

The second patient (case 7) was a 16-year-old girl who, after drinking alcohol, attempted suicide by ingesting about 4.5 grams of propoxyphene. She convulsed shortly thereafter and on admission one hour later was comatose and apneic. She was severely acidotic. Systolic blood pressure was 100 mm Hg, and the ECG revealed sinus tachycardia, widened QRS (0.12 seconds), and prominent S waves (except in lead III). Mechanical respiration was instituted, and subsequent seizures were controlled with intravenous diazepam. She responded well to treatment, acidosis subsided, and the ECG was normal in six hours. She was discharged after two days. Her plasma propoxyphene concentration was 0.51 micrograms/ml; and her norpropoxyphene concentration, 0.79 micrograms/ml, 2.5 to 3 hours after ingestion.

Propoxyphene and norpropoxyphene analyses were carried out utilizing the gas chromatograph-mass spectrometer technique of Wolen (Toxicol. Appl. Pharmacol, 19:480, 1971). Highest plasma concentrations were found in the fatal case; and the patient with the second-highest concentration, over 0.5 micrograms/ml, had very severe symptoms. In discussing the clinical symptomatology the authors note that cardiac arrest may occur secondary to respiratory depression and apnea and that QRS widening and ventricular bigeminy have been observed in humans taking excessive doses of propoxyphene.

Comment: The development of respiratory depression and apnea, when excessive propoxyphene has been ingested either alone or with CNS-depressant agents, results in severe anoxia and acidosis. While the use of a narcotic antagonist to reverse the opiate-induced respiratory depression is of prime importance, the need to correct acidosis needs emphasis. Acidosis depresses myocardial contractility, diminishes cardiac responsiveness to catecholamines, and predisposes to ventricular fibrillation. The importance of correcting acidosis under conditions of anoxia with acute cardiopulmonary failure cannot be overemphasized. The use of intravenous sodium bicarbonate in cardiopulmonary resuscitation is described in *The Heart*, J. Willis Hurst, Ed., 4th Edition, 1978, McGraw Hill, New York.

FINKLE STUDY

In a review of 1,022 medical examiner cases associated with propoxyphene overdose, Finkle *et al.* (J. Forensic Sci., 21:706-742, 1976) observed a small group of cases exhibiting a common pattern of symptoms prior to death, the most striking of which was a survival time of 15 minutes or less, that is, "sudden death." He examined various toxicologic and epidemiologic aspects in 52 cases, in all of which death apparently occurred within 15 minutes (interval from time last seen alive until death) of unexplained cause or causes.

Age and sex distributions differed from those observed for the total study population, inasmuch as the greatest proportion of males was noted in the 21-25 and 46-50 age groups. Body weights were not remarkable. In 4 of the 10 cases for which there was a medical history, "a heart condition" was noted. Single instances of hypertension, asthma, epilepsy, paraplegia, ulcers, and "recent head injury" were also noted. The drug abuse histories were noteworthy in that 44% had a documented history of abusing some substance (34% for total study group). Respiratory arrest, the predominant symptom (85%), was almost twice as frequent. Seizure frequencies were about the same. Coma was observed less frequently (15% vs. 40%), but this may be due to the brief survival. The authors concluded that "the final collapse is centrally mediated and rarely cardiovascular."

There was a very high incidence of the use of other drugs in these "sudden death" cases; 85 percent had some other drug in addition to propoxyphene, in contrast to 76 percent for all cases. In the sudden death group, 52 percent had alcohol involved, in contrast to 42 percent in the total group. The other drugs, determined by case investigation or by chemical analysis, were predominantly central nervous system depressants. In 40 percent of the cases, concentrations of drug (by laboratory analysis), other than propoxyphene or alcohol, were significantly high in and of themselves. Diazepam was the most frequent. The data indicate that alcohol and other drugs played a major role in these cases. The particular importance of alcohol in the sudden death cases is attested to by the fact that blood alcohol concentrations were predominantly associated with lower propoxyphene concentrations. In 75 percent of the sudden death cases associated with alcohol, plasma propoxyphene concentrations were less than 2.5 micrograms/ml., whereas in the total study group 72 percent of the sudden death cases associated with alcohol had values less than 7.0 micrograms/ml.