J Forensic Sci, Jul. 1974, Vol. 19, No. 3

W. Q. Sturner,[1] *M.D.; F. G. Spruill,*[2] *M.D.; and J. C. Garriott,*[3] *Ph.D.*

Two Propylhexedrine-Associated Fatalities: Benzedrine® Revisited

The Benzedrine® inhaler, long used as a local vasoconstrictor for nasal congestion, and at one time a readily available source of amphetamine, was replaced some years ago with the Benzedrex® inhaler, containing propylhexedrine. It was known that abuse had occurred with the prior constituent, but few toxic episodes and no fatalities have been documented with the latter agent. We have recently observed two deaths involving propylhexedrine which are the subject of this report.

Case Reports

Case 1

A 19-year-old female returned to her residence at 8:30 p.m. with a cut over her left eye. She told her mother that she had been fighting with her boyfriend, a rather regular occurrence, and proceeded to leave the house at 11:00 p.m. She returned home approximately 1½ h later, indicating that she had been "drinking alcoholic beverages." She then ate a bologna sandwich, following which she became "sick to her stomach." Her brother took her outside to "get some fresh air," but the decedent collapsed in a parking lot and fell over the hood of an automobile. An Emergency Rescue Unit was called as no signs of life were apparent, and she was pronounced dead on arrival at a local hospital. The family indicated that she "drank a lot," but was not a known drug user.

Postmortem examination revealed multiple parallel scars of the arms, buttocks, and posterior thighs, believed to be indicative of ritualism, rather than attempted self-destruction. White frothy fluid was present in the mouth and nose. There were no signs of recent needle marks. Callous formation covered the knuckles of both hands. No characteristic odor was detected about the body. The internal examination revealed extensive hemorrhagic edema of both lungs with frothy white foam in the trachea and bronchi. Focal pulmonary consolidation revealed sarcoidosis upon microscopic examination. Similar changes in one hilar lymph node were seen, but the remainder of the parenchymal organs was free from granuloma formation. The liver showed no evidence of fatty change or cirrhosis. Mild chronic pelvic inflammatory disease was observed. No significant blunt

Received for publication 9 Nov. 1973; accepted for publication 3 Dec. 1973.

[1] Assistant professor, Department of Pathology, University of Texas Health Science Center at Dallas, and Medical Examiner, Dallas County, Institute of Forensic Sciences, Dallas, Texas 75235.

[2] Instructor, Department of Pathology, University of Texas Health Science Center at Dallas, and Assistant Medical Examiner, Dallas County, Institute of Forensic Sciences, Dallas, Texas 75235.

[3] Instructor, Departments of Pathology and Pharmacology, University of Texas Health Science Center at Dallas, and chief toxicologist, Institute of Forensic Sciences, Dallas, Texas 75235.

force injuries were demonstrated. Sections of skin beneath the scarred areas revealed healed fat necrosis, but no granuloma formation or polarizable foreign material. Gas chromatographic analysis of postmortem specimens revealed propylhexedrine in the following concentrations: blood, 0.27 mg percent; kidney, 0.95 mg percent; liver, 1.18 mg percent; and stomach contents, 1.15 mg total in 280 ml, 0.54 mg percent. The procedure utilized *n*-butyl chloride as an extractant [*1*] and subsequent analysis of the extract using a 5 percent KOH, 5 percent Apiezon L column at a temperature of 125°C. No urine was available for analysis. The blood ethyl alcohol level was 0.122 percent. No other drugs, including narcotics, were detected.

Case 2

A 29-year old Negro man collapsed at home after working in his yard. He expired in the hospital in spite of efforts at resuscitation, including open heart massage. A history, reluctantly given by his wife, revealed "spells" for a long time, described as "breaking out in a cold sweat and passing out." Additional history revealed imprisonment on at least two occasions and friends of the deceased indicated that he "knew about using drugs and stuff" and did purchase inhalers from the drug store.

Postmortem examination revealed cor pulmonale with right ventricular hypertrophy (1 cm) and chronic lung disease with pulmonary congestion and edema. The hallmarks of chronic intravenous narcotism were present in the form of pulmonary vascular granulomata with polarizable foreign material and triaditis of the liver. The chronic lung disease exhibited features of bullous emphysema, fibrosis secondary to sickle cell disease, and scarring secondary to narcotism. There were multiple subcutaneous nodules of the extremities with occasional surface ulceration, but there was no evidence of infection. Hemoglobin electrophoresis revealed SC hemoglobin. Gas chromatographic analysis of postmortem specimens revealed propylhexedrine in the following concentrations: blood, 0.18 mg percent; urine, 1.26 mg percent; kidney, 0.15 mg percent; liver, 0.28 mg percent; and vitreous humor, 0.17 mg percent. Gastric contents were not analyzed. There was no evidence of alcohol, narcotics, or other drugs. In this case, it was felt that the pressor effect of propylhexedrine added the final stress to a cardiorespiratory system already compromised by severe disease processes.

Discussion

Propylhexedrine is a potent local vasoconstrictor, but is said to have only one twelfth the central nervous system stimulatory effect and less than one eighth the pressor action of racemic amphetamine sulfate [*2*]. It is used as an appetite suppressant (Obesin®) in Europe and a nasal decongestant (Benzedrex®) in the United States. The latter item contains 250 mg of propylhexedrine mixed with aromatics [*3*].

In previously reported instances, intoxication from 375 mg of propylhexedrine ingested by a 3-year-old child elicited symptoms of restlessness, tremor, hyperactivity, and inability to sleep. The child recovered in three days. Loss of appetite was not evident [*4*]. In another case, a 22-year-old man who swallowed 250 mg of propylhexedrine from an inhaler experienced violent palpitation, headache, and severe chest pain. Shock ensued and an ECG revealed an anterior myocardial infarct. The patient recovered after lengthy hospital treatment for additional complications [*5*]. Myocardial infarction has previously been observed after the administration of sympathomimetic amines and psychosis has been precipitated after chronic use of the contents of the inhaler [*6–8*].

Death resulting from use or abuse of this compound has not, to our knowledge, been previously observed and consequently the lethal dose is not known. It is suggested as a result of the herein reported cases that the use of propylhexedrine in the quantity found in Benzedrex® inhalers may result in or contribute to severe and occasionally lethal toxic reactions.

References

[1] Foerster, E. H. and Mason, M. F., "Preliminary Studies on the Use of *n*-Butyl Chloride as an Extractant in a Drug Screening Procedure," *Journal of Forensic Sciences*, JFSCA, Vol. 19, No. 1, Jan. 1974, pp. 155–162.
[2] Anlage, H. J., Smith, Kline and French Laboratories, Philadelphia, Pa. personal communication, 1973.
[3] *Physicians' Desk Reference*, 27th ed., Medical Economics Co., Oradell, N.J., 1973, p. 1301.
[4] Polster, H., "Uber eine Vergiftung mit dem Appetitzügler Propylhexedrin, Obesin, bei einem 3-jährigen Kinde," *Archiv fuer Toxikologie*, Vol. 20, 1965, pp. 271–273.
[5] Marsden, P. and Sheldon, J., "Acute Poisoning by Propylhexedrine," *British Medical Journal*, Vol. 1, No. 5802, 18 March 1972, p. 730.
[6] Anderson, E. D., "Propylhexedrine (Benzedrex) Psychosis," *New Zealand Medical Journal*, Vol. 71, 1970, p. 302.
[7] Johnson, J., Johnson, D. A. W., and Robins, A. J., "Propylhexedrine Chewing and Psychosis," *British Medical Journal*, Vol. 3, No. 5825, 26 Aug. 1972, pp. 529–530.
[8] Pallis, D. J., Barraclough, B. M., Tsiantis, Jr., "Psychosis and Nasal Decongestants," *Practitioner*, Vol. 209, No. 1253, Nov. 1972, pp. 676–678.

Department of Pathology
University of Texas Health Science Center at Dallas
5323 Harry Hines Blvd.
Dallas, Texas 75235