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Review
Titanium: the implant material of today

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The use of metals for the replacement of structural components of the human body has been with us for some considerable time. The metals originally used were stainless steels which have gradually been replaced by cobalt–chromium alloys. Although titanium has been used since the late forties, it is only relatively recently that it has gained widespread interest. Titanium and its alloys are being used more and more in preference to the cobalt–chromium alloys and has broadened the field of applications. The features which make titanium such an interesting material are its excellent corrosion resistance in the biological environment, combined with an exception degree of biocompatibility which it shares with only a handful of other materials. In this review the background to the clinical use of titanium is discussed with particular attention to the biological aspects of the material. While there are now many clinical uses for titanium and its alloys their main areas of application are in the field of dentistry and orthopaedics and these are described in some detail.

1. Introduction

The field of biomaterials has been expanding rapidly over the last 25 years such that now it constitutes an important area of the medical industry. A wide variety of metals, polymers and ceramics have found application to the extent that many are now part of the routine armamentarium of the medical profession. The success of the hip joint prosthesis, of which some 20,000 are implanted each year in the UK alone, is but one example [1]. Thus the clinical application of materials is no longer a matter of academic interest but a matter of great concern to us all.

Much has been written about titanium both in the scientific and medical literature and this review is not intended to be all inclusive of all that has been published on titanium for clinical applications. Rather it is meant to present an overview of the progress made in the clinical application of titanium and to highlight some of the major areas of advance in the last few years. It is hoped that this article will stimulate the reader's interest and provide some insight into the important clinical aspects of the use of titanium.

Titanium was first introduced into the medical field in the early 1940s with the publication of an article by Bothe, Beaton and Davenport [2] on the reaction of bone to multiple metallic implants. They implanted a number of metals including titanium, stainless steel and cobalt–chromium alloy in the femur of a rat and noted no adverse reaction. Further studies during the 1950s [3, 4] confirmed the lack of any adverse reaction to titanium. Nevertheless titanium had a slow beginning since a number of other metals, notably stainless steel and cobalt–chromium, were already very popular at the time. Over the years cobalt–chromium has gradually replaced stainless steel because of the recognition of the superior corrosion resistance of cobalt–chromium in the biological environment. Now the dominance of cobalt–chromium as the metal of choice is being challenged by titanium.

A great variety of implants of many different designs are now made from this metal in either its pure or its alloyed form [5]. The metal is finding great favour with orthopaedic and dental surgeons alike and more and more implants made of titanium are appearing on the market. In order to appreciate why this has come about it is necessary to look more closely at the interaction between titanium and the biological environment and see what features of this interaction makes this a material of such interest.

2. Theory

2.1. Titanium and its alloys

2.1.1. Background

The discovery of the element titanium has been attributed to the Reverend William Gregor in 1798 [6]. It is the ninth most abundant element in the lithosphere as it is a constituent of practically all crystalline rock. The reason why titanium has not become more widely used until the latter half of the twentieth century is because the production of pure titanium is extremely difficult due to its high reactivity. It was not until 1910 that the first pure form of titanium was produced and even now titanium is still very expensive compared with, for example, stainless steel.

Pure titanium is a white, lustrous metal which has the attraction of low density, good ductility and constitutes an important alloying element with many other metals. Alloys of titanium are widely used in the aircraft industry and have military applications

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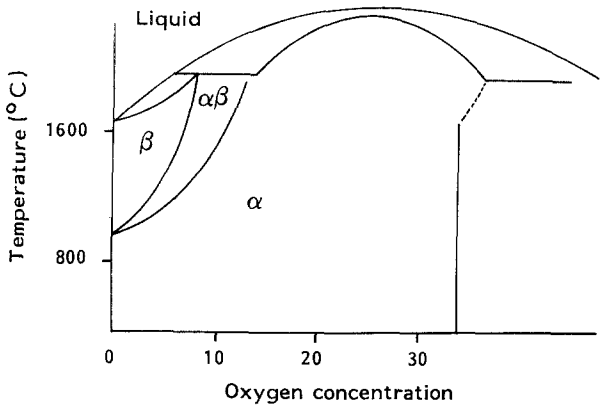

Figure 1 Phase diagram of titanium and oxygen.

because of their light weight, strength and ability to withstand high temperatures. Clinically two forms of titanium have received the most interest, one is the commercially pure form of titanium (Ti-160) and the other is an alloy of Ti–6% Al–4% Va (Ti-318). (N.B. all alloys are given in wt %).

2.1.2. Commercially pure titanium

Commercially pure titanium (c.p.Ti) is in fact an alloy of titanium and oxygen. To satisfy the British Standard specification for use in surgical implants the oxygen content must be less than 0.5% [7]. In this form the alloy has a close packed hexagonal structure. A partial binary phase diagram of titanium and oxygen is shown in Fig. 1. The oxygen is in solution so that the metal is single phase. Elements such as oxygen, nitrogen and carbon have a greater solubility in the close packed hexagonal structure of the alpha-phase than in the cubic form of the beta-phase. These elements form interstitial solid solutions with titanium and help to stabilise the alpha-phase. Transition elements such as molybdenum, niobium and vanadium act as beta stabilisers.

2.1.3. Ti–6% Al–4% V

When aluminium and vanadium are added to titanium in only small quantities the strength of the alloy is much increased over that of c.p.Ti. Aluminium is considered to be an alpha-stabiliser and with vanadium acting as a beta-stabiliser, the temperature at which the alpha–beta transition occurs is depressed such that both the alpha and beta forms can exist at room temperature [6]. Ti–6% Al–4% V has a two-phase structure of alpha and beta grains. In situations where extra hardness is needed Ti-550, an alloy of Ti–4% Mo–4% Al–2% Sn, is being used instead of Ti-318 [8]. A new wrought Ti–6% Al–7% Nb has recently been developed which is showing great promise as an implant material [9].

2.2. Mechanical properties

The Young's modulus of c.p.Ti is 110 GPa which is only half that of stainless steel or cobalt–chromel alloy. Some consider the lower modulus to be a distinct advantage because it helps to overcome the mechanical incompatibility with bone. But since bone has a modulus of some 10 GPa this value of the modulus of titanium is still considerably higher than that of bone and is unlikely to have any major significance. The reader is referred to an excellent text on the problems of mechanical compatibility for a detailed discussion [10].

For the Ti–6% Al–4% V alloy considerably higher tensile properties [11] are achievable than for pure titanium which makes it attractive for use in high stress-bearing situations, such as the hip prosthesis and artificial knee joint. Nevertheless c.p.Ti is widely used for dental implants and so far the lower strength has not proved to be a problem [12]. Perhaps more important is the fatigue resistance of these materials and it is here that the superior properties of the titanium alloy really come to the fore. Both c.p.Ti and Ti–6% Al–4% V have a well defined fatigue limit with the S–N curve levelling out after 10^7 to 10^8 cycles of stress reversal at a tensile strength reduced by 45 to 50%. Thus c.p.Ti should not be used in situations where the tensile stress may exceed 100 MPa. In contrast for the Ti–6% Al–4% V the fatigue limit is approximately 620 MPa. This provides a much increased safety margin against the possibility of fatigue failure and makes it a much better candidate material for hip prostheses than c.p.Ti.

2.3. Corrosion resistance

Corrosion can be a serious problem in implant applications [13] and an example of a material which has not stood the test of time is stainless steel which is now gradually being replaced by the cobalt–chrome alloys. Titanium has become popular because it is one of the most corrosion resistant metals known to man [7] and this applies equally to the alloys. Its resistance to attack by seawater is well known [14]. Although titanium is a highly reactive metal this is also one of its strengths because the oxide formed on the surface (TiO_2) is extremely stable and has a passivating effect on the metal. Passivation does not by itself mean that the metal will not corrode but the rate of corrosion is much reduced in the presence of a stable oxide layer. The potential for corrosion of titanium in the biological environment has been studied and has confirmed its excellent corrosion resistance [7, 15, 16]. There is always some anxiety that failure may occur due to a combination of factors such as occurs with stress corrosion cracking. Such cracking is virtually unknown for titanium and although the alloys may be more susceptibile to this phenomenon as yet there are no reports of this type of failure in orthopaedic implants employing the alloy [7]. Neither is titanium susceptible to crevice and pitting corrosion [17]. The fatigue limit of some materials can be seriously compromised in the presence of a corrosive environment and a solution of 0.9% saline as occurs in the body is just that. Studies on a number of titanium alloys have shown that the fatigue limit of Ti–6% Al–4% V is unaffected by the presence of seawater [18, 19]. Since seawater and body fluids are very similar it can reasonably be assumed that corrosion fatigue is unlikely to be a problem with Ti–6% Al–4% V. In a study which included Ti-318, Ti-550 and cobalt–chromium alloys, Dobbs and Robertson [8] concluded that, where high corrosion

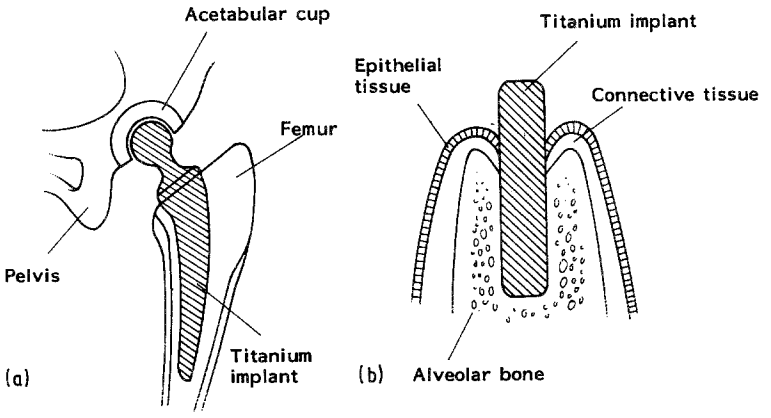

Figure 2 Diagrammatic representation of (a) a hip prosthesis and (b) a dental implant with its surrounding structures.

fatigue strength was required, titanium alloys would be the materials of choice.

Many of the attributes ascribed to titanium and discussed above make it a highly desirable material for implant applications. It has mechanical properties which are more than adequate for most implant uses and its corrosion resistance is a real asset. But to be a successful implant material its effect on the biological environment both at the local and systemic level is of the utmost importance and this will be considered next.

3. The biocompatibility of titanium

The clinical requirements for a successful implant material are both stringent and exacting. Not only does it have to perform the function for which it is intended, but it has to do so in a way which causes no damage to the biological environment in which it is asked to perform. Under no circumstances should the patient come to any harm so that a successful implant should not lead to dysthesia (loss of sense), discomfort, pain, infection, resorption of bone or psychological effects related to the implant [21]. Given these conditions one can imagine that the use of an implant is not taken lightly and the surgeon must be convinced that the procedure adopted is in the best interest of the patient.

It has already been mentioned that the early results with titanium implants showed the material to be well accepted by the biological environment. Titanium has been described as a physiologically indifferent metal and toxicologically appears to be very benign [22]. One of the most important features of an implant is that it will be in contact with the living tissues of the body, thus creating an interface between them. What happens at this interface is a matter of great interest since it will largely determine the success or failure of the implant, both in terms of the immediate reaction and the longer term response. Consequently, much attention is now being paid to the study of the biological response to titanium local to the site of implantation. It is only recently that more detailed studies have been undertaken to define more accurately the interfacial properties of titanium.

3.1. Tissue–implant interface

The biological response at the interface between the implant and the host tissues is highly dependent on the site of implantation and the surface properties of the implant. With reference to Fig. 2, it can be seen that for the hip prosthesis the interface consists almost entirely of bone while for a permucosal dental implant the material will be in contact with bone, connective tissue and epithelium. Hence in order to assess the interfacial response to titanium and judge its acceptability as an implant material, a knowledge of the effects of titanium when in contact with each of these living tissues is required.

3.1.1. Bone–titanium interface

A common biological response to a foreign object such as an implant is to isolate it from its immediate surroundings by an encapsulating layer of fibrous tissue. This response typically occurs with silicone polymers and the material is then generally described as being inert [23]. However, when the implant is to perform as a load bearing device, which is nearly always the case for titanium, this type of response would not be considered acceptable since it has a destabilizing influence on the implant. Excessive movement of the implant can lead to dislocation if used as a joint replacement or more seriously cause bone resorption around the implant. What makes titanium such an exciting implant material is that it is one of only a handful of materials which will not produce a fibrous tissue barrier when placed in contact with healthy bone [24]. To the contrary it allows bone to grow so close to the surface of the implant that the titanium is in virtual contact with the bone. Since the bone will actually grow into any spaces on the surface of the implant, it becomes firmly embedded in the bone. This situation is now commonly described as *osseointegration* [20]. The various stages of the process of osseointegration are shown diagramatically in Fig. 3 and can be described as follows:

Stage 1: Immediately upon placement the implant is not perfectly congruent with the bone. The threads in the implant are there to allow bony ingrowth and so anchor the implant in the bone. Haematoma is present in the recesses of the screw threads and there is a layer of damaged bone resulting from the thermal and mechanical trauma during operation.

Stage 2: During healing the haematoma is gradually transformed into new bone and the damaged bone also heals by a process of revascularization and de- and re-mineralization.

Stage 3: When the healing has completed, new bone is in virtual direct contact with the implant without any intermediate layer of fibrous tissue.

Much of the work confirming this phenomenon

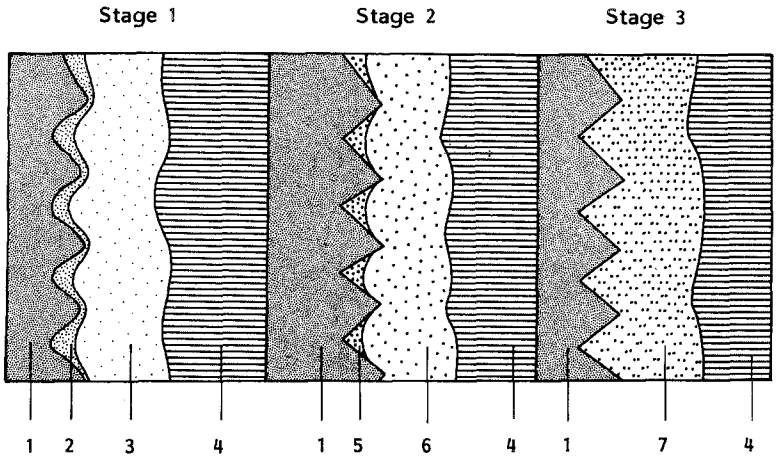

Figure 3 Representation of the process of osseointegration adapted from Branemark [20] where the numbers denote (1) Titanium implant, (2) Haematoma, (3) Damaged bone, (4) Healthy bone, (5) Haematoma transforming into new bone, (6) Damaged bone healing itself by de- and re-mineralization, (7) New healthy bone.

must be attributed to Branemark and his team at the University of Goteborg, who have been studying the biological response to titanium since the 1950s [20]. One of their earliest studies involved a microscopic examination of bone and marrow response to screw-shaped titanium chambers in rabbit fibula. They observed that the titanium chambers could not be removed from the bone once it had healed because it had grown right into the spaces of the screw threads [20]. An example of the close adaptation of bone to titanium is shown in Fig. 4. Further studies of tooth root implants in dogs confirmed these findings since again the fixtures could not be removed from the mandible without cutting away the bone first. Any attempt to extract the implant only resulted in fracture of the bone at sites well away from the interface. The importance of these findings cannot be over emphasized since it forms the basis of the principles underlying many of the applications of titanium currently being explored.

Figure 4 Microstructure around the screw thread of a titanium implant showing the close apposition of bone to the surface of the implant. Note the absence of a fibrous capsule. (Courtesy of Professor T. Albrektsson, University of Goteborg, Goteborg, Sweden).

A detailed examination of the interface at the cellular and sub-cellular level is desirable [25] but does present problems since it is not possible to produce thin sections on a microtome for TEM with the implant present [24, 26]. If the implant is removed before embedding the tissue in resin, the interface will be damaged and potentially valuable information lost, but by careful removal of the implant after embedding it is possible for the interface to remain intact. Using such a procedure Thomsen and Ericson [26] and Hansson *et al.* [27] have been able to study the tissue morphology close to a commercially pure titanium implant. The method involves the removal of the titanium implant and the surrounding tissue by using a trephine so that a collar of bone is attached to the implant. The specimen is then fixed, decalcified, dehydrated and embedded in epoxy resin. The block is cut into several pieces and the segments containing the interface tissue carefully separated from the implant. SEM examination of the surfaces of the interface revealed no damage to the implant or the resin embedded tissue [26]. Having eliminated the implant the ultrastructural features of the interface could subsequently be examined by optical and TEM. The results showed that new bone forms very close to the surface of the implant and consists of a haversian system of regularly organised bone lamellae [27]. A narrow, electron-lucent layer was observed separating the collagen fibrils or cell membranes from the implant [26]. Using a different technique, involving the evaporation of titanium on to the surface of an epoxy resin implant, Albrektssen [28] showed that the bone-implant interface consisted of a fibrous tissue-free zone with a 20–40 nm thick proteoglycan coat immediately adjacent to the titanium oxide surface of the implant. In contrast, bone cement which does not induce a fibrous capsule formation either when placed in contact with bone, has been shown to have a proteoglycan layer separating it from the bone of the order of 2000 nm [29]. Thus it would appear that the formation of this proteoglycan layer is all important and needs to be as thin as possible to ensure close

apposition of bone to the implant. Why titanium should have such a favourable response compared with almost all other metals is not as yet clear but it is believed that a major contributing factor is the high stability of the titanium oxide on the surface of the metal [30]. Much of the discussion so far has been concerned with the biological response to commercially pure titanium since little is known of the biological response to the alloys of titanium. It would not be unreasonable to accept the suggestion that what happens at the interface is not a function of the metal but is governed by the surface oxide coating on the metal [30]. Since the alloys of titanium used for implants have the same titanium dioxide coating as the commercially pure titanium their behaviour is likely to be similar. However this ignores the possible role played by metallic ions which are released into the surrounding tissues. High levels of titanium have been recorded in the tissues adjacent to titanium implants which cannot be attributed to wear [31]. How these high levels of titanium arise is not clear although it has been suggested that the source could be needle-like oxides which project from the surface and which are readily dissolved into or abraded by the surrounding tissues [7]. As yet there are no reports of similar high levels of aluminium or vanadium but this does not mean that these are not released and their presence may modify the local tissue response for the alloys compared to c.p. titanium. The reports so far would indicate that the alloys of titanium are equally as biocompatible as the pure titanium.

3.1.2. Soft tissue–titanium interface

Some of the earliest detailed data of the soft tissue response to titanium were gathered from the tissues around titanium implants in orthopaedic patients [31]. Using neutron activation analysis, significant amounts of titanium were detected in some of the tissue sections taken from the soft tissues adjacent to titanium implants. Dense, patchy accumulations of particulate titanium were observed but appeared to have had no harmful effect on the local tissues or caused any systemic reactions in the patients concerned [7]. This would indicate that there is a significant release of metal ions from the surface of the implant and it has been reported that this can lead to discolouration of the tissue around a titanium implant [32, 33]. Nevertheless the excellent biocompatibility of titanium is confirmed yet again.

The formation of a fibrous tissue layer around an implant placed in the soft tissues and the thickness of this fibrous layer can be considered as indicative of the biological acceptability of a material [7]. Recent studies [34–38] have shown that under certain circumstances no fibrous tissue layer is formed between titanium and connective tissue but a genuine attachment is created. This attachment, which is discussed in more detail in the section on dental implants, has been observed for other metals too but appears to be more organised in the case of titanium [28]. Even when a fibrous capsule does form such as reported by Laing [33], who implanted Ti–6% Al–4% V in rabbit muscle, the thickness of this capsule was found to be thinner for the titanium alloy when compared with cobalt–chromium–molybdenum alloy or 316 stainless steel.

3.2. The surface of the implant

It has been known for some time that the interfacial bond between an implant and the bone can be improved by creating a rough, or better still a porous surface coating on the implant. If the pores are of the right size (between 100 to 300 μm) [39] and the implant material has good biocompatibility with bone then bone will grow into these pores, thus providing an extremely rigid fixation of the implant. An example of this is the use of cobalt–chromium alloy to which has been sintered a layer of spheres so creating a porous surface coating [40]. Titanium does not lend itself readily to this form of treatment because powder preparation for sintering is difficult, compacting has to be carried out at extremely high pressures and the sintering has to be done in a vacuum furnace [11]. Nevertheless porous surface coatings have been produced [40]. Alternative surface treatments aimed at increasing the surface roughness are being explored such as acid-etching [41] and the use of flame-sprayed titanium powder [36] which creates a porous surface with pores of 25 to 100 μm. Another approach is the use of titanium wire, surface bonded to the solid implant made of titanium alloy [42, 43]. By a suitable choice of wire, pore sizes of around 100 μm are easily produced [44], although there is always the danger of the fibre mesh separating from the implant [45].

A potentially more serious problem with the concept of porous surface-coated implants is that the surface porosities act as ideal local stress intensifiers which can dramatically affect the fatigue life of the material. Also the sintering process itself may adversely affect the fatigue strength by causing changes in the microstructure. Yue *et al.* [46] and Cook *et al.* [47] have shown a significant reduction, by as much as a factor of four, in the fatigue limit of Ti–6% Al–4% V down from 620 to 140 MPa. This increases the potential for fracture of the implant, particularly in the young and active patient.

Another potential concern with the use of porous titanium implants is the increase in the surface area of the implant exposed to the biological environment [48, 49]. The pigmentation of tissue around a titanium implant has already been commented on and this increased surface area will result in more titanium being released into the surrounding tissues. This release of titanium may alter the local tissue response to the implant to the detriment of its function or the metallic ions may give rise to systemic effects not previously encountered. Although titanium is a non-essential element to the human body, an excessive presence of the metal could trigger some as yet undefined toxicological or carcinogenic reactions [49, 50].

The information gathered to date shows that titanium is well tolerated by the biological environment. In fact one can go so far as to say that it is well accepted by bone and soft tissues as opposed to being isolated as an unwanted foreign body.

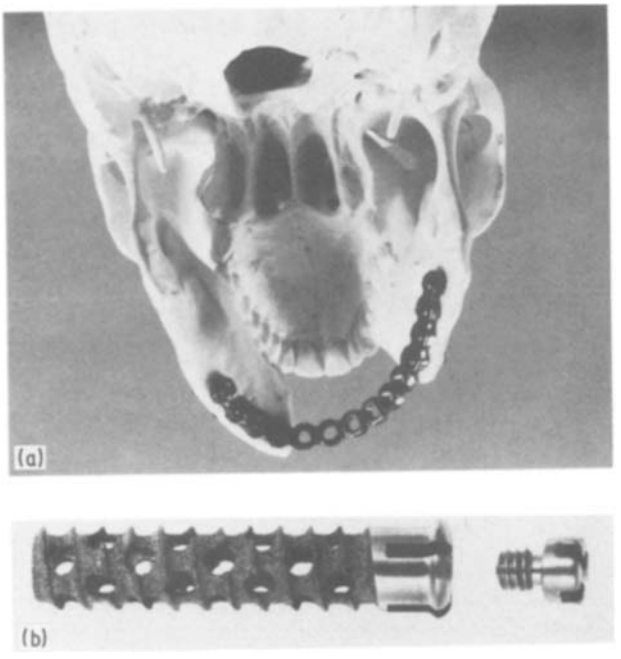

Figure 5 A titanium alloy bridge shown on a model (a) and a close up of the titanium screw (b) used for fixation of the bridge. (Courtesy of Dr. J. Raveh, University of Berne, Berne, Switzerland).

4. Clinical applications of titanium

The clinical application of implants presents a particularly difficult challenge to the medical and dental professions. Factors which need to be taken into account are the biocompatibility of the material, the design of the implant, the site of implantation, whether its supportive or functional, operative procedure and post-operative care of the patient to name but a few. Nevertheless there are many applications of titanium such as pacemaker casings and electrode tips [51, 52], auricular implants [53, 54] and heart valves [7], but the two most prominent applications of titanium are the joint prostheses and the dental implants. Since most of the attention in the published literature has been focused on these two latter applications of titanium, only these will be considered in this section.

4.1. Dental implants

A number of oral diseases such as the growth of tumours and large cysts or osteomyelitis require surgical procedures in which there is extensive loss of bone from the mandible. This results in a severe impairment of the natural oral function giving rise to speech difficulties and the inability to eat properly. The preferred method of dealing with this situation is to use autogenous bone, that is the patient's own bone being taken from another site. Unfortunately this is not always possible and under those circumstances an implant may be considered [55]. The implant shown in Fig. 5 is an example of Ti–6% Al–4% V used to bridge a large defect in the mandible [56]. The superstructure is held in position by hollow screws with a plasma-sprayed surface allowing direct bone contact and new bone formation in the lateral perforations of the screw. The early clinical results are highly encouraging [57].

Another problem related to the mandible is denture instability. In the case of the edentulous patient the mandible will gradually resorb such that there comes a point when insufficient residual ridge remains to hold the denture in place. A number of options are available for dealing with this problem but the one with most appeal to the patient is the use of permucosal implants, two examples of which are shown in Fig. 6. The use of these implants represent a particularly severe problem because they have to penetrate through the mucosa in order to support either a denture or a bridge structure. Yet if a successful implant could be developed it would help many thousands of middle aged and elderly patients. We are in fact witnessing a rapid increase in the elderly population, a large number of whom are edentulous. In Britain in 1968 over 50% of the population over fifty were edentulous rising to 90% for those over the age of seventy [58], so demand is likely to rise.

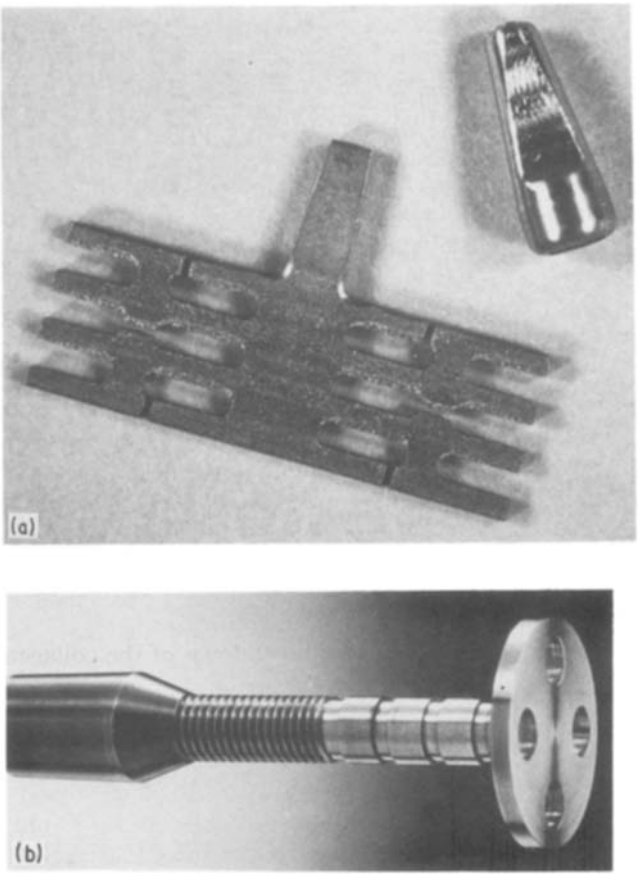

Figure 6 Two designs of dental implant showing in (a) a blade-vent design made of titanium alloy and (b) a disc implant. (Courtesy of AMBITEC SA, Vevey, Switzerland).

In order to appreciate the complexity of the problem it is warranted to look first at the way the natural tooth deals with this situation. From Fig. 7 the various tissues in contact with the surface of the tooth can be identified. The junctional epithelium is attached to the tooth via an extracellular mucopolysaccharide cementing substance [59]. At the ultrastructural level this involves hemi-desmosomes which are structural membranes. Desmosomes are membranes which attach the individual epithelial cells to one another, one half of each of the desmosomes being formed by the two contacting epithelial cells. Hemi-desmosomes are found when an epithelial cell contacts a surface other than another epithelial cell. Thus they are found where

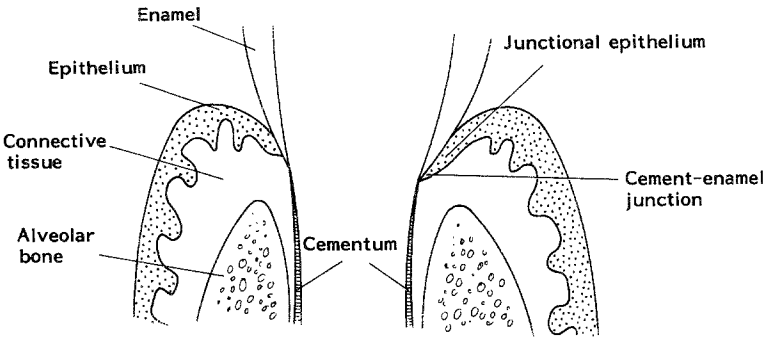

Figure 7 The anatomical arrangement of the tissues around the neck of a natural tooth.

the junctional epithelium joins on to the connective tissue and on to the enamel and cementum of the tooth. The gingival connective tissue is attached to the root cementum by collagen fibers extending into the cementum. In this way a double defence mechanism against the invasion of bacteria is presented. If bacterial toxins were allowed to establish themselves in the gingival crevice, then the attachment of the junctional epithelium will break down. This loss of attachment is then followed by breakdown of the collagen fibers bonded to the cementum and inflammation of the soft tissues. In response the junctional epithelium begins to migrate towards the apex of the tooth which results in the formation of a pocket and eventually loss of the tooth. Thus for a permucosal implant to be successful, it must be able to bond to bone to provide rigid fixation and to connective tissue and epithelial tissue in order to prevent the ingress of bacteria. If it is incapable of doing this then the implant will be lost in the same way as the natural teeth were probably lost.

In ultrastructural studies of the interface between titanum and epithelium and connective tissue it has been shown that attachments similar to those of the natural tooth are created [35–38]. It is even suggested that the attachment of epithelium to titanium is stronger than the adhesion between the cells [34]. Hemi-desmosomes have been observed between the titanium and epithelium so creating a tightly bonded collar around the neck of the implant, which will prevent the ingress of bacteria as long as the attachment is maintained. Thus by combining the ability of titanium to induce osseointegration and also create an epithelial attachment, it would seem that titanium has all the attributes necessary for the application as a permucosal implant.

A consensus conference on dental implants held in 1978 made the recommendation that for a particular implant material and design to be considered successful it must show that it is able to provide functional service for 5 years in 75% of cases [60]. In 1979 there were no dental implants which could claim to be able to meet this criterion. The clinical results reported by Adell *et al.* [61] using an implant design made of titanium represent a major advance in oral implantology. The procedure is as outlined in Fig. 8 and involves a two-stage technique. The first stage in the surgical procedure is the insertion of the implant into the bone and is represented as steps 1 to 6. A flap is raised and a space created for the implant with specially designed titanium instruments. Titanium is used throughout the procedure to avoid the possibility of contamination of the site of implantation with metals other than titanium. The implant is inserted and the flap is closed (steps 7 to 10). The site of implantation is then allowed to heal and at no stage during this phase of the procedure is the implant being loaded or disturbed in any way.

Osseointegration is allowed to take place and once the implant has become fully osseointegrated the implant is again accessed via a small incision and an abutment is attached which protrudes through the mucosa and to which the superstructure of the bridge or the denture will eventually be attached. This is shown by steps 11 to 15. During a period from 1965 to 1980 Adell *et al.* [61] implanted some 2768 titanium screw-type fixtures in 410 edentulous jaws of 371 consecutive patients. Disregarding the early results obtained during the learning phase and only considering those implants inserted during the last 5 to 9 years, they found that 91% of the implants placed in the mandible and 81% of those in the maxilla were successful and able to support a fixed bridge structure. These results more than meet the requirements laid

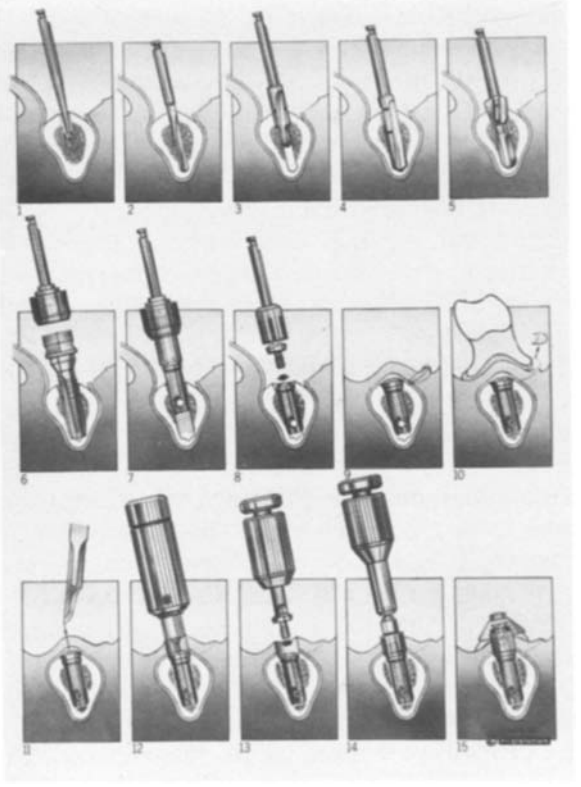

Figure 8 Schematic of the operative procedure adopted for the placement of a titanium screw implant. For explanation see the text. (Courtesy of Nobelpharma AB, Goteborg, Sweden).

down and further studies have confirmed the excellent performance of this implant [61–64]. The good results obtained by some research groups have encouraged the dental profession to adopt the use of titanium implants with great enthusiasm. Nevertheless their application should be approached with great caution because the successful application of an implant is not merely a matter of choosing the right material and the right design. The insertion technique can be deceptively simple and there is a danger that they will be used in situations where the prognosis may be poor [65]. Correct operative procedures and intensive patient management post-operative are also vitally important to the success of the implant. No doubt, as familiarity with the implants and the operative procedures is improved and as patients suitable for this type of treatment are recognised, so the experience gained will ensure that the success rate with titanium dental implants will increase.

4.2. Orthopaedic implants

As stated by Williams [7] the two basic reasons for the use of implants in orthopaedic surgery are for the fixation of bones and joints or for their replacement. The artificial hip joint is now widely used and can justifiably claim to be one of the success stories of the medical application of materials. Nevertheless the failure of orthopaedic implants is still a matter of concern since there are a small but significant number of failures related to the material [8]. Such failures require total revision surgery which is both painful for the patient and costly to the health service.

The mechanical performance of joint prostheses depends on many factors such as the design of the prosthesis, the surgical technique as well as the choice of material. Originally the two alloys most used were cobalt–chromium alloy and wrought stainless steel, which are still used to this day. The commercially pure titanium (Ti-160) was introduced during the 1950s but has since been replaced by the alloys of titanium (Ti-318 and Ti-550), because of their superior strength [66]. Material related failure of the hip prosthesis may manifest itself in one of three ways. An obvious case is that of fracture. But two factors of major interest are wear of the articulating surfaces and loosening of the implant [67].

Fracture of the metallic components of hip joint prostheses is most commonly associated with fatigue failure of the femoral stem [67]. The excellent fatigue strength of titanium and titanium alloy should help to alleviate this problem. Although few fractures of titanium have been reported it is still important to know why these arise so that solutions can be found. Hughes and Jordan [68] have demonstrated the susceptibility of Ti-160 to the presence of surface imperfections, acting as stress concentrations. Examination of the fracture surface of an implant showed the presence of surface flaws and the fracture was more indicative of an impact failure than fatigue. This problem can be overcome by paying more attention to the surface finish of the final product and impressing upon the surgeons that every care should be taken not to damage the implant surface during the operation. Such surface defects may also act as ideal sites for the onset of fatigue especially for Ti-160 which has a much lower fatigue strength than Ti-318. Thus the introduction of Ti-318 should help to overcome this problem and as Dobbs reports [66], does appear to give a better performance compared with Ti-160, although he admits that this observation is based on few clinical data. He did report on one fatigue failure of a Ti-318 stem prosthesis but felt this was due to a design fault. It would appear that the problems associated with the early failure of hip prosthesis have now been resolved. However the trend towards porous surface coated implants which have a significant effect on the fatigue strength means that a careful watch must be kept for any signs of potential trouble.

Friction and wear are also important aspects of the behaviour of the implant material when used for joint replacement [7, 67]. It is extremely important that the friction between the articulating surfaces is as low as possible so that a smooth gliding action results. In addition the potential for damage of the articulating surfaces which may manifest itself as surface loss, creep or fatigue should be kept to a minimum. Release of wear debris into the surrounding tissues may adversely affect the biocompatibility of the whole implant by inducing a local tissue reaction. Titanium moving over itself has a low coefficient of friction when tested at low loads but this increases rapidly as the load is increased. At high loads disruption of the oxide coating occurs and because of the high reactivity of titanium local welding results. Thus titanium has a tendency for galling and seizing which makes it a poor bearing surface [11]. The application of lubricants

Figure 9 A total hip prosthesis system with titanium wire mesh sintered on to the surface of the stem and the acetabular cup for fixation by ingrowth of bone. (Courtesy of Zimmer Limited, Swindon, UK).

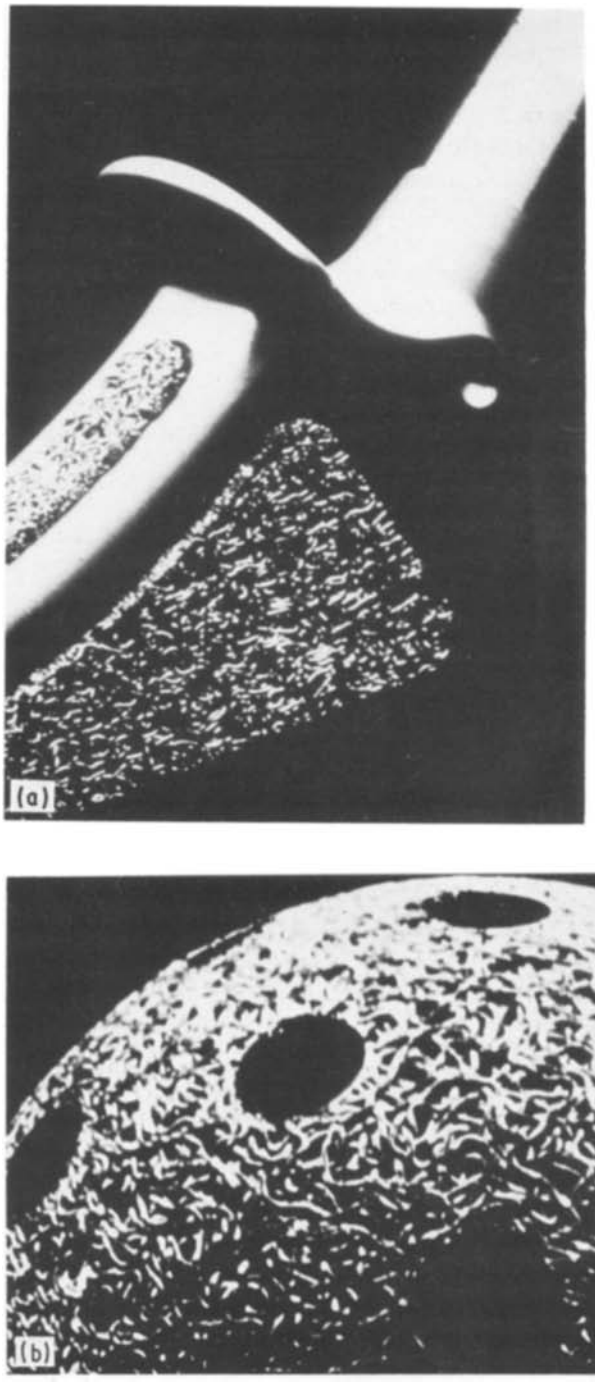

Figure 10 Close-up views of titanium fibre mesh sintered on to the femoral stem (a) and the acetabular cup (b) of a hip prosthesis. (Courtesy of Zimmer Ltd., Swindon, UK).

does not alleviate this problem because of the failure of titanium to form a physically or chemically absorbed layer of the lubricant. An alternative approach is the application of surface coatings but these can have an adverse effect on the fatigue strength or the corrosion resistance and are likely to compromise the excellent biocompatibility of titanium. Consequently the use of titanium for articulating surfaces was originally not recommended. The way this problem was overcome was by the use of a coupled prosthesis, where the main body of the prosthesis would be made of titanium alloy and the bearing surface consist of cobalt–chromium alloy or alumina (Fig. 9). However it has been shown by Miller *et al.* [69] that titanium performed no worse than stainless steel or cobalt–chromium alloy when abraded against ultra-high-molecular-weight-high-density (UHMWHD) polyethylene, now extensively used as one of the bearing surfaces. This would suggest that in situations where titanium articulates against a UHMWHD polyethylene bearing surface no wear of the titanium should arise and has encouraged the wider application of titanium as a direct articulating surface, making the implant design considerably less complex.

Because of continuing concern about the potential for wear of titanium alloy a recent development is the ion implantation of nitrogen of the articulating surfaces [70]. This is a high energy process in which many of the atoms are displaced from their original position by collisions such that implanted atoms occupy regular substitutional sites in the crystal lattice. In the case of titanium and its alloys the implantation of nitrogen creates a very fine dispersion of hard second-phase nitride (less than 0.1 μm in size) within the metal. These tiny nitride particles prevent the movement of dislocations resulting in a two-fold increase in the micro-hardness of the surface layer and it has been claimed to show a dramatic reduction in the rate of

wear of nitrogen-implanted titanium alloy against UHMWPE. The technique of ion bombardment has the advantage that it is fast compared with thermal diffusion processes.

Loosening of the hip prosthesis has been cited as one of the main reasons for revision surgery. In a recent article of a long term study of 230 McKee-Farrar hip arthroplasties, August *et al.* [71] reported that 50% of cases showed loosening of the femoral stem or the acetabular cup. Of the 64 which needed revision, loosening accounted for 78%, stem fracture for 8% and infection for 4.8%. This high incidence of loosening in long term patients has also been observed by others [72–74] and has become a matter of great concern, especially as the problem is more prevalent in young adults who wish to lead a full and active life [75]. Conventionally, implant fixation is achieved by the use of a bone cement of poly (methyl methacrylate) and considerable effort has gone into improving the cement technique [76], so improving the quality of fixation of the prosthesis. But with the excellent results for bony ingrowth into porous surfaces of some materials the idea of cementless fixation is being explored with great enthusiasm. There are also a number of patients, estimated at 0.8% of the patient population [77], who have an allergy to the cement for whom cementless fixation would be the best solution. Titanium, because of its excellent biocompatibility with bone is an obvious candidate for this approach. Not that the concept of cementless fixation is new, far from it, the first reported case of cementless fixation of a joint prosthesis was by Moore and Bohlman [78] way back in 1943.

Much of the work on porous coated implants for orthopaedic applications have concentrated on the cobalt–chromium alloys which lend themselves readily to the production of porous surface coatings [40]. Nevertheless ways of producing a porous-surface titanium alloy implant are being explored [40, 79, 81–83] because it offers many of the same features as the cobalt–chromium alloys as well as light weight and excellent fatigue strength. The examples shown in Fig. 10 are close-ups of the c.p.Ti fibre pads sintered onto the stem and the acetabular cup of the titanium alloy hip prosthesis depicted in Fig. 9. A judicious design of the femoral component is of paramount importance. In the case shown, the porous mesh is only situated at sites away from regions of high stresses and where the stem is thick in cross-section to counteract the reduced fatigue strength. As yet these new prostheses have not undergone extensive clinical trials. Since the objective is to seek improvement in the long term performance, that is in excess of five years, compared with the cemented prostheses it will be some time before their clinical performance can be judged with any degree of certainty.

5. Conclusions

The evidence presented in this review shows that titanium and its alloys are well tolerated by the biological environment. They have mechanical properties which are at least adequate for the applications used and because of their corrosion resistance they rank among the best metallic materials for clinical use. The interactions between titanium and the body tissues which allow osseointegration when placed in contact with bone and produce a strong attachment to epithelial and connective tissue are features of the material which have opened up many new possibilities. The cementless fixation of hip prosthesis components and the retention of dentures by oral implants are but two exciting examples of the clinical application of titanium and undoubtedly more will follow.

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