Metal particles and tissue changes adjacent to miniplates

A retrieval study

Sissel Torgersen, Nils Roar Gjerdet, Egil S. Erichsen and Gisle Bang

Departments of Dental Biomaterials, Oral Surgery and Oral Medicine, Oral Pathology and Forensic Odontology, and Laboratory for Electron Microscopy, School of Dentistry, University of Bergen, and Department of Oral and Maxillofacial Surgery, Haukeland Hospital, Bergen, Norway

Torgersen S, Gjerdet NR, Erichsen ES, Bang G. Metal particles and tissue changes adjacent to miniplates. A retrieval study. Acta Odontol Scand 1995;53:65–71. Oslo. ISSN 0001–6357.

Peri-implant soft tissue and bone from 12 patients undergoing removal of stainless steel miniplates and screws after healing of jaw fractures were studied with regard to histomorphology and metal content. Three patients with titanium plates were also included. Light microscopy and scanning electron microscopy with energy-dispersive X-ray microanalysis were used. Non-osseous tissue adjacent to devices of both materials showed fibrosis, including areas of mild chronic inflammation. The cellular picture was dominated by fibroblasts with small aggregates of lymphocytes and scattered macrophages. A connective tissue collar was found between the bone tissue and the screws of both stainless steel and titanium. Bone formation was also evident adjacent to screws of both materials. Stainless steel or titanium particles 5–50 μm in diameter were found in both soft tissue and bone next to implants of their corresponding bulk material. The amount of metal impregnation varied between individual sections, and fewer particles were found in the bone specimens than in soft tissue. The mild inflammatory changes were not restricted to areas of metal impregnation. □ *Biomaterials, adverse reactions; metallosis; stainless steel; titanium*

Sissel Torgersen, Department of Dental Biomaterials, School of Dentistry, Årstadveien 17, N–5009 Bergen, Norway

The biocompatibility of metallic materials for internal fixation is under discussion (1). Stainless steel has so far formed the backbone of osteosynthetic devices; however, the introduction of titanium has reduced the use of Ni-Cr-containing alloys. Still, no implant material can be judged as inert. The major elements of stainless steel are iron (Fe), chromium (Cr), and nickel (Ni), whereas commercially pure titanium consists of more than 99% titanium (Ti). Corrosion and wear products from stainless steel may accumulate in the tissue surrounding implants and contribute to local tissue changes (2–9). Similar conditions may occur around titanium implants (3–13). The possible reactions to metal implants and their degradation products by the biologic environment may involve both local and generalized reactions (1, 4, 14). Both nickel and chromium are elements suspected of causing hypersensitivity (1, 15). Recently, titanium has also been found to be capable of eliciting immune reactions in humans (14, 16). Most of these studies have been performed on orthopedic implants. At present there is a lack of information about local tissue changes around maxillofacial fixation devices. It was the objective of this study to evaluate histomorphologically the tissue surrounding maxillofacial miniplates and screws of both stainless steel and titanium and to ascertain the nature of the particulate material observed within the tissue at the implant bed.

Materials and methods

Soft tissue and bone in contact with miniplates and screws were obtained at removal of the implants from the mandible of 12 patients with stainless steel devices and 3 patients with titanium ones. Soft-tissue specimens were taken from all the patients, whereas bone tissue was harvested from six patients with stainless steel implants and from two patients with titanium implants. The mean age of the patients was 29 years (16–75 years) in the stainless steel group, which comprised 10 males and 2 females. The mean age of the patients, 2 males and 1 female, with titanium osteosynthesis was 30 years (16–54 years). All patients but one were fully dentate; the latter was edentulous. Seven patients with body fractures and five with angle fractures were treated by stainless steel fixation. The titanium plate/screw devices were used in two patients with body fracture and one patient with angle fracture. Four-hole plates with two screws on both sides of the fracture line were used (Fig. 1). The plates and screws of both materials were manufactured by Martin Medizin-Technik, Tuttlingen, Germany. The fixation devices had been inserted in the mandible by experienced surgeons as an aid to stabilize fractures. The time elapsed between fracture and treatment was less than 48 h in all cases. Rigid intermaxillary fixation was used during the operation, except for the edentulous case. Intermaxillary elastics were often used for about a week postoperatively. Primary complications, presenting as minor occlusal instability, occurred in two patients with stainless steel fixation devices. Routine removal of the stainless steel implants was performed 15–47 weeks (mean, 34 weeks) postoperatively. Titanium plates and screws are not rou-

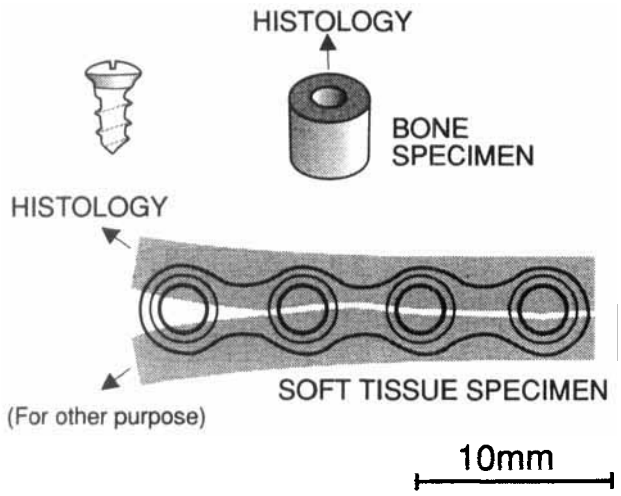

Fig. 1. Size and shape of plates and screws together with soft tissue and bone specimens.

tinely removed in our hospital. The titanium implants included in this study were removed after 39–41 weeks (mean, 40 weeks) on the patient's request. The fixation devices were removed by one operator (S. Torgersen). Bony union was found at all the fracture sites on removal of plates and screws. No clinical complications were observed in relation to the implant devices at removal. All the patients were healthy. The procedures were approved by the Regional Committee of Medical Research Ethics.

A soft-tissue biopsy specimen about 3 mm thick was taken from the area overlying the plate before the implant was removed and fixed in 4% formaldehyde (Fig. 1). The biopsy specimens were divided longitudinally, and about half of each specimen was assigned for a future immunohistochemical study (Fig. 1). After screw removal, a trephine bur (Meisinger, Germany; diameter, 4 mm) was used to obtain bone biopsy specimens surrounding and including a screw hole (Fig. 1). The bone specimens were fixed in 4% formaldehyde and decalcified in 18% formic acid (Merck) for 14 days. Both soft tissue and decalcified bone were embedded in paraffin, sectioned to a thickness of 6 μm, and stained with hematoxylin (Shandon Instant Hematoxylin). Staining with Preussian blue was used to disclose hemosiderin (blood-derived ferric ion). The soft-tissue specimens were sectioned parallel to the surface of the plates, enabling evaluation of the tissue in contact with the implant. The bone specimens were cut perpendicular to the long axis of the screws. The stained sections of both soft tissue and bone were examined by light microscopy (Ernst Leitz Wetzlar, Germany; magnification, 35×, 100×, 450×). The area of the sections was measured with a light microscope connected to an image analyzer unit (Cue2 Image Analyzer, Olympus). The mean size of the soft-tissue sections from stainless

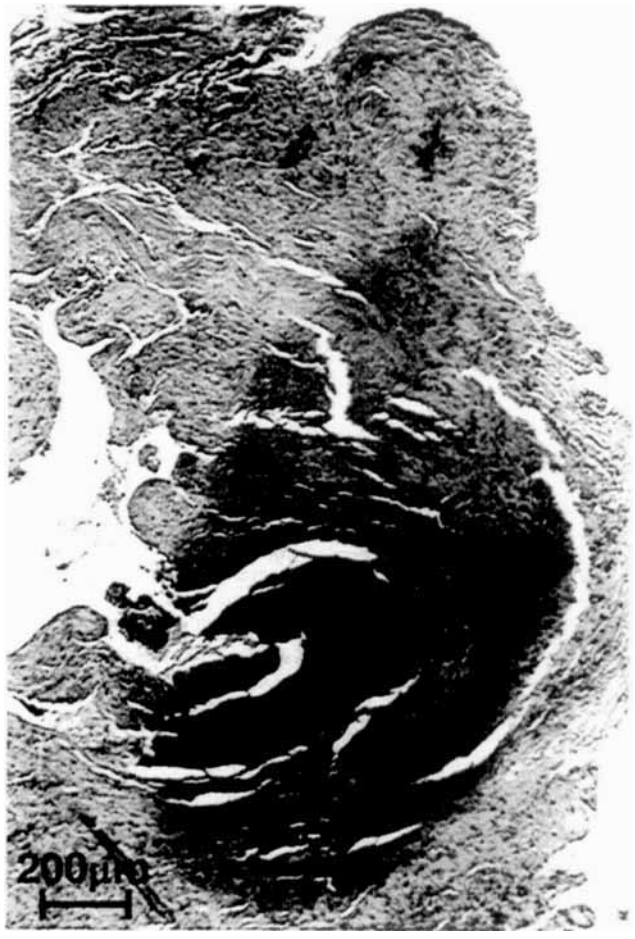

Fig. 2. Fibrous tissue adjacent to a titanium miniplate. Note the accumulation of metal particles (black areas).

steel cases was 15 mm^2 and from titanium cases 18 mm^2. The mean size of the bone section was 7 mm^2.

Soft-tissue sections (7 μm thick) from six stainless steel specimens and from the three titanium specimens were prepared for metal content analysis. The specimens chosen for this purpose displayed macroscopically visible discoloration. The sections were stretched in water at 40°C for a few seconds, subsequently fixed to carbon discs (Nordiska Baltzers A/B, Gentofte, Denmark), and subjected to drying for 3 min at 60°C. The tissue sections were then sputter-coated with carbon. A scanning electron microscope (SEM) (JSM 6400, Jeol Ltd., Tokyo, Japan) in the back-scatter mode was used for energy-dispersive X-ray microanalysis (EDXA) (Series II X-ray Analyzer, provided with SQ Standardless Quantitative Analysis Program; Tracor Northern, Middleton, Wisc., USA), and the information was processed by a particulate recognition and characterization software (PRC; Tracor Northern). The magnifications used were 100× and 200×. Elements with atomic number higher than 5 (boron) could be

Fig. 3. Fibrous tissue with proliferation of capillaries next to a stainless steel miniplate. Accumulation of metal particles in the tissue (m). A mild perivascular lymphocyte infiltration is observed together with small metal particles in the vicinity of the vessels (some of which are indicated by arrows).

identified, and particles with an average diameter of 2 µm and greater could be characterized. The diameter of the particles was measured by calculating the mean equivalent circle diameter (MECD) of the particles (17). No contamination of relevant metals was found by atomic absorption spectrophotometry of the reagents used for preparation or by screening the paraffin wax by EDXA before use.

The chi-square test was used to test for statistical significance (Minitab Inc., State College, Pa., USA). A p value of 0.05 or less was considered statistically significant.

Results

At removal of the implants, firm and fibrous-appearing soft tissue was found to cover the plates and screwheads in 13 of 15 cases. Highly vascular, loose connective tissue was observed in association with stainless steel plates and screws in two patients, of whom one had a total loosening of the multicomponent device. Single loose screws were found in five patients with stainless steel implants. One of the titanium plates was partly covered by bone, whereas no stainless steel device showed bone overgrowth.

Macroscopically visible discoloration, postulated to be metal impregnation of the tissue, appeared adjacent to the implants in six patients with stainless steel plates and in all three patients with titanium plates. Neither loose implant components nor implant time in situ could be related to the presence of tissue discoloration at the implant bed ($p > 0.1$).

Soft-tissue specimens

The most consistent findings were those of dense connective tissue or collagen with black discoloration regardless of the implant material (Figs. 2 and 3). Histologic examination of the 15 soft-tissue specimens confirmed the macroscopic observation of a fibrous or collagen capsule, which separated the normal tissue from the implant in 13 (87%) of the cases. Fibrous tissue covered the implants of both materials. The remaining two cases were dominated by granulation tissue. There were in general no substantial differences in the soft-tissue morphology between specimens taken adjacent to stainless steel and titanium implants. Both the density of fibroblasts and the presence of collagen fibers varied between individual specimens.

Proliferation of capillaries and small aggregates of perivascular lymphocytes was sometimes observed in the fibrous capsule around stainless steel devices (Fig. 3). Edema of the vessel walls occurred occasionally. All specimens contained lymphocytes, and macrophages were present in most specimens from tissue covering both stainless steel implants and titanium ones. Multinucleated giant cells were absent.

On a microscopic level black particles, found to be stainless steel or titanium material by EDXA, were apparent in all the soft-tissue specimens (Figs. 2 and 3). There were no differences in the particle distribution between stainless steel and titanium. Hemosiderin was not observed in the tissue sections. The metal deposits were localized nearby small vessels (Fig. 3) or embedded in the fibrous tissue (Figs. 2 and 3). Particles localized perivascularly were regularly associated with lymphocyte aggregates, but the lymphocytes were not only restricted to the areas of metal impregnation (Fig. 3). Small particles could be observed within the cytoplasm of fibroblasts and macrophages in the soft tissue next to both materials. Large particles had been encapsulated by the connective tissue, and a mild or no cellular reaction was present in the surrounding tissue (Fig. 2). In areas with a high concentration of metal particles,

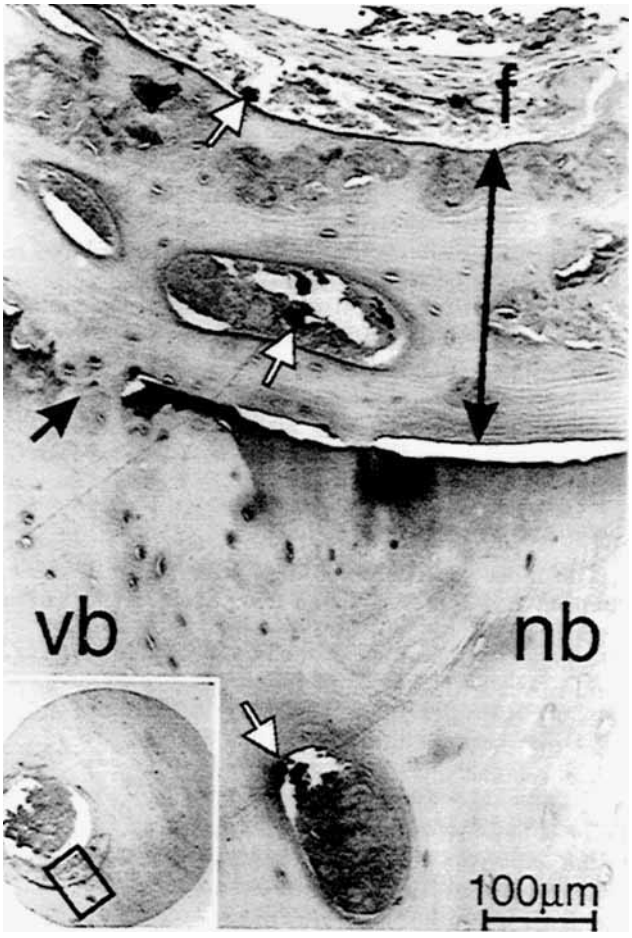

Fig. 4. Bone tissue specimen taken from the surroundings of a stainless steel screw. Fibrous tissue next to the screw (f). Bone formation in the periphery of the screw hole (distance between black arrowheads), with vital bone (vb) bridging (black arrow) between the newly formed bone and an area of non-vital bone (nb), tending to replace the non-vital bone. Metal impregnation (white arrows) in the fibrous tissue next to the screw, in the postoperatively formed bone, and distant from the screw, in the preoperative bone.

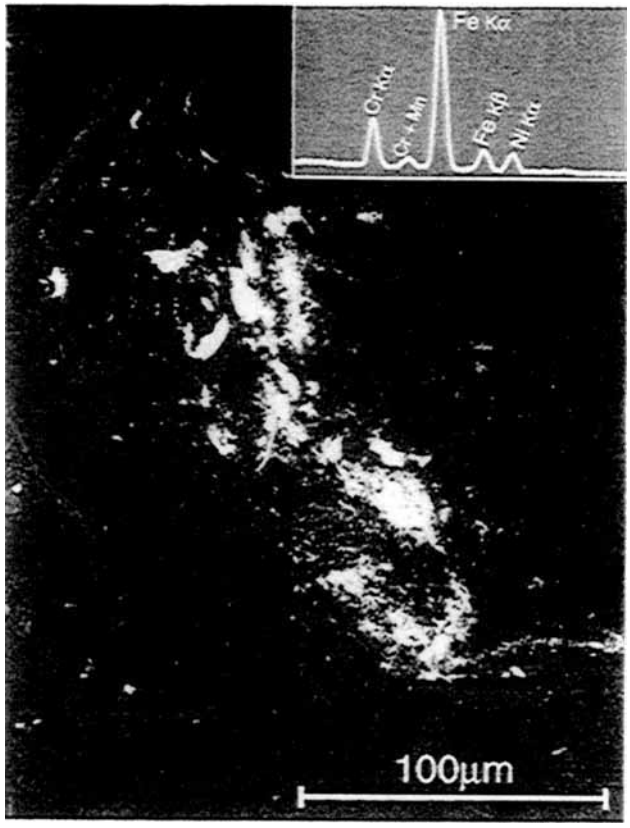

Fig. 5. Scanning electron microscopy of the soft tissue next to a stainless steel miniplate showed metal particles accumulated in the tissue (white areas). Energy-dispersive X-ray microanalysis showed that the particles had the same composition as the implant material.

the black deposits masked the cellular structure of the tissue (Fig. 2).

Bone specimens

Production of connective tissue was evident in the periphery of screwholes next to both the stainless steel screws and the titanium screws (Fig. 4). The amount of fibrous tissue between screw and bone varied from specimen to specimen. The mean width was 0.44 mm in the stainless steel specimens and 0.07 mm in the titanium ones. Inflammatory cells were rare, except in the cases of loose screws, in which lymphocytes and macrophages occurred frequently. Osteoblastic activity with osteoid and bone formation adjacent to the screws was observed in five of the six specimens associated with stainless steel screws and in the two with titanium. Vital and mature bone tissue with a normal histomorphology was found in the vicinity of both stainless steel and titanium screws (Fig. 4). However, non-vital bone with loss of osteocytes in the lacunae was frequently found in restricted areas around stainless steel screws (Fig. 4). The bone formation next to the screws tended to replace the surrounding non-vital bone tissue (Fig. 4).

All specimens taken around screws included metal particles, regardless of the material (Fig. 4). Particles were observed in the periphery of the screw holes and in the marrow spaces of the bone tissue distant from the screw hole (Fig. 4). The amount of metal particles in the bone specimens was less than in the soft-tissue specimens. Rather than dense deposits of metal, the particles were scattered throughout the connective tissue and bone surrounding the screw holes. Metal particles could be identified intracellularly in fibroblasts in the connective tissue or in macrophages, similar to what was seen in the soft-tissue specimens.

Metal analysis

By SEM small and scattered deposits of metal particles were detected throughout the soft-tissue sections and in the periphery of the screw holes in the bone sections. The particles were irregular in shape, and the diameter (MECD) ranged from 5 to 49 μm (mean, 15 μm) for stainless steel particles (Fig. 5) and from 9 to 20 μm (mean, 13 μm) for the titanium ones (Fig. 6). Some titanium particles with a greatest diameter of 100–200 μm occurred in the soft-tissue specimens obtained from positions next to titanium implants (Fig. 6). Particles of that size were never seen in the specimens next to stainless steel devices. EDXA analysis of these deposits showed iron (Fe), chromium (Cr), nickel (Ni), and molybdenum (Mo) in the tissue in contact with the stainless steel devices (Fig. 5). Titanium (Ti) and aluminium (Al) were found next to the commercially pure titanium devices (Fig. 6). The chemical composition of the particles resembled that of the bulk material of the plates and screws. Large amounts of metal particles (covering >50% of the section area) were found in the soft-tissue specimens from two patients, one from each material group.

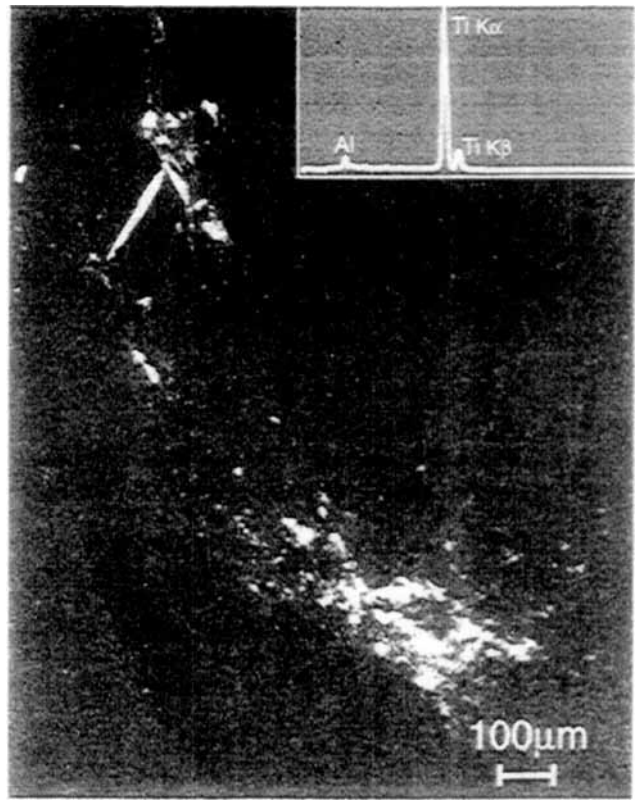

Fig. 6. Scanning electron microscopy of the soft tissue next to a titanium miniplate showed metal particles accumulated in the tissue (white areas). Energy-dispersive X-ray microanalysis showed that the particles had the same composition as the implant material.

Discussion

All implant materials interact with the biologic environment they are exposed to. The present study demonstrates metal particles and changes in the tissue in contact with miniplates and screws of stainless steel and titanium designed for use in the maxillofacial region. Metal impregnation could be present and visible on the microscopic level despite the absence of macroscopic tissue discoloration, a finding that is supported by the results of a recent report (12). Differences were observed between individual specimens with regard to the amount of metal particles in the tissue, and the amount of metal content varied independently of implant time in situ (2, 5, 9, 10). As reported previously, bone overgrowth of a titanium plate was observed, whereas in none of the 12 patients with stainless steel devices did bone tissue cover the implant (10). However, because of the small number and selection of patients, the results dealing with the titanium cases should be interpreted with caution.

A connective tissue capsule containing metal particles in most cases covered the surface of the devices of both stainless steel and titanium implants. A fibrous capsule is believed to be formed as a non-specific response to the implant solely as a foreign body regardless of the material implanted (4, 8). The thickness of the fibrous tissue or the pseudomembrane surrounding the implant has been proposed to reflect the biocompatibility of the material (3, 6, 18). The cellular and vascular changes most clearly observed with stainless steel implants may represent a mild chronic inflammation, occasionally with a stenosing vasculitis (4, 6, 8).

Perivascular infiltrates of mononuclear cells, as found in the soft-tissue specimens around stainless steel implants, were more than a decade ago associated with a delayed-type hypersensitivity reaction (19). The mild tissue alterations found in this study do not fully agree with the changes observed next to orthopedic implants, where macrophages were a constant feature and multinucleated giant cells appeared regularly (4, 6, 7, 8). The discrepancy might be due to the fact that many of the orthopedic studies have been performed on failed metal implants, such as loosened fixation devices and loosened hip joint prostheses. The present study, on the other hand, was carried out on a non-symptomatic population. The longer time elapsed between insertion and removal of the orthopedic implants compared with the maxillofacial fixation devices may also be taken into consideration when discussing differences in tissue reactions. The amount of metal implanted together with different loading conditions in the maxillofacial skeleton compared with that of long bones may contribute to a different biologic response (8). It should also be borne in mind that a tissue response in the vicinity of plates and screws may be due to factors other than the biocompatibility of the implant material. Tissue trauma, hematoma, healing processes with scarring, and insta-

bility between the implant and the surrounding tissue may be partly responsible for the histologic changes observed in the tissue (4, 20, 21). The original bone–biomaterial interface is distorted by separation of the implant devices from the biopsy specimens before removal, thereby hampering the possibility of studying the cellular picture at the interface.

A study comparing the tissue response to stainless steel and titanium showed significantly more lymphocytes in the connective tissue around stainless steel plates than with pure titanium ones, and the cells near stainless steel had a greater volume (6). No such differences could be outlined from the present study, in which scattered areas of lymphocytes were observed close to both materials.

The postoperative bone formation in the periphery of screwholes in the vicinity of both implant materials was in most cases separated from the screws by a fibrous zone. The osseoadaptation by deposition of bone on the screw surface may not be dependent on the implant material but rather on the stability of the implant during healing and on the roughness of the implant surface (20, 22, 23). In contrast, animal experiments have shown that stainless steel implants present a wider soft-tissue interface than titanium ones (18).

Corrosion and wear of implant devices cause metal particle impregnation of tissues adjacent to stainless steel or titanium fixation devices (2–13, 16). Stainless steels for implantation are susceptible to crevice corrosion (4, 5, 7, 8). In addition, fretting between different components of the devices or between plate/screws and cortical bone may occur both with stainless steel and titanium multicomponent devices (4, 5). It has been suggested that instability between bony fragments and delayed fracture healing give rise to increased fretting and more metal deposits in the tissue than does a stable fixation with primary bone healing (5). The observation of metal particles located intracellularly or in association with vessels may represent a biologic response aimed at eliminating the foreign material (4, 5, 9, 10, 13).

Metal particles of variable size were found in the the tissue. It is most likely that metal particles form aggregates in the tissue, making it difficult to measure the actual particle size (Figs. 5 and 6). Small particles may be phagocytized by macrophages (4, 6, 9). The particle size and the amount and reactivity of the ions released may be essential for the development of the host response. It has been proposed that the local tissue reaction and the potential of eliciting an immune reaction could be dependent on whether the degradation products are released in oxidized or ionized form and on the protein adhesion on the surface of the metal, rather than on the chemical composition of the material liberated to the tissues (5).

Direct osteofixation with miniplates and screws in the maxillofacial region has been of great advantage to the patient, especially due to the shortening of intermaxillary fixation period. Changes in the tissue at the implant bed are most likely direct or indirect consequences of plate and screw insertion. The observed histomorphologic changes of the soft tissue and bone may, however, not be of clinical importance. Despite the release of potentially bioactive degradation products, it appears that both the stainless steel and the titanium devices studied are well tolerated by adjacent tissue. Possible consequences of long-term implantation have not been evaluated. Implants that are meant to be left permanently in the host must be thoroughly analyzed for potentially adverse reactions. The present study did not disclose local tissue changes that speak in favor of handling patients with stainless steel and titanium implants differently with regard to removal or not of plates and screws.

Acknowledgements.—The excellent technical assistance of Gunnvor Øijordsbakken, Department of Oral Pathology and Forensic Odontology, and Grete Moe, Department of Dental Biomaterials, is highly appreciated. We are also grateful to Steiner Ørbeck Stølen at the Department of Anatomy, University of Oslo, for advice during the EDXA analyses. Kate Frøland at the Department of Dental Biomaterials is acknowledged for secretarial assistance. The staff at the Department of Maxillofacial Surgery, Haukeland Hospital, receive our thanks for their contribution in collecting the material. Financial support from the Meltzer Foundation is highly appreciated.

References

1. Black J. Does corrosion matter? J Bone Joint Surg 1988;70-B:517–20.
2. French HG, Cook SD, Haddad RJ Jr. Correlation of tissue reaction to corrosion in osteosynthetic devices. J Biomed Mater Res 1984; 18:817–28.
3. Laing PG, Ferguson AB Jr, Hodge ES. Tissue reaction in rabbit muscle exposed to metallic implants. J Biomed Mater Res 1968; 1:135–49.
4. Meachim G, Pedley B. The tissue response at implant sites. In: Williams DF, editor. Fundamental aspects of biocompatibility. Vol I. Boca Raton (FL): CRC Press, 1981:107–44.
5. Pohler OEM. Degradation of metallic orthopedic implants. In: Rubin LR, editor. Biomaterials in reconstructive surgery. St. Louis (MO): Mosby, 1983:158–228.
6. Riede UN Von, Krekeler G, Häring M, Schilli W. Die Metallose bei kieferchirurgischer Osteosynthese. Eine histomorphometrische studie an menschlichem Gewebe. Dtsch Z Mund-Kiefer-Gesichts-Chir 1981;5:30–7.
7. Simpson JP, Geret V, Brown SA, Merritt K. Retrieved fracture plates: Implant and tissue analysis. In: Weinstein AM, Gibbons D, Brown S, Ruff W, editors. Implant retrieval: material and biological analysis. Proceeding of a conference held at the National Bureau of Standards; 1980 May 1 and 2; Gaithersburg (MD). Washington (DC): National Bureau of Standards, 1981:395–422.
8. Skinner H, Weinstein AM, Clemow AJT, McPhillips-Meade M, Klawitter JJ, French G. Corrosion, materials characteristics and local tissue reaction associated with osteosynthesis devices. In: Weinstein AM, Gibbons D, Brown S, Ruff W, editors. Implant retrieval: material and biological analysis. Proceeding of a conference held at the National Bureau of Standards 1980; May 1 and 2; Gaithersburg (MD). Washington (DC): National Bureau of Standards, 1981:423–47.
9. Williams DF, Meachim G. A combined metallurgical and histological study of tissue-prosthesis interactions in orthopedic patients. J Biomed Mater Res Symposium 1974;5:1–9.
10. Meachim G, Williams DF. Changes in nonosseous tissue adjacent to titanium implants. J Biomed Mater Res 1973;7:555–72.

11. Moberg L-E, Nordenram Å, Kjellmann O. Metal release from plates used in jaw fracture treatment. A pilot study. Int J Oral Maxillofac Surg 1989;18:311–4.
12. Rosenberg A, Grätz KW, Sailer HF. Should titanium miniplates be removed after bone healing is complete? Int J Oral Maxillofac Surg 1992;22:185–8.
13. Schliephake H, Lehmann H, Kunz U, Schmelzeisen R. Ultrastructural findings in soft tissues adjacent to titanium plates used in jaw fracture treatment. Int J Oral Maxillofac Surg 1993;22:20–5.
14. Lalor PA, Revell PA, Gray AB, Wright S, Railton GT, Freeman MAR. Sensitivity to titanium. J Bone Surg 1991;73:25–8.
15. Rostoker G, Robin J, Binet O, Blamoutier J, Paupe J, Lessana-Leibowitch M, et al. Dermatitis due to orthopaedic implants. A review of the literature and report of three cases. J Bone Joint Surg 1987;69:1408–12.
16. Panigutti MA, Merritt K, Bruner RJ, Kraay MJ, Brown SA. Correlation of allergy, metal levels, implant alloy, and implant damage in patients undergoing revision joint arthroplasty. Transactions of the Implant Retrieval Symposium, Society for Biomaterials; 1992 September 17–20; St. Charles (IL). Volume XV, Abstract 7.
17. Gjerdet NR, Hegdahl T. Porosity of resin filling materials. Acta Odontol Scand 1978;36:303–7.
18. Albrektsson T, Hansson H-A. An ultrastructural characterization of the interface between bone and sputtered titanium or stainless steel surfaces. Biomaterials 1986;7:201–5.
19. Kumar V. Diseases of immunity, basic immunology. In: Robbins SL, Cotran RS, editors. Pathologic basis of disease. 2nd ed. Philadelphia: W.B. Saunders, 1979:286–7.
20. Aspenberg P, Goodman S, Toksvig-Larsen S, Ryd L, Albrektsson T. Intermittent micromotion inhibits bone ingrowth, titanium implants in rabbits. Acta Orthop Scand 1992;63:141–5.
21. Spiessl B. Internal fixation of the mandible. A manual of AO/ASIF principles. Berlin: Springer-Verlag, 1989:19–37.
22. Donath K, Kirsch A, Osborn J-F. Zelluläre Dynamik um enossale Titanimplantate. Fortschr Zahnaerztl Implantol 1984;1:55–8.
23. Linder L. Osseointegration of metallic implants. I. Light microscopy in the rabbit. Acta Orthop Scand 1989;60:129–34.

Received for publication 19 May 1994
Accepted 12 August 1994