Human spermatogenesis and fertility following exposure to dibromochloropropane (DBCP)

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1,2-Dibromo-3-chloropropane (DBCP) is a highly effective nematocide and soil fumigant which was widely used in agriculture between 1955 and 1977. The first report of its gonadotoxic effect in animals appeared in 1961 (Torkelson, et al., 1961), but it was only during the summer of 1977 that epidemiological studies conducted at chemical plants manufacturing this compound indicated that employees who had been exposed to it showed oligospermia or azoospermia and infertility (Potashnik et al., 1978; Whorton et al., 1977). A thorough investigation was initiated and the suppressive effect of OBCP on human testicular function was confirmed. It was not clear at that time whether this compound selectively affects the seminiferous tubules or whether it also exerts some toxic effect on the interstitial (Leydig) cells, leading to peripheral testosterone depletion and sexual disturbances, as initially claimed by some of the affected individuals. In addition, the questions relating to the mechanism of this gonadal effect and its possible reversibility could not be answered at that time.

Periodic follow-up of the affected workers for more than five years and intensive clinical and experimental research has improved our understanding of these questions. This chapter presents the latest information and data accumulated on this subject.

CHEMICAL CHARACTERIZATION AND COMMERCIAL USE

Until 1977 DBCP was available on the market under the trade names, Fumazone, Nemazone and Nemaset. The compound is a dark yellow or amber liquid with a pungent odour. The molecular structure of DBCP is presented in Fig. 19.1. The compound has a specific gravity of 2.08 (at 25°C), a boiling point of 195°C and a vapour pressure of 0.8 mm Hg (at 20°C). DBCP is slightly soluble in water and miscible in methanol, acetone, carbon tetrachloride and dimethylsulphoxide (DMSO).

DBCP was used on a variety of crops, including cotton, soybeans, fruits,
nuts, vegetables and ornamentals. DBCP is not phytotoxic and can be applied directly to the soil. It was applied to the soil by injection, granular deposition, or sprinkler irrigation. The combination of its relatively low vapour pressure and high density ensured a long residence time of the compound in soil. Its fumigation action in the soil was attributed to its slow rate of volatilization.

EXPERIMENTAL STUDIES

Effect on the reproductive system

In 1961 DBCP was found to exert acute and chronic toxicological effects on the rat, guinea pig, rabbit and monkey. Respiratory exposure to DBCP vapour at a concentration of 10 or more parts/10⁶ over a period of more than 7 weeks resulted in a significant decrease in sperm count, degeneration of the seminiferous tubules and severe atrophy of the testes (Torkelson et al., 1961). Oral ingestion of DBCP similarly reduced sperm count and motility, increased the rate of formation of morphologically abnormal sperm cells and caused testicular atrophy (Faydysh et al., 1970).

The suppressive effect of DBCP on rat testes is reversible. In a recent study fertile male rats were injected subcutaneously with DBCP, dissolved in DMSO, at a dosage of 20 mg DBCP per kg body weight, once a week for three consecutive weeks. One testis of each rat was removed 3–7 weeks after the last injection. The second testis was removed 27 weeks later. About 70% of the animals with atrophy of the seminiferous tubules in the first testis showed reversibility of the suppressive effect. Active spermatogenesis was observed on histological sections of the second testis (Shemi et al., 1981).

Other toxicological effects of DBCP

A bioassay for the possible carcinogenicity of DBCP was conducted on rats and mice of both sexes (Olson et al., 1973; Powers et al., 1975). DBCP dissolved in corn oil was administered by gavage five days a week for a total of 78 weeks. As early as 10 weeks after the study was initiated, squamous cell carcinomas of the stomach were detected in both male and female rats and mice. The incidence of adrenocarcinoma of the mammary gland was statistically significant only in female rats. Based on these data, under certain bioassay conditions, DBCP is a stomach carcinogen in rats.