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### Effect of Growth and Lactogenic Hormone on Tumor Induction by Methylcholanthrene in 4-Month-Old Female Rats.\*† (31016)

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An optimum yield of mammary tumors occurs when methylcholanthrene (Mc) is administered *per os* to female rats 30-60 days of age(1); successive daily doses of the carcinogen, including those given after the rats are 4 months of age or older, continue to contribute to the final tumor yield(2). If, however, administration of the initial dose is delayed until the rats are 4 months of age, the tumor yield is markedly reduced(3). These data indicate that the age of the animal when the carcinogen is first administered, governs its tumor-inducing, but not its growth-promoting, properties. Since the period of greatest susceptibility to tumor induction is coincident with the period of greatest growth rate, an attempt was made to increase tumor induction in 4-month-old female rats by addition of growth hormone to the daily regimen. Prolactin was administered to control rats since it is the only one of the minute quantities of contaminating hormones not normally found in virgin rats(4).

*Method.* Female Wistar rats were divided into 4 groups of 20 animals each and treated according to the plan in Table I. The rats were caged singly in wire mesh cages and were given Wayne Lab-Blox *ad libitum*.

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† The growth hormone and lactogenic hormone used in this study were generously supplied by the Endocrine Study Section, Nat. Inst. Health.

TABLE I. Tumor Incidence in 4 Groups of Experimental Female Rats.

Group	Age (mo)	Treatment*	No. of animals	No. of animals with tumor	No. of tumors
A	4	GH & Mc	19	9	35
B	4	Prolactin & Mc	19	9	25
C	4	Mc	16	11	38
D	1	Mc	19	18	108

\* Growth hormone ovine. NIH-GH-S6.  
Prolactin ovine. NIH-P-S6.

Methylcholanthrene dissolved in olive oil was administered five days weekly through an esophageal catheter. All 4-month-old rats received doses of 5 mg daily whereas the 30-day rats received 2 mg daily for the initial 30 days of experiment, after which the dose was increased to 5 mg daily. Hormones were administered subcutaneously twice daily for the initial 4 months of the experiment. The total daily dose of growth hormone was 3.2 USP units and that of prolactin of 0.8 I.U., the latter an estimate of prolactin contamination in the growth hormone preparation. The experimental plan and results are shown in Table I.

*Results and discussion.* The administration of growth hormone resulted in a constant increase in weight of the recipient adult rats, whereas the animals receiving prolactin failed to gain at the same rate as those treated with methylcholanthrene alone (Fig.

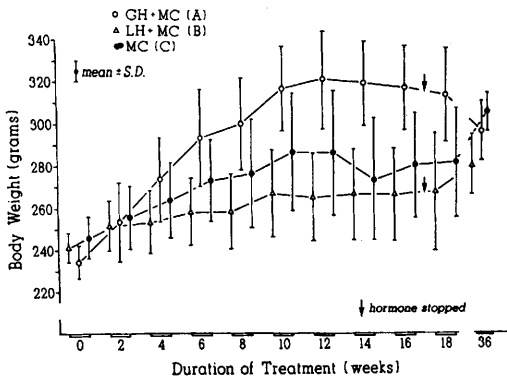


FIG. 1. Body weight curves of rats of groups A, B and C (4-month-old females) showing alterations in the rate of change of body weight caused by administration of growth hormone and prolactin.

1). The experimental results are listed in Table I. These data confirm our prior observations that tumor induction by methylcholanthrene is significantly diminished if the initial treatment is withheld until the animals are 4 months of age. They also demonstrate that neither growth hormone nor prolactin

increases the rate of tumor induction by methylcholanthrene.

Despite the fact that the amount of contaminating prolactin is insufficient to inhibit the weight gain caused by GH, the experiment fails to resolve the possibility, however remote, that it impeded a potentiating effect by GH in tumor induction.

**Summary.** Four-month-old female rats are resistant to carcinogenesis by methylcholanthrene when compared to female rats 30-60 days of age. Neither growth hormone nor prolactin potentiate tumor induction by methylcholanthrene in mature female rats.

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### Effect of Parabiosis on Tumor Induction with Methylcholanthrene in Rats.\* (31017)

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A maximum yield of mammary tumors occurs when methylcholanthrene is administered *per os* to female rats 30-60 days of age(1). If administration of the initial dose is delayed until rats are 4 months of age, a drastic reduction in the number of induced tumors results (2). The purpose of this experiment was to determine whether or not a humoral substance exists in 30-60-day rats that will increase susceptibility of rats to tumor induction, or conversely, whether a circulating substance is present in 4-month-old rats that will inhibit tumor induction.

**Method.** Female rats of the histocompatible Lewis strain were paired by the modified Bun-

ster & Myer procedure(3) according to the following scheme.

**Group A.** 30-day-old females were paired with 4-month-old female rats and methylcholanthrene was administered to the 4-month-old twin.

**Group B.** 30-day-old females were paired with 4-month-old female rats, and methylcholanthrene was administered to the 30-day-old twin.

**Group C.** 30-day-old females were paired with each other, and methylcholanthrene was administered to one of each of the pairs.

Methylcholanthrene, in doses of 5 mg daily 5 times weekly was administered *via* an esophageal cannula as a .5% solution in olive oil for a period of 8 weeks. The experiment was

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