

DISINFECTANTS AND ASTHMA: PART II

The Winter 2008-2009 SENSOR newsletter (Vol. 20, No. 1) reviewed the medical literature that demonstrates quaternary ammonium chloride compounds can cause asthma. These disinfecting agents are commonly found in home cleaning products. In response to readers' questions about whether other types of disinfectants can also cause asthma, particularly those used in health care settings, this issue of PS News presents information about additional disinfectants.

Table I summarizes the literature on some key chemical disinfectants and their potential to cause asthma. Sufficient medical documentation shows that individuals can become sensitized and develop asthma from exposure to formaldehyde, glutaraldehyde and the quaternary ammonium chloride compounds as well as the chlorine-containing compounds of chloramine-T, chlorhexidine and hexachlorophene. In addition, acute high level exposure to chlorine-containing compounds and formaldehyde and possibly peracetic acid can cause Reactive Airways Dysfunction Syndrome

TABLE I. CHEMICAL DISINFECTANTS

Disinfectant	Evidence of		
	Sensitization	Asthma from Sensitization	RADS
Alcohol			
Ethyl or Isopropyl	No	No	No
Chlorine			
Hypochlorite	No	No	Yes
Chloramine T	Yes	Yes	No
Chlorhexidine	Yes	Yes	No
Hexachlorophene	No	Yes	No
Aldehydes			
Formaldehyde	Yes	Yes	Yes
Glutaraldehyde	Yes	Yes	No
Ortho-Phthalaldehyde (OPA)	Yes	No	No
Peroxide			
Hydrogen Peroxide	No	No	No
Peracetic Acid	No	?	?
Iodophors	?	No	No
Phenolics	No	No	No
Quaternary Ammonium Chloride	Yes	Yes	No

(RADS).

A recent CDC publication reviewed ten chemical disinfectants used in health care facilities (Rutala et al, 2008). *Disinfection* is defined as the elimination of most if not all microbial life except for spores, while *sterilization* eliminates all microbial life including spores.

The mechanism for the development of asthma is indicated in Table I as either: (1) immunologically mediated with sensitization or (2) secondary to an irritant reaction that occurs after high level exposure.

The determination of whether a substance causes asthma was based on the Association of Occupational and Environmental Clinics (AOEC) Exposure List of Asthmagens. The AOEC is an organization of more than 60 occupational and environmental medicine clinics; this group has developed criteria and set up a review process to designate whether a substance causes asthma. Separate criteria have been developed for sensitizers and the irritants that cause RADS (http://www.aoec.org/content/Asthmagen_Protocol_10-25_08.pdf).

SPECIFIC DISINFECTANTS

ALCOHOL

Both ethyl and isopropyl alcohol are bactericidal. Neither has been approved as the main ingredient in any liquid sterilant or high level disinfectant by the FDA.

There are no studies to suggest they can cause asthma.

CHLORINE

Both sodium and calcium hypochlorite are commonly used disinfectants. They are usually used in aqueous solutions of 5.25% - 6.15% (bleach). Chloramine-T and sodium dichloroisocyanurate are other examples of chlorine-based disinfectants.

Exposure to high levels of bleach (hypochlorite) can cause RADS. Mixing bleach with an acid, which releases chlorine, or mixing bleach with ammonia which releases chloramine has also been shown to cause RADS.

Chloramine-T is well-documented to cause sensitization and asthma with at least ten peer-reviewed publications showing positive specific antigen bronchoprovocation and positive skin or specific IgE tests.

Although not mentioned in the CDC review, both chlorhexidine and hexachlorophene are both chlorine-based disinfectants. For each of these substances there is a single peer-reviewed publication showing that the compound caused asthma in health care personnel. In addition, for chlorhexidine there are multiple publications on cases of anaphylaxis with positive skin tests to chlorhexidine.

ALDEHYDES

Formaldehyde is commonly used as a water-based solution called formalin, which is 37% formaldehyde. Both positive specific antigen bronchoprovocation and specific IgE testing are well-documented, although more recent studies have suggested that an allergic reaction to formaldehyde occurs less frequently than originally suspected. Acute high level exposure to formaldehyde has also been reported to cause RADS.

For glutaraldehyde, there are at least 44 well-documented cases of occupational asthma from seven peer-reviewed publications. These publications include positive specific antigen bronchoprovocation and skin and specific IgE tests.

Ortho-phthalaldehyde (OPA) has been introduced as a less toxic, more efficient substitute for glutaraldehyde. There is one poorly documented case report of *occupational* asthma after exposure to OPA. The subject in this one case report had symptoms of asthma which improved away from work; however, this individual had no pulmonary function testing. There are, however, reports of anaphylaxis in *patients* who had endoscopic procedures using equipment that had been disinfected with OPA. These patients had positive skin tests or specific IgE tests to OPA.

IODOPHORS

Iodophors are a combination of iodine and a carrier agent. There are no FDA approved liquid chemical sterilants or high-level disinfectants with

iodophor as the active ingredient.

There are no reports that iodophors cause asthma although exposure to iodine as a contact agent or after ingestion is associated with allergic reactions.

PEROXIDES

Hydrogen peroxide at high exposures is irritating to mucosal surfaces. There are no reports that it causes asthma.

Peracetic acid (peroxyacetic acid) is manufactured from acetic acid and hydrogen peroxide and is sold in solution with acetic acid and hydrogen peroxide to maintain its stability. When dissolved in water it forms hydrogen peroxide and acetic acid. Glacial acetic acid, which is pure acetic acid, has been shown to cause asthma both as a sensitizer with specific antigen bronchoprovocation and as an irritant after a large spill. There are no studies showing asthma after exposure to more dilute solutions such as vinegar (4-8% acetic acid). There are no studies showing the development of asthma after the use of peracetic acid.

KEY REFERENCES

- Kivity S, Fireman E, Lerman Y. Late asthmatic response to inhaled glacial acetic acid. *Thorax* 1994; 49:727-728.
- Kujala VM, Reijula KE, Ruotsalainen E-M, et al. Occupational asthma due to chloramine-T solution. *Respir Med* 1995; 89:693-695.
- Beaudouin E, Kanny G, Morisset M, Renaudin JM, Mertes M, Laxenaire MC, Mouton C, Jacson F, Moneret-Vautrin DA. Immediate hypersensitivity to chlorhexidine: literature review. *Eur Ann Allergy Clin Immunol* 2004; 36:123-6.
- Nagy L, Orosz M. Occupational asthma due to hexachlorophene. *Thorax* 1984; 39:630-631.
- Fujita H, Ogawa M, Endo Y. A case of occupational bronchial asthma and contact dermatitis caused by ortho-phthalaldehyde exposure in a medical worker. *J Occup Health* 2006; 48:413-416.
- Gannon PF, Bright P, Campbell M, O'Hickey SP, Burge PS. Occupational asthma due to glutaraldehyde and formaldehyde in endoscopy and x ray departments. *Thorax* 1995;50:156-9.
- Bernstein JA, Stauder T, Bernstein DI, Bernstein IL. A combined respiratory and cutaneous hypersensitivity syndrome induced by work exposure to quaternary amines. *J Allergy Clinical Immunol* 1994; 94:257-259.
- Rutala WA, Weber DJ and the Healthcare and Infection Control Practices Advisory Committee. Guideline for disinfection and sterilization in healthcare facilities, 2008. www.cdc.gov/NCIDOD/dhqp/pdf/guidelines/disinfection_Nov_2008.pdf.

PHENOLICS

Two phenol derivatives commonly used as disinfectants are ortho-phenylphenol and ortho-benzyl-para-chlorophenol. These substances are irritants. There are no reports of phenolic compounds causing asthma.

QUATERNARY AMMONIUM CHLORIDE COMPOUNDS

These compounds were the subject of the Winter 2008-2009 Volume 20, No. 1 issue of this newsletter. Published peer-reviewed articles documented positive specific antigen bronchoprovocation and positive skin testing.

SUMMARY

A number of chemical disinfectants are potential causes of asthma in hospital workers. As always, we are interested in receiving reports of such cases and are happy to provide assistance in diagnosing and managing individual patients. Kenneth Rosenman, MD can be reached at 1-800-446-7805 to discuss individual patients.

*Project
S E.N.S.O.R.

News

Michigan State University
College of Human Medicine
117 West Fee Hall
East Lansing, MI 48824-1316
Phone (517) 353-1846

Address service requested.

In this issue:
v20n2: Disinfectants and Asthma: Part II

*Remember to report all cases of occupational disease!

Printed on recycled paper.

Michigan Law Requires
the Reporting of
Known or Suspected
Occupational Diseases

Reporting can be done by:

Web

www.oem.msu.edu

E-Mail

ODREPORT@ht.msu.edu

FAX

(517) 432-3606

Telephone

1-800-446-7805

Mail

Michigan Occupational Safety &
Health Administration (MIOSHA)

Management and Technical

Services Division

P.O. Box 30649

Lansing, MI 48909-8149

Reporting forms can be obtained by

calling (517) 322-1817

Or

1-800-446-7805

Project SENSOR Staff

*At the Michigan Occupational
Safety & Health Administration
(MIOSHA)*

Douglas J. Kalnowski, M.S., C.I.H.,
Director MIOSHA, Project SENSOR,

Co-Director

John Peck, M.S., Director MTS Division

Byron Panasuk, C.I.H., C.S.P.,
Project SENSOR Specialist

*At Michigan State University—
College of Human Medicine*

Kenneth D. Rosenman, M.D.,
Professor of Medicine

Project SENSOR, Co-Director

Mary Jo Reilly, M.S.,
Project SENSOR Coordinator

Melissa May, Ph.D.,
Project SENSOR Office Staff:

Tracy Carey

Amy Krizek

Ruth VanderWaal

Patent Interviewers:

Mario Espindola

Michael Moffat

Maureen O'Brien

Sarah Schauben

Liz Wilson

Advisory Board

John J. Bernick, M.D., Ph.D.,
Representative, Michigan Occupational

& Environmental Medical Association

James Blessman, M.D., M.P.H.,
Wayne State University

Kevin Flaherty, M.D.,
President, Michigan Thoracic Society

Michael Harbur, M.D., M.P.H.,
Center for Occ. and Env. Medicine

AFL-CIO, Medical Advisor

Edward Zoratti, M.D.,
President, Michigan Allergy and

Asthma Society

Thomas G. Robins, M.D., M.P.H.,
University of Michigan

School of Public Health

Division of Occupational Medicine

The Project SENSOR News is published
quarterly by Michigan State University-College
of Human Medicine with funding from the
National Institute for Occupational Safety and
Health and is available at no cost. Suggestions
and comments are welcome.

(517) 353-1846
MSU-CHM
117 West Fee Hall
East Lansing, MI 48824-1316