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Metal Release from Stainless Steel Mandibular Plates Used in the Treatment of Mandibular Fractures

by

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A treatise submitted in partial fulfilment of the requirements for the degree of Master of Dental Science.

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ABSTRACT

Since the 1960s, surgery of the facial skeleton was revolutionised by the introduction of plates and screws for fixation. This method counteracted the dynamic biomechanical forces to maintain anatomical alignment of the fragments in function and allowed mobilisation of the mandible in the early phases of healing.

The two fundamentally different systems were that of compression plates based on the AO-ASIF for long bones and modified for mandibles and monocortical plate system as introduced by MICHELET and refined by CHAMPY. Due to functional and biocompatibility requirements, the material of choice for the plates and screws were metal alloys. In the early stages stainless steel based alloys were introduced followed by titanium.

One of the problems encountered with the earlier alloys is corrosion. This was especially true for the stainless steel alloys and highlighted by the condition "metallosis". The types of corrosion encountered were classified into pitting, crevice, surface and fretting corrosion. With refinement of the alloy by introducing elements such as chromium and molybdenum and improving mechanical properties such as surface finish the corrosion rates were reduced to the point where it was not clinically obvious. The corrosion rate in the orthopaedic literature is established at 0.15-0.3 μ/cm2/day.

The biological effects of these released ions have been categorised into metabolic, oncogenic and immunologic. While the metabolic, and oncogenic effects need to be further characterised and established, the hypersensitivity rate is established at 4%. Under septic conditions the hypersensitivity rate is further increased to 10%. These figures warrant hypersensitivity testing prior to placement of these implants.

In case of miniplates used in the treatment of fractures there has been limited research carried out looking at corrosion.

The aim of this study was to establish whether stainless steel miniplates in this system underwent corrosion. The corrosion was investigated by analysing the surrounding tissues for any release of corrosion products such as CHROMIUM (Cr), MOLYBDENUM(Mo) and NICKEL(Ni).

The plates involved in this study were stainless steel monocortical plates commonly referred to as CHAMPY plates. The alloy concerned is the AISI 316L alloy with the composition of Cr, Mo and Ni which complies with ASTM.
Biopsies of overlying soft tissue and underlying bone were obtained from 20 male patients with an age range of 18-67 yrs (mean age 23.6). As controls and for comparison biopsies of soft tissue and bone were obtained from 25 male patients undergoing lower third molar surgery and with no prior history of exposure to implants or environmental factors which might influence their levels of Cr, Mo and Ni at the time of surgery.

RESULTS

The biopsies obtained were analysed for tissue levels and the pattern of release in relation to the time the plates have been in situ. The time period was divided into 0-9, 10-18 and 19-27 months. The position of the plates were also analysed by comparing anterior vs body/angle region and against the controls. Wilcoxon rank sum test and ANOVA were employed for statistical analysis. Both methods gave the same conclusions.

In the case of nickel the bone levels were not accurate due interference by calcium oxide. There is a significant increase in levels of Cr and Mo, and an increased level of Ni are released from the miniplates. In relation to the time the plates have been in situ the mean levels were variable with no significant difference when compared to the controls or within each group. For the position of the plates only Ni for soft tissue and Mo were significant.

CONCLUSION

In conclusion, in spite of the rather small sample size, this study provides the scientific evidence for removal of these plates as soon as there is clinical and radiographic healing.
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Dedicated to....

My teachers, my family and my friends, Peter A., Ashleigh J.
CHAPTER 1

REVIEW OF THE LITERATURE

1 TREATMENT OF MANDIBULAR FRACTURES

1.1 INTRODUCTION

The event of a fracture, is the sudden loss of continuity of bone due to a direct or indirect force applied to that bone. The extent and the nature of this fracture is determined by the type of trauma experienced and the nature of any pathological process affecting the bone. In the case of the mandible, additional factors such as the anatomy of the bone and the dentition it houses, influence the nature of the fracture. This event of a fracture causes a sequence of biological events as the body responds to the mechanical destabilisation of the bone. The significant initial biological event is the formation of a haematoma by the extravasation of blood from the surrounding soft tissues and bone. The haematoma not only acts as a splint for the fractured segments but also plays a protective role against infection. The inherent elasticity of the soft tissues aids in the mechanical splinting with the exception of those instances where the action of the attached muscles determine the extent and direction of displacement of the fractured bony segments.

1.2 PRINCIPLES OF TREATMENT

The healing of the fractured bone is a biological event determined by the intrinsic response of the body directed towards restoring tissue integrity and full functional capacity. The surgical treatment is purely a mechanical process that aids this biological event by providing anatomical continuity and/or stabilisation of the fractured segments.
The goals of treatment of mandibular fractures are defined as (a) to achieve anatomical reduction and stabilisation, (b) to re-establish the pretraumatic functional occlusion (c) to restore facial contour and symmetry and (d) to balance facial height and projection (Sinn, 1989). These goals are achieved by the time-honoured principles of REDUCTION, FIXATION, IMMOBILISATION and REHABILITATION.

Traditionally the methods of treatment of mandibular fractures are classified as shown in Table 1 (Laskin and Best, 1988). The conservative management includes rest, soft diet and antibiotics and analgesics as required. The fracture is usually undisplaced or with minimal displacement. There is no derangement of the occlusion. Closed reduction implies the use of materials to align the fractures and the occlusion without any direct surgical intervention. Some of the methods used include the use of maxillomandibular fixation, wiring of teeth, Gunning splints, plaster caps and chin straps. Open reduction is where there is surgical intervention using wires or plates to reduce and fix the fractured segments. The last method involves the use of a combination of closed and open reduction techniques.

**TABLE 1**

<table>
<thead>
<tr>
<th>CLASSIFICATION OF TREATMENT</th>
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<tbody>
<tr>
<td>1. CONSERVATIVE MANAGEMENT</td>
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<tr>
<td>2. CLOSED REDUCTION</td>
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<tr>
<td>3. OPEN REDUCTION</td>
</tr>
<tr>
<td>4. OPEN/CLOSED REDUCTION</td>
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1.3 HISTORICAL PERSPECTIVE

The questions of how, when, and where the first successful treatment of the fractured mandible took place is most probably lost to antiquity. The earliest writing in relation to treatment of fractures can be found in the times of the Sumerians in the year 5000 BC when their king, Hamurabi, had a code written on clay tablets (Ring, 1985). In part, this code stipulates that "If a physician sets a broken bone for a man or cures his diseased bowels, the patient shall give five shekels of silver to the physician". It further stipulates that "If a physician shall make a severe wound with a bronze operating knife and kill the
patient, his hand shall be cut off”. The philosophy of treatment was limited to conservative management of suitable fractures that were not infected and reflected the limited knowledge at that time of the human body and the materials available. In fact, it is stated that the belief that all efforts should be expended in an attempt to save any patient is said to have begun under the influence of Christian philosophy around 400 or 500 AD. According to Sinn (1989), the earliest recorded treatment of mandibular injury can be found in the Edwin Smith Papyrus, c.1650 B.C. This document describes reduction of a dislocated mandible in Egypt some 3600 years ago. The Etruscans in the seventh century B.C. used gold wire for fixation of fractures. Hippocrates (460-370 BC) recommended that, in the treatment of jaw fractures, the teeth be ligatured, so that immobility and correct positioning of the fractured segments may be achieved. Rowe mentions the description of tracheostomy by Anthills in 150 AD as the only remarkable advance in the two millennia after Hypocrates (Rowe, 1971).

In India, the system of Ayurvedic Medicine which was probably developed in the first millennium A.D. was based on the material taught by two practitioners, CHAKRA, who wrote on medicine and SUSHTRA, who wrote on surgery. Surgical procedures were performed with strict attention to an elaborate system of religious rituals. First, the heavenly auspicious (time) had to be favourable. Then, the god of fire was propitiated with offerings of food, drink and jewels. Finally, the patient was seated facing the east and the surgeon the west. Food was given to the patient for strength and wine for anaesthesia. Fractures were treated by relocating the bite and using a complicated system of bandaging for stabilisation. After surgery the practitioner recited a series of incantations requesting protection from the gods (Ring, 1985).

Avicenna (980-1037), one of the early Islamic physicians, emphasised the need for proper reduction by placing the patients into proper occlusion and stabilisation by supportive bandages and wiring of teeth. In Western Europe, in the late middle ages, Hieronymus Brunschag (c.1450-1533) designed chin straps for support of the fractured jaw and also advocated wiring of teeth in badly displaced fractures. Ambroise Pare (c.1517-1590) advocated
gold wires for stabilising jaw fractures (Ring, 1985).

In 1780, two Parisian surgeons, Chopard and Desault, introduced a combined intraoral and extraoral treatment of mandibular fractures. Their device sandwiched the mandible between a metal splint covering the dental arches and a wooden plate secured under the chin. The two segments were held together by a screw device. This appliance was uncomfortable and underwent many modifications, with the final modification being made by Hartig in 1830 (Leonard, 1990). Direct wiring of bony fragments was achieved in 1846 by Buck (Sinn, 1989). Gilmer pioneered maxillomandibular fixation (but the first mention of tying the teeth of injured jaw to the uninjured is credited to William Saliceto from Italy in 1275) and credits Black with the first use of circumferential wiring of fractured mandible in the United States in 1881 (Ivy, 1969). Batons (1807-1877) in Paris was the first to use circummandibular wiring in a dentate patient (Leonard, 1990). Gilmer’s original technique has since been modified by Oliver, Winter and Ivy. T.B. Gunning introduced splints for stabilisation of mandibular fractures in 1861 (Ivy, 1969).

As mentioned above, the majority of the early surgeons tended to treat fractures conservatively due to the limited resources and technology available at that time. The high rate of infection with the associated morbidity such as non-union, and the lack of knowledge of the biology of bone and healing were also important determinants of the type of treatment offered. The desire to treat fresh fractures by open reduction and direct fixation techniques stems from the need for treatment of non-union of fractures.

The concept of surgical resection and the approximation of fresh bleeding bone to fresh bleeding bone for osseous consolidation of long standing non-union was an important ideological breakthrough and this was put forward by Charles White of Manchester, England in 1759 (Robinson, 1978). It also reflects the advancement in the understanding of bone biology. With the
advent of: local anaesthesia in 1890, general anaesthesia in 1846, radiography in 1895, antiseptic surgery in 1867, followed by the introduction of aseptic techniques in 1879 and rubber gloves in 1890, the surgeon became more adventurous and utilised more direct fixation techniques in the treatment of fractures (Fig 1).

The two world wars gave maxillofacial surgeons the opportunity to manage a vast number of facial fractures and the research stimulated led to further important discoveries such as antibiotics in 1937, blood replacement in the late 1930's and these with better understanding of surgical haemostasis, led to a rapid advancement in the number of techniques available to the surgeon today (Rowe, 1971).

1.4 INTERNAL FIXATION

1.4.1 Introduction

The concept of whether a fracture should be treated as an open reduction or closed reduction has created one of the most heated philosophical debates in the history of surgery. According to Ellis, the first published debate over open reduction dates back to August 1775 in THE FRENCH SURGICAL JOURNAL where one prominent surgeon castigated another over a disastrous result of an open reduction (Ellis, 1991). Over the next 200 years surgeons aligned themselves, one of two camps of thinking, those who favoured non-operative technique as opposed to those who favoured operative management.
Open reduction is defined as an operative technique where the fracture site is surgically exposed to provide reduction and/or fixation (immobilisation). Its introduction led to the introduction of many internal fixation techniques which can be broadly classified into RIGID and NONRIGID internal fixation. By definition, Internal Fixation implies the placement of wires, screws, plates, rods, pins and other hardware directly onto bone for stabilisation. Any form of internal bone fixation which is not strong enough to permit active use of the affected skeleton during the healing phase and requires other forms of fixation including immobilisation is considered nonrigid.

Rigid internal fixation is defined as any form of bone fixation in which otherwise deforming biomechanical forces are either countered or used to advantage to stabilise the fractured fragments and to permit loading of bone so as to permit active motion during the healing phase.

1.4.2 Bone Healing

The provision of internal fixation allows for direct osteosynthesis of the apposed fractured segments. In osteosynthesis the bone heals primarily by either contact healing or gap healing (Ochs et al,1991). Both forms of healing are considered to be primary bone healing. There are two barriers that have to be overcome in primary bone healing. The first barrier is the dense avascular cortical bone which acquires its nutrients from outside sources and the second is the fact that a portion of the bone that is directly adjacent to the fracture site may be rendered nonviable. In case of contact healing, there is direct cortical bone contact and healing takes place from the periphery to the centre with the osteoclasts widening the haversian canals on either side of the fracture. The canals are oriented longitudinally towards the fracture site, with the osteoclasts excavating across the fracture line (cutting cones). Capillary ingrowth takes place, followed by laying down of osteoid bone by the osteoblasts lining the haversian tunnels( also referred to as intra canicular osteogenesis). The osteoid bone matures directly into lamellar bone. Cortical bridging occurs by eight weeks and is completed at 16 weeks after stabilisation. The tunnelling directly towards the fracture site is thought to be similar to normal physiological
remodelling associated with growth. The clinical union is due to cancellous bone healing and bridging, rather than cortical bone healing.

Gap healing takes place by new bone being deposited at right angles to the normal direction of the bone at the fracture site which is then remodelled along the functional axis of the bone through normal haversian remodelling. In fractures where rigid internal fixation is used, both types of healing take place at various sites in the fracture. Although direct osteosynthesis does not involve the intermediate stages of tissue differentiation (callus formation) as involved in bone healing by secondary intention, it is not considered to be faster, but is more efficient with high levels of bone integrity restored at an earlier phase in the healing process.

The process of direct osteosynthesis is therefore influenced by the osteogenic potential of the bone involved and the osteointegrative capability of the implant used for the internal fixation. The osteointegrative capability is defined as the process by which bone tissue incorporates the implant so that the implant can accept functional demands without mechanical failure or rejection over a period of time.

1.4.3 Historical Perspective

The use of rigid internal fixation was first achieved in 1886, when Hansmann introduced unhardened nickel plated steel strips with screw holes drilled at various intervals (Robinson, 1978). The screws were left to protrude from the wound after fixation for easy removal. As mentioned earlier, with the introduction of radiology in 1895 the surgeons were able to visualise the malunions of closed reductions and this contributed to the acceleration of development and application of internal fixation techniques. In Europe, König, Matti and Kuntscher made great strides introducing metallic fixation on the surface or into the medullary cavity of bone. In England, Arthur Lane introduced the Lane plates for long bone fractures. The Lane plates were modified later by Sherman of Pittsburg in 1912.
In Belgium, the Lambotte brothers advocated internal fixation and contributed to its understanding especially in the area of composition of the implants. Robert Danis (1880-1962), is considered to have made the greatest contribution in the field of internal fixation (Ellis, 1991). He introduced certain requirements for internal fixation which form the basis of modern theories of internal fixation. The first concept was that of early mobilisation following fixation which he believed prevented regressive alterations that took place in bone as a result of immobilisation. He believed in this concept to the point of even advocating fixation of undisplaced fractures so that cast fixation may not be used. The second concept was that of perfect anatomical reduction so that the original shape of the bone is restored. He argued that the restoration of the original shape would obtain the optimal functional capacity as defined by the bone prior to the injury. His third concept was that of the union of the bone fragments without callus formation as he believed that callus was pathological and considered it to be the body's way of providing a splint.

In providing the above concepts, Danis established the following principles of internal fixation:

(a) The treatment should be carried out in an aseptic environment with minimal trauma to the tissues involved.

(b) The implant or graft used should not be chemically or electrically active and should not cause mechanical irritation.

(C) The internal fixation used should provide absolute interfragmentary rigidity until the fracture has united.

(d) The internal fixation should create and maintain sufficient interfragmentary pressure directed along the bone axis. Thus the concept of compression at the fracture site was introduced.
In the United States, Clay Murray (1890-1947) made contributions in developing the concept of internal fixation (Robinson, 1978). His often repeated ideal of fracture treatment: "To wish the fragments into place, to hold them there by moral persuasion and send the patient on about his business while the fracture heals". Other notables, William Halstead in Baltimore and Marius Smith-Peterson in Massachusetts, who contributed toward surgical techniques.

1.4.4 Internal Fixation of Fractured Mandible

The controversy between closed and open reduction of mandibular fractures parallels that for other skeletal fractures. The local anatomical factors, the dynamic forces involved due to the muscles of mastication and facial aesthetics influenced the fixation of the mandible and have contributed to the delay of the use of internal fixation of mandibular fractures. The anatomical factors included the following:

(a) the dentition, which provided an excellent means of reduction of the fractures.

(b) the fact that the mandible is a bone with two joints articulating with the cranium meant the reduction of the mandibular fractures must be perfect or the condyles will slip out of the fossa resulting in malocclusion.

(C) the presence of the neurovascular bundle coursing through the middle of the mandible restricted the types of fixation device able to be used.

The dynamic forces from the muscles of mastication, including the pterygomandibular sling and the infrahyoid muscles, provided the forces which had to be neutralised before the fixation could be applied.

Another factor which was important in the consideration of the type of fixation used was the aesthetic results of the treatment of the fractures. Probably the most important contribution was the fact that the dentition was used for easy reduction by the use of intraosseous, intradental and interdental wires.
(maxillomandibular fixation). In the edentulous cases the problem was compounded due to the fact that the dentition was not available for easy reduction.

Gordon Buck, in the United States in 1847, is credited with being the first to place an intraosseous wire in a mandibular fracture as mentioned above. Following this, there were sporadic attempts at internal fixation by using examples of fixation such as internal pin fixation (Fig 2) as highlighted by the use of Steinman pins and Kirschner wires. The stability provided by the pins was not adequate for fixation of mandibular fractures and usually necessitated the use of maxillomandibular fixation. An alternative was the use of metallic mesh implants which provided some fixation but they were mainly used to provide a framework into which autogenous cortico-cancellous bone could be packed, in cases of malunion or nonunion. The mesh was not an ideal source of fixation for the fractures. John Converse introduced the use of external pin fixation during the second world war. He adapted Roger Anderson's orthopaedic external pin fixation kit for use in the mandibular fractures of English soldiers. Unfortunately the external pin fixation was restricted to selective cases to achieve adequate success. Another innovation was the use of bone clamps which applied forces on both the lingual and buccal cortices of the mandible at the inferior border. They were ideal for oblique fractures but involved exposure of the lower border of the mandible which included stripping of extensive areas of periosteum. The Samson pericortical clamp system (Pittsburg, PA) is a classic example of the type of bone clamps used in oral and maxillofacial surgery. One of the common complication caused by the clamps was their slippage, hence its unreliability in providing fixation.
Bone plates had been originally introduced to maxillofacial surgery by Christensen in 1945 (Ellis, 1991). He used tantalum plates to provide interfragmentary stability of unstable mandibular fractures. Others attempted to use modified bone plates including metacarpal plates. In the early days many failures resulted probably owing to the lack of knowledge of the biomechanics of the system with combined function of the jaw and the improper use of antibiotics. A system which gained notoriety was the Robinson and Yoon L-shaped plate which was further modified by Professor Schilli. While the L-plates were satisfactory in certain cases, again they involved stripping of large portions of the mandible and were unreliable due to the inflexibility of the plate to adaptation to the bony surface even after the Schilli modification.

Thoma, in his review of methods of internal fixation of jaw fractures, states that many fractures which are multiple, compound, and complicated by fracture or absence of teeth or infection cannot be adequately treated by the use of most of the simple types of fixation and intermaxillary wiring (Thoma, 1948). He goes on to describe the methods available at that point in time, being transosseous wiring, use of bone plates (the early plates as described above), internal wiring fixation and transf ixation and skeletal fixation with pins and clamps. The use of rigid internal fixation hence came to the forefront in the early sixties to seventies.

Professor Hans Luhr, who carried out extensive experimentation with mandibular fractures, contributed significantly towards the introduction of bone plates. In fact, he is credited with introducing the compression plating system to maxillofacial surgery. His other contributions include the important observation, in the case of fractures, that the healing takes place by a combination of gap and contact healing as compared to the observations made by the Association of Osteosynthesis/Association for the Study of Internal Fixation (AOASIF) group who, because of their method of experimentation (osteotomising long bones of sheep), only observed contact healing. Another important contribution by Professor Luhr towards internal fixation was the popularisation of self tapping screws which he used in the 1960's by introducing
the 2.7mm self tapping screw. Later, he made a further contribution by the invention of the microfixation system.

During this period the AOASIF technique for mandibular fractures was also introduced and extensively researched by Professor Spiessl (1976). In 1973 Schmoker and Niederdollmann, two AOASIF investigators, further developed the plating system by introducing the eccentric dynamic compression plate, a modification of the standard dynamic compression plate (Schmoker, 1976). The 1970's also saw the introduction by Professor Michelet of the monocortical plating system which was further researched and modified by Professor Champy and his colleagues in France (Michelet et al., 1973; Champy et al., 1978). Another internal fixation technique which was introduced in the seventies by Brons and Boering was the use of lag screws (Leonard, 1987). Again Niederdollmann further modified the lag screw technique in 1981 (Niederdollmann and Shetty, 1987). Currently the types of internal fixation methods available for fixation of the fractured mandible include:

1. The single plate rigid fixation which involves placement of the plate with extreme rigidity (the heavy mandibular plates as used for reconstruction) at the lower border of the mandible. The plate has to be rigid enough to neutralise the tension and compression forces created by the fracture. One of the disadvantage of the system is that of stress shielding.

2. Stabilisation of the inferior border using compression and tension band stabilisation which was popularised by Professor Spiessl. This involved a rigid plating technique which provided stabilisation by combining both compression and tension (Spiessl, 1972). The compression was provided by a compression plate and the tension was neutralised by use of either a smaller monocortical plate or fixation of the dentition by the use of arch bars or a bone plates in those instances where the fractured segments did not involve dentition.

3. The stabilisation of fractures through use of eccentric compression plates which only required fixation at the lower border. Due to the position of the screw holes and the direction in which the screw holes were constructed, the rigid bone plate was applied to the lower border and this had a
neutralising effect in the tension band and enhanced the compression band.

(4) Stabilisation using the area of tension only. This was popularised by Michelet and Champy.

The use of these varieties of fixation techniques involves the neutralisation of the tension and compression bands which are created when the mandible is fractured. This is best explained by the beam flexion model (Fig 3) as outlined by Tucker and Ochs. The beam flexion model involves application of force (axial compressive force) to objects such as a metal tube or bone (Tucker and Ochs, 1991). The opposing sides of the object are subjected to different types of stress. On one side of the object the major force is compression as compared to the opposite side where there is an area of tension. The tension side involves elongation and the compression side involves shortening of the bone or metal tube. When a fracture occurs, the forces initially result in closing of the fracture gap on the side of the compression and opening or widening of the gap on the side of the tension. Further force on the object eventually results in distraction at the site of tension and displacement of the fractured segments. In the mandible, the tension and compression zones are introduced by the muscles of mastication. The superior and anterior rotation of the posterior segment of the mandible is provided by the pterygomasseteric sling and temporalis muscle. The compression band is provided by the suprathyroid and infrahyoid muscles. This results in contact at the inferior border and distraction of the superior border of the fracture site which is referred to as the tension zone (Fig 4).
In his argument for the case for mandibular plating Roberts outlines the advantages of open reduction and fixation (Roberts, 1964). These include:

(1) Accurate reduction of the fracture is more easily achieved when the bone fragments are exposed and he highlights the fact that reduction is particularly helpful when dealing with displaced edentulous mandibular fractures.

(2) Surgical debridement of the wound can be carried out more efficiently and small fragments of bone, interposing muscle and foreign bodies can be removed as well as the intervening blood clot which can be evacuated.

(3) The treatment time is shortened in that both reduction and fixation can be accomplished at one operation as compared to, for example, cap splinting where one has to take impressions in the first instance and then apply permanent fixation when the cap splints are cemented.

(4) Jaw movement can be maintained until the patient is fully conscious following general anaesthetic which is an advantage especially in multitrauma cases, children and also in those instances where an edentulous mandible is involved.

(5) Early mobilisation of the jaws is possible leading to less morbidity to the temporo-mandibular joints as compared to when the patient is in maxillomandibular fixation and earlier feeding is made possible with the reduction in the rate of weight loss.

(6) Operating time is reduced.
His disadvantages of open methods of fixation are:

(1) A general anaesthetic is almost essential.
(2) A scar is inevitable in those instances where an external incision is involved.
(3) The mandibular branch of the facial nerve could be damaged.
(4) The inferior dental nerve can be damaged.
(5) Foreign bodies, such as wires and plates, when left buried are potential sources of infection and recommends the use of antibiotics and early fixation of the fractures.
(6) Gross comminution is a contraindication for wires and plates due to the increased danger of sepsis and sequestration.
(7) The extensive stripping of periosteum and also the possible effects of stress shielding in those instances where heavy mandibular plates are used.
(8) A flat area of bone is necessary unless special plates are used. This is especially difficult in the area of symphysis or in those instances of edentulous mandible where there is less than 1cm of bone available.

1.5 BONE PLATE OSTEOSYNTHESIS

In bone plate osteosynthesis the fractured segments of bone are reduced and fixed by applying the bone plates to the surface of the bone thus reducing interfragmentary mobility while maintaining adequate blood supply so that the fractured bone heals by primary intention. The systems available are those of large bone plates and small bone plates. The large bone plates can be categorised as those plates which accept or are designed for use
with screws 2.7mm in diameter or larger, and these include the noncompression plate, dynamic compression plate and eccentric dynamic compression plate. These plates are mainly used for reconstruction and also, as described earlier, for application along the lower border of the mandible which in turn neutralises the tension zone in the upper border. The small bone plate systems are used with screws which are less than 2.7mm in diameter. These plates can be categorised into compression and non compression monocortical plates.

2 MONOCORTICAL PLATING SYSTEM

The monocortical plating system was originally introduced by Michelet in 1973. In his article (Michelet et al,1973), he described the technique as an original technique of osteosynthesis for reduction and immobilisation of fractures and osteotomies of the facial skeleton. The plates used were stellite plates (of 12, 18 and 25mm in length and 4mm in width). They had four holes, except the 12mm length plate which had only 2 holes. These were applied in a juxta-alveolar portion of the mandible. He outlined the advantages of this technique to be that of:

(1) An intraoral access to the site, hence absence of a skin scar.

(2) The possibility of watching simultaneously the reduction of fragments and restoration of the occlusion.

(3) Excellent tolerance of the osteosynthesis material. The strength of the device being adequate to withstand the dynamic forces of the mandible involved.

His paper also included the presentation of 300 cases which had been treated in his unit and they reported a complication rate of 5% which consisted of gradual exposure of the plate, whether or not associated with infection and sequestration around the screw.

The monocortical plating system was then further developed by Professor Champy. As stated by Champy (Champy et al,1978; Worthington and
Champy, 1987), the therapeutic objectives for developing these monocortical systems were:

(1) A perfect anatomical reposition.
(2) A complete and stable fixation of the fracture.
(3) A painless mobilisation of the broken extremity bones with the surrounding joints.
(4) Reproduction of the occlusion and of the individual articulation must be guaranteed at the same time as the exact anatomical reposition of the bone fragments.
(5) Opening of the mouth should be guaranteed during the bone healing phase.
(6) Extraoral scars are avoided as far as possible.
(7) Especially in the lower jaw, the osteosynthesis procedures must take into account typical trajectory courses which are restricted by mastication and speech.
(8) Roots and the inferior alveolar nerve must not be injured by the surgical manipulation.

The original plates which were introduced were malleable for easy adaptation to the bony surfaces. Their limits of elasticity were 70 to 90 daN / mm² and a breaking point of 95 to 100 daN / mm². The miniplates varied in length from 2-9cm and consisted of a thickness of 0.9mm. The number of holes involved varied. The screws used were of self tapping variety with a cruciate head type and they were available in lengths ranging from 5mm to 15mm. The screws were designed allowing insertion at a 30 degree slant with respect to the plate surface.
The extensive biomechanical research carried out by Professor Champy and his colleagues showed the ideal osteosynthetic line along which the monocortical plates were to be applied (Fig 5). This line defined the region along which the tension and torsional forces were neutralised.

2.1 COMPOSITION

2.1.1 Introduction

The introduction and development of the principles of internal fixation ensured the need for development of the materials used as fixatures. This is especially true when the principle of internal fixation progressed from that of approximation of the fractured segments to true rigid fixation using biocortical screws and plates. Some of the earlier materials that were used include gold and German silver (Robinson, 1978). The materials involved were biocompatible and were thought to provide some antiseptic or self-sterilising value to the wound, but were not strong enough to withstand the forces generated especially when it involved bicortical fixation. Some of the earlier iron and steel materials that were introduced also caused increased tissue reaction, especially discolouration of the tissue and also loosening of the implants. Dr. William O'Neill Sherman from the United States, introduced in 1910, Vanadium steel which was supposed to be less brittle than the tool steel. While Vanadium steel was less brittle it was still found to corrode very easily.

The 1920's saw an increased interest in biocompatibility and research in metallurgy in relation to internal fixation. Many materials were used. Some of these included gold, silver, aluminium, zinc, lead, copper, nickel, high carbon steel and stellite. The copper showed much discolouration and marked
overgrowth of bone. The gold, silver and aluminium produced excessive periosteal growth of bone. Lead caused non specific bone reaction. Nickel produced marked irritation and some stimulation of new bone. Iron and steel caused the most discoloration and soft tissue reaction. Gold and stellite were readily tolerated by bone and became encapsulated early. Silver and lead, which easily corroded, caused collective tissue reaction. Zinc corroded easily and interfered with bone regeneration. Stellite, an alloy which contained 58% cobalt, 35% chromium and 4% tungsten, with small amounts of iron and carbon had unacceptable levels of corrosion but increased strength. This was the forerunner to chrome cobalt alloys for human metal implants of which vitallium is an example.

The intense research carried out in the area of metallurgy and biocompatibility is yet to establish an ideal biocompatible material with an ideal implant life history. The inertness of the material is a relative matter. Exchange of ions between all implant materials and the surrounding tissue can be demonstrated if tests are sufficiently critical. While metals are relatively inert in themselves, they do cause local reaction which are chemically, electrically and/or physically mediated. The need for the ideal biocompatible implant also accelerated the study in terms of the implant surface, finish, size, shape as these factors were also shown to influence the reaction between the implant and the tissues. The 1950's saw the introduction of titanium and its various alloys and the 1970's saw the

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<tbody>
<tr>
<td><strong>MATERIALS</strong></td>
</tr>
<tr>
<td><strong>STAINLESS STEEL ALLOYS</strong></td>
</tr>
<tr>
<td><strong>COBALT/ CHROMIUM ALLOYS</strong></td>
</tr>
<tr>
<td><strong>TITANIUM</strong></td>
</tr>
<tr>
<td><strong>RESORBABLE POLYMERS</strong></td>
</tr>
</tbody>
</table>

TABLE 3 COMPOSITION OF METALS AND ALLOYS CURRENTLY USED AS SURGICAL IMPLANTS

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>Ti</th>
<th>Cr</th>
<th>Fe</th>
<th>Co</th>
<th>Ni</th>
<th>Mo</th>
<th>Si</th>
<th>P</th>
<th>S</th>
<th>W</th>
<th>H</th>
<th>N</th>
<th>Al</th>
<th>V</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>AISI type 316 stainless steel</td>
<td>0.08max</td>
<td>18.5</td>
<td>rem</td>
<td>12.0</td>
<td>3.0</td>
<td>0.75</td>
<td>0.03</td>
<td>0.03</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cast cobalt-chromium alloy</td>
<td>0.36max</td>
<td>28.5</td>
<td>0.75max</td>
<td>rem</td>
<td>2.5max</td>
<td>6.0</td>
<td>1.0max</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrought cobalt-chromium alloy</td>
<td>0.15max</td>
<td>20.0</td>
<td>3.0max</td>
<td>rem</td>
<td>2.5max</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.3</td>
</tr>
<tr>
<td>Unalloyed titanium</td>
<td>0.10</td>
<td>rem</td>
<td>0.30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.015</td>
<td>0.07</td>
<td></td>
<td></td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td>Ti-6Al-4V</td>
<td>0.08</td>
<td>rem</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0125</td>
<td>6.0</td>
<td>4.0</td>
<td></td>
<td></td>
<td>0.13</td>
</tr>
</tbody>
</table>

(a) rem - remainder.
(b) The composition is stated in percentage.
(C) Individual variations exist due to the manufacturing process hence the composition can vary not only between each batch in production but also between manufacturers.
introduction of resorbable materials as implant materials.

Currently, the biomaterials used are stainless steel, cobalt chrome based alloys, titanium and resorbable materials as shown in Table 2 above.

Titanium appears to be the most acceptable in terms of biocompatibility but the implant life history for titanium is yet to be established. The composition of the materials shown in Table 2 are outlined in Table 3 above. The figures are expressed in percentage of the total weight and is the recommendation of the American Iron and Steel Institute and the American Society for Testing and Materials specifications. The composition of individual brand alloys vary according to the manufacturer’s specifications and needs. The composition of the resorbable polymers is not readily available and is broadly discussed in the relevant section.

The mechanical properties of the above materials are presented in Table 4. The mechanical properties presented are average figures and are

<table>
<thead>
<tr>
<th>TABLE 4 MECHANICAL PROPERTIES OF MATERIALS USED IN INTERNAL FIXATION</th>
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<tbody>
<tr>
<td>TENSILE STRENGTH (MPa)</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>BONE(CORTICAL)</td>
</tr>
<tr>
<td>BONE(CANCELLOUS)</td>
</tr>
<tr>
<td>316 STAINLESS STEEL(ANNEALED)</td>
</tr>
<tr>
<td>316 STAINLESS STEEL(COLD WORKED)</td>
</tr>
<tr>
<td>CAST COBALT-CHROMIUM ALLOY</td>
</tr>
<tr>
<td>WROUGHT COBOLT-CHROMIUM ALLOY</td>
</tr>
<tr>
<td>PURE TITANIUM</td>
</tr>
<tr>
<td>Ti-6Al-4V(ANNEALED)</td>
</tr>
<tr>
<td>RESORBABLE POLYMERS</td>
</tr>
<tr>
<td>polyactides</td>
</tr>
<tr>
<td>polyactides(oriented)</td>
</tr>
<tr>
<td>polyactides/glass fibre</td>
</tr>
</tbody>
</table>
variable depending on the manufacturer's specifications. The properties may be varied by the amount of additives and/or impurities present.

The cobalt-chrome based alloys are stronger than the stainless steel alloys. Then follows titanium and the resorbable materials. In terms of malleability titanium is the most malleable and the resorbable polymers the least.

2.1.2 Stainless Steel

The surgical stainless steel belongs to the group referred to as austenitic stainless steel (Davison et al., 1987). The Austenitic steels have a crystal structure which has a face-centred cubic crystal structure. The detrimental effects of carbon and nitrogen in ferrite is overcome by the structure and is accomplished by adding austenitic stabilisers, such as nickel, manganese and nitrogen. It is a non-magnetic steel with relatively low yield strength and high ductility, rapid work hardening rates and excellent toughness. The fabrication process is simpler for most austenitic grades. The processing difficulties tend to limit increases in chromium content which are important for creating a passive film, hence resistance to corrosion. The addition of molybdenum and nickel increases the level of corrosion resistance. The use of nitrogen as an intentional alloy addition, stabilises the austenitic phase particularly with regard to precipitation of intermetallic compounds. The nitrogen and the addition of molybdenum could be controlled as it plays an important role in corrosion resistance, especially in chloride environments.

The austenitic stainless steels can be sensitised to intergranular corrosion by welding or longer term thermal exposure, which in the biomedical environment has limited application. These thermal exposures lead to precipitation of chromium carbide in the grain boundaries and to the depletion of chromium adjacent to these carbides. Sensitisation can be greatly delayed or prevented by use of lower carbon grade. In practical terms, the surgical steel 316 is more susceptible to chloride induced corrosion.

The degree of protection afforded by the chromium oxide layer is a function of the thickness of the oxide layer, its continuity, its coherence and adhesion to the metal. As mentioned earlier the amount of impurities in the
processing influences the mechanical properties and corrosion resistance of the alloy. Other factors such as the fabrication, external treatments and the design of the alloy influence the mechanical properties.

2.1.3 Titanium

Titanium was introduced as a biomaterial in the early 1950's as mentioned earlier and has become one of the established metal alloys to be used. Commercially available pure titanium is the basic material for purposes where lower mechanical strength is required and titanium alloys such as TiAl6V4, Ti318 and Ti350 are used in applications when higher strength is desirable. The passive oxide (Titanium oxide) layer it forms offers excellent corrosion resistant properties and shows excellent tissue integration and adaptability. To increase the surface resistance, nitrogen or carbon are introduced to form titanium nitride and titanium carbide respectively in the outer most layers of the surface (Tengvall and Lundstrom,1992). The nitrides and the carbides formed, prevent movement of dislocations and result in greater microhardness of the surface. This hardness leads to wear reduction and improved fatigue properties of the titanium surfaces. Barium ions implanted into the oxide layer also provide increased wear and fretting resistance and improves cyclic fatigue resistance of the titanium implants.

While surface modifications improves the mechanical properties of titanium, it has been shown that pure titanium has better integration, less solubility and appears to be more compatible with synthetic hydroxyapatite and calcium based ceramic coating materials.

2.1.4 Resorbable Implants

Due to the limitations imposed by metallic implants, a need for an alternative was established. The limitations included metal implants being too stiff for adapting to bone surfaces, sensitisation, mutagenicity and the need for removal (which requires a second operation). Currently, for internal fixation devices, the polyester group of resorbable polymer implants have shown some favourable results. Of the polyester polymers, the polyglycloide, the polylactide and polydioxanone are the materials which have been extensively investigated (Bostman,1991; Williams,1992; Hofmann,1992). The polylactide, polygalactide
and their co-polymers are more applicable to fixation devices due to their mechanical properties. While their Youngs modulus is greater than cancellous bone, the limitation is that they are brittle, hence the inability to adapt to bone and the inability to withstand functional loads following fixation.

The degradation of the polymers is believed to be via hydrolysis of the Ester bonds. The pathway involves breakdown through glycolic and lactic acid pathways to pyruvic acid which is then converted to water and carbon dioxide via the tricarboxylic acid cycle (Williams, 1992). The factors which determine the breakdown are the water content, pH and temperature of the environment. Other factors which influence degradation are the composition of the polymers; higher molecular weight and high crystallinity and orientation lead to lower degradation rate. Large sized implants degrade slower than implants with small cross-sections. Porous materials containing impurities and additives degrade faster than non-porous ones which are free from additives and impurities. Co-polymers usually degrade faster than homopolymers, although there are many variations from this trend. It has also been shown that degradation is accelerated by stress and load. In general, degradation is faster in soft tissue than bony tissue, which seems to result from differences in vascularity.

The monomer byproducts formed by the polymer degradation are believed to be broken down by the tissue enzymes. The implants demonstrate initial hydrolysis in the amorphous regions and, in a later stage, the crystalline regions are degraded. During the initial hydrolysis, the overall crystallinity is increased. The total degradation time, however, is variable depending on the molecular weight of the polymer used, as well as the other factors described above. It ranges from 2 weeks to 2-3 years.

The enhancement of bone growth and fracture healing by some biodegradable polymers has produced some contradictory results based on in-vitro and in-vivo studies and is controversial (Hofmann, 1992).

The mechanical properties of the polymers are strongly dependent upon their molecular weight, orientation and crystallinity, material purity, presence of defects, voids and re-enforcing elements in the material and the inherent
chemical structure. The yield strength and Youngs modulus increases with increasing molecular weight up to a certain value and differs with different polymers. The increase in polymer crystallinity and orientation accompanied by fibrillation enhances mechanical properties and in the direction of the orientation of the material. The presence of re-enforcing structures, such as fibres in polymers, improves their mechanical properties, while the presence of impurities and additives decreases these properties.

The standard methods of production of biodegradable polymers are by injection moulding, compression moulding, metal extrusion and machining of extruded polymers and compression moulded polymerised polymeric blocks.

Currently, the biodegradable internal fixation devices are appropriate for instances where fixation devices are used for approximation rather than extreme rigid fixation. This applies regardless whether it is in the field of orthopaedic surgery or oral and maxillofacial surgery (Suuronen, 1993). Numerous studies have been carried out where the biodegradable materials have been applied to stress bearing areas where it has shown that additional support, such as plaster or intermaxillary fixation, is required for support. Based on these studies, the limitations of using biodegradable materials is that they should not be used in those instances where there is a large functional load requirement.

Complications for the biodegradable polymers are partly the same as those for conventional metal implants (Bostman, 1991; Schakenraad and Dijkstra, 1991; Suuronen, 1993). They include fracture dislocation of the implant, superficial wound infections and deep infections. A further complication arising from biodegradable implant, has been the development of a sterile inflammatory process in 4-8% of the cases treated. This appears to develop about 8 weeks to 2-3 years following the use of the implant and is variable upon the breakdown rate of the polymers. The inflammatory process eventually forms a chronic sinus which lasts until the implant has been removed or is totally degraded. The inflammatory reaction appears to be a foreign body type reaction and currently is believed to be related to the biodegradation pathway. The incidence of the reaction appears to be related to the anatomical position of the plate; for example, the highest rate has
been encountered in the distal part of the radius and in the scaphoid, whereas the lowest rate has been reported in the ankle. The reaction is not influenced by the volume of implanted polymer, the location of the implant in terms of whether it is subcutaneous or deep, or the bathing of the implant in body fluids. The histological characteristics of the specimens obtained are abundant with macrophages and debris from the polymer.

Other limitations of using the biodegradable material include technical problems such as the restriction in adaptability of the implant and the need for multiple instrumentation. The other factor is the unpredictability in the resorption rate and also the brittleness of the implant as outlined earlier. A further, important drawback, is the current high pricing of the fixation system.

2.2 CONCLUSION

The choice of which material to use in the osteosynthesis using monocortical plates is not only dependent on the physical properties of the material in relation to the functional demands, but also the biological response of the implant, the experience of the surgeon, the availability of a given plating system and current trends.

3 BIOLOGICAL RESPONSE

Once the fractured mandible is treated using an internal fixation device two issues are raised. The first issue is that of what response the host tissues have on the implant device. The second issue is that of what impact the implant material itself has on the immediately surrounding tissues and the host in general. It is the outcome of these two factors which determine whether a treatment procedure is successful or not.

3.1 Definitions

Historically biocompatibility refers to the effect of the material on the biological system. The effects of the biological process on the materials are rarely included unless the results of the material changes elicit a change in the
biological response. The effect of the biological system on the material is usually referred to as biodegradation. The limitation of these traditional definitions are that basically it does not accommodate the dynamic processes involved in the interaction of the biomaterial of the implant device used and the host. The consensus conference sponsored by the European Society of Biomaterials which was held in 1986 (Williams, 1987), defined biomaterial as a nonviable material used in a medical device, intended to interact with the biological system. The biocompatibility was defined as the ability of the material to perform with the appropriate host response in a specific situation. The host response is referred to as the reaction of a living system to the presence of a material. These definitions at least accept the effect of the host response on the systems involved.

One of the earliest authors to take into consideration the physiological factors in the interaction of biomaterials was Osborn in 1979 who classified biomaterials as (1) biotolerant meaning the biomaterial had negative effect but tolerable, (2) bioinert meaning absence of host response and (3) bioactive meaning positive local host response.

Black (1992) prefers to use the biological performance as a description of materials in order to replace the present idea of biocompatibility. The biological performance infers interaction between materials and living systems and the two aspects of the performances are (a) host response meaning local and systemic response rather than the intended therapeutic response of living systems to material and (b) the material response which is the response of the material to living systems. He further states that the generality of these terms is obvious, there are no valued judgements of their definition nor do they suggest absolute qualities. He also goes on to define a reference material as a material that by standard tests has been determined as a reproducible, quantifiable host or material response which does not imply good or bad behaviour on the part of the material. The level of the host response is defined as the nature of the host response in a standard test with respect to the response obtained with a reference material.
The definitions are crucial from the point of view that they can limit the approach to study of the concept of biomaterials and their interactions on the living systems. In the following sections pertinent aspects of the host response and the material response will be outlined.

4 HOST RESPONSE

The host response to an internal fixation device is not only determined by the mechanical, chemical and electrical properties of the implant but also the local and systemic environments of the host. These effects are also related to time. In figure 6 an outline of the various outcomes of the host response is given.

The ideal response would be for the surgical site to heal uneventfully but because of the presence of a foreign material the usual outcome is the formation of a fibrous capsule. In some instances the reaction by the host is that of an immune response or tumorigenic in nature.

4.1 Initial Response

The initial response to an implant device is that of an acute inflammatory process. The acute inflammatory process is due to the traumatic
incident of the fracture, surgical handling and the implant device. The inflammatory response is a non-specific physiological response to tissue damage and follows the haematoma formation alluded to earlier (Spector et al, 1991; McCormick and Hudson, 1994). There are a number of systemic and local factors which influence this process. The systemic influences include age, nutrition, haematological and metabolic derangements, hormones and steroids.

The local factors are determined by the type of cell population present at the site of injury, the nature of the extent of injury and the chemical, mechanical and surface factors of the implant material involved. The type of cell population present at the site of injury is normally classified as stable, labile and permanent cells based on their capacity to regenerate. In traditional thinking the inflammatory response is a series of events made up of chemical and cellular activities which eventually lead to the protection of the damaged tissue. The protection is in terms of clearing the necrotic tissue as well as the toxic agents and providing a scaffold on which normal healing could take place. Complete regeneration of the area involved would take place provided the local cell population is labile or stable.

In the case of implanted materials, the cellular invasion initially consists of neutrophils followed by macrophages. The role of the neutrophils is primarily that of phagocytosis. This not only involves engulfing, degradation and digestion of foreign material but also releasing other chemical mediators to improve the efficiency of the clearing system by fellow neutrophils and other types of cells. However, in some situations there is a predominance of lymphocytes and this is normally considered to be a reflection of a non-specific immune reaction rather than a specific immune reaction which improves the efficiency of the phagocytic process. The second type of cell to arrive at the site of injury are the monocytes. The monocytes again are involved in clearing the damaged or injured site of necrotic tissue and this is carried out mainly by the process of phagocytosis. The activated macrophage under conditions of persistent irritation progresses to form a multinuclear foreign body giant cell (Rae, 1985). This is a common finding in situations where there is an implant involved. The presence and activity of
monocytic cells is particularly correlated to the presence of small particles. The relationship between size and stimulus is not understood (Curtis and Clark, 1990). The maximum stimulus seems to occur when the average particle size is in the 0.1 - 1 micron range. Larger particles bigger than 50 microns do not excite a reaction greater than that compared to bulk materials.

The end result of this initial acute inflammatory process, as stated earlier, is to clear the local irritants and to remove the damaged tissue. In those instances where an implant is not involved, this would lead to resolution in terms of formation of granulation tissue. In the case of bone, the outcome is formation of either normal bone or granulation tissue (fibrous union) depending on the environment. The other extreme is articular cartilage which never completely remodels but is repaired by formation of loose tissue called fibrocartilage. This remodelling process is the primary mechanism involved in tissue adaptation.

The maturation of the scar tissue which marks the end of the inflammatory process is dependent on the presence of the implant. The implant prevents the collapse of the capsule which forms around the injured tissue and its eventual maturation. The degree of capsule formation is dependent upon the degree of the original insult, the subsequent cell death, the location of the implant and the type of implant (McNamara, 1981). The exploration of an implant site four or more weeks following implantation usually reveals a relatively acellular fibrous capsule (Pizzoferrato et al, 1988). This capsule is maintained by the continuing presence of the implant. Spindle shaped fibroblasts are usually associated with the capsule with a small number of macrophages and foreign body giant cells. The presence of foreign body giant cells suggests production of small particles by corrosion, depolymerisation, dissolution or wear and a continuing general tissue response. Observation of large numbers of lymphocytes suggests specific immune response as opposed to the non-specific immune response alluded to in the inflammatory process.

The thickness of the fibrous capsule is consequent to several factors which include the chemical nature of the implant material such as metals which corrode freely or polymers which leach their constituents. The formation of the
thick capsule is directly proportional to the rate of release of these molecules. The chemical nature of the molecules released will determine the extent of necrosis associated with the capsule. In other words, whether the molecules released were cytotoxic, inhibitory or neutral, influences the outcome. Other factors which influence the formation and the size and shape of the capsule are mechanical factors such as the shape of the implant, the design of the implant (for example sharp edges tend to promote a thicker capsule as compared to smooth edges). Another factor which is not clearly understood but is shown to influence the thickness of the capsule is the micromotion involved at the implant site (Linder and Lundskog, 1975). This is in relation to the increased relative motion between implant and tissue. There is also evidence that the electrical currents set up by local pH as well as oxygen tension changes from corrosion products will influence the thickness of the capsule. Increased current density in a given area increases the thickness of the capsule. Another factor which is thought to be involved in humans is the age of the person. Generally it is believed that the older the host the slower the reaction but there is no clinical or epidemiological data to support this conclusively.

The final factor involved in determining the response of the fibrous capsule is the type of tissue involved at the surgical site. In case of muscle the thickness of the fibrous capsule is usually much smaller compared to an implant placed in normal connective tissue. In bone there is a spectrum from normal bone healing and apposition (osseointegration) to a formation of fibrous capsule (Linder and Lundskog, 1975; Pazzaglia et al, 1991). The fibrous capsule again would have a spectrum of cells ranging from fibroblasts to foreign body cells depending on the implant.

The signals which mediate this local host response is still unclear. It is believed that they are mediated through chemical, mechanical and electrical means. The initial acute response is thought to be mainly mediated through chemical activity. The mechanical and electrical factors play a major role in the establishment of the type of fibrous capsule.
Once resolution is reached a balance is established at the implant site. The possible outcomes of resolution are fibrous capsule formation, an immunologically based response and a neoplastic response depending on the implant. In case of resolution through fibrous capsule formation there is a fine balance established at the implant site which would have four possible outcomes as shown in table 5.

(1) Extrusion- If the implant is in contact with epithelial tissue, the local host response will be formation of a pocket or a pouch continuous with the adjacent epithelial membrane. This process will lead to marsupialisation and eventual extrusion of the implant from the host.

(2) Resorption- If the implant is resorbable then the implant site eventually resorbs and the surrounding fibrous tissue collapses and is remodelled.

(3) Integration- This occurs in a very limited number of cases such as implantation of pure titanium in bone, where possibly, a close chemical adhesion between bone and implant is achieved without any intervening fibrous capsule or inflammatory cells.

(4) Encapsulation- This is the usual response where the fibrous capsule formed is maintained. If the implant is placed in a location where bone may form such as within medullary space, the capsule may become mineralised and the structure is then referred to as a sequestrum.

### Table 5

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<th>Resolution Outcomes</th>
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<td>Extrusion</td>
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#### 4.2 Immune Response

Von Pirquet in 1906 defined allergy as a pronounced reaction of an individual to a substance when the latter is reintroduced into the individual (Hildebrand *et al*, 1989). As time progressed this definition has been modified and the sensitising substance is now called an antigen.
The types of immunological response that have been identified at a cellular level can be classified into (a) humoral mediated or (b) cell mediated responses. On a clinical level these fall into the categories of immediate type hypersensitivity and delayed type hypersensitivity. Immediate hypersensitivity is further subdivided into (1) anaphylactic, (2) cytotoxic reactions and (3) toxic complex syndrome. These three reactions are clinically referred to as type I, II and III and the delayed type hypersensitivity is referred to as type IV reaction. There is a further classification of type V which is a mixed response of delayed type and immediate type hypersensitivity. In relation to metal implants the type of reactions which have been reported can be divided into those which show systemic manifestations, especially skin reactions and mucosal reactions, and those which show implant site inflammation.

4.2.1 Skin sensitivity

The action of metals released on the immune system is contradictory. Given the fact that the ions released are of low molecular weight it is unlikely they stimulate the immune system directly. It is thought that they combine with organic molecules such as albumin to form complexes referred to as haptens which possess antigenic qualities. Amongst the general population, the metals’ sensitivity is yet to be fully established.

The incidence of sensitivity in the general population is estimated to be between 1-5%. Within this population as much as 10% are sensitive to at least one metal (Hildebrand et al, 1989). The most common metals involved are chromium, cobalt and nickel. The incidence rate also differs between men and women and this is possibly a reflection of the differences in work, industrial exposure and the ornaments worn. It has been shown that in addition to formation of haptens, metals used in implants can influence the response of the host immune system to other antigens, for example chromium and nickel have been shown to suppress antibody production. Iron, chromium and nickel have also been shown in vitro to bind with T cell surface antigens and this may change the specificity of the previously formed receptors.
4.2.2 Systemic Hypersensitivity

The most common clinical manifestation of systemic hypersensitivity reaction has been that of contact dermatitis which can involve the skin or mucosa. Hildebrand et al define contact dermatitis as consisting of three criteria (Hildebrand et al, 1989). These criteria are:

(1) a clinical manifestations in the form of asthma, redness, ulceration.
(2) healing after removal of the allergen and
(3) positive skin reaction after epicutaneous or subcutaneous test. The most common metals involved in sensitivity reactions are cobalt, chromium and nickel. Cross sensitivity between nickel and cobalt has been reported. In case of chromium, the chromate ion (Cr\textsuperscript{6+}) appears to be more relevant as opposed to the divalent and trivalent ionic forms in nickel. In people who have established hypersensitivity there appears to be a threshold concentration for topical application of metal salts. In recent years isolated cases of contact hypersensitivity to titanium have also been reported (Lalor et al, 1990).

4.2.3 Implant Site Inflammation

There have been a number of cases reported regarding implant loosening without any clinical or pathological evidence of infection (DiCarlo and Bullough, 1992; Clarke et al, 1992). This loosening could possibly be due to a local sensitivity reaction. Initially it was thought to be a simple inflammatory response associated with relatively high corrosion rates of alloys, but with improvements in the type of alloy used and the finish of the alloy, interest has shifted to a possible local immune response to these metals. One of the earlier studies to investigate this aspect of hypersensitivity was that by Evans et al. They showed that out of 39 patients who had a clinically loose prosthesis, nine showed hypersensitivity to chromium, cobalt or nickel. Of the nine patients, the majority were hypersensitive to cobalt but interestingly there was no cross reactivity with nickel. Of those patients who clinically showed no loosening of the prosthesis there was no hypersensitivity expressed. While histology in their study showed bone necrosis and fibrosis, unfortunately they did not report the type of cell population which was
present in the region (Evans et al, 1974). Lalor et al (1991) showed an increased lymphocyte cell population in the region of a loosened implant. In an extensive study by Hierholzer and Hierholzer on internal fixation and metal allergy, they found an allergy rate of 4% in patients with internal fixtures and this was increased to approximately 10% in association with septic or aseptic complications (Hierholzer and Hierholzer, 1992). Further they confirmed the finding of Lalor et al in relation to the type of cell population which showed an increase in lymphocyte populations in those patients who showed allergy. This cell population was further increased in those patients who showed septic complications. Histopathology in those patients who showed allergic reactions was characterised by increased necrosis surrounding the implants. The majority of the patients showed an increased hypersensitivity to nickel as compared to chromium or cobalt.

In relation to monocortical plates used in Oral & Maxillofacial surgery there is limited information available regarding hypersensitivity reactions. Torgersen et al in their study of 15 patients who had stainless steel miniplates, showed a significant increase in lymphocyte transformation to nickel stimulation but no clinical features of delayed hypersensitivity were seen (Torgersen et al, 1993).

4.2.4 Conclusion

While there have been clinical reports and studies showing hypersensitivity reactions to metal implants there is limited knowledge available in relation to the pathophysiology and the mechanisms involved. Black (1992), makes the following conclusions:

1. There is significant level of immune hypersensitivity to metals in the general population.
2. Groups of patients who have nickel, chromium and cobalt bearing implants display higher than expected incidences of hypersensitivity.
3. There are specific documented incidences of symptoms consistent with type IV delayed hypersensitivity reaction which is specifically
related to the presence of a metallic implant.

(4) There is general correlation between hypersensitivity to metal and other clinical symptoms, especially device loosening. However, which is cause and which is effect is unclear at this time.

Another point to be made in relation to hypersensitivity, is the mode of testing as the majority of the studies to date have used epicutaneous (patch test) tests which might not be a sensitive probe for allergy testing. Recently in vitro tests such the lymphocyte transformation (Bjurholm et al, 1990) and leucocyte histamine release tests have been developed which are non-invasive and probably more reliable. The sensitivity and selectivity of these tests are yet to established.

4.3 Tumour Response

The concept of metal implants and/or their released products causing malignant changes in the surrounding tissues is yet to be established. While there have been a number of case reports of malignant fibrous histiocytoma (Bago-Granell et al, 1984; Swann, 1984), osteosarcoma (Penman and Ring, 1984) and animal studies (Sinbadli et al, 1976; Memoli et al, 1986) suggesting tumour growth surrounding implants, the cause and effect of these tumours in relation to the metal implants is less clear. Gillespie et al reviewed the incidence of remote site tumours in a population of 1,358 humans who had undergone total hip replacement. They found the incidence of tumours of the lymphatic and haemopoetic system to be higher and interestingly found the incidence of breast, colon and rectum to be lower than expected (Gillespie et al, 1988). When one compares the number of case reports that are published to the number of metal implants that are placed in the human body (hip replacement, knee replacement, joint replacement, as well as internal fixation devices), the incidence certainly appears to be extremely low, but there are a number of other factors associated.
4.3.1 Carcinogenesis

Black (1992) identifies two possible types of carcinogenesis in relation to metal implants. They are chemical carcinogenesis and foreign body carcinogenesis.

4.3.1a Chemical Carcinogenesis

Furst proposed strict criteria which the material involved had to meet before it could be considered carcinogenic (Furst and Haro, 1969). These criteria were: (1) the tumour must appear both at the site and at a distance from the point of application, (2) more than one route of application (injection, implantation and surface exposure) must be affective, (3) more than one species must respond, (4) the growth should be transplantable and, if malignant, invasion and metastasis must be noted. These criteria, although, almost 30 years old, are still applicable and relevant today.

Based on the above criteria, Black (1992) has drawn the following conclusions from studies published. Nickel appears to be a metal for which both the pure form and its compounds are carcinogenic. Cobalt appears to be carcinogenic in the pure metal form, but no carcinogenic compounds of cobalt are known. Chromium, iron, titanium and manganese are not carcinogenic in pure form but have carcinogenic compounds. It is not established clearly whether the metal involved is a complete carcinogen, procarcinogen or a cocarcinogen. Epidemiological studies (Sprince et al, 1988; Hayes, 1988) based on industrial workers show some evidence that chromium, cobalt, nickel and perhaps iron are carcinogenic in humans. Some of the problems associated with the animal and human studies are, that it is still unclear whether the latency period is long enough and whether there is a threshold effect in relation to chemical carcinogenesis. While it is normally assumed that there is a direct linear relationship between the concentration of the carcinogens and the carcinogenic effect, it is still not clearly established in humans. Another factor is that the tissues which normally surround the implant tend to be muscle and bone and they, generally speaking, have a much lower incidence of tumours.
4.3.1b Foreign Body Carcinogenesis

Oppenheimer (1955), carried out a number of studies in relation to foreign body carcinogenesis, and the conclusions were that solid materials without chemical carcinogenic activity can induce a variety of neoplasms in very small rodent species. The induction activity generally increases with the size of the implant and also varies inversely with the inflammatory response. In other words, well-tolerated materials are, in the long run, better foreign body carcinogens. Porosity with an average diameter of 0.22 microns reduces the risk of transformation. It appears that there are a number of other factors which play an important role in the foreign body carcinogenesis, and these are mainly the geometry of the implants (the size and shape of the implant), and also the chemical and electrical conditions near an implant tissue interface. It has been shown that if the implant has a high electric charge, especially with sharp points, then it appears to be more tumorogenic than if it was smooth or colloidal in form (Black, 1992).

A review by Bischoff (1964), made the following conclusions. On the basis of the responses to rather stable unrelated substances, there is a type of non-specific carcinogenesis in rodents that is dependent on a minimum surface requirement. In case of humans, there is a low reported incidence of neoplasm associated with implants, natural deposits such as cholesterol plaques, gallstones and chronic low level inflammatory processes. With the exception of asbestosis and silicosis, there does not appear to be any other carcinogenesis from foreign bodies. A further factor to be considered, is whether a particular tumour seen is purely foreign body carcinogenesis or chemical carcinogenesis, or a combination of these, as yet there is no mechanism to differentiate the two at an experimental level.

Brand (1983), in his studies, has made the following conclusions about foreign body carcinogenesis. (1) The most probable target cell in foreign body carcinogenesis is the pericyte, a small cell associated with small blood vessels. After implantation, the transformation needed to produce a neoplastic parent cell with all the genetic information for later expression in the active neoplasm occurs quite rapidly.
In mice, he noted that this happened within four to eight weeks. (2) While transformation occurs near the foreign body tissue, actual close contact with the foreign body is not required. (3) Transformation is quite uncommon. (4) While neoplasms will occur in the capsule after foreign body removal, a significant period of implantation after the initial transformation event is required. (5) The latent period always occurs between transformation and neoplastic expression. However, this period is characterised by more inactivity of macrophages than of the transformed parent cell which may be cloning. (6) When the latent period is over, rapid neoplastic growth begins although daughter cells, even if transplanted, appear to act in synchrony.

He cited six proposed mechanistic origins of foreign body carcinogenesis which include:

(1) The physical and chemical surface properties of the foreign body.
(2) The chemical activity of the components of the foreign body, which he feels may play a moderating or modifying role.
(3) The interruption of cellular contact or communication.
(4) Tissue anoxia and insufficient exchange of metabolites.
(5) The virus influence as the unseen contaminant of foreign body.
(6) Disturbances of cellular growth regulation.

Another factor to bear in mind regarding foreign body carcinogenesis, is the possibility that it is a form of carcinogenesis where the material is external to the cell and the method of carcinogenesis, as far as the cells are concerned, is yet to be established.

In humans, the number of published cases point towards a latent period of about five to seven years, which could be too short when considering the latent period for tumours in humans is around 15 to 25 years. Another problem with carcinogenesis in humans is the fact that there is an association between
chronic irritation, infection and mechanical trauma in relation to carcinogenesis. In the case of the implant, wear debris may also play a role in formation of the tumour. Another factor which one has to consider is whether a benign tumour which developed in the region of the implant was converted to a malignant tumour.

4.3.2 Conclusion

While there is no conclusive evidence of a causal effect relationship between metal implants and carcinogenesis in humans, one has to take a more sensible approach to artificial implantations in relation to how long the implants are in the human body (Hamblen and Carter, 1984). Also, based on the information available from animal studies, the smallest possible size of implants should be used, and regular examination or review of the patients with implants.

5 MATERIAL RESPONSE

The material response, as defined earlier, is the response of the material to the living system. It is the reaction in function and degradation (wear and tear) of the implant material to the living tissues. The following sections will deal with wear debris and corrosion which are pertinent to this study.

5.1 Wear Debris

Since the introduction of total hip replacement by Charnley, debris generation has been a significant concern (Clarke et al, 1992; Collier et al, 1994). The concern has not only been from the point of view of the dimensional changes and the effect the affected prosthesis has on function, but also the biological activity which is produced in the immediate surrounding tissues (Pizzatoferrato et al, 1991; Williams and McQueen, 1992).

The types of wear patterns which are usually described are those of adhesive wear, abrasion, fatigue, three body wear and anomalous wear (table 6) (Black, 1992; Collier et al, 1994).
5.1.1 Adhesive Wear

When interatomic forces between the mating wear surfaces become greater than the intrinsic forces between the molecules of the bulk matter in the prosthesis, wear debris is produced. The opposing forces which are perpendicular to the surfaces may be generated by compressive or gravity forces. Other factors which influence adhesive wear are the coefficient of friction which is a ratio usually expressed between 0 and 1. A coefficient friction of 0 implies no friction and a friction of 1 is maximum. This coefficient describes the relationship of the frictional restraining force to the perpendicular force. Other factors which influence wear are the surface composition, the surface finish of the materials involved and the effect of lubrication.

5.1.2 Lubrication

The principle of lubrication is to provide a film or a layer to separate the two surfaces during relative motion, for example during function, in order to reduce both frictional restraining forces and wear. The lubrication processes are normally classified according to:

(1) Hydrodynamic lubrication where the motion of one body relative to the other draws a continuous film of lubricant into the contact area. This is perhaps the most common process and the characteristic surface separation for typical lubricants is between $10^{-3}$ and $10^{-4}$ cm.

(2) Elastohydrodynamic lubrication which occurs at smaller separations between $10^{-4}$ and $10^{-5}$ cm. In this case the motion of one body of the prosthesis is able to transmit force through the lubricant to generate sufficient stress for transient elastic deformation of the other body. In the long term this may lead to localised fatigue failure on one of the surfaces which then increases wear rate.

(3) Squeeze Film lubrication which occurs in either hydrodynamic or elastohydrodynamic conditions if the lubricant is sufficiently viscous to respond
elastically to temporarily increased normal loads.

(4) Boundary lubrication which occurs where the lubricant coats the opposing surfaces rather than acting as a low shear interface. This coating acts to modify the frictional character of the surface reduced by restrictive straining forces and wear.

(5) A mixture of the above mentioned processes.

5.1.3 Abrasive Wear

This takes place when a soft surface is abraded by a rougher harder surface resulting in debris. The abrasive wear is dependent on contact stress, the surface hardness and the surface finish. Other factors which influence abrasive wear are the contact angle of the bearing surfaces which can be important in reducing the adhesive wear and lubrication of the surfaces to prevent abrasive wear.

5.1.4 Fatigue wear

In fatigue wear, due to repeated stress cycles, the material involved undergoes fatigue leading to crack formation and production of wear debris. The three body wear takes place in those instances where a metal oxide layer is transferred onto a softer material and this transferred oxide layer in turn becomes the abrasive material. This also enhances production of further reduces the surface strength of the articulating surface.

5.1.5 Corrosive Wear

This form of wear occurs secondary to physical removal of the passive or protective layer. The exposed surface leads to softer and more chemically reactive surface which in turn accelerates the wear process. This may lead to a repetition of cycles of passive film formation and mechanical removal.

5.1.6 Anomalous Wear

The final type of wear which one should consider is referred to as the anomalous wear, where a softer material abrades the harder surface. For example such wear occurs when tendons move over bone rapidly forming grooves while appearing unchanged. This change reflects a dynamic remodelling process.
In the case of artificial implants where there is no remodelling process, the harder surface, such as a metal surface, can be worn away producing wear debris.

The outcome of these wear patterns is the production of metal particles which can cause osteolytic reactions in the body. An example of this is referred to as cement disease where the combined generation of cement debris as well as other debris produced by the articular components in a hip prosthesis, leads to an osteolytic process. The effects of wear debris are thought to be local as well as systemic and are determined not only by the factors described above, but also the size of the wear debris and the concentration of wear products which appear to play a major role in the extent of the reaction.

The finding of wear debris particles either at implant sites or in the regional lymph nodes where they were deposited by diffusion and phagocytosis are quite variable (Pizzoferrato et al, 1991). This would suggest that several wear processes are taking place either simultaneously or at different times and that the mechanical and environmental factors of each application involves the type of particles produced. Usually the metal particles produced tend to be less than one micron in size and appear to be susceptible to high dissolution rate and transfer to distant sites as compared to polymer particles which tend to be in the order of 0.25 microns to 1mm in diameter and induce a foreign body reaction rather than an inflammatory reaction.

These reactions are characterised radiographically in terms of radiolucent zones surrounding the implants, calcar resorption, lytic lesions, cysts and granulomatous pseudotumours. The precise mechanism by which the osteolytic process takes place is yet to be established (Clarke et al, 1992). There have been a number of theories put forward in terms of mechanical theories of implant loosening and foreign body reaction. The mechanical theories include understressed or overstressed mechanical movement. In the case of understressed mechanical movement, the porosity of bone is believed to be due to stress shielding (Clarke et al, 1992; Mjoberg, 1994).

In the case of overstressed mechanical movement, the interfaces appear to break down (Clarke et al, 1992). In the mechanical theories, debris and
biological foreign body reactions have traditionally played little or no part, and therefore the role of polymer debris and osteolysis has not been universally recognised as an important loosening mechanism. Other theories include foreign body reaction and a combination of mechanical and foreign body reaction.

It appears that there is a spectrum of wear debris determined by various factors including the type of materials and the size of the debris in the joint (Salvanti et al,1994). The knowledge of the factors that determine the tissue response is incomplete. Based on the clinical studies macrophages appear to play a common role in stimulating bone loss at implant site but the role of the foreign body giant cell is unclear. It could be that the aseptic implant loosening does indeed begin as a mechanical problem that is initiated and propelled by normal motion and interface micromotion. The intermediary formation of particles of the order of 10 microns and smaller will result in stimulation of the macrophages (the biological process). Thus the implant loosening mechanism could be a combination of mechanical and biological processes. The functional demands placed by the patient in terms of high stresses, frequent cyclic motion and large joint exertion and the greater quantities of debris produced in terms of materials size, shape and numbers will produce a faster and more aggressive macrophage driven osteolytic process (Clarke et al,1992).

6 CORROSION

(Murata,1988;Davison et al,1987;Brettle,1970;Harris,1979;Black,1992)

The word corrosion is derived from the Latin word *rodere* meaning to gnaw. It implies chemical attack on solid materials, especially metals. For the lay person it means breakdown of steel or iron (rusting); for the building constructor it means the effects on the structure and stability of the building. For the shipping magnate, it means the amount of money that has to be spent in terms of maintenance of the ship at sea in order to prevent attack by sea water and the inhabiting micro-organisms; for the biomaterial scientist, it means assessment of stability and function of the biomaterials involved.
While metals are commonly involved in reference to corrosion in the broader sense of the word chemical attack on glass and polymers do resemble corrosion in the physical result. Regardless of the agent causing the corrosion, the basic underlying mechanism is electrochemical in nature and is a process of reaction and/or dissolution in the presence of an aqueous environment. There are four generic chemical reactions that are usually involved:

1. Ionisation where there is reduction of a metal ion in an acidic or oxygen poor environment.

2. Oxidation which involves the direct reaction of metal with oxygen in either gaseous or dissolved form, usually in water.

3. Hydroxylation is where there is a reaction of metal with water under alkaline or oxidising conditions to yield a hydroxide or hydrated oxide compounds. This process is usually involved in formation of a passive film on the metal surface.

4. The mixed reaction in terms of combination of metal or metallic ions with other cation and ions which does not necessarily have to be of metallic origin and is termed complex formation.

The end result of this process is to reduce the mass of the object which in turn alters the dimensions, the physical properties and the stability of the object involved. The environment in which corrosion takes place can be thought of as an electrochemical cell in which the metal which gets oxidised (gives out the electrons) can be considered the anode and the region or electrode where reduction takes place (gain of electrons) is considered to be the cathode. The anode and cathode are in an aqueous medium which is referred to as the electrolyte and it is normally a conductor of metallic ions. In other words a current could flow through the electrolytes. The path between the anode and cathode which completes the circuit in the system is referred to as the metallic path which is usually the electrolyte or it could be the metal substance involved.
The whole system is driven by change in the energy of the system. The energy change takes place through an electromotive force and the tendency of the system is to go from a high energy state to a low energy state. In practical terms that implies the metal goes from a solid high energy state to a dissolved low energy state. The dissolved material can be individual ions or under certain circumstances small particles of metal. The potential for the energy change in the electrochemical cell is determined by the balance between the effect of the potential energy accumulated (enthalpy) and the effect of probability towards tendency of disorder (entropy). In other words, it is the potential for progression of the chemical state of the system towards a lower energy system in a fashion where by the ions from the breakdown of the metal are distributed in a number of possible ways within the system. This potential energy is referred to as the free energy and each metal has a potential energy in relation to water and is normally referred to as the electromotive force series.

The outcome of this potential energy is that the wider the spectrum between a metal acting as the anode and substance acting as the cathode, the more likely the tendency towards corroding and also at a faster rate. The system can be measured in terms of change in potential which gives a qualitative assessment of the potential for corrosion and in terms of current flow within the system which gives the rate of corrosion.

6.1 Factors Affecting Corrosion

The electrochemical cell is affected by the properties of both the metal or alloy involved and the environment (Silverman and Puyear, 1987; Black, 1992).

6.1.1 Environmental Factors

The environmental factors which influence corrosion are acidity (pH), the oxidising power (potential for oxidation), temperature of the system, velocity in terms of the flow of the electrolyte medium or the metallic path, and the concentration of the solutions involved.
6.1.1a pH

At low pH the corrosion mechanism is dependent not only on the hydrogen ion concentration but also on the counter ions present. The metal dissolution rate at very low pH is equal to the mass transfer rate of the ion from the saturated anode. The mass transfer rates are also sensitive to fluid velocity hence sensitive to fluid flow of the electrolyte system. The corrosion rates can vary depending on the acid environment and the availability of the type of acid. This is also influenced by the nature of the metals involved. In strongly basic conditions the tendency is to form hydroxides hence the formation of the passive layer.

6.1.1b Oxidation Power

The oxidation power or potential is the ability to remove electrons from the metals so as to oxidise or reduce the surface. There are a number of ways in which this oxidising potential can be altered. For example, increasing the passivity of the surface oxide layer of the anode (anode protection) will decrease the corrosion process. An alternative method of preventing corrosion is by supplying electrons to the cathode that would normally be yielded by the oxidation reaction of the anode. This is referred to as cathodic protection. The changes to the anodic surface is achieved by anodic protection of the metal surface by means of imparting passivity or altering the constituents of the environment in such a way that a passive film is formed on the surface of the anode. Another method is to alter the electrolyte content which again will either form a passive film on the anode because the potential of the system is such that the anode becomes more noble than the cathode. Yet another method is direct electrical coupling of the metal to a more active metal by using cathodic potentials to affect corrosion, for example coupling zinc to steel to protect steel in industrial applications.

6.1.1c Temperature

Temperature can affect not only the potential for corrosion but also the corrosion rate. It affects the system in a number of ways: (1) the oxygen solubility is influenced by the temperature. (2) The ionisation constant of the water increases with temperature which in turn will influence the pH, hence the reaction
rate in corrosion. (3) It can also affect the polarity in galvanic corrosion. This usually takes place due to the corrosion potential of the anode being more sensitive to temperature than the cathode and which in turn makes the anode potential more noble with respect to the cathode hence the reversal of polarity, as for example, iron zinc coupling. (4) It can also affect the onset of localised attack of passive alloys, as for example 316 stainless steels. This is dependent on the constituents of the electrolyte as for example, in those instances where the electrolyte has a large constituent of chloride ions the time to initiate the crevice corrosion has been shown to be a function of temperature. The temperature influence is not only in terms of a critical crevice temperature for setting off the reaction but also in terms of the ongoing rate of the reaction. (5) Another way temperature can affect corrosion rate is to affect the fluid flow in the electromotive cell system. The fluid flow is usually affected by the natural convection currents that enhance mass transfer, hence fluid flow.

6.1.1d Fluid Flow Rate (Velocity)

The fluid flow rate is also a complex variable which influences the corrosion process. Its influence on corrosion is dependent on the alloy, fluid constituents, fluid physical properties, geometry and corrosion mechanism. The rate at which the constituents are changed will drastically influence the potential in a given system. This happens not only by removal of oxidised ions but in biological system in terms of changing the electrolyte constituents. For example in tissues, in case of inflammatory or infective process, where the local environment is changed by the alteration of the concentrations of the electrolytes involved in the tissue and the influence of the incoming protein molecules. The fluid flow usually affects pitting and crevice type corrosion in a given environment. Another possible method which is less likely in biological systems is the erosion of the surface through the mechanical force of fluid itself. This process is called impingement and it involves mechanical removal of the surface layer hence exposing the underneath metal for increased corrosion.
6.1.1e Concentration

The concentration of constituents within the electromotive force cell mainly influences how the other variables manifest themselves. They affect pH in terms of the concentration of ions by introducing other ions into the system, as for example chloride ions, and protein molecules as in the initial response. Also the initial response could introduce impurities into the system which will reduce or cease the corrosion process. It can also alter the oxidation state (passivation) via nitrites, sulfites or chromates. These are all examples of factors which influence corrosion rate. In biological systems the presence of a biological film or environment on a corroding metal surface does not introduce a new type of corrosion but it influences the occurrence and/or the rate of the known types of corrosion. The mechanisms in which this influence can take place are by: (1) production of differential oxygenation or chemical concentrations of cells such as, for example, the oxygenation in a given tissue sample or the chloride content or the pH. (2) Production of organic or inorganic acids as by products from metabolism or other reactions. For example where there is influence of bacteria, the production of sulphuric acid through their metabolism and also the production of sulfides and nitrides under oxygen free conditions which can cause passivation.

6.1.2 Alloy Factors

The factors which influence the metal or metal alloy is dependent on the composition of the implant, in particular variations within the implant which do affect corrosion rates. Manufacturing variables such as casting conditions, metal purity, the amount of cold work and the degree and type of heat treatment all influence corrosion rates. Other factors such as handling both in delivery and insertion can influence corrosion in terms of physical damage hence creating surface defects or stress fractures and also by introducing contaminants. Other factors are anatomical location in terms of the application of the metal, for example, in internal fixation devices where positioning of the implant influences stress upon it leading not only to creation of stress cycles and fatigue failure, but also in terms of exposure to its local environment. The anatomical location also influences the wear rate or production of wear particles as discussed earlier and this
again will influence the type of corrosion and corrosion rate.

6.2 Types of Corrosion

The types of corrosion that have been categorised (Harris, 1979; Fracker, 1987; Black, 1992) are shown in Table 7.

6.2.1 Uniform Attack

Uniform attack is generally referred to as surface corrosion and is a very common form of corrosion. It is the process that takes place in the corroding region and by oxide and hydroxide dissolution, in the passivation region. In the absence of equilibrium concentrations of the constituent ions in the bathing solution all metals will have surface corrosion. Even in the immunity region (as defined by the Pourbaix diagram on page 60) uniform attack will result in the slow removal of metal from implants. This form of corrosion is usually measured in terms of surface recession in mls/m² (surface area). Modern design and production of implants are such that it is extremely rare to see uniform corrosion.

6.2.2 Galvanic Corrosion

Galvanic corrosion or couple corrosion takes place when two different metals are in physical contact. The electrochemical reaction that results when two dissimilar metals are in contact depends on the difference in potential of the two metals with the less noble metal becoming the anode and the other the cathode. This usually occurs when different metals are in contact or immersed in an ionic conducting fluid medium such as serum or interstitial fluid or when there is variation in composition within the same metal, for example, if there is a difference in composition along an internal fixation plate from one end of the plate to the other, as this could set up an electromotive force cell. Another example is when
screws are used to fix plates on bone and there is dissimilarity between the screw and the plate this will also set up an electromotive cell. The extent of the corrosion and the corrosion rate is dependent on factors such as the relative size of the areas of electronic and ionic contact, the pair of dissimilar metals involved (in relation to their position in the electromotive force series) and the corrosion rate which is increased in an acidic environment.

6.2.3 Crevice Corrosion

Crevice corrosion is related to structural details. The basic requirement for occurrence of this process is the presence of a crevice, which is a narrow deep crack, either an interface between parts of a device such as between plate and screw or a defect within a component such as fatigue or stress cycle crack. The initiation of crevice corrosion is not clear but once started is characterised by oxygen depletion in the crevice and anodic metal corrosion along the metal surfaces and the cathodic protective conditions on the metal surface around the opening of the crevice. A static non-flowing condition of the electrolyte medium seems to favour crevice corrosion. This form of corrosion is easily seen at interfaces such as plates and screws or in those instances where there has been damage to the plate or screw on insertion. This form of crevice corrosion is also influenced by cyclic loading as mentioned earlier. Crevice corrosion is a localised attack and can be eliminated by changing the design of the implant or components of the implant, reducing the fatigue to the implant and avoiding damage to the implant during insertion and fixation.

6.2.4 Pitting Corrosion

Pitting corrosion is a severe form of localised corrosion attack that results in extensive damage to the implant part and in the release of significant amounts of metal ions. Pits may be initiated at breaks in the protective film, defects in the material or protective film, inclusions, voids and dislocations. The break in the protective film or voids tends to expose the metal to the body fluids which in turn initiates the corrosive process. The restriction in flow of the fluid in the pits created also leads to an increase in concentration of hydrogen ions at the base of the pit which in turn will accelerate the corrosion process. Pitting corrosion is
hazardous to implants as they constitute points of stress concentration and may serve as the starting points for mechanical cracks. When very small they change the surface finish producing a frosted or matt appearance. The larger more developed pits often have accumulations of coloured corrosion products. The appearance of the pit corrosion can easily be confused with burr damage to the screw head or shaft during insertion and/or removal.

6.2.5 Intergranular Corrosion

Intergranular corrosion occurs when grain boundary becomes anodic or cathodic to the rest of the grain. The change in composition in the grain boundaries may be due to precipitated grain boundary phases, concentrated impurities or elemental depletion near the grain boundary area. The high energy of the grain boundaries also provides a means for collecting second phases or contaminating materials which can lead to corrosion. It is more common in cast alloys and once initiated they progress rapidly because the grain boundaries are physically small. The process can eventually, through cavitation, be converted to crevice corrosion which will then accelerate the corrosive process. It is fairly common in implants constructed from alloy material and also at welding joints which are not commonly used in biomaterial implants.

6.2.6 Leaching

Leaching is a form of corrosion, where the various components of the alloy are bound weakly with differing chemical reactivity. This leads to a difference in the rate of loss of the alloy components by uniform attack. Attack of this kind removes metal with a regular periodic variation of effect at the microscopic level. The surface changes are similar to that of pitting and intergranular corrosion. It can only be verified by analysis of the surface concentrations of the products released. Leaching usually takes place in multiphase alloys. It is not common in surgical alloys as they are single phase alloys.
6.2.7 Erosive Corrosion

Erosive corrosion is a rare form of corrosion, which takes place when there is an acceleration of attack on implants because of fluid flow on the surface of the implant. This process tends to enhance the rate of other forms of corrosion by removing the corrosion products. The physical damage is that of elongated pits in the direction of the flow. The flow rate alters the position in the Pourbaix diagram by shifting to a more corrosive region.

6.2.8 Stress and fatigue Corrosion

Stress corrosion is form of localised corrosion that takes place when an implant is simultaneously subjected to a static tensile stress and a corrosive medium. This has the effect of producing a difference in electrochemical potential that renders the convex (tensile stressed) surface anodic in respect to the concave surface. It is a complex interaction of electrochemical, mechanical and material factors.

Any stress cracks formed due to the tensile stress, is accelerated by this process. The cracks tend to extend along the grain boundaries and are branched compared to fatigue cracks where the cracks are more linear with some striations. The rate of corrosion can be reduced by selecting materials which are not susceptible to flexion, to remove surface flaws that could act as crack initiators and change the surface of the implant (by design) to reduce tensile stress.

Fatigue corrosion takes place when the tensile stress becomes cyclic during function. The cracks formed can initiate from hidden imperfections, surface damage during transport and insertion and chemical attack. The effects of corrosion increase with decreased frequency of the stress cycle. The fatigue strength is dependent on the medium in which the test is carried out. It plays a role in production of wear debris.

6.3 CORROSION PRODUCTS

Once the implant corrodes, the released products are usually in the form of oxides, hydroxides, phosphates and sulphates (Hanawa et al, 1992). Usually
the particles are not more than one micron in size (Finnegan, 1989). Wear debris can be larger in size but they also undergo corrosion, especially those particles which are 50 microns or greater in size and cannot be removed from the local environment. The fate of these released particles are not fully understood. They may complex with proteins (Williams and Williams, 1988), be engulfed by macrophages (Rae, 1985) or lie dormant in the tissues and eventually get walled off by the fibrous capsule. Lux and Zeisler, assessed the levels of ions in the vicinity of the implant using Neutron activation analysis and found a gradient in the tissue concentrations with exponential decrease in concentration with increase in distance from the implant (Lux and Zeisler, 1974). He further analysed the metabolism of the released products adjacent to the implant and found that there was a decrease in concentration of chromium and nickel with time (Lux et al, 1976). Numerous prospective studies have also shown that the chromium, nickel and molybdenum are excreted in serum, urine, lungs, liver and kidneys. The homeostasis of these trace elements is not fully established.

6.3.1 HOMEOSTASIS

(Merian, 1991; Frausto da Silva and Williams, 1991; Black, 1992)

Chromium, molybdenum, nickel and titanium are considered to be trace elements. With the exception of titanium, all other elements are essential trace elements and the role of each is characterised by:

(1) Amplification- All known essential trace elements exert their biological actions through a succession of regulatory and biosynthetic steps which produces a meaningful amplification function which leads to an effect on the whole body.

(2) Specificity- Each essential trace element has a specific role as a core molecule or as an enzyme cofactor. This specificity depends both on the ionic size and the valence state.

(3) Homeostatic regulation- Each essential trace element is under strict metabolic regulation where the absorption, transport, storage and excretion mechanisms are regulated in relation to the concentration required by the body and is kept within an optimum range. With the exception of chromium,
knowledge of the metabolic role of nickel, chromium and molybdenum in humans is limited. A brief summary of the homeostatic regulation is presented in the following sections.

6.3.1a Chromium

Chromium has an atomic number of 24 and an atomic mass 51.996 and exists in oxidation states ranging from -2 to +6 but only the trivalent and hexavalent compounds and metallic chromium are of practical importance in humans. The uptake of chromium is through the gastrointestinal system and through lungs and skin in industrial workers. The Cr\(^{+4}\) can easily cross cell membranes where the phosphate sulphur carrier also transports the chromate anions. In contrast, Cr\(^{+3}\) does not utilize any specific membrane carrier and its entrance into the cell is through simple passive diffusion. In the case of animals it is through endocytosis. Cr\(^{+3}\) uptake depends on the nature of the molecules it is complexed with, to such an extent that in some instances cell membranes are practically impermeable to Cr\(^{+3}\) complexes. The exception to this is the lipophilic ligands which allows the chromium to diffuse into cells with relative ease. This reflects the fact that Cr\(^{+3}\) is the most stable state for chromium in nature, whereas Cr\(^{+4}\) is unstable and highly toxic to tissues exposed.

The absorption of chromium through lungs is facilitated by the mechanisms mentioned above and the alveolar macrophages (lining the epithelial surfaces of the lung alveoli) are the most active in reduction of Cr\(^{+6}\) and are the main defence against the carcinogenic form of chromium. The lung secretions also have some reducing ability. In the case of skin, the exposed chromium has to be converted to a soluble form before it is absorbed through into the body. The absorbed or released chromium is transported in the body by blood. Cr\(^{+3}\) is bound to plasma proteins, especially transferrin and Cr\(^{+4}\) is accumulated inside the red blood cell where it is reduced to Cr\(^{+3}\). This reducing ability of the erythrocyte represents an important mechanism of detoxification. The second factor which influences transport is the solubility of the compound involved and this is determined by the valence state, the complexes it has formed in the tissue fluid or blood and the size of the ion involved.
The transported chromium is then distributed to tissues and organs which have different retention capacity. The highest levels of chromium are found in liver, kidneys, spleen and lungs. In the case of corrosion of implants, not only is there distribution of the chromium through blood, but it is also thought to be distributed through the lymphatic system. In the liver, chromium is stored linked to proteins and smaller peptides such as glutathiones. While in the spleen in accumulates in the debris of red blood cells. In humans other tissues which have significant levels of chromium are brain, skin, hair and local depositions around implants. Placental transport of chromium is established in animals where it is shown to cross the placenta by diffusion mechanisms. However, it is dependent upon the time of administration during pregnancy and has been shown to induce genetic and teratogenic effects in the offspring of treated mice. In humans it is yet to be established whether there is placental transfer. The main route of excretion of chromium is through the kidneys but there is some excretion through skin, sweat and possibly saliva.

6.3.1b Nickel

Nickel has an atomic mass of 58.71 and its valence states range from -1 to +4 with the valence of 0 as nickel metal and its alloys. The valence state of +2 is predominant in biological systems. The uptake of nickel is by the GIT system and in industrial workers the lung and skin. Transport is mediated by binding to albumin and ultra filterable low molecular weight molecules. The major nickel binding site of serum albumin has been identified and characterised. This is characterised by the absence of nickel binding site in certain persons with certain types of bisalphunaemia which is a congenital abnormality characterized by the presence of two distinct serum albumins that differ in mobility when using electrophoresis. The ultra filterable molecules in plasma include amino acids, such as histidine and small polypeptides. Although a major fraction of plasma nickel is bound to nickeloplasmin and alphamacroglobulin the nickel content of nickeloplasmin is not readily exchangeable with exogenous nickel 2+ and it does not appear to play an important role in extracellular transport of nickel. Nickel carbonide is an important derivative of nickel which is highly liquid soluble and is
highly toxic. Nickel is eliminated by the kidneys. It also has been found in skin, saliva and sweat. In humans the elimination is dependent on the physical and chemical properties of specific nickel compounds to which they are exposed.

6.3.1c Molybdenum

Molybdenum has an atomic number of 42 and an atomic mass of 95.94. The valance states range from +2 through to +6 with questionable existence of +4 and +5. Molybdenum is thought to be absorbed in humans through the gastrointestinal tract and the elimination is through the kidneys. The transport of molybdenum in the body is not fully established and is thought to be mediated through blood products. Placental transfer for molybdenum is not established. Molybdenum appears to be the least toxic of the three trace elements.

6.3.2 Toxicity

The response of tissues to these released metals appear to range from minimal response to overt toxicity. This spectrum of reactions is dependent on the valence state and molecular weight of the ion, the concentration, the type of tissue involved, and whether the ion is bound to protein. At the cellular level the response has been assessed for the osteoblast (Puleo et al, 1991; Vrouwenvelder et al, 1993), fibroblast (Evans and Thomas, 1986; Wataha et al, 1992), muscle (Therin et al, 1991), neutrophils (Remes and Williams, 1990) and macrophages (Rae, 1985). With the exception of molybdenum, chromium and nickel are toxic to cells at high concentrations. There appears to be a threshold effect where after a given

![Figure 7 Graph Showing the Effect of Concentration on Function]
concentration the toxic effects rise exponentially (Fig 7). The effects vary from necrosis to effects on cellular function such as chemotaxis, teratogenesis and carcinogenesis.

The following table outlines the known and suspected toxic effects of chromium, nickel and molybdenum in humans. The hypersensitivity reactions and carcinogenic effects have been discussed previously.

**Table 10 showing the known and suspected effects of chromium, nickel and molybdenum in humans**

<table>
<thead>
<tr>
<th></th>
<th><strong>ACUTE TOXICITY</strong></th>
<th><strong>DEFICIENCY</strong></th>
<th><strong>OTHER EFFECTS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>CHROMIUM</td>
<td>0.5-1gm fatal, diarhoea, bleeding from stomach and intestine, liver damage, kidney damage and cramps</td>
<td>decreased glucose tolerance, diabetes elevated serum lipids and corneal opacities.</td>
<td>allergy (contact dermatitis, asthma, skin ulcers and eczema) lung cancer</td>
</tr>
<tr>
<td>NICKEL</td>
<td>nickel carbonyl poisoning—neuropathic syndrome hypomickelemia</td>
<td>growth depression, impaired reproduction and decreased activity of calcineurin ?</td>
<td>contact dermatitis, lung cancer, nasal polypsos, anosmia, asthma, bronchitis, pneumoconiosis</td>
</tr>
<tr>
<td>MOLYBDENUM</td>
<td>anaemia, gout like syndrome</td>
<td>growth depression, night blindness, Keshan disease</td>
<td>molybdenosis</td>
</tr>
</tbody>
</table>

**6.4 MEASUREMENT OF CORROSION**

Black (1988) estimated the total corrosion for a typical total hip replacement prosthesis to be around 11-22 mg/year based on the corrosion rate of 0.3 microns/cm²/day. This is only an estimate as the measurement of corrosion is extremely complex. About 60 years ago, corrosion of implants was confirmed by staining the surrounding tissues for iron using Prussian blue. The corrosion was referred to as metallosis and characterised by pain, black staining of tissues, and an inflammatory reaction. The study of corrosion and its rate can be divided into in vitro and in vivo. For in vitro studies, the methods employed are (1) weight loss measurements on specimens which have been standing in simulated body fluids for variable length of time and (2) the study of the implant under simulated physiological conditions using potentiostatic techniques. The in vivo methods
involve (1) surface analysis of retrieved implants and (2) staining of tissue biopsies to assess corrosion products present and the type of tissue reaction that has taken place and (3) prospective analysis of release of corrosion products from implanted materials in animals and humans.

6.4.1 Potentiostatic Techniques

Potentiostatic techniques measure the electromotive potential (E) and the current density (I) flowing through the implant solution interface. The two common methods used are CYCLIC VOLTAMETRY with a linear potential sweep and CHRONOAMPERMETRY at constant potential (Bellier et al, 1990; Viegas et al, 1990). In cyclic voltametry the general behaviour of the implant within a given potential range is assessed. Chronoampermetry allows for some quantitative determinations on corroded products and must be used in conjunction with the voltametry method. The results are usually expressed in terms of polarization curves. The curves represent the relationship between the current and the potential for the given set of conditions of pH, temperature and the constituents of the solution medium. Other types of electrochemical methods that have been used are (a) Zero current test, where the metal is simply immersed with or without stress in a given solution and the influence of time on the potential is measured. (b) Linear polarization tests and impedance tests. The limitation with the Potentiostatic methods is that the dynamic physiological conditions cannot be imitated for a given type of implant with the functional requirements and the physiological conditions in the body for that implant.

The results are usually expressed in terms of amps/cm². An alternate is to represent the possible reactions between the implant and the solution (aqueous based) in Pourbaix diagrams as popularized by Marcel Pourbaix (Pourbaix, 1984). These are pH- potential plots for a given solution at a particular temperature, fluid flow and concentration based on the polarization curves.

Once the conditions are changed a new diagram has to be drawn. Fig 8 below shows an idealised Pourbaix diagram. There are three important regions in the diagram: (a) Immunity- where the dominant reaction is ionization. In
this region, although there is release of ions, the implant is considered to be stable. (b) Passivation - where the dominant reactions lead to formation of oxides and hydroxides, leading to formation of the passive layers and reduction of the reactions. (c) Corrosion - the dominant reactions lead to formation of corrosion products. The diagrams are graphical representations of the stability of metal oxides and other species in solution. They offer a framework for kinetic interpretation but do not provide precise information on rates.

There have been a number of in vitro studies that have assessed not only the corrosion of various metal alloys (Brown and Merritt, 1981; Cahoon and Holte, 1981; Bundy et al, 1983; Griffin et al, 1983) but also stainless steel alloys under different physiological conditions. Further, Bundy reviewed the effects of pH in tissue culture (Bundy et al, 1985), Williams studied the influence of proteins on corrosion (Williams and Williams, 1988), Kuhn studied the influence of the various aqueous environments such as acidic, alkali and chloride media (Kuhn, 1981) and Brune the effect of passivation with chromium of stainless steel in artificial saliva (Brune and Hultquist, 1985).

6.4.2 Retrieval Analysis

Retrieval analysis involves the assessment of the implant performance in tissues. The assessment involves not only a clinical and radiographic survey but also microbiological studies of the implant site, histological studies of the tissues using light and electron microscopy, assessment of tissue levels of corrosion products and surface analysis of the implants.

Patric et al have outlined the protocol to be followed for retrieval analysis in order to standardise the studies (Patric et al, 1988). The studies show that stainless steel implants mainly exhibit surface corrosion and pitting and crevice
corrosion (Brettle, 1970; Smethurst and Waterhouse, 1978; Cook et al, 1985; Harding et al, 1985; Betts et al, 1992). Surface corrosion involves the smooth surfaces of the implants and pitting and crevice corrosion, the regions of the screw hole and screw heads. While the microbiological assessment showed no bacterial growth with the exception of infected plates, the histological assessment showed that the severity of the tissue reaction in terms of histiocytic reaction and tissue necrosis correlated with the extent of the corrosion.

Corrosion also showed significant correlation to the grain size of the implant and nonmetallic inclusions. The tissue levels of the various metal ions ranged from 2.7-250 micrograms per gram of tissue. The levels were increased in those instances where the reason for removal of the implant was infection (Hildebrand et al, 1989).

6.4.3 Prospective Studies

The prospective studies involve the assessment of the release of metal ions following implantation. As outlined earlier there have been a number of studies that have shown increased levels of chromium, nickel and molybdenum in serum, urine, lungs, liver, kidneys and pancreas (Dobbs and Minski, 1980; Bartolozzi and Black, 1985; Pazzaglia et al, 1986; Ishihara et al, 1987; Sunderman et al, 1989; Jacobs et al, 1991).

6.4.4 Monocortical plates

In case of the monocortical plates used in Oral & Maxillofacial surgery there is limited information available regarding the corrosion process (Bessho et al, 1988; Moberg et al, 1989). The local environment in which these plates are placed could influence the rate at which corrosion takes place. While the plates are applied to the surface of bone and covered by soft tissue as in the case of internal fixation devices in orthopaedic surgery, the functional load placed on these plates are different. The other factor which could influence the local environment is the micro-motion during the use of the jaws in speech, swallowing and mastication.

Moberg's study investigated corrosion by analysing the tissue levels of corrosion products. The in-vivo study consisted of applying plates to surfaces of the mandible in monkeys. Biopsy of bone and soft tissue surrounding the plates
were obtained and analysed for the various elements using atomic absorption spectrometer and neutron activation analysis. The surface of the plates were examined using an electron microscope and the tissues studied under a microscope. Their conclusion was that while there were increased tissue levels of corrosion products, there was no evidence of corrosion on the surface of the plates.

Bessho et al carried out an in-vivo study where they removed Stainless Steel plates from patients and analysed the surface of the plates for evidence of corrosion and made a naked eye assessment for presence of corrosion products by noting the extent of discoloration. They confirmed the presence of the corrosion products by the use emission spectral analysis (qualitative analysis).

6.5 AIM

The aim of this study was to measure the levels of chromium, nickel and molybdenum in the soft tissue and bone surrounding the stainless steel monocortical plates (Champy Plates) used in the treatment of fractured mandibles. In addition to the metal ions detected, it was hoped to establish time related patterns to their release. The tissue concentrations of metal ions were then compared to those of patients having their third molars removed and any differences analysed for statistical significance.
Part 1 of the study consisted of establishing the soft tissue and bone levels of chromium, nickel and molybdenum in the control group of subjects matched by age and sex for the plate group.

Part 2 of the study was the retrospective analysis of chromium, cobalt and molybdenum detected in soft tissue and bone surrounding the metal plates in the plate group.

Ethical committee approval was obtained for this study.
CHAPTER 2

MATERIALS AND METHOD

2.1 SUBJECTS

2.1.1 Control Group

The subjects for the control group consisted of male (25) and female (21) patients who were having their lower third molar teeth removed under local anaesthetic. The patients’ ages ranged from 16 to 67 years (mean 24.9) and selection criteria were applied. The selection criteria involved exclusion of those patients who:

1. Lived outside the Sydney metropolitan area.
2. Had occupations involving mining (especially mining of trace elements), electroplating, battery manufacture, tannery, production of dyes, bleaches and detergents and hairdressers.
3. Those patients who had the following medical history were also excluded from the study (Versieck, 1985):
   a) Liver disease (alcoholism, hepatitis)
   b) Diabetes
   c) Chronic renal failure
   d) Undergoing renal dialysis
4. Subjects with history of previous exposure to metal implants.
5. Those subjects who had known history of allergy to chromium and nickel.
2.1.2 Plate Group

The plate group subjects were volunteers from a group of patients at the Sydney United Dental Hospital for whom stainless steel monocortical plates had been used for treatment of their fractured mandibles. The composition of these plates as supplied by the manufacturers (Martins) is expressed in percentages in Table 1. The normal time for the removal of the plates is three to six months based on the inherent healing properties of the bone. In this group of subjects the plates had not been removed for two and a half years, mainly because the option for removal of the plates was not offered to the patients by the practising Maxillofacial Surgeons. Another reason for plates not being removed was failed attendance. The patient population consisted of 22 male patients for whom biopsies of soft tissue and bone were obtained.

<table>
<thead>
<tr>
<th>Stainless Steel</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>IRON</td>
<td>64.18</td>
</tr>
<tr>
<td>CHROMIUM</td>
<td>17.20</td>
</tr>
<tr>
<td>NICKEL</td>
<td>13.98</td>
</tr>
<tr>
<td>MOLYBDENUM</td>
<td>2.72</td>
</tr>
<tr>
<td>MANGANESE</td>
<td>1.650</td>
</tr>
<tr>
<td>SILICON</td>
<td>0.24</td>
</tr>
<tr>
<td>CARBON</td>
<td>0.02</td>
</tr>
<tr>
<td>PHOSPHORUS</td>
<td>0.14</td>
</tr>
<tr>
<td>SULPHUR</td>
<td>0.002</td>
</tr>
</tbody>
</table>

2.2 PROCEDURE

Informed consent was obtained from all subjects included in the study. The biopsies were carried out under local anaesthesia. Attempts were made to create an environment whereby the contamination of chromium, molybdenum and nickel was reduced (Versieck and Cornelis, 1989). This was achieved by creating a positive laminar air flow in the surgery where the biopsies were obtained. Also, the surgeons and the assistants wore non-powdered latex gloves and mask and headcap. Any jewellery, wristwatch and ornaments were removed prior to the surgical procedure, from the patient as well as the operator and the assistants. The number of staff in the surgery was reduced to the minimum. All surgical procedures were carried out with minimal involvement of stainless steel instruments. The tissue samples which were used for analysis were removed with specially constructed titanium instruments (knife, chisels, curette and periosteal
elevators). The bone was initially removed using tungsten carbide burs and the edges were shaved using a Carborundum disc. The solution for irrigation during the procedure was purified deionised water. The biopsy material was placed into acid washed plastic containers and sealed. The materials were then weighed to obtain the weight of the tissue involved in the analysis. Following the procedure the area was irrigated and the flaps sutured using multiple polyglactin 910 (vicryl) sutures.

The patients were followed-up for review of healing and to assessment of any post-operative complications.

2.2.1 Control group

Biopsies were obtained prior to the removal of the lower third molar teeth. The soft tissue samples involved periosteum and overlying connective tissue from the buccal aspect in the third molar region and buccal cortical bone was obtained for the bone samples (Fig 1).

Figure 1 Biopsy of Bone and Soft Tissue in the Control Group
2.2.2 Plate group

Access to the region was gained via a buccal incision. The soft tissue surrounding the plates was isolated and biopsy was obtained from the second screw hole from the midline of the face in relation to the plate. The plate was then removed and biopsy of the underlying bone was obtained. The plates that were removed were initially gently washed in deionised water and then soaked in acetone for removal of the protein and surface materials. Following this, the plates were again washed in deionised water and then absolute alcohol for removal of any water contamination. The plates were then dried and placed in vacuum containers for surface analysis.

Following the removal of the plates, the bone biopsy was obtained (Fig 2). The bone obtained was from the region of the second screw hole and involved cortical and cancellous bone. The bone was removed using tungsten carbide burs followed by the use of a Carborundum disc for removal of any contamination from the edge of the biopsied bone. The region of the biopsy from the plate group was directly adjacent to the plates as Lux and Zeisler (Lux and Zeisler, 1974) have shown the concentration of the released products to be maximum in the immediate vicinity of the implant. The biopsy material was placed into preweighed acid-washed polycarbonate containers for weighing of the tissue sample and transport of the tissue sample for analysis.

Following the bone biopsy, the area was debrided and the incision closed using multiple polyglactin 910 (vicryl) sutures. The patients were followed-up for healing, as well as for any post-operative complications.
2.3 MATERIALS

2.3.1 Biopsy material containers

The biopsy material was weighed and transported in thirty ml polycarbonate containers. In order to reduce contamination, the containers were soaked for 24 hours, rinsed using Milli-Q water, air-dried and sealed. The containers were handled using non-powdered gloves in order to minimise any further contamination of organic materials or trace elements on the inside and outside surfaces. The containers were pre-weighed, and once the sample was placed, were weighed again to obtain the mass of the biopsied tissue.

2.3.2 Sample preparation

The biopsy material was dissolved in order to inject the material into the mass spectrometer using a flow meter. The material was dissolved in the containers using high purity nitric acid by standing overnight and the samples that were not completely dissolved were then further digested by heating in a microwave oven for 10 minutes to complete the digestion (Gillman and Engelhart, 1988; Grillo, 1988).

2.3.3 INDUCTIVELY COUPLED PLASMA MASS SPECTROMETER

In this study, the inductively coupled plasma mass spectrometer (ICP-MS) was used for analysis of the biopsy tissue. The original concept of ICP-MS developed from a requirement, expressed in the 1970's, for the next generation of multi-elemental analytical instruments to follow the then established but not commercially used ICP-Atomic Emission Spectrometry. The problems with the ICP-AES was the lack of capability of multi-elemental analysis. Other factors such as solids and liquids being not good matrices to work with (difficult to efficiently ionise solids and liquids) and the broad spectral interferences by Ca, Al and Fe compounded these problems. The ICP-MS was developed to provide wide elemental coverage, element specificity and relatively uniform sensitivity. Hence this instrument was selected based on its multi-element analysis capability, its low
sensitivity limits (Dale, 1990; Lugowski et al, 1990; Schmit, 1991), reduced spectral or background interferences, ease of sample preparation and cost of the analysis. The instrument involved was a VG PLASMA QUAD PQ2+ with argon plasma. Figure 3 shows the various components involved in the analytical process and Table 2 the various stages of operation of the ICPMS.

In the stage of ion production the sample is nebulised (Brower and Zhu, 1987; Wiederin et al, 1991) and fed into the mass spectrometer using peristaltic pump (GILSON MINIPLUS 3) at a flow rate of 0.7 mls/min. The argon plasma provides the ionising source (Houk, 1986) under the following conditions: Plasma argon flow rate of 14 L/min; auxiliary argon flow rate of 0.95 L/min. The nebuliser argon flow rate was set at 0.8 L/min. The radio frequency (r.f) power was set at 1348 Watts and the reflected power at 0 Watts. Ionising temperatures reach up to ten thousand degree Celsius (Wilson et al, 1987). The sampling time for stabilisation was 10 seconds.

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<tbody>
<tr>
<td>STAGES OF OPERATION</td>
</tr>
<tr>
<td>ION PRODUCTION</td>
</tr>
<tr>
<td>ION EXTRACTION</td>
</tr>
<tr>
<td>ION SEPARATION</td>
</tr>
<tr>
<td>ION MEASUREMENT</td>
</tr>
</tbody>
</table>
In the ion extraction stage the ions are removed from the plasma under a vacuum pressure and at a constant rate by the sampling cones. The low pressures also help to maintain the ions from further changes or decay in ionic states. There is however some oxide and polyatomic ion formation between the two cones. There is also a disc which prevents photon emission from the plasma reaching the mass spectrometer. From this stage the ions are accelerated through a series of optical lenses into the Quadropole mass spectrometer (Denoyer, 1991). The mass analyser is maintained at low pressures (1-2x10⁻⁴ Pa). The cones are made of nickel with the aperture width for the sampler cone at 1.0 mm and the skimmer cone at 0.7 mm.

The accelerating voltage of the optical lens directs the ion beam along the central axis of the quadrapole. The quadrapole consists of four cylindrical rods in a square array and diagonally paired in terms of the polarity and magnetic fields. This enables the voltages of the cylinders to be varied so that only ions of certain mass to charge ratio to reach the detector (ion separation stage). The quadropole acts as a narrow-band pass mass filter. The complete mass spectrum can be scanned rapidly (30 ms). The particles are directed toward the lenses by sampler cones under vacuum conditions. Once the particles have reached the detector, it then passes the information on the computer (COMPAQ 386/25e) which processes the information and provides a readout in the ion measurement stage. The analyte was scanned 50 times per analysis and an average of the peaks of chromium, nickel, molybdenum was obtained. Due to interference by calcium oxide, bone levels of nickel were not included in the study.

The concentrations were expressed in terms of milligrams of the trace element per kilogram of tissue (mg/Kg). Before the samples were analysed, standard solutions at 1000 ppm were used to calibrate the mass spectrometer. In between samples a solution of 1% nitric acid was used to wash the system with a rinse time of one minute.
2.4 Statistical Analysis

The tissue levels obtained was analysed using descriptive and inferential statistics. The data were analysed using descriptive and inferential statistics. The following null hypothesis was proposed:

(1) There is no significant difference in tissue levels of chromium, nickel and molybdenum in soft tissue and bone from the mandible between males and females.

(2) There is no significant difference between the tissue levels from the plate group as compared to the control group.

(3) There is no time related pattern of release of the above mentioned products in the plate group.

The confidence level was set at 0.05.
CHAPTER 3

RESULTS

3.1 INTRODUCTION

The raw data are presented in table form in Appendix A. The data were analysed using descriptive and inferential statistics. The inferential statistics used in this study were Linear Regression analysis, One Way ANOVA and Mann Whitney U Test which is a Non Parametric test. The Non Parametric Test was chosen because of the right skewness of the data from a small sample size with six out of the ten variables measured on a nominal scale. In the case of the continuous quantitative data, they were transformed to \( \log_{10}(x) \) to obtain a more symmetric distribution.

3.2 DESCRIPTIVE STATISTICS

In the control group there were twenty one females \( (n_f=21) \) and twenty five males \( (n_m=25) \). In the plate group, there were twenty one plate patients \( (n_p=21) \), all of whom were males. The following Tables present the mean, minimum and maximum, and standard deviation for the above group for the age distribution and tissue levels. The tissue levels presented are the soft tissue levels of nickel (NIST), bone levels of chromium (CRBO), soft tissue levels of chromium (CRST), soft tissue levels of molybdenum (MOST) and bone levels of molybdenum (MOBO). Bone levels for nickel were not included because of background interference from calcium oxides in bone which reduced the sensitivity of the measurements. Variables such as side, location, gender and age of the plates were assigned integer values in rank order for the purpose of analysis.
Table 1 above and table two and three below describe the age in years and the tissue levels for Nickel, Chromium and Molybdenum in mg/Kg. For nickel, only values for soft tissue were obtained. In Table three, the time the plates were in the patients are also summarised in months.
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>NUMBER</th>
<th>MEAN</th>
<th>MINIMUM</th>
<th>MAXIMUM</th>
<th>STD.DEV</th>
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<td>21</td>
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<td>16</td>
<td>54</td>
<td>9.292</td>
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<td>.030</td>
<td>3.6</td>
<td>.805</td>
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<tr>
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<td>.400</td>
<td>16</td>
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<tr>
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<td>.165</td>
<td>.010</td>
<td>1.5</td>
<td>.319</td>
</tr>
<tr>
<td>TIME (PLATE IN)</td>
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<td>11.33</td>
<td>3</td>
<td>25</td>
<td>7.631</td>
</tr>
</tbody>
</table>

Figures (1-2) show the distribution of the side in the mandible from which the biopsies were obtained for female and male patients from the control group and figure (3) the site distribution for the biopsies from the plate group.

Figure 1 Distribution of Side in Female Patients
Figures (4-6) show the distribution for location in terms of industrial or residential for the female, male and the plate groups (pages 76-77) and Fig 7 the time the plates were *in situ* (page 77).
Figure 4 Distribution of Female Patients According to Location

Figure 5 Distribution of Male Patients According to Location
Figure 6 Distribution of Plate Patients According to Location

Figure 7 Distribution of the Plates According to the time the Plates were In Situ
The measure of variability for the above data is reflected in the following graphs (Fig 8-13). The box plots show the median, the 25 and the 75 percentile, the outliers and the extreme values for the female, male and the plate patients involved in the study. The coefficient for the outlier value is 1.5 (1.5 x SD) and for the extremes is 3 (3 x SD). The standard deviations for the variables are included for comparison. The outlier is represented by a red circle and the extreme values by a blue square. In the case of the bone levels of chromium for males, there is a tendency towards bimodal distribution with three values above and equal to 4.5 mg/Kg. These values are extremes given the standard deviation of 1.47 and hence treated as extremes. Also they represent three values in a small sample size.

![Age Distribution Diagram](image)

Figure 8 Box Plots of Age Distribution for Male, Female and Plate Patients

In the age distribution for the male control group the extreme is aged 67 years. This value was discarded in the final analysis.
Figure 9 Box Plots of Nickel Levels in Soft Tissues for Male, Female and Plate Patients

Figure 10 Box Plots of Chromium Levels in Soft Tissues for Male, Female and plate Patients
Figure 11 Box Plots of Chromium Levels in Bone for Male, Female and Plate Patients

Figure 12 Box Plots of Molybdenum Levels in Soft Tissues for Male, Female and Plate Patients
The mean is greater than the median for the soft tissue and bone values of the trace elements indicating right skewed distributions. As mentioned earlier these continuous quantitative data were transformed to $\log_{10}(x)$ to obtain a more symmetric distribution. The transformed data were used for the inferential analysis. Figure 14 shows the transformed data.
3.3 INFERENTIAL STATISTICS

As stated earlier, using the log scores, correlation matrices were setup with the tissue levels as the predictor variables and the age, sex, side (left / right) and location (industrial / residential) as the outcome variables. This was followed by linear regression analysis to establish any relationships between the predictor and outcome variables. This was further tested for significance by comparing the variations in the means by using the nonparametric analysis.

3.3.1 Control group

3.3.1a Chromium

Figure 15 below shows the correlation matrices for bone and soft tissue for chromium.

Figure 15 Correlation Matrices for Bone and Soft Tissue Levels for Chromium with Gender, Date of Biopsy, Age, Side and Location. Gender is Male and Female Patients. The Predictor Variable (X axis) is the Tissue Levels of Chromium Except for when Bone and Soft Tissue Levels are Compared.
Bone

There was no significant difference between the sexes, sides, locations and ages for chromium levels in bone. For the Wilcoxon rank sum test the p values were:

- sex - 0.205
- side- 0.892
- location - 0.828

Soft Tissue

There was a correlation between sex and soft tissue levels. The one way ANOVA gave a p value of 0.003 and for Wilcoxon rank sum test, p value of 0.002. Hence there was a significant difference between males and females for soft tissue levels. The side and location showed no differences (p=0.869 and p=0.982 respectively for Wilcoxon rank sum test).

3.3.1b Molybdenum

Fig 16 below shows the correlations for the tissue levels of molybdenum.

Bone

There was no correlation established for sex, side location and age.

The p values for Wilcoxon rank sum test were:

- Sex- 0.828
- Side - 0.847
- Location - 0.109

Soft Tissue

The correlation showed a significant relationship between sex and soft tissue levels (one way ANOVA: p=0.039; Wilcoxon rank sum test: p= 0.019). For side (Wilcoxon rank sum test: p=0.226) and location (Wilcoxon rank sum test: p=0.42) there was no correlation.
Correlations (Molybdenum tissue levels)

Figure 16 Correlation Matrices for Bone and Soft Tissue Levels of Molybdenum with Gender, Date of Biopsy Age, Side and Location. Gender is Male and Female Patients. The Predictor Variable (X axis) is the Tissue Levels of Molybdenum Except for when the Bone and Soft Tissue Levels are Compared.

Correlations (Nickel tissue levels)

Figure 17 Correlation Matrices for Soft Tissue Levels of Nickel with Gender, Date of Biopsy, Age, Side and Location. Gender is Male and Female Patients. The Predictor Variable (X axis) is the Tissue Levels of Nickel.
3.3.1c Nickel

The figure 17 above shows the correlations for nickel levels for soft tissue. There was no correlation between side (Wilcoxon rank sum test: $p=0.322$), location (Wilcoxon rank sum test: $p=0.14$), sex and the soft tissue levels for nickel.

3.3.2 PLATE GROUP

The mean trace element values were compared across the male control group and the plate group. The female group was not included in the analysis of the plate group because of the significant differences between the male control group and the female control group (soft tissue levels for chromium and molybdenum). Also there were no female patients involved in the plate group. With the exception of nickel, the plate group had higher mean values.

3.3.2a Chromium

Soft tissue

Following the removal of the extreme value of 45 mg/Kg for the plate population, the one way ANOVA and Wilcoxon rank sum test gave $p$ values of 0.005 and 0.006 respectively. Hence the plate group has a significantly higher level of chromium than the male controls in the soft tissue samples.

Bone

Following the removal of the extreme value of 16 mg/Kg for the plate group, the one way ANOVA and Wilcoxon rank sum test gave $p$ values of 0.006 and 0.014 respectively. Hence the plate group has a significantly higher level of chromium in bone samples than the male controls.

3.3.2b Molybdenum

Soft Tissue

After deleting the extreme value of 1.5 mg/Kg for the plate population, the one way ANOVA and Wilcoxon rank sum test gave $p$ value of 0.033 respectively. Hence the plate group have a significantly higher levels of
molybdenum in soft tissue samples compared to the control male group.

**Bone**

One way ANOVA and Wilcoxon rank sum test gave p values of less than 0.000 and 0.000 respectively. The bone values indicating a significant increase in the bone samples compared to the control male group.

**3.3.2c Nickel**

For nickel only the soft tissue samples were analysed as indicated earlier. The one way ANOVA and Wilcoxon rank sum test gave p values of 0.614 and 0.7 indicating no significant difference in the soft tissue levels.

**3.3.3 PERIOD OF INSERTION OF PLATES**

The relationship of the overall age the plates were in situ and the tissue levels were analysed following removal of case number three for the plate group who had extreme soft tissue reading for chromium, molybdenum and nickel. There was no significant relationship between the age of plate and tissue levels.

The plate patient group was subdivided into three groups according to the duration between insertion and removal of the plates (0-6, 7-13, 18-25 months) and analysed for any variations. The control group served as the fourth group for comparison. The Kruskal-Wallis test was chosen rather than Wilcoxon rank sum test in the analysis of age of the plate because of the small numbers in each group. For nickel there are no differences between the three groups as compared to the controls (one way ANOVA, p-value = 0.608 and the Kruskal-Wallis test p-value = 0.611). The bone levels for chromium showed, following removal of extremes, marginal significance with p values of 0.041 for one way ANOVA and 0.06 for the Kruskal-Wallis test. The soft tissue levels showed no significant difference for chromium (p-value = 0.061 for the Kruskal-Wallis test and p-value of 0.066 for one way ANOVA). Molybdenum showed no significant differences between the groups for soft tissue levels following deletion of the extremes (p-value=0.24 for the Kruskal-Wallis and p-value =0.25 for one way ANOVA). For bone levels the control group was significantly lower (p value of
less than 0.00 for both tests) compared to other groups but there was no difference within the plate groups.

3.3.4 PLATE POSITION

The plate positions were grouped into anterior and posterior. The anterior group included the midline and parasympyseal regions, The posterior group included the body and angle groups. Only the two groups were chosen because of the sample size being too small. One way ANOVA (p=0.02) and Wilcoxon rank sum test (p= 0.036) showed a significant difference between the mean nickel soft tissue levels for the two positions. In the case of chromium, there was no significant difference for bone (one way ANOVA: p=0.314 ; Wilcoxon rank sum test: p=0.325) and soft tissue (one way ANOVA: p=0.88; Wilcoxon rank sum test: p=0.341) levels. For molybdenum, the anterior plate group showed higher levels in bone (one way ANOVA: p=0.039; Wilcoxon rank sum test: p=0.036) and no significant difference for soft tissue levels (one way ANOVA: p=0.128; Wilcoxon rank sum test: p=0.094) following removal of the extreme value of 1.5 mg/Kg for the plate patient from the posterior group.
CHAPTER 4

DISCUSSION

Metallosis, the clinical manifestation of corrosion is considered to rare in modern times. This is due to the fact that the improvement in the knowledge of alloying has resulted in improved surface finish and implant design.

In oral and maxillofacial surgery, with the introduction of monocortical plates in the 1970s, metallosis has not been reported as a complication. In general the symptom of pain reported by the patient could be attributed to infection, hypersensitivity reaction or impingement of the implant on the periosteal tissues. In current materials, there is no association established, between pain and metallosis. While histological studies report occasional discolouration of the surrounding tissues, this is not associated with chronic inflammation and tissue necrosis. The most common finding is that of fibrous capsule formation.

Another important factor to consider is the local environment in which the monocortical plates are utilised. In the case of the mandible, there are number of factors that makes this system unique:

1. The miniplates are not exposed to saliva and bacteria during the initial response and the healing phase that follows.

2. The miniplates are applied to regions where the functional loads are in the region of 150-350N, compared to the ankle (790N) during walking, ankle during standing (2000N) and the hip (2800N) during standing in a 80 Kg man (Simon, 1986).

3. The miniplates are applied to the surface of bone and covered by soft tissue such as periosteum, mucosa and muscle.

4. The miniplates are not in contact with dissimilar metals or materials.

5. The miniplates are in an area of increased vascularity compared to the long bones or joints.
The influence of the above factors in relation to corrosion is yet to be established. Another factor is micromotion during healing. With the current philosophy of not placing the patient into intermaxillary fixation following internal fixation, the stress placed on the plates and screws during normal function is yet to be investigated. While the plates have been tested for their limits in terms of strength under laboratory conditions (Haug, 1993; Ellis and Laskin, 1994) they have not been investigated under normal loads in the physiological environment in vivo.

One of the limiting factors towards the understanding of corrosion has been the analysis of the tissue levels of the corrosion products. In recent times, the measurement of these products has been feasible with the introduction of instruments such as ICP-AES and ICPMS. A further factor has been the limitation in the understanding of the metabolism of these products in the human body. While qualitative analysis of implants in the body has been straightforward with the use of surface analysis of retrieved implants, histological studies and naked eye assessment for tissue discoloration, quantitative analysis has been limited. The introduction of the above instrumentation has improved the efficiency and reliability of the measurement of the tissue levels.

This study utilised ICPMS to analyse the released products in the tissues surrounding stainless steel monocortical plates used in the treatment of mandibular fractures.

4.1 METHOD

The method applied in this study is the standard approach used in previous studies of the released products during corrosion (Moberg et al., 1989; Bessho et al., 1988). The difference in this study is that the ICPMS was used to measure the ion levels in the tissues. The ICPMS, which was only introduced in the last 15 years, is considered to be more efficient in the analysis in terms of the complexity of the tissue preparation, the time involved in the analysis, cost effectiveness and sensitivity (Dale, 1990). The previous studies analysing tissue levels of trace elements did not use ICPMS as the analytical instrument.
Strict criteria were applied for patient selection and the biopsy procedure in order to minimise contamination. No attempts were made to quantify the effectiveness of the selection criteria. The tissue levels obtained are comparable to other parts of the body. Unfortunately, there are no data available for the normal tissue levels of Cr, Mo and Ni in the jaw region.

The method of preparation of the sample (acid digestion followed by further microwave digestion as required) is considered to be an acceptable method but there are no data available to compare the accuracy. The precision (reproducibility for the ICPMS is 5% and the drift allowed is less than 10%). Unfortunately, the accuracy for the biopsy method was not tested for this study due to the availability of the amount of sample during biopsy and the ethical issue of the amount of tissue that could be obtained during biopsy.

4.2 RESULTS

The results for the control population were unusual because there was a significant difference between males and females for Cr (one way ANOVA, p =0.003; Wilcoxon rank sum test, p =0.002) and for Mo (one way ANOVA, p =0.039; Wilcoxon rank sum test, p =0.019). The Cr levels are especially highly significant. This result is difficult to explain when considering the fact that the patients were only matched for age, with no correlation for the place of residence or place of work or the site of biopsy (the side the wisdom tooth was removed from) and the sexes. Since the males have the highest mean levels, facial make up is not an explanation. One possibility is the sample size of 21 females and 25 males being too small. There are no sex differences in the normal tissue levels of Cr and Mo. Further study is required to not only confirm our finding but also to explain the above differences.

Due to the sex differences for the control figures, only the values for males were used for comparison with the plate group which consisted of only male plate patients. For tissue levels, while the overall mean levels were higher compared to the control group, only Cr (bone and soft tissue) and Mo (bone and soft tissue ) showed significant differences. These results are not consistent with
that of Moberg et al as they found Ni levels to be significant but for Cr and Mo there was no significant difference between Champy plates and control tissues. There are a number of explanations one could consider to explain these differences. Moberg et al used AAS for the tissue analysis which is considered to be less sensitive. Their sample size is made up of seven monkeys. In our study, human tissues were used. One could argue, in the light of limited knowledge of the metabolism of trace elements in animals generally, there might be significant differences between humans and other animal species.

When the data were analysed for the age the plate has been in situ there were no significant differences for the trace elements. The marginal significance for bone levels of Cr is difficult to interpret due to the small sample size. While Lux and Zeisler (1976) showed that there was a decrease in the concentration of tissue levels with time, our study failed to establish this relationship. Again a prospective study might offer an explanation.

In the case of plate position, there were significant differences for Ni (soft tissue) and Mo (bone). Given the small sample size, these results are difficult to interpret. The important limitation in our study is that it is not a prospective study where it would have been ideal to have established the pre-insertion tissue levels in the human subjects and then to have monitored the levels over a period of time.

The implications of these findings are still a contentious issue (Black, 1988). Apart from the hypersensitivity reactions (Hierholzer and Hierholzer, 1992; Suuronen, 1993) there is no association between tissue levels and carcinogenesis or metabolic effects. The finding of hypersensitivity warrants hypersensitivity testing especially in cases where there is infection because of the associated increased incidence of hypersensitivity (Hierholzer et al, 1984).

### 4.3 Conclusion

In spite of the rather small sample size, this study has shown that there is a statistically significant increase in tissue levels of Cr and Mo, and an increased soft tissue level of Ni surrounding the miniplates used to fix mandibular
fractures. While this does not prove that the release is due to corrosion, other workers have shown that metal implants may corrode. There is also sufficient evidence that release of such ions leads to increased sensitisation among patients compared to the normal population. More research should be undertaken to investigate whether corrosion and sensitisation occur (and if so how frequently) following insertion of Champy stainless steel miniplates in the mandible.
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APPENDIX A

The raw data are presented in the following tables. Table one presents the data for the female sample of the control group. Table two presents the data for the male sample of the control group and table three the data for the plate group. Ethical committee approval was obtained for the study and informed consent from the patients before biopsy.

The column date is the time when the biopsy was carried out. The column side refers to the side the biopsy was done which in this study is right (r) or left (l). In case of the plate patients the site of biopsy is recorded as anterior (ant), parasymphysis (para) or angle (ang) and included the body region of the mandible due to small sample size. The side the biopsy was taken was recorded as right (r) or left (l). The column suburb refers to the residential area where the patient has lived for at least six months and the column location classifies the suburbs as industrial (I) or residential (R) based on information obtained from The Industrial and Commercial map for the Sydney Metropolitan area, 8th edition.

The tissue levels for the soft tissue and bone are presented under the categories of Chromium, Nickel and Molybdenum. The values are in mg/Kg. In Table three the time the plates have been in situ are presented in months and the column plate numbers refers to the number of plates that were removed at the time of the biopsy.
<table>
<thead>
<tr>
<th>PT NO</th>
<th>DATE OF BIOPSY</th>
<th>AGE</th>
<th>M/F</th>
<th>SIDE L/R</th>
<th>SUBURB</th>
<th>LOCATION</th>
<th>NICKEL</th>
<th>CHROMIUM</th>
<th>MOLYBDENUM</th>
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</thead>
</table>
|       |               |     |     |          |           |          | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSUE | BONE | SOFT TISSU
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Table 3 Plate group
Appendix B

In appendix B the following are included:

(1) The human ethical committee approval for this study.

(2) The consent form used.

(3) The list of presentations associated with this study.

(4) The list of publications associated with study.
The University of Sydney

N.S.W. 2006
Australia

Mr Sri Kathirgamathamby
13/116 Tyrrell Street
NEWCASTLE NSW 2300

Reference: Mr Wilson/rj

22 October 1990

Dear Mr Kathirgamathamby

I am pleased to advise that the Human Ethical Review Committee of the Faculty of Dentistry has approved the following protocol application for 1990:

'Metal Release from Stainless Steel Plates used in Treatment of Mandibular Fractures'

Yours sincerely

[Signature]

H Wilson
for
Keith Jennings
Registrar and Deputy Principal
FACULTY OF DENTISTRY
THE UNIVERSITY OF SYDNEY
DEPARTMENT OF ORAL AND MAXILLOFACIAL SURGERY

STUDY: Metal release from stainless steel plates used in treatment of mandibular fractures

INFORMED CONSENT FORM

I, ................................................ of ................................................
................................................, consent to participate in this research project.

All aspects of the project have been explained to me including the surgical procedure, the possible complications and associated morbidity.

I understand that with the exception of the age and sex no other personal information will be used and this confidentiality will be preserved in the publication of any research results.

Signed: ................................................
Date: ................................................

Witnessed: ................................................

I have explained to the patient the details of the experimental procedures and any adverse effects associated with the biopsy of tissue and removal of the plate/plates.

Investigator - Signed: ................................................
Date: ................................................
PRESENTATIONS

(1) "Metal Release from Champy Plates"
   Champy plating course
   United Dental Hospital
   December 1990.

(2) "Metal Release from Stainless Steel Miniplates used in the Treatment of Fractured Mandibles"
   Poster Presentation
   14th A.N.Z.A.O.M.S. Conference
   Adelaide

(3) "Metal release from Stainless Steel Miniplates used in Treatment of Mandibular Fractures"
   I.A.D.R. Regional Committee Meeting (NSW)
   United Dental Hospital - Sydney
   Won The Colgate Palmolive Travel Grant

(4) "Metal Release from Stainless Steel Miniplates used in Fracture Fixation"
   Poster Presentation
   I.A.D.R. National Meeting
   Brisbane
   October 1991.

(5) "Metal Release from Stainless Steel Plates used in the Treatment of Mandibular Fractures"
   Registrars's Day
   Westmead Hospital

(6) "Corrosion of Stainless Steel Miniplates used in Fixation of Mandibular Fractures"
   15th A.N.Z.A.O.M.S. Conference
   Melbourne
   February 1993.

(7) "Corrosion of Metallic Implants used in the Treatment of Jaw Fractures"
   A. Punnia-Moorthy, S. Thamby
   R.A.C.D.S. Convention
   Canberra
   March 1994.

(8) "Corrosion of Metallic Implants used in the Oro-Facial Region"
   A. Punnia-Moorthy, S. Thamby
   International Meeting of the Iranian Dental Association
   Tehran, Iran
PUBLICATIONS

(1) S. Thamby, A. Punnia-Moorthy, L. Dale.
Metal Release from Stainless Steel Miniplates used in Treatment of Mandibular Fractures

(2) S. Thamby, A. Punnia-Moorthy, L. Dale.
Metal Release from Stainless Steel Miniplates used in Fracture Fixation

Metal Release from Stainless Steel Miniplates used in Treatment of Mandibular Fractures

(4) A. Punnia-Moorthy, S. Thamby.
Corrosion of Metallic Implants used in the Treatment of Jaw Fractures