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Alternative medicine

One of the few growth industries in contemporary Britain is alternative medicine. An apparently endless stream of books, articles, and radio and television programmes urge on the public the virtues of treatments ranging from meditation to drilling a hole in the skull to let in more oxygen.[1] Patients readily tell their doctors that they have flirted with the competition: one recent study found that 33% of patients with rheumatoid arthritis and 39% of those with backache admitted to having consulted an alternative practitioner.[2] Increasingly often doctors themselves are becoming interested in alternative treatments: a survey (p 337) of general practitioner trainees showed that 70 of the 86 wanted training in techniques such as hypnosis, acupuncture, manipulation, homoeopathy, and herbalism. Twelve of the doctors had referred their patients for treatment to non-medical practitioners—a step which only a few years ago could have led to an appearance before the General Medical Council disciplinary committee.

Attitudes among doctors to alternative medicine seem to have become polarised. Either they welcome moves to include all therapists within the health professions and argue that doctors should be open minded about alternatives to drugs, or they reject the range of alternative therapies as "rubbish" and regret the change in attitudes that has given them so much public acceptance.

The truth lies, I believe, somewhere in the middle ground. No one would want to return to the days when patients who had consulted an osteopath or a herbalist dared not tell their doctor what they had done. Caring doctors will be sympathetic when one of their patients with multiple sclerosis or rheumatoid arthritis wants to go on a pilgrimage or try some modification to the diet. Nevertheless we need to remember that improvements in the results of treatment of diseases such as tuberculosis or leukaemia have come from the acceptance by clinicians of the need for controlled clinical trials. Such trials are the only way to disprove widely held convictions such as the need for radical mastectomy in early breast cancer or for prolonged bed rest for patients with tuberculosis or cardiac infarction. However discomforting it may be to their proponents, the gluten free diet and the sunflower oil diets for multiple sclerosis have failed to pass the test of the controlled trial: doctors should be aware of negative results of this kind and pass the information on to inquiring patients.[3-5]

Informed scepticism seems, indeed, to be the most useful approach by the doctor to alternative treatments. He should be able to tell his patients which have been evaluated by objective tests and which have not—applying the same standards of trial design and assessment as those applied to studies of new drugs. If treatments have not been evaluated he should say so—while not denigrating the undoubted benefits that many patients gain from a treatment they believe in given by caring therapists.

Stricter standards should be required, however, by a doctor proposing himself to use alternative treatments. If the treatment he proposes using has not been validated by a clinical trial then he is in just the same position as a clinical pharmacologist with a new drug. Treating a few patients to see how they get on is scientifically—and I believe ethically—unacceptable. Patients given new treatments (or old treatments that have not been formally tested) should be entered into some sort of formal trial. Enthusiasts who claim that acupuncture has been used by hundreds of millions of people for 4000 years ignore the need for Western clinicians to know how it compares with, say, analgesics, muscle relaxants, or physiotherapy and in which conditions it can be shown to be superior.[6]

Much of the appeal to the public of alternative medicine lies in the setting in which most such treatments are given. Practitioners give their patients time, courtesy, and individual attention; and they listen. Healing is not the same as curing: patients with chronic or terminal diseases may have many of their symptoms relieved by a skilled, compassionate healer who does nothing to arrest the disease process. Conversely, compassion is no barrier to research. One of the important achievements of the hospice movement has been its demonstration that compassion can mix with scientific evaluation of drug regimens and other procedures for controlling pain.

At the heart of the matter is the reality that the public sees doctors as scientifically trained clinicians; and that means they have a professional obligation to their patients to help guide them through the claims and counterclaims of practitioners on the medical fringe. Uncritical enthusiasm has no place in such an evaluation; the crucial tests are the objective ones.

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Acetate or bicarbonate for haemodialysis?

Early dialysis systems used bicarbonate to correct the acidosis of renal failure, and this required carbon dioxide to be bubbled continuously through the dialysis fluid to prevent a rise in pH and the subsequent formation of insoluble salts of calcium and magnesium. Mion *et al* in 1964[1] showed that patients could rapidly metabolise acetate to bicarbonate, and since then acetate, which is more stable and convenient to use than bicarbonate, has become the source of buffer in haemodialysate. Recent evidence,[2-7] however, suggests that some patients metabolise the acetate load more slowly than others and may develop high concentrations of acetate in the blood during dialysis. Hyperacetataemia has been linked with unpleasant symptoms[2] such as nausea, malaise, and sudden hypotension[8-11] as well as accelerated atherogenesis due to diversion of acetylcoenzyme A formed during acetate metabolism to lipid biosynthesis.[12] These reports have coincided with the production of new dialysis systems capable of delivering bicarbonate in the dialysate. It is therefore important to examine the evidence on which the concept of so called acetate "intolerance" is based.

The normal blood acetate concentration ranges between 10 and 400 μmol/l (0·6 and 23·6 mg/l).[4-6 13-15] It can be measured by gas chromatography,[4 13 15] isotachophoresis,[10 16] and enzymatic methods,[14] provided that the generation of acetate from glucose in the preparative stage[15] is avoided. Some claims of acetate toxicity must be treated cautiously, either because blood concentrations were not actually measured[8 9] or because unsatisfactory methods were used.[2 15 17] During dialysis the arterial concentration of acetate remains at about 2-4 mmol/l (12-24 mg/100 ml) in about three quarters of patients, though in those who metabolise acetate slowly it may increase to 15 mmol/l (89 mg/100 ml) or more.[5 7] The usual concentration of acetate in the dialysate is 35 mmol/l (207 mg/100 ml) and hyperacetataemia is more likely to occur if this is increased[3] or if dialysers with very large surface areas ($>1·5$ m^2) are used.[3 6] The maximum rate of utilisation of acetate is roughly 2-5 mmol/min/70 kg,[18] and may be impaired[18 19] in the presence of renal failure, diabetes, liver disease, and poor tissue perfusion. After conversion to acetylcoenzyme A most acetate is metabolised by way of the Krebs cycle,[3] producing increased concentrations of some intermediates[16] and organic acids,[3 6 20] although there is little evidence[21] of enhanced lipid formation.

Haemodialysis is associated with hypotension in about a quarter of patients, which is important because it limits ultrafiltration and contributes to the morbidity of the procedure. Normally the reduction in circulating volume due to removal of fluid is compensated for by changes in peripheral resistance and cardiac output and by vascular refilling.[22] In some patients, however, peripheral resistance may fail to increase, possibly because the sympathetic response to volume depletion is inhibited, or because of an increase in body temperature.[23] Similarly, the production of a compensatory tachycardia may be impaired[24] because of autonomic neuropathy, diminished activity of the baroreceptors, or postsynaptic unresponsiveness. Vascular refilling may be restricted if the sodium concentration in the dialysate is inappropriately low.[25]

It has been suggested that acetate may contribute to the hypotension associated with dialysis by causing vasodilatation[10 22] and impaired myocardial contractility.[8 11 26 27] Though acetate does reduce peripheral resistance,[28] the effect in an individual patient is unpredictable,[29] and vasodilatation is usually accompanied by an increase in cardiac output.[7 22] The evidence for a specific "cardiodepressant" effect of acetate is open to debate. For example, the impairment of myocardial function during acetate dialysis inferred by Aizawa *et al*[8] may merely reflect a fall in peripheral resistance. In any case, these authors used indirect methods to study cardiac function, which may not be appropriate for patients having dialysis.[22 30] Kirkendol *et al* showed that massive bolus injections of acetate (and bicarbonate) reduced the contractile force of the myocardium,[26] but the relevance of this particular observation is not clear, particularly as later work using an infusion of acetate showed the opposite effect.[27] Furthermore, other clinical[7 30] and laboratory[31] studies have shown that an infusion of acetate increases cardiac output and that acetate alone can provide a satisfactory source of energy for the mammalian heart, even under ischaemic conditions.[32] Nevertheless, many workers have claimed that the incidence of hypotensive episodes is reduced if dialysate containing bicarbonate, rather than acetate, is used.[8 9 11 29 33]

Complex changes in acid base balance occur during haemodialysis.[20] In the early stages metabolism of acetate may not keep up with the loss of bicarbonate from the patient into the dialysate so that a fall in arterial bicarbonate and pH may result. Influx of acetate and generation of bicarbonate continue during dialysis, and an appreciable alkalosis may develop by the end of a dialysis. These changes may be compounded by hyperventilation due to the fall in pH, hypoventilation secondary to loss of carbon dioxide through the dialyser,[34] and hypoxaemia resulting from plugging of the pulmonary circulation with microthrombi consisting of leucocytes, which are caused by contact with the dialyser membrane.[35] The combined effect of these changes on blood gases and pH may be hard to predict, especially since there are secondary changes in the affinity of haemoglobin for oxygen. Symptoms such as fatigue and nausea have been ascribed to tissue hypoxia and may be relieved by the administration of oxygen.[36] Bicarbonate dialysis prevents some of the changes,[11 20 29] perhaps because ventilation is maintained by the high partial pressure of carbon dioxide in the dialysate.

Instability of the circulation must therefore reflect not only the presence of the acetate ion but also changes in blood volume, acid-base balance, and autonomic dysfunction. Many of the adverse effects attributed to acetate appear only when large and highly efficient dialysers are used—generally because of the pressure to dialyse large numbers of patients in the shortest possible time. The problem of overload with acetate encountered in the United States may, therefore, be of limited interest in Britain, where dialysers with large surface areas are seldom used.

The function of the cardiovascular system during haemodialysis is attracting much attention, and the various factors which lead to vascular instability are being defined. The new bicarbonate dialysers provide a stimulus to this research and