BLOOD FLOW IN THE CANINE ILEUM AS AFFECTED BY LUMINAL ISOSMOTIC AND HYPEROSMOTIC SOLUTIONS

Thesis for the Degree of M. S.
MICHIGAN STATE UNIVERSITY
WANG-TSAU CHEN
1970


LIBRARY
Michigan State
University


BINDING BY
HOAG & SONS'
BOOK BINDERY INC.

ABSTRACT

BLOOD FLOW IN THE CANINE ILEUM AS AFFECTED BY LUMINAL ISOSMOTIC AND HYPEROSMOTIC SOLUTIONS

By

Wang-Tsau Chen

The naturally occurring ions of sodium, potassium, magnesium and calcium, may be important agents in regulating and maintaining normal vascular resistance. These ions are normally present in the gut lumen and regularly move between the intestinal blood and lumen contents. The primary purpose of the present study was designed to answer the question whether or not the placement of these ions in the intestinal lumen can affect the local blood flow and intestinal wall activity. This was accomplished by measuring total venous outflow, its osmolarity and cation concentration and monitoring luminal pressure from two naturally perfused adjacent in situ ileal segments in anesthetized dogs. Isosmotic polyethylene glycol (I-PEG) served as the pre- and post-control solution for the salt solution in the test segment. The other segment contained PEG and served as a continual control for systemically induced and spontaneous changes in the test segment.

Isosmotic solution of $NaCl_2$, $MgCl_2$ or $CaCl_2$ in the ileal lumen decreased ileal venous outflow while isosmotic KCl caused a variable effect on venous outflow. Venous cation concentration was significantly raised by all isosmotic solutions of $CaCl_2$, KCl and $MgCl_2$ but not by NaCl. Only KCl ever induced an increase in ileal wall activity.

All hyperosmotic (1500 mOsm/liter) solutions of the four salts increased ileal venous outflow, its osmolarity, cation concentration and luminal fluid volume. The increase in blood flow and luminal fluid volume by KCl was greater than that caused by any of the other three. The increase in blood flow by $MgCl_2$ was greater than that by NaCl or $CaCl_2$ while the increases by NaCl and $CaCl_2$ were not different from each other. Again, only KCl regularly produced an increase in intestinal motility. Hyperosmotic PEG in the ileal lumen also caused an increase in venous outflow, its osmolarity, and luminal fluid volume. But this increase in venous outflow and luminal fluid volume was minimal and the elevation in venous osmolarity was not different from those caused by $MgCl_2$ or $CaCl_2$. An <u>in vitro</u> study on the relationship of osmolarity to concentration of PEG and NaCl showed that serial dilution of hyperosmotic PEG and NaCl (1450 mOsm/liter) decreased the osmolarity of PEG more rapidly than that of NaCl.

It is concluded that the luminal placement of salt solutions, either isosmotic or hyperosmotic, did, in most cases, cause a local change in ileal blood flow. Isosmotic

solutions of NaCl, $MgCl_2$ or $CaCl_2$ caused a small decrease while isosmotic KCl had a variable effect on local blood flow. All hyperosmotic salt solutions caused an increase in blood flow and this increase in flow was, apparently, caused by one or more factors in addition to an increased osmolarity and ion concentration. Luminal pressure and motor activity was increased only by KCl solution, either isosmotic or hyperosmotic; this increase seems to be caused by the action of potassium on visceral smooth muscle and/or local intestinal nerves. The increase in luminal fluid volume produced by hyperosmotic PEG was less than the increase by any hyperosmotic salt solution. This can be attributed to a greater decline in osmolarity of the H-PEG than of H-salt when both are equally diluted.

BLOOD FLOW IN THE CANINE ILEUM AS AFFECTED BY LUMINAL ISOSMOTIC AND HYPEROSMOTIC SOLUTIONS

By

Wang-Tsau Chen

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Physiology

1970

ACKNOWLEDGMENTS

The author wishes to express his sincere appreciation to Dr. J. M. Dabney and Dr. C. C. Chou for their invaluable encouragement and guidance during the course of this study. Sincere appreciation is also extended to Dr. W. D. Collings for his service on the examination committee. The author also wishes to express his special thanks to Mrs. Jodi Johnston for her patient work on the chemical analyses in the present study.

TABLE OF CONTENTS

	Page
ACKNOWLEDGMENTS	ii
LIST OF TABLES	iv
LIST OF FIGURES	v
Chapter	
I. INTRODUCTION	1
II. METHODS AND MATERIALS	3
Osmolarity-Concentration Relationship of Polyethylene Glycol (PEG) and Sodium Chloride (NaCl)	9
Statistical Analysis of Results	10
III. RESULTS	12
Control Venous Outflows with I-PEG in the Ileum	12
Venous Outflow and Ileal Motility with I-Salt Solutions in the Ileum	14
Venous Outflow and Motility with Hyperosmotic Salt Solutions in the Ileum	22
Summary of Changes in Blood Flow by Solutions in the Ileum	38
Osmolarity-Concentration Relationship of Polyethylene Glycol (PEG) and Sodium Chloride (NaCl)	41
IV. DISCUSSION	43
V. SUMMARY AND CONCLUSION	63
BIBLIOGRAPHY	67

LIST OF TABLES

Table		Page
1.	Osmolarity and Concentration of Solutions . .	7
2.	Venous Outflows from Paired Ileal Segments During the First Two Periods of Study with I-PEG in the Lumen	13
3.	Effect on Venous Outflow (gm/min) from Ileal Segments of Placing Isosmotic Salt Solutions in the Lumen	18
4.	Cation Concentration (mEq/liter) in Venous Outflow from Ileal Segments with Isosmotic Salt Solutions in the Lumen	19
5.	Fluid Volume (ml) Recovered from Ileal Segments 15 Minutes After Placing 10 ml Isosmotic Salt Solutions in the Lumen. . .	20
6.	Effect on Venous Outflow (gm/min) from Ileal Segments of Placing Hyperosmotic Salt Solutions in the Lumen.	24
7.	Cation Concentration (mEq/liter) in the Venous Outflow from Ileal Segments with Hyperosmotic Salt Solutions in the Lumen . . .	25
8.	Plasma Osmolarity (mOsm/liter) in the Venous Outflow from Ileal Segments with Hyperosmotic Salt Solutions in the Lumen . . .	26
9.	Fluid Volume (ml) Recovered from Ileal Segments 15 Minutes After Placing 10 ml Hyperosmotic Solutions in the Lumen . . .	28
10.	Venous Outflow (gm/min) from Paired Ileal Segments as Affected by Two Different Osmolarities of PEG (N = 11) or by Hyperosmotic Solutions of Two Different Salts (N = 8).	35

LIST OF FIGURES

Figure		Page
1.	The Double-Segment Preparation of the Dog Ileum	5
2.	Effects of Placing Isosmotic Salt Solutions in the Ileal Lumen on Venous Outflow, Cation Concentration and Recovered Luminal Fluid Volume.	17
3.	Effects of Placing Hyperosmotic KCl and NaCl in the Ileal Lumen on Venous Outflow, Cation Concentration, Osmolarity and Recovered Luminal Fluid Volume.	23
4.	Pressure in the Ileal Lumen Containing Hyperosmotic KCl	30
5.	Effects of Placing Hyperosmotic $MgCl_2$ and $CaCl_2$ in the Ileal Lumen on Venous Outflow, Cation Concentration, Osmolarity and Recovered Luminal Fluid Volume	31
6.	Effects of Placing Isosmotic and Hyperosmotic Polyethylene Glycol Solutions in the Ileal Lumen on Venous Outflow, Venous Osmolarity and Recovered Luminal Fluid Volume . . .	34
7.	Venous Outflow and Recovered Luminal Fluid Volume from Paired Ileal Segments Containing Different Hyperosmotic Salt Solutions .	37
8.	Summary of Changes in Venous Outflow After Placing Various Solutions in the Ileal Lumen	39
9.	Relationship of Osmolarity to Concentration of Polyethylene Glycol (PEG) and Sodium Chloride (NaCl).	42

CHAPTER I

INTRODUCTION

The naturally occurring ions, Na^{+}, K^{+}, Ca^{++}, and Mg^{++}, may have important roles in regulating and maintaining normal vascular resistance (12,14,26). In addition to their vascular effects, these ions also have distinct actions on the gastrointestinal smooth muscle. Local intra-arterial infusions of isosmotic KCl, $MgCl_2$, or $CaCl_2$ produce characteristic changes in local vascular resistance and wall tension of the small intestine (9). $MgCl_2$ decreases both vascular resistance and wall tension; $CaCl_2$ decreases wall tension but has a variable effect on vascular resistance. KCl has a biphasic action on both vascular resistance and wall tension, first lowering then increasing as a function of its plasma concentration.

These ions are normally present in the gut and regularly move between blood and lumen. Absorption or secretion of these ions can alter intestinal tissue concentration as well as plasma concentraion of these ions. Since changes in plasma concentration of these cations can affect both vascular and visceral smooth muscle and thereby affect

intestinal blood flow, absorption of these ions may play a role in regulation of local intestinal blood flow. A review of the literature reveals that no study has been done on the effect of placing ions into the intestinal lumen on local blood flow. The present study was, therefore, designed to investigate whether the placement of these naturally occurring ions, sodium, potassium, calcium and magnesium, in the intestinal lumen can affect the local blood flow and intestinal wall activity.

CHAPTER II

METHODS AND MATERIALS

Mongrel dogs, weighing from 10 to 15 Kg, of both sexes were used. They were anesthetized with sodium pentobarbital (30 mg/Kg) and ventilated with a positive pressure respiration pump (Harvard, model 607, Dover, Mass.) via an endotracheal tube. Heparin sodium (5 mg/Kg) was given intravenously as an anticoagulant. The abdominal cavity was opened through a midline incision and a loop of ileum about 20 cm proximal to the ileo-cecal junction was exteriorized. Utilizing the natural vascular pattern as a guide, two adjacent segments were chosen such that the venous outflow from each segment drained through a single vein. Leaving the artery and extrinsic nerves undisturbed, both of these single veins were cannulated with polyethylene tubing. A rubber tube was placed into the lumen of each segment through which fluids were put into or removed from the segments. At other times the tube was utilized for monitoring luminal pressure of the segment. The segments were tied at both ends and the mesentery cut to exclude collateral flow. Thus, two separate and naturally perfused <u>in situ</u>

ileal segments were formed and placed outside the abdominal cavity (Figure 1). They were kept warm and moist by a heating lamp and by covering them with plastic film. The venous outflows from these two segments were directed into a reservoir and the blood was continuously pumped back to the dog via a femoral vein. The venous outflows were collected periodically in beakers and weighed on a top loading precision balance, accurate to ± 50 mg. (Mettler, model P1200, Hightstown, N.J.). Hence, flow was recorded as grams of blood per minute. A femoral artery was cannulated for monitoring systemic pressure. Both arterial and luminal pressures were measured with pressure transducers (Statham, model P23 Gb, Hato Rey, Puerto Rico) and recorded on a direct writing oscillograph (Sanborn, Model 7714A, Waltham, Mass.).

All experiments consisted of three successive periods, i.e., pre-control, test and post-control. In each period (control or test), the agents (control or test) were introduced into the lumen and remained there for 15 minutes. Venous outflows were then collected for 4 three-minute periods with three one-minute intervals between them. The blood of the three-minute collection was weighed and returned to the reservoir. The first three-minute flow value was not included in the results because the flow was often influenced by the previous manipulation of the gut segment (washing of the gut lumen and introduction of solutions). Blood samples for measurement of ion concentration and osmolarity were taken from the last flow collection. After

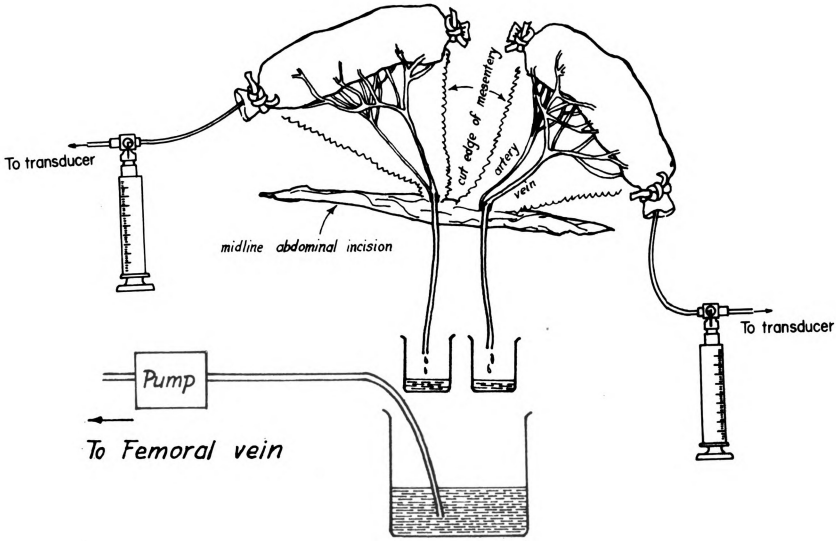

Fig. 1.--The double-segment preparation of the dog ileum.

a 15-minute period, the luminal contents were then withdrawn and its volume was measured with a 10 ml syringe. The lumen was gently washed with normal saline and the next solution was then introduced into the lumen. Na^+ and K^+ concentrations were analyzed with a flame photometer (Beckman, model 105, Fullerton, California); Mg^{++} and Ca^{++} were analyzed with an atomic absorption spectrophotometer (Perkin-Elmer, model 290B, Norwark, Conn.). Osmolarity was determined by the technique of freezing point depression with an osmometer (Advanced Instruments, model 67-31LAS, Newton Highlands, Mass.).

Effects of luminal placement of 10 solutions (Table 1) on local blood flow, venous osmolarity and cation concentration, luminal fluid volume, and intestinal wall activity were studied in 5 combinations. They were: (1) isosmotic polyethylene glycol solution (I-PEG) in one segment vs. ambient air in the other, (2) isosmotic salt solution (I-Salt) in one segment vs. I-PEG in the other, (3) hyperosmotic PEG (H-PEG) in one segment vs. I-PEG in the other, (4) hyperosmotic salt solution (H-Salt) in one segment vs. H-PEG in the other, (5) one H-Salt in one segment vs. another H-Salt in the other, e.g., H-KCl vs. H-$MgCl_2$. All solutions were kept in a constant temperature water bath at 37°C before placing them into the lumen.

TABLE 1.--Osmolarity and concentration of solutions.

Solutions	Concentration		Osmolarity measured
	grams/100 ml	mEq/liter	mOsm/liter
I-NaCl	0.9	154	290
I-KCl	1.2	164	309
I-$MgCl_2$	1.1	233	308
I-$CaCl_2$	1.3	233	298
I-PEG	8.8	--	303
H-NaCl	4.5	770	1450
H-KCl	6.0	800	1480
H-$MgCl_2$	5.6	1170	1460
H-$CaCl_2$	6.5	1170	1480
H-PEG	24.0	--	1480

1. I-PEG vs. Air

This experiment was designed to test the vasoactivity of I-PEG when it was placed in the ileal lumen. Three dogs were used. During the control (pre- and post-) periods, 10 ml of ambient air were placed into both segments. During the test periods, 10 ml of I-PEG were placed into one segment and 10 ml of air into the other as volume control for I-PEG.

2. I-Salt vs. I-PEG

The I-Salt solutions were isosmotic sodium chloride (I-NaCl), potassium chloride (I-KCl), magnesium chloride (I-$MgCl_2$) and calcium chloride (I-$CaCl_2$) (Table 1). In this experiment, 10 ml of I-PEG were placed into both segments during the control periods. During the test period, 10 ml of an isosmotic salt solution were placed into one segment and 10 ml of I-PEG into the other as volume and osmolarity control for I-Salt. Ten dogs were used. All four I-Salt solutions were tested in each dog in random sequence.

3. H-PEG vs. I-PEG

This experiment was designed to test the effect of H-PEG in the ileal lumen on both venous outflow and venous osmolarity using I-PEG as the control. Eleven dogs were used. During the control periods, 10 ml of I-PEG were placed into both segments. During the test period, 10 ml of H-PEG were placed into one segment and 10 ml of I-PEG into the other.

4. H-Salt vs. H-PEG

The effects of hyperosmotic solutions (1500 mOsm/liter) of the four salts were studied on 8 dogs. During the pre- and post-control periods, 10 ml of I-PEG were placed into both segments. During the test period, 10 ml of one hyperosmotic salt solution were placed into one segment and 10 ml of H-PEG into the other as volume and osmolarity control for the salt solution. All these four H-Salt solutions were tested on each dog in random sequence.

5. H-Salt vs. H-Salt

Eight dogs were used for the study of H-KCl vs. H-$MgCl_2$, H-NaCl vs. H-$MgCl_2$, and H-NaCl vs. H-$CaCl_2$. These three comparisons were performed in random sequence in each dog. In each comparison, I-PEG was placed into both segments during the control periods (pre- and post-) and the two H-Salt solutions to be compared were placed into the two segments during the test period.

Osmolarity-Concentration Relationship of Polyethylene Glycol (PEG) and Sodium Chloride (NaCl)

This study was designed to compare the changes in osmolarity of 1500 mOsm/liter PEG solution with those of 1500 mOsm/liter NaCl when both solutions were equally diluted with water. Empirically, 24% PEG solution (600 mM/liter) and 4.5% NaCl solution (770 mM/liter) have the same osmolarity, i.e., 1450 mOsm/liter (Table 1). Eight

diluted solutions were made by adding water into 24% PEG or 4.5% NaCl solution in the following proportions: (1) 1.5 ml water to 8.5 ml 24% PEG or 4.5% NaCl, (2) 2.5 ml water to 7.5 ml 24% PEG or 4.5% NaCl solution, (3) 3.5 ml water to 6.5 ml 24% PEG or 4.5% NaCl solution, (4) 5.0 ml water to 5.0 ml 24% PEG or 4.5% NaCl, (5) 6.5 ml water to 3.5 ml 24% PEG or 4.5% NaCl, (6) 7.5 ml water to 2.5 ml 24% PEG or 4.5% NaCl, (7) 8.5 ml water to 1.5 ml 24% PEG or 4.5% NaCl, and (8) 9.5 ml water to 0.5 ml 24% PEG or 4.5% NaCl. The osmolarity of all these solutions was measured by the technique of freezing point depression with an osmometer (Advanced Instruments). This same experiment was repeated five times. New solutions were made for each experiment.

Statistical Analysis of Results

In every experiment, all data (flow, cation concentration, osmolarity and luminal fluid volume) which were gathered from the three time periods (pre-control, test and post-control) in either the test segment or control segment were compared from one period to the next period using Student's t-test modified for paired comparison between two sample means (30). For example, the effect of I-NaCl on blood flow was analyzed by comparing the amount of flow that occured while I-NaCl was in the lumen of the test

segment with the flow collected when I-PEG was in the test segment (pre- or post-control period). The same statistical analysis (Student's t paired comparison) was also used to compare a change in flow, cation concentration or osmolarity from the pre-control or post-control value in the test segment with the concomitant change in the control segment. For example, the change in flow from the pre-control value produced by I-NaCl in the test segment was compared to the concomitant change in the control segment which contained I-PEG.

When data on blood flow using any given solution were pooled from all experiments, then these pooled flow data were analyzed with Student's t-test for unpaired comparison between two sample means (30). For example, using I-PEG as the control, the per cent change in flow produced by a given solution was compared to the change produced by any other solution (Figure 8).

CHAPTER III

RESULTS

Several experiments were performed on each dog. In no case did the experimental procedure alter, significantly, the systemic arterial pressure. The average arterial pressure was 125 mmHg.

Control Venous Outflows with I-PEG in the Ileum

In order to find out the degree of spontaneous change of blood flow in the present preparation, twenty experiments were randomly chosen to compare blood flow from two segments in two successive periods. I-PEG was placed into both segments in both periods. In 15 minutes blood flow fell by 1.27 $\pm$ 0.27 gm/min in Segment A and 1.35 $\pm$ 0.26 gm/min in Segment B (Table 2). These spontaneous changes were statistically significant. However, the fall in Segment A was not significantly different from the fall in Segment B (0.08 $\pm$ 0.37 gm/min). This result supports the concept that one segment can be reasonably used as a control for the spontaneous changes in blood flow with time in the other segment.

TABLE 2.--Venous outflows from paired ileal segments during the first two periods of study with I-PEG in the lumen. (N = 20)

Segment	1st 15 min. gm/min	2nd 15 min gm/min	Change (2nd-1st) gm/min/15 min	Per cent change (2nd-1st) x 100/1st
A	15.57	14.30	- 1.27 ± 0.27*	- 8.2 ± 1.7*
B	14.63	13.28	- 1.35 ± 0.26*	- 9.2 ± 1.8*

*Denotes a significant change at p value < 0.05.

Venous Outflow and Ileal Motility with I-Salt Solutions in the Ileum

I-PEG vs. Air

In the test segment which contained air (pre-control), I-PEG (test), and then Air (post-control), the average venous outflows were 11.21, 11.13 and 10.92 gm/min respectively for the three consecutive periods. In the control segment which contained Air during all three periods these values were 11.39, 11.09 and 10.81 gm/min respectively. The flow changes caused by I-PEG in the test segment (- 0.09 $\pm$ 0.41 gm/min from pre-control and + 0.21 $\pm$ 0.29 gm/min from post-control) were not significantly different from the concomitant flow changes that occurred in the control segment (-0.30 $\pm$ 0.27 gm/min from pre-control and + 0.28 $\pm$ 0.07 gm/min from post-control). These results show that I-PEG in the lumen has no vasoactivity when Air is used as its control.

I-NaCl vs. I-PEG

The effect on venous outflow of placing isosmotic NaCl (I-NaCl) into the ileal lumen is shown in both Table 3 and Figure 2. As compared to pre-control value (14.17 gm/min) with I-PEG in the lumen, I-NaCl significantly decreased (- 1.41 $\pm$ 0.32 gm/min) venous outflow, but did not cause a statistically significant decrease (- 0.31 $\pm$ 0.37 gm/min) when compared with the post-control value (13.07 gm/min). However, the concomitant flow changes in the

control segment (I-PEG segment) were - 0.27 ± 0.17 gm/min from pre-control value and + 0.86 ± 0.23 gm/min from post-control value. Thus, the decrease in flow by I-NaCl in the lumen may be overestimated when only compared to the pre-control flow value and underestimated as only compared to the post-control value. Therefore, the differences between the changes in the test segment (I-NaCl segment) and control segment (I-PEG segment) as shown in the last column on Table 3 were attributable to placing I-NaCl in the lumen. Both pre- and post-control differences were statistically significant ($p < 0.05$).

The sodium concentration in venous outflow was not significantly altered (+ 1.0 ± 2.4 mEq/liter) by placing I-NaCl in the lumen for 15 minutes (Table 4 and Figure 2).

Both I-PEG and I-NaCl lost some fluid volume in the ileal lumen. On the average, I-PEG lost a greater amount than did I-NaCl (Table 5).

As indicated by the intraluminal pressure neither I-NaCl nor I-PEG affected ileal wall motility.

I-KCl vs. I-PEG

I-KCl in the ileal lumen had a variable effect on the venous outflow. As compared to the concurrent changes in the control segment (I-PEG segment), I-KCl increased flow in 5 of 10 dogs, decreased in 3 dogs, and caused no change in 2 dogs. On the average, I-KCl gave a nonsignificant increase on venous outflow (Figure 2 and Table 3).

The venous concentration of potassium was significantly increased from 3.6 to 5.8 mEq/liter (Figure 2 and Table 4). The increment occurred in each of the 10 experiments with an average rise of 2.21 ± 0.26 mEq/liter. There was no significant change in potassium concentration of the venous outflow from the control segment which contained I-PEG (Table 4).

The volume recovered from the lumen after placing I-KCl in the lumen for 15 minutes was significantly greater than that with I-PEG in the lumen (Table 5 and Figure 2). On the average, I-PEG lost 1.6 ml of volume while I-KCl lost only 0.2 ml. The difference in the loss of volume was statistically significant between I-KCl and I-PEG as shown in Table 5.

I-KCl in the lumen of closed ileal segments occasionally altered the ileal wall activity as indicated by the luminal pressure. An increase in both rhythmic contraction and luminal pressure was found in 3 of 10 dogs studied.

I-$MgCl_2$ vs. I-PEG

Like I-NaCl, I-$MgCl_2$ placed in the ileal lumen significantly decreased ileal venous outflow (Figure 2 and Table 3) accompanying a small but consistent and significant rise (0.4 ± 0.06 mEq/liter) in its venous concentration (Figure 2 and Table 4). After considering the spontaneous change (usually a fall) in flow with time by using the change in the control segment as an index, I-$MgCl_2$ decreased

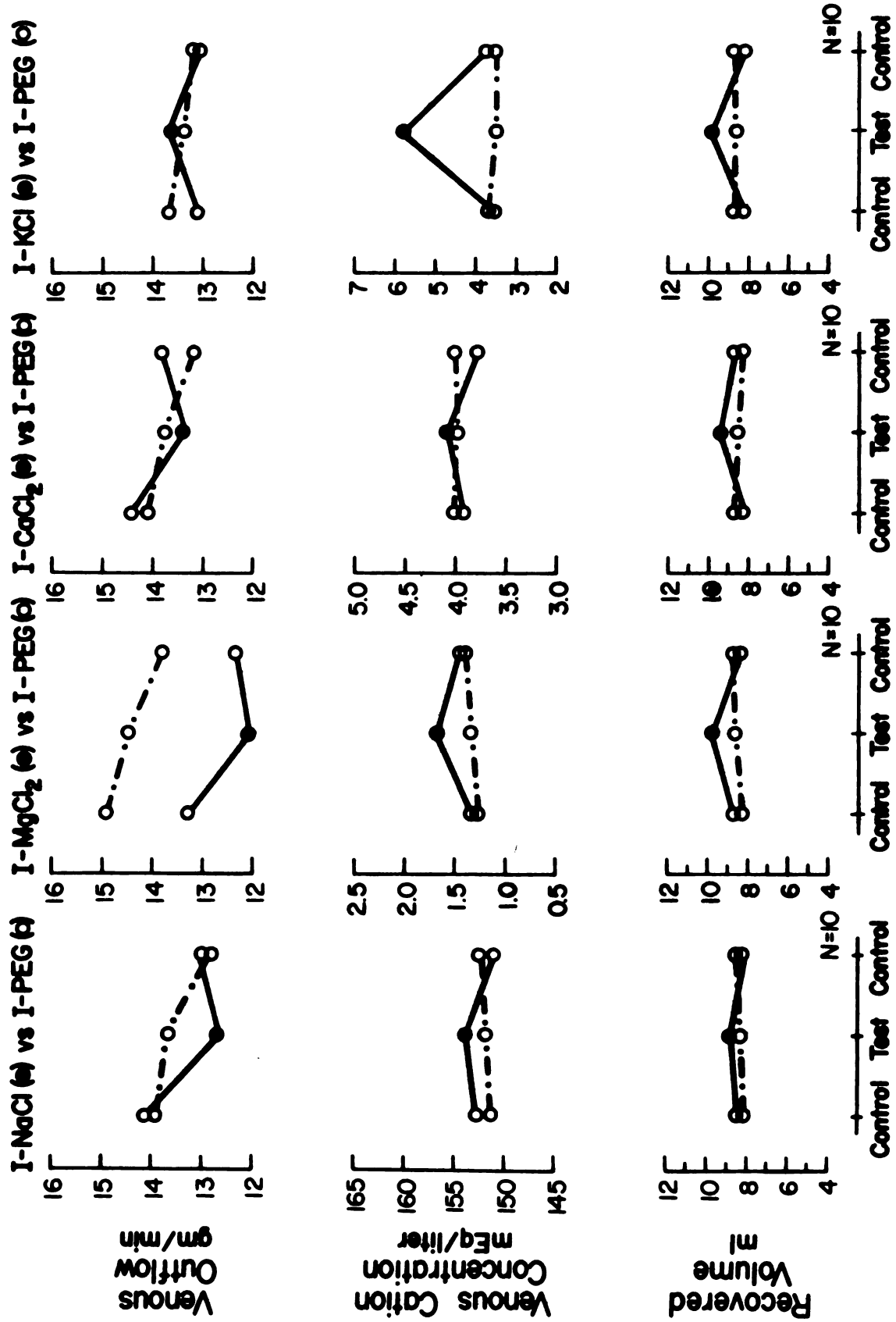

Fig. 2.--Effects of placing isosmotic salt solutions in the ileal lumen on venous outflow, cation concentration and recovered luminal fluid volume. [The abscissa shows the three successive periods.]

TABLE 3.--Effect on venous outflow (gm/min) from ileal segments of placing isosmotic salt solutions in the lumen. (N = 10)

Test Solution (mEq/liter)	Control Period	Segment A (Test)		Segment B (Control)		Change in Segment A Relative to Change in Segment B (A-B)
		I-PEG (Control)	Test Solution (Change from Cont.)	I-PEG (Control)	I-PEG (Change from Cont.)	
NaCl(154)	pre	14.17	- 1.41 ± 0.32*	13.98	- 0.27 ± 0.17	- 1.14 ± 0.36*
	post	13.07	- 0.31 ± 0.37	12.85	+ 0.86 ± 0.23*	- 1.17 ± 0.47*
KCl(164)	pre	13.14	+ 0.47 ± 0.55	13.69	- 0.29 ± 0.24	+ 0.76 ± 0.71
	post	13.15	+ 0.46 ± 0.36	13.18	+ 0.22 ± 0.14	+ 0.24 ± 0.61
$MgCl_2$(233)	pre	13.30	- 1.21 ± 0.41*	14.98	- 0.45 ± 0.33	- 0.76 ± 0.23*
	post	12.31	- 0.22 ± 0.44	13.85	+ 0.68 ± 0.26*	- 0.90 ± 0.42*
$CaCl_2$(233)	pre	14.44	- 1.01 ± 0.51*	14.15	- 0.37 ± 0.27	- 0.64 ± 0.42
	post	13.86	- 0.43 ± 0.43	13.17	+ 0.61 ± 0.24*	- 1.04 ± 0.53*

*Denotes that the change from control value or the difference between two changes compared is statistically significant at $p < 0.05$.

TABLE 4.--Cation concentration (mEq/liter) in venous outflow from ileal segments with isosmotic salt solutions in the lumen. (N = 10)

Test Solutions (mEq/liter)	Test Segment			Control Segment		
	I-PEG	Test Solution	I-PEG	I-PEG	I-PEG	I-PEG
I-NaCl (154)	153	154	151	152	152	153
I-KCl (164)	3.6	5.8*	3.8*	3.6	3.5	3.7
I-$MgCl_2$ (233)	1.3	1.7*	1.5*	1.3	1.3	1.4
I-$CaCl_2$ (233)	3.9	4.1	3.8*	4.0	4.0	4.0

*Denotes that the value is significantly different from the preceding value at $p < 0.05$.

TABLE 5.--Fluid volume (ml) recovered from ileal segments 15 minutes after placing 10 ml isosmotic salt solutions in the lumen. (N = 10)

Test Solutions (mEq/liter)	Test Segment			Control Segment		
	I-PEG	Test Solution	I-PEG	I-PEG	I-PEG	I-PEG
NaCl(154)	8.5 ± 0.4[a]	8.8 ± 0.3	8.2 ± 0.3*	8.5 ± 0.4	8.5 ± 0.4	8.7 ± 0.3
KCl(164)	8.4 ± 0.4	9.8 ± 0.3*	8.3 ± 0.4*	8.6 ± 0.3	9.0 ± 0.4	8.7 ± 0.3
$MgCl_2$(233)	8.4 ± 0.4	9.8 ± 0.2*	8.6 ± 0.5*	8.4 ± 0.3	8.7 ± 0.4	8.7 ± 0.3
$CaCl_2$(233)	8.3 ± 0.4	9.4 ± 0.3*	8.8 ± 0.3*	8.4 ± 0.4	8.7 ± 0.4	8.7 ± 0.3

[a]Denotes mean ± S.E.

*Denotes a significant difference from the preceding value at $p < 0.05$.

flow in 8 of 10 dogs and increased flow in the other two dogs. On the average, I-$MgCl_2$ decreased flow 0.7 ± 0.23 gm/min from pre-control value and 0.90 ± 0.42 gm/min as compared to flow during post-control period (Table 3).

I-$MgCl_2$ in the ileal lumen for 15 minutes had a greater recovered volume than I-PEG (Figure 2). On the average, I-$MgCl_2$ lost 0.2 ml out of 10 ml while I-PEG lost 1.6 ml. The difference in loss of volume between I-$MgCl_2$ and I-PEG was statistically significant as shown on Table 5.

Intestinal wall activity was not altered by I-$MgCl_2$ in the lumen as judged from the tracings of the intestinal luminal pressure.

I-$CaCl_2$ vs. I-PEG

The effect of placing I-$CaCl_2$ in the ileal lumen on venous outflow was more variable than those of I-NaCl or I-$MgCl_2$. As compared to I-PEG in the pre-control period, $CaCl_2$ caused a decrease in flow in five of 10 dogs, an increase in three dogs, and no change in the remaining two dogs. As compared to post-control value, six of 10 dogs had a decrease, two an increase, two no change. On the average, I-$CaCl_2$ in the ileal lumen either did not significantly decrease ileal venous outflow (as compared to pre-control) or significantly decreased flow (as compared to post-control) (Table 3). The concentration of Ca^{++} in the venous outflow was significantly increased but was minimal (+ 0.2 ± 0.09 mEq/liter) (Table 4).

I-$CaCl_2$ in the ileal lumen for 15 minutes had a greater volume recovered from the lumen than did I-PEG (Figure 2 and Table 5). On the average, I-$CaCl_2$ lost 0.6 ml from 10 ml of solution while I-PEG lost 1.7 ml. The loss of volume was statistically different between I-$CaCl_2$ and I-PEG (Table 5).

Venous Outflow and Motility with Hyperosmotic Salt Solutions in the Ileum

H-NaCl vs. H-PEG

Figure 3 illustrates the average effect of H-NaCl in the ileal lumen on the venous outflow (Table 6), venous Na^+ concentration, venous osmolarity and luminal volume recovery in comparison to that of H-PEG. The venous outflow with H-NaCl in the lumen increased from 10.74 gm/min to 13.05 gm/min and returned back to 10.57 gm/min in the post-control period with a significant elevation in Na^+ concentration (+ 10 $\pm$ 3.6 mEq/liter) (Table 7) and plasma osmolarity (+ 9 $\pm$ 2.7 mOsm/liter) (Table 8). H-PEG in the control segment did not significantly alter the venous outflow or venous Na^+ concentration, but significantly increased the osmolarity (+ 4.0 $\pm$ 1.0 mOsm/liter) of the venous blood. However, the increase in venous osmolarity by H-NaCl was significantly greater (+ 5.0 $\pm$ 2.0 mOsm/liter) than that by H-PEG. Both H-PEG and H-NaCl in the ileal lumen produced a greater intraluminal fluid volume than did I-PEG

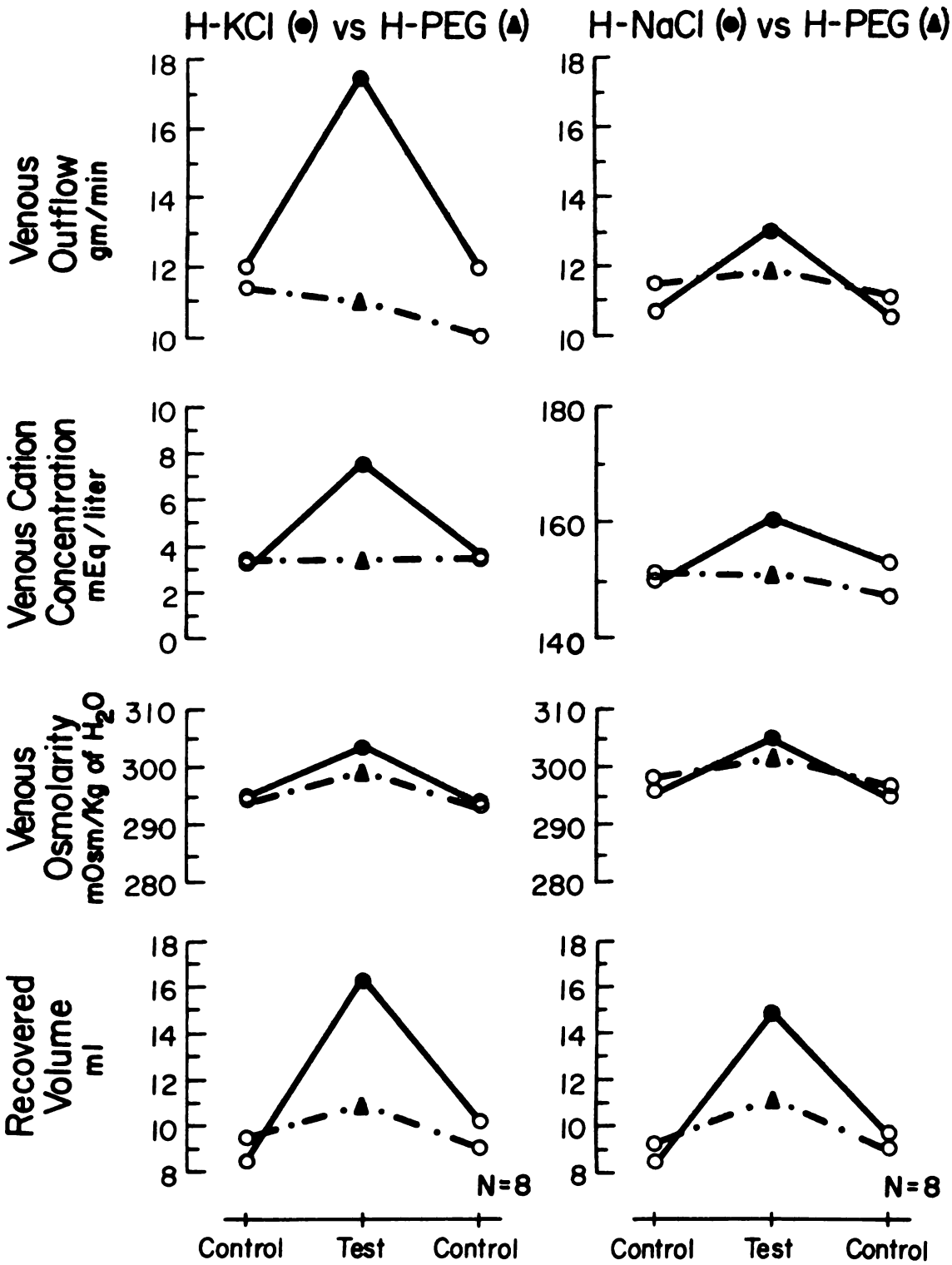

Fig. 3.--Effects of placing hyperosmotic KCl and NaCl in the ileal lumen on venous outflow, cation concentration, osmolarity and recovered luminal fluid volume. [Open circles represent the average value with control solution, I-PEG in the lumen.]

TABLE 6.--Effect on venous outflow (gm/min) from ileal segments of placing hyperosmotic salt solutions in the lumen. (N = 8)

Test Solution (mEq/liter)	Control Period	Segment A (Test)		Segment B (Control)		Change in Segment A Relative to Change in Segment B (A-B)
		I-PEG (Control)	Test Solution (Change from Cont.)	I-PEG (Control)	H-PEG (Change from Cont.)	
H-NaCl(770)	pre	10.74	+ 2.31 ± 0.28*	11.60	+ 0.23 ± 0.19	+ 2.08 ± 0.27*
	post	10.57	+ 2.48 ± 0.30*	11.18	+ 0.65 ± 0.29*	+ 1.83 ± 0.18*
H-KCl(800)	pre	12.08	+ 5.32 ± 0.66*	11.51	- 0.39 ± 0.18*	+ 5.71 ± 0.77*
	post	12.02	+ 5.38 ± 0.86*	10.07	+ 1.05 ± 0.23*	+ 4.33 ± 0.80*
H-$MgCl_2$(1170)	pre	11.12	+ 2.15 ± 0.65*	11.55	+ 0.40 ± 0.24	+ 1.75 ± 0.61*
	post	11.19	+ 2.08 ± 0.48*	10.62	+ 1.33 ± 0.22*	+ 0.75 ± 0.48
H-$CaCl_2$(1170)	pre	12.46	+ 1.79 ± 0.29*	12.78	- 0.01 ± 0.32	+ 1.80 ± 0.43*
	post	12.75	+ 1.50 ± 0.29*	11.87	+ 0.90 ± 0.30*	+ 0.61 ± 0.43

*Denotes that the change from control or the relative difference between two changes compared is statistically significant at $p < 0.05$.

TABLE 7.--Cation concentration (mEq/liter) in the venous outflow from ileal segments with hyperosmotic salt solutions in the lumen. (N = 8)

Test Solution (mEq/liter)	Test Segment			Control Segment		
	I-PEG	Test Solution	I-PEG	I-PEG	H-PEG	I-PEG
H-NaCl(770)	151	161*	154*	151	151	148
H-KCl(800)	3.3	7.5*	3.6*	3.4	3.4	3.6
H-$MgCl_2$(1170)	1.5	6.3*	1.7*	1.6	1.5	1.6
H-$CaCl_2$(1170)	4.3	5.2*	4.3*	4.3	4.2	4.1

*Denotes that the value is significantly different from the preceding value at $p < 0.05$.

TABLE 8.--Plasma osmolarity (mOsm/liter) in the venous outflow from ileal segments with hyperosmotic salt solutions in the lumen. (N = 8)

Test Solutions (mEq/liter)	Test Segment			Control Segment		
	I-PEG	Test	I-PEG	I-PEG	H-PEG	I-PEG
H-NaCl(770)	297	306*	295*	298	302*	297*
H-KCl(800)	295	303*	293*	295	300*	295*
H-$MgCl_2$(1170)	293	300*	293*	293	296*	293
H-$CaCl_2$(1170)	292	298*	291*	294	297	293*

*Denotes that the value is significantly different from the preceding value at $p < 0.05$.

(Table 9). H-NaCl also produced a significantly greater luminal volume (+ 3.8 ± 0.4 ml/15 min) than did H-PEG.

As with I-PEG, neither H-PEG nor H-NaCl caused a significant change in the intestinal wall activity as indicated by the intraluminal pressure.

H-KCl vs. H-PEG

The average effect of H-KCl on the flow, K^+ concentration and osmolarity of the ileal venous outflow as compared to that of H-PEG is shown on Figure 3. H-KCl raised the ileal venous outflow from 12.08 gm/min (pre-control value) to 17.04 gm/min. Flow returned to 12.02 gm/min during the post-control period. H-PEG in the control segment showed a small decrease in flow (Table 6) which was not different from the decrease in flow in the segment which contained I-PEG in three successive periods (Table 3). The potassium concentration of the venous outflow was elevated from 3.30 mEq/liter to 7.52 mEq/liter by H-KCl (Table 7). The H-PEG did not significantly change potassium concentration of the venous blood. Both H-KCl and H-PEG caused an increase in the venous osmolarity but H-KCl produced a greater increase (+ 3.0 ± 1.0 mOsm/liter) than did H-PEG (Table 8).

Both H-KCl and H-PEG gained luminal fluid volume (Figure 3 and Table 9). However, H-KCl gained much more (5.4 ± 0.4 ml/15 min.) than did H-PEG.

TABLE 9.--Fluid volume (ml) recovered from ileal segments 15 minutes after placing 10 ml hyperosmotic solutions in the lumen. (N = 8)

Test Solutions (mEq/liter)	Test Segment			Control Segment		
	I-PEG	Test	I-PEG	I-PEG	H-PEG	I-PEG
NaCl(770)	8.6 ± 0.4	15.0 ± 0.4*	9.9 ± 0.3*	9.2 ± 0.6	11.2 ± 0.5*	9.1 ± 0.4*
KCl(800)	8.6 ± 0.2	16.4 ± 0.6*	10.3 ± 0.5*	9.6 ± 0.3	11.0 ± 0.2*	9.1 ± 0.3*
$MgCl_2$(1170)	8.6 ± 0.3	14.6 ± 0.9*	10.1 ± 0.4*	9.2 ± 0.5	11.6 ± 0.4*	9.4 ± 0.3*
$CaCl_2$(1170)	8.5 ± 0.3	14.2 ± 0.3*	10.8 ± 0.3*	9.2 ± 0.4	10.8 ± 0.2*	9.1 ± 0.3*

*Denotes that the value is statistically different from the preceding value at $p < 0.05$.

H-KCl in the ileal lumen regularly caused a change in the intestinal luminal pressure. A typical recording is shown in Figure 4. H-KCl caused an increase in luminal pressure (PL) with rhythmic increases in pressure to 15-35 mm Hg by the eighth minute. At this time, the potassium concentration in the plasma was 7.4 mEq/liter. Blood flow increased as soon as H-KCl was introduced into the lumen but this increase had started to wane by the time that lumen pressure and venous potassium showed an increase. I-PEG or H-PEG did not significantly alter intestinal wall activity, blood flow or plasma K^+ concentration.

H-$MgCl_2$ vs. H-PEG

In Figure 5 are shown the average effects on venous outflow, venous Mg^{++} concentration, venous osmolarity and recovered luminal fluid volume of placing H-$MgCl_2$ in one lumen vs. H-PEG in the other. H-$MgCl_2$ raised the venous outflow from 11.12 to 13.27 gm/min, while H-PEG raised flow from 11.55 to 11.95 gm/min. H-$MgCl_2$ in the ileal lumen caused a four-fold rise in venous Mg^{++} concentration while H-PEG did not alter the concentration of the magnesium ion (Table 7). However, both H-$MgCl_2$ and H-PEG caused the same degree of increase in venous osmolarity (Table 8).

Both H-$MgCl_2$ and H-PEG caused a gain in luminal fluid volume after the placement of these solutions in the lumen for 15 minutes (Table 9). H-$MgCl_2$ caused a significantly greater increase in luminal fluid volume

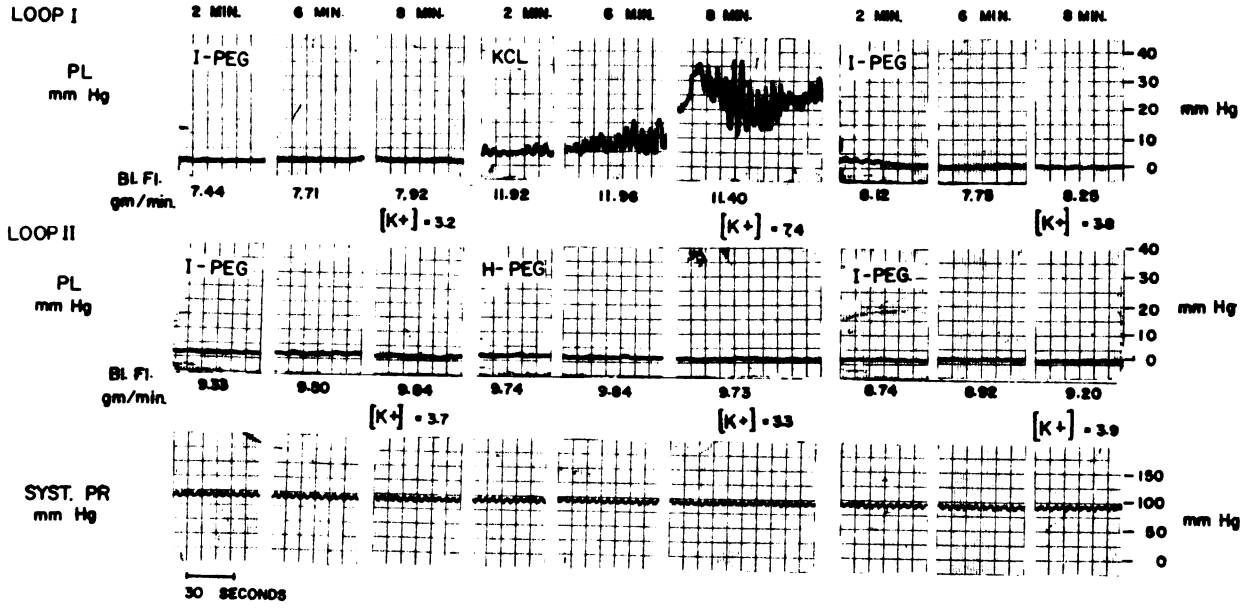

Fig. 4.--Pressure in the ileal lumen containing hyperosmotic KCl. [Lumen pressure (PL) in both segments and systemic blood pressure (SYST. PR), were recorded simultaneously. Venous outflow (Bl. Fl.) and the accompanying potassium ion concentration are shown in numbers below tracings of lumen pressure.]

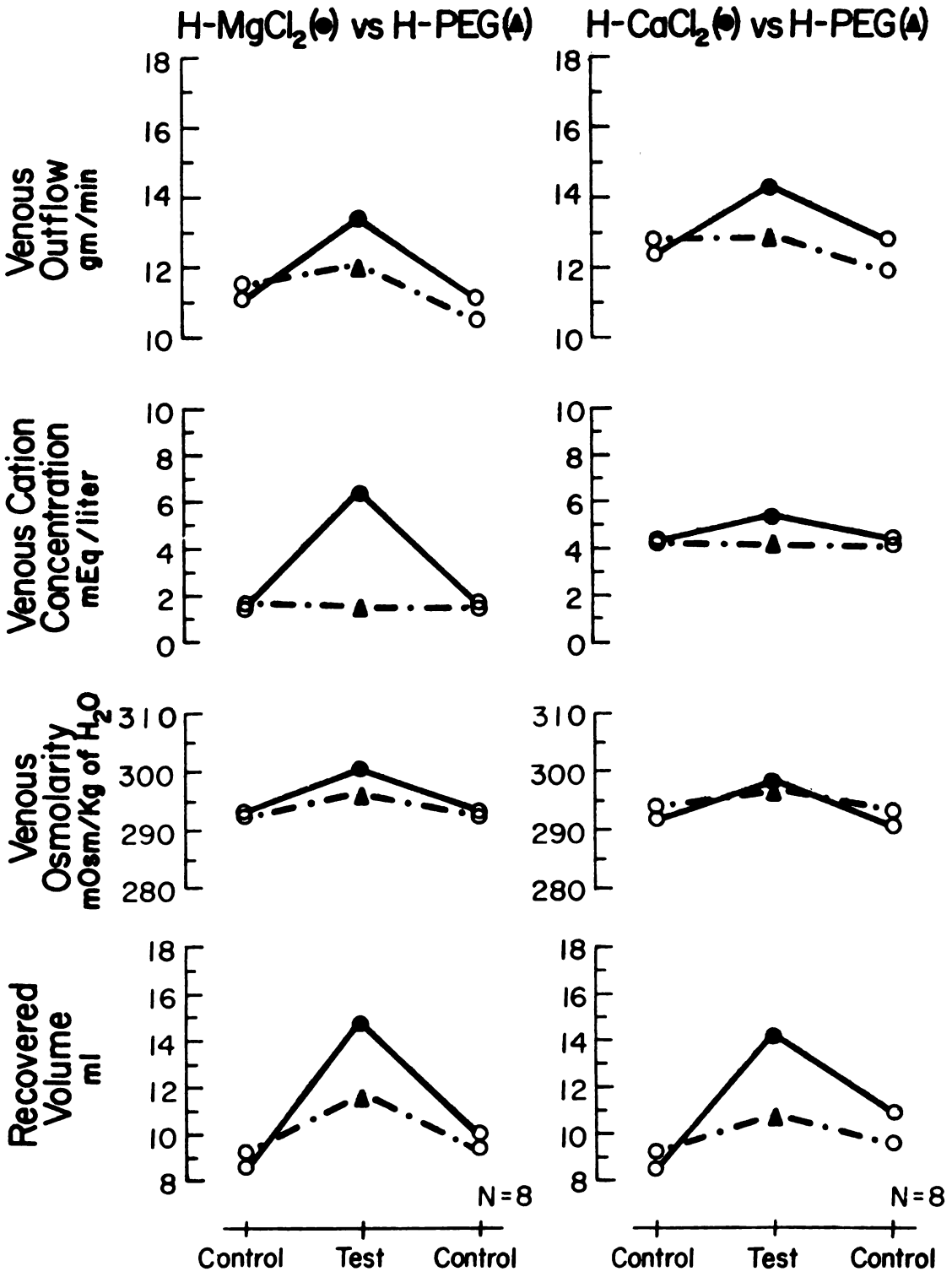

Fig. 5.--Effects of placing hyperosmotic $MgCl_2$ and $CaCl_2$ in the ileal lumen on venous outflow, cation concentration, osmolarity and recovered luminal fluid volume. [Open circles represent the average value with control solution, I-PEG in the lumen.]

(+ 3.0 ± 0.5 ml/15 min) than did H-PEG. H-$MgCl_2$ or H-PEG in the ileal lumen rarely altered the intestinal luminal pressure or wall activity.

H-$CaCl_2$ vs. H-PEG

The result of this study was essentially the same as those in the study of H-$MgCl_2$ vs. H-PEG for all the measured parameters, excepting that the increase in venous Ca^{++} concentration was not as great as that of Mg^{++} concentration (Figure 5). H-$CaCl_2$ increased ileal venous outflow from 12.46 to 14.25 gm/min, while H-PEG remained at the control level (12.78 gm/min) (Table 6). H-$CaCl_2$ in the ileal lumen did cause a rise in Ca^{++} venous concentration in every case (N=8), while H-PEG caused no change in Ca^{++} concentration in the control segment. However, the rise in Ca^{++} concentration caused by H-$CaCl_2$ in the lumen was small, on the average only 0.95 mEq/liter in the venous outflow (Table 7).

The rise in venous osmolarity by H-$CaCl_2$ was not different from that caused by H-PEG (Figure 5 and Table 8). H-$CaCl_2$ and H-PEG both showed a gain of luminal fluid volume (Figure 5), but H-$CaCl_2$ gained a greater volume than did H-PEG (Table 9). H-$CaCl_2$ gained 4.2 ml during 15 min in the lumen while H-PEG gained 0.76 ml.

Neither H-$CaCl_2$ nor H-PEG caused a measurable change in the ileal luminal pressure or wall activity.

H-PEG vs. I-PEG

Figure 6 and Table 10 show that on the average, H-PEG in one segment did not cause a significant change in venous outflow (- 0.21 ± 0.41 gm/min) as compared to the pre-control value (13.36 gm/min) but caused a significant increase in flow (+ 0.58 ± 0.20 gm/min) from the post-control value (12.57 gm/min). The concomitant flow changes occurring in the other segment which contained I-PEG during all three successive periods were a significant fall in flow (- 0.85 ± 0.33 gm/min) from pre-control (13.66 gm/min) and a nonsignificant increase in flow (+ 0.18 ± 0.17 gm/min) from post-control (12.64 gm/min). Comparing the flow changes in the test segment (H-PEG) to the concomitant flow changes in the control segment (I-PEG), H-PEG caused a significantly greater flow (+ 0.63 ± 0.25 gm/min) from pre-control than did I-PEG but did not show a significantly greater flow (+ 0.41 ± 0.32 gm/min) from the post-control (Table 10). The venous osmolarity was significantly raised by H-PEG (+ 3.5 ± 1.2 mOsm/liter) while it was significantly decreased (- 3.7 ± 1.2 mOsm/liter) in the control segment which received I-PEG (Figure 6).

The volume recovered from the lumen containing H-PEG is also shown in Figure 6. H-PEG gave a greater volume recovery than I-PEG as compared to both pre- and post-control values while there was no difference among the recovered volumes from 3 successive periods with I-PEG

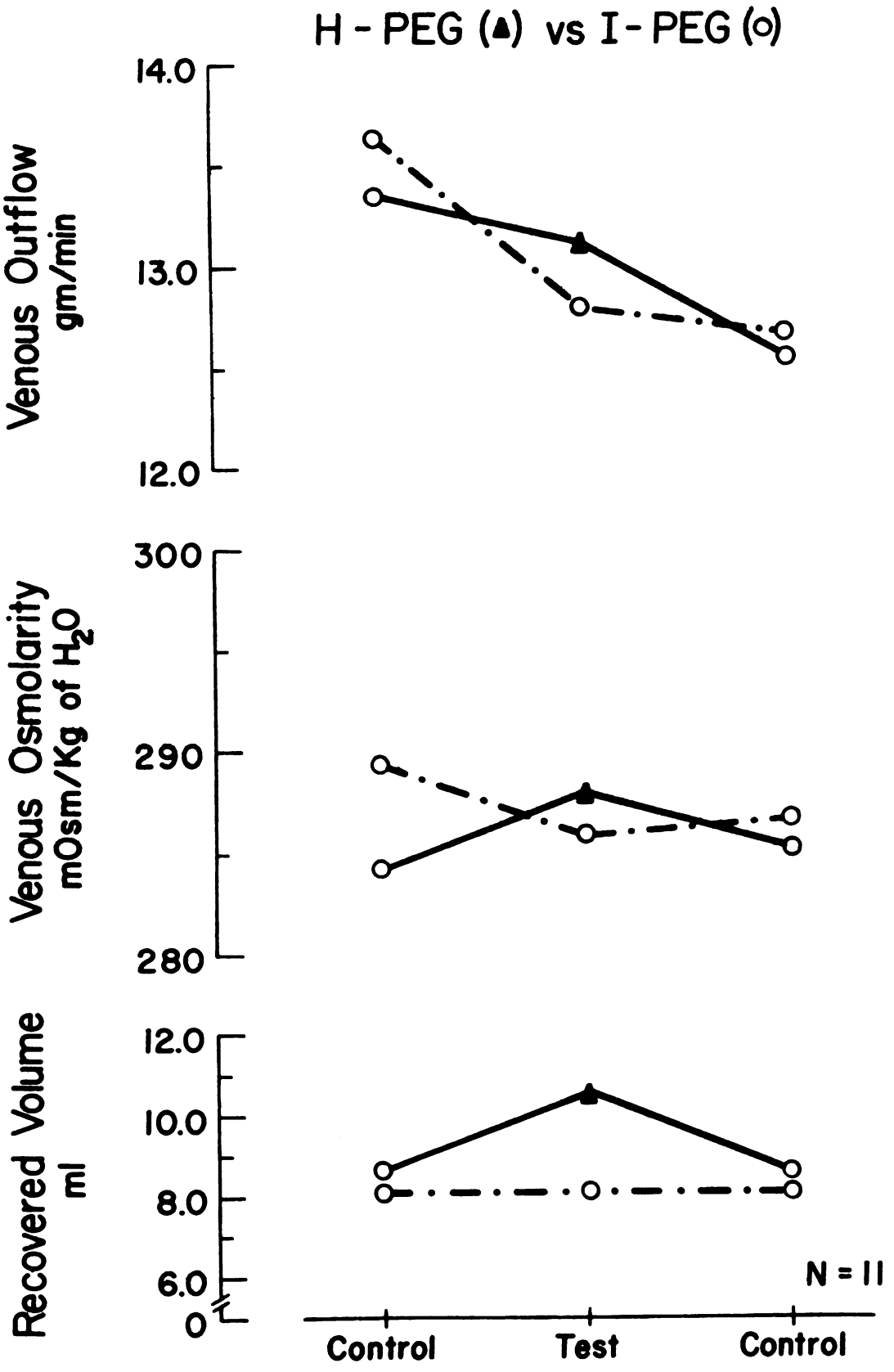

Fig. 6.--Effects of placing isosmotic and hyperosmotic polyethylene glycol solutions in the ileal lumen on venous outflow, venous osmolarity and recovered luminal fluid volume.

TABLE 10.--Venous outflow (gm/min) from paired ileal segments as affected by two different osmolarities of PEG (N = 11) or by hyperosmotic solutions of two different salts (N = 8).

Test Solution During Test Period		Control Period	Segment A		Segment B		Change in Segment A Relative to Change in Segment B (A-B)
Segment A	Segment B		I-PEG (Control)	Test Solution (Change from Cont.)	I-PEG (Control)	Test-Solution (Change from Cont.)	
H-NaCl	H-$CaCl_2$	pre	10.40	+ 2.28 ± 0.37*	11.32	+ 3.03 ± 0.70*	- 0.75 ± 0.71
		post	9.31	+ 3.37 ± 0.43*	11.01	+ 3.34 ± 0.68*	+ 0.03 ± 0.76
H-NaCl	H-$MgCl_2$	pre	10.50	+ 3.24 ± 0.88*	11.17	+ 4.41 ± 0.77*	- 1.17 ± 0.94
		post	10.89	+ 2.85 ± 0.95*	10.65	+ 4.93 ± 1.15*	- 2.09 ± 0.90*
H-KCl	H-$MgCl_2$	pre	11.33	+ 5.53 ± 0.79*	12.03	+ 2.17 ± 0.76*	+ 3.36 ± 0.93*
		post	10.68	+ 6.18 ± 0.83*	10.66	+ 3.54 ± 0.62*	+ 2.64 ± 0.71*
H-PEG	I-PEG	pre	13.36	- 0.21 ± 0.41	13.66	- 0.85 ± 0.33*	+ 0.63 ± 0.25*
		post	12.57	+ 0.58 ± 0.20*	12.64	+ 0.18 ± 0.17	+ 0.41 ± 0.32

*Denotes that the change or the difference between two values compared is statistically significant at $p < 0.05$.

in the lumen. These data show that H-PEG had no volume loss (- 0.02 ± 0.23 ml/15 min) while I-PEG had about the same volume loss (- 1.86 to - 1.54 ml/15 min) in the series of isosmotic studies (Figure 6 and Figure 2).

H-PEG in the ileal lumen did not significantly change the wall activity as indicated by the luminal pressure recording (Figure 4).

H-NaCl vs. H-$CaCl_2$

Figure 7 and Table 10 show that H-$CaCl_2$ and H-NaCl caused similar magnitudes of increase in venous outflow or luminal fluid volume. Rarely did either change the intestinal luminal pressure.

H-$MgCl_2$ vs. H-NaCl

H-$MgCl_2$ caused a greater venous outflow than did H-NaCl (Figure 7 and Table 10). Neither H-$MgCl_2$ nor H-NaCl in the ileal lumen altered the intestinal luminal pressure, but both caused the same degree of gain in the recovered luminal fluid volume (Figure 7).

H-KCl vs. H-$MgCl_2$

Using I-PEG as a control, H-KCl caused a significantly greater flow increase than did H-$MgCl_2$ (Figure 7 and Table 10). H-KCl also caused a greater gain in recovered luminal fluid volume than H-$MgCl_2$. Again H-KCl caused an increase in intestinal luminal pressure while H-$MgCl_2$ did not.

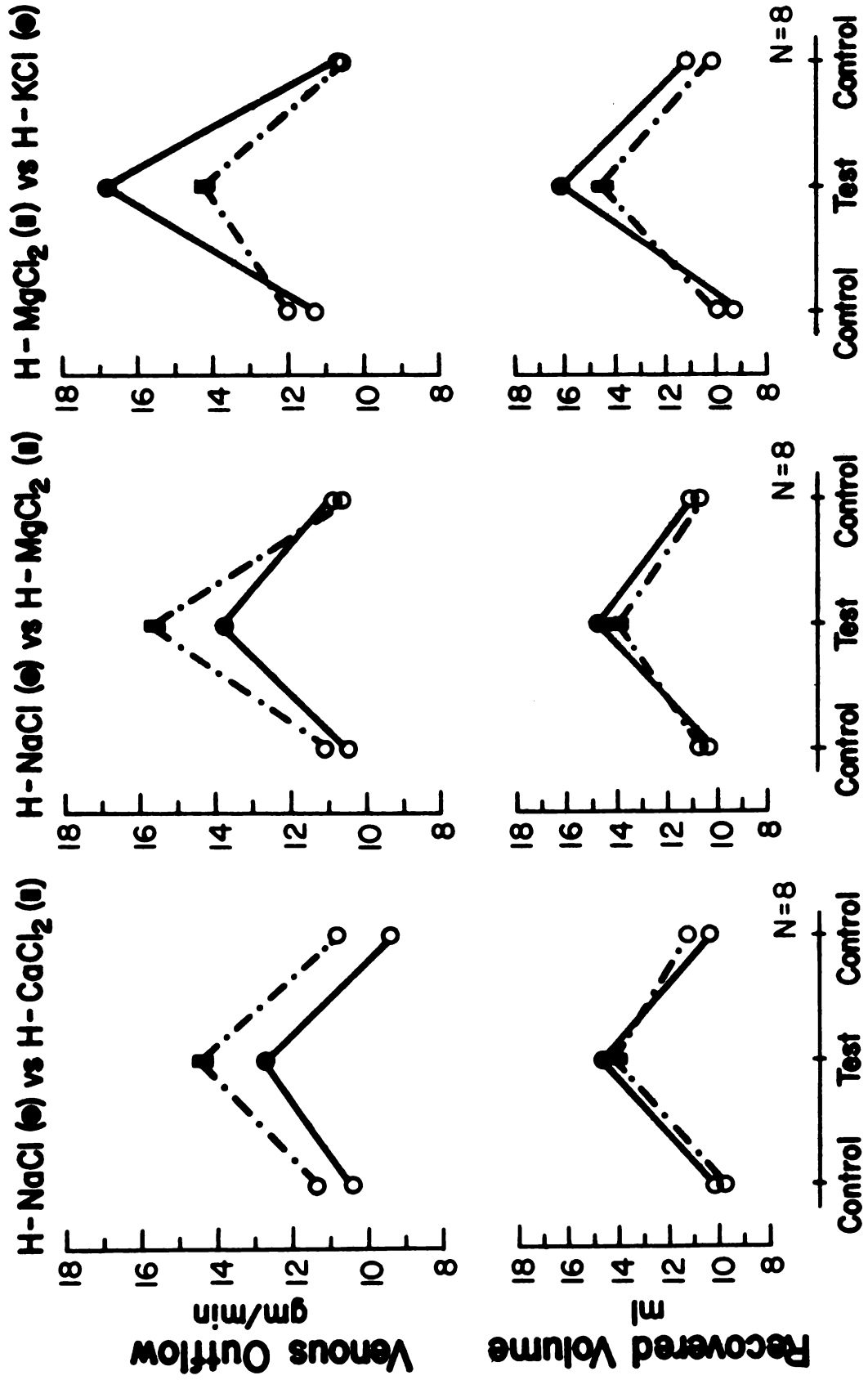

Fig. 7.--Venous outflow and recovered luminal fluid volume from paired ileal segments containing different hyperosmotic salt solutions. [Open circles represent the average value with control solution, I-PEG in the lumen.]

Summary of Changes in Blood Flow by Solutions in the Ileum

The average per cent changes in venous outflow from the pre-control flow caused by various solutions in the ileal lumen are shown in Figure 8. The data for each solution were pooled from all the experiments presented in the previous sections. The pre-control value for each solution was obtained with I-PEG in the lumen just preceding the placement of the test solution into the lumen. I-PEG *per se* had a significant fall in flow of 2.5 ± 0.9% (N=41) below the pre-control flow. As shown in Table 2 the fall in flow with I-PEG in the lumen was 8.2 ± 1.7% in one segment and 9.2 ± 1.8% in the other segment. The flow values for I-PEG in Table 2 were collected in the early periods of all experiments while the flow values for I-PEG in Figure 8 were pooled from data gathered from every stage of experiments. Thus, these data show that the rate of fall in flow (spontaneous change) was greater during the early stages of experiments than during the later stages.

All the isosmotic salt solutions in the ileal lumen except I-KCl caused a significant decrease in venous outflow. I-NaCl caused a 9.9 ± 2.3% fall in flow below the pre-control; H-$MgCl_2$ a 9.2 ± 3.1% fall; and I-$CaCl_2$ a 7.0 ± 3.5% fall. These falls in flow were not significantly different from each other. However, these decreases were all significantly different from the fall in flow caused

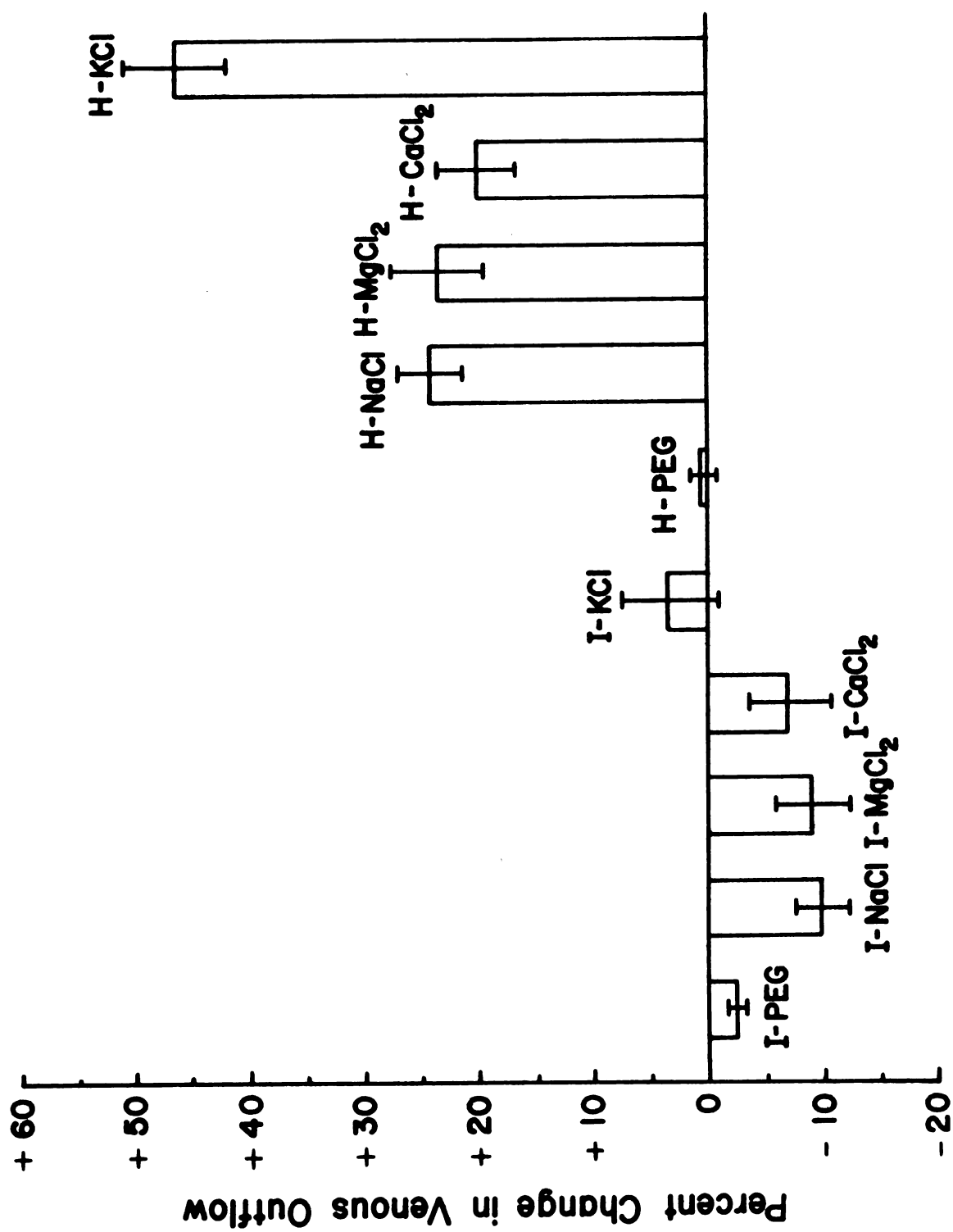

Fig. 8.--Summary of changes in venous outflow after placing various solutions in the ileal lumen. [Bars represent the mean of per cent change ± S.E. from the pre-control value with I-PEG in the lumen.]

by I-PEG (- 2.5 ± 0.9%). I-KCl in the lumen did not cause a significant change in venous outflow (+ 3.5 ± 4.2%) from the pre-control value. As compared to the overall flow change caused by I-PEG (- 2.5 ± 0.9%, N = 41), I-KCl however caused a significant increase in flow.

The analysis of the pooled data in Figure 8 with Student's t-test for unpaired comparison reveals that the flow change by H-PEG (+ 0.5 ± 1.1%, N = 32) was obviously not significantly different from the pre-control value but was significantly different from the pooled flow change caused by I-PEG (- 2.5 ± 0.9%, N = 41). This analysis also reveals that all the hyperosmotic salt solutions caused a much greater increase in flow (+ 20 - + 47%) than that caused by H-PEG (+ 0.5 ± 1.1%, N = 32). H-KCl caused a greater increase in flow (+ 47.0 ± 4.4%, N = 18) than did any other hyperosmotic salt solution. The pooled data show further that changes in flow caused by H-NaCl (+ 24.0 ± 2.8%, N = 22), H-$MgCl_2$ (+ 24.0 ± 4.0%, N = 24), and H-$CaCl_2$ (+ 20.0 ± 3.4%, N = 16) were not different from each other. However, in experiments specifically designed to allow a simultaneous comparison of H-$MgCl_2$ *vs.* H-NaCl in the same dog, it was found that H-$MgCl_2$ did cause a small but significantly greater increase in flow than did H-NaCl (Figure 7 and Table 10). A similar experimental comparison of H-KCl *vs.* H-$MgCl_2$, H-$CaCl_2$ *vs.* H-NaCl (Figure 7 and Table 10) or H-PEG *vs.* I-PEG (Figure 6

and Table 10) allows the same conclusions regarding their relative effects on blood flow as can be made from the pooled data in Figure 8.

Osmolarity-Concentration Relationship of Polyethylene Glycol (PEG) and Sodium Chloride (NaCl)

Figure 9 illustrates the results of five different sets of experiments. Empirically, 24% PEG solution (600 mM/liter) has about the same osmolarity (1450 mOsm/liter) as 4.5% NaCl solution (770 mM/liter). As shown in Figure 9, the osmolarity-concentration relationship of NaCl was different from that of PEG. The PEG curve about 790 mOsm/liter was steeper than that of NaCl in the range of 790-1450 mOsm/liter. This indicates that with the same dilution, the decrease in osmolarity of PEG was greater than that of NaCl. For example, when 2.5 ml of water was added to 7.5 ml of 1450 mOsm PEG (600 mM/liter) or NaCl (770 mM/liter) solution, the osmolarity of the diluted PEG solution (450 mM/liter) was 860 mOsm/liter whereas that of the diluted NaCl solution (580 mM/liter) was 1060 mOsm/liter. This dilution is equivalent to adding 3.3 ml of water to 10 ml of 1450 mOsm/liter PEG or NaCl solution. According to Figure 9, an addition of 5 ml of water into 10 ml of 1450 mOsm/liter NaCl (H-NaCl, Table 9) will make a 930 mOsm/liter solution (510 mM/liter), and an addition of 1.2 ml of water into 10 ml of 1450 mOsm/liter PEG (H-PEG, Table 9) will make a 1180 mOsm/liter solution (540 mM/liter).

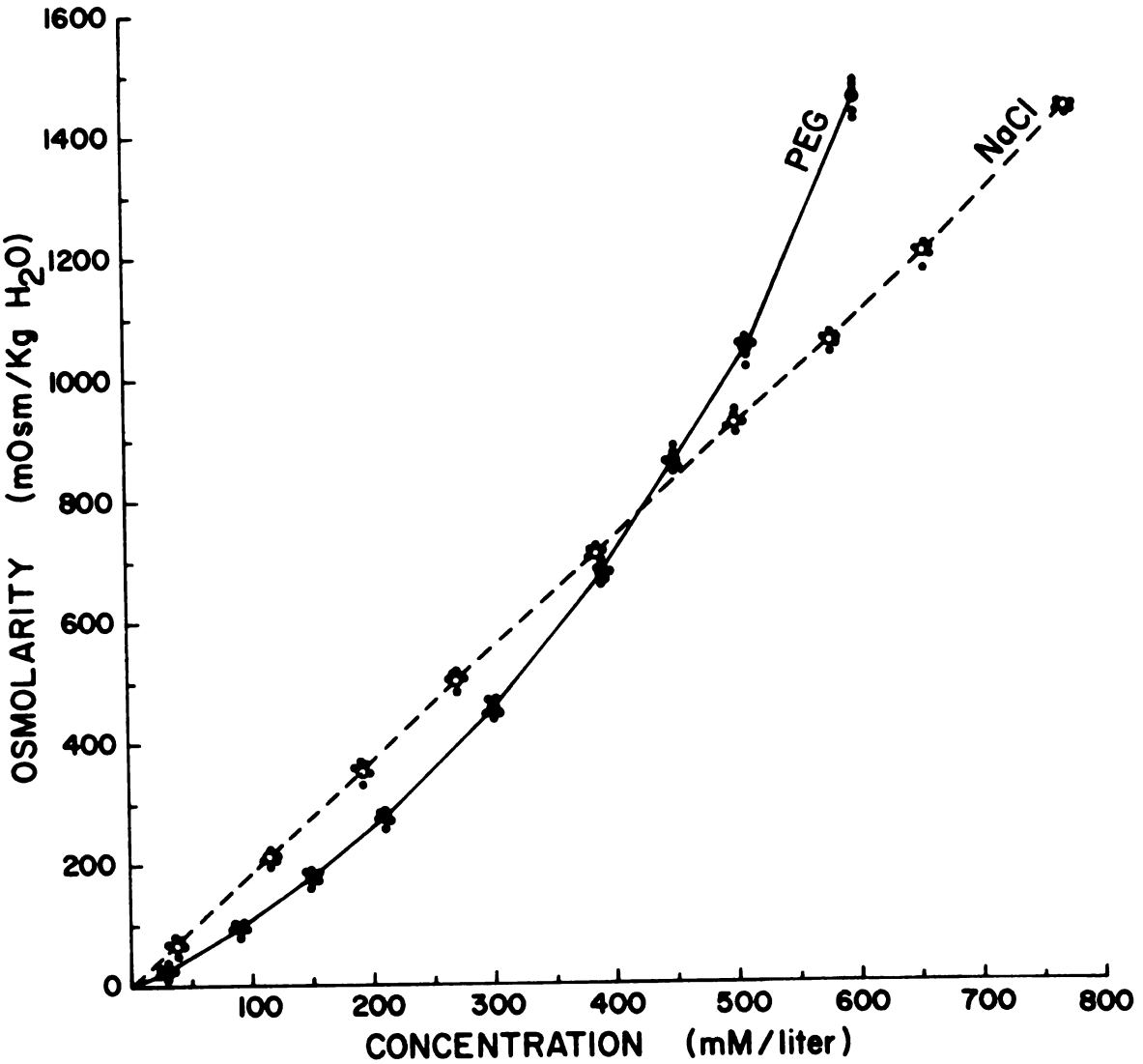

Fig. 9.--Relationship of osmolarity to concentration of polyethylene glycol (PEG) and sodium chloride (NaCl).

CHAPTER IV

DISCUSSION

This study was designed to investigate the effects of placing isosmotic (300 mOsm/liter) and hyperosmotic (1500 mOsm/liter) solutions of sodium chloride, potassium chloride, magnesium chloride and calcium chloride into the lumen of the ileum on local blood flow, venous osmolarity and cation concentration, luminal fluid volume and intestinal wall activity. These parameters were measured in two adjacent *in situ* segments of the ileum which were naturally perfused through their intact arteries. Control solution was placed in one segment and test solution in the other and their effects on the above parameters were simultaneously measured in the two segments.

Blood flow through a vasculature is determined by its resistance to flow and the pressure gradient across the vasculature. Since pressure gradients along the vasculature of the two segments are the same, difference in flow changes between two segments indicates difference in changes in their vascular resistance. Therefore, in the present study a decrease in flow indicates an increase

in vascular resistance and an increase in flow a decrease in resistance.

It is usually observed that a natural or spontaneous fall in flow with time occurs in a preparation of a naturally perfused vasular bed. Thus, in the present study the purpose of using two adjacent segments, one as control and the other as test, was to separate this natural fall in flow with time from the experimental or test effect. Therefore, it was necessary to test whether this natural or spontaneous change in flow between the two segments is different or the same. As shown in Table 2, when both segments contained the same solution (I-PEG) the fall in blood flow was essentially the same. This indicates that spontaneous changes (i.e., a natural fall in flow with time) that occurred in the two segments were the same. It is, therefore, valid to use one of these two segments as control for the spontaneous change that occurred in the other segment. Thus, in the analysis of the data, flow changes that occurred in the test segment were always compared with a simultaneous changes that occurred in the control segment.

These studies show that isosmotic solutions of NaCl, $MgCl_2$ or $CaCl_2$ in the ileal lumen decreased ileal venous outflows and isosmotic KCl caused variable changes in venous outflow. Venous concentration was significantly raised by all isosmotic solutions of $CaCl_2$, KCl and

$MgCl_2$ but not by NaCl. Only isosmotic KCl occasionally induced an increase in ileal wall activity. The other isosmotic salt solutions rarely changed the lumen pressure and motor activity. All isosmotic solutions in the ileal lumen for 15 minutes lost some of their luminal fluid. Isosmotic PEG lost a greater volume than any of the isosmotic salt solutions.

All of the four hyperosmotic salt solutions increased the venous outflow. The increase by KCl was greater than that by any of the other three. $MgCl_2$ caused a greater increase than did NaCl or $CaCl_2$. Increases caused by NaCl and $CaCl_2$ were not different. All hyperosmotic salt solutions significantly elevated the cation concentration and osmolarity of the venous outflow. Again only hyperosmotic KCl regularly produced an increase in the intestinal wall activity and intra-luminal pressure. The other hyperosmotic salt solutions rarely altered the intraluminal pressure. All the hyperosmotic salt solutions gained luminal fluid volume. Potassium chloride was the greatest and the other three had no difference in their volume gains. Hyperosmotic PEG gained much less volume than any of the hyperosmotic salt solutions.

Placement of these salt solutions in the gut lumen will likely increase intestinal tissue concentration when they are absorbed. Increasing the concentration of these ions by intra-arterial infusion of the isosmotic solution

of these salts has been shown by Dabney, Scott and Chou (9) and Texter et al. (32) to cause notable changes in intestinal blood flow. Dabney et al. found that in a naturally perfused ileal segment $MgCl_2$ increases blood flow as a function of its plasma concentration; $CaCl_2$ produces a variable effect on blood flow over the same range of rise in plasma Ca^{++} concentration as Mg^{++}; KCl causes a biphasic effect on blood flow, first increasing then decreasing as a function of its plasma concentration and NaCl has no effect. The findings in a constant flow perfusion of the superior mesenteric vasculature by Texter et al. were generally in agreement with those found by Dabney et al. in a naturally perfused ileal segment except that infusion of $CaCl_2$ caused increased vascular resistance. Texter et al. found that $CaCl_2$ caused an increase in resistance when its concentration was 2.2 mEq/liter or more above control. They also found that $MgCl_2$ with an increase of 0.48 mEq/liter in plasma Mg^{++} concentration significantly decreased the resistance of the superior mesenteric vasculature; K^+ at an increase of 4.8 to 9.6 mEq/liter decreased resistance.

The effects of luminal placement of isosmotic solutions on blood flow obtained in the present study are quite different from those obtained when these solutions were given intra-arterially. Luminal placement of I-NaCl consistently decreased blood flow while intra-arterial

infusion caused a small increase. Magnesium chloride when placed in the ileal lumen caused a decrease in flow while intra-arterially $MgCl_2$ always caused a large increase in flow in ileal or superior mesenteric vascular bed (9, 32). Potassium chloride had a variable effect on blood flow when placed in the ileal lumen but it increased ileal blood flow when given intra-arterially into an ileal segment over the low concentration range of postassium. In considering the reasons for this difference, several possibilities need to be evaluated. First, the control solutions were different. I-PEG was used as control in the present study while I-NaCl was used as control in the intra-arterial infusion study. Second, it is conceivable that tissue ion concentration might not be raised enough to exert direct vascular effects with I-Salt solutions in the lumen. Third, it is possible that luminal placement of salt solutions could affect local blood flow through mechanisms other than the mechanisms which determine the results when ions are given intra-arterially.

I-PEG was used as the control solution for all these I-Salt solutions and the changes in local blood flow caused by I-NaCl, I-$MgCl_2$ or I-$CaCl_2$ were very small. It is, therefore, possible that these I-Salt solutions actually do not alter blood flow and the apparent decrease in flow by these salt solutions might result from using I-PEG as the control solution. If I-PEG in the lumen

caused a small rise in blood flow and I-Salt solutions did not change blood flow, then a comparison of the blood flow caused by the I-Salt solution to I-PEG as the control would show a small decrease by the I-Salt solution. The vasoacivity of I-PEG in the lumen was tested and the results showed that local blood flow did not change when the luminal content was changed from I-PEG to ambient air and vice versa. This result supports the possibility that I-PEG in the lumen does not have a vascular effect and tends to validate I-PEG as an adequate control. If it is, then the effects on venous outflow of isosmotic salt solutions in the lumen did not result from using I-PEG as the control solution but were due to some real action of these salt solutions when they were placed in the ileal lumen.

Although plasma cation concentration of the venous outflow was significantly raised by I-KCl, I-$MgCl_2$ and I-$CaCl_2$, it is possible that the cation concentration in the tissue fluid bathing the resistance vessels was not raised sufficiently to cause direct vascular effects. I-$MgCl_2$ in the ileal lumen raised plasma Mg^{++} concentration by 0.4 mEq/liter. I-$CaCl_2$ raised Ca^{++} concentration by 0.2 mEq/liter, I-KCl raised K^{+} by 2.2 mEq/liter and I-NaCl did not significantly change plasma sodium concentration. It is not known whether these increments in venous cation concentrations also occurred around the resistance vessels. But as compared to the effect of cations when given intra-arterially (9, 32), it is

reasonable to consider that the increase in local ion concentration in the present study was not enough to cause a detectable vascular effect. On the other hand, the direction of these vascular effects in the present study was opposite to that of the intra-arterial studies especially in the case of $MgCl_2$ and NaCl. Therefore, the effects of the luminal placement of these salt solutions may have been caused through mechanisms other than the direct effect of ions on the vasculature.

In speculating on other mechanisms whereby these isosmotic salt solutions in the ileal lumen affect the local blood flow, several possibilities are worth consideration. These are: (1) a change in motor activity and luminal pressure, (2) a mild decrease in K^+ concentration around the vessels during the placement of isosmotic salt solutions, (3) a change in metabolism of the intestinal tissue, and (4) a neural mechanism leading to the vasoactivity.

It has been demonstrated that intestinal blood flow is profoundly influenced by motor activity of the intestine (6). A rise in luminal pressure or strong contractions of the intestine decrease the inflow of blood and lessening of the intestinal wall tension augments intestinal blood flow (2, 11, 28). But none of the isosmotic salt solutions except KCl caused any measurable change in motor activity and luminal pressure. The first

possibility is, therefore, not likely to be the mechanism whereby I-NaCl, I-$MgCl_2$ or I-$CaCl_2$ decreased local blood flow. That I-KCl occasionally increased luminal pressure and motor activity, however, may be one of the reasons why I-KCl in the ileal lumen caused a variable effect on local blood flow. The direct vasodilation of the potassium ion may be counteracted by the rise in luminal pressure and motor activity (5, 13). This counteraction can be seen in Figure 4, blood flow was first increased by KCl, but this increase had started to wane as the luminal pressure rose.

During the placement of isosmotic salt solutions other than KCl, a diffusion of intestinal tissue potassium into the lumen in exchange for other ions might occur. Such an exchange could produce a small decrease in the concentration of K^+ in the plasma or interstitial fluid in the intestinal wall. A mild deficit in potassium concentration either of plasma or of interstitial fluid could cause a small degree of vasoconstriction (14, 23) and, thus, a small decrease in local blood flow. Such a mechanism might explain, in part, why all I-Salt solutions in the lumen except I-KCl caused a small decrease in venous outflow.

A change in local tissue metabolism can cause a change in local blood flow (18, 24). During the placement of isosmotic salt solutions, the metabolism of the intestinal tissue might be changed. Thus, a change in

local blood flow might consequently occur. This parameter, however, was not measured in the present study.

A neural mechanism, sensitive to nutrients like glucose and amino acids, has been demonstrated in the intestine. Zamiatina (37) in 1957 first studied the frequency and amplitude of impulses in the intestinal nerve as affected by various states of the digestive tract in anesthetized adult cats. He reported that high activity of afferent impulses was observed in small intestinal nerves during intestinal digestion of boiled meat. He also reported that with either a perfusion of glucose or amino acids into the intestinal lumen or with intramuscular injection of glucose or amino acids there was a marked increase in afferent impulse activity of small intestinal nerves. Sherma and Nasset (27) in 1962 also demonstrated that the activity of mesenteric afferent nerves was increased when foodstuffs were perfused through the intestinal lumen both in anesthetized cats and in conscious dogs. Furthermore, the size of the nerve affected was relatively specific to the class of substances used. Vasilevskaya (33) also has reported that enteroceptive "chemoreceptors" can react selectively to the intraluminal introduction of acid or to glucose perfusion. Thus, it is possible that the placement of salt solutions in the lumen, in the present study, might have stimulated "chemoreceptors" and this excitation could possibly bring

about changes in alimentary behavior. A change in the local blood flow in the presence of salt solutions in the lumen might be one of these responses.

In contrast to the isosmotic solutions, luminal placement of hyperosmotic solutions caused a significant rise in local blood flow. This rise in flow may be attributable to: (1) a rise in osmolarity of the fluid surrounding the vasculature of the intestinal wall, (2) a rise in local cation concentration and (3) mechanisms other than a direct effect of hyperosmolarity or ions on the vasculature.

It has been demonstrated that when given intra-arterially, hyperosmotic solutions cause a decrease in vascular resistance (21, 22) and hyposmotic solutions cause an increase in vascular resistance (21). Read, Johnson, Vick and Meyer (22) found that when plasma osmolarity, was increased more than 25 mOsm/liter, a maximal dilation was observed. Plasma osmolarity higher than 700 to 800 mOsm/liter caused intravascular red-cell agglutination and hence the blood flow through that area decreased. Thus, in the present study, all the hyperosmotic solutions including H-PEG raised local intestinal blood flow concomitant with a rise in venous osmolarity so that a rise in local osmolarity around the blood vessels may be a factor causing the increase in flow.

It is not known whether the change in tissue osmolarity is the same as the change in venous osmolarity. However, it is reasonable to speculate that at least the tissue osmolarity of the mucosa which was exposed to a 1500 mOsm solution is some higher than the venous osmolarity. Thus depending on the osmolarity, blood flow through the mucosa may have increased or decreased. It might also be expected that the intestinal tissue would become hyperosmotic owing to both the insorption of solutes into tissue and/or the exsorption of water from tissue into lumen. Thus, an osmotic gradient would exist in the intestinal tissue, higher in the mucosal layer and lower in the serosal layer.

The present study showed that hyperosmotic PEG caused the same degree of rise in venous osmolarity as that by H-$CaCl_2$ or H-$MgCl_2$. Thus, H-PEG may have produced about the same degree of rises in local tissue osmolarity as those by H-$CaCl_2$ or H-$MgCl_2$. However, the rise in blood flow caused by H-PEG was minimal as compared to 20 to 25% rise in flow by H-$CaCl_2$ or H-$MgCl_2$ (Figure 8). If PEG <u>per se</u> has no direct action on vessels, then the rise in blood flow by H-PEG appears to be due to the rise in local osmolarity. Therefore, these data indicate that the rise in local osmolarity produced by placing 1500 mOsm solutions in the lumen may contribute minimally to the rise in local blood flow. Thus, it appears that most

of the increase in local blood flow caused by the hyperosmotic salt solutions was through mechanisms other than the rise in local osmolarity.

All the hyperosmotic salt solutions in the ileal lumen caused a significant rise in venous concentration of cations. It is, therefore, possible that the direct vascular effect of ions is in part responsible for the increase in local blood flow. The data showed that H-$CaCl_2$ raised calcium ion concentration in the venous outflow from a control value of 4.3 to 5.2 mEq/liter, H-NaCl, from 151 to 161 mEq/liter, H-KCl, from 3.3 to 7.5 mEq/liter, and H-$MgCl_2$ from 1.5 to 6.3 mEq/liter. In view of the effects of intra-arterial infusions, it might be expected that H-KCl or H-$MgCl_2$ in the ileal lumen would cause an increase in local blood flow; while H-$CaCl_2$ would cause a decrease or a variable effect and H-NaCl would cause little effect on local blood flow. However, the results were that all the hyperosmotic salt solutions raised local blood flow by 20-47% over the control flow value (Figure 8).

In the study of hyperosmotic salt vs. hyperosmotic salt solutions, it was found that H-KCl produced a greater rise in blood flow than did H-$MgCl_2$. H-$MgCl_2$ produced a greater rise in flow than did H-NaCl, while H-NaCl and H-$CaCl_2$ had the same degree of rise in flow. Therefore, these data suggest that the greater rise in ileal blood flow by H-KCl or H-$MgCl_2$ than that by H-NaCl or H-$CaCl_2$

was due to a direct dilating effect of potassium or magnesium ion on the blood vessels. In other words, the increases in flow caused by H-$MgCl_2$ or H-KCl might be in part, through the direct vascular effect of ions. However, the rise in flow caused by H-$CaCl_2$ or H-NaCl can not be explained by the direct effect of ions on vessel.

The possibility that mucosal chemoreceptors may play a role in flow change has been described (p. 51). In addition to a chemoreceptor a mucosal osmoreceptor may also be involved in the flow changes. Since osmoreceptors have been demonstrated to exist in the intestine (10, 29), it is possible that osmoreceptors in the intestine are stimulated by the hyperosmotic salt solutions and are, in part, responsible for the rise in local blood flow. Vogt (36) in his in vitro study on isolated jejunal segments of rabbits suggested that the response in motility of the circular smooth muscle to the hyperosmolarity of various sodium salts was through the stimulation of Auerbach's plexuses by the hyperosmolarity of these sodium salts. Therefore, it is reasonable to speculate that hyperosmotic salt solutions might stimulate the intrinsic nerve plexuses to raise blood flow.

An increase in local tissue metabolism is accompanied by a decrease in local vascular resistance (18, 24). In the present study there was no data to show that the metabolic rate of the intestinal tissue was raised during

the luminal placement of hyperosmotic salt solutions. However, Brodie and his associates in 1910 (3, 4) observed an increase in oxygen uptake by the intestinal segment during the placement of distilled water, 10% peptone solution or NaCl solutions of 0.9% to 4.6%. Furthermore, Chou, King and Dabney (7) have shown that placing 20% or 50% glucose solution in a canine jejunal segment raised the local blood flow while PEG solution of equal osmolarity to these glucose solutions caused much less rise in local blood flow than did glucose solution. PEG is presumably a nonabsorbable substances while glucose is actively absorbed with the expenditure of energy. Thus, it is possible that an increase in metabolic rate through mucosal transport or absorptive process may be involved in the rise in local blood flow caused by the hyperosmotic salt solutions.

In the present study, only KCl, either isosmotic or hyperosmotic, in the ileal lumen caused an increase in intestinal wall activity, i.e., increase in lumen pressure and rhythmic contractions. Other salt solutions either isosmotic or hyperosmotic in the lumen rarely altered the lumen pressure. The mechanisms for this potassium effect on the intestinal wall activity of placing isosmotic KCl solutions in the lumen is not clear. But it seems possible that the potassium ion affects both visceral smooth muscle and intrinsic nerve plexuses. Other studies have shown

that KCl causes a biphasic action on intestinal wall activity; low concentration of potassium inhibits whereas high concentration stimulates intestinal motility (1, 5, 9, 36).

In addition to KCl effect, hyperosmolarity itself might cause some motility effect. Helft et al. (15) have reported that perfusion of 50% glucose into Roux-Y jejuno-cutaneous preparation in conscious dogs inhibited the jejunal motility. However, Vogt (36) has found that in an in vitro study on an isolated intact jejunal segment hyperosmolarity elicited a potent stimulating effect on the intestinal circular smooth muscle. But he suggested that this effect of hyperosmolarity is through the action of hyperosmolarity on the intestinal Auerbach's plexus. Thus, hyperosmolarity has two actions, one is inhibitory and the other is stimulatory. No significant change in the intestinal lumen pressure (except with KCl) was found with luminal placement of hyperosmotic solutions in this present study. This disagreement with the previous studies of Helft et al. and Vogt may be due to: (1) different technique and different experimental conditions, e.g., different osmolarity, (2) the less sensitivity of the intraluminal pressure tracing to detect a small stimulating or inhibiting effect. In the present study, the ileal segment during the control period was very quiescent. Therefore, it would have been difficult to detect

inhibitory effect of hyperosmolarity in the present study. However, a stimulating effect of the hyperosmolarity was also not seen in the present study, possibly because osmolarity in the intestinal tissue was not raised sufficiently to alter motility. The stimulatory effect of hyperosmotic KCl solution on the motility, thus, seems to be due to the potassium or chloride ion itself.

All isosmotic solutions of salts and polythylene glycol lost some luminal fluid volume (Figure 2 and Table 5), and all the hyperosmotic solutions gained luminal fluid volume (Figures 3, 5 and 6 and Table 9). Isosmotic polyethylene glycol lost greater fluid volume than did any isosmotic salt solution and hyperosmotic PEG gained much less fluid volume than any hyperosmotic salt solution. PEG has been reported as being a reliable indicator for estimating intestinal water volume in perfusion studies (17) and therefore has been used regularly as an indicator of net water movement between the intestinal blood and lumen. It has been found that isosmotic PEG neither gains nor loses luminal fluid volume in the jejunum (7). Thus, if PEG is not absorbed in the small intestine, water was absorbed from isosmotic PEG solution in the dog ileum against osmotic gradient but not in the dog jejunum. Vischer et al. (34) have found that water was absorbed against an osmotic pressure gradient to about 130 mOsm greater than isosmolarity, when isosmotic NaCl is placed

in the dog ileum. A similar relation between water movements across the intestine and the total osmotic pressure is obtained if mannitol is used instead of NaCl (16). The present findings with isosmotic polyethylene glycol in the dog ileal segment are in accord with these findings by the others (16, 34) that water can be absorbed against osmotic gradient to a certain limit in the dog ileum. However, why isosmotic PEG in the ileum lost greater fluid volume than any of isosmotic salt solutions is puzzling.

A body of evidence shows that sodium is actively absorbed in the small intestine (8, 35). There is also evidence showing that calcium is probably actively absorbed (19, 25). But there is still no evidence showing that magnesium or potassium is actively absorbed in the small intestine. In the present study, all the isosmotic salt solutions except isosmotic NaCl in the ileal lumen had a much higher cation concentration than that of plasma or interstitial fluid. Therefore, no matter whether the cation is actively or passively absorbed, the cation was absorbed from the lumen due, at least, to the concentration gradient. This was evidenced by the rise in the venous concentration of these cations when they were placed in the lumen (Figure 2). Therefore, if water flow across the intestinal mucosa depends on the osmotic pressure but not the nature of the osmotically active substance, the isosmotic salt solutions in the dog ileum would be expected

to lose a greater fluid volume than the nonabsorbable isosmotic PEG because more water would be absorbed accompanying the absorption of salt particles. But the findings in the present study were just the opposite. Therefore, there may be some other physical or biological phenomena related to the handling of this fluid movement in the dog ileum.

Intestinal secretion is stimulated by the contact of foodstuffs with the mucosa and both chemical and mechanical factors are reported to exert the stimulation of secretion (31). In the present study, salt solution, as compared to PEG, might have had greater chemical stimulation of secretion, especially of mucus. Visual inspection of the recovered fluid revealed that luminal fluid from the segment receiving a salt solution was more viscous than that from the PEG segment. Thus, the greater recovered fluid volume of the salt solution may have resulted from a greater mucus secretion.

The gain in the luminal fluid volume after the placement of hyperosmotic solutions in the ileal lumen can be expected from the high osmotic pressure in the lumen. This result agreed with previous studies. As early as 1910, Brodie and Vogt (3) have found that with hyperosmotic NaCl solutions (2-4.6%) in the ileal lumen the luminal fluid was increased in the early stage (about 10 to 20 minutes) of the placement, but was gradually

absorbed later on. By using isotopes to measure the bidirectional movement of solutes and water Visscher et al. (34) and Hindle and Code (16) have also found that with a hyperosmotic solution (480 mM/liter of NaCl or 600 mOsm/liter of mannitol) in the dog ileum a net water movement occurred within the first 30 mintues but this fluid was reabsorbed thereafter.

This present study showed that hyperosmotic nonabsorbable polyethylene glycol solution gains much less luminal fluid volume than the hyperosmotic absorbable salt solutions. If PEG is nonabsorbable, it might be expected to gain more volume than absorbable ions since absorption of ions would reduce the number of osmotically active particles in the lumen. This present study however, showed the effect opposite to what would be expected from theoretical consideration based on osmosis and absorption. This unexpected findings might be explained in two ways. Moody and Durbin (20) have shown that in the stomach the osmotic effect of luminal solutes is greater for solutes with low molecular weight than for those with high molecular weight. Thus, the findings in the present study in the dog ileal segment are very similar to their findings in the stomach. The molecular weight of PEG is greater than those of cations used. The other explanation is that osmolarity-concentration relationship of PEG is nonlinear and is different from that of NaCl. As shown in Figure 9,

when both PEG and NaCl solutions of about 1450 mOsm/liter were equally diluted, the osmolarity of the PEG solution decreased more rapidly than did NaCl. Thus, even though the osmotic force of 1450 mOsm PEG was the same as that of 1450 mOsm NaCl, the osmotic force of PEG solution would become less than that of NaCl as soon as the same amount of fluid moves into the lumen as a result of hyperosmolarity. Therefore, a 1450 mOsm PEG solution in the lumen would be expected to gain less volume than a 1450 mOsm salt solution.

It is also possible that, as with isosmotic salt solutions, hyperosmotic salt solutions in the ileal lumen might cause a larger amount of mucus secretion than hyperosmotic PEG solution (31). This would tend to produce a larger recovered luminal fluid volume with the salt solution than that with PEG.

CHAPTER V

SUMMARY AND CONCLUSION

The present study was designed to investigate whether or not the luminal placement of NaCl, KCl, $MgCl_2$, or $CaCl_2$ solutions can affect the local blood flow and intestinal wall activity. This was accomplished by measuring total venous outflow and monitoring luminal pressure from two naturally perfused adjacent in situ segments of the dog ileum. It was found that:

1. The double-segment technique used in the present study was adequate and better than the single-segment technique in separating the flow change caused by the test agent from that occurred spontaneously with time.
2. All isosmotic solutions of NaCl, $MgCl_2$ and $CaCl_2$ in the ileal lumen when compared to isosmotic polyethylene glycol decreased the ileal venous outflow while isosmotic KCl caused a variable effect.

3. All the isosmotic salt solutions except NaCl in the lumen raised the venous cation concentration.
4. All the hyperosmotic solutions (1500 mOsm/liter) of these four salts significantly raised the ileal venous outflow with concomitant elevations of venous osmolarity and cation concentration.
5. Hyperosmotic PEG produced the same degree of elevation in venous osmolarity as that by hyperosmotic $MgCl_2$ or $CaCl_2$ but the increase in venous outflow by H-PEG was much less than the increase by hyperosmotic salt solutions.
6. Among these salt solutions, only KCl solution altered the luminal pressure and wall activity. Isosmotic KCl solution occasionally induced rhythmic contractions and elevation of luminal pressure. Hyperosmotic solution of KCl regularly produced these changes.
7. The volume of isosmotic solutions including PEG were decreased while in the ileal lumen; but all hyperosmotic solutions gained luminal fluid volume during 15-minute luminal placement. Isosmotic PEG lost greater volume

than did isosmotic salt solutions but hyperosmotic PEG gained less volume than did any hyperosmotic salt solution.

8. The *in vitro* study on osmolarity-concentration relationship of PEG and NaCl showed that when both PEG and NaCl solutions of 1450 mOsm/liter were equally diluted the osmolarity of PEG solutions decreased more rapidly than that of NaCl solutions. Thus, in order to reach to the same osmolarity PEG required less dilution than did NaCl.

In conclusion, the present study indicates that:

1. The luminal placement of salt solutions, either isosmotic or hyperosmotic, cause local change in ileal blood flow and these changes in the local blood flow were caused by one or more factors in addition to the direct effect of ions and tonicity on the local blood vessels. One of these additional factors may be through local nerves.
2. The increase in the intestinal wall activity or the lumen pressure induced by the potassium chloride solution in the lumen may have been caused either by the direct action of potassium ion on the visceral smooth muscle and/or by the stimulating effect of the

potassium ion on the nerves which innervate the visceral smooth muscle.

3. It seems probable that the smaller gain in the luminal fluid volume caused by hyperosmotic PEG than that caused by any hyperosmotic salt solution was due to the fact that the osmolarity of a PEG solution is decreased more than is the osmolarity of a salt solution when both are equally diluted.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Ambache, N. Interaction of drugs and the effect of cooling on the isolated mammalian intestine. J. Physiol. 104:266-287, 1946.

2. Anrep, G. V., Cerqua, S., and Samaan, A. The effect of muscular contraction upon the blood flow in the skeletal muscle, in the diaphragm and in the small intestine. Proc. Roy. Soc. London, B 114:245-257, 1934.

3. Brodie, T. G., and Vogt, H. The gaseous metabolism of the small intestine. Part I. The gaseous exchanges during the absorption of water and dilute salt solutions. J. Physiol. 40:135-172, 1910.

4. Brodie, T. G., Cullis, W. C., and Halliburton, W. D. The gaseous metabolism of the small intestine. Part II. The gaseous exchanges during the absorption of Witte's peptone. J. Physiol. 40:173-189, 1910.

5. Chou, C. C. Intestinal compliance and blood flow. Ph.D. Thesis. Univ. of Oklahoma, Oklahoma City, 1966.

6. Chou, C. C., and Dabney, J. M. Interrelation of ileal wall compliance and vascular resistance. Am. J. Dig. Dis. 12:1198-1208, 1967.

7. Chou, C. C., King, P. N., and Dabney, J. M. Intestinal blood flow with glucose in the lumen. Fed. Proc. 26:715, 1967.

8. Curran, P. F., and Solomon, A. K. Ion and water fluxes in the ileum of rats. J. Gen. Physiol. 41:143-168, 1957.

9. Dabney, J. M., Scott, J. B., and Chou, C. C. Effects of cations on ileal compliance and blood flow. Am. J. Physiol. 212:835-839, 1967.

10. Day, J. J., and Komarov, S. A. Glucose and gastric secretion. Am. J. Dig. Dis. 6:169-175, 1939.

11. Dragstedt, C. A., Lang, V. F., and Millet, R. F. The relative effects of distension on different portions of the intestine. Arch. Surg. 18:2257-2263, 1929.

12. Haddy, F. J. Role of chemicals in local regulation of vascular resistance. Cir. Res. 18 and 19 (suppl. I):14-22, 1966.

13. Haddy, F. J., Chou, C. C., Scott, J. B., and Dabney, J. M. Intestinal vascular responses to naturally occurring vasoactive substances. Gastroenterology 52:444-451, 1967.

14. Haddy, F. J., and Scott, J. B. Effects of electrolytes and water upon resistance to blood flow through intact vascular beds. In: Electrolytes and Cardiovascular Disease, edited by Bajusz. White Plains, New York: Karger, 1965. Pp. 383-400.

15. Helft, A. E., Brandwein, C. J., McNally, E. F., Neel, H. B., and Dennis, C. Effects of hypertonic glucose on small bowel motility and absorption. Minnesota Medicine 48:1601-1604, 1965.

16. Hindle, W., and Code, C. F. Some differences between duodenal and ileal sorption. Am. J. Physiol. 203:215-200, 1962.

17. Jacobson, E. D., Bondy, D. C., Broitman, S. A., and Fordtran, J. S. Validity of polyethylene glycol in estimating intestinal water volume. Gastroenterology 44:761-767, 1963.

18. Kontos, H. A., Richardson, D. W., and Patterson, J. L., Jr. Blood flow and metabolism of forearm muscle in man at rest and during sustained contraction. Am. J. Physiol. 2ii:869-876, 1966.

19. Krawitt, E. L., and Schedl, H. P. In vivo calcium transport by rat small intestine. Am. J. Physiol. 214:232-236, 1968.

20. Moody, F. G., and Durbin, R. P. Effects of glycine and other instillates on concentration of gastric acid. Am. J. Physiol. 209:122-126, 1965.

21. Overbeck, H. W., Molnar, J. I., and Haddy, F. J. Resistance to blood flow through the vascular bed of the dog forelimb. Local effects of sodium, potassium, calcium, magnesium, acetate, hypertonicity and hypotonicity. Am. J. Cardiol. 8:533-541, 1961.

22. Read, R. C., Johnson, J. A., Vick, J. A., and Meyer, M. W. Vascular effects of hypertonic solutions. Cir. Res. 8:538-548, 1960.

23. Roth, S. A., Anderson, D. K., Radawski, D. P., Scott, J. B., and Haddy, F. J. Effects of acute hypokalemia on resistance to blood flow through the gracillis muscle in the dog. Physiologist 12:343, 1969.

24. Rudko, M., Scott, J., and Haddy, F. Flow to metabolism ratio (F/M) and vascular resistance (R). Fed. Proc. 24:458, 1965.

25. Schachter, D., Dowdle, E. B., Schenker, H., and Kimberg, D. V. Vitamin D and the active transport of calcium. J. Clin. Invest. 39:1025, 1960.

26. Scott, J. B., Daugherty, R. M., Jr., Overbeck, H. W., and Haddy, F. J. Vascular effects of ions. Fed. Proc. 27:1403-1407, 1968.

27. Sharma, K. N., and Nasset, E. S. Electrical activity in mesenteric nerves after perfuson of gut lumen. Am. J. Physiol. 202:725-730, 1962.

28. Sidky, M., and Bean, J. W. Influence of rhythmic and tonic contraction of intestinal muscle on blood flow and blood reservoir capacity in dog intestine. Am. J. Physiol. 193:387-392, 1958.

29. Sircus, W. Studies on the mechanisms in the duodenum inhibiting gastric secretion. Quart. J. Exptl. Physiol. 43:114-133, 1958.

30. Steel, R. G. D., and Torrie, J. H. Principles and Procedures of Statistics. McGraw-Hill Book Co., Inc., N. Y., 1960.

31. Texter, E. C., Jr., Chou, C. C., Laureta, H. C., and Vantrappen, G. R. Physiology of the Gastrointestinal Tract. C. V. Mosby Co., Saint Louis, 1968. P. 202

32. Texter, E. C., Jr., Laureta, H. C., Frohlich, E. D., and Chou, C. C. Effects of major cations on gastric and mesenteric vascular resistances. Am. J. Physiol. 212:569-573, 1967.

33. Vasilevskaya, N. E. The selective effect of acid and sugar loading on interoceptive conditioned reflexes. Sechenov. Physiol. J. USSR, English Transl. 43:790-799, 1957.

34. Visscher, M. B., Fetcher, E. S., Jr., Carr, C. W., Gregor, H. P., Bushey, M. S., and Barker, D. E. Isotopic tracer studies on the movement of water and ions between intestinal lumen and blood. Am. J. Physiol. 142:550-575, 1944.

35. Visscher, M. B., Varco, R. H., Carr, C. W., Dean, R. B., and Erickson, D. Sodium ion movement between the intestinal lumen and the blood. Am. J. Physiol. 141:488-505, 1944.

36. Vogt, M. The site of action of some drugs causing stimulation of the circular coat of the rabbit's intestine. J. Physiol. 102:170-179, 1943.

37. Zamiatina, O. N. Electrophysiological investigation of the afferent impulsation in intestinal nerves. Sechenov. Physiol. J. USSR, English Transl. 43:412-420, 1957.