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Brief Communication

Adverse Reactions Associated With Respirator Fit Testing of Healthcare Workers in British Columbia, Canada: A Review of Compensation Claim Cases

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ABSTRACT. Thousands of healthcare workers in British Columbia are being fit tested for respirator use as a part of respiratory protection programs emanating from the SARS outbreak in 2003. The author reviews 8 claims submitted to the Workers' Compensation Board of British Columbia for adverse reactions related to denatonium benzoate fit testing. The adverse effects varied in severity. Most claims involved respiratory symptoms and 3 dermatitis or angioedema symptoms. One asthmatic required hospitalization for a severe asthmatic reaction. These cases indicate that there may be potentially significant health risks associated with denatonium benzoate-based fit testing at least for a small group of susceptible individuals. More systematic research is required.

KEYWORDS: adverse reactions, denatonium benzoate, fit testing, healthcare workers, respirators

During the coronavirus SARS outbreak in Toronto, Canada, in early 2003, a significant proportion of the afflicted individuals were healthcare workers (HCWs) who contracted this serious respiratory tract infection from their patients.[1] This incident clearly demonstrated the vulnerability of the healthcare system[2] and the need to better protect healthcare providers.

The use of respiratory protection is a commonly recommended method for protecting HCWs from SARS and other airborne infectious agents such as tuberculosis.[3–6] Respiratory protection programs typically include a respirator fit testing component.[7–9] The primary purpose of fit testing is to ensure that the respirator being used by the individual forms a tight enough seal so as to adequately protect the person from unwanted airborne hazard exposures.

Fit testing HCWs in British Columbia (BC), Canada, typically involves qualitative testing using denatonium benzoate as the detection agent. This method is similar to the saccharine testing method against which it has been validated and produces nearly identical results.[10] The test takes a few minutes to perform and relies on the individual's ability to perceive the extremely bitter taste of the agent. A plastic testing hood with a clear visor is placed over the individual's head to the shoulders, and a small anterior port permits the insufflation of the denatonium benzoate solution into the hood using a nebulizer. The first part of the test screens for the individual's ability to detect (taste) aerosolized droplets of a dilute solution of denatonium benzoate. The individual puts on the respirator for the second part of the test, and a more concentrated solution of the denatonium benzoate is sprayed into the hood while the individual performs a set of maneuvers such as talking or grimacing. An acceptable respirator fit test occurs when the individual fails to taste the denatonium benzoate.[11–13]

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Over the past few years, thousands of HCWs in BC have undergone respirator fit testing with this method. The Workers' Compensation Board of BC (WorkSafeBC) has received a number of claims for adverse reactions that have been attributed to qualitative respirator fit testing based on denatonium benzoate as the detection substance. I summarize these cases in this article; I then discuss the occupational and public health implications.

Case Summary

A total of 8 claims, all from persons aged between 33 and 58 years (5 from women and 3 from men) were filed with WorkSafeBC between 2003 and 2005. These included 7 HCW and 1 non-HCW claim.

Six of the 8 individuals had a history of allergies. One individual was allergic to latex, and one was allergic to shellfish. Four had allergies to dust mites, grass, pollen, or hay fever; one was also allergic to sulfites as well as seafood, and another was also allergic to cedar. Three individuals had a history of asthma, 2 had diabetes, and 2 had hypothyroidism.

Seven of the 8 claimants were actually fit tested, and one was in the same room where fit testing occurred. Exposure to denatonium benzoate was by inhalation in all cases, although one individual who developed delayed skin symptoms also had direct skin contact with the liquid.

In 7 cases, the symptoms occurred immediately or within minutes of testing. In one case with predominantly dermal manifestations, the onset of symptoms was delayed by 8 hours posttesting. Five of the 8 claimants had predominantly respiratory symptoms, whereas 3 of the 8 had predominantly dermal or soft-tissue symptoms. Two individuals had exacerbation of their underlying asthma; one had an anaphylactic reaction including angioedema and severe bronchospasm. Two other individuals may have had bronchospasm and one individual may have had angioedema; it is not possible to be more definite with the available clinical information. In at least 2 of the 8 cases, anxiety was an important component of the symptom presentation.

Seven of the 8 individuals developed no significant complications. One individual with preexisting asthma required hospitalization and treatment in the ICU for a severe asthmatic/anaphylactic reaction. Four cases involved paid time loss from work, varying in duration from 1 to 25 days.

COMMENT

Qualitative respiratory fit testing methods are commonly preferred over quantitative methods when testing large number of people repeatedly because they are simple, rapidly performed, easily transportable, easy to teach to testers, and relatively inexpensive, requiring minimal material.[10,11] There are 3 commonly used qualitative fit-testing methods for particulate air purifying respirators, and all rely on the ability of the individual being tested to detect the testing substance.[11,12] The oldest method uses an airflow indicator or smoke tubes, which are commonly used to evaluate ventilation systems. These tubes emit visible stannic chloride aerosol, which produces hydrogen chloride when it interacts with moisture on mucous membranes. Hydrogen chloride is a potent respiratory tract irritant, and detecting the irritation is the basis of the test. However, during testing, concentrations of hydrogen chloride are difficult to control, and occasionally significantly elevated levels can be produced. The US National Institute for Occupational Safety and Health considers the fumes of hydrogen chloride produced by irritant smoke tubes a health risk and recommends against this method of respirator fit testing.[14,15] The second method uses saccharine as a detection agent. However, this method was also called into question when saccharine was suspected of being carcinogenic.[15] The newest method based on denatonium benzoate was approved by the Occupational Safety and Health Administration (US) in 1998 as an as a safe third alternative.[16]

Denatonium benzoate ($C_{28}H_{34}N_2O_3$; *N*-[2-[(2,6-dimethylphenyl)amino]-2-oxoethyl]-*N*,*N*-diethylbenzenemethanaminium benzoate) is a lignocaine derivative that was discovered accidentally in 1958 by W. Barnes while searching for a more powerful local anesthetic. It is manufactured and sold by Macfarlan Smith Ltd., in the United Kingdom, under the brand name Bitrex. It is one of the bitterest substances known, and most people are able to detect it at concentrations as low as 10 ppb; at 10 ppm, it is unpleasantly bitter.[17,18] This characteristic of denatonium benzoate has made it useful as a taste-aversion agent—commonly used to prevent accidental or harmful consumption, especially by children—of a variety of consumer products.[18] Animal toxicity studies suggest a low toxicity profile for denatonium benzoate,[19] but the data related to chronic toxicity and hypersensitivity potential for humans are limited.[20] Repeated inadvertent exposure of the population occurs through a variety of consumer products such as suntan lotions, beauty products, and household cleaning products. Adverse reactions to these exposures would be difficult to recognize given that denatonium benzoate is not listed on most products because of its low percentage content.[20] A search of the medical literature provided only one case report of an individual with severe allergic reactions, including urticaria and asthma, resulting from exposure to a variety of products containing denatonium benzoate.[21] The material safety data sheet for Bitrex fit sensitivity solution (0.01%) and the fit testing solution (0.2%) do not report any significant adverse health effects.[22] This, as far as I am aware, is the first series of cases reporting adverse reactions to respirator fit testing with denatonium benzoate.

The cases presented in this report raise a number of important occupational and public health issues related to the use of denatonium benzoate for fit testing. The primary issue involves determining the nature of the adverse reactions. Several of the cases describe adverse reactions that are likely due to an irritant effect, whereas others are more consistent with an allergic mechanism. Although most of the individuals presented with fairly rapid onset of

symptoms or immediate reactions in relation to the testing, one case raises the possibility of a delayed response. Some of the adverse effects may be more psychological than toxicological in nature. In at least 2 of the cases submitted to WorkSafeBC, the presentation was consistent with a psychological reaction. Wearing a respirator is distressing for some individuals because it can provoke claustrophobic feelings. Adding the hood over the head and shoulders to perform the fit testing can significantly exacerbate these sensations to the level of acute anxiety or panic. Most of the adverse reaction cases, however, cannot be attributed simply to an anxiety response. Some of adverse effects were serious, including angioedema and asthmatic episodes. In fact, one individual had a potentially life-threatening reaction, requiring intensive care unit admission for severe bronchospasm and anaphylaxis.

Another issue that needs clarification concerns the possibility that some individuals may be more susceptible than others to adverse reactions. In the cases presented, the majority of individuals (6 of 8) had a history of allergies, and 3 of the 8 had pre-existing asthma. Are atopic individuals or asthmatics more susceptible to developing adverse reactions from fit testing with denatonium benzoate? Should such individuals be precluded from this type of fit testing?

From the public health perspective, it is essential to obtain an estimate of the rates of adverse reactions in the population being tested and the severity of these reactions. Relative risk estimates may permit benefit-risk analysis and high-risk group identification. There is also the need to consider the absolute risk given the size of the population of workers undergoing testing. In BC, thousands of HCWs and other workers are being tested. Even if the relative risk for adverse effects of fit testing using denatonium benzoate is small, the absolute number of workers with adverse reactions may nevertheless be sizeable.

The frequency of testing workers is another important issue that requires consideration and study. Annual fit testing has been recommended[8] or required by regulation in certain jurisdictions,[9] including BC.[23] Under these circumstances, a large number of HCWs (and other workers) may undergo several fit tests over their working careers. Does annual testing increase the risk of adverse effects? For example, can repeated exposure to denatonium benzoate result in sensitization of certain individuals? If so, what are the health consequences for these individuals given the ubiquity of denatonium benzoate in consumer products?

Conclusions

Qualitative fit testing with denatonium benzoate has a number of advantages, and it can serve a useful role in the protection of HCWs. However, it may not be the method of choice for all individuals. The cases summarized in this report indicate that denatonium benzoate testing may produce adverse effects at a low rate, but nevertheless, the small fraction of the population affected may be susceptible to serious reactions. Researchers must evaluate this issue in a more systematic and comprehensive fashion.

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References

1. Varia M, Wilson S, Sarwal S, et al. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ*. 2003;169:285–292.
2. MacKay B. SARS: "a domino effect through the entire system." *CMAJ*. 2003;168:1308.
3. Health Canada. *Infection Control Guidance for Respirators (Masks) Worn by Health Care Workers-Frequently Asked Questions. Severe Acute Respiratory Syndrome (SARS)* [revised June 6, 2003]. Ottawa, Canada: Health Canada. http://www.phac-aspc.gc.ca/sars-sras/pdf/sars-respiratormasks-0606_e.pdf. Accessed May 5, 2006
4. Centers for Disease Control and Prevention. *Interim Domestic Guidance on the Use of Respirators to Prevent Transmission of SARS*. Atlanta, GA: May 3, 2005. http://www.cdc.gov/ncidod/sars/respirators.htm. Accessed May 5, 2006.
5. Lange JH. SARS respiratory protection. *CMAJ*. 2003;169:541.
6. Carmine J, Bozzi D, Burwen R, et al. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care facilities. *MMWR Recomm Rep* 1994;43(RR13):1–132.
7. Health and Safety Executive. *Fit Testing of Respiratory Protective Equipment, Facepieces*. Information Document 282/28. Sudbury, England: HSE Books; 2003. http://www.hse.gov.uk/pubns/fittesting.pdf. Accessed May 1, 2006.
8. Canadian Standards Association. Standard Z94.4-02: Selection, use, and care of respirators. CSA Publication Update. 2004;2.
9. Occupational Safety and Health Administration. Respiratory Protection. *OSHA Regulations, Standards - 29 CFR Part 1910-134*. April 3, 2006. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=12716. Accessed May 1, 2006.
10. Mullins HE, Danisch SG, Johnston AR. Development of a new qualitative test for fit testing respirators. *Am Ind Hyg Assoc J*. 1995;56:1068–1073.
11. Colton CE, Nelson TJ. Respiratory protection. In: Dinardi SR, ed. *The Occupational Environment—Its Evaluation and Control*, 2nd ed. Fairfax, VA: AIHA; 2003:931–953.
12. Occupational Safety and Health Administration. Fit-testing procedures (mandatory). *OSHA Regulations Standards - 29 CFR 1910.134 Appendix A*. 2004. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9780. Accessed May 1, 2006.
13. Nelson TJ, Janssen LL, Luinenburg MD, Mullins HE. Development of an abbreviated qualitative fit test using bitter aerosol. *J Int Soc Respir Protect*. 2003;20:102–109.
14. Lenhart SW, Burroughs GE. NIOSH Health Hazard Evaluation Report No. 93-040. Washington, DC: NIOSH; 1993. http://www.cdc.gov/niosh/hhe/reports/pdfs/1993-0040-2315.pdf. Accessed July 12, 2007.
15. Bollinger N. NIOSH Respirator Selection Logic 2004. Washington, DC: NIOSH; 2005. DHHS (NIOSH) publication No. 2005-100. http://www.cdc.gov/niosh/docs/2005-100/pdfs/05-100.pdf. Accessed July 12, 2007.
16. Occupational Safety and Health Association. Qualitative Fit Test (QLFT) [Appendix A, paragraphs B3 and B4]. *Fed Reg*. 1998;63:1230.
17. O'Neil MJ, ed. *The Merck Index—An Encyclopedia of Chemicals, Drugs, and Biologicals*, 14th ed. Whitehouse Station, NJ: Merck; 2006.
18. Payne HAS. Bitrex—a bitter solution to safety. *Chem Ind*. 1988;22:721–723.

19. Hansen SR, Janssen C, Beasley VR. Denatonium benzoate as a deterrent to ingestion of toxic substances: toxicity and efficacy. *Vet Hum Toxicol*. 1993;35:234–236.
20. Klein-Schwarts W. Denatonium benzoate: review of efficacy and safety. *Vet Hum Toxicol*. 1991;33:545–547.
21. Bjorkner B. Contact urticaria and asthma from denatonium benzoate (Bitrex). *Contact Derm*. 1980;6:466–471.
22. Allegro Industries. Material Safety Data Sheet [Bitrex Fit Sensitivity Solution #1 and Bitrex Fit Test Solution #2]. http://allegrosafety.com/docs/Respirators/BtxFitTstKitMSDS.pdf.Accessed July 12, 2007.
23. WorksafeBC. *OHS Regulations Part 8 Personal Protective Clothing and Equipment: Subsection 8.40, Fit tests*. 2006. http://www2.worksafebc.com/publications/OHSRegulation/Part8.asp#SectionNumber:8.40. Accessed May 1, 2006.