REGULATION OF SALT AND WATER ABSORPTION BY THE CANINE ILEUM DURING HEAD UPWARD TILTING

A Thesis

Presented to

the Faculty of the Department of Biology

University of Houston

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

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by

Roberto San Martin

August 1969

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ABSTRACT

Head upward tilting causes a compensatory reduction in blood flow to the gut. The purpose of this investigation was to determine if head upward tilting could alter the rate of intestinal absorption of salt, water, and sugar by virtue of reflex action on the cardiovascular system and also to determine which aspect of intestinal transport is primarily affected.

Mongrel dogs of both sexes were used in this study. Unidirectional fluxes of ^{22}Na, $^{3}H_2O$, and 3-O-$^{14}CH_3$-D-glucose were measured from a ten inch segment of terminal ileum which had been isolated with its nerve and blood supply intact. Despite reduced blood flow to the gut, net salt and water absorption increased. A decrease in the absorption of 3-O-methyl-glucose was noted. Increased transmural potential, with the mucosa becoming more positive, was observed during the head upward tilting period.

The changes in net flux of Na were due to the combined effects of changes in the influx and outflux of Na, neither one by itself being significantly altered. The increased net absorption of water was due to an increased difference between the influx and outflux of water, both of which decreased significantly. Reduction of the sugar absorption could be accounted for by the decreased blood supply to the segment. This reduction in blood supply can decrease transport by failing to supply sufficient oxygen and nutrients to maintain a normal level of activity for all transport processes. Increased transmural potential could be accounted for by the decrease in NaCl concentration in the intestinal lumen.

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I. INTRODUCTION

INTRODUCTION

A change from the supine to the vertical position is accompanied by an increase in heart rate, diastolic pressure, and peripheral vascular resistance along with a decrease in cardiac output and stroke volume (1, 2). Sympathetic nervous system activity is increased to compensate for the reduced cardiac output and stroke volume, and may extend to peripheral organs as well as the heart.

Abbrecht and Malvin (3) have shown that a decreased blood flow to the kidney causes the excretion of a hypertonic urine due to the increased relative reabsorption of water. This change in reabsorptive capacity has been attributed to counter-current mechanisms within the kidney (4,5). Similar effects due to decreased blood flow may be present in the gut since the gut has a functional counter-current system (6).

Effects of decreased blood flow to the denervated small intestine have been studied by Varro et al (7). Reduction of blood flow to about 50% of normal caused no significant change in oxygen consumption or glucose absorption. Reduction of blood flow below 50% resulted in a proportionate decrease in oxygen consumption and glucose absorption. This direct correlation between oxygen consumption and glucose absorption suggests that the decreased absorption is due to an inadequate oxygen supply to the gut. It was, therefore, of interest to study the relationships between an apparent blood loss to the head and thorax, produced by head upward tilting, with a homeostatic

activation of increased gut absorption. Mailman (8) has shown that the canine intestine may act as a homeostatic organ, along with the kidney, for the regulation of water and salt due to a real or apparent blood volume reduction. Hemorrhaging or tilting an animal head upward increased reabsorption of salt and water by the gut. Infusion of isoncotic dextran to an animal had no effect on absorption of salt and water by the intestine. Therefore, it was concluded that the initiation of some homeostatic mechanism rather than the change in extracellular volume caused the increased reabsoprtion during hemorrhage or head upward tilting.

The intestinal vascular bed is a complex arrangement of vessels specialized to cope with the metabolic and transport functions of the gut. The arteriolar area, together with the precapillary sphincter area, are primarily responsible for the control and distribution of blood supply to the intestinal capillaries. The homeostatic control of blood flow to the viscera during head upward tilting is probably mediated at this level.

The surface area across which exchange can occur in the intestine is large. The capillary filtration coefficient, a measurement of the magnitude of the available capillary surface area, varies from a value of 0.1 at rest to a maximum of 1.0 indicating full opening of all the capillaries or maximum vasodilation. At a capillary filtration coefficient of 1.0 and at a maximal blood flow to the intestinal smooth muscle, the mucosal blood flow would fall in the

range of 500 ml per minute per 100 grams wet gut weight (6, 9). This value represents a potentially large blood supply that must have fine channels of regulation. Vasoconstriction is mediated by sympathetic activity of the alpha adrenergic fibers and is primarily responsible for the redistribution of blood from the mucosal regions to the submucosal regions (6). Histological examination of the intestinal villi suggests the presence of a counter-current exchanger formed by the hairpin loop of the ascending artery with the descending vein and the capillary network in between. Only 10 to 30 micra separate the two blood flows; a distance not posing a great barrier to diffusion of small molecules (6). Reduction in net absorption may be caused by the counter-current transfer of a substance from the venous effluent back to the arterial affluent. The counter-current system may also be able to concentrate molecules within the serosal compartments during reduced blood flow to the gut mucosa, thereby producing a hypertonic effluent.

Autoregulation of blood flow to the intestine implies the presence of homeostatic mechanisms to provide the gut with an adequate supply of blood even though either the arterial pressure or the vascular resistance of the vessels may vary. This concept is especially important during postural changes since decreases in the vascular resistance of the vessels would lead to increased blood flow to areas of need in the gut. Both the aortic and the carotid baroreceptors play important roles in the regulation of systemic and cerebral blood flow. Their primary mode of action is through control

of heart rate and stroke volume. On the assumption of the head upward position, the fall in arterial pressure stimulates the baroreceptors. Stimulation of other receptors in other vascular areas occurs since anesthetized dogs are capable of producing compensatory blood pressure changes even after sectioning of the vagus and the aortic and carotid sinus nerves (10). Green (11) has shown that the intestinal vascular bed contains in addition to alpha receptors, very powerful beta adrenergic vasodilator receptors. Bond and Green (12) have demonstrated that the intestinal vascular bed is capable of active participation in the homeostatic regulation of blood adjustments when stimulated by the carotid sinus pressure receptors. Thus, homeostatic control of intestinal blood flow is known to exist but its precise mode of action has not been determined.

Mean blood flow through the canine ileum has been calculated by Geber (13) to be 83 ml per minute per 100 grams wet gut weight. Studies by Delaney and Custer (14) on the gastrointestinal blood flow in the dog indicate that the small intestine received a mean of 72 ml per minute per 100 grams gut weight or 6.48% of the cardiac output.

Correlation of the homeostatic effects of head upward tilting with salt, water, and sugar absorption may provide further insight into the complex mechanism of gut action. Blood flow to the gut may or may not be the primary factor determining the absorption capacities of the gut. Decreases in blood flow to the gut during head upward tilting may play a secondary role in absorption or may serve to activate a change in the net flux of substances by acting on either

the influx, the outflux, or both. Changes in the ionic and aqueous contents of the gut lumen may provide vital clues to the possible involvement of gut action in a homeostatic mechanism of control of the body fluids.

Absorption of salt, water, and sugar from the intestine is an important physiological function. Absorption involves passage of the substance in question from the luminal or mucosal side of the intestinal epithelial cell, through the cell, and to the basal or serosal end to be transported to the circulatory or lymphatic systems. In addition to the nutrient function of the intestinal epithelial cell, the cell must be able to maintain its internal environment in a different state from that of its mucosal and serosal compartments.

Ussing in 1949 (15) presented an equation to describe simple or passive diffusion. He considered the process of passive diffusion across membranes as being due exclusively to the concentration and electrical potential differences across the membrane. Any process that met the requirements of the equation was considered to be passive diffusion. Processes of membrane transport that do not meet the requirements of Ussing's equation are due to one or more of the following: exchange diffusion; single-file diffusion; solvent drag; active transport; reactions within the membrane.

The concept of exchange diffusion was proposed by Ussing in 1947 (16, 17) to explain increases in unidirectional fluxes across membranes with no increase in the net flux. This mechanism is explained as the exchange of a molecule on one side of a membrane with an identical molecule on the other side. The

presence of a carrier in the membrane is not an absolute prerequisite for the process to occur.

Hodgkins and Keynes (18) proposed the concept of single-file diffusion to explain certain transport processes that always occur in the direction of the electrochemical gradient. They postulated that membrane pores were lined by cations and that cations of the same species would pass in single-file through the pores in the direction of the electrochemical gradient.

Solvent drag has been demonstrated in the intestine by Hakin and Lifson (19). This transport process may be defined as the transfer of solute as a direct consequence of solvent transfer. Anderson and Ussing (20) have shown that an uncharged molecule may be transferred against an electrochemical gradient by this process.

Active transport may loosely be defined as any process that results in the net transfer of a substance against its electrical and chemical gradients. Active transport must be specific for its particular carrier; must be capable of being competitively inhibited; must be able to be saturated; must require metabolic energy which, when inhibited, is capable of completely stopping the process; and must not be explained by the above theories of passive or facilitated diffusion. Osterhout and Lungergardh (21-24) first proposed the concept of carrier mediated transport. Molecules may enter the intestinal epithelial cell either by diffusion or by complexing themselves with a specific carrier. Once inside the cell, a concentration gradient carries the complex to the internal surface where dissociation

occurs and the molecule either diffuses or is pumped out of the cell. The carrier diffuses back to the mucosal surface where it is capable of combining with another molecule constituting a cyclic system of transport. The end result is that the molecule is transported from the lumen of the gut to the blood. Diffusion or active transport may also transfer a molecule from the serosal to mucosal end.

Ingraham and Vissher (25) in 1938 showed that Na was capable of being transferred by the canine intestine against its concentration gradient. All evidence seems to point to the fact that Na transport across the small intestine is due primarily to an energy dependent process rather than to a passive diffusion process. Sodium transport can occur from the mucosal to serosal surfaces of the intestinal epithelial cell in the absence of either an electrical or chemical gradient. Studies by Curran (26,27) on *in vivo* and *in vitro* rat ileum have shown that the observed net fluxes for Na are similar regardless of the method used. The calculated Ussing ratio for Na was different from the observed Ussing ratio for Na suggesting that passive forces are not responsible for Na movement. Curran also studied the effects of metabolic inhibitors on the Na fluxes. He found that the serosal to mucosal flux of Na was not affected by the inhibitors while the mucosal to serosal flux was significantly reduced. These studies suggest that the mucosal to serosal flux for Na seems to be due to active transport while the serosal to mucosal flux for Na seems to depend upon passive diffusion.

Curran (26-30) proposed that solvent drag had no significant effect on the Na fluxes across the everted sacs of rat intestine. Schultz and Zalusky (31, 32) in similar studies suggested that if solvent drag did have an effect on Na transport across the membrane then it should follow that the solute being transferred should be NaCl along with the aqueous solvent. Since the transfer of Cl was negligible, solvent drag could not have an important role in Na transport.

Chloride has been shown to be actively transported by the canine ileum in vivo (33). Application of the Ussing equation and the use of acetazolamide as an inhibitor indicated that passive transport of Cl does not occur in the canine ileum. Bicarbonate and hydrogen ion fluxes maintain electrical neutrality and must be taken into account whenever Cl is transported across the intestinal epithelial cell. The exact nature of Cl transport still remains uncertain.

Absorption of K occurs in the canine ileum whenever the luminal concentration of K is greater than 5-6 mEq/L (34). Insorption of K in the small intestine can be explained by passive processes and is concentration dependent.

Water transport across epithelial membranes has been extensively investigated. Several proposals for the transport of water seem to indicate that the process is coupled to active solute transport and can be blocked by metabolic inhibitors. Curran (28) proposed a double membrane model for water transport. In 1938 Ingraham proposed the fluid circuit theory for water transport (35). Diamond proposed the standing gradient

osmotic theory for water transport across the rabbit gall bladder epithelium (36). Ingraham's theory is essentially one of active water transport with a concomitant passive solute transfer. Two flows across the membrane are proposed with one being hypertonic to the other. Thus a difference in the net flux of solute is accomplished. Curran's theory of water transport by the intestine is one of passive water transfer coupled to active solute transport. This process requires the transport of solute from the mucosal end of the cell which has a membrane lined with small pores. The transport of solute into the compartment of the cell creates an osmotic gradient which is responsible for the movement of water into the compartment passively. On the serosal end of the cell, a second membrane with large pores allows the passage of the water with little resistance to flow. Net flow is from mucosa to serosa due to the differences in membranes and the active solute transport creating an osmotic gradient in a rigid compartment. Diamond's theory is similar to that of Curran. Diamond suggested that the solute is actively transported across the lateral borders of the cells which, in turn, sets up a standing gradient or concentration gradient of solute in the lateral cell space with the mucosal end being hypertonic and the serosal end being nearly isotonic to plasma. Water is pulled in passively by the gradient from the cell interior in an effort to dilute out the concentration difference of solute. This process is dependent on metabolic energy and not only explains the net transport of water from the mucosal to serosal end

of the cell but also explains a mechanism for solute transport past the brush border.

A transmural potential can be taken to be indicative of ion transport. Potential differences or changes may be due to two types of ionic movement. The first is the active transport of a neutral salt such as NaCl from one end of the cell to the other with the concomitant back diffusion of one ion species down its electrochemical gradient. The second type of ionic movement is electrogenic whereby a potential difference is created directly by the transport of unpaired ions. A diffusion potential may be created in the ileum as the concentrations of the various ionic species are changed.

The intestinal epithelial cell, the kidney tubule, and the epithelial cell of the toad bladder have been shown to be capable of actively transporting Na, and in some cases Cl against an electrochemical gradient, and of transporting water passively. Recent investigations on toad bladders (37) have shown that the potential difference can be accounted for by the active transport of Na ions from the mucosal to the serosal end of the epithelial cell. The apical end of the cell is permeable to Na while the basal end is permeable to K. Alterations in these relative permeabilities due to factors such as the pH of the luminal contents, the passive transport of water or some other ionic species, and the formation of bicarbonate in the gut lumen may tend to change the potential difference across

the gut (38).

Observed transepithelial potential difference is the result of the net difference between two potentials: from lumen to cell interior and from cell interior to blood. Increases in the serosal membrane potential are observed when actively transported substances such as glucose or alanine are added to the luminal contents of the intestine. Phlorizin reduces this effect. Mucosal membrane potential is not affected by these actively transported molecules (39).

Crane (40) has shown that the D form of glucose is preferentially transported in the rat intestine. Faust (41) demonstrated that, in the hamster jejunum, the preferential binding of D-glucose to the brush border of the epithelium is probably the intial step in the active transport of the sugar. Interaction of glucose transport with Na transport has been observed by Nelson and Beargie (42) and by Schultz and Zalusky (39). Taylor (43) suggested that actively transported sugars increase the rate of active Na absorption regardless of the extent to which the sugars are metabolized by the tissues. Increased Na flux may in turn be related to the change in the transmural potential. Active Cl transport may or may not be coupled in some fashion to the active Na transport. Coupling of Cl to Na may play an indirect but significant role in the development of the transmural potential.

The intestinal epithelial cell is functionally polarized with respect to sugar transport. Cocco et al (44) have shown the presence of a selective barrier affecting the movement of sugars from the

serosal to mucosal ends of the intestinal epithelial cell where the ratio of 20:1 is seen for mucosal to serosal: serosal to mucosal fluxes. Evidence seems to indicate that the brush border area is intimately associated to the entry and accumulation of the sugar during active transport. Crane (45) has proposed the existence of a mobile carrier to account for sugar transport across the intestine. His model postulates that the carrier is like an enzyme with active sites which can be inhibited by ionic species or by monosaccharides with an affinity for the same carrier. Miller and Crane (46) proposed that the primary driving force behind the mobile carrier is the sodium gradient which is maintained by the Na pump. Under normal conditions the Na pump maintains a high extracellular Na concentration with a high intracellular K concentration. Crane proposed that the Na binds to the carrier which in turn increases the affinity of the carrier to the sugar molecule and vice versa. The loaded carrier now diffuses to the interior surface of the cell membrane where the sugar is released together with the Na. The unloaded carrier now has a high affinity for K and the K-carrier complex diffuses toward the outside where K is released and the carrier is now able to pick up Na and sugar. The net effect of this process is to transport sugar from the mucosa to the serosa, in addition to increasing the internal Na which in turn activates the Na pump; thus the indirect effect of the ionic gradient provides the energy to drive the mobile carrier from mucosa to serosa and back. The affinity between the carrier and the sugar has been

found to be directly related to the concentration of the Na present.

Taylor (47) has demonstrated the presence of a Na-K dependent ATPase in the brush border of the guinea pig small intestine. This ATPase is of the same kind proposed by Skou (48) which activates the membrane Na pump. Although other investigators (49) have demonstrated that inhibition of the ATPase system at the serosal end of the cell completely blocks Na transport, the available evidence for the brush border pump must be kept in mind.

Kohn (50) has demonstrated that both glucose and galactose are transported by the same carrier since their rates of transport are similar and the two sugars are competitive inhibitors for each other. Crane (40) has shown that the D form of glucose is preferentially absorbed over the L form although both forms of the sugar are actively transported. 3-O-CH_3- D-glucose is actively transported by the same carrier that transports glucose and galactose but of the three, only glucose is metabolized by the small intestine.

Tidball (51) has presented evidence for a direct cholinergic effect on intestinal absorption in dogs. Crocker and Munday (52) have shown an effect of aldosterone and angiotensin on water absorption in the rat jejunum but the rats had to be on high sodium diets to demonstrate this. Torphy (53) has noted a rise in urinary excretion of norepinephrine when human subjects were tilted to a 44 degree angle from the supine position. Bastide and Jard (54) have studied the effects of norepinephrine on the active transport of Na across the

isolated frog skin. They found that norepinephrine stimulates active transport of Na which is due to an increase in the influx of Na with no effect on the outflux. Aulsebrook (55) also demonstrated an increased absorption of both salt and glucose by the everted rat gut due to the action of catecholamines. Work by Mailman and Eddings suggests the possible role of a hormonal or humoral agent in the regulation of intestinal absorption in the everted rat ileum (56). The release of this blood borne substance may be mediated by nervous stimulation in response to a reduced blood volume to the head and thorax.

II. STATEMENT OF THE PROBLEM

STATEMENT OF THE PROBLEM

Little work has been done on intestinal blood flow and its relation to intestinal absorption. Considering the importance of an adequate supply of nutrients and oxygen to the gut, experimentation in this area has been neglected. Regulation of intestinal blood flow by gut contents is little affected unless the contents are strongly hyperosmotic. Lack of regulation indicates that any changes in blood flow to the gut would be caused by changes in the physiological state of the animal. Head upward tilting causes a compensatory reduction in blood flow to the gut. The purpose of this investigation was to determine if head upward tilting alters the rate of intestinal absorption of salt, water, and sugar by virtue of reflex action on the cardiovascular system and also to determine which aspect of intestinal transport is primarily affected.

III. METHODS AND MATERIALS

METHODS AND MATERIALS

ANIMALS

Mongrel dogs of both sexes weighing between 13.5 and 17.5 kilograms were used. The animals were obtained from Baylor University Medical School and dewormed one week before being delivered. The animals were maintained on hospital diet and were allowed water *ad libitum*. After an overnight fast, the dogs were anesthetized with sodium pentobarbital (30 mg/kg) intravenously and then transferred to the University of Houston.

SURGICAL PROCEDURES

Subsequent doses of Nembutal were administered as needed to maintain the proper level of anesthesia. The trachea was cannulated to facilitate respiration and the femoral artery and vein of the left leg exposed. A polyethylene catheter (PE 240) was threaded up the femoral artery to a level near the superior mesenteric artery. The catheter was connected to a blood pressure transducer and to an ink writing polygraph (E&M Instrument Co.). The femoral vein was cannulated with a saline-filled-polyethylene tube to the end of which was attached a three-way valve.

An eight inch midline abdominal incision was made using an electrocautery knife (National) and the intestinal area was prepared in such a way as to cause minimal displacement and disturbance of the arrangement of the gut *in situ*. A ten inch segment of terminal ileum a few inches from the ileocolic artery was isolated with its nerve and blood supply

intact. Two small incisions through the segment were made with the cautery knife. At one end of the segment a rubber tube was inserted which was connected to a glass funnel while the other end served as the drainage. The entire segment was flushed with warm isotonic NaCl and then with isosmotic NaCl (9 gm/l)-$MgSO_4.7H_2O$ (64 gm/l), (v/v), until the effluent was clear. Both ends of the gut were closed off with rubber stoppers. Two plastic tubes extended through one of the stoppers and into the lumen of the gut. One of these tubes was a salt bridge consisting of a 1M KCl- 4% agar electrode. The other tube was perforated and was connected to a valve extending outside the rubber stopper. Gut samples were obtained through the valve.

One of the mesenteric veins draining the segment was cannulated with a Jelco IV catheter. The Jelco was connected to the femoral vein cannula so blood leaving the intestine was immediately returned via the femoral vein. Previous to cannulation the animal was injected with 200 units/kg of heparin (Sigma). Doses of the same amount were given every additional 1/2 hour by means of the three-way valve.

The KCl-agar electrode along with a reference electrode were used to complete the circuit to a high impedence electrometer (Keithy) which was used to measure transmural electrical potentials. The cannula, gut, and reference electrode were placed in a lucite trough filled with warm saline and surrounded by a heating pad. During all surgical procedures the gut was wrapped with Saran Wrap over gauze and kept warm and moist.

SAMPLING

The gut was then filled with a solution of equal volumes of isotonic NaCl and isosmotic $MgSO_4$ to which had been added 2uC/100 ml of ^{22}Na, 2uC/100 ml of 3-O-$^{14}CH_3$-D-Glucose, 30uC/100ml of $^{3}H_2O$ (New England Nuclear) and phenol red at a concentration of 8 mg/100ml. The segment was filled with a known volume and in a manner so as not to induce excess stretching. Samples (1.5-2.0 ml) were taken every 15 minutes for one hour. Blood flow from the gut segment was measured by collecting blood in a graduated test tube for one minute. At the end of the period the gut was emptied (and the volume noted), flushed, and refilled with fresh isotope solution. The same procedure was followed during three periods: Control; Experimental (where the entire animal was tilted head upward at a 45^{o} angle); and Recovery (where the animal was returned to the supine position). The periods will be referred to as I, II, and III, respectively.

CHEMICAL DETERMINATIONS

Chemical determinations were carried out by standard methods on all gut and blood samples. Of the samples, 0.2 ml was used for the analysis of osmotic pressure by a freezing point osmometer (Precision Instruments). Sodium and Potassium concentrations were determined by flame photometry (Eppendorf) from a 0.1 ml sample. An equal portion of the sample was used in the determination of chloride concentration by the coulombmetric titration with a Cotlove choridometer (Buchler Instruments). An aliquot which was collected anaerobically was employed

in the determination of pH and P_{CO_2} in a pH-P_{CO_2} analyzer (Instrumentation Laboratories). Radioactive isotopes were counted from a 0.1 ml sample. The sample was dissolved in 10 ml of scintillation cocktail consisting of 1700 ml of Toluene (Mallinckrodt), 300 ml Bio-Solv III (Beckman), and 12 grams PPO (Beckman). Quench curves were generated with phenol red and with plasma. Counting was carried out in a tri-channel ambient temperature Beckman LS 150 scintillation counter. Samples were corrected for quenching and spillover by suitable equations. Phenol red concentrations employed as indicators of the volume of luminal contents were determined spectrophotometrically in both acid (HAc,pH 2.2) and basic (NaOH,pH 12.0) pH at a wavelength of 560 millimicrons to correct for chromogenic compounds in the gut samples. Any chromogens present at acidic pH were in negligible concentrations. Unidirectional fluxes of water and Na were calculated by the method of Berger and Steele (57). All calculations were carried out by an S.D.S. Sigma 7 computer using a computer program in the Fortran language.

STATISTICS

Differences between periods were determined by analysis of variance (ANOV) and paired t tests. The Control period was compared to the Experimental period by paired t tests to determine if head upward tilting had a significant effect on parameters. The Control and Experimental periods were compared to the Recovery period by ANOV to determine if head upward tilting had any prolonged effects on gut absorption. These

comparisons are independent as required by ANOV. Relationships between parameters were determined from the least squares regression line.

IV. RESULTS

RESULTS

The amount of Na absorbed during head upward tilting (Table I) was significantly increased ($p<1\%$) from the amount of Na absorbed during the Control period. A net secretion of Na in period I occurred while in the other periods net absorption of Na was present. The influx of Na into the gut decreases slightly after head upward tilting but the decrease was not significant (Table I). Na outflux did not change greatly after head upward tilting (Table I). Average Na influx for the entire Control period was 0.97 uEq/gm/15 min while the average Na influx during the Experimental period was 0.73 uEq/gm/15min. Na outflux during period I averaged 0.77 uEq/gm/15min while in period II Na outflux averaged 0.80 uEq/gm/15min.

Water was secreted in all three periods indicating that $MgSO_4$ was pulling water into the gut lumen. The flux of water into the gut (Table II) remained fairly constant during the Control period and showed a significant decrease during the Experimental period ($p<1\%$). Influx of water during the Recovery period continued to decrease due to some long lasting effects of the Experimental Period ($p<1\%$). Average influx of water during the Control period was 19.2 ul/gm/min while the average water influx during the Experimental period was 11.5 ul/gm/min. The Recovery period influx of water averaged 10.6 ul/gm/min.

TABLE I

Unidirectional and Net Fluxes of Sodium from the Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

	Time (Minutes)			
Period	0-15	15-30	30-45	45-60
		Na Absorbed (uEq/gm wet gut wt/15 min)		
I	-6.77±(4.71)	-3.32±(5.00)	-1.22±(5.14)	-0.42±(5.01)
**II	-2.00±(6.14)	3.15±(2.96)	1.08±(3.28)	1.61±(1.26)
III	-2.64±(4.40)	0.25±(1.96)	4.33±(3.28)	0.07±(2.02)
		Na Flux In (uEq/gm wet gut wt/min)		
I	1.10±(0.13)	1.00±(0.27)	1.03±(0.23)	0.74±(0.32)
II	1.31±(0.67)	0.69±(0.24)	0.50±(0.17)	0.44±(0.06)
III	0.97±(0.26)	0.61±(0.14)	0.55±(0.14)	0.43±(0.17)
		Na Flux Out (uEq/gm wet gut wt/min)		
I	0.65±(0.13)	0.78±(0.18)	0.94±(0.14)	0.71±(0.13)
II	1.18±(0.26)	0.90±(0.07)	0.57±(0.07)	0.54±(0.07)
III	0.80±(0.05)	0.63±(0.18)	0.84±(0.09)	0.44±(0.17)

Values are mean ±(SEM) at times indicated. *,**, represent a significant difference at the 5% and 1% level respectively. Significance at period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

Outward flux of water (Table II) during the Control period did not vary. Period II outflux of water was significantly decreased ($p<1\%$) from that of the Control period. Average outflux of water during the Control period was 15.9 ul/gm/min. Average outflux of water during the Experimental period was 10.8 ul/gm/min. Water outflux during the Recovery period was also significantly reduced indicating a prolonged effect of head upward tilting ($p<1\%$). Average outflux of water during the Recovery period was 9.3 ul/gm/min.

The amount of water secreted (Table II) during period II declined significantly ($p<1\%$) when compared to the secretion observed in period I. Average water secreted during period I was 49.3 ul/gm/15 min while the average secretion of water during period II was 11.8 ul/gm/15 min. The average secretion of water was 20.6 ul/gm/15 min during period III.

The outflux of 3-0-$^{14}CH_3$-D-Glucose (Table III) decreased during the Control period from 0.040 to 0.014 muMoles/gm/15 min. Experimental period values fell significantly ($p<5\%$) as compared to the Control period values. Absorption of the sugar during the Recovery period was similar to the absorption during the Experimental period but no significant long lasting effects were observed. Average outflux of 3-0-methyl-glucose during period I was 0.027 muMoles/gm/15 min. Average outflux of the sugar during period II was 0.021 muMoles/gm/15 min and during period III average outflux was 0.020 muMoles/gm/15 min.

TABLE II

Unidirectional and Net Fluxes of Water from the Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

Period	Time (Minutes) 0-15	15-30	30-45	45-60
		H_2O Flux In (ul/gm wet gut wt/min)		
I	19.03±(1.88)	19.24±(2.21)	21.12±(3.32)	17.55±(6.01)
**II	14.95±(2.47)	12.03±(1.97)	10.57±(1.88)	8.59±(3.03)
**III	13.57±(0.57)	8.84±(2.14)	10.34±(1.49)	9.65±(2.53)
		H_2O Flux Out (ul/gm wet gut wt/min)		
I	13.62±(1.43)	15.68±(1.37)	17.75±(1.51)	16.73±(3.76)
**II	12.51±(0.94)	11.92±(1.04)	10.05±(0.66)	8.54±(2.24)
**III	10.54±(2.21)	7.56±(1.80)	10.69±(1.93)	8.28±(2.12)
		H_2O Absorbed (ul/gm wet gut wt/15 min)		
I	-81.6±(44.9)	-53.8±(29.4)	-51.0±(37.1)	-10.8±(46.8)
**II	-36.3±(44.6)	- 1.8±(16.9)	- 6.7±(27.9)	- 2.3±(11.9)
III	-45.6±(29.9)	-20.6±(15.8)	5.9±(11.3)	-22.3±(23.9)

Values are mean ±(SEM)at times indicates. *,**, represent a significant difference at the 5% and 1% level respectively. Significance at period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

Chloride absorption (Table III) followed that of Na but at a greater rate. Net absorption was noted in all three periods with the Experimental period averaging a greater amount than the Control period ($p<5\%$). Chloride absorption during the Control period averaged 0.7 uEq/gm/15 min as compared to 2.8 uEq/gm/15 min during the Experimental period and 2.2 uEq/gm/15 min during the Recovery period. Chloride concentration in the lumen at the end of all three periods was lower than the Na concentration in the lumen at the end of the periods.

Potassium was secreted into the gut lumen in all three periods (Table IV). Since the solution placed in the gut contained no K, secretion occurred due to K following its concentration gradient. A decrease in the amount of secretion from the beginning to the end of each of the three periods was observed. Secretion of K during period I averaged 0.95 uEq/gm/15 min. The amount of K secreted in period II was significantly lower ($p<5\%$) than the amount of K secreted in period I. Period II averaged 0.61 uEq/gm/15 min of K secretion. Period III was not significantly different from the first two periods and averaged 0.73 uEq/gm/15 min of K secreted.

Bicarbonate secretion into the lumen of the gut was calculated from the Henderson Hasselbalch equation employing the pH and P_{CO_2} of each sample. Secretion in all periods tapered off near the end of each period and approached similar values (Table IV). Both Experimental and Recovery periods averaged 1.3 uEq/gm/15 min of bicarbonate secretion.

TABLE III

Net Absorption or Secretion of 3-0-methyl glucose and Cl from the Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and A Recovery (III) Period.

Period	Time (Minutes) 0-15	15-30	30-45	45-60
	Flux Out 3-0-$^{14}CH_3$-D-Glucose (muMoles/gm wet gut wt/15 min)			
I	0.040±(0.006)	0.033±(0.001)	0.023±(0.002)	0.014±(0.002)
*II	0.031±(0.006)	0.024±(0.003)	0.017±(0.003)	0.011±(0.003)
III	0.030±(0.008)	0.019±(0.005)	0.021±(0.004)	0.012±(0.002)
	Cl Absorbed (uEq/gm wet gut wt/15 min)			
I	-2.83±(6.31)	2.34±(4.82)	1.81±(4.54)	1.48±(3.45)
*II	0.28±(6.72)	4.96±(3.20)	2.41±(3.12)	3.54±(0.54)
III	0.73±(4.66)	1.46±(2.45)	5.66±(2.84)	1.12±(2.62)

Values are given as average over 15 minutes ±(SEM). *,**, represent significant difference at the 5% and 1% level respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

TABLE IV

Net Absorption or Secretion of Potassium and Bicarbonate from the Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

Period	Time (Minutes) 0-15	15-30	30-45	45-60
	K Secreted (uEq/gm wet gut wt/15 min)			
I	1.42±(0.27)	0.87±(0.19)	0.93±(0.17)	0.64±(0.17)
*II	1.34±(0.21)	0.46±(0.30)	0.38±(0.12)	0.27±(0.08)
III	1.09±(0.33)	0.48±(0.15)	0.64±(0.20)	0.70±(0.31)
	HCO_3 Secreted (uEq/gm wet gut wt/15 min)			
I	2.02±(0.33)	2.80±(0.27)	0.87±(0.50)	1.68±(0.50)
II	1.48±(0.71)	1.26±(0.50)	0.73±(0.19)	1.65±(0.43)
III	1.57±(0.43)	0.45±(0.29)	1.88±(0.42)	1.30±(0.29)

Values are given as average over 15 minutes ±(SEM). *,**, represent significant difference at the 5% and 1% level respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

Period I averaged a slightly higher amount of HCO_3 secretion (1.8 uEq/gm/15 min). The differences were not significant.

Blood pressure (Table V) during the Experimental period was corrected for tilting by subtracting the hydrostatic pressure due to head upward tilting from the recorded blood pressure. The average value of 24 mm Hg hydrostatic pressure was calculated from the perpendicular distance from the tip of the blood pressure cannula to the pressure transducer. This distance averaged 12.8 inches. Relative stability in blood pressure was observed in each period. Mean blood pressure during head upward tilting was significantly lower ($p<1\%$) than the mean blood pressure during the Control period (Table VI). No significant prolonged effects of head upward tilting on mean blood pressure were observed during the Recovery period.

Blood flow through the isolated gut segment was calculated from the average flow through the cannulated vein draining the segment times the number of veins in the same generation. This value was divided by wet gut weight to obtain an estimate of mean blood flow per gram of wet gut. A significantly lower mean blood flow ($p<1\%$) from the gut was observed during head upward tilting when it was compared to the Control period mean blood flow (Table VI). An approximate 50% reduction in average blood flow from Control values (63.2 ml/100 gm/min) was noted in the Experimental period (33.3 ml/100 gm/min). Average blood flow during period III was 53.4 ml/100 gm/min.

Luminal Na concentration in period II was significantly lower ($p<5\%$) when compared to luminal Na concentration in period I (Table VII).

TABLE V

Cardiovascular Changes During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

Period	Time (Minutes) 0-15	15-30	30-45	45-60
		Systolic Pressure (mmHg)		
I	175.0±(9.6)	173.8±(8.5)	172.5±(7.5)	157.5±(11.8)
*II	131.0±(18.5)	131.0±(18.4)	123.5±(21.4)	122.2±(23.0)
III	136.2±(10.7)	133.8±(10.7)	130.0±(10.0)	127.5±(11.1)
		Diastolic Pressure (mmHg)		
I	125.0±(5.0)	123.8±(3.8)	112.5±(7.5)	97.5±(11.8)
II	93.5±(17.5)	86.0±(20.3)	82.2±(20.1)	83.5±(20.9)
III	90.0±(10.0)	90.0±(10.0)	82.5±(12.5)	82.5±(12.5)

Values are mean ±(SEM) at times indicated. *,**, represent a significant difference at the 5% and 1% level, respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

TABLE VI

Cardiovascular Changes During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

Period	Time (Minutes) 0-15	15-30	30-45	45-60
		Mean Blood Pressure (mmHg)		
I	141.7±(6.3)	140.4±(5.1)	132.5±(7.5)	117.5±(11.8)
*II	106.0±(17.8)	101.0±(19.6)	96.0±(20.6)	96.4±(21.6)
III	105.5±(10.0)	104.6±(10.2)	98.3±(11.7)	97.5±(12.0)
		Blood Flow (ml/100gm gut wt/min)		
I	61.4±(5.4)	64.0±(9.9)	70.7±(9.9)	56.7±(8.5)
**II	44.0±(11.8)	24.5±(5.1)	28.1±(3.3)	36.5±(1.0)
III	58.7±(1.4)	48.6±(4.9)	51.3±(1.6)	50.6±(6.4)

Values are mean ±(SEM) at times indicated. *,**, represent a significant difference at the 5% and 1% level, respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Sixteen observations were made on four animals in each of three periods.

Chloride concentrations in the luminal contents were not significantly different among the periods (Table VII). Potassium concentrations (Table VII) in the luminal contents was significantly smaller ($p<5\%$) in period III when compared to period I plus period II, indicating a lasting effect of tilting into the Recovery period. No significant difference between the first two periods was noted with respect to K concentration. Potassium concentration averaged 4.1 mEq/1 in period I and 4.3 mEq/1 in period II. Period III K concentration averaged 3.3 mEq/1.

The pH in the lumen (Table VIII) decreased significantly ($p<5\%$) during the Recovery period when compared to periods I plus II. No significant changes among the periods was established with respect to P_{CO_2} (Table VIII).

Osmotic pressure (Table IX) decreased from an average value of 328 mOsm to a level close to the osmolarity of isotonic saline (300 mOsm). Period II was significantly lower with respect to osmotic pressure when compared to period I ($p<5\%$). Period III indicated a sustained effect of the Experimental period ($p<1\%$).

Transmural potential (Table IX) with the given values representing the polarity of the mucosa, tended to increase in all three periods. The transmural potential was greater in period II than that observed during period I ($p<1\%$). All three periods reached a similar potential difference at the end.

TABLE VII

Ion Concentrations in The Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

	Time (Minutes)				
Period	0	15	30	45	60
			Na(mEq/liter)		
I	85.25±(1.93)	86.13±(3.81)	82.75±(6.71)	76.00±(8.97)	72.25±(10.71)
*II	86.50±(3.99)	82.92±(6.38)	75.88±(9.10)	70.63±(10.78)	65.63±(11.76)
III	89.13±(4.09)	86.25±(5.75)	82.50±(7.02)	74.50±(9.53)	71.63±(11.47)
			Cl (mEq/liter)		
I	80.63±(1.03)	74.20±(4.43)	63.00±(8.51)	52.92±(11.25)	46.13±(12.57)
II	77.38±(3.47)	70.50±(7.52)	60.25±(10.66)	52.38±(12.70)	44.13±(12.65)
III	84.75±(3.04)	76.88±(4.92)	71.25±(6.44)	60.50±(9.46)	53.25±(11.46)
			K (mEq/liter)		
I	1.02±(0.34)	3.00±(0.39)	4.15±(0.73)	5.37±(1.02)	6.75±(1.39)
II	1.60±(0.70)	3.65±(0.79)	4.47±(0.86)	5.30±(1.01)	5.90±(1.14)
*III	0.80±(0.49)	2.42±(0.52)	3.22±(0.34)	4.50±(0.54)	5.75±(0.78)

Values were given as average ±(SEM) at times indicated. *,**, represents a significance difference at the 5% and 1% level, respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Twenty observations were made on four animals in each of three periods.

TABLE VIII

Ion Concentrations in The Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

	Time (Minutes)				
Period	0	15	30	45	60
			pH		
I	7.03±(0.05)	7.24±(0.09)	7.34±(0.08)	7.45±(0.09)	7.37±(0.10)
II	6.99±(0.09)	7.17±(0.04)	7.32±(0.10)	7.37±(0.07)	7.30±(0.08)
*III	6.92±(0.10)	7.17±(0.16)	7.16±(0.15)	7.24±(0.09)	7.25±(0.11)
			P_{CO_2}		
I	5.88±(3.47)	19.13±(4.36)	24.40±(3.44)	37.50±(11.45)	46.75±(13.71)
II	11.52±(6.77)	21.27±(5.99)	28.52±(5.69)	32.52±(4.86)	41.63±(7.04)
III	6.32±(3.67)	19.07±(4.66)	23.27±(6.85)	28.30±(7.26)	34.38±(9.69)

Values were given as average ±(SEM) at times indicated. *,**, represents a significant difference at the 5% and 1% level, respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Twenty observations were made on four animinals in each of three periods.

TABLE IX

Osmotic Pressure and Transmural Potential in The Canine Ileum During a Control (I) Period, a Head Upward Tilting (II) Period, and a Recovery (III) Period.

Period	Time (Minutes) 0	15	30	45	60
			Osmotic Pressure (mOsm)		
I	328.0±(1.4)	318.8±(1.8)	312.0±(3.7)	306.0±(2.9)	297.5±(3.2)
*II	324.8±(2.0)	316.0±(1.4)	303.2±(3.6)	300.5±(3.5)	294.8±(3.3)
**III	330.8±(6.0)	324.8±(3.5)	322.2±(2.3)	312.5±(1.9)	310.2±(1.7)
			Transmural Potential (mVolts)		
I	1.0±(4.0)	1.0±(4.4)	1.5±(4.3)	7.0±(1.7)	8.0±(1.7)
**II	5.9±(1.7)	6.8±(2.2)	9.8±(3.6)	8.0±(5.8)	9.1±(6.8)
III	3.4±(5.4)	4.5±(6.2)	4.8±(6.3)	9.5±(3.2)	8.8±(2.8)

Values are mean ±(SEM) at times indicated. *,**, represent a significant difference at the 5% and 1% level, respectively. Significance at Period II indicates the significance between Period I and Period II. Significance at Period III indicates significance between Period I and Period II versus Period III. Observations were made on four animals in each of three periods. A total of twenty observations was made in each period.

V. DISCUSSION

DISCUSSION

Despite reduced blood flow to the ileal segment during head upward tilting, net NaCl and water absorption increased. The gut responds to an apparent reduction in blood volume by increasing the volume of saline in circulation. However, the absorption of 3-O-CH_3-D-Glucose decreased indicating that the response of the gut was relatively specific for NaCl and water as compared to sugar. The changes in net flux of Na were due to the combined effects of changes in the influx and outflux of Na, neither one by itself being significantly altered. The increased net absorption of water was also due to an increased difference between the influx and outflux of water, both of which decreased significantly.

A relatively large fraction of normally available energy is required to drive the Na pump in tissues which actively transport Na. The gut is capable of increasing its uptake of oxygen in the face of reduced blood flow (7) and, therefore, the Na pump may have sufficient energy available to keep Na transport at a normal level.

Purely physical factors could also affect transport. Reduction of blood flow to the gut decreases the area of intestine being perfused per unit time. This reduction can alter transport by failing to supply sufficient oxygen and nutrients to maintain a normal level of activity. In addition, adequate removal of absorbed products and metabolic wastes may tend to lower transport. Reduction of blood pressure may decrease the influx of water through large pores.

The reduced Na concentration in the intestinal lumen during period II, when considered with the increase in the net NaCl and water absorption, indicates that the Na pump can increase the concentration difference against which it can pump Na. However, the luminal potential became more positive in period II and thus tended to decrease the electrical gradient. Figure 1 indicates that the observed Ussing ratio for Na is greater than the calculated Ussing ratio for Na in all three periods. Active transport of Na is probably taking place but there is little difference among the three periods with respect to the observed Ussing ratio for Na. This lack of change indicates that the pump for Na has not altered its efficiency during the three periods.

Lack of decreased absorption by the ileum after isoncotic dextran infusion indicates that the increased blood volume does not by itself alter the final Na and Cl concentration against which salt can be absorbed (8).

The ability of the Recovery period to show a continued and significant decrease in both influx and outflux of water when compared to the Control plus the Experimental periods is indicative of a prolonged effect of head upward tilting which may be due to a hormonal or humoral agent.

Increases in transmural potential were observed in all periods with the Experimental period having a greater positive (mucosal) potential. Curran and Solomon (27) have shown in the <u>in vivo</u> rat ileum that the luminal potential becomes more positive as the concentration of NaCl

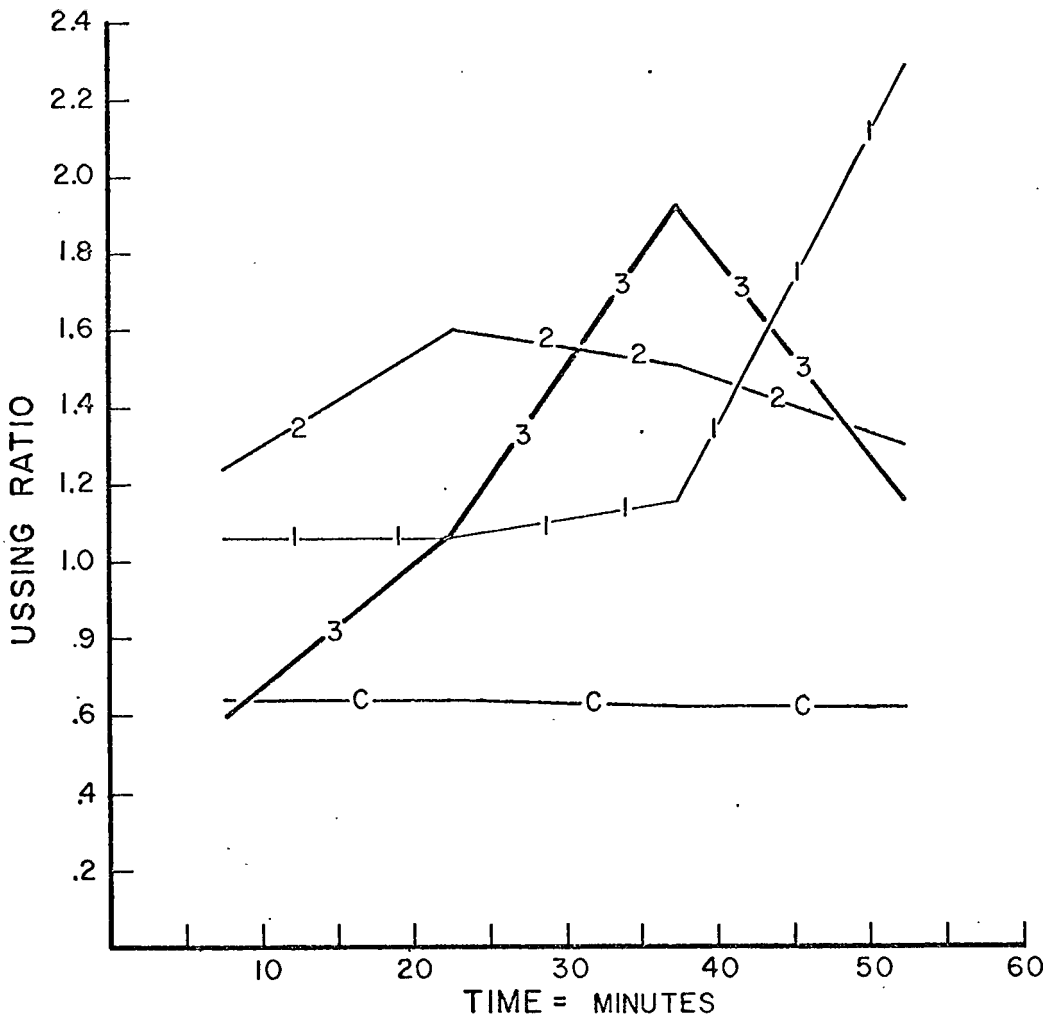

FIGURE 1

USSING RATIO FOR SODIUM

$$\text{USSING RATIO} = \frac{(Na)\ \text{LUMEN}}{(Na)\ \text{PLASMA}}\ e^{F(P.D.)/RT}$$

e = 2.718
F = FARADAY
P.D. = TRANSMURAL POTENTIAL DIFFERENCE
R = GAS CONSTANT
T = ABSOLUTE TEMPERATURE

decreases; such was the case in the present experiments. An excess of Cl transport would create a net positive mucosal potential. Clarkson and Rothstein (58) have stated that as the negative Cl ion is removed, another negative ion, probably bicarbonate, moves in to maintain electrical neutrality. In addition, a positive ion such as hydrogen ion, may move out of the intestinal lumen. This effect was observed as the bicarbonate concentration in the intestinal lumen increased while the luminal pH approached basic values. The potential was significantly ($p<5\%$) correlated with pH and P_{CO_2} in all three periods. The pH and the P_{CO_2} determine the bicarbonate concentration. The bicarbonate concentration in turn represents, together with K, the difference between Na and Cl. Potassium, in addition to hydrogen ion, might also be responsible for exchanging with sodium as Cl is removed from the intestinal lumen. An electrogenic Cl pump, therefore, might account for the potential difference across the gut. Other possibilities for this observed transmural potential exist (31,32).

Autoregulation of blood flow refers to the ability on an organ to adjust its blood supply in accordance with its needs. When mean blood pressure is reduced, intestinal blood flow decreases and then tends to return to control values (59). Vascular resistance to blood flow is initially increased but decreases as the mean blood pressure is reduced below 100 mm Hg (59). This autoregulatory mechanism may be of primary importance during postural changes, from the supine position to the vertical position, in order to maintain adequate blood

flow to the intestine. Figure 2 demonstrates these responses of autoregulation of blood flow to the intestine. A relative increase in the resistance to flow is initially present but tends to decrease at about 20 minutes. This time (20 minutes) corresponds to a mean blood pressure of 104.6 (Table VI) which is at the level predicted where resistance begins to decrease. Blood flow to the intestine (Table VI) initially decreases and then tends to return to Control values.

Sodium was absorbed at an average concentration of 114.4 uEq/ml during period I (Table X) while sodium absorption during period II was increased to 132.7 uEq/ml. Absorption of Na during period III was also increased from Control values and averaged 130.8 uEq/ml. Period I had 2.7 uEq of Na absorbed independent of water absorption. Period II had 2.5 uEq of Na absorbed independent of water but the significant finding in period II is that Na was absorbed in a hypertonic solution when compared to the Control period. Period III also showed a hypertonic absorption of Na when compared to the Control period and had a larger amount of Na absorbed in the absence of water than did the other two periods.

Chloride was absorbed during the Control period at an average concentration of 105.3 uEq/ml which was similar to the concentration of Na absorbed. Hence, no differences in the activity of the respective transport mechanisms was evident. Chloride absorption during period II averaged 132.6 uEq/ml which increased from the Control values. It can

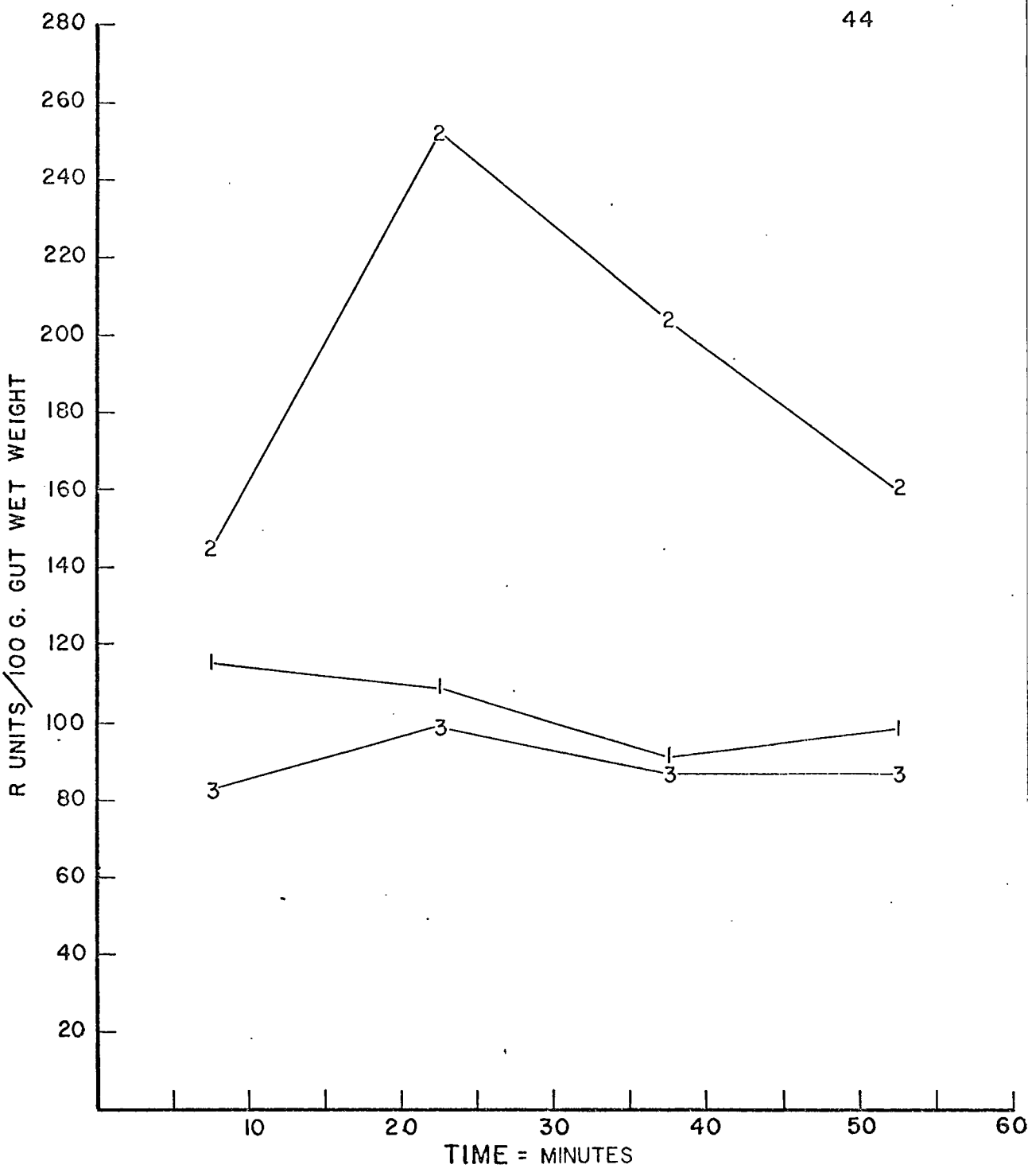

FIGURE 2

INTESTINAL VASCULAR RESISTANCE

$$R = \frac{\text{BLOOD PRESSURE (mm Hg)}}{\text{BLOOD FLOW (ml/sec)}} \Big/ \text{100 grams WET GUT WEIGHT}$$

TABLE X

Regression Equations

Period	$\bar{Y}$	= Slope (uEq/ml) ·	$\bar{X}$	+ Intercept (uEq)
	Na Absorbed (uEq)		H_2O Absorbed (ml)	
I	-2.93±(2.31)	114.4±(10.5)	-0.049±(0.019)	2.71
II	0.96±(1.78)	132.7±(7.2)	-0.012±(0.013)	2.52
III	0.50±(1.52)	130.5±(15.1)	-0.020±(0.011)	3.13
	Cl Absorbed (uEq)		H_2O Absorbed (ml)	
I	0.70±(2.25)	105.3±(14.1)	-0.049±(0.019)	5.89
II	2.80±(1.86)	132.6±(13.1)	-0.012±(0.013)	4.36
III	2.24±(1.53)	133.9±(13.6)	-0.020±(0.011)	4.94
	Cl Absorbed (uEq)		Na Absorbed (uEq)	
I	0.70±(2.25)	0.93±(0.08)	-2.93±(2.31)	3.42
II	2.80±(1.86)	1.02±(0.06)	0.96±(1.78)	1.82
III	2.24±(1.53)	0.97±(0.07)	0.50±(1.52)	1.76

*Values are given as mean ±(SEM) for a control period (I), a Head Upward Tilting Period (II), and a Recovery Period (III). Regression equations were calculated by the least squares method from sixteen observations in each of three periods for four animals. Linearity of regression was significant at $p<1\%$.

be noted that both transport mechanisms during head upward tilting increased an equal amount since both Na and Cl were transported at an average concentration of 133 uEq/ml. Chloride transport during the Recovery period (Table X) was similar to Cl transport during the Experimental period. The difference between total Na and total Cl absorbed is represented by the difference in intercept between Na absorbed versus water absorbed and Cl absorbed versus water absorbed.

Chloride absorption when compared to Na absorption showed no significant differences among the three periods; Table VI (page 33) illustrates these findings. All three periods showed a similar slope, close to 1, indicating that approximately equal amounts of Na were absorbed with Cl when water absorption was occurring concomitantly. The only difference among the periods was that period I showed a slightly greater amount of Cl absorbed in the absence of Na absorption.

Increased salt and water absorption by the gut during head upward tilting suggests that the gut is capable of acting as an homeostatic organ with respect to the fluid balance of the dog. This mechanism may be due to neural or humoral agents. In addition, activation of the carotid and aortic baroreceptors may activate the sytem to increase the fluid in circulation during the apparent reduction of blood volume to the head and thorax.

Reduction of the absorption of 3-O-methyl-glucose suggests that the mechanism for the homeostatic control of the body fluids may not be the same mechanism for the control of sugar absorption. Reduction of sugar fluxes could also be explained by the failure of the reduced blood

supply to the gut during head upward tilting to provide adequate nutrients and oxygen since the blood supply approached the 50% limit measured by Varro (7).

Further investigations into the possible role of the above agents of homeostatic control will provide vital clues that will lead to a more fruitful understanding of gut function.

VI. SUMMARY

Summary

The canine ileum was shown to possess an autoregulatory response to head upward tilting. Despite reduced blood flow to the gut, net NaCl and water absorption increased. A decrease in the absorption of 3-O-methyl-glucose with reduced blood flow was noted. Increased transmural potential, with the mucosa becoming more positive, was shown during the experimental period. Changes in the rates of influx and outflux have been observed which are responsible for the changes in net absorption during head upward tilting.

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