J.Physiol. (1971), **214**, *pp.* 1–13
With 3 text-figures
Printed in Great Britain

THE EFFECT OF SPLANCHNIC NERVE STIMULATION ON GASTRIC ACID SECRETION AND MUCOSAL BLOOD FLOW IN THE ANAESTHETIZED CAT

BY J. D. REED, D. J. SANDERS AND VALERIE THORPE

From the Department of Physiology, Medical School, The University, Newcastle upon Tyne NE1 7RU

(*Received 20 July 1970*)

SUMMARY

1. Electrical stimulation of the vagus nerves produced a parallel increase in gastric acid secretion and gastric mucosal blood flow.

2. Gastric acid secretion and mucosal blood flow, stimulated by pentapeptide infusions or by vagal stimulation, were markedly and equally reduced by electrical stimulation of splanchnic nerve fibres.

3. The splanchnic stimulated reduction in acid and mucosal blood flow occurred only when the rise in blood pressure, normally associated with splanchnic stimulation, was prevented by inclusion of a pressure reservoir in the circulation.

4. There was evidence that the effect of the splanchnic nerves was not mediated by release of adrenaline from the adrenal medulla.

INTRODUCTION

Stimulation of acid secretion by histamine, gastrin extracts and synthetic pentapeptide, has recently been shown to be accompanied by a parallel increase in gastric mucosal blood flow (Jacobson, Linford & Grossman, 1966; Jacobson, Eisenberg & Swan, 1966; Swan & Jacobson, 1967; Jacobson, Swan & Grossman, 1967; Moody, 1967; Cowley & Code, 1967; Harper, Reed & Smy, 1968; Reed & Smy, 1968; Cowley, Code & Fiasse, 1969).

Reductions of acid secretion by adrenaline, posterior pituitary extract and secretin (Jacobson *et al.* 1966), thiosulphate solutions (Moody, 1967), large doses of pentapeptide and gastrone (Cowley *et al.* 1969), noradrenaline and prostaglandin E_1 (Jacobson, 1970) have been shown to be associated with decreases in mucosal blood flow.

Although there appears to be parallelism between mucosal blood flow

and acid secretion during both stimulation and inhibition of acid secretion, there is neither evidence of a causal relationship between the two, nor evidence of the relationship.

This study was undertaken in part to clarify the role of the splanchnic nerves in gastric function. It was, furthermore, argued that if the splanchnics do cause vasoconstriction, as they have long been assumed to, then this might provide some insight into the mechanism of acid secretion and its relationship to mucosal blood flow.

METHODS

All the cats were starved for 36 hr before the experiment, although allowed water. Anaesthesia was induced with ether, maintained by a single I.V. injection of chloralose (80 mg/kg body wt.) and a glass cannula was inserted into the trachea. An indwelling cannula was placed in the right saphenous vein. A nylon catheter with the tip directed towards the heart was inserted into a carotid artery in the neck to allow measurement of arterial blood pressure by a mercury manometer, and collection of arterial blood samples. Both vagus nerves were sectioned in the neck.

The stomach was exposed through a mid line incision and the pylorus occluded with a tape ligature. A wide bore rubber catheter (i.d. 8 mm) was inserted through an incision in the cervical portion of the oesophagus, passed into the stomach and secured so that the tip lay in the pyloric antrum. The 8th rib on the right side was removed and through this aperture the dorsal and ventral vagal trunks were dissected free and sectioned. Small insulated ring electrodes were placed on the distal nerve ends. Respiration in these animals was maintained by a Starling Ideal Pump. In all animals the splanchnic nerves were cut extraperitoneally on both sides through incisions in the flanks. Ring electrodes were also placed on the distal ends of these nerves. The suprarenal glands were ligated in a group of four cats in which hydrocortisone succinate (5 mg/kg body wt.) was injected I.M. at the beginning of each experiment.

An hour was allowed between completion of the surgical procedures and the beginning of each experiment. During this time a priming dose of amidopyrine (30 mg/kg body wt.) was given I.V. followed by an infusion of 10 mg/kg . hr. Routinely 50 ml. of 1/5 vol./vol. mixture of isosmolal glycine and mannitol adjusted to pH 3·5 by addition of 0·15 N-HCl were placed in the stomach at the beginning of each 10 min collection period, drained between 9·5 and 10 min and replaced by a further 50 ml. Acid content was determined by electrometric titration of a 25 ml. sample to pH 7·0 using 0·02 N-NaOH and a pH meter with glass electrode system. Arterial blood samples were collected every 20 min throughout the experiments, centrifuged, 1 ml. plasma stored for amidopyrine extraction and the R.B.C.S returned to the animal via the indwelling cannula. Gastric mucosal blood flow was measured by the amidopyrine technique described for use in the anaesthetized cat by Harper *et al.* (1968).

Gastric activity was stimulated either by electrical stimulation of the vagal trunks (10 V, pulse duration 1 msec, 10 Hz, 20 sec of stimulation being alternated with 40 sec of rest) or by I.V. infusion of pentapeptide (Peptavlon I.C.I. 50123), 1 μg/10 min. The splanchnic nerves were continuously stimulated (10 V, pulse duration 1 msec, 10 Hz) for two consecutive 10 min collection periods. A 5 l. air reservoir with a small compartment containing 5 ml. heparinized saline was connected to the lower aorta of fourteen animals in which the splanchnic nerves were stimulated. The pressure in the reservoir was adjusted to that recorded in the carotid

artery before splanchnic stimulation. After stimulation and when blood in the reservoir had returned to the animal, the reservoir was closed to the circulation.

Experiments were in five groups, five cats in each group, and in all experiments three successive collection periods were carried out before stimulation to ascertain the basal levels of acid output and mucosal blood flow. Acid output was expressed as H^+, μ-equiv/10 min, and as the increase in H^+ output (ΔH^+) above the basal level of H^+ secretion. Similarly mucosal blood flow (MBF) was expressed as ml./10 min and as the increase in mucosal blood flow (ΔMBF) above basal MBF.

The mucosal blood flow and acid responses to prolonged vagal stimulation (series 1) were compared with the responses to identical vagal and simultaneous splanchnic stimulation producing either a rise in B.P. (series 2) or no rise in B.P. (prevented by inclusion of the pressure reservoir, series 3). The responses to infusions of pentapeptide (series 4) were compared to those with identical pentapeptide and simultaneous splanchnic stimulation (series 5). In series 5 experiments, which were repeated in four animals in which the adrenals had been ligated, the rise in B.P. during splanchnic stimulation was prevented by inclusion of the pressure reservoir in the circulation.

Statistical analysis

In the test experiments (series 2, 3, and 5) the splanchnic nerves were stimulated for two consecutive periods between the 6th and 11th periods of vagal or pentapeptide stimulation. These experiments were randomly paired with their appropriate controls (series 1 or 4). The individual ΔMBF responses in each experiment were calculated either as a % of the observed value in the period before splanchnic stimulation, or in the case of control experiments (series 1 and 4) as a % of the ΔMBF observed in the equivalent stimulation period. The % ΔH^+ responses were similarly calculated. Comparison of the mean % responses for corresponding periods were made using Student's t test for paired data. Results are presented as the mean $\pm$ 1 S.E.

RESULTS

Vagal stimulation

During the first 70 min of prolonged vagal stimulation (series 1) the % ΔH^+ and % ΔMBF responses increased progressively and subsequently remained more or less constant during the period of stimulation studied (Fig. 1). The means of actual ΔH^+ and ΔMBF responses during the control periods were 259 ± 51 μ-equiv/10 min and $54{\cdot}8 \pm 17{\cdot}9$ ml./10 min respectively.

During the two consecutive 10 min periods of splanchnic nerve stimulation (series 2) the mean arterial blood pressures were 160 and 138·5% of that observed before stimulation, which in twelve cats was a mean of $131 \pm 8{\cdot}3$ mm Hg. However, inclusion of the 5 l. pressure reservoir into the circulation during identical splanchnic stimulation (series 3) resulted in mean arterial pressures of 109 and 95·6% of those recorded before stimulation. Splanchnic nerve stimulation in these experiments in which the usual rise in blood pressure was largely prevented (series 3), produced marked reductions of % ΔH^+ and % ΔMBF responses (Fig. 2*A*). The mean actual ΔH^+ and ΔMBF responses during control periods in these

experiments were 299·6 ± 48·7 μ-equiv/10 min and 34·7 ± 4·5 ml./10 min and were not significantly different to those in the control series 1 ($P > 0{\cdot}05$ in each case). The greatest reduction of mean % ΔMBF and % ΔH^+ compared to the mean % values in the paired control experiments occurred during the second 10 min period of splanchnic stimulation. Subsequent to this, i.e. the end of splanchnic stimulation, these responses gradually returned to the values expected had there been no splanchnic stimulation (Fig. 2*A*).

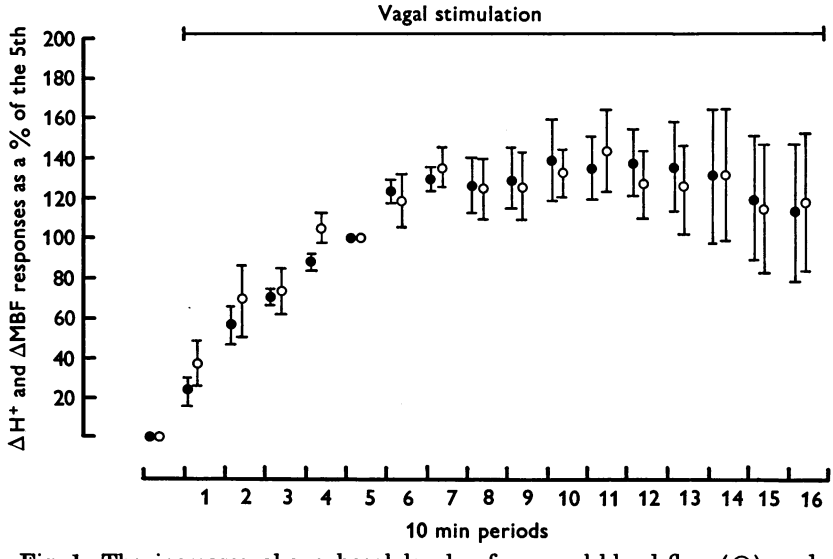

Fig. 1. The increases above basal levels of mucosal blood flow (○), and H^+ (●) responses during electrical stimulation of the vagus trunks in the thorax. The responses are expressed as a % of the appropriate responses occurring during the 5th period of vagal stimulation and represent the means ± 1 S.E. of observations in five cats.

However, in those experiments in which the B.P. rose during splanchnic stimulation (series 2) there was very little reduction of acid or blood flow (Fig. 2*B*). The means of actual ΔH^+ and ΔMBF responses during the control periods were 226·6 ± 29·0 μ-equiv/10 min and 30·6 ± 4·9 ml./10 min and were not significantly different to those in control periods of series 1.

In three experiments inhibition of vagal stimulated acid secretion and mucosal blood flow were produced by prolonged stimulation of the splanchnic nerves, the rise in blood pressure being prevented by use of the reservoir. When the inhibition was well established I.V. injections of 3 mg guanethidine (Ismelin, Ciba) were given and in each case resulted in an increase in H^+ output and mucosal blood flow. One of these experiments is illustrated in Fig. 3.

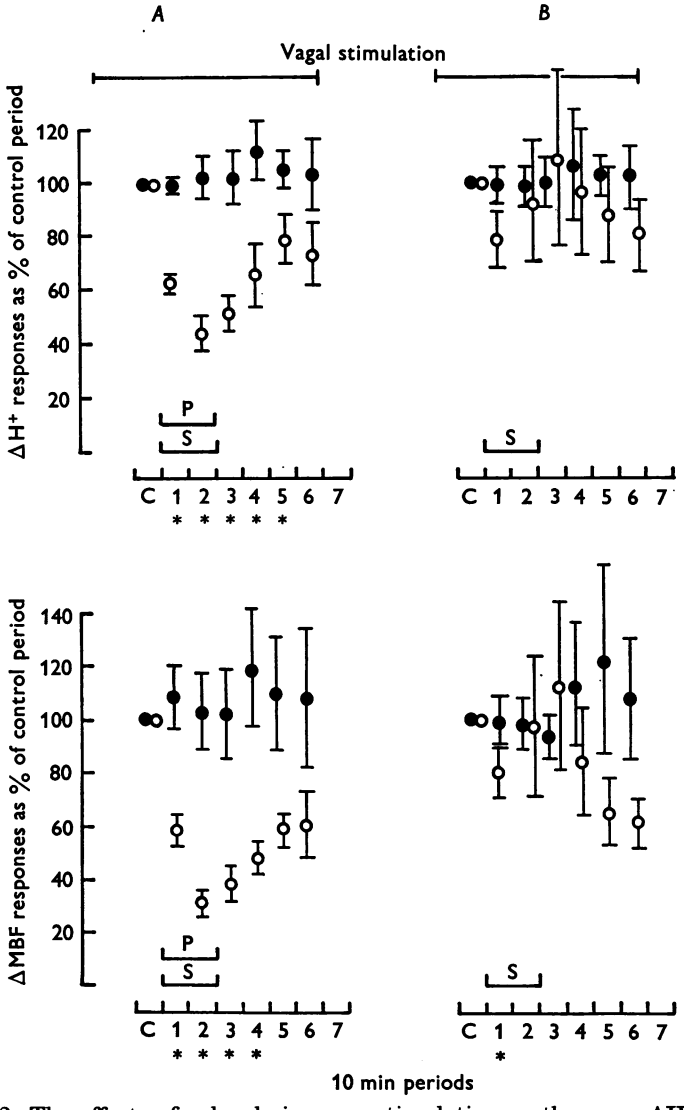

Fig. 2. The effects of splanchnic nerve stimulation on the mean ΔH^+ and mean ΔMBF responses to repeated electrical stimulation of the vagus nerves.

A. A comparison of five paired experiments. Controls (●) without splanchnic stimulation, the test experiments (○) with two consecutive periods of splanchnic stimulation (S) during which time a pressure reservoir was included in the circulation (P).

B. A comparison of five paired experiments. Controls (●) had no splanchnic stimulation whereas test experiments had two periods of electrical excitation of the splanchnic nerves (S).

All results are expressed as a % of the appropriate control responses. The bars represent ± 1 S.E.

* Indicates significant differences between means at 5% level.

Pentapeptide stimulation

The mean absolute rates of ΔH^+ secretion (332 ± 91 μ-equiv/10 min) and ΔMBF ($35{\cdot}9 \pm 12{\cdot}3$ ml./10 min) during the control periods of pentapeptide stimulated secretion (series 4) were not significantly different to those during vagal stimulation ($P > 0{\cdot}05$ in each case).

Splanchnic nerve stimulation produced a marked reduction in % ΔH^+ output and % ΔMBF. The difference between the means of the control experiments (series 4) and the paired test experiment with splanchnic stimulation (series 5) are shown in Table 1*A*.

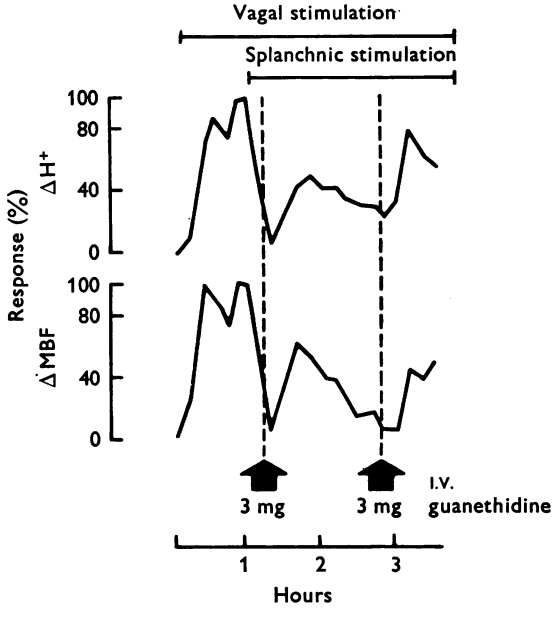

Fig. 3. An experiment in which vagally stimulated H^+ and MBF were reduced by concomitant splanchnic nerve stimulation with a 5 l. pressure reservoir included in the circulation. 3 mg guanethidine were injected I.V. at each of the arrows followed in each case by an increase in H^+ and MBF responses.

The inhibitions of vagal and pentapeptide stimulated % ΔH^+ and % ΔMBF, by splanchnic stimulation, when the rise in blood pressure normally associated with splanchnic stimulation was prevented, were very similar (Table 1). The differences between % means in control and test experiments in the vagal stimulation group were not significantly different from those in corresponding periods in the pentapeptide stimulation group ($P > 0{\cdot}05$ in each case). In both groups % ΔH^+ was reduced during

TABLE 1. The difference between % mean responses in control and splanchnic stimulation experiments (with pressure reservoir) during pentapeptide and vagal stimulation

	Splanchnic stimulation							
	1	2	3	4	5	6	10 min periods	
ΔH^+ Difference between means (%)	−37·0	−61·0	−45·4	−53·0	−45·6	−40·6	*A*	Pentapeptide stimulation
S.E. of difference	19·1	14·2	9·5	14·5	15·7	19·6		
Significance P =	< 0·05	< 0·02	< 0·001	< 0·05	< 0·05	> 0·05		
ΔMBF Difference between means (%)	−35·4	−70·0	−50·0	−63·6	−52·0	−54·8		
S.E. of difference	12·6	20·0	11·4	24·6	24·8	28·6		
Significance P =	< 0·05	< 0·02	< 0·001	> 0·05	> 0·05	> 0·05		
ΔH^+ Difference between means (%)	−36·7	−58·4	−50·2	−45·8	−30·4	−31·2	*B*	Vagal stimulation
S.E. of difference	3·4	6·9	5·5	5·3	8·6	12·7		
Significance P =	< 0·05	< 0·05	< 0·05	< 0·05	< 0·05	> 0·05		
ΔMBF Difference between means (%)	−49·8	−72·2	−63·2	−71·2	−70·2	−47·6		
S.E. of difference	10·4	9·5	13·5	23·9	32·8	22·7		
Significance P =	< 0·05	< 0·05	< 0·05	< 0·05	> 0·05	> 0·05		
	Splanchnic stimulation							

splanchnic stimulation and remained significantly so during the three 10 min collection periods subsequent to the end of splanchnic stimulation. The mean % ΔMBF was significantly reduced in both groups during both periods of splanchnic stimulation, and for 10 min subsequently in the pentapeptide experiments and for 20 min subsequently in the vagal stimulation experiments.

In four experiments the splanchnic nerves were stimulated in adrenalectomized animals during pentapeptide stimulation with the pressure reservoir in the circulation. During the 1st and 2nd periods of splanchnic stimulation the mean reductions in % ΔH^+ of 35·5 ± 17·0 %, and 48 ± 9·3 %, and in % ΔMBF of 37·0 ± 16·0 %, and 48·8 ± 18·0 %, were not significantly different to those observed with splanchnic stimulation during pentapeptide stimulated secretion in animals with the adrenals intact (Table 1*A*, $P > 0{\cdot}05$ in each case).

The % reductions of ΔMBF were usually greater than the % reductions of ΔH^+ during splanchnic stimulation (Table 1). However, these differences were not statistically significant.

DISCUSSION

It is clear that electrical stimulation of the vagus nerve produces a parallel increase in gastric acid secretion and gastric mucosal blood flow (Fig. 1). Previous workers have reported little or no effect on gastric blood flow during vagal stimulation (Burton-Opitz, 1910; Lim, Necheles & Ni, 1927; Freisen & Hemingway, 1952), although Martinson (1964) has reported an increase in total gastric blood flow measured by a drop counter. Swan & Jacobson (1967) have shown a marked rise in mucosal blood flow associated with acid secretion stimulated by insulin and 2-deoxy-D-glucose. A parallel rise in mucosal blood flow and gastric acid secretion has been shown when acid secretion is stimulated with histamine (Jacobson *et al.* 1966; Moody, 1967; Harper *et al.* 1968) or gastrin (Jacobson *et al.* 1966; Harper *et al.* 1968; Cowley *et al.* 1969).

A reduction in gastric acid secretion and MBF was produced by splanchnic stimulation. However, significant reduction of vagal stimulated % ΔMBF and % ΔH^+ only occurred when the rise in blood pressure normally associated with splanchnic nerve stimulation was prevented by inclusion of a pressure reservoir in the circulation (Fig. 2). The greatest reduction in mean % ΔH^+ or mean % ΔMBF occurred during the second 10 min period of splanchnic stimulation, being 58 and 72 % respectively. Following the end of splanchnic stimulation both % ΔH and % ΔMBF responses returned toward the control values, the acid responses being significantly reduced for 30 min and the mucosal blood flow

reduced for 20 min. There was an isolated significant reduction of the % ΔMBF (19 %) during the first period of splanchnic nerve stimulation in those experiments in which the blood pressure was allowed to rise (Fig. 2*B*).

Splanchnic stimulation during pentapeptide stimulation produced a similar pattern of reduced % ΔH^+ and % ΔMBF to that observed to splanchnic stimulation during vagal stimulation (Table 1).

It is perhaps strange that the maximum inhibition occurs during the 2nd period of splanchnic stimulation. The majority of sympathetic nervous stimulation effects are immediate and usually decline during continuous stimulation. Indeed, in the experiments in which the blood pressure rose during splanchnic stimulation, the greatest rise occurred during the first 10 min period of stimulation, declining from 160 % response to 138 % during the 2nd period. The progressive inhibition of acid and MBF during splanchnic stimulation may suggest that this mechanism is not a direct nervous influence on secretion. It may indicate that the site of action is at some intermediate level between the secretory stimulus and the secretion of acid. This intermediate site could involve gastric mucosal blood flow. However, it is doubtful whether the complex phenomenon of inhibition of gastric acid secretion and the related gastric blood flow can be directly equated to a single end organ effect, such as the sympathetic effect on the pupillary muscle.

It has long been assumed that the splanchnic nerves exert a vasoconstrictor effect on gastric blood vessels, and that in turn this may produce a reduction in gastric secretion. Such evidence as exists is largely inferred from results of experiments in which infusions of catecholamines have resulted in a reduction of acid secretion (Forrest & Code, 1954). Recently Jacobson (1970) reported that I.V. infusion of noradrenaline in conscious dogs during either histamine or gastrin stimulated acid secretion, produced a reduction in both acid output and mucosal blood flow. The ratio *R* of

$$\frac{\text{(gastric juice amidopyrine)}}{\text{(arterial plasma amidopyrine)}} = \frac{\text{clearance}}{\text{volume rate of secretion}}$$

fell during this period, a fact the author suggests indicates a primary action of noradrenaline on the gastric vasculature, leading to a secondary reduction in acid secretion. However, to interpret *R* as the ratio of blood flow to acid secretion requires the assumption that acid concentration remains constant during all forms of stimulation and inhibition. Indeed Jacobson's results, when calculated as the ratio of gastric clearance to acid secretion, show a rise during noradrenaline inhibition of pentapeptide stimulated acid secretion.

Thompson & Vane (1953) showed that splanchnic stimulation produced a reduction of total gastric blood flow in their viviperfused preparation

of the histamine stimulated cat stomach. A reduced output of gastric acid accompanied the reduction in blood flow. That the splanchnic nerves probably do exert a physiological effect on gastric secretion is indicated by the studies of Oberhelman, Woodward, Smith & Dragstedt (1951) and Schafer & Kittle (1951). Both groups of workers used total pouch preparations in dogs and compared secretion with, and without splanchnic innervation. Oberhelman *et al.* (1951) showed that sympathectomy produced a significant increase in 24 hr gastric acid secretion in five of seven dogs with good vagal innervation of the stomach and fed a fairly normal diet, whereas four dogs with poor vagal innervation showed no such increase following sympathectomy. The gastric secretory response to a standard insulin hypoglycaemia was more than doubled when the gastric sympathetic supply was destroyed and two of three dogs showed an increased response to histamine post-sympathectomy.

Schafer & Kittle's results were similar in that acid and pepsin secretion collected during a standard 60 min period were markedly increased by sympathectomy and reduced by aortic neurectomy, a procedure giving rise to a generalized sympathetic hyperactivity.

This work, together with that cited above, provides direct evidence of a probable role of splanchnic-induced inhibition of gastric secretion and mucosal blood flow. What has not been evaluated is the nature of this inhibition. There are at least four mechanisms whereby splanchnic stimulation could bring about reduction of gastric secretion:

1. A direct antisecretory mechanism.

2. A vasoconstriction and reduction of mucosal blood flow giving rise to a decreased nutrient supply such that, in spite of a constant level of stimulation, the secretory mechanism is no longer capable of secreting H^+ in the same amount; a decreased mucosal blood flow decreasing the amount of stimulant arriving at the stimulatory sites; or a combination of both mechanisms.

3. Either 1 or 2 could be brought about by circulating catecholamines released by splanchnic stimulation from the adrenal medulla.

4. It has been suggested (Jansson & Martinson, 1966) that splanchnic inhibition of vagally stimulated excitatory gastric motor tone is brought about by action on vagal ganglion cells rather than on the smooth muscle itself. Such a mechanism might be extended to include the effect on secretory and blood flow responses and would account for the greater effect splanchnotomy had on secretion in pouches with good vagal innervation reported by Oberhelman *et al.* (1951).

It is significant that the reduction in acid secretion during splanchnic stimulation only occurred if the blood pressure rise was prevented. This suggests that the rise in systemic arterial pressure counteracts the

splanchnic-induced reduction of secretion, an effect which could be brought about in a number of ways. Inhibition by splanchnic stimulation may be as a result of vasoconstriction, a primary reduction in mucosal blood flow leading to a secondary reduction in acid secretion. This inhibitory mechanism would obviously be reduced by an increased arterial pressure tending to increase the blood flow. Similarly, if inhibition of acid secretion is primarily produced by nervous action against the secretory mechanism, i.e. a direct antisecretory effect, this would reduce mucosal blood flow, assuming mucosal blood flow to be controlled by acid secretion. However, it has been shown (Harper *et al.* 1968) that under certain conditions an increase in mucosal blood flow potentiates acid secretion. Therefore, if a rise in central B.P. tends to increase MBF the overall effect could be one of little or no change as illustrated in Fig. 2*B*.

Jansson & Martinson's (1966) suggestion of splanchnic stimulation resulting in a block of vagal transmission at an intramural ganglion is supported by the physiological observations of Kewenter (1965) on intestinal motility. The anatomical studies of Jacobowitz (1965) on the stomach and Norberg (1964) on the intestine, show that the majority of sympathetic fibres end on the intramural vagal ganglia. However, Martinson (1964) suggested that gastric vagal efferent fibres could be split into two groups; first, those with lowest threshold being responsible for excitatory gastric motor changes and secondly a group of higher electrical threshold controlling a 'peripheral pattern of response' of gastric acid and pepsin secretion, gastric blood flow and muscle relaxation. Jansson & Martinson did not report the effect of splanchnic stimulation on gastric secretion and blood flow and no evidence has been put forward as to whether splanchnic fibres penetrate the mucosa or whether inhibition of these activities might also be at the intramural ganglion level.

Celander (1959) and Kock (1959) showed that the inhibitory effect of supraspinal reflex increase of sympathetic activity on intestinal motility was not due to direct inhibitory fibres, but to release of catecholamines from the adrenal medulla. However, it was observed in this study that guanethidine largely removed the splanchnic nerve induced inhibition of vagal stimulated gastric function. There is no evidence that this drug either blocks the release of catecholamine from the adrenal medulla or interferes with the end-organ action, its effect being to prevent release of noradrenaline from post-ganglionic sympathetic nerve endings (Abercrombie & Davies, 1963). Moreover, the reduction of pentapeptide stimulated acid and mucosal blood flow by splanchnic stimulation was the same whether the adrenal glands were removed or not. It therefore seems unlikely that circulating catecholamine is responsible for the observed inhibitions.

The similarity in the pattern of inhibition of acid and mucosal blood flow produced by electrical stimulation of the splanchnic nerves during gastrin and vagal stimulation suggests a common inhibitory mechanism. Atropine produces almost total abolition of the gastric responses to electrical stimulation of the efferent vagus but, at least in the anaesthetized cat, has no effect on gastrin stimulated secretion (Blair, Harper, Lake & Reed, 1961; Blair, 1965). It is unlikely that vagal ganglion cells situated on the atropine sensitive vagal pathway would provide a common site for splanchnic nerve inhibition of gastrin and vagal stimulated gastric function. Such a common site might exist in the vicinity of the parietal cell representing an antisecretory function of the splanchnic nerves. It is probably more likely that the common site of action is a reduction of mucosal blood flow and a subsequent reduction of secretion as a result of either nutrient supply or reduced amount of stimulant. The work reported here would not differentiate between these possibilities. The dose of gastrin was not sufficient to produce maximal secretion and we have no knowledge of the extent of the vagal stimulation other than that the rates of acid secretion produced by the gastrin and vagal stimulation were not significantly different. Presumably alterations in mucosal blood flow would alter the amount of gastrin arriving at the stomach during either pentapeptide or vagal stimulation.

We would like to thank the M.R.C. for the award of a Scholarship for Training in Research Methods to D. J. Sanders and for an Award to Miss Valerie Thorpe to enable her to take an Intercalated Course in Physiology.

REFERENCES

ABERCROMBIE, G. F. & DAVIES, B. N. (1963). The action of guanethidine with particular reference to the sympathetic nervous system. *Br. J. Pharmac.* **20**, 171–177.

BLAIR, E. L. (1965). The effects of tissue extracts on the stomach. *Gastric Secretion Mechanisms and Control*, p. 263. London: Pergamon Press.

BLAIR, E. L., HARPER, A. A., LAKE, H. J. & REED, J. D. (1961). The effect of atropine upon gastrin-stimulated acid section. *J. Physiol.* **159**, 73*P*.

BURTON-OPITZ, R. (1910). Über die Strömung des Blutes in dem Gebiete der Pfortader. III. Das Stromvolum der Vena gastrica. *Pflügers Arch. ges. Physiol.* **135**, 205–244.

CELANDER, O. (1959). Are there any centrally controlled sympathetic inhibitory fibres to the musculature of the intestine? *Acta physiol. scand.* **47**, 299–309.

COWLEY, D. J. & CODE, C. F. (1967). Gastric mucosal blood flow during secretory inhibition by gastrin pentapeptide (abstr.). *Gastroenterology* **52**, 1131.

COWLEY, D. J., CODE, F. C. & FIASSE, R. (1969). Gastric mucosal blood flow during secretory inhibition by gastrin pentapeptide and gastrone. *Gastroenterology* **56**, 659–666.

FORREST, A. P. M. & CODE, C. F. (1954). The inhibitory effect of epinephrine and norepinephrine on secretion induced by histamine in separated pouches of dogs. *J. Pharmac. exp. Ther.* **110**, 447–450.

FREISEN, S. & HEMINGWAY, A. (1952). The vascular response of the stomach to experimental alterations in the autonomic nervous system of the dog. *Am. Surg.* **18**, 195–200.

HARPER, A. A., REED, J. D. & SMY, J. R. (1968). Gastric blood flow in anaesthetized cats. *J. Physiol.* **194**, 795–807.

JACOBOWITZ, D. (1965). Histochemical studies of the autonomic innervation of the gut. *J. Pharmac. exp. Ther.* **149**, 358–364.

JACOBSON, E. D. (1970). Comparison of prostaglandin E_1 and norepinephrine on the gastric mucosal circulation. *Proc. Soc. exp. biol. Med.* **133**, 516–519.

JACOBSON, E. D., EISENBERG, M. M. & SWAN, K. G. (1966). Effects of histamine on gastric blood flow in conscious dogs. *Gastroenterology* **51**, 466–472.

JACOBSON, E. D., LINFORD, R. H. & GROSSMAN, M. I. (1966). Gastric secretion in relation to mucosal blood flow studied by a clearance technic. *J. clin. Invest.* **45**, 1–13.

JACOBSON, E. D., SWAN, K. G. & GROSSMAN, M. I. (1967). Blood flow and secretion in the stomach. *Gastroenterology* **52**, 414–420.

JANSSON, G. & MARTINSON, J. (1966). Studies on the ganglionic site of action of sympathetic outflow to the stomach. *Acta physiol. scand.* **68**, 184–192.

KEWENTER, J. (1965). Vagal control of the jejunal and ileal motility and blood flow. *Acta physiol. scand.* **65**, suppl. 251, 3–68.

KOCK, N. G. (1959). An experimental analysis of mechanisms involved in reflex inhibition of intestinal motility. *Acta physiol. scand.* **47**, suppl. 164, 3–54.

LIM, R., NECHELES, H. & NI, T. (1927). The vasomotor reactions of the (vivi perfused) stomach. *Chin. J. Physiol.* **1**, 381–395.

MARTINSON, J. (1964). The effect of graded vagal stimulation on gastric motility, secretion and blood flow in the cat. *Acta physiol. scand.* **62**, 256–262.

MOODY, F. (1967). Gastric blood flow and acid secretion during direct intra-arterial histamine administration. *Gastroenterology* **52**, 216–224.

NORBERG, K. A. (1964). Adrenergic innervation of the intestinal wall studied by fluorescence microscopy. *Int. J. Neuropharmac.* **3**, 379–382.

OBERHELMAN, H. A., WOODWARD, E. R., SMITH, C. A. & DRAGSTEDT, L. R. (1951). Effect of sympathectomy on gastric secretion in total pouch dogs. *Am. J. Physiol.* **166**, 679–685.

REED, J. D. & SMY, J. R. (1968). *Proc. int. Union Physiol. Sci.*, vol. VII, XXI Int. Cong., Washington D.C., abstract 1084. Washington: Fed. Am. Soc. Expt. Biol.

SCHAFER, P. W. & KITTLE, C. F. (1951). The relation of the autonomic nervous system to gastric secretion with particular reference to the sympathetic nerves. *Surgery* **29**, 1–10.

SWAN, K. G. & JACOBSON, E. D. (1967). Gastric blood flow and secretion in conscious dogs. *Am. J. Physiol.* **212**, 891–896.

THOMPSON, J. E. & VANE, J. R. (1953). Gastric secretion induced by histamine and its relationship to the rate of blood flow. *J. Physiol.* **121**, 433–444.