Occupational Airways

A quarterly newsletter of the Occupational Health Surveillance Program, Division of Environmental Epidemiology and Occupational Health (EEOH), Connecticut Department of Public Health, 150 Washington Street, Hartford, CT 06106 (860) 240-9029

March 1996

This issue:

Isocyanates & Asthma

by Juanita Estrada, MSPH, Department of Public Health, Renae Reese, MPH, University of CT Health Center & Eileen Storey, MD, MPH, University of CT Health Center

Occupational asthma has become the most prevalent occupational lung disease in developed countries. In the United States, it is estimated that up to 15% of diagnosed asthma cases in adults are due to workplace exposure. Of the approximately 250 known work-related asthmagens, isocyanates are the most common cause of occupational asthma. The prevalence of isocyanate-induced asthma in exposed workers has been documented to be between 5-10%.[1,2,3]

In CT, respiratory diseases and disorders are the fourth most commonly reported occupational conditions. Occupational asthma accounts for approximately 30% of the respiratory diseases and disorders reported. Of the asthma cases (including Reactive Airways Dysfunction Syndrome-RADS) reported to the Departments of Labor and Public Health, 17% are isocyanate-induced.[4]

Isocyanates are highly reactive low molecular weight compounds which have an -N=C=O group attached to a radical. The most commonly used isocyanates are toluene diisocyanate (TDI), 4,4'-diphenylmethane diisocyanate (MDI), and hexamethylene diisocyanate (HDI). Other isocyanates include 1,5-naphthylene diisocyanate (NDI), isophorone diisocyanate (IPDI), and 4,4'-dicyclohexylmethane diisocyanate (hydrogenated MDI, HMDI).[1,5]

Isocyanates are mainly used in industry, especially in automobile, airplane, and train manufacturing and foundries. Isocyanates are a key ingredient in the production of polyurethane products. These products include rigid and flexible foams, synthetic rubbers, spandex fibers, protective coatings for electrical wiring and cables, liners for mine and grain elevator chutes, casts and molds, and adhesives and binders used in foundries. Isocyanates are also used in the production of paints, varnishes, lacquers, and caulking. TDI and MDI are both used in the manufacturing of polyurethanes, and HDI is used in spray paints.[1,2,5,6]

Occupations at risk of isocyanate exposure include polyurethane foam makers, plastic molders, upholstery and furniture workers, spray painters, wire coating workers, rubber workers, insulation installers, and workers in foundries and transportation equipment manufacturing.[1,2,5]

Exposure to isocyanates occurs by vapor inhalation. Acute exposure can cause irritation to the skin, mucus membranes and eyes. The dose (concentration and length of exposure) of isocyanates that will induce asthma is unknown. However, it has been documented that once a worker has been sensitized to TDI, very low levels can trigger an asthma attack.[8]

According to Amdur et. al., both immunological and nonimmunological mechanisms appear to be operative in isocyanate-induced asthma. Unlike protein allergens, isocyanates induce asthma through a non-IgE-dependent mechanism. Specific antibodies have been found in only a small percentage, 10-30%, of patients with diagnosed

WE'RE MOVING!

We are scheduled to move on March 29th. Our new mailing address will be as follows:

CT Department of Public Health
410 Capitol Ave., MS#11OSP
P.O. Box 340308
Hartford, CT 06134-0308
Phone: 860/509-7744 Fax: 860/509-7785

asthma. RADS can also occur following exposure to high levels of isocyanates as in spill situations. There is continuing research to determine the mechanism by which isocyanates and other low molecular weight compounds, such as wood dusts, metal salts, acid anhydrides and antibiotics, induce asthma.[1,2,3,6,7]

TDI has been the isocyanate most studied. In addition to asthma, TDI has been shown to cause a variety of respiratory problems, including chemical bronchitis, hypersensitivity pneumonitis, and chronic deterioration in lung function. MDI has also been associated with occupational asthma. It is being substituted for TDI because of its lower vapor pressure. The health hazards of other isocyanates have not been studied in detail.[9]

Studies have shown that patients with isocyanate-induced asthma may continue to be symptomatic for months and even years after removal from the exposure. Cross reactivity between isocyanates is also documented. Personal or family history of atopy, smoking status, and pre-existing asthma do not appear to be related to the development of isocyanate-induced asthma.[7,9,10]

Prevention is the key. The National Institute of Occupational Safety and Health (NIOSH) and the American Conference of Governmental Industrial Hygienists (ACGIH) recommend that isocyanate exposure not exceed an 8 hr. time weighted average of 0.005 ppm. Engineering controls, personal protective equipment and/or substitution with other chemicals when possible should be employed to limit worker exposure to isocyanates. Once a worker has become sensitized to isocyanates, early diagnosis and medical management, along with exposure control or removal from the offending source are imperative. (See page 3 for an outline of asthma diagnostic techniques.) [1,5,11]

Summary of Number of Cases of Selected Respiratory Diseases
CT DPH Occupational Disease Surveillance Data

	11/91-12/93	1994	1995*	ODSS** Total
Asthma	41	14	30	85
RADS	6	1	1	8
Silicosis	2	4	1	7
Asbestosis	27	3	5	35
Asbestos-related pleural diseases	90	17	8	115
Total	166	39	45	250

* As of February 29, 1996
**Occupational Disease Surveillance System (ODSS)

CASE REVIEW

Asthma in a Mold Developer: Worksite Evaluation Reveals Likely Culprit

After approximately fifteen months of work creating molds and plastic parts, and demonstrating the casting machine for customers, worker B, a 37-year-old male, developed hay fever symptoms - sneezing, sniffles, itching eyes and congestion. Two months later he started experiencing chest tightness, shortness of breath, and difficulty speaking. He had no history of asthma or allergies and had quit smoking five years prior to the onset of symptoms.

In reporting his history, he noted that his advancing symptoms always occurred at work and always during some aspect of the casting process. The Material Safety Data Sheet (MSDS) for the polyurethane resin used to make the prototype parts indicated that 4,4'-diphenylmethane diisocyanate (MDI), a well documented sensitizer, was a component.

Suspecting occupational asthma, Worker B was asked to use a peak flow meter eight times a day, both at work and away from work, for two weeks. Review of the peak flow diary showed a consistent drop of expiratory flow of more than 15 percent during the work day, with recovery at night and by the next morning. Pre- and post-shift spirometry were not performed, as efforts were already underway to eliminate his exposure at work.

With asthma symptoms temporally related to work, exposure to MDI, a known asthma sensitizer, and peak flow tracings indicating expiratory flow declines at work, Worker B was diagnosed with occupational asthma.

During a workplace evaluation, an industrial hygienist recommended controlling MDI vapor using local exhaust ventilation for all casting and molding operations. When emissions could not be directly vented, Worker B was advised to wear respiratory protection. Ventilation improvements, designed by Worker B, and respiratory protection relieved the symptoms. Moving Worker B's office away from the casting area and promoting him, with subsequent change in duties further reduced his exposure to MDI. However during demonstrations of processes away from the shop when ventilation systems were not in place and respiratory protection would inhibit communication, Worker B continued to experience asthma symptoms.

Because sensitization is progressive and can lead to chronic asthma, additional job function changes were recommended to eliminate direct exposure to MDI. While Worker B's employer attempted to implement these changes, it was not practical, and the patient continued to be exposed and symptomatic. He left his job. In this case, control of MDI emissions with local exhaust ventilation at all sites where the casting machine is demonstrated or used was recommended to prevent asthma for other potentially exposed workers.

For more information about occupational asthma & isocyanates, contact DPH/EEOH at (860) 509-7744.

REFERENCES:

1. Chan-Yeung, M. and J-L. Malo. Aetiological agents in occupational asthma. *EUR Respir J* 1994; 7:346-371.
2. Chan-Yeung, M. and J-L. Malo. Occupational asthma. *N Engl J* Med 1995, 333:107-112.
3. Alberts, W.M. and S. Brooks. Occupational asthma. *Postgrad Med* 1995, 97:93-104.
4. Occupational disease surveillance system summary data. State of Connecticut, Department of Public Health, Environmental Epidemiology and Occupational Health Division, Occupational Health Surveillance Program, Hartford, CT.
5. MA Department of Public Health Occupational Health Surveillance Program and the MA Thoracic Society. Isocyanate exposure and occupational asthma. *SENSOR Occupational Lung Disease Bulletin* December 1994.
6. Herd, Z., D. Berstein. Antigen-specific stimulation of histamine releasing factors in diisocyanate-induced occupational asthma. *Am J Respir Crit Care Med* 1994, 150:988-994.
7. Amdur, M., J. Doull, C. Klaassen. *Casarett and Doull's Toxicology: The Basic Science of Poisons* , 4th ed. (New York: Pergaman Press, 1991), pp. 305-6.
8. Vandenplas, O., A. Cartier, H. Ghezzo, Y. Cloutiers and J.L. Malo. Response to isocyanates: effect of concentration, duration of exposure, and dose. *Am Rev Respir Dis* 1993, 147:1287-1290.
9. Fuortes, L., S. Kiken, M. Makowsky. An outbreak of naphthalene di-isocyante-induced asthma in a plastics factory. *Arch Environ Health* 1995, 50:337-340.
10. Pisati G., A. Baruffini, S. Zedda. Toluene diisocyanate induced asthma: outcome according to persistence or cessation of exposure. *Br J Ind Med* 1993, 50:60-64.
11. Doull, J., C. Klaassen, Amdur, M. *Casarett and Doull's Toxicology: The Basic Science of Poisons* , 2nd ed. (New York: MacMillan Publishers Co. Inc., 1980).

Occupational Asthma: Diagnostic Techniques

by Eileen Storey, MD, MPH & Renae Reese, MPH,
University of CT Health Center

The following is an outline of diagnostic techniques utilized by the University of CT's Occupational Health Unit when work-related asthma is suspected.

Document asthma

- **Record symptoms**
  - -Wheezing
  - -Cough
  - -Chest tightness
  - -Shortness of breath

- **Conduct pulmonary function tests**
  - -Peak flows recorded 8 times daily for 2 wks
  - -Spirometry with and without bronchodilators
  - -Methacholine challenge for strong history and negative pulmonary function tests

Document work-relatedness

- Determine if symptoms are temporally related to work.

- Obtain work history
  - - Duration of exposure
  - - Exposures in previous jobs

- Assess work exposures
  - - Processes
  - - Substances/Materials used

- Evaluate physiology
  - - Peak flows recorded 8 times daily for 2 weeks
  - - Spirometry before and after working with the suspected agent on a Monday or equivalent. Repeat on Friday afternoon if no drop on Monday.

- Identify other cases from same workplace

Document work exposures

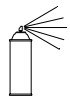
- Obtain Material Safety Data Sheets
- Conduct worksite visit
- Identify known asthma agents in the workplace or work processes known to cause asthma
- Identify suspected asthma agents

Control or eliminate worksite exposures and note improvement

(In long established cases improvement may not be possible)

For more information, contact Dr. Eileen Storey at the University of CT Health Center, Section of Occupational & Environmental Medicine at (860) 679-2893.

Yale Clinic Begins Study of Asthma Due to Spray Paints



by Mark Cullen, MD, Yale School of Medicine

A significant problem of isocyanate-induced asthma has been the lack of recognition by both workers and their physicians. The symptoms often start very subtly with a cough and chest discomfort before more classic symptoms like wheezing and shortness of breath ensue. When the possibility of asthma is finally considered, no simple symptom or test can be used to point towards the workplace or the particular culprit, isocyanates. Only a clear history of exposure coupled with evidence of worsening symptoms during or shortly after work help distinguish isocyanate asthma from every other variant of asthma.

Investigators from the Yale Occupational Medicine Program have begun a clinical study to address this problem. The study involves a bronchoscopy and blood tests immediately after an exposure to isocyanates, looking for T-lymphocytes migrating to the lungs in response. Early tests have shown that there is a brisk response of these cells, comparing the lung before and after the exposure. The next step will be to try to isolate the T-cells which "recognize" the isocyanate molecule and are stimulated by the exposure to react. Although there has not been success in isolating such cells in the preliminary tests, a method has been identified which will be used in the future. At the same time, Yale has collaborated with toxicologists at the University of Pittsburgh to identify the binding of the highly reactive isocyanates throughout the lining of the airway, which has never been previously shown in workers' lungs.

The most important aspect of the trial should begin sometime later in the year. Physicians from the clinic, along with industrial hygienists, will be visiting auto body shops where spray painting occurs and occupational asthma is a significant problem. They will be looking for simpler ways to diagnose this disorder, as well as for preventive measures. Blood and lung lavage fluid from the auto body workers who have asthma due to isocyanates will be further studied in the lab in hope of finding the elusive immune cells at the heart of the disease.

For more information, contact Dr. Mark Cullen at the Yale Occupational and Environmental Medicine Program, at (860) 785-5885.

Turning Diagnosis into Prevention

A Day Long Occupational Medicine Conference

Rescheduled to Wednesday, June 26, 1996

Connecticut Hospital Association
110 Barnes Road
Wallingford, CT

For more information call, DPH/EEOH at (860) 240-9029

Sponsored the Departments of Health & Labor and CT's Occupational Medicine Clinics

Occupational Airways is produced by the Occupational Health Surveillance Program, Division of EEOH, Connecticut Department of Public Health.

Editor:
Juanita Estrada, Epidemiologist

Staff:
Carolyn Jean Dupuy, Director
Betty Jung, Epidemiologist
Marian Heyman, Epidemiologist/Industrial Hygienist

Contributors to this edition:
Mark Cullen, MD
Renae Reese, MPH
Eileen Storey, MD, MPH

Connecticut Department of Public Health
Division of Environmental Epidemiology & Occupational Health
150 Washington Street
Hartford, CT 06106

TO: