of purified growth hormone. When this occurred an impairment of glucose tolerance, *i.e.*, a diabetic state, was also present. Evans and his colleagues(6) have shown that growth hormone produces nitrogen retention and lowers the blood amino nitrogen. In our experiments, therefore, increased gluconeogenesis, as a factor accounting for the loss of hypersensitivity and the diabetic state, can be minimized. The alteration in carbohydrate metabolism effected by growth hormone must be attributed to decreased carbohydrate utilization. That peripheral utilization of carbohydrate is diminished by purified growth hormone, is supported by the work of Stadie *et al.*(7) and Park *et al.*(8). These investigators found a decrease in carbohydrate utilization in the isolated diaphragm of growth hormone treated rats. It is apparent from our work that a physiological antagonism exists between growth hormone and insulin. In view of this latter phenomenon, the effects of growth hormone administration to intact animals are in all likelihood greatly modified by compensatory adjustment of the insulin-secreting cells of the pancreas. If the islets of Langerhans of growth hormone treated animals had been able to adequately adjust themselves to the peripheral inhibition of carbohydrate utilization by increasing their insulin output, no impairment of glucose tolerance would have been observed.

It is our opinion that in the hypophysectomized animal the absence of endogenous growth hormone is an important factor in causing the insulin hypersensitivity. If we had succeeded in obtaining physiological levels by hormonal replacement therapy, we certainly should not have observed a diabetic state. We consider the impairment of glucose tolerance induced by growth hormone to be the result of overdosage, an exaggerated manifestation of a physiological process.

Summary. The insulin hypersensitivity characteristic of hypophysectomized dogs was completely abolished by purified anterior pituitary growth hormone. Concomitantly an impairment of glucose tolerance, *i.e.*, a diabetic state, was produced.

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Effects of B-Diethylaminoethyl Xanthene 9-Carboxylate Methobromide (Banthine*) on Human Gastrointestinal Function.† (17961)

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(Introduced by C. M. Carpenter)

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Medical therapy in peptic ulcer has relied to a considerable extent upon agents that will neutralize or buffer the acid gastric juice which appears to be so important in the production of peptic ulcer. In searching for medication to prevent or diminish the production of acid gastric secretion, the belladonna derivatives, notably atropine, have been used because of their effect as para-sympathetic antagonists. The usefulness of this group of drugs has been limited because depression of gastric secretion is not affected unless other physiological side effects are produced(1,3). There are also unpredictable individual tol-

* Banthine furnished by courtesy of G. D. Searle Co., Chicago, Ill.

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erances(3). Atropine has been found to depress the volume of gastric secretion but the acidity is not affected until the volume has been reduced to 40-60%(2). B-Diethylaminoethyl xanthene 9-carboxylate methobromide (Banthine) has recently been therapeutically employed largely as a depressant of gastric secretion. This drug is a quaternary ammonium compound and may be classed as an anti-cholinergic drug. In moderate dosage it seems to have a muscarine effect, blocking the post-ganglionic parasympathetic nerve endings. In large doses a nicotine or curariform response is noted(4).

Procedures. The studies reported here have been concerned with 3 phases of gastrointestinal function: (1) gastric secretion, (2) gastric motility, and (3) small intestinal motility. Gastric secretion has been studied in the fasting state, at least 12 hours following the last meal. Eight patients had duodenal ulcers and 2 had no demonstrable gastrointestinal disease having been admitted to the hospital for other unrelated conditions. Continuous gastric aspiration was performed and samples divided into 15 minute fractions. The volume of the specimen was measured and the acid values were determined by titration with 0.1 N sodium hydroxide within a few minutes of aspiration. When a control period of a reasonably constant secretory level had been obtained, 100 mg of Banthine was given by mouth with 30 cc of water. Aspiration was discontinued for 30 minutes and then resumed in the manner described for the control period. No gastric secretagogues were used in this study. Gastric motility was recorded on a kymograph by means of an intra-gastric balloon containing from 100-150 cc of air connected to a water manometer and an ink-writing tambour. Following a control period of 30-45 minutes 100 mg of Banthine with 30 cc of water was administered by mouth, and

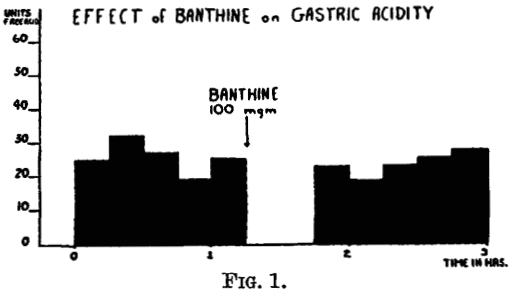

FIG. 1.
Composite chart of acidity values obtained in 10 patients. Following administration of Banthine, aspiration was discontinued for 30 min. and then resumed.

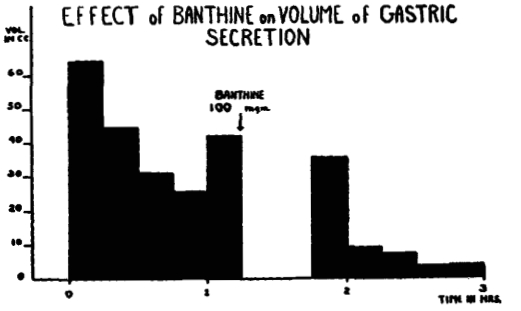

FIG. 2.
Composite chart of volume of gastric secretion obtained in 10 patients. Aspiration of the gastric contents was withheld for 30 min. following the oral administration of Banthine.

the recording continued. Small intestinal motility was recorded in a similar manner but a balloon containing 20 cc of air was used, being guided into the upper jejunum under fluoroscopic control. Gastric motility studies were made on 2 patients, both of whom had duodenal ulcers. Small intestinal motility records were obtained in 2 patients with regional enteritis.

Results. 1. Gastric secretion. 100 mg of Banthine diminished the volume of gastric secretion but produced no significant change in the titratable gastric acidity. The depression in volume occurred within 30-45 minutes following oral administration and persisted from 1.5 to 4 hours. In this small series no detectable difference in response was noted between the 2 control cases and the 8 ulcer patients. Fig. 1, a composite chart of gastric free acidity determinations obtained in the 10 patients before and after giving Banthine, shows little difference in the two periods. Fig. 2, a composite chart of gastric secretory

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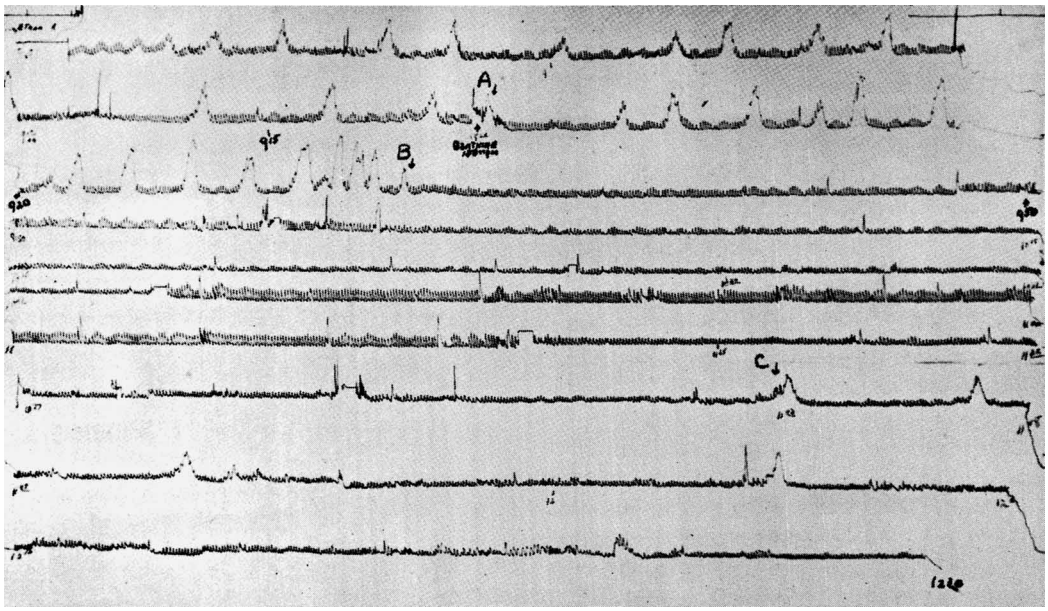

FIG. 3.
Gastric motility tracing obtained in patient with duodenal ulcer. 100 mg Banthine given orally at A. Gastric contractions were absent from B to C (approx. 2 hr). One line on the graph represents 20 min.

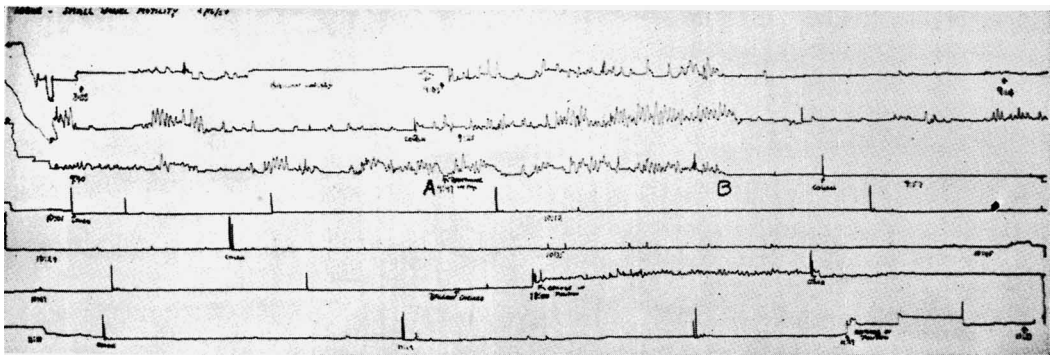

FIG. 4.
Tracing of upper jejunum motility obtained in patient with regional enteritis. Banthine (100 mg) administered at A with prompt cessation of contractions at B. One line on the graph represents 20 min.

volume, demonstrates a marked fall in the volume of secretion after Banthine.

2. Gastric motility. Banthine markedly reduced gastric motility, Fig. 3. Within 20-30 minutes following 100 mg orally, gastric contractions ceased and remained absent for approximately 2 hours. In one patient secretion and motility were recorded simultaneously and appearance of the depression of volume and motor activity were found to occur at the same time.

3. Small intestinal motility. In both patients in whom small intestinal motility records were obtained, marked depression of motor activity was found. Changes were apparent within 15 minutes after oral administration of the drug and persisted for as long as 2 hours, Fig. 4.

Summary. In 10 patients Banthine decreased the volume of gastric secretion without significantly altering gastric acidity. Gastric and small intestinal motor activity

was markedly diminished in 2 studies. Banthine depressed gastric secretion in a manner similar to atropine, but side effects were less pronounced. 100 mg of Banthine produced no undesirable side effects other than dryness of the mouth.

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Effect of Cortisone and Adrenocorticotropin Therapy on Serum Proteins in Disseminated Lupus Erythematosus. (17962)

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The serum proteins in patients with *disseminated lupus erythematosus* have been investigated electrophoretically. They appear to have a characteristic protein pattern. About 800 sera from patients with a great variety of diseases have been examined in our laboratory, and except for an occasional specimen from an unrelated condition, we have found no consistent duplication of this particular protein pattern (Fig. 1).

The serum was diluted with barbiturate buffer of pH 8.6 and an ionic strength of 0.1, and dialyzed either with mechanical stirring at room temperature(1), or without stirring for 48-72 hours in the refrigerator. An Aminco-Stern electrophoresis apparatus equipped with the cylinder lens-diagonal diaphragm optical system of Philpot-Svensson was employed. Both the ascending and descending boundaries were recorded, but for the sake of simplicity, only the ascending boundaries are shown (Fig. 1 and Table I). While the total protein content of the sera is generally within normal limits(2), the albumin concentration is decreased; the α_2- and γ-globulins are increased, but the α_1 and β-globulin fractions remain in the normal range. This causes a reversal of the A/G ratio.

The γ-globulin may be increased to 50% of the total protein content. Hyper-γ-globulinemia is usually encountered either in infectious diseases or in some involvement of the liver *e.g.* cirrhosis. As the condition of the patient improves temporarily either under treatment or during a spontaneous remission of the disease, the amount of γ-globu-

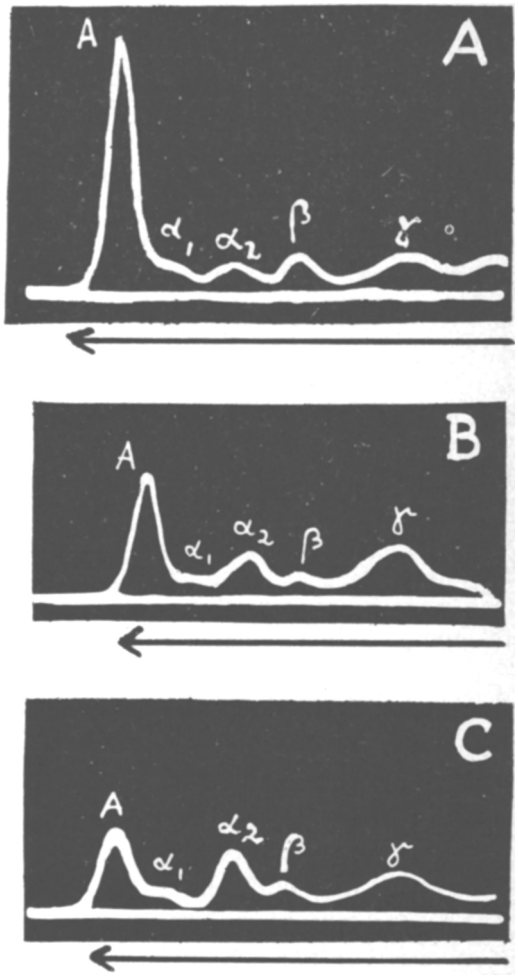

FIG. 1.

Representative electrophoretic patterns of normal serum (A), and of 2 sera from patients with *disseminated lupus erythematosus* (B, C).

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