IN BRIEF

- Eugenol has a long history of successful therapeutic use in dentistry, but has the capacity to cause adverse effects
- Eugenol is cytotoxic at high concentrations and can cause allergic reactions in sensitised patients
- This paper illustrates cases of such reactions occurring in general dental practice

Adverse reactions associated with the use of eugenol in dentistry

N. Sarrami[1] M. N. Pemberton[2] M. H. Thornhill[3] E. D. Theaker[4]

Eugenol is a material commonly used in dentistry with few reported side effects. It is not however, a bio-friendly material when in contact with oral soft tissues. It can produce both local irritative and cytotoxic effects, as well as hypersensitivity reactions. Here we report on two cases of adverse local reaction to eugenol, contained within a temporary restorative material and a temporary cementation material respectively, which illustrate these problems.

Allergy to materials used in dentistry is a topical issue and has been the subject of recent papers[1,2] and an editorial.[3] This interest may be due to an increasing public/practitioner awareness of the ability of dental materials to cause adverse reactions or a reflection of an increase in the population's potential for hypersensitivity type reactions. Some reports concern reactions to increasingly used materials such as hydroxyethyl methacrylate,[2] however traditional materials such as dental amalgam[1] also have the potential for allergic and other adverse reactions, although rarely. This paper describes two cases of adverse reactions to eugenol, another traditional dental material, and serves to remind colleagues of the need for care in its use.

CASE 1

A 40-year-old woman presented to her GDP for routine conservative treatment on the UL7 (27). A resin-reinforced zinc-oxide eugenol temporary dressing (Kalzinol) was initially placed over the deep cavity in the UL7 (27) followed by an amalgam restoration. Two days later an ulcer was noted buccal to the UL7 (27). A diagnosis of mechanical trauma was made and the lesion resolved over the following month. Over the next 2 months with progressive symptoms suggestive of a loss of vitality, root canal treatment of the tooth was instigated followed by a resin-reinforced zinc-oxide eugenol temporary dressing. Within 48 hours of placement of this dressing, a painful ulcer with surrounding erythema, had erupted on the adjacent buccal mucosa. A diagnosis of mechanical trauma was again made but when the ulcer showed no sign of healing a referral was made to the University Dental Hospital of Manchester.

The patient attended the Dental Hospital approximately 5 weeks after the dressing had been placed. Her medical and dental histories were unremarkable, she had no known allergies and her only medication was ibuprofen for the relief of pain from the oral ulcer. Intra-oral examination revealed a shallow ulcer with surrounding erythema in the buccal mucosa. This lay adjacent to the UL7 (27) when the mouth was closed (Fig. 1).

Given the history and the close spatial association, a provisional diagnosis of a hypersensitivity reaction to the temporary dressing material was made. The patient underwent epi-cutaneous patch testing using the Dental Materials Series (Trolab Biodiagnostics Ltd., Worcestershire, UK). A positive response to 1% eugenol was noted after 72 hours.

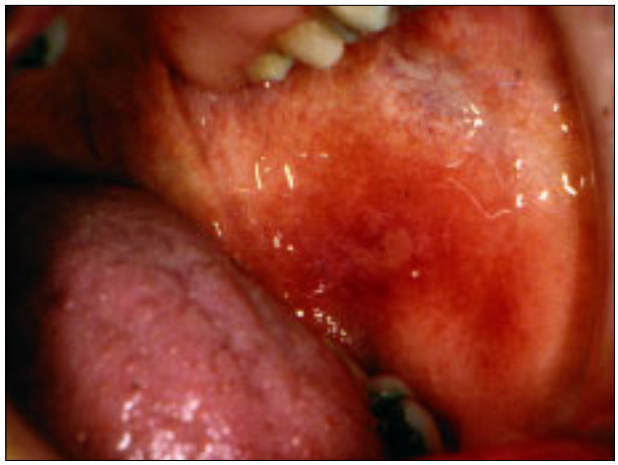

Fig. 1 Erythema and ulceration in left buccal mucosa, adjacent to UL7 (27) on closure of the mouth

[1]Staff grade, Unit of Primary Dental Care; [2*]Consultant, [4]Lecturer, Unit of Oral Medicine, University Dental Hospital of Manchester, Higher Cambridge Street, Manchester M15 6FH [3]Professor of Clinical Oral Sciences, Oral Disease Research Centre, Bart's and the London, Queen Mary School of Medicine and Dentistry, Clinical Sciences Building, 2 Newark Street, London E1 2AD
*Correspondence to: Dr M.N Pemberton, Unit of Oral medicine, University Dental Hospital of Manchester, Higher Cambridge Street, Manchester M15 6FH
E-mail: mike.pemberton@man.ac.uk

Refereed Paper
Received 02.10.01; Accepted 21.02.02

A diagnosis of type IV-delayed type hypersensitivity to eugenol was made. The restoration in the UL7 (27) was replaced with a non-eugenol containing material and the ulcer rapidly resolved thereafter.

CASE 2

A 53-year-old man attended his GDP with a fractured porcelain jacket crown (PJC) which had been in place on the UR1 (11) for about 30 years. The GDP replaced this with an acrylic temporary crown, which was cemented in place with zinc-oxide eugenol cement (Sedanol™).

One week later the temporary crown was removed, the tooth was prepared, an impression with an elastomeric material was taken, and the existing temporary crown was recemented as before with the same zinc-oxide eugenol cement.

On his return to the surgery a further week later, the patient complained of acute pain in his gums that had started soon after his last visit. On examination the GDP noted marked erythema and destruction of the interdental papillae. The temporary crown was removed and the permanent PJC cemented with a polycarboxylate cement. The patient was prescribed a short course of metronidazole. Upon review a further 2 days later, the patient was only a little improved and so was referred to the University Dental Hospital of Manchester for further management.

The patient presented to the Dental Hospital on the same day. His medical and dental histories were unremarkable and he had no known allergies. His only medication was the metronidazole prescribed by his GDP. On examination, swelling of the upper lip and erythema of its inner aspect was noted. Intra-orally destruction of the interdental col and surrounding gingivae was present (Fig. 2). The patient was prescribed benzydamine hydrochloride mouthwash and triamcinolone in orobase for relief of his acute symptoms. A full blood count was performed, and a latex specific IgE titre was assayed. Both results were normal. Two weeks later the patient underwent epi-cutaneous patch testing (Trolab Biodiagnostics Ltd, Worcestershire, UK) against the most likely allergens to which he had been exposed, including the Dental Material Series (the impression material was not available for testing). At the reading 72 hours later there was a positive reaction to 1% eugenol. By this visit the gingival and mucosal conditions were improved (Fig. 3) and the symptoms had disappeared. The results were consistent with a hypersensitivity response to eugenol. The patient and the GDP were both informed of its implications and the need for avoidance of products containing eugenol in the future.

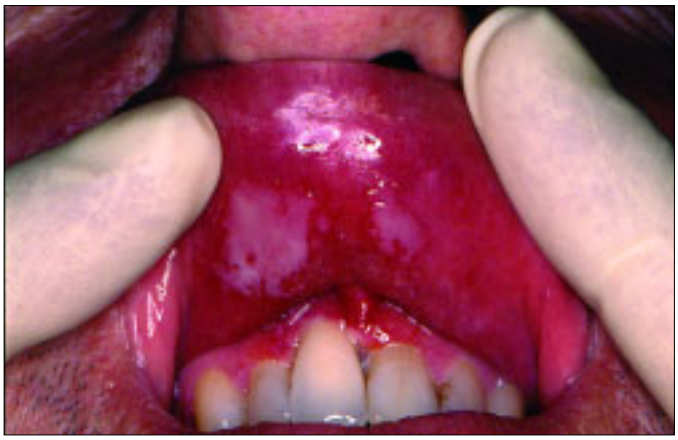

Fig. 2 Erythema and ulceration on the inner surface of the upper lip and around the gingival margin of UR1 (11)

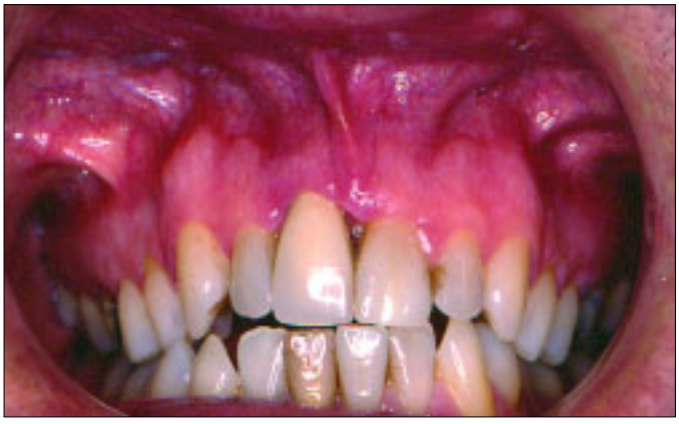

Fig. 3 Healed gingival margin around UR1 (11), showing loss of interdental papilla between the central incisors

DISCUSSION

Oil of cloves (eugenol in its unrefined form) has been a popular remedy for toothache for over a century. Chisholm[4] in 1873 described its mixture with zinc oxide to form a plastic mass and its therapeutic uses. It has sedative and anodyne effects[5] as well as antibacterial properties.[6] Eugenol is found as a major ingredient in a variety of dental materials such as impression materials, filling materials, dental cements, endodontic sealers, periodontal dressing materials and dry socket dressings.

These materials rely on a setting reaction between zinc oxide and eugenol, which produces zinc eugenolate. This substance however is not stable in the presence of water. The surface of the set material readily undergoes hydrolysis with the release of free eugenol. This release is initially rapid and then decreases exponentially, as all the surface eugenol is hydrolysed. The free eugenol can interact with other dental materials[7–9] and hence eugenol-containing materials are not used in conjunction with composite luting cements or resin composite restorative materials.

Free eugenol can also be of detriment to human soft tissues. Adverse effects of eugenol in the oral cavity have been reported in association with its use in surgical and periodontal packs,[10] root canal sealers,[11,12] mouthrinses,[13] and in impression pastes.[14] Adverse reactions to eugenol amongst dental personnel are also well documented. These reactions range from localised irritation of the skin to allergic contact dermatitis.[15–18]

The type and extent of oral soft tissue reactions to eugenol vary, but can be thought of in three ways:

1. Eugenol is generally cytotoxic at high concentrations and has an adverse effect on fibroblasts and osteoblast-like cells.[19–21] Thus at high concentrations it produces necrosis and reduced healing. This effect is dose related and will potentially affect all patients.
2. In lower concentrations, eugenol can act as a contact allergen evoking a localised delayed hypersensitivity reaction.[10,13,14]
3. Rarely, eugenol when placed in the mouth, can cause a more significant generalised allergic response.[12] One particularly sensitive patient is reported to have developed anaphylactic-like shock subsequent to a pulpotomy in which zinc-oxide and eugenol cement was used.[22]

In the 1960s eugenol was a common constituent of dressings used after periodontal surgery. As eugenol was a well known contact allergen in dermatology,

investigation soon centred on its ability to sensitise patients after dental use. Koch *et al.*[10] found that the majority of patients who experienced stomatitis following the placement of a surgical dressing containing eugenol, were found to be sensitised to eugenol and/or colophony on patch testing.

In further experiments Koch *et al.*[23] assessed the risk of inducing sensitisation to eugenol, secondary to the placement of a surgical dressing containing eugenol. Out of 133 patients who had patch tested negative to eugenol prior to periodontal surgery, 12 tested positive post-operatively. The results indicated a sensitisation rate of almost 10% and as such the use of eugenol-free periodontal dressings became favoured.

Everyone is vulnerable to hypersensitivity although individual susceptibility varies. Fragrances and perfumes are widely encountered in our daily environment and are a common cause of contact allergy. Eugenol is regarded as one of the most common sensitizers of the fragrance group. In a group of 5,202 patients tested for contact dermatitis by epicutaneous patch testing, 43 (0.8%) gave a positive response to eugenol.[24] Amongst the general population the prevalence of hypersensitivity to eugenol is unknown, however the figure is likely to be lower than this. Reassuringly, there does not appear to have been any increase in eugenol hypersensitivity over the past two decades.[25] Furthermore, the oral implication of epi-cutaneous patch testing of dental materials is unclear. In general, the mouth and the oral mucosa appear to be less sensitive to contact allergens than the skin, possibly because allergens are constantly diluted and washed away by the saliva.

In the cases reported here, the history of the lesions, their clinical relationship to eugenol containing dental material, coupled with the evidence of a positive patch test result would indicate that a genuine hypersensitivity reaction to eugenol was involved in the aetiology of the oral lesions.

In Case 1 the patient was exposed to eugenol and on two separate occasions showed a reaction that took 2–3 days to appear and resolved only after removal of the eugenol containing material. The reaction was typical in its presentation of a localised reaction confined to a small area, analogous to allergic contact dermatitis.

Case 2 probably displays a mixture of eugenol's allergic, irritant, and cytotoxic effects. Eugenol in high enough concentrations to be cytotoxic may explain the direct tissue damage and necrosis (as evident circumferentialy around the gingival col). The more widespread inflammation of the lip may have been allergic in nature.

CONCLUSIONS

Eugenol is widely used in dentistry. It is generally used without incident however in a sensitised individual it can cause a range of tissue effects, from low-grade local reactions to the rare, but serious, anaphylactic reaction. Eugenol is not a bio-friendly material and patients should be discouraged from using it in its pure form, either to alleviate toothache or dentine hypersensitivity. Eugenol containing materials need to be used in the appropriate amounts and manufacturer's instructions should be followed. For patients who are allergic to eugenol, eugenol-free alternatives are available.

1. McGivern B, Pemberton M, Theaker E D, Buchanan J A, Thornhill M H. Delayed and immediate hypersensitivity reactions associated with the use of amalgam. *Br Dent J* 2000; **188:** 73-76.
2. Moore M M, Burke F J T, Felix D H. Allergy to a common component of resin-bonding systems: A Case report. *Dent Update* 2000; **27:** 432-434.
3. Burke T F J. Allergic to dentistry? *Dent Update* 2000; **27:** 421.
4. Chisholm E C. Proceedings of the Tennessee Dental Association, 7th annual meeting- Nashville . *Dent Regist October* 1873; **27:** 517.
5. Hume W R. The pharmacological and toxicological properties of zinc oxide-eugenol. *J Am Dent Assoc* 1986; **113:** 789-791.
6. Newman M G, Hulem C, Colgate J, Anselmo C. Antibacterial susceptibility of plaque bacteria. *J Dent Res* 1979; **58:** 1722-1732.
7. Mayer T, Pioch T, Duschner H, Staehle H J. Dentinal adhesion and histomorphology of two dentinal bonding agents under the influence of eugenol. *Quintessence Int* 1997; **28:** 57-62.
8. Al-Wazzan K A, al-Harbi A A, Hammad I A. The effect of eugenol-containing temporary cement on the bond strength of two resin composite core materials to dentin. *J Prosthodont* 1997; **6:** 37-42.
9. Millstein P L, Nathanson D. Effects of temporary cementation on permanent cement retention to composite resin cores. *J Prosthet Dent* 1992; **67:** 856-859.
10. Koch G, Magnusson B, Nyquist G. Contact allergy to medicaments and materials used in dentistry. II. Sensitivity to eugenol and colophony. *Odontol Revy* 1971; **22:** 275-289.
11. Hensten-Pettersen A, Orstavik D, Wennberg A. Allergenic potential of root canal sealers. *Endo Dent Traumatol* 1985; **1:** 61-65.
12. Barkin M E, Boyd J P, Cohen S. Acute allergic reaction to eugenol. *Oral Surg Oral Med Oral Pathol* 1984; **57:** 441-442.
13. Vilaplana J, Grimalt F, Romaguera C, Conellana F. Contact dermatitis from eugenol in mouthwash. *Contact Dermatitis* 1991; **24:** 223-224.
14. Goransson K, Karltorp N, Ask H, Smedberg O. Nagra fall av eugenoloverkanslighet (some cases of eugenol hypersensitivity). *Svensk Tandlakaretidskrift* 1967; **60:** 545-549.
15. Jacobsen N, Hensten-Pettersen A. Occupational health problems and adverse patient reactions in periodontics. *J Clin Periodontol* 1989; **16:** 428-433.
16. Hensten-Pettersen A, Jacobsen N. Perceived side effects of biomaterials in prosthetic dentistry. *J Prosthet Dent* 1991; **65:** 138-144.
17. Rudzki E, Rebandel P, Grzywa Z. Patch tests with occupational contactants in nurses, doctors and dentists. *Contact Dermatitis* 1989; **20:** 247-250.
18. Kanerva L, Estlander T, Jolanki R. Dental nurse's occupational allergic contact dermatitis from eugenol used as a restorative dental material with polymethylmethacrylate. *Contact Dermatitis* 1998; **38:** 339-340.
19. Lindqvist L, Otteskog P. Eugenol: liberation from dental materials and effect on human diploid fibroblast cells. *Scand J Dent Res* 1980; **88:** 552-526.
20. Alpar B, Gunay H, Geurtsen W, Leyhausen G. Cytocompatibility of periodontal dressing materials in fibroblast and primary human osteoblast-like cultures. *Clin Oral Investig* 1999; **3:** 41-48.
21. Kozam G, Mantell G M. The effect of eugenol on oral mucous membranes. *J Dent Res* 1978; **57:** 954-957.
22. McCarter R F. An unusual allergy. *Midwest Dent* 1966; **42:** 20.
23. Koch G, Magnusson B, Nobreus N, Nyquist G, Soderholm G. Contact allergy to medicaments and materials used in dentistry. (IV). Sensitizing effect of eugenol-colophony in surgical dressing. *Odontol Revy* 1973; **24:** 109-114.
24. Broeckx W, Blondeel A, Dooms-Goossens A, Achten G. Cosmetic intolerance. *Contact Dermatitis* 1987; **16:** 189-194.
25. Buckley D A, Wakelin S H, Seed P T, *et al.* The frequency of fragrance allergy in a patch-test population over a 17-year period. *Br J Dermatol* 2000; **142:** 279-283.