Humidifier Disinfectant–associated Interstitial Lung Disease and the Ardystil Syndrome

To the Editor:

In their recent letter, Park and colleagues (1) demonstrated that humidifier disinfectant–associated interstitial lung disease affected children and women in Korea between 2006 and 2011 (2–4) was probably caused by the biocide polyhexamethylene guanidine (PHMG). Recently, PHMG has also been shown to be highly toxic after intratracheal instillation in mice (5) and to be cytotoxic for various types of cells, including lung cells (6). Yet PHMG was considered to be a safe disinfectant, causing little skin irritation (7), and it was even claimed that it was harmless (8).

The Korean PHMG-associated interstitial lung disease outbreak is strikingly reminiscent of the history of the Ardystil syndrome in the 1990s. The Ardystil syndrome is an interstitial lung disease that appeared first in Spain (mainly in a factory named Ardystil) (9) and then in Algeria (10) among textile workers who had applied paints of the Acramin type by air-spraying. These paints were considered to be nonhazardous because of their very low oral toxicity and low dermal irritation potential in experimental animals. The first two compounds are components of the Acramin paint system implicated in the Ardystil syndrome, and the third compound is a disinfectant (polyhexamethylene guanidine) implicated in the Korean outbreaks of humidifier disinfectant–associated interstitial lung disease. These polymers are characterized by the presence of multiple nitrogen atoms that are positively charged at physiologic pH.

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Figure 1. Structural formulae of the polymers implicated in the causation of interstitial lung disease and subsequently found to be toxic by inhalation in experimental animals. The first two compounds are components of the Acramin paint system implicated in the Ardystil syndrome, and the third compound is a disinfectant (polyhexamethylene guanidine) implicated in the Korean outbreaks of humidifier disinfectant–associated interstitial lung disease. These polymers are characterized by the presence of multiple nitrogen atoms that are positively charged at physiologic pH.
valid whether or not chemicals are designed or manufactured to be aerosolized, and it applies to a wide variety of circumstances such as, for example, components and natural or synthetic ingredients in electronic cigarettes, as well as cleaning agents and biocides for use in homes, hospitals, swimming pools, paints, metal working fluids, and so on. In other words, potentially inhaled agents must be deemed hazardous until proven innocent.

Author disclosures are available with the text of this letter at www.atsjournals.org.

Benoit Nemery, M.D., Ph.D.
Peter H. Hoet, Ph.D.
KU Leuven Center for Environment and Health
Leuven, Belgium

References


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Reply: Is Every Inhalant Safe?

From the Authors:

We appreciate the thoughtful comments provided by Nemery and Hoet on our study of humidifier disinfectant-associated interstitial lung disease (HD-ILD) in an animal model, induced by polyhexamethylene guanidine (PHMG) aerosol (1).

First, they point out that there is a common clinical and pathologic background between HD-ILD in Korea and the Ardystil syndrome in Spain. With the Ardystil syndrome, a bronchiolitis obliterans (BO) manifestation associated with exposure to aerosols containing Acramin FWN, and it was noted that the polymeric compound also has a polycationic nature, and this characteristic explains this resemblance (2). In fact, we already discussed the pulmonary toxicity of PHMG, in contrast to its safety on cutaneous or oral exposure (3). Polymers are generally a safe material, and many restriction authorities exempt these materials from toxicity

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