Brief Communication

Behavioral Sensitization to Irritants/ Odorants After Acute Overexposures

Considerable controversy has arisen recently regarding individuals who react acutely with multiple somatic complaints when exposed to very low levels of airborne chemicals. The term "multiple chemical sensitivities" has been coined to describe such patients, and an entire volume was recently published addressing this phenomenon.[1] We report on two cases of recurrent panic/hyperventilation symptoms after acute overexposures to chemicals having both irritant and odorant properties. In each case, the offending chemical's odor was tolerated prior to the acute overexposure, but acted as a trigger for recurrent anxiety or hyperventilation symptoms thereafter. An explanation is offered from classical (Pavlovian) conditioning theory, and a new diagnostic label is suggested.

Case 1

A 34-year-old male laborer was seen in consultation 9 months after an acute overexposure to a liquid phenol-formaldehyde resin. Before the incident, he experienced occasional transient upper respiratory irritation when he pumped formaldehyde (without respiratory protective equipment) from supply trucks to holding tanks; he was otherwise unaffected by his work duties (which included pumping liquid phenol and dumping resorcinol flakes and sulfuric acid into reaction kettles). On the day of the acute overexposure, he was sprayed on the legs and face with liquid phenol-formaldehyde resin, resulting in self-limited upper respiratory irritation symptoms, nausea, and a burning sensation of the tongue, without skin burns or wheezing. He completed the work day after a decontamination shower and a change of clothing. Medical evaluation at 1 and 2 weeks after the overexposure revealed only a resting tachycardia and warm, moist skin, evidence of what the treating physician termed a "hyperadrenergic state of questionable etiology." Pulmonary function and thyroid function tests were within normal limits, and the patient reported nearly complete resolution of symptoms over a 2-week period.

Subsequent to the above acute overexposure, the patient began noting fleeting chest pains, acrodigital and perioral paresthesias, lightheadedness, and air hunger on an intermittent basis, all occurring acutely when he perceived transient formaldehyde odors on the job. He was able, however, to tolerate the odor of a variety of other chemical agents without manifesting symptoms. His personal physician was unable to answer his questions of whether he had suffered permanent injury, and this uncertainty served only to increase his level of anxiety. As in the acute situation, he continued to deny wheezing or skin rash, both possible indicators of physiologic sensitization to formaldehyde.

At consultative examination, the patient again exhibited warm, moist skin and a fine resting tremor (the patient explained that he had always had sweaty palms and a fine tremor, dating back at least to his high school days). The examination was otherwise unremarkable, including the lack of skin rashes or wheezing on forced expiration. The explanation that his symptoms resembled those of hyperventilation syndrome, and that he had apparently associated the odor of formaldehyde with his acute overexposure (thus triggering repeated episodes of hyperventilation), was reassuring to the patient, who was worried about possible organic impairment. He believed that, with the aid of pursed-lip breathing to control his hyperventilation, he could learn to tolerate occasional formaldehyde odors on the job, and declined behavioral science intervention or reassignment. At follow-up 3 months later, the patient indicated that his symptoms had improved, even without pursed-lip breathing, because he felt "more relaxed" on the job after the consultation. Given the intervening promulgation of a stricter formaldehyde exposure standard by the federal Occupational Safety and Health Administration, however, discussion was initiated toward obtaining industrial hygiene evaluation of the workplace.

Case 2

A 43-year-old female electronics worker was seen in consultation 3 months after an acute overexposure to

From the Occupational Health Clinic, San Francisco General Hospital, San Francisco, CA 94110 (Dr Shusterman, attending physician; Dr Balmes, attending physician; Dr Cone, Medical Director).
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phosphine gas. Before this incident, the patient reported that she occasionally smelled the characteristic garlic-like odor of phosphine during her work in semiconductor fabrication, but experienced no adverse symptoms on these occasions. On the evening of the overexposure, she opened the cover of a wafer diffusion apparatus (in which an exhaust tube had apparently become plugged) and experienced a strong odor, with accompanying "pressure sensation in the head," dizziness, and shortness of breath. She was taken to a nearby emergency room, where she was observed overnight. Aside from obvious acute anxiety and injected conjunctivae, the physical examination, including auscultation of the chest, was within normal limits. Arterial blood gases obtained on room air showed evidence of mild hyperventilation, with pH 7.45, pCO_2 30 mmHg, PO_2 99 mmHg, and HCO_3 21 mEq/L. The chest roentgenogram was normal, as were the hemogram and liver function panel.

Upon consultative examination, the patient reported that she was no longer able to tolerate the intermittent and faint garlic-like odor of phosphine which had caused her no problems at work before the incident. On occasions when she smelled phosphine, she reported experiencing anxiety, nausea, lightheadedness and dyspnea (not wheezing), although she denied acrodigital or perioral paresthesias. Identical symptoms began to occur after she smelled hydrochloric or sulfuric acid vapors. Although no evidence was obtained that she experienced bronchoconstriction, the patient reported that she had used bronchodilators intermittently at the suggestion of her primary physician during this time, with no effect upon her symptoms. Her physical examination and pulmonary function tests were unremarkable on three occasions, including at the time of consultation. A diagnosis of "psychological sensitization to the work environment" was made, and vocational rehabilitation was suggested, as the patient had already voluntarily terminated her employment. She subsequently had no recurrence of symptoms in her employment as a counter clerk in a dry-cleaning establishment.

Discussion

In both of these cases, the chemical agent involved possessed both dose-related irritant properties and a distinct odor. In each case, the odor was tolerated before an acute overexposure, but acted as a trigger for recurrent anxiety or hyperventilation symptoms thereafter. In behaviorist terms, a chemical agent at irritant levels can be said to constitute an *unconditioned stimulus* for a panic or hyperventilation response.[2] Subsequent to an acute overexposure, the same chemical's characteristic odor (typically perceived at sub-irritant concentrations) becomes a *conditioned stimulus* for the same response. Far from a neurotic process, this constitutes an adaptive or protective psychophysiologic response with minimal, if any, volitional or personality component.[3] We therefore advocate the use of the diagnostic designation "*behavioral sensitization to odorant*" for this disorder, in preference to such terms as "phobic state,"[4] "acute reaction to stress,"[4] "panic disorder,"[5] "posttraumatic stress disorder,"[5] or "psychological sensitization," all of which have not only behavioral, but also psychiatric connotations.

Superimposed upon the above phenomenon may be varying degrees of stimulus generalization. *Stimulus generalization* occurs if more than one odor comes to serve as a conditioned stimulus, without aversive conditioning to that particular chemical agent.[3] This occurred to a limited degree in Case 2, in which the patient reacted to the odors of sulfuric and hydrochloric acids in the same workplace where she was overexposed to phosphine, but this same person was able to tolerate the odor of perchloroethylene in her subsequent employment in a dry-cleaning establishment.

Potential interventions for uncomplicated behavioral sensitization include improved industrial hygiene controls (sufficient to maintain airborne exposures below the odor threshold),[6] reassignment of the affected worker,[7] biofeedback/breathing training,[8] and supportive therapy.[9] Emphasis, of course, should be upon industrial hygiene controls when odor threshold information suggests that exposure standards are being approached or exceeded.[6] Most important is the proper labeling of this condition in nonjudgmental terms, since insight into the underlying mechanism of behavioral sensitization is desirable for rehabilitation, and might be obscured by the use of stigmatizing or judgmental psychiatric labeling. It is for this reason that the present terminology is advocated.

The syndrome of "multiple chemical sensitivities" has been defined as a "history of recurrence of [nonallergic] symptoms involving multiple organ systems following exposure to low levels of multiple environmental stimuli."[10] Most case series of patients identified as having multiple chemical sensitivities contain subsets of patients whose troubles began when they were acutely overexposed to one or more irritant chemicals.[9,10] It is possible that some of these cases represent behavioral sensitization to an odorant *with stimulus generalization*.[11] Although we made the point that behavioral sensitization itself was probably both involuntary and not personality-dependent, the potential contribution of personality to the process of stimulus generalization is probably greater. At the extreme, such traits as somatization or hypochondriasis may enter the picture.[12] Therapeutic considerations in such cases should be tailored accordingly.

Dennis Shusterman, MD, MPH
John Balmes, MD
James Cone, MD, MPH
Occupational Health Clinic
San Francisco General Hospital
San Francisco, CA 94110

References

1. Cullen MR (ed): Workers with Multiple Chemical Sensitivities. *Occupational Medicine: State of the Art Reviews.* 1987;2:655–806.

2. Dager SR, Holland JP, Cowley DS, et al: Panic disorder precipitated by exposure to organic solvents in the work place. *Am J Psychiatry* 1987;144:1056–1058.

3. Dawson ME, Schell AM: Human autonomic and skeletal classical conditioning: The role of conscious cognitive factors, in Davey G (ed): *Cognitive Processes and Pavlovian Conditioning in Humans. New York, Wiley, 1987, pp 27–55.*

4. *Commission on Professional and Hospital Activities: The International Classification of Diseases, 9th Revision, Clinical Modification.* Ann Arbor, MI, Commission on Professional and Hospital Activities, 1978.

5. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, ed 3, revised.* Washington, DC, American Psychiatric Association, 1987.

6. Amoore J, Hautala E: Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *J Appl Toxicol* 1983;3:272–290.

7. Swezey CL: Workers' compensation law, in La Dou, J (ed): *Occupational Health Law.* New York, Marcel Dekker, 1981, pp 20–21.

8. Grossman P, de Swart JCG, Defares PB: A controlled study of a breathing therapy for treatment of hyperventilation syndrome. *J Psychosomat Res* 1985;29:49–58.

9. Lewis BM: Workers with multiple chemical sensitivities: Psychosocial intervention, in Cullen MR (ed): Workers with Multiple Chemical Sensitivities. *Occupational Medicine: State of the Art Reviews.* 1987;2:791–799.

10. Cone JE, Harrison R, Reiter R: Patients with multiple chemical sensitivities: Clinical diagnostic subsets among an occupational health clinic population, in Cullen MR (ed): Workers with Multiple Chemical Sensitivities. *Occupational Medicine: State of the Art Reviews.* 1987;2:721–738.

11. Schottenfeld RS: Workers with multiple chemical sensitivities: A psychiatric approach to diagnosis and treatment, in Cullen MR (ed): Workers with Multiple Chemical Sensitivities. *Occupational Medicine: State of the Art Reviews.* 1987;2:739–753.

12. Kellner R: Hypochondriasis and somatization. *JAMA* 1987;258:2718–2722.