Effects of ethylene dimethanesulphonate on reproductive function in rats

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Ethylene dimethanesulphonate (EDS), a diester of ethylene glycol and methane sulphonic acid, belongs to the homologous series of esters of general formula: $(CH_2)_n(OSO_2CH_3)_2$. Unlike other members of the series, which suppress bone marrow activity, EDS appears to have no such action, at least in rats and mice, although showing inhibitory activity against tumours. Its antispermatogenic effects also differ strikingly from the homologues and involve the intermediate range of spermatogenic cells—meiotic spermatocytes and spermatids (Jackson, 1966), whereas related diesters predominantly attack spermatogonia in the early stages of spermatogenesis. However, repeated oral courses of EDS (5×25 mg/kg orally) at 5 week intervals eventually produce irreversible sterility in rats.

Again, in the rat, EDS produces marked inhibition of the accessory sexual structures (prostate and seminal vesicles), indicating pharmacological action on the androgenic function of the Leydig cells. This may be central or peripheral in origin and is not a feature of the antispermatogenic action of the homologous diesters. Single injections of EDS have now been observed to produce spermatoceles in the epididymis within a few days, which may be important in relation to antifertility action of this compound. These lesions are cystic spaces evidently formed by rupture of the thin wall of the tube, leading to extravasation of fluid containing sperm. These spermatoceles may be visible to the naked eye or microscopic and multiple but there is no evidence that vascular damage is the cause. It is tempting to infer that Leydig cell damage is responsible since the epididymis is androgen-dependent. Only one other organic compound, α-chlorohydrin (U-5897) has been implicated in the production of epididymal damage and spermatocele formation (Ericsson & Baker, 1969; Ericsson, personal communication).

The question is whether the various changes induced in the reproductive tract by EDS are due primarily to interference with androgen control or result from more than one pharmacological activity.

REFERENCES

ERICSSON, R. J. & BAKER, V. F. (1969). Male antifertility compounds: biological properties of U-5897 and U-15,646. *J. reprod. Fert.*, in the Press.

JACKSON, H. (1966). *Antifertility Compounds in the Male and Female.* Springfield: Charles C. Thomas.

The occurrence of pharmacologically active substances in, and the action of drugs on, preparations of the sea anemone *Actinia equina*

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Mathias, Ross & Schachter (1960) found histamine, tetramethylammonium and a pharmacologically active polypeptide in extracts of *Actinia equina*. They were unable to demonstrate the presence of 5-hydroxytryptamine or esters of choline, but their extraction and bioassay techniques may have led them to overlook small amounts of these substances. Indeed, it is known that the choice of solvent system may influence the recovery of choline esters (Aprison, 1967). In this study, therefore, five different solvent systems have been used for the extraction of anemones and the active substances identified by chromatographic, colorimetric, fluorometric and bioassay methods. In general the results of Mathias *et al.* (1960) have been confirmed