CP*a* and CP*b* may be, respectively, the pro-carboxypeptidase and carboxypeptidase of Anson(9). To test this, a portion of kidney supernatant was treated with trypsin according to Anson's method for assay of the enzyme and zymogen. The treated and untreated portions were then assayed for CP*a* and CP*b*. The only effect of the trypsin treatment was an overall diminution in both enzymes; the ratio of the two was unaffected. It is thus apparent that CP*a* is not a trypsin-activatable precursor of CP*b* and so is not identical with Anson's pro-carboxypeptidase.

Preliminary experiments indicate that if a kidney homogenate is permitted to stand at room temperature for several days under a layer of toluene, the amount of CP*b* increases at the expense of CP*a*, which decreases to an approximately equivalent degree. This interconversion is apparently enzymatic in nature and occurs only at certain pHs, of which 8.5 appears to be optimum. The reverse reaction has not been detected.

Summary. Evidence is presented that the enzyme carboxypeptidase is more widely distributed throughout mammalian tissues than is commonly realized. The reasons for previous failure to detect the enzyme are: a) the existence of a natural cellular inhibitor, the effect of which is to mask the enzymatic activity, and b) the fact that two carboxypeptidases probably co-exist in many tissues; the pH optima of these two are different, and one is activated, the other inhibited, by cysteine. The natural cellular inhibitor affects only one of the carboxypeptidases, and does so in a non-competitive fashion.

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Development of Sarcomas in Marsh-Albino Mice Following Injection of Desoxycorticosterone Acetate in Sesame Oil.* (20250)

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While investigating strain differences in mice, an incidental observation was made in the Marsh strain, namely the development of tumors following prolonged injections of a mineral corticoid, desoxycorticosterone acetate (DCA; Organon's Doca Acetate) in sesame oil. This development has interest in view of the numerous reports that the administration of DCA in various forms has no tumorigenic effect [Kuhlman *et al.*(1), Carnes *et al.*(2), Ludden *et al.*(3), Shimkin and Grady(4), Shimkin and White(5), Burrill and Greene(6), Forbes(7), Rakoff *et al.*(8), Rodard and Freed(9), Gineste *et al.*(10), Sarason(11), Selye and Hall(12), Selye *et al.*(13), Bruzzone *et al.*(14), Segaloff(15), and Lipschutz(16)]. Shimkin and Wyman(17), however, implanted DCA pellets in C3H mice, and mammary tumors developed. These authors considered the results to be insignificant in view of the small number of animals involved; furthermore, the C3H strain is known to produce spontaneous mammary adenocarcinomas at an early age. Woolley

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TABLE I. Summary of Experimental Procedure on Marsh-Albino Mice. 12 animals in each series.

Sex	Treatment	Duration of treatment, mo	Animals surviving 3 mo after termination of treatment		Incidence of tumor development 6 mo after termination of treatment	
			No.	%	No.	%
♀	None	—	12	100	0	0
♀	Doca acetate, .2 mg	3	11*	91	10†	91
♂	None	—	12	100	0	0
♂	Doca acetate, .2 mg	3	9*	75	9	100

* Four died during treatment; cause of death unknown.
† One killed 3 mo after termination of treatment; no tumor evident.

and Chute(18) concluded that DCA, provided in pellet form, does not restrict the development of adrenal tumors. The work of Houssay *et al.*(19) indicates that DCA restricts adrenal carcinoma development.

Procedure. Six-week-old female and male Marsh-albino mice, weighing 20-25 g, were used. All animals were fed Purina Laboratory Chow and water *ad lib.* DCA in sesame oil (0.2 mg/0.1 cc) was given subcutaneously daily except Saturdays and Sundays for 3 months. The injections were made alternately into the left and right flanks. After the 3-month period of injections, the animals were examined periodically. At death the animals were autopsied; the tissues, fixed in formalin and stained with Hematoxylin and Eosin, were then studied histologically.

Results. The results of this experiment are shown in Table I. Of the 24 mice injected, 4 died within 3 weeks of the initiation of the experiment. Toward the end of the period of inoculation and for several weeks thereafter, all the mice showed fairly large subcutaneous swellings on the dorsal and lateral surfaces; these fluctuated on palpation. The swelling in one animal sacrificed during this period was found to be an oil-filled cyst the wall of which, upon microscopic examination, was found to be devoid of tumor. The remaining mice were kept under observation for several months.

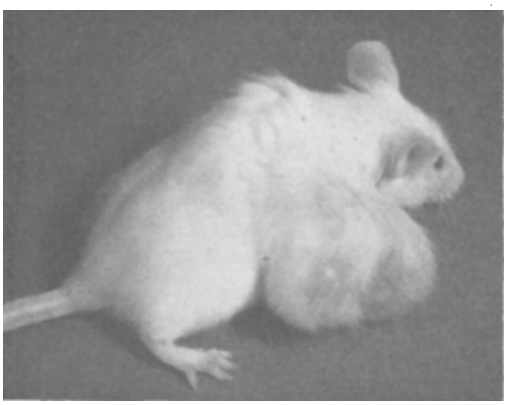

FIG. 1. Tumor masses evident on dorsal and lateral regions of a Marsh mouse. The dorsal mass was diagnosed as a fibrosarcoma and the lateral mass as a myosarcoma.

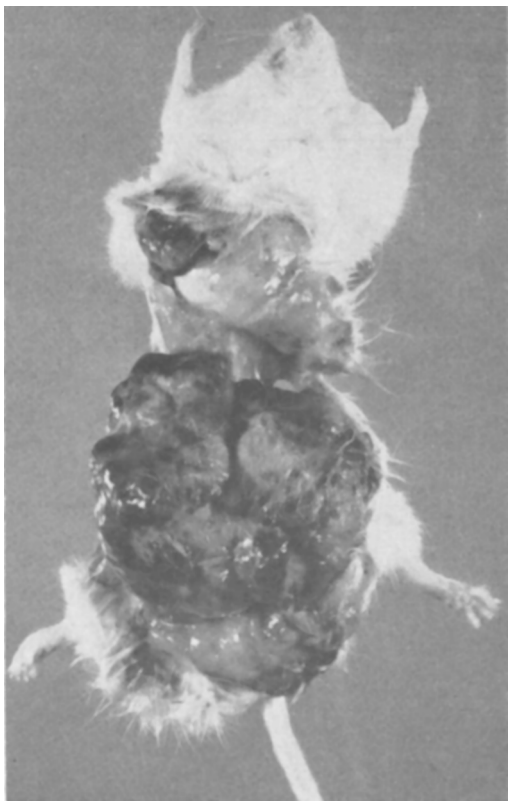

FIG. 2. Tumor mass evident on the dorsal region of a Marsh mouse. This tumor mass comprised 48% of total body wt of the animal.

TABLE II. Transplantation of DCA-Induced Sarcomas in Marsh-Albino Mice.

Tumor No.	Tumor	No. of transplantations ♂	♀	No. of takes* (F_1 generation)	% takes (F_1 generation)
1	Fibrosarcoma	15	4	19	100
2	"	10		10	100
3	"	5	5	10	100
4	Myosarcoma	5	15	20	100
5	"	10		8	80
6	Fibrosarcoma	10	10	20	100
7	"	12	8	20	100
8	Myosarcoma	4	4	8	100
9	Fibrosarcoma	9	1	10	100

* Showing progressively enlarging tumors.

During this period the oil cyst persisted, becoming smaller but gradually harder, until they presented a hard, firm mass with no evidence of a liquid content on palpation. Approximately 6 months after the cessation of inoculations (9 months after the initiation of the experiment), all of the mice showed large, firm masses as shown in Fig. 1 and Fig. 2. In some cases the induced tumor comprised as much as 50% of the total body weight of the animal.

Nine of the mice having the largest masses were sacrificed and, upon autopsy, showed well-circumscribed subcutaneous firm masses which were adherent to the overlying skin. The masses, when cut, were pearl gray in color; in some, small oil pockets were found in the center. These masses were examined microscopically. All were diagnosed as malignant tumors: 3 as myosarcoma and 6 as fibrosarcoma. In many instances the cells of these tumors were arranged in interlacing bundles, while other tumors or other regions of the same tumor contained cells that were round or irregular in shape. Mitoses and giant multinucleated cells were evident throughout most of the tumors. In some, the blood channels were prominent and indicative of a hemangiomatous structure. The tumors were encapsulated, and there was no evidence of metastasis in the lungs, heart, liver, spleen, kidneys, adrenals, reproductive organs, etc.; however, the liver and kidney in some animals showed definite evidence of hypertrophy. The ovaries showed evidence of stimulation.

Fragments of the tumors from 9 animals were transplanted into mice of the same strain. To date, all of the transplants except two are growing. (Table II).

The remaining 10 mice all have firm tumors up to 4 cm in diameter. They are being watched for signs of metastasis.

Because of the original intent of this experiment, there were no control animals which received inoculations of sesame oil only. However, in other experiments, mice of the Marsh strain have received sesame-oil injections for a shorter period of time without showing any evidence of tumor formation.

Summary. Twenty-four mice of the Marsh-Albino strain were injected daily for a period of 3 months with desoxycorticosterone acetate (0.2 mg/0.1 cc) in sesame oil. Of these, 1 was killed 3 months after termination of treatment but showed no evidence of tumor, while 9 others, killed 6 months after termination of treatments had subcutaneous tumors of two histological types, fibrosarcoma and myosarcoma. The remaining 10 mice are still alive; all show gross evidence of tumor formation, which became evident 6 months after completion of treatment.

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Effect of Orally Administered Penicillin-Resistant Microorganisms on Growth of Chicks.*† (20251)

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The exact mechanism of antibiotic stimulation of chick growth is still not clearly understood. Most theories concerning this mechanism explain it through changes in the intestinal microflora. These have been reviewed by Briggs(1). In experiments by Romoser *et al.*(2), definite changes occurred in the number and types of bacteria found in the ceca of four-week-old chicks following the oral administration of procaine penicillin G. The numbers of *Escherichia coli* and *Aerobacter aerogenes* present in the ceca were increased when penicillin G was fed at a level of 150 ppm of the diet. The growth rate was also improved. The addition of 5-15% lactose, in combination with the antibiotic, further increased chick growth and the numbers of these organisms. Anderson *et al.*(3) observed an increase in the coliform bacteria as a result of feeding penicillin to chicks. Similar increases, though less marked, were also secured by March and Biely(4) who used aureomycin. These workers also noted a marked decrease in the lactobacilli. Preliminary reports indicate that oral administration of *A. aerogenes*(5) or *E. coli*(6) increase the growth rate of chicks fed diets containing penicillin. From this it would appear that the growth-promoting action of antibiotics may result from: 1) the elimination of fastidious organisms which compete with the host for essential known or unidentified nutrients and/or, 2) the stimulation of other organisms which affect the host beneficially through the *in vivo* synthesis of one or more growth factors.

In this study the intestinal microflora was modified by feeding viable penicillin-resistant organisms to chicks, in order to investigate further the effect on chick growth.

Materials and methods. In all experiments, 15-20 day-old New Hampshire chicks of both sexes were used per experimental group. In Exp. 1, the chicks used were the progeny of dams housed on raised wire floors and fed a ration which was complete in all known nutrients but contained no animal protein supplements. Based on other studies, these chicks were considered to have a suboptimal "carry-over" of unidentified chick growth factors. In

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