Sodium metabisulphite induced airways disease in the fishing and fish-processing industry

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Background
Sodium metabisulphite (SMBS) is recognized as a potential cause of airway irritation and possibly occupational asthma, but awareness of its use in the fishing and fish-processing industry is low.

Aims and methods
To describe three cases of occupational airways disease due to SMBS exposure and to review the literature.

Results
Three patients, one trawlerman and two prawn processors, developed work-related airways disease due to exposure to SMBS, one with irritant-induced asthma with a positive-specific bronchial challenge associated with very high sulphur dioxide exposures, one with occupational asthma and one with vocal cord dysfunction and underlying asthma. Of the nine cases recorded in the literature, most were non-atopic and responses to specific bronchial challenge when undertaken showed an immediate response. Exposures to sulphur dioxide in these settings are very high, in excess of 30 ppm.

Conclusion
SMBS should be regarded as a cause of occupational airways disease and its use in the fish and prawn-processing industry investigated further to better identify risks from exposure and handling of the agent in the workplace.

Key words
Asthma; bronchial challenge; fish-processing industry; occupational exposures; sodium metabisulphite; sulphur dioxide.

Introduction
Sodium metabisulphite (SMBS) and its close relative sodium disulphite have been described as causing occupational asthma [1–4] or ‘asthma-like syndrome’ [5], either by single or repeated exposures, and also dermatitis both in occupationally exposed workers and in the general population [6,7]. It is widely used in the food and beverage industry and in the fishing industry as a preservative, antioxidant and bleaching agent. However, the mechanism whereby exposure to SMBS causes asthma is unknown, an IgE-mediated mechanism being unlikely because of the small size of the molecule. It has been suggested that it occurs through an irritant mechanism following release of sulphur dioxide [2], although the lack of information on the level of occupational exposure makes this difficult to assess. While in all reported cases of occupational asthma where specific bronchial challenge was undertaken, an immediate marked fall in FEV1 was seen, in no cases were sulphur dioxide measurements made during exposure. Epidemiologically, occupational exposure to sulphur dioxide in sulphite mill workers has been shown to be associated with an increased risk of asthma [8], perhaps an example of low-dose irritant-induced asthma.

Three patients were referred to the occupational lung disease clinic at Aberdeen Royal Infirmary between March 2004 and October 2006 with episodes of increased breathlessness and symptoms typical of asthma. All three had been working in the fishing or fish-processing industry, and none had had asthma prior to working in the industry. In one subject, bronchial challenge was associated with extremely high levels of generated sulphur dioxide which suggests that the mode of action of SMBS in inducing airway inflammation and irritability is through an irritant mechanism.

Case 1
A 44-year-old man had worked as a trawlerman for many years fishing for prawns and white fish. He had been exposed to SMBS (used as a preservative for prawns) in dry and in liquid form for ~3 years in this job. The powdered form was stored in sacks on deck which were often inadvertently punctured releasing powder onto the
deck. Solutions were made up by the trawlermen in an approximate fashion using seawater as the diluent and an empty baked bean can as a scoop to 'measure' the powder. The made-up solutions were then put into the holds with the prawns. When off loading the catch, substantial re-exposure occurred as the fume was released from the hold and on occasion the prawns were further dipped into SMBS solution on the quayside at offloading. He developed symptoms of breathlessness, chest tightness and waking at night with a clear work-related pattern for ~18 months. He had been advised to stop work before referral. His asthmatic symptoms remained constant for 2 years after leaving work and were only partly controlled by anti-asthma therapy (inhaled corticosteroids and long- and short-acting beta-agonists). He also complained of itching and a sore scalp (suggestive of scalp dermatitis) and itching of the hands and arms when exposed, although these dermal symptoms had settled at the time he was seen in the clinic. He had had intermittent sore throats and occasional blood-stained sputum during periods of exposure which improved away from work. He had smoked 15–20 cigarettes per day for 20 years.

On investigation, total IgE was normal and radioallergosorbent test (RAST) levels to a range of allergens, including shrimp protein, were negative.

No peak flow records during occupational exposure were possible as he had left work by the time of referral, but serial peak flows away from work confirmed significant variability compatible with asthma (range 400–550 l/minute) over a 2-month period.

Bronchial responsiveness to methacholine showed no change in FEV$_1$ but when repeated following SMBS challenge showed a 10% reduction in FEV$_1$ (Figure 1).

Specific bronchial challenge to seawater and to SMBS in seawater (2.5% solution) was undertaken in an exposure chamber. SMBS handling tasks were simulated for 5, 10, 15 and 60 min by tipping SMBS solution between two beakers. Concentrations of sulphur dioxide were measured during this process. Exposure to SMBS resulted in a 30% decrement in FEV$_1$ at the highest exposure concentration (Figure 2) accompanied with symptoms of wheezing, chest tightness and itching of the scalp. Additionally, he experienced a sore throat and blood-stained sputum the following day. Sulphur dioxide concentrations in the exposure chamber reached 40 ppm after only 15 min exposure (Figure 3). There were no lung function changes or symptoms reported following seawater challenge.

He is now working onshore without exposure to SMBS. His symptoms have improved but he still has asthma, although better controlled on lower doses of fluticasone/salmeterol (Seretide™ 500) and less frequent use of rescue salbutamol.

**Case 2**

A 43-year-old woman employed in a prawn-processing factory for 16 years, latterly as a supervisor. For an unknown period, she had been exposed to SMBS for ~1 h a day while making up the preservative solutions and during prawn dipping for many years. She reported a stronger smell of SMBS in the processing hall on warmer days. Six months before referral, she developed work-related symptoms of wheezing and palpitations and had been treated...
with inhaled corticosteroids and relief beta₂-agonists with partial benefit. She had smoked 15–20 cigarettes per day for the previous 20 years.

On investigation, total IgE was negative and RAST levels were negative to prawns and to a range of inhaled and ingested allergens.

Occupational peak flow records showed a work-related pattern in peak flow with an OASYS [16] work effect index of 3.67 (Figure 4). Her FEV₁ was 2.5 l (96% predicted) and forced vital capacity (FVC) 3.25 l (93% predicted). Tests for non-specific bronchial responsiveness were not undertaken.

Standard treatment for asthma did initially reduce her symptoms both at and away from work. Her employer changed the process substituting SMBS with another commercial product (Xyrex®), a complex formulation of inorganic and organic salts. Her symptoms improved considerably and her dose of inhaled steroid was reduced from 1000 mcg/day of fluticasone to 500 mcg/day, her peak expiratory flow (PEF) at that time being 370 l/min (88% predicted, range 340–400). However, her employer decided to reintroduce SMBS for financial reasons and her symptoms worsened. She still works in the same post but is using respiratory protective equipment.

**Case 3**

A 39-year-old woman was referred 8 years after her symptoms first began and 5 years after she had ceased working as a prawn packer. She had been smoking one ounce of hand-rolled tobacco a week (3–5 cigarettes per day). She first became exposed to SMBS 6 weeks after she began this work, her job involving collecting prawns as they arrived from the dipping tank and packing them in caskets according to size. On each occasion, she experienced immediate symptoms, notably a severe, dry cough. After 2 days with these symptoms, she developed breathlessness and coughing on exposure. Despite provision of a simple face mask, her symptoms deteriorated but the severity of her symptoms led to two work-related hospital admissions. These exposures were typically repeated and there were no large exposures just before onset of symptoms. Typical triggers for her symptoms were smells, paint fumes and perfumes.

Investigations revealed that her total IgE was normal and RAST levels for common allergens (done 5 years previously) were negative.

Peak flow records performed long after leaving the workplace showed no significant diurnal variability although mean levels were markedly reduced (380 l/min, predicted value 530 l/min). FEV₁ and FVC were 2.25 and 2.95 l, respectively (predicted 2.69 and 3.12 l), when seen initially after the incident (8 years ago). When seen in our clinic, the respective values were 1.90 and 2.20 l. Earlier spirometry had shown significant reversibility to bronchodilator (pre/post-FEV₁ 2.03/2.34 l and FVC 3.16/3.27 l). The flow volume curve showed airflow obstruction but was also suggestive of vocal cord dysfunction with truncation of the expiratory peak and flattening of the inspiratory limb along with dysphonia and inspiratory dyspnoea. Recently, irritable larynx has been described in

![Figure 4. Serial PEF record (OASYS 2) for Patient 2 with improvement during a fortnight work break and subsequent deterioration on return to work.](https://academic.oup.com/occmed/article-abstract/58/8/545/1467381/538)
<table>
<thead>
<tr>
<th>Author/year</th>
<th>Age (years)/ gender</th>
<th>Occupation</th>
<th>Smoking status</th>
<th>Atopic status</th>
<th>Specific bronchial challenge</th>
<th>BHR baseline</th>
<th>BHR post-specific challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malo et al. [1]</td>
<td>27/male</td>
<td>Agricultural developer</td>
<td>Never smoker</td>
<td>Non-atopic</td>
<td>35% fall in FEV₁ at 10 min after exposed to 35 sec 10% SMBS powder and 52% fall in FEV₁ at 50 min after exposed to 1% SMBS powder for 4 min</td>
<td>PC₂₀ metacholine &gt;128 mg/l before exposure (non-reactive)</td>
<td>PC₂₀ metacholine &gt;128 mg/l before and 7 h after exposure ended (non-reactive)</td>
</tr>
<tr>
<td>Madsen et al. [3]</td>
<td>31/male</td>
<td>Lobster fisherman</td>
<td>NK</td>
<td>Non-atopic</td>
<td>21% fall in FEV₁ at 10 min</td>
<td>PC₂₀ histamine 7.8 mg/ml</td>
<td>Not repeated</td>
</tr>
<tr>
<td>Merget et al. [2]</td>
<td>37/female</td>
<td>Radiographer</td>
<td>NK</td>
<td>Atopic</td>
<td>33 and 25% fall in FEV₁ to SMBS concentrations of 49 μg respectively 96 μg after 1 min each</td>
<td>PD₂₀ methacholine 16 μg</td>
<td>Not repeated</td>
</tr>
<tr>
<td>Agard et al. [4]</td>
<td>29/female</td>
<td>Vineyard worker</td>
<td>NK</td>
<td>Atopic</td>
<td>57% fall in FEV₁ at 3 min</td>
<td>Not repeated</td>
<td>Not repeated</td>
</tr>
<tr>
<td></td>
<td>52/female</td>
<td>Hospital laundry worker</td>
<td>NK</td>
<td>Non-atopic</td>
<td>31% fall in FEV₁ at 2 min</td>
<td>Not repeated</td>
<td>Not repeated</td>
</tr>
<tr>
<td></td>
<td>28/female</td>
<td>Laundry worker</td>
<td>NK</td>
<td>NK</td>
<td>47% fall in FEV₁ at 3 min</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Steiner et al., 2008*</td>
<td>44/male</td>
<td>Trawlerman</td>
<td>Current smoker</td>
<td>Non-atopic</td>
<td>30% fall in FEV₁ at 60 min</td>
<td>Non-reactive to methacholine</td>
<td>Increased slope suggesting change in reactivity</td>
</tr>
<tr>
<td></td>
<td>43/female</td>
<td>Prawn packer (supervisor)</td>
<td>Current smoker</td>
<td>Non-atopic</td>
<td>Not done</td>
<td>Not done</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>39/female</td>
<td>Prawn packer</td>
<td>Current smoker</td>
<td>Non-atopic</td>
<td>Not done</td>
<td>Patient unable to perform the test (due to cough)</td>
<td>NA</td>
</tr>
</tbody>
</table>

BHR, broncho-hyperresponsiveness; NK, not known; NA, not applicable.

*Subjects from this paper.
a large series of workers exposed to chemicals [9] with identical clinical features to this case.

Non-specific bronchial challenge with histamine was not possible due to coughing with repeated forced expiratory manoeuvres.

As a diagnosis of bronchiolitis was considered, a high-resolution computer tomogram (CT) scan was undertaken, which showed no evidence of gas trapping or bronchiolitis.

This patient changed her job shortly after her second hospital admission to a workplace without SMBS exposure. However, her symptoms of breathlessness and cough continued and when last reviewed, 9 years after onset of symptoms, she still suffered exertional breathlessness and incapacitating episodes of cough unresponsive to a range of different medication approaches including high-dose inhaled steroid treatment.

**Discussion**

We report three cases of SMBS-induced occupational airways disease, which we contend comprise one of irritant-induced asthma (Case 1), one of occupational asthma (Case 2) and one of vocal cord dysfunction with underlying asthma (Case 3). Vocal cord dysfunction, or irritable larynx syndrome in the occupational setting [9], is now recognized as a condition which is frequent in association with exposure to chemicals at work. Demographic, clinical and challenge data of these three cases and the six other reported cases of sulphite-induced airways disease [1–4] are shown in Table 1.

Marked bronchial hyperresponsiveness is not a consistent association in these individuals (where measured) suggesting that in SMBS-induced airways disease bronchial responsiveness may not be a critical factor either in terms of susceptibility or as a result of exposure. Most reported subjects were non-atopic but smoking history has been poorly reported, so little conclusion can be drawn as to the importance of smoking as a cofactor. In the case we challenged, levels of sulphur dioxide during challenge were extremely high, very much higher than those experienced by workers exposed to sulphites during apricot processing [3] but comparable to one of the laundry workers reported by Agard et al. [4] where workplace sulphur dioxide levels reached 37 ppm. This suggests that in some circumstances, levels of exposure in the fishing and fish-processing industries and in other industries may be well in excess of the old UK occupational exposure limit for sulphur dioxide (1 ppm). The reasons for this are likely to be related to lack of awareness of the risks of SMBS exposure and poor work practices. We do not believe that in our first case using seawater as a diluent enhanced the release of sulphur dioxide.

SMBS is widely used in the food and beverage industry but occupational exposure also occurs in fish processing where it is used extensively as a preservative but has only been reported once before in a lobsterman [3]. SMBS is known as a respiratory irritant in its own right and has been used as an agent to assess non-specific bronchial reactivity [10]. It also decomposes to produce the irritant gas sulphur dioxide, which can lead to respiratory symptoms, with workers in a sulphite-pulp mill exposed to the gas showing a high prevalence of irritant-induced asthma [8]. Neither SMBS nor sulphur dioxide, however, can be regarded as classical sensitizers. Sulphur dioxide is a very soluble gas which is thought to reach the lower respiratory tract only when lung ventilation rates are high [11]. It has been suggested that sulphur dioxide exerts its effect through upper airway irritant receptor stimulation [12] which was one reason behind the use of SMBS as a challenge molecule for measuring bronchial responsiveness [10]. However, sulphur dioxide can potentiate the inactivation of α1-anti-proteinase caused by peroxynitrite, thus potentially leading to the formation of protein-modifying sulphite radicals [13]. If so, this could lead to more important structural changes in the respiratory epithelium and a potential mechanism for persistent symptoms as typically seen in irritant-induced asthma [14].

The true prevalence of SMBS-induced airways disease in the fish-processing industry is likely to be high if the anecdotal evidence from two of our cases is to be believed. Currently, in the UK there is no workplace exposure limit for sulphur dioxide. The previous limit of 1 ppm was withdrawn in 2003 and a review process [15] established. The current advice for workplace exposure to sulphur dioxide is to use Control of Substances Hazardous to Health Essentials to follow good practice in any task involving its use or production. However, there is now sufficient evidence to support further investigation and control of SMBS in this industry.

In summary, we report three cases of SMBS-induced airways disease associated with different jobs in the fishing industry. It would appear that high exposures to SMBS and thus sulphur dioxide occur in these industries and that study of the use of this agent in relation to respiratory and probably dermal disease alongside accurate exposure measurement is needed. In the meantime, advice with respect to better control of use of SMBS should be provided if suitable alternatives are unavailable.

**Key points**

- Use of SMBS as a preservative in the fishing and fish-processing industries is associated with an increased risk of respiratory disease.
- Exposure to sulphur dioxide generated by SMBS dissolved in water can be substantial and much higher than existing recommended exposure limits.
- Better characterization of the use of this agent and its broader capability to cause lung disease in these occupations is needed.
Conflicts of interest

None declared.

References