Bioactive ceramics

The modern era of joint reconstruction using low-friction arthroplasty represents a surgical success story that ranks second to few. As with any human activity, however, success spawns attempts to do even better, and in this instance there is a case for improvement. The aims of the pioneers were to relieve pain and restore joint movement, and the techniques which they developed achieved these goals. The method of fixation, however, suffered from limitations, both theoretical and real. Bone cement can fragment and the formation of particles at the cement-bone interface can result in osteolysis and loosening. Osteolytic reactions have also been related to wear debris from ultra-high-molecular-weight polyethylene, another key material of the pioneering days. Since current methods fall short of achieving a lifetime of function, particularly when arthroplasty is performed in younger patients, it is of interest to review the future potential of bioactive ceramics in this and other fields.

The bioactive properties of ceramics such as hydroxyapatite, some calcium phosphates and various types of bioactive glass, are well known. When placed in bone tissue, these materials promote bone formation, and bond to bone at various rates. To assess their potential for long-term, successful performance, we need to understand the mechanism of this interaction. Over the last few years evidence has been mounting that there is a gradual change at the ceramic surface by dissolution, precipitation and ion-exchange reactions which result in a carbonate-containing, calcium-deficient hydroxyapatite with small crystal dimensions (Daculsi, Le Geros and Dendon 1990; Ducheyne et al 1990; Kokubo et al 1992). This change is the first step in the cascade of events which underlies bioactive behaviour and is accompanied by parallel reactions, such as solution-mediated and substrate-controlled effects on cellular activity, organic matrix deposition and mineralisation. Absorption and incorporation of proteins and other biological molecules occur and surrounding cells become attached to the changing material surface. All these phenomena lead to the gradual incorporation of the ceramic into developing bone tissue.

Calcium phosphate ceramics include several materials which differ not only in their chemical composition, but also in their specific surface area, crystal structure and macro- and microporosity. There are differences due to variations in the calcium to phosphate ratio; tricalcium phosphate, hydroxyapatite and tetracalcium phosphate have Ca/P ratios of 1.5, 1.67 and 2 respectively, and there are other materials with ratios in between these (de Groot 1980). Furthermore, hydroxyl ions may be missing from the structure, as in oxyhydroxyapatite, and other trace ions may be present.

The importance of these compositional variations is not merely academic; they affect the biological response as the following examples show. Dense, stoichiometric hydroxyapatite (Ca$_{10}$(PO$_4$)$_6$(OH)$_2$), for instance, is among the more stable of the calcium phosphates and in vitro, the rate of precipitation on the ceramic surface is slow and the initial precipitate is very deficient in calcium. In animals, this material bonds to bone tissue present in the immediate vicinity. However, multinuclear giant cells can be seen resorbing the material for as much as two years after implantation (Schepers et al 1991). The second
example relates to plasma-sprayed hydroxyapatite coatings. Plasma spraying can have a profound effect on the chemical and physical characteristics of the deposited coating and few commercial coatings are alike. Fortunately, the compositional and structural changes which result from the spraying usually enhance the bone-forming properties of hydroxyapatite, but at the price of increasing the rate of progressive resorption of the coating with time. This would not necessarily be detrimental if the function of the coating was simply to stimulate bone formation and shorten the time to osseointegration. As long as the ceramic coating is not involved in transmitting stresses from tissue to prosthesis, plasma-sprayed coatings can provide clinical benefits but if the coating must also transmit loads between the host and the prosthesis, it cannot be reasonably expected that the mechanical function will last for the patient’s lifetime.

A simple tenet which must not be overlooked when considering the effect of bioactive ceramics is that tissue is formed as the result of cellular activity. The metabolic state of the patient must therefore have an effect on the outcome of treatments which use these materials either as coatings or as artificial bone grafts. It must also be borne in mind when assessing the clinical relevance of experiments performed on healthy, young animals. We have shown that a calcium-phosphate coating which had a good bone-growth enhancement effect in normal bone, failed in osteopenic bone. Such coatings act at short range only and although the bone ingrowth was more abundant with the calcium phosphate coating than without, the struts of trabecular bone that reached from the cortex to the porous coating were neither thicker nor more numerous. Since it is these that support the implant, no increase in mechanical fixation was observed (Ducheyne et al. 1992).

The incorporation of growth factors or bone morphogenetic protein into a calcium-phosphate coating has been envisaged in order to enhance the tissue response of the host, and several recent studies have shown that the use of such substances can produce dramatic alterations in the potential for bone growth (Mohan and Baylink 1991; Cornell and Lane 1992; Chesmel et al. 1993). The development, however, of a cost-effective treatment employing these genetically-engineered molecules, released in a time- and site-controlled fashion from carrier materials, may require resources of an order of magnitude greater than those previously needed by manufacturers of orthopaedic devices for the development of new products.

Some ceramic materials can themselves have a direct effect on cell function. Bioactive glass for instance can cause stem cells to differentiate into osteoblasts (Schepers et al. 1991). The bioactive behaviour of implant materials, as it is now understood, covers a spectrum of reactions ranging from non-reactivity at one extreme (titanium approaches this behaviour) to the highly reactive materials at the other. It is towards the reactive, resorbable end of the spectrum that one would look for materials to serve as artificial grafts. The rate of resorption can be controlled by restricting the size range of bioactive glass granules, the absorption of which leads to the formation of protective pockets in which osteoprogenitor cells differentiate into osteoblasts. Bone formation can then take place throughout a defect, in contrast to the repair starting from the pre-existing bone-tissue walls as observed with the apatites mentioned above.

When made in porous form with a surface having the characteristics of the bone mineral phase, bioactive glass can be seeded with cells capable of expressing the osteoblastic phenotype. The result is the rapid and abundant synthesis, in vitro, of extracellular matrix with most of the characteristics of bone tissue (El-Ghannam, Ducheyne and Shapiro 1994). It is an appealing idea that the next generation of bioactive materials may serve as templates for in vitro synthesis of bone tissue from cells aspirated from the patient’s own marrow (Nakahara, Goldberg and Caplan 1991). In an in vitro system, osteoprogenitor cells, and bone cells themselves, can rapidly dedifferentiate and the substrate must therefore promote the expression of the bone-cell phenotype. Ideally, it must provide a template for bone deposition while gradually resorbing as new bone tissue is laid down. Bioactive glass may well be the material that best combines these requirements of the ideal template for in vitro synthesis of bone tissue.

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REFERENCES


