Advances in Cancer Research Vol IV 1956

initial displacement of a lipid from a lipoprotein. Indirect evidence for the implication of cell lipids stems from the pronounced cocarcinogenic action of the polyglycol detergents (Spans and Tweens), as well as certain "association colloids" and lipoproteins (Ekwall, 1954), which may owe this action to the possession of both water-soluble and lipid-soluble properties. In effect, these substances, as vehicles, may facilitate the passage of the water-insoluble carcinogens into the aqueous environment of the cell. In addition to this obvious mechanism, the detergents may function in a different manner, namely, to inhibit lipase of the sebaceous glands. Such inhibition would amount to a true cocarcinogenic action since the polycyclic hydrocarbons actually cause the disappearance of this lipase (Kung, 1949) (see Section II,1,C).

b. *Sarcoma production by subcutaneous injection.* When sarcoma is produced by the subcutaneous injection of the carcinogenic hydrocarbons, the influence of the solvent may be complicated (Berenblum, 1954). However, out of a confusing array of experimental evidence, certain solvents emerge as stimulatory, others as inhibitory, to carcinogenic action. Dickens (1946–47) summarizes the solvents that had been found to lead to a relatively high incidence of tumors, namely, sesame oil, arachis (peanut) oil, olive oil, paraffin, several synthetic glycerides, benzene, and some samples of lard; cholesterol may also belong to this group. Likewise, the solvents that had inhibited the carcinogenic response were, in chickens, egg yolk fat and chicken fat; in mice, ethyl ether or mouse fat; and rat fat in rats. Lipid solvents, such as vegetable oils, lard, and paraffin, which were commonly used in the past with variable responses, have been largely superseded by synthetic tricaprylin, an inert or neutral vehicle in the sense that it neither promotes nor retards carcinogenesis.

Recently, the stimulatory action of sesame oil has been uniquely demonstrated. This oil has been extensively employed as a vehicle for the subcutaneous injection of various compounds related to or derived from cholesterol. Of special interest in this connection is the observation that a steroid can be noncarcinogenic when administered in aqueous colloidal solution but carcinogenic when injected in sesame oil (Bischoff *et al.*, 1955; Fieser *et al.*, 1955). The sesame oil is considered essential in the carcinogenic process (see Section II,2). A possibly relevant result was that of Mirand *et al.* (1953) who obtained malignant tumors in mice upon the subcutaneous injection of deoxycorticosterone acetate (noncarcinogenic heretofore) dissolved in sesame oil. These interesting results with this oil merit further investigation of its role in carcinogenesis and comparative studies of other lipid vehicles.

On the other hand, the inhibitory effects of homologous fat on benzpyrene carcinogenesis in the mouse did not result from the high degree of unsaturation of the fat; cod liver oil did not inhibit (Dickens,

LIG- 39629

LG 2022035