CASE REPORT

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Oral Overdose of Propylhexedrine

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ABSTRACT: We present a case of an oral overdose of cotton pledgets saturated with propylhexedrine, the active chemical in Benzedrex® inhalers. The tissue levels are included for reference purposes.

KEYWORDS: pathology and biology, toxicology, propylhexedrine, drug abuse, overdose

Twelve deaths associated with intravenous abuse of propylhexedrine, the active agent in Benzedrex® nasal inhalers, have been reported since 1974 [*1-5*]. However, only two cases of a toxic reaction from oral ingestion of the drug have been reported [*6, 7*]. No fatal oral overdose of propylhexedrine has been documented. Recently, we investigated a case of fatal propylhexedrine intoxication from ingestion of multiple cotton pledgets obtained from dismantled Benzedrex inhalers (Fig. 1). The tissue levels of the drug are included for reference purposes.

Case Report

A 30-year-old white male was found dead at his residence, slumped over the side of an empty bathtub. According to the informants, the decedent had used marijuana steadily for at least 15 years, had occasionally ingested amphetamines, but was never known to have injected drugs of any sort. A high-school dropout, the decedent had worked occasionally as a laborer. A week prior to his death, he had returned from a two-month journey through the Southwestern United States, where he was described by a relative as "being on a death trip." He had been depressed because of rejection of his poetry for publication.

At the scene, in the dining room, which served as living and sleeping quarters for the decedent, multiple disassembled Benzedrex nasal inhalers and stubs of marijuana cigarettes were scattered over a table in front of the sofa where the decedent slept. Additional inhalers were lying on the mantlepiece of the room, and still more were strewn across the floor in an

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upstairs room. In total, 49 inhalers were identified; 15 had been disassembled. No syringes or other paraphernalia for intravenous injection were discovered. A friend, who owned the house, said that he had never known the decedent to abuse propylhexedrine and that the inhalers had been present when he had last seen him alive two days previously.

At autopsy, there was no cutaneous evidence of intravenous or subcutaneous drug usage. A highly aromatic odor emanated from the sectioned tissues. The heart weighed 350 g and had a normal configuration. All three major coronary arteries had widely patent lumina. The lungs weighed 1200 g and were edematous and congested, as were the other viscera. The most striking findings were the highly aromatic gastric contents, consisting of mucus mixed with ten 5.0-cm cylindrical cotton pledgets identical to those found within intact Benzedrex inhalers (Fig. 2). Both the esophageal and gastric mucosal surfaces were hyperemic and edematous.

Microscopically, all organs were acutely congested. The architecture of the lungs was unremarkable. There was no anatomic evidence of pulmonary hypertension. There were, however, several foci of foreign body granulomas containing polarizing material scattered throughout the lung fields. There were increased numbers of mononuclear cells in the hepatic portal triads.

Toxicological screening analysis for alcohols and acidic, basic, and neutral drugs demonstrated only the presence of propylhexedrine. Column 2 of Table 1 lists the concentrations of the drug found in the autopsy specimens.

Toxicological Methods

Propylhexedrine in body fluids and organs was identified and quantitated by gas chromatography on OV-1, OV-17, and Apiezon L potassium hydroxide columns following alkaline ether extraction of tissues obtained at autopsy. The pure propylhexedrine standard was obtained by extraction of the cotton pledget from a new Benzedrex inhaler.

Discussion

The development, uses, and potential abuse of propylhexedrine have been discussed [*1-5*]. The Benzedrex inhaler contains a cotton pledget saturated with 250 mg of propylhex-

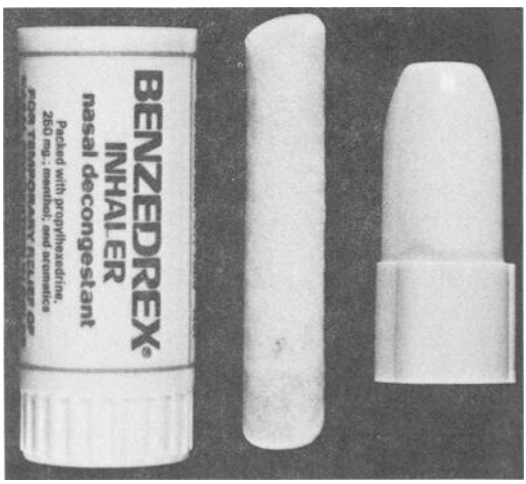

FIG. 1—*Dismantled Benzedrex inhaler with cotton pledget saturated with propylhexedrine in the center.*

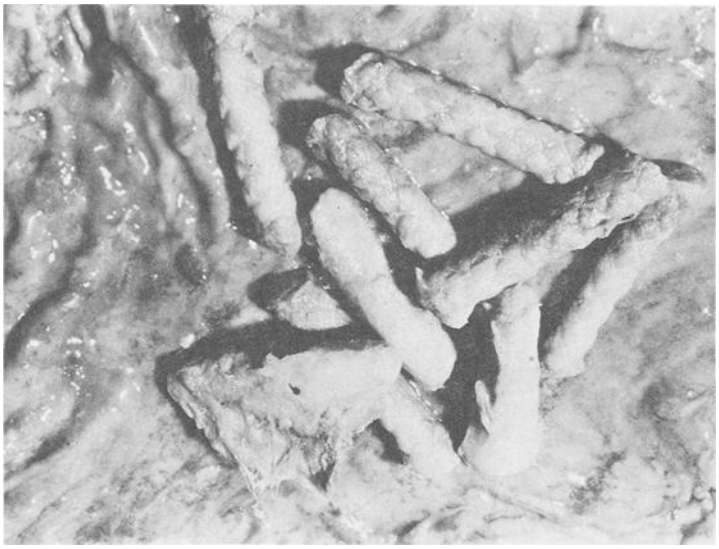

FIG. 2—*Opened stomach with gastric contents of cotton pledgets from Benzedrex inhalers.*

TABLE 1—*Tissue distribution levels of propylhexedrine in fatal cases.*

	Case 1	Cases from Institute of Forensic Sciences, Dallas, Tex.					
	from D.C.	2[a]	3[a]	4[b]	5[b]	6[b]	7[b]
Age and sex	30, m	19, f	29, m	19, m	17, f	24, m	23, m
Propylhexedrine levels							
Blood, mg/dL	3.6	0.27	0.18	0.20	0.03	0.16	0.25
Urine	6.0	NA[c]	1.26	6.95	NA	NA	NA
Bile	2.0	NA	NA	0.94	NA	NA	0.57
Vitreous	NA	NA	0.17	0.11	0.05	0.22	0.05
Liver	3.6	1.18	0.28	0.74	0.13	0.58	0.44
Lung	5.0	NA	NA	NA	NA	NA	NA
Kidney	3.0	0.95	0.15	0.40	0.18	0.053	0.21
Brain	2.4	NA	NA	NA	NA	NA	NA

[a]Cases reported by Sturner et al [*3*].
[b]Cases reported by DiMaio and Garriott [*4*].
[c]NA = not available.

edrine, 4.5 mg of menthol, and various other aromatic compounds. Experimental observations by DiMaio and Garriott [*4*] have established the blood concentration of 0.001 mg/dL as the maximal quantity detected 10 min following inhalation. Abusers of the drug dismantle the inhaler and either swallow the cotton plugs or heat them in water, dissolving the propylhexedrine for injection. The maximum blood concentration recorded from such intravenous use is 0.27 mg/dL [*4*].

Oral ingestion of the drug has produced severe adrenergic effects in a three-year-old child and in a 22-year-old man who suffered a myocardial infarction [*6, 7*]. No deaths from oral ingestion have thus far been reported.

The blood concentrations of the drug and the pathologic findings in the 15 reported cases of propylhexedrine abuse are given in Table 2. The drug distribution concentrations in all tissues and body fluids for the cases in which the information is available are listed in Table 1. In their analysis of the first six reported cases (Cases 2 to 7, Tables 1 and 2), DiMaio and Garriott [*4*] indicate that they presented a spectrum of fatal responses to the drug ranging from acute toxic effects to chronic pulmonary and cardiac lesions associated with long-term intravenous drug abuse. Anderson et al's extensive review [*1*] confirms this. In only two of the cases (Cases 2 and 4, Tables 1 and 2) can the toxic effect of the drug be considered the primary cause of death, and in one of these (Case 2) there was a blood ethanol concentration of 122 mg/dL. All the other cases have important pathologic changes. Three died from trauma. Of the other twelve, nine had changes of pulmonary hypertension including right ventricular hypertrophy resulting from chronic intravenous drug abuse or stimulation with adrenergic drugs or both [*1*]. Others have a variety of pathologic lesions. Since several of these deaths occurred during physical stress, Anderson et al [*1*] reason that the terminal mechanism may have been a cardiac dysrhythmia resulting from the combined effects of the endogenous adrenergic mediators and the propylhexedrine. In the present case there was neither the history of nor the cutaneous stigmata of long-term chronic intravenous drug abuse, nor was there any underlying natural disease, including the pulmonary arterial changes and the associated right ventricular hypertrophy attributed to chronic α-adrenergic stimulation. Finally, the scene displayed no evidence that the subject had been engaged in any strenuous physical activity.

We conclude that the subject from the District of Columbia died from the toxic effects of the propylhexedrine. (This conclusion does not preclude that the lethal mechanism may be a cardiac dysrhythmia.) The tissue levels of propylhexedrine in this case are several times higher than those of any other reported case. Also, the presence of pulmonary and cardiac disease in most of those cases confounds any interpretation of the dose response of the subjects. Based on the findings of the case reported here, we consider a blood concentration of 3.0 mg/dL lethal. Moreover, the urine concentration of 6.0 mg/dL in this case correlates well with the 6.95 mg/dL in the urine of DiMaio and Garriott's case report (Case 4) [*4*], the only other case in which no other drug or natural disease could be implicated.

All the reported fatalities associated with intravenous propylhexedrine abuse have occurred in Dallas, Tex. The decedent in the present case had just returned from a trip to the Southwestern United States, where he had visited Dallas. This is intriguing in light of the fact that this is the only fatality involving propylhexedrine in the eight years' existence of the Office of the Chief Medical Examiner of the District of Columbia, where a screen for amphetamine-type drugs is routinely conducted on the majority of cases. A sample of institutions routinely conducting similar drug screens, the Office of the Chief Medical Examiner in Westchester County, New York, the Office of the Chief Medical Examiner of North Carolina, the Center for Human Toxicology in Salt Lake City, and the Office of the Chief Medical Examiner of San Francisco, revealed that no fatal cases associated with propylhexedrine abuse had been recently encountered [*7*].[3] The Office of the Chief Medical Examiner of San Francisco has noted fatalities in the past. The only other locale in which there is known widespread abuse of this drug is London, England. Anderson et al [*1*] suggest that the problem may be indigenous to Dallas or a subculture within Dallas or that forensic pathologists and toxicologist in other locales are missing these cases. The present survey, although limited, would indicate that the former reason is more likely. Dr. J. C. Garriott, chief toxicologist at the Institute of Forensic Services in Dallas, offers no explanation for the cases being clustered in that city.

[3]Personal communications with L. L. S. Roh, Page Hudson, Michael Peat, and Boyd Stephens.

TABLE 2—*Propylhexedrine-associated deaths.*[a]

Case	Age, Race, and Sex	Blood Level, mg/dL	Other Drugs	Pulmonary Granulomas	Pulmonary Vascular Changes	Pulmonary Edema	Right Ventricular Hypertrophy	Other Pathologic Changes
			DISTRICT OF COLUMBIA CASE					
1	30, w, m	3.0	—	+	—	+	—	...
			CASES FROM INSTITUTE OF FORENSIC SCIENCES, DALLAS, TEX.					
2	19, b, f [3]	0.27	BA, 122 mg/dL	+	—	+	—	focal sarcoid
3	29, b, m [3]	0.18	—	+	—	+	+	SC Hgb, emphysema
4	19, b, m [4]	0.20	—	—	—	+	—	...
5	17, b, f [4]	0.03	—	+	+	+	+	...
6	24, b, m [4]	0.16	—	+	+	+	+	...
7	28, b, m [5]	0.16	—	—	+	+	—	...
8	34, b, f [1]	0.23	NA	+	+	+	+	LVH
9	27, b, m [1]	0.22	NA	—	+	+	+	LVH
10	22, b, m [1]	0.12	NA	—	+	+	+	70% narrowing of LAD coronary artery
11	29, b, m [1]	0.07	NA	+	+	+	+	focal myocardial fibrosis
12	22, b, m [1]	0.12	NA	—	+	+	+	interstitial pulmonary fibrosis
13	26, b, m [1]	0.14	NA	+	—	+	+	...
14	27, b, m [4]	0.08	—	+	—	—	—	multiple gunshot wounds
15	23, b, m [4]	0.25	BA, 186 mg/dL	+	—	—	—	suicidal hanging
16	25, b, m [1]	0.11	NA	—	—	—	—	gunshot wounds

[a]LVH = left ventricular hypertrophy; LAD = left anterior descending artery; SC HgB = sickle cell C hemoglobinopathy; BA = blood alcohol; and NA = not available.

Summary

A case of an oral overdose of propylhexedrine in a 30-year-old white male is presented, and the findings are contrasted with previously reported fatal cases from intravenous abuse. The blood concentrations of 3.0 mg/dL is offered is a reference for the toxic level of this drug.

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