glucose or saline may be given as rewarming proceeds. Otherwise there should be minimal interference with the patient. In particular measures that may precipitate ventricular fibrillation should be avoided, such as unnecessary cardiac massage or laryngeal intubation, or, worst of all, intravenous injection of adrenalin.

More active treatment has long been known to produce recovery after hypothermia has caused ventricular fibrillation or arrest, but it is often forgotten that it can do so after arrest lasting an hour and sometimes considerably longer.[4] In Sweden anyone found apparently dead in cold air or water is routinely regarded as a candidate for emergency treatment rather than a casualty for the mortuary. This is particularly necessary as complicating factors such as "paradoxical undressing" by victims as hypothermia develops[5] may mislead a rescuer into thinking that they were victims of assault and injury rather than simple hypothermia. The problem is less common in countries with less cold winters, but the same principles should clearly be adopted in cold weather anywhere.

Simple external warming, with or without external cardiac massage and artificial ventilation, has seldom revived adults from hypothermic cardiac arrest or ventricular fibrillation. This is probably because rewarming is so slow that many hours may elapse before cardiac temperature rises to the point at which spontaneous cardiac rhythm restarts or defibrillation can succeed. Extracorporeal circulation—to provide vascular rewarming as well as maintenance of circulation—is therefore the treatment of choice in hypothermic arrest. It may be achieved by femoral or cardiopulmonary bypass and succeeds in a high proportion of suitable cases.[4,6]

The effort and resources needed for such invasive treatment have prompted a search for means of identifying victims capable of being revived. A recent paper suggests that hyperkalaemia may be a marker for non-recoverable hypothermia as hypothermic victims of avalanches had very high plasma potassium concentrations (mean 14·5 mmol/l) and could not be revived.[7] Patients with similar core temperatures after drug intoxication or simple exposure to cold had lower plasma potassium concentrations (mean 3·5 mmol/l) and could be revived, though some died later from other conditions. The high plasma potassium concentration probably reflected asphyxia as well as cardiopulmonary arrest in the avalanche group, all of whom were clinically dead. All of the 15 patients in the second group seem to have had a heart beat and respiration when found, although two had a brief arrest at some stage. The value of a very high serum potassium concentration as a prognostic indicator in uncomplicated hypothermia is therefore uncertain, but it may provide a guide to cases in which resuscitation cannot succeed for other reasons. Early measurements of plasma potassium concentrations might help in focusing attention on those victims who could be revived by the heroic measures needed in hypothermic cardiopulmonary arrest.

Most cases of urban hypothermia in Britain are not due to simple exposure and need different management.[8] Most of these people have collapsed as a result of serious disease and have cooled as a result of the illness and immobility, often in heated rooms.[9] Blankets and warm air inhalation can be used to prevent further cooling in any hypothermic person.[10] More active rewarming of people who have collapsed in their homes, however, is usually best delayed until admission to hospital, where the underlying disease, which is often masked by hypothermia, can be diagnosed and treated effectively.

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Cyclosporin: use outside transplantation

Promising, but long term follow up is essential

The success of cyclosporin A in allograft transplantation stems from its selective immunological action on T lymphocytes and its much lower ratio of risk to benefit than cytotoxic drugs. Enthusiasm for the drug is tempered by its potential toxicity, particularly nephrotoxicity,[1] and by the risks associated with chronic immunosuppression. Nevertheless, cyclosporin's potential is being investigated in a wide variety of autoimmune diseases.[2,3] A recent symposium organised by the Royal Society of Medicine reached some consensus on the use of cyclosporin outside transplantation and on its relative efficacy and potential.

Cyclosporin inhibits T lymphocyte activation and proliferation but is not cytotoxic. Unlike corticosteroids, azathioprine, and other cytotoxic drugs, it inhibits selectively both antigen induced activation of CD4+ (T helper) lymphocytes and the production by these cells of interleukin 2 and other cytokines.[4,5] Cyclosporin can also interrupt active immune responses, as shown by its efficacy in treating autoimmune diseases—presumably by blocking the secretion of cytokines by lymphocytes. The drug inhibits the in vivo transcription of genes encoding interleukin 2 and interferon γ[6] and blocks the expression of interleukin 2 receptors, whose induction is essential to T cell proliferation.

It is now clear that cyclosporin reversibly inhibits early, calcium dependent events in T lymphocyte activation and that there are probably several molecular targets within the cell membrane, cytosol, and nucleus.[4] The most exciting new developments concern the uptake and concentration of cyclosporin in cystolic and nuclear target sites mediated by cyclophilin, a recently discovered enzyme (peptidylprolyl isomerase). The relation between T cell activation and the function of this enzyme is unknown, but, by interfering with cyclophilin's role in the folding of regulatory peptides, the drug may prevent the formation or function of nuclear factors that regulate the expression of cytokine genes.[7] Recent evidence suggests that cyclosporin blocks the function of a gene termed NF-AT (nuclear factor of activated T cells), which may be the immediate or early regulator of T cell activation.[8] These properties of cyclosporin are shared by the novel anti-T cell agent FK-506, which may also have important clinical potential.[9,10]

In view of its molecular action not surprisingly cyclosporin will induce and maintain remission in many autoimmune disorders, particularly those with mechanisms mediated by T cells. Cyclosporin's effectiveness has been established in

randomised controlled studies in psoriasis,[11] insulin dependent diabetes mellitus,[12] and uveitis[13]; and promising results have been obtained in rheumatoid arthritis,[14] myasthenia gravis,[15] primary biliary cirrhosis,[16] and Crohn's disease.[17] Its efficacy has also been shown in uncontrolled trials in the nephrotic syndrome, systemic lupus erythematosus, and various dermatological and haematological disorders, although not in multiple sclerosis.[18] In psoriasis in particular, cyclosporin has been shown to be effective and safe for up to one year provided that the guidelines for treatment are strictly observed.[19] Long term experience in these conditions is still limited.

Several features are common to these studies in different conditions. Cyclosporin has a quick onset of effect (within two to 12 weeks, depending on dosage), but relapse after withdrawing it is almost universal and is in keeping with the reversible inhibitory action of cyclosporin on cytokine synthesis by T lymphocytes. Cyclosporin does not affect the clinical course of the disease. Nevertheless, many patients who are unresponsive to or intolerant of conventional drug treatment may benefit from cyclosporin or achieve a useful reduction in their steroid dosage.

Cyclosporin may do far more than simply act on T cells. It seems to be effective in some autoimmune disorders associated with antibodies—for example, pemphigus and pemphigoid and myasthenia gravis. In skin diseases it may well have an anti-inflammatory action through inhibiting eicosanoid synthesis, while in the nephrotic syndrome it may act predominantly through a haemodynamic action to reduce excretion of protein. Because of the possible drug interactions and other adverse effects careful review of all patients is mandatory. Among the guidelines for its safe use are an initial dosage of no more than 5 mg/kg a day, unless a rapid effect is critical, and the maintenance of trough blood concentrations of cyclosporin at 200 ng/ml or less (as measured by radioimmunoassay). If serum creatinine concentrations rise more than 30% above baseline the dose should be reduced. The use of cyclosporin in less advanced disease—for example, in acute type 1 diabetes—has to be individually and carefully balanced against the risks of both the disease and alternative treatment. Drug toxicity may outweigh the apparent benefit of improved efficacy. Long term follow up is essential to monitor blood pressure and to ascertain the risk of chronic irreversible renal impairment and the consequences of chronic immunosuppression.

Though further clinical trials of cyclosporin, both alone and in combination, are justified in autoimmune disease, these must be restricted to formal investigations conducted by experienced clinicians skilled in using cyclosporin and with facilities for monitoring the long term risks. Only then will it be possible to pass valid judgment on its value for autoimmune disease.

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Child health computing

A springboard for a community health register

One of the unsung successes of British child health services has been the development of computerised health information systems, pioneered in West Sussex in the early 1960s.[1] By exploiting surplus capacity on the county council's computer, West Sussex's public health department computerised its birth notifications and thus formed the basis for recording immunisation data. The system was developed so that it would organise appointments, produce invitations with appointment times, record the immunisation details, and then write a cheque for the doctor who did the immunisations. Soon West Sussex found that its immunisation rate had risen to at least 15% above that of neighbouring districts using manual recording methods.[2] Other districts adopted similar systems and found not only that their immunisation performance improved but that morbidity—as measured by measles notifications—was reduced.[3] Subsequently, the development of a national child health computer system was taken on by the NHS, along with the child health services themselves, and has now reached the point at which the system could form the basis of a total community register, forging links with primary care and recording events into adulthood.

When the NHS took over child health services in 1974 its computerised vaccination and immunisation system was based on the ICL mainframe computers operated by regional computer centres. The first two modules of the system—child register and immunisation—were generally available by 1977 and operational in 60% of districts in England and Wales by 1983.[4] A system for scheduling preschool surveillance checks was implemented in 1984, followed by an extension to school health checks in 1985.[5] In 1984 an alternative version of the system, written in MUMPS (Massachusetts University Medical Programme Systems) language and based on DEC equipment, provided an opportunity to move away from centralised batch processing to an on line system based in districts, and the ICL system soon followed suit in allowing direct data entry. Although the ICL and MUMPS systems have developed at different rates, both versions have a common core specification. Meanwhile some regions have