Update over beroepsmatige longopathologie

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Take home message

Inhalation of “non toxic” chemicals may lead to (severe) lung disease ...
Outline

- One recent case
- Some recent examples from the literature
Case

- **September/October 2014**
  - Male, 46 y, ex-smoker (stop 2 y ago, 2 PY)
    - Allergic rhinitis & asthma since adolescence, well-controlled
    - Mild obstructive sleep apnoea
    - Nasal septum correction; orthopaedic surgery (shoulder)
  - Since early 2014: shortness of breath, fatigue, productive cough, R/ antibiotics for bad “airway infection” (April 2014), no other systemic symptoms
  - Fine basal crepitations, no clubbing, no arthritis, no adenopathies; restrictive impairment + low diffusion; HRCT, bronchoscopy/BAL, surgical lung biopsy

➢ Referred to clinic of occupational disease UZ Leuven: etiology, management?
### Pulmonary function

30.09.2014

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>% Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>3.06 L</td>
<td>64%</td>
</tr>
<tr>
<td>FEV₁</td>
<td>2.73 L</td>
<td>71%</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>PEF</td>
<td>9.54 L/s</td>
<td>104%</td>
</tr>
<tr>
<td>TLC</td>
<td>4.12 L</td>
<td>58%</td>
</tr>
<tr>
<td>TLco</td>
<td>5.62 U</td>
<td>52%</td>
</tr>
<tr>
<td>Kco</td>
<td>1.41 U</td>
<td>93%</td>
</tr>
</tbody>
</table>

- **Restrictive impairment with reduced diffusing capacity**
Bilateral interstitial changes, peripheral, mainly basal, but also towards apical
Bilateral traction bronchiectases, mainly basal/posterior
Non-Specific Interstitial Pneumonia (NSIP)
(DD atypical UIP, HP)

10/01/2015
Laboratory + Bronchoscopy/BAL

- Blood: no abnormalities, incl. auto-immune serology
- No endobronchial abnormalities
- BAL
  - 221 WBC/µL (low)
  - 84% macrophages
  - 7.5% lymphocytes
  - 4.5% neutrophils
  - microbiological investigations (bacteria, TB, viruses, fungi): all negative
Surgical lung biopsy (Right Lower Lobe)

- Interstitial inflammation (lymphocytes + plasmocytes); some fibrosis; no granulomas
- Translobular and homogenous distribution across all lobules
- Hyaline material (PAS+) and cholesterol crystals + foamy macrophages in some alveoli
- No vasculitis
- Ziehl – / Grocott –; no particles/fibres

➤ Fibrosing NSIP (+ secondary alveolar proteinosis)
Other findings

- Laboratory:
  - Auto-immune screening: negative
  - GM-CSF antibodies: none detected
  - IgGs (fungi): not increased above normal
  - Serum LDH: minimally increased (266 U/L)
- Capillaroscopy: normal findings
Exposure history

- Electrician
- Various jobs in buildings
- Since age 24 y: work in theater, philharmonic orchestra, ...: operating various machines, stage décor, ...
- Past 8 y: work as light and sound technician in a busy cultural centre
- Home: no dampness
- Hobby: bass trombone (2 h/week) since 3 y, no sports
Light technician

- Use of “theatrical haze/fog”
- Since 2 y: new device “ANTARI fog machine”, at least once a week (rehearsals and shows)
- Initial information: “harmless water-based product”
Onderwerp: HZ 500 vloeistof JB systems

Hallo,

Ik werk in CC en ben op zoek naar de samenstelling van boven vernoemde vloeistof. Ik heb geprobeerd om antari zelf te mailen maar krijg daar geen reactie op. Het zou kunnen dat ik daar allergisch voor ben en zit nu al van oktober thuis met een zware allergische reactie op mijn longen. De bus die we hebben is dezelfde als die jullie verkopen, om de hazen vloeistof uit te sluiten zoek ik dus de samenstelling.

Deze vloeistof is zeker niet toxisch, ... maar dit wil niet zeggen dat jij er niet allergisch voor kunt zijn. Een kat is ook niet toxisch, maar er zijn er toch heel wat allergisch aan.

Wat ik weet

- Dit is watergebaseerd, dus geen solventen, geen alcoholen
- Is op basis van diglycolen: is een verbinding die tussen vetten en alcohol ligt.
- Het kan bij inademing wel een olieachtige film nalaten, maar dit alleen bij langdurige en zeer geconcentreerde blootstelling.
Theatrical smoke and fog
From Wikipedia, the free encyclopedia

• Smoke: pyrotechnic materials, smoke cartridges, incense, ...
• Low lying fog effect: liquid or solid CO$_2$ or N$_2$
• Fog machine: pumping glycol or glycol/water mixtures into heat exchanger $\rightarrow$ vapour cloud
• Haze machine: homogeneous cloud (fine mist) intended to reveal lighting beams
  • Glycol/water mixture
  • Mineral oil
HAZE LIQUID HZL-5

HAZER LIQUID

This Haze Liquid is specially designed for Hazer. It contains high quality chemical liquid that can be dispersed into haze for entertainment use. It leaves no residue or contamination and increases the life span of your Hazer considerably. This Haze Liquid is colorless, odorless, non-toxic, non inflammable, oil based liquid that can be dispersed into a long-lasting, non irritating haze with no health hazard.

CAUTION
Keep out of reach of children.
Non-edible. Do not drink it.
Please do not mix it with any other Liquid.

HAZER-FLUID

Dieses Hazer-Fluid wurde speziell für Hazer-Nebelmaschinen entwickelt. Es besteht aus hochwertigen Chemikalien und kann zu Unterhaltungszwecken verdampft werden. Das Fluid hinterläßt keinerlei Rückstände und erhöht die Lebensdauer Ihrer Hazer-Nebelmaschine.

DIFFUSEUR-LIQUIDE

Ce liquide est spécialement développé pour les machines à diffusion de brouillard léger. Il contient une composante chimique de haute qualité diluée dans de l'eau distillée pour être utilisé à la formation de brouillard léger, presque invisible à des fins d’effets spéculifs pour spectacles et animations.
Il ne contient aucune matière ou résidu ce qui permet une durée de vie extrême du diffuseur.
Ce liquide est incolore, inodore, ininflammable, non toxique à base d’huile.
Ce qui le rend non nocif pour la santé.

ATTENTION
Certaines précautions sont tout de même nécessaires, telles que garder hors de portée des enfants.
A ne pas boire.
Ne pas mélanguer avec d’autre liquid.

Made in Taiwan by Antari Lighting & Effects Ltd.
www.antari.com
I. IDENTIFICATION

PRODUCT NAMES: “HZL-1 Haze Liquid” and “HZL-5 Haze Liquid” Where data differs discretely by product (not over a range) it will be presented in the above product order.

FORMULA: Pure grade Lubricating Base Oil.

III. INGREDIENTS

These products are all "Oil-based" Mineral oil solutions. As such, toxicity is minimal. These products have been shipped internationally for more than 5 years under the Antari name, and are considered "non-hazardous" by most national health and safety regulatory bodies.

Tests conducted by independent laboratories have confirmed the non-hazardous nature of these liquids.
V. HEALTH HAZARD DATA

No exposure limits have been determined for these products, nor for any of the ingredients from which they are formulated.

Swallowing has no adverse effects in low doses. Higher doses may induce nausea and vomiting, but with no long-term toxicity. **Inhalation produces no adverse effects when used according to standard practices.** Continuous exposure to highly concentrated fog may lead to throat/respiratory tract irritation. Under such conditions, irritation should subside immediately upon moving to an area of low fog concentration. The fog produced by these products will be adequately filtered by any 10 - 20 micron filtration system. Contact with the liquid may cause minimal, temporary irritation to exposed skin areas. Eye contact with the liquid may also cause minimal, temporary irritation. In all cases of contact with the liquid, flushing of the exposed area with water is sufficient. No contra-indications may be determined, as the ingredients have no independently toxicological effects, even when considered combinatively with possible pre-existing physical conditions or dietary/medicinal regimens. Treatment of egregious overexposure may be determined by health personnel, with principal attention given to the control of symptoms and overall clinical status.
Haze liquid 1% in CS$_2$
GC-MS

mineral oil
(no glycols)
Final diagnosis & management

- Interstitial lung disease: NSIP
- Probably caused by chronic high (?) exposure to mineral oil (theatrical haze)

- stop exposure
- reported to FBZ
Follow-up

- Complete work stop
- No specific treatment (except asthma meds)
- Some clinical improvement; still cough +++ (muscle pains) & dyspnoea on exercise
- No functional improvement
- No changes in HRCT (MAY 2015)
- BAL + transbronchial biopsies (MAY 2015): no PAP, “normal tissue”
# Follow-up

(Stop exposure; no specific treatment)

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OCT</td>
<td>JAN</td>
</tr>
<tr>
<td>FVC</td>
<td>64%</td>
<td>61%</td>
</tr>
<tr>
<td>TLC</td>
<td>58%</td>
<td>55%</td>
</tr>
<tr>
<td>TLco</td>
<td>52%</td>
<td>54%</td>
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<td>6MWT</td>
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</tr>
<tr>
<td>SaO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAL M</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Ly</td>
<td>7.5%</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>4.5%</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other cases?

- Possibly one other case of subacute lung injury in a job student exposed to haze (to be confirmed).
- No similar cases in literature.
Exposures to Atmospheric Effects in the Entertainment Industry

Kay Teschke,¹ Yat Chow,² Chris van Netten,¹ Sunil Varughese,² Susan M. Kennedy,² and Michael Brauer²

¹University of British Columbia, Health Care and Epidemiology, Vancouver, BC, Canada
²University of British Columbia, School of Occupational and Environmental Hygiene, Vancouver, BC, Canada
TABLE I. Summary of Area Inhalable Aerosol Concentrations

<table>
<thead>
<tr>
<th></th>
<th>All Fog Fluids</th>
<th>Glycol Only</th>
<th>Mineral Oil Only</th>
<th>Glycol and Mineral Oil</th>
<th>Dry Ice</th>
</tr>
</thead>
<tbody>
<tr>
<td>All productions (n)</td>
<td>32</td>
<td>14</td>
<td>14</td>
<td>3</td>
<td>(1)</td>
</tr>
<tr>
<td>Minimum, mg/m³</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.60</td>
<td>n/a</td>
</tr>
<tr>
<td>Maximum, mg/m³</td>
<td>17.1</td>
<td>3.47</td>
<td>6.56</td>
<td>17.1</td>
<td>n/a</td>
</tr>
<tr>
<td>Arithmetic mean, mg/m³</td>
<td>1.36</td>
<td>0.57</td>
<td>1.21</td>
<td>6.18</td>
<td>0.08</td>
</tr>
<tr>
<td>Arithmetic SD, mg/m³</td>
<td>3.16</td>
<td>0.91</td>
<td>1.74</td>
<td>9.45</td>
<td>n/a</td>
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<tr>
<td>Geometric mean, mg/m³</td>
<td>0.41</td>
<td>0.24</td>
<td>0.55</td>
<td>2.05</td>
<td>0.08</td>
</tr>
<tr>
<td>Geometric SD</td>
<td>4.21</td>
<td>3.37</td>
<td>3.71</td>
<td>6.32</td>
<td>n/a</td>
</tr>
<tr>
<td>Movie and TV productions (n)</td>
<td>16</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>(0)</td>
</tr>
<tr>
<td>Minimum, mg/m³</td>
<td>0.05</td>
<td>0.11</td>
<td>0.05</td>
<td>n/a</td>
<td>n/a</td>
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<tr>
<td>Maximum, mg/m³</td>
<td>17.07</td>
<td>3.47</td>
<td>2.71</td>
<td>n/a</td>
<td>n/a</td>
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<tr>
<td>Arithmetic mean, mg/m³</td>
<td>1.86</td>
<td>0.76</td>
<td>0.90</td>
<td>17.09</td>
<td>n/a</td>
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<tr>
<td>Arithmetic SD, mg/m³</td>
<td>4.20</td>
<td>1.33</td>
<td>1.00</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Geometric mean, mg/m³</td>
<td>0.47</td>
<td>0.30</td>
<td>0.43</td>
<td>17.09</td>
<td>n/a</td>
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<tr>
<td>Geometric SD</td>
<td>4.90</td>
<td>3.71</td>
<td>3.96</td>
<td>n/a</td>
<td>n/a</td>
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<tr>
<td>Theater, music, and other productions (n)</td>
<td>16</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>(1)</td>
</tr>
<tr>
<td>Minimum, mg/m³</td>
<td>0.05</td>
<td>0.05</td>
<td><strong>0.41</strong></td>
<td>0.60</td>
<td>n/a</td>
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<tr>
<td>Maximum, mg/m³</td>
<td>6.56</td>
<td>1.49</td>
<td><strong>6.56</strong></td>
<td>0.85</td>
<td>n/a</td>
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<tr>
<td>Arithmetic mean, mg/m³</td>
<td>0.86</td>
<td>0.42</td>
<td>1.77</td>
<td>0.72</td>
<td>0.08</td>
</tr>
<tr>
<td>Arithmetic SD, mg/m³</td>
<td>1.57</td>
<td>0.47</td>
<td>2.69</td>
<td>0.18</td>
<td>n/a</td>
</tr>
<tr>
<td>Geometric mean, mg/m³</td>
<td>0.35</td>
<td>0.20</td>
<td>0.88</td>
<td>0.71</td>
<td>0.08</td>
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<tr>
<td>Geometric SD</td>
<td>3.68</td>
<td>3.32</td>
<td>3.24</td>
<td>1.28</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Notes: Results for all productions and all fluid types in **bold**. Concentrations measured using the 7-hole sampler. SD = standard deviation; n/a = not applicable.
Effects of Theatrical Smokes and Fogs on Respiratory Health in the Entertainment Industry

Sunil Varughese, MSc,1 Kay Teschke, PhD,1,2 Michael Brauer, ScD,1 Yat Chow, MSc,1 Chris van Netten, PhD,1,2 and Susan M. Kennedy, PhD1,2*

Background Theatrical fogs (glycol or mineral oil aerosols) are widely used in the entertainment industry to create special effects and make lighting visible.

Methods We studied 101 employees at 19 sites using fogs and measured personal fog exposures, across work shift lung function, and acute and chronic symptoms. Results were also compared to an external control population, studied previously.

Results Chronic work-related wheezing and chest tightness were significantly associated with increased cumulative exposure to fogs (mineral oil and glycols) over the previous 2 years. Acute cough and dry throat were associated with acute exposure to glycol-based fogs; increased acute upper airway symptoms were associated with increased fog aerosol overall. Lung function was significantly lower among those working closest to the fog source.

Conclusions Mineral oil- and glycol-based fogs are associated with acute and chronic adverse effects on respiratory health among employees. Reducing exposure, through controls, substitution, and elimination where possible, is likely to reduce these effects. Am. J. Ind. Med. 47:411–418, 2005. © 2005 Wiley-Liss, Inc.
Theatrical smoke and fog, also known as special effect smoke, fog or haze, is a category of atmospheric effects used in the entertainment industry. The use of fog can be found throughout motion picture and television productions, live theatre, concerts, at nightclubs and raves, amusement and theme parks and even in video arcades and similar venues. These atmospheric effects are used for creating special effects, to make lighting and lighting effects visible, and to create a specific sense of mood or atmosphere. If an individual is at an entertainment venue and beams of light are visible cutting across the room, that most likely means smoke or fog is being used. Theatrical smoke and fog are indispensable in creating visible mid-air laser effects to entertain audiences. Recently smaller, cheaper fog machines have become available to the general public, and fog effects are becoming more common in residential applications, from small house parties to Halloween and Christmas.

Theatrical fog and theatrical fog machines are also becoming more prevalent in industrial applications outside of the entertainment industry, due to their ease of use, inherent portability and ruggedness. Common popular applications for theatrical fog in include environmental testing, such as HVAC inspections, as well as emergency personnel and disaster response training exercises.

Militaries have historically used smoke and fog to mask troop movements in training and combat, and the techniques and technology used for generating smoke and fog in theatre and film are similar.
When you find one case of occupational disease, there are likely more around ...  
**In occupational medicine, n is nearly always >1**

Modified From  LEVY BS, WEGMAN DH. Occupational health (3rd ed), p.60
Other examples of ILD caused by “non toxic” agents

- Ardystil syndrome: spray paints used in textile industry (Spain, Algeria)
- Flock worker’s lung: nylon flock (USA, Canada) + other polymers (Turkey, Spain)
- Popcorn worker’s lung / Food flavourer’s lung
- Korea: biocides used in domestic humidifiers

- Novel materials
Popcorn worker’s lung
(Food flavourer’s lung)
Popcorn worker’s lung


  ➢ cause = “butter flavor” (GRAS)
  
  predominant compound:

\[
\text{diacetyl} = 2,3\text{-butanedione} \\
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{CH}_3\text{- C - C - CH}_3
\end{array}
\]
“POPCORN” LUNG

Proximity to the butter flavoring increased the risk of developing disease.

Histologic finding: Constrictive bronchiolitis

Slide courtesy of T.V. Colby
Production of diacetyl

van Rooy FBGJ et al. Bronchiolitis obliterans syndrome in chemical workers producing diacetyl for food flavourings. AJRCCM 2007,176, 498-504

• Retrospective study among 102 process operators in a Dutch chemical plant producing diacetyl (1960-2003)

• 3 (4) cases consistent with Bronchiolitis Obliterans
“Food flavourer’s lung”


- Man, 36 y, nonsmoker
- Exposed to diacetyl in factory producing food flavouring for potato crisps/chips
- Rapidly evolving fixed airways obstruction
Obliterative Bronchiolitis in Workers in a Coffee-Processing Facility — Texas, 2008–2012

• Two nonsmoking workers (W 34 y, M 39 y)
• Respiratory symptoms < 18 months of working in flavoring room
• Severe obstructive impairment (FEV$_1$ < 35% pred.)
• Diacetyl present in facility

• More cases ? (ATS 2013)
Respiratory Morbidity in a Coffee Processing Workplace With Sentinel Obliterative Bronchiolitis Cases

Rachel L. Bailey, DO, MPH, Jean M. Cox-Ganser, PhD, Matthew G. Duling, MS, Ryan F. LeBouf, PhD, Stephen B. Martin Jr., PhD, Toni A. Bledsoe, MS, Brett J. Green, PhD, and Kathleen Kreiss, MD

- Bronchiolitis Obliterans in 5/13 former workers
- Possible Bronchiolitis Obliterans or Occupational Asthma in 11/75 current workers
SiO$_2$ in “novel” materials
“New materials”
Kitchen and bathroom countertops, ...
Artificial Stone Silicosis

Disease Resurgence Among Artificial Stone Workers

Mordechai R. Kramer, MD, FCCP; Paul D. Blanc, MD, MSPH, FCCP; Elizabeth Fireman, PhD; Anat Amital, MD, FCCP; Alexander Guber, MD, FCCP; Nader Abdul Rahman, MD; and David Shitrit, MD

• Israel, 1997-2010: retrospective analysis of 25 cases of silicosis referred for lung transplantation (n=10)
• Dry cutting of synthetic decorative stone “Caesarstone®” >85% quartz (+ resin + pigments) → kitchen & bathroom countertops
“Artificial marble”


- Galdakao, Bizkaia, Spain: 6 cases of silicosis among 11 workers of family-run “marble” workshop ("innovative silica product" = quartz)


- Cadiz, Spain, 2009-2012: 46 cases of silicosis in men making kitchen countertops (quartz countertops)

Silicosis and autoimmune disease

Straichman et al. Occup Med 2015, 65, 444-50

- Israel: institute for pulmonary transplantation
- “advanced silicosis databank” 9/40 patients with various autoimmune diseases [7.5 x expected] [3 with features of PAP]

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptoms</th>
<th>Physical findings</th>
<th>Relevant serologies</th>
<th>Clinical diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Raynaud’s; Dysphagia</td>
<td>Sclerodactyly; Telangiectasia; Serositis</td>
<td>Anti-Scl-70 (+); SSA (anti-Ro) (+)</td>
<td>SSc</td>
</tr>
<tr>
<td>2</td>
<td>Raynaud’s; Arthritis</td>
<td>Digital pitting; Arthritis; Serositis</td>
<td>ANA &gt; 1:160; RNP (+); SSA (anti-Ro) (+)</td>
<td>MCD</td>
</tr>
<tr>
<td>3</td>
<td>Raynaud’s; Dysphagia</td>
<td>Sclerodactyly; Digital pitting</td>
<td>ANCA (+)</td>
<td>SSc</td>
</tr>
<tr>
<td>4</td>
<td>Raynaud’s</td>
<td>Digital pitting; Arthritis; Serositis</td>
<td>Anti-Scl-70 (+); RNP (+); SSA (anti-Ro) (+); SSB (anti-La) (+)</td>
<td>SSc</td>
</tr>
<tr>
<td>5</td>
<td>Arthritis, Xerostomia</td>
<td>Arthritis</td>
<td>ANA &gt; 1:160; SSA (anti-Ro) (+)</td>
<td>Sjogren’s syndrome</td>
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<td>7</td>
<td>Arthritis</td>
<td>Arthritis; Serositis</td>
<td>ANA &gt; 1:160; RF (+)</td>
<td>RA</td>
</tr>
<tr>
<td>8</td>
<td>Arthritis</td>
<td>Arthritis</td>
<td>RF (+)</td>
<td>RA</td>
</tr>
<tr>
<td>9</td>
<td>Arthritis, Myalgia</td>
<td>Arthritis: Myositis</td>
<td>ANA (+); SSA (anti-Ro) (+); SSB (anti-La) (+); anti-JO-1 (+)</td>
<td>Polymyositis—anti-synthetase syndrome</td>
</tr>
</tbody>
</table>
Humidifier disinfectants and ILD
Toxic Inhalational Injury-Associated Interstitial Lung Disease in Children

Eun Lee,1,2,3,* Ju-Hee Seo,4,* Hyung Young Kim,5 Jinho Yu,1,2 Won-Kyoung Jhang,1 Seong-Jong Park,1 Ji-Won Kwon,6 Byoung-Ju Kim,7 Kyung-Hyun Do,8 Young Ah Cho,8 Sun-A Kim,9 Se Jin Jang,9 and Soo-Jong Hong1,2,3

Interstitial lung disease in children (chILD) is a group of disorders characterized by lung inflammation and interstitial fibrosis. In the past recent years, we noted an outbreak of child in Korea, which is possibly associated with inhalation toxicity. Here, we report a series of cases involving toxic inhalational injury-associated chILD with bronchiolitis obliterans pattern in Korean children. This study included 16 pediatric patients confirmed by lung biopsy and chest computed tomography, between February 2006 and May 2011 at Asan Medical Center Children’s Hospital. The most common presenting symptoms were cough
• Nationwide retrospective study

Kim K.W., Ahn K. et al. AJRCCM 2014, 189, 48-56
Inhalation Toxicity of Humidifier Disinfectants as a Risk Factor of Children’s Interstitial Lung Disease in Korea: A Case-Control Study

Hyeon-Jong Yang1,9, Hwa-Jung Kim2,9, Jinho Yu3, Eun Lee3,4, Young-Ho Jung3,4, Hyung-Young Kim3,4, Ju-Hee Seo5, Geun-Yong Kwon6, Ji-Hyuk Park6, Jin Gwack6, Seung-Ki Youn6, Jun-Wook Kwon7, Byung-Yool Jun6,7, Kyung Won Kim8, Kangmo Ahn9, Soo-Young Lee10, June-Dong Park11, Ji-Won Kwon12, Byoung-Ju Kim13, Moo-Song Lee14, Kyung-Hyun Do15, Se-Jin Jang16, Bok-Yang Pyun1,*, Soo-Jong Hong3,4,*

- 16 pediatric patients matched 1:3 with controls (lobar pneumonia, asthma, healthy)
- Questionnaire (with photographs) on humidifiers + many other indoor & outdoor environmental factors
  - use of humidifier disinfectants only significant risk factor (16/16 vs 11/47)
<table>
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<tr>
<th>물산코웨이</th>
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<tr>
<td>① CHP-08AL</td>
<td>② CP-078LO</td>
<td>③ P-220L</td>
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<td>④ 열っております</td>
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<td>⑥ 디지털 납품정수기</td>
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<td>교원L&amp;C, 웰스정수기</td>
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<td>⑧ KW-P03W1</td>
<td>⑨ KW-P01W1</td>
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<td>⑩ WPU-8230C</td>
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<td>⑤가습기메이트</td>
<td>⑥홈플러스가습기청정제</td>
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<td>⑧아토세이프</td>
<td>⑨아토오가닉 가습기실균제</td>
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<td>⑩에코후레쉬 가습기용품</td>
<td>⑪엔위드 가습기 전용 실균제</td>
<td>⑫기타</td>
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</table>
Humidifier disinfectants
- PGH = oligo [2-(2-ethoxy) ethoxyethyl] guanidinium chloride
- PHMG = polyhexamethyleneguanididine
- DDAC = didecyldimethylammonium chloride

• widely used biocides for water systems and consumer products
• “non toxic” by oral or dermal route
• little or no data on toxicity by inhalation!
Humidifier Disinfectant–associated Children’s Interstitial Lung Disease

Kyung Won Kim¹*, Kangmo Ahn²+, Hyeon Jong Yang³, Sooyoung Lee⁴, June Dong Park⁵, Woo Kyung Kim⁶, Jin-Tack Kim⁷, Hyun Hee Kim⁸, Yeong Ho Rha⁹, Yong Mean Park¹⁰, Myung Hyun Sohn¹¹, Jae-Won Oh¹¹, Hae Ran Lee¹², Dae Hyun Lim¹³, Ji Tae Choong¹⁴, Man Yong Han¹⁵, Eun Lee¹⁶, Hyung-Young Kim¹⁷, Ju-Hee Seo¹⁸, Byoung-Ju Kim¹⁹, Young Ah Cho²⁰, Kyung-Hyun Do²⁰, Sun-A Kim²¹, Se-Jin Jang²¹, Moo-Song Lee²², Hwa-Jung Kim²³, Geun-Yong Kwon²⁴, Ji-Hyuk Park²⁴, Jin Gwack²⁴, Seung-Ki Youn²⁴, Jun-Wook Kwon²⁵, Byung-Yool Jun²⁶, Bok Yang Pyun³⁺, and Soo-Jong Hong¹⁶⁺

Am J Respir Crit Care Med Vol 189, Iss 1, pp 48–56, Jan 1, 2014

Deterding R.R., White C.W. Humidifier and environmental “chILD” risks (Editorial). AJRCCM 2014, 189, 10-2
Kim K.W., Ahn K. et al. AJRCCM 2014, 189, 48-56

- Nationwide retrospective study
- 138 children with chILD; 80 (58%) died
- some household clustering

- epidemic stopped after suspension of sale of humidifier disinfectants in 2011
Kim K.W., Ahn K. et al. AJRCCM 2014, 189, 48-56

• Nationwide retrospective study

![Graph showing number of patients over time with a peak in 2011 following the suspension of sale of humidifier disinfectants.](image)
A cluster of lung injury associated with home humidifier use: clinical, radiological and pathological description of a new syndrome

Sang-Bum Hong, Hwa Jung Kim, Jin Won Huh, Kyung-Hyun Do, Se Jin Jang, Joon Seon Song, Seong-Jin Choi, Yongju Heo, Yong-Bum Kim, Chae-Man Lim, Eun Jin Chae, Hanyi Lee, Miran Jung, Kyuhong Lee, Moo-Song Lee, Younsuck Koh, Korean Unknown Severe Respiratory Failure Collaborative, the Korean Study Group of Respiratory Failure

A cluster of lung injury cases associated with home humidifier use: an epidemiological investigation

Hong S.-B. et al. Thorax 2014, 69, 694-702

- 2011 (spring)
- 17 adults, 28-49 y, 15 women
- 6 pregnant, 4 delivery < 2 weeks
- 13/17 admitted to hospital
- 10/13 severe respiratory distress → ICU
- 5 deaths, 5 lung transplants
- Viral infection (avian flu, SARS, ...)?
- Yellow dust?
- Some familial clustering
- Humidifier disinfectants

- 2004-2011 (spring)
- Detailed environmental questionnaire of 18/28 confirmed cases (15 women / 3 men) vs 121 matched controls
- Significantly more use of humidifier disinfectants (detergents) in cases (17/18) than controls (32/121): aOR = 53 [6-444]
- Majority (~80%) used PHMG
- Inhalation of PHMG (100 nm) caused acute pulmonary injury in experimental animals
Polyhexamethyleneguanidine (phosphate, hydrochloride)

**Material Safety Data Sheet**

**SKYBIO 1100**

**HEALTH : 3  FLAMMABILITY : 1  REACTIVITY : 0**

**DATE ISSUED DEC 02, 2002**

**SUPERSEDES FEB 27, 1995**

**IX. TOXICOLOGY INFORMATION**

**ACUTE/CHRONIC TOXICITY TEST DATA**

- oral LD$_{50}$ (rat) : 857mg/kg
- dermal LD$_{50}$ (rat) : 2000mg/kg
- eye irritation (rabbit) : Mild irritation to the eyes
- skin irritation (rabbit) : No Irritation
- skin sensitization (Guinea-Pig) : No Sensitization
Take home message

Inhalation of “non toxic” chemicals may lead to (severe) lung disease ...
Thank you for your attention

ben.nemery@med.kuleuven.be
Obliterative bronchiolitis in fibreglass workers: a new occupational disease?


- 6 workers [1987-2007, UK & Taiwan]
  - preparing fibreglass-reinforced plastic (5 boatbuilders)
  - 34 y (25-51y); onset of symptoms < 12 months
- obliterative (constrictive) bronchiolitis
  - well documented, severe (1 death, 2 lung Tx)
- exact cause?
  - styrene-based resin
  - accelerator (methylethylketoneperoxide, dimethylphthalate)
  - other chemicals, solvents

Chen et al. OEM Sept 2013 + 2 patients (MEKPO?)