anterior lobe of the pituitary of immature and adult guinea pigs and rabbits. 2. Inconsistent results were obtained with ovary. Adrenal tissue and capsule invariably underwent degeneration. 3. Evidences of growth (areas of proliferation and mitotic figures) were observed only in the case of the pituitary. 4. It is concluded that the conditions under which one endocrine organ may be successfully maintained *in vitro* are not necessarily the same as those required by another.

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Failure of Histaminase to Prevent Anaphylactic or Histamine Shock in Guinea Pigs.

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The increasing interest in the hypothesis that anaphylactic shock and allergy depend on the liberation of histamine has directed attention to the possibility of destroying this physiologically active substance *in vivo*. Best and McHenry[1] in discussing the enzyme, histaminase, suggest as its possible rôle the inactivation of histamine *in vivo*. In a more recent note, these authors[2] object to the misinterpretation of this suggestion and deny that available preparations of histaminase are, in their experience, effective *in vivo*.

Karady and Browne[3] were able to protect guinea pigs from the intraperitoneal injection of histamine by earlier intraperitoneal injection of histaminase. They were also able to protect sensitized guinea pigs from anaphylactic shock by treating the animals with histaminase prior to giving the shocking dose of antigen. These injections were given intraperitoneally.

The purpose of this report is to present experiments dealing with the *in vivo* action of a commercial preparation of histaminase* on anaphylactic and histamine shock in guinea pigs.

Methods. Guinea pigs averaging 350 g were sensitized by in-

1 Best, C. H., and McHenry, E. W., *J. Physiol.*, 1930, **70**, 349.

2 Best, C. H., and McHenry, E. W., *J. A. M. A.*, 1940, **115**, 235.

3 Karady, S., and Browne, J. S. L., *J. Imm.*, 1939, **37**, 463.

* The histaminase used was a preparation of the Winthrop Chemical Company (Torantil-T360), obtained through the courtesy of the Department of Medical Research of that company.

jecting 1.0 ml of 10% egg white intraperitoneally. At the time of giving the shocking dose of antigen, 3 weeks later, the guinea pigs were anesthetized by an intraperitoneal injection of nembutal. The trachea was exposed and a glass T-tube inserted. One outlet of this tube was partially closed by means of rubber tubing and a screw clamp, and the other connected to the tambour of a kymograph which recorded breathing continuously until bronchospasm occurred. This method is a modification of that of Auer and Lewis[4] used in studying anaphylaxis. A record of breathing during anaphylactic shock is an important aid in differentiating anaphylactic death from that due to emboli or hemorrhage. The sudden spasm of the bronchi with resulting arrest of breathing despite respiratory effort is a very striking and characteristic feature of anaphylactic or histamine shock in guinea pigs. Air does not pass in or out of the respiratory tract of shocked guinea pigs even when pressure is applied to the chest wall.

Histaminase was injected intracardially into some of the animals 15 minutes or 24 hours before testing their reaction to the sensitizing antigen. The guinea pigs, their breathing having been recorded, were then injected with 0.5 ml of 10% egg white intracardially. Also the effect of the administration of histaminase on the subsequent injection of histamine hydrochloride dissolved in 0.85% NaCl

TABLE I.
Effect of Administration of Histaminase on Production of Anaphylactic Shock in Guinea Pigs.*

Units† histaminase administered	Time between administration of histaminase and shocking dose of egg white	Amt of 10% egg white sol. inj. intracardially as shocking dose, ml	Time in sec. before bronchospasm after inj. of egg white
5	15 min.	1.0	17
5	15 "	0.5	27
8	15 "	0.5	65‡
10	15 "	0.5	25
12	15 "	0.5	20
6	24 hr	0.5	23
6	24 "	0.5	21
10	24 "	0.5	22
10	24 "	0.5	20
0		0.5	25
0		0.5	21

*The guinea pigs were sensitized 3 weeks previously by the administration of 1.0 ml of 10% egg white intraperitoneally.

†One unit of histaminase was defined by the manufacturer as the amount required to neutralize 1.0 mg histamine hydrochloride *in vitro*.

‡Questionable intracardial injection.

[4] Auer, J., and Lewis, P. A., *J. Exp. Med.*, 1910, **12**, 151.

was tested in normal animals. Varying amounts of the histamine salt were injected intracardially. The smallest amount which consistently killed the animals was 0.2 mg. By making all injections directly into the blood stream, the uncertainty of varying absorption rate from the peritoneal cavity or subcutaneous tissue was eliminated. On the other hand, the rapidity of onset of shock, either anaphylactic or more particularly histamine shock, requires a rapid action of histaminase if it is to be effective.

Results. The data in Table I indicate that histaminase injected 15 minutes or 24 hours prior to giving the shocking dose of egg white did not prevent or alter the response of the sensitized animals. When normal guinea pigs were treated with varying amounts of histaminase at different time intervals before they were injected intracardially with histamine hydrochloride, it was found (Table II) that the histamine shock was unaltered by the previous treatment with large doses of the enzyme preparation. Fig. 1 illustrates the type of record of breathing obtained with guinea pigs during anaphylactic or histamine shock. During bronchospasm, indicated by the straight line portion of the record, the animals made sporadic respiratory efforts. During such efforts occasional, or no evidence of breathing is noted, depending on the severity of the shock. There was no observed alteration in the breathing pattern as a result of previous treatment with histaminase in sensitized animals injected with egg white or in normal animals injected with histamine. The *in vitro* activity of the histaminase preparation employed was verified after the completion of the experiments reported.

TABLE II.
Effect of Administration of Histaminase on Production of Histamine Shock in Guinea Pigs.

Units* of histaminase administered	Time between administration of histaminase and histamine	Amt of histamine inj. intracardially, mg	Time in sec. before bronchospasm after histamine inj.
5	2 min.	1.0	2
5	2 "	0.1	2
2	12 "	0.1	3
5	18 "	0.2	3
5	22 "	0.4	4
12	15 "	0.4	4
6	1 hr	0.4	3
6	3 "	0.4	3
6	24 "	0.4	3
6	24 "	0.4	3
0		0.4	3

*See Table I.

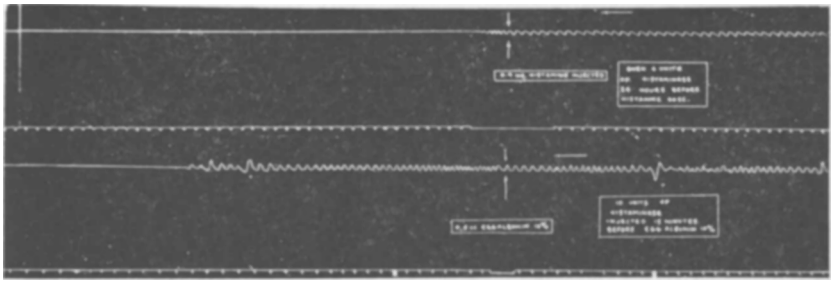

FIG. 1.

Conclusion. No evidence was obtained of *in vivo* activity of histaminase in preventing anaphylactic or histamine shock. There is still a possibility, however, that histaminase might act *in vivo* if the release of histamine into the body were slow and small in amount, thus allowing more time for the enzyme to act.

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Treatment of Experimental Hydrofluoric Acid Corrosion.

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In the experiments here presented hydrofluoric acid corrosions in rats were infiltrated hypodermically with a 3% solution of calcium gluconate in distilled water.

Adult rats were treated on the lateral aspect of the front paws just below the shoulder or on the lateral aspect of the thigh. The method was to clip but not shave the skin and to apply a drop of 40% hydrofluoric acid on the tip of a wax applicator to a spot of skin 7 mm in diameter. After a variable time interval, 0.5 cc of the calcium gluconate solution was injected subcutaneously under the lesion (or intramuscularly if the skin had sloughed off) in some animals, while in some the lesion was left untreated to serve as controls.

All the lesions, both treated and untreated, eventually healed, but there was a marked difference in healing time between the two groups. The criterion of healing was the complete disappearance

* Crile Scholar, Summer, 1939.