Next, when acupuncture is compared with conventional treatments some sort of physical placebo will be needed. Several studies have compared acupuncture with random needling, assuming it to have only a placebo effect. Such an assumption is probably incorrect. Any noxious stimulus can attenuate pain elsewhere in the body through the mechanism of diffuse noxious inhibitory control.^{24 25} Probably the best available placebo is mock transcutaneous nerve stimulation, which produces a placebo response of the order of 30%²⁶⁻²⁸—similar to that expected from placebo medication.^{26 29 30} The machine may be defunctioned simply by stopping the transmission of current to the patient while allowing its “black box” to produce audio or visual signals. It may therefore be a more suitable physical placebo than random needling, which has a 40% response rate.

Should a study to compare acupuncture with mock transcutaneous nerve stimulation have different therapists providing the two different treatments? Such a design might, in effect, compare the charisma of the therapists rather than the treatments. If the same therapist provided both treatments he or she might “sell” one particular treatment in a less convincing way than the other. Both options have faults, but it is difficult to devise a valid placebo which may be used consistently, without the therapist’s knowledge.

A further problem with most of the published clinical trials is that too few patients have been entered for a statistically significant result to emerge. Trial size need not be large, however, if two widely different treatments as acupuncture, with a predicted 60% response rate, versus a physical placebo, with a predicted 30% response rate, are compared. Clear definitions of success or failure of treatment must be made at the start of the study. Pain returns almost invariably after treatment with acupuncture, and it may be more appropriate to use a survival analysis rather than a comparative statistical test.³¹

Another criticism of some of the previous studies is that they have evaluated the effect of acupuncture on pain without analysing the natural history of different types of pain.¹⁶ Ideally a single disease should be studied, and the entry criteria should define a relatively homogeneous group of patients.

Acceptable studies of effects of acupuncture as an analgesic should, then, be single blind, comparative trials, initially using a physical placebo, perhaps later comparing the effects of acupuncture with more conventional treatment. If acupuncture is to become an accepted treatment objective scientific studies must be carried out.³²

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Letters to the editor

One of the reasons for publishing a scientific paper is to hold it up for critical scrutiny and comment. We believe this comment should be public and immediate, which is why we devote so much space to correspondence. So we are pleased to be receiving more letters for publication, but like all bonanzas it is creating problems. Ten years ago we published more than three quarters of all the letters we received, but now we can publish only half—despite devoting more pages to correspondence. In order to stop the proportion we publish from dropping any lower (and maybe even to raise it) we are going to change our policy. From now on we will shorten some letters ourselves unless authors specifically state that we may not, and authors’ willingness to have their letters shortened will inevitably be one factor we will consider when deciding which letters to publish.

A second policy change is that we will no longer consider for publication letters that are not typed with double spacing between the lines. We have stated for the past two years in our instructions to authors that letters should be prepared in this way, but most of the letters we receive are not. Indeed, many of them are very poorly presented—in a way that would not be acceptable if they were papers. Many authors seem not to realise that their letters have to be subedited and then read by a printer who sets them in type.

While embarked on this moan, I want to point out two other policies that we have for our correspondence columns and to which many of our readers seem oblivious. Firstly, unlike many other scientific publications our correspondence columns are reserved primarily for letters that relate to articles that we have published. We try to avoid original publications (what we call “out of the blue”)—these we consider as papers or short reports and so referee in the normal way. This rule does not apply to letters on political and policy matters.

Secondly, we are unenthusiastic about publishing letters more than six weeks after the article to which they refer. If a writer wants to take part in the argument about an article then he must be quick. One corollary to this policy is that our overseas readers who want to have letters published will need to make sure that they have access to an airmail edition of the journal.

We are not inflexible bureaucrats, and all of these rules may be broken. But their aim is to make our correspondence columns more readable and immediate and to give as many people as possible a chance to have their say. We hope, therefore, that our readers will cooperate.

RICHARD SMITH
Assistant editor

Cytomegalovirus infections in renal transplant recipients

After renal transplantation up to 60% of seronegative recipients and nearly 90% of seropositive recipients may show evidence of cytomegalovirus infection.¹ While many such patients remain clinically asymptomatic, the infection is associated with considerable morbidity and mortality.¹⁻³

Impairment of renal function developing after transplantation may be due to rejection or cytomegalovirus infection, and the distinction is vital clinically, since the former requires an increase in immunosuppressive drugs whereas in the latter the dose has to be decreased.⁴ Studies from Boston have shown that about half the patients with cytomegalovirus viraemia and renal impairment have diffuse glomerular lesions with only minimal interstitial damage. This finding helps to differentiate patients with cytomegalovirus infection from those having rejection episodes.⁴⁻⁵ Changes in the ratio of T lymphocyte subset populations may also help since the ratio of OKT4 (helper/inducer) to OKT8 (suppressor/cytotoxic) cells may be increased in rejection⁶ and reduced in clinically apparent cytomegalovirus infection.⁵ Some workers, however, have failed to confirm this finding⁷; the type and degree of immunosuppression may affect the OKT4:OKT8 ratio.⁸ Indeed, the degree of immunosuppression has a direct influence on cytomegalovirus infection—and in particular

treatment with antithymocyte globulin increases the risk of severe cytomegalovirus infection,⁹ possibly by causing T cell depression.¹⁰

Which patients, then, are at risk of developing severe cytomegalovirus disease? Firstly, reactivation of virus among patients who were seropositive before receiving their transplants is the more common form of infection and is usually less severe than primary infection.¹¹⁻¹⁴ The source of cytomegalovirus in primary infection is probably the donor kidney, since infection is rare in seronegative recipients given grafts from seronegative donors.¹¹⁻¹⁴⁻¹⁵ Orsi *et al* isolated cytomegalovirus from donor kidneys¹⁶ and Wertheim *et al* showed by DNA restriction enzyme analysis that two recipients of kidneys from the same donor excreted cytomegalovirus strains with identical DNA profiles.¹⁷ Kidneys obtained from cadavers and parents carry a greater risk of infection among recipients than those obtained from child or sibling donors¹⁴—probably because the incidence of cytomegalovirus infection increases with age.

The risk of cytomegalovirus infection may, therefore, be lessened by careful matching of donor and recipients with respect to cytomegalovirus state. With the shortage of donor kidneys in Britain and with over half of all donors being seropositive this group cannot be excluded; but whenever possible allografts from seropositive donors should not be given to seronegative recipients.¹³ Surprisingly the protocols for neither UK Transplant nor Eurotransplant make any reference to cytomegalovirus state. All renal units have access to virology services for testing markers of hepatitis B virus infection, however, so they should be able also to determine the cytomegalovirus state of donors and recipients.

Another approach to preventing cytomegalovirus infection is to use relatively low dose steroid regimens.¹⁸ McGeown *et al* noted that though infections caused 37.5% of deaths after renal transplantation reported to the European Dialysis and Transplant Association none of their 100 patients died of infection.¹⁹ One of the reasons suggested for this disparity was the sparing use of steroids. Whether or not the use of cyclosporin will reduce the incidence of cytomegalovirus infection is not clear. Since cyclosporin acts primarily on T cell functions one might expect that cytomegalovirus infection would occur more frequently and perhaps be more severe.²⁰ So far, however, the findings have been variable. Dummer *et al*²¹ and the European Multicentre Trial Group²² found no difference in the incidence of cytomegalovirus infection between patients treated with cyclosporin and azathioprine. Petersen *et al* reported that patients given cyclosporin had responded beneficially—but they used antilymphocyte globulin in the control group.²³

High titre globulin has been used for the prophylaxis and treatment of cytomegalovirus infection; three reports all found a beneficial effect.²⁴⁻²⁶ Meyers *et al* found that bone marrow recipients who had received prophylactic globulin had significantly fewer infections than controls, provided that the granulocyte transfusion donors were seronegative for cytomegalovirus.²⁵ Winston *et al* showed that, though giving cytomegalovirus immune plasma resulted in a similar incidence of cytomegalovirus infection in the treated and control groups of bone marrow recipients, the infection was less severe in the treated group.²⁴ Recipients of bone marrow transplants are more profoundly immunosuppressed than renal transplant recipients, in whom comparable results might be expected: Condie *et al* treated 52 such patients with high titre globulin in an uncontrolled trial and concluded that some benefit had occurred.²⁶