protein bound than propranolol,9 but the value of this procedure has not been assessed.

The optimum management of these patients requires intensive supportive care with facilities for continuous cardiac monitoring and ventilatory support. Transvenous electrical pacing may be useful,10 though it is not always successful,1 and ideally all patients with serious overdosage from beta-blockers should have a pacing catheter inserted. Intravenous atropine, 2-3 mg in divided doses, should be given to reduce unopposed vagal activity, and isoprenaline should be given by intravenous infusion with the dose monitored according to the response of the pulse and blood pressure. Because beta-blocking drugs are competitive antagonists of isoprenaline, massive doses may have to be given: in one recent report a total of 115 mg was infused over 65 hours.10 The effects of beta-blocking drugs on the body last longer than their chemical half life in the plasma, and so intensive care may have to be continued for several days. Theoretically, other catecholamines such as dopamine or dobutamine11 may have some advantages over isoprenaline, especially in poisoning with selective drugs such as atenolol or metoprolol—when the haemodynamic effects may be modified by beta-receptor selectivity, unopposed alpha-adrenoreceptor stimulation, and baroreceptor reflexes.12 Further developments of specific beta-adrenoreceptor agonists are awaited with interest.

Intravenous glucagon may also be of value in treatment13 14 and in severe overdosage with beta-blocking drugs it should be given early. Glucagon is thought to activate myocardial adenyl cyclase by a different mechanism from the beta-adrenergic catecholamines,15 and its inotropic effect is not blocked by propranolol.16

Individual clinicians are unlikely to gain much experience in treating self-poisoning with beta-blockers, and hence these emergencies require close collaboration between the cardiologist and the clinical pharmacologist.

Plasmapheresis

Removing of antibody from the circulation of patients with antibody-mediated hypersensitivity diseases sounds a rational remedy. In practice, however, it is not quite so simple. Sudden withdrawal of antibody from the circulation stimulates a brisk compensatory increase in its synthesis, and subsequent antibody concentrations may exceed or even double those before plasmapheresis.1 2 Plasmapheresis needs to be combined with treatment with immunosuppressive drugs such as cyclophosphamide or azathioprine to suppress this response. Even then such a regimen achieves only partially suppression of antibody synthesis.3

Plasma exchange has been used with success in the management of Goodpasture syndrome,4 5 an autoimmune disease in which antibodies are formed against glomerular and pulmonary basement membranes.6 Removal of these antibodies may not, however, be the factor that induces remission—for improvement has been reported in other forms of acute glomerulonephritis associated with renal failure7 and in patients with the Goodpasture syndrome in whom antibodies are not detectable in the serum.5 Plasmapheresis certainly produces profound defibrination,8 and fibrin deposition is well established as part of the renal lesion in the Goodpasture syndrome and is also thought to play a part in crescent formation.9

In systemic lupus erythematosus the clinical manifestations are caused by immune complexes (made up of DNA and anti-DNA) becoming deposited in the kidney, blood vessels, and skin. Plasmapheresis is an effective way of reducing the amounts of circulating immune complexes, and may be associated with clinical improvement.10 Plasma exchange is also an effective way of lowering anti-D concentrations in Rhesus immunised women,11 though the authors could not conclude that it contributed to the successful deliveries.

Myasthenia gravis has long been suspected of having an immune basis, and recent animal studies in which the disease was reproduced by immunisation with purified acetylcholine receptor12 gives this hypothesis strong support. Furthermore, circulating antibodies specific for the acetylcholine receptor are found in nearly 90% of patients with myasthenia gravis.13 Further evidence that the circulating antibodies might be the cause of the neuromuscular disorder has come from studies in which the passive transfer of serum fractions from patients with myasthenia gravis induced the disease in mice14 and from experience with plasma exchange, which shows that there is an inverse relationship between the clinical state and the antibody titre.15 16

What, then, is the place of plasmapheresis in the treatment of myasthenia gravis? Pinching et al17 described improvement in two patients during a series of plasma exchanges and Finn and Coates18 noted transient improvement in one patient. A larger series has recently been reported from the United States.19 Combined with corticosteroids and azathioprine, plasmapheresis produced striking improvement in five patients who were still severely disabled despite thymectomy, corticosteroids, and optimal doses of anticholinergic drugs. The drop in the titre of antibody to acetylcholine receptor was steep during the first three plasma exchanges, falling to about 40% of the initial value, but the maximum clinical response was delayed for a further several weeks. Possibly since the neuromuscular junction had been subjected to antibody attack for several years the resulting structural damage might take time to recover. Alternatively, the response might be the effect of the administration of azathioprine. Dau et al20 believe that plasmapheresis offers a valuable new treatment for myasthenic patients with major disability or life-threatening weakness. Nevertheless, such a conclusion is premature, and the warning of Pinching et al17 against the premature acceptance of uncontrolled results in only a few patients is pertinent. Controlled studies are under way,19 and these may provide a more secure basis for recommending the use of plasma exchange in myasthenia gravis.

In general, the applications of plasma exchange are limited. It is time consuming, expensive, and cumbersome, and there may be practical difficulties in gaining access to the circulation. Though the procedure seems to be reasonably safe,20 an
amount of plasma equivalent to the patient’s total plasma volume needs to be removed at roughly weekly intervals, and this has to be replaced with plasma substitutes. Many factors, moreover, probably contribute to the benefits of plasma exchange and we need further trials under controlled conditions to establish its real value.


**Hyperbaric oxygen**

Although hyperbaric oxygen has a firmly established if small place in clinical practice, most doctors know little about it or where it can be obtained. The single-patient chamber filled with pure oxygen came into use in the United Kingdom during the 1960s. Sixteen of these are in radiotherapy centres in the UK with 27 other chambers in 22 hospitals throughout Britain. A move to establish regional centres has resulted in three—at Heatherwood Hospital, Ascot, for the Oxford Region; at Whipp Cross Hospital for North London; and at Peterborough District Hospital for the Cambridgeshire area. Large, walk-in, multiplace chambers exist in Aberdeen, Wroughton, Glasgow, and Newdale upon Tyne, and at the Institute of Naval Medicine at Alverstoke. In these the patients receive hyperbaric oxygen by face mask, the staff being pressurised with air. This type of chamber is more expensive to run. Britain is behind other countries in exploiting this method of treatment. Japan has over 100 treatment chambers in 80 centres, the Soviet Union at least 69, and Spain 33 (the most in terms of chambers per head of population). Over 70 units have been sold to the United States by British manufacturers. In the last two decades hyperbaric oxygen systems have been exported from Britain to 40 countries, during which time the numbers in the UK have not substantially increased.

The established indications for the use of hyperbaric oxygen include burns,\(^1\) carbon monoxide poisoning,\(^2\) decompression sickness,\(^3\) air embolism, and anaerobic infections— notably gas gangrene.\(^4\) Despite many published accounts of its dramatic effects on *Clostridium welchii* infections, surgeons still prefer the scalpel to the pressure chamber as the first line of attack in this lethal condition. The high PO\(_2\) within the chamber—about 2250 mm Hg (299 kPa)—at a pressure of three atmospheres absolute—immediately stops the organism multiplying and inactivates the toxin while maintaining the viability of the damaged tissues. Carbon monoxide poisoning is much less common than it was in Britain, because the North Sea gas now used contains no carbon monoxide. Paradoxically, however, the advent of North Sea gas, though it has reduced the need for hyperbaric oxygen as a treatment for gas poisoning, has increased the demand for hyperbaric facilities in hospitals close to the offshore rigs because of the conditions of pressure in which the divers work.

There is a small demand for the method for handling sickle-cell crises and improving the viability of pedicle skin grafts, and a wider demand (with less predictable results) for treating ulcers of ischaemic origin and pressure sores. Hyperbaric oxygen has also been used successfully in chronic osteomyelitis\(^5\) even though the causative organisms are aerobic. The results of studies using the technique for treating myocardial infarction,\(^6\) for improving cognitive functioning in the aged,\(^7\) and for neurosurgery\(^8\) have proved encouraging. For these conditions, however, the place of oxygen at pressure remains uncertain.

Hyperbaric oxygen has thus earned itself a place in orthodox clinical practice. The method is not fully exploited in Britain but existing facilities would probably be adequate if they were properly coordinated throughout the country. Setting up the three regional centres is a move in the right direction.

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