tion. 4. *0.01 N HCl*: One hundred cubic centimeters of 0.01 N HCl was instilled into the duodenum of 3 patients and resulted in a gastric motor inhibition lasting 5 to 8 minutes. In 1 patient, 50 cc of this solution inhibited gastric activity for 5 minutes; in 2 patients, 25 cc of the same solution inhibited gastric contractions for only 3 minutes.

In the 3 patients with persistent histamine achlorhydria, 0.1 N HCl instilled into the duodenum resulted in prompt and profound inhibition of gastric motility. It was indistinguishable in latent period, degree, and duration from that occurring in subjects with normal gastric secretion.

*Conclusions.* 1) Duration of inhibition of gastric motility varies directly with volume and concentration of HCl solutions introduced into the duodenum. 0.075 N HCl produces definitely shorter inhibition than was previously found with equal volumes of 0.1 N HCl. When concentration of HCl is reduced to 0.01 N and volume reduced to 25 cc, the inhibitory period is very brief, lasting only 3 minutes. 2. In 3 patients with complete histamine achlorhydria, the inhibitory effect of intraduodenal acid on gastric motility was the same as that in individuals with normal gastric secretion.

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## Organ-Specific Effects of Cortisone on Protein Synthesis in Protein Depleted Rats.* (22310)

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The mechanism of action of cortisone and other adrenocortical steroids on protein metabolism has been the subject of many investigations. The theories and observations of some investigators(1-3) seem to favor a primary anti-anabolic effect while other workers(4-6) favor a primary catabolic mechanism. Still other reports(7) support a more complex interpretation.

Previous work(8) indicated that rats maintained on a completely protein-free diet offered a unique situation in which to study the effects of cortisone. The present communication is a preliminary report of results obtained from a study of the incorporation *in vitro* of glycine-2-$C^{14}$ into protein fractions of liver slices and intact isolated diaphragms from protein depleted rats treated with cortisone. The liver and diaphragm were studied in the hope that they might show differences in their ability to incorporate labeled amino acids and that these changes would reflect the influence of cortisone on protein synthesis or breakdown.

*Material and methods.* Young male rats were maintained on 3 experimental regimens (8). These regimens included: 1) normal synthetic diet; 2) protein-free synthetic diet; 3) protein-free synthetic diet plus daily subcutaneous injections of 2.5 mg of cortisone/100 g body weight. All groups were maintained on the experimental regimens for 12 to 17 days. Following the period of treatment the rats were lightly anesthetized with ether and sacrificed by exsanguination from the heart. The livers and diaphragms were removed, weighed, and placed immediately in chilled Krebs-Hensleit media equilibrated with 95% oxygen and 5% $CO_2$. The incu-

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TABLE I. *In Vitro* Incorporation of Glycine-2-$C^{14}$ into Protein Fractions of Rat Liver Slices and Intact Isolated Diaphragms. (Values are expressed as the mean of the individual values ± the standard error of the mean.)

| Treatment | Incorporation of glycine-2-$C^{14}$ into LIVER protein fractions | | Incorporation of glycine-2-$C^{14}$ into DIAPHRAGM protein fractions | |
|---|---|---|---|---|
| | Without added non-labeled amino acids (cpm/mg protein) | With added non-labeled amino acids* (cpm/mg protein) | Without added non-labeled amino acids (cpm/mg protein) | With added non-labeled amino acids* (cpm/mg protein) |
| Normal controls | 260 ± 37.2 (4)† | No observations | 38 ± 5.7 (3) | 36 — (1) |
| Protein-free diet controls | 128 ± 9.0 (7) | 201 ± 11.7 (5) | 41 ± 5.6 (7) | 60 ± 10.7 (5) |
| Protein-free diet + cortisone | 164 ± 7.0 (7) | 149 ± 11.9 (5) | 61 ± 3.8 (7) | 82 ± 6.6 (5) |

* Final concentration of L-isomer, 10 μg/ml.
† The No. of animals in which duplicate observations were made are shown in parentheses.

bation and isolation of the protein fraction was essentially as described by Krahl(9) except for minor technical changes. Approximately 400 mg of liver slices or one hemidiaphragm was placed in screw-cap incubation bottles. These bottles contained Krebs-Hensleit media (liver, 2 ml; diaphragm, 1 ml) and glycine-2-$C^{14}$, 11.6 μg/ml (specific activity, 1.25 mc/mM). A mixture of non-labeled amino acids was also added to some of the flasks in addition to glycine-2-$C^{14}$. This mixture contained l-cysteine, dl-lysine, l-histidine, dl-leucine, dl-threonine, dl-phenylalanine, dl-valine, l-arginine, dl-methionine, dl-isoleucine, and dl-tryptophane and was adjusted to pH 7.0 with $NaHCO_3$. The tissues were incubated with shaking for 2 hours at 37°C. Radioactivity in protein fractions was determined in an internal gas flow counter. All samples were counted at maximum self-absorption. Protein content was determined by the method of Lowry *et al.*(10).

*Results.* In confirmation of our earlier findings(8) the animals on the normal synthetic diet gained weight, those on the protein-free diet lost about 20% of their initial body weight, and those on the protein-free diet plus cortisone lost 40% of their starting weight ($P<0.001$). Liver weight/body weight ratios were significantly increased ($P<0.001$) in the animals receiving the protein-free diet plus cortisone. The protein-free diet caused a 30% decrease in the mean diaphragm weight when compared to normal values ($P<0.001$). The increase in liver weight in the cortisone treated animals was due in part to an increased protein content. Whereas cortisone treatment caused no change in the diaphragm weight/body weight ratio the liver weight/body weight ratio increased. Thus while the diaphragm suffered with other tissues from the wasting effects of cortisone, the liver was spared.

Liver slices from animals on a protein-free diet showed a decreased utilization of glycine-2-$C^{14}$ compared with that of liver from normal controls ($P = 0.01$) (Table I). Krahl (9) observed a similar effect in fasted rats. It was possible to increase utilization of glycine-2-$C^{14}$ by the addition of a mixture of essential non-labeled amino acids ($P<0.001$). Liver slices from animals on a protein-free diet plus cortisone showed an increased utilization of glycine-2-$C^{14}$ compared with that of liver from protein-free dieted animals ($P = 0.01$); in this case the addition of other amino acids had no stimulatory effect.

In the diaphragms, the diet had no effect on the utilization of glycine-2-$C^{14}$ (Table I). Treatment with cortisone caused an increased utilization of glycine-2-$C^{14}$ by the diaphragms ($P = 0.01$). Addition of non-labeled amino acids to the diaphragms from the cortisone treated animals caused a still further increased utilization of glycine-2-$C^{14}$ ($P<0.02$).

*Summary and conclusion.* In these experiments cortisone had no antisynthetic effect; its effect on protein synthetic reactions was to increase synthesis in the diaphragm. Since liver is spared and diaphragm is not spared against the wasting effects of cortisone, the chief effect of cortisone according to our ob-

servations must be its influence on catabolic reactions. Thus the organ-specific effects of cortisone can be explained on the basis of increased catabolism in diaphragm but not in liver.

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## Effect of Serotonin on Renal Excretion of Sodium; Possible Relation to Rauwolfia Action.* (22311)

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The administration of reserpine has been found to be associated with a decrease in the concentration of serotonin in brain, platelets and intestines(1). It has also been demonstrated that rauwolfia alkaloids can produce occasional salt and water retention even to the point of congestive failure(2). The present study was undertaken to investigate the possibility that this effect of rauwolfia might be mediated through serotonin.

*Materials and methods.* Forty convalescent patients free of cardiovascular, renal, metabolic or endocrine disease were selected for the study. All but 3 were bed patients, and all were afebrile and on a regular diet. All were given an infusion of 250 ml of 5% glucose and water. One or 2 mg of serotonin base‡ were added to the infusion of 18 subjects, the remaining 22 serving as controls. Those receiving serotonin were unaware that any drug had been added to their infusion, and did not experience any blood pressure change or discernible local or systemic reaction. Comparable conditions and identical procedures were employed in both groups. Each subject emptied his bladder as completely as possible in the sitting or standing position. One hour after breakfast the patients voided and then drank 200 ml of water. Exactly one hour later, they again voided and were immediately given the infusion which was administered at a constant rate to require one hour for its completion. Urine specimens were obtained at the close of the infusion and at exactly hourly intervals for 2 additional hours. All hourly urine specimens, beginning with those obtained at the start of the infusion, were measured and analyzed for sodium, potassium (by flame photometer), and chloride. For the purposes of this study, the excretion rates in the hour's specimen obtained at the end of the infusion were compared with excretion rates per hour in the combined 2 hourly specimens subsequently collected.

*Results.* The mean excretion of sodium in mEq/hr in the control group was 7.7 at the start of the infusion, rose to 9.4 at its close, with a further increase to 9.6 in the 2-hour period after the infusion. In the serotonin group the initial value was 5.9, rose to 7.2 at

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