Contact allergy to sodium metabisulfite: an occupational problem

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Sodium metabisulfite (SMB), also known as sodium disulfite, can be found in several products such as food (E223), beer, wine, cosmetics including hair colours, medications, photographic chemicals, and leather, but also in swimming pool water. It is also used as an antioxidant in mineral extraction and in chemical and rubber manufacture (1). In medications, there is considerable exposure to SMB used as a stabilizer in anaesthetic
preparations, in antifungal and haemorrhoidal creams, rectal suspensions and in different parenteral, ophthalmic, nasal, and intravenous solutions (2).

Published patch test studies have shown the frequency of positive reactions varying from 1.4% to 4.1% (1, 3–9). Over the last decade, there has been discussion about whether SMB is a true contact allergen or not, and if so, about its relevance (1, 3, 4, 10, 11). As SMB occurs in such a vast variety of products, it is also of interest as a possible occupational contact allergen.

In 1997, at our Department of Occupational and Environmental Dermatology we observed three cases with positive patch test reactions to SMB and SMB-containing products. All three had occupational exposure to SMB (one dentist, the other kitchen worker, and the third working with photograph development) and the current relevance of the positive patch test reactions was considered in all three cases. Because of this, SMB was tested routinely from November 1998.

The aim of this retrospective study was to investigate the prevalence of positive patch test reactions to SMB in our patients and to evaluate the clinical relevance of positive patch test reactions.

Materials and Methods
A retrospective study was performed at the Department of Occupational and Environmental Dermatology in patients with positive patch test reactions to SMB (CAS-nr 7681-57-4 alternatively 7757-74-6).

From November 1998 to April 2007, a total of 1518 consecutive patients were patch tested to 2% SMB in pet. Of these patients, 839 (55.3%) were females and 679 (44.8%) males. The most common diagnosis was hand eczema.

SMB was purchased from Sigma-Aldrich Company Ltd. (St Louis, MO, USA). The patch test material was prepared in our laboratory. Pet. as vehicle was chosen because of SMB’s stability.

The tests were performed according to International Contact Dermatitis Research Groups criteria using Finn Chamber® on Scanpor® tape and occluded for 2 days. Patch test readings were undertaken at D3 and D7. For those showing positive reactions to SMB, patient records were reviewed.

Results
A total of 51 out of 1518 patients (3.4%) showed positive patch test reactions to SMB (Table 1). Forty-three (84.3%) were males aged 24–74 years (mean 48) and 8 (15.7%) were females aged 36–62 years old (mean 50). In addition to the 51 patients, another 10 showed weak reactions, interpreted as irritant reactions. Sixteen cases (31.3%) had ++/− reactions (Table 1) and 35 patients (68.6%) had strong patch test reactions (++ or +++). Furthermore, 14 out of 51 patients (27%) had positive reactions to other contact allergens beside SMB, but no special concomitant reaction pattern was ascertained.

All but 2 patients who tested positively had manual jobs (current or previous) and there was a predominance of metal work and exposure to oils among the males (10/51 patients; 19.6%).

The patch test reactions were considered of current relevance in two cases; in a third case, a previous relevance was probable. In 14 cases (27%), the relevance was considered questionable and no relevance was found in 24 patients (47%). In 10 cases, the relevance could not be evaluated because of incomplete patient records.

Among the patients with positive patch test reactions and known relevance, the first one was a male photographer, 39 years old, with hand eczema. He proved to have contact allergy to photodeveloping chemicals (containing SMB) as well as SMB. The second patient was a 43-year-old male textile dyer, also with hand eczema. He mainly dyed linen yarn and he used to clean his hands with a SMB-containing skin cleanser. After replacing this with a non-SMB-containing cleanser his hand eczema resolved. The third patient was a 57-year-old female dentist diagnosed with hand eczema. She had previously been developing X-ray films and handling photograph developing chemicals containing SMB, therefore past relevance was probable.

Discussion
We performed a retrospective study of patients consecutively tested to SMB at the Department of Occupational and Environmental Dermatology over nearly 9 years. The majority of the patients were referred to us for investigation of hand eczema.

A high prevalence of positive patch test reactions to SMB (3.4%) was found. The highly significant male dominance is interesting and is in contrast to the results in a recently published British study where there was a female preponderance (1). This might indicate a difference in occupational exposure between the sexes resulting in contact allergy, although this hypothesis was difficult to evaluate retrospectively from our records. The significant predominance of manual jobs further indicates SMB being an occupational contact allergen.

Seventy-three percent had no contact allergy to other substances tested beside SMB and this is important to emphasize. Although the question of relevance has to be further evaluated, these cases would have been missed if SMB had not been included in the patch test series.

Out of 51 positive cases, we found only 3 with a clearly relevant contact allergy to SMB. This reflects a minimum frequency of relevant contact allergy because not all patient records enabled complete evaluation, as this was a retrospective study. It is difficult to trace SMB as it occurs in a wide variety of products, including

Table 1. Number of patients with positive patch test reactions among 1518 tested to sodium metabisulphite

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total positive reaction</th>
<th>+ Reaction</th>
<th>++ Reaction</th>
<th>+++ Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femalesa (n = 839)</td>
<td>8</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Malesa (n = 679)</td>
<td>43</td>
<td>12</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>Total (n = 1518)</td>
<td>51</td>
<td>16</td>
<td>28</td>
<td>7</td>
</tr>
</tbody>
</table>

The strongest reaction at either reading is presented.

aStatistically significant difference between positive cases observed in females and males (P < 0.001).
medicaments (1, 2). Historically, the relevance of positivity to another contact allergen, thiomersal, used as a preservative in vaccines, has been difficult to interpret. The use of thiomersal in vaccines is thought to have caused iatrogenic contact allergy (12).

Furthermore, there is some ambiguity about both the name of the used substance and the substance itself. We have chosen to use the INCI name sodium metabisulfite throughout the paper. There are several other trivial names and disused CAS numbers adding to the uncertainty of the identity of the compound. Furthermore, in aqueous solution, disulfite exists in a complex equilibrium with hydrogen sulfite, sulfite, and sulfur dioxide that may further add to the ambiguity of the identity of the test compound (Figure 1). During storage, sulfur dioxide, which is a volatile gas, evaporates thereby affecting the amount and concentration of disulfite. As a consequence, patch testing SMB in water may be compromised. This has been suggested as an explanation of the relatively low number of positive reactions to SMB (3). To circumvent this problem, we performed the study by using pet. as the vehicle.

Regarding the EU risk-phrase classification, SMB is classified as R22, R31, and R41, i.e. dangerous to ingest. Furthermore, it may develop a toxic gas in contact with acid and may constitute a risk of severe eye damage. It is not classified as skin irritant or contact allergen (R38, R43) (13).

To conclude, we found a high prevalence of positive patch test reactions to SMB, the majority in males. The difference between the sexes was statistically significant. Because of this statistically significant male predominance and also the high frequency of manual jobs among the patients testing positively, we regard SMB as an important occupational contact allergen.

We also found the majority of the positive patch test reactions being strong. On the other hand, there were few with an obvious current or past relevance. However, the relevance was difficult to interpret as this was a retrospective study. We recommend pet. as the patch test vehicle. More studies on the relevance of contact allergy reactions to SMB and detailed investigations of possible exposure sources are needed.