titative relationship existing between histamine concentration and skin wheal size suggests the possibility of using histamine as a standard reference material in comparing various skin irritants.

Summary. There is a species variation in the local reaction to intradermal injections of histamine. The dog, goat, and man show a marked skin whealing, but no such response is obtainable in the guinea pig, rabbit, or cat.

The diameter of the skin wheal produced by intradermal injection is a function of the concentration of histamine used, the threshold being 0.001%. In the presence of an extraneous histamine-like substance, this relationship still exists, but the threshold of histamine sensitivity is elevated to 0.01%.

A practical application to the field of experimental dermatology is suggested involving the proper selection of test animals and the use of histamine as a standardizing agent.

15057

Ulcer Production in Intestines of Dogs by Various Enzymes Under Hydrostatic Pressure.

ROBERT L. DRIVER. (Introduced by Emmett B. Carmichael.)

From the Department of Physiological Chemistry, School of Medicine, University of Alabama, University, Alabama.

In a previous paper from this laboratory the effect of hydrostatic pressure on the production of ulcers was described.[1] In another paper it was reported that ulcers could be produced in the intestines of dogs by an alkaline solution of pancreatin under a hydrostatic pressure of 90 cm H_2O.[2]

The purpose of the experiments reported here was to study the effect produced on the intestines by the following enzymes: rennin, trypsin, erepsin, steapsin, and amylopsin. The enzyme solutions were at pH ranges corresponding to those under which the enzymes act in the normal animal.

The procedure was the same as that described in [1] except that in these experiments only one pressure (90 cm H_2O) was used. The severity of damage to the loops was graded according to a scheme adopted in this laboratory which is described here: (1) represents a condition in which there is a slight surface necrosis of the mucosa; (2) designates a deeper necrosis involving at least $\frac{1}{3}$ of the thickness of the mucosa of the entire area with smaller areas (from $\frac{1}{2}$ cm^2 to 2 cm^2) showing necrosis as deep as the submucosa; (3) indicates necrosis of practically all the mucosa with some patches extending into the circular muscle; (4) was applied to a loop having areas of necrosis extending to the serous coat or to a frank perforation. Each loop was scored in this manner and the average taken for each group of experiments. The results are given in Table I.

Discussion. Rennin (0.1%) in N/10 HCl produced perforating ulcers in 114 minutes while N/10 HCl alone caused perforation in 174 minutes and pepsin (0.1%) in N/10 HCl in 82 minutes.[2] These data show that rennin has a marked digestive effect on the mucosa of the intestine but not so great an effect as pepsin.

Of the other enzymes studied only the proteolytic ones were active. The necrosis produced by trypsin was about twice as severe as that caused by erepsin, but not even trypsin digested the mucosa to an extent comparable to that of rennin and pepsin, and was only about one-half as effective as pancreatin.[2]

Neither steapsin nor amylopsin caused any necrosis of the mucosa, alkaline solutions of these enzymes behaving like controls where the loops of intestine were exposed to the

[1] Driver, R. L., Chappell, R. H., and Carmichael, E. B., *Am. J. Dig. Dis.*, 1945, **12**, 168.

[2] Driver, R. L., *Arch. Path.*, in press.

TABLE I.
Ulcer Formation in Intestines by Enzyme Solutions under 90 cm H_2O Pressure.

Dog No.	0.1% solution of	pH	Time exposed (min.)	Remarks	Severity
1-12	rennin* in N/10 HCl	1.2	60-180	perforated ulcer in all dogs	4.0 in all dogs
13	trypsin† in N/10 $NaHCO_3$	8.1	580	necrosis through ½ thickness of mucosa entire area	2.0
14	" " " "	"	698	necrosis through ⅓ thickness of mucosa over entire area, 10 small spots into submucosa	2.0
15-17	" " " "	"	326-384	normal mucosa	0
18	" " " "	"	696	necrosis through ⅓ thickness of mucosa entire area, 5 small spots into submucosa	2.0
19	" " " "	"	694	surface necrosis over ¾ area of loop	1.0
20-21	" " " "	"	690-692	normal mucosa	0
22	erepsin† in N/10 $NaHCO_3$	"	640	surface necrosis	1.0
23-24	" " " "	"	636-638	normal mucosa	0
25	" " " "	"	634	necrosis entire mucosa, some patches into muscle	3.0
26-30	" " " "	"	284-632	normal mucosa	0
31-41	steapsin† in N/10 $NaHCO_3$	"	458-810	" "	0
42-53	Amylopsin† in N/10 $NaHCO_3$	"	290-745	" "	0
54-65	N/10 HCl	1.0	91-320	perforated ulcer in all dogs	4.0 in all dogs

* Armour, Rennet, N.F.
† Pfanstiehl.

alkaline solution alone.

Summary. 1. The proteolytic enzymes, rennin, trypsin, and erepsin, under hydrostatic pressure of 90 cm H_2O produced necrosis of the intestines of dogs, rennin being the most active of the three. 2. The average time required to produce a perforation with N/10 HCl alone was about 50% more than with rennin in N/10 HCl. 3. Neither steapsin nor amylopsin caused necrosis under the above condition.

15058

Effect of Infused Penicillin in the Bovine Mammary Gland.*

F. J. WEIRETHER, D. E. JASPER, AND W. E. PETERSEN.
From the Divisions of Veterinary Medicine and Dairy Husbandry, University of Minnesota.

Reports[1-3] have been published dealing with the therapy of bovine mastitis by infusion of penicillin but none has been found that deals with the physiologic behavior of this antibiotic when introduced into the mammary gland. This report deals primarily with studies on the rate of decline and irritating effects of infused penicillin. A knowledge of both of these aspects is essential to a rational approach to the use of the drug in therapy.

For the majority of experiments the sodium salt of penicillin was made up with sterile distilled water so that 1 ml of solution contained 5,000 Oxford Units. Immediately after

* Paper No. 2240, scientific journal series, Minnesota Agricultural Experiment Station. The work reported in this paper was made possible by a special legislative grant for the study of mastitis.

1 Kakavas, J. C., *North Am. Vet.*, 1944, **25**, 408.

2 Klein, L. A., Crissman, D. W., and Moor, J. W., *Am. J. Vet. Research*, 1945, **6**, 3.

3 Bryan, C. S., Horwood, R. E., and Huffman, C. F., *Vet. Med.*, 1945, **40**, 87.