organs. MCA increases the amino acid incorporating activity in the liver of male rats (9) and stimulates the formation of thyroxine glucuronide by the microsomal fraction of hepatic cells in males and females (10). The chemical also releases prolactin from the pituitary gland of sexually mature females (11).

Thyroiditis in rats given s.c. or oral MCA was more frequent in females than in males. This finding is similar to that in human beings, since the lesion is seen more often in women than in men (12).

Summary. Buffalo strain rats were given a single s.c. injection of 4 mg of MCA in corn oil. Thyroiditis was observed in 10 of 13 females and 3 of 14 males. The glands were larger in the females. The thyroiditis could not be correlated with the presence of s.c. tumors.

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Received June 14, 1968. P.S.E.B.M., 1968, Vol. 129.

Proximal to Distal Secretory and Absorptive Gradients of the Rat Small Intestine* (33358)

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Absorption and secretion in the small intestine vary along its length (1). This systematic study of net movements of water, sodium, and chloride further defines the functional characteristics of mucosa in the various regions of the rat small intestine.

Materials and Methods. Male albino rats (200–400 g) were fasted with free access to water for 18 hr. They were anesthetized with intraperitoneal sodium pentobarbital (Nembutal) and the abdomen was opened. The common bile duct was ligated, and inlet and exit cannulas were introduced into the small intestine through small incisions and tied in place. Two or 3 gut segments were studied simultaneously by recirculation of 16 or 26 ml of solution from separate reservoirs through each segment for 3 hr. Blood was drawn from the vena cava at the beginning and at the end of some experiments. During the procedure the rats were warmed with heating lamps and the abdomen was kept moist with saline-soaked gauze. At the end of the experiment the entire small gut was stripped from the mesentery. The length and wet weight were measured immediately on all segments from pylorus to ileocecal value, whether perfused or not.

Transmural potential differences (PD) were measured during some studies with agar–saline bridges in contact with mucosal and serosal fluids. The mucosal bridge was placed intraluminally through the entry can-

* Supported in part by Research Grant AM02354 from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health.

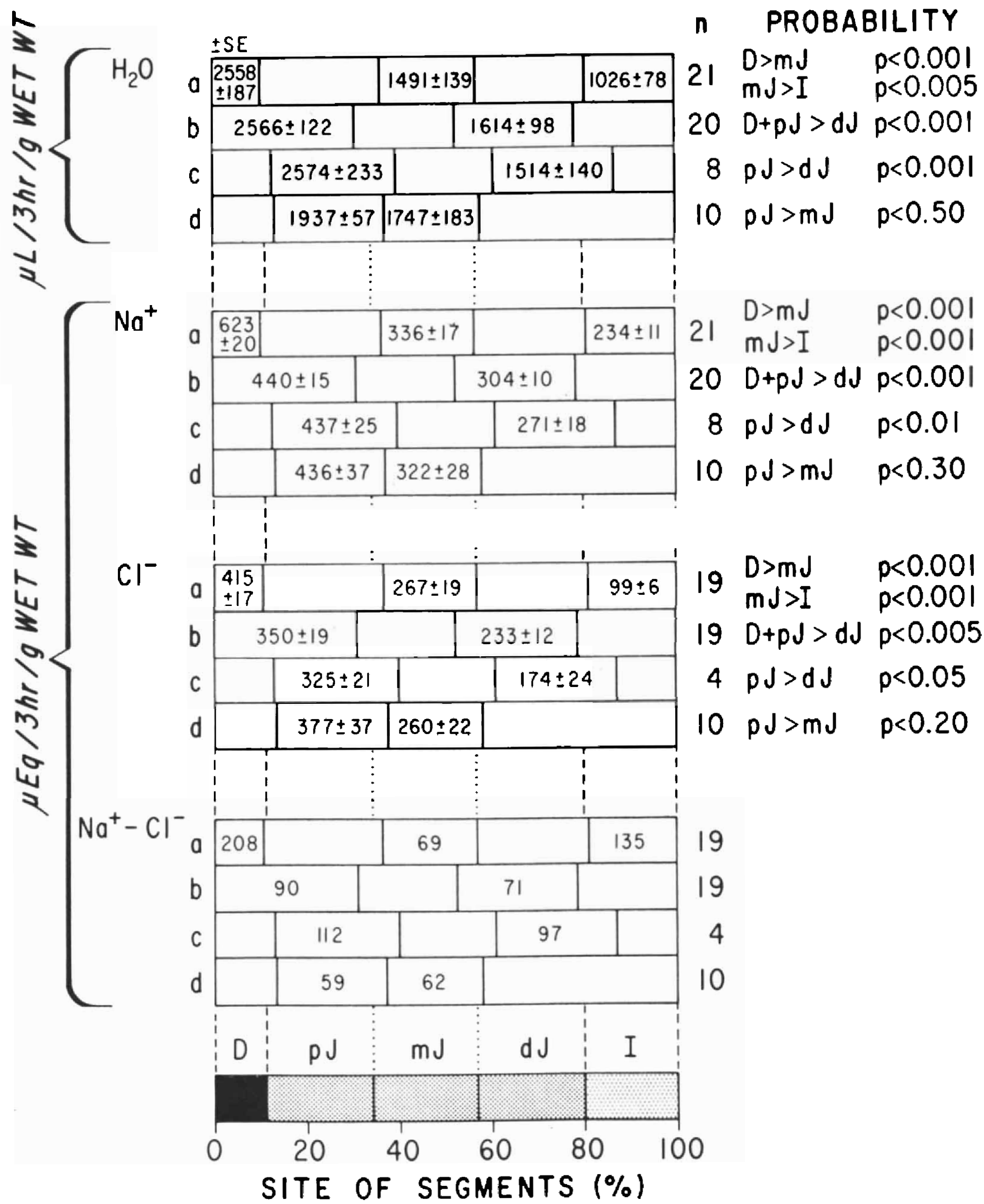
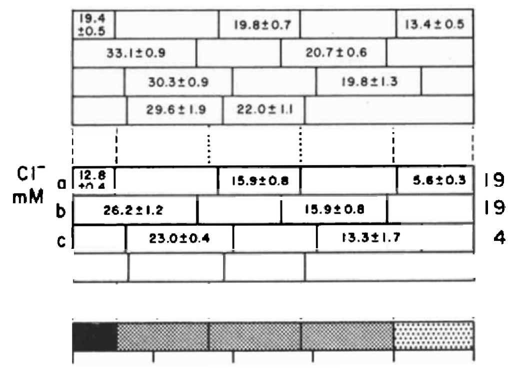


FIG. 1. Secretion of water, sodium, and chloride by segments of rat small intestine during 3 hr of recirculation of 300 mM (315 milliosmoles/kg) mannitol. Values are mean with one standard error. The small intestine was divided into 5 segments as shown by the bar graph at the bottom of the figure: duodenum (D), proximal, mid, and distal jejunum (pJ, mJ, dJ), and ileum (I). The segments and their locations are expressed in terms of their wet weights relative to total wet weight of the small intestine and are indicated by corresponding lengths on the bar graphs (a,b,c,d). Thus, the duodenum (the segment from the pylorus to the ligament of Treitz) was the proximal 11%, and the distal 20% was taken as ileum. The intestine between these segments was divided approximately into thirds. The following types of studies are represented: (a) short D

segments studied simultaneously with mJ and I segments weighing approximately twice as much as D; (b) studies in which a long proximal segment (D plus most of pJ) was compared with a dJ segment of similar weight; (c) and (d) 2 segment studies in which J segments of nearly equal weight were compared. The number of animals (n) for each type of study is shown at the right of each bar graph next to the p values for significance of differences between the segments. Except for adjacent segments, all differences are significant. The secretion rates for H_2O, Na^+, and Cl^- were highest in D and showed a progressive distal decrease. The difference, Na^+ less Cl^-, was always positive, indicating more rapid secretion of sodium than of chloride.



nula of each segment, and the serosal bridge was in the abdominal cavity. The bridges were led to a pair of matched calomel cells (Radiometer, Copenhagen) which were connected to an expanded scale pH meter (model 76, Beckman Instruments, Inc., Fullerton, California). The PD was measured at 0.5 hr intervals during the experiment. The solutions circulated were 300 mM mannitol or 152 mM sodium chloride. All solutions contained PEG (polyethylene glycol, Carbowax 4000, Union Carbide Corp., New York, New York) in a concentration of 2 mg/ml. Initial solutions, reservoir contents, and serum were anlayzed for sodium (Baird internal standard flame photometer) and chloride (Buchler-Cotlove chloridometer) at the end of the study period. The PEG was analyzed by an automated modification of the method of Hyden (2).

Secretion is defined as the measured net entry and absorption as the measured net disappearance of sodium, chloride, and water from the intestinal lumen. Data were calculated as follows: (i) Secretion (μmoles/3 hr/g) $= 16 \times C_f \times$ PEG R/g; (ii) Absorption (μmoles/3 hr/g) $= 26 \times [C_i - (C_f \times \text{PEG } R)]$/g; where the subscripts i and f refer to initial and final values, 16 or 26 = initial volume (ml) of fluid circulated; C = concentration of sodium or chloride (μmoles/ml), or PEG (mg/ml); g = segment wet weight (g); PEG $R = C_i/C_f$ for PEG. Since PEG is essentially nonabsorbed, PEG R is the ratio of final to initial volume.

Results and Discussion. Figure 1 shows the location of the intestinal segments studied and their secretion of water, sodium, and chloride into a 300 mM solution of mannitol. Final sodium and chloride concentrations in the luminal solution are shown in Fig. 2. Absorption by the segments when 152 mM

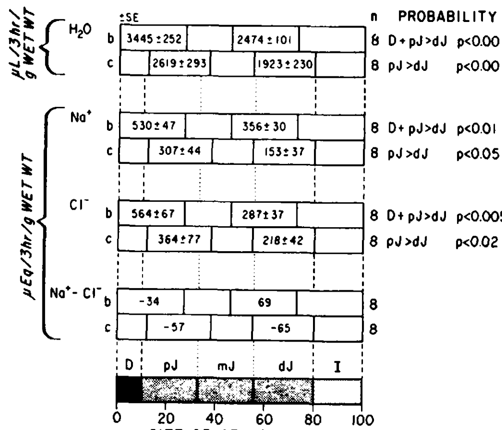


FIG. 3. Absorption of water, sodium, and chloride from rat small intestine during 3 hr of recirculation of 152 m*M* (283 milliosmoles/kg) sodium chloride. Relative positions of segments and their proportionate part of the intestine are indicated as in Fig. 1. Studies correspond to (b) and (c) of Fig. 1: b circulation of a long proximal segment (D+pJ) simultaneously with a dJ segment of similar weight; c comparison of 2 J segments of nearly equal weight. As shown by *p* values on the right, absorption rates were significantly higher in the proximal than in the distal segments. The difference, Na^+ less Cl^-, was usually negative, showing more rapid absorption of chloride than of sodium.

cally along the length of the small intestine. Sodium and water secretion by the distal duodenum and the ileum (a segment 16-cm proximal to the cecum) was studied in the dog by Hindle and Code (3). When 300 m*M* mannitol was placed in the isolated segments of dog intestine, sodium accumulated in the lumen: 3.5 meq in the duodenum and 0.5 meq in the ileum during a 4-hr period. Mean serosal surface area data of Hindle and Code (3) (duodenum 89 cm^2, ileum 102 cm^2) can be used to calculate sodium secretion rates in the dog of 39 μeq/4 hr/cm^2 for the duodenum and 5 μeq/4 hr/cm^2 for the ileum. To compare our rat studies with those done in the dog, we converted our rat data (Fig. 1) to μeq/3 hr/cm^2 using our mean value of 18.2 cm^2 of serosal surface/g of intestine: proximal sodium secretion rates were 34 and 24 μeq/3 hr/cm^2 in the duodenum and proximal jejunum, respectively; the ileal secretion rate was 13 μeq/3 hr/cm^2. Thus, proximal secretion rates in the two species were similar but ileal rates were higher in the rat. Final sodium concentrations in the dog were 105 m*M* in the duodenum and 20 m*M* in the ileum. In the rat we found the proximal sodium concentrations to be 19–33 m*M* and distal to be 13–21 m*M* (Fig. 2). Thus, the initial high plasma-to-lumen concentration gradient was less well preserved in the dog than the rat.

The pattern of water movement differed in the 2 species. With 300 m*M* mannitol in the dog, intraluminal volume was unchanged after 4 hr in the duodenum, whereas in the ileum the solution was almost completely absorbed. The rat showed a 10–20% increase in the initial 16-ml volume in proximal and a 5–10% increase in distal segments (Fig. 1). Thus, there was always net water secretion in the rat, whereas in the dog, ileal mannitol absorption permitted essentially complete water absorption.

Absorption of sodium, chloride, and water has been studied along the length of the rat small intestine, although the anion composition differed from that used in the present studies. Parsons (4) used a solution containing sodium (160 m*M*), chloride (135 m*M*), and bicarbonate (25 m*M*) to compare jejunal (30-cm segment distal to the duodenum) and ileal (30-cm segment proximal to the cecum) absorption in the rat. He found net absorption of water, sodium, and chloride (4) as we did in our studies with 152 m*M* sodium chloride. Water and sodium absorption were most rapid from the jejunum. Chloride absorption did not differ between the segments. To compare our data with Parsons (4) we recalculated his data using the values for wet and dry weights of intestine given in the paper. Parsons' absorption rates per 4 hr/g of wet weight were as follows: jejunum; water, 12,203 μl; sodium, 2220 μeq; chloride, 1303 μeq. Our absorption rates per 3 hr/g of wet weight in a comparable segment (Fig. 3) were as follows: water, 2619 μl; sodium, 307 μeq; chloride, 364 μeq. Thus, Parsons' values are substantially greater than would be expected simply from comparison of 4-hr with 3-hr data. In another study of rats by McHardy and Parsons (5), phosphate was substituted for bicarbonate.

The perfusion solution contained sodium (160 m*M*), chloride (120 m*M*), and phosphate (25 m*M*). Recalculation of their jejunal data, as above, gave the following comparison between their absorption rates at 1 hr (given first) and our values at 3 hr: water 4559 and 2619 μl; sodium 481 and 307 μeq; and chloride 315 and 364 μeq. Thus, except for chloride, McHardy and Parsons' absorption rate per hour was greater than our rate per 3 hr. It is unlikely that the more rapid absorption rates observed by the previous investigators can be explained by the higher intraluminal sodium concentration nor by the presence of the bicarbonate or phosphate in the solution placed in the lumen. Although our loops were distended by the intraluminal solution under a pressure of 15 cm of water, Parsons (personal communication) has suggested that his higher absorption rates may have been caused by the higher intraluminal pressure in his circulation system.

Code *et al.* (6) compared absorption of water and sodium from the duodenum and ileum of the dog from Tyrode's solution and measuring fluxes isotopically. They interpreted their studies as demonstrating a net water and sodium absorptive function for the ileum, and equilibration with little net absorption in the duodenum. This contrasts with the present and previous findings (4) in the rat of higher proximal than distal absorption of water and sodium.

The transmucosal potential differences were lumen negative with the sodium chloride solution (duodenum, —4.3 mV; midjejunum, —4.4 mV; ileum, —5.3 mV; mean values, $n = 4$). The pattern of the potentials does not parallel the absorption rates which were greater in the more proximal segments. Potentials were lumen positive with the mannitol solution (duodenum, +19.9 mV; midjejunum +26.9 mV; ileum +28.1 mV; mean values, $n = 4$). The positive intraluminal potential is consistent with a sodium ion diffusion potential. There is no evident correlation between the PD and the ion movements (Fig. 1). The lowest potential was in the duodenum, where sodium secretion and the difference between sodium and chloride secretion rates were greatest. There was little difference between potential difference values in midjejunum and terminal ileum, even though the secretion rates differed significantly.

Summary. Secretion of sodium, chloride, and water was most rapid in the proximal small intestine and showed a progressive distal decline when osmotic and concentration gradients were imposed by intraluminal 300 m*M* mannitol. Like secretion, absorption of sodium, chloride, and water from 152 m*M* sodium chloride solution was highest proximally and showed a progressive distal decrease. The pattern of transmucosal potential differences showed no correlation with absorption and secretion rates.

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Received June 18, 1968. P.S.E.B.M., 1968, Vol. 129.