

under the conditions of the experiments described herein the rate of change of the chloride excretion is considerably greater than that of the water output over a practicable working range of 5-25 milli-units of U.S.P. post-pituitary extract.

11765 P

1-Proline and Tumor Incidence in Mice.

FREDERICK S. HAMMETT.

From the Research Institute of the Lankenau Hospital, Philadelphia.

It has been demonstrated that l-proline is a specific participant in some process concerned in differentiation expression of obelia.¹

It is our purpose and practice to test the repeatability or non-repeatability of the uncomplicated and unequivocal findings from lower forms on growth of spontaneous mammary tumors in female mice. Such has been done with l-proline.

Preliminary trials for toxicity level were made on some 20 test and 20 control mice by Mr. McDevitt at the Marine Experimental Station in North Truro. More secondary tumors appeared in the proline mice. These were separate new tumors. The small number of animals and the changing dosage made this observation inadequate for conclusion.

The measure of non-toxicity commonly used in these growth studies is absence of body weight loss of tests in terms of controls on prolonged administration of the amino acid.

Having established the safe dosage the regular series of trials was run in the mouse colony at Philadelphia. Here 78 mice were daily given by intrascapular subcutaneous injection 0.2 cc of an M/125 solution of l-proline in distilled water from the time of appearance of the first tumor until death. Seventy-six untreated mice served as controls. These lived, grew, produced their tumors and died contemporaneously with the others under like environmental and nutritive conditions.

Here, too, the mice given l-proline had more multiple primary tumors than the controls. All mice, both tests and controls, had primary tumors of course. A second tumor appeared in 56.4% of the proline group, and in but 44.7% of the controls. A third tumor appeared in 20.5% of the proline series and in but 13.2%

¹ Hammett, F. S., and Collings, W. D., *Growth*, 1937, 285.

of the controls; and a fourth tumor came in 9.0% of the proline mice, and in but 2.6% of the controls.

Since we are here dealing with *more* instead of *larger* tumors it is well to distinguish between tumor production and tumor growth. Tumor production depends on the change from body cell to cancer cell. Tumor growth depends to a large degree on cell proliferation. It is conceivable that more tumors are produced, not because more cells are stimulated to divide; but because more body cells or nests of body cells are stimulated to undergo specialization into cancer cells.

If the argument is logically sound, it follows that these mouse tumor results are consistent with those obtained with obelia, since both may be interpreted as indicating a stimulation of cellular specialization or differentiation by l-proline.²

No less noteworthy is the fact that l-proline—a naturally occurring tissue component of general distribution—is perhaps a significant factor in tumor production.

Conclusion. Tumor incidence in mice is enhanced by l-proline, probably through its favoring action in some process concerned in cellular differentiation.

11766

Influence of Amorphous Fraction from Adrenal Cortex on Efficiency of Muscle.

DWIGHT J. INGLE AND EDWARD C. KENDALL.

From the Division of Biochemistry, The Mayo Foundation, Rochester, Minnesota.

An extract of the adrenal cortex which is free from epinephrine and contains the physiologically active steroid derivatives characteristic of the adrenal cortex can be separated into a surprisingly large number of crystalline compounds and an amorphous fraction. The crystalline compounds A, B, E, and F, which have an atom of oxygen attached to C₁₁, have a marked effect on the efficiency of muscle¹ and on carbohydrate metabolism,^{2, 3} but relatively large

² Hammett, F. S., *The Nature of Growth*, Science Press and Printing Company, Lancaster, Pa., 1936.

¹ Ingle, D. J., *Endocrinology*, 1940, **26**, 472.

² Long, C. N. H., Katzin, B., and Fry, Edith G., *Endocrinology*, 1940, **26**, 309.

³ Ingle, D. J., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 176.