Occupational Asthma
New Deleterious Agents at the Workplace

Catherine Lemiere, MD, MSc[a,*], Jacques Ameille, MD[b], Piera Boschetto, MD, PhD[c], Manon Labrecque, MD, MSc[a], Jacques-André Pralong, MD, MSc[d]

KEYWORDS

• Occupational asthma • Irritant-induced asthma • RADS • Occupational agents
• High-molecular-weight agents • Low-molecular-weight agents • Irritant agents

KEY POINTS

- This article summarizes the main new categories of occupational agents responsible for causing occupational asthma, with and without a latency period reported in the last 10 years.
- This article also reports examples of occupational agents for which the fabrication processing or use have influenced the outcome of occupational asthma.

INTRODUCTION

Occupational asthma (OA) refers to de novo asthma or the recurrence of previously quiescent asthma (ie, asthma as a child or in the distant past that has been in remission) induced by either sensitization to a specific substance, which is termed sensitizer-induced OA, or by exposure to an inhaled irritant at work, which is termed irritant-induced OA.

More than 400 distinct agents have been documented as causing OA.[1,2] The agents responsible for OA are classically divided according to their molecular weight. High-molecular-weight (HMW) agents (>10 kDa[3]) include proteins and microorganisms of animal and vegetable origins. Low-molecular-weight (LMW) agents include wood dust, drugs, metals, and other chemicals. The list of agents that cause OA is constantly growing[4] (www.asthme.cssst.qc.ca). The causes of irritant-induced asthma (IIA; OA without a latency period) are also steadily increasing.[5] Ammonia, chlorine, and sulfur dioxide are the most frequent causes of IIA.

Many agents, especially LMW agents can have both sensitizing and irritant properties. For example, isocyanates can induce OA by an immunologic mechanism but, at higher concentrations, they have been reported to induce irritant-induced asthma.[6]

Publications continue to report new causes of OA. This article reviews the new causes of sensitizer-induced OA and IIA reported in the last 10 years. It describes how interventions such as surveillance programs or changes in the fabrication process can influence the incidence of OA.

ALLERGIC OA

Newly Identified HMW Agents

HMW agents encountered at the workplace are natural proteins, derived from animal or plant

Disclosures: Catherine Lemière, Jacques Ameille, Piera Boschetto, Manon Labrecque, and Jacques-André Pralong do not have any conflict of interest in relation to this article.

[a] Chest Department, Sacré-Coeur Hospital, Montreal, 5400 Gouin Ouest, Montreal, Quebec H4J 1C5, Canada; [b] AP-HP, Unité de pathologie professionnelle, Hôpital Raymond Poincaré, Université de Versailles, 104 Boulevard Raymond Poincaré, Garches 92380, France; [c] Department of Clinical and Experimental Medicine, University of Ferrara, Via Fossato di Mortara, 64B, Ferrara 44100, Italy; [d] Research Center, Sacre-Coeur Hospital, Montreal, Université de Montréal, 5400 Gouin Ouest, Montreal, Quebec H4J 1C5, Canada
* Corresponding author. Hôpital du Sacré-Coeur de Montréal, 5400 Gouin Ouest, Montreal, Quebec H4J 1C5, Canada.
E-mail address: catherine.lemiere@umontreal.ca

Clin Chest Med 33 (2012) 519–530
http://dx.doi.org/10.1016/j.ccm.2012.06.003

sources that induce classic immunoglobulin (Ig) E–mediated sensitization after months or years of exposure.[4] HMW agents act as complete antigens and cause an allergic or immunologic asthma by producing specific IgE antibodies. Some newly recognized HMW agents that induce OA are discussed in this article.

Laboratory animals

Small animals represent a frequent cause of OA in laboratory technicians and veterinarians. Proteins excreted in urine, especially those produced by male rats, are the most potent source of sensitization.[7] A new gerbil allergen (*Meriones unguiculatus*) of 23 kDa has been identified in the gerbil urine, epithelium, hair, and airborne samples. Partial characterization of this allergen suggests that it could be a lipocalin.[8] Inhalation of bovine serum albumin (BSA) powder, commonly used in research laboratories, has been shown to cause OA and rhinitis in a laboratory worker in whom an IgE-mediated response was shown.[9] The patient had a high serum-specific IgE level to BSA, and a 66-kDa IgE-binding component was detected within the BSA extract on immunoblot analysis. During a bronchial provocation test with a BSA solution, the patient experienced severe systemic reactions, including eye itching, conjunctivitis, rhinorrhea, nasal obstructions, sneezing, shortness of breath, and bronchospasm, with a 30% decrease in forced expiratory volume in 1 second (FEV_1), 52% of predicted, and decreased blood pressure.

Allergens derived from flour, cereal, and vegetable matter

Cereals and flour are the oldest and most commonly identified causes of OA.[1,4] Purified wheat proteins either in natural or recombinant forms have been implicated in the pathogenesis of baker's asthma. The thaumatinlike protein and lipid transfer protein 2G were identified to be newly identified allergens associated with baker's asthma in a group of 20 patients with baker's rhinitis, asthma, or both who had positive skin-prick test reactions and specific IgE antibodies to wheat flour.[10] The recombinant wheat lipid transfer protein (Tri a 14) has also recently been recognized as a potential novel tool for the diagnosis of baker's asthma.[11] The possibility of discriminating baker's asthma, wheat-induced food allergy, and grass pollen allergy was investigated by serologic tests based on microarrayed recombinant wheat seed and grass pollen allergens.[12] Recombinant wheat flour allergens, specifically recognized by patients suffering from baker's asthma, but not from patients with food allergy to wheat or pollen allergy, were identified.

The first known case of an IgE-mediated OA to malt has been reported in a machine operator in a malt manufacturing plant.[13] Pirson and colleagues[14] described a case of a patient employed in a factory producing inulin from chicory who developed rhinoconjunctivitis and asthma to the dust of dry chicory roots. A specific inhalation challenge (SIC) with dry chicory was performed and an acute rhinoconjunctivitis and an immediate asthmatic response was seen. This case documents occupational rhinoconjunctivitis and asthma caused by IgE sensitization to inhaled chicory allergens, including one identified for the first time as a 17-kDa Bet v 1 homologous protein.

In addition, the first case of IgE-mediated occupational allergy (rhinitis and asthma) to marigold flour has been reported.[15] Marigold flour has been largely used by the food additive industry as poultry feed colorant. The sensitization was confirmed by a skin-prick test, a nasal challenge test, and specific IgE determination.

Food and fishing industry

Various foods, food additives, and contaminants have been associated with OA.[16] In the commercial fishing industry, crustaceans are the main source of sensitization, followed by mollusks and fin fish.[17] Patients who are allergic to fish can suffer asthma attacks when they breathe airborne particles from fish. Rosado and colleagues[18] described the first case of OA caused by handling and exposure to aerosolized octopus allergens in a seafood processing worker. Immunoblotting revealed IgE-binding bands of 43 and 32 kDa that likely correspond with tropomyosin (38–40 kDa) as the culprit allergen. Three workers experienced symptoms of rhinoconjunctivitis and bronchial asthma while classifying fish by size at the same fish farm.[19] Although they could eat turbot, they were sensitized to this fish probably by inhalation. Parvalbumin was identified as the causal allergen in 1 of the cases. Simultaneous type I and type IV allergic reactions (asthma and contact dermatitis) caused by occupational contact with fish parasitized by *Anisakis simplex* have been reported.[20] *A simplex* is a nematode that is a parasite of several marine organisms during its life cycle. It is known as an accidental gastrointestinal parasite in subjects who had ingested raw fish, but it has also been suggested to be the cause of allergic reactions in subjects who frequently eat or manipulate parasitized fish.

Pests and arthropods

Molds have been identified as causal agents of OA in workers exposed to coffee grounds (*Chrysonilia sitophila* [asexual state of *Neurospora*