Common and Unrecognized Allergens in the Health Care Workforce

Karin Pacheco, MD, MSPH
Division of Environmental & Occupational Health Sciences
Allergic disease in the healthcare workplace can be difficult to diagnose, and identifying the allergic trigger even harder.

The goals of this talk are:

- To recognize the most common allergic exposures,
- To distinguish the diseases these can cause, and
- To learn how to make the association between exposure and disease.
Outline

► Who are the exposed workers
► Where do they work
► Primary routes of exposure
► Health endpoints
► Common allergens
► Uncommon allergens
► Diagnosis and Prevention

http://www.newberry.edu/academics/areasofstudy/nursing
Who are exposed?

A. **Primary exposed** – direct use of allergen
   - Physicians, Surgeons
   - RN, LPN, nurses’ aides
   - Surgical technicians, respiratory technicians, endoscopy technicians
   - Dentists, dental technicians and nurses
   - Pharmacists, pharmacy technicians
   - Cleaners, maintenance workers

B. **Secondhand exposed**
   - Administrative, clerical personnel
Where do they work?

- OR
- ICU
- ED
- Floor
- Clinics
- Pharmacy
- Respiratory department
- Central supplies
- Maintenance/household
Contact allergies in healthcare workers


- N=13,849 patch tested patients with eczema
  - 1992-1995
  - Occupational subgroup n = 2,234: nurses, nurses aides, OR nurses, dental nurses and technicians, lab workers, receptionists, masseurs, surgeons, physicians, dentists.
- Among healthcare workers, nurses are most affected by hand dermatitis (~30%), both irritant or allergic.

Most frequent allergens in women with medical occupations compared to controls

<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thimerosol</td>
<td>12.6%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Glutaraldehyde</td>
<td>9.9%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Thiuram-mix</td>
<td>6.7%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>3.6%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Glyoxal*</td>
<td>4.2%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

*p<0.05

*cross-links polymers, acts as biocide & disinfectant

http://www.chemspider.com/Chemical-Structure

di(n-propyl)thiuram disulfide
Leading allergens by job group:
Relative risk of sensitization compared to controls

- Nickel  1.3 receptionists (physicians 0.7)
- Fragrance  1.5 masseurs, 1.2 RNs
- Thimerosol  5.3 dentists, 3.2 MDs, 2.8 RNs
- Thiuram  4.8 dentists, 3.1 MDs, 2.8 RNs
- Glutaraldehyde  10.1 dental RNs, 4.5 RNs
- Glyoxal*  5.2 dental RNs, 4.1 RNs
- Formaldehyde  2.1 masseurs, 2.0 RNs and Lab techs
- Benzalkonium  2.1 dental RNs, 1.5 RNs

*cross-links polymers, acts as biocide & disinfectant
What are the main routes of exposure?

- Skin
- Lung
What are the health outcomes?

- Hives
- Rhinitis, sinusitis
- Asthma
- Contact Dermatitis: Type IV allergy
Type 1 immune reactions

► Based on IgE to a specific allergen, with acute symptoms that begin minutes after exposure.
► Diagnosed by prick skin test.
Type IV immune reactions

- Based on sensitized T cells migrating into the area of allergen exposure; reaction comes on gradually over 24 to 48 hours after exposure.
- Diagnosed by patch testing.
What are some of the common allergens?

- Latex, rubber accelerators
- Biocides
  - Glutaraldehyde
  - Formaldehyde
How are latex objects made?

- Chemicals are added to the sap from the Hevea brasiliensis tree to polymerize the latex, and allow it to be formed into objects.
- Also used in non-latex gloves
Rubber accelerators

- Benzothiazoles
  - 2-Mercaptobenzothiazole (MBT)

- Carbamates
  - Dithiocarbamates
  - Diphenylguanidine

- Thiurams

- Hexamethylenetetramine (methenamine)

All of these are potential sensitizers
Common allergens: latex, rubber accelerators

- 24% (316/1294) HCW reported glove-related skin symptoms; 295 had skin and patch testing.
  - 9% (27/295) latex PST +
  - 10.5% (31/295) thiurams / carba mix patch test +

- 93% (275/295) contact dermatitis: irritant or allergic
  - 4% (13/295) contact urticaria,
  - 4% (7/295) had both.

Type I allergy to NRL and type IV allergy to rubber chemicals in HCW with glove-related symptoms. Clin Exp All 2002; 32: 441-7.
Common allergens:
laxet, rubber accelerators

► 11.5% (59/512) OR staff reported latex glove symptoms.
► 83% (49/59) PST or RAST + to latex.
► 48/59 were patch tested:
  ▪ 25% (12) + latex
  ▪ 27% (13) + rubber additives (thiuram mix)
  ▪ 8.5% (5) both type I and type IV allergy.

Prevalence of type I allergy to NRL and type IV allergy to latex/rubber additives in OR staff with glove-related symptoms.
Common sensitizing biocides affecting the hands

- **Glutaraldehyde**: powerful biocide in sterilizing solutions, disinfectants, waterless hand soaps, fabric softeners, radiograph developers.
  - Dentists and maintenance workers are most likely to be sensitized.

- **MCI/MI** (methyl chloro isothiazolinone, methyl isothiazolinone): baby wipes, moist toilet paper, topical meds, creams and cosmetics.

Common allergens: Biocides

► **Chloroxylenol**: (Aero-Otic™ HCCortane B™ AqueousCortane B™ OticCortane™) cleaning fluids used in medical facilities, preservative for paints, adhesives, MWF, hand washes, skin disinfectants. Reported as one of the top 4 causes of hand dermatitis in HCW.

► **Parabens** (para-hydroxybenzoic acid – most common are methyl and propyl): topical meds.

Common allergens: Formaldehyde and formaldehyde releasers

- **Formaldehyde** – found in disinfectants/skin care products, topical medications.
  - **Quaternium-15**: adhesives, cleansers/disinfectants
  - **DMDM hydantoin** (Glydant)
  - **IMID** (imidazolidinyl urea, Germall 115): topical meds
  - **DIAZ** (diazolidinyl urea): cleaning agents, detergents, topical meds.
  - **Bronopol/Myacide BT or AS**
    - (2-bromo-2-nitropropane-1,3-diol): topical meds
Occupational exposures and asthma in HCW

► Mail-in questionnaire response 3,650/5,387 (68%)
  ▪ Occ therapists 73%, RNs 70%, Resp therapists 65%, MDs 54%

► Two outcome variables:
  ▪ MD dx asthma with onset after entry into health care
  ▪ Chest symptoms predicting methacholine reactivity <4 mg/mL
    ▶ trouble breathing, wheezing, shortness of breath, nocturnal cough or chest tightness, allergy sx with animals, dust, trees, grasses, pollen, etc. in past 12 months

► Developed job exposure matrix (JEM)
  ▪ Job axis: job title and main practice setting
  ▪ Exposure axis of 4 main exposure classes: a) cleaning products, b) powdered latex gloves, c) aerosolized medications, and d) adhesives/solvents/gases.

### Odds Ratios for risk of asthma with specific exposures*

<table>
<thead>
<tr>
<th>Cleaning agents</th>
<th>MD dx asthma</th>
<th>BHR sx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient care</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Instrument cleaning</td>
<td>2.22</td>
<td>ns</td>
</tr>
<tr>
<td>Surface cleaners</td>
<td>2.02</td>
<td>1.63</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Pre-1992</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>1992-2000</td>
<td>2.17</td>
<td>ns</td>
</tr>
<tr>
<td>After 2000</td>
<td>ns</td>
<td>ns</td>
</tr>
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*adjusted for seniority (in quartiles), race/ethnicity BMI, atopy

G Delclos et al. AJRCCM 2007; 175: 667-75.
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<tr>
<td>Adhesives/Solvents/Gases:</td>
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<tr>
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<td></td>
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<tr>
<td>On surfaces</td>
<td>ns ns</td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>0.53 ns</td>
<td></td>
</tr>
<tr>
<td>Aerosolized meds</td>
<td>1.72 1.40</td>
<td></td>
</tr>
<tr>
<td>Spill at work</td>
<td>ns 2.02</td>
<td></td>
</tr>
</tbody>
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G Delclos et al. AJRCCM 2007; 175: 667-75.
Instrument Cleaning/Disinfection Products

- Glutaraldehyde
- Isopropanol
- Orthophthaldehyde (Cidex OPA)
- Sodium sesquicarbonate
- Subtilisins (enzymatic cleaners)

G Delclos et al. AJRCCM 2007; 175: 667-75.
Building surface cleaners

- Acetic acid
- Ammonia/ammonium hydroxide
- Bleach (sodium hypochlorite-NaClO)/hydrochloric acid
- Butyl, ethyl, methyl parabens
- Diethanolamine
- Phosphoric acid
- Quaternary ammonium compounds
- Sodium sulfate / sulfuric acid

G Delclos et al. AJRCCM 2007; 175: 667-75.
Adhesives used in patient care

► Adhesive removers
  - Acetone, ethanol, isopropanol
  - Dipropylene glycol methyl ether

► Stoma care products
  - Carboxymethyl ether
  - Hexane-based skin bond
  - Methylbenzene

► Other: methylene chloride, (trichloroethane)

Most are solvents and irritants, not asthmagens

G Delclos et al. AJRCCM 2007; 175: 667-75.
Asthma related to cleaning agents

► N=44 patients with Specific Challenge (SIC) to cleaning products 1992-2011, positive in 17 (39%).
► ++SIC → 3x fall in PC20 FEV-1, Sputum EOS 1.8% → 10% at 7 hrs post challenge
► Cleaning products:
  ▪ QACs (n=10)
  ▪ Glutaraldehyde (n=3)
  ▪ Both (n=1)
  ▪ Ethanolamines (n=2).

Vandenplas O et al. Asthma related to cleaning agents. BMJ Open 2013;3:
What are some uncommon allergens?

- Quaternary ammonium compounds (QACs)
- Bacterial cleaners: enzyme solutions
- Orthopedic and dental cements
HEALTH EFFECTS

► Acute
- Swallowed: Considered an unlikely route of entry in commercial / industrial environments. May be irritating to gastro-intestinal tract.
- Eye: May cause irritation and reddening.
- Skin: May cause irritation.
- Inhaled: Inhalation of mist may cause irritation.

► Chronic
- Swallowed: No effects known.
- Eye: No effects known.
- Skin: No effects known
- Inhalation: No effects known.

Details
Commercial grade lemon disinfectant, contains 2.5% quaternary ammonium compounds. Use for cleaning around toilets, showers, floors and walls.

TOXICITY DATA: Not available.
Uncommon Allergens: Quaternary Ammonium Compounds

- Used as disinfectants in many cleaning products and topical medications.
- Ex: Benzalkonium chloride
- Products: Virex II 256, Cavicide
VIREX II 256 SUPER CONCENTRATE DISINFECTANT CLEANER

► One-Step Broad-spectrum, 1:256 neutral quaternary disinfectant cleaner for use in health care facilities; where cross-contamination control is critical. The #1 name in hospital hard surface disinfection. EPA registered.

► Ingredients:
  ▪ n-Alkyl Dimethyl Benzyl Ammonium Chloride 8.2%
  ▪ Didecyl Dimethyl Ammonium Chloride 8.7%

► Health hazards:
  ▪ Eyes: Corrosive. May cause permanent damage including blindness.
  ▪ Skin: Corrosive. May cause permanent damage.
  ▪ Inhalation: May cause irritation & corrosive effects to nose, throat, respiratory tract
  ▪ Ingestion: Corrosive. May cause burns to mouth, throat, and stomach.
‘CaviCide™ is a convenient, ready-for-use, broad-spectrum multi-purpose disinfectant for the cleaning and disinfection of hard surfaces of medical and dental devices and instruments.’

‘CaviCide™ is the recommended disinfection solution by numerous medical device manufacturers.’

Active Ingredients: Di-isobutyl phenoxy ethoxy ethyl dimethyl benzyl ammonium chloride 0.28% and Isopropanol 17.20%. Inert ingredients 82.52%.

QACs not mentioned on MSDS.
Occupational Asthma to benzalkonium chloride (BAC)

► Case report of 3 nurses with rhinitis and cough with wheezing when cleaning with BAC, or entering areas that had been cleaned with BAC.

► All had asthma based on methacholine challenge and work-related declines in peak flow rates.

► Two were atopic, one was not.


Bronchial challenge test to detergent with BAC (patient 2), exposed to solution of 10 ml/L for 30 min.
Uncommon allergens: bacterial enzymatic cleaners

- **Medicine**
  - Pharmacology & drug manufacture
  - Laundry & dishwashing detergents (#1)
  - Hard surface / instrument cleaning
  - Contact lens cleaning formulations: Ultrazyme, ReNu-step, Unizyme

- **Waste treatment**

- **Industrial applications**
  - Fermentation (fuel EtOH, etc.)
  - Chondroitin & heparin production

- **Animal feed additives**

- **Digestive supplements**

- **Food processing**
Instrument Cleaning Solutions

- MetriZyme – Metrex: YES*
- Klenzyme - Steris Corp: YES
- Endozime Ruhof: NO
- emPower™ Metrex: YES
- Enzol - J&J: YES

- Enzy-Clean – Alliance: couldn’t find MSDS
- Asepti-zyme – Ecolab: YES
- ProEz – Cottrell: NO
- Sklar Enzymatic Detergent: NO

*MSDS mentions bacterial subtilisin as ingredient
Occupational asthma and rhinitis due to detergent enzymes

- 6 cases from 3 different worksites

Jobs:
- 4 sterile services technicians
- 2 nurses in GI lab, wiped down scopes after use

Symptoms:
- rhinitis
- new onset asthma
- worsening asthma
- skin rash

Peak flow rates in endoscopy nurse at work and away from work

Case E: OASYS plot of serial peak flow rates. Hashed areas indicate work periods. Daily mean (solid black line), minimum and maximum PEFs are shown in lower plot; diurnal variation is in uppermost plot.

Uncommon allergens: orthopedic cements

Many orthopedic implants require use of methacrylate based bone cements.

- Liquid component: methyl methacrylate, n,n-dimethyl-p-toluidine, hydroquinone.
- Powder: poly methyl acrylates, benzoyl peroxide.
Uncommon allergens: dental cements

- Dental cements
  - Zinc oxide eugenol
  - Cyanoacrylates
  - Methacrylates and polyacrylates
  - Eugenol
  - Benzoyl peroxide
  - Bis-GMA (Bisphenol A glycidylmethacrylate)
Occupational asthma to cyano-acrylate and methacrylate based cements

Jobs: instrument assemblers, dental technician, orthopedic OR nurse.


Case

- 38 y/o nurse, prior history of mild asthma and hay fever as a child, on no meds as adult.
- Worked as telemetry nurse for many years, switched jobs to work as endoscopy nurse for hospital-based GI practice.
- Sx began after 6 months in her new job, with onset of cough and hoarseness at work.
Work-related symptoms

- In the cleaning room, she does not feel well with headache and cough. She also feels sick in the negative pressure room, where bronchoscopies to rule out TB and other procedures are performed.
- She has worsening cough when she enters the cleaning room, with hoarseness and sore throat during the rest of the day.
- However, she does not report a runny, itchy nose or sneezing in the area.
Job duties

► Sets up scopes for procedures, administers conscious sedation and monitors during procedures, and performs biopsies.
► She then places biopsy samples into formalin.
► May have to retrieve endoscopes soaking in a container of cleaning solution, rinse these in a blue solution, and then air dry them.
► On call, she may also have to wipe down scopes with a cleaning solution, soak them in a tub with Cidex OPA, and then place them in a washer for about 40 minutes.
Work practices

► The cleaning room has certain use rules, including keeping the door closed and using hoods while cleaning scopes.
► However, the door frequently remains open, and the washers are not opened under flexible hoods as recommended.
► The predominant chemical used in the cleaning room is Cidex-OPA, a substitute for glutaraldehyde.
► She reports that co-workers also develop a cough when cleaning scopes, and another co-worker has developed skin sensitization, perhaps to the OPA.
Diagnostic work-up

► Does she have asthma?
  ▪ Methacholine challenge PC20 FEV-1 = 0.36 mg/mL.

► Does she have work-related asthma?
  ▪ Predicted PFR = 445 ± 85.
  ▪ PFR at home and during work week = 385 to 425.
  ▪ PFR on call on weekend fell to 220, improved to 275 after bronchodilator.
Potential exposures

- Formaldehyde
- Glutaraldehyde
- Cidex OPA
- Enzyme solutions
- QACs?
Specific Challenges

- Cidex OPA

![Graph showing specific challenges with Cidex OPA with data points at 33%, 55%, and 21% on the Albuterol axis.](image)
Specific Challenges

Biozyme

After two Albuterol nebs

33%
Final diagnoses and treatment

- Asthma
- Occupational asthma to Cidex OPA
- Occupational asthma to Biozyme and other enzymatic cleaners
- Asthma treated with inhaled steroids and bronchodilators
- Restricted from exposure to Cidex OPA and enzymatic cleaners
How do we prevent disease?

► **Primary**: prevent exposure to prevent disease
  - Substitution
  - Reduced inhalational exposures
  - The right skin protection
  - The right respiratory protection
  - Appropriate ventilation, hoods, etc.

► **Secondary**: surveillance to pick up early cases

► **Tertiary**: treatment for workers with disease

*only primary prevention actually prevents disease*
Thank you!

Questions?