The intercept with the abscissa is therefore the reaction constant of the first order reaction that is approximated at low substrate concentrations.

Under physiological conditions, where the substrate concentration may be low, the reaction rate will be determined by $\frac{V_m}{K_M}$, in which expression $\frac{1}{K_M}$ is related to the affinity of the substrate for the enzyme. In this respect comparison of the rates at which two substrates are attacked has little meaning if only one arbitrarily chosen substrate concentration has been used. It is clear from the above that the complete concentration curves must be determined. If these curves cross, the situation at relatively high concentrations may be the reverse of that at low concentrations. In view of these considerations, the intercept with the abscissa, when Plot III is used, may give directly the most important constant of an enzyme system. In terms of Equations I and II, this intercept equals $\frac{k_3}{K_M}$ or $\frac{k_1 k_3}{k_2 + k_3}$ per amount of enzyme.

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Manuscript received April 1, 1952.

Inhibition of Methylcholanthrene Carcinogenesis by Hypophysectomy[1]

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The significance of pituitary function in neoplastic disease is indicated by the many and diverse neoplasms that develop in the rat following the prolonged administration of growth hormone (*1–4*) and the absence of both growth hormone–induced and spontaneous tumors in the hypophysectomized rat (*5*). The present report is concerned with the inhibitory effect of hypophysectomy in methylcholanthrene carcinogenesis.

For this study 60 adult female rats of the Long-Evans strain were divided into four groups and treated as follows: (1) 15 rats were implanted with methylcholanthrene pellets into the right gastrocnemius muscle; (2) 15 rats were maintained without treatment as controls; (3) 15 rats were hypophysectomized; two weeks following hypophysectomy methylcholanthrene pellets were implanted into the right gastrocnemius muscle; (4) 15 rats were hypophysectomized and maintained without further treatment as controls. All animals were weighed and examined for tumors every 5 days for a maximum period of 316 days.

During the period of observation it was noted that 12 of the 15 rats treated with methylcholanthrene developed a palpable increase in connective tissue at the site of implantation as early as 3½ months and that 8 of these developed rapidly growing tumors after periods varying from 195 to 299 days following the implanting of methylcholanthrene. Prior to the completion of the experiment it was necessary to sacrifice 4 of these animals because of large tumors. Histologic examination of these tumors showed all of them to be sarcomas arising in skeletal muscle.

None of the normal controls developed comparable lesions.

Of the group of 15 hypophysectomized rats treated with methylcholanthrene, only one developed a sarcoma at the site of implantation. There was little or no connective tissue reaction to the methylcholanthrene pellet in the others. Nine of this group survived for more than 199 days, and of these there were 6 which survived for the total experimental period of 316 days.

There were no tumors in the hypophysectomized control group.

Although the numbers of animals used in these experiments are not great enough to warrant a definite conclusion at this time, nevertheless it is considered that the results are sufficiently important to deserve a preliminary note. Additional animals subjected to identical, as well as similar, conditions are now being investigated, following which studies a final report will be made.

[1] Aided by grants from the U. S. Public Health Service, GG409(C3) and C 1098, and the University of California Cancer Grant.

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Manuscript received May 5, 1952.