

lation of the parietal cell-bearing mucosa. The outpouring of cortisol in the response to the hypoglycaemia presumably plays some part in determining the size of the secretory response of the parietal cells to the activated vagus in the first post-insulin phase. In the absence of repeated blood

letting, however, the cortisol level in the plasma is basal during the period of time in which the second phase of the post-insulin gastric secretory response appears. The second phase therefore is unlikely to be due to the stimulation of the adrenals by the action on the pituitary of hypoglycaemia.

3 The effect of bilateral adrenalectomy

It has been claimed that in monkeys (French *et al.*, 1953) and man (Shay and Sun, 1954) the second or delayed phase of the gastric secretory response to insulin-induced hypoglycaemia is abolished by bilateral adrenalectomy.

In our studies in parts 1 and 2 on the biphasic nature of the gastric secretory response to hypoglycaemia in dogs we failed to demonstrate any relation between the delayed phase of gastric secretion and the level of endogenous cortisol in the plasma. It was therefore considered necessary to examine in dogs the effect of removal of the adrenal glands upon the biphasic phenomenon.

METHODS

Two dogs were equipped with Pavlov-type innervated gastric pouches and the gastric secretory response to insulin hypoglycaemia was determined in the manner reported in part I. After suitable control experiments had been carried out bilateral adrenalectomy was performed

in one stage, using the technique described by Freud, Uyldert, and Waterman (1938).

The dogs were subsequently maintained in good health by a daily intramuscular injection of 25 mg. cortisone acetate (Glaxo), and when they were fully recovered from the operation the effect of insulin hypoglycaemia upon the gastric secretion was again studied. In both dogs following the removal of the adrenals a much smaller dose of insulin was required to induce a satisfactory level of hypoglycaemia. After the conclusion of the experiments the animals were sacrificed and a careful search of the abdominal cavity failed to reveal any residual adrenal tissue in either.

RESULTS AND DISCUSSION

No change appeared in the phasic character of the gastric secretory responses to hypoglycaemia in either dog following the adrenalectomy (Fig. 1a and b). In both dogs there appeared an increase in the volume and acid content of the gastric juice secreted,

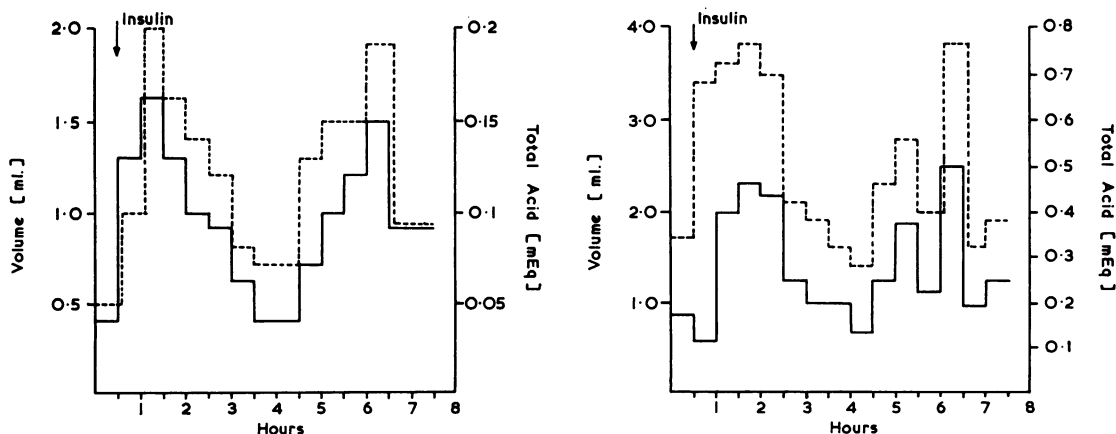


FIG. 1a. The effect of bilateral adrenalectomy on the secretory response to insulin hypoglycaemia of an innervated gastric pouch in dog A. (Data are for the means of five experiments before and two after adrenalectomy for each half-hour period.)

Continuous line = total acid

Broken line = volume

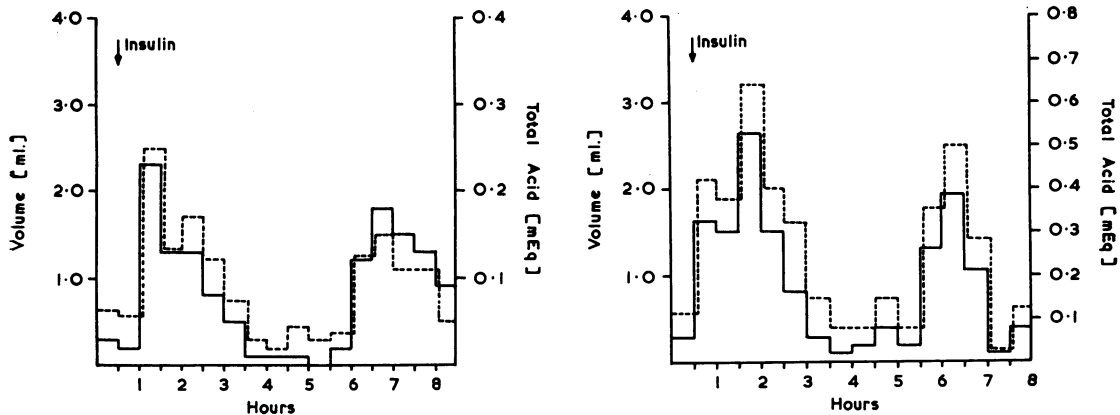


FIG. 1b. The effect of bilateral adrenalectomy on the secretory response to insulin hypoglycaemia of an innervated gastric pouch in dog B. (Data are for the means of three experiments before and three after adrenalectomy.)

Continuous line = total acid Broken line = volume

and in one dog in the fasting state there was a continuous secretion of acid from the pouch. These features are explained as the sequel to the daily administration of cortisone which we have shown in dogs to augment the gastric secretion from pouches, both in the fasting state and to a variety of stimuli.

The results reported here, together with the absence of any relationship between plasma cortisol levels and the second phase of insulin-induced gastric secretion, indicate that in dogs the second phase is not due to the stimulation of a pituitary-adrenal

mechanism of gastric secretion as postulated by previous authors.

The results do not affect established observations on the influence of corticosteroids on the secretory activity of the parietal cells, in which they would appear to have both a permissive and an augmentation role. The mechanism of the biphasic response to hypoglycaemia requires another explanation than that suggested by French *et al.* (1953), and the results of our subsequent studies are reported in part 4.

4 The interrelationship of the phases of the response and the role of the antrum

It is possible that the phasic nature of the gastric secretory response to hypoglycaemia may be due either to the operation of different excitatory mechanisms after different intervals of time or to the temporary depression of a single excitatory mechanism by the operation of an inhibitory one. It was therefore considered prudent to examine both the influence of an anticholinergic compound upon the secretory responses to insulin and the role of the antrum in the pattern of the response to hypoglycaemia.

EFFECT OF ATROPINE UPON THE PATTERN OF THE GASTRIC SECRETORY RESPONSE TO INSULIN HYPOGLYCAEMIA

METHODS Twelve experiments were made on three dogs, two of which had an innervated and one a denervated gastric pouch.

In each experiment insulin was used to stimulate gastric secretion and, as previously described, the responses collected over seven to nine hours. In six experiments an intramuscular injection of 1/50 gr. of atropine was given simultaneously with the insulin. In