

## Short communication

# Occupational conjunctivitis associated with type IV allergy to methacrylates

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On rare occasions, exposure to methacrylates (MAs) may induce mucosal symptoms. Three patients, two dental laboratory workers and one hearing aid laboratory worker, are presented. All three had allergic contact dermatitis from MAs which disappeared after avoidance of contact with uncured MA compounds. Two of the patients, the dental laboratory assistant and the hearing aid worker, had also developed symptoms of conjunctivitis. Both were exposed to chemically curable and light-curable MAs. The association between their conjunctivitis and type IV allergy to MAs was supported by the following observations: 1) sensitization to several MAs including methylMA, 2-hydroxyethylMA, ethyleneglycol diMA, triethyleneglycoldiMA, tetrahydrofurfuryldiMA, and 1,4-butanedioldiMA, as well as to pentaerythritol triacrylate; 2) simultaneous appearance of their eye symptoms and allergic contact dermatitis; 3) high exposure to MAs because of disturbances of ventilation; 4) disappearance of the eye symptoms during holidays; and 5) ophthalmologist's findings of follicular conjunctivitis with some papillae, eosinophilia, and lymphocytosis in conjunctival scrapings corresponding to allergic contact conjunctivitis. In addition, the activation of eosinophils in the conjunctival scrapings was demonstrated with the monoclonal antibody technique, and an elevated level of eosinophilic cationic protein was found in the tear fluid. Our cases suggest that conjunctivitis may be caused by type IV allergy to MAs, although type I allergy (even though prick tests were negative), other hypersensitivity mechanisms, or irritation cannot be excluded. 4H-Gloves® seem to give adequate hand protection even to allergic patients. More attention should be paid to ventilation systems if MA exposure occurs. In some cases, patients with eye symptoms need to be patch tested.

**Key words:** contact dermatitis; dental laboratory assistant; ethylene glycoldimethacrylate; hearing aid worker; methylmethacrylate; pentaerythritol triacrylate; triethylene glycoldimethacrylate; 2-hydroxyethylmethacrylate.

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Working with methacrylates (MAs) may lead to an exposure which is sufficient on rare occasions to induce asthma (1–3) or mucosal symptoms (4). The reported asthma patients also had rhinitis, but not eye symptoms. The mechanism of sensitization in these cases has not been defined. In the case of pharyngitis, the patient had only pharyngeal symptoms. Type IV sensitization to several MAs and other acrylate compounds was revealed though no skin symptoms appeared. Contact dermatitis associated with eye symptoms and caused by type IV allergy to ophthalmic drugs and contact lens solutions is well known and has been reviewed by Herbst & Maibach (5) and de Groot et al. (6). As a result of airborne exposure to MAs, the eyes

could be one of the shock organs also in patients with delayed-type sensitivity to MAs.

We report on two dental laboratory workers, a dental laboratory assistant and a dental technician, as well as on a hearing aid worker who developed allergic contact dermatitis. The laboratory assistant and the hearing aid worker also had work-related eye symptoms.

## Material and methods

### Patients

Thirty cases of allergic contact dermatitis and one case of pharyngitis from MAs in dental restorative

and prosthetic materials were diagnosed during 1974-94 at the Finnish Institute of Occupational Health. Five of the patients worked in dental laboratories. In addition, one patient was diagnosed as having allergic contact dermatitis from the preparation of in-the-ear hearing aids.

Two of the five dental laboratory workers were employed by the same dental laboratory (patients 1 and 2). The man (patient 1) had handled chemically curable MA for 3 years and light-curable MA for about 1 week (Table 1). The woman (patient 2) had used only chemically curable MAs for 8 years. The hearing aid worker (patient 3) had prepared in-the-ear hearing aids from chemically curable MA for 9 years and had covered the devices with a light-curable acrylic lacquer for 3 years (Table 1).

### Skin tests and other investigations

Epicutaneous tests were conducted using the Finn Chambers (Epitest Ltd Oy, Finland) and read and scored as previously described (7, 8). They included the European standard series, a dental screening series, and a (meth)acrylate series, all from Chemotechnique Diagnostics AB, Sweden. Patch tests were also carried out with acrylate and other products used at the workplaces. Prick tests included a series of environmental allergens and a latex allergen (Allergologisk Laboratorium A/S, Denmark). They were also done with two other latex prick test solutions prepared as described by Turjanmaa et al. (9), and with methylmethacrylate (MMA) and 2-hydroxyethylmethacrylate

(2-HEMA) conjugated with human serum albumin (HSA) (4, 10). Other investigations consisted of an ophthalmologist's examination of the eyes including conjunctival scrapings, and, in one case, demonstration of the activation of eosinophils with the monoclonal antibody (EG2, Pharmacia Diagnostics AB, Sweden) technique, and determination of eosinophilic cationic protein (ECP) in tear fluid. The investigations also included an industrial hygienist's inspection of the dental laboratory, determinations of airborne MMA concentrations with the charcoal method (SFS standard 3861), and gas chromatographic analyses of MMA in two cured hearing aids.

### Case reports and Results

The dental laboratory assistant (patient 1) had developed, after fingertip dermatitis, eye symptoms, which appeared soon after he had started to handle light-curable MA liquids. The redness, stinging, and itching of his eyes were worst during the last days of the working week and after he had polished light-curable materials. He had neither nasal nor chest symptoms. During holidays, his eyes were symptomless, without any medication. He continued in the same work, and the half-year follow-up confirmed the clinical association of his eye symptoms with his work. An ophthalmologist's findings (Table 2) included follicular and papillary conjunctivitis in lower lid conjunctiva and hyperemic bulbar and tarsal conjunctivae. The corneas were quite clear, and no signs of corneal inflammation were seen. His conjunctival scrapings showed strong lymphocytic reaction and activated eosinophils. The tear ECP was elevated (7 µg/l) compared to the levels found in healthy nonatopic subjects. The patient was atopic and prick test positive to grass pollen, mugwort (*Artemisia*), and a house-dust mite (*Dermatophagoides farinae*). He had had

Table 1. Acrylate compounds used in work of patients according to information from material safety data sheets

| Dental laboratory<br>(patients 1 and 2) | Hearing aid laboratory<br>(patient 1) |
|-----------------------------------------|---------------------------------------|
| <i>Chemically curable material</i>      | <i>Chemically curable material</i>    |
| Liquid:                                 | Liquid:                               |
| MMA                                     | MMA                                   |
| N,N-dimethyl-p-toluidine                | Oimethacrylate                        |
| Ethylene glycol dimethacrylate          | Aromatic amine                        |
| Hydroquinone                            |                                       |
| Terpinoline                             |                                       |
| Powder:                                 | Powder:                               |
| Polymethylmethacrylate                  | Polymethylmethacrylate                |
| Dibutylphthalate                        | Dibenzoylperoxide                     |
| <i>Light-curable material</i>           | <i>Light-curable material</i>         |
| Liquid 1:                               | Acrylic lacquer:                      |
| Diacylurethane monomer                  | MMA                                   |
| 1,6-Hexanediol dimethacrylate           |                                       |
| Initiators, accelerators                |                                       |
| Liquid 2:                               |                                       |
| MMA                                     |                                       |
| Tetrahydrofurfuryl methacrylate         |                                       |
| 1,6-Hexanediol dimethacrylate           |                                       |
| Initiators, accelerators                |                                       |

Table 2. Ophthalmologist's findings on two conjunctivitis patients with type IV allergy to (meth)acrylates

| Finding                                                       | Dental laboratory<br>assistant<br>(patient 1) | Hearing aid<br>worker<br>(patient 3) |
|---------------------------------------------------------------|-----------------------------------------------|--------------------------------------|
| Redness of conjunctiva                                        | Yes                                           | Yes                                  |
| Negative conjunctival bacterial culture                       | Yes                                           | Yes                                  |
| Follicular and papillary reactions of conjunctiva             | Yes                                           | No                                   |
| Eosinophilia and lymphocytosis in one or both eyes            | Yes                                           | Yes                                  |
| Activation of eosinophils                                     | Yes                                           | ND                                   |
| Elevated level of eosinophilic cationic protein in tear fluid | Yes (7 µg/l)                                  | ND                                   |
| Corneal changes                                               | No                                            | No                                   |
| Lomudal® relieves the symptoms                                | Yes                                           | Yes                                  |

ND: not done.

eye symptoms during the pollen season, but not during the past 15 years. The dental technician (patient 2) had pulpitis on her fingers only. The skin symptoms of both dental laboratory workers disappeared when they used finger protectors made of 4H-Gloves® (Safety 4 A/S, Denmark). On patch testing, in addition to MMA, the man (patient 1) reacted to many other MAs (Table 3), to a liquid containing MMA, and slightly to polymethylmethacrylate powder (Table 4). The dental technician (patient 2) was clearly 2+ positive only to 2-HEMA and the liquid containing MMA, but reacted with a weak ?+reaction to ethyleneglycol dimethacrylate (EGDMA).

The hearing aid worker's (patient 3) eye symptoms had begun at the same time as her fingertip dermatitis; i.e., 3 years after she had started to use a light-curable acrylic lacquer. She also continued her work after her sensitization to MAs was confirmed. Her eye symptoms were at first mild and occasional, but got worse during the 4-year follow-

up period. No nasal or chest symptoms appeared. Her eye findings included eosinophilia and moderate neutrophilic and lymphocytic reaction in the conjunctival scrapings. She had neither follicular nor papillary conjunctival hypertrophy, and the tarsal conjunctiva was mildly hyperemic (Table 2). She was nonatopic and prick test negative to environmental allergens, but had atopic dermatitis in her family. She was patch test positive to several MAs and dimethacrylate compounds (Table 3), as well as to a liquid containing MMA, a cured ear device (contained free MMA up to 3.3 mg/g), and light-curable acrylic lacquer (Table 4). Prick tests with MMA-HSA and 2-HEMA-HSA were negative in all three patients.

The ventilation system was inadequate in both workplaces. The air there was not replaced satisfactorily, and possibly part of the removed air returned to the working room. The MMA values in the air of the dental laboratory were 13–32% of the Finnish hygienic reference values (100 ppm/m<sup>3</sup> air/8 h and 150 ppm/m<sup>3</sup> air/15 min) (Finnish Ministry of Labour, Safety data sheet no. 25/1993).

Table 3. Patch test results of two conjunctivitis patients with (meth)acrylate series

| (Meth)acrylate                       | Dental laboratory assistant (patient 1) | Hearing aid worker (patient 3) |
|--------------------------------------|-----------------------------------------|--------------------------------|
| Methylmethacrylate (MMA)             | 3+                                      | 2+                             |
| Ethylmethacrylate                    | 2+                                      | 1+                             |
| 2-Hydroxyethylmethacrylate (2-HEMA)  | 3+                                      | 2+                             |
| 2-Hydroxypropylmethacrylate (2-HPMA) | 3+                                      | 2+                             |
| Ethylacrylate                        | NT                                      | 2+                             |
| 2-Hydroxyethylacrylate               | NT                                      | 2+                             |
| 2-Hydroxypropylacrylate              | NT                                      | 2+                             |
| Ethyleneglycol dimethacrylate        | 3+                                      | 2+                             |
| Triethyleneglycol dimethacrylate     | 3+                                      | 1+                             |
| Triethyleneglycol diacrylate         | Neg                                     | 2+                             |
| Tetrahydrofurfuryl dimethacrylate    | 2+                                      | NT                             |
| 1,4-Butanediol dimethacrylate        | 2+                                      | Neg                            |
| 1,4-Butanediol diacrylate            | Neg                                     | 2+                             |
| 1,6-Hexanediol diacrylate            | Neg                                     | 2+                             |
| Diethyleneglycol diacrylate          | Neg                                     | 2+                             |
| Urethane diacrylate, aromatic        | Neg                                     | 2+                             |
| Pentaerythritol triacrylate          | Neg                                     | 2+                             |

NT: not tested; Neg: negative.

Table 4. Positive patch test results of two conjunctivitis patients tested with (meth)acrylate products used in their work

| Product                                    | Dental laboratory assistant (patient 1) | Hearing aid worker (patient 3) |
|--------------------------------------------|-----------------------------------------|--------------------------------|
| Methylmethacrylate (MMA) liquid 2% pet     | 2+                                      | 2+                             |
| Polymethylmethacrylate powder as such      | 1+                                      | Neg                            |
| Cured in-the-ear hearing aid* as scrapings | NT                                      | 1+                             |
| Light-curable acrylic lacquer              | NT                                      | 2+                             |

NT: not tested; Neg: negative; pet: petrolatum.

\* Analyzed by gas chromatography; contains up to 3.3 mg/g free MMA.

## Discussion

The workers in dental and hearing aid laboratories are usually exposed to mixtures (11) of numerous chemicals (Table 1). The compounds are of commercial grade; i.e., they may also contain many impurities. Both of the patients who had conjunctivitis had type IV sensitization to several MAs including MMA. In addition, the hearing aid worker was sensitive to several diacrylates and pentaerythritol triacrylate (PETA), an allergen found in UV-curable acrylic compounds (12). PETA may have been included in the acrylic lacquer though the material safety data sheet mentioned MMA only. However, most of the several patch reactions to acrylate compounds could be explained by cross-sensitization, but concomitant sensitization was also possible because of impurities. In agreement with the reported case of pharyngitis (4), mucosal symptoms may be associated with extensive sensitization to acrylate compounds. The third patient (patient 2) reacted to two dimethacrylates only, and she also had the least clinical symptoms and no mucosal symptoms. Acrylate compounds are volatile, and disturbances in the ventilation may have periodically caused the peaks of airborne MMA concentrations to be even higher than the values found in the determinations. Free MMA was found in the chemically cured, in-the-ear hearing aid, and the scrapings of the device gave a positive patch test reaction to the sensitized hearing aid worker. Sensitization to MMA has also been reported from the use of such a device (13).

The eye symptoms of the two patients were associated with their exposure to both chemically curable and light-curable materials. Newer light-curable acrylic compounds may be even more potent allergens, as well as irritants, than the older ones (4, 11). This may have contributed to the patients' sensitization and the appearance of their eye symptoms. When examined immediately after their work, the two patients displayed eye findings (Table 2) that correspond to allergic contact conjunctivitis reactions associated with type IV allergy (14, 15). Langerhans' cells, the key cells of type IV allergy, are present in the human conjunctiva (16) and also in the cornea after various stimuli and inflammation of the cornea (17). However, the eye findings in allergic contact conjunctivitis partly resemble those found in late-phase type I allergic reactions (18). Thus, type I reactions cannot be excluded even though prick tests with the two MA compounds were negative (4). The preparation of HSA-conjugates entails many problems (4), and acrylates other than the two used in prick tests may be responsible for the reactions. Corresponding to a type I allergic conjunctival reaction, the activation of eosinophils was demonstrated, and in agreement with this finding, an elevated level of ECP was found in the tear fluid of patient 1 (18). On the other hand, eosinophilia can also be a manifestation of type IV allergy, as is seen in allergic blepharoconjunctivitis caused by ophthalmic drugs (19). In addition, other hypersensitivity mechanisms or irritation must also be kept in mind.

All three patients have continued their work, including the handling of dental or hearing aid acrylates. The ventilation systems have been repaired, and the conjunctivitis patients use Lomudal® (sodium chromoglycate) eye-drops when at work, and the dental workers wear on their fingers 4H-Gloves protectors.

Our cases suggest that light-curable MAs may be even more hazardous than chemically curable MA; this is in accordance with our previous experience. The findings also suggest that conjunctivitis may be caused by type IV allergy to MAs, although type I allergy, other hypersensitivity mechanisms, and irritation cannot be excluded. 4H-Gloves seem to give adequate protection even to allergic patients. More attention should be paid to ventilation systems if MA exposure occurs. In some cases, patients with respiratory and eye symptoms need to be patch tested.

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