enveloping impermeable exhaust-ventilated suits in addition to working in an ultraclean environment the rate of deep sepsis fell even further, to only 0.9%. With the wisdom of hindsight (and the example of the gases) it is a pity that we do not know how effective exhaust-ventilated suits would have been if used in conventionally ventilated operating rooms.

The rates noted so far were achieved without prophylactic perioperative antibiotics. The use of prophylactic antibiotics was not controlled during the experiment, but a retrospective examination of the data showed that when they were used during operations done in conventional operating rooms the deep sepsis rate was 0.8%. In ultraclean conditions there was a further but insignificant improvement to 0.7%, and when exhaust-ventilated suits were worn as well deep sepsis was reduced to a near-perfect 0.06% (one in 1584 operations). This dramatic effect has been confirmed by an independent study in which use of antibiotics was fully controlled.³

If ultraclean air more than halves the rate of sepsis in prosthetic orthopaedic surgery, why not perform all such operations in these conditions? The implications of an affirmative answer need careful consideration. The available data suggest that prophylactic antibiotics are at least as effective as ultraclean air and exhaust-ventilated suits in reducing deep sepsis. Close attention to the choice of prophylactic agents—and the timing of their administration—might possibly improve their effectiveness still further.

When all three measures are used simultaneously the final improvement is less than 1%. So the cost of equipping large numbers of orthopaedic operating rooms with ultraclean air delivery and exhaust-ventilated suits could be justified only if deep sepsis rates after prosthetic surgery in conventionally ventilated operating rooms had already been reduced to the minimum possible; the further improvement of a fraction of 1% might then be thought worth while. In the mean time attention directed to general measures and more efficient use of antibiotics seem likely to produce greater benefit at a fraction of the cost of providing ultraclean air delivery and exhaust-ventilated suits.

Should these results be extended to the rest of surgery? Could infection rates of 5% or 10% be better than halved by operating in ultraclean air conditions? The strongest reason for doubting the validity of this extrapolation is that the infection rates under discussion are of deep sepsis, the kind which threatens the integrity of an implanted joint. "Ordinary" wound sepsis has been excluded from the figures available at present from the MRC trial, and we shall have to wait for details to be published before a proper judgment can be made. The idea cannot, however, be dismissed out of hand. Further information is provided by a double-blind study of the effects of ultraviolet irradiation in operating rooms in 14 854 operations performed over two years in five American hospitals.⁴ Like ultraclean air, ultraviolet irradiation achieved an impressive reduction in the number of airborne bacteria, but the overall rates of infection were 7.4% in irradiated rooms compared with 7.5% in unirradiated. Only in operations classed as "refined clean" did irradiation show any advantage, and that was comparatively small—a reduction of infection from 3.8% to 2.9%. These results, like those of the MRC study, show that the total contribution of airborne micro-organisms to postoperative sepsis is very small, and their removal, or killing, can be important only when the more important causes of sepsis have been eliminated or considerably reduced. It follows that in classes of surgery with higher infection rates any benefit from the provision of ultraclean air is likely to be small.

The message seems to be clear. The presence of micro-organisms in the air of operating rooms is relevant to the production of deep postoperative sepsis in the special circumstances of prosthetic orthopaedic surgery. The observation might cautiously be extended to other types of surgery where very low rates of infection have already been achieved, but more data are needed to establish this. These findings are overshadowed by the deduction that prophylactic antibiotics have an effect at least as dramatic as clean air in the circumstances under review. A rational appraisal suggests that the benefit to be derived from this very much cheaper alternative should be exhausted before any of the substantially more expensive provisions are considered.

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Skin replacement after burn injury

Burnt servicemen—quite rightly—attract public sympathy and attention. Their injuries are not, however, necessarily more severe than burns resulting from injuries in civilian life. In reality, losses amounting to hectares of full-thickness and partial-thickness skin occur daily throughout the world. The improved management of hypovolaemic shock by early intravenous infusion has led to more injured patients surviving the injury itself. This still leaves the patient and the clinician to cope with the problems of immunoincompetence, the prevention and treatment of infection, and the management and repair of the extensive wounds.

Large full-thickness burns rarely heal spontaneously but almost invariably need covering with new skin from another source. The surgeon treating an extensive burn has to prepare the surface of the wound to accept the new cover and find a source of the new skin itself. The only possible source of new permanent skin cover remains the patient's own skin, usually applied as a sheet of split-thickness skin which is harvested from an unburnt area and applied to the wound as soon as the wound bed is ready to accept the graft. In extensively burnt patients the same donor area may have to be used several times.

The management and surgical techniques used to achieve skin cover for burns vary from centre to centre. Some surgeons advocate early excision of the wound with immediate grafting of the excised wound bed, but others equally strongly advocate conservative treatment, waiting for spontaneous separation of the eschar before proceeding to immediate or delayed grafting. Both approaches are likely to benefit from some exciting recent developments in preparing the wound bed and the supply of new skin.

Skin obtained from unrelated donors (allograft or homograft) has been used for many years as temporary cover, so cutting down the loss of fluid and heat from the wound, and, more nebulously, "preparing" the wound bed for final autografting. The immunosuppressed state of most severely burnt patients ensures that such allografts survive for considerably longer than they would in normal recipients. A recent and promising development in the use of full-thickness cadaver skin as an allograft has been to seed tiny patches of autograft through holes punched in the allograft cover. By the use of this method some very extensive burns, up to 95% of the body-surface area, have been successfully treated.¹

Skin from unrelated species, usually pigs (xenograft), has also been used to treat burn wounds. Pigskin is used solely to provide a temporary cover for the wound; it is said to be suitable for applying as a dressing to partial-thickness and superficial burns and has been claimed to provide analgesia and, possibly, to improve the final outcome of the injury. The claims made for pigskin are not, however, substantial enough to merit its widespread adoption for treatment.

More promising are methods being used to augment the supply from the patient himself. The process of harvesting the split skin causes additional injury and upset especially when very little has been left unburnt. The introduction of the mesh graft allowed expansion of the available skin by a factor of up to five.² Recent developments promise to improve greatly on this figure. O'Connor *et al*³ have reported the use of cultured epithelial cells for grafting. In this system a small split-skin sample is taken when the patient is admitted and cells are cultured to confluence by using a complex culture system.⁴ These sheets of differentiated epithelium may then be used to provide epithelial cover some four to six weeks after the initial sample has been taken. Potentially this method might enormously expand small donor areas, but simpler culture systems than those described by Green *et al*⁴ will need to be developed if the method is to come into widespread use.

One disadvantage to using split-thickness skin for full-thickness wounds is that it provides no new dermis, so that the grafted area may later contract. This problem is particularly important in reconstructive surgery and in attempting to make up losses in tissue caused by the contraction of existing scars. Burke *et al*⁵ have recently reported the use of an artificial dermis produced as a copolymer of collagen and mucopolysaccharide to provide fibrous infilling. This material requires to be over-grafted with split-thickness meshed grafts, but it may well prove effective in producing a stable, contracture-free closure. It should be accepted by the body since the collagen is non-antigenic.⁶ Indeed, the dermal collagen preparation described by Oliver *et al*⁶ has recently proved an effective implant substrate in preliminary studies in man.⁷

So surgeons can now provide their patients with new skin cells as sheets of cultured epithelium and an acceptable "dermis" either from a synthetic copolymer or from unrelated human tissue. The most exciting development will be to combine these two methods to provide a skin substitute tailored to the patient's own requirements. This goal is now in sight: Yannas *et al* have reported that burn wounds can be closed by the use of synthetic dermis seeded with epithelial cells to provide a complete skin substitute.⁸

Prospects are bright for research and development in practical skin substitutes that improve on existing methods of treatment. For some time yet these developments will be in the hands of the units with laboratory facilities for carrying out the demanding culture and preparation techniques. Though current methods of treatment are certainly adequate to treat

most patients with burn injury, at least in Britain, these recent developments promise great hope for the most severe burn injuries, where the treatment process itself poses considerable hazards.

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Artificial blood

The group of substances named perfluorochemicals enhance the oxygen carrying capacity of the circulation in mammals, including man.¹ These perfluorochemicals act as simple carriers of oxygen, but they have to be given as emulsions containing particles with diameters of around 0.1 micron to pass through the capillary nets. The dissolved oxygen is given up by diffusion in hypoxic tissues. So great is the oxygen carrying potential of perfluorochemicals, especially in hyperbaric conditions, that complete exchange perfusions have been performed in rats, which have then been kept alive with no red blood cells in their circulation.² In studies on animals some of the properties of the blood other than oxygen transport have been provided by glucose, bicarbonate buffer, electrolytes, and hydroxyethylstarch.

Much of the early work with perfluorochemicals was done in Japan and the United States.³ Recently Tremper and his colleagues in Los Angeles have reported their experience with Fluosol-DA, a 20% emulsion of two perfluorochemicals made by the Green Cross Corporation of Japan (Alpha Therapeutic Corporation).⁴ Seven severely anaemic patients were given Fluosol-DA before surgery. At ambient oxygen tensions there was little change, the emulsion acting simply as a non-toxic volume expander, but at higher tensions a substantial amount of oxygen was taken up and delivered to the tissues. The authors suggested several clinical conditions in which perfluorochemicals might be valuable including carbon monoxide poisoning, myocardial infarction, cerebral vasospasm, and sickle cell crisis.

One very obvious use for the perfluorochemicals is as oxygen carrying substitutes in the rare but difficult problem of religious objection to blood transfusion.¹ Other uses which have been explored are as initial treatment in haemorrhagic