Anti-uterotrophic Response of Immature Mice to 3-Methylcholanthrene

As well as its ability to induce cancer in various tissues, the polycyclic hydrocarbon 3-methylcholanthrene (MCA) is capable of affecting the activity of certain endocrine glands[1–3] and altering the metabolism of several hormones[4–7]. Indirect evidence from several sources[6,8–12] indicates that, in various experimental conditions, MCA may be capable of inhibiting, potentiating or mimicking the activity of certain steroid hormones. We have conducted preliminary experiments aimed at testing more rigorously the alleged steroidal activity of MCA. In the experiment reported here, MCA was tested for oestrogenic (uterotrophic) activity in a four point assay using oestrone as the reference standard.

Immature female Swiss Webster mice each received a total dose of either 0·08 or 0·32 μg of oestrone. Mice of the same age and strain each received a total dose of either 0·15 or 3·00 mg of MCA. The total dose of either oestrone or MCA was administered to each mouse in three equal, daily subcutaneous injections of 0·1 ml., beginning when the mice were 19 days old. Control mice received either no treatment or daily subcutaneous injections of 0·1 ml. of the solvent (10 per cent benzyl alcohol in sesame oil) in which oestrone and MCA were administered. All animals were killed on the fourth day and their uteri were rapidly removed, trimmed and weighed.

Two identical experiments were performed. The results of these experiments did not differ significantly from each other, and so both sets of data are combined in Table 1. Injections of oestrone produced the expected uterotrophic response. In this biological assay system, MCA failed to exhibit the oestrogenic activity observed by other investigators[12] in different experimental conditions. In our case, uterine weight was significantly depressed in mice receiving the higher dose of MCA.

Although Huggins *et al.*[12] provided evidence that MCA could substitute for oestrogen in the initiation of mammary growth, Jackson and Robson[11] found that local application of MCA to the vaginae of ovariectomized mice antagonized the effects of concurrently administered oestradiol on vaginal cornification. Jull[10] observed that MCA mimicked the action of progesterone with respect to acinar growth in the mammary gland. Our data tend to support the concept that MCA exerts an anti-oestrogenic or progestational activity, and further experiments are in progress to test this hypothesis.

Whether the ability of MCA to effect endocrine alterations in the recipient animal is related to its carcinogenic properties is largely a matter of speculation. As a general hypothesis, Jull[10] suggested that MCA is sufficiently similar to some steroid hormone, progesterone in the case of his own experiments, to mimic its normal physiological activity, but that the difference in the structure of MCA and the hormone might produce an abnormality in the hormonal mechanism concerned, which could result in malignant proliferation. Yang *et al.*[13] and Huggins and Yang[14] extended this concept to include a general mode of action common to the carcinogenic polycyclic hydrocarbons and involving close steric similarity between the carcinogenic hydrocarbons, the steroid hormones and the base pairs of nucleic acids. Assuming that the structure of MCA is sufficiently similar to that of certain steroid hormones to permit access and steric fit of the carcinogen into various molecular receptor sites, it is certainly conceivable that much of the biological activity of MCA could be accounted for in this way.

Table 1. ASSAY OF MCA FOR OESTROGENIC (UTEROTROPHIC) ACTIVITY

Injectate (total dose)*	No. of mice	x̄ Final body weight (g)	x̄ Uterus weight (mg/100 g body weight)
None	12	14·7	80·0 ± 7·0†
Solvent only	8	13·5	85·2 ± 7·1
0·08 μg of oestrone	10	13·6	118·4 ± 19·0
0·32 μg of oestrone	10	13·8	232·7 ± 22·3
0·15 mg of MCA	10	14·9	79·0 ± 5·3
3·00 mg of MCA	10	13·7	54·6 ± 4·6

* Total dose administered to each mouse in three equal, daily subcutaneous injections of 0·1 ml., beginning when the mice were 19 days old.
†x̄ ± standard deviation.

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Short Half-times of Caesium-137 in Pregnant Women

BENGTSSON *et al.*[1] reported a patient with a shorter biological half-time for caesium during pregnancy than afterward. Prompted by this finding, and by the marked individual variation in body burden[2] and biological half-time[3] seen in our own studies, we evaluated the equivalent biological half-times in twenty-four pregnant women while the environmental levels of fall-out caesium-137 were still sufficiently high that artificial administration of radioactivity was not required. The equivalent biological half-time is defined as 0·693 times (observed body content/observed excretion rate). Our technique has been described previously[4].

Fig. 1 and Table 1 show that the average half-time of 49 days in twenty-four pregnant women was only 58

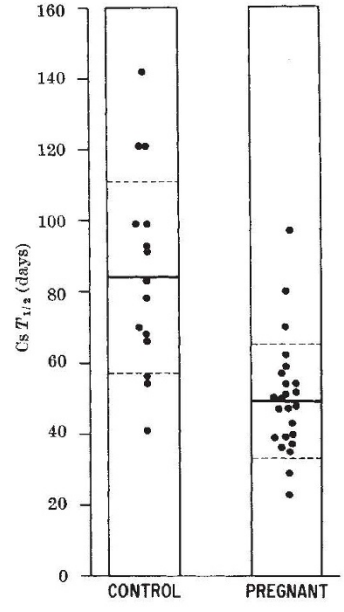

Fig. 1. The distribution of individual half-times. The means (solid lines) and standard deviations (broken lines) are shown.