knee (Lidwell et al. 1982, 1983). Their conclusions may be summarised as follows: (1) Bacterial contamination of wounds during operation was closely related to the level of air contamination. (2) Operating in ultraclean air reduced the incidence of deep sepsis to about half of that in a standard operating environment: when a body-exhaust suit was also worn it was reduced to less than one quarter. (3) Prophylactic antibiotics, known to be effective in reducing the incidence of sepsis in a conventional operating environment (Hill et al. 1981), were also effective in reducing still further the already low sepsis rate of an ultraclean environment.

The sepsis rates calculated by Lidwell and his colleagues seem to show that the case for ultraclean air is incontrovertible. But this view has been challenged on two main counts. Firstly, it has been argued (Meers 1983) that alternative methods of calculation give less convincing differences – and since this view derives from the Public Health Laboratory Service it cannot be lightly disregarded. The second challenge concerns antibiotics: the MRC study was not designed primarily to assess their prophylactic value and in any case more effective antibiotics have emerged since the MRC trials. Operation clothing also has improved greatly; new materials such as that developed by Whyte et al.* (1983), are far more acceptable to many surgeons than the cumbersome body-exhaust systems and are equally impervious to bacterial penetration. When combined with modern antibiotics in a conventionally ventilated operating environment, such clothing may well give sepsis rates as low as those with ultraclean air, antibiotics and conventional clothing.

It seems clear that each of the three adjuncts alone reduces the rate of deep infection significantly so that, in any statistical study, the third factor can have only a small effect. Moreover, to measure this effect with precision would require a further trial of massive proportions (probably over 10 000 cases) followed for several years, during which time any fresh advances would need to be prohibited!

So new and reliable statistics are probably a pipe dream and yet the practising orthopaedic surgeon needs to decide where he stands now. It seems clear that, however competent and careful he is, he must provide systemic antibiotic cover; and he would be wise to use modern relatively impervious operation clothing. As for ultraclean air, it would be absurd to restrict joint replacement to centres where it is available and thereby further delay an operation which so transforms the patient's life. Where ultraclean air can be provided without great difficulty it is desirable; but where it is not available, the surgeon can still continue to perform joint replacements with confidence, fortified by the low sepsis rates which care and antibiotics can achieve. His confidence will be even greater if he also uses impervious operation clothing.

So how hard should he press for ultraclean air? The writer of this annotation is no more capable than anyone else of giving the final authoritative answer, but if he himself ever needs a joint replacement he will certainly not insist on ultraclean air; faced with a choice between a good surgeon working in an ultraclean environment and a superb surgeon in a conventional one he would opt for human excellence.

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REFERENCES


HEAD INJURY, FRACTURE HEALING AND CALLUS

Persistent in orthopaedic folklore is the idea that the production of callus and the healing rate of fractures are increased by head injury. Is this so, or is it yet another clinical myth? If it is true what could be the possible mechanisms, and would they apply equally to fracture healing and to ectopic ossification? Is there anything (apart from anatomy) which connects the brain to the skeleton, and does recent research on osteogenesis provide us with any clues?

* Fabric 450, made by Surgikos Limited.
healing response was measured by the ratio of the maximum external width of the callus at the site of fracture to that of the unfractured bone. The most abundant healing response was found in those with the most severe head injury, and the significantly increased healing response and accelerated fracture union time in head injuries were directly correlated.

Internal fixation of fractures may modify the osteogenic response but it certainly prevents undue mobility at the fracture site, itself a known cause of excessive callus and a likely feature in head-injury patients. For this reason Perkins and Skirving (1987) chose to compare two groups of 22 patients, with or without head injury, in both of which fractures of the femoral shaft had been fixed by intramedullary nailing. The calculated volume of callus was significantly greater in the head-injured group, and the average time to radiological union less.

The suggestion (Spencer 1987), based on limited histology, that the excessive callus in brain-injured patients is in fact a form of ectopic ossification is useful. The evidence that injury to the brain and spinal cord predisposes to the formation of bone in the soft tissues supports that on fracture healing and is far more convincing (Smith and Triffitt 1986). Although the healing of fractures and the formation of bone in ectopic sites may differ clinically, both must depend on the activity of osteogenic cells.

It is now recognised that the healing of wounds and fractures begins with a complex inflammatory cascade. Within minutes of injury platelets adhere to the wound, interact with collagen and produce platelet-derived growth factor (Smith 1985; Grotendorst et al. 1985). This factor is chemotactic and mitogenic to fibroblasts and smooth muscle cells. Before the arrival of connective tissue cells polymorphic leucocytes are attracted into the wound to be followed by monocyte macrophages which have a phagocytic role and also produce interleukin 1, a mitogenic messenger for lymphocytes. Lymphocytes are attracted to the site of injury and themselves produce lymphokines which have important later effects including bone remodelling. Subsequently myofibroblasts begin cellular healing and in fractures bone tissue is laid down, vascularised and remodelled. During fracture healing many processes occur, involving changes in vitamin D metabolites (McEwan et al. 1985; Lidor et al. 1987), in prostaglandin production and in different genetic collagens. Although simple fractures or osteotomy wounds may heal with very little callus, in the majority of fractures callus forms apparently from bone marrow cells (internal) and periosteal cells (external).

Both skeletal and extraskeletal osteogenesis depend on the presence of bone-forming cells, the osteoblasts. Normal fracture repair probably depends on the presence of osteoblasts already present at the fracture site. Heterotopic ossification, and probably excessive callus, will result from induction of additional mesenchymal cells into the osteogenic pathway. Of the cells potentially capable of forming bone some will do so without an inducing agent (such cells within the bone marrow stromal system have been termed “determined osteoprogenitor cells”), whilst others require an inducer (inducible osteoprogenitor cells). The former cells are not usually migratory, but the latter can be found at distant as well as local sites and are presumed to migrate and circulate through the body (Owen 1980). If we assume that there is a population of potentially inducible osteoprogenitor cells, it is important to know what these inducers are.

Most recent work has been concerned with identifying local inducers already present in bone. In tissue culture such osteo-inductive factors lead to the production of cartilage in vitro, an important step in osteogenesis; and in vivo a bone morphogen (BMP), whose exact structure is unknown, can be demonstrated by the implantation of acid-deminalised bone matrix into responsive sites.

If such an inducer (or inducers) exists it may act locally or through the bloodstream to be effective at distant sites and produce both excessive callus and soft-tissue ossification. The mystery which concerns us here is why head (and presumably brain) injury should influence osteogenesis at a site distant from the injury. Is there any evidence that the environment in the fracture site is influenced by head injury, or that head injury influences production of a putative bone inducer?

It has often been suggested that the ectopic ossification in paraplegics is related to immobilisation and to passive movements but experimental studies on rabbits do not support this (Izumi 1983).

Early biochemical measurements on the plasma and the fracture haematoma site (at operation and derived from local drainage samples) in brain-injured adults and children and in adults without brain injury were inconclusive (Heuwinkel 1979; Heuwinkel and Schneider 1979).

Nuclear magnetic resonance (NMR) provides a non-invasive way of measuring biochemical changes – particularly in phosphate metabolism – in the region of healing fractures, and also enables calculation of pH changes within the tissue. Animal experiments show that the local pH increases as callus is deposited. Since patients with head injuries may develop a respiratory alkalosis due to hyperventilation, it has been suggested that this contributes to the formation of callus and also to its mineralisation (Stone, Newman and Mukherjee 1987). Unfortunately neither direct analysis of healing tissues nor the use of NMR will provide information about the changes in cellular activity which form the basis for abnormal osteogenesis.

Head injury can be associated with marked endocrine changes but there is no evidence to relate them to abnormal osteogenesis; interestingly fracture healing in the somatomedin-deficient Snell dwarf mouse is normal.


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