make it so, and we firmly believe that this is quite fundamental in an efficacy study. As researchers and clinicians with a good knowledge of acupuncture, we as a profession have the responsibility to present the clearest possible evidence, and we do not believe that it is in the consumer’s best interest to further propagate more confusion if such confusion already exists.

We would also like to make it clear that we have not at any point accused White and Ernst (or indeed anyone else) of misrepresenting the truth and, as pointed out in the letter by White and Ernst, pulling out a ‘sound-bite’ such as this can be a risky business. The paragraph in which this phrase was used in our paper related to the general use of scoring mechanisms and the inherent problems thereof. White and Ernst’s letter then draws attention to a neck pain trial that we have conducted ourselves. This trial is not the focus of our attention and indeed the finished paper is in submission and therefore cannot be commented upon. We would agree, however, with the comment that the placebo effect of sham TENS (transcutaneous electrical nerve stimulation) could indeed be different from that of sham acupuncture. This is a very valuable point and suggests that more research into acupuncture controls is vital. We are ourselves planning such research. The advantage of sham TENS, however, is that, in terms of efficacy, it is inert whereas sham acupuncture may not be. The use of sham TENS as a control has been well validated [2–5] and there is no evidence to show that, when used in conjunction with the proper outcome measures, it is inferior to any other currently used acupuncture control.

Lastly, White and Ernst have drawn attention to their use of the Jadad scoring mechanism. Whilst we would in no way doubt the calculations made by White and Ernst, our point was that the system has poor intertester reliability and sensitivity, as explained in our paper [1], and it is therefore not surprising that our scoring of the same trials was different from theirs.

We would like to thank Dr. White and Professor Ernst for pointing out and highlighting two valuable points. First, we are glad to report that our use of the Jadad scoring mechanism is in line with White and Ernst, who also used this mechanism. However, we disagree with their statement that our use of Jadad was ‘arbitrary’ and ‘inappropriate’ [1]. We believe that our use of Jadad was appropriate and that it is a reliable and valid tool for assessing the quality of clinical trials. Second, we are glad to report that our results are consistent with White and Ernst’s findings, and we are in complete agreement with their statement that “the results of our review are consistent with those of White and Ernst” [1]. We would therefore like to express our sincere thanks to White and Ernst for their comments, which will help to improve our methodology and the quality of our future research.

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Pancytopenia in a patient with scleroderma treated with infliximab

Sir, We read with interest the report by Marchesoni et al. [1] of life-threatening reversible bone marrow toxicity in a rheumatoid arthritis patient treated initially with methotrexate and later switched to leflunomide plus infliximab. The authors suggest that leflunomide may have been responsible for the pancytopenia in their case.

We took care of a 45-yr-old female nurse with scleroderma diagnosed 5 yr earlier when she presented with arthralgias, sclerodactyly and a history consistent with Raynaud’s phenomenon. She was anaemic (haemoglobin 10.5 gm/dl), had positive antinuclear antibodies (ANA) at a titre of 1:160, and had renal insufficiency (blood urea nitrogen 37 mg/dl, creatinine 1.7 mg/dl). Initial therapy included d-penicillamine 125 mg daily and enalapril 10 mg twice daily. Three months later she developed renal crisis and had worsening of renal function that required haemodialysis for approximately 14 months. Renal function stabilized with a serum creatinine level at around 3 mg/dl. She did well for the next 2 yr, until she suddenly developed severe dyspnoea that worsened over the ensuing few weeks. Chest radiographs showed interstitial lung disease and pulmonary function tests showed a restrictive pattern. Transthoracic echocardiography showed a pulmonary artery pressure of 45 mmHg. Her underlying renal failure limited the use of cytotoxic and immunosuppressive agents. Therefore, infliximab therapy was discussed with the patient and, after agreeing to it, she received an infusion of infliximab (300 mg intravenously over 2 h). Six days after receiving the infusion, the patient reported a late hypersensitivity reaction that lasted 3 days and was characterized by sore throat, malaise and severe arthralgias, and she refused further infliximab infusions. Two weeks later she was hospitalized with nausea, vomiting and progressive weakness. She was found to be hypotensive and dehydrated. Blood tests...
revealed pancytopenia [white blood cell count (WBC) \(2.3 \times 10^3/\text{mm}^3\), haemoglobin (Hb) 6.8 g/dl, haematocrit (Hct) 17.5, platelets 37000/mm\(^3\)]. Prior to infliximab therapy her WBC was \(8.0 \times 10^3/\text{mm}^3\), Hb 11 g/dl, Hct 35 and platelet count 200000/mm\(^3\). She developed fever up to 102°F (38.9°C) and abdominal pain over the next 24 h, and ascites was present. Peritoneal fluid was cloudy, with 322 red blood cells/mm\(^3\), 4950 white blood cells/mm\(^3\) and 96% neutrophils. Fluid cultures later grew Candida albicans. According to the patient’s wishes, only blood transfusions, antibiotics and supportive care were given, and she expired the next day. No autopsy was done.

Tumour necrosis factor (TNF) inhibitors are being investigated in the treatment of a variety of rheumatic disorders, including scleroderma [2, 3]. Early results with etanercept indicate marginal clinical improvement, especially of skin involvement. Due to the severity of the patient’s clinical picture, infliximab therapy was given. This was followed by pancytopenia and fungal infection. She was not receiving any other therapy that may have induced her haematological complication, which led us to implicate infliximab as an important contributor. This case should be added to the cases of existent pancytopenia already reported in association with anti-TNF-α therapy [4, 5].

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Reply

We read with interest this letter from Menon et al. [1] reporting another case of pancytopenia following infliximab infusion, but this case was a bit different from ours. It concerned a patient with scleroderma (our patient was affected by rheumatoid arthritis), and the pancytopenia was strictly linked to infliximab treatment, whereas the bone marrow toxicity occurring after the infliximab infusion in our patient may have been partially due to the fact that he was being treated with methotrexate and allopurinol and had been receiving leflunomide until a few weeks before the infliximab infusion. As it was not clear which drug(s) or combination of drugs was responsible for the severe adverse reaction, we stressed the importance of careful patient monitoring when switching from one anti-rheumatic drug to another, especially in the case of the new and powerful immunosuppressive agents. It is interesting to note that both patients had impaired renal function and, although we cannot know whether this condition may be relevant in such cases, in our opinion it must clearly be kept in mind when starting infliximab therapy. At least one lesson that can be learned from these two cases of pancytopenia following infliximab infusion is that such powerful biological agents should be used with caution in rheumatic patients debilitated by other conditions and years of drug therapy.

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Fate of inflammatory neutrophils within the joint

Sir, We agree with Ottonello et al. [1] that the fate of neutrophils at inflammatory sites, especially within the rheumatoid joint, is an important issue which needs to be clarified. Their study, recently reported in this journal, is one of a very few which examines the influence of inflammatory synovial fluid on apoptosis in neutrophils [1, 2]. In their studies, joint fluid from eight of 11 RA patients produced inhibition of spontaneous and stimulated apoptosis in cultured neutrophils. Evidence is presented that this effect relates to adenosine levels within the joint fluids. The authors suggest that their findings support the view that, within the inflamed rheumatoid joint, synovial fluid factors (especially adenosine) tend to inhibit apoptosis and prolong neutrophil lifespan, thus maintaining the inflammatory response.

Their results appear to conflict with some of our own findings [2] in which we reported that synovial fluids from a variety of arthritic patients generally promoted neutrophil apoptosis, a finding at odds with...