THE EFFECT OF MASSIVE SMALL INTESTINAL RESECTION OR BYPASS ON JEJUNAL TRANSPORT OF WATER AND ELECTROLYTES

by

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SUMMARY

Absorption in Thiry-Vella loops of proximal small intestine was investigated in female mongrel dogs following massive intestinal resection or bypass. A control group underwent only laparotomy and intestinal transection. Bidirectional fluxes of Na, K and H_2O were determined preoperatively and for three months postoperatively. Massive intestinal resection or bypass had no effect upon the bidirectional fluxes of these substances in the defunctioned fistulae. The remaining intestine in continuity following resection or bypass underwent villus hypertrophy but the defunctioned bowel did not participate in this response. Therefore the hypothesis that hormonal factors mediate the adaptive response is rejected because of the lack of anatomical and functional compensation in the bypassed intestine. The factors mediating such a response presumably are intralumenal.

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INTRODUCTION

Prior to 1940 quantitative measurements of small intestinal absorption were limited to the measurement of the rate of change of the concentration of the test solute within the intestinal lumen. Visscher and his co-workers with the aid of radioisotopes then demonstrated the bidirectional movement of water and electrolytes across intact intestinal mucosa in vivo.[91, 92, 93] This work was further expanded by Berger et al.[7] in 1960.

SEMANTICS

Prior to Visscher's contribution, the movement of fluid and electrolytes was considered to be either absorption (loss of test substance) or secretion (gain in test substance). This concept required revision and the following definitions were proposed by Code in 1960.[23]

a. insorption: the movement of a substance out of the intestinal lumen.

b. exsorption: the movement of a substance into the intestinal lumen.

c. absorption: positive value of insorption minus exsorption; i.e. insorption $>$ exsorption.

d. secretion: negative value of insorption minus exsorption.

It is apparent that absorption and secretion, the previously measured parameters, will give no estimate to the absolute amount of substance movement across the intestinal mucosa.

TECHNIQUE

With the assumption that radiosodium ^{24}(Na) and D_2O are handled in a similar fashion to ^{23}Na and H_2O, Visscher concluded:

a. Net absorption ^{24}Na = insorption ^{24}Na

and

b. Insorption Na = $\dfrac{\text{change in concentration Na}}{\text{Arithmetic mean of the specific activity of } ^{24}\text{Na.}}$

This consideration of the relationship of net absorption of ^{23}Na to the determination of insorption ^{23}Na will not be further considered here, for even though similar techniques have been used in successive occasions, there are serious methodological errors in their assumptions and approximations.

Indeed, the mechanics of this system have been fully described by Berger et al.[6] in a theoretical model and then in an experimental situation. It can be demonstrated that:

$$\beta = \frac{A - Ao}{t} \qquad \frac{\ln \dfrac{\theta A - \theta B}{\theta A - \theta Bo} + \ln \dfrac{B}{Bo}}{\ln \dfrac{B}{Bo} - \ln \dfrac{A}{Ao}}$$

and

$$\alpha = \frac{A - Ao}{t} \qquad \frac{\ln \dfrac{\theta A - \theta B}{\theta Ao - \theta Bo} + \ln \dfrac{B}{Bo} - 1}{\ln \dfrac{B}{Bo} - \ln \dfrac{A}{Ao}}$$

If $\alpha \neq \beta$ and if α and β are constant in time for any substance in a two compartment system not in dynamic equilibrium where the symbols represent:

	Time	Compartment I	Compartment II
Amount of Material (labelled + unlabelled)	0	Ao	Bo
Specific Activity	0	oAo	oBo
Exchange I-II	t	$\xrightarrow{\qquad\alpha\qquad}$	

Exchange II-I	t	$\xleftarrow{\qquad\beta\qquad}$	
Amount of Material	t	$A = Ao + (\beta - \alpha)t$	$B = Bo + (\alpha - \beta)t$
Specific Activity	t	θA_t	θB_t
Exchange of Material	t	$\xrightarrow{\qquad\alpha \Delta t\qquad}$ $\xleftarrow{\qquad\beta \Delta t\qquad}$	
Exchange of Tracer		$\xrightarrow{\qquad\theta_A \alpha \Delta t\qquad}$ $\xleftarrow{\qquad\theta_B \beta \Delta t\qquad}$	

It can be seen that in our terminology, if compartment I = intestinal lumen and compartment II = blood, then:

α = insorption

β = exsorption of the test substance.

Similarly under these circumstances, $B \gg A$, then:

(1) $\frac{B}{Bo} \simeq 1$ and $\frac{(\alpha - \beta)t}{Bo} \simeq 0$

(2) And when the test substance is placed intralumenally; i.e. compartment I, the period of observation relatively short, then $\theta_A \gg \theta_B$.

If a non-absorbable volume marker is used (e.g., polyethylene glycol = PEG)

then:

$$\alpha = \frac{A-Ao}{t}\left[\frac{\ln\ (\theta A/\theta A^{o})}{-\ln \frac{[S]/[PEG]}{[So]/[PEG]}} - 1\right]$$

S = concentration of test substance

and

$$\beta = \frac{A-Ao}{t}\left[\frac{\ln \frac{\theta A}{\theta Ao}}{-\ln \frac{[S]/[PEG]}{[So]/[PEG]}}\right]$$

Visscher's formulae may now be seen to be a gross over-simplification; however, in practice the results are nearly identical for changes in specific activity less than 40 per cent.[7, 24]

EXPERIMENTAL TECHNIQUE

Bidirectional fluxes have been measured both in vivo and in vitro and although most analyses have not been statistically compared, it is generally accepted that the results are comparable for acute experiments, and also between species in a similar segment of intestine.[70] On a contrary note is the brief communique of Love et al.[51] that there is a difference in transport of water, glucose and sodium in vivo and in vitro of rabbit ileum. The significance of this report awaits further experimentation. The correlation of the various in vivo techniques has not been subjected to scientific enquiry, and thus the significance of the following experimental results is open to debate.

Visscher's original technique was based upon the fluxes of sodium and water across isolated canine intestine.[91] The intestine was isolated by the formation of a Thiry-Vella fistula, whereby both cut ends of an intestinal loop of standard size are led out to the surface of the abdominal wall, the intestinal continuity being re-established by anastomosis of the proximal and distal cut ends. Absorption tests then being carried out by the instillation of a solution with suitable markers, withdrawn and analysed, the results then substituted in the previously described formulae and flux rates calculated. Although this technique yields results of high variability, it remains the standard experimental technique.

ERRORS INHERENT IN TECHNIQUE

(A) METHOD:

Methodological errors have not been evaluated. Specifically, it is unknown at present whether the formation of the fistula affects the absolute flux rates, although the degree of variability between tests in time intervals up to five years are no different than the degree of variability between experiments hours or days apart.[7]

(B) ANALYTIC:

Analytical errors have significant effects on the accuracy of the derived flux rate. This results because the estimate of rate of flux may in some time intervals depend upon a small difference between two large numbers (e.g., $\theta A - \theta Ao$) each of which is subject to analytical errors.

Calculation of the specific activity of more than one radioisotope by differential counting depends upon satisfactory discrimination of the emissions of the isotopes.[65] For example, the discrimination between ^{24}Na and ^{42}K depends upon the fact that ^{24}Na emits gamma radiation of different energy than ^{42}K. Under experimental conditions, the error in ^{24}Na activity was found to be 3 per cent and the error in ^{42}K activity was 1 per cent.[73]

Analytical errors also affect the estimation of sodium and potassium by flame photometry (e.g., 1.3 and 2.5 per cent) and of deuterium oxide by infra-red spectrophotometry. (0.86 per cent)[73]

The volume marker utilized also is a source of error. The qualities necessary for the volume marker are:[52]

(1) estimated simply and accurately.

(2) estimated in small concentration to have minimal osmotic effect.

(3) neither absorbed nor adsorbed.

(4) mixes homogeneously.

Polyethylene glycol has been investigated and found to fulfill these criteria, as well or better than any other substance, in experiments utilizing Thiry-Vella fistulae, but not without significant errors in perfusion experiments.[41, 52, 102] The calculation of the concentration of polyethylene glycol by Malawer's modification of Hyden's technique has an error of 6 per cent.[54]

The effect of an analytical error upon the calculation of flux rates may be determined by the following formulae:[6]

$$\frac{\Delta\beta}{\beta} = \frac{1}{\ln \frac{\theta A - \theta B}{\theta Ao - \theta Bo} + \ln \frac{B}{Bo}} \times \frac{\theta A}{\theta A - \theta B}$$

$$\frac{\Delta\alpha}{\alpha} = \frac{1}{\ln \frac{\theta A - \theta B}{\theta Ao - \theta Bo} + \ln \frac{A}{Ao}} \times \frac{\theta A}{\theta A - \theta B}$$

$$\frac{\Delta\beta}{\beta} = \left[\frac{A}{A - Ao} + \frac{1}{\ln \frac{B}{Bo} - \ln \frac{A}{Ao}} \right] \frac{\Delta A}{A}$$

$$\frac{\Delta\alpha}{\alpha} = \left[\frac{A}{A - Ao} + \frac{1}{\ln \frac{\theta A - \theta B}{\theta Ao - \theta Bo} + \ln \frac{A}{Ao}} + \frac{1}{\ln \frac{B}{Bo} - \ln \frac{A}{Ao}} \right] \frac{\Delta A}{A}$$

$$\frac{\Delta\beta}{\beta} = - \frac{\Delta t}{\Delta t}$$

$$\frac{\Delta\alpha}{\alpha} = - \frac{\Delta t}{t}$$

The order of magnitude of the effects of analytical errors may be seen from a hypothetical calculation; e.g., if $\beta = 35$, $\alpha = 60$, Ao = μEq 2800, $\theta o = 1.0$ then a 2 per cent error of θ would affect β by 15 per cent at 10 min, and 1.3 per cent at 60 min.

More rapid transfers, smaller pools and longer time intervals tend to minimize errors.

VARIATIONS IN FLUX RATES - CAUSES

As has been demonstrated, the flux rates must remain constant for the duration of each experiment. However it has been demonstrated repeatedly that the flux rates will vary depending upon the nature of the experimental conditions.

A. EFFECT OF THE INTRALUMINAL SOLUTION

In general absorption studies are carried out with isotonic solutions. Under these circumstances the effects of osmosis are minimized.

The effect of changes in osmolality have been investigated. Absorption of water occurs from a hypertonic solution against a lumen to blood gradient of $<$ 50mOsm.[10, 39] This absorption occurs in a linear relationship to the absorption of other solutes (mainly sodium) and it is believed the movement of the water is passive secondary to active solute transport.

Billich et al.[10] also studied the effects of varied electrolyte compositions in absorption from the human colon. They demonstrated a linear relationship between luminal sodium concentration and rate of net water, Na and Cl absorption. There was no water absorption when the sodium concentration was less than 20 mEq/l. In addition, water and Na absorption were decreased when chloride was replaced by bicarbonate.

Sladen et al.[77] demonstrated that glucose in the intestinal fluid enhanced net sodium and water absorption in the human small intestine. This effect is more marked and the rate of glucose absorption increased when the concentration of luminal glucose has been chemically increased prior to the acute experiment, likely as a result of substrate induction. It would seem that the active transport of sodium and glucose are related with interdependent mechanisms.

B. VARIATION BETWEEN INTESTINAL SEGMENTS

Some substances absorbed by active transport are selectively absorbed (e.g., Vitamin B_{12} and bile salts in the terminal ileum) only in specific locations in the intestinal tract. All portions of the intestinal tract have the capacity for insorption and exsorption of fluids and electrolytes but vary in degree. The more distal the intestinal segment, the greater is the value for exsorption of potassium and greater for the insorption of sodium and water.[7, 24, 73]

C. EFFECT OF BLOOD FLOW

Williams[98] in a short communique reported that ischemia of intestinal loop by arterial occlusion for two hours was followed by a "slight" decrease in insorption and exsorption for sodium.

Varro et al.[90] correlated blood flow, oxygen consumption and activity of active transport processes. They demonstrated that a 50 per cent reduction in blood flow (afferent obstruction) had no demonstrable effect. Greater reductions in blood flow caused a proportionate reduction in oxygen consumption and glucose absorption while sorbose absorption was unaffected. They did not measure sodium or water fluxes but owing to the interrelationships of sodium and glucose absorption (q.v.) a similar decrease in absorption of sodium and thus water could be inferred.

Williams[98] also investigated the effect of 30 min. of total venous occlusion and demonstrated that insorption of sodium was subsequently decreased while exsorption was unchanged.

D. AUTONOMIC INFLUENCES

The effect of the autonomic nervous system specifically upon the absorption of fluid and electrolytes has not been investigated. However, less precise techniques have demonstrated that the autonomic nerves have some influence upon intestinal function.

Ballinger et al.[4] demonstrated weight loss, increased fecal fat and villus atrophy following post ganglionic sympathectomy in canine intestinal loops.

Mori[56] investigated the effects of vagotomy in rats and demonstrated that vagotomy caused increased glucose absorption, increased ^{131}I triolein absorption and increased azo dye absorption. The increased glucose absorption was reversed by splanchnicectomy but not the absorption of triolein or azo dye absorption. It was suggested that these results were due to an increase in intestinal blood flow secondary to the vagotomy. However, Tiblin et al.[84] demonstrated that vagotomy increases intestinal blood flow for only 5 minutes following and does not alter the normal post prandial hyperemia.

Thus the autonomic influences await clarification.

E. <u>EFFECT OF MOTILITY</u>

Barriero et al.[5] investigated the effects of motility in humans with relation to transit time. They noted that increased motility per minute resulted in shorter transit time. The shortened transit time in turn was associated with decreased absorption of xylose.

Yagasaki et al.[107] suggest that strong peristalsis causes transient local decrease in absorption as a result of decreased blood flow.

In general, the effect of motility upon absorption has been ignored aside from intuitive statements relating to transit time.

F. HORMONAL INFLUENCES

In general, those hormones known to act upon the renal excretion of salt and water have similar but not as pronounced effects in the intestinal tract.

1. A.D.H. (Pitressin)

Soergel et al.[78] documented the effects of pitressin upon bidirectional fluxes in the human small intestine. They noted that ADH had no effect upon exsorption of sodium or water, but significantly decreased the insorption of water. This is the only well controlled study on the subject and seems to suggest that the action of ADH is to relatively increase the intestinal loss of sodium and water.

In contradistinction are two reports which have opposite conclusions but suffer in experimental design. Blickenstaff[13] reported that net absorption in dogs from an Omi fistula perfused with normal saline at 15 cm H_2O pressure was increased after .01 pitressin/Kg but not with .005 Kg. However, no labelling techniques were used and this may represent only incomplete emptying of the intestinal loop or alternatively may reflect the constant perfusion pressure. Arlen and Levowitz[2] measured portal venous ^{22}Na as a measure of sodium insorption following insertion of ^{22}Na in the bowel and administering ADH; they concluded that insorption of sodium was increased.

Therefore, the action of ADH upon intestinal absorption of fluids and electrolytes is uncertain and merits further investigation.

2. Adrenal Steroids

(a) That the adrenals influence absorption was demonstrated in vitro by Levin et al.[48] by measuring absorption in everted rat intestine following adrenalectomy. They demonstrated that adrenalectomy resulted in decreased net absorption of glucose, glycine and water and that this reduction was proportional to the loss of intestinal weight. Furthermore oral feeding of 1 per cent Na Cl restored both intestinal weight and absorption.

A further stimulus to the question in relation to total body sodium depletion was supplied by Clarke and Shields.[21] Using isolated intestinal loops they demonstrated that under conditions of sodium depletion that exsorption of sodium and water was decreased and of potassium increased; insorption was unaffected. This effect was noted in the colon only and was unaffected by spironolactone.

(b) Effect of Desoxycorticosterone Acetate (DOCA)

Berger et al[8] investigated the effect of DOCA upon isolated canine intestinal loops and found no effect on the transfer rates in the small intestine. In the colon however, they demonstrated that DOCA has no effect on Na exsorption, increases sodium insorption and markedly increases both insorption and exsorption of K (exsorption more than insorption so that net secretion occurs).

Tilson et al[86] also noted increased net absorption of water in DOCA treated rats and in addition noted villus hypertrophy and increased cellular Na-K ATP'ase activity.

(c) Effect of aldosterone

Although aldosterone is more potent than DOCA and represents the physiological mineralocorticoid several authors found no effect of aldosterone in their absorption studies.

Levitan and Ingelfinger[49] perorally perfused human colons with normal saline. Polyethylene glycol was used as the marker but bidirectional fluxes were not calculated as tracers were not used. Following 1 mg. aldosterone intraveneously, testing 24 hours later was followed by increased net absorption of Na, Cl and H_2O. They did not observe increased secretion of K. Levitan and Goulston[50] performed similar experiments on patients with ileostomies and found no appreciable change following administration of aldosterone. Both of these experiments are incapable of detecting alterations in bidirectional fluxes and in both cases the aldosterone was given as a single dose.

Spat et al.[80] in a short communique evaluated the effect of aldosterone upon the ileum of adrenalectomized rats. Their paper is difficult to evaluate as their semantics (absorption-secretion) seem variable. They conclude that aldosterone increases ^{24}Na absorption, decreases ^{42}K absorption, increases Na secretion and decreases K secretion. They do not mention if their animals received supplemental saline or the details of their calculations.

However, Shields et al.[71, 73] have repeatedly reported that the action of aldosterone is to increase the exsorption of K from the ileum and colon. The effect is best demonstrated with an aldosterone infusion and they noted that increasing the dose had no additive effect.

Low dosage aldosterone infusions were blocked by spironolactone while higher doses of aldosterone were not. In addition, Shields et al.[75] documented the results of perfusion studies in the colon of a patient with a functioning adrenal adenoma, demonstrating that pre-operatively K exsorption was increased while following resection of the adenoma K exsorption was in the range of normal controls.

Further insight into the action of aldosterone was provided by Castles and Williamson.[19] They demonstrated that in the rat kidney the action of aldosterone is to increase RNA synthesis. This effect was blocked by Actinomycin D. The work of Tilson et al.[86] previously referred to, demonstrating that DOCA results in increased intestinal mucosal Na-K ATP'ase, raises the possibility of similar effects in the gut.

In summary the action of aldosterone is to increase intestinal exsorption of K, and possibly insorption of Na. This effect may be mediated via DNA directed synthesis of messinger RNA which in turn stimulates enzyme synthesis.

3. <u>Ovarian Steroids</u>

Crocker[26] utilizing everted sacs of rat jejunum demonstrated that net absorption of water and Na varies with the estrus cycle. She noted a significant increase in absorption at pro-estrus and estrus compared to diestrus and metestrus. Moreover the infusion of aldosterone was followed by increased water and sodium absorption at diestrus only, and then only at 28 hours post injection. The infusion of angiotensin was followed by a similar increase in water and sodium absorption at diestrus only.

Following adrenalectomy and oophorectomy, administration of estradiol was followed by increased water absorption 28 hours post injection.

She concluded that the action of ovarian steroids was due to increased activity of the adrenal cortex and the renin-angiotensin system. There are no reports of similar experiments in other species.

G. Effect of Drugs

The effect of various drugs upon water and electrolyte absorption has not been extensively studied. Those experiments that have been performed rarely included calculation of bidirectional fluxes.

1. Atropine

Blickenstaff and Lewis[12] investigated the effects of atropine upon net absorption in dogs with an Omi fistula. Tracers or volume markers were not used. The experiments were performed under conditions of constant pressure (thus intraluminal volume varied) or constant volume. They noted that atropine resulted in increased net absorption of water and chloride that was most marked under conditions of constant pressure.

These experiments have not been repeated with more precise absorption studies, but in general are compatable with the effects of vagotomy reported by Mori.[56]

2. Carbonic Anhydrase Inhibitor

Acetohexamide (Diamox) a known carbonic anhydrase inhibitor has been shown to have definite effects on chloride absorption. Kinney and Code[43] demonstrated that Diamox specifically inhibits the insorption of chloride by preventing its substitution by bicarbonate. These results were confirmed by Madson.[53]

3. <u>Diuretics</u>

Little investigation has been devoted to the effects of diuretics. Rummel and Stupp[69] noted that in isolated rat jejunum of nephrectomized rats, mercurial diuretics (Mersalyl) decrease the net absorption of sodium, potassium, water and glucose, but increase net absorption of calcium. Thiazide diuretics (hydrochlorothiazide) cause decreased absorption of all these substances including calcium.

These effects await confirmation utilizing kinetic studies.

4. <u>Barbiturates</u>

Many absorption studies have been carried out under pentobarbital anesthesia while others are performed on conscious animals or in vitro. Little investigation has been undertaken to determine the effect of barbiturates or other anesthetic agents.

Code et al.[24] investigated the effects of anesthesia upon isolated ileal or duodenal loops in the dog. They demonstrated that pentobarbital anesthesia (25 mg./Kg.) had no effect on ileal absorption. In the duodenum the exsorption of sodium and water was decreased while insorption was not affected.

Cramer et al.[25] demonstrated that pentobarbital anesthesia increased the net absorption of calcium from intestinal loops in dogs. However this result may reflect only incomplete recovery of the test solution as no volume markers or tracers were used.

Thus the effect, and possible mechanisms, of anesthesia upon intestinal absorption are unclear.

H. Effect of Surgery

The effect of surgery is obviously multifactorial, ranging from the effect of the stress response (adrenal), dehydration, drugs (anesthetic, analgesic, etc.) to the effect of surgical trauma to the bowel itself. Thus the interpretation of variations in absorption is fraught with difficulty; moreover the absence of variation in absorption may only represent the result of antagonistic influences. Coupled with this are the variations and difficulties inherent in various techniques, particularly those relying on net absorption.

1. Operations Without Intestinal Manipulation

Shields[72] noted that laparotomy under anesthesia followed 24 hours later by studying absorption under anesthesia was associated with decreased insorption (and absorption) of sodium and water and with increased exsorption (and secretion) of potassium in isolated canine intestine.

Shoemaker and Wright[76] with a catheter perfusion technique measured the change in net absorption pre and post-operatively in 5 patients. Their first measurement at 6 hours post-operatively disclosed decreased absorption of sodium and water. Water absorption was consistently decreased up to 48 hours post-operatively but was rising to pre-operative levels. Bunch and Shields[16] assessed 9 patients utilizing perfusion techniques with radioactive tracers. They noted no change in insorption or exsorption if their patients received "prolonged" intravenous fluids. Six patients who received only 500 ml. of fluid intravenously had abnormal absorption studies. These latter patients demonstrated decreased net sodium absorption as a result of marked decrease in Na exsorption with a less marked decrease in insorption. The net secretion of potassium decreased as a result of decreased exsorption greater than decreased insorption. Water absorption at 6 hours was normal but by 30 hours post-operatively exsorption had increased to such an extent that net secretion occured.

2. <u>Intestinal Anastamosis Without Resection</u>

Glucksman et al.[37] investigated the effect of intestinal anastomosis with dogs, measuring net absorption of glucose and insorption of ^{22}Na in the duodenum. At 2 hours post-operatively all dogs had significantly decreased absorption of glucose and insorption of ^{22}Na. After 2 hours only those dogs which regurgitated had decreased values, those not regurgitating had normal or slightly increased values. No mention is made of intravenous supplements.

Grace and Shields[38] however, demonstrated the maximum deviation in absorption values to occur at 24 hours post-operatively. They demonstrated a net decrease in absorption of sodium and water at 24 hours which at 48 hours and 72 hours had returned to normal. The net secretion of potassium was increased at 24 hours and likewise then fell to normal values.

None of these experiments have been followed for periods greater than 72 hours. There is some evidence to suggest that a further change in absorption will occur. Nygaard[58] demonstrated that, in rats, laparotomy and intestinal transection with anastomosis resulted, within 2-4 weeks, in shortening of the intestine and a significant loss of total absorptive surface. The intestinal anastomosis resulted in a zone of villus hypertrophy 5 cm. proximal and distal to the anastomosis. The mediating factors for these changes and the result on fluid and electrolyte absorption is unknown.

3. Effect of Bowel Obstruction

Shields[72] produced experimental obstruction in dogs by transecting the ileum 30 cm. from the ileocecal valve, suturing the ends closed, and studying absorption characteristics under the same or subsequent anesthetic.

The proximal segment immediately above the obstruction absorbed water for 12 hours and then secreted water. This was due to a progressive fall in insorption. Exsorption of water was unchanged until 48 hours and then exsorption markedly increased. The insorption of sodium progressively fell with time until by 12 hours net secretion occured. Potassium exsorption markedly increased with time to such an extent that by 60 hours potassium exsorption was 6 times normal.

One hundred cm. above the obstruction the absorption of sodium and water was decreased but there was no increase in potassium exsorption.

The distal segment showed a slight decrease in water and sodium absorption due to increased exsorption and increased potassium excretion due to increased exsorption.

Wright et al.[106] created a closed segment obstruction in patients with ileoostomies by means of suitable balloon catheters placed through the stoma. They related changes in absorption to intraluminal pressure. At pressures of 10-20 cm. of H_2O absorption of water was increased due to an increase in insorption with a smaller increase in exsorption. At pressures greater than 20 cm. H_2O insorption markedly fell but exsorption continued to rise resulting in net secretion and a further rise in intraluminal volume and pressure. They postulated these effects were due to venous occlusion but Williams [98] found venous occlusion did not effect exsorption.

4. Effect of Bowel Resection

Experiments to assess the effects of bowel resection on fluid and electrolyte absorption have not been performed. All experiments have measured other chronic effects of resection, days to months post-operatively.

(a) Pathophysiology of Bowel Resection

It has been established that once a critical amount of intestine has been resected a characteristic syndrome of undernutrition, steatorrhea and acidic diarrhea may follow.[68] These effects result from loss of specific and general absorptive sites but other factors are known to contribute to the decrease in absorption.

The effect of the type of anastomosis and the presence of bacterial proliferation has been investigated by Nygaard.[58, 62] Resection with an end to end anastomosis resulted in a moderate increase in lactobaccilli at all levels; however, fecal fat excretion was normal even with 75% resections. Resection with an end to side anastomosis caused similar effects. Side to side anastomosis resulted in a moderate increase in coliforms proximal to the anastomosis but a marked increase in the distal coliform count. The fecal fat excretion was increased, but this latter effect was normalized by administering chloramphenicol.

By-passed intestinal loops had a more pronounced effect. A side to side bypass resulted in steatorrhea, reversable by chloramphenicol, but prevented if the anastomosis was less than 7 mm. in diameter.

Long self-emptying blind pouches also caused steatorrhea, not reversable; the effect being more pronounced when the pouch was in the proximal intestine rather than the distal intestine.

Resection has also been shown to influence transit time. Small bowel resections decrease transit time the effect being more marked with distal resections than proximal resections. Ileocecal bypass also results in decreased transit time.[82, 99]

(b) Secondary Effects of Resection: Gastric Hypersecretion

Gastric Hypersecretion following small bowel resection has been well documented in man and experimental animals.[35] The effect of the hypersecretion is to further reduce absorption as a result of:

1) Direct injury of the proximal intestinal mucosa by the acid

2) lowering of the intraluminal pH below the optimum pH of lipase and trypsin and

3) delivery of a high solute load to the remaining intestine.

The degree of hypersecretion is proportional to the extent and location of resection,[35] since resection of the proximal small intestine is associated with a greater increase in secretion than a distal resection.[47]

The etiology of the hypersecretion has been extensively investigated yet is still unclear.

The role of the vagus nerve in the syndrome has not been investigated.

The role of the antrum is controversial. Landor[45] demonstrated a marked rise in 24 hour secretion following enterectomy in dogs having a previous antrectomy, suggesting the antrum has no effect. However, Stafford and Schnaufer[81] and Kerr et al.[42] demonstrated that antrectomy has a protective influence.

Evidence for a gastric secretogogue was first advanced by Westerheide et al.[97] who demonstrated that exclusion of the proximal small bowel caused greater acid secretion than excision of the small bowel. Such a conclusion was supported by Kerr et al.[42] who demonstrated that in antrectomized dogs, the hypersecretion produced by a Thiry fistula is normalized by excision of the fistula. Orloff et al.[64] demonstrated a potent secretogogue liberated from the jejunum responsible for the gastric hypersecretion following portacaval shunting. On the other hand Konturek et al.[44] demonstrated that the increased gastric secretion produced by duodenal exclusion is further increased by duodenal excision.

The loss of an inhibitor of gastric secretion produced in the small intestine is the most likely explanation for the hypersecretion following resection. Both fat[27] and acid[44] when placed in the small intestine inhibit gastric secretion. Paradoxically, fat has been shown to be necessary in the diet for the increase in gastric secretion following resection.[46]

Whether such substances affect fluid and electrolyte absorption in the remainder of the intestine has not been evaluated.

(c) <u>Secondary Effects of Bypass</u>

As mentioned bypass results in gastric hypersecretion by direct stimulation and/or loss of inhibitor.

In addition bypass in some manner as yet unknown often results in fatty infiltration of the liver occasionally leading to cirrhosis and/or death.[15, 31, 62] Jejunocolic bypass is more lethal than jejunoileal bypass.[15]

The influence of various lengths of intestine bypassed upon liver morphology and function is unknown.

(d) Adaptation Following Resection

1) Functional Compensation

Dowling and Booth demonstrated by a perfusion technique in humans that net absorption of glucose was increased following small bowel resection.[29] Weinstein et al. similarly demonstrated that the net absorption of sodium and water was increased following bowel resection.[94] Nygaard demonstrated that adaptation occurs more rapidly following proximal resections than distal ones.[62]

2) Compensatory Hypertrophy

Porus[66] demonstrated in humans that resections greater than 50% of the small intestine were followed by epithelial hyperplasia of the remaining intestine. Booth et al.[14] and Nylander and Olerud[63] noted post anastomotic dilation following resections in rats. Dowling and Booth[30] noted mucosal hypertrophy following resection in rats. This change was more marked in the ileal segment following proximal resection than vice versa. Nygaard[61, 62] described hypertrophy of the whole remaining intestinal tract following resections or bypass, regeneration being more rapid following proximal resection than distal resection.

3) Cellular Adaptation

Weser and Hernandez[96] could detect no increase in active transport of glucose and leucine one month following 50% resection in rats, and concluded that the increased uptake following resection is due primarily to hypertrophy. However Tilson and Wright[87] demonstrated increased mucosal Na-K ATP'ase following the adaptation hypertrophy of transposed ileum.

The contribution of the individual cell to the adaptive process is still uncertain.[40]

(e) Mechanisms of Adaptation

Although the factors which mediate the adaptive response have not been rigourously examined current evidence would indicate there may be two mechanisms.

1) Intraluminal factors:

Altman and Leblond[1] presented detailed evidence concerning factors controling normal villus height in rats. Villi in the jejunum were found to be of greater height than those in the ileum. This difference was shown, by a series of transposition experiments, to result from a villus enlarging factor present in the pyloro-duodenal region and a villus reducing factor present in the ileal chyme. Removed from these influences the villi tended to become intermediate in height.

This latter effect was also noted by Menge et al,[55] who, after partially excluding the small intestine in rats demonstrated a decrease in villus height with a corresponding decrease in glucose absorption.

Similar experiments have not been performed following intestinal resection. However the presence of a villus enlarging intraluminal factor would explain the pronounced hypertrophy of the ileum following jejunectomy, as in these circumstances the ileum would receive such factors more quickly. The presence of additional synergistic factors remains a possibility.

2) Systemic Factors:

a) Nutrition

Wilmore and Dudrick[100] noted that the maintenance of nutrition following 95% resection resulted in a greater degree of hypertrophy than in controls. This extra nutrition was accomplished by intravenous alimentation although the animals also received oral intake. They conclude that the extent of hypertrophy is not dependant upon the amount of oral intake but upon the nutritional status of the animal.

b) Hormonal or Neural

If following a massive resection the terminal ileum is left in situ but bypassed by a jejunocolostomy, it is found that the ileum participates in the adaptive response.[85] The explanation proposed has been the presence of neural or humoral factors mediating this response. Such a hypothesis has also been invoked by Touloukian et al[88] to explain the lack of benefit from an elemental diet during the first 6 weeks following massive resection.

Similarly following total colectomy the terminal ileum has also been demonstrated to adapt and consequently absorb more water.[105] Such an observation is difficult to explain on other than a neural or hormonal mechanism.

These conclusions however are not warranted at this stage, because the intestinal tract is still exposed to those intraluminal factors which were previously discussed.

I. Effect of Bowel Pathology

In addition to infectious diseases[34, 67] which are known to affect intestinal absorption several other pathological states affect absorption.

Active ulcerative colitis has been shown to decrease absorption of water, sodium and chloride in the jejunum[11] and decrease insorption of sodium and water in the colon.[32] Regional enteritis had no effect on net absorption of sodium and water in the colon, bidirectional fluxes not being measured.

The effect of various adenomata has been investigated. Villous papillomata result in marked increase in exsorption of sodium (5 times normal), potassium (7 times normal) and water (2 times normal): insorption being unaffected.[3, 74] With multiple polyposis although net absorption was unchanged, the bidirection fluxes were 4 times normal.[74] Localized polyps resulted in increased exsorption of potassium (4 times normal) that was not corrected by polypectomy, other values being normal.[74]

RESTATEMENT OF THE PROBLEM

RESTATEMENT OF THE PROBLEM

Massive intestinal resection or bypass is followed by villus hypertrophy and increased absorption per unit length in the remaining small intestine. Potential factors which mediate this response are unknown but current evidence supports two hypotheses. viz.

1) intralumenal factors and/or food are essential.

or 2) neural or humoral factors are the essential contributing elements to adaptation.

The latter hypothesis was investigated by determining if a change in mucosal transport could be demonstrated in a chronically defunctioned portion of the intestine following massive intestinal resection or bypass.

MATERIALS AND METHODS

MATERIALS AND METHODS

Sixteen healthy female mongrel dogs immunized against distemper, dewormed with two 2.5 ml. doses of tetrachlorethylene given one week apart, were trained to lie still for periods up to one hour.

THIRY-VELLA FISTULA

All animals, under pentobarbital anesthesia and via a midline incision, underwent isolation of a 40 cm. segment of jejunum with minimal disturbance of blood supply. The proximal point of isolation was 30 cm. from the ligament of Treitz: all measurements were performed on the antimesenteric aspect of the intestine.

Both ends of the isolated loop were brought through the left lateral abdominal wall and fixed in place as matured jejunostomies. Such an isolated loop is known as a Thiry-Vella fistula.

Intestinal continuity was reestablished by anastomosing the remaining proximal and distal cut ends in an end to end fashion.

Biopsies were taken of liver and small intestine.

PREPARATION OF TEST SOLUTION

a) Standard Solution

Code's modification of Tyrode's solution was used throughout the experiments.[22] It was prepared as follows:

To make 4.0 litres.

Solution A:

To a 2.0 L. flask the following were added:

Glass distilled H_2O	500 ml.
NaCl	32 G.
KCl (10% w/v)	10ml.
$CaCl_2$ (10% w/v)	6 ml.
$MgCl_2$ (10% w/v)	4 ml.
Dextrose	3.6 G.
Na_2HPO_4	0.2 G.
Glass distilled H_2O to	2.0 L.

Solution B:

To a 2.0 L. flask the following were added:

Na HCO_3	4 G.
Glass distilled H_2O to	2.0 L.

Solutions A and B were then mixed. The pH of the resultant solution was adjusted to 7.4 by the addition of 0.2 HCl.

b) Test Solution

On the day of an absorption test the following materials were added to the standard solution:

Polyethylene Glycol (PEG) to a concentration of approximately 800 ml. %.

Radioactive sodium ^{24}(Na) to a concentration of approximately 480 µc/l.

Radioactive potassium ^{42}(K) to a concentration of approximately 240 µc/l.

Deuterium oxide (D_2O) to a concentration of approximately 4.8 Gm%.

Since ^{24}Na and ^{42}K have short half-lives, fresh supplies were obtained weekly. The amount of each isotope to be added on a given test day was computed from the known amount supplied by introducing correction for radioactive decay.

REAGENTS

The radioactive isotopes were supplied as the chloride salts of ^{24}Na and ^{42}K dissolved in water at pH 6-8. Both isotopes had greater than 99% radiochemical purification and were supplied by New England Nuclear of Canada.

The deuterium oxide was obtained from Merck Sharp and Dohme Canada Ltd., Isotope Division, and supplied in lots having 99.7% isotopic purity.

Polyethylene Glycol 4000 (PEG) was obtained from BDH Canada Ltd.

CARE OF THIRY-VELLA FISTULA

At weekly intervals following creation of the Thiry-Vella Fistula, the fistulae were rinsed with 200 ml. of the standard Tyrode's solution.

ABSORPTION TESTS

The dog was placed on its side on the restraint table and a multiperforate catheter modified by having a balloon 16 cm. from the tip (Fig. 1) was placed into the afferent stoma. A second Foley catheter was placed into the efferent stoma. Both balloons were inflated with 2 - 5 ml. of liquid and retracted against the abdominal wall to minimize leakage. (Fig. 2)

Fig. 1

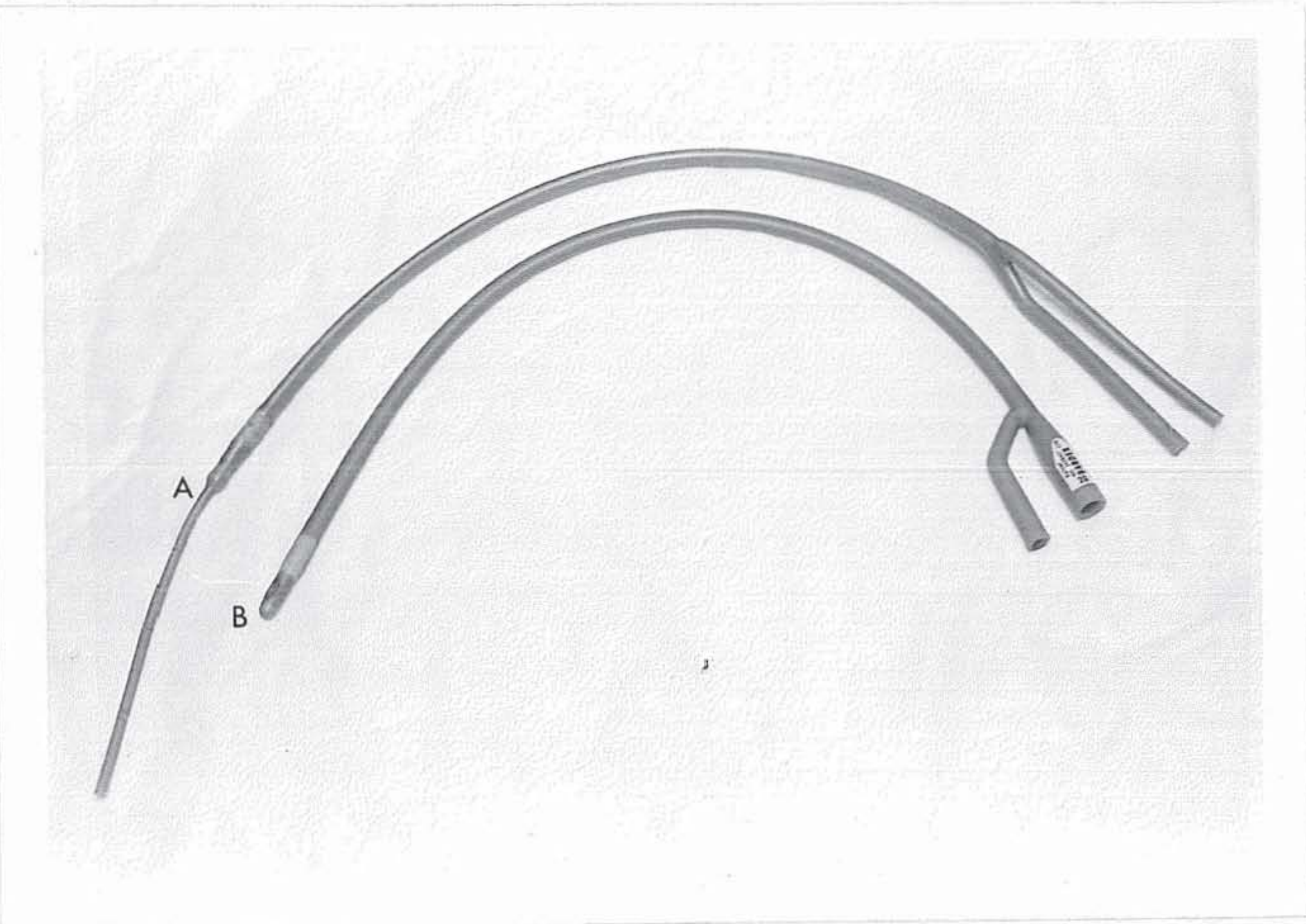


FIG. 1 A. MODIFIED MULTIPERFORATE CATHETER (PLACED IN THE AFFERENT STOMA)

B. FOLEY CATHETER (PLACED IN THE EFFERENT STOMA)

Fig. 2

FIG. 2 CATHETERS INFLATED IN AFFERENT AND EFFERENT STOMA

A sample of the test solution was reserved for measurement of PEG concentration. Exactly 10 ml. of the test solution was then introduced via the afferent catheter and gently mixed with the intraluminal contents for one minute. A sample (1.5 - 2.0 ml.) was then taken. This was the t = 0 sample and at this time a stop-watch was started. Similar samples were taken at approximately t = 10, 15, 20, 25, and 30 minutes, but the exact time of sampling was noted.

Adequate mixing was ensured by aspirating a greater amount than was needed, re-introducing the aspirate and then taking the sample.

For each sample was recorded a) the time the sample was obtained and b) the volume of the sample. For each sample 1.0 ml. was transferred to a separate sealed vial for radioactive counting. The remaining sample was also placed in a separate sealed vial.

Sampling continued until a large enough sample ($\geq$ 1.0 ml) could not be aspirated. At that time 100 - 200 ml. of standard Tyrodes solution (rinse) was circulated through the fistula and the fluid stored in a sealed vial.

The time at which the t = 0 sample was taken was recorded for calculation of radioactive decay. During the test the animal's body temperature was maintained at 37 $^{\circ}$C by use of a heating pad placed beneath the animal. All solutions were also maintained at 37 $^{\circ}$C.

DIRECTLY MEASURED DATA

The following were measured on each sample:

1) time of sample
2) volume
3) PEG concentration
4) Na concentration
5) K concentration
6) D_2O concentration
7) Two channel synchronous counting of radioisotopes

As well, for the sample of the test solution and the rinse the PEG concentration was measured; also the volume of the rinse.

a) Radioisotope Counting

All counting was performed in the well of a thallium activated sodium iodide crystal connected to a photomultiplier and a Picker Nuclear Twinscalar II model 600 - 125. The following instrument settings were used:

preset count 200 K
preset time 1.00 minute
Channel A
lower level range - 2
lower level control - 550
window - In
window width 200

Channel B
lower level range 4
lower level control 575
window In
window width 125

Preliminary isotope energy curves were plotted for ^{24}Na and ^{42}K and the channel widths were chosen to include the main energy peaks of each isotope.[20] (Appendix) Each day samples were counted separate 5 µC samples of ^{24}Na and ^{42}K were also counted. Background counts were also obtained.

For each sample synchronous counts were obtained on two channels N_1 = Channel A and N_2 = Channel B.

The time from t = 0 to the time of counting was determined in hours for each absorption test.

Following the radioisotope counting the samples were sealed and placed in a separate room for 2 weeks. Absence of radioactivity was confirmed with a Geiger-Mueller tube and the samples released for further analysis.

Each sample was then centrifuged at 3000 r.p.m. for 10 minutes and the supernatent analysed for Na, K and PEG. concentrations.

b) Sodium Analysis

Sodium analysis was performed with a Unicam SP90 Atomic Absorption Spectrophotometer with the following instrument conditions:

wavelength: 581 mu
slit width: 0.07 mm.
burner: acetylene emission head
burner height: 1.0 cm.
fuel: acetylene - pressure 10 lb/in^2
- flow 1 L./min.
air - pressure 30 lb/in^2
- flow 5 L/min

All operations were performed after an initial warm up time of 30 minutes. The instrument was calibrated with freshly prepared standards such that 100 m Eq/l. and 175 m Eq/l resulted in spectral absorbance of 11% and 97% respectively.

Following centrifugation 0.1 ml. of the supernatant was diluted to 10 ml. with distilled water and mixed. The spectral absorbance of this mixture was determined and by comparison with the absorbance of the standard solution the concentration in m Eq/l. determined.

Laboratory control sera were also analysed.

(For calibration curve see appendix)

c) Potassium Analysis

The same instrument was used as in sodium analysis with the following changes in instrument conditions:

wavelength: 766.5 mu
slit width: 0.09 mm.

Operation of the instrument was also similar except that 0.2 ml. of the supernatent was used and the instrument was calibrated such that control standards of 0mEq/1 and 8 m Eq/1 corresponded to absorbance of 0% and 60% respectively. (For calibration curve see appendix)

d) PEG Analysis[54]

Into a 50 ml. Erlenmeyer flask containing 0.5 ml. of supernatant the following were added:

5.0 ml. of distilled water
0.5 ml. of 10% w/v $Ba Cl_2$
1.0 ml. of 0.3 N $Ba (OH)_2$
1.0 ml. of 5% w/v $Zn SO_4 . 7 H_2O$

Between each addition the contents were mixed by swirling the flask. After addition of the $Zn SO_4$ the flasks were capped with parafilm and shaken vigorously then let stand for 10 minutes. The solution was then filtered through double-thickness Whatman #42 filter paper. From the filtrate, 1.0 ml. was transferred to 16 x 150 mm test-tubes and the remainder sealed and reserved for D_2O analysis.

To the test tubes were added 3.0 ml. of gum arabic solution and the mixture gently agitated. Trichloracetic acid (4.0 ml of 30% w/v) containing 5% barium chloride was then added, the tubes capped and mixed by inversion five times.

The tubes were allowed to stand 60 - 90 minutes and the optical density then measured using a Unicam SP 500 series 2 spectrophotometer at a wave length of 650 mu and with a 12.5 mm. light path.

The optical density was compared to a previously constructed standard curve and the PEG concentration determined.

d) D_2O Analysis[9, 83]

The filtrate from the PEG analysis was microdistilled[89] and the distillate placed in sealed ampoules.

The D_2O analysis was performed on a Perkin-Elmer Model 21, double beam infra-red spectrophotometer. Standard instrument settings were:

pen speed - 5
path width - .2mm.
Gain - 4.8
slit width 250 microns
resolution 106.5
response 1
auto suppress 1
scan 2650 cm^{-1} to 2450 cm^{-1}

Matched CaF_2 cells with spacers of 0.025 mm. were used. Distilled water was used in the reference beam and the same cell was used throughout for this beam. The cells, samples and machine were maintained at 32 ^{o}C and an on machine equilibration of 5 - 15 minutes was allowed before a scan was performed.

Calibration curves were constructed from standards supplied by Atomic Energy of Canada Ltd., Whiteshell Research Establishment. The minimum percent transmittance in the scanning range was used throughout.

Comparison of the sample per cent transmittance to the calibration curve allowed determination of the sample wt % D_2O (Appendix)

DERIVED DATA

a) Correction for Sampling [6]

Calculations were performed on an Olivetti Programma 101. The total amount of PEG instilled was calculated from the concentration of PEG of the test solution times the volume instilled (10 ml.). The intraluminal volume of the test solution was computed by dividing the PEG instilled by the PEG concentration of the t = 0 sample. The sample size of the t = 0 sample times the PEG concentration was subtracted from the PEG instilled to give PEG residual. Successive samples were handled in a similar fashion allowing computation of the intraluminal volume at the time of each sample. The final residual PEG was compared to the PEG recovered in the rinse and the per cent recovery of PEG determined.

Multiplication of the Na and K concentration by the intraluminal volume equalled the amount of Na and K in the intestine at the time of sampling. To each value was added the amount of Na or K removed in sampling allowing a measure of what these amounts would be had no sampling occurred. Similarly the volumes were corrected by adding the sample sizes to successive intra-luminal volume calculations.

b) Radioisotope Separation [65]

Each time the samples were counted separate samples of ^{24}Na and ^{42}K were also counted.

If N1 = counts from low energy channels (minus background) and N2 = counts from high energy channels (minus background) then r (channel ratio) is defined as N2/N1. For ^{24}Na alone r has a distinctive value m whereas the ratio for ^{42}K is n.

During sample analysis, N1 and N2 receive contributions from both ^{24}Na and ^{42}K. The physical ratio.

$$S = \frac{m - r}{r - n} = \frac{I_2}{I_1}$$

where I_1 = number of counts due to ^{24}Na in N1.
and I_2 = number of counts due to ^{42}K in N_1 allows separation of the counts of each isotope.

A suitable program was written for the Olivetti Programma 101 to perform the calculations and arrive at separate c.p.m. for ^{24}Na and ^{42}K.

Each value obtained was then corrected for radioactive decay using the relationship $Ro = \frac{R}{e^{-\lambda t}}$

where R = cpm after decay
Ro = cpm at t = 0
λ = disintigration constant ie

^{24}Na λ = .046209
^{42}K λ = .055898

t = time of decay in hours

c) Calculation of Flux Rates[6]

Another program for the Olivetti Programma 101 was written to compute insorption and exsorption for Na, K and H_2O by the following formulae:

$$\text{insorption} = \alpha = \frac{A - Ao}{t} \quad \frac{\ln \theta A / \theta Ao}{\begin{array}{c}[S]/[PEG]\\ -\ln [So]/[PEG_o]\end{array}} \quad -1$$

$$\text{exsorption} = \beta = \frac{A - Ao}{t} \quad \frac{\ln \theta A / \theta Ao}{\frac{[S]/[PEG]}{[So]/[PEG_o]}}$$

where Ao = amount of substance at t = 0
PEGo = concentration of PEG at t = 0
θAo = specific activity at t = 0
i.e. cpm./uEq/ of Na or K
wt % D_2O for H_2O
So = concentration of test substance at t = 0
t = time sample was taken
A = amount of substance corrected for sampling at t = t
PEG = concentration of PEG at t = t
0A = specific activity at t = t
S = concentration of test substance

EXPERIMENTATL DESIGN

At least 4 weeks following creation of the Thiry-Vella fistula all animals underwent 3 absorption tests at the same time of day for each animal and 1 week apart.

At the fourth week an absorption test was not performed but the animals were randomly assigned to one of 3 groups.

Group A underwent laparotomy under pentobarbital anesthesia. The intestine in continuity was divided 5 cm. distal to the ligament of Treitz and reanastomosed. This was the control group.

Group B also underwent laparotomy with division of the intestine 5 cm distal to the ligament of Treitz. The distal bowel was closed and the bowel further divided 5 cm proximal to the ileocecal valve. The distal end of this area was anastomosed to the proximal end at the point of proximal division thus reestablishing intestinal continuity and bypassing most of the small intestine. The bypassed small intestine was decompressed by leading the distal bypassed intestine through a separate incision in the right flank as a matured ileostomy.

Group C underwent an identical operation to Group B except the small intestine thus isolated was excised.

In all groups the Thiry-Vella fistula was not disturbed.

In the week following the operations all animals underwent absorption tests in a fashion identical to preoperatively. The absorption tests were repeated at weekly intervals for 19 weeks or until the animal's death.

OTHER TESTS COMMON TO ALL ANIMALS

The animals were weighed at weekly intervals and a blood specimen obtained for determination of total serum proteins.

The serum proteins were determined by adding 9.5 ml. of 28% w/v of sodium sulfite solution to 0.5 ml. of serum. Two (2.0) ml. of the mixture were transferred to a separate tube, 5 ml. biuret reagent added; and the mixture allowed to stand for 30 minutes. The optical density at 550 mμ was determined on a Unicam SP 500 series 2 Spectrophotometer. Comparison of this optical density to a similarly prepared standard allowed determination of the protein concentration of the sample.

At the time of death or upon sacrifice all animals were autopsied. Histological specimens were prepared from liver, Thiry-Vella fistula, and intestine 10 cm. proximal to the anastomosis.

For each animal the intestinal biopsies from a) time Thiry-Vella fistula constructed b) proximal intestine at autopsy and c) Thiry-Vella fistula at autopsy were photographed at 10 x magnification. The villus height was measured on the film in mm.

STATISTICAL METHODS

For each dog the flux rates were analysed over the duration of the study by an analysis of variance.[79] The Duncan multiple range test was used to detect any pattern of variability with time.[79]

To assess the effect of bypass or resection upon the flux rates a factorial analysis of variance was performed for a repeated measures design.[101] The independant factor was treatment ie. sham, bypass or resection. The correlated factor was date of measurement ie. at weekly intervals pre or post-operatively. Dates having missing values were analysed in two ways, ie. estimation of the value and by excluding all other values on the date of the missing value.

To assess the effect on villus height an analysis of variance was used to compare biopsy heights between dogs and groups, rather than a paired t-test since the biopsies originated from different sites within a dog but at approximately the same site between dogs.

RESULTS

RESULTS

A) CHARACTERISTICS OF TREATMENT GROUPS

1) Size of Group

Random allocation of 16 dogs to three groups resulted in five dogs undergoing sham operation, five dogs undergoing resection and six dogs undergoing bypass operations.

2) Time From Fistula to Treatment

There was no significant difference in the time interval from creation of the Thiry-Vella fistula to either sham, resection or bypass operations (unpaired t-test). The interval (mean $\pm$ S.E.M.) for the sham group was 37 $\pm$ 3.7 weeks, while for the resection and bypass groups the intervals were 37 $\pm$ 3.6 weeks and 40 $\pm$ 4.3 weeks respectively.

3) Morbidity and Mortality

The sham animals remained healthy and there were no deaths during the duration of the study. The mean weight for the group was 24.8 $\pm$ 1.63 Kg. and did not change significantly with time. Total serum proteins also did not change with time the overall mean being 6.4 $\pm$ .21 Gm%.

In contrast the bypass and resected groups significantly lost weight with time, falling from mean pre-operative weights of 21.1 $\pm$ .29 Kg. and 19.1 $\pm$ .32 Kg. to 11.4 $\pm$ .29 Kg. and 11.7 $\pm$ .32 Kg. respectively at 10 weeks postoperatively. The overall group mean of weights of the bypass group was 15.2 $\pm$ 1.63 Kg and of the resected group was 14.0 $\pm$ 1.83 Kg. Both of these values were significantly different from the value of the sham group. (Table 1)

Total serum proteins in the bypass and resected groups also fell with time. Initially the values in the bypass group were 7.1 ± .27 Gm% falling to 4.5 ± .27 Gm% by the tenth post-operative week. Similar values in the resected group were 6.65 ± .31 Gm% and 4.83 ± .31 Gm%. The overall group means in the bypass and resected groups were 5.27 ± Gm% and 5.57 ± .24 Gm%. Again these group means were significantly different from the sham group. (Table 2)

The fall in weight and serum proteins in the bypass and resected groups was reflected in the clinical condition of the animals. Three dogs in the bypass group died of obvious malnutrition at 7, 12 and 16 weeks postoperatively. The three remaining animals were excluded from the experiment and sacrificed at 12 weeks postoperatively on humane grounds as they were weak and had developed ulcers.

Three animals in the resected group also died in the postoperative period. One animal died during the first postoperative week of unknown cause. The other two died of malnutrition at 16 and 22 weeks. The remaining two animals were healthy for the duration of the experiment.

4) Pathology

All animals were autopsied. There was no gross abnormality of any of the sham operated dogs. The intestine in continuity of the bypass and resected group was dilated with grossly obvious mucosal thickening. No ulcers were present in the gastroduodenal region. The Thiry-Vella fistulae of all animals and the bypassed intestine of the bypassed group was contracted and distinctly different from the intestine in continuity.

Villus height as measured from biopsies obtained at the time of Thiry-Vella fistula construction demonstrated insignificant differences between groups. The over all mean height was .89 $\pm$ .009 mm. Following resection or bypass there was a significant increase in villus height of intestine in continuity compared to the sham group. In the bypass group the height was 1.63 $\pm$ .063 mm. and the height in the resected group was 1.55 $\pm$ .023 mm. The sham group had a height of 1.16 $\pm$ .072 mm. Villus height in the Thiry-Vella fistula was unchanged post resection or bypass, the mean height being .864 $\pm$ .027 mm. (Tables 9, 10, 11) (Figures 3, 4, and 5)

Histological examination of the liver was normal in all animals before and after sham, bypass and resection operations.

B) <u>ABSORPTION TESTS - VARIABILITY OF MEASUREMENT</u>

1) <u>Analytical Technique</u>

During sodium analysis by atomic absorption spectrophotometry three control sera were analysed. The sample with a known value of 121 mEq/1. was calculated to have a concentration of 127 $\pm$ 1.0 mEq/1. The second sample with a predicted value of 142 mEq/1 was calculated as a concentration of 145 $\pm$ 1.2 mEq/1. The third sample, a specimen of human serum, had a calculated concentration of 144 $\pm$ 1.9 mEq/1.

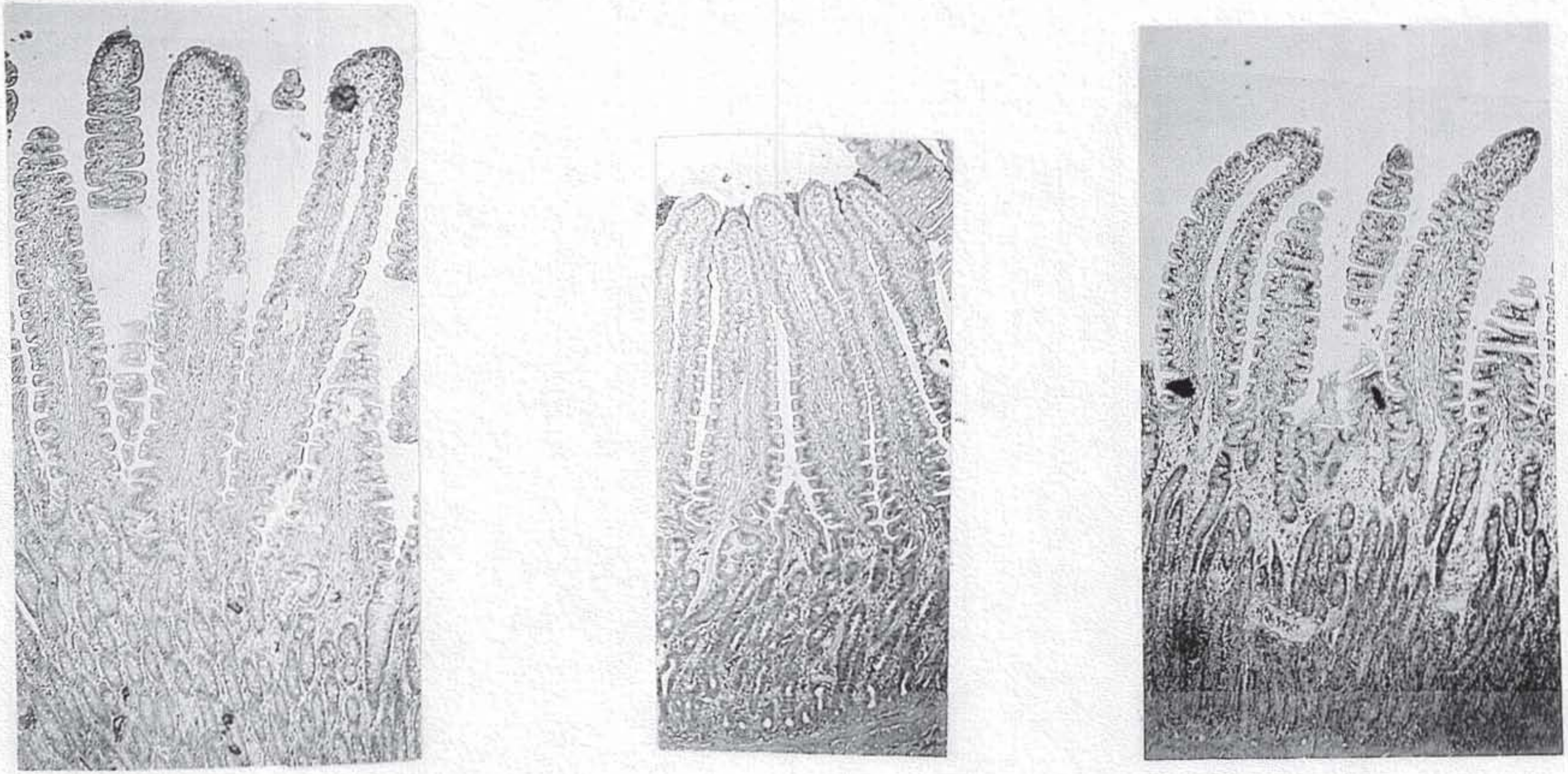
Similarly control samples for potassium with predicted concentrations of 6.0 and 4.5 mEq/1 resulted in calculated concentrations of 6.1 $\pm$ .08 and 4.95 $\pm$ .09 mEq/1. The control human serum had a calculated concentration of 4.55 $\pm$ .12 mEq/1.

2) <u>Radioisotope Discrimination</u>

The overall value of the channel ratio for ^{24}Na was 0.598 $\pm$ .0100 while the ratio for ^{42}K was 0.006 $\pm$ .0010.

Fig. 3

Villus Height - Before Treatment



SHAM RESECTION BYPASS

FIG. 3. ANALYSIS OF VARIANCE OF VILLUS HEIGHTS DEMONSTRATING NO SIGNIFICANT DIFFERENCE BETWEEN TREATMENT GROUPS.

Fig. 4

Villus Height - Intestine in Continuity

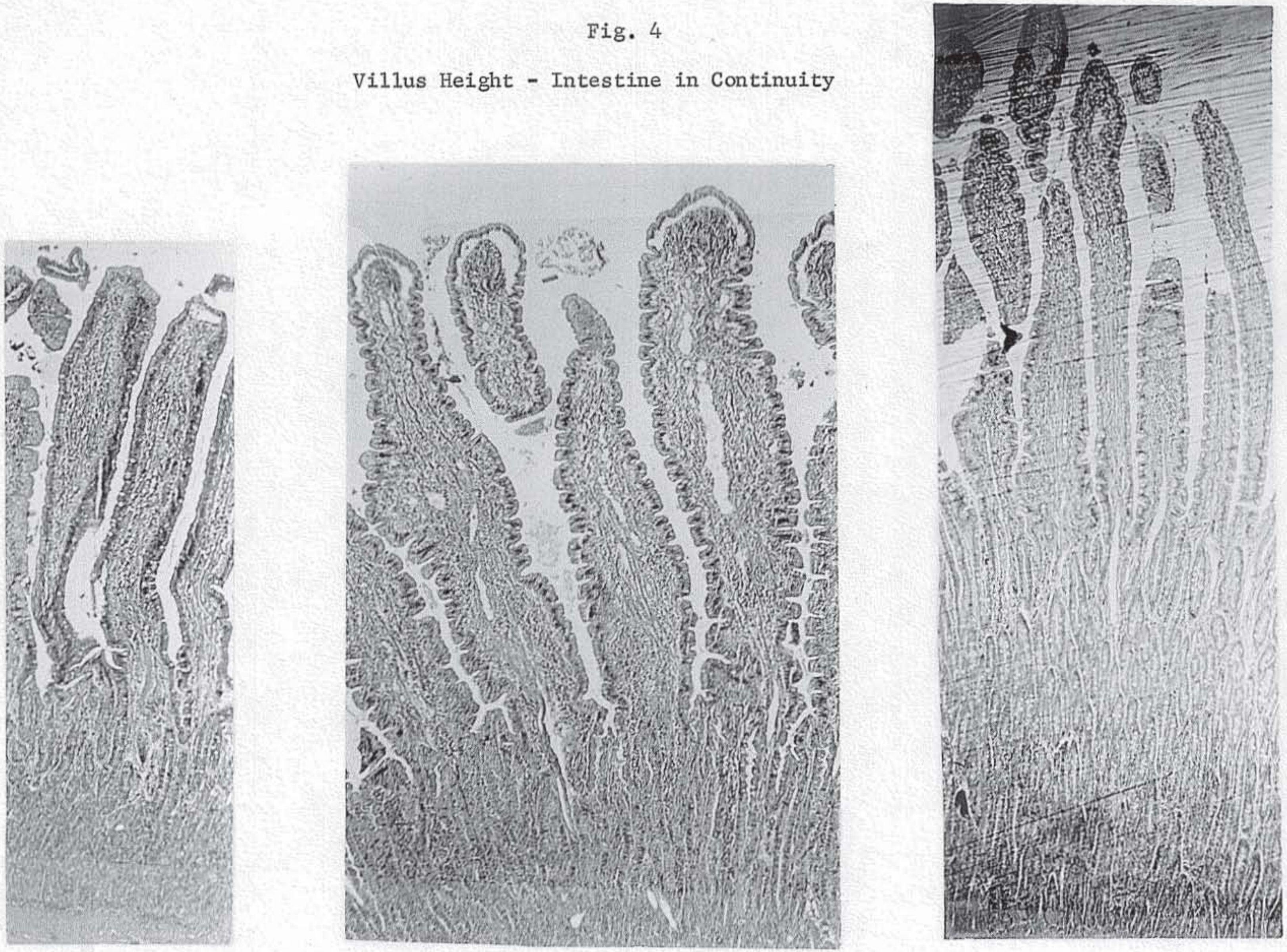
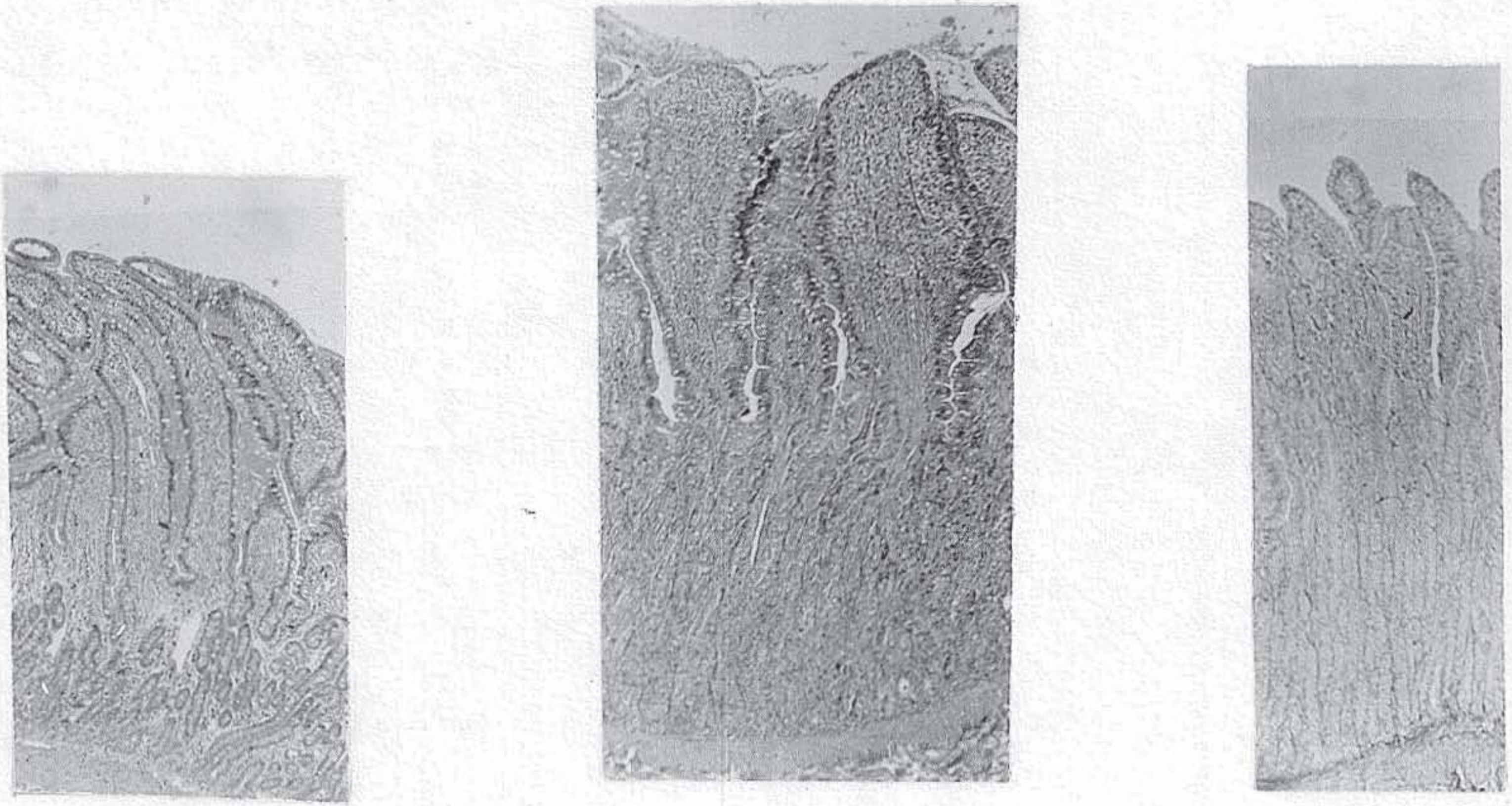


FIG. 4 ANALYSIS OF VARIANCE DEMONSTRATES A SIGNIFICANT TREATMENT EFFECT ON VILLUS HEIGHT OF THE INTESTINE IN CONTINUITY

Fig. 5

Villus Height - Thiry-Vella Fistula



SHAM RESECTION BYPASS

FIG. 5 ANALYSIS OF VARIANCE DEMONSTRATING NO SIGNIFICANT DIFFERENCE OF VILLUS HEIGHTS BETWEEN THE TREATMENT GROUPS.

3) PEG Recovery

The recovery of PEG was numerically incomplete but not significantly different between groups. For the sham group the mean recovery was 83 $\pm$ 1.4% while the recovery for the resection and bypass group was 83 $\pm$ 1.7% respectively.

However at no time was leakage from the stomae of the fistula observed to be greater than a few drops.

C) ABSORPTION TESTS - VARIABILITY WITH TIME

1) Sodium Fluxes

The overall group mean for insorption was 37.9 $\pm$ 2.38 uEq/min./unit length and the value for exsorption was 47.8 $\pm$ 2.52 uEq/min./unit length. All dogs in each group demonstrated a significant difference with time. The Duncan multiple range test also disclosed this variability but failed to distinguish any pattern over the course of the experiments. In other words the variability was random.

2) Potassium Fluxes

Insorption of potassium occurred at a rate of 1.39 $\pm$ .085 uEq/min/unit length while for exsorption the value was 2.05 $\pm$ .095 uEq/min./unit length. Statistical analysis disclosed a random variation of both these values with time.

3) Water Fluxes

Insorption of water was found to be 0.85 $\pm$ 0.036 ml/min./unit length and the value for exsorption was 0.90 $\pm$ 0.036 ml/min/unit length. Both of these values also displayed a significant random variation with time.

D) ABSORPTION TESTS - VARIABILITY BETWEEN GROUPS

1) Sodium Fluxes

Insorption of sodium in the sham, resected and bypassed groups was 43.3 $\pm$ 3.98, 32.2 $\pm$ 4.45 and 38.1 $\pm$ 3.98 uEq/min/unit length respectively. These differences are not statistically significant (Table 3)

Exsorption of sodium in the sham, resected and bypassed groups was 50.6 $\pm$ 4.29, 45.6 $\pm$ 4.78 and 47.6 $\pm$ 4.29 uEq/min/unit length respectively. These differences are also not statistically different. (Table 4)

2) Potassium Fluxes

Insorption of potassium in the sham, resected and bypassed groups was 1.48 $\pm$ 0.143, 1.44 $\pm$ 0.160 and 1.24 $\pm$ 0.143 uEq/min/unit length respectively. These differences are not statistically significant. (Table 5) Exsorption of potassium in the sham, resected and bypassed groups was 2.2 $\pm$ .16, 2.03 $\pm$ .18 and 1.93 $\pm$ .16 uEq/min/unit length respectively. These differences are not statistically significant (Table 6).

3) Water Fluxes

Insorption of water in the sham, resected and bypassed groups was 0.80 $\pm$ .061, 0.88 $\pm$ .068 and 0.87 $\pm$ .061 ml/min/unit length respectively. These differences are not statistically significant. (Table 7)

Exsorption of water in the sham, resected and bypassed groups was 0.86 $\pm$ .060, 0.95 $\pm$ .067 and 0.91 $\pm$ .060 ml/min/unit length respectively. These differences are not statistically significant. (Table 8)

DISCUSSION

DISCUSSION

A) ANALYTICAL TECHNIQUES

When dealing with derived functions every effort must be made to reduce the error of measurement as even small errors in measurement will introduce marked variability in the derived answer.[6]

In this study the greatest sources of variability in measurement were in the discrimination of the radioisotopes of sodium and potassium and the determination of PEG concentrations.

Since the contribution of ^{42}K to Channel B was small the channel ratio n exhibited high variability. The ultimate effect of this variability may be ascertained with a multiple sampling technique using the statistical tools of analysis of variance.

However since the measurement of potassium fluxes added little information the present study would have been improved if potassium fluxes were not measured.

A more serious source of error was in the PEG measurement. The volume marker is the cornerstone for all further measurements and errors in PEG measurement would affect all the calculated flux rates. Incomplete recovery of PEG may be caused by adsorbtion of PEG in the loop, unobserved leakage of test solution or imprecise analytical techniques. Leakage around the catheters was never observed in quantities greater than a few drops but as this leakage was not quantitated it remains a possibility. Adsorbtion of PEG has been investigated by others and not thought to occur.[52]

The most likely cause for the low recovery of PEG in these experiments was in the analytical technique. Turbidimetric measurements are always imprecise even though Malawer's method of stabilizing the emulsion reduces analytical error.[54] In addition the graph of PEG concentration vs. optical density is non-linear at low concentrations. (Appendix) Since the final measurement of PEG in the rinse used to detect the remaining PEG not removed by sampling, was always of low concentration, the nonlinearity of the curve introduced significant error. This error could not be corrected by altering the dilution of the test sample during PEG analysis.

However if the low recovery of PEG in this study only reflects the difficulty of measuring PEG in the rinse, then this error would not affect the eventual calculation of fluxes. Recently radioactively labelled ^{14}C-PEG has been introduced and found to eliminate these errors in the turbidimetric measurement.[28] This substance is the obvious choice for future experiments and will serve to clarify these difficulties.

B) <u>VARIATIONS IN FLUX RATES WITH TIME</u>

Berger has previously noted that the flux rates in Thiry-Vella fistulae of dogs vary significantly with time. He found a coefficient of variation of 25%.[7]

In the present study the result of variation with time and variation between animals was a coefficient of variation of approximately 60%. The result of such a great variation is to make it difficult to detect any other source of variability during chronic experiments.

Any experiment which did not have a large number of observations with time, and an estimate of the magnitude of such variation, would be liable to interpretation of such variation as being due to treatment effects.

The present experiment quantitated this source of variability in an effort to eliminate such errors.

C) EFFECT OF MASSIVE SMALL BOWEL RESECTION OR BYPASS

Massive loss of intestinal absorptive surface area results in systemic and intestinal changes.

As in the present study the animals lose weight and as a measure of caloric insufficiency become hypoproteinemic. These results are progressive until a plateau is reached when net absorption improves.

Clinically dogs undergoing bypass operations fared less well than the resected group. They were so cachectic and weak it would have been inhumane to persist in including them in the experiment. The resected group were always more active even though by objective parameters of weight and serum proteins the magnitude of the absorptive deficit was identical in the two groups.

Nevertheless in all dogs in both the resected and bypassed groups there was gross anatomic and histologic evidence of adaptation of the bowel in continuity.

In no animal, however, was there evidence of such hypertrophy in bowel that was not in continuity.

Many investigators have previously demonstrated that accompanying the villus hypertrophy of the adaptive response there is a functional compensation of increased absorption.[18] It is reasonable to suppose that the intestine in continuity of the bypassed and resected dogs would have demonstrated this increased absorption.

The defunctioned bowel (Thiry-Vella fistula) was not demonstrated to undergo any functional adaptation. Recognizing that lack of statistical change does not mean that no change occurred, only that observed differences could be accounted for by the variability with time, the lack of anatomic adaptation lends support to the conclusion that functional adaptation did not occur.

Since the Thiry-Vella fistula retained its normal blood supply a hormonal factor mediating the adaptive response is unlikely. There is no direct evidence that this portion of the intestine retained normal innervation so any neural involvement in the adaptive response is still possible, but since the nerves in this area follow the blood vessels,[4] a neural component is also unlikely.

Tilson and Wright[85] believed that the adaptation of bypassed terminal ileum which they observed following small bowel resection resulted from hormonal factors. However the bypassed ileum was still connected distally to the colon and thus was not completely defunctioned. In addition the ileum is known to respond to E.C.F. volume depletion by villus hypertrophy,[86] presumably as a result of aldosterone.[73] Since such a reaction does not occur in the jejunum,[73] a jejunal loop would not be sensitive to such a stimulus. The operative procedures and their sequelae of the present study presumably represented a stimulus to aldosterone secretion and the lack of change in histology or flux rates is compatible with the conclusion that the changes observed by Tilson and Wright were due to aldosterone.

The inescapable conclusion of this study is that the factor or factors responsible for the adaptive response are in, or act via, the intestinal lumen. Glucose and water are not likely agents since the Thiry-Vella fistulae received regular, although intermittent, supplies of glucose in the test and rinse solutions.

Furthermore, Wilmore and Dudrick,[100] noted hypertrophy when their resected animals received nutrition intravenously. However it is possible that some specific substrate, not supplied in the present study, and supplied unknowingly by Wilmore and Dudrick is essential to trigger the adaptive response.

In the light of the present study, Altman and Leblond's observations and their postulation of the presence of a villus enlarging factor in the pyloro-duodenal region gain added importance. Such a substance originating proximal to jejunum, would explain all the observations of the present experiment. This substance would not be present in the lumen of a Thiry-Vella fistula; nor in the bypassed gut, hence villus hypertrophy would not occur, in these segments. Indeed neither hypertrophy nor absorptive compensation did occur.

Of course such a substance may not act in isolation. Following massive resection or bypass, villus height is increased far beyond normal limits.

Nevertheless the indisputable fact remains that whatever is occurring in the lumen of the intestine is the "sine qua non" of the adaptive response and should be the area of future research.

TABLES

Table I

Factorial Analysis of Variance - Dog Weights

Source of Variation	d.f.	SS.	M.S.	F
Treatment	2	3904.7	1952.3	12.22 **
Error I	11	1758.1	159.8	
Dates	11	600.4	54.6	134.2 **
Trt. x Dates	22	336.4	15.3	37.6 **
Error 2	121	49.2	.407	
Error due to approximation		116.6		
Total	167	6765.3		

** = $p < .01$

Table I: ANOVA for dog weights from week 1 to 13, excluding week 3 (missing values). There is a significant difference between treatment groups and between dates. A significant interaction between treatment and dates is also present.

Table 2

Factorial Analysis of Variance - Serum Proteins

Source of Variation	d.f.	S.S.	M.S.	F.
Treatment	2	37.4	18.7	7.62 **
Error I	11	26.98	2.45	
Dates	10	58.91	5.89	15.88 **
Treatment x Date	20	9.36	.468	1.26
Error 2	110	40.8	.371	
Error due to approximation	3.59			
Total	153	177.02		

** = $p < .01$

Table ANOVA of serum proteins to week 13 excluding weeks 1 and 3 (missing values). There is a significant difference between the treatment groups and with time.

Table 3 (a)

Factorial Analysis of Variance - Insorption of Sodium

Source of Variation	d.f.	S.S.	M.S.	F
Treatment	2	2266.96	1133.48	1.792
Error I	11	6955.89	632.35	
Dates	7	3579.49	511.34	2.28*
Treatment x Dates	14	1926.99	137.64	.614
Error 2	77	17260.88	224.17	
Error due to approximation	94.89			
Total	111	32085.05		

* = $p < .05$

Table 3 (a) ANOVA for insorption of sodium to week 12 excluding weeks 2,6,11 and 12. There is no treatment effect but there is significant variation with time.

Table 3 (b)

Factorial Analysis of Variance - Insorption of

Sodium with Estimation of Missing Values

Source of Variation	d.f.	S.S.	M.S.	F
Treatment	2	1347.47	673.7	0.834
Error I	11	8890.73	808.25	
Dates	11	4877.29	443.39	2.24 *
Treatment x Dates	22	4759.46	216.34	1.13
Error 2	117	23200.92	198.29	
Error due to approximation 360.34				
Total	163	43436.21		

* = $p < .05$

Table 3 (b) ANOVA for insorption of sodium with estimation of missing values. There is no change in patterns of significance compared to table 3 (a).

Table 4

Factorial Analysis of Variance - Exsorption of Sodium

Source of Variation	d.f.	S.S.	M.S.	F.
Treatment	2	510.99	255.49	.310
Error I	11	9058.74	823.52	
Dates	8	6041.44	755.18	2.143 *
Treatment x Dates	16	3700.46	231.28	.656
Error 2	88	21017.52	352.47	
Error due to approximation - 56.70				
Total	125	50272.45		

$* = p < .05$

Table 4: ANOVA for exsorption of sodium. There is no difference between treatment groups but there is significant variation with time.

Table 5

Factorial Analysis of Variance - Insorption

of Potassium

Source of Variation	d.f.	S.S.	M.S.	F
Treatment	2	1.29	.643	.786
Error I	11	8.99	.818	
Dates	7	13.45	1.92	4.66 **
Treatment x Dates	14	7.94	.567	1.38
Error 2	77	31.76	.412	
Error due to approximation				
Total	111	.805		

** = $p < .01$

Table 5: ANOVA for insorption of potassium. There is no difference between treatment groups but there is significant variation with time.

Table 6

Factorial Analysis of Variance - Exsorption of Potassium

Source of Variation	d.f.	S.S.	M.S.	F
Treatment	2	1.35	.676	.663
Error I	11	11.21	1.02	
Dates	7	12.95	1.85	3.39 **
Treatment x Dates	14	6.16	.439	.807
Error 2	77	41.97	.545	
Error due to approximation	.685			
Total	111	74.33		

** = $p < .01$

Table 6: ANOVA for exsorption of potassium. There is no significant difference between treatment groups but there is significant variation with time.

Table 7

Factorial Analysis of Variance - Insorption of Water

Source of Variation	d.f.	S.S.	M.S.	F.
Treatment	2	.189	.095	.509
Error I	11	2.05	.186	
Dates	9	1.33	.148	2.26 *
Treatment x Dates	18	.576	.032	.498
Error 2	97	6.35	.066	
Error due to approximation		.05		
Total	137	10.55		

* = $p < .05$

Table 7: ANOVA for the insorption of water. There is no significant difference between treatment groups but there is significant variation with time.

Table 8

Factorial Analysis of Variance - Exsorption of Water

Source of Variation	d.f.	S.S.	M.S.	F
Treatments	2	.183	.092	.506
Error I	11	1.99	.181	
Dates	9	1.399	.156	2.17 *
Treatment x Dates	18	.654	.036	.516
Error 2	97	6.96	.0718	
Error due to approximation .027				
Total	137	11.22		

* = $p < .05$

Table 8: ANOVA for the exsorption of water. There is no significant difference between treatment groups but there is significant variation with time.

Table 9

Analysis of Variance - Villus Height of

Pretreatment Intestinal Biopsy

Source of Variation	d.f.	S.S.	M.S.	F
Treatments	2	1.39	.697	.469 (n.s.)
Dogs	11	16.34	1.49	
Total	13	17.73		

Table 9: Analysis of variance of villus heights demonstrating no significant difference between treatment groups.

Table 10

Analysis of Variance of Villus Height

of Intestine in Continuity

Source of Variation	d.f.	S.S.	M.S.	F
Treatment	2	58.24	29.12	31.49 **
Dogs	11	10.17	.925	
Total	13			

** = $p < .01$

Table 10: Analysis of variance demonstrates a significant treatment effect on villus height of the intestine in continuity

Table 11

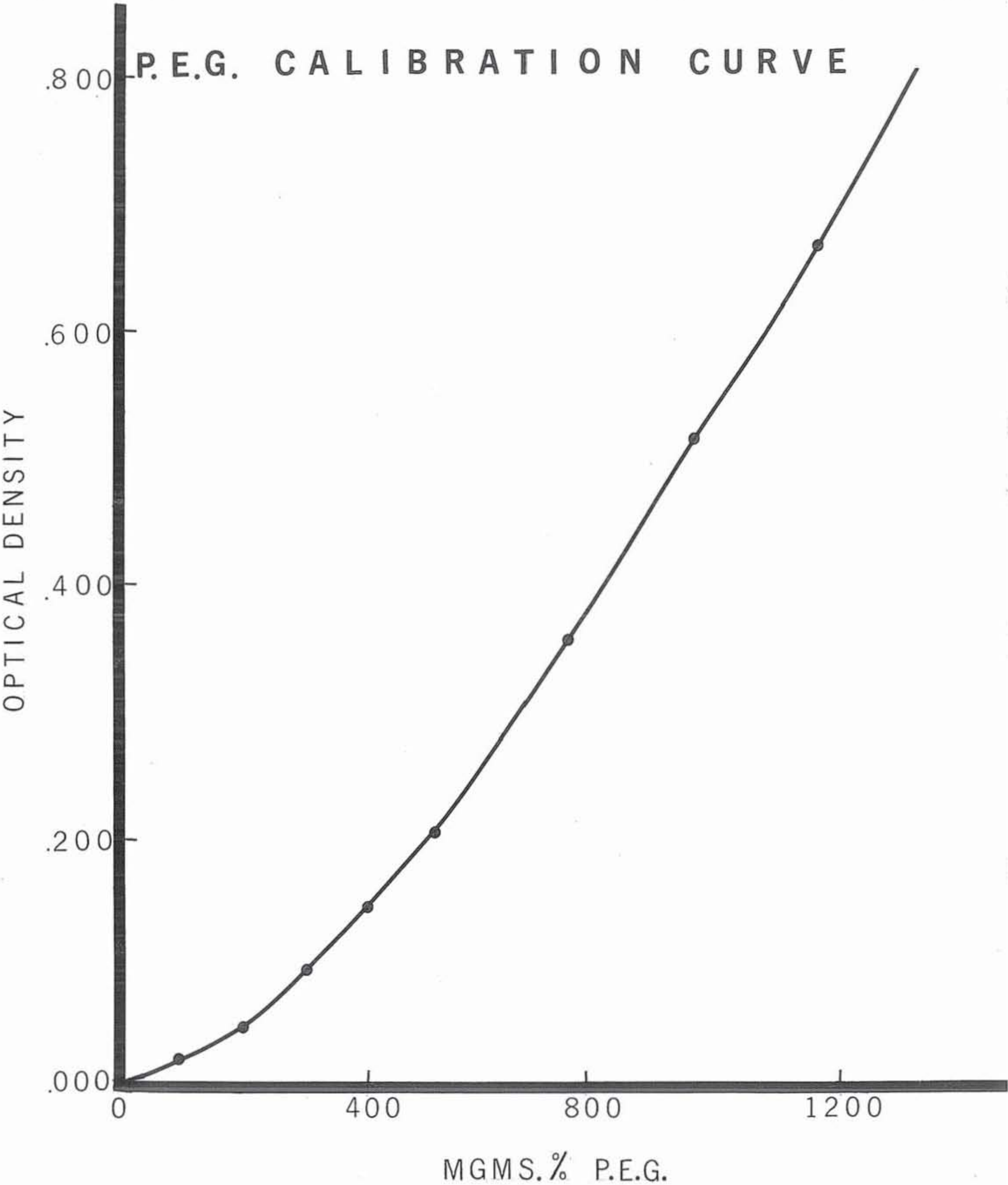
Analysis of Variance - Villus Height of

Thiry-Vella Fistula

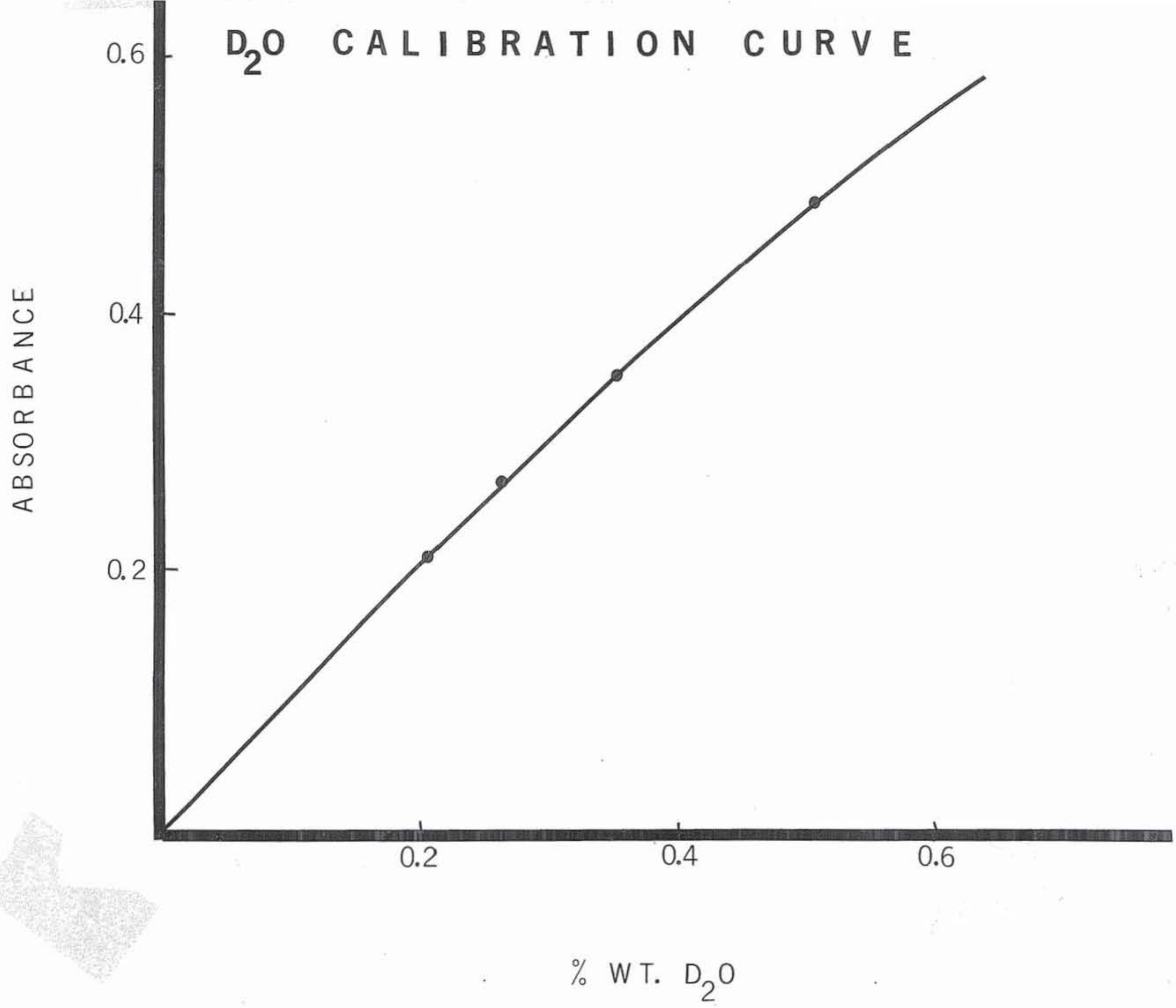
Source of Variation	d.f.	S.S.	M.S.	F.
Treatment	2	.055	.027	.011
Dogs	11	28.14	2.56	
Total	13	28.19		

Table 11 Analysis of Variance demonstrating no significant difference of villus heights between the treatment groups.

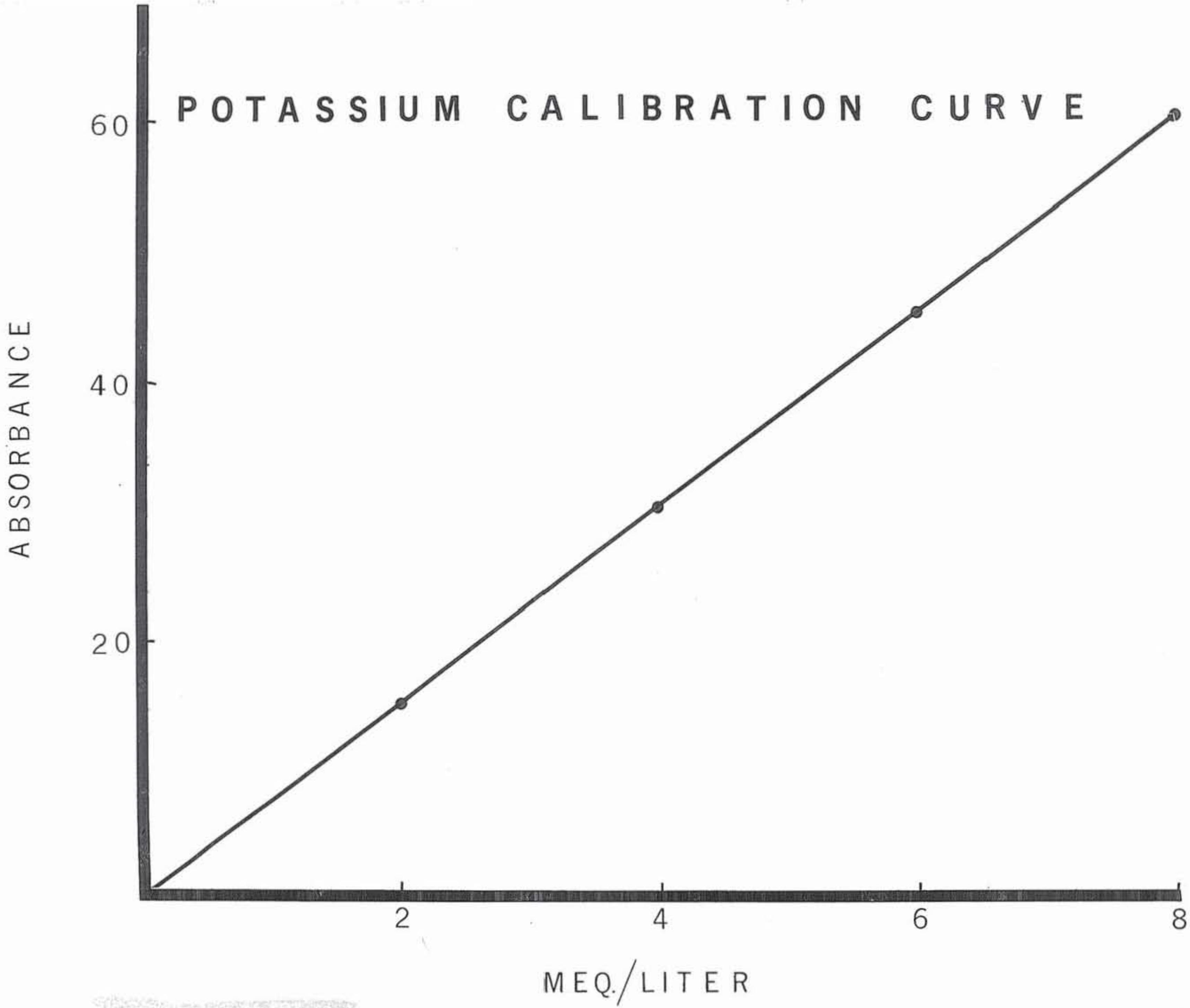
APPENDIX

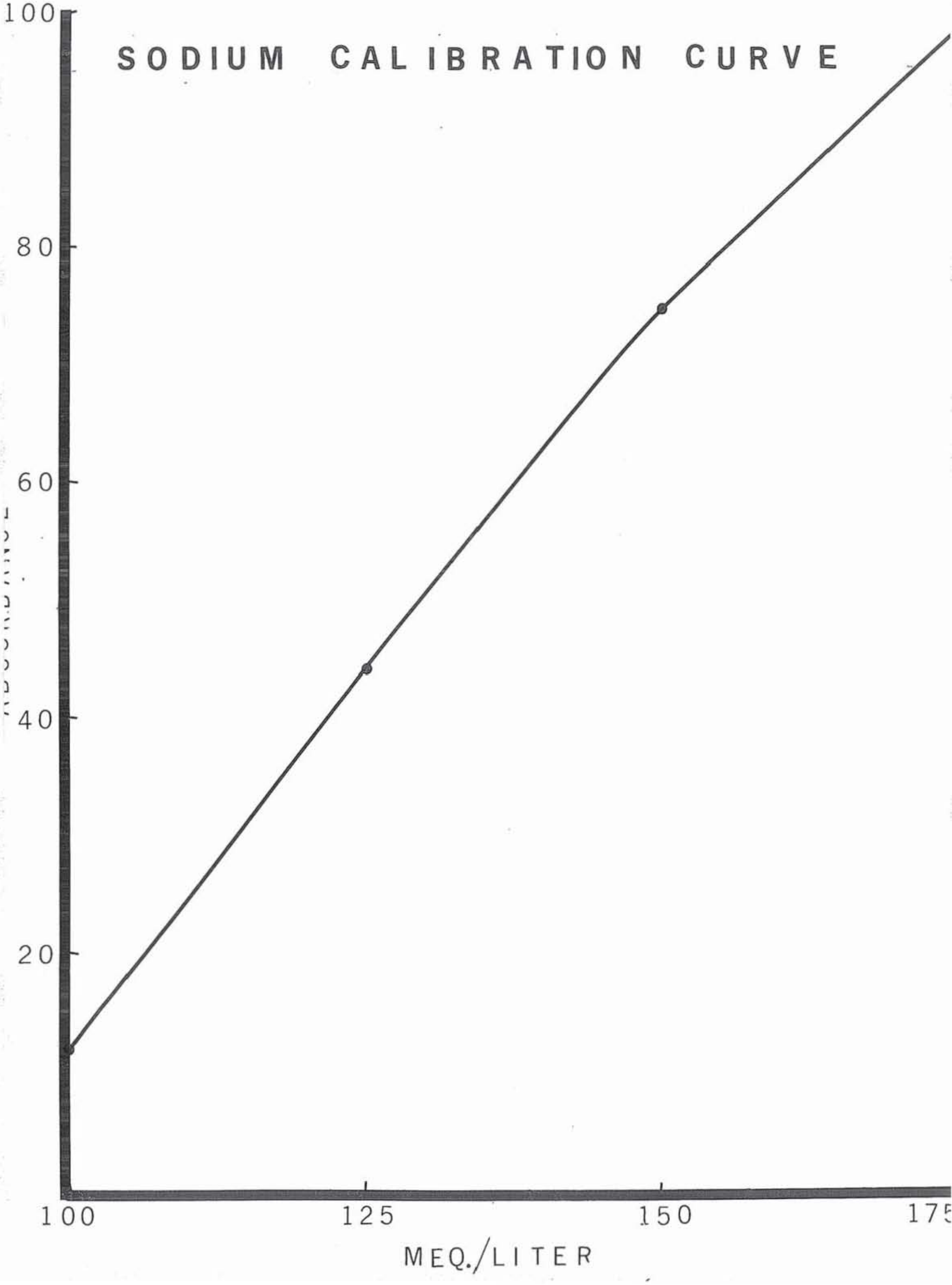


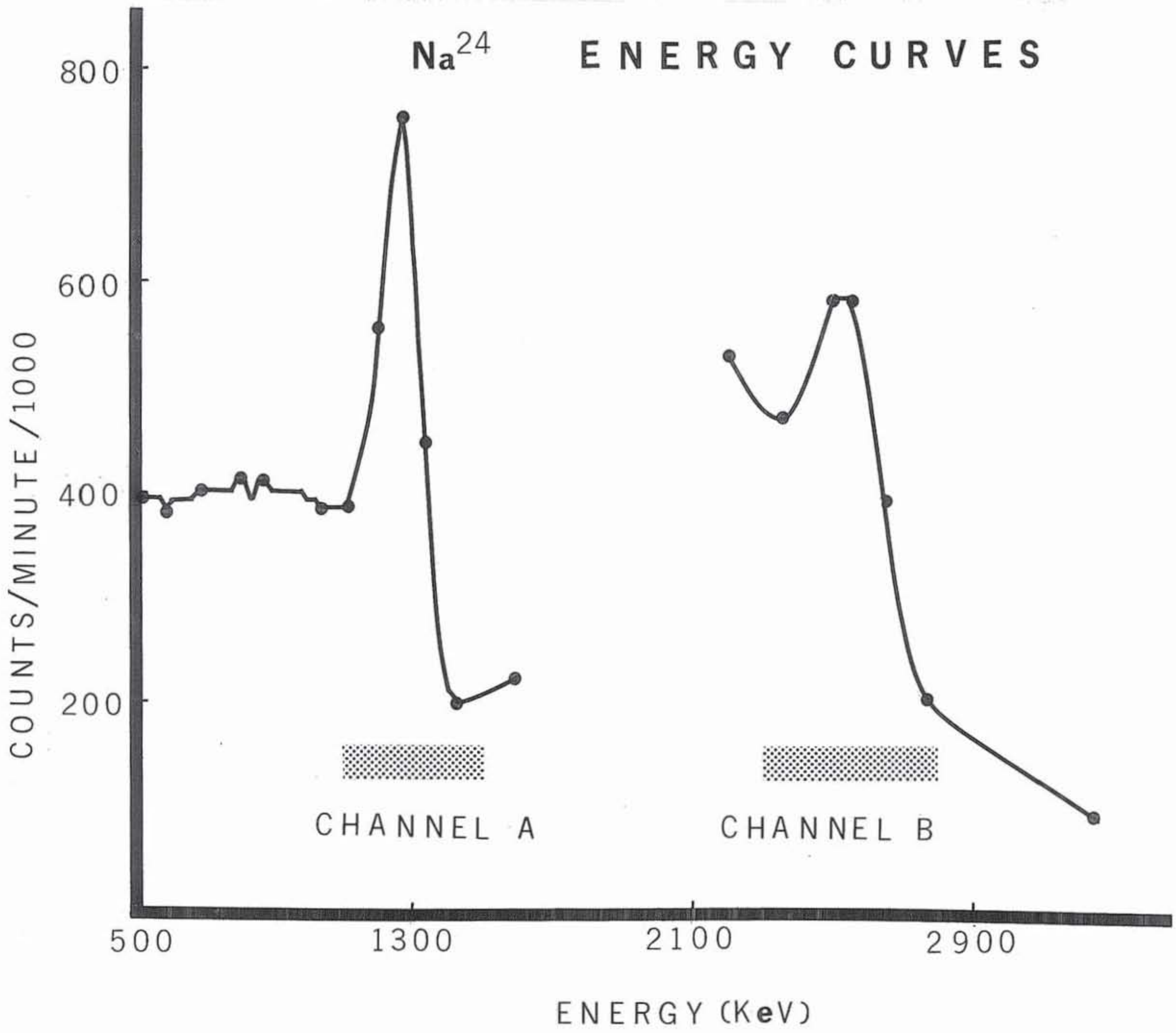
P.E.G. CALIBRATION CURVE
OPTICAL DENSITY
.800
.600
.400
.200
.000
0
400
800
1200
MGMS.% P.E.G.

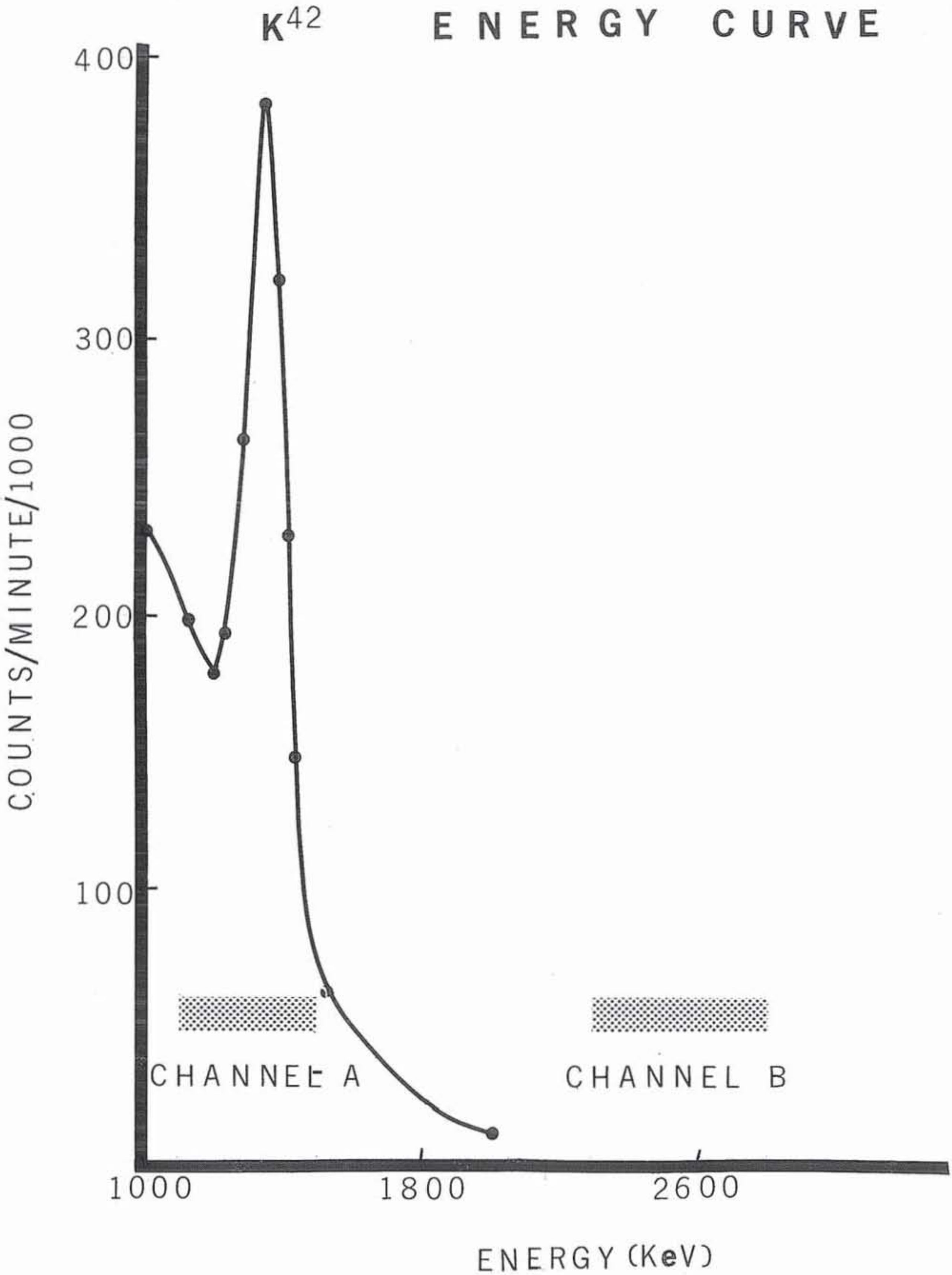


D2O CALIBRATION CURVE
ABSORBANCE
0.6
0.4
0.2
0.2
0.4
0.6
% WT. D2O


POTASSIUM CALIBRATION CURVE
ABSORBANCE
60
40
20
2
4
6
8
MEQ./LITER


SODIUM CALIBRATION CURVE
100
80
60
40
20
100
125
150
17
MEQ./LITER


Na24 ENERGY CURVES
800
600
400
200
COUNTS/MINUTE/1000
CHANNEL A
CHANNEL B
500
1300
2100
2900
ENERGY (KeV)



K42
ENERGY CURVE
400
300
200
100
COUNTS/MINUTE/1000
CHANNEL A
CHANNEL B
1000
1800
2600
ENERGY (KeV)

DOG # ____________ DATE: ________________

79

t	Sample Size	(PEG) mg/ml	Resid. PEG	Vol.	(Na)	Total Na	Na Prev. Removed	Correct Na	Rel. Amt.	(K)	Total K	K Prev. Removed	Correct K	Rel. Amt.

PEG (rinse) = ________

% Recovery PEG = ________

VOLUME

t	Correct Vol.	Ratio

DOG # ________ DATE: ________________

t	Tracer cpm/ml	Natural Isotope UEq/ml	(PEG) mg / ml	A UEq (Corrected)	(A - Ao)t UEq/min.	Θ cpm/UEq	$\frac{\ln \Theta^n/\Theta_1}{\ln \frac{(S^n)/(PEG)^n}{(S_1)/(PEG_1)}}$	Insorption	Exsorption

WATER FLUXES Dog # ________ Date: ____________

t	Corrected Volume	% D_2O	$\frac{A - A_o}{t}$	$\frac{O_n}{O_o}$	$\ln \frac{O_n}{O_o}$	$\frac{A_n}{A_o}$	$\ln \frac{A_n}{A_o}$	α	β

$$\alpha = \frac{A - A_o}{t}\left(\frac{\ln \frac{O_n}{O_o}}{-\ln \frac{A_n}{A_o}} - 1\right)$$

$$\beta = \frac{A - A_o}{t}\left(\frac{\ln \frac{O_n}{O_o}}{-\ln \frac{A_n}{A_o}}\right)$$

Dog #:
Date:

ISOTOPES

Test:

Na

N_1 N_2

$m =$

K

N_1 N_2

$n =$

1) $t = 0$
$N_1 =$
$N_2 =$
$r = N_2/N_1 =$

$S = \frac{m - r}{r - n} =$

$Na = I_1 = \frac{N_1}{1 + S} =$

log R =

= λt log e =

log Ro =

antilog Ro = Ro =

cpm / ml of Na^{24}

Time of Decay =

anti log:

(Na) $\lambda t \log e = (.0462)(.434297)t$

(K) $\lambda t \log e = (.05428)(.434297)t$

$K = I_2 = N_1 - I_1 =$

log R =

+ λt log e =

log Ro =

Ro =

cpm / ml of K^{42}

---

2) $t =$
$N_1 =$
$N_2 =$
$r =$

$S =$

$Na = I_1 \quad \frac{N_1}{1 + S} =$

log R =

+ λt log e =

log Ro =

Ro =

cpm / ml of Na^{24}

$K = I_2 = N_1 - I_1 =$

log R =

+ λt log e =

log Ro =

Ro =

cpm / ml of K^{42}

3) $t =$
$N_1 =$
$N_2 =$
$r =$

$S =$

$Na = I_1 = \frac{N_1}{1 + S} =$

$\log R =$

$+ \lambda t \log e =$

$\log Ro =$

$Ro =$

cpm / ml of Na^{24}

$K = I_2 = N_1 - I_1 =$

$\log R =$

$+ \lambda t \log e =$

$\log Ro =$

$Ro =$

cpm / ml of K^{42}

4) $t =$
$N_1 =$
$N_2 =$
$r =$

$S =$

$Na = I_1 = \frac{N_1}{1 + S} =$

$\log R =$

$+ \lambda t \text{ Log } e =$

$\log Ro =$

$Ro =$

cpm / ml of Na^{24}

$K = I_2 = N_1 - I_1 =$

$\log R =$

$+ \lambda t \log e =$

$\log Ro =$

$Ro =$

cpm / ml of K^{42}

5) $t =$
$N_1 =$
$N_2 =$
$r =$

$S =$

$Na = I_1 = \frac{N_1}{1 + S} =$

$\log R =$

$+ \lambda t \log e =$

$\log Ro =$

$Ro =$

cpm / ml of Na^{24}

$K = I_2 = N_1 - I_1 =$

$\log R =$

$+ \lambda t \log e =$

$\log Ro =$

$Ro =$

cpm / ml of K^{42}

DERIVED DATA - UNANALYSED

VILLUS HEIGHT mm x 10 $^{-1}$

	DOG	PRETREATMENT BIOPSY	INTESTINE IN CONTINUITY	THIRY-VELLA FISTULA
	9	9.8	10.5	8.5
	11	9.5	13	7.5
SHAM	15	9.0	12.5	9
	17	11.1	12	10
	21	7	10.2	7.8
	5	8.1	15	6
	6	8	15.2	9
BYPASS	10	8	16	9.5
	12	10	16.5	12
	19	10	15	7
	22	-	-	7.5
	8	7.5	15.5	8.5
	13	8.2	17.5	9.2
RESECTION	14	- excluded - early death		
	18	8.5	16	9.5
	20	9.8	16	7.5

DOG #	I_1	I_2	I_3	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9	D_{10}
							WEIGHT						BYPASS
5	21.4	21.7	21.3	16	14.9	14	13.1	12.7	12.2	11.6	11.1	10.5	9.9
6	21.9	21.4	21.6	17.8	17.5	16.7	16.2	15.1	14.7	14.5	13.8	12.1	12.0
10	22	22	-	17.8	16.7	16	15.4	13.9	13.8	13.4	12.7	11.8	11.6
12	22.3	24.5	24.5	19.6	19.5	18.8	17.8	17.2	16.5	15.8	15.2	15.1	14.4
22	17.8	17.8	17.4	13.4	12.6	11.8	11.4	10.9	10.1	9.9	9.1	9.1	9.0
19	19.5	20.5	19.4	15.8	14.5	13.3	13.3	12.1	10.4	died			

WEIGHT — BYPASS CONT'D

DOG #	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21
5	9.6	- reconnected									
6	11.7	-	10.8	11.0	11.0	10.7	10.6	9.2	9.5	died	
10	11.2	- reconnected									
12	14.4	13.9	resected								
22	-	died									
19											

DOG	WEIGHT										RESECTION		
#	I_1	I_2	I_3	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9	D_{10}
8	19.1	19.3	19.3	16.4	15.5	14.8	14	13.2	13.2	13.1	13	13.4	11.8
13	19.8	19.8	20.1	16.2	15.7	14.2	13.7	12.9	13.1	12.1	11.9	11.7	11.6
18	16.7	16.4	-	11.6	10.9	10.6	10.7	9.3	11.2	8.8	8.4	7.9	8.4
20	20.6	20.6	20.6	17.6	17.1	16.4	15.9	15.5	14.8	14.4	13.4	13.8	13.8
14	22.6	22.6	22	died									

DOG WEIGHT RESECTION CONT'D

#	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21	D 22	D 23	D 24
8	12.6	12.4	11.6	11.2	12.1	11	10.2	9.9	9.9	8.8	10.8	10.7	9.2	9.5
13	11	11.6	11.1	11	10.6	11	10.8	10.7	9.4	11.3	10.9	10.4	9.8	
18	8.4	8.5	died											
20	13.1	12.6	13.5	12	11.5	10.6	9.6	died						
14														

DOG							WEIGHT							SHAM
#	I_1	I_2	I_3	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9	D_{10}	D_{11}
9	23.2	24.6	24.6	22.7	22.2	20.1	21.6	21.8	22	22.1	22.3	22.2	22.2	22
11	32.2	32.6	32.6	33	32.8	32	34.2	33.3	34.2	34	34.4	34.3	34.4	35
15	19.4	19.4	18.9	19.1	19.2	19.2	19.3	20.2	20.1	20.4	20.2	19.6	18.8	19
17	23.3	26.8	-	24	25.3	25.3	25.6	25.6	26	25.6	25.8	25.4	25.3	25
21	23.8	24.3	23.5	22.8	23.2	23.8	24.2	23.1	24.6	23.8	23.2	22.8	23.6	23.7

DOG | WEIGHT | SHAM CONT'D

#	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21	D 22	D 23	D 24
9	22.5	22.1	21.9	21.4	21.3	21.2	20.9	19.7	20.7	21.1	20.9	20.9	21.2
11	34.8	34.2	35	34.3	34	33.8	33.2	33.1	33.6	33.8	34	34.2	33.5
15	18.9	19.3	18.8	17.9	17.1	18.4	18.3	17.3	20.6	20.1	19.4	19.2	
17	26	26	25.2	26.3	25.1	25.2	23.7	26.6	26.7	25.7	24.8		
21	23.7	23.6	23.8	23.9	23.2	23.2	23.7	24.6	25.1	23.6	23.7		

PROTEINS RESECTION

DOG #	I_1	I_2	I_3	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9	D_{10}
8	-	6.3	-	6.2	6.2	6.1	5.8	4.9	5.3	5.3	5.7	5.1	5.2
13	-	7.4	-	6.6	6.2	6.0	4.8	5.1	5.8	5.7	5.0	4.8	4.6
18	-	6.4	-	7.2	5.1	3.9	4.5	4.4	6.1	4.1	4.1	4.6	3.9
20	-	6.5	-	7.0	6.0	5.3	5.5	5.9	6.1	5.9	6.6	6.1	5.6
14	-	7.4	-	died									

PROTEINS RESECTION CONT'D

DOG #	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21	D 22	D 23	D 24
8	5.3	5.0	5.8	5.4	4.4	5.1	5.2	4.8	4.6	5.0	5.5	5.4	5.9	5.9
13	4.8	4.4	4.7	4.6	4.6	4.1	4.2	5.5	4.8	4.9	4.6	6.0	6.0	
18	4.6	died												
20	5.7	6.0	5.0	5.4	5.7	5.5	5.6	died						
14	5.7	6.0												

PROTEINS BYPASS

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D 12
5	-	7.8	-	6.6	5.3	6.8	4.8	3.9	4.4	4.7	4.8	4.0	4.4	4.2	-
6	-	6.3	-	5.7	5.6	6.4	5.0	4.4	5.0	5.3	5.5	5.2	5.1	5.4	-
10	-	7.5	-	7.4	9	5.1	4.6	4.8	5.2	5.0	5.2	5.4	5.0	5.4	-
12	-	7.0	-	6.2	5.5	4.9	4.7	4.1	4.4	4.8	4.7	4.3	4.1	4.5	4.6
22	-	6.8	-	6.0	5.7	5.0	4.2	4.6	4.1	5.6	4.1	3.9	3.9	-	
19	-	7.8	-	7.8	5.6	4.9	4.7	4.9	5.4	died					

PROTEINS

BYPASS CONT'D

DOG #	D_{13}	D_{14}	D_{15}	D_{16}	D_{17}	D_{18}	D_{19}
5							
6	4.9	5.4	4.8	5.1	4.6	5.7	5.3
10							
12							
22							
19							

DOG #	I_1	I_2	I_3	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8	D_9	D_{10}	D_{11}	D_{12}
						PROTEINS							SHAM		
9	-	6.9	-	7.0	6.4	6.8	5.9	4.7	5.8	6.2	6.4	5.5	5.9	5.7	6.0
11	-	9.4	-	8.6	7.4	7.5	8.1	6.0	6.3	6.2	7.5	7.1	6.4	6.5	7.0
15	-	6.5	-	7.2	7.2	7.0	5.3	6.0	6.4	6.6	6.1	6.1	5.4	6.1	5.2
17	-	6.4	-	6.3	5.6	5.2	6.1	6.1	6.3	5.4	5.3	5.7	5.8	5.1	5.9
21	-	7.6	-	6.7	6.3	5.8	6.6	7.1	7.4	6.1	6.1	6.0	6.3	6.3	5.2

PROTEINS — SHAM CONT'D

DOG #	D_{13}	D_{14}	D_{15}	D_{16}	D_{17}	D_{18}	D_{19}	D_{20}	D_{21}	D_{22}	D_{23}	D_{24}
9	4.6	5.9	5.2	5.8	5.3	5.2	5.5	5.1	6.7	6.1	6.2	5.7
11	5.7	7.2	6.4	7.2	6.7	5.9	4.7	5.4	7.3	8.6	6.8	5.9
15	6.0	5.1	5.3	5.5	4.9	5.4	5.1	6.7	6.2	6.2	6.5	
17	5.5	5.8	6.2	5.6	5.5	4.6	6.0	6.6	6.2	6.3		
21	6.1	6.3	6.0	5.5	5.6	5.5	6.4	6.3	7.9	6.4		

DOG							Na $\propto$						SHAM	
#	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11
	25.28	57.89	42.17	111.52	22.32	-	42.42	37.95	26.73	3.56	35.81	-	5.17	12.28
11	32.54	47.40	87.00	-	36.86	-	51.86	39.75	30.48	26.50	25.93	-	17.26	18.92
	35.68	72.29	-	-	30.48	-	37.52	-	42.15	28.39	36.34	-	26.32	43.80
	-	21.84	-	-	24.62	-	-	-	29.70	17.98	35.60	-	24.06	75.15
21	53.15	31.86	48.52	36.14	76.55	39.74	56.44	19.14	16.76	31.77	28.50	37.12	20.21	-
	89.08	44.66	54.58	22.09	69.89	59.47	-	45.55	41.20	28.48	25.04	23.46	18.52	-
	66.04	48.60	50.74	28.32	-	52.70	-	46.48	48.41	34.67	40.47	21.14	29.35	-
	-	63.16	56.70	-	-	36.06	-	-	36.21	30.50	38.62	22.12	37.95	-
	-	-	-	-	-	-	-	-	-	-	-	18.31	-	-
17	6.12	40.73	33.51	66.24	52.58	17.59	62.59	36.59	34.73	29.47	-	19.17	6.98	7.39
	17.86	52.31	49.21	66.46	33.34	18.60	62.06	46.58	29.87	36.87	-	27.41	21.86	-
	6.35	36.39	-	-	-	36.52	58.84	50.27	28.68	55.75	-	17.23	36.83	-
	-	30.07	-	-	-	-	-	35.61	-	44.93	-	-	16.35	-
	51.74	28.72	77.89	55.92	42.07	42.59	33.61	13.28	13.03	45.33	35.20	21.66	-	15.13
15	35.21	32.57	78.56	72.13	40.30	41.20	-	-	7.79	57.85	27.83	46.72	9.56	43.72
	37.57	-	-	98.85	32.66	29.04	-	-	21.68	165.99	27.21	112.85	8.43	41.75
	-	-	-	-	29.74	-	-	-	-	-	-	-	7.03	30.05
	29.58	7.80	20.33	24.38	24.08	21.90	35.17	23.83	21.48	18.62	-	29.96	15.81	5.27
9	37.55	29.86	22.92	32.87	17.65	-	36.87	16.45	46.03	62.91	6.47	25.88	24.80	20.97
	40.15	39.99	32.98	14.12	23.97	-	42.02	30.95	38.78	37.45	27.76	32.87	49.13	16.58

SHAM CONT'D

DOG #	D 12	D 13	D 14	D 15	D 16	D 17	Na α D 18	D 19	D 20
	13.13	23.96	19.55	16.68	17.30	9.76	44.98	23.34	32.18
11	17.29	11.31	13.30	19.85	13.83	25.60	11.58	29.34	23.86
	29.64	68.72	3.23	33.08	13.86	25.28	20.70	41.76	81.39
	25.91	14.77	-	22.51	24.85	24.48	24.76	36.95	33.40
	23.22	-	-	-	20.10	-	19.55	-	-
	18.16	53.56	10.48	11.17	32.70	12.07			
21	42.06	50.38	12.36	22.81	34.11	21.38			
	54.05	82.73	11.00	35.54	33.74	28.47			
	94.68	-	23.07	33.88	40.10				
	-	-	-	33.70	26.19				
	10.60	46.99	24.55	37.20	-	24.53			
17	27.19	53.32	39.08	34.75	-	24.58			
	27.44	-	-	44.55	-	24.43			
	30.91	-	-	42.18	-	15.22			
	13.37	46.88	-	28.88	27.71	-	23.96		
15	10.81	23.78	3.44	25.29	-	-	-		
	35.37	29.47	10.93	39.51	-	-	-		
	26.49	20.01	-	32.84	-	55.15	-		
	2.03	27.59	19.41	40.00	-	4.87	17.80	8.00	
9	1.05	33.81	17.19	-	11.73	11.26	17.74	8.76	
	9.23	24.19	33.98	-	22.84	11.45	22.65	24.36	
	9.90	27.07	-	-	22.83	7.73	18.47	20.52	

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	Na D 4	D 5	D 6	D 7	D 8	D 9	RESECTION D 10
	12.49	55.46	17.56	44.91	37.06	44.78	28.08	38.57	44.04	19.64	60.65	81.82	-
8	25	31.46	29.31	41.64	22.39	40.57	27.05	22	27.44	27.78	98.5	44.87	-
	-	34.02	-	-	-	-	27.68	19.11	36.05	41.87	-	19.29	-
	-	-	-	-	-	-	-	-	25.25	-	-	-	-
	80.89	18.85	50.53	54.18	36.92	26.49	40.22	18.77	38.28	27.70	46.69	20.61	14.19
	43.43	26.64	60.76	-	30.43	35.99	48.49	18.38	28.43	22.99	36.77	28.25	12.27
	59	32.26	58.75	-	56.71	27.85	35.07	32.55	27.27	23.27	36.48	27.11	11.48
13	-	27.32	-	-	-	26.75	-	-	23.8	23.72	-	31.72	-
	55.02	31.68	31.11	24.51	42.52	19.27	27.81	26.06	10.75	41.64	26.85	44.36	31.71
	45.48	33.68	31.19	33.23	31.54	18.54	20.78	25.21	13.73	33.47	33.49	28.28	31.03
	41.02	25.6	33.47	42.75	29.62	28.35	28.4	24.18	18.26	32.51	44.81	33.05	20.27
18	38.59	31.78	26.77	-	-	33.44	19.3	21.52	19.88	-	24.86	19.6	-
	19.89	29.81	50.01	20.92	22.21	16.52	52.32	10.49	18.82	32.19	9.22	17.03	25.72
	30.24	22.78	28.83	19.89	-	25.33	-	16.93	24.37	31.99	9.44	27.06	17.78
20	18.77	20.48	24.19	-	-	28.71	-	29.61	30.22	33.34	31.36	30.50	26.77
	30.05	19.11	-	-	-	-	-	-	5.84	33.97	19.16	-	-
		21.51	-	-	-	-	-	-	13.74	-	-	-	-
	20.71	14.86	41.02	-	-	-	-	-	-	-	-	-	-
	30.6	13.69	33.4										-
	21.44	-	32.23	died									-
	29.42	-	28.41										-
14													

Na

RESECTION CONT'D

DOG #	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	
	28.12	5.38	11.21	26.95	44.06	-	31.01	26.78	25.99	
8	39.4	10.79	10.2	-	28.36	-	-	60.33	50.4	
	34.68	18.3	-	-	17.56	-	-	15.99	33.17	died
	-	15.01	-	-	-	-	-	-	-	
13	18.41	10.93	5.84	36.17	4.12	26.05	30.34	24.24		
	15.23	34.81	17.01	10.18	13.18	26.85	21.2	25.6		
	19.47	35.5	5.28	27.12	11.62	6.79	26.13	30.15		
	18.58	19.36	4.96	22.56	15.88	10.08				
	17.4	-	-	15.4	13.74	-	-	-		
	15.26	3.50	-	-	-	-	-	-		
18	20.49	7.20	-	-	-	-	-	-		
	20.01	13.22	died							
	11.42	11.26								
	10.64	4.14								
	14.1	8.52	12.38							
20	26.01	-	22.8							
	21.93	-	-							
	24.94									

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	Na D 4	D 5	D 6	D 7	BYPASS D 8	D 9
5	-	31.48	13.29	41.37	45.26	20.87	27.12	32.14	18.37	22.26	20.39	11.38
	-	30.36	22.34	54.42	34.88	69.34	36.03	47.65	24.53	19.93	16.21	25.49
	38.24	31.12	26.86	36.64	-	27.83	-	34.4	26.34	30.6	17.32	-
	-	21.84	27.08	-	-	32.17	-	63.3	-	26	-	25.31
	-	-	30.95	-	-	-	-	-	-	-	-	-
6	27.94	10.79	18.2	54.62	18.95	31.68	19.87	30.45	27.05	31	19.02	31.21
	23.71	38.16	22.57	-	26.93	29.4	28.48	36.94	28.23	23.4	22.6	20.07
	16.57	18.42	19.88	-	30.51	79.86	47.18	24.69	-	37.56	21.39	28.76
	-	-	-	-	-	-	39.54	29.15	-	-	23.96	29.64
											25.07	
10	32.35	51.37	46.99	42.93	15.26	36.37	42.68	37.02	29.96	18.07	11.92	36.03
	34.21	27.95	50.54	46.67	23.47	17.32	68.93	-	38.22	12.24	27.01	39.47
	28.99	26.31	32.91	38.50	35.03	23.2	86.93	-	39.61	20.14	71.55	29.91
	-	-	45.09	-	30.09	-	45.92	-	-	16.32	-	-
12	-	71.54	67.51	65.14	55.02	67.39	44.33	75.52	48.4	32.3	15.42	48.99
	59.44	27.55	-	70.07	61.49	-	54.01	53.91	94.02	47.54	-	59.36
	-	-	-	44.69	-	-	-	48.51	51.3	-	-	57.08
												65.13
22	29.22	-	38.48	31.98	39.44	13.65	33.04	-	14.5	31.04	7.45	28.84
	30.32	-	25.53	34.7	34.41	57.11	26.44	-	11.05	-	10.79	10.8
	35.93	-	-	-	28.07	-	-	36.42	13.99	-	21.53	10.69
								44.86			18.65	5.8
								16.6				

Na α

BYPASS CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	
	19.99	18.77	7.82					
	15.55	24.31	10.21					
5	21.12	18.15	14.21	sacrificed				
	38.04	24.27	17.66					
	5.68	16.3	40.82	-	19.05	27.99	25.81	
	17.72	19.5	36.13	-	21.87	33.14		died
	-	27	41.41	-	20.65	-	-	
6	-	23	25.87	-	-	-	-	
	15.85	31.83	29.35					
			14.35					
10			21.51					
			14.2	sacrificed				
	-	29	23.18					
		13.58	14.18					
12		20.41	19.54	resected				
			27.45					
	10.5	17.8						
	16.9	21.59						
22	26.68	14.6	died					
		15.05						
		10.15						

DOG #	I 1	I 2	I 3	D 1	D 2	Na - β D 3	D 4	D 5	D 6	BYPASS D 7	D 8
	85.93	33.65	21.41	51.77	49.65	45	53.26	56.05	39.61	31.9	23.79
		30.72	38.75	58.8	32.64	79.58	60.24	55.5	39.94	36.45	25.85
5		37.91	37.72	45.4		47.97		44.55	38.61	39.72	23.31
		31.8	36.64			45.79		69.32		34.66	
			39.46								
	42.36	24.5	25.83	88.3	43.02	50.19	36.18	28.71	31.83	29.64	24.15
	48.13	63.41	35.9	-	48.58	40.3	48.94	34.86	34.18	31.94	48.16
6	37.28	58.46	29.59	-	48.66	85.21	57.82	21.33	-	41.03	44.79
							49.29	25.58			41.19
											39.28
	28.1	55.29	57.78	37.97	24.68	36.65	65.98	50.95	43.07	24.48	
10	38.15	25.49	55.54	42.0	39.9	29.73	77.92	-	53.22	25.64	15.65
	23.38	23.56	39.86	32.45	44.77	35.51	92.93	-	46.89	32.95	34.82
	94.25		54.68		39.4		53.18			26.95	74.19
	55.49	64.26	58.35	62.75	37.23	52.79	51.74	75.76	34.8	56.79	26.3
		32.24	-	64.75	46.77	-	81.17	57.03	90.73	62.64	-
12				37.92				51.38	44.77		
	30.0	-	40.97	45.21	30.88	35.16	37.27	38.92	33.24	64.53	9.44
	25.07	-	24.18	47.35	27.29	62.95	31.43	46.12	28.88	-	28.83
22	32.34	-	-	-	16.12	-	-	15.42	28.78	-	38.35
											42.43
	64.4	45.9	31.92	35.73	39.51	43.85	-	47.79	38.19		

Na - β

BYPASS CONT'D

DOG #	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	35.23	25.82	32.9	23.44				
	59.66	27.17	33.8	26.92				
5	55.29	32.03	27.14	27.5				
		46.9	32.45	28.96				
	35.54	13.41	29.73	59.13		32.35	48.95	45.5
	56.49	27.11	34.83	51.01	-	49.92	48.1	
6	63.59	32.91	38.58	53.9	-	43.88		
	60.4							
	59.46	-	37.27	40.02				
	35.75	8.98	49.54	26.02				
	47.56			18.22				
10	35.35	-	-	21.09				
	-	-	-	27.0				
	118.19	-	26.46	43.86				
	113.89	-	20.72	37.37				
12	94.49	-	23.34	33.91				
	96.17	-	-	40.02				
	22.28	15.32	32.04					
	16.71	19.95	32.54					
22	14.79	28.9	32.44					
	13.79	-	32.07					
			$\boxed{29.47}$					

DOG #					Na β						SHAM	
	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
	54.25	36.77	23.13	22.88	14.01	36.16	44.89	12.44	34.01	12.37	22.2	25.01
9	53.83	48.22	31.06	27.79	21.37	-	48.83	29.36	58.37	61.47	36.88	46.78
	50.09	55.19	38.61	15.44	28.78	-	51.62	38.67	50.95	34.68	-	58.32
			31.22				48.38	32.3				63.86
	44.96	58.03	50.8	117.82	34.25	-	66.65	51.91	8.21	46.39	-	28.39
	49.08	53.85	90.24	-	47.84	-	65.9	48.13	35.62	42.08	-	49
11	48.86	79.42	-	-	41.65	-	58.4	59.95	35.17	46.72	-	44.56
		27.0			36.05		60.32	53.83	30.26	45.46		47.21
							62.93					
	44.06	30.6	66.75	76.26	47.89	52.62	43.85	17.12	6.52	62.33	30.03	16.2
15	37.79	19.49	64.83	83.81	49.08	36.57	-	-	13.79	72.4	32.18	43.55
	42.83	-	-	105.19	41.49	31.19	-	-	23.46	171.63	33.37	111.17
					37.85							
	45.27	59.62	53.11	84.23	52.37	28.48	61.92	58.09	64.37	40.46	-	19.68
17	50.15	60.89	61.26	79.03	39.32	48.63	59.32	63.48	51.87	52.39	-	29.75
	37.83	50.87	-	-	-	60.54	56.71	64.06	48.16	68.46	-	13.66
		45.28	-	-	-	-	-	54.63	-	61.01		
	98.43	109.62	77.99	37.46	88.7	52.98	66.72	36.7	33.51	43.19	49.16	32.7
21	110.69	93.74	71.24	35.28	105.89	68.74	-	60.87	61.99	45.66	46.54	34.03
	99.71	82.53	74.75	39.76	-	63.52	-	69.97	58.58	48.81	54.4	37.04
		86.35	76.35			49.22			46.08	47.98	50.52	36.48
												[illegible]

Na β SHAM CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
		28.01	5.07	34.82	19.12	21.52	31.27	13.43	28.48	31.65
		34.84	13.18	41.16	23.22		36.61	36.99	34.74	33.77
9		29.65	19.29	35.3	37.29		34.24	38.87	37.47	49.62
		31.01	20.43	34.4				38.27	35.62	48.12
								42.74		35.67
		26.51	21.73	29.63	20.41	20.03	20.89	44.79	41.7	45.91
		34.82	16.91	36.75	28.02	26.67	36.5	28.56	50.59	42.8
11		44.18	70.08	14.86	38.76	25.04	33.78	36.75	54.83	89.14
		40.64	18.58		28.1	32.62	33.33	38.84	49.49	40.38
		37.96				27.58		35.16		
		44.27	21.82	50.53	28.38	41.24	44.77	89.6	43.93	
		54.19	38.97	27.74	24.27	49.54				
15		52.27	53.46	32.65		58.18				
		40.73	53.14	22.94		48.9				
		27.63	22.2	67.03	32.22	35.47	-	54.97		
			37.78	63.14	45.36	49.1	-	69.07		
17			36.1			57.86	-	57.37		
			37.95			55.5	-	61.49		
		-	32.95	139.31	28.48	24.74	50.64	18.39		
		-	53.06	160.48	37.92	44.36	52.66	34.21		
		-	61.4	273.93	45.68	52	56.28	41.42		
21			99.67		53.79	51.54	62.81			
						49.5	55.12			

DOG #	I 1	I 2	I 3	D 1	D 2	Na - β D 3	D 4	D 5	D 6	D 7	RESECTION D 8	D 9
	13.82	47.41	27.06	44.13	30.03	39.99	26.99	41.75	39.62	38.18	48.74	81.98
8		34.34	38.46	45.52	27.55	42.92	32.31	20.55	34.35	39.6	95.32	51.24
	19.42	34.08	-	-	-	-	35.78	19.3	38.89	48.44	-	17.99
									29.8			
	83.58	22.29	63.04	56.36	43.78	37.37	68.22	26.99	39.78	41.62	64.5	31.88
	54.72	52.05	70.47	-	38.76	48.3	60.05	32.14	38.05	37.9	60.51	41.59
13	65.77	49.75	67.52	-	61.1	42.89	56.74	40.88	37.81	46.24	55.81	40.32
		45.63	-	-	-	39.45	-	-	32.47	46.91	-	43.2
	84.1	55.8	49.1	41.88	52.49	39.28	49.14	30.04	33.49	41.24	43.94	79.41
	74.79	74.16	48.11	53.12	56.14	42.34	48.84	32.24	31.03	34.66	54.54	60.58
	70.12	102.84	43.5	55.22	55.74	41.35	49.07	34.2	32.28	35.67	55.89	65.09
18	67.87	111.72	37.29	-	-	45.73	40.98	29.11	32.25	-	37.89	54.24
	26.73	38.26	42.83	28.32	44.2	24.04	127.51	28.1	26.03	65.7	28.3	18.4
	44.43	63.15	36.24	32.77	-	40.08	-	30.42	42.69	62.33	30.07	37.49
20	41.43	54.32	22.46	-	-	38.94	-	40.4	45.05	68.41	43.83	37.65
	48.79	52.79	-	-	-	-	-	-	31.38	63.65	31	
		52.5							41			
	18.27	10.18	52.52									
	42.63	34.4	52.32									
14	40.58		47.25									
	44.03		43.37	died								

Na - B

RESECTION CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	-	32	29.44	33.89	24.06	54.08	-	62.88	35.28	41.11
8	-	57.2	31.52	23.3	-	32.78	-	-	62.31	61.3
	-	51.02	28.59	-	-	30.04	-	-	13.91	40.99
	29.89	27.56	22.84	11.41	47.68	25.7	16.61	33.47	35.9	
	23.86	36.4	39.92	10.08	32.76	38.51	21.09	26.51	36.8	
13	21.72	36.85	38.94	9.72	39.83	43.54	11.35	19.86	35.66	
	-	35.51	25.73		35.8	48.91	14.34			
	-	32.18			28.52	52.26				
	37.05	39.62	8.06							
	35.99	41.92	17.48							
18	26.66	37.81	22.71							
		35.63	22.25							
		37.99	14.37							
	56.47	52.22	20.35	43.1						
	60.41	74.29		55.27						
20	60.79	71.29								
		68.17								
		55.24								

DOG #	I 1	I 2	I 3	D 1	D 2	D 3 (K – α)	D 4	D 5	D 6	D 7	D 8 (BYPASS)	D 9
	-	1.18	.87	1.36	-	.94	.82	.18	.55	.78	1.99	1.1
5	-	3.25	1.1	1.27	-	2.15	1.71	.95	.57	.87	.64	.92
	-	2.39	1.39	1.46	-	1.55	1.88	1.72	.74	.84	.29	.64
			1.42									
	-	1.92	1.39	3.19	-	1.23	-	2.24	.71	.76		
	1.59	.24	.75	1.19	.68	1.02	1.05	1.0	.58	1.53	.42	1.15
6	1.05	.97	.69	1.88	.95	1.06	1.93	1.1	1.05	1.21	.83	.97
	1.14	.63	.64	-	-	-	1.85	-	1.16	1.31	1.41	1.03
							1.58				.86	1.2
											.73	.79
	1.73	2.37	2.02	1.30	.32	.26	2.69	1.87	1.0	.16	.81	-
10	1.94	1.43	1.59	1.51	.71	.95	1.54	1.41	1.08	.52	1.09	-
	4.21	-	1.25	1.42	.99	.71	3.02	.73	.59	.47	1.30	-
	5.7	-	-	-	.71	-	1.28	.59	-	-	-	-
	.69	.59	1.95	2.2	1.71	2.18	1.98	1.25	2.09	1.25	.42	1.97
12	1.45	2.46	-	3.01	1.64	1.55	2.35	1.43	1.51	1.3	.21	1.71
	2.15	2.08	-	-	-	1.66	-	1.96	2.13	1.75	.02	1.62
	1.09										.25	1.96
	1.29	-	1.29	1.09	1.07	1.01	.7	.38	.55	.58	.87	1.06
22	1.79	-	1.85	1.52	1.14	1.23	-	.57	.63	1.34	.74	.65
	1.73	-	-	-	3.82	1.17	-	.84	-	1.09	1.12	.36
										.55	1.1	.19
	1.41	1.34	.09	1.00	.92	1.1	-	1.33	.68			

BYPASS CONT'D

K - α

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16
5	.66		.33				
	.38	-	.02				
	.76	-	.36				
	1.13	-	.49				
6	.02	.34	.01	.73	.17	1.11	.97
	.16	.79	1.33	.41	.55	1.5	.65
	.72	.75	1.67	.6	.16	-	1.01
	-	.79	1.36	.34	.31	-	.92
					.3		.37
10	.42	.81	.94				
		1.02	.64				
		.58	.46				
		.82	.68				
12	-	1.14	1.15				
	-	.43	.27				
	-	.43	.6				
	-	.69	.81				
22	3.22	.36					
	2.38	.5					
	2.09	.32					
	1.21	.34					

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
						K				RESECTION		
	0.66	3.37	-	1.25	1.21	1.95	.82	0.90	1.15	.82	2.34	1.52
8	1.89	2.29	-	1.90	1.17	1.97	.77	2.19	.99	.87	1.1	1.54
		2.20	-					9.89	.86	.88	1.09	1.60
									.80			
	2.58	1.05	1.69	2.14	1.18	1.43	.92	1.91	1.39	1.04	1.25	.75
	1.80	1.09	2.35	-	.87	1.97	1.07	1.20	1.02	.7	1.7	1.00
13	2.16	1.24	2.34	-	1.17	1.23	-	.59	.95	.93	1.01	1.06
		.98	-	-	-	.96	-	-	.67	.88		
	2.4	.57	1.35	.07	1.89	2.13	1.29	1.79	.3	1.36	.71	.19
	1.65	.78	1.01	1.41	1.51	.91	1.29	1.02	.37	.83	.81	.67
18	1.74	.84	1.11	1.63	.55	1.01	1.04	.75	.34	1.01	.9	.45
	1.48	.55	.93	-	1.07	1.8	.76	.68			.91	
	.64	.91	1.82	.72	.94	2.08	1.88	.15	.67	1.00	.2	.84
20	1.3	1.29	9.81	.86	1.73	3.29	-	.42	1.17	.99	.44	1.00
	1.06	1.17	.87	-	2.14	2.49	-	.4	1.04	1.32	.29	1.04
	1.13	.8							. .21	.74	.75	2.78
		.94							.53		.53	
	.81	.53	1.28									
14	1.02	.55	1.45									
	1.01		1.24									
	1.38		.97									

RESECTION CONT'D

Kα

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	-	.53	.22	.66	.59	1.03	.26	1.17	.79	.56
8	-	1.28	.27	-	.81	.57	.30	.61	.77	1.12
	-	1.30	.56	-	.86	.50	.32	1.23	3.12	.58
			.62				.62	1.13		
	.52	.7	.72	.23	1.08	.39	.85	.69	.71	
	.23	.2	1.02	.65	.44	.29	.65	.51	.84	
13	.48	.37	-	.21	.65	.15	.4	-	.72	
		.43	-	.3	.6		.58	-	.67	
		.6		.2	.42					
	1.05	1.04	.12							
	1.15	.64	.06							
18	.52	.34	.11							
		.4	.08							
	.69	.32	.22							
	.47	.68	1.06	.67						
20	.51	.5	.85	.33						
		1.11		.35						
		1.12		.4						
				.33						

DOG #	I 1	I 2	I 3	D 1	D 2	K - α D 3	D 4	D 5	D 6	SHAM D 7	D 8	D 9
	.68	.38	.6	1.31	.74	.6	1.09	1.58	1.87	1.01	.45	.75
	1.85	1.15	.96	1.77	.67	1.11	1.16	.41	1.85	.89	.95	.87
9	1.35	1.29	1.14	1.42	1.2	1.61	1.78	.23	1.12	1.37	.86	1.11
			1.04			1.11	1.25	1.14	1.34			.9
	.95	1.98	.92	-	.64	.46	1.43	.41	.24	1.07	.81	.12
	1.94	2.65	1.35	-	1.37	1.04	1.74	.31	1.06	1.53	2.39	.34
11	1.21	1.79	-	-	.83	1.07	1.34	-	.96	1.63	1.62	.79
	-	-	-	-	.64	-	1.34		.78	1.11		.76
							1.48					
	1.89	2.48	2.9	2.74	1.66	1.82	1.87	.59	.82	1.59	.1	.64
	1.7	-	3.15	3.32	1.6	2.57	-	1.22	.38	2.34	-	1.69
15	1.75	-	-	-	1.12	1.52	-	1.08	.42	4.84	-	.31
					1.13							
	.41	2.15	1.69	1.83	-	.55	2.17	1.87	1.03	-	.45	1.09
	.85	2.2	1.3	-	-	3.88	2.92	2.22	1.54	2.17	.76	1.04
17	.83	1.65	-	-	-	-	3.13	1.82	1.1	1.14	.85	1.53
	-	1.39	-	-	-	-	-	1.37	-	1.22		
	4.28	1.76	2.07	1.12	2.89	3.22	2.62	.72	.45	1.01	.95	1.38
	2.63	1.76	2.67	.86	3.25	1.14	2.47	1.68	1.41	1.39	.92	1.1
21	3.66	2.84	2.21	1.11	-	4.55	1.50	-	1.42	1.27	1.28	1.2
			2.35			5.73			1.03	1.28	1.08	1.02

K - α SHAM CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	.98	.53	.17	1.19	.32	.15	.07	.09	.47	.2
	1.31	.86	.07	1.19	.15	.41	.08	.56	.75	.55
9	1.35	.67		.8	.53	.53	.67	.77	.8	1.01
	1.73	.53		1.93			.52	.25	.61	.87
								.26		.62
	.28	.71	1.11	.3	.32	.08	.11	1.38	.87	1.41
	.58	.62	.82	.3 .82	.68	.55	1.16	.42	1.05	.91
11	1.4	.98	.76	.8	.79	.34	1.26	.63	1.41	2.28
	1.12	.92	.99	.67	.73	.55	1.05	.61	1.19	.91
		.64				.49		.5		
	.69	.48	.89	1.47	.48	.33	.67	1.78	1.07	
	.61	.87	.87	.76	.53	.53	.62		1.64	
15	.5	.86	2.01	.91	.4	.98	.94	-	1.25	
	.73	.73	1.02	.5		.7	.57			
	.75	.65	.43	.71	.27	1.23	.93	.85		
	1.13	1.5	.44	.91	.95	1.4	1.57	.78		
17	.99	1.03	.43			1.28	1.48	.84		
	.85	.92	.66			1.12	1.46			
	.35	-	.54	.9	.29	.29	.76	.53		
	.47	-	1.22	1.25	.93	.72	1.23	1.0		
21	.62	-	1.08	2.6	.61	.96	1.39			
	.68	-	.94		.91	1.03	1.31			

DOG #	I 1	I 2	I 3	D 1	D 2	K - B D 3	D 4	D 5	D 6	BYPASS D 7	D 8	D 9
	-	3.39	3.26	1.81	-	1.5	2.43	1.27	1.24	1.24	2.07	1.79
5	-	4.86	3.39	1.82	-	3.0	3.16	1.67	1.12	1.46	.9	1.93
	-	3.56	2.99	2.06	-	2.49	2.89	2.49	1.24	1.30	.45	1.73
	-	3.11	2.63	3.54	-	2.01		2.75	1.16	1.23		
			2.42									
	2.21	.27	1.44	2.87	1.62	1.75	1.81	1.09	.75	2.04	1.4	2.21
	2.03	2.13	1.73	3.71	2.14	1.46	2.75	1.18	1.54	1.78	1.43	2.92
6	2.67	2.96	1.57				2.57		1.43	1.78	2.02	3.24
							2.16				2.43	3.09
											1.6	2.67
	3.61	2.7	2.44	1.69	.92	.81	3.49	2.74	1.38	.74	1.57	
	3.33	1.54	2.08	1.8	1.38	1.54	1.86	2.3	1.26	1.0	1.82	
10	4.82		2.0	1.71	1.5	1.42	3.34	1.49	.81	.84	1.93	
	6.18				1.18		1.57	1.32				
	.75	.48	2.55	2.43	1.91	2.48	3.76	2.51	2.44	2.26	1.13	5.06
12	2.02	2.92		3.23	1.93	2.31	4.21	2.32	1.99	2.25	.97	4.05
	2.49	3.27				2.14		2.95	2.51	2.35	.65	3.47
	1.5										.86	3.30
	2.64		1.70	1.48	1.52	1.73	1.36	.67	1.5	.73	2.29	.96
	2.56	-	2.47	2.05	1.42	1.63		1.02	1.42	1.38	2.17	.98
22	2.4				3.96	1.59		1.27		1.67	2.32	.63
										.81	2.42	.62
	4.43	2.03	1.59	2.32	2.24	1.81	-	3.29	1.85			
19		2.09	1.3	2.55	1.68	2.1	-	2.24	1.54			

BYPASS CONT'D

K - B

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16
5	1.3		.94				
	1.16	-	.56				
	1.34	-	.91				
	1.66	-	.98				
6	1.0	.81	.03	.78	.31	2.73	2.15
	1.23	1.48	2.65	.66	1.2	2.36	2.2
		1.43	2.71	.81	.71		2.51
	1.53	1.66	2.42	.55	.97		2.39
					.93		1.79
10	.85	1.77	1.51				
		1.69	1.19				
		1.2	1.18				
		1.35	1.38				
12	-	1.42	1.85				
	-	1.1	1.28				
	-	.91	1.35				
	-	1.06	1.45				
22	3.73	.74					
	2.82	1.04					
	2.38	1.07					
	1.5	1.07					

DOG #	I 1	I 2	I 3	D 1	D 2	K β D 3	D 4	D 5	D 6	RESECTION D 7	D 8
8	1.05	4.33	-	1.76	1.59	1.92	1.26	.61	1.39	1.76	2.47
	1.95	3.11	-	2.73	2.13	2.33	1.47	1.83	1.50	1.34	1.41
		2.75	-	-	-	-	-	9.79	1.27	1.34	1.49
									1.23		
	3.22	1.03	3.52	3.14	1.85	1.81	1.44	2.24	1.54	1.31	1.99
13	2.71	1.97	3.48		1.41	2.11	1.73	1.66	1.41	1.51	2.51
	2.84	2.18	3.46		1.73	1.53		.96	1.39	1.66	1.79
		1.89				1.32			1.03	1.85	
	4.35	2.73	2.66	.23	2.76	3.52	2.06	2.42	1.41	2.64	2.35
18	2.91	3.32	1.84	2.6	2.9	2.15	2.19	1.62	1.31	1.48	2.31
	3.06	4.47	1.81	2.94	2.24	1.99	1.87	1.42	1.18	1.85	2.04
	2.85	4.39	1.6		2.57	2.69	1.65	1.28			1.96
	.94	1.68	1.29	1.61	1.66	2.71	5.00	.8	1.15	2.50	1.28
20	2.04	3.11	9.73	1.78	2.48	3.83	-	1.02	2.04	2.07	1.37
	2.33	2.68	.98		2.78	3.00	-	.93	1.82	2.45	1.08
	2.62	2.37							1.47	1.92	1.34
		2.68							1.72		1.08
	1.36	.97	3.1								
14	1.63	1.71	2.53								
	2.4		2.25								
	2.54		1.9								

K β RESECTION CONT'D

DOG #	D 9	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	2.68	-	1.34	.98	1.15	.81	1.73	.28	2.81	1.04	1.09
8	2.54	-	2.60	1.17		1.24	1.21	2.62	2.58	1.23	1.96
								1.53			
	2.31	-	2.49	1.21		1.23	.98	1.63	2.30	3.26	1.54
				1.31				1.62	2.16		
	1.48	.91	1.32	.17	.48	2.03	1.19	.99	1.11	1.35	
	1.83	.67	.76	.73	.85	1.41	1.33	1.00	.91	1.40	
13	1.86	.9	.96		.48	1.36	1.25	.98		1.36	
			.88		.65	1.18		.18		1.22	
			1.02		.53	1.00					
	1.48	1.44	2.3	.65							
	2.05	1.51	1.64	.62							
18	2.00	1.31	1.21	.64							
			1.62	.56							
	1.34	2.03	2.24	.2	.24						
	1.53	1.79	2.62	2.23	.5						
20	1.45	1.37	2.43	1.95	.56						
	3.01		2.42		.75						
			2.07		.73						

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DOG						K - B				SHAM		
#	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
	1.31	1.26	.97	1.66	.69	1.15	1.48	1.32	2.55	1.47	.93	.94
	2.16	2.07	1.45	2.11	1.13	1.73	1.81	.96	2.56	1.37	1.50	1.65
9	1.68	2.40	1.75	1.95	1.5	2.23	2.37	.72	1.94	1.92	1.36	1.94
			1.53			1.98	1.87	1.9	2.3			1.99
	1.48	2.83	2.5	-	1.26	1.72	2.3	2.08	1.4	2.34	1.53	.85
	2.67	3.86	2.61	-	1.8	1.83	2.51	1.75	2.14	2.3	3.96	1.55
11	2.18	2.65	-	-	1.47	2.39	2.56		1.92	2.25	2.77	1.79
					1.41		2.56		1.92	1.74		1.84
							2.53					
	2.3	4.36	2.72	4.11	2.77	3.23	2.03	1.04	.91	2.36	.97	.49
	2.62	-	3.03	4.03	2.55	3.3	-	1.77	.68	2.97	-	1.61
15	2.7	-	-	-	2.03	2.44		1.54	.75	5.09		.33
					1.93							
	2.65	3.13	1.84	2.82	-	1.77	2.74	2.91	2.61	1.98	1.62	1.66
17	2.76	2.87	1.17	-	-	5.92	3.44	3.09	2.75	1.42	1.75	1.5
	2.69	2.37	-	-	-	-	3.4	2.63	2.07	1.83	1.94	1.81
		2.15						2.22				
	7.53	4.59	4.19	1.79	4.51	4.09	4.13	1.64	1.33	2.61	1.88	2.05
	4.92	3.91	3.87	1.93	5.51	2.09	3.92	2.98	2.18	2.75	2.02	1.92
21	6.43	4.35	4.03	2.16	-	5.37	2.54	-	1.97	2.66	2.08	2.29
			3.87			6.54			1.67	2.67	1.89	1.95
												[illegible]

K - β SHAM CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
	1.41	1.02	.80	1.16	.24	1.12	.83	.79	.92	.92
	2.0	1.38	.77	1.0	.27	1.21	.62	1.59	1.37	1.64
9	1.98	1.2		1.12	.63	-	1.16	1.74	1.48	2.17
	2.17	1.16		2.16			.93	1.16	1.23	2.2
								1.5		1.6
	1.34	.74	1.4	.66	.7	.53	1.42	2.18	2.42	2.61
	1.47	1.12	1.36	.83	1.12	1.12	2.01	1.68	2.24	2.11
11	1.92	1.73	1.22	1.56	1.3	.76	1.95	1.54	2.37	2.98
		1.46		1.53		.93				
	1.65	1.46	1.52	1.29	1.22	.88	1.76	1.55	2.3	1.59
	1.13	1.25	2.03	1.77	.71	1.05	1.23	3.46	1.81	
	.96	1.36	2.52	1.2	1.25	1.55	1.3		2.02	
15	.74	1.34	3.16	1.17	1.18	1.67	1.54		1.9	
	.91	1.19	2.36	.76		1.34	1.14			
	1.0	.51	.47	.86	1.1	1.71	2.64	2.92		
	1.65	2.07	.94	1.15	1.56	2.35	2.97	3.02		
17	1.41	1.61	.9			2.19	2.53	2.74		
	1.76	1.48	1.0			1.94	2.44			
	.74		1.45	2.56	1.17	1.1	1.58	1.19		
	1.03	-	2.06	5.74	2.17	1.66	2.58	2.02		
21	1.22	-	1.73	9.08	1.96	1.71	2.38			
	1.16	-	1.5		2.13	1.72	2.75			

DOG #	$H_2O - \alpha$										BYPASS	
	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
5	1.34	.45 .63 .66 .59	.31 .44 .51 .55 .6	.68 1.49	.83 1.09	.83 1.15 1.04 .98	.37 .97 .74	.82 .91 .98 1.29	.61 .82 .96 1.18	.6 3.0 1.55	.57 .75 .85	.52 .73 .93
6	0.52 0.52 0.51	.12 .32 .39	.28 .44 .47	.98	.47	.51 .61 .79	.79 .94 .96	.61 .72 .76 .88	.98 .89 1.12	.65 .68 .77	.36 .86 .71 .66	.36 .61 .82 .85 .91
10	- - -	.87 .9 1.04	.85 .75	.82 .95 1.0	.56 .78 .8 .96	.33 .52 .61	1.13 1.33 1.29 1.23	.73 .87 1.09 .91	.63 .7 .75	.32 .51 .55 .61	.42 .72 .89	.83 1.00
12	.12 .72 .96 .84	1.89 .89 1.05	1.16 1.52 1.41	- - -	1.37 1.49	1.39 1.49 1.21	.92 1.15	.77 .99 1.12	.94 1.17 1.25	.22 .50 .84	.05 .21 .21 .23 .25	.95 1.31 1.45 1.57
22	- -	- -	1.03 1.24	.75 .99 1.02	.81 .74 .88	.84 1.00 1.01	.68 .79	.78 .95 1.04	.56 .52 .54	.89 .99 1.09 1.19	.65 .92 1.16	.46 .56 .42 .68
19	.69	1.15 1.21 .99	.48 .68	1.01 1.03	.57 1.00 1.21 1.00	.51 .7	- -	1.23 .81 .99	.23 .35			

H_2O - α

BYPASS CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16
	.5	.45	.44				
5	.72	.62	.60				
	.89	.71	.78				
	1.08	.88	.89				
	.38	.59	.22	.52	.34	.49	.47
6	.65	.69	.65	.40	.65	.61	.65
	.63	.72	.91	.39	.70		.69
	.72	.83	.97	.38	.62		.70
					.60		.64
	.05	.72	.55				
10		.75	.45				
		.80	.54				
		.72	.72				
	-	.37	.28				
12	-	.47	.41				
	-	.46	.54				
	-	.59	.69				
	.25	.50					
22	.39	.57					
	.48	.73					
	.53	.66					

DOG #	H_2O									RESECTION		
	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
	.01	1.23	.43	1.01	.98	.71	.77	.76	1.14	.56	.60	.70
8	0.66	1.19	.61		1.23	1.27	1.00	.82	1.05	.79	.90	.87
	0.79	0.98	.69				1.08	1.07	1.02	.82	.89	1.11
									.97			
	-	.42	1.09	1.2	.84	.87	1.05	.98	.65	.48	.85	.70
	-	.82	1.55	-	.88	1.04	1.14	1.1	.94	.87	.96	.95
13	-	.91	1.74	-	1.07	1.12	1.17		1.08	1.04	1.01	1.09
	-	.97				1.31			.82	1.28		1.15
	.95	.64	.61	.92	.73	.51	.90	.57	.57	1.09	.7	.35
	.98	.78	.69	1.28	.87	.67	.91	.66	.56	1.09	.98	.46
18	.92	.83	.59	1.56	.96	.67	.91	.75	.67	1.21	.95	.56
	.92		.68		1.11	1.02	.93	.77	.88		.76	.62
	.22	.40	.76	.80	.52	.64	.95	.37	.38	.76	.40	.33
	.47	.89		.93	.76	.67		.55	.61	.85	.50	.49
20	.64	.95			.97	.81		.69	.78	1.15	.56	.72
	.76	.42							.86		.67	1.00
		.82							.83			
	-	.27	.48									
	-	.51	.55									
14	-	.48	.57									
			.59									

$H_2O - \alpha$ RESECTION CONT'D

DOG #	D_{10}	D_{11}	D_{12}	D_{13}	D_{14}	D_{15}	D_{16}	D_{17}	D_{18}	D_{19}	D_{20}	D_{21}
	-	.73	.25	.67	.03	.70	.45	.79	.50	.82	.49	.33
8	-	1.00	.40	.89	.02	.72	.53	.84	.68	.98	.63	.44
	-	.86	.53	1.04	.02	.85	.56	.88	.79		.69	.53
	-		.61				.56	.99				.70
							.55					
	.37	.75	.36	.30	.74	.27	.79	.66	.96	.46	.76	
	.48	.76	.70	.57	.87	.51	.76	.68	.89	.49	.79	
	.56	.81	.74	.60	.91	.59	.82	.72	1.16	.54	.78	
13	.61	.84	.83	.73	.94	.70	.94				.93	
		.77		.78		.75						
	.42	.35	.03									
	.61	.45	.23									
18	.89	.49	.36									
		.61	.76									
			.48									
	.57	.49	.60	.60	.24	.47						
20	.67	.59	.84	.77	.59	.61						
	.79	.63		.98	.96	.69						
		.83		.88		.68						
				.86		.81						

DOG							H_2O -					SHAM
#	I	I	I	D	D	D	D	D	D	D	D	D
	1	2	3	1	2	3	4	5	6	7	8	9
	.34	.29	.28	.01	.47	.41	.57	.32	.50	.34	.30	.31
	.71	.64	.58		.75	.80	.83	.56	.82	.56	.48	.62
9	.75	.78	.64		.84	1.02	.87	.72	.95	.86	.68	.83
			.66			.96	.93	.75	.96			1.06
	.55	1.04	1.09	1.18	.39	1.20	.96	.58	.59	.62	.34	.26
	.40	1.11			.67	1.04	1.19	.51	.87	.73	.90	.45
11	.87	1.08			.74		1.32		.84	.88		.56
		.94			.77		1.26		1.08	1.01		.77
							1.32					
		.67	1.24	1.07	.80	.98	.31	.22	.20	.87	.40	.44
		.97	1.36	1.34	.72	1.24	.65	.34	.30	1.00	.58	.74
15				1.20	.71	1.20	.87	.36	.31	1.06	.73	.78
					.64		.75					
	.61	.91	.77	1.14	.38	.43	1.12	.11	.55	.50	.23	.50
	.74	.78	.93	1.19	.66	.60	1.03	.82	.60	.74	.37	.74
17	.72	.75			.64	.66	1.12	.87	.57	.86	.45	.64
		.67						.93		.89	.57	
											.77	
	1.06	1.28	-	.64	1.24	.74	1.06	.55	.55	.62	.50	.60
	1.38	1.33	-	.83	1.67	1.23	1.45	1.07	.46	.90	.78	.78
	1.25	1.61	-	.85		1.29	1.32	1.44	.85	.98	.93	.79
		1.62	-			1.48			.86		1.06	.86
21						1.30						

SHAM CONT'D

H_2O - α

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21
	.34	.18		.51	-	.22	.06	.18	.26	.23	.16	.20
9	.68	.44		.96	-	.58	.35	.13	.44	.52	.33	.31
	.67	.45		.89	-	.61	.47	.52	.54	.66	.47	.41
	.62	.58		.89	-			.61		.50	.57	.40
										.54	.42	
	.99	.46		-	.00	.25	.47	.42	.72	.78	.02	.53
	.91	.54		-	.56	.46	.61	.51	.90	.96	.15	.63
11	1.03	.79		-	.69	.55	.70	.62	1.07	.84	.18	.65
	1.05	.82		-	.80	.61	.73	.71	1.06	.84	.16	1.30
		.88				.70		.89				
	.10	.51		-	.14	.58	.32	.04	.74	.52	.32	
	.13	.63		-	.31	.76	.57	.37	.77	.67	.44	
15	.10	.77		-	.45	.97	.67	.55	.85	.74	.67	
		.78		-		.80	.69	.79			1.11	
	.16	.35		.56	.30	.61	.50	.32	.36	.30		
	.46	.62		.84	.59	.65	.76	.51	.57	.57		
17	.46	.84				.79	.87	.40	.55	.71		
	.64	.79				.89	.89	.61	.54	1.02		
	.54	-		1.02	.22	.30	1.03	.23	.42	.53		
				1.68	.53	.65	1.20	.55	.67	.81		
	.65				.68	.89	1.34	.68	.88	.99		
21	.55				.78	1.09	1.38					
	.83						1.30					

DOG #						H_2O - B					BYPASS	
	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
		.51	.41	.68	.84	.84	.54	.9	.71	.67	.56	.62
5	1.67	.7	.54	1.49	1.07	1.17	1.11	1.09	.88	3.17	.77	.89
		.71	.6			1.1	.84	1.03	1.03	1.63	.87	1.09
		.66	.62			1.04		1.31	1.23			
	.55	.2	.31	1.13	.56	.53	.89	.65	.97	.69	.41	.41
6	.6	.45	.48			.63	.99	.73	.91	.74	.99	.81
	.59	.65	.52			.77	1.01	.77	1.12	.8	.81	1.00
								.86			.74	1.03
												1.08
	-	.82	.86	.77	.64	.32	1.24	.77	.69	.34	.45	.83
10	-	.85	.76	.92	.89	.59	1.39	.92	.72	.57	.75	1.03
	-	.99		.97	.85	.67	1.34	1.13	.78	.6	.89	1.06
	-	-	-	-	1.01	-	1.28	.96	-	.67		
	.16	1.83	1.06	-	1.28	1.31	.98	.85	.86	.34	.04	1.38
12	.73	.86	1.51	-	1.39	1.46	1.26	1.03	1.12	.59	.30	1.57
	.95	1.11	1.38	-		1.19		1.17	1.20	.89	.32	1.68
	.84										.33	1.76
	-	-	1.01	.8	.73	.92	.69	.77	.65	.98	.71	.39
			1.22	1.04	.66	.99	.82	.96	.6	1.04	1.01	.54
22				1.01	.79	.99		1.04	.6	1.15	1.24	.43
										1.24		.72
	.86	1.16	.59	1.1	.6	.63	-	1.26	.42			
19		1.23	.76	1.1	1.05	.77		.83	.48			
		1.03			1.36			1.04				

H_2O - B

BYPASS CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17
	.57	.56	.55					
5	.79	.69	.70					
	.96	.78	.87					
	1.18	.94	.96					
	.45	.62	.26	.60	.37	.55	.53	
	.74	.73	.70	.46	.74	.67	.75	
6	.73	.74	.95	.44	.81		.81	
	.79	.88	1.02	.43	.71		.83	
					.69		.79	
	.01	.75	.48					
10		.78	.44					
		.83	.57					
		.74	.77					
	-	.36	.37					
12	-	.51	.52					
	-	.48	.62					
	-	.60	.77					
	.35	.53						
22	.44	.61						
	.51	.81						
	.55	.74						

H_2O - β RESECTION

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
	.05	1.19	.47	1.02	.93	.62	.78	.75	1.07	.68	.57	.73
	.65	1.16	.63		1.33	1.22	1.02	.79	1.04	.85	.90	.90
8	.76	.97	.68				1.12	1.06	1.00	.87	.90	1.12
									.98			
	-	.44	1.17	1.19	.81	.9	1.17	1.00	.59	.57	.96	.79
	-	.97	1.59	-	.88	1.09	1.18	1.12	.97	.96	1.06	1.04
13	-	.99	1.79		1.07	1.14	1.29		1.12	1.15	1.12	1.18
	-	1.06				1.39			.86	1.42		1.22
	1.12	.84	.7	1.04	.76	.63	1.04	.63	.75	1.13	.81	.56
	1.1	1.08	.77	1.42	.99	.8	1.06	.72	.69	1.06	1.08	.64
18	1.08	1.33	.65	1.68	1.13	.76	1.03	.81	.76	1.24	1.03	.75
	1.08		.74		1.27	1.08	1.05	.82	.93		.83	.84
	.26	.45	.74	.89	.61	.63	1.33	.49	.46	.93	.50	.35
	.53	1.08		1.02	.80	.74		.67	.71	1.01	.61	.53
20	.76	1.16			.99	.86		.79	.89	1.33	.66	.76
	.88	.64							1.02		.73	1.02
		1.02							.99			
	-	.27	.74									
14	-	.6	.75									
	-	.59	.74									

$H_2O - \beta$ RESECTION CONT'D

DOG #	D_{10}	D_{11}	D_{12}	D_{13}	D_{14}	D_{15}	D_{16}	D_{17}	D_{18}	D_{19}	D_{20}	D_{21}
	-	.79	.33	.71	.01	.74	.69	.90	.52	.85	.51	.42
8	-	1.10	.50	.96	.00	.82	.98	.99	.70	1.02	.70	.55
	-	.95	.61	1.06	.01	.94	.93	.95	.76		.75	.63
							.81					
			.68				.78	1.06				.77
	.46	.82	.41	.36	.72	.45	.81	.66	.97		.72	
	.55	.86	.71	.62	.98	.68	.74	.70	.91	.63	.80	
13	.63	.90	.77	.68	.98	.82	.88	.74	1.14	.63	.78	
	.67	.93	.86	.81	1.00	.93	1.00			.66	.96	
		.85		.85		.97				.69		
	.43	.48	.05									
18	.61	.58	.29									
	.93	.60	.43									
		.75	.83									
			.55									
	.63	.55	.84	.88	.29	.60						
	.69	.70	1.14	1.04	.67	.77						
20	.81	.76		1.30	1.24	.86						
		.95		1.15		.82						
				1.12		.93						

DOG #	I 1	I 2	I 3	D 1	D 2	D 3 (H_2O - B)	D 4	D 5	D 6	D 7	D 8 (SHAM)	D 9
9	.39	.46	.33	.02	.41	.44	.55	.28	.55	.34	.30	.26
	.70	.74	.65		.76	.87	.89	.64	.87	.58	.52	.71
	.79	.87	.70		.85	1.06	.94	.77	1.01	.88	.72	.97
			.71			1.02	.99	.80	1.02			1.24
11	.61	1.10	1.12	1.97	.46	1.28	1.03	.73	.63	.67	.44	.37
	.47	1.15			.70	1.09	1.25	.62	.91	.81	1.01	.60
									.90			
	.96	1.11			.80		1.44		1.17	.93		.66
		.98			.84		1.38			1.05		.90
							1.45					
15	-	.71	1.15	1.17	.83	1.08	.40	.25	.12	.97	.40	.41
	-	.97	1.26	1.36	.76	1.25	.74	.35	.29	1.07	.60	.71
				1.21	.76	1.23	.90	.39	.29	1.08	.76	.76
					.68		.78					
17	.85	.97	.88	1.18	.40	.61	1.13	.22	.74	.57	.43	.50
	.92	.83	.96	1.23	.70	.83	1.03	.92	.72	.83	.56	.74
	.94	.83			.64	.85	1.12	.95	.68	.93	.60	.62
		.76						1.04		.97	.71	
											.92	
21	1.30	1.77	-	.63	1.25	.80	1.06	.67	.63	.68	.57	.54
	1.47	1.63	-	.91	1.32	1.30	1.45	1.14	.59	.97	.87	.83
	1.46	1.85	-	.91		1.34	1.31	1.60	.92	1.08	.98	.86
		1.76				1.54			.92		1.12	.93
						1.37						.95

$H_2O - \beta$ SHAM CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	D 20	D 21
	.37	.27	.14	.50	-	.33	.18	.23	.30	.41	.24	.15
	.75	.52	.29	.96	-	.67	.42	.28	.50	.66	.44	.33
9	.71	.53	.38	.94		.70	.51	.71	.62	.80	.57	.45
	.64	.66	.49	.91				.82		.66	.68	.46
										.68	.50	
	1.14	.54	.53	-	.05	.35	.60	.47	.82	.84	.09	.56
	1.05	.63	.66	-	.62	.58	.70	.66	1.00	1.07	.29	.81
	1.11	.87	.82	-	.74	.66	.79	.73	1.14	.89	.29	.81
11	1.10	.90	.84	-	.84	.69	.81	.81	1.13	.88	.25	1.92
		.90		-		.79		1.01				
	.11	.67	.43	-	.20	.68	.42	.75	.89	.58	.37	
15	.15	.73	.53	-	.46	.89	.63	.80	.82	.78	.54	
	.12	.84	.70	-	.65	1.06	.73	.97	.89	.84	.72	
		.86		-		.89	.75	1.01			1.23	
	.18	.52	.33	.63	.35	.64	.65	.51	.50	.35		
	.51	.67	.56	.91	.61	.76	.86	.75	.70	.64		
17	.48	.89	.57			.89	.96	.60	.68	.73		
	.72	.84	.63			1.00	.97	.89	.63	1.04		
	.63		.62	1.73	.35	.46	1.12	.27	.61	.71		
	.74		.96	2.71	.72	.78	1.32	.62	.83	.93		
	.63	-	1.30		.89	1.00	1.46	.78	1.02	1.08		
21	.88	-	1.25		.99	1.21	1.52					
							1.48					

DOG #						PEG - % RECOVERY					BYPASS	
	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
5	-	80	131	100	65	91	72	81	83	95	96	58
6	-	81	105	57	77	87	87	88	76	70	108	84
10	112	89	89	87	96	68	85	96	82	88	71	86
12	-	61	109	93	65	85	49	55	72	85	95	57
22	95	-	69	76	84	72	68	71	85	85	72	117
19	78	76	79	66	68	76	-	85	72			

PEG - % RECOVERY

BYPASS CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16
5	84	89	96				
6	82	85	90	99	96	55	81
10	40	95	87				
12	-	87	88				
22	96	94	-				
19							

PEG - % RECOVERY

RESECTION

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
8	-	73	132	74	66	53	68	67	84	91	66	66
13	76	98	70	53	91	82	83	81	107	76	62	103
18	88	70	90	75	67	80	75	91	100	63	86	71
20	107	81	69	65	71	78	39	89	96	72	113	86
14	97	83	96									

DOG #	PEG - % RECOVERY D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19	RESECTION
8	91	77	-	76	87	87	88	93	88	90	
13	99	94	78	102	98	90	83	84	96		
18	83	90	92								
20	63	89	78	94							
14											

PEG - % RECOVERY

SHAM

DOG #	I 1	I 2	I 3	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9
9	-	83	145	93	81	93	78	82	77	76	89	66
11	-	90	105	90	97	80	86	75	81	90	69	70
15	79	67	77	87	99	75	91	83	84	85	69	96
17	85	75	68	63	74	56	80	90	79	69	90	79
21	60	67	77	75	44	88	101	76	85	75	96	93

PEG - % RECOVERY

SHAM CONT'D

DOG #	D 10	D 11	D 12	D 13	D 14	D 15	D 16	D 17	D 18	D 19
9	86	87	93	88	96	62	95	84	97	92
11	81	94	95	94	96	96	89	91	99	98
15	100	92	72	94	64	85	88	78	93	
17	87	81	90	45	58	84	91	64		
21	95	103	40	76	92	87	92	94		

REFERENCES

REFERENCES

1) Altman G.G. and Leblond C.P.; Factors influencing villus size in the small intestine of adult rats as revealed by transposition of intestinal segments.

Am. J. Anat. 127:15:1970.

2) Arlen, M. and Levowitz; Effect of Pitressin on intestinal ionic transport.

Surg. Forum 18:323:1967.

3) Atwell, J.D. and Duthie, H.L.; Changes in absorption of water, sodium and potassium produced by villous papillomas.

Brit. J. Surg. 50:768:1963.

4) Ballinger, W.F., Christy, M.G., and Ashby, W.B.; Autotransplantation of the small intestine: the effect of denervation.

Surg. 52:151:1962.

5) Barreiro, M.A., McKenna, R.D., and Beck, I.T.; The physiologic significance of intraluminal pressure changes in relation to propulsion and absorption in the human jejunum.

Am. J. Dig. Dis. 13:234:1968.

6) Berger, E.Y., and Steele, J.M.; The calculation of transfer rates in two compartment systems not in dynamic equilibrium.

J. Gen. Physiol. 41:1135:1958.

7) Berger, E.Y., Kanzaki, G., Homer, M.A. and Steele, J.M.; Simultaneous flux of sodium into and out of the dog intestine.

Am. J. Physiol. 196:74:1960.

8) Berger, E. Y., Kanzaki, G., and Steele, J.M.; The effect of deoxycorticosterme on the undirectional transfers of sodium and potassium into and out of the dog intestine.

J. Physiol. (London) 151:352:1960.

9) Berglund-Larson, U.; Determination of small amounts of deuterium oxide in water by infra-red spectroscopy.

Acta. Chem. Scand. 10:701:1956.

10) Billich, C.O., and Levitan, R.; Effects of sodium concentration and osmolality on water and electrolyte absorption from the intact human colon.

J. Clin. Invest. 48:1336:1969

11) Binder, H.J., and Ptak, T.; Jejunal absorption of water and electrolytes in inflammatory bowel disease.

J. Lab. Clin. Med. 76:915:1970

12) Blickenstaff, D.D. and Lewis, L.J.; Effect of atropine on intestinal absorption of water and chloride.

Am. J. Physiol. 170:17:1952.

13) Blickenstaff, D.D.; Increase in intestinal absorption of water from isosmotic saline following pitressin administration.

Am. J. Physiol. 179:471:1954.

14) Booth, C.C., Evans, K.T., Menzies, T., and Street, D.F.; Intestinal hypertrophy following partial resection of the small bowel in the rat.

Brit. J. Surg. 46:403:1959.

15) Bondar, G.F., and Pisesky, W.; Complications of small intestinal short-circuiting for obesity.

Arch. Surg. 94:707:1967.

16) Bunch, G.A. and Shields, R.; Absorption of water and electrolytes by the human small intestine after surgical operations.

Brit. J. Surg. 56:708:1969.

17) Bunch, G.A.; Jejunal permeability to sodium, potassium and water immediately after surgery.

18) Bury, K.D.; Carbohydrate digestion and absorption after massive resection of the small intestine.

Surg. Gynec. Obstet. 135:177:1972.

19) Castles, T.R. and Williamson, H.E.; stimulation in vivo of renal RNA - synthesis by aldosterone.

20) Chase, G.D. and Rabinowitz, J.L. Principles of radioisotope methodology

Burgess Publishing Co. Minneapolis 3rd Ed. 1967.

21) Clarke, A.M. and Shields, R.; The role of the intestine in fluid and electrolyte conservation during sodium depletion.

Brit. J. Surg. 50:768:1963.

22) Code, C.F. and McIntyre, F.C.; Quantitative determination of histamine.

Methods of Biochem. Analysis 3:49:1956 pg. 66

23) Code, C.F.; The semantics of the process of absorption.

Perspect. Biol. Med. 3:560:1960.

24) Code, C.F., Bass, P., McClary, G.B., Newnum, R.L., and Orvis, A.L.; Absorption of water, sodium and potassium in the small intestine of dogs.

Am. J. Physiol. 199:281:1960.

25) Cramer, C.F., Sadder, S.J. and Schulz, R.G.; A plastic-cannulated intestinal loop to study effects of anesthesia on Ca. absorption.

J. Appl. Physiol. 22:1149:1967.

26) Crocker, A.D.; Variations in mucosal water and sodium transfer associated with the rat oestrus cycle.

J. Physiol. (London) 214:257:1971.

27) Debas, H.T., Bedi, B.S., and Gillespie, M.B., Mechanism by which fat in the upper small intestine inhibits gastric acid.

Gastroenterology 56:483:1969.

28) Domschke, S.; Demling, J., Domaschke, W., Hacker, J., Classen, M., and Demling, L.; Gastric nonabsorbable indicator in man: a comparison of phenol red and polyethylene - 14C glycol.

Scand. J. Gastro. 8:17:1973.

29) Dowling, H.R. and Booth, C.C.; Functional compensation after small bowel resection in man.

Lancet 2:146:1966.

30) Dowling, H.R. and Booth, C.C.; Functional compensation after small bowel resection in man.

Lancet 2:146:1966

30) Dowling, H.R., and Booth, C.C.; Structural and functional changes following small intestinal resection in the rat.

Clin. Sci. 32:139:1967.

31) Drenick, E.J., Simmons, F., and Murphy, J.F.; Effect on hepatic morphology of treatment of obesity by fasting, reducing diets and small bowel bypass.

New England J. Med. 282:829:1970.

32) Duthie, H.L., Watts, J.M., de Dombal, F.T., and Goligher, J.C.; Serum electrolytes and colonic transfer of water and electrolytes in chronic ulcerative colitis.

Gastroenterology 47:525:1963.

33) Emslie, R.G., Mulholland, A.T., and Shields, R.; Blocking by spironolactone (SC9420) of the action of aldosterone upon the intestinal transport of potassium, sodium and water.

Gut 7:697:1966.

34) Field, M., Fromm, D., Al-Awqati, Q., and Greenborough, W.B.; Effect of cholera enterotoxin on ion transport across isolated ileal mucosa.

J. Clin. Invest. 51:796:1972.

35) Frederick, P.L., Size, J.S., and Osborne, M.P.; Relation of massive small bowel resection to gastric secretion.

New England J. Med. 272:509:1965.

36) Glucksman, D.L. and Warren, W.D.; Small intestinal absorption in the immediate post-operative period.

Surg. Forum 16:354:1965.

37) Glucksman, D.L., Kalser, N.H., and Warren, W.D.; Small intestine absorption in the immediate post-operative period.

Surgery 60:1020:1966.

38) Grace, R.H. and Shields, R.; The effect of operation on the intestinal handling of water, sodium and potassium.

Brit. J. Surg. 57:862:1970.

39) Grim, E.; Water and electrolyte flux rates in the duodenum, jejunum, ileum and colon and effects of osmolarity.

Am. J. Dig. Dis. 7:17:1962.

40) Hanson, W.R. and Osborne, J.W.; Epithelial cell kinetics in the small intestine of the rat 60 days after resection of 70 per cent of the ileum and jejunum.

Gastroenterology 60:1087:1971.

41) Jacobsen, E.D., Bonday, D.C., Broitman, S.A., and Fordtram, J.S.; Validity of polyethylene glycol in estimating intestinal water volume.

Gastroenterology 44:761:1963.

42) Kerr, G., Elliot, D.W. and Endahl, G.L.; Effect of antrectomy on gastric acid hypersecretion induced by isolation of the proximal small bowel.

Am. J. Surg. 115:157:1968.

43) Kinney, V.R., and Code, C.F.; Canine ileal chloride absorption; effect of carbonic anhydrase inhibitor on transport.

Am. J. Physiol. 207:998:1964.

44) Konturek, S.J., Dubiel, J., and Gabrys, B.; Effect of exclusion, acidification and excision of the duodenum on gastric acid secretion and the production of pentagastric induced peptic ulcers in cats.

Gastroenterology 56:703:1969.

45) Landor, J.H.; Intestinal resection and gastric secretion in dogs with antrectomy.

Arch. Surg. 98:645:1969.

46) Landor, J.H., Wild, R.A., and Behringer, B.R.; The influence of dietary fat on the gastric secretory response to pancreatic duct ligation or small bowel resection.

Surgery 68:831:1970.

47) Landor, J.H., Behringer, B.R. and Wild, R.A.; Postenterectomy gastric hypersecretion in dogs; the relative importance of proximal versus distal resection.

J. Surg. Res. 11:238:1971.

48) Levin, R.J., Hewey, H., and Smyth, D.H.; The effects of adrenalectomy and fasting on intestinal function in the rat.

J. Physiol. (london) 177:58:1965.

49) Levitan, R. and Ingelfinger, F.J.; Effect of d-aldosterone on salt and water absorption from the intact human colon.

J. Clin Invest. 44:801:1965.

50) Levitan, R. and Goulston, K.; Water and electrolyte content of human ileostomy fluid after d-aldosterone administration.

Gastroenterology 52:510:1967.

51) Love, A.H.G., Mitchell, T.G. and Neptune, E.M.; Transport of sodium and water by rabbit ileum, in vivo and in vitro.

Nature 206:1158:1965.

52) Maddrey, W.C., Serebro, H.A., Marcus, H., and Iber, F.L.; Recovery, reproducability and usefulness of polyethylene glycol, I^{131} Rose Bengal, sulfo-bromophthalein and indocyanine green as markers.

Gut 8:169:1967.

53) Madson, P.O.; The etiology of hyperchloremic acidosis following uro-intestinal anastomosis: an experimental study.

J. Urol. 92:448:1964.

54) Malawer, S.J. and Powell, D.W.; An improved turbidimetric analysis of polyethylene glycol utilizing an emalsifier.

Gastroenterology 53:250:1967.

55) Menge, H., Bloch, R., Schaumloffel, E., and Riecken, E.O.; Transport studies, morphological, histochemical and morphometric findings on the excluded small intestinal loop in the rat.

Z. Ges. Exp. Med. 153:74:1970.
Excerpta Medica (Physiol.) 24:2174:1971.

56) Mori, H.; Influence of the autonomic nerves on intestinal absorption.

Jap. J. Gastroent. 63:131:1966. Excerpta Medica 20:1763:1968.

57) Nunn, A.S. and Ellert, M.S.; Absorption and electrolyte changes of intestinal mucosa following substrate induction.

Am. J. Physiol. 212:711:1967.

58) Nygaard, K.; The effect of intestinal anastomosis on the intestinal flora and fat absorption in rats.

Acta. Chir. Scand. Suppl. 357:306:1966.

59) Nygaard, K.; Resection of the small intestine in rats: I Nutritional Status and adaptation of fat and protein absorption.

Acta. Chir. Scand. 132:731:1966.

60) Nygaard, K.; Resection of the small intestine in rats: II Absorption of Vit. B12 with special regard to adaptation of absorption.

Acta. Chir. Scand. 132:743:1966.

61) Nygaard, K.; Resection of the small intestine in rats: III Morphological changes in the intestinal tract.

Acta. Chir. Scand. 133:233:1967.

62) Nygaard, K.; Nutrition and absorption after resections and bypass operations on the small intestines in rats.

Acta Chir. Scand. 134:66:1968.

63) Nylander, G. and Olerud, S.; Intestinal adaptation following extensive resection in the rat.

Acta Chir. Scand. 123:57:1962.

64) Orloff, M.H., Chandler, J.C., Alderman, S.J., Keiter, J.E. and Rosen, H.; Gastric secretion and peptic ulcer following portacaval shunt in man.

Am. Surg. 170:515:1969.

65) Orvis, A.L. and Albert, A.; Gamma counting of radiosodium and radio-potassium in the bioassay of aldosterone and related steroids.

Endocrinology 56:218:1956.

66) Porus, R.L.; Epithelial hyperplasia following massive small bowel resection in man.

Gastroenterology. 48:753:1965.

67) Powell, D.W., Plotkin, G.R., Maenza, R.M., Solberg, L.I., Cotlin, D.H. and Formal, S.B.; Intestinal water and electrolyte transport in rat salmonella enteritis.

Gastroenterology 60:1053:1971.

68) Reynell, P.C. and Spray, G.H.; Small intestinal function in the rat after massive resections.

Gastroenterology. 31:361:1956.

69) Rummel, W. and Stupp, H.F.; The influence of diuretics on the absorption of salts, glucose and water from the isolated small intestine of the rat.

Experientia 18:303:1962.

70) Shultz, S.G. and Curran, P.E.; Intestinal absorption of sodium chloride and water.

Chapter 66. Handbook of Physiology. Sect 6 Vol III Code, C.F. Editor.

American Physiological Society Washington 1968.

71) Shields, R. and Elmslie, R.G.; The effect of aldosterone on absorption of water and electrolytes from the ileum and colon of the dog.

Brit. J. Surg. 50:96:1962.

72) Shields, R.; The absorption and secretion of fluid and electrolytes by the obstructed bowel.

Brit. J. Surg. 52:774:1965.

73) Shields, R., Mulholland, A.T., and Elmslie, R.G.; Action of aldosterone upon the intestinal transport of potassium, sodium and water.

Gut. 7:686:1966.

74) Shields, R.; Absorption and secretion of electrolytes and water by the human colon, with particular reference to benign adenoma and papilloma.

Brit. J. Surg. 53:893:1966.

75) Shields, R., Miles, J.B., and Gilbertston, C.; Absorption and secretion of water and electrolytes by the intact colon in a patient with primary aldosteronism.

Brit. Med. J. 1:93:1968.

76) Shoemaker, C.P. and Wright, H.K.; Rate of water and sodium absorption from the jejunum after abdominal surgery in man.

Am. J. Surg. 119:62:1970.

77) Sladen, G.E. and Dawson, A.M.; Interrelationships between the absorption of glucose, sodium, and water by the normal human jejunum.

Clin. Sci. 36:119:1969.

78) Soergel, K.H., Whalen, G.E., Harris, J.A. and Genen, J.E.; Effect of antidiuretic hormone on human small intestinal water and solute transport.

J. Clin. Invest. 47:1071:1968.

79) Sokal, R.R. and Rohlf, F.J.; Biometry,

W. H. Freeman and Co. San Francisco. 1969.

80) Spat, A., Saliga, M., Sturcz, J., and Solyom, J.; Effect of aldosterone on intestinal transport of sodium and potassium.

Lancet. 2:96:1963.

81) Stafford, E.S. and Schnaufer, L.; Studies on the isolated circular intestinal loop - III ulcerogenic effect of isolated duodenum.

Arch. Surg. 82:167:1961.

82) Stahlgren, L.H., Umana, G., Roy, R., and Donnelly, J.; A study of intestinal absorption in dogs following massive small intestinal resection, and insertion of an antiperistaltic segment.

Ann. Surg. 156:483:1962.

83) Thorton, U. and Condon, F.E.; Infrared spectrometric determination of deuterium oxide in water.

Anal. Chem. 22:690:1950.

84) Tiblin, S., Burns, G.P., Hahnloser, P.B., Schenk, W.G.; The influence of vagotomy on superior mesenteric blood flow.

Surg. Gynec. Obstet. 129:1231:1969.

85) Tilson, M.D. and Wright, H.K.; Adaptation of functioning and bypassed segments of ileum during compensatory hypertrophy of the gut.

Surgery. 67:687:1970.

86) Tilson, M.D., Phillips, S., and Wright, H.K.; Effect of DOCA upon the ileum.

Clin. Res. 18:390:1970.

87) Tilson, M.D. and Wright, H.K.; Augmented ileal sodium and potassium stimulated adenosine triphosphatase after jejunal transposition.

Surg. Forum 21:326:1970.

88) Toulowkian, R.J., Mitruka, B., and Hoyle, C; Growth and nutrition of enterectomized rats fed on elemental diet.

Surgery 69:637:1971.

89) Turner, M.D., Neely, W.A., and Hardy, J.A.; Rapid determination of deuterium oxide in biological fluids.

J. Appl. Physiol. 15:309:1960.

90) Varro, V., Blaho, G., Csernay, L., Jung, I. and Szarvas, F; Effect of decreased local circulation on the absorptive capacity of a small intestinal loop in the dog.

Am. J. Dig. Dis. 10:170:1965.

91) 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. 141:488:1944.

92) Visscher, M.B., Fetcher, E.S., Carr, C.W., Gregor, H.P., Bushy, M.S. and Barker, D.E.; Isotopic tracer studies on the movement of water and ions between intestinal lumen and blood.

Am. J. Physiol. 142:550:1944.

93) Visscher, M.B. and Roepke, R.R.; Osmotic and electrolyte concentration relationships during absorption of salt solutions from ileal segments.

Am. J. Physiol. 144:468:1944.

94) Weinstein, D.L., Shoemaker, C.P., Hersh, T. and Wright, H.K.; Enhanced intestinal absorption after small bowel resection in man.

Arch. Surg. 99:560:1969.

95) Weser, E. and Hemandez, M.; Effect of small bowel resection on glucose and leucine uptake by rat intestinal epithelial cells.

Gastroenterology. 56:1206:1969.

96) Weser, E. and Hernandez, M; Studies on small bowel adaptation after intestinal resection in the rat.

Gastroenterology. 60:69:1971.

97) Westerheide, R.L., Elliot, D.W., and Hardacre, J.M.; The potential of the upper small bowel in regulating acid secretion.

Surgery. 53:73:1965.

9') Williams, L.F.; Intestinal electrolyte transport.

Surg. Forum. 18:321:1967.

99) Wilmore, D.W. and Johnson, C.J.; Metabolic effects of small bowel reversal in treatment of the short bowel syndrome.

Arch. Surg. 97:784:1968.

100) Wilmore, D.W. and Dudrick, S.J.; Effects of nutrition on intestinal adaptation following massive small bowel resection.

Surg. Forum. 20:398:1969.

101) Winer, B. J., Statistical Principles in Experimental Design.

McGraw Hill, New York 1962.

102) Worning, H. and Andrup, E.; Experimental studies on the value of the reference substances polyethylene glycol, bromsulphthalein and ^{51}Cr as indicators of the fluid content in the intestinal lumen.

Gut. 6:487:1965.

103) Wright, H.K., Poskitt, T., Cleveland, J.C. and Herskovic, T.; The effect of total colectomy on morphology and absorptive capacity of ileum in the rat.

J. Surg. Res. 9:301:1969.

104) Wright, H. K., Poskitt, T., Cleveland, J.C. and Herskovic, T.; The effect of total colectomy on morphology and absorptive capacity of ileum in the rat.

J. Surg. Res. 9:301:1969.

105) Wright, H.K., Cleveland, J.C., Tilson, M.D. and Herskovic, T.; Morphology and absorptive capacity of the ileum after ileostomy in man.

Amer. J. Surg. 117:242:1969.

106) Wright, H.K., O'Brien, J.J., and Tilson, M.D.; Water absorption in experimental closed segment obstruction of the ileum in man.

Amer. J. Surg. 121:96:1971.

107) Yagasaki, O. and Yamagiya, I.; The effects of intestinal movement upon absorption.

Folia Pharmacol. Jap. 63:1:1967.
Excerpta Medica 21:889:1968.