

# Investigation of reactions to dental materials

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## Summary

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Patients undergoing dental treatment can be exposed to a wide range of potential allergens, but adverse events seem infrequent. Patients with symptoms or signs of stomatitis, burning, tingling, cheilitis, oral lichenoid lesions, lip and facial swelling may relate their problems to dental treatment or to the use of dental products. Investigation for immediate type or delayed type hypersensitivity is indicated using patch testing, prick testing and blood tests for allergen-specific IgE. The main allergic reactions found in patients include contact allergy to metals, cosmetics, food additives, flavours and acrylates, and immediate type allergy to latex. Adverse reactions following the administration of local anaesthetics are seen in about 0.5% of cases, but immediate type allergy to these agents is rare. In dental staff, occupationally related problems are common and usually take the form of hand or facial dermatitis or respiratory disease. The most common allergic reactions in dental staff are immediate type allergy to latex, and contact allergy to rubber additives, fragrances, acrylates and formaldehyde. Occupational irritant problems causing hand dermatitis are probably more common in dental personnel than is dermatitis caused by contact allergy. Patch testing and tests for immediate type allergy are useful investigative methods in the investigation of patients who present with oral or facial symptoms possibly related to dental treatments and are also beneficial in dental personnel who present with hand or facial dermatitis or respiratory symptoms.

The incidence of adverse reactions to dental treatment and dental products is difficult to estimate but seems to be low considering the number of dental treatments undertaken in westernized countries. The best estimates come from the Scandinavian reporting schemes, which suggest that some sort of adverse event may occur with an incidence of between 1 in 700 and 1 in 2600 dental procedures and which may tend to be more common in specialized practices.<sup>1-3</sup>

Dentists and their staff use many potential allergens and irritants in the course of their work. These materials include antiseptics, metals, impression materials, local anaesthetics, ultraviolet radiation, cements, latex gloves, rubber dams, acrylics, adhesives, mouthwashes and other dental hygiene materials. Many of these materials can be allergens, irritants or sometimes both. It is not uncommon for a patient to give a history of having a reaction after dental treatment, within minutes, hours or weeks. Dentists use many metals in amalgam restorations, most notably mercury, which may give an oral lichenoid eruption, and use gold and platinum group metals for inlays, crowns or bridges, which may give allergic reactions. Dentists use acrylate resins extensively for dentures, and even traces of these plastics can sometimes give rise to allergic symptoms, although most cases of apparent reactions to dentures are not 'allergic' in origin. The presentation of

oral complaints can include stomatitis, lichenoid changes, burning in the mouth, cheilitis and lip swelling, facial swelling, general symptoms and anaphylaxis.

Dental personnel have a high frequency of occupational skin problems and may complain of hand dermatitis or itching, facial eruptions or respiratory symptoms. With regard to oral lichenoid lesions, the proportion of patients allergic to mercury on patch testing varies according to series. Studies show that even in patients with oral lichenoid changes not allergic to mercury on patch testing, removal of adjacent amalgam can improve the lichenoid change, suggesting that in some patients the mechanism might be irritant as well as allergic, although the mechanism remains unknown in these cases. Gold, often regarded by dentists as inert, can cause lichenoid eruption or other changes. The role of palladium, used extensively in dental alloys and commonly found as positive on patch testing usually in combination with nickel, is still very difficult to judge.

Cheilitis is particularly difficult to investigate, as there are many causes. The aetiology is irritant (lip lick) in a third, allergic contact dermatitis in a quarter (e.g. to medicaments, toothpaste materials or colophonium in dental floss) and atopic eczema in a fifth.<sup>2</sup> Benzoates, antioxidants or flavourings in foods are sometimes found to cause lip swelling. Hand

dermatitis is common in dental personnel: about two-thirds give a history of having had it at some time,<sup>4</sup> 14% in the last year.<sup>5</sup> Common causes are irritancy, latex contact urticaria, and allergic contact dermatitis to acrylates, Myroxyton, fragrance, thiuram and colophonium. The investigation of reactions in dental patients is difficult as many things need to be considered and quite often the cause is not related to the dental materials suspected.

The hypersensitivity reactions can be a type I (immediate, IgE-mediated) reaction, e.g. as seen with latex, latex-fruit allergy, formaldehyde or, very rarely, local anaesthetics, or a type IV (cell-mediated, delayed) reaction, e.g. allergic contact dermatitis to a toothpaste flavouring, metal used in a dental prosthesis, rubber in gloves worn by a dental technician, or mercury in some cases of oral lichenoid reaction, or occasionally a mixture of the two types of reaction (e.g. to latex). In some cases, the mechanisms of the hypersensitivity reactions are unknown. In this article, the potential allergens used in dental practice will be outlined, the types of reaction that patients may have after dental treatment considered, the occupational syndromes that may be seen in dental personnel discussed and an outline will be given on how these problems can be investigated.

### Potential allergens and irritants used by dentists

General materials that might be irritant or occasionally allergenic to staff or patients include antiseptics used for cleaning and disinfecting, and hygiene products, such as mouthwash, toothpaste, hand wash and lip products. Other possible irritants include etching gels, astringents and acids.

Impression materials, usually made of silicone or polyether, can occasionally be suspected of causing a reaction. Local anaesthetics are often suspected by patients and sometimes by dentists of causing problems, but the incidence of true allergy is very low. Cements occasionally cause symptoms.

The main allergens used by dentists are metals, rubber products, acrylates and resins. Metals are used for amalgams, inlays, crowns, bridges, posts, cores and braces. The metals employed in amalgam include mercury, tin, silver and copper. Gold alloys contain varying amounts of gold mixed with silver, copper, and smaller amounts of platinum, palladium and zinc. Silver-palladium alloys are used and contain zinc and copper as well as the palladium and silver. Other metals used include cobalt, chromium, molybdenum, beryllium, gallium, rhodium and iridium. Positive patch tests to gold correlate with the amount of gold in dental prostheses, but the presence of cell-mediated allergy does not bear a relationship to oral lesions.<sup>6</sup>

Rubber is usually encountered in the form of latex gloves worn by staff<sup>7</sup> or as rubber dams. Resins, usually acrylates, are employed in composites for filling teeth, as bonding agents and in the manufacture of dentures. Acrylates are commonly used for dentures, composite restorations and bonding materials.<sup>8</sup> Commonly used compounds include methyl methacrylate

(MMA), triethylene glycol dimethacrylate (TGDMA) and polymethyl methacrylate. Occasionally, problems are suspected from traces in the denture of the initiator benzoyl peroxide, or the inhibitor hydroquinone, or the plasticizer dibutyl phthalate. Other potential allergens in dentures include pigments, dyes, nylon fibre and titanium/zinc oxides.

Patients may complain of sore mouth (stomatitis) or mouth ulceration, soreness in the mouth from oral lichenoid lesions, burning or tingling in the mouth, an eruption on the lips (cheilitis) or lip swelling, facial eruption or more systemic and extreme problems such as anaphylaxis.

### Oral lichenoid reactions

Patients with oral lichenoid lesions complain of soreness or discomfort in the mouth, or have oral ulceration (Fig. 1). Several studies have demonstrated an association with delayed type hypersensitivity to mercury or occasionally to other metals, although the proportion of patients with this allergy depends on the series reported. Laine *et al.* found that of the 118 patients with oral lichenoid lesions they patch tested, 80 had an allergy to a metal, with 78 reacting to mercury, 11 to gold, four to cobalt, three to tin, two to silver, two to palladium and one to chromium (with 17 being nickel allergic).<sup>9</sup> By contrast, others have found smaller proportions of patients with oral lichenoid lesions to be allergic to mercury; of 55 patients patch tested in Sheffield, 22 were allergic to mercury, four to both mercury and gold, one to gold alone and one to gold and palladium.<sup>10</sup> The proportion was only 1 in 12 in another study.<sup>11</sup>

Occasionally, oral lichenoid lesions may be due to other metals in dental prostheses, e.g. chrome and cobalt.<sup>12</sup> When assessing for metal allergy by patch testing, it may be necessary to undertake a late reading at 10 or more days, as up to a third of patients with mercury allergy have negative patch tests at 4 or 7 days.<sup>13</sup>

Removal of the amalgam restoration adjacent to the area of oral lichenoid reaction produced healing or much improvement in 102 of 105 cases.<sup>14</sup> Others have shown similar benefits.<sup>15</sup> Lesions on the sides of the tongue improve best and



Fig 1. Oral lichen planus (patch testing was positive for mercury).

lesions in patients with cutaneous lichen planus do not respond well.<sup>14</sup> Some authors suggest that the problem may be irritant (and the cause of oral lichenoid reaction) in certain cases as removal of the amalgam can be beneficial even when the patient is patch test negative to mercury.<sup>14,16</sup>

### Burning mouth syndrome

Patients who complain of burning in the mouth without any physical sign of mucosal disease are difficult to evaluate and the symptom seems akin to burning experienced at other sites of the body, e.g. vulvodinia. Most patients are denture wearers; a few have iron or folate deficiency, or infection with *Candida albicans*, but in others 'psychological factors' are thought to be most important. It is felt that, in most cases, burning mouth symptoms are not due to allergic mechanisms.<sup>17</sup> If a patient has signs, e.g. redness in the mouth, the term 'burning mouth' should not be used. Patch testing to dental materials is often performed in patients with burning mouth symptoms and usually shows negative results,<sup>18</sup> although in one series six of 22 cases apparently had a contact allergy to acrylates.<sup>19</sup>

### Red mouth

If there is redness in the mouth (Fig. 2) and the patient has had exposure to dental materials such as metals or plastics (e.g. dentures), it is worth investigating for contact allergy. Acute gingivostomatitis has been reported due to allergy to methacrylate in a dental restorative material,<sup>20</sup> and painful redness of the mouth has been observed due to allergy to 2-hydroxyethyl methacrylate (HEMA) in a denture.<sup>21</sup> Prolonged boiling of the denture resulted in reversal of the symptoms, presumably as the offending acrylate was 'cured'. Acrylates in composite restorations may cause irritant or allergic reactions in the adjacent mucosa.<sup>22</sup> Metals such as palladium, gold or manganese in a partial denture can sometimes cause stomatitis. Contact allergy, demonstrated by patch testing to manganese, used in a partial denture, resulted in redness and soreness of

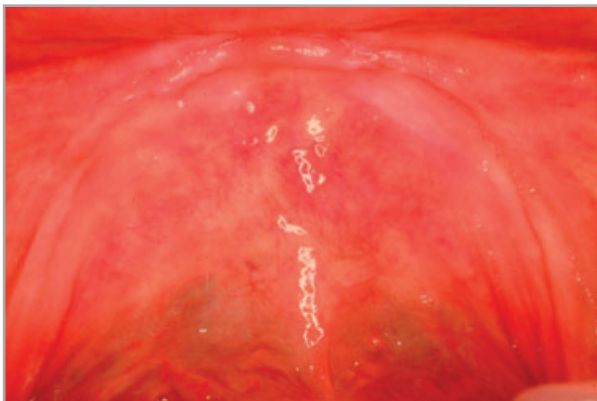


Fig 2. Red mouth showing erythema on the palate in an edentulous patient due to contact allergy to an acrylate (courtesy of Dr C. M. Yeoman).

the oral cavity with signs at areas of denture contact.<sup>23</sup> Contact allergy to dyes used in the manufacture of a denture has been reported, with the patient apparently having systemic symptoms.<sup>24</sup> Food additives (e.g. benzoic acid) and flavourings (e.g. cinnamaldehyde) may cause mucosal inflammation, and avoidance can be curative.<sup>25</sup> Allergy to acrylates in dental prostheses has occasionally been found to be the cause of tingling or jaw pain.<sup>22</sup>

Intraoral exposure of young girls to nickel as a component of dental braces, at an age before they have had their ears pierced, results in a reduced prevalence of nickel allergy (which is accepted as being linked to ear piercing) compared with those who never wore a dental brace, suggesting the possibility of the induction of immune tolerance, as opposed to sensitization.<sup>26</sup>

### Cheilitis and lip swelling

Cheilitis is an inflammatory eruption on the lip that can have many causes (Fig. 3).<sup>27</sup> A comprehensive study that included patch testing in 75 cases of cheilitis revealed that 27 (36%) were due to irritancy, e.g. lip lick, 19 (25%) to contact allergy, 14 (19%) to atopic dermatitis, and in the remainder the cause was unknown or was not an eczema.<sup>4</sup> Allergens reported to cause cheilitis include medicaments, toothpaste ingredients (including sodium lauryl sulphate), potassium persulphate (in denture cleanser: the potassium persulphate seemed to be absorbed by the prosthesis),<sup>28</sup> colophonium (in dental floss), nail varnish, cosmetics (e.g. castor oil in lipsticks) and nickel (in the mouthpiece of a musical instrument).<sup>4,28-30</sup>

If lip swelling is acute, i.e. if it occurs within minutes or a few hours of dental treatment, immediate type allergy to latex (from handling of the mouth by the dentist) should be suspected and investigated. Lip swelling unrelated to dental treatment may be due to allergens in dental products such as cinnamaldehyde, mint or eugenol in toothpaste, or to allergens in foods or cosmetics.<sup>4,25,31</sup> It may be necessary to investigate for both immediate and delayed type allergies.



Fig 3. Cheilitis (patch testing revealed contact allergy to nickel: the patient had been wearing wire braces).

Granulomatous cheilitis (Fig. 4) can be complicated by coexisting type IV allergy to foodstuffs: most recently allergy to chocolate was described in this context.<sup>32</sup>

### Facial eruption

Acute swelling of the face after dental treatment may be a manifestation of immediate latex allergy.<sup>33</sup> Swelling of the face within a few hours of dental treatment is often regarded as being due to immediate type allergy to the local anaesthetic used. In practice, investigation rarely reveals this to be the case, and true allergy to local anaesthetic agents is rare. Prolonged dental treatment might be sufficient to induce delayed type contact dermatitis due to rubber additives in the dentist's glove.

Intraoral metal is sometimes postulated as a cause of chronic facial swelling. This was confirmed in one case where patch testing was positive for palladium and removal of the crowns that contained palladium produced a cure.<sup>34</sup> Gold is commonly used for dental restoration and has been held responsible for different sorts of oral complaints including facial dermatitis, as well as oral soreness and oral lichenoid reactions. Sometimes removal of the gold will alleviate the problem but this is not invariable.<sup>35</sup> It is not uncommon to find that patients who have gold crowns or inlays are positive to gold on patch testing without any symptoms or signs to indicate a clinical problem.<sup>35</sup> Only occasionally has facial dermatitis or a lichenoid reaction on the oral mucosa been convincingly related to contact allergy to dental gold.<sup>36</sup>

There are few reports of generalized skin problems related to dental allergies. Occasionally nickel (or sometimes chrome) in a dental prosthesis has been thought to cause a dermatitis or to exacerbate dermatitis usually around the mouth,<sup>37</sup> but sometimes in a more widespread distribution, e.g. on the hands or feet.<sup>38</sup> Interesting, the use of crowns or bridges containing 66% nickel in patients known to be nickel-allergic in Poland did not produce any adverse reaction in 16 patients followed up for 3 years.<sup>39</sup> Organic polymer orthodontic



Fig 4. Granulomatous cheilitis in orofacial granulomatosis (courtesy of Dr C. M. Yeoman).

appliances have been developed for use in patients with metal allergies.<sup>40</sup>

### Reactions to local anaesthetics

Local anaesthetics are used extensively in dentistry and are normally well tolerated. Sometimes reactions of different kinds are observed. These may range from simple vasovagal episodes to tachycardia (due to intravascular administration of epinephrine), to apparent 'collapse'. It is estimated that an adverse reaction of some sort is seen with 0.5% of all dental local anaesthetics administered.<sup>41</sup> In a series of 5018 patients reported from Uruguay, there were 25 reactions following a dental local anaesthetic, of which 22 were diagnosed as being vasovagal or psychogenic in origin.<sup>41</sup> One case was due to defective administration; in the other two, provocation tests with the local anaesthetic concerned were negative. One methodology for undertaking investigation of a possible reaction to a local anaesthetic is described by Ruzicka *et al.*<sup>42</sup>

A recent study from Israel evaluated 236 patients who were referred having had some sort of reaction following administration of local anaesthetic: skin prick tests and intradermal injection tests followed by subcutaneous injection using the local anaesthetic agents (containing preservative) were uniformly negative, leading the authors to conclude that true immediate type (type I) allergy to local anaesthetics was very rare and that tests could omit the intradermal injection and use local anaesthetic containing preservative.<sup>43</sup> Cell-mediated (type IV) allergy to lidocaine and other local anaesthetics is well recognized, but the risk of an anaphylactic reaction to an injected local anaesthetic is felt to be low.<sup>42</sup> Latex allergen can be released into pharmaceutical solutions from latex-stoppered vials,<sup>44</sup> and 'skin reactions' can be seen from this source.<sup>45</sup>

### Immediate type reactions and anaphylaxis due to dental products

The most common cause of systemic symptoms such as wheezing or, at the extreme, anaphylaxis, and due to contact with a dentally related material, is immediate allergy to latex. Atopics are at higher risk of developing latex allergy. A systematic history will usually define other features that are highly suggestive of latex allergy, e.g. lip swelling on blowing up balloons, latex-fruit allergy syndrome (often to banana) or reactions to condoms.<sup>46</sup> Immediate type latex allergy, and also delayed type hypersensitivity to rubber additives, may be manifest as swelling of the face or mouth following dental treatment due to contact of the dentist's latex rubber glove with the patient's skin or mucosa.<sup>33</sup> The allergen-specific IgE to latex can give false-positive reactions and false-negative reactions: the prick test for latex allergy is the best test to use.<sup>46</sup> Skin prick tests are most reliably done using commercially supplied preparations, e.g. those of ALK Abelló (UK) Ltd (Hungerford, U.K.).

Formaldehyde, used as a disinfectant for root canal treatment, has been recorded to cause anaphylaxis within minutes

of exposure in a patient who subsequently was found to have immediate type allergy to formaldehyde.<sup>46</sup> Confirmation of immediate type allergy is by prick test or allergen-specific IgE test.

### Occupational dermatitis in dental personnel

In dental personnel, the most common complaints are of hand dermatitis (Fig. 5), an eruption on the face, swelling on the hands or face, or rarely of more systemic symptoms such as wheezing or collapse. In a survey of dentists in Sweden, 191 of 3500 (15%) reported having had hand dermatitis at some time in the previous year.<sup>47</sup> The diagnosis of eczema was confirmed in 94% of the 158 who attended a consultation, with irritant dermatitis being diagnosed in two-thirds and allergic contact dermatitis diagnosed in the other third.<sup>48</sup> In another study authors found a 1-year prevalence of hand dermatitis of 14% in a survey of 527 dental personnel:<sup>7</sup> of the 72 patients, 41 were patch tested and four were allergic to one or more acrylates. Other allergens identified on patch testing include nickel, fragrance, gold and thiurams.<sup>47</sup> In further study of 700 dental personnel, the prevalence of work-related skin allergy was 8%.<sup>49</sup>

Immediate type latex allergy was reported in 10% of dentists, 6% of dental nurses and 4% of dental hygienists, in a study from 2000, although this may become less problematic with the use of nonpowdered gloves and now the use of latex-free gloves.<sup>7,50</sup> In dentists and dental technicians with hand dermatitis patch tested to both a European standard and a specific dental series of allergens (suppliers: Chemotechnique Diagnostics AB, Malmö, Sweden and Hermal Trolab, Hamburg, Germany), the commonest relevant positives were to acrylates, nickel, cobalt, palladium, Myroxylon, fragrance, thiuram and colophonium.<sup>5</sup> It was found that the standard series gave relevant positive results in 77 of 131 patients, with the dental series giving relevant positives in 44 of 109, suggesting that testing to both series is needed.

A report from Poland showed that of 46 dental nurses with suspected occupational dermatitis, on patch testing 12 (26%) were allergic to glutaraldehyde, six (12%) to formaldehyde

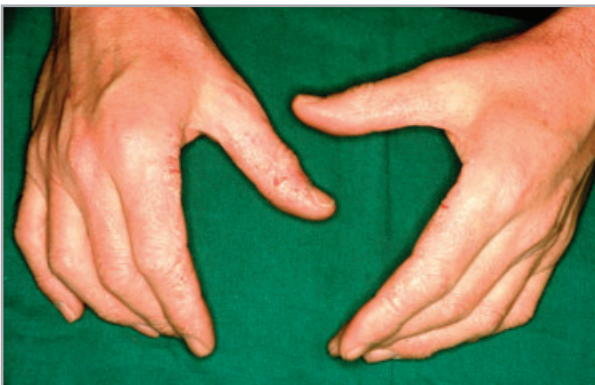


Fig 5. Hand dermatitis in a dental technician (patch testing revealed contact allergy to thiuram chemicals).

and five (11%) to thimerosal.<sup>51</sup> All three substances (or related chemicals) are used as disinfectants in Poland. Colophonium has also been described as an allergen in dental nurses.<sup>52</sup>

Contact allergy to acrylates is a particular problem in dentists and dental technicians, typically presenting with dermatitis on the fingertips (sometimes with facial or eyelid involvement). There is cross-reactivity between the monomers, so it is not uncommon to find that patients react to several of the acrylates when they are patch tested. One survey of Swedish dentists, dental nurses and dental technicians found that 3% overall had a dermatitis due to acrylate allergy.<sup>49</sup> Acrylate contact allergy was identified on patch testing in seven of 149 (5%) dentists with hand dermatitis, with HEMA and ethyleneglycol dimethacrylate (EGDMA) being the predominant allergens.<sup>47</sup> Other important acrylate allergens include MMA and TGDMA.<sup>53</sup> Two-thirds of dental personnel with occupational hand dermatitis, allergic to an acrylate, were also positive to one of the standard series allergens, most commonly nickel, cobalt, palladium, fragrance, colophonium or thiuram.<sup>5</sup> Some patients develop respiratory signs of an occupational asthma in association with their eczema.<sup>54</sup>

Colophonium, present at 7.5% concentration in dental baseplate moulding material, is another allergen which may cause an occupational hand and forearm dermatitis in dental technicians.<sup>55</sup>

### Adverse reaction reporting

There are several schemes for the reporting of adverse reactions to dental materials: one of the first to be instigated was that in Norway.<sup>56</sup> Over the last 4 years there has been a British reporting scheme for adverse reactions to dental materials based at the Dental School at the University of Sheffield. The experiences have been reported.<sup>57</sup> There have been 831 responses, including 390 patient events and 440 occupational events in dental personnel. Of the patient reactions, 68% were intraoral, 47% involved the lip or face and 20% were generalized. The suspect materials were, in order of frequency, rubber (latex), followed by metals, resins and hygiene products. In dental staff, rubber latex gloves were the single biggest problem.

In the U.K., the dental Adverse Reactions Project has found latex glove allergy to be the biggest problem in dental personnel,<sup>50</sup> and in patients, reactions to metals were the most common adverse event reported—mainly lichenoid changes associated with amalgam.<sup>57</sup>

### Recommended dental series of patch test allergens

The assessment of patients who present with oral or facial symptoms that may be due to dental materials requires first an evaluation of the history, as most presentations will fall into one of the categories mentioned above. An examination of the face, lips, oral cavity and teeth will give more information. It may be necessary to enquire of dental surgeons exactly what procedures they have undertaken and what materials they have

used (especially regarding metal prostheses and crowns). If the patient is a dental care professional, additional factors need consideration, e.g. occupational-type exposures.

Once the presentation has been decided, potential allergens can be identified. Immediate type allergy (type I) always needs to be considered in addition to delayed type (cell-mediated; type IV), and allergen-specific IgE tests or prick tests may be requested or performed, e.g. to latex or to some foods.

All patients presenting with symptoms possibly related to dental allergens should be tested to the British Contact Dermatitis Society's standard series (details can be obtained via the BCDS website <http://www.bad.org.uk/groups/bcds/>). Additional series depend on the clinical situation but may include:<sup>25,58</sup> (i) extra metals, e.g. mercury, palladium, gold, silver, platinum, copper, tin and perhaps some metals rarely used in patch testing; (ii) flavourings, antioxidants or preservatives, e.g. eugenol, cinnamaldehyde, menthol, peppermint oil, benzoyl peroxide, glutaraldehyde, benzoic acid and thiomersal; and (iii) acrylates, epoxy resins and associated chemicals, e.g. MMA, HEMA, EGDMA, TGDMA, urethane dimethacrylate, bisphenol A and others.

The allergen preparations are available from the usual suppliers, i.e. Chemotechnique Diagnostics AB (Malmö, Sweden) and Hermal Trolab (Hamburg, Germany). Interpretation of the results, as for all patch testing, requires skill in the reading of the patches (taking care to recognize irritant reactions that are of no clinical relevance), coupled with demonstration (which may involve some detective work) of the relevance of an allergic positive reaction in the affected individual, and liaison with colleagues in dental surgery or oral medicine regarding how best to tackle the patient's problem. The interpretation of some results may seem difficult, e.g. how to advise a patient who has gold dental restorations with no apparent adverse reaction who has an apparently allergic-positive patch test (most contact dermatologists would agree that there is no need to remove the dental gold).

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