Effects of Intraperitoneally Injected Arginase on Growth of Mammary Carcinoma Implants in the Mouse. (18568)

OZRO B. WISWELL. (Introduced by Ira R. Telford)

From the Department of Anatomy, University of Texas School of Dentistry, Houston.

Arginine has been reported to influence nuclear activity of cells *in vitro*(1). There are also indications that this amino acid induces mitosis in the normal cells and stimulates such activity in tumor cells grown *in vitro*. Its enzyme however, tends to inhibit this phenomenon (2). There is also evidence that the usable amount of arginase in the animal carcass varies with the sex or that the enzymatic-activator (or deactivator of an inhibitor) is sex-linked(3). Additional effects of intraperitoneally injected arginase have been observed on Hamilton and C_3H strain mice(4). While pursuing another phase of work involving the enzyme arginase it was thought that intraperitoneal injections of arginase into *normal* Swiss mice, and those exhibiting spontaneous adenocarcinomas would be of some interest. Injecting various amounts of enzyme we observed reductions, ranging from 30 to 90%, in the size of existing tumors. A few tumor mice received injections directly into the tumor mass with similar results. Histological examinations of the effected tumors in both direct tumor and intraperitoneal injections showed cytoplasmic and nuclear changes occurring in the tumor cells with increased fibrosis throughout the mass. In many instances the connective tissue response of the tumor resulted with almost entire disappearance of the neoplastic cells.

A preliminary experiment using C_3H strain mice implanted with locally available mammary carcinomas was set up to study the effect of arginase on induced tumors. These implants were made by a trochar in the flank of 30 (mixed) C_3H strain mice. After 11 days the tumors were established and the animals were separated at random into 3 groups of 10 each. Group "A" was designated as control. Group "B" received daily intraperitoneal injections of 1 cc of 0.16 M arginine monohydrochloride in 0.1 M phosphate buffer at pH 7.5. Group "C" received daily intraperitoneal injections of arginase. This solution was obtained by extraction of beef liver and activated with cobalt acetate (1.25 mg Co^{++} per cc) for 3 hours at 40°C. Each injection was 1 cc and contained 60 arginase units(5). Every animal in each group was weighed daily and its tumor measured with calipers. The experiment was terminated at the end of the tenth treatment day. At this time all mice of groups "A" and "B" had died of the tumor, while all animals receiving the arginase (Group "C") were still alive. This was 21 days after successful tumor implantation.

TABLE I.

Group	"A" (Control)	"B" (Arginine IP)	"C" (Arginase IP)
Body wt 11th day after implant	29.5	32.6	31.4
Body wt at necropsy	35.0*	34.8*	34.8
Tumor length 11th day after implant	15.2	21.7	18.8
Tumor length at necropsy	37.1*	38.8*	26.7
Tumor wt at necropsy	6.4*	6.2*	6.1
% growth compared to group "A"	100	104.5	72.0
Ratio tumor length/wt expressed in %	100	107.9	74.1

* Animals died at various intervals after 11th day of implant. Length (L) expressed in mm. Wt (W) expressed in g. Growth refers to length increase in mm. IP—intraper.

Table I presents the average tumor growth from day of implant, per cent growth as compared to group "A", and ratio of tumor

1. Irons, W. G., *Dental Research,* 1946, v25, 180.

2. Bach, S. J., and Lasnitzki, J., *Enzymologia,* 1947, v12, 198, 205.

3. Wiswell, O. B., *Science,* 1950, v112, 117.

4. Irons, W. G., and Wiswell, O. B., *Science,* 1947, v106, 393.

5. Mohamed, M. S., and Greenberg, D. M., *Arch. Biochem.,* 1945, v8, 349.

length to weight in percent of each group over the 10 day treatment period. A liver factor other than arginase might possibly have been responsible for this growth phenomena; however, it is known that the procedure for arginase extraction and purification from beef liver produces a substance of relative high purity(5). Therefore it was assumed that the active factor could have been arginase.

Summary of results. 1. Animals receiving arginase treatment did not die of their implanted tumors during the 21-day period. The controls (Group "A") and those receiving arginine (Group "B") died within this period. 2. Those animals receiving arginine indicate a tumor length weight ratio increase of 7.9% over group "A". 3. The group receiving arginase (Group "C") exhibited a 28% decrease in size as compared to the controls in group "A". 4. The ratio of tumor length to weight was 26% lower in the group receiving arginase. 5. Tumor specific volume (tumor length to weight) is offered as an accurate tumor measurement method.

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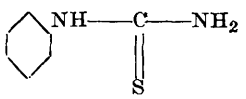
Ability of Infants to Taste PTC: Its Application in Cases of Doubtful Paternity. (18569)

HUGO M. CARDULLO AND L. EMMETT HOLT, JR.

From the Department of Pediatrics, New York University College of Medicine and the Children's Medical Service, Bellevue Hospital, New York.

In 1930 while working with phenyl thio carbamide (PTC), Fox(1) observed that the compound was tasteless to some individuals but extremely bitter, even to the point of nausea, for others. Approximately 40% of the subjects tested were "taste blind" to this material. He investigated a number of chemically similar substances and concluded that the characteristic taste of PTC and related compounds was due to the C = S linkage, *viz.*:



He postulated that this difference must be an inherent property of the individual's saliva, a concept recently proved by Cohen and Oydon(2). The observations of Fox were promptly confirmed and extended by others. Snyder(3) studied 440 individuals from 100 families and observed an incidence of 68.5% tasters (T) and 31.5% non-tasters (t), and Blakeslee(4-6) investigating 103 families, encountered 66.5% tasters and 33.5% non-tasters. The ability to taste PTC appeared to follow Mendelian laws, tasting being an inherited as a dominant characteristic and non-tasting as a recessive. Thus, the union of two tasters invariably produced tasters and the union of non-tasters produced all non-tasters. The union of a taster and a non-taster may produce both tasters and non-tasters, but if the offspring is a taster, at least one parent must be a taster.

It occurred to us that the ability to taste PTC might profitably be applied in cases of doubtful paternity. Before doing so, however, it would be necessary to establish: (1) that the ability to taste PTC was differentiated at an early age and (2) that it could be satisfactorily determined by an objective test. The observations of Fisher, Ford and Huxley(7) on chimpanzees indi-

1. Fox, A. L., *Proc. Nat. Acad. Sci.*, 1932, v18, 115.
2. Cohen, J.. and Oydon, D. P., *Science*, 1949, v110, 532.
3. Snyder, L. H., *Science*, 1931, v74, 151.
4. Blakeslee, A. F., *Proc. Nat. Acad. Sci.*, 1932, v18, 120.
5. Salmon, T. N., and Blakeslee, A. F., *Ibid.*, 1935, v21, 78.
6. Blakeslee, A. F., and Salmon, T. N., *Ibid.*, 1935, v21, 84.