I have often been asked by my clinical colleagues, “Does corrosion matter?” More explicitly, they ask: “Is corrosion of metallic implants a clinically important phenomenon?” This is not a simple question with an easy answer. The answer lies in a consideration of the various phenomena of metal release in vivo, the biological roles which the released metal-bearing species may play and any associated clinical observations.

In the world around us, evidence of corrosion, that is, oxidation of fully reduced metals to compound forms including chlorides, oxides and hydroxides, is plentiful. Rust, tarnish, scaling, even the beautiful patina on copper roofs are all easily visible examples. Less obvious is the more gradual loss of material from all metal surfaces through the combined attack of oxygen, moisture and atmospheric pollutants such as hydrochloric and sulphuric acids.

Alloys used in implants are derived from three materials systems: iron-base stainless steels, cobalt-base alloys and titanium-base alloys. These have been selected and adapted from marine and aerospace applications because of their combination of high strength, relative workability and, especially, resistance to corrosion. However, they do corrode.

We are most familiar with the frank evidence of corrosion seen in fracture fixation devices. Apart from obvious massive attack, as seen in late retrievals as much as half a century after implantation (Danzig et al. 1980) of early, poorly-manufactured hardware, evidence of pitting and crevice corrosion is seen in more than 75% of all stainless steel components in retrieval studies (Cook et al. 1985). In some cases, electrical potential differences between portions of multipart devices, such as mismatched plate/screw combinations or older designs of proximal femoral fracture fixation devices, such as the Jewett nail/McLaughlin sideplate, can produce galvanic corrosion and well-localised pain. The gross appearance of the typical symptomatic implant site, with local “tattooing” of soft tissues by corrosion products, mild inflammation and accumulations of grey, brown or black sterile sero-sanguinous fluid, gives rise to the descriptive terms “metallosis” and “sterile abscess”.

Although such overt symptoms are rare, the recognition of the frequency of frank corrosion in such circumstances has led to a growing practice of the routine removal of implants after one to two years, especially in younger patients, if other considerations do not argue against it.

The evidence for corrosion of cobalt-base and titanium-base alloys used as permanent implants for partial and total joint replacement is less easy to discern. Modern devices, made in accordance with sound metallurgical practice, using “clean” material and fabrication processes, rarely if ever show visible signs of corrosion. However, studies in animals, with passive implants in soft tissue (Ferguson et al. 1960, 1962; Koegel and Black 1984; Woodman, Black and Jimenez 1984; Smith and Black 1985; Wapner, Morris and Black 1986; Black et al. 1987), segmental bone replacements (Woodman, Jacobs et al. 1984) and total joint replacements (Woodman, Black and Nunamaker 1983), reveal a pattern of elevated metal content in serum, urine and remote tissue locations. Furthermore, some studies show evidence of the interaction of these metallic species with systemic physiology including time dependent increases in high molecular serum protein pool sizes (Woodman et al. 1983) and in concentrations of metal in remote tissue stores (Ferguson et al. 1962; Woodman, Jacobs et al. 1984; Smith and Black 1985). In particular, chromium (from stainless steels and cobalt-base alloys) and aluminium (from Ti6Al4V alloy) accumulate in a variety of remote soft tissues.

From these and related in vitro studies one can estimate the corrosion rates for these alloys to be 0.15 to
0.3 μ/cm²/day (Steinemann 1980, 1985). For the typical metallic femoral component of a total hip replacement, this suggests a total release of 11 to 22 mg/year. This does not appear to be a large amount until it is realised that the total body burden for a 70 kg man for most of the metals involved is below 10 mg, and normal concentrations in body fluids and tissues are probably in the 0.1 to 1.0 ng/ml range. Furthermore, friction and wear phenomena as well as details of design and fabrication of complex joint replacement components, including the use of high specific surface area coatings in the absence of a PMMA cement mantle, may raise these rates as much as tenfold (Black 1986).

Very limited studies in patients, made possible by the recent advent of highly sensitive neutron activation analysis (Michel et al. 1984) and atomic absorption spectroscopy (Black et al. 1983; Bartolozzi and Black 1985; Hildebrand et al. 1987), demonstrate elevated metal concentrations in serum and urine, and in local and remote soft tissues in patients with conventional PMMA-cemented cobalt-base alloy/polyethylene total hip replacements. These studies are extremely difficult to perform without large random contamination of specimens and are complicated by the wide variation in expected “normal” concentrations due to differences in heredity, occupation, diet, and other factors (Michel 1987).

What is clear, however, is that all of the released metals (Al, Cr, Co, Fe, Mn, Ni, Ti, V), with the possible exception of titanium, have biological roles in the human body. Some are essential in normal processes (Mertz 1981), such as chromium in sugar metabolism and cobalt in vitamin B₁₂ synthesis. Others are frankly toxic, such as aluminium, which is a neurotoxin (McLachlan et al. 1983). Most other metals display both characteristics, depending upon their concentration.

These biological effects may be classified under four main headings: metabolic, bacteriological, immunogenic and oncogenic (Smith and Black 1977). Examples of metabolic processes are widespread; two are cited above and it is likely that most of these metals will eventually be seen to play normal metabolic roles at trace concentrations. Most are already recognised as toxic in overload situations. Of great current concern is the emerging evidence that aluminium competes with magnesium, a normally occurring catalyst, in polymerising tubulin, one of the primary structural proteins in the central and peripheral nervous system (MacDonald, Humphreys and Martin 1987). Aluminium rich/magnesium poor neurofibrillary tangles have been reported in the cerebral cortex of deceased individuals who suffered from Alzheimer’s dementia (Perl and Brody 1980), suggesting a possible causal relationship.

There is continuing concern about the effect of foreign materials upon both immediate and late infections at implant sites, but the emerging view is one of physical mediation, related to the competition between host cells and invading bacteria during colonisation of the implant-tissue interface (Gristina 1987) rather than of chemical mediation, related to implant composition. However, the role of metals in immunological and in oncogenic processes is much clearer.

Chromium (in both +3 and +6 valence states), cobalt and nickel are haptens capable of binding with proteins to form immunogenic complexes. Studies of normal (non-implant) populations (Fregert and Rorsman 1966) suggest around 10% incidence of sensitivity to these metal ions as a group, with wide variations depending upon dose, sex, home and workplace exposure, and other factors. Study of immune responses to metallic orthopaedic implants has been somewhat neglected after a brief flurry of reports confirming (Evans et al. 1974) or denying (Brown et al. 1977) a possible relationship to loosening of metal-on-metal total hip replacements. More recently, Merritt and Brown (1985), using sensitive in vitro cell migration inhibition tests, have demonstrated high rates of sensitivity (>50%) in patients presenting for removal of either fracture fixation or joint replacement components. Of particular interest is a study of 32 patients who had internal fixation of a fracture with stainless-steel components (Merritt, K, personal communication). Before implantation, 13 (41%) were sensitive to chromium and/or nickel. At routine removal of the implant, three of the original 19 non-sensitive patients were found to be sensitive, all the previously sensitive ones remained so but nine of these sensitive patients (28% of all studied) were sensitive and reacting, as demonstrated by full suppression of leucocyte chemotactic capabilities. It is interesting to note, in the light of the equivocal nature of many studies of acquired hypersensitivity which used conventional patch testing, that these latter patients (who might be regarded as being at risk for immune complications) would demonstrate negative patch tests, due to chemotactic suppression. Thus, it is clear that conventional stainless-steel and cobalt-base alloy components in use today can sensitise patients as well as elicit immune system responses in previously sensitised individuals. The clinical significance of these observations remains to be seen; there have been no controlled prospective studies relating acquired orthopaedic implant-related “metal” sensitivities to local and remote symptoms.

Chromium (+6 valence state), cobalt and nickel and many of their compounds are oncogenic in animals (Sax 1981). The veterinary literature reports many cases of implant site tumours related to the use of stainless-steel internal fixation devices (Stevenson et al. 1982). These cases show some correlation with implant site infection (presumably through increased release of corrosion products secondary to local acidosis). The most common tumours are osteosarcomas and fibrosarcomas occurring generally three to eight years after implantation.
Tumours at implant sites in patients are rare. There are seven known reports in the English literature of tumours associated with fixation devices (McDouggall 1956; Delgado 1958; Dube and Fischer 1972; Tayton 1980; McDonald 1981; Dodion et al. 1982; Ward et al. 1988) but, until three reports in the same year (Bagó-Granell et al. 1984; Penman and Ring 1984; Swann 1984), there were none of association with total joint replacements. Discussing these latter three reports in this Journal, Hamblen and Carter (1984) commented that “...the number of reported cases is so minute...that no surgeon or patient should feel undue concern...”. However, since then there have been at least three additional reports (Weber 1986; Bauer et al. 1987; Ryu et al. 1987). Bauer et al. 1987 report a telangiectatic osteosarcoma 10 years after the implantation of a conventional PMMA-cemented metal-on-polymer total hip replacement. This is disturbing, as is the case reported by Weber (1986), which suggests that there was malignant transformation of a previously benign fibrous histiocytoma at the site of a total knee replacement.

Before these later cases were reported, I had pointed out that there were three additional reasons for concern, despite the apparently low incidence of tumours at the site of partial and total joint replacements (Black 1984). First, primary tumours of bone and cartilage are quite rare, showing an incidence rate (in all musculoskeletal locations) of about one-quarter of 1% of all tumours reported in England, Sweden and the USA, producing an occurrence rate of just over one case per million adult population per year in these three countries. Even without consideration of latency effects, rates of primary tumour genesis associated with implants would have to be greatly elevated over those normally expected in the hip or knee (a small fraction of the whole rate for the musculoskeletal system) for their presence to be easily perceived.

Second, related to evidence previously cited of metal transport and storage in sites remote from the implant, it is possible that excess tumours are occurring in implant patients in more sensitive tissues. A report in this issue of the Journal (p. 539) provides some evidence to support this supposition. Gillespie et al. (1988) identified 1 358 patients who had total hip replacements in New Zealand between 1967 and 1973. They investigated over one thousand of these patients who had been followed up for an average of more than 10 years, and demonstrated a 70% excess incidence (p < 0.05) of tumours of lymphatic and haemopoetic origin over that expected from the appropriate morbidity and mortality statistics. While expressing reasonable reservations about the validity of their pioneering study, the authors conclude that the results were consistent with “chronic stimulation of the immune system, encouraging the emergence of lymphoreticular malignancies...”, as might be expected from chronic exposure to immunogens or carcinogens.

Finally, it is known, from both animal studies and the epidemiology of human workplace exposure, that metal-bearing chemical carcinogens typically have long latencies, with a five- to 10-year minimum exposure required and a typical 20-year delay to mean tumour expression in man. Until recently, there was no significant human population with implants of greater than ten years' duration. Thus, present reports of tumours at implant sites and at remote sites in patients with implants may be harbingers of future problems.

The benefits of metallic implants in orthopaedic surgery are clear and cannot be denied by even the greatest pessimist. However, we are living in an increasingly risk-aversive society; we are asked daily to balance benefit with risk in decisions affecting ourselves, our family, the environment and, in the practice of orthopaedic surgery, the patient. It is becoming clear that there are real risks associated with the use of metals as chronic implants. Prudence suggests that steps should be taken to limit risk by minimising the exposure of patients to corrosion products.

Yes, corrosion does matter. All metallic implants corrode. The corrosion products are biologically active. Patients do exhibit symptoms relative to corrosion products from implants.

The magnitude and clinical significance of these symptoms remains to be seen. However, all orthopaedic surgeons should reflect that, as they wait for further intelligence, corrosion continues. Second by second, minute by minute, day by day, week by week, month after month, year piled upon year, metal is released and permeates every tissue of the bodies of patients with metallic implants.

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REFERENCES


