metoclopramide. There was no history of ischaemic heart disease, but a routine ECG performed in April 2006 showed first-degree heart block, at a rate of 70 beats/min.

Patients having infliximab in our unit are admitted overnight for the first three infusions. The first infusion was uneventful at week 0. Following the second infusion 2 weeks later, she then gave a history of dry cough for 3–4 months. A chest X-ray was performed, which showed an increased number of nodules (which were of varying sizes) in comparison to a chest X-ray taken 2 months previously, which had been initially reported as ‘normal’ but on review showed a small number of opacities. A high-resolution computed tomography (HRCT) chest scan was then performed, which confirmed the presence of these opacities, but excluded hilar lymphadenopathy or interstitial lung disease. The patient refused a lung biopsy to confirm that these were rheumatoid nodules (RhN). However, a multidisciplinary meeting involving the rheumatologist, respiratory physician and radiologist concluded that these nodules were most likely rheumatoid in nature taking into account the rapidity with which the opacities increased, and the clinical condition of the patient.

A third dose of infliximab was given at 6 weeks. Routine observations carried out immediately post-infusion picked up a pulse rate of 42 beats/min. She continued to remain bradycardic, and by 18h post-infusion, her pulse rate had dropped to 25 beats/min. She maintained an adequate blood pressure with an average of 180/90mmHg. She had no cardiorespiratory symptoms or signs of heart failure. A 12 lead ECG confirmed the bradycardia at a rate of 35–40 beats/min and CHB. Urea and electrolytes, thyroid function tests, cardiac enzymes including troponins were all normal. After cardiology review, she was discharged home, and a permanent pacemaker was inserted at a later date. Review of her RA at 3 months did not show an improvement in disease activity score (DAS)-28 and no further infliximab was given.

Bradycardia [1] and heart failure are recognized side-effects of infliximab, and there are two case reports of patients developing second-degree atrioventricular block during the infliximab infusion [2]. To our knowledge there are no reports in the medical literature of CHB following infliximab infusion or treatment with any other anti-TNF.

Conduction disturbances, including CHB, are well recognized within the RA population [3]. Cardiac RhN are reported to be present in between 1% and 3% of RA patients [4–6]. Pizzarello and Goldberg [3] suggest that RhN could cause conduction disturbances at the sino-atrial or atrioventricular (AV) nodes or His-Purkinje system. The conduction tissue could be compressed by RhN, or directly invaded, or be compromised by impaired blood supply.

In this patient, it was noticed that she had increased pulmonary nodulosis after commencing infliximab. It was at this stage that she developed complete heart block. It is probable that the CHB was due to a RhN at the AV node. Our patient did not have any subcutaneous nodules.

There are case reports of accelerated nodulosis (subcutaneous and pulmonary) following etanercept [7, 8] and infliximab therapy [9]. The authors postulate that this could have been due to autoimmune phenomena occurring with anti-TNF therapy or due to the natural history of RA. Other authors hypothesize that the mechanisms of nodulosis are largely TNF-α-independent [10].

Given that the onset of CHB in this patient was immediately following her third infliximab infusion, it is likely that infliximab played a role in the development of CHB in this case, probably by exacerbating a nodule at the AV node. Unfortunately, we were unable to prove the presence of nodules in this patient’s heart as we were unable to obtain a magnetic resonance imaging scan prior to pacemaker insertion. HRCT scanning of our patient is not justified on clinical grounds.

We recommend that all patients have an ECG performed prior to anti-TNF to exclude cardiac conduction abnormalities. It would seem prudent to be vigilant in patients with pre-existing cardiac conduction problems or nodulosis elsewhere if the decision to treat with infliximab is made.

**Rheumatology key message**

- Be vigilant if using infliximab with co-existing cardiac conduction problems.

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**Comment on:** Failure of anti-TNF therapy in TNF receptor 1-associated periodic syndrome (TRAPS)

Sir, We read with interest the report by Jacobelli et al. [1] about their experiences with anti-tumour necrosis factor (TNF) therapy in TNF receptor 1-associated periodic syndrome (TRAPS). In particular, they describe a severe paradoxical reaction following infliximab infusion, which has previously been noted in other patients [2, 3].

We report a patient with TRAPS who developed a similar inflammatory exacerbation following infliximab, but who subsequently responded well to etanercept, and discuss these apparently divergent responses to anti-TNF therapy. We have previously reported on the signalling effects in a 50-year-old woman with the TRAPS phenotype and a C43S TNFRSF1A mutation [4]. This patient experienced recurrent attacks of inflammation every 4–5 weeks, characterized by high fevers, pharyngitis and arthritis, accompanied by a migrating skin rash and myalgia. These episodes

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It has become increasingly evident that there are important differences between the various anti-TNF agents [6]. We postulate that these differences could account for the differential effects seen with etanercept and infliximab in our patient. Further study of these differential effects in TRAPS could help explain the underlying mechanisms of this condition and advance our understanding of how the anti-TNF agents work.

Furthermore, while there are no published reports on the use of the fully humanized anti-TNF monoclonal antibody adalimumab in TRAPS, the above responses to infliximab caution against its use in TRAPS. We suggest that the monoclonal anti-TNF antibodies, infliximab and adalimumab, should be avoided in TRAPS. While the results with etanercept are mixed, anakinra, a recombinant IL-1 receptor antagonist has shown promise and is undergoing further evaluation and could also yield interesting mechanistic information [3].

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**Comment on: A prospective double-blind placebo-controlled randomized trial of ultrasound in the physiotherapy treatment of shoulder pain**

Sir, Ainsworth et al. [1] included 221 patients with unilateral shoulder pain, and randomized them into two groups that received (on average) six treatments in 6 weeks. Both groups received the interventions information and manual therapy; the intervention group further was ‘applicated with’ real ultrasound (US) (that is indeed something totally different from ‘treated with’) and the control group with sham US (average 4.5 min).

Let us mention three major diagnoses for the included patient group: instability, impingement and frozen shoulder. In case of instability, US has no treatment rationale. Michener et al. [2] describe seven aetiological factors for impingement. In just one of the seven factors (tendinosis), US therapy is indicated. In fact,