

Medications and Work-Related Asthma

Awareness about allergic reactions to medications, particularly penicillin and cephalosporin, is widespread. Less appreciated is that workers who are involved in the manufacturing or handling of pharmaceuticals may be at risk of becoming allergic to these substances. Four examples of cases reported in Michigan with work-related asthma developing from exposure to pharmaceuticals are summarized below.

CASE REPORT #1 - A woman in her 20's developed wheezing, cough, and chest tightness in relation to work a few months after beginning to package psyllium powder at a pharmaceutical company. She was diagnosed with asthma and began taking Albuterol and Advair. She had a positive specific IgE to psyllium. She had no personal or family history of allergies or asthma. She had smoked a few cigarettes a day for four years, quitting a year before her symptoms began. Her symptoms persisted, although decreased after she was transferred away from the psyllium processing area. Two additional cases of work-related asthma were reported from the same facility of individuals who worked around the process (i.e. maintenance) but not directly with psyllium.

CASE REPORT #2 - A woman in her 40's developed cough, chest tightness and shortness of breath one year after beginning to work in a pharmacy. She was prescribed Ventolin, Advair and Singulair. Her symptoms occurred when she counted hydrocodone pills in an unventilated part of the pharmacy. She quit work because of her symptoms. Her respiratory symptoms persisted after she stopped working at the pharmacy, although they were less severe. She had smoked five cigarettes a day for three years in her 20's. She had a personal history of allergies and asthma. She had a child with asthma. She had a positive methacholine challenge test.

CASE REPORT #3 - A nurse in her 20's developed wheezing, cough and shortness of breath at a nursing home while mixing, or being in the room when a psyllium laxative was prepared. She had never smoked cigarettes. She was prescribed ProAir and Symbicort. She had allergic rhinitis and asthma as a child, and had been treated with allergy shots. She had been asymptomatic for over 10 years when her symptoms in relation to psyllium began. She had a positive specific IgE to psyllium. Her spirometry was normal.

CASE REPORT #4 - An aide in her 30's, who worked at an assisted living facility, developed wheezing and shortness of breath after mixing a psyllium powder to prepare a laxative for the residents. She had no history of allergies and had never smoked cigarettes. She was prescribed Albuterol and given Prednisone after an emergency department visit for her respiratory symptoms.

Table I lists the medications which have been categorized as causing work-related asthma. Fourteen of the medications have been reported to cause work-related asthma to individuals involved in manufacturing of the medication. In addition to manufacturing, six medications (Enflurane, Isoniazid, Isoflurane, Piperacillin, Psyllium and Sevoflurane) have caused work-related asthma in health care personnel, nurses, pharmacists or anesthesiologists, preparing or administering the medication (Table I).

Table I. Human Medications Known to Cause Work-Related Asthma

Medication	Workers at Risk	Other Conditions	Key Reference
Cefaclor Ceftazidime Cefadroxil Cefmetazole Cefoperazone Cefotetan	Pharmaceutical Manufacturers	Anaphylaxis in patients	Stenton SC, Dennis JH, Hendrick DJ. Occupational asthma due to ceftazidime. <i>Eur Respir J</i> 1995; 8:1421-3.
Cimetidine	Pharmaceutical Manufacturers	Anaphylaxis in patients	Coutts II, Lozewicz S, Dally MB, et al. Respiratory symptoms related to work in a factory manufacturing cimetidine tablets. <i>Brit Med J</i> 1984; 288:1418.
Colistin	Pharmaceutical Manufacturers	Contact Dermatitis, Rhinitis Bronchospasm in cystic fibrosis patients	Gomez-Olles S, Madrid-San Martin F, Cruz M-J, et al. Occupational Asthma due to colistin in a pharmaceutical worker. <i>Chest</i> 2010; 137:1200-1202.
Enflurane	Anesthetists, Nurses		Schwettmann RS, Casterline CL. Delayed asthmatic response following occupational exposure to Enflurane. <i>Anesthesiology</i> 1976; 44:166-169.
Hydralazine	Pharmaceutical Manufacturers	Lupus and Vasculitis in patients	Perrin B, Malo J-L, Cartier A, et al. Occupational asthma in a pharmaceutical worker exposed to hydralazine. <i>Thorax</i> 1990; 45:980-981.
Isoniazid	Pharmacists		Asai S, Shimoda T, Hara K, Fujiwara K. Occupational asthma caused by isonicotinic acid hydrazide (INH) inhalation. <i>J Allergy Clin Immunol</i> 1987; 80:578-582.
Isoflurane	Anesthetists, Nurses	Contact dermatitis	Vellore AD, Drought VJ, Sherwood-Jones D, et al. Occupational asthma and allergy to sevoflurane and isoflurane in anesthetic staff. <i>Allergy</i> 2006; 61:1485-1486.
Methyl dopa	Pharmaceutical Manufacturers	Coombs antibodies and hemolytic anemia in patients	Harries MG, Taylor AN, Wooden J, MacAuslan A. Bronchial asthma due to alpha-methyldopa. <i>Brit Med J</i> 1979; 1:1461.
Opiates	Pharmaceutical Manufacturers	Asthma in patients	Biagini RE, Bernstein DM, Klinecicz SL, et al. Evaluation of cutaneous responses and lung function from exposure to opiate compounds among ethical narcotics-manufacturing workers. <i>J Allergy Clin Immunol</i> . 1992; 89:108-118.
Penicillamine	Pharmaceutical Manufacturers		Lagier F, Cartier A, Dolovich J, Malo J-L. Occupational asthma in a pharmaceutical worker exposed to penicillamine. <i>Thorax</i> 1989; 44:157-158.
Penicillin and Ampicillin	Pharmaceutical Manufacturers	Anaphylaxis in patients	Davies RJ, Hendrick DJ, Pepys J. Asthma due to inhaled chemical agents: ampicillin, benzyl penicillin, -6 amino penicillanic acid and related substances. <i>Clin Allergy</i> 1974; 4:227-247.
Piperacillin	Pharmaceutical Manufacturers Nurses		Moscato G, Galdi E, Scibilia J, et al. Occupational asthma, rhinitis and urticarial due to piperacillin sodium in a pharmaceutical worker. <i>Eur Respir J</i> 1995; 8:467-469.
Psyllium	Pharmaceutical Manufacturers Nurses	Anaphylaxis in patients	Malo J-L, Cartier A, L'Archeveque J, et al. Prevalence of occupational asthma and immunologic sensitization to psyllium among health personnel in chronic care hospitals. <i>Am Rev Respir Dis</i> 1990; 142:1359-1366.
Salbutamol	Pharmaceutical Manufacturers		Agius RM, Davison AG, Hawkins ER, Newman Taylor AJ. Occupational asthma in salbutamol process workers. <i>Occup Environ Med</i> 1994; 51:397-399.
Sevoflurane	Anesthetists, Nurses	Contact dermatitis	Vellore AD, Drought VJ, Sherwood-Jones D, et al. Occupational asthma and allergy to sevoflurane and isoflurane in anesthetic staff. <i>Allergy</i> 2006; 61:1485-1486.
Spiramycin	Pharmaceutical Manufacturers, Farmers (used as a feed additive)	Urticaria Rhinitis	Malo J-L, Cartier A. Occupational asthma in workers of a pharmaceutical company processing spiramycin. <i>Thorax</i> 1988; 43:371-377.
Tafenoquine	Pharmaceutical Manufacturers		Cannon J, Fitzgerald B, Seed M, et al. Occupational asthma from tafenoquine in the pharmaceutical industry: implication for QSAR. <i>Occup Med</i> 2015; 65:256-258.
Tetracycline	Pharmaceutical Manufacturers	Anaphylaxis in patients	Menon MPS, Das AK. Tetracycline asthma—a case report. <i>Clinical Allergy</i> 1977; 7:285-290.
Thiamine	Fortified Cereal Manufacturers	Contact dermatitis, anaphylaxis in patients	Drought VJ, Francis HC, Niven R, McL, Burge PS. Occupational asthma induced by thiamine in a vitamin supplement for breakfast cereals. <i>Allergy</i> 2005; 60:1213-1218.
Vancomycin	Pharmaceutical Manufacturers		Choi GS, Sung JM, Lee JW, et al. A case of occupational asthma caused by inhalation of vancomycin powder. <i>Allergy</i> 2009; 64:1391-1392.

Consistent with workers who manufacture pharmaceuticals being at increased risk are the five substances listed in Table II where work-related asthma was reported from exposure to intermediaries in pharmaceutical manufacturing.

Table II. Pharmaceutical Intermediates Known to Cause Work-Related Asthma

Pharmaceutical Intermediary	Used to produce	Key Reference
Phenylglycerine Acid Chloride	Ampicillin, cephalexin, cephaloglycin	Kammermeyer JK, Mathews KP. Hypersensitivity to phenylglycine acid chloride. <i>J Allergy Clin Immunol</i> 1973; 52:73-84.
7-aminocephalosporanic acid (7-ACA) Tosylate dihydrate (7-CTD) 7-Amino-3-thiomethyl-3-(7-TACA) Cephalosporanic acid	Cephalosporins	Pala G, Pignatti P, Perfetti L, Cosentino R, Moscato G. Occupational asthma and rhinitis induced by a cephalosporin intermediate product: description of a case. <i>Allergy</i> 2009; 64:1390-1391.
Chicory	Inulin	Pirson F, Detry B, Pilette C. Occupational rhinoconjunctivitis and asthma caused by chicory and oral allergy syndrome associated with Bet v 1-related protein. <i>J Investig Allergol Clin Immunol</i> 2009; 19:306-310.
Potassium Tetrachloroplatinate	Cisplatin	Thanasias E, Polychronakis I, Van Kampen V, et al. Occupational immediate-type allergic asthma due to potassium tetrachloroplatinate in productions of cytotoxic drugs. <i>Adv Exp Med Biol</i> 2013; 755:47-53.

Four medications (Spiramycin, Thiamine, Amprolium and Tylosin Tartrate) have caused work-related asthma in workers exposed to animal feed or cereal with medication additives. Amprolium and tylosin tartrate are exclusively used in veterinary practice (Table III).

Table III. Veterinary Medications Known to Cause Work-Related Asthma

Medication	Workers at Risk	Other Conditions	Key Reference
Amprolium	Feed Manufacturers, Farmers (used as a feed additive)		Greene SA, Freedman S. Asthma due to inhaled chemical agents—amprolium hydrochloride. <i>Clin Allergy</i> 1976; 6:105-108.
Tylosin Tartrate	Farmers, Veterinarians Pharmaceutical Manufacturers	Contact Dermatitis	Lee HS, Wang YT, Yeo CT, et al. Occupational asthma due to tylosin tartrate. <i>Brit J Ind Med</i> 1989; 46:498-499.

We are interested in hearing from you if you have a patient with recurrent symptoms in association with work exposure to a medication. Ways to notify us are listed on the back page of this newsletter, or you can call Ken Rosenman, MD at 1-800-446-7805 to discuss.



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S Remember to report all cases of occupational disease!

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