

daily. 3. Keep screen raised so that roots clear the bottom of the pan.

7th day after planting: Cut and feed the green portion of the plants. In order to insure a uniform supply of fresh grass, only the first cutting is used. Seeds are planted at intervals to correspond to the days on which the grass is to be fed.

Kohler, Elvehjem and Hart³ reported one experiment in which 5 g of greenhouse-grown oat grass per guinea pig per day did not furnish appreciable amounts of the grass juice factor. However, we have found that grass grown as described above and fed *ad libitum* in addition to the basal diet of Kohler and associates⁴ completely protected guinea pigs against a deficiency of this dietary essential. Details of these experiments will be reported at a later time.

Although we were particularly interested in having a regular supply of the grass juice factor, grass for various purposes may be grown by this method.

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Effect of Rammstedt Operation on Incidence of Cinchophen Ulcer.

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This study of the effect of the Rammstedt operation on the incidence of gastro-duodenal ulcer caused by the administration of large doses of cinchophen was undertaken for several reasons. First, it was observed that the ulcer caused by cinchophen is frequently located at the site of the pyloric sphincter, as well as in the duodenum, and along the lesser curvature of the stomach as has been observed by others.¹ Second, it was found that the intravenous injection of from 10 to 25 mg per kilo body weight of cinchophen caused an increase in the activity of the pyloric sphincter in 6 out of 14 dogs. The activity of the pylorus was recorded by a balloon made for the purpose. The increased activity of the pyloric sphincter, illustrated in Fig. 1, was abolished by atropine, but not by bilateral section of the vagi in the neck. Third, the results of studies by us on the effect of cinchophen (100 mg per kilo per day) on bilirubin clearance (4

¹ Churchill and Van Wagoner, *Arch. Path.*, 1932, **14**, 860; Bollman and Mann, *Proc. Staff Mayo Clin.*, 1935, **10**, 580.

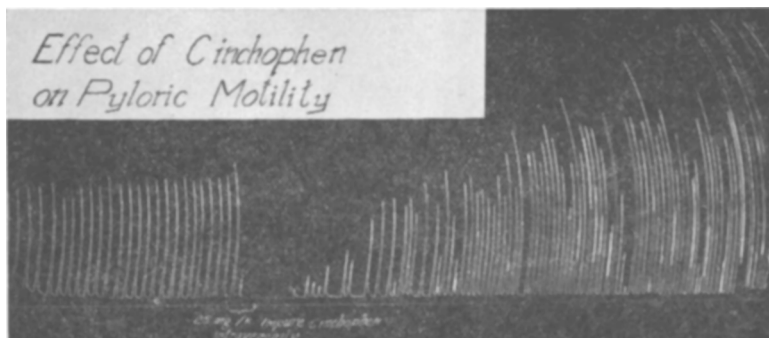


FIG. 1.

dogs) and serum phosphatase (4 dogs) failed to reveal any evidence of liver damage which might account for the ulcers. Fourth, when the excretion of cinchophen into gastric juice or pyloric secretion was examined by the method of Bradley,² a maximum excretion of 1.5 mg per hour was obtained. This was done to ascertain whether circulating cinchophen might be excreted into the lumen of the stomach in quantities sufficient to irritate, since it has been found that cinchophen introduced by routes other than the oral causes gastro-duodenal ulcer.^{3, 4} Finally, we failed to observe a significant change in the gastric secretory response to a test meal in 3 Pavlov and 4 Heidenhain pouch dogs to occur after the daily administration of 100 mg of cinchophen per kilo body weight, though 5 of the animals developed ulcer. The averaged results are shown in Table I. These results do not necessarily disagree with those of Stalker, Bollman and Mann⁵ who observed a hypercontinuous secretion rather than an increased response to a meal. We did not follow the output of secretion during 24 hours as they did.

The observations just referred to suggested that if a Rammstedt operation was performed, it might prevent ulcers from occurring at the site of the pyloric sphincter by preventing pylorospasm and might reduce the incidence of ulcer in the stomach by tending to promote enterogastric regurgitation and gastric evacuation.

Methods. The Rammstedt operation was performed by the usual surgical technic, the muscle being separated widely from the mucosa. Those dogs in which the mucosa was accidentally incised were discarded from the series.

² Bradley, W. B., to be published.

³ Churchill and Manshardt, *Proc. Soc. Exp. Biol. and Med.*, 1932, **30**, 825.

⁴ Stalker, Bollman and Mann, *Arch. Surg.*, 1937, **35**, 290.

⁵ Stalker, Bollman and Mann, *Arch. Surg.*, 1937, **34**, 1172.

TABLE I.
Effect of Cinchophen "B" on Gastric Secretary Response to a Meal in Pavlov and Heidenhain Pouch Dogs.

Dog No.	Control Avg of 7-11 test meals		1st week		2nd week		3rd week		4th week		5th week	
	cc of		cc of		cc of		cc of		cc of		cc of	
	Vol. cc	N/10 HCl	Vol. cc	N/10 HCl	Vol. cc	HCl N/10	Vol. cc	HCl N/10	Vol. cc	HCl N/10	Vol. cc	HCl N/10
1	42.8	37.0			39.8	43.1						
2	79.7	87.4			79.1	86.9						
3*	36.9	32.3	21.2	14.9	20.0	15.5						
4*	19.7	6.4	15.2	5.9	15.2	5.9	24.3	11.1				
5*	19.5	8.2	19.7	7.1	21.6	6.0	27.0	8.2	18.1	5.3		
6*	12.0	7.9	6.6	2.0	22.2	10.5	14.3	7.2				
7*	12.6	8.1	14.4	6.3	22.0	11.5	16.8	7.5	13.7	7.8	11.1	7.1

*These dogs had an ulcer at autopsy.

Dogs 1, 2 and 3 were typical Pavlov pouches and Dogs 4, 5, 6 and 7 were Heidenhain pouches, according to the curve of secretion. 2 to 5 test meals were given per week.

A maximum of 1.5 mg of cinchophen was secreted per hour in the gastric juice. For Dog No.:

1. No ulcer. 6 test meals. 1.5 mg cinchophen secreted in juice per hour.
2. " " " 5 " " Max. of 1.5 mg cinchophen secreted in juice per hr.
3. 4 test meals each week. Ulcer at autopsy.
4. 5 " " " " " " " " " "
5. 2 " " " " " " " " " "
6. 2 " " " " " " " " " "
7. 2 or 3 test meals each week. Ulcer at autopsy.

Two different cinchophen preparations were used. Cinchophen "A" had physical properties analogous to the cinchophen which was used in ulcer studies prior to 1935,^{1, 3, 6} and was available on the market at that time. It had a greyish cream color and contained some phenolquinolin and an alkali-insoluble residue. Cinchophen "B" was a white powder and contained no impurities that we could detect. The cinchophen preparation used in our laboratory prior to 1935 was apparently more toxic than cinchophen "B", in that it produced lethal effects more rapidly. For example, 100 mg per kilo daily of the cinchophen prior to 1935 produced death with ulcers in 23 of 26 dogs in from 3 to 59 days, or in an average of 14.5 days. All had a gastritis.

One hundred mg per kilo body weight of cinchophen A and B was fed daily to 16 and 14 dogs respectively. The same quantity of cinchophen A and B was fed daily to 16 and 8 dogs respectively after a Rammstedt operation had been performed.

Results. The results are shown in Table II. It is evident that cinchophen A, the "impure" product, produced death with ulcer more

⁶ Reid and Ivy, PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 142.

TABLE II.
Effect of Rammstedt Operation on Incidence of Ulcer Produced by Cinchophen.

Product	No. of dogs used	No. with ulcer	No. with gastric erosions	Normal sacri- feed after 90 days	Avg survival time in days
Control.					
Cinchophen A, an "impure" product	14	12	2	0	21.5
Cinchophen B, a "pure" product	16	12	3	1	35
Total	30	24	5	1	
Rammstedt Operation.					
Cinchophen A	16	7	0	9	48.4
Cinchophen B	8	4	0	4	64
Total	24	11	0	13	

rapidly than cinchophen B. It is also clear that the Rammstedt operation reduced the incidence of ulcer by almost one-half. In the control group the incidence of ulcer was 80% (24 of 30 developed ulcer), and of ulcer and hemorrhagic erosions 96%. In the Rammstedt group the incidence of ulcer was 46% (11 of 24 developed ulcer) and of ulcer and hemorrhagic erosions 46%. A marked difference in the general condition between the control and Rammstedt animals was apparent, which was especially true of those Rammstedt animals that did not develop ulcer. These latter animals appeared to be healthy and only occasionally manifested anorrhexia and emesis, and their weight loss was slight. This was apparently due to the absence of gastritis revealed by autopsy.

Observations were made in regard to the location of the ulcer. In all the control animals, approximately 10% of the ulcers were located in the duodenum, 70% at, or in contact with, the pyloric ring, and the remainder along the lesser curvature. In the Rammstedt animals no duodenal ulcers were observed and none in relation to the pyloric ring. They were located along the lesser curvature near the incisura and were of the chronic, penetrating and cicatricial type, rather than of the acute, hemorrhagic and perforating type observed in the controls.

Conclusion. The Rammstedt operation decreases the incidence of gastritis, hemorrhagic erosions and ulceration that follows cinchophen administration in dogs. This indicates that pylorospasm plays a significant but not an all inclusive rôle in the genesis of cinchophen ulcers.