The majority of deaths are suicidal in North Carolina when the manner of death could be determined (2). Many of the deaths attributed to overdoses of propoxyphene involve other drugs including alcohol and diazepam. In the deaths we have attributed to propoxyphene there was in our opinion a sufficient quantity of the drug to cause death in the absence of the other drugs but the other drugs may have been contributory factors in the deaths. Of the 183 deaths attributed to propoxyphene at least 145 or about 80% did not have enough alcohol or other drug to have caused death; in each sufficient propoxyphene to cause death was found. In 7 cases greater than 20 mg/dl of salicylate was found. This could come from a propoxyphene-aspirin containing product. Most of our cases involved deaths of middle-aged individuals and not the younger drug abusers.

Although propoxyphene was introduced in 1957, it wasn't until around 1970 that analytical procedures for adequately detecting and measuring it in the relatively low concentrations present in the blood of those fatally poisoned began to be reported. Twelve articles (3) on propoxyphene overdoses published from 1960–1970 reported 4 fatalities. Eighteen articles (3) published from 1971–1975 reported 117 fatalities. A survey published in 1976 (4), reported 1022 propoxyphene-associated cases in the years 1969 through July 1975. There were only 2 in 1969, 7 in 1970, and 11 in 1971 for a total of 20 cases; 1002 cases were reported for the 3½ years 1972–July 1975. In the same nine years, 1970–1978 we have discovered 228 fatal overdoses in North Carolina. In spite of greatly improved analytical procedures which allow for the identification and quantitation of not only the parent drug propoxyphene but also its longer-lived pharmacologically-active metabolite, norpropoxyphene, many laboratories either do not detect the drug or are unable to quantitate it and its metabolite. In establishing that the drug is a cause of death it is essential that about 1 microgram of propoxyphene be found in a milliliter of blood and not be confused with the usually greater concentration of norporpoxyphene. A therapeutic dose of 130 mg (2 65-mg doses) of propoxyphene hydrochloride produces concentrations of the order of 0.1 mcg/ml of blood. This is about one-tenth what we consider a lethal blood concentration.

In a national proficiency testing program in 1978 which involved 273 laboratories, 120 laboratories reported that propoxyphene was identified and norpropoxyphene was identified by 32. Only 67 reported quantitative results for propoxyphene with a rane of 0.7–13.0 mcg/ml for a serum containing 5 mcg/ml and 13 reported a range of 0.3–3.0 mcg/ml of norpropoxyphene for a serum containing 2 mcg/ml. The specimen which contained about five times the lethal concentration was identified by about only 44% of the laboratories and quantitated by about 25% with a very wide range of results. This could serve as an evaluation of the state of the art of analysis for the drug in 1978. We infer that many cases are missed because of generalized inadequacy of the laboratories.

In 1971 when the patent on propoxyphene expired, propoxyphene napsylate was introduced. It was hoped that its lower solubility would prevent poisoning of overdoses, unfortunately we have seen no evidence of this. In 1978 in North Carolina where 31 deaths were attributed to propoxyphene, the tradenames were given in the histories on 17 reports. Thirteen had the tradenames of one manufacturer; 8 were for a propoxyphene hydrochloride product and 6 were for a propoxyphene napsylate product (one case had both named).

Our attention was attracted to the drug in 1972 when we applied a specific method of analysis developed in our laboratory to specimens submitted from a number of unexplained deaths. If an adequate method of analysis for the drug had existed in 1957, it is interesting to speculate whether overdose deaths would have been detected and if they had, would the use of the drug have been discouraged. If propoxyphene were not legally available, it is our opinion that there would be no incentive to prepare the compound or to traffic in this drug for the illicit market.

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