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ANTRAL MUSCLE SENSITIVITY AFTER VAGOTOMY IN THE RAT*

C. G. BREMNER, CH.M., F.R.C.S., *Department of Surgery, General Hospital, Johannesburg, and University of the Witwatersrand*

When vagotomy without a drainage procedure is performed in the experimental rat, gross gastric stasis results (Fig. 1). The enormous stomach may take several days to empty its contents.

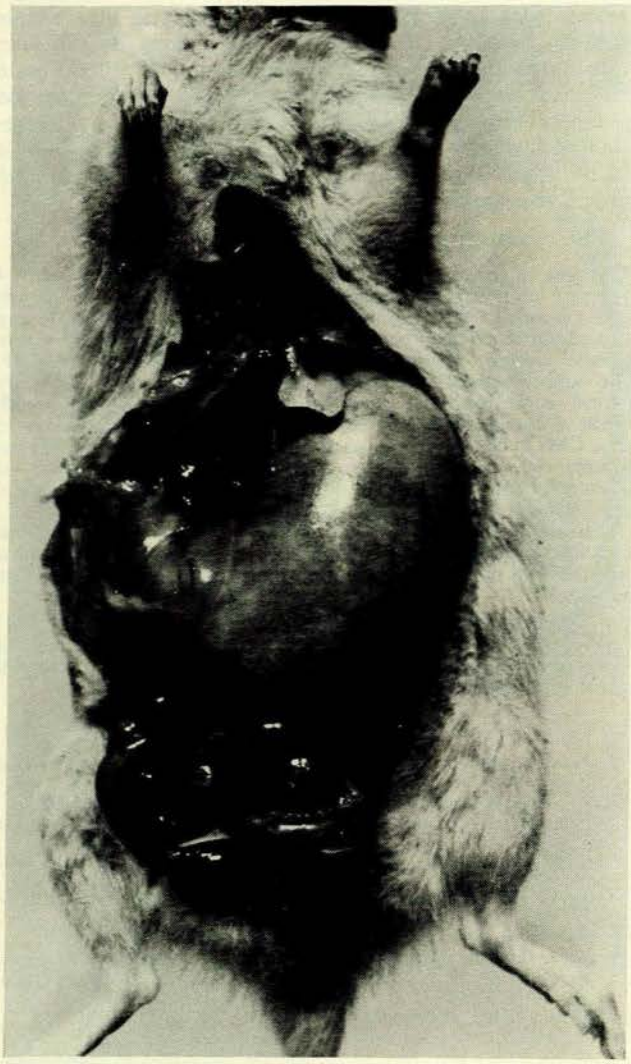

Fig. 1. Enormous gastric stasis following vagotomy in the rat.

There is adequate evidence to show that gastric motility in man is diminished after vagotomy, and because of gastric stasis some form of drainage procedure is mandatory. The stasis following vagotomy in man and animals is believed to be due to smooth-muscle atony.[1-3] A dilated, slowly emptying, weak-waved stomach is mentioned in 14 papers in a review of vagotomy.[4]

In rabbits, however, cervical or thoracic vagotomy is followed by a brief cessation of motility (12 - 48 hours), and subsequently abnormal hypermotility and retention results.[5]

The experiments described in this paper show that the rat stomach behaves in a similar manner to the rabbit's stomach after vagotomy and that the muscle of the rat is not hypotonic after vagotomy performed 5 - 30 days previously.

MATERIALS AND METHODS

Three methods were used to assess the muscle sensitivity *in vitro*.

Method 1

Longitudinal strips of muscle taken from the greater curvature of freshly sacrificed rats were suspended in an oxygenated Tyrode bath at 37°C. The muscle strips were cut to measure approximately 1·5 cm. × 0·5 cm. and included the muscle of the pylorus. A balanced tambour (ratio 5:1; 0·5 G), attached to the muscle, recorded muscle contractions on a blackened revolving drum.

Muscle strips were also prepared from sham-operated rats and rats which had undergone vagotomy, 5 - 31 days after operation. Two identical 50-ml. immersion compartments were used synchronously, so that normal and sham-operated gastric muscle could be compared with gastric muscle after vagotomy under identical conditions. When the immersed muscle strips had stabilized (20 - 30 minutes), acetylcholine chloride 0·5 ml. × 10^{-3} was added to each bath and the contractions were recorded simultaneously.

Method 2

A modification of a previously described rat preparation was used.[6] Glass cannulae were tied into the antrum and duodenum at equal distances from the pyloric ring. The stomach was immersed in oxygenated Tyrode solution at 37°C and perfused through the cut oesophageal end at a pressure of 10 cm. Tyrode (Fig. 2). The cannulae were connected via transducers (Statham 0 - 50 mm.Hg) to an electrical recording unit. The outflow was measured electrically, but is not considered in the results.

Baseline recordings were made from 10 sham-operated rats of equal weight range (200 - 250 G). The mean antral pressure rise in mm. water was calculated over a period of 5 minutes recording in each rat. The duration of each contraction was measured, and the percentage duration of spontaneous contractions was also calculated. The antral activity was calculated by the product of the mean height of antral pressures and the percentage duration of contractions.[7] Transmural electrical stimulation, using coaxial platinum electrodes, was used,[8] and 10-volt and 30-volt stimulation was given for 1-minute periods (1 msec. pulse duration, 6 cycles/sec. frequency). The antral activity was again calculated for each period of stimulation. The same method of stimulation was used in 11 rats studied 7 - 66 days after abdominal vagotomy, and the results were compared with the sham-operated group.

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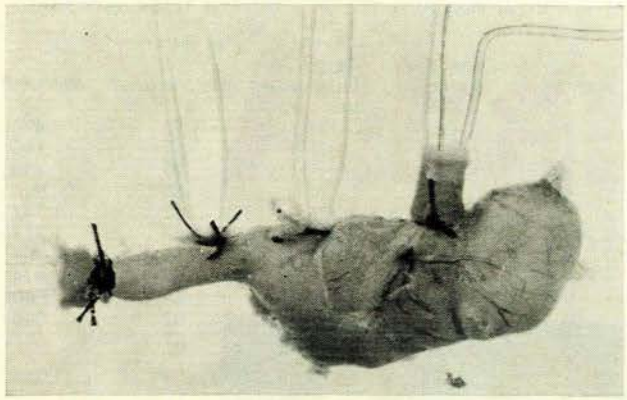


Fig. 2(a). Rat's stomach cannulated for pressure recording.

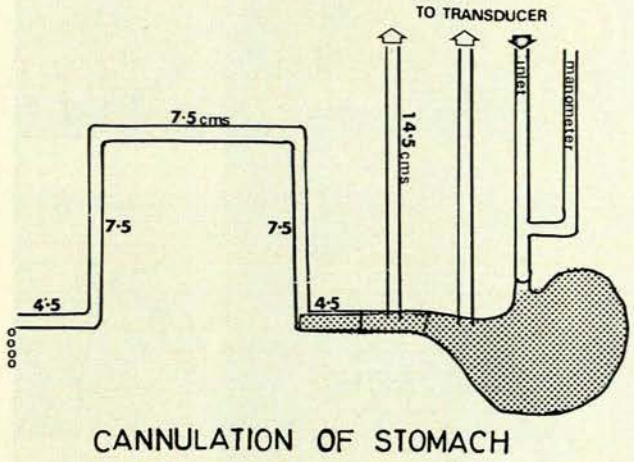


Fig. 2 (b). Diagrammatic illustration of the cannulation of a rat's stomach for pressure recording.

Method 3

The same *in vitro* model was used. Acetylcholine chloride 1 ml. × 10^{-3} and 1 ml. × 10^{-5} was added to the Tyrode bath. The resulting rise in antral pressure was recorded in 11 sham-operated rats. The experiment was repeated in the rats which had undergone vagotomy, and the results were compared.

RESULTS

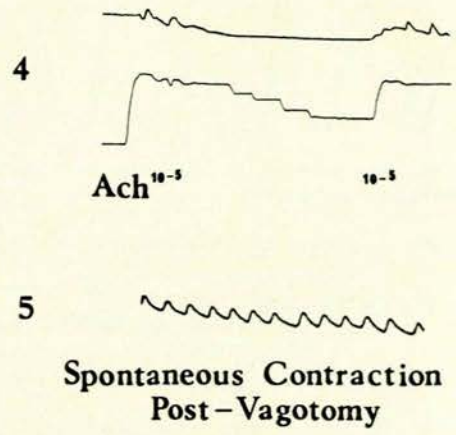
Muscle-Strip Sensitivity

Sensitivity was assessed by the presence or absence of spontaneous muscle contractions and the response to acetylcholine stimulation in the stomachs of 5 rats which had undergone vagotomy at 5, 12, 12, 12 and 30 days after the operation, respectively. Table I summarizes the results.

Spontaneous contractions were demonstrated in the normal and chronic vagotomy specimens, but not in the sham-operated muscle (Figs. 3 and 4). The over-all response to acetylcholine was as good in the normal rat as in the specimens from rats which had undergone vagotomy. Following vagotomy, specimens definitely gave a better response to acetylcholine than did the muscle from the sham-operated rats.

TABLE I. MUSCLE-STRIP SENSITIVITY

	Experiment No.	*Normal*	*Sham*	*Vagotomy*
Spontaneous contractions	1	−		−
	2	+		++
	3	+		−
	4		−	+
	5		−	−
Acetylcholine response	1	++		+
	2	++		+
	3	+		++
	4		+	++
	5		+	++



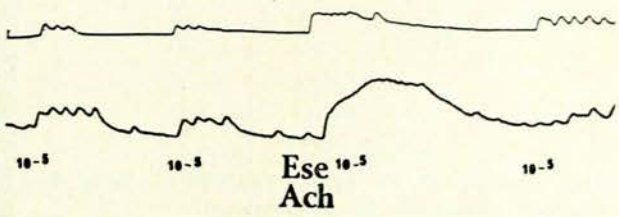


Fig. 3. Muscle-strip sensitivity *in vitro*, showing vagotomy and sham comparisons. *Top*: Upper sham-operated rat, lower vagotomized rat. *Bottom*: Upper sham-operated rat, lower vagotomized rat.

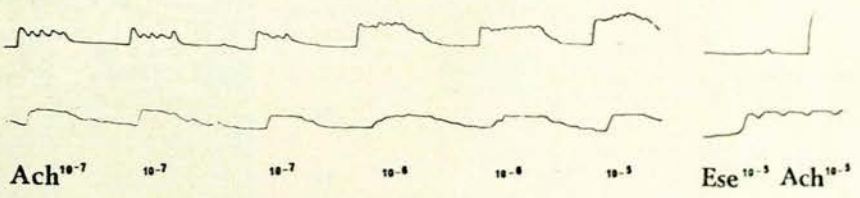


Fig. 4. Muscle-strip sensitivity *in vitro*, showing vagotomy and normal comparisons.

Spontaneous Activity

The antral activity of 11 sham-operated rats was calculated and compared with the antral activity of rats after vagotomy. Typical pressure recordings are shown in Fig. 5. The results are shown in Tables II and III.

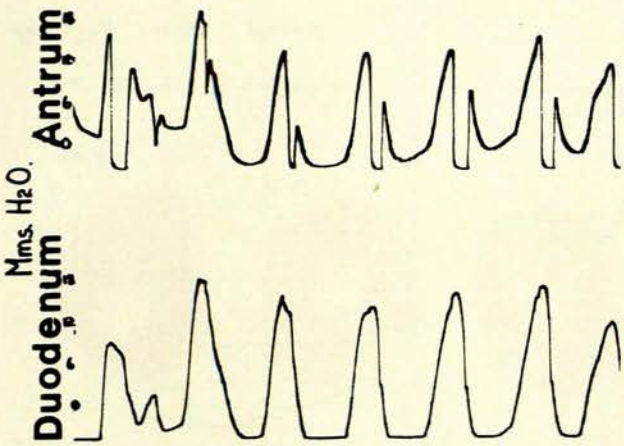


Fig. 5. A pressure recording of the spontaneous motility of a stomach, after vagotomy.

TABLE II. ANTRAL ACTIVITY OF SHAM-OPERATED STOMACHS

Rat No.	*Days after operation*	*Average height of contractions (mm. water)*	*% duration of contraction*	*Activity**
1	20	3·8	36	137
2	20	2·9	72	209
3	20	2·5	52	130
4	23	1·4	48	67
5	17	2·2	47	104
6	21	1·9	38	72
7	21	2·7	55	147
8	22	1·8	64	115
9	22	1·8	45	81
10	22	2·8	61	170
		$\bar{x}$=2·4	$\bar{x}$=51·8	$\bar{x}$=123

*See text.

TABLE III. ANTRAL ACTIVITY OF STOMACHS AFTER VAGOTOMY

Rat No.	*Days after operation*	*Average height of contractions (mm. water)*	*% duration of contraction*	*Activity**
1	25	13·1	52	676
2	25	21·5	57	1,146
3	66	7	70	490
4	26	24·9	40	996
5	26	26	67	1,742
6	14	21	63	1,323
7	14	38·7	58	2,268
8	16	22	67	1,474
9	30	30·6	68	2,080
10	7	8·8	62	546
11	30	13	47	611
		$\bar{x}$=25·4	$\bar{x}$=20·6	$\bar{x}$=59	$\bar{x}$=1,214

*See text.

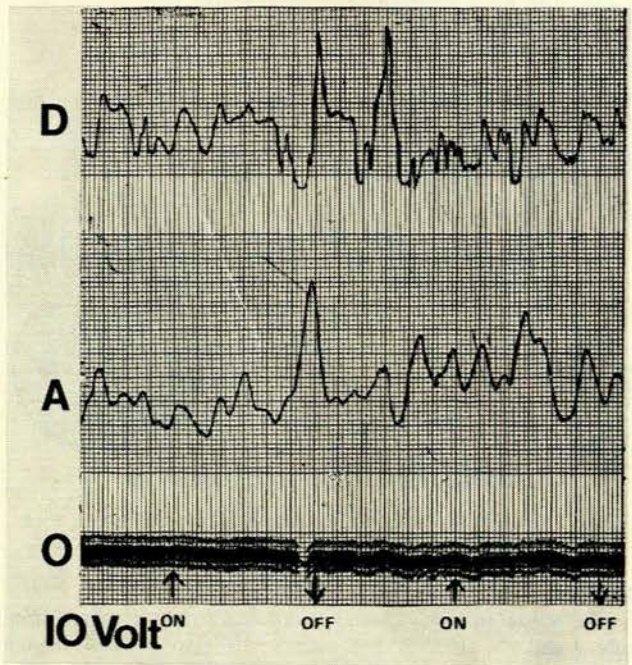


Fig. 6. The effect of electrical stimulation on antral motility. D=duodenal contractions, A=antral contractions, O=outflow.

Effect of Electrical Stimulation (Fig. 6)

The antral activity was again calculated following stimulation with 10-volt and 30-volt currents.

The comparison of results with sham-operated rats and those which had undergone vagotomy is summarized in Table IV.

The Effect of Acetylcholine Stimulation (Fig. 7)

Acetylcholine added to the Tyrode bath resulted in an immediate rise in antral pressure in all specimens. The

TABLE IV. EFFECT OF ELECTRICAL STIMULATION

	Spontaneous activity in 'sham' rats	*Spontaneous activity in vagotomy rats*	*Activity after 10-volt stimulation*		*Activity after 30-volt stimulation*	
			Sham	*Vagotomy*	*Sham*	*Vagotomy*
Mean height of contraction (mm. water)	2·4	20·6	3·7	21·6	10·7	15·6
% duration of contraction	52	59	47	61	58	79
Activity	127	1,214	174	1,317	591	1,231
% increase in activity		855	37	8·5	365	1

rise in antral pressure was compared in the sham-operated rats and those which had undergone vagotomy. The results are given in Table V.

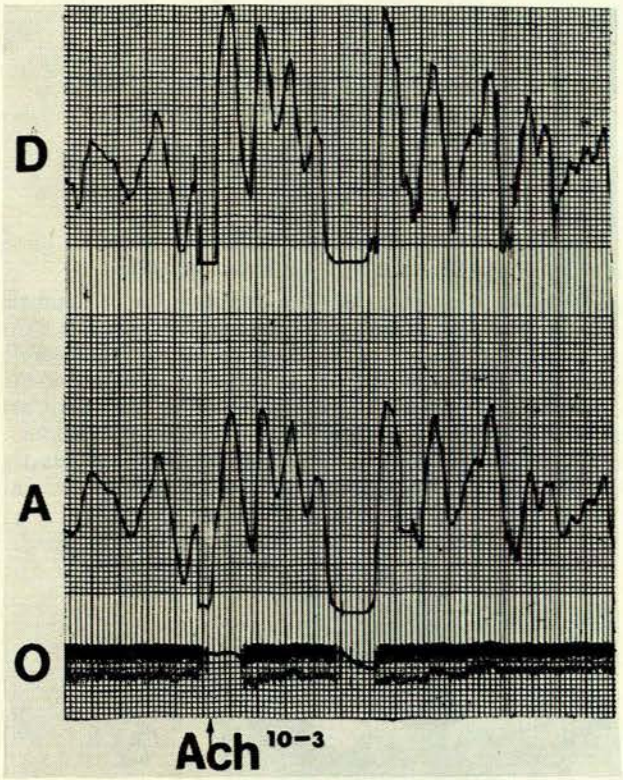


Fig. 7. The effect of acetylcholine on antral pressure.

TABLE V. EFFECT OF ACETYLCHOLINE STIMULATION

	Acetylcholine 1 × 10^{-3} concentration		*Acetylcholine 1 × 10^{-5} concentration*	
Mean rise in antral pressure	*Sham*	*Vagotomy*	*Sham*	*Vagotomy*
	13 cm.	20 cm.	9·6 cm.	14 cm.
Degrees of freedom	38		14	
t	2·4		3·3	
p	$·01 < p < ·02$		$p < ·01$	

DISCUSSION

Following vagotomy the antral activity of the stomachs studied *in vitro* is markedly increased, when compared with the sham-operated stomach. The sham-operated specimen is, in fact, an acutely denervated structure, and the poor spontaneous activity recorded may be due to an acute vagotomy effect. Acute vagotomy results in an immediate hypotonic stomach in rabbits,[5] and after 48 hours hypermotility develops. Antral activity depends on the efficiency of the antral pump and the resistance to the outflow at the pylorus. If the muscle is hypotonic or the outflow resistance removed, the antral pressure recordings would be poor. Therefore, the marked rise in antral pressure shown in these studies is due either to an increase in the antral muscle efficiency or to pyloric obstruction.

The muscle-strip sensitivity to acetylcholine was as good as in the normal unoperated group, but better than in the sham-operated group. This suggests a slight increase in muscle sensitivity after vagotomy, but the increase is not enough to explain the 855% increase in activity. Therefore some pyloric dysfunction must result, causing a mechanical obstruction to the outflow. The stretched wall of intestine produces larger amounts of acetylcholine than the non-stretched wall.[9] Stasis after vagotomy causing stomach stretching should therefore result in a release of acetylcholine. This could explain the increased activity. However, one of the effects of decentralization of ganglion cells is that they become spontaneously active,[10] and this could be an additional explanation for the increased activity after vagotomy in the rat.

The initial hypotonia after vagotomy may also be only a temporary phenomenon in the dog.[11,12] The diminished gastric motility after vagotomy in man also improves later.[3,13] There is still a possibility of some pyloric obstructive effect after vagotomy in man.

The change in antral activity following electrical stimulation was minimal in the rats which had undergone vagotomy. However, the organ is possibly already contracting to its capacity and unable to shorten its muscle fibres any further. A platinum electrode dipping into the Tyrode solution makes the whole bath a diffuse external electrode. Coaxial electrodes permit a fairly uniform excitation over the whole stomach.[8] Contractions during stimulation result from stimulation of cholinergic nerves in the substance of the muscle.[14] Since stimulation of cholinergic nerves releases acetylcholine, the failure to respond to electrical stimulation after vagotomy indicates a possible depletion of acetylcholine.

The significant rise in antral pressure on the addition of acetylcholine to the waterbath shows that the muscle has in fact further capacity to contract. This increased response after vagotomy has 2 possible explanations. Firstly, it may indicate an increased sensitivity to acetylcholine in denervated smooth muscle. However, denervation hypersensitivity occurs only with adrenergic stimuli.[15] Secondly, an increase in the size of the stomach and protein mass following vagotomy[16] means an increase in muscle bulk which probably accounts for the increased response.

Using a radioactive marker to assess gastric emptying in the rat, vagal denervation has been shown to affect only the pylorus, leaving motility of the small intestine untouched.[17]

SUMMARY

In vitro antral pressure studies in the rat show that there is a marked increase in antral activity following vagotomy. Reasons are given suggesting that this increased activity is due to pyloric dysfunction causing mechanical obstruction. Muscle-strip studies *in vitro* show that the antral muscle is not hypotonic after vagotomy performed 5 - 30 days previously.

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