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THE SMALLER HALOGENATED
ALIPHATIC HYDROCARBONS

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The chemical substances to be considered in this review are those compounds containing from 1 to 4 carbon atoms and 1 or more halogen atoms. Because of current interest, halogenated ethers are included, although they are not, strictly speaking, hydrocarbons. Compounds containing other functional groupings obviously excluded themselves.

The period, 1955 to June, 1961, is covered as accurately as space and frailty permit. The reader would be well-advised to study both sections, for some widely different view points are held by anesthesiologists and toxicologists.

ANESTHETIC ASPECTS

The production of general anesthesia is at least as much an art as it is pharmacological engineering. The primary criteria; that the patient should feel no pain and recover undamaged from the anesthetic and that the surgeon should be able to perform the necessary procedures, can be met by the skilled practitioner with any one of a wide variety of agents, whereas the neophyte can expect trouble with them all.

Local conditions and the skills and prejudices of the anesthetist and surgeon have as much to do with the outcome and evaluation of the anesthesia as does the special pharmacology of the anesthetic vapor employed. In truth, "What is one man's poison is another's meat."

K-2511 Chloroform.—Despite its classic reputation for evil-doing, chloroform has reacquired supporters, particularly as more reliable methods of administering powerful anesthetics have been recently developed. Although earlier than our general coverage, one should still begin with the detailed Wisconsin study (1). More recently, Duncan *et al.* (2) reported some 17,000 obstetrical patients receiving chloroform alone as their obstetrical anesthetic. These investigators were well pleased with the results and reported no deaths or late toxic manifestations of hepatic and renal damage in this series. The well-known tendency of chloroform to decrease the strength of uterine contraction can indeed at times be an advantage. That the agent has intrinsic hazard even in the best hands today is indicated by the report of Siebecker & Orth (3) who attempted seven administrations in open thoracic operations. Two of the seven patients died due to acute centrilobar necrosis of the liver, and two more presented clinical and laboratory evidence of toxic hepatitis. It is probable that the poor ventilation consequent upon intrathoracic exploration was a considerable factor and they caution against the use of chloroform under such conditions. The light touch with chloroform is again emphasized by Davison (4). Lately, Dobkin, Johnston & Skinner (5) have examined chloroform using a modern temperature-compensated vaporizer. With this

to our attention. The abstract indicates that the chemical was liberally applied to the shaven thighs of white rats. Edema of subcutaneous tissue and effects upon muscle and nerve fibers were noted. Nervous tissue became normal 10 days after exposure ceased, coinciding with the reduction of the inflammatory reaction. Widespread clinical use attests to the relative innocuousness of cutaneous application.

K-1711 Vinyl chloride.—Of the short-chain halogenated hydrocarbons utilized as monomers for polymerization, vinyl chloride is probably the most important. Several recent papers have helped to delineate the toxicological picture.

Danziger and co-workers (332) recently studied the effects of acute exposures to anesthetic concentrations of vinyl chloride after 2 accidental deaths in industry. Danziger (333) described the circumstances involved in these two cases. The pathological findings in both were cyanosis, conjunctival burns, congestion of internal organs, especially lungs and kidneys, and failure of the blood to clot. Since no vinyl chloride could be detected at autopsy 3 and 8 hr. after death, mice, rats, and guinea pigs were exposed to levels of 10 to 40 per cent vinyl chloride in air for periods of time up to 30 min. A concentration of 10 per cent produced injury in rats and mice, while 30 per cent caused death. Guinea pigs were less susceptible, 3 of 5 surviving at a concentration of 40 per cent for 30 min. The principal pathological changes noted were congestion in the lungs, liver and kidneys, pulmonary edema and hemorrhage, and failure of the blood to clot. These results tended to confirm the cause of death in the overexposure of humans.

The effects on rats, rabbits, guinea pigs and dogs, of repeated exposures to vinyl chloride were reported by Torkelson *et al.* (334). After exposing animals 7 hr per day, 5 days per week, for up to 6 months, to air concentrations of 500, 200, 100 and 50 ppm, it was only at the last concentration, 50 ppm, that all species were completely free of deleterious effects. At a concentration of 100 ppm, there was only a slight increase in the average weight of the rat livers. From these studies, the authors have recommended that the maximum allowable concentration for repeated exposures in the workroom be 100 ppm and that the timeweighted average for daily exposure should not exceed 50 ppm. From this work, the present recommended threshold limit of 500 ppm as set by the American Conference of Governmental Industrial Hygienists appears to be too high. K-1717 K-1985

Dichloroethane.—There are two structural isomers of dichloroethane, 1,1- and 1,2-dichloroethane. The 1,2-dichloro compound, usually called ethylene dichloride, has been studied much more extensively than the 1,1-dichloro compound, which is sometimes called ethylidene chloride. The authors were unable to find reference within the last five years to any work which specifically named 1,1-dichloroethane as the subject compound. Several papers concerning 1,2-dichloroethane are cited. Where the authors of papers did not specify the isomers, the term dichloroethane will be used.

Loscalzo *et al.* (335) studied the effects of 1,2-dichloroethane upon the heart, arterial pressure and respiratory activity of rats which had received