Chapter 27: Biomaterials

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Biomaterials are synthetic or treated materials employed to replace or augment tissues and organs. The potential usefulness of alloplastic materials in the fabrication of prostheses has been known for a long time; however, the adaptation of materials technology for the purposes of surgical implant manufacture did not take place until about 25 years ago (Calman, 1963).

Biomaterials science is the study of living and non-living materials. Biomaterials themselves have always been of interest to the otologist concerned with reconstructive middle ear surgery (Grote, 1984a). In the past, the results obtained from using alloplastic implant materials in the middle ear have been disappointing because of the problems associated with extrusion (Guilford, 1964; Portmann, 1967). Nevertheless, it is worth noting that the most successful middle ear reconstruction in otosclerosis patients has been that performed with alloplastic implants (Shea, 1969). The recent advances in biomaterials science and the concomitant increase in knowledge have effected a revival in the development of middle ear prostheses. Furthermore, in maxillofacial surgery, implants are being used for the reconstruction of bony defects. In cases of head and neck surgery and in rhinology, the use of biomaterials has so far been reported only in experimental studies.

Scientific methods and surgical criteria must be applied if good results with alloplastic materials are to be achieved; the interrelationship between these criteria, however, necessitates their combined application. The dissimilarity between the surgical aims and the demands to be made on the implants used in orthopaedics and those used in otology will obviously be reflected in the different implant materials employed by surgeons in these respective fields. The same is true in the case of middle ear reconstruction, where the requirements for the reconstruction of the canal wall are different from those for an ossicular chain reconstruction.

The selection of alloplastics for reconstructive surgery is based on aspects derived from a variety of physical, chemical, biomechanical and surgical concepts (Homsy, 19700. With the ever increasing number of implants on the market, it is essential that the otolaryngologist has a fundamental knowledge of biomaterials science to complement his surgical aims.

Biocompatibility

The reaction of the body to the implant has to be studied in terms of both local and general reactions - the cytotoxicity of the implant material; however, the influence of the body on the prosthesis is also of importance. These reactions can eventually lead to degradation and loss of function. This phenomenon is called the biofunctionality of the implant.

Biocompatibility is the first prerequisite for a useful implant material and this must be tested extensively in vitro, in animal experiments, and in clinical studies with long postoperative follow-up periods. The interaction between the implant and the body must ultimately lead to a good and permanent integration. Such a successful integration is
dependent on the surface activity of the implant material, and on the breakdown and likely remodelling of the implant by the body.

Surface activity

An implant material can be regarded as bioinert if the body does not react at all to the implant material; as biotolerant if the body regards the implant material as a foreign body but, after incorporation, ceases to react to the implant; and as bioactive if the body has an active surface compatibility with the implant material, which leads to a firm integration between the body and the foreign material.

An implant material will always be placed in a wound, and thus normal wound reactions will inevitably take place (Silver, 1980). A foreign body will be encapsulated by a fibrous capsule with a varying number of reactive cells, particularly foreign body giant cells. In the case of bioinert material, where no reaction of the surface to the body occurs, the encapsulation will be in the form of only a small fibrous capsule, without further reaction taking place. A biotolerant material will have a good fibrous capsule around the implant material, an indication of cellular activity; giant cells, in particular, can be present even after longer postoperative periods, but the integration will be stable. A bioactive material will achieve a real bond with the surface of the surrounding tissue, because of active ion exchange, leading to a firm bond between the implant material and the body.

Structure

In the past, implant materials had a solid structure. However, during the last decade, several investigators have developed porous materials which enable the host tissue to grow into the porous part of the implant, resulting in a good integration with the body (Friedenberg, 1963; Klawitter and Hulbert, 1971; Homsey and Anderson, 1976; Spector, Fleming and Kreutner, 1976). It was found that micropores of 100 μm were ideal for the ingrowth of fibrous tissue, especially of bone tissue, if adjacent to the implant material. Micropores of several micrometres seemed to be essential, particularly if the implant materials had to be resorbed and remodelled in living tissue. In contrast, the micropores can be a problem in those materials which are not meant for degradation.

It is important to understand, however, that all materials will be affected by the body and will be resorbed to some degree, depending on the surface activity. If there is a large surface area, the response of the body tissue to the implant material will be greater, with the production of large numbers of macrophages and giant cells (Brown, Neel and Kern, 1979; Kern, 1981). The corrosion of implants can lead to the release of potentially harmful substances into the body, for example metals such as nickel, cobalt, chromium and aluminium which can be released from metal implants, may cause allergic responses, for which nickel, in particular, is notorious (Barranco and Solomon, 1972; Benson, Goodwin and Brostoff, 1975). Polymers can undergo degradation as a result of water or lipid absorption, by leaching of low-molecular-weight molecules, or by chain scission through oxidation or hydrolysis. It is probable that some additives, which are necessary for the stability of the polymer, will be released from the implant material, and some of these can be very toxic (US Pharmacopeia 1975, XIX). Even ceramics, such as alumina, which are very inert, can release substances into the body, and a characteristic of alumina is that it can be stored in the brain. Small particles
from the implant can stimulate a non-specific fibrocytic response, which leads to the destruction of surrounding tissue.

A most important criterion is the potential carcinogenic property of some substances which may be released - in particular from certain polymers. It has been demonstrated in animal experiments that large smooth surfaces may enhance the development of sarcomata, but the same is not reported from clinical studies (Oppenheimer et al, 1964).

A foreign body placed in a wound can attract bacteria which colonize the surface of the implant in a protected environment that is ideal for the proliferation of such organisms, thereby rendering conventional antibiotic treatment ineffectual (Gristina et al, 1976). Therefore, the behaviour of the implant material should also be studied in an infected surrounding.

An aspect of the structure of the material which must be considered is the density, including the porosity which will indicate the macropores and micropores, as this will have an influence on both the integration capacity and the wound reaction and remodelling capacity. In the case of ceramics, the crystallographic structure must also be indicated.

Generic names

Many implants are marketed with trade names, which give no information on the capacity of the material; therefore, the generic name of the material used must be indicated.

In addition to the generic names of the materials, the additives which might be part of the implant material must also be listed. The generic names can give the information on biocompatibility.

Specific materials

In reconstructive surgery, three classes of biomaterials are used: metals, polymers and ceramics. The different classes of biomaterials have both advantages and disadvantages with regard to biocompatibility, integration capacity and surgical application.

Metals

Metals are used less frequently in otolaryngology than in other disciplines. Over 100 years ago, it was noticed that metal, in the form of bullets, gave rise to inflammation, but occasionally the metal would be walled off in a pocket of scar tissue, thus creating few problems. However, metal implants were a considerable infection risk and caused a great deal of wound reaction; the exceptions were gold and silver devices, although their applicability had been restricted by the softness of these two metals. Metallurgic developments have rise to a large variety of alloy steels (the patent for stainless steel was recorded in 1913), but none of the steels had sufficient resistance to corrosion.

Cobalt-chromium allow - first invented by Haines - were developed before 1930, and in the late 1930s a cobalt-chromium allow (Vitalium) began to be used, particularly in arthroplasty. After the Second World War, when knowledge about corrosion resistance had
increased, metal implants achieved a wide application, especially in the field of orthopaedics. There are three classes of alloys: the cobalt-chromium group, the stainless steel group and the titanium group. The cobalt-chromium alloy group is especially popular, and is covered by several trade names, Vitalium being used most frequently. All cobalt-chromium alloys are corrosion resistant to tissues (Cohen, 1983). These types of prosthesis are generally not used in the middle ear but can be used in maxillofacial surgery.

According to the patent description of 1930, the definition of stainless steel is a steel that has a chromium content of between 11 and 30%, with the higher amount of chromium giving the steel a relative resistance to many corrosive fluids. The most corrosion resistant are those such as 316 low carbon steel and these are the most widely used. Stainless steel prostheses, especially in the form of wire prostheses, are well known in middle ear surgery and have proven to be reliable, particularly when integrated into a mobile middle ear chain (Schuknecht, 1958). Stainless steel plates for the purpose of reconstruction are also used in maxillofacial surgery.

The development of a metal alloy based on titanium began during the Second World War when it was used in the airplane industry. These metals are mostly used in orthopaedic devices. There is a reasonable level of corrosion resistance, but experience has shown that tissue surrounding the implant can be dark, indicating an initial loss of titanium to the tissues. Titanium wires are also used in middle ear surgery.

In some metals, corrosion products can be observed in the cells around the implant. As with all implant materials, one important consideration is that concerning the possibility of inducing malignancy. In orthopaedics, in particular, there are large numbers of individuals who have had metal implants for long periods of time, and there is no evidence to support an aetiological connection between the use of these metals and any type of neoplasm. A second very important aspect is that of hypersensitivity reactions to implants. Dermatologists are well aware of the sensitivity of some patients to certain metals, particularly nickel. However, whether that sensitivity also applies in the case of implants under the skin is not known. The conclusion must be that metal implants should not be widely used in otolaryngology, apart from their application in maxillofacial surgery, especially for reconstruction of the middle ear chain. Integrated into a mobile middle ear chain remnant, these implants are reliable; placed against a mobile tympanic membrane, they are extruded (Plester, 1968).

**Polymers**

Large quantities of plastics were being manufactured as early as the 1930s and 1940s. The application of these industrial polymers to surgical procedures was dictated by both the availability of the product and the intuition of the clinician. The first use of a biomaterial in reconstructive middle ear surgery was by Wullstein in 1952. He implanted a columella of Palavit in the middle ear for the reconstruction of the middle ear chain. Initial hearing results were good, but the implant was extruded. At that time, commercial plastics such as polyethylene, Teflon, and Silastic were used. Only a few polymers had been designed and tested specifically for surgical application. Later, many polymers were used for different types of columella reconstruction. At the end of the 1960s, the use of plastic implant materials was abandoned, particularly in reconstructive middle ear surgery, because of the high extrusion
rate (Sheehy, 1965). Apart from the body's reaction to the different polymers, many materials, which were originally intended for industrial use, frequently demonstrated the presence of low-molecular-weight impurities and pharmacologically active trace components in the polymer system.

Many classes of polymers are unsuitable for reconstructive surgery. In otolaryngology, the principal generic classes of interest are low density polyethylene (LDPE or LDP), high density polyethylene (HDPE or HDP), polytetrafluoroethylene (PTFE, also called Teflon) and polydimethyl-xylolene (Silastic).

Some polymers may also consist of more than one chemical entity. To test the different polymers for their potential application in the field of reconstructive surgery, classic procedures are a necessity, depending on either intradermal reaction tests or systemic toxicity tests, the latter of which uses extracts of the materials. These tests are not very sensitive methods for testing biocompatibility; therefore, testing procedures in tissue culture and in cell growth inhibition are more appropriate alternatives (Autian, 1977). Long-term animal and clinical studies are essential. Following the implantation of polymer implants, chemical reactions, as well as wound reaction, will take place, leading to the formation of a fibrous capsule. The thickness of this capsule is an indication of the level of tolerance of the material. In the cellular reaction around the implant, the foreign body reaction with giant cells and macrophages is of primary importance. It has been shown that giant cell reaction around polymers will continue for a long time. This foreign body reaction will also take place in the case of more tolerant materials, especially at sites where there is mechanical irritation (Kuijpers, 1984).

At the beginning of the 1970s, a new concept for implant materials was invented, namely the concept of the porous implant materials. Friedenberg, in 1963, was the first to report on the possibility of adapting an open pore sponge material which, in this case, was made of polytetrafluoroethylene, especially for surgical reconstructive use. This initial work generated a great deal of further research into porous implant materials, especially where ingrowth was apparent when the material was in contact with the bony skeleton. Two porous alloplasts, Proplast and Plastipore, have been promoted in otolaryngology (Janeke and Shea, 1975; shea, 1976). Proplast is a composite of polytetrafluoroethylene and carbon, and Plastipore is a trade name for a porous polyethylene polymer. These materials show ingrowth of fibrous tissue and capillaries during the first month and, if exposed to bone, bony ingrowth as well. During the implantation periods, the giant cells predominate in the transitional areas between implant and soft tissue. After longer survival periods, hyalinization of the fibrous tissue in the pores has been demonstrated in some studies (Kuijpers, 1984). The resorption of these materials by macrophages has also been demonstrated (Kerr, 1981). It has to be expected that a variety of other polymers will be developed in porous and solid form, and the same test results can be expected. Of the porous materials, total ossicular replacement prostheses (TORPs) and partial ossicular replacement prostheses (PORPs), which are used as columellae between the footplate and the tympanic membrane, or between the stapes superstructure and the tympanic membrane, have been used in middle ear reconstructive surgery. In the absence of cartilage between the tympanic membrane and the prosthesis, an increase in extrusion rate has been reported (Smyth et al, 1978). Whether this can be blamed only on the materials or whether surgical procedures with regard to the columella technique are also culpable, has not yet been established.
Porous materials have also been used in maxillofacial surgery. Apart from these materials, Silastic has also been used in otolaryngology, especially as plastic sheeting in the middle ear (Sheehy, 1973). Teflon is used in different situations in the middle ear as well as in head and neck surgery for stenting of the larynx and trachea. It must be stated that a precise knowledge of the chemistry and physics of the surface of different polymer implants does not yet exist. The chemical and physical reactions that take place in those areas where the implant is in contact with surrounding tissue, as well as with blood, must be understood. Better physical criteria have to be established in order to facilitate an optimum selection of polymer materials for implantation.

Ceramics

Biologically ceramics can be classified as bioinert materials (most oxide ceramics or a different modification of carbon) and reactive materials (glass ceramics and calcium phosphate ceramics). Some of these ceramics are used in otolaryngology.

Bioinert ceramics

The Al₂O₃ ceramic is a bioinert ceramic which is used in otolaryngology. It is a polycrystalline material consisting of corundum crystals. The advantage of this material is that it can be used under full load application. Although this is not of importance in the middle ear, it may be of significance in maxillofacial surgery. It has already been demonstrated in animal experiments that the implant is covered with a delicate membrane within 3 weeks; there is also a normal subepithelial cell layer with active fibroblast-collagen fibres and blood vessels. Because it is a bioinert ceramic, integration will be less than with other implant materials, although there will be the fibrous capsule. Prostheses of corundum crystals are very hard and not easy to shape; however, as has been proven in long-term clinical studies with columella prostheses, these bioinert materials behave well in the middle ear (Jahnke, Plester and Heimke, 1979). Other applications in maxillofacial surgery are being developed.

Bioactive ceramics

Glass ceramics

Glass ceramics were developed in order to achieve a direct chemical bond between the implant and the living tissues. They are available in different compositions of surface active glasses (Ceravital, Bioglass, and Macor). Each glass ceramic has its own distinct composition, and the different reactivity can be explained in terms of this individual composition. The basic reactivity depends on the ion exchange at the surface of the implant material. The surface of glass ceramics is lysed after implantation, and is coated with an amorphous gel layer, which probably contains SiO₂, CaO and P₂O₅ and is about 0.1 μm thick. Into this gel layer, the osteoblasts lay down and embed collagenous fibres. Calcium phosphate precipitates as apatite on the surface of the implant, thereby preventing its further corrosion. All glass ceramics will be degradable to a certain extent (Hench and Paschall, 1973).

Glass ceramics are used in otolaryngology mainly for reconstruction of the middle ear chain, in the form of columella prostheses (Reck, 1984). Glass material can be difficult to shape during surgery.
Calcium phosphate ceramics

Because their composition resembles that of bone tissue, calcium phosphate ceramics have been studied for many years. These materials are used to fill defects in the bone, Dreesman (1984) being the first to publish the clinical results. The problem is that the biomaterial usually disappears faster than new bone can fill the empty spaces. Different calcium phosphates of the bone matrix have been studied and used, for example B-whitlockite (Ca₃(PO₄)₂) and hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂) in otolaryngology. Hydroxyapatite is present in the bony tissue and B-whitlockite is present in the body in only a soluble form and can, by means of sintering techniques, be reproduced in ceramic. A selection has to be made according to the reactivity of the body, but there is general agreement that calcium phosphate ceramics are very compatible with the body, especially with bony tissues (de Groot, 1981).

B-whitlockite

Tricalcium phosphates, as a bioactive implant material, behave in the same manner as all calcium phosphates in viable tissues. However, the control on degradation and remodelling is less than with hydroxyapatite, particularly when some impurities are present in the ceramic, the remodelling cannot be controlled and trace elements of the implant may be found in the macrophages around the implant. The degradation process takes place in two stages. As a result of the physicochemical dissolution of the necks between sintered powder particles, individual particles are released, which are subsequently digested and presumably dissolved by cells. If degradation occurs rapidly, the cells cannot dissolve all particles intracellularly before these reach the lymph nodes. This will result in a temporary presence of tricalcium phosphate crystals in the lymph nodes.

Tricalcium phosphates (B-whitlockite) have been used for the obliteration of mastoid cavities (Zöllner et al, 1983; Wullstein, Schindler and Döll, 1984).

Hydroxyapatite

Hydroxyapatite has been studied extensively both in vitro and in vivo, and in long-term clinical studies (van Blitterswijk et al, 1986a, b; Grote, 1984b, 1986). It has proven to be a bioactive material which achieves a real integration with bone tissue, without any encapsulation. There is controlled remodelling if a porous material is used. These calcium phosphate ceramics can be made in porous as well as in dense forms, depending on the surgical requirements. The continuation of remodelling of the porous forms is also compatible in infected surroundings. The interaction with epithelium and connective tissue has been shown to be excellent, with a direct bond and then integration between the material and the tissue in continuity with the surrounding materials. The attachment of epithelium to dense apatite surfaces has been shown to take place by means of hemidesmosomes, while connective tissue fibres do not encapsulate the implant but run perpendicular to the ceramic surface.

Biologically, B-whitlockite or tricalcium phosphate ceramics behave in the same manner as hydroxyapatite, the one difference being that the B-whitlockite ceramic may be more biodegradable than the hydroxyapatite. This means that an implant in bony tissue will be degraded in an uncertain way. Calcium phosphate materials are resorbed and remodelled in the same way as a living bone tissue matrix; thus they are released and resorbed by
macrophages. The resorption and remodelling is not only dependent on the macropores, but also on the micropores, and this in turn is dependent on the crystallography and stoichiometry of the calcium phosphate materials and on the sintering procedures. The disadvantage of calcium phosphate ceramics is their brittleness. As it has insufficient tensile strength, this type of ceramic is not useful as a replacement in large bony defects; only smaller defects in the bone and maxillofacial surgery can be repaired. The use of this ceramic in long-term clinical studies in middle ear surgery has validated its biocompatibility and usefulness. An extensive application in the fields of nasal and maxillofacial surgery has now begun.

Conclusions

Many criteria must be met before an implant can be used effectively. Apart from the biomaterial criteria, a combined application of these with good surgical criteria is a prerequisite for a lasting result. The site where the implant is to be used will determine the selection of the material. The ideal implant material will closely resemble the tissue it is designed to replace in such factors as the size, shape and consistency of the defect. It will be structured in such a way that neither infection nor healing response will alter its characteristics. As the implant becomes established it will assume the characteristics of the tissue which it replaces or augments, thereby ensuring its permanent toleration by the body.

Autologous and homologous materials are often considered to be ideal for the reconstruction of defects in the body. However, after preservation techniques have been carried out, the remodelling of the body with these materials will take place in the same way as with alloplastic implant materials. Advances in biomaterials science will increase the fundamental knowledge of the surface activity of these alloplastic implant materials and of their interaction with the body. The more the material resembles the human body, the better will be its compatibility with the body. The surgical criteria employed in implantation techniques have to be developed and refined for the different surgical areas. It is obvious that the increase in knowledge will lead to the development of innovative implant materials, devices and artificial organs in the near future. The prefabrication of these reliable materials will more than compete with all the problems associated with the transplantation of autologous materials and with the preservation and shaping of homologous materials. A critical evaluation of the materials concerned and some fundamental knowledge of biomaterials science are necessary for the successful use of alloplastic implant materials in the field of reconstructive surgery.