

suggestive evidence that  $\beta_2$  adrenergic therapy might be able to enhance alveolar lung epithelial repair.

The results of this study are important. They provide a new mechanism to potentially explain the beneficial effects of  $\beta_2$  adrenergic agonist therapy in patients with acute lung injury. The data suggest that repair of the injured alveolus might be accelerated by  $\beta_2$  agonists, an effect that could provide a functional epithelial barrier that might be better able to remove alveolar oedema fluid in patients with acute lung injury. Although not tested in this study, other investigators have suggested that  $\beta_2$  adrenergic agonists might also decrease injurious inflammatory responses<sup>17</sup> and reduce lung endothelial injury.<sup>18</sup>

In summary, the investigators should be commended for an elegant translational study that tests a novel mechanism by which  $\beta_2$  agonists might benefit the injured lung. Large well powered randomised clinical trials are needed to test the potential value of  $\beta_2$  agonist therapy in patients with acute lung injury. In the USA, treatment with aerosolised  $\beta_2$  agonist is currently being tested in a 1000 patient trial by the ARDS Network supported by the National Heart Lung

and Blood Institute. Hopefully, a trial of intravenous salbutamol will be carried out with the support of the Medical Research Council in the UK in the near future.

**Competing interests:** None.

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# Standards of care for occupational asthma

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Work-related asthma has been reported to be frequent among adults with asthma.<sup>1,2</sup> Most cases (>90%) of occupational asthma (asthma caused by work) are caused by specific sensitisation to a workplace agent<sup>3</sup> (rather than irritant-induced occupational asthma), and it is this sensitiser-induced occupational asthma that is addressed in this issue of *Thorax* in a paper from the British Thoracic Society recommending standards of care for occupational asthma (*see page 240*).<sup>4</sup> It is especially important that occupational asthma is recognised early with appropriate intervention (including removal from further exposure to the causative workplace sensitiser when possible), since early recognition and such management improves the possibility that

the asthma will clear or significantly improve.<sup>5,6</sup>

Identification of occupational asthma in an individual can also serve as a “sentinel event”, offering the opportunity to alert workplaces and public health agencies that there may be an increased risk to co-workers in the same workplace and to other workers with similar exposures which can result in intervention measures to reduce or eliminate this risk.

Unfortunately, there has often been a period of several years between the onset of symptoms from occupational asthma and diagnosis.<sup>7,8</sup> Potential reasons for delay in diagnosis include workers’ lack of awareness of work-related asthma and of the association between their symptoms and workplace exposures. This is especially likely when the sensitiser is a low molecular weight (chemical) sensitiser which may cause isolated late asthmatic responses occurring several hours

after exposure. Symptoms may then be worst after leaving a work shift or during sleep after work. Even if they do recognise a work association, workers may be afraid to report this to their physician for fear of losing their job or transfer to a lower paid job (especially if working in a small company and/or without support from a union). Also, when seen by a healthcare worker, they may not be asked about the job and work-relatedness of symptoms. In a North American study of barriers to diagnosis of occupational asthma,<sup>7</sup> the median time to suspicion by the physician of the diagnosis was 2 years and to final diagnosis was 4 years. Most patients reported that they only saw a physician when symptoms worsened or became unbearable, and only a minority had been aware of an agent at work potentially causing asthma. Only 57% of primary care physicians surveyed in Ontario, Canada reported always or usually taking a history of workplace exposures, citing time constraints as the most frequent reason for not doing this.<sup>9</sup> In this and an earlier survey of members of the American College of Chest Physicians,<sup>10</sup> a high proportion of physicians recognised the need for further education in occupational lung diseases.

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To diagnose occupational asthma after suspicion is raised from the clinical history, the presence of asthma must be objectively confirmed and a probable causal relationship to work shown (from timing of symptoms, work exposures, functional assessment of asthma during periods of exposure versus periods without exposure, immunological response to a workplace sensitiser and/or specific laboratory exposure testing with the suspected causal agent, depending on the feasibility of these tests). Such testing may be initiated by a primary care health practitioner but often also requires specialist referral. The current document from the British Thoracic Society<sup>4</sup> is therefore very timely and it is hoped that it will improve awareness and appropriate care. It supplements a recent evidence-based review of occupational asthma performed by the British Occupational Health Research Foundation<sup>11</sup> as well as a Delphi consensus report<sup>12</sup> by providing practical advice for those involved in practice, both in the primary care setting and in specialist practice, as well as potentially for those in government and workplaces.

As noted recently by Nicholson,<sup>13</sup> there are few high quality systematic reviews in occupational health topics, since it is usually not feasible or ethical to perform a randomised trial of diagnostic tests or management. Systematic or evidence-based reviews of the diagnosis and management of occupational asthma with meta-analyses requiring high quality studies can address relatively few questions,<sup>5</sup> and many of the resulting recommendations have been limited in grade of evidence.<sup>11</sup>

In contrast, practical standards of care can be based on the best available evidence, and for some aspects this may be solely based on expert opinion. The current standards on occupational asthma contain some excellent practical features including reference to several useful British web-based resources for the practitioner, a worker information leaflet and a suggested form for clinical assessment. The standards are based in large part on the previously published evidence-based recommendations<sup>11</sup> and Delphi process<sup>12</sup> as well as consensus expert opinion from the authors. Although associated editorial articles for both previous documents questioned some of their conclusions/opinions,<sup>14, 15</sup> the writing panel for the current standards elected to keep these statements/emphasis (eg, they suggest less value/role for non-specific and specific challenge tests than suggested by others<sup>14, 15</sup>).

Such differences in some recommendations or in the emphasis given to some tests compared with other statements or reviews on occupational asthma from other countries may not be surprising in a document which includes aspects based on expert opinion from one nation. These differences may pertain to the British practice of the authors. In comparison with other statements<sup>16-18</sup> and a "state of the art" review,<sup>19</sup> this document places more weight on computer analysis of serial peak flow readings in the diagnostic process (rather than visual interpretation), despite the initial validation of the computerised method by comparing results with expert visual interpretation and the indication in the standards of current availability only in 12% of selected secondary care facilities.<sup>4</sup> It may be questioned how frequently computer analysis will be applied; perhaps the recommendations will lead to greater use of this. These standards of care also place more weight on in vitro assessment of specific serum IgE antibodies to a workplace agent (rather than skin prick testing with extracts of occupational allergens<sup>16-19</sup>), which might relate to differences in timely accessibility to allergy testing. One potential advantage of these two British recommendations is that both data for peak flows and serum for specific IgE could be collected by a primary care health provider without need for expertise in the visual interpretation of work-related peak flow recordings and without expertise in skin testing, and could then be sent for interpretation/analysis in a central location for which sources are provided.<sup>4</sup> However, it may be expected that most patients with suspected occupational asthma would require specialist evaluation in centres with expertise, so this theoretical advantage may not be highly relevant.

In contrast, there is no evidence that current computer interpretation relates better to the gold standard of specific challenge testing than expert visual interpretation of peak flow recordings, and in a recent study the computer analysis actually resulted in lower sensitivity (35% vs >63%) although higher specificity (65% vs 48-62%) when both were compared with a specific challenge.<sup>20</sup> Although there is no accepted simple formula which can be used by the healthcare practitioner for the interpretation of serial peak flow recordings,<sup>21, 22</sup> expert visual interpretation of plotted graphs with the additional consideration of recorded as-needed short-acting bronchodilators, symptoms and exposures has been recommended as an option in other European and North American documents.<sup>16-19</sup> Skin prick testing with extracts

of high molecular weight work allergens (when available)—as with common aeroallergens—are more sensitive and are similar in specificity to a gold standard of specific challenge than in vitro specific IgE assays.<sup>23</sup> Skin tests have been assessed in this manner more frequently than in vitro tests as identified by systematic review,<sup>5</sup> are simple to perform and provide a rapid result, so there is a rationale for these as an option when available to healthcare practitioners.

Other statements and reviews<sup>16-19</sup> have also given more weight to the initial objective confirmation of asthma (by assessing bronchodilator response on spirometry or, if this is normal, by assessing methacholine or histamine challenge during a period when the patient has recently been symptomatic) to exclude conditions that may mimic asthma such as upper airway syndromes. Conclusions in this document that airway responsiveness measures are frequently normal in occupational asthma as determined from the previous British evidence-based review were based on responses immediately prior to the specific challenge when the worker may have been away from exposure for some time and may have had clearing of asthma (rather than testing within a day or two after relevant work exposure or post-specific challenge).<sup>14</sup>

The new standards of care also address management and prevention of occupational asthma.<sup>4</sup> As noted by the authors, the diagnosis should lead to the consideration of co-workers to detect additional cases of occupational asthma and to prevent future cases where possible. The authors state that "exposures in the workplace should be low enough to prevent the onset of asthma in all workers, irrespective of individual susceptibility". Although this would be ideal and may be attainable for some jobs/sensitisers, it is very unlikely to be currently realistic for workers such as bakers or animal care workers. As noted in the standards, pre-existing risk factors should not be used to exclude employment, so the observed reality that primary preventive measures are not always successful to always prevent exposure to work sensitiser indicates current needs for additional secondary and/or tertiary preventive measures to detect occupational asthma early and to provide appropriate advice as to work exposures and asthma treatment.

It is hoped that this British Thoracic Society Standards of Care document will achieve its aims of improving practice related to occupational asthma caused by workplace sensitiser. However, it should not be forgotten that there are other

forms of work-related asthma. Irritant-induced asthma is caused by a high level irritant exposure in the workplace and has different diagnostic criteria and management.<sup>17–24</sup> Finally, work exposures/conditions can exacerbate or aggravate asthma either via common sensitizers which may be present at work such as animals or fungal allergens, by physical factors such as cold air or exercise, or by (non-specific) effects of dusts, fumes or sprays—and this has been reported to be at least as common as occupational asthma.<sup>25</sup> The criteria for diagnosis are less clear than for occupational asthma, but worsening of symptoms and of serial peak flow changes related to work have also been described from this.<sup>26</sup> In some case series work-exacerbated asthma has also had a significant socioeconomic impact similar to that of occupational asthma, but only in a few jurisdictions is it currently compensable.<sup>25–27</sup> Thus, when patients report worsening asthma at work but are found not to have occupational asthma, rather than continuing with “standard asthma care” (as recommended in the document), consideration should also be given to a diagnosis of irritant-induced occupational asthma or to work-exacerbated asthma. Although there are no currently published evidence-based guidelines or standards of care for work-exacerbated asthma, suggested management has included measures to reduce exacerbating exposures at work and outside the work environment, and optimising pharmacological management of asthma.<sup>24</sup>

The prevention, diagnosis and management of occupational asthma and work-exacerbated asthma is of significant importance to workers, and these British standards are a significant step forward to

assist in better physician, worker and employer recognition of this problem and familiarity with an approach to take.

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**Competing interests:** Dr Tarlo has a clinical practice that includes seeing and/or performing file reviews of workers with suspected occupational asthma for consultation at the request of other physicians, the Ontario Workplace Safety and Insurance Board and occasionally at the request of employers.

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