



FIG. 8.

Appearance of the liver in a mouse injected subcutaneously twice with .05 cc of necrosin. The mouse succumbed 4 days following the second injection. Note the severe degree of injury to the liver in the form of marked vacuolation within the hepatic cells. $\times 560$.

were C H and dba mice.[§] Repeated subcutaneous injections of necrosin were³ likewise followed by some degree of tumor necrosis with concomitant necrotizing effect on some of the lung metastasis. In these animals, however, many more injections of this toxic material were necessary, and the effect was generally not as pronounced as on the Swiss strain of mice. The extensive initial vascularity of the tumor has probably something to do with the ultimate effect of necrosin administration. Finally, in view of Shear's⁹ recent work on bacterial polysaccharides necrosin was tested for the Molisch reaction, and it was found on a sample utilized to be negative. Culturing necrosin for bacteria in broth yielded negative results within eleven hours,

⁹ Shear, M. J., *J. National Cancer Inst.*, 1944, **4**, 461.

and negative growth on agar slants within 24 hours. The necrosin samples employed ranged from fresh material (only several hours old) to material prepared over 2 years previously and preserved in a refrigerator. The effects obtained were identical. Finally, the subcutaneous injections of 0.2 cc of a slightly acid exudate (pH 6.9 to 7.0), in which presumably necrosin was present, induced hemorrhagic necrosis in the tumor and in some of the metastatic foci of Swiss mice.^{||}

Conclusions. Necrosin is a substance associated with the euglobulin fraction of usually acid inflammatory exudates. Its liberation by injured cells offers a reasonable explanation for the basic pattern of injury in inflammation.

The subcutaneous injections of canine necrosin, at a distance from the site of spontaneous tumors, in a strain of Swiss mice produce, after varying intervals, hemorrhagic or other types of necrosis in the tumor substance.

A necrotizing effect is also seen to occur in some of the metastatic lesions encountered in the lung.

Necrosin injections in these mice induce severe injury to the liver.

None of the effects on the tumor or on its metastasis are usually encountered with the use of the euglobulin fraction of canine blood serum, the leukocytosis-promoting fraction of canine exudates, or with one of the proteolytic enzymes adequately studied, namely papain.

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Effect of Adrenocorticotrophic Hormone on Anaphylaxis in the Guinea Pig.

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Adrenal cortical hormones are known to cause dissolution of lymphoid tissue,^{1,2} and it

has recently been shown that in sensitized animals, the rate of lymphocyte disintegration is paralleled by an increase of circulating antibodies.³⁻⁶ This phenomenon may be elici-

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¹ Dougherty, T. F., and White, A., *Proc. Soc. Exp. Biol. and Med.*, 1943, **53**, 132.

² Selye, H., *J. Clin. Endocrinol.*, 1946, **6**, 117.

TABLE I.
Influence of A.C.T.H. on Anaphylactic Shock.

Animals	Sensitizing dose, cc	Incubation period, days	Control group.		Symptoms	% shock
			Shocking dose, cc	A.C.T.H. mg		
1	.25	12	0.5		Severe	
2	.25	12	0.5		Fatal	
3	.25	12	1.0		"	
4	.25	12	1.0		"	
5	.25	12	1.0		"	12 died
6	.25	12	1.0		"	
7	.25	12	1.0		"	
8	.25	17	0.5		"	
9	.25	17	0.5		Mild	100% shock
10	.25	17	0.5		Fatal	
11	.25	17	0.5		Severe	
12	.25	17	0.5		Fatal	
13	.25	17	0.5		Severe	
14	.25	17	0.5		Fatal	
15	.25	17	0.5		Mild	
16	.25	17	0.5		Fatal	
17	.25	17	0.5		"	
Experimental group.						
1	.25	13	1.0	4	Fatal	
2	.25	13	0.5	4	"	
3	.25	13	1.0	4	Severe	
4	.25	13	1.0	4	Fatal	
5	.25	13	1.0	4	"	12 died
6	.25	13	1.0	4	Mild	
7	.25	13	1.0	4	Fatal	
8	.25	13	0.5	3.5	"	
9	.25	17	0.5	3.5	Severe	100% shock
10	.25	17	0.5	3.5	Fatal	
11	.25	17	0.5	3.5	Mild	
12	.25	17	0.5	3.5	Fatal	
13	.25	17	0.5	3.5	Severe	
14	.25	17	0.5	3.5	Mild	
15	.25	17	0.5	3.5	Fatal	
16	.25	17	0.5	3.5	"	
17	.25	17	0.5	3.5	"	
18	.25	17	0.5	3.5	"	

Mild shock denotes symptoms of dyspnea, sneezing, diarrhea and restlessness.

Severe shock denotes symptoms of dyspnea going on to convulsions and unconsciousness.

Fatal refers to death.

ted by administration of adrenal cortical hormones, or by stimulation of the adrenal cortex by means of A.C.T.H. (adrenocorticotrophic hormone). The following investigation was carried out in order to study the effect of A.C.T.H. on anaphylactic shock in the guinea pig.

Methods. Thirty-five male and female

³ Dougherty, T. F., Chase, J. H., and White, A., *Proc. Soc. Exp. Biol. and Med.*, 1944, **57**, 295.

⁴ Dougherty, F. F., White, A., and Chase, J. H., *Proc. Soc. Exp. Biol. and Med.*, 1944, **56**, 28.

⁵ Dougherty, T. F., Chase, J. H., and White, A., *Proc. Soc. Exp. Biol. and Med.*, 1945, **58**, 135.

⁶ Dougherty, T. F., and White, A., *J. Lab. and Clin. Med.*, 1947, **32**, 584.

guinea pigs weighing between 200 - 400 g were injected intraperitoneally with 0.25 cc of undiluted horse serum. These animals were submitted to a re-injection of $\frac{1}{2}$ to 1 cc of the same antigen after an incubation period varying between 12 to 17 days. The readministration was performed via the jugular vein, which had been exposed by dissection in the unanaesthetized animal. The animals were divided into two groups, Group I comprising 17 control guinea pigs, and Group II comprising the remaining 18 animals. The animals of Group II were given $3\frac{1}{2}$ to 4 mg of A.C.T.H. (s.c.) 6 to 8 hours prior to the shocking dose of the antigen. Since Dougherty and his colleagues used 1

mg A.C.T.H. for mice, 60 to 80 days of age and 10 mg of A.C.T.H. for 4-month-old rabbits, it was considered that weight for weight $3\frac{1}{2}$ to 4 mg of A.C.T.H. would be a suitable dose for the guinea pigs used. The animals were carefully observed for the appearance of anaphylactic shock which was graded as follows: mild shock, severe shock, and death.

Results. The results of this experiment are summarized in Table I. The animals in both groups showed a similar response to the shocking dose of the antigen. Group I, the control group, all showed varying degrees of shock, which was fatal in 12 of 17 animals, with 3 showing severe shock and 2 showing symptoms of mild shock. Group II, the experimental group, also showed 100% reactivity, there being 12 instances of fatal shock, 3 cases of severe shock, and mild shock in 3

animals. The time of death occurred at approximately the same time interval following the shocking dose in both groups of animals. Therefore, one may conclude that A.C.T.H. in the dose administered, and under these experimental conditions, does not seem to have any effect on anaphylactic shock as elicited in guinea pigs by the procedure outlined above.

Summary. The administration of adrenocorticotrophic extract to sensitized guinea pigs prior to injection of a shock dose of antigen failed to influence the course of anaphylactic shock in a group of 18 animals.

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In vitro Studies of Aureomycin, a New Antibiotic Agent.*

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Samples of a new antibiotic, designated as A377 and later named aureomycin, were received from the Lederle Laboratories Division of the American Cyanamid Company, in November 1947. Since preliminary trials showed that the product had considerable activity *in vitro* against both a gram negative bacillus and a gram positive coccus, it was decided to test it further.

Description. According to information received from the Lederle Laboratories, aureomycin is derived from a strain of *Streptomyces aureofaciens*. The partially purified hydrochloride which was sent us is a bright yellow, fluffy, crystalline material. A 10%

solution can be prepared in distilled water but the solubility is lowered by the presence of sodium chloride. The pH of a 0.1% aqueous solution is approximately 4. Dilute broth solutions pass through Berkefeld N and Seitz filters with but little loss of activity.

Range of Action. The least amount of aureomycin which prevents visible growth for 24 hours was determined for a variety of gram positive and gram negative bacteria. Polymyxin¹ and penicillin were used as standards of comparison in parallel tests. Serial 2-fold dilutions of the drugs in Difco Heart Infusion Broth, with 0.075% dextrose added, were inoculated with equal volumes of 18 hour old cultures so diluted as to result in approximately 200,000 organisms per cc. The diluent for the gram negative bacilli was

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¹ Stansly, P. G., Shepherd, R. G., and White, H. J., *Bull. Johns Hopkins Hosp.*, 1947, **81**, 43.