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Role of the Vagus Nerve in Experimental Cinchophen-Ulcer.

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By giving the drug cinchophen, it is possible to produce a peptic ulcer in the dog pathologically identical with that found in man,[1] and, furthermore, procedures which have benefited one have been equally helpful in the other,[2-6] and vice versa.[7,8] Cinchophen produces an ulcer in almost 100% of dogs without grossly disturbing the normal physiology of the gastro-intestinal tract,[9] and provides an ideal means for observing the effect of various proposed measures on peptic ulcer.

Numerous studies on cinchophen-ulcer have been conducted by Stalker, Bollman and Mann.[1,3,5,10] They came to the conclusion that cinchophen produced an increase in the total volume of gastric secretion and that the increase was chiefly acid.[10] Thus, it was assumed that cinchophen caused an ulcer by producing hyperacidity.

If cinchophen-ulcer is caused by an increase in the total volume of acid, it is clear that transthoracic vagotomy, by its reduction of gastric acidity,[11] should have a marked beneficial effect on this ulcer. To verify this inference, transthoracic supradiaphragmatic vagotomy was performed in 15 dogs. These vagotomized animals were then given sufficient cinchophen to produce an ulcer over varying lengths of time.

Procedure. The vagus nerves were observed in the thorax and abdomen at autopsy in 42 dogs and were found to pursue a constant course. Operations were performed under positive intratracheal pressure and morphine-pentobarbital anesthesia. The right chest was opened in the 7th interspace and a 1.5 to 3.0 cm section removed from the anterior and posterior vagus nerves just before they pierced the diaphragm. The chest was closed by interrupted cotton sutures throughout.

Two groups of vagotomized dogs were used. The first, Group A, comprising 4 dogs, received 2 g of cinchophen 4 times a week for at least 30 days (this has been reported as giving the greatest incidence of chronic cinchophen-ulcer[3]) to allow an ulcer to form. Then, 2 g of the drug were given every day to try to perforate the ulcer if present.

The second group, Group B, comprising 11 dogs, received approximately 2 g of cinchophen 6 days a week. This method had been used previously in this laboratory to produce cinchophen-ulcer.[6,7,8]

Results. All the dogs in Group A developed ulcer. Nine dogs in Group B developed ulcer; however, in 2 of these animals the vagi had not been completely severed in the thorax: in one, the posterior branch of the right vagus was intact; in the other, the anterior vagus was intact. The 2 animals in Group B that failed to develop an ulcer received cinchophen for an insignificant period of time—2 to 9 days respectively. All dogs had excellent appetites throughout cinchophen administration until the last day or so before

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TABLE I.
Cinchophen Administration to Vagotomized Animals.

Dog	Total grams of cinchophen	Days	Results
1*	4	2	Stomach and duodenum normal
2*	18	9	" " " "
3*	60	39	4 pyloric antral ulcers
4*	64	32	3 " " "
5*	12	6	Numerous antral ulcers
6*	16	9	3 antral ulcers, 1 fundic ulcer
7*	46	26	3 pyloric antral ulcers
8*	6	4	2 pin-point antral ulcers
9*	18	10	Antral ulcers
10*	74	43	Numerous antral ulcers
11*	50	29	3 large antral ulcers
12†	92	60	Large antral ulcer, large annular pyloric ulcer
13†	114	72	Large annular pyloric ulcer.
14†	118	74	Perforated antral ulcer, healed annular ulcer
15†	113	83	Perforated pyloric ulcer, antral ulcers

* Creighton regime.
† Modified Stalker regime.

death.

Discussion. In dogs, vagotomy produces a decrease in total volume of acidity[11] and also a marked decrease in motility[11,12] which persist for at least 5½ months.[13] Meek[14] reported a peptic ulcer in 2 out of 13 vagotomized dogs but Beazell and Ivy[15] failed to find an ulcer in 60 vagotomized dogs. It is evident, therefore, that vagotomy alone is not capable of producing peptic ulcer in a high percentage of cases. In view of our results, this probably means that merely the increased exposure of the gastric mucosa to gastric contents is not the prime factor in the formation of cinchophen-ulcer in vagotomized dogs.

Since vagotomy decreases the total volume of acidity, it may be that cinchophen produces an ulcer, not by producing an hyperacidity, but by inactivating one of the protective mechanisms of the stomach. Possibly it affects mucus in some way so as to render it incapable of preventing hydrochloric acid and pepsin from attacking the stomach wall. The importance of mucus as a protective mechanism was pointed out by Whitlow[16] and conclusively demonstrated in man[17] merely by allowing a normal amount of acid and pepsin to attack an area of mucosa deprived of mucus.

Summary and Conclusions. Surgical interruption of the vagus nerves above the diaphragm had no effect whatsoever on the incidence of peptic ulcer produced by cinchophen.

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13 Vanzant, F. R., *Am. J. Physiol.*, 1932, **99**, 375.

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16 Whitlow, J. E., quoted by Fogelson, S. J., *J. A. M. A.*, 1931, **96**, 673.

17 Wolf, S., and Wolff, H. G., *Human Gastric Function*, Oxford University Press, New York, London, Toronto, 1943, p. 168.