Furthermore, different populations of cultured bone cells seemed to be specifically stimulated by certain intensities of electrical fields. Such electrical stimuli might circumvent the prostaglandin $E_2$ system, triggering adenyl cyclase directly and inducing DNA synthesis.

How prostaglandins might convert a mechanical stimulus into an osteogenic one is uncertain. Prostaglandin $E_2$ is a powerful bone resorber, but its effect depends on its amount, and it may also enhance osteogenesis. The study of the behaviour of bone cells in culture—and in other experimental systems—may be said to have little present relevance to man; but it does suggest how mechanical forces might act on the osteoblast and provides a way forward for future investigation.

If this extraordinary cell, the osteoblast—which synthesises bone matrix, mineralises it, and controls the activity of other cells[9]—is in fact sensitive to mechanical (and electrical) stimuli, why is exercise not universally successful in increasing bone mass? Some reasons are obvious. One is the coupling of bone formation to resorption; another, as in the athletes with amenorrhoea, is oestrogen deficiency. Doubtless there are many unrecognised limitations to the osteogenic effect of exercise on bone. Clues may come from the striking effect of immobilisation or satellite travel on the skeleton, where there appears to be an uncoupled decrease in osteoblastic and increase in osteoclastic activities, and where in neither case is the loss of bone alleviated by exercise.[10]

Should we therefore recommend exercise as a treatment for osteoporosis? Certainly some are not impressed by its efficacy.[11] But in the elderly, where osteoporosis may be partly due to sleepy osteoblasts, the answer is probably yes.[12] In the young the answer is not so clear, and where exercise is so excessive that it produces amenorrhoea loss of bone from the spine will be aggravated rather than prevented. In this regard we must remember the differences in the behaviour of weight bearing, predominantly cortical bones and that of predominantly trabecular bones.[13]

We still have a lot to learn about the effects of mechanical forces on the skeleton. As jogging and space travel become more popular and the population ages, the answers will be sought more avidly. The search will not only be advancing our knowledge of bone disease but also throwing light on an important problem in cell biology.

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# *Regular Review*

# Is peritoneal dialysis a good long term treatment?

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Long term treatment for terminal renal failure with peritoneal dialysis was first achieved successfully by Boen and colleagues.[1] The technique did not become suitable for general use, however, until a satisfactory permanent peritoneal catheter was developed.[2] Since then very many patients have received intermittent peritoneal dialysis. Continuous ambulatory peritoneal dialysis was first developed in 1975.[3] This technique is now used widely, particularly in Britain, where 1104 patients were undergoing treatment at the end of 1982.[4] In 1983 nearly half of all children in Britain having dialysis were receiving continuous ambulatory peritoneal dialysis[5]; in Canada, too, nearly half of all new patients are being offered this treatment.[6] Continuous ambulatory peritoneal dialysis has helped individual units in Britain to increase the numbers of new patients they can take on.[7]

Despite the phenomenal growth in the use of this form of treatment, the long term prognosis for patients receiving peritoneal dialysis remains uncertain. In the June 1984 issue of the *Peritoneal Dialysis Bulletin* Oreopoulos described a patient maintained in reasonable health for over 10 years with intermittent peritoneal dialysis alone and then continuous ambulatory peritoneal dialysis.[8] This woman may well be the longest survivor on peritoneal dialysis in the world to date.

More patients have received intermittent peritoneal dialysis than continuous ambulatory peritoneal dialysis, since the treatment is often used as a temporary measure

before haemodialysis or transplantation. It may also be used as a last resort.[9] Little is known about the long term results of intermittent peritoneal dialysis, though individual patients have survived over six years. Much more data are available for continuous ambulatory peritoneal dialysis.

One of the major benefits of continuous ambulatory peritoneal dialysis is that most patients have a rise in haemoglobin concentration owing to an increase in red cell mass.[10 11] This haematological response may be of particular value in children and contrasts with the need for repeated transfusion during haemodialysis. A postal survey of patients having continuous ambulatory peritoneal dialysis in the United States suggested that they were capable of more physical activity than recipients of haemodialysis.[12] The data for the latter group were taken from a separate study, however, and thus did not form a comparable population.[13]

Haemodialysis is well known to be associated with stress in both patients and families. A comparison of patients receiving continuous ambulatory peritoneal dialysis and haemodialysis, matched for demographic variables and time on dialysis, suggested that the former were more satisfied with relations at home than patients receiving haemodialysis.[14] Certainly in the short term most patients who transfer from haemodialysis to continuous ambulatory peritoneal dialysis prefer the latter. Children are said to prefer peritoneal dialysis, not least because of the absence of needles.[15] Teenagers and young adults may choose haemodialysis, however, simply because it allows them freedom between treatment sessions.

One problem with any form of peritoneal dialysis is loss of protein through the peritoneum. This may be serious during peritonitis, when hypoalbuminaemia may develop rapidly. Patients having haemodialysis need 1 g protein/kg/day but adults having continuous ambulatory peritoneal dialysis need at least 1·3 g/kg/day.[16] In practice many patients do not take sufficient protein and have a fall in total body nitrogen.[17] A survey of children receiving continuous ambulatory peritoneal dialysis has shown that their intake of protein and energy is often less than prescribed and that they show evidence of poor nutrition.[18] Children with chronic renal failure grow poorly, and treatment with a transplant gives better results than haemodialysis. The response to continuous ambulatory peritoneal dialysis is still uncertain, owing partly to the small numbers so far treated. Their growth velocity was reduced in one study,[19] but in another the increase in height was said to be as fast with continuous ambulatory peritoneal dialysis as with a graft.[20]

Some patients with chronic uraemia have raised triglyceride concentrations. Treatment with continuous ambulatory dialysis is associated with a rise in the serum concentrations of both total cholesterol and very low density lipoprotein cholesterol,[21] whereas in haemodialysis these values remain normal. Whether this increase in cholesterol will be associated with an increased risk of cardiovascular disease remains uncertain.

The main complication of any form of peritoneal dialysis is peritonitis due to micro-organisms. If the infection is not adequately treated sufficient adhesions may occur to obliterate the peritoneal cavity. This is particularly likely if the organism is a fungus or yeast. Removal of the catheter and temporary transfer to haemodialysis may be necessary. Repeated bacterial peritonitis may lead to loss of the cavity from sclerosing peritonitis.[22]

Renal physicians have worried that the peritoneal membrane had not evolved to be "insulted" by man made fluids for years on end so that long term treatment would be a rare occurrence or impossible. Clearly the experience of Oreopoulos's patient shows that 10 years is feasible, but she had spent half that time having intermittent peritoneal dialysis before switching to continuous ambulatory peritoneal dialysis. Apparently in the absence of severe peritonitis the clearance or removal rate of metabolites shows no sign of reduction in the first few years of continuous ambulatory peritoneal dialysis. The possible loss of ultrafiltration capacity is another matter. Slingmeyer and colleagues suggested that by two years a third of patients receiving continuous ambulatory peritoneal dialysis had lost a substantial proportion of that filtration capacity and that eventually they needed to change their treatment.[23] An international study has shown that the use of acetate is far more likely to lead to this problem than lactate.[24] Part of the phenomenon may be artefactual because of a falling urine output and excess fluid intake.[25] Even with lactate solutions, however, a few patients develop fluid retention within two to three years of starting treatment. Sometimes "resting" the membrane by switching to haemodialysis for a period allows recovery.

Any programme of continuous ambulatory peritoneal dialysis requires support by haemodialysis facilities. Perhaps as many as 80% of patients having had more than two years' treatment will have needed haemodialysis at some time.[26] Even if that estimate is too high the need is sufficient to prevent continuous ambulatory peritoneal dialysis being developed on a large scale by district general hospitals with no haemodialysis facilities. The underprovision of dialysis facilities in Britain cannot, therefore, easily be solved by encouraging further growth of continuous ambulatory peritoneal dialysis.

Survival is clearly what concerns patients most. A study from Canada suggested that at two years the survival of non-diabetics having continuous ambulatory peritoneal dialysis was the same as those receiving haemodialysis.[6] A report from seven renal units in Britain found no gross differences between the two treatments over the first two years.[27] The registry of the European Dialysis and Transplant Association, however, has recently analysed the interval mortality for over 1000 patients receiving continuous ambulatory peritoneal dialysis. They were matched with patients receiving haemodialysis of the same age, sex, primary diagnosis, country, body weight, and starting date of treatment. During the first year there was no difference but thereafter there was increasing interval mortality in those having continuous ambulatory peritoneal dialysis.[9] Since the patients were not randomly selected for the various treatments, however, the difference may possibly have been determined by other prognostic factors rather than the treatment itself.[28] Most studies have found a higher proportion of patients having continuous ambulatory peritoneal dialysis with pre-existing cardiovascular disease or diabetes than those having haemodialysis.

A further concern is the relatively high drop out rate owing to technical failure. The United States continuous ambulatory peritoneal dialysis registry reported that two thirds of patients were still using this treatment after one year,[29] and the European Dialysis and Transplant Association noted that by two years only 40% were continuing with continuous ambulatory peritoneal dialysis. After exclusion of transplants, loss to follow up, and recovery of function there remained a technical failure rate of 38%.[9] Most patients had transferred to haemodialysis.

These seemingly poor results have directed attention to the selection of patients. A report from Manchester

concluded that those who would otherwise have been suitable for home haemodialysis had fewer problems with continuous ambulatory peritoneal dialysis.[30] An American study found that patients whose training took a long time had an increased risk of peritonitis.[12] Younger patients did less well, possibly because they were in too much of a hurry—a phenomenon not confined to those having dialysis. A further consideration has been whether certain people are more or less susceptible to infection. Recent work suggests that patients having high opsonic activity against *Staphylococcus epidermidis* in their peritoneal effluent have a lower chance of peritonitis.[31] If confirmed this may prove a valuable way of predicting a high risk group.

Clearly the best way of comparing the results of treatment would be a prospective randomised trial, but none has been reported. Furthermore, it is doubtful if any such study could be performed since it would deny patients the right to choose. How, then, should the nephrologist advise a patient? There seems little doubt that in the short term (two to three years) certain patients do better with continuous ambulatory dialysis—for example, those with serious cardiovascular disease, diabetes,[32 33] very small children, and those who fear machines. Patients having problems with training for continuous ambulatory peritoneal dialysis or who have repeated peritonitis should be transferred to haemodialysis.

The question that needs to be answered is whether younger patients should be offered peritoneal dialysis as a first treatment. Quite possibly continuous ambulatory peritoneal dialysis might give as good results as haemodialysis in selected groups, but clinicians will remember that haemodialysis has kept patients alive for 20 years[4] with 57% of those aged 15 to 34 surviving 10 years,[34] whereas no such data are available on the results of peritoneal dialysis. Rubin and colleagues have commented that so far there is no evidence that peritoneal dialysis offers any lower morbidity or mortality than haemodialysis.[35] One must, therefore, conclude that for the younger patient with good family support and no other serious medical problems home haemodialysis gives the best chance of longevity and least chance of serious morbidity (short of a successful transplant).

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