Inflammatory Response to Dental Polishing and Prophylaxis Materials in Rats

Jose Luis Tapia[1], Mirdza E. Neiders[1], Alfredo Aguirre[1], WD McCall, Jr.[1] and Robert E. Cohen[2]
Departments of [1]Oral Diagnostic Sciences and [2]Periodontics and Endodontics, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY

Abstract

Objective: To describe the tissue response to implanted polishing and prophylaxis materials using a rat model system. **Material and methods:** Two polishing pastes (diamond polishing paste and aluminum polishing paste), two prophylaxis materials (prophylaxis paste with fluoride and air polishing prophylaxis powder) and negative and positive controls were subcutaneously implanted in rats. Tissue specimens obtained after 2 days, 1, 4, 6 and 8 weeks after implantation were processed for routine hematoxylin and eosin staining and polarized light evaluation. **Results:** Air polishing prophylaxis powder produced a mild inflammatory response. A more intense inflammation was elicited by diamond polishing paste, and the prophylaxis paste with fluoride elicited an even greater response. The aluminum polishing paste produced the most severe and persistent tissue response, which was of the granulomatous type. **Conclusions:** This finding suggests that foreign body reaction should be considered in a gingivitis that does not respond to plaque control or does not represent a mucocutaneous lesion.

Key words: Inflammation, polishing paste, prophylaxis paste, foreign body gingivitis

Introduction

Dental materials commonly used in periodontal and restorative procedures may be inadvertently implanted in the oral soft tissues and may lead to a tissue reaction. The most commonly implanted dental material in the oral soft tissues is dental amalgam (Cataldo and Santis, 1974). Implanted amalgam in the oral mucosa results in pigmented macules known as amalgam tattoos (Buchner and Hansen, 1980). Clinical and experimental studies have demonstrated that the soft tissue reaction to implanted dental amalgam could be variable, ranging from no tissue response to granulomatous inflammation (Buchner and Hansen, 1980; Nadarajah *et al.*, 1996). It appears that the tissue reaction is related to several factors such as particle size and elemental composition (Buchner and Hansen, 1980; Eley, 1982; Forsell *et al.*, 1998).

Another widely used restorative dental material that can be embedded in oral tissues is composite resin (Goodman, 1984; Moore and Barker, 1986). It may be accidentally implanted in oral mucosa during finishing, shaping or removing procedures (Nadarajah *et al.*, 1997). Clinically, this reaction may present as an asymptomatic nodular lesion and as granulomatous inflammation on histologic examination (Moore and Barker, 1986). Experimental studies also have suggested that composite resins have the potential to induce a persistent tissue reaction. Using a rat model, it was demonstrated that granulomatous inflammation occurred a week after implantation of composite resin (Hansasuta *et al.*, 1993). Based on a comparative experimental study, it appeared that composite resin might produce a more severe inflammatory response than implanted dental amalgam (Nadarajah *et al.*, 1996).

Similarly, it has been speculated that particles of polishing and prophylaxis pastes may be incorporated into the gingival connective tissue causing foreign body reaction (Daley and Wysocki, 1990; Gordon and Daley, 1997a). Clinically, this lesion has been described as a red or red-and-white macule, or as a diffuse erythematous inflammation. At the microscopic level it is characterized by the presence of a moderate to severe inflammatory infiltrate. Nearly half the cases of this type of non-plaque induced gingivitis exhibited granulomatous inflammation (Gordon and Daley, 1997a). Energy dispersive X-ray microanalysis of

Corresponding author: Mirdza E. Neiders, DDS, MS
355 Squire Hall, Department of Oral Diagnostic Sciences, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY 14214
e-mail: neiders@buffalo.edu

gingival foreign bodies revealed a number of elements, including silicon and aluminum (Gordon and Daley, 1997b). The authors concluded that those elements are constituents of dental materials, especially abrasives. Consequently, the authors suggested that abrasives, such as prophylaxis and polishing pastes, should be used only when the gingival epithelium is intact.

The ability to induce an inflammatory response by prophylaxis and polishing materials has not been studied extensively. Pistoia and de Figueiredo (2002) implanted a variety of dental abrasive materials in rat tongues and found that those containing abrasive particles induced a marked tissue response. The aim of this study was to assess the inflammatory response of four commercially available polishing and prophylaxis materials in an animal model.

Materials and methods

Animals and implanted materials

Twenty-five female adult Wistar rats (200-224 g, Harlan Sprague Dawley Company, Indianapolis, IN, USA) were used for the study. The animals were maintained on Purina food pellets and water *ad libitum* and housed in air-conditioned, humidity-controlled facilities. The experimental protocol and procedures used in this study were reviewed and approved by the Institutional Animal Care Use Committee, State University of New York at Buffalo. Every effort was made to minimize animal suffering and reduce the number of animals used in this study.

Two of each prophylaxis and polishing materials used in our institution were selected as experimental implant materials. The prophylaxis materials were prophylaxis paste with fluoride (Nupro Supreme®, Dentsply Preventive Care, York, PA, USA) and air polishing prophylaxis powder (Prophy-Jet® Dentsply International, Long Island, NY, USA). The prophylaxis paste with fluoride contained fine grit pumice with sodium saccharin and sodium fluoride. The contents of the air polishing prophylaxis powder were sodium bicarbonate, food grade silica, spearmint and sodium saccharin. The polishing materials were diamond polishing paste (Ultradent Diamond Polishing® Ultradent, South Jordan, UT, USA), and aluminum polishing paste (Prisma Gloss Extra Fine® Dentsply International, Milford, DE, USA). Diamond polishing paste included diamond particles as the active ingredient. The manufacturer did not disclose the other ingredients of this paste. The composition of the aluminum polishing paste included aluminum oxide, glycerine and hydrophobic amorphous fumed silica.

A composite resin based on quartz silica (Concise® composite resin, 3M ESPE, St. Paul, MN, USA) was used as positive control based on previous studies that showed that it produces a persistent inflammatory response (Hansasuta *et al.*, 1993). A solution of sterile 0.9% sodium chloride (Baxter Healthcare Corporation, Deerfield, IL, USA) was used as a negative control.

Preparation of implanted materials

Three grams of each paste were measured under sterile conditions using an electronic calibrated scale (Mettler Instruments Corporation, Hightstown, New Jersey, USA). The material was placed in a plastic container (Baxter Healthcare Corporation, Deerfield, IL, USA) and 6 ml of 0.9% NaCl were added and mixed to achieve a final concentration of 500 mg/ml.

For the positive control, 2 cm of each composite resin paste A and B were mixed and formed into 1 mm thick blocks. Twenty-four hours after polymerization, the blocks were ground into powder under sterile conditions with a diamond bur using a high-speed handpiece with a sterile water coolant spray. A sterile plastic enclosure served as a collection hood. Water was then removed from the composite slurry by gentle evaporation at room temperature until a dry powder was obtained. Three grams of the powder were suspended in sterile 0.9% sodium chloride to a concentration of 500 mg/ml.

Implantation and sampling procedures

For implantation, rats were placed in an induction chamber and anesthetized with a constant flow of isoflurane (Terrell® isoflurane (MINRAD INC., Bethehem, PA, USA, 1-3% mg/kg body weight). Once rats were anesthetized, isoflurane was administered with a mask. A 5 x 10 cm area on the back of the rats was shaved using a hair clipper. The shaved area was swabbed with alcohol, and 0.2 ml of each experimental and control suspensions were implanted by subcutaneous injection using sterile 1 cc syringes (Becton Dickinson, Rutherford, NJ, USA) with 18 or 20 g needles. All the materials were implanted/injected in each rat at six different sites.

Samples were obtained at 2 days, 1, 2, 4, 6 and 8 weeks after implantation. All rats were euthanized with an overdose of pentobarbital (Fatal Plus® pentobarbital, Vortech Pharmaceuticals, Dearborn, MI; 100 mg/kg) i.p. Four rats each were euthanized at 2 days, 1, 2, 4 and 6 weeks after implantation. Five rats were euthanized at 8 weeks after implantation.

Individual tissue specimens were obtained from the six sites for each specific time period and fixed in 10% buffered formalin.

Polarized and light microscopy

Smears were prepared from the materials used as experimental and control agents. Each smear was air dried for 24 hours at room temperature. The smears were immersed in xylene, and mounted in a xylene-based mounting medium (Cytoseal®, Kalamazoo, MI, USA).

Table 1. Summary of inflammatory response of all materials at all experimental periods.

Material	2 days	1 week	2 weeks	4 weeks	6 weeks	8 weeks
Positive control composite resin	+++ Subacute	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous
Negative control 0.9% NaCl solution	0	0	0	0	0	0
Prophylaxis paste with fluoride	+ Subacute	+ + Subacute	+++ Subacute/ granulomatous	++ Granulomatous	++ Granulomatous	++ Granulomatous
Air polishing prophylaxis powder	+ + Subacute	+ + Subacute	+++ Granulomatous	+ Granulomatous	0	0
Diamond polishing paste	++ Chronic	++ Chronic	++ Chronic	+ Chronic	+ Chronic	+ Chronic
Aluminum polishing paste	++ Chronic	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous	+++ Granulomatous

0, absence of inflammation; +, mild inflammation; ++, moderate inflammation; +++, severe inflammation

After fixation for 24 hours, the tissue samples were prepared for microscopic examination. The samples were embedded in paraffin and 5 μm step sections were prepared and stained with hematoxylin and eosin (H&E). The smears and sections were evaluated for conventional light microscopy and polarized light microscopy at x200 and x400 (Olympus®, Cainta Rizal, Metro-Manila, Philippines). Polarized light was used to detect double refraction (birefringence), which occurs when the rays of light pass through certain anisotropic materials.

Two observers analyzed the H&E-stained sections and a descriptive analysis was performed. The presence or absence of implanted material and the size of the identified particles were recorded.

The inflammatory response was evaluated following a modification of The Fédération Dentaire Internationale (FDI) criteria for evaluation of inflammatory response (1980). A mild inflammatory response was defined as the presence of scarce and scattered inflammatory cells. A moderate inflammatory response was defined as the presence of non-confluent patches of inflammatory cells. A severe inflammatory response was defined as the presence of uninterrupted dense sheets of inflammatory cells.

In addition, the inflammation was described as subacute, chronic or granulomatous. The designation of subacute inflammation was rendered if the predominant inflammatory cells were neutrophils intermixed with macrophages and lymphocytes. The category of chronic inflammation was assigned if the predominant inflammatory cells were lymphocytes, macrophages and plasma cells. Granulomatous inflammation consisted of epithelioid and giant cells. The presence of abscess formation, granulation tissue, fibrinous exudate, capsule, myositis, panniculitis, and phagocytosis also were recorded.

The Friedman test was used to compare the mean ranks of the five materials. Pairs of materials were compared using the Wilcoxon signed ranks test and a Bonferroni correction for the 10 pairs.

Results

Composite resin (positive control)

Using conventional light microscopy, the smear preparation exhibited colorless polymorphic particles of varying sizes ranging approximately from 0.5 to 80 mm in diameter. Polarized light examination of the smear showed birefringence of some particles.

Light microscopic examination of H&E sections after two days of implantation revealed a severe inflammatory infiltrate surrounding irregular colorless particles (*Table 1*). The inflammatory infiltrate consisted of neutrophils, macrophages and, occasionally, lymphocytes. At one week, a thin fibrous capsule consisting of irregularly arranged layers of collagen fibers with interspersed fibroblasts was seen surrounding the area of inflammation. In addition, areas of inflammatory response composed of epithelioid cells and occasional multinucleated giant cells were also noted. Some of the giant cells contained intracytoplasmic particles ranging from 0.5 to 2 mm in diameter (*Figure 1*). Interspersed focal areas of acute inflammation were still evident at one week. At two weeks, a typical granulomatous inflammation

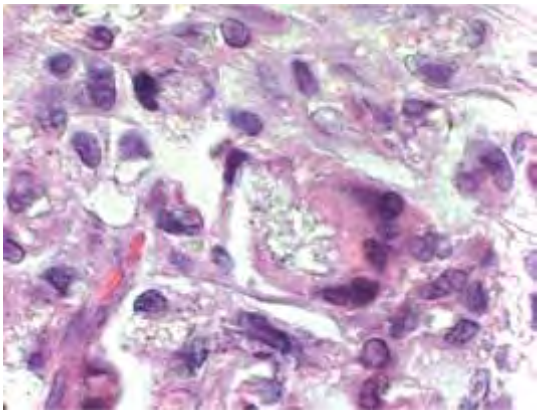

Figure 1. Photomicrograph of a tissue specimen obtained one week after the implantation of composite resin showing areas of granulomatous inflammation consisting of epithelioid cells and occasional multinucleated giant cells with intracytoplasmic particles of the material (H&E, original magnification x400).

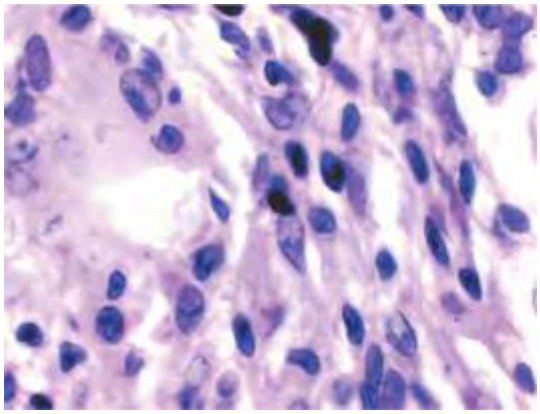

Figure 2. Photomicrograph of a tissue specimen obtained eight weeks after the implantation of prophylaxis paste with fluoride showing granulomatous inflammatory response composed of macrophages, epithelioid cells and occasional lymphocytes (H&E, original magnification x400).

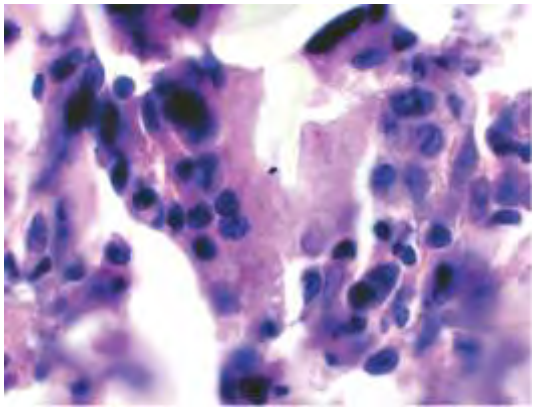

Figure 3. Photomicrograph of a tissue specimen obtained two weeks after the implantation of air polishing prophylaxis powder showing granulomatous inflammation composed of epithelioid cells with multinucleated giant cells showing intracytoplasmic crystals (H&E, original magnification x400).

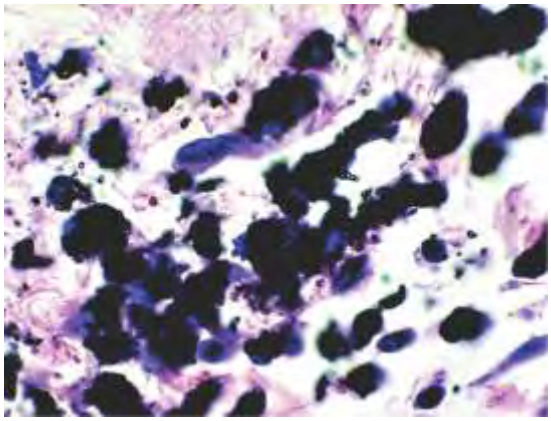

Figure 4. Photomicrograph of a tissue specimen obtained one week after the implantation of diamond polishing paste showing macrophages with intracytoplasmic black granules (H&E, original magnification x400).

containing large colorless particles was present and persisted until the end of the experiment at eight weeks.

Polarized light microscopy of the specimens revealed numerous birefringent particles in the connective tissue at all time periods examined.

NaCl 0.9% (negative control)

Examination of the smear preparation of NaCl solution using light microscopy revealed colorless crystals. Polarized light examination of the smear did not show any birefringent particles. Microscopic examination of the H&E stained sections from areas injected with saline revealed normal structures without inflammatory response at all experimental periods (*Table 1*).

Prophylaxis paste with fluoride

The smear preparation demonstrated three different particles when analyzed by conventional light microscopy. The smaller ones were rounded colorless particles measuring approximately 7 to 9 mm. The larger ones were polymorphic colorless crystals measuring approximately 30 to 50 mm. Intermixed with these were brown needle-like particles. Polarized light microscopy showed birefringence only of the needle-like particles.

Two days after implantation of the prophylaxis paste there was a mild subacute inflammatory response consisting of neutrophils with occasional macrophages and lymphocytes on examination in light microscopy (*Table 1*). Areas of edema also were noted. At one week,

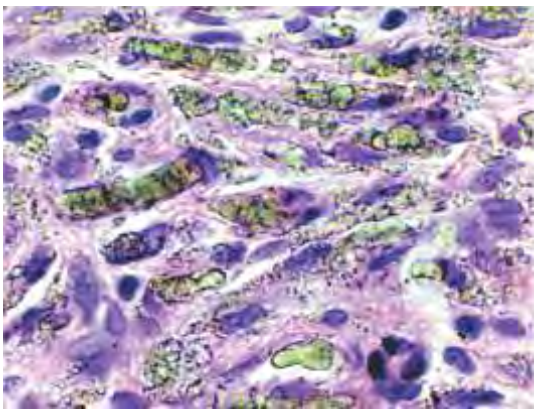

Figure 5. Photomicrograph of a tissue specimen obtained eight weeks after the implantation of aluminum polishing paste showing granulomatous inflammation with prominent phagocytic activity (H&E, original magnification x400).

the inflammatory response increased in intensity and consisted of neutrophils, lymphocytes and macrophages. At two weeks, the subacute inflammatory response was severe with abscess formation. In focal areas, larger particles were surrounded by macrophages and epithelioid cells. At four weeks, a thin fibrous capsule surrounded the particles and the intensity of the inflammatory infiltrate had decreased. The inflammatory response represented granulomatous inflammation. This type of inflammation persisted to the eighth week (*Figure 2*).

Polarized light examination of the specimens at all periods did not show the presence of the needle-like particles that were seen in the smears.

Air polishing prophylaxis powder

Under conventional light microscopy, the smear preparation of air polishing prophylaxis powder was characterized by the presence of two different particles. The smaller particles were star-like colorless crystals measuring approximately to 10 to 40 mm. The larger ones were colorless rectangular crystals of different sizes ranging from 50 to 300 mm. Polarized light examination of the smear showed birefringence of both particle types.

Microscopic examination of the H&E stained specimens in light microscopy obtained after two days and one week revealed a moderate inflammatory response composed of neutrophils and lymphocytes (*Table 1*). At two weeks, severe granulomatous inflammation with multinucleated giant cells showing intracytoplasmic crystals was observed (*Figure 3*). In addition, large extracellular crystals were also seen. At four weeks, only a mild inflammatory response consisting of lymphocytes, macrophages and occasional epithelioid cells were associated with the crystalline material. At six and eight weeks, there was no inflammatory response or evidence of residual foreign material in the sections examined. Birefringent particles were present in specimens up to four weeks.

Diamond polishing paste

Under conventional light microscopy, the smear of diamond polishing paste showed aggregates of fine dark black granules measuring 0.5 mm, as well as colorless needle-like particles. Under polarized light, only the needle-like particles demonstrated birefringence.

Microscopic examination of the 2-day specimens stained with H&E in light microscopy revealed scattered large dark aggregates and numerous small black granules. There was a moderate inflammatory response composed of lymphocytes and macrophages surrounding the foreign particles (*Table 1*). Macrophages with phagocytized intracytoplasmic black granules also were also observed. A moderate inflammatory response was observed in one- (*Figure 4*) and two-week specimens. At four weeks, a decrease of inflammation was noted with further decrease at six and eight weeks. Intracytoplasmic black granules were present in sections taken at all time periods. Polarized light examination of the specimens at every single experimental time period failed to reveal the presence of the birefringent particles observed in the smear.

Aluminum polishing paste

Using conventional light microscopy examination, the smear of aluminum polishing paste showed the presence of 0.5 mm brown granules either in a solitary arrangement or forming aggregates. These granules were not birefringent under polarized light examination.

Microscopic examination of 2-day specimens with H&E in light microscopy revealed brown aggregates and brown granules in the connective tissue. There was a moderate inflammatory infiltrate consisting of

Table 2. Comparison of pairs by Wilcoxon signed ranks tests.

	Mean Rank	Aluminum polishing paste	Prophylaxis paste with fluoride	Diamond polishing paste	Air polishing prophylaxis powder	NaCl 0.9%
Aluminum polishing paste	4.75		2.724 3	3.022 1	2.873 2	3.276 0
Prophylaxis paste with fluoride	3.38			1.292 4	2.070 7	2.719 3
Diamond polishing paste	2.88				0.541 6	2.972 2
Air polishing prophylaxis powder	2.54					2.232 6
NaCl 0.9%	1.46					

Top row: Z score, must be greater than 2.81 to be significant. The integer under the Z score is the number of tied ranks.

macrophages and lymphocytes with conspicuous active phagocytosis of the resident macrophages (*Table 1*). The intracytoplasmic foreign material phagocytosed by macrophages measured approximately 0.5 mm. At one week, a severe granulomatous inflammation composed of epithelioid and giant cells was observed. This severe granulomatous inflammation with prominent phagocytic activity was still evident at the end of the experiment at eight weeks (*Figure 5*).

Polarized light examination of the specimens at every experimental period failed to show the presence of birefringent particles.

Statistical analysis

The ranks of the inflammation differed significantly among the five materials (Friedman Test, 4 df, $p < 0.001$). The paired comparisons showed significantly more inflammation for: aluminum polishing paste (Prisma Gloss Extra Fine) compared to diamond polishing paste (Ultradent Diamond Polishing), air polishing prophylaxis powder (Prophy Jet) or negative control; and diamond polishing paste (Ultradent Diamond Polishing) compared to negative control (*Table 2*).

The pairs that differed significantly had 0 to 2 tied ranks whereas the pairs that failed to differ significantly had 3 to 7 tied ranks, thus the small sample size likely contributed to the non-significant differences between some pairs (*Table 2*).

Discussion

In 1990 Daley and Wysocki described a persistent type of gingivitis that was refractory to conventional treatment (plaque removal) and was microscopically characterized by chronic or granulomatous inflammation. The lesion was termed foreign body gingivitis (classified as non-plaque induced gingival lesion–foreign body reaction, Armitage, 1999) because foreign material could be identified in the biopsy specimens from these cases (Daley and Wysocki, 1990). Gordon and Daley (1997a) described 61 cases of this foreign body reaction and other cases also have been described by various authors (Lombardi *et al.*, 2001; Gravitis *et al.*, 2005). On microscopic examination the cases showed opaque fine granules in the tissue (Gordon and Daley, 1997a). The authors concluded that those granules represented particles of abrasive materials used for polishing the teeth or restorations (Gordon and Daley, 1997b).

We found that all polishing and prophylaxis materials used in this study produced an inflammatory response. The response was characterized by granulomatous inflammation after the first or second week. Our findings are similar to those reported by Gordon and Daley (1997a) in foreign body reaction of gingiva in patients and support their conclusion that abrasives may cause non-plaque induced gingival lesions.

Polarized light has been used as an adjunct in identifying foreign material in gingiva. About 86% of the gingival specimens examined by Gordon and Daley (1997b) showed particle birefringence. Other published cases also relied on the use of polarized light (Lombardi *et al.*, 2001; Gravitis *et al.*, 2005). In our study, only one of the pastes showed refractive particles under polarized light examination of tissue.

Prophylaxis and polishing materials are complex materials. It is difficult to determine which components produce the tissue response. Gordon and Daley (1997b) examined 61 cases of foreign body reaction in gingiva with energy dispersive x-ray microanalysis. They found that most common elements were silicon (61%), aluminum (46%) and iron (43%). Koppang *et al.* (2007) found that the most common elements in gingiva were silver (67%),

aluminum (66%) and silicon (61%) using the same technique. Silicon and aluminum are components of silica and aluminum oxide, which are frequently found in dental abrasives (Gordon and Daley, 1997b). Both prophylaxis materials and one of the polishing pastes used in our studies contained silica and it is the substance that has been implicated in the etiology of foreign body reactions by several authors (Gordon and Daley, 1997b; Pistoia and de Figueiredo, 2002).

Further studies are needed to further elucidate the etiologic agent(s) implicated in granulomatous inflammation, and it cannot be automatically assumed that the presence of particles in granulomatous inflammation of gingiva on H&E examination represent the causative agent. The particles in the gingiva may be inert and the patient may have a granulomatous inflammation due to systemic diseases, such as tuberculosis, Crohn's diseases or sarcoidosis (Rees, 1999; Alawi, 2005). It has been also shown that skin sarcoidosis lesions may contain foreign bodies and it is thought that the foreign body may induce granuloma formation in selected cases of sarcoidosis (Kim *et al.*, 2000). In order to make a diagnosis of foreign body reaction, other diagnoses of granulomatous diseases have to be eliminated.

Our studies show that incorporation of polishing and prophylaxis materials in tissue may produce an inflammatory tissue response. Consequently, it is reasonable that efforts should be made to minimize gingival incorporation of prophylaxis and polishing materials.

References

Alawi, F. Granulomatous diseases of the oral tissues: differential diagnosis and update. *Dental Clinics of North America* 2005; **49**:203-221.

Armitage, G.C. Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology* 1999; **4**:1-6.

Buchner, A. and Hansen, L.S. Amalgam pigmentation (amalgam tattoo) of the oral mucosa. A clinicopathologic study of 268 cases. *Oral Surgery Oral Medicine and Oral Pathology* 1980; **49**:139-147.

Cataldo, E. and Santis, H. Response of the oral tissue to exogenous foreign materials. *Journal of Periodontology* 1974; **45**:93-106.

Daley, T. D. and Wysocki, G. P. Foreign body gingivitis: an iatrogenic disease? *Oral Surgery Oral Medicine and Oral Pathology* 1990; **69**:708-712.

Eley, B.M. Tissue reactions to implanted dental amalgam, including assessment by energy dispersive x-ray micro-analysis. *Journal of Pathology* 1982; **138**:251-272.

Forsell, M., Larsson, B., Ljungqvist, A., Carlmark, B. and Johansson O. Mercury content in amalgam tattoos of human oral mucosa and its relation to local tissue reactions. *European Journal of Oral Sciences* 1998; **106**:582-587.

Goodman, J.R. Fractured composite restoration embedded in the lip. *British Dental Journal* 1984; **156**:293-294.

Gordon, S.C. and Daley, T.D. Foreign body gingivitis: clinical and microscopic features of 61 cases. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* 1997a; **83**:562-570.

Gordon, S.C. and Daley, T.D. Foreign body gingivitis: identification of the foreign material by energy-dispersive X-ray microanalysis. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* 1997b; **83**:571-576.

Gravitis, K., Daley, T.D. and Lochhead, M.A. Management of patients with foreign body gingivitis: report of 2 cases with histologic findings. *Journal of the Canadian Dental Association* 2005; **71**:105-109.

Hansasuta, C., Neiders, M.E., Aguirre, A. and Cohen, R.E. Cellular inflammatory responses to direct restorative composite resins. *The Journal of Prosthetic Dentistry* 1993; **69**:611-616.

Kim, Y.C., Triffet, M.K. and Gibson, L.E. Foreign bodies in sarcoidosis. *The American Journal of Dermatopathology* 2000; **22**:408-412.

Koppang, H.S., Roushan, A., Srafilzadeh, A., Stolen, S.O. and Koppang, R. Foreign body gingival lesions: distribution, morphology, identification by X-ray energy dispersive analysis and possible origin of foreign material. *Journal of Oral Pathology & Medicine* 2007; **36**:161-172.

Lombardi, T., Kuffer, R. and Dubrez, B. Polishing-paste-induced silica granuloma of the gingiva. *Dermatology* 2001; **203**:177-179.

Moore, D.L. and Barker, B.F. A foreign body lesion of the gingiva subsequent to the placement of a composite resin restoration. *Quintessence International* 1986; **17**:785-787.

Nadarajah, V., Cohen, R.E., Neiders, M.E. and Aguirre, A. Cellular inflammatory responses to implanted dental materials. *The Journal of Prosthetic Dentistry* 1996; **75**:552-561.

Nadarajah, V., Neiders, M.E. and Cohen, R.E. Local inflammatory effects of composite resins. *Compendium of Continuing Education in Dentistry* 1997; **18**:367-368.

Recommended standard practices for biological evaluation of dental materials. Fédération Dentaire Internationale, Commission of Dental Materials, Instruments, Equipment and Therapeutics. *International Dental Journal* 1980; **30**:140-188.

Pistoia, A.D. and de Figueiredo, M.A. Submucous implant of abrasive dental materials in rat tongues: clinical and histological evaluation. *Brazilian Dental Journal* 2002; **13**:103-108.

Rees, T.D. Orofacial granulomatosis and related conditions. *Periodontology 2000* 1999; 21:145 157.