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Web based listing of agents associated with new onset work-related asthma

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Summary
Background: Work-related asthma is common and yet remains a challenge to diagnose. Access to a listing of agents associated with work-related asthma has been suggested as useful in assisting in the diagnosis.
Methods: The Association of Occupational and Environmental Clinics (AOEC) developed criteria that were used to review the peer-reviewed medical literature published in English. Based on this review, substances were designated either as a sensitizing agent or an irritant. The reviews were conducted by a board certified internist/pulmonologist/occupational medicine specialist from 2002 to 2007 and a board certified internist/occupational medicine physician from 2008-date. All reviews were then reviewed by the nine member AOEC board of directors.
Results: The original list of agents associated with new onset work-related asthma was derived from the tables of a text book on work-related asthma. After 13 years of review, there are 327 substances designated as asthma agents on the AOEC list; 173 (52.9%) coded as sensitizers, 35 (10.7%) as generally recognized as an asthma causing agent, four (1.2%) as irritants, two (0.6%) as both a sensitizer and an irritant and 113(34.6%) agents that still need to be reviewed.
Conclusions: The AOEC has developed a readily available web based listing of agents associated with new onset work-related asthma in adults. The listing is based on peer-reviewed criteria. The listing is updated twice a year. Regular review of the peer-reviewed medical literature is conducted to determine whether new substances should be added to the list. Clinicians should find the list useful when considering the diagnosis of work-related asthma.

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Introduction

Work exposures are an important component of the development of asthma in adults, and controlling them represents an opportunity for prevention [1]. In 2003, the American Thoracic Society published a consensus statement that concluded: "A careful review of the literature demonstrates that approximately 15% of both asthma and COPD is likely to be work related," [2]. Work-related asthma remains a challenge for physicians to diagnose and manage. To assist physicians, the American College of Chest Physicians published a consensus statement on the Diagnosis and Management of Work-Related Asthma, which included the statement that clinicians "should focus particularly on exposures occurring at the time that asthma started or worsened at work" [3]. To assist clinicians in assessing the work exposures of their patients, the consensus statement referred to the ASMANET website that contained a listing of "workplace sensitizers" based on reports in the published literature up to 2002. Although the ASMANET website can still be found on the internet, the list of "workplace sensitizers" has not been available for the past four years.

This paper describes an active web site, which is regularly updated, that lists substances that meet specified criteria for causing work related asthma by sensitization or acute irritant-induced asthma. This manuscript also describes the criteria used for a substance being included on the listing as a sensitizer or irritant. Clinicians can use this web site to assist them when evaluating patients they suspect have new onset work-related asthma.

Methods

The Association of Occupational and Environmental Clinics (AOEC) maintains an exposure code list (http://www.aoecdata.org/ExpCodeLookup.aspx). The AOEC Exposure Code List was first developed in 1995, for use by AOEC members in order to help identify emerging occupational and environmental health concerns [4]. The AOEC Exposure Code List is not an official document of any governmental agency. The AOEC is registered with the United States Internal Revenue Service as a non-profit, 501(c) 3 organization made up of approximately 60 occupational and environmental clinics. AOEC encourages use and has open access to all practioners for all the information and resources it has developed.

A supplemental designation for asthmagens (indicated by an "A") was added the same year the AOEC list was developed to facilitate analysis of data by the four states in the United States doing work-related asthma surveillance [4]. The designation of an "A" was mainly derived from substances listed in either of the two tables in Chapter 35 of the second edition of the medical textbook *Asthma in the Workplace*, which was published in 1999, Agents Causing Occupational Asthma with Key References or Low-Molecular-Weight Agents Causing Occupational Asthma [5]. The chapter was written by two experts in occupational asthma, Moira Chan-Yeung and Jean-Luc Malo. No formal criteria were described by the authors for the agents included in these two tables. Inclusion was based on published journal articles "derived mostly from English-language journals, but other languages were also included." (The most recent edition of this text was published in 2013, which includes an updated listing of substances causing occupational asthma, as well as detailed chapters on selected categories of substances). This table can be found at http://www.asthme.csst.qc.ca/document/Info_Med/IdCauses/Bernstein/AgentsAnglais.pdf.

The AOEC developed formal criteria for the asthmagen designation for sensitizer-induced asthma in 2002 (Table 1) and for acute irritant-induced asthma (RADS) in 2008 (Table 2). These criteria were developed by the second author in consultation with others in occupational and pulmonary medicine. Both sets of criteria were reviewed and approved by the AOEC Board of Directors, which consists of nine members: five are clinics representatives, usually physicians and four individual members, at least one of whom must be non-physicians (i.e. nurse, industrial hygienist).

Beginning in 2002, with the development of these criteria, a formal review process was begun to use the new criteria to evaluate substances on the list previously designated as causing occupational asthma and to add new substances that met the criteria. The reviews have been conducted by the two authors, one a board certified internist/pulmonologist/occupational medicine specialist did the reviews from 2002 to 2007 and second a board certified internist/occupational medicine physician did the reviews from 2008- date. Not all of the substances reported to be asthmagens in the 1995 AOEC list have yet been formally evaluated against the AOEC criteria, however the AOEC has been reviewing approximately 20 substances per year to determine which substances meet the criteria. Each year, exposures are selected for review based on recommendations from AOEC members, asthma researchers, industry representatives, or other stakeholders. These annual reports are available from the AOEC office by request (aoec@aoec.org). The Exposure Code List has two columns to identify asthmagens. The first column indicates an "A" once a substance has been designated as an asthmagen. The second column indicates which criteria were used for determining that designation. Substances reviewed and meeting criteria for sensitizer-induced asthma are designated "Rs"; those reviewed and meeting criteria for RADS are designated "Rr"; those reviewed and meeting both sets of criteria are designated "Rrs"; those reviewed and not meeting either set of criteria are designated "R". A substance that has an "R", meaning it has been reviewed but does not meet either criteria, will not have an A in the first column. Substance may not have originally had an "A" in the first column because a review may have been requested and conducted on a substance never previously designated as an asthmagen. Exposures that are still scheduled to be reviewed will be blank in the second column. Exposures that are generally accepted as an asthmagen, such as toluene diisocyanate where the medical evidence is so extensive that a review is not felt to be needed, have a "G" in the second column.

A systematic search of the English peer reviewed medical literature is conducted for each agent. This search consists of a U.S. National Library of Medicine (NLM) PubMed search including a search of TOXNET (NLM Toxicology Data Network), review of references in the articles identified and