not seem to be any doubt that the patient had both a myocardial infarction and a patent foramen ovale (PFO) but:

- The presentation of the assumed stroke is atypical and there is no reported neurological abnormality after the event.
- Lacunar infarction is an unlikely cause of seizure.
- The images from the CT brain scan in this patient are not included in the paper, but in the absence of MRI with diffusion-weighted imaging² I do not think that acute ischaemic stroke can be diagnosed with confidence in this case. Given that, comment about an embolic aetiology seems a matter of conjecture.
- No distant source of thrombus was identified.
- PFO may be found in a significant proportion of the adult population.

Is it not more likely that the patient had a transient arrhythmia and/or hypotension leading to seizure?

Regarding the subsequent approach to treatment of the PFO, the authors will be aware of the results of the CLOSURE I trial³ and a subsequent systematic review of the available literature.⁴

The CLOSURE I trial did not demonstrate any statistical benefit from PFO closure with a STARFlex device compared with medical treatment in patients aged 60 and under with transient ischaemic attack (TIA) or stroke. The trial did show that PFO closure with this device was associated with an increased incidence of atrial fibrillation, thereby replacing a debatable stroke risk factor with one for which there is no doubt.

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References

- 1 Grogono J, Fitzsimmons SJ, Shah BN *et al*. Simultaneous myocardial infarction and ischaemic stroke secondary to paradoxical emboli through a patent foramen ovale. *Clin Med* 2012;12:391–2.
- 2 Durkin C, Briley D, Meagher T. Diagnosis and management of transient ischaemic attack and ischaemic stroke in the acute phase. *BMJ* 2011;342:d1938.
- 3 Furlan AJ, Reisman M, Massaro J *et al*. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. *N Engl J Med* 2012;366:991–9.
- 4 Kitsios GD, Dahabreh IJ, Abu Dabrh AM *et al*. Patent foramen ovale closure and medical treatments for secondary stroke prevention. A systematic review of observational and randomized evidence. *Stroke* 2012;43:422–431.

Response

Editor – We thank Dr Durkin for his interest in our recently published 'Lesson of the month'. We agree that the diagnosis of paradoxical embolism cannot be made with certainty; however we wished to use this case to remind physicians to consider this as a possibility, especially in younger stroke patients. Dr Durkin correctly highlights the unusual association of lacunar

cerebral infarction and seizure, and raises the possibility of transient arrhythmia and/or hypotension leading to seizure-like activity (presumably secondary to the myocardial infarction). However, we believe it is equally unlikely that a fit, active and healthy 39-year-old with no cardiovascular risk factors would suffer a large anterior myocardial infarction (MI). Additionally, the presence of an occluded left anterior descending (LAD) coronary artery and fresh thrombus in its diagonal branch – as well as neurological symptoms with confirmed cerebral infarction on CT brain scan – are all in keeping with embolic phenomena. We agree that diffusion-weighted MRI brain imaging is superior to CT scanning and acknowledge this would have been a valuable additional test.

This case occurred prior to the publication of the CLOSURE I trial¹ but, as always, the risks and benefits of PFO device closure and anticoagulation were discussed with the patient. The patient is a high level competitor in martial arts, and is therefore not ideally suited to long-term anti-coagulation. The patient therefore opted for percutaneous PFO closure. The clinical value of percutaneous PFO closure has been a controversial field for many years and the release of the only randomised control trial, CLOSURE I, has failed to resolve many of the outstanding issues. However, the CLOSURE I trial has not been without its own criticism, including the long time to recruitment, the inadequate power to identify small differences between device closure and medical therapy, the high non-closure rates (15%) and the exclusion of 'high risk' patients or patients thought to represent the population seen in daily practice.^{2–4} The study does, however, remind us that vascular complications and atrial fibrillation should always be discussed with patients being considered for PFO closure.

The recently published RESPECT and PC Trials did not provide good direction on whether prevention of further stroke by PFO closure is effective, but the totality of results supports the use of PFO closure in a select group of patients at risk of secondary stroke following cryptogenic stroke.^{5,6}