PART A

EFFECTS OF RESECTION OF MASSIVE SEGMENTS OF LARGE AND SMALL BOWEL UPON FLUID AND ELECTROLYTE BALANCE

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INTRODUCTION

It was proposed to study in man and dogs the type and degree of alterations in fluid and electrolyte balance which occur after resection of massive segments of the intestinal tract. In human beings, this might be encountered as a result of trauma or disease.

The specific aspects of metabolism under consideration in this study were to be:

1. Water balance
2. Sodium balance
3. Chloride balance
4. Potassium balance
5. Nitrogen balance
6. Hematologic findings

It was also intended to record clinical signs and symptoms for correlation with the laboratory findings. Necropsy findings were to be included in the animal studies as well as in the human studies whenever possible.

It was hoped that, with a better understanding of the deviations from normal of fluid and electrolyte balance, produced by the loss of massive segments of intestine, the post-operative fluid and electrolyte supportive therapy might be better designed; and that the general management of the patient could be better planned in the light of deviations from normal resulting from loss of intestine. With more accurate replacement methods, permitting more precise maintenance of normal fluid and electrolyte balance, it seemed likely that both mortality rate and degree of morbidity could be significantly reduced.

When this problem was undertaken in July 1951, it was our good fortune to have for study a patient, in the Queen Mary Veteran's Hospital, who had recently undergone a resection of the intestine of massive proportions, in which were left only the first and second portions of the duodenum, anastomosed to the mid transverse colon. This man survived for a period of almost ten months during which time we observed him as carefully as facilities and the patient would permit. Dr. John Martin, research fellow at this hospital, was directly responsible for the observations in this case and generously consented to allow us access to the records and patient at any time.

Dogs were prepared in the Donner Building in such a way as to duplicate, as closely as possible, the massive resection seen in the human case mentioned above. For comparison and contrast, other dogs were prepared with less extensive resections of the small intestine.

PHYSIOLOGY OF DIGESTION AND ABSORPTION

A characteristic feature of the mucosal surface of the small intestine is the transverse plica circularis or Kerkring's folds, which are circular or spiral ridges or elevations formed by permanent duplications of the mucosa and submucosa (2). These anatomic projections from the mucosa are more prominent in the terminal duodenum and gradually become smaller towards the terminal jejunum until, in most subjects, they disappear entirely before the terminal ileum is reached. The intestinal villi are creases or elevations in the mucosal surface. The plicae circulares give the jejunum its herring bone, feathery appearance on Barium film study. The villi are numerous in the duodenum and decrease in number in a caudad direction toward the ileum. Each villus is covered by epithelium and supplied with blood and nerve supply. The functions of digestion and absorption are increased many times by the presence of these folds and villi because of the extensive surface area.

Most foodstuffs contained in the human diet are colloidal substances of high molecular weight which cannot be utilized directly for purposes of growth, tissue maintenance or the liberation of energy. They must be disintegrated into simpler compounds, that is, proteins into amino acids, carbohydrates into simple monosaccharides, and fats into fatty acids and glycerol. This is accomplished by enzymes elaborated by the stomach, pancreas and intestine.

The movement of dissolved food across the mucous membrane of the intestine is accomplished by simple diffusion, osmosis and filtration. Another factor is the pumping movement of the villi. These mechanisms of transfer are, as yet, not clearly understood and much remains to be learned about food absorption.

In the case of fat absorption, it has been held for many years that the fat must be hydrolysed to its component fatty acids before absorption occurs. Recent work has shed new light on the mechanism. It now seems evident that some neutral fat is absorbed into the lymph channels and carried to the peripheral blood, whereas other true fats are hydrolysed by bile acids and other enzymes (e.g., pancreatic lipase) to fatty acids and absorbed as such directly into the portal blood stream.

Intestinal, pancreatic and biliary enzymes are necessary for the preliminary breakdown of protein, carbohydrate and fat molecules to their component parts, namely, amino acids, monosaccharides and fatty acids, respectively. Water is quickly absorbed in the upper small bowel. Absorption of food is practically completed in the small intestine. It is said that the jejunum absorbs more fluid and sugar than the ileum, and that the ileum absorbs more protein and fat.

Massive resection in human beings leads to severe impairment of fat absorption, moderate impairment of protein and usually normal carbohydrate absorption (44). Jensenius (26) observed fat absorption to be greater in the distal loops of the small intestine. Therefore he felt that, since fat absorption is the first to suffer in shortening of the intestine, loss of the ileum is more serious than loss of proximal segments.

THE NATURE OF NON PROTEIN NITROGEN (32)

Definition:

Non protein nitrogen refers to the nitrogen of blood, tissues, urine or excreta which is not precipitated by the usual protein - precipitating reagents. It is a mixture of protein components, all of small molecular size and readily diffusible. They represent intermediary products of protein metabolism in process of transportation, or end products of metabolism en route for excretion. As such, the blood concentrations of these compounds, and the quantities excreted, serve as criteria of the state of protein metabolism and as measures of the rate of protein metabolism.

Urea:

Urea is the most completely oxidized nitrogenous product of protein metabolism and the one most properly termed an end product, suited only for excretion. Urea is the product of the deamination of the amino acids of which protein is composed, and is the most significant index of the rate of destruction of protein.

Ammonia:

Ammonia participates actively in the formation of nitrogenous compounds in the body. In the urine it is an end product substituted for inorganic bases when there is a demand for excessive excretion of acid. Because of its chemical reactivity and toxicity, its concentration in the blood and body fluids is negligible.

Creatine:

Creatine appears in low concentration in the blood; presumably it is being conveyed to the tissues or has escaped from them.

Creatinine and Uric Acid:

They can be regarded as end products of creatine and purine metabolism, respectively, which have not been as completely oxidized as urea. Their concentrations and the amounts excreted are quite constant compared with those of urea.

Amino Acids:

Little is known of their mode of excretion. Their appearance in the urine is taken as inevitable leakage through the glomeruli.

Undetermined Nitrogen:

This consists of polypeptides and other aggregations of amino acids, glutathione, and probably purine and pyrimidine compounds. Enzymes and nucleotide nitrogen compounds such as adenosine-tri-phosphate are also in this group.

Nitrogen Balance:

An individual is said to be in nitrogen equilibrium when the daily loss of nitrogen from his body equals the nitrogen content of his diet. Practically, only urine and faeces need be considered as avenues of nitrogen loss. In many metabolism experiments where the stool is normal in amount and consistency, an average value of 1.3 grams of nitrogen per day may be assumed and only urine specimens analysed for their total nitrogen.

If the nitrogen excretion exceeds the intake, the nitrogen balance is said to be negative; a subject is said to be in positive nitrogen balance when intake exceeds excretion, i.e., nitrogen is retained in the body.

NITROGEN EXCRETION

Fecal Nitrogen: This is often estimated as one-tenth of ingested nitrogen. However, in animals it diminishes little even on protein-free diet, so faecal nitrogen represents more than unabsorbed food nitrogen. It may increase slightly when a high nitrogen intake is given. Its amount is distinctly related to the bulk of the stool and therefore to the weight of the indigestible food.

In human subjects, the above does not necessarily obtain. In starvation faecal nitrogen is negligible. If neither the weight of the diet nor the weight of the dry matter it contains are known, it is more correct to use a constant figure for the faecal nitrogen of a normal adult than to estimate it as a fixed proportion of the nitrogen intake.

Average faecal nitrogen of a normal adult on ordinary diets amounts to 1 to 2 grams daily.

Non Protein Nitrogen in Sweat: In temperate climates, an average adult probably loses 0.3 grams of nitrogen or less per day. In tropical climates, this may rise to 0.9 grams of nitrogen per day. Ordinarily, this avenue of nitrogen loss is negligible.

Loss of Nitrogen in Other Excreta: Menstrual flow - 1.5 to 3.3 grams of nitrogen per day. Vomitus - 25 mgm. nitrogen per 100 cc.

The Partition of Non Protein Nitrogen in the Urine: Under ordinary circumstances, the average adult excretes an amount of nitrogen roughly equivalent to that ingested during the same period. It is all non protein nitrogen because proteinuria is a pathological condition. The urinary nitrogen may be used as a measure of nitrogen catabolism and, also, of the amount of nitrogen ingested.

Average values for a healthy adult male on an unrestricted normal diet:

	Grams Per Day	% Total Urine Nitrogen
Feces Nitrogen	1.02	
Total Urine Nitrogen	12.03	100
Urea	10.20	83
Ammonia	0.50	4
Ammonia + Urea	10.52	87
Uric Acid	0.15	1
Creatinine	0.68	6
Undetermined	0.68	6

Blood NPN - 27 mgm/100 cc.

Urea may be regarded as the ultimate ash of burned protein. The other components of the non protein nitrogen excretion are less completely oxidized nitrogenous compounds and represent products of specialized activities.

Normally, the free alpha amino acids appear in the urine in small amounts, not usually exceeding 1 to 2 per cent of the total urine nitrogen.

Urea: Urea is formed in the liver. Amino acids are deaminated by all tissues and the released ammonia is conveyed to the liver in an amide form by certain other amino acids, notably arginine where, by virtue of the enzyme arginase, the arginine is converted to ornithine liberating urea. This latter step occurs only in the liver. Urea is the chief end product of protein metabolism and serves no nutritive purpose. The urea clearance by the kidney measures the capacity of the kidney to eliminate the chief excretory product of metabolism.

Ammonia: When acids accumulate in the human body, the kidneys can form as much as 5 to 6 grams of ammonia per day, to excrete the acids as ammonium salts, thereby preserving the inorganic bases of the body. In all tissues it is continually released from deaminated amino acids and taken to the liver, incorporated as an amide of other amino acids, e.g., arginine to be reconverted to ornithine with urea liberation. Some ammonia is also used to resynthesize amino acids. Glutamine liberates ammonia in the kidneys where it serves as a defense against acid intoxication.

Urea formation by the liver can be regarded as a defense against poisoning by ammonia which is a toxic material. The kidney is the site of formation of urinary ammonia and glutamine is the chief source. Average ammonia excretion in urine amounts to 0.3 to 1.2 grams of ammonia nitrogen per day.

Creatine: Creatine is not found in the urine of most normal adults. It exists in muscle as phosphocreatine and provides the phosphoric acid for the phosphorylation of hexoses derived from glycogen. So long as plasma creatine remains below 0.6 mg. per cent, none will appear in the urine. With higher plasma concentrations it will appear in the urine.

The amount of creatine converted to creatinine is relatively constant and creatine in excess of this is disposed of in some other manner. Glycine, arginine and guanidoacetic acid form creatine in the normal animal.

Urine of most normal adult males does not contain sufficient creatine to be demonstrated by the usual methods. Pathological creatinuria exists when more than 50 to 60 mg. of creatine appear in the urine in 24 hours when a normal diet is eaten. It is indicative of a fundamental disturbance of muscle metabolism. Pathological creatinuria is distinguished from physiological creatinuria by the fact that in the former, preformed creatinine is excreted in normal amounts whereas, in the latter, creatine is excreted at the expense of creatine.

Creatinine: Creatinine is both filtered and secreted by the kidney. It is an end product of most of the creatine. It is generally assumed that creatinine is a waste product of metabolism. The urine creatinine is remarkably constant even in the face of changes in diet, exercise of urine volume. The daily excretion of creatinine is often used to check the accuracy of 24 hour urine collections. Some authors believe that urinary creatinine is proportional to muscle mass, while urinary creatine is an expression of some metabolic pecularity. The specific gravity of the urine is often an aid in the differentiation of pre-renal azotemia from azotemia due to primary renal disease. In pre-renal azotemia, the specific gravity is greater than 1.020; in primary renal disease with oliguria, the specific gravity is usually fixed around 1.010. A blood creatinine value, disproportionately low as compared with the elevation of the NPN (creatinine : NPN greater than 1 : 20), is often indicative of pre-renal azotemia. The disproportion is probably due to the fact that urea is eliminated solely by glomerular filtration, while creatinine is excreted by both filtration and tubular excretion (28).

normal NPN: 20-40 mgm/100 cc.

creatinine: 1-2 mgm/100 cc.

Summary of Facts Concerning Creatine and Creatinine: Creatine is chiefly synthesized in the liver from which it passes into the blood: a necessary and ordinarily constant amount is taken up by the muscles to form creatine phosphate. This is constantly converted to creatinine, most of which is excreted in the urine. The quantity of creatine that enters the muscles is, within wide limits, independent of the supply of creatine. In diseases affecting the general musculature, creatinuria is common. It is usually associated with a diminished excretion of creatinine. In wasting diseases, creatinuria is common: this may be related to the disease process or to some disorder associated with the disease. Until these are clarified, the value of urine creatine levels in diagnosis is very limited.

Uric Acid: In birds and reptiles, uric acid represents the final product of protein catabolism. Ammonia combines with some oxidation product of lactic acid to form uric acid. In substituting uric acid for urea as a means of excreting waste nitrogen, birds and reptiles conserve water. Their uric acid is precipitated out in the cloaca. They lack the ability to convert ammonia to urea.

The daily uric acid excretion in the normal human adult on a purine free diet is fairly constant and is usually between 0.3 and 0.5 grams. This represents the degradation products of nucleoproteins metabolized during the 24 hour period. It appears as endogenous uric acid.

Exogenous uric acid has been assumed to bear a relation to the amount of purine in the food; assuming that the purines of the food are directly oxidized to uric acid. This is in some dispute and conflicting reports have appeared on the relation of dietary purines to uric acid excretion in the urine. It should be noted that there are other avenues of uric acid excretion, e.g., bile, and gastric juice.

INTERPRETATION OF POSITIVE AND NEGATIVE NITROGEN BALANCES

There is a continuous exchange between endogenous and exogenous nitrogenous materials. Nitrogen balances then may serve for the over-all accounting of protein metabolism but it is improper to identify the items of income with the items of expenditure.

A positive nitrogen balance is interpreted as storage of nitrogen for the formation of protein and a negative balance as evidence of tissue destruction. Such interpretations are only justified if it is known that the non protein nitrogen of the blood and tissues has not undergone important change.

The body appears to have little capacity for the storage of surplus nitrogen as protein. Normal adults on unlimited diets containing adequate protein will have nitrogen catabolism and urine nitrogen vary with the amount of nitrogen in the diet.

It is always essential that there be sufficient carbohydrate and fat in the diet to supply adequate calories before nitrogen equilibrium can be attained. Factors leading to negative nitrogen balance in human subjects are:

1. Inadequate protein intake
2. Impaired digestion of protein
3. Impaired absorption of protein derivatives

   It is possible, from recent experiments, that the protein sparing action of carbohydrate may not be due to its energy contribution but to the fact that, when fed with protein, the latter is absorbed more slowly and more completely.

4. Impaired synthesis of protein, e.g., hyperthyroidism, diabetes mellitus

5. Defective quality of protein ingested

   It must contain the essential amino acids.

6. Inadequate caloric intake

   The protein will be deaminated to fat to produce energy.

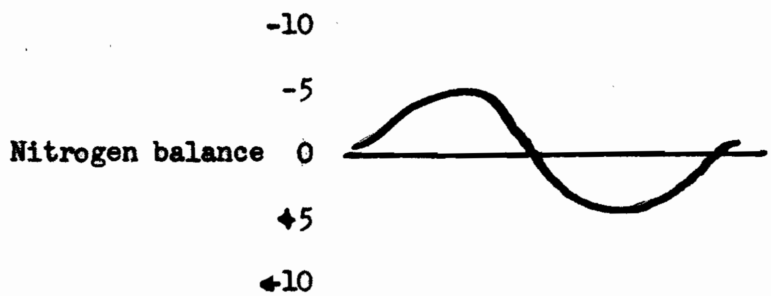
7. Trauma

Browne (7) described the concept of the catabolic and anabolic period of protein metabolism following acute or chronic disease states. He observed an increased excretion of nitrogen, as compared with the amount excreted by normals on similar diets, following trauma; this was referred to as the catabolic period. Merging with this there followed a period of nitrogen retention with less rise in nitrogen excretion than normals on similar diets. He considered it probable that both periods occur at the same time and that the nitrogen excretion rate is a differential between these two processes. In chronic illness he found that nitrogen retention might occur even in the presence of inadequate caloric intake. He concluded that the degree of retention of the same protein may thus differ markedly in the same individual depending on his metabolic state. Those adrenal cortical substances that act on carbohydrate and nitrogen metabolism render the protein of certain tissues more readily mobilized. The fate of this mobilized protein, whether it be catabolized, or translocated to other organs or tissues, will depend upon homeostatic mechanisms acting at the time. If the adrenal cortex is repressed or underactive as in chronic disease states, mobilization and translocation of protein from one tissue to another is more difficult and the catabolic anabolic phenomena may not be evident.

Mechanisms which determine whether food or body protein will be broken down and the constituents used for energy or other special metabolic purposes, or will be retained and built into tissues, are unknown.

In the healthy, well-nourished organism stress seems to lead to marked catabolism but, after the protein content of the body is depleted, other homeostatic mechanisms seem to come into play so that food or other body protein tends to be retained even under conditions of stress.

Werner and Randall (42) have challenged this hypothesis of protein metabolism under stress. Using subnormal caloric diets and subnormal nitrogen diets both pre- and post-operatively, they were unable to demonstrate an anabolic period of protein metabolism following the trauma of operation. Accurate metabolic balance studies were done. They concluded that simple caloric lack explains the post-operative nitrogen loss found following operation uncomplicated by infection. However, in this connection it must be remembered that observation periods of 7 to 10 days following the trauma of operation may not be sufficient time to recognize the gradual swinging over from the catabolic to the anabolic period illustrated below.



Variations in stress and variations in the previous homeostasis of the individual may lead to a period of weeks before the complete nitrogen balance picture represented is realized. Hence we must not accept the sub-caloric origin of the phenomena until further studies are done using longer periods of post-operative balance periods.

Factors leading to positive nitrogen balance are:

1. Growth
2. Anabolic phase in response to trauma
3. Pregnancy

    Negative nitrogen balance in first trimester, positive in last two trimesters of pregnancy.

4. Malnutrition or chronic disease states

DISEASE STATES REQUIRING MASSIVE RESECTION OF THE SMALL INTESTINE

It must be remembered that the removal of intestine is not always an elective procedure and the surgeon at operation must resect heroically, in certain instances, or allow the patient to die.

Haymond (20) summarizes the commonly encountered conditions from a survey of 254 cases gathered from the literature:

1. Volvulus 31%
   Knotenbildung 17%
   (Knot of ileum around Sigmoid)
   Ileum alone 13%

2. Hernia 16%
   (Inguinal, femoral, umbilical, incisional)

3. Mesenteric thrombosis of Embolus (equal) 15%

4. Female Pelvis 10%
   (Curette damage to mesentery)

5. Mesentery 10%
   (Tumors etc.)

6. Miscellaneous 18%
   (Injuries, tuberculosis, etc.)

Cattell (9) lists the indications for massive resection:

1. Regional enteritis

2. Mesenteric thrombosis and embolism

3. Volvulus and intussusception

4. Primary carcinoma or carinoma infiltration

5. Granulomas, e.g., tuberculosis

6. Extensive incisional hernia

7. Obscure gastro-intestinal bleeding

8. Multiple intestinal and abdominal fistulae

A.

REVIEW OF THE LITERATURE CONCERNING RESECTION OF MASSIVE SEGMENTS OF BOWEL

Hans Jensenius (26), working in Denmark, reported a large series of experiments in resections of the small intestine on dogs and this remains one of the most detailed studies to be found in the literature today. This work had its origin in experiments designed to unearth the etiological significance of the digestive canal in pernicious anemia and degenerative changes in the central nervous system. Jensenius continued the experiments to inquire into the morbid condition arising from the resection of the small intestine and to compare these observations with the clinical signs and symptoms of the sprue syndrome. The investigation of the anemic state of the animals was merely an essential and natural part of the work. He prepared 25 animals, some with resections of the proximal two-thirds of the small intestine and others with resections of the distal two-thirds of the small intestine. His conclusions are enumerated below:

1. The limit of resection compatible with the maintenance of life is two-thirds of the small intestine.

2. It seems reasonable to expect that survival is more likely after a proximal resection because of fat absorption studies, which suggest that the ileum serves better in this capacity than the jejunum.

3. Resection of the distal two-thirds of the small

intestine resulted in death, within 60 to 299 days, of all five animals so prepared. Resection of the proximal two-thirds of the small intestine resulted in death, of two out of five animals so prepared, by the 322nd day.

4. Both the proximal and distal resection groups developed anemia, but not a true pernicious anemia. He noted macrocytosis in some and occasionally hyperchromia in others but never any hyperplastic bone marrow. Generally the anemia was of a hypochromic normocytic type, not responding to liver therapy and occasionally influenced favourably, for a time, by iron therapy.

5. Fat and nitrogen absorption studies: pre-operatively the animals showed an average loss of 4.5% of nitrogen and 4.79% of fat. Post-operatively, the losses of fat ranged from 30-45% in the distal resection group and 7 to 18% in the proximal resection group. The loss of nitrogen was proportionately much less after such resections.

6. Sugar tolerance curves were generally flattened indicating a decreased and slow absorption from the intestine.

7. No definite consistent histological abnormalities were noted in the remaining gastro-intestinal tract, except for one instance of atrophy of the fundic mucosa of the stomach. Atrophy of the intestinal mucosa and slight lymphocytic infiltration, indicative of mild chronic enteritis, were noted in a few animals.

8. A conclusion is reached that, in comparing the total clinical picture of the resected animals with that of the sprue syndrome, it is probable that the pathogenesis of sprue has its origin in the small intestine and that the absorptive aspects characteristic of sprue, especially that of steatorrhea, are fully explained by impairment of intestinal function.

9. Compensatory changes, hyperplasia or hypertrophy of intestinal mucosa, were not observed with certainty in any of the experiments. However, no special examinations were adopted with a view to these possibilities, e.g., counting and measuring the villi.

DEFINITION OF TERMS

1. <u>Massive Resection of Bowel</u>:

Cattell (9) has defined this term as the removal from an adult, of seven feet or more of small bowel. It seems appropriate that those cases reported under the term 'Massive Resection' be limited to this definition. However, in a subsequent paragraph we will see where even this definition is not specific enough, but will probably have to suffice.

2. <u>Measuring the Intestine</u>:

a) <u>Length of the small intestine</u>: This elementary question must be settled first. Treves (38) gives the following:

average adult male:	22 feet 6 inches
average adult female:	23 feet 4 inches

Other reports (11) quote figures of 20 feet 6 inches and 18 feet 26 inches. It has been stated that the small intestine is longer in vegetarians than in meat-eaters, as in the Japanese who live almost entirely on rice. It is evident that there is considerable variation in the length of human small intestine, but a probable average might be taken as being 20 to 22 feet. It should be noted that the duodenum is not included in these measurements; it usually measures about 12 inches.

In the dog, wide variation exists. Jensenius (26) quotes from the literature the following measurements:

2.1 metres to 7.3 metres or 6 feet 8 inches to 23 feet 8 inches

Another rough measurement is four and four-fifths times the length of the animal which, in our experimental animals, would equal approximately 10 feet of small intestine. The duodenum in the dog is proportionately longer than in man, measuring on the average, 12 inches.

Alvarez (2) states that the small bowel of man is so short compared with the body length that there can be no question about man being a carnivorous type. In Herbivores, the bowel after death is from 25 to 75 times the length of the animal, whereas in the cat and dog it is from four to eight times that length. In man the small intestine has always been supposed, from measurements on the cadaver, to be about 20 feet long, but recent stueies show that during life the whole tract, from mouth to anus, measured by a rubber tube, is from eight to ten feet long.

Further studies quoted by Alvarez must alter our concept of the length of intestine in the living dog. Tube studies on living dogs revealed a mesenteric border length of the small intestine to be five feet! These animals were operated upon and no gathering of the bowel on the tube was noted. Upon removal of this five feet, the length gradually increased, without handling the bowel, until four hours later when it measured 12 to 13 feet!

In summary, we may say that the average lengths of small intestine in man and the dog are the following:

1)	Cadavers	Man	20 feet
		Dog	10-12 feet
2)	Living Subjects	Man	10 feet

Dog 5 feet

b) <u>Sources of error in measuring the small intestine</u>:

As will be seen in subsequent sections, there is a wide divergence in the consequences attending the resection of small intestine and not a little of this is due to inaccuracy in measurement of the gut. The contraction of the longitudinal musculature of the intestine will decrease its observed length quite markedly; the presence of gangrenous or atonic gut will be longer than the aforementioned. Immediately upon removal, the gut will contract maximally and its measurement will be about one-half of the non-contracted gut. Intestine at autopsy is atonic and longer. After fixation in formalin it is much shorter than fresh gut.

Thus we can see the many variables: Situations favoring lengthening of the gut are measurements in the intact animal, measurements on atonic gut at autopsy, measurements on gangrenous intestine; situations favoring shortening of the gut are measurements on the gut after removal from the intact animal or after fixation in formalin. A further error in measuring the gut is encountered when a certain degree of traction is exerted when laying it on a floor or table for measurement. It might be better, as Jensenius suggests, to measure intestine along the mesenteric border where less likelihood of variations in tonus would occur. Clinical investigators who do report the length of remaining intestine after resection, have often used primitive indices of measurement such as the span of the hand or the length of the index finger.

Another important measurement that is all too frequently omitted from the reports of clinical investigators concerns the length of small intestine and duodenum remaining after resection. Glowing accounts of survivals after resections of 10 or 20 feet of small intestine leave no idea of the absorptive length remaining which is the really important consideration. Twenty feet removed in an individual, whose normal length of intestine was 21 feet, is naturally more incapacitating than a 20 foot resection in an individual whose total length was 24 feet. The margin of survival may rest upon six inches to 12 inches of jejunum. Other reports do describe the surgeon's impression of how many inches or feet of gut remain, but fail to state what proportion of the remainder constitutes duodenum or whether duodenal length is omitted entirely from the remaining portion quoted.

It will be readily seen that these many variables in the measurement of the small intestine make for not a little difficulty in assessing the reports to follow. These facts must be borne in mind when one comes to answer the common question: What is the limit of resection compatible with the maintenance of life?

A more accurate point of reference would be the ampulla of vater in the second stage of the duodenum rather than the more variable ligament of Treitz.

ANATOMY OF THE DUODENUM

The name duodenum (from duodeni, twelve each) was applied to the first portion of the small intestine because of its length, twelve fingers breadth. It is the shortest, widest and most fixed portion of the small intestine.

Average cadaver measurements in the human are:

Length -		8 to 12 inches (20-30 cm.)
Width -	Average	4 cm.
	1st Stage	5 cm.
	Ampulla Vater	10 cm.

The mucosa of the superior portion of the duodenum is devoid of transverse plicae circulares. The remainder of the duodenum shows the circularly disposed folds of the mucosa to a very marked degree. These large transverse folds are permanent and are seldom obliterated, even when the duodenum is markedly distended.

CHART I

AUTHOR & YEAR	DISEASE	AGE	EXTENT OF RESECTION (in feet)	REMAINING SMALL BOWEL EXCL. DUODENUM	WEIGHT LOSS lbs.	OBSERVATION PERIOD	CLINICAL COURSE & REMARKS
DOOLAN 1951	OPERATIVE INJURY IN CANCER PANC.	63		0 GASTRO-COLOSTOMY		66 DAYS	DEATH AFTER TOTAL I.V. ALIMENTATION
GARDNER 1952	MESENTERIC EMBOLISM	45	TOTAL SMALL GUT AND RIGHT COLON	8 inches DUODENUM	170 to 95	10 MONTHS	DEATH
SHONYO & JACKSON	CANCER JEJUNUM	41		4.5 ins. JEJ.	165 to 85 ↓ 90	1½ YEARS	B DEFICIENCY INANITION & DEATH SERUM ELECTROLYTES NORMAL NO COMPENSATORY HYPERTROPHY
ALTHAUSEN 1947	MESENTERIC THROMBOSIS	47		6 ins. JEJ.	140 ↓ 88	1 YEAR	3-6 SOFT FOUL STOOLS/DAY MALNUTRITION & MORBIDITY
WILKIE 1950	INTERNAL HERNIA	28		6 ins. JEJ.	135 ↓ 90	1½ YEARS	DEFICIENCIES PSYCHOSIS
WECKESSER 1949	VOLVULUS GASTRO-ENTEROSTOMY	40		1 FT. OR 12% JEJ.	127 ↓ 88	10 MONTHS	HYPOCHROMIC ANEMIA DIED OF STARVATION
DOERFLER 1917	VOLVULUS	52		1 FT. JEJ.		6 YEARS	RECOVERY
COGSWELL 1948	MESENTERIC EMBOLISM			14 ins. JEJ.	95	6 MONTHS	LOW BLOOD CHOLESTEROL & INDICANURIA
WECKESSER 1948	REGIONAL ENTERITIS	26		1½ FT.	118 ↓ 75	8 MONTHS	HYPOCHROMIC ANEMIA DIED OF STARVATION
MEYER 1946	MESENTERIC THROMBOSIS	19		1½ FT.		10 MONTHS	NO ANEMIA HIGH CHO. LOW FAT NORMAL PROTEIN DIET 2 SOFT STOOLS/DAY GENERAL CONDITION GOOD
BOWEN 1936	VOLVULUS	9		2 FT.			2-3 LIQUID STOOLS/DAY NORMAL GROWTH & DEVELOPMENT
COLEMAN 1942	SHOTGUN WOUND 1940	18	15	2½ FT.	140 ↓ 90 ↓ 117	2 YEARS	JEJUNUM DILATED REGAINED SOME WEIGHT DID HEAVY WORK AS FISHERMAN
BERMAN 1945	MESENTERIC THROMBOSIS	31	20	3 FT.		1 YEAR	NORMAL DIET 3 STOOLS / DAY GOOD HEALTH
ELMAN	REGIONAL	32		3 FT.	140 ↓ 90 ↓ 140		3 STOOLS / DAY JEJUNUM DILATED UNRESTRICTED DIET
WEST 1938		40		3 FT. JEJ.		12 YEARS	LOW CA COMP. HYPERTROPHY WELL 12 YRS. LATER
CROOT 1952	CANCER CECUM	41	14	4-5 FT	120 ↓ 98	1 YEAR	REASONABLY WELL RECURRENCE OF CANCER
CROOT 1952	INTERNAL HERNIA	29	11	4-5 FT.	130 ↓ 85	10 YEARS	COMPLETE RECOVERY
STANLEY 1951	INTERNAL HERNIA	32	18	4-5 FT.	154 ↓ 125 ↓ 154	6 MONTHS	RECOVERY WORKING NORMAL
WECKESSER	MESENTERIC THROMBOSIS	37		5½ FT.	165 ↓ 132	1 YEAR	RECOVERY & WELL
JERRAULD 1926	MESENTERIC EMBOLISM	36	19	8 FT.	140 ↓ 134		RECOVERY

A summary of certain reports collected from the literature. It is not intended to be complete.

N.B. 1) Gardner 1952. To be reported in this thesis.
2) Elman - Regional enteritis

SOME INTERESTING CASES GATHERED FROM THE RECENT LITERATURE

1. Stanley (34) reported survival of a man, aged 32 and weighing 154 lbs., who, in 1951, had a resection of 18 feet of gangrenous bowel resulting from an internal hernia. His remaining small bowel consisted of duodenum plus four or five feet of jejunum. One month later he was having 8 bowel movements per day and weighed 125 lbs. Six months later he returned to work weighing 154 lbs. and having normal formed stools twice a day. Barium reached the cecum in one and one-half hours. His protein absorption was normal.

2. Croot (12) in 1952 reported two cases. One was that of a man, aged 29, who had a resection of 14 feet of gangrenous bowel in an internal hernia, leaving approximately 4 to 5 feet of jejunum. His weight decreased in five weeks from 130 lbs. to 85 lbs., with diarrhea 10 times daily. He improved gradually but developed symptoms of duodenal ulcer which he had previously suffered from. A partial gastrectomy was done. He recovered and went on to normal activity and work for the next ten years. At the end of this time his bowels moved once daily and he was in good health.

The other case reported by Croot concerned a 41 year old woman who had a resection of 11 feet, leaving between 4 and 5 feet of jejunum anastomosed to the colon. The reason for the resection was carcinoma of the cecum with spread to the mesenteric glands and superior mesenteric vessels. Her weight fell from 120 lbs. to 98 lbs. in one month, during which she had three semi-formed stools daily. She returned to active housework and one year later developed recurrence of carcinoma.

3. Shonyo and Jackson (35) reputedly hold the record for survival beyond a year of a patient with the least intestine. However, the record is a dubious honor and, measurements being so variable, accurate comparison is sometimes difficult when a matter of one inch is at stake.

This case was a woman, aged 41 and weighing 165 lbs., with adenocarcinoma of the jejunum involving many loops and extending into the base of the mesentery. A jejuno-ileostomy was established and the bowel intervening between the ligament of Treitz and the cecum measured 4.5 inches. Three months later she was doing light work but had developed cheilosis and mild stomatitis which disappeared with Vitamin B Complex therapy. Eight months later she weighed 100 lbs. At this time blood cholesterol, HCO_3, prothrombin time, serum sodium, potassium and chloride were all normal. Ten months after operation, her weight reached 85 lbs. and remained there. One year after operation, on limited social activities, she ate three to four meals daily and had two to three stools per day. A barium meal revealed normal stomach emptying with barium reaching the cecum in five minutes.

The patient died 16 months post-operatively, after onset of progressive irreversible emaciation. The duodenum and remaining small bowel measured 15.3 inches. No compensatory hypertropy was noted by the pathologist in the gastro-intestinal tract.

4. Wilkie (45), in 1950, reported the survival of a patient who had a resection of all but six or seven inches of jejunum plus the duodenum, for massive gangrene due to a strangulated internal hernia. His weight fell from 135 lbs. to 106 lbs. in three months. Nine months later he developed malnutrition, pellagra, and multiple vitamin deficiencies. His weight at this time was 90 lbs. He had survived 18 months at the time of Wilkie's report. Jackson and Linder (25) reported a number of metabolic studies in this case and, at the time of their report, March 1951, more than one year later, the man was still alive. He had actually returned to work six months after operation but was forced to give it up.

At the time of his readmission and the beginning of metabolic study, the man was found to have the following disturbances:

1. Weight - 87 lbs.
2. Irregular brown pigmentation of forehead, face and neck, back of the hands, palm of the hands.
3. Skin of the back was coarse and thickened.
4. Generalized peri-follicular hyperkeratosis.
5. Cheilosis
6. Tongue was smooth and deep red.
7. Unable to walk unaided.

On the following therapy, much of the pigmentation, hyperkeratosis, dryness of skin and smoothness of the tongue disappeared.

1. High protein, low residue diet with amino acid supplements
2. Thiamine - 100 mg. per day
3. Riboflavine - 50 mg. per day . . . Parenterally
4. Nicotinamide - 400 mg. per day
5. Crude liver extract - 4 cc. per day

Curiously, this man then developed a psychotic condition with convulsions, apparently on a nutritional basis while receiving parenterally large doses of the only food factors (thiamine and nicotinamide) whose lack is known to produce mental derangement in man. Pyridoxine in heroic doses had no clear effect on his condition.

Intestinal State:

One year after operation, a barium meal revealed rapid passage of barium into the colon (15 minutes), accentuated mucosal pattern of duodenum and remaining segment of jejunum, with dilatation of duodenum and jejunum. There was no evidence of colitis on sigmoidoscopic examination.

Diet:

An attempt was made to have him eat a high protein, low fat, low residue diet supplying 3000-4000 calories, but he soon refused all synthetic substitutes and pureed foods, preferring whole foods. On these he did better, raising the question whether the digestive ferments are more copiously secreted when preferred foods are eaten. He ate, by choice, 150 gms. of fat daily. It was only on a lower fat diet, with intravenous amino acid supplements that he gained some weight.

Gastro-intestinal Secretions:

He showed a deficiency of pancreatic enzymes. This led to a low intestinal pH. The pH of his gastric contents was also low (5.7), yet there was no free HCl present. The stool pH was also quite acid (4 to 5) whereas the normal is from 6 to 7. It was suggested that he might be one of those fortunate individuals who do well in the absence of pancreatic external secretion, e.g., the occasional individuals who do well after total pancreatectomy.

Intestinal Absorption:

Five day periods of metabolic balance study were done on five occasions.

I High Fat Diet (P 180, F 170, CHO 340, CAL 3270)

The following were noted:

1. PROTEIN - Maintenance of a small positive nitrogen balance by absorbing 33 1/3% of ingested protein, which contained 5 grams of nitrogen.

2. FAT - Although a fat content of 170 grams is ordinarily high, it was a restricted amount according to the patient's tastes. On this regime he excreted 90-95% of the ingested fat: 53% of faecal fat was unsplit, indicating

defective fat digestion as well as poor or negligible fat absorption.

3. CALCIUM and PHOSPHORUS - On an adequate intake of 1400 mg. of calcium, and calcium-phosphorus ratio of 0.78 adequate for satisfactory calcium absorption, there was a normal urine calcium excretion and an over-all slight negative calcium balance. Urine phosphorus normally exceeds stool phosphorus but in this case, the ratio was reversed to 1:7. The phosphorus balance was about even.

II <u>Very Low Fat Diet</u> (40 gms.)

On a very low fat diet and the same amount of protein and carbohydrate as during the previous period, 112 gms. and 370 gms., respectively, balance studies were done.

1. PROTEIN - Absorption was 43% of ingestion, an increase of 10%. The positive balance of nitrogen increased to 3.3 gms. a day.

2. FAT - The percentage of fat absorbed was increased but the actual amount was not.

3. CALCIUM and PHOSPHORUS - There was less phosphorus in the faeces without change in the urinary output. The phosphorus balance became positive. Calcium absorption was not improved.

On the low fat diet the utilization of the calories provided improved from 46% to 75%. The calcium balance was negative to such a small extent that it would take a very long time to demineralize the bones radiologically.

Vitamins:

A. There were no signs of Vitamin A deficiency except, possible, for the dry skin and areas of perifollicular hyperkeratosis. It is doubtful whether A-deficiency was the cause of this condition.

B Group. There was no doubt of the pellagrous state. The angular stomatitis suggested riboflavin deficiency. Massive therapy did not completely cure his deficiency, suggesting that angular stomatitis is not curable if present for any length of time.

C. Gross Vitamin C absorption defect. Twenty-four hour urine specimens contained only 5 mg. and the plasma level was below 0.4 mg. per 100 cc. (normal above 0.9).

It appeared that the patient could absorb the fat-soluble Vitamin A better than Vitamin C, for which there was no explanation.

Faeces:

Consistency - semi-fluid

Volume - 1500 cc. per day

The combined volume of urine and faeces constantly exceeded the recorded fluid intake, but this did not take into consideration the volume of fluid in the food and the water formed by its metabolism: This was taken as approximately equal to the weight of the food eaten, and amounted to 2 kg. a day.

REACTION - Always acid, between pH of 5 and 6, due to the absence of alkaline succus entericus, absence of pancreatic enzymes and presence of much free fatty acid.

PROTEIN - The bulk of the nitrogen lost in the faeces appeared to have been in the form of undigested and undissolved protein, such as meat fibres. The loss of nitrogen as ammonia and amino acid was much smaller, although considerable.

FAT - With a high fat diet (160 gms.) the absorption was 3-5%, and the percentage of split fat was 54 (40% fatty acid and 14% soap). It seemed likely that the defect in fat absorption was concerned largely with a failure in the absorption of neutral fats, and that a large proportion of the fat was passed on into the colon with some lipases, where fatty acid was set free.

<u>Biochemical</u>:

1. Serum proteins remained within normal limits
2. Serum cholesterol remained low, e.g., 123 mg. per 100 cc.
3. Serum calcium remained normal.
4. Serum phosphorus was low (2.1 and 2.6 mg. per 100 cc.).

    Serum calcium is easily maintained at expense of bone while low serum phosphorus is an important index of inadequate absorption. Hence the normal calcium and low phosphorus is some evidence of a strain on normal calcification.

5. Serum levels of Vitamin A and C were low.

6. BMR depression (53%)

   This suggests the patient's remarkable compensation by reduction of combustion, and hence reduction in caloric and other metabolic requirements was largely responsible for his survival.

7. Creatine.

   Small amount of creatinuria (70 mg. a day) and high serum creatine level (0.93 mg. per 100 cc.:normal below 0.6 mg.).

8. Creatinine.

   The creatinine coefficient (mg. urinary creatinine per kilo per day) was 10, the normal being 20 to 26. Serum creatinine level was normal.

   Creatine and creatinine findings indicate some abnormality of muscle metabolism with a large overall depression. The very low creatinine production is related to the generally diminished muscle mass.

Fluid Balance:

The patient failed to demonstrate any diuresis whatsoever following ingestion of 840 cc. of water after a 12-hour fast. Normal controls have a diuresis, losing most of this ingested fluid within 2½ hours. Furthermore, it was noted that he voided urine mainly at night and the volume of urine equalled the fluid intake.

Hence all ingested fluids were completely absorbed, retained in the extracellular space for a time; then followed a delayed nocturnal diuresis with loss of the ingested fluid. He took most of his fluids during the day, yet voided the majority of the daily urine at 6 a.m. the following day.

e.g.,	urine volume 8 am - 8 pm:	506 cc.
	urine volume 8 pm - 8 am:	839 cc.
	TOTAL	1445 cc.
	Total Fluid Intake . .	1500 cc.

Further, it was found that diuresis would not follow intravenous fluids given rapidly in 2-litre quantities.

There was no increase in stool water content during these test periods.

Two extracellular fluid space measurements were done using the thiocyanate space method with the following results:

a) 12.8 litres one day

b) 15.0 litres another day, after drinking as much as he could

What was the mechanism of this lack of diuresis?

a) It was not due to dehydration.

b) It was not due to low serum sodium (132-138 meq/L while admittedly low normal is not excessively low, as in Addison's disease).

They surmised an excess of pituitary anti-diuretic hormone and/or a depression of the adrenal cortex capable of causing abnormal distribution of water excretion.

Was it due to abnormal renal function?

The patient's urea and creatinine clearances were half normal but these findings are found in low protein assimilation. His blood urea was normal.

Urine formation was more rapid at night than during the day (1.3 cc. versus 0.6 cc. per minute). Urea and creatinine clearances were reversed indicating the possibility that water and urea excretion were depressed at night. It could be explained by a posterior pituitary secretion which was greater by day than by night. Although there was no demonstrable renal pathology, the kidneys certainly showed the functional depression of activity normally occurring with a low protein diet.

Salt Excretion and Acid Base Balance:

Chloride was excreted in high concentration (250 meq/L of urine) in the presence of high salt intake. His serum sodium and chloride remained at just below normal most of the time and the pH of the blood and the serum HCO_3 were normal.

Haematology:

The bone marrow was normal. Blood volume was normal for his weight. Mild anemia occurred occasionally, which was normochromic, e.g., packed cells 36%. His serum iron level was normal. It has been found that the duodenum absorbs most of the ingested iron and, even in the absence of iron absorption, the body is capable of re-using its iron supply.

Ketosteroid Excretion:

Loss of libido was marked. Secondary sexual characteristics remained prominent. Two 24-hour urine ketosteroid excretions measured 6.4 mg. and 5 mg. Both suggest lowered output (normal 10-20 mg. for normal adult male). However, under-nutrition alone is able to reduce the 17-ketosteroid excretion in animals.

Liver:

Function tests and biopsy were normal.

DISCUSSION

In summary, this man was able to maintain life at a minimum level on an absorbed diet of 100% carbohydrate, 42% of protein and about 5% of fat. The protein absorption of 47 grams per day is said to be the bare minimum for nitrogen balance. Fat in the diet impaired protein, calcium, and phosphorus absorption. He absorbed 1800 calories per day. Protein hydrolysate supplements by mouth did not improve the absorptive situation. The glucose tolerance curve was flat due to a delay in absorption. The frequency of bowel motions was low, one or two a day, but the bulk was enormous (1½ gallons). A depression of pancreatic exocrine secretion was noted. Inability to produce a water diuresis and storage of absorbed fluid in the extracellular space was noted.

His prognosis may depend on avoiding intercurrent infection.

PSYCHOSIS

One year after operation, following readmission for a pellagrous state with multiple vitamin deficiencies, he developed a psychosis described as a mixed type and characterized by epileptiform seizures, normal electro-encephalogram tracing, hallucinations, paranoid ideas, depression and suicidal tendencies. Exacerbations and remissions continued during the next year unaffected by massive vitamin therapy. It was felt that the cause of the psychosis was the personality impact of the resection plus its complications and the vitamin deficiencies persisting a long time before massive therapy was begun.

Jackson and Linder later reported a case of "loop syndrome" which resulted in a number of observations not unlike those reported in their previous case of massive resection. A duodeno-jejunal fistula developed following a perforated ulcer, thereby creating an ill-used loop from the first stage of the duodenum to mid-jejunum. The abnormalities discovered consisted of clinical pellagra, emaciation, edema, abnormal mental attitude, low plasma protein and calcium, an inability to absorb the water-soluble Vitamin C and to produce a water diuresis, slight defect in fat and phosphorus absorption, and doubtful partial deficiency in pancreatic exocrine function. These authors concluded that remarkable though it may appear, resection of the small gut by itself does not produce the complete picture of jejuno-ileal insufficiency or sprue-like state which may be found in celiac disease, steatorrhea, malignancies of the small gut, gastrocolic fistula, multiple strictures and "the loop syndrome". They further warn that it is metabolically unsound to by-pass a diseased segment of small gut or to leave in situ a blind-ended length of intestine. Furthermore, they suggest that gastroenterostomy and partial gastrectomy be suspect and a Billroth I gastrectomy be substituted. They give no explanation for this phenomenon other than to suggest that amino acids, calcium and haematinic factor may be absorbed in the absence of jejunum and ileum and that some (? toxic) agency other than pure deficiency of jejuno-ileal absorptive function must be at work in those conditions which produce a sprue syndrome.

OTHER REPORTED CASES OF VERY EXTENSIVE RESECTION

1. Althausen (3) reported digestion and absorption studies on a case of massive resection in 1949. As outlined in the chart, it was a 47 year old man who had a resection of his entire small bowel except for 12 inches of duodenum and 6 inches of jejunum. His weight had decreased from 140 lbs. to 88 lbs. by ten months later. He then regained about 8 lbs. and remained at that weight. There is no further progress report beyond one year from the date of operation, January 1947. He was given a diet of 2125 calories: protein - 150 grams, fat - 65 grams, carbohydrate - 200 grams. He was also given vitamins daily: A - 15,000 units, D - 3,000 units, B complex and C - 300 mg. He was given calcium gluconate - 12 grams per day, and ferrous sulphate - .6 grams per day. He complained of dizziness, hypotension, abdominal pain with bloating and nausea. He had 3 - 6 stools per day, foul-smelling, usually soft but not liquid.

2. Doolan et al (15), in 1951, reported a case of gastro-colostomy in a 63 year old woman. The patient was undergoing a radical pancreaticoduodenectomy for cancer of the pancreas when the superior mesenteric artery was inadvertently injured beyond repair. Accordingly, a resection of the entire small intestine and right colon was performed with a gastrocolostomy and cholecyst-gastrostomy. She survived 66 days on total intravenous alimentation, during which time several interesting biochemical abnormalities arose.

Intermittent gastric suction was employed for all but a 3-day period. The pancreatic duct was not joined to the gastrointestinal tract. Accurate balance studies were not done. Her fluid balance remained normal for 30 days on the following intake:

a) 1000 cc. Aminosol + 5% glucose

b) 1000 cc. 10% dextrose in water . . 1200 calories
7 grams Nitrogen

c) 1000 cc. 10% dextrose in normal saline

d) With added vitamins B complex, C, K

e) 40 meq. K per day

She developed a hypokalemic, hypochloremic, metabolic alkalosis on the 19th day which responded to potassium therapy.

Nitrogen Balance: She did not manifest a negative nitrogen balance but balance records were not begun until the 16th day, by which time the catabolic period may well have ended. Furthermore, being under chronic stress, one might have expected a catabolic phase but it is known that, under chronic stress, an individual may remain in an anabolic phase, storing nitrogen, even in the face of fever or inadequate nitrogen intake. They also suggested that a high adrenal cortex function in this patient may have led to greater mobilization of ingested and tissue proteins but that these were commandeered by the anaplastic focus which had a higher priority rating and the over-all result would be progressive depletion of tissue protein in the presence of a small urinary excretion of nitrogen. The foregoing hypothesis seemed substantiated by the following: 1) only slightly negative nitrogen balance 2) muscular wasting 3) flourishing cancer at autopsy.

It should be remembered that the status of the tissue stores of protein are a factor in the catabolic response. The authors were unable to state which of the following, or what combination of the following, were acting:

1) restricted protein and caloric intake imposed by the intravenous route

2) variations in adrenal activity

3) state of protein depletion

They found only coincidental correlation between the administration of potassium to correct the hypokalemia and the occurrence of the one period of positive nitrogen balance.

3. West et al (43) report the case of a man of 40 in whom three feet of jejunum were left. Ten years after operation he developed tetany with serum calcium ranging from 5 - 7 mg. per 100 cc. Laparotomy performed for persistent distension at this time revealed jejunal hypertrophy and dilatation to the size of the colon. Approximately 50% fat wastage was noted, the majority in the form of split fat.

COMPENSATION FOR THE LOSS OF INTESTINE

Resections of the small intestine not exceeding one-third, may result in little if any untoward symptoms. This implies that the bowel possesses considerable "reserve power". Other cases of more extensive resection may begin with diarrhea which later subsides.

Greeley (19) noted no growth in length of the remaining bowel, but an increase in absorbing surface through hypertrophy which, in some cases, reached 400%. He noted no regeneration in crypts or villi. Although complete compensation did occur in some cases, a later breakdown under stress or disease could occur. He also commented on the wide individual variation in the extent of compensation.

Coleman (11) felt that massive resections, no matter how little in excess of 7 feet, interfere markedly with metabolism in most cases until compensatory hypertrophy is established. Experimental work on dogs, notably by Flint (17), demonstrated marked compensatory hypertrophy of the remaining small bowel with all layers participating in the hypertrophy. Providing there is an adequate remnant, the remaining bowel may attain the epithelial surface area of the original gut and the digestion of the animal or human subject return to normal.

The rate of intestinal absorption can increase to twice the normal above the resection, but not below it. There is as yet no evidence that of absorption rates the distal ileum and colon can increase.

Flint further showed that, whereas dilatation, hypertrophy and hyperplasia of the remaining gut could occur, there was no increase in length. He felt that this was certainly in keeping with physiological laws.

In estimating hypertrophy by the height of the mucosa, post-mortem autolysis might obscure the presence of such mucosal thickening.

It has often been wondered whether or not the colon or the stomach might take over some of the function of the resected intestine. A few observed cases of dilatation of the stomach have been noted, but no evidence of any compensatory changes occurring in the colon has yet appeared.

ANEMIA FOLLOWING MASSIVE RESECTION

Jensenius (26) reported anemia in all of his dogs, which was mainly a hypochromic anemia occurring shortly before death of the animals. Occasionally he noted macrocytic anemia.

Martin (29) performed resections on 12 dogs, leaving four inches of jejunum and four inches of ileum. Eight dogs died in 10 days of malnutrition and dehydration. Four animals survived a sufficient length of time for study. His findings are enumerated below:

1. Hemoconcentration due to initial diarrhea and low fluid intake in the early postoperative period.
2. Normal erythrocyte counts when fluid intake was resumed.
3. Three to four weeks later, the hemoglobin and red cell count dropped to low levels and remained there. Reticulocytes were absent or low.
4. Weight declined 25 to 40%, then remained there.
5. Developed pellagra-like changes in the integument.
6. Changes in volume and color indices were not constant.
7. No response to folic acid.
8. Retained good appetites: normal intake: semi-solid stools.

He concluded that perhaps wider resections might produce macrocytic anemias like those seen in human subjects, but these dogs did not show it.

Weckesser (41), in resections in 12 dogs, observed normochromic or hypochromic anemia but no cases of macrocytic anemia.

EFFECT OF VAGOTOMY

Weckesser et al (41) reported an experimental study to determine whether or not vagotomy would prolong transit time and thereby allow a longer period for absorption. Proximal and distal resections of two-thirds of the small intestine were done, followed by vagotomy a few weeks later. They found that "late" vagotomy, i.e., 23 weeks after extensive resection, was not beneficial and was even detrimental in some dogs. "Early" vagotomy, i.e., 5 weeks after resection, had a temporary beneficial effect on fat and nitrogen absorption but this effect was not permanent. Transit time remained prolonged only in the stomach; there was no effect on that of the intestine or colon. They found no difference between the proximal and distal resections, contrary to Jensenius' observations that proximal resections were tolerated better than distal resections. Anemia, when it developed, was normochromic or hypochromic. Gastric ulceration with death occurred in two out of 14 dogs, four to eight months after vagotomy.

THE LENGTH OF INTESTINE NECESSARY FOR THE MAINTENANCE OF LIFE

In cases of gangrenous bowel, the surgeon will not be faced with answering this question. In tumors of the mesentery or in regional enteritis or adherent loops of bowel, the choice may have to be made between leaving bowel which may not be sound, and performing a more extensive resection. In these latter cases, it is of direct practical importance to know how large a part of the small intestine can be safely resected with maintenance of life.

One has two sources of appraisal; the experimental work in the literature and the reported cases in the literature. The latter are difficult to interpret for three reasons. First, the majority of investigators report only the immediate survivors and no mention is made of the operative of hospital mortality from the procedure. Second, as previously mentioned, few reports include an accurate description of the length of remaining bowel. Third, few reports have sufficient follow-up periods to indicate the subsequent course of patients after the initial observation period is completed.

All told, the result of the clinical experiences has been uncertain and variable, and while a number of authors have arrived at the conclusion that the limit for the maintenance of life - or for the maintenance of a tolerable state - varies between the removal of one-third and four-fifths or even more of the gut, many others hold that it is impossible to give any limit.

In the accompanying table on page 29 a group of cases is listed which contains information reported by the respective authors. It can be seen that some cases recovered with as little as two feet of small bowel, 12 inches of which would presumably be duodenum. It must be remembered that some of all of these cases might have died after the reported observation time. There is so much variation in individual tolerance that we cannot do more than cite extraordinary cases reported in the literature as an index of how much loss of bowel an individual can tolerate and survive.

Again it might be mentioned that all measurements referred to in this section are based on cadaver averages of 20 feet of small intestine.

Haymond (20), in 1935, reviewed the literature and collected 257 cases with more than 9 feet of small bowel resected. Taking 21 feet as an average, he calculated the following:

86 cases with good results after having 47% removed, i.e., approximately 10 feet

21 cases with fair results after having 55% removed, i.e., approximately 12 feet

He considered that 50% resection of small intestine was the upper limit of safety. Discounting the dangers of the operation itself and its possible concomitant complications, a patient can withstand a massive resection of 33% of the length of the small intestine and expect the digestive tract of maintain normal function. Fifty per cent removal constitutes the upper limit of safety in extensive enterectomy, and resections above 50% must necessarily obtain poorer results even though an exceptional case may be better than predicted.

Certainly the general health and age of the individual, and the state of the remaining segment of bowel are all important factors.

DIET

Most authors agree on the following general principles of diet - high carbohydrate, moderate to high protein, low fat, low cellulose, bland, low residue, high calorie with supplementary vitamins and calcium.

A diet rich or even normal in fat may result in loss of 66% of ingested fat in the stool with the accompanying disadvantage of foul smell and bulkiness of faeces. Hence an easily absorbable diet, rich in carbohydrate and poor in fat and waste products, is desirable.

It has been reported that both human subjects and dogs develop voracious and peculiar appetites with strange and exotic tastes.

CALCIUM

If the animal or patient, after very large resection, is fed a diet high or even normal in fat content, the calcium in his diet will form soaps and be excreted in foul-smelling fat containing faeces. This can lead to a calcium deficiency and tetany. Supplementary calcium intake will not be absorbed in the presence of anything but a low fat intake.

CONCLUSIONS

According to the literature concerning extensive resections, the prognosis depends only in part upon the amount of intestine remaining. Diminished fat absorption appeared in all cases. Loss of protein nitrogen in the stool occurred to a lesser extent and carbohydrates were apparently sometimes normally absorbed. Tetany occurred in some cases and anemia occasionally; anemia is more common in short-circuiting, "loop" conditions than in extensive resections.

Modern surgical techniques combined with chemotherapy and control of fluid balance have made it possible to resect progressively more intestine during the past decade. The problem of maintaining adequate nutrition subsequent to operation appears to be the greatest hazard in the procedure. Intractable diarrhea, which materially decreases water and food assimilation, does not appear to be inevitable in cases of massive resection of the bowel. Perhaps the remaining portion of bowel may undergo compensatory physiological adjustments to insure a normal existence in the absence of large portions of the small bowel.

Massive resection of the small gut is not frequently necessary and the indications for it may appear unexpectedly in the course of a laparotomy for intestinal obstruction. A decision must be made on the spot, and the cases reviewed in this article may serve to increase the optimism one may have with regard to this operation. Extensive resections give better results than one might expect and should not be allowed to fail through being insufficiently radical.

In conclusion, resection of more than three-quarters of the small bowel is apt to be followed by serious permanent metabolic defects, but there is considerable variation between individuals. As much as one-half of the intestine may be resected without fear of metabolic disturbance.

METHODS

EXPERIMENTAL METHODS

Material:

Five adult mongrel dogs, weighing about 27 lbs. each at the beginning of the experiment, were used.

One adult male patient (No. V33038) at the Queen Mary Veteran's Hospital, Montreal, was studied on the research ward of that hospital under the direct care of Dr. J. R. Martin and the supervision of Dr. C. J. Pattee. The operations performed on this man were under the direction of Dr. Campbell Gardner, Surgeon-in-Chief, Queen Mary Veteran's Hospital.

Experimental methods concerning the animal experimentation will be described first.

Care of Animals:

The animals were kept in metabolism cages. It was necessary to remove them daily for a short period to allow the cages to be cleaned. At this time they were placed on the top of each cage to discourage the voiding of any excreta while out of their cage.

Diet:

A standard dog biscuit was fed. Purina Dog Chow was obtained in 100 lb. bags. Each animal was also allowed one-half pint of plain milk per day. Water was allowed ad libitum. Early in the experiments, the Chow was analysed on several occasions and found to contain standard proportions of solids and minerals. Aliquots from different lot bags gave particularly constant values on analysis.

A neglibible quantity of electrolytes existed in the tap water so the early feeding of only distilled water was replaced by tap water.

Purina Dog Chow Analysis - Company's report:

	Crude %	Digestible %
Protein	23.0	19.0
Fat	5.0	4.7
Fibre	4.0	
Ash	7.0	
Nitrogen free Extract	54.0	48.0
Moisture	7.0	
	100.0	71.7

<u>Vitamins</u>:

A	4,000 I.U./lb.
B	275 Sherman units/lb.
C	low
D	500 I.U./lb.
E	high
G	300 Sherman units/lb.

1400 calories per lb. - Nutritive Ratio 3 to 1

Minerals:	%	mgm/kgm	meq/gm
Iron	0.018	180	
Silica	0.23	2300	
Magnesium	0.09	900	0.075
Sodium	0.67	291.3	0.291
Chloride	0.68	6800	0.192
Potassium	0.56	5600	0.144
Phosphorus	1.17	11,700	0.676
Calcium	2.22	22,200	1.110

Calcium Phosphorus ratio: 1.9 to 1.0

Analysis by Donner Laboratories of Chow aliquots:

1. Water soluble	meq/gram			Average
Potassium	0.18	0.1852	0.1912	0.187
Sodium	0.207	0.189	0.1933	0.195
Chloride	0.224	0.216	0.220	0.220

2. After Digestion

Potassium	0.192	0.208	0.200
Sodium	0.224	0.224	0.22
Protein	22.5%		
Nitrogen	42.0 mgm/gram		

3. Analysis of Milk

Protein	3.5%
Nitrogen	4.9 gm/litre
Sodium	20.0 meq/litre
Chloride	28.7 meq/litre
Potassium	37.39 meq/litre

The animals were presented with more than they could usually eat and the quantity remaining was subtracted from the amount given each day. Five hundred cc. of water were also offered daily.

Collections of Specimens:

BLOOD

Venipuncture was done when possible, otherwise the femoral artery puncture was used to obtain samples. The needle was filled with a small quantity of heparin for obtaining samples of blood destined for biochemical determination. Unheparinized blood was obtained for the hematology determinations which was immediately transferred from the syringe to a test tube containing oxalate and gently inverted.

Blood samples were drawn at various times pre- and postoperatively but no set time intervals were used.

URINE

Voided urine was conducted down the inclined pan and out a spigot into specimen bottles and collected daily. If pooled as three day or six day samples, they were kept in the refrigerator and a drop of xylol added as a preservative.

Weight:

Dogs were weighed periodically.

Laboratory Determinations:

These were done by Miss Hope Thompson and her staff at the Donner Experimental Surgery Laboratory. The following methods were used:

Serum and Urine Sodium and Potassium	Flame Photometer
Serum and Urine Chloride	Van Slyke and Hiller modification of Sendroy's Iodometric method
Serum Bicarbonate	Manometric Van Sleyke
Blood N. P. N.	Nesslerization method
Blood Sugar	Folin Wu method
Urine Nitrogen	Semi micro Kjeldahl
Haemoglobin	
Red cell count	
Haematocrit	
Urinalysis	

Discussion of Difficulties:

It was felt from the beginning that an accurate record could be kept of the intake and output but difficulties soon presented themselves. The analysis of the Dog Chow and milk was close enough on several aliquot determinations to allow us to assume accuracy in this respect. There was considerable difficulty in collecting excretory specimens accurately. All the animals developed copious diarrhea which contaminated each urine specimen. This, in the most extensive resections, reached a stage where the specimens consisted principally of faeces. The finest wire mesh platforms did not prevent the very fluid stool from penetrating it.

The considerable alkalinity of the resulting speciman and presence of ammonia precluded an accurate nitrogen assay.

The performance of a cystotomy and the use of a pezzar catheter, draining into a bag strapped to the animal, was considered but disregarded because these preparations are only feasible in short term experiments with the animal strapped in harness 24 hours a day.

Accordingly, it was deemed inadvisable to pursue any further balance studies after December, 1951 but to continue with general observations such as weight, haematology and serum electrolyte values.

In retrospect, it might have been possible to fashion some receptacle for urine collections and suspend the animal for short term periods such as three days, during which time an accurate balance study might have been conducted. However, the animals with more extensive bowel resections were constantly in a weakened condition and might not have tolerated this procedure.

Autopsy:

Autopsies were performed on all dogs after sacrificing them by a lethal dose of nembutal intravenously. In all animals but one, the autopsy was performed on the day of anticipated death of the animal as judged by its moribund state. The only exception was an animal in extremely good health who was sacrificed in the same manner to complete the project.

EXPERIMENTAL METHODS - HUMAN CASE

This man was admitted to the Queen Mary Veteran's Hospital in June 1951. He had two operations subsequently and was then transferred to the Research Ward of the hospital in September 1951, where he remained until his death in April 1952.

During the period from September until April, metabolic balance studies were attempted but failed for the following reasons:

1. The patient developed personality changes, including irresponsibility, which prevented the research dietitian from keeping an accurate tabulation on the quantity and content of the food eaten.

2. Careful serum and haematological determinations could not be done regularly due to the state of the man's peripheral veins and his refusal to allow venipuncture on several occasions.

Other factors entered the picture of which I am not aware, since it was my position only to have access to the records of the patient.

Accordingly, the following determinations were recorded periodically:

a) serum electrolyte values

b) haemograms

c) urine determinations for sodium, potassium, chloride, and fractioned non-protein nitrogen

d) stool analysis for fat and nitrogen content

CHARTS

In each section the intake is charted downwards from the zero line. The faecal excretion is charted upwards from the line representing the intake and the urinary excretion is above the faecal. When the urinary and faecal excretion exceed the intake (negative balance), the column projects above the zero line; when they are less than the intake, a blank space is left below the zero line (positive balance).

Most of the data is charted according to the method described by Albright, Reifenstein et al (1).

PROCEDURE

Animal Experiments

I OPERATIONS - All dogs were operated on under intravenous nembutal anesthesia.

Dog # 1 was operated upon on September 19, 1951, and a resection of the small intestine was carried out. An estimate of two-thirds of the small intestine was made from the jejunum, four inches distal to the ligament of Treitz to the ileum and the bowel resected between these two points. After removal it measured approximately five feet. This animal was sacrificed on May 1, 1952 (eight months later), at which time it was in excellent health. Results of the course of this animal and the autopsy findings are recorded.

Dog # 2 was operated upon on October 11, 1952, and a resection of the small intestine was carried out leaving only four inches of jejunum, measured distal to the ligament of Treitz, and four inches of ileum; these were united by end to end anastomosis. This animal reached a moribund state on February 19, 1952, approximately four months later, at which time it was sacrificed. Results on this animal are reported.

Dog # 3 was operated upon on December 5, 1951, and the following procedure was carried out. A Heidenhain pouch was fashioned from the greater curvature of the stomach and anastomosed end to end between the transected duodenojejunal junction and the distal four inches of ileum. All of the small bowel between these points was resected. This operation was performed in an attempt to lengthen the remaining gut by means of a tube of stomach. The animal died in four days with necrosis and gangrene of the proximal anastomosis. In retrospect, had this operation succeeded for a time, a peptic ulcer may well have developed in the terminal ileum segment. No results are reported.

Dog # 4 was operated upon on February 2, 1952, and a resection similar to that of Dog # 2 was carried out. This animal died of pneumonia four days later. No results are reported.

Dog # 5 was operated upon on February 5, 1952, and a resection similar to Dogs # 2 and 4 was done, i.e., massive small bowel resection, except for duodenum, four inches of jejunum and four inches of ileum. This animal reached a moribund state on May 1, 1952, three months later, and was sacrificed. Results are reported.

Dog # 6, a normal animal of similar weight and size, was sacrificed to obtain a normal gastrointestinal tract for comparison. An autopsy was performed on May 10, 1952.

RESULTS

ANIMAL EXPERIMENTS

Dog # 1:

General Remarks:

This animal was subjected to resection of two-thirds of the small intestine. The area resected extended from a point on the jejunum, four inches distal to the ligament of Treitz, to a point on the ileum at about its mid-portion. An end-to-end anastomosis was then established. The resected bowel weighed 380 grams and in its atonic state measured 4½ feet.

Two months after the operation, the animal was noted to have ulcers of the extremities situated on the extensor aspects of joints. The texture of the hair was abnormal and the loss of hair, especially on the extremities, was marked. Without specific treatment, the abnormal skin and hair changes completely disappeared by the time the animal was sacrificed.

For the first two postoperative weeks the animal was in fair condition but its oral intake was poor and erratic. Thereafter it behaved normally and, by about the 180th day, began to manifest more activity, to gain weight and generally to appear in better health. At the time it was sacrificed it was, if anything, in better condition than before operation.

Fluid Balance: (Chart # 2)

Moderate dehydration existed for the first postoperative week. For the rest of the period, hydration was normal with the fluid intake averaging 750 cc. per day and the urine output 150-175 cc. per day. Bowel movements were occasionally semi-solid early in the observation period, but later they were always well-formed. There was no steatorrhea and no diarrhea.

Electrolyte Balance: (Chart # 2)

1. SODIUM. For a few days after operation the balance was negative but thereafter it remained positive. The serum sodium value was low on the fifth day (130 meq/L) but rose to normal limits during the remainder of the study (140-160 meq/L).

2. CHLORIDE. This balance followed a pattern similar to the sodium balance, being negative postoperatively for a few days and then remaining positive. The serum chloride value was also low (106 meq/L) on the fifth day but then remained within normal limits (110-120 meq/L).

3. POTASSIUM. This balance was irregular in the immediate postoperative period but remained positive throughout the remainder of the period. The serum potassium ranged between 4 and 5 meq/L throughout the study, except for one value of 3.6 meq/L on the 133rd day.

4. BICARBONATE. Serum values for this dog remained within the normal range.

Nitrogen Balance: (Chart # 2)

a) Calories. The caloric intake remained below 500 calories per day until the 31st day, when it reached an average of 700-1000 calories per day and remained in that range.

b) Weight. Pre-operatively the animal weighed 25 lbs. He reached his lowest weight on the 20th day (18 lbs.). A gain in weight became manifest on the 56th day and increased gradually until, on the 231st day, the weight was 26 lbs., an increase of one pound over the pre-operative weight.

c) Food Intake. The Dog Chow intake averaged 100 gms. per day until the 22nd day, when the dog began to eat an average of about 250-300 gms. per day in addition to a half-pint of milk.

<u>Peripheral Blood Picture</u>: (Chart # 3)

Pre-operatively, the haemoglobin level was 100%, the red cell count 4,600,00 per cu.mm., and the haematocrit 46%. A gradually increasing hypochromic anemia developed and was most marked about the 38th day when the following results were obtained:

haemoglobin	68%
red cell count	4,200,000 per cu. mm.
haematocrit	29%

A gradual return to normal then began without specific treatment. At the time the animal was sacrificed the following results were obtained:

haemoglobin	118%
red cell count	6,000,000 per cu. mm.
haematocrit	50%

This represented an improvement in the blood picture over the pre-operative status. There were no abnormalities noted in the blood smear.

Autopsy Findings: (Dog # 1)

N.B. Dog # 6 was a normal healthy adult animal of similar weight and size to the preoperative weight and size of Dogs # 2 and 5. Dog # 6 weighed 26 lbs. He was sacrificed to obtain a basis of comparison for the other animals and will henceforth be referred to as Dog # 6, implying normality.

1. GENERAL REMARKS. This animal (Dog # 1) was very well nourished and had normal skin and hair. The thoracic viscera were not abnormal. The abdominal viscera were in contact with a healthy fat-containing omentum.

2. GASTRO-INTESTINAL TRACT. a) Gross: The esophagus, stomach and duodenum were of normal size and in their normal sites. The site of the anastomosis was difficult to detect because of minimal tissue reaction. The stoma was adequate. The duodenum appeared somewhat dilated and the mucosa slightly thickened. Photographs of the tract after removal in toto, and with the gut opened along the mesenteric border, are illustrated in Photograph # 3 and # 4 respectively, and can be compared with Dog # 6, illustrated in Photograph # 1 and # 2.

Peyer's patches were quite evident in the ileum. The ileum appeared slightly thickened. The colon was not remarkable.

b) Microscopic: Sections of the stomach revealed a little thickening of the muscularis only. The pyloric antrum was normal. The duodenum showed a thickened lamina propria.

The ileum revealed moderate epithelial hyperplasia, evidenced by broadening and elongation of villi, as compared with that of the control animal, and the total thickness of the lamina propria was $1\frac{1}{2}$ times the control. The glands were deeper and the cells showed an increase in mitotic activity. Superficial erosion of the tips of some villi were considered artefacts. Peyer's patches were large but not remarkable.

3.	KIDNEY.	a)	Gross	no changes
		b)	Microscopic	no changes
4.	LIVER.	a)	Gross	no changes
		b)	Microscopic	no changes
5.	ADRENAL.	a)	Gross	no changes
		b)	Microscopic	no changes
6.	PANCREAS.	a)	Gross	no changes
		b)	Microscopic	no changes

7. SPLEEN a) Gross The organ was enlarged and engorged with blood.

b) Microscopic There was an increase in the amount of red pulp and congestion with red blood cells.

N.B. The spleen and kidney of Dog # 1 are compared with those of Dog # 5 in Photograph # 8. The enlarged spleen of Dog # 1 may also be compared with that of Dog # 6, the normal, in Photograph # 6. Photomicrograph # 10 reveals the changes mentioned in the SPLEEN of Dog # 1.

Dog # 2:

General Remarks:

A massive resection was performed on this animal on October 11, 1951, leaving the proximal four inches of jejunum, measured from the ligament of Treitz, anastomosed end-to-end to the distal four inches of ileum. A progressive decline in weight and strength occurred in the first two weeks and then the animal sustained this substandard existence for approximately 2½ months, after which a further decline occurred terminating two weeks later in a moribund state of inanition, at which time the animal was sacrificed. Death was imminent on the day he was sacrificed.

Apart from the last two weeks, the animal maintained moderate activity and would run about quite actively and respond quickly. Total survival time was about four months (130 days). Towards the end of the observation period, the hair was noted to be sparse and the skin very scaly with the epidermis heaped up in areas.

<u>Fluid Balance</u>: (Chart # 4)

This animal remained in a poor state of hydration. Diarrhea was frequent and foul-smelling. There were occasional formed stools. The fluid intake averaged 300-500 cc. per day, seldom more. The urine output ranged from 100-150 cc. per day.

<u>Electrolyte Balance</u>: (Chart # 4)

1. SODIUM. The balance of sodium was erratic and unpredictable. Although not negative, accurate studies were hampered by the constant contamination of urine with faeces and undigested food. The serum sodium values remained within a normal range.

2. CHLORIDE. The balance was again erratic and inconclusive. The serum values remained within a normal range.

3. POTASSIUM. The balance was strongly negative at various times in the first month but technical difficulties precluded any further observation. The serum potassium was low in the immediate postoperative period but then rose to and remained within normal limits.

4. BICARBONATE. The serum bicarbonate was normal for the most part. On one occasion in the second month it was quite low: 15.5 meq/L.

Nitrogen Balance: (Chart # 4)

a) Intake. The caloric intake was usually quite low, ranging from 100-400 calories per day. The intake of dog food was erratic. The animal seldom consumed more than 150 grams per day, and frequently no solid food was taken. It is interesting to note that, although ordinary milk was liked by this animal, a milk of high fat content, such as Jersey milk, was strongly rejected.

b) Nitrogen. The balance was negative in the early period coincident with poor intake and loss of weight. It later remained in equilibrium but again accuracy in the balance is questioned.

c) Weight. The initial weight was 25 lbs. This decreased to 19 lbs., by about the 18th day and remained there until the 32nd day. Thereafter it ranged between 19 and 21 lbs. until the 115th day, when it began to fall, reaching 15 lbs. at the time the animal became moribund on the 130th day.

<u>Peripheral Blood Picture</u>: (Chart # 5)

Preoperative findings - haemoglobin 108%

red cell count 5,300,000 per cu.mm.

haematocrit 46%

Immediately following operation there was a marked rise in all the values coincident with the postoperative dehydrated state. A return to the initial values occurred by the 18th day. A normal blood picture then persisted until about the 50th day. Thereafter there was a gradual decline until there was a marked hypochromic anemia by the 130th day, at which time, just before sacrificing the animal, the following values were obtained:

haemoglobin 72%

red cell count 4,000,000 per cu.mm.

haematocrit 32%

<u>Autopsy Findings</u>:

1. GENERAL REMARKS. The animal was extremely emaciated. There were ulcers over the extensor aspect of the fore-legs. The skin was scaly and thickened. The hair texture was silky and sparse. The ears and sternal area were markedly involved with these abnormalities. There was complete absence of body fat.

2. GASTRO-INTESTINAL TRACT. a) <u>Gross</u>: The stomach was only slightly dilated and the mucosa normal. The duodenum was moderately dilated and felt thicker than normal. The site of the anastomosis was not remarkable and the stoma was adequate.

The colon was not remarkable.

b) Microscopic:

a) Stomach: The only change noted was an increase in the number of parietal cells in the pyloric antrum.

b) Duodenum: Marked hyperplasia was noted with broad club-shaped villi covered with wavy tall columnar epithelium. The total depth of the lamina propria was twice that of the control animal. The glands were also deeper and more numerous. There was a definite increase in the number of mitoses, especially in the basal parts of the glands. The individual cells were taller and possessed more cytoplasm than those of the control animal (Dog # 6). Photomicrograph # 2 reveals the changes of the duodenum from Dog # 2.

c) Jejunum: The four inches of proximal jejunum, which was anastomosed to the distal ileum, revealed a marked epithelial hyperplasia similar to that described above in the duodenum (as compared with that of the control animal). The total depth of the lamina propria was again twice that of the control. The myenteric plexus of Auerbach was prominent. Photomicrograph # 6.

d) Colon: There was slight thickening of the lamina propria in the ascending colon but otherwise no changes.

3. KIDNEY.	a)	Gross	much reduced in size
	b)	Microscopic	no changes
4. ADRENALS.	a)	Gross	no changes
	b)	Microscopic	no changes
5. PANCREAS.	a)	Gross	no changes
	b)	Microscopic	no changes

6. LIVER. a) Gross There was the suggestion of patchy areas of lighter color.

b) Microscopic Diffuse vacuolization of hepatic cells, probably with glycogen.

7. SPLEEN. a) Gross Shrunken and about one-fifth the size of normal.

b) Microscopic no changes

8. SKIN. Microscopic This showed infestation with a parasite enclosed in a thickened papillary keratinized layer. The underlying epidermis was acanthotic and the superficial dermis possessed a fairly marked small round cell inflammatory infiltrate. Photomicrograph # 13.

Dog # 5:

General Remarks:

This animal was operated upon February 5, 1952, and a resection of small intestine, similar in extent and location as Dog # 2, was performed. At this time, however, the decision to forego balance studies of electrolytes or nitrogen had been made. This animal was no exception to the rule and for the most part had diarrhea throughout the observation period.

The animal recovered from the operation quite well and, although it lost a great amount of weight, maintained a normal state of activity until just prior to the 85th day when lassitude, weakness, a stumbling gait and dehydration occurred. The animal was sacrificed on May 1, 1952, in a moribund state of inanition.

<u>Weight</u>: (Chart # 6)

Preoperative weight	29 lbs.
Weight at autopsy	11 lbs.

<u>Serum Electrolytes</u>: (Chart # 6)

Serum sodium, potassium, chloride and bicarbonate remained within normal limits.

<u>Peripheral Blood Picture</u>: (Chart # 6)

Preoperative findings -	haemoglobin	110%
	red cell count	6,300,000 per cu. mm.
	haematocrit	50%

There was then a marked fall in all findings so that on the 85th day the findings were:

haemoglobin	60%

red cell count 2,000,000 per cu. mm.
haematocrit 25%

Autopsy Findings:

1. GENERAL REMARKS. The animal was emaciated and possessed skin lesions similar to Dog # 2. Inanition and dehydration were severe at death.

2. GASTRO-INTESTINAL TRACT. (Photographs # 5,6 and 8)

a) Gross: The stomach was moderately dilated and contained a large hair-ball. The duodenum was only moderately dilated. The colon was not remarkable.

b) Microscopic:

i)	Stomach	no changes
ii)	Duodenum	no changes (Photomicrograph # 4)
iii)	Colon	no changes

3. KIDNEY. a) Gross Very small with complete absence of perirenal fat.

b) Microscopic Slight vacuolation of scattered groups of distal convoluted tubules.

4. LIVER. a) Gross No changes other than small size.

b) Microscopic A few hepatic cells contain small fatty droplets.

5. ADRENAL. a) Gross no changes

b) Microscopic slight hyperplasia

6. PANCREAS. a) Gross small

b) Microscopic no changes

7. SPLEEN. (Photomicrograph # 12)

a) Gross Very shrunken and about one-tenth the size of normal.

b) Microscopic Decrease in red pulp with approximation of trabeculae and slight atrophy. The malpighian corpuscles were small.

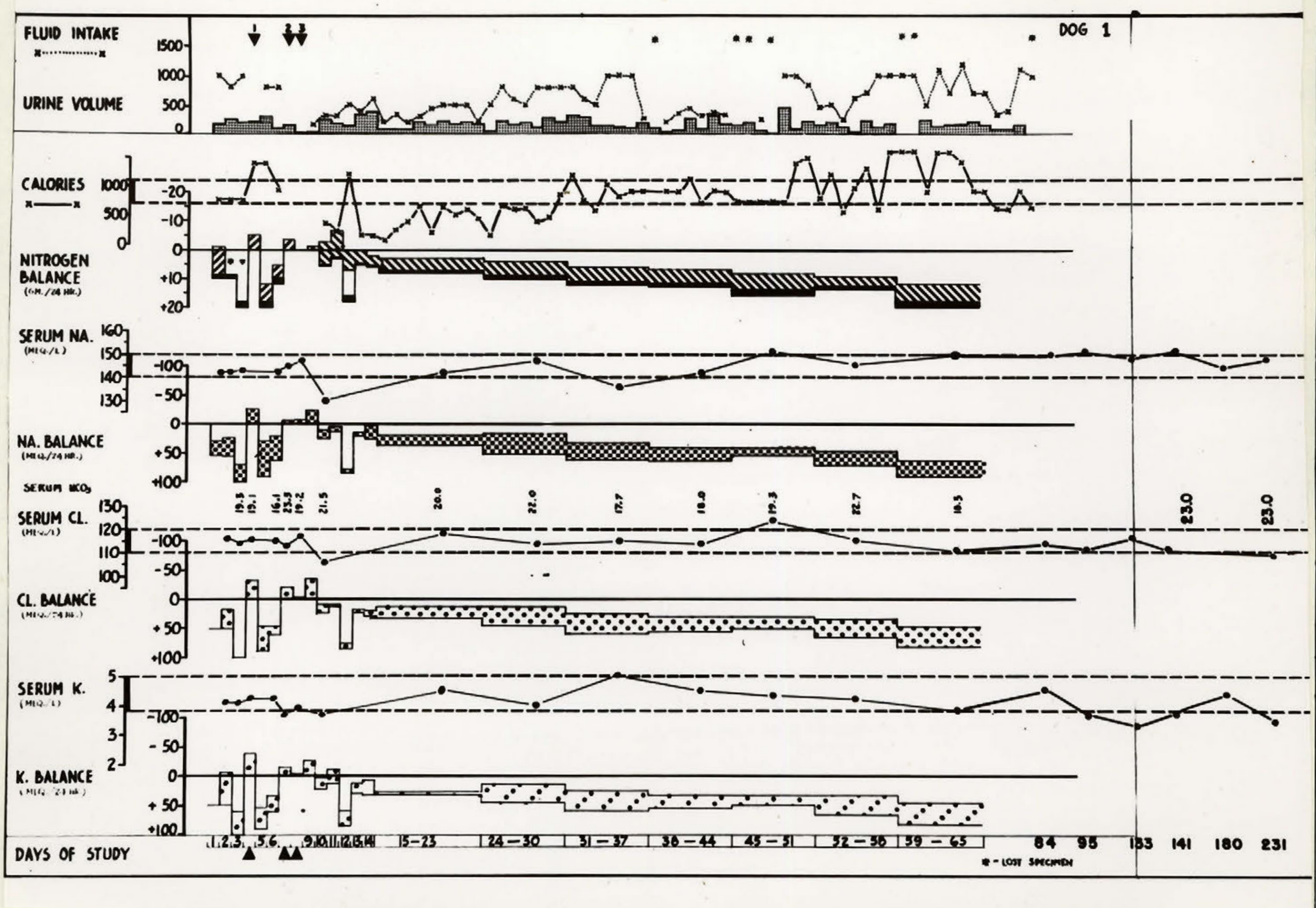


CHART # 2

Dog # 1: 1 - Anesthesia for de-vocalizing

2 - Pre-operative fast

3 - Day of resection

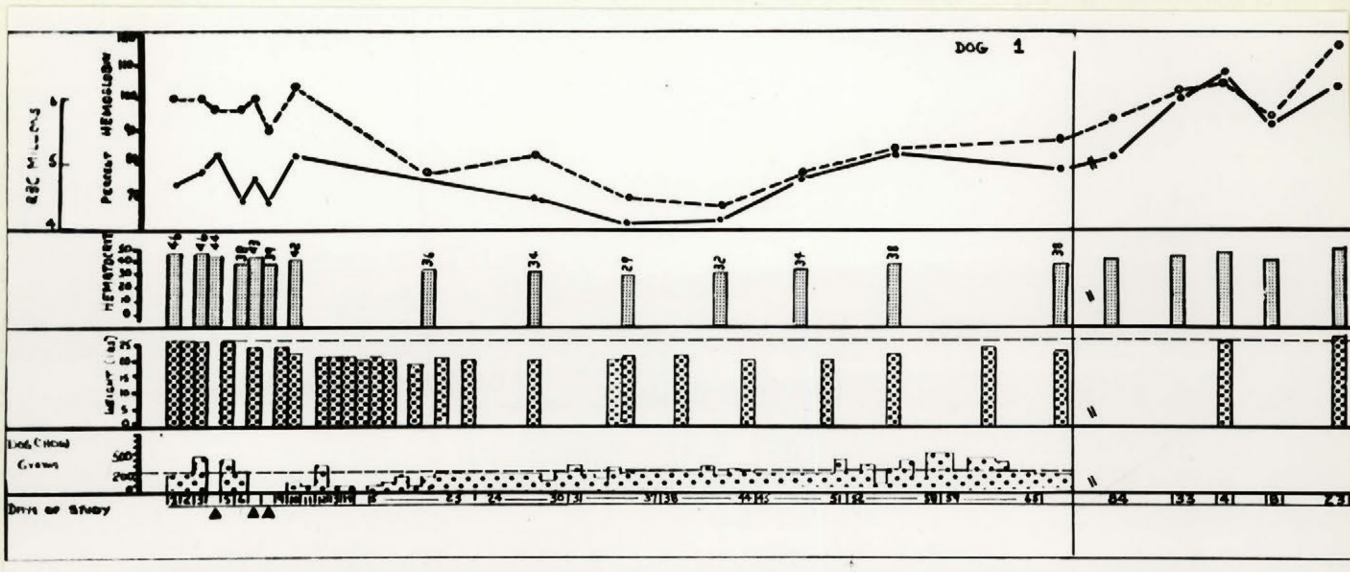


CHART # 3

Dog # 1: The upper portion depicts the haemoglobin in dotted lines and the red cell count in solid lines.

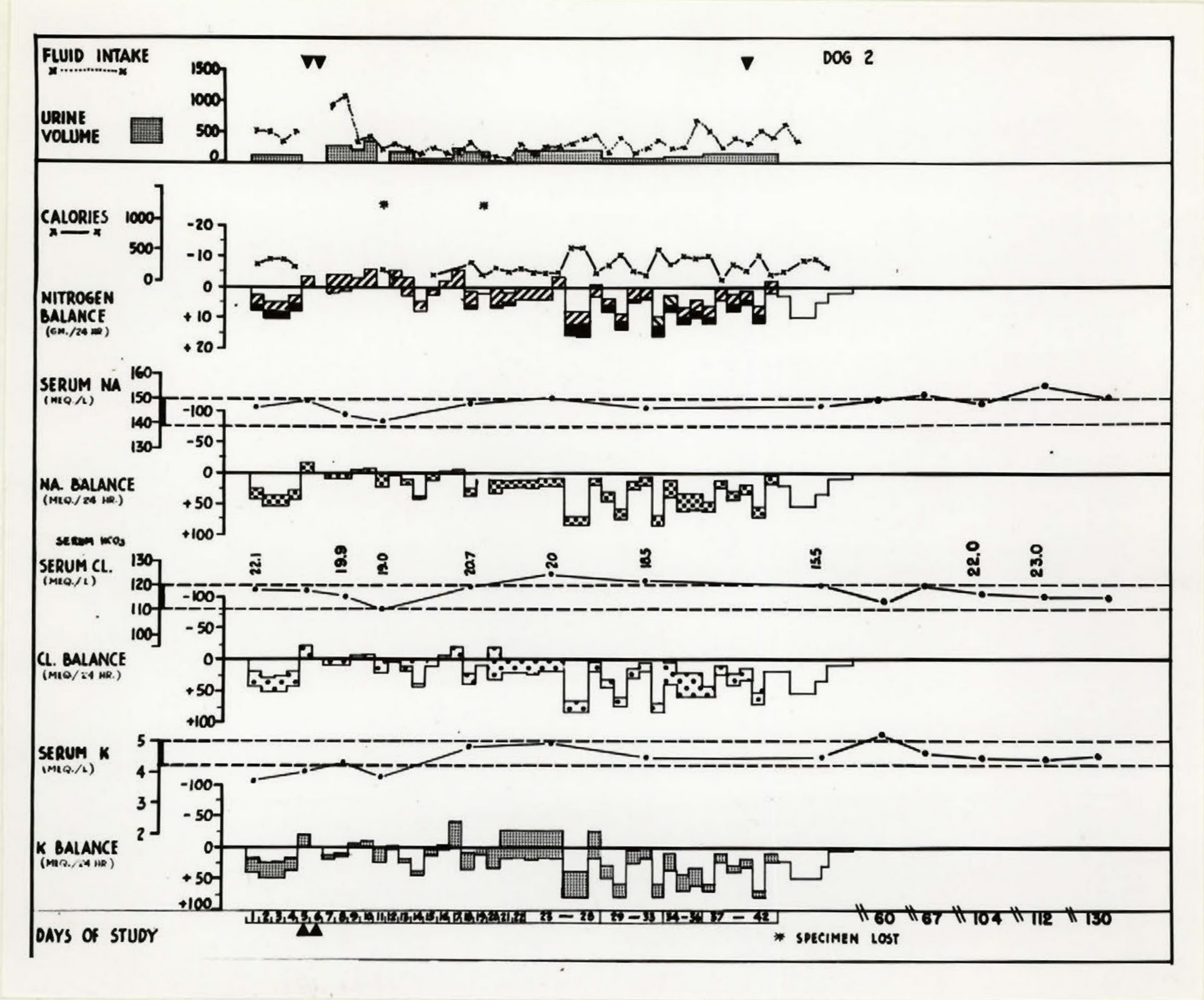


CHART # 4

Dog # 2: Operation.

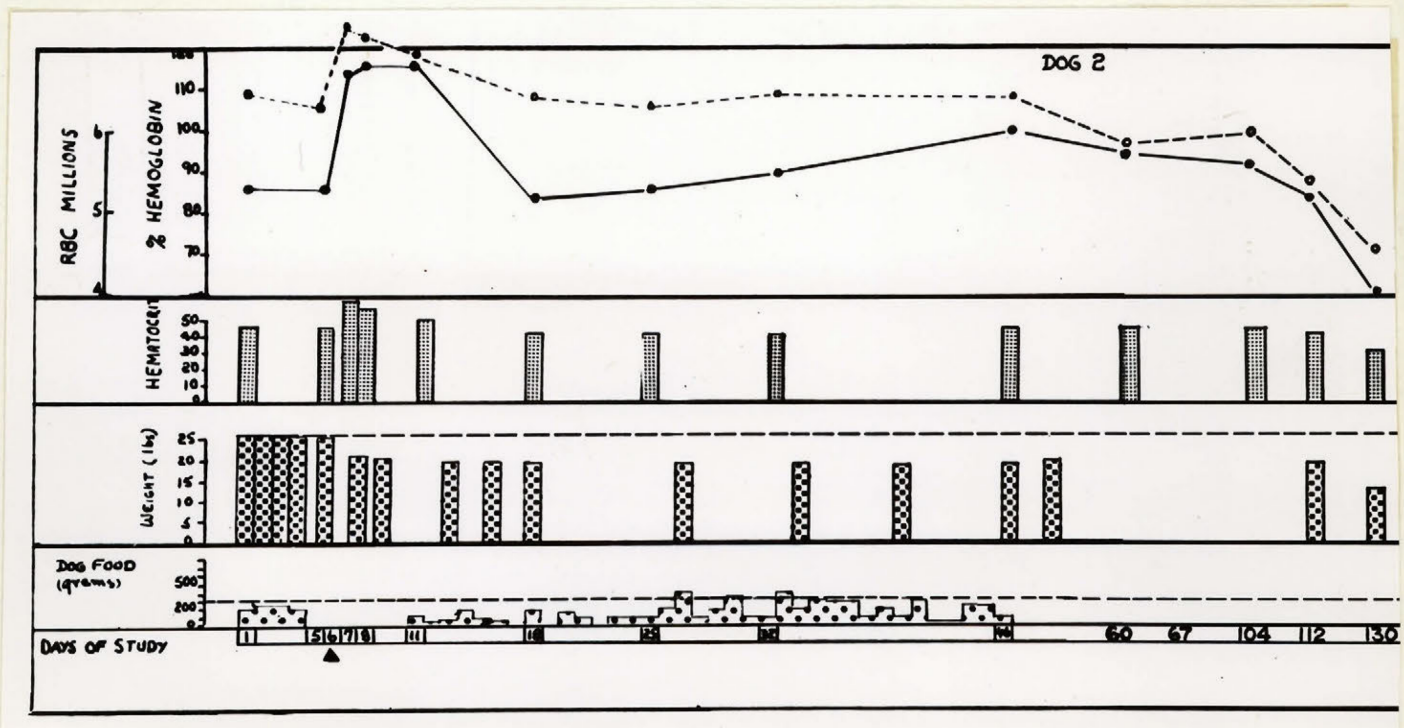

DOG 2
RBC MILLIONS
% HEMOGLOBIN
HEMATOCRIT
WEIGHT (lbs)
DOG FOOD (grams)
DAYS OF STUDY
60
67
104
112
130

CHART # 5

Dog # 2.

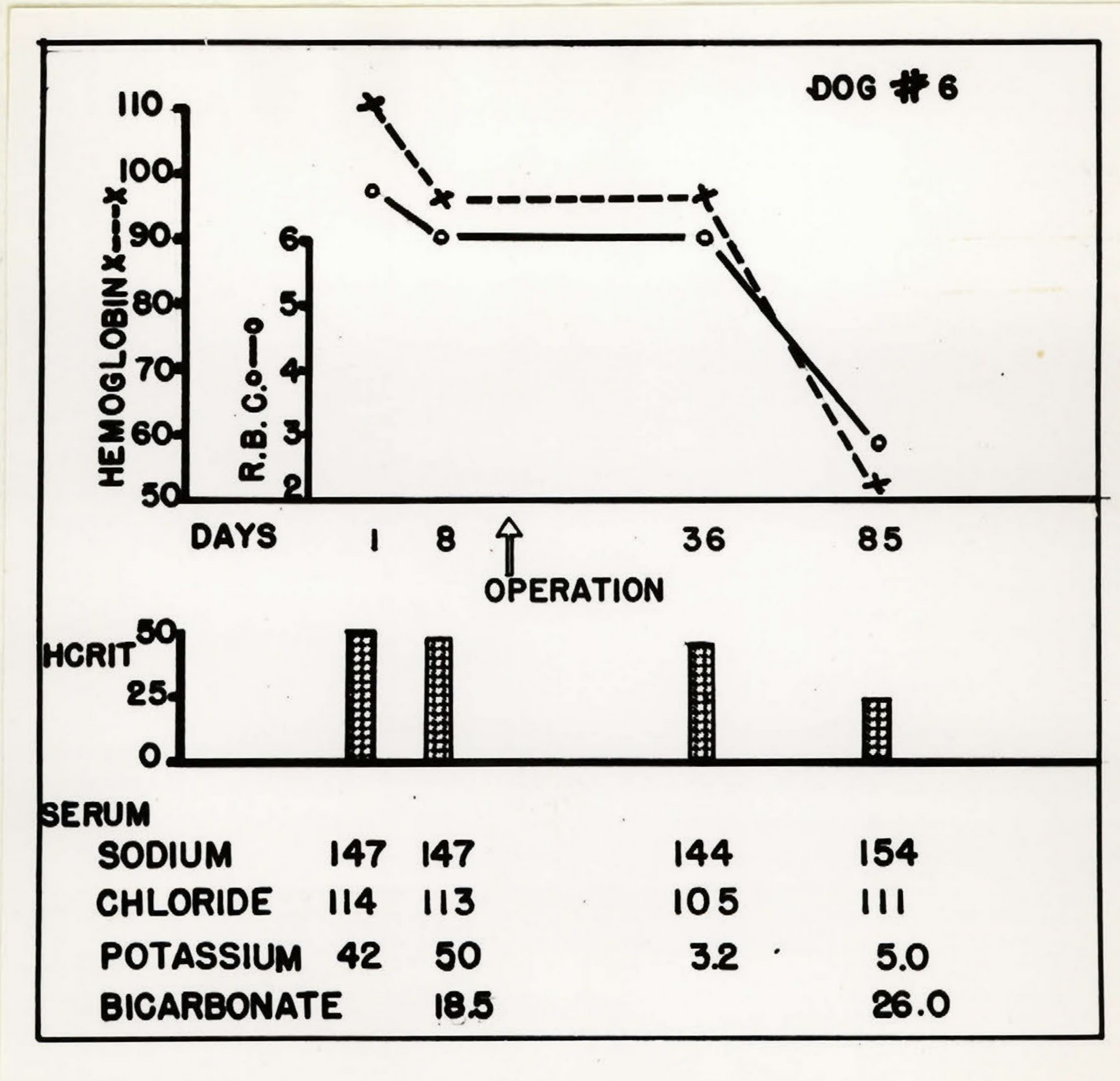

DOG # 6
HEMOGLOBIN X---X
110
100
90
80
70
60
50
R.B.C. o—o
6
5
4
3
2
DAYS
1
8
36
85
OPERATION
HCRIT
50
25
0
SERUM
SODIUM 147 147 144 154
CHLORIDE 114 113 105 111
POTASSIUM 42 50 3.2 5.0
BICARBONATE 18.5 26.0

CHART # 6

Dog # 5.

PHOTOGRAPH # 1

Dog # 6: Gastro-intestinal tract of normal adult dog.

1. Pylorus

3. Duodeno-jejunal junction

5. Ileo-caecal valve

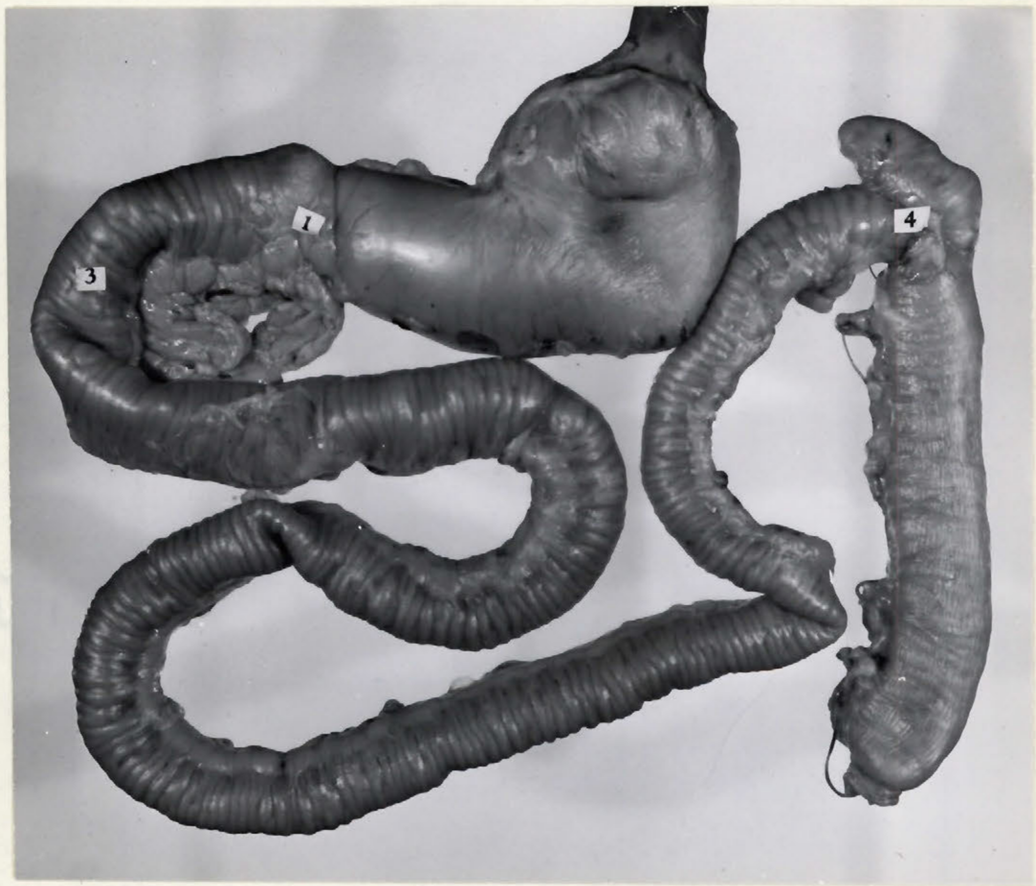
PHOTOGRAPH # 2

Dog # 6: Gastro-intestinal tract of normal dog. The duodenum is opened from the pylorus

1. To the duodeno-jejunal junction

3. A segment of jejunum, ileum and colon are also opened

5. Represents the ileo-caecal area.



PHOTOGRAPH # 3

Dog # 1: Gastro-intestinal tract after resection of one-half the small intestine.

1. Pylorus

3. Ampulla of Vater area

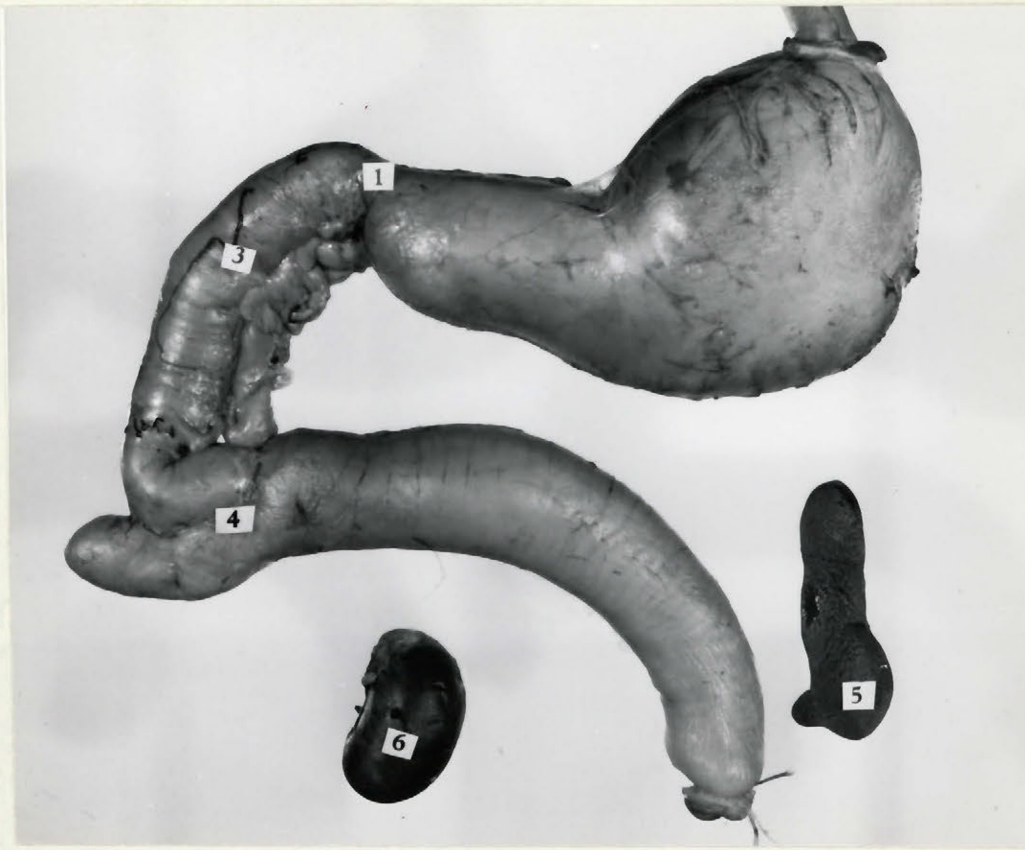
5. Ileo-caecal area

PHOTOGRAPH # 4

Dog # 1: Gastro-intestinal tract after resection of one-half of the small intestine. The entire gut has been laid open along the anti-mesenteric border.

1. Pylorus

4. Ileo-caecal area



PHOTOGRAPH # 5

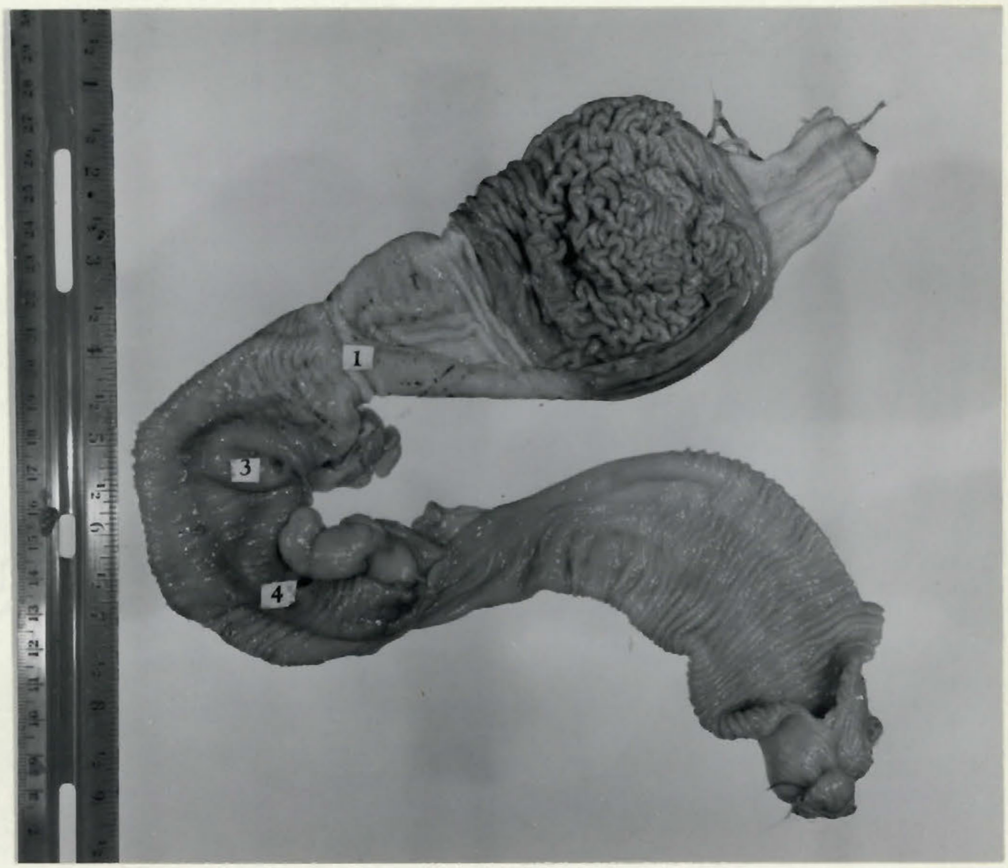
Dog # 5: Gastro-intestinal tract of dog after resection of total small intestine.

1. Pylorus

2. Ampulla of Vater area

4. Ileo-caecal area

The spleen (5) and kidney (6) are also shown.



PHOTOGRAPH # 6

Dog # 5: Gastro-intestinal tract of dog after removal of entire small intestine. The gut has been laid open along anti-mesenteric border.

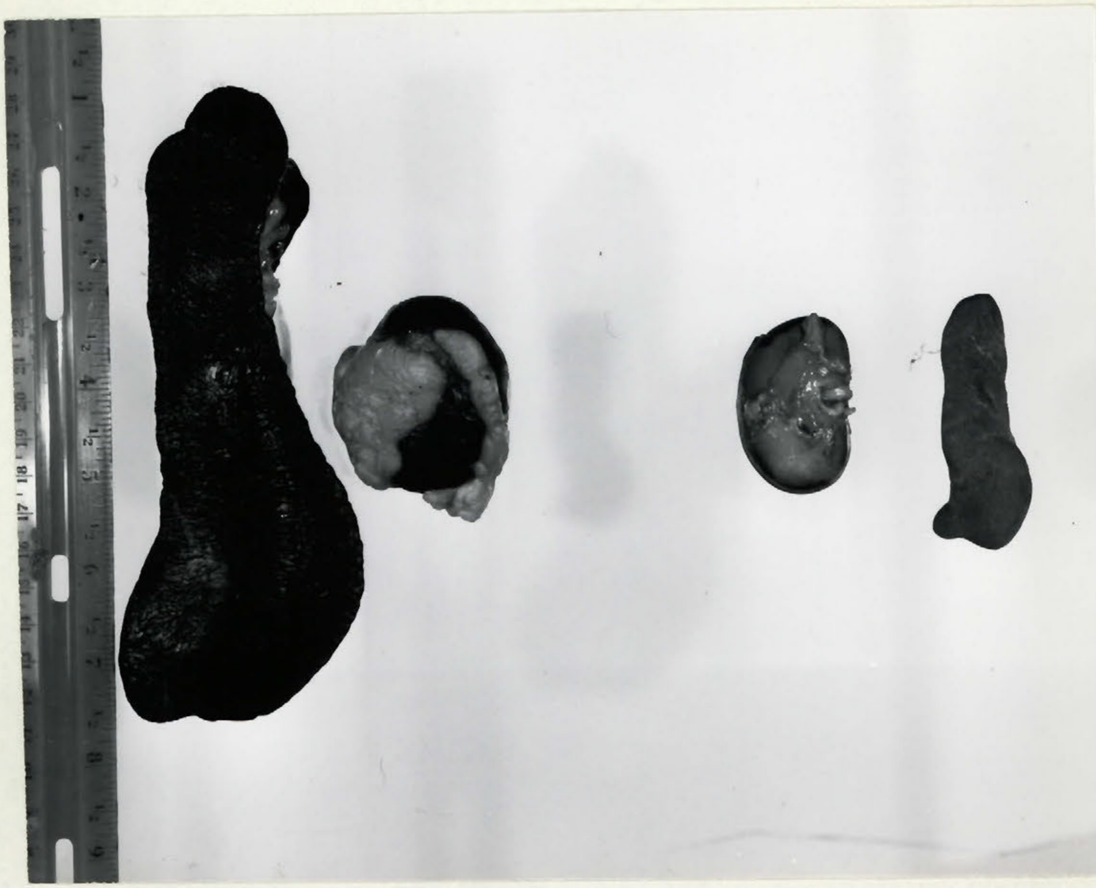
1. Pylorus

3. Ampulla of Vater area

4. Site of anastomosis

PHOTOGRAPH # 7

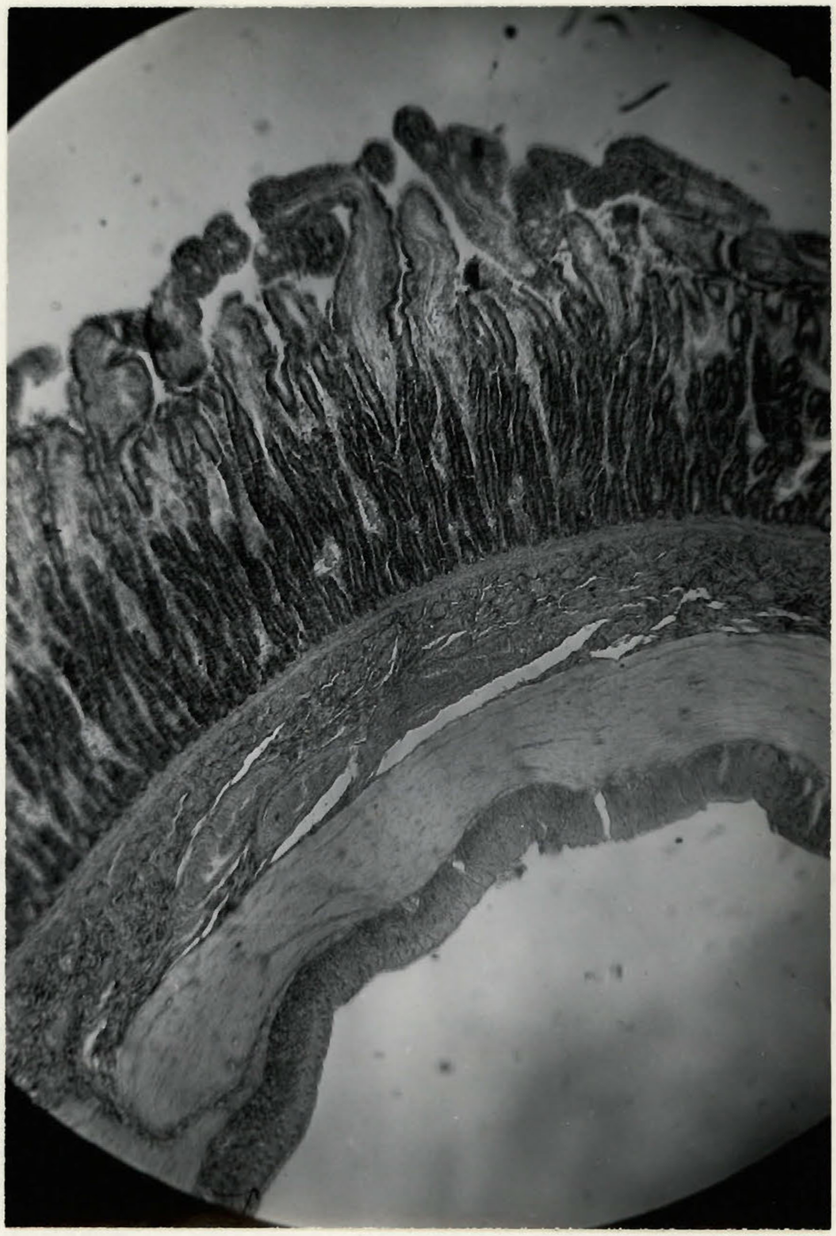
Spleen and kidney of normal dog # 6.



PHOTOGRAPH # 8

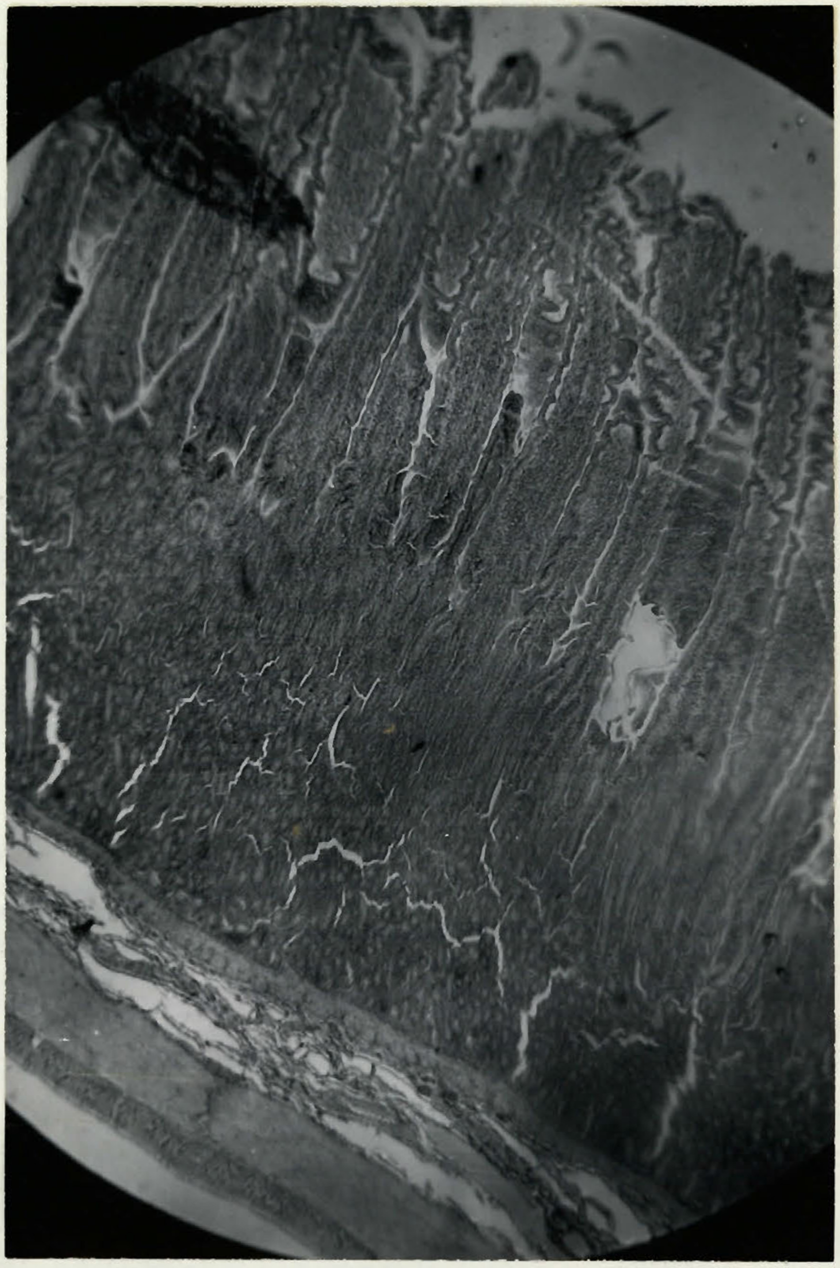
Spleen and kidney of Dog # 1 - on the left

Spleen and kidney of Dog # 5 - on the right



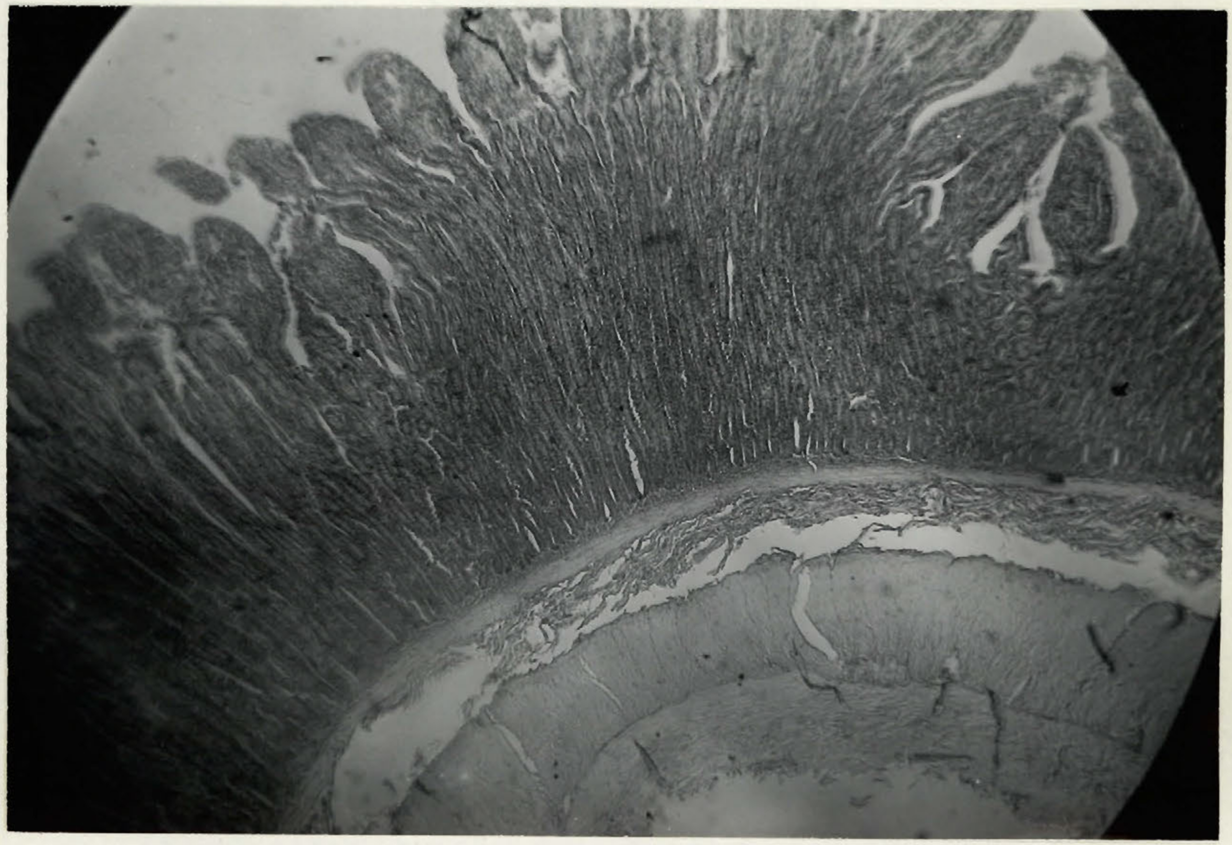
PHOTOMICROGRAPH # 1

Dog # 6: Duodenum - normal x 22



PHOTOMICROGRAPH # 2

Dog # 1: Duodenum x 22.

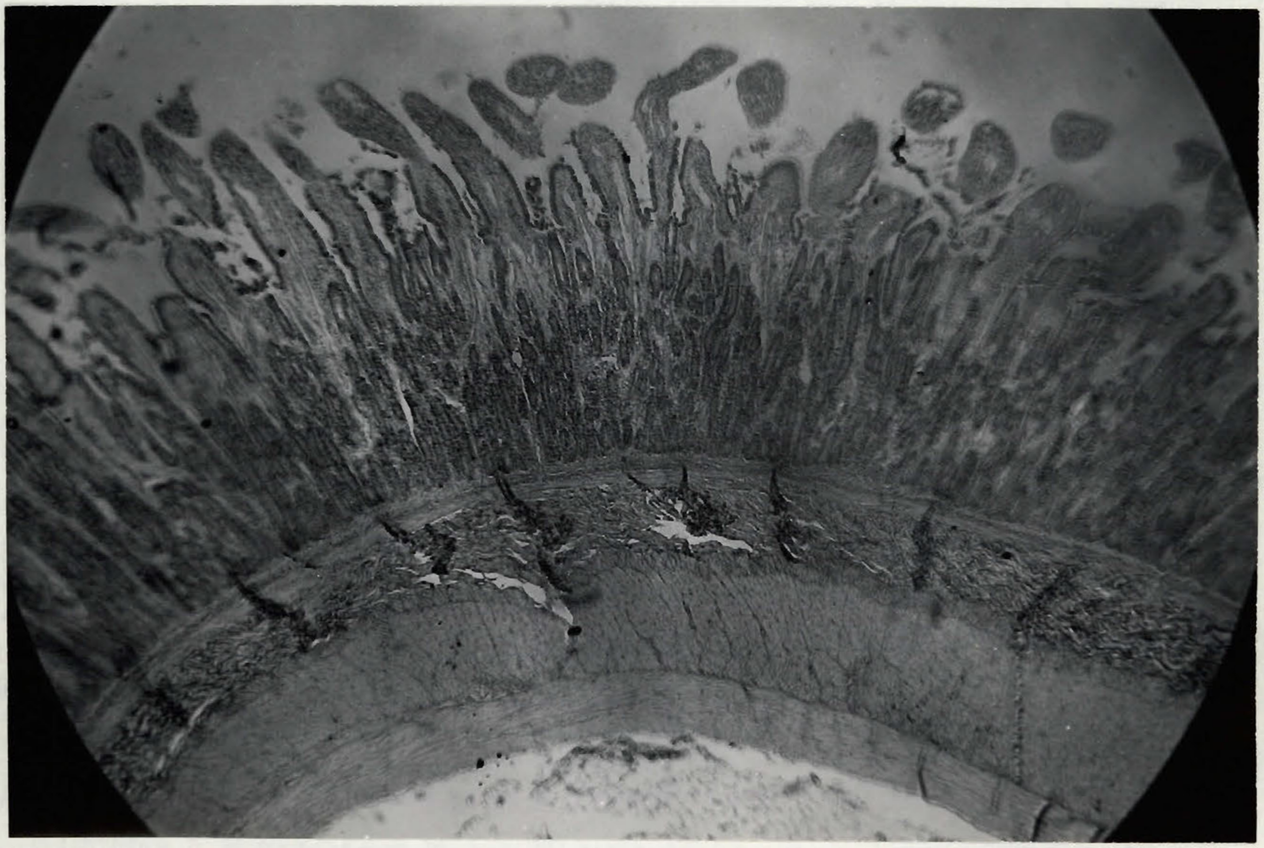


PHOTOMICROGRAPH # 3

Dog # 2: Duodenum x 22.

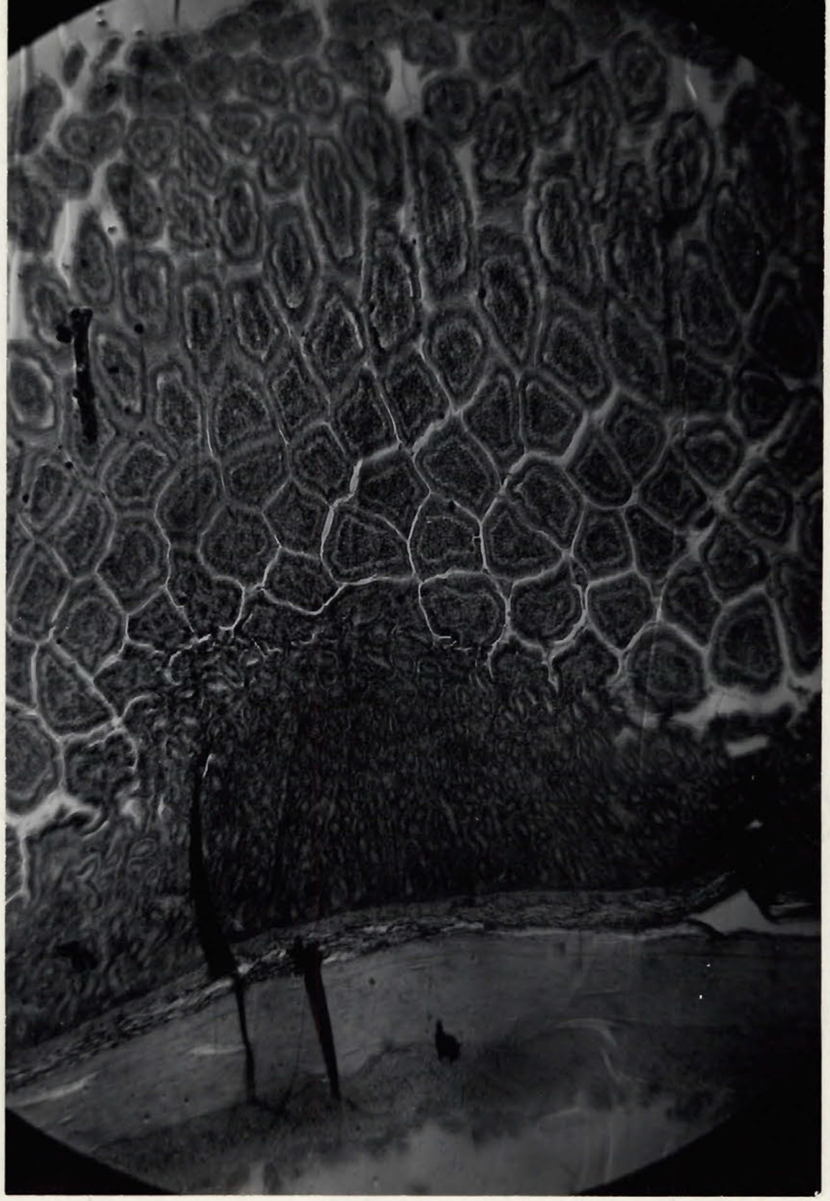
PHOTOMICROGRAPH # 4

Dog # 5: Duodenum x 22.



PHOTOMICROGRAPH # 5

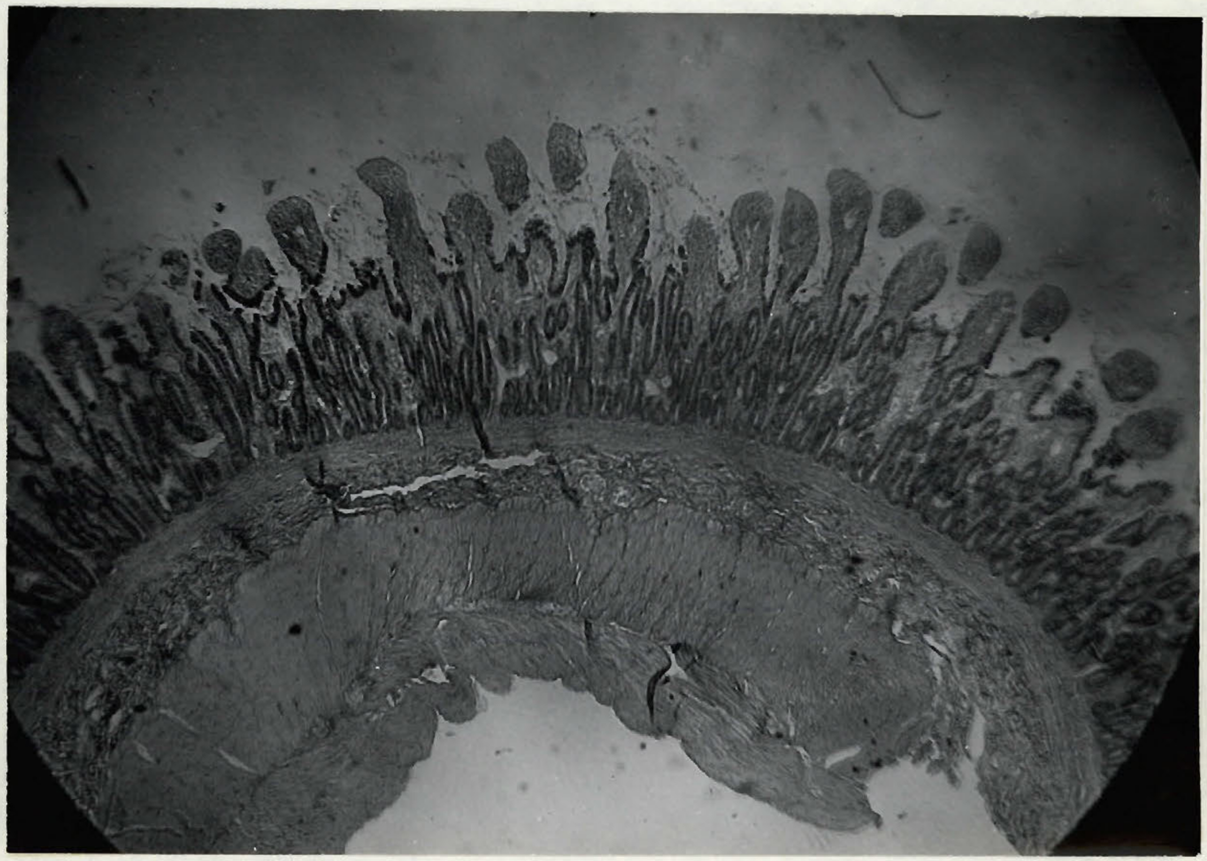
Dog # 6: Jejunum x 22 - Normal dog



PHOTOMICROGRAPH # 6

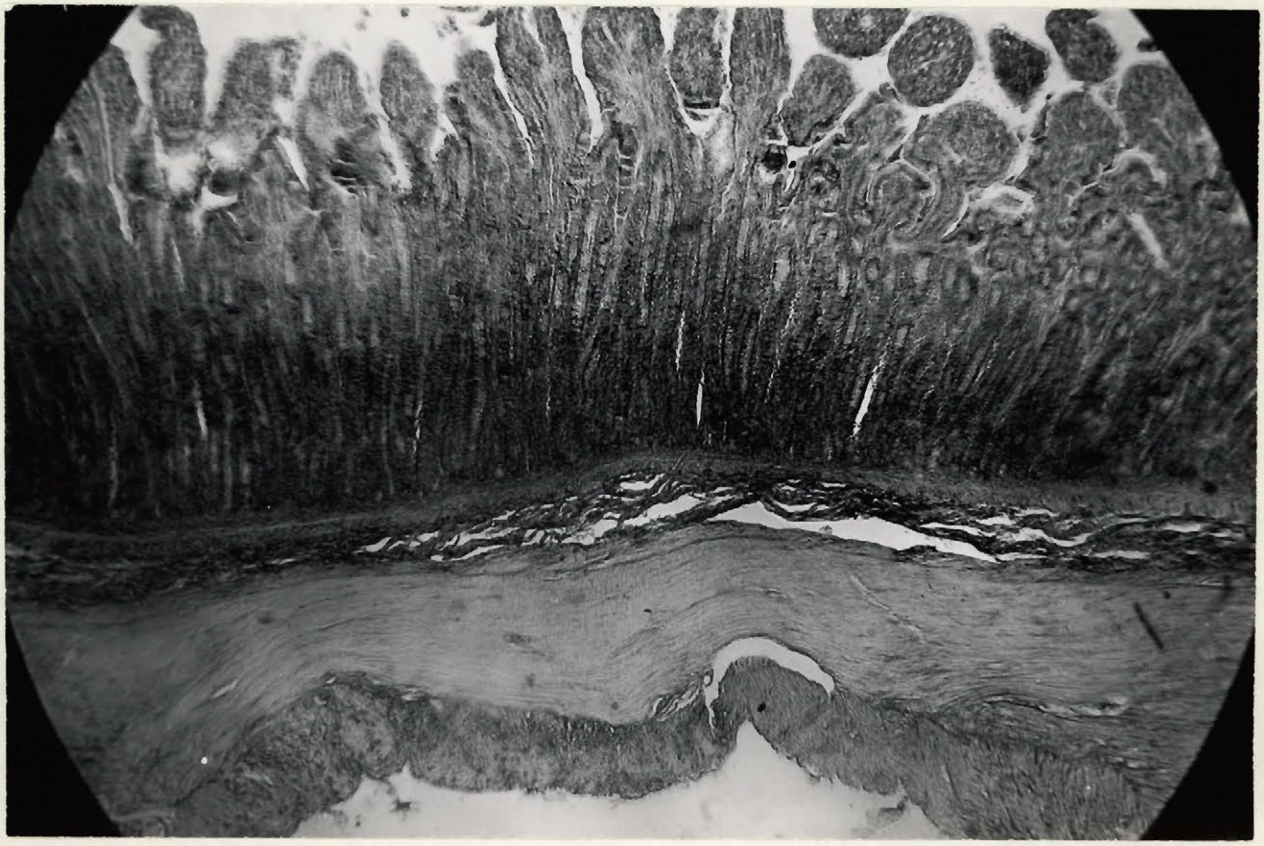
Dog # 2: Jejunum - Magnification x 22

This section is a tangential one and is therefore not very good for comparison.



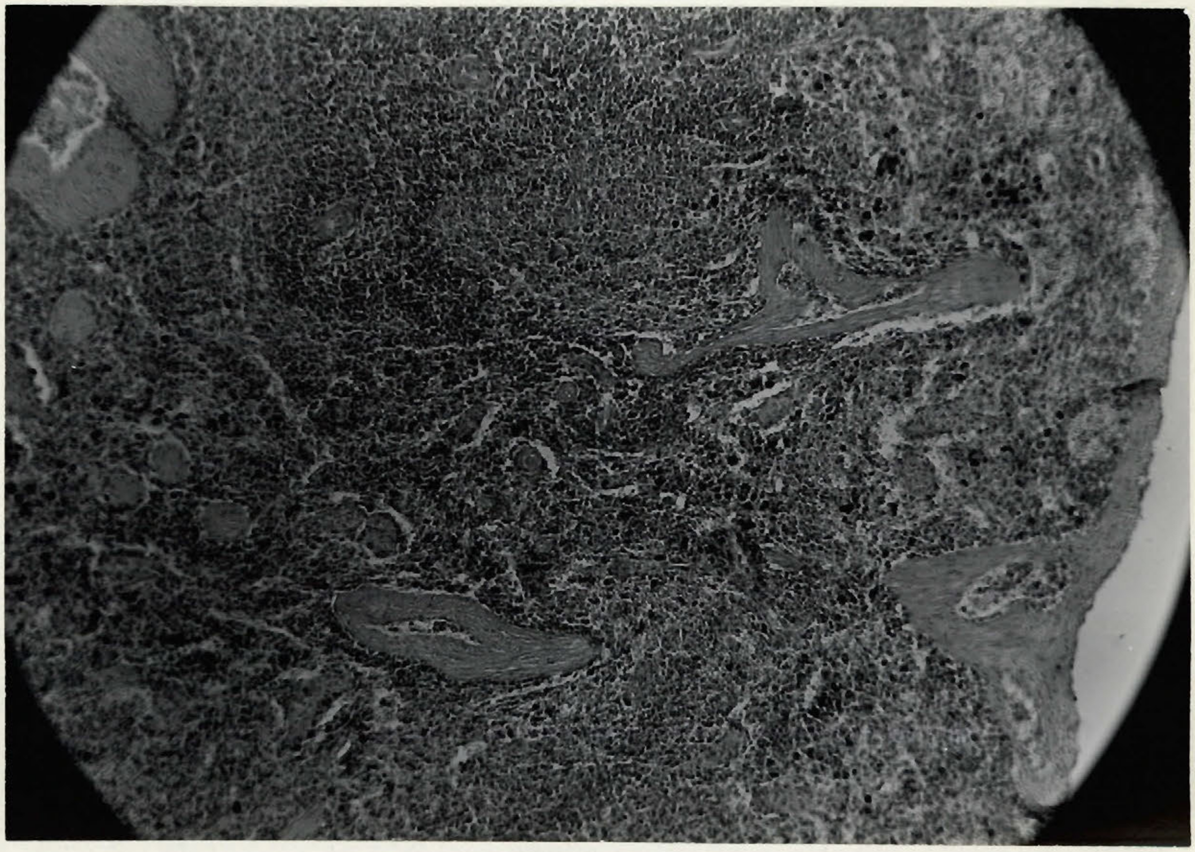
PHOTOMICROGRAPH # 7

Dog # 6: Ileum - Normal dog x 22



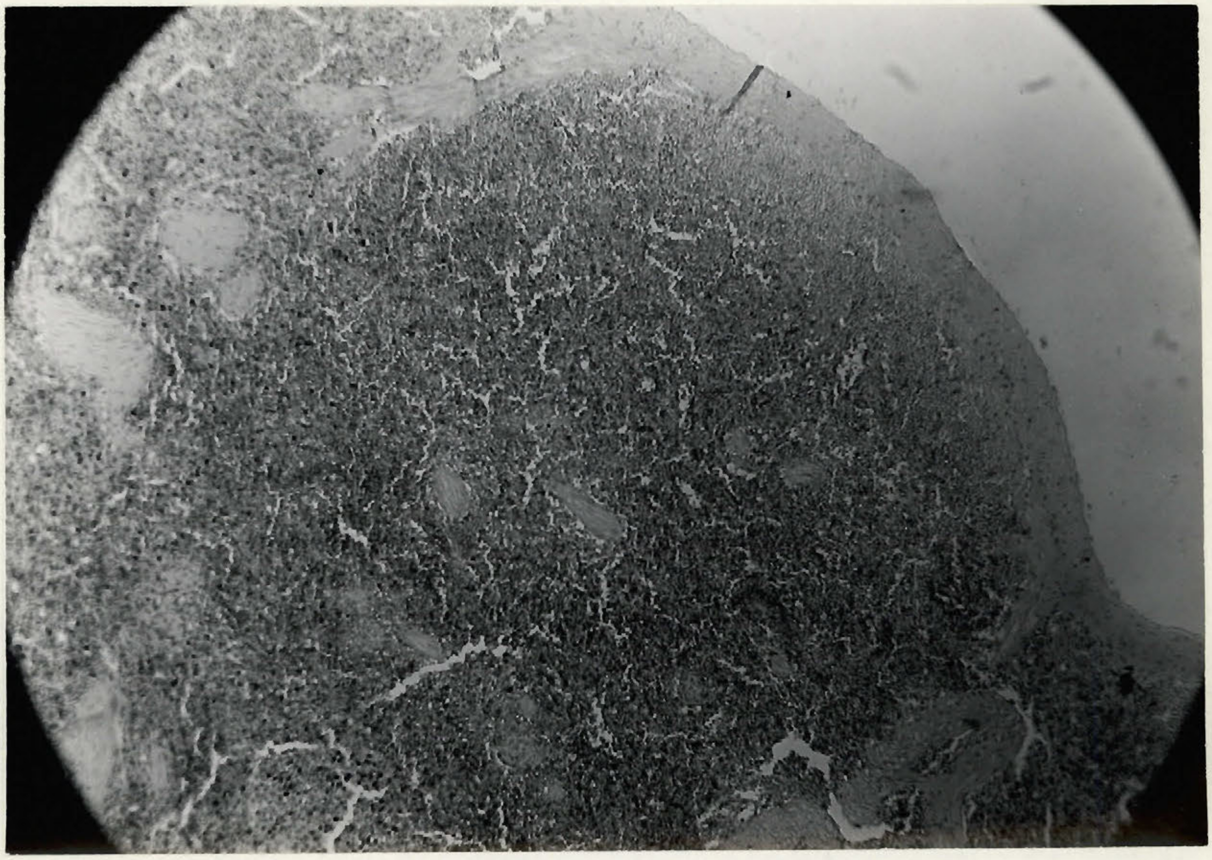
PHOTOMICROGRAPH # 8

Dog # 1: Ileum x 22.



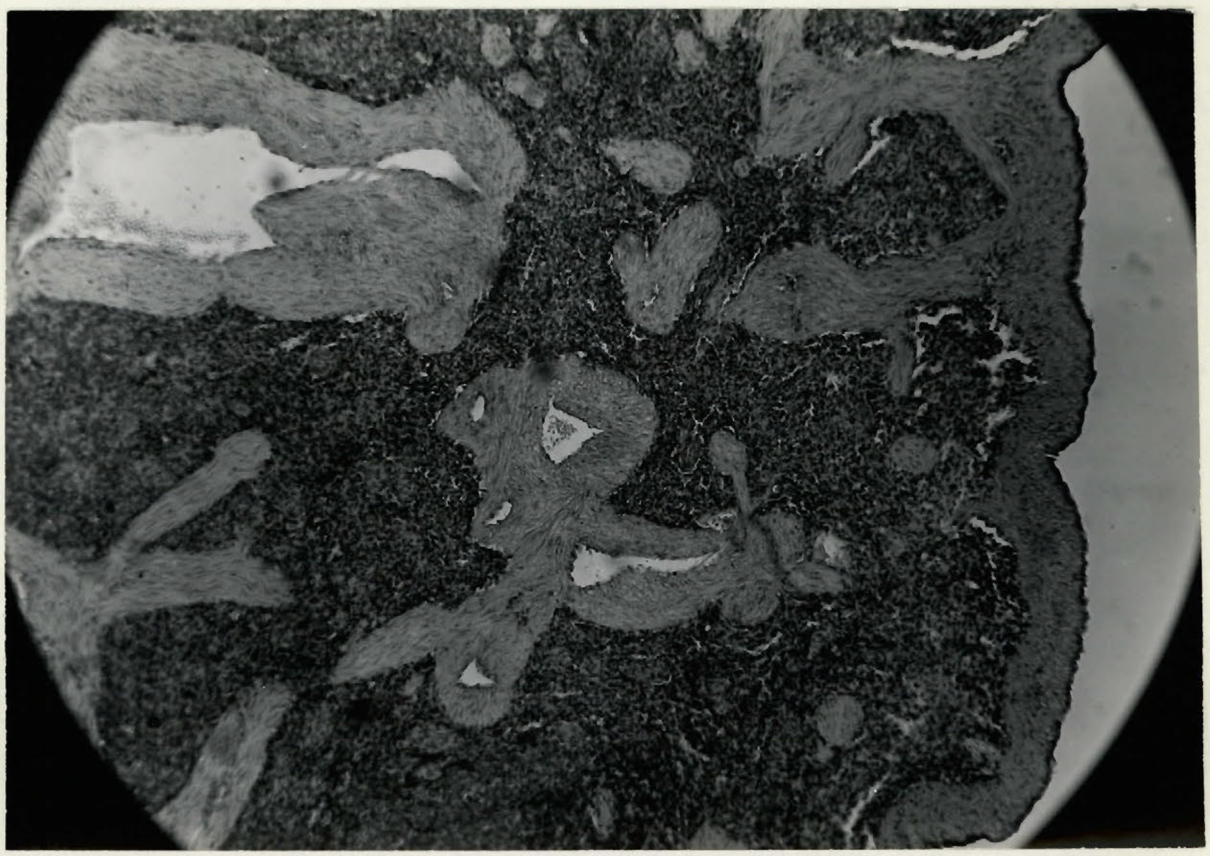
PHOTOMICROGRAPH # 9

Dog # 6: Spleen x 22.



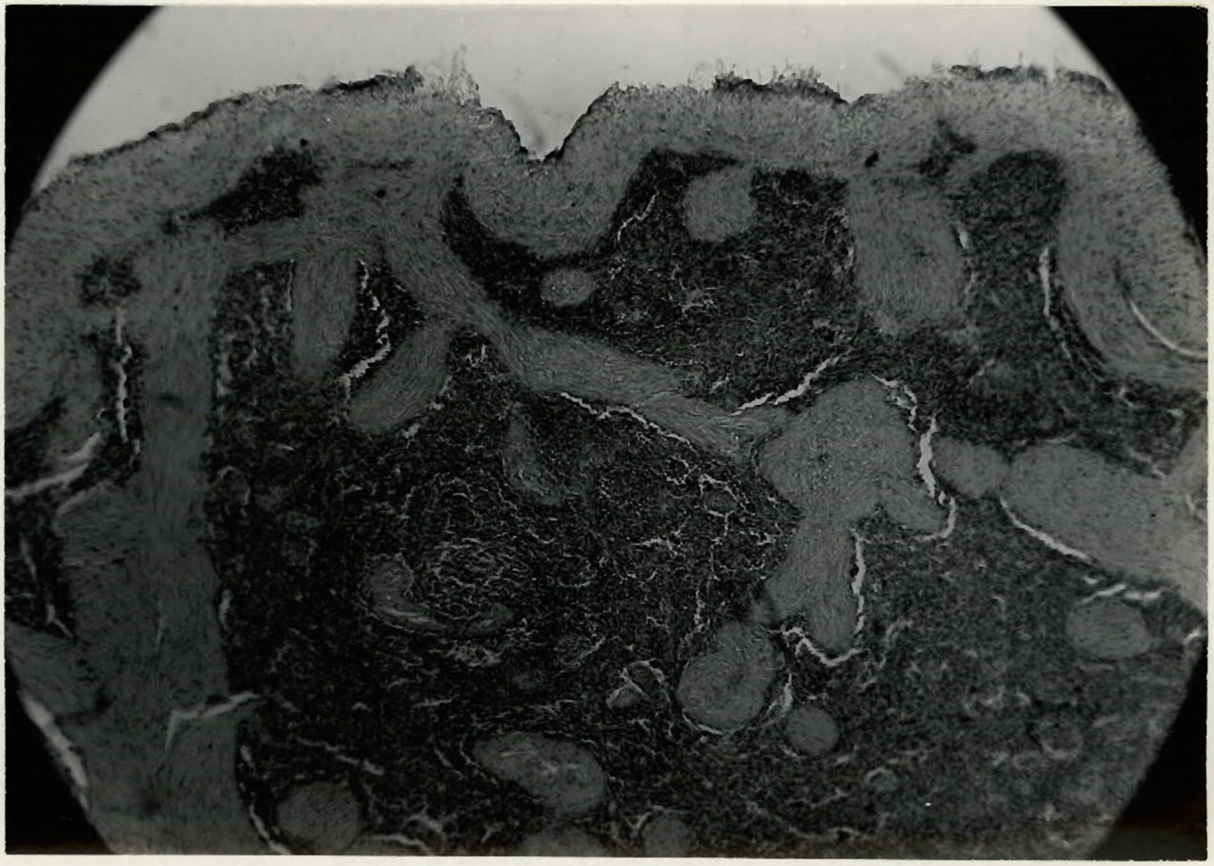
PHOTOMICROGRAPH # 10

Dog # 1: Spleen x 22.



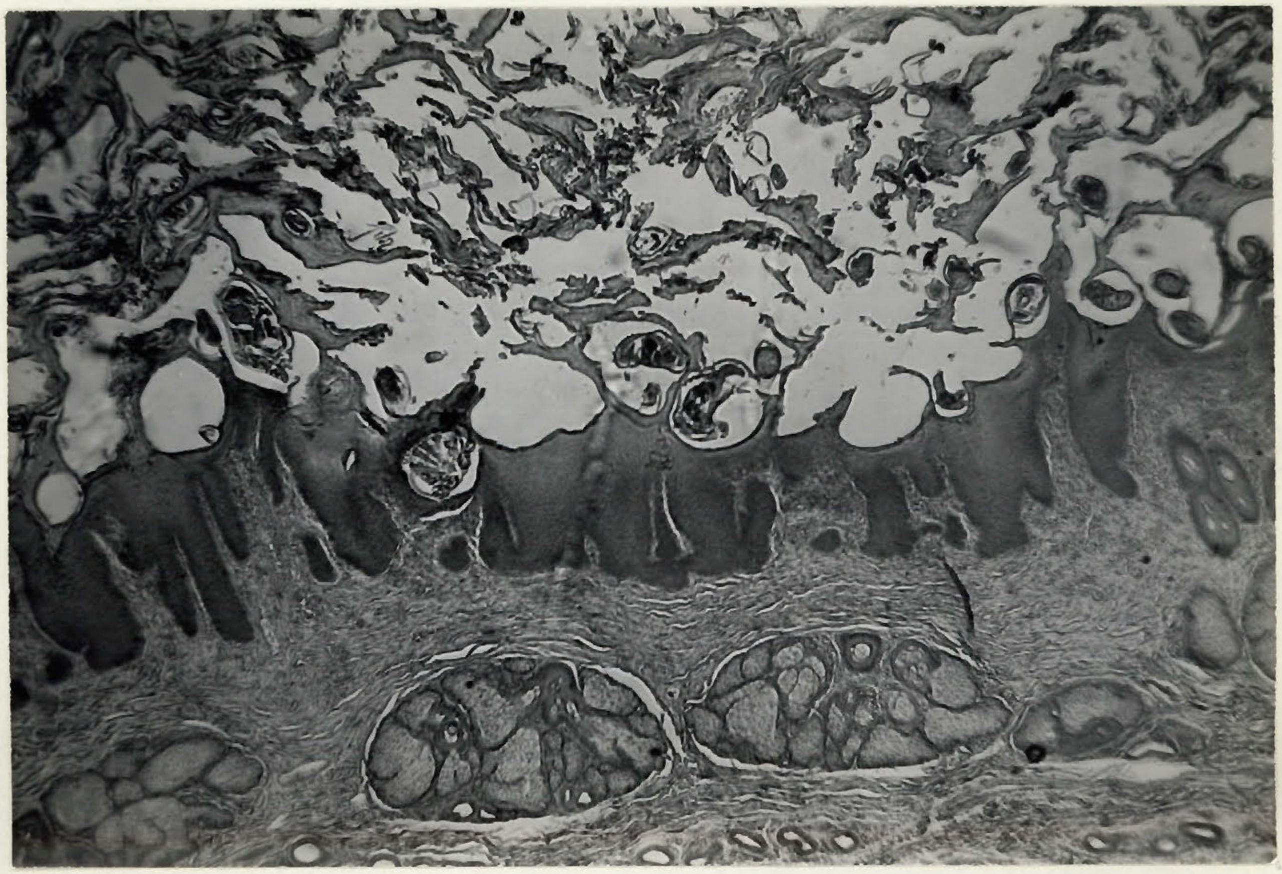
PHOTOMICROGRAPH # 11

Dog # 2: Spleen x 22.



PHOTOMICROGRAPH # 12

Dog # 5: Spleen x 22.



PHOTOMICROGRAPH # 13

Dog # 2: Skin of the sternal area showing acantholic epidermis and parasites enmeshed in keratin layer. x 58.

CASE NO. V-33038 QUEEN MARY VETERAN'S HOSPITAL

CLINICAL SUMMARY

This man, aged 46, was admitted to the QMVH on June 10, 1951, suffering from rheumatic heart disease. He was found to have mitral valve stenosis and insufficiency, aortic valve insufficiency and auricular fibrillation. Three days later he developed acute abdominal pain, and the diagnosis of mesenteric artery embolism was entertained. The following day a laparatomy revealed massive gangrene extending from the third portion of the duodenum to the right transverse colon; this area was resected and a duodenostomy and colostomy performed. He astounded everyone by actually improving somewhat in the next month, so an end-to-end anastomosis between the terminal portion of the second stage of the duodenum and the transverse colon was made on July 27, 1951. He remained essentially bedridden for the entire period of hospitalization and expired on April 25, 1951, a little over 10 months from the date of his admission. He was bedridden for the entire time except for a short period each morning when his bed was made up.

He was very difficult to handle, being unco-operative in almost everything he was asked to do. He never manifested a frank psychosis but psychologically his illness altered his previous personality to one of a complaining and demanding type.

He became quite irresponsible in many ways, which made accurate intake and output records difficult to keep. He was profoundly weak on many occasions. He ate large meals but largely of his own choosing, high in fat content by preference. He developed peculiar tastes and food fancies.

He complained bitterly of anal and rectal pain about September 22nd, and a hemorrhoidectomy afforded him some relief. This complaint reappeared in April, 1952, and a second hemorroidectomy was done April 18, 1952, just seven days before his death.

Thrombosis of the peripheral veins early in the patient's course precluded any extensive serum or whole blood investigations. Furthermore, the man frequently refused any venipuncture whatever or even parenteral injections.

Weight: (Chart # 10)

Pre-operatively the man reported his weight as being 78 kilograms. At death he weighed 42 kilograms, representing a loss of approximately one-half the body weight. Hiw weight had fallen to 62 kg. by August, then decreased to about 50 kg. by September. Thereafter, his weight remained fairly constant with small fluctuations of one or two kilograms (presumably due to fluid retention and diuresis as a consequence of his heart disease) until February, 1952. A further gradual decrease in weight occurred in the next two months reaching 42 kg. at the time of death.

Fluid Balance: (Chart # 10)

The fluid intake ranged from two to three litres per day. The measured fluid output equalled the intake on many occasions but was seldom less. As shown on the chart, the proportion of total fluid output that represented stool volume was always two or three times the urine volume. The urine volume seldom exceeded 500 cc. per day. In March and April the volume of intake was not calculated as the patient had become totally unreliable in his handling of fluids. The stool : urine ratio of output remained similar but the total volume was considerably less, ranging from one to two litres. This, presumably, was because of a diminished intake compared with the previous months.

Protein Metabolism:

1. NITROGEN BALANCE. A rough and admittedly not very accurate nitrogen balance was computed on various days in the period from September 1st to November 1st. Generally the balance remained in equilibrium during this period on an intake of about 10 to 15 grams of nitrogen The proportion of faecal nitrogen to urine nitrogen was found to be in the vicinity of 3 : 4 during the month of August but then changed to a ratio of 3 : 1 in October. Normally this ratio is 1 : 10. It can be seen in the chart that faecal nitrogen represented almost two-thirds to three-quarters of the ingested nitrogen. Occasionally the balance was negative to the extent of four grams and on other days it was positive to the same degree. A typical example

of a negative balance of nitrogen can be seen in Chart # 10, in the first two weeks of November when the following results were obtained:

Dietary nitrogen per 24 hours	18 grams
Calorie intake	3200
Faecal nitrogen per 24 hours	18 grams
Urine nitrogen per 24 hours	3.8 grams
Net negative balance of	3.8 grams

On those days when the balance was maintained, it could be seen that the total urine nitrogen just represented the amount of nitrogen actually absorbed from the diet, and hence the absorption of protein equalled the breakdown of protein.

2. CALORIC INTAKE. During the period of dietary calculations (September, October, November) the caloric intake ranged from 2000 to 3000 calories per day. Prior to this period, and in the latter two months of his illness, the caloric intake was more in the region of 1000 to 1500 calories per day.

3. URINE. (Chart # 7, # 10)

Urinalysis on several occasions revealed a specific gravity range of 1010 to 1015 with rarely any albuminuria. There were no abnormal crystals, red blood cells or casts. The reaction was usually slightly alkaline.

The total urinary nitrogen per 24 hours seldom exceeded six grams and often was about four grams. The fractionated urinary nitrogen was interesting. Whereas the total volume of urine nitrogen was understandably low in view of the subnormal urine output per day, the urea fraction represented less than 50% the total non protein nitrogen (normal 80%). The remainder consisted of a slightly increased uric acid proportion, a relatively normal amount of creatinine, a pathological presence of creatine and an excessive amount of ammonia and undetermined nitrogen.

4. SERUM PROTEIN. The albumin globulin ratio did not alter but, as may be seen in Chart # 8, the total serum protein value became progressively lower, reaching a value of 4.8 grams per cent in early April, 1952. The decrease was due to a fall in both the albumin and globulin fraction.

Electrolyte Metabolism: (Chart # 9)

Balance studies were not possible in this case. Serum electrolyte determinations were made on various occasions. The serum sodium was low in September (136 meq/L) but not unduly so. The serum chloride was normal in August and September. Serum calcium remained below normal from October until April (8 mgm./100 cc.). Serum potassium remained essentially within normal limits except for a value of 3.74 meq/L in February.

Urinary excretion of electrolytes, Chart # 7. The 24-hour urine sodium excretion was usually low. The urine chloride was more normal on the four occasions when it was determined. The urine potassium excretion was also low. The urine calcium excretion ranged from 56 to 188 mgm. per 24 hours, whereas normal adult excretion averages 200 mgm. per day.

Peripheral Blood Picture: (Chart # 8)

A hypochromic anemia developed in October and became more severe with time until, in early April, the following values were obtained:

haemoglobin	68%
red cell count	3,300,000 per cu. mm.
haematocrit	35%

In July the findings were similar to the above, but improved during the months of August and September only.

The white cell count remained normal throughout the period except for the initial leucocytosis associated with the gangrenous bowel.

A sternal marrow puncture finding, after the development of the hypochromic anemia, was in keeping with the changes expected in such an anemia.

Diet:

During the period of attempted balance studies, the intake was carefully recorded. This period extended from September to November. An average daily intake in November consisted of the following:

calories	3000-3500
carbohydrate	300-350 grams
fat	140-200 grams
protein	150 grams (20-25 grams nitrogen)
calcium	0.5-1.3 grams

fluids	3000 cc.

From November to March the intake was a little less:

calories	2500-3000
carbohydrate	250-300 grams
fat	100-150 grams
protein	100-125 grams

During the months of March and April the diet became insufficient with the patient refusing a great deal and seldom eating more than a 1000 calorie diet.

Vitamins:

A multivitamin mixture was administered in tablet form three times a day. Each tablet contained the following:

B_1	1.5 mgm.
B_2	0.5 mgm.
B_6	0.1 mgm.
Niacinamide	5.0 mgm.
Brewer's yeast	75 mgm.

Vitamin C, 200 mgm. per day, was also administered. In February the man developed cheilosis, which was thought to be due to a Vitamin B deficiency even though he was receiving daily vitamin supplements. He was then given a double dose of the Vitamin B group tablets but the fissures at the angle of the mouth failed to improve. There were no other overt skin changes except perhaps, for a suggestion of pigmentation and darkening of the face and hands. There was no detectable jaundice.

Fat Metabolism:

Only one complete faeces analysis was made. On November 29, 1951, while on a diet containing 180 gms. of fat, the following analysis of 24 hour stool volume was done:

Volume of Faeces	820 cc.
Solids	11.2% - very high
Total fat	43.6 gms. % dry weight - slightly high
Combined fatty acids	0
Free fatty acids	25.2 gms. % - high
Neutral fats	20.4 gms. % - high

All this indicated a defective fat absorption but lack of accurate balance data prevents one from determining the percentage of ingested fat that was absorbed.

Cardiovascular System:

Digitalis gr. one and one-half per day controlled cardiac irregularities and cardiac output. After the development of hypochromic anemia, there were fruitless attempts to add supplementary iron to the diet. He would not tolerate ferrous gluconate or ferrous sulphate. His diet was calculated to contain 12 mgm. iron per day, but how much of this was absorbed could not be determined. There was persistent hypotension, blood pressure, ranging from 90/60 to 60/40 mm. of mercury.

Miscellaneous:

Testosterone was given in doses of 50 mgm. daily by intramuscular injection to encourage protein utilization and deposition, but this therapy did not result in any weight gain after one month so the therapy was discontinued. Seventeen ketosteroid excretion on one occasion was subnormal - 0.74 mgm/24 hour urine (655 cc. volume).

<u>Autopsy Findings</u>:

The man was very much emaciated. The secondary sex characteristics were normal for an adult male. The extremities revealed moderate pitting edema about the ankles.

<u>Thoracic Organs</u>:

A. LUNGS. There was no abnormal free fluid in the pleural cavity. The right lung showed some congestion in the lower lobe and weighed 620 grams. The left lung revealed an infarct in the lower lobe; it weighed 630 grams.

B. HEART. This organ weighed 290 grams. There were numerous calcareous deposits overlying the stenotic mitral valve and the aortic valve revealed retraction of the cusps and welding of the commissures. The left auricle was dilated. The aorta was slightly atheromatous in its thoracic portion only. No embolus could be found in the remnant of the superior mesenteric artery. Microscopically there was no evidence of active myocarditis.

C. LIVER. This organ weighed 1010 grams but externally appeared normal. On section there was atrophy of lobules and hepatic cells but no fatty change was present.

D. SPLEEN. It weighed 80 grams but otherwise appeared normal. On section the malpighian corpuscles were small and atrophic with disappearance of the germinal centers. The red pulp contained brownish pigment, probably haemosiderin.

E. KIDNEYS. The right weighed 80 grams and the left, 150 grams. The right certainly appeared hypoplastic. On section the left kidney appeared normal and the right revealed several old healed infarcts.

F. ADRENALS. They appeared normal grossly and on section some narrowing of the cortex with the cells staining darkly suggesting some loss of lipid content.

G. BONE MARROW. On section diffuse hypoplasia was noted but all the normal cellular elements were present.

H. BRAIN. The brain weighed 1400 grams. No gross abnormalities were observed.

I. GASTRO-INTESTINAL TRACT. (Photographs # 9,10,11 and 12)
Photographs of the gastro-intestinal tract were taken after removing the anterior abdominal wall with the organs in situ, then with the gut removed, and finally with the entire tract laid open along the ante-mesenteric border.

1. Gross. At autopsy the stomach and duodenum were enormously dilated. The colon formed large dilated segments when seen in situ. Upon removal of the gut, its contents were

emptied and the dilatation was still evident. The duodenum was very large and measured about 8 to 10 inches in length. The site of the anastomosis to the transverse colon is indicated by # 3 in the intact specimen and # 4 in the opened specimen.

No gross lesions were observed except for erosions of the esophagus which were probably due to post-mortem autolysis. Gross thickening of the gut was not observed and the mucosa appeared stretched but not hyperplastic.

B. Microscopic. Unfortunately the autopsy was not performed until 12 hours after death, at which time considerable autolysis had occurred. The junction of the cardia and esophagus revealed partial loss of epithelial surface with some round cell exudation. The fundus of the stomach was not remarkable except for some atrophy of gastric glands with near absence of parietal cells. The duodenum failed to reveal hyperplasia. Considerable autolysis of the mucosa was present. The muscularis was not attenuated. A section at the line of anastomosis showed replacement of muscle layers with fibrous scar. The colon showed a flat autolysed mucosa but the muscle layers were normal. The rectum revealed similar mucosal autolysis with a slight round cell infiltration.

<u>Summary and Pathological Diagnosis</u>:

1. Rheumatic heart disease

2. Rheumatic endocarditis (mitral and aortic valves)

3. Embolism of superior mesenteric artery and infarction of small bowel and right colon - June, 1951.

4. Dilatation of intestine - stomach - slight

   duodenum - marked

5. Cachexia

6. Broncho-pneumonia

7. Recent infarct left lower lobe

8. Old infarcts of the kidney

9. Liver atrophy - 1010 grams

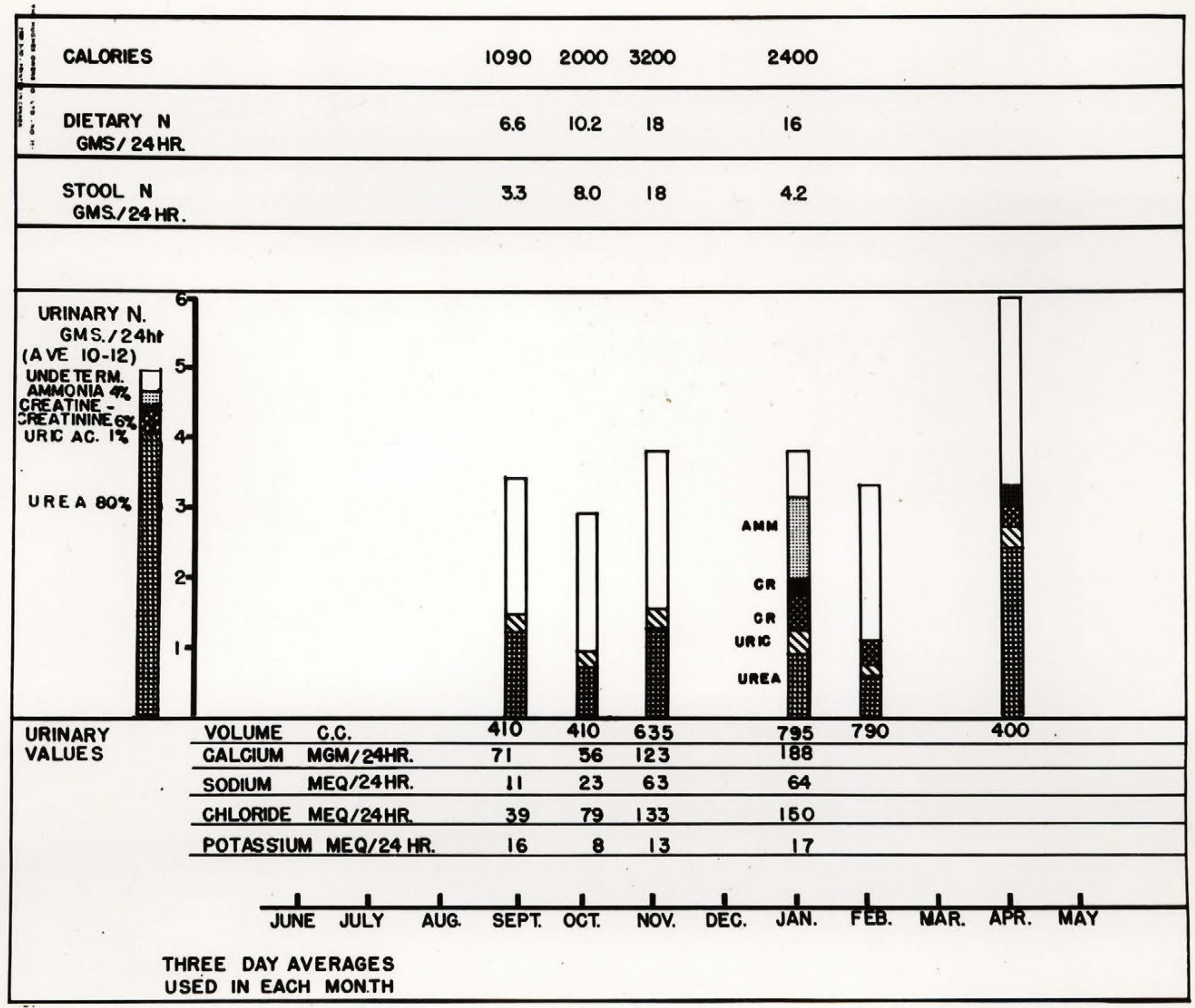


CHART # 7

Mr. J. - # V33038: Approximate normal proportions of the components of non protein nitrogen, when the total NPN is 5 grams, is illustrated in the left margin.

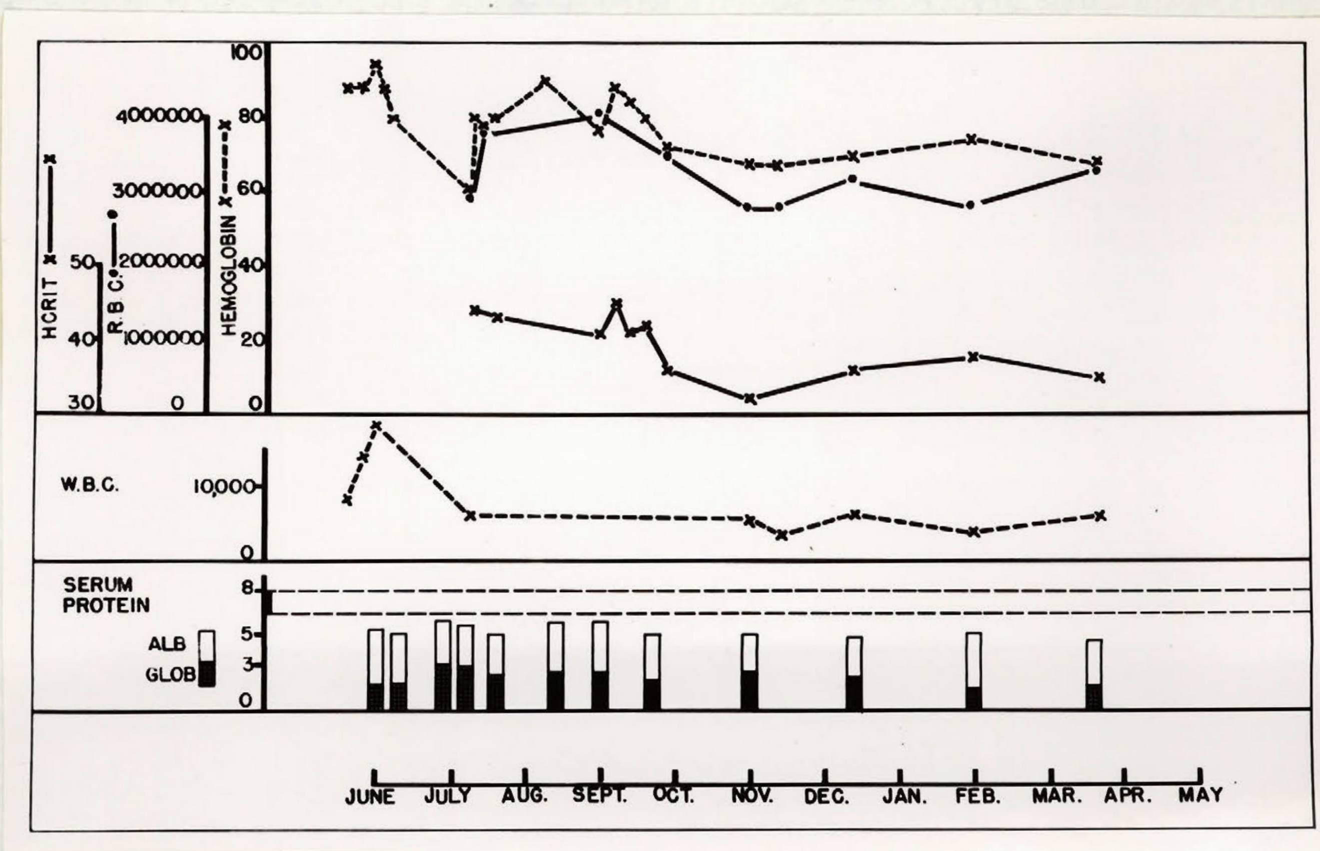


CHART # 8

Mr. J. - # V33038

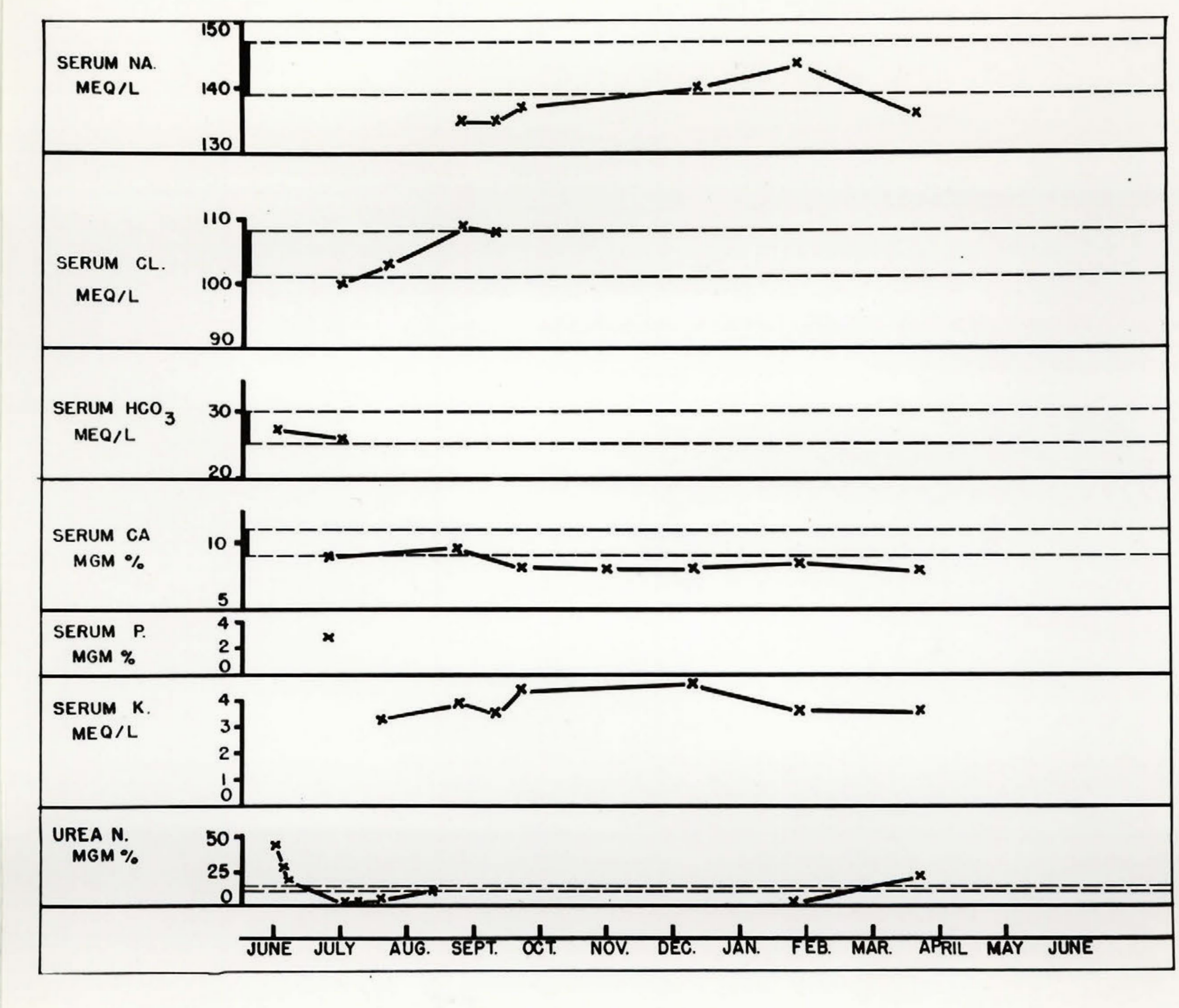


CHART # 9

Mr. J. - # V33038

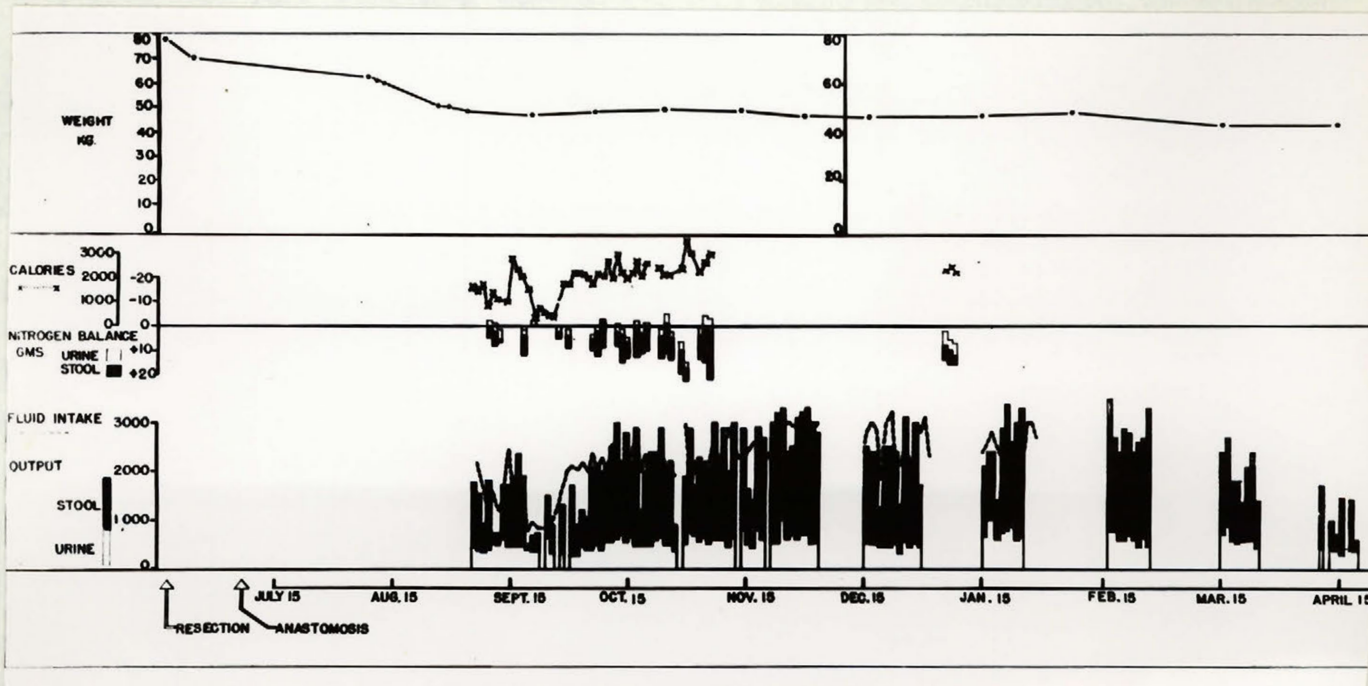
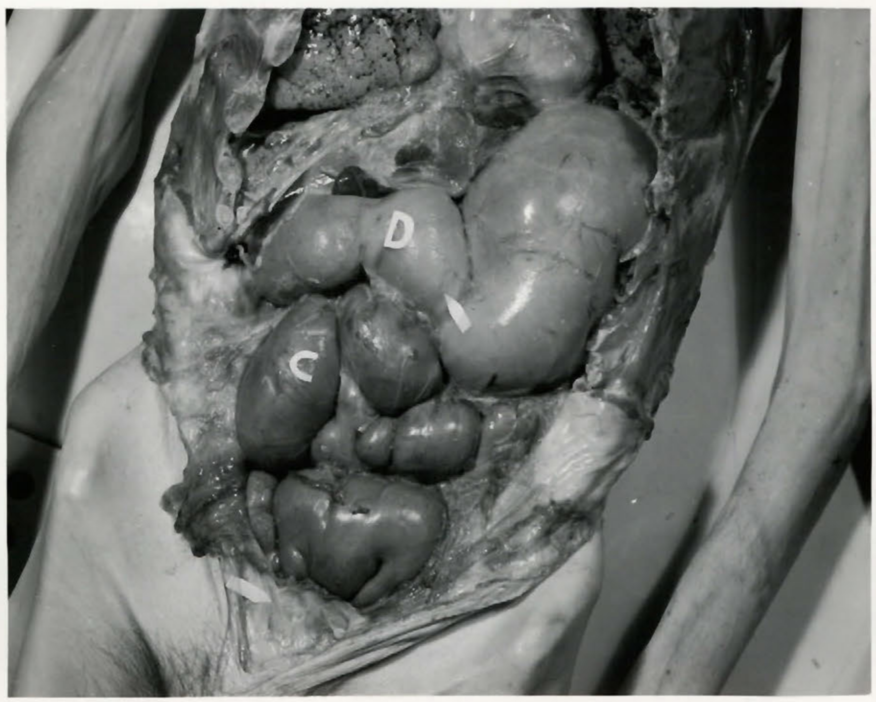


CHART # 10

Mr. J. - # V33038



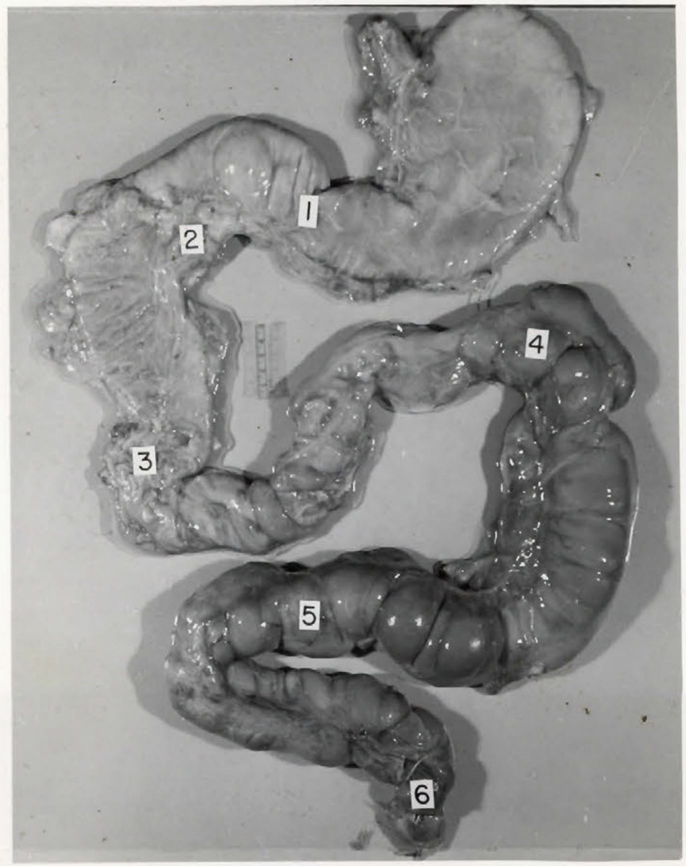
PHOTOGRAPH # 9

Mr. J. - # V33038: Abdominal viscera in situ at autopsy.

D. Duodenum

C. Colon

The white arrow is placed at the pylorus.



PHOTOGRAPH # 10

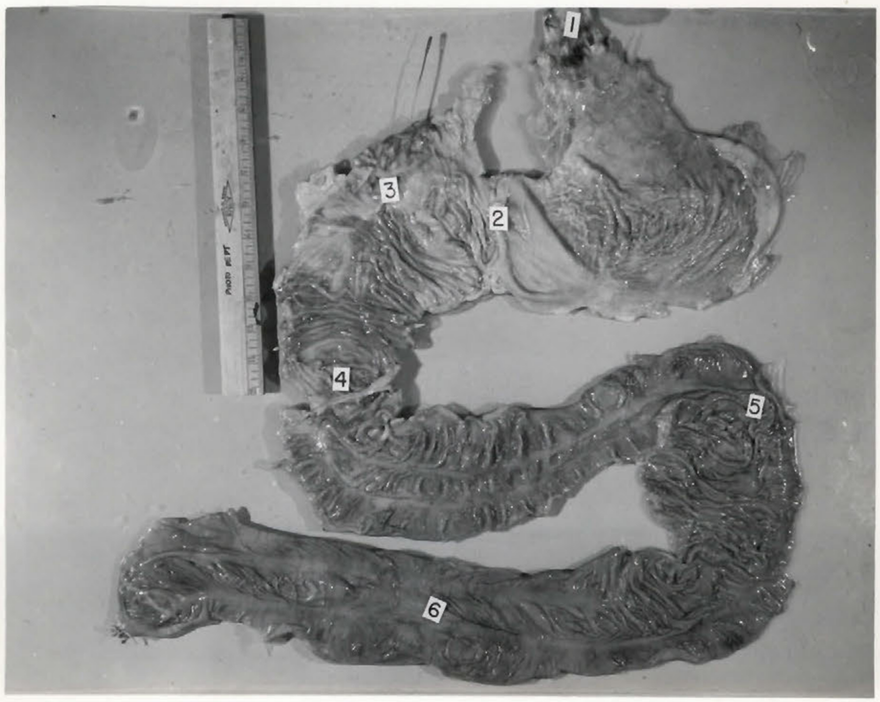
Mr. J. - # V33038: Gastro-intestinal tract unopened but partially emptied.

1. Pylorus 2. Ampulla of Vater

3. Site of anastomosis, duodenum to transverse colon

4. Splenic flexure colon

5. Sigmoid colon 6. Rectum



PHOTOGRAPH # 11

Mr. J. - # V33038: Gastro-intestinal tract laid open.

1. Cardia 2. Pylorus

3. Ampulla of Vater

4. Site of anastomosis

5. Splenic flexure of colon

6. Sigmoid colon

PHOTOGRAPH # 12

Mr. J. - # V33038: Barium Meal study September, 1951. The large gas filled area to the right of the vertebral column contains some barium and represents the dilated duodenum. Immediately below and to the left can be seen the stoma entering the transverse colon.

DISCUSSION OF RESULTS

A. Animal Experiments:

It is realized that the number of animals studied was small, but the purpose of this was to observe each animal carefully rather than to have a large series of animals which would overtax the facilities and time available.

Dog # 1 survived a resection of the proximal two-thirds of the small intestine. There was a gradual deterioration in the animal's condition which lasted about six weeks. The animal then gradually improved and surpassed its pre-operative status by the sixth month. Adequate fluid balance was maintained except for a temporary post-operative dehydration. The electrolyte balances and the serum concentrations of sodium, potassium, chloride and bicarbonate were not altered. A hypochromic anemia developed in the second month but a gradual return to a normal hematological state occurred in the succeeding four months. Initially, the animal lost about one-fifth of its weight, but later regained it entirely. At autopsy, positive findings included a mild dilatation of the duodenum, a moderate epithelial hyperplasia of the ileum, and a markedly enlarged spleen, engorged with blood. It would appear that the dog can tolerate a resection of the proximal two-thirds of the small intestine, and after a temporary decline in weight and health, can return to a healthy state. This assumption is, admittedly, based on the findings in only one animal. The temporary period of weight loss and malnutrition was not attended by any abnormality in the electrolyte metabolism of the animal. Fat absorption seemed to be unimpaired during the recovery phase, at least as judged by the appearance of the faeces. Apparently a Vitamin B deficiency developed at the second month when ulcers of the extremities and sparseness of body hair became evident; this was only temporary and disappeared without any specific therapy.

A resection of most of the small intestine, leaving only four inches of jejunum and a cuff of ileum, was not compatible with long survival in Dog # 2 and Dog # 5. The former survived 130 days, and the latter, 85 days. Each animal lost almost 50% of its pre-operative weight. They developed gross evidence of Vitamin B deficiencies and died in a severe state of malnutrition. A very severe hypochromic anemia was present. No abnormalities of electrolyte metabolism developed. Absorption of fat was very poor. The faeces were almost always liquid and bowel movements occurred several times a day. The fluid balance remained in equilibrium. In Dog # 2 the positive findings at autopsy consisted of a marked epithelial hyperplasia of the duodenum and the remnant of jejunum. Gastrointestinal changes with epithelial hyperplasia were not observed in Dog # 5, probably because the survival period was insufficient for some compensatory change in the remaining small intestine to occur. No changes in the colon were observed in either Dog # 2 or Dog # 5. The spleen was very small and atrophic in both animals.

It becomes clear that resection of at least two-thirds of the small intestine will lead to a hypochromic anemia, similar in nature to that described by Martin et al (29). A more extensive resection will lead to a more severe anemia. The severity of the anemia seems to vary inversely with the length of remaining intestine. When it is short, the absorption of iron is deficient. If the anemia corrects itself, a marked hyperplasia of the spleen occurs.

The renal and respiratory regulation of electrolyte metabolism remain unaltered after extensive resection of the small intestine in animals.

In view of the complete recovery of Dog # 1, and the death of Dogs # 2 and # 5, it might appear that the dog can survive a resection of slightly more than two-thirds of the small intestine and remain in good health.

Marked emaciation and avitaminosis can be expected to attend the resection of massive segments of small intestine which leave only a few inches of jejunum or ileum remaining in the animal.

B. Mr. J. - Case # V33038:

This case remains as the longest survival with so little intestine yet reported in the literature. Shonyo and Jackson (35), Wilkie (45), and Althausen (3), all reported cases surviving over one year with less then one foot of jejunum. Mr. J. survived 10 months with a segment of duodenum that comprised the first and second stages and measured about eight inches in length.

He subsisted on oral feedings alone with supplementary vitamin tablets. It is true that he remained in a lethargic, weakened state throughout most of this 10 month period, but it is still remarkable to observe a human being with so little intestine survive that long a time.

He developed personality changes which consisted of immature, unco-operative behavious, but not a frank psychosis as occurred in "Toni", the survival reported by Wilkie (45), and later by Jackson and Linder (25).

A weight loss of almost one-half his previous weight occurred mainly in the first two months. So much of the lean body mass was metabolized in the first few months, that little muscle or fat tissue remained to be lost in the succeeding months.

His hydration was maintained by a very narrow margin with the intake of fluid barely exceeding the fluid output; in fact, the fluid balance was negative on certain days. The stool output comprised two-thirds of the total fluid excretion. Urinary excretion seldom exceeded 500 cc. per day, which is ordinarily the minimum urine secretion necessary for removal of waste products of metabolism. The non protein nitrogen level of the blood remained within the normal range. Fractionated urine nitrogen analysis revealed a small proportion or urea and a larger than normal amount of undetermined nitrogen. There was some occasional albuminuria which might account for the excessive undetermined nitrogen. The presence of creatine indicated a disturbed protein metabolism. The large amount of ammonia found in the sample obtained in the eight month might indicate a base conservation by the kidney; at this time the sodium concentration of the urine was much lower than the chloride concentration.

Following the initial loss of weight in the first two months, the absorption of nitrogen just equalled the excretion of urinary nitrogen. This amount of nitrogen was never in excess of six grams even though the diet contained from 15 to 20 grams of nitrogen. The total serum protein value progressively decreased throughout the ten months, reaching a value of 4.8 grams per cent shortly before death.

Electrolyte balance studies were not made but occasional serum determinations revealed a slight fall in the potassium level (3.7 meq/L) in the seventh month and a persistently low serum calcium (8 mgm. %). The low serum calcium value was probably due to the fat content of the diet which was normal to high at the patient's insistence; this would lead to the formation of calcium soaps and interference with calcium absorption.

Hypochromic anemia gradually developed and persisted throughout the ten month period. The patient was unable to tolerate iron therapy either by mouth or parenterally. The effect or iron therapy upon the anemia could not be ascertained.

Intensive vitamin therapy did not prevent the development of an angular stomatitis suggestive of Vitamin B deficiency. The 17 ketosteroid excretion was low. Defective fat absorption was evident throughout the study period.

The positive autopsy findings consisted of a marked state of emaciation, a greatly dilated duodenum and a moderately dilated colon. Post-mortem autolysis prevented the detection of any change in the mucosa of the intestine. Rheumatic heart disease was clearly evident.

It is quite true that this man was never expected to survive with so little intestine. Nevertheless, we were encouraged by the length of time that he did survive. It is not expected that a man can maintain a homeostatic state with an absorptive surface of only eight inches of duodenum but, through observation of such cases, much may be learned. Application of such knowledge in cases where there is slightly more intestinal absorptive surface will reduce both morbidity and mortality.

The personal idiosyncrasies of the individual often mitigate against the use of the proper diet in a situation of massive intestinal resection. A low fat, high carbohydrate, high protein diet is recommended by most authors. One danger of fat in the diet is the development of a low serum calcium and tetany, as previously explained. The only other electrolyte abnormality to be guarded against is a decrease in the serum potassium, probably as a result of the constant tissue breakdown. Vitamin deficiencies are to be guarded against, especially of the B. group. The precarious existence that these individuals lead may predispose them to personality changes of severe degree; these could be guarded against by a psychological preparation of the patient for his difficulties.

Marked dilatation of the small intestinal remnant can be expected. The animal experiments suggest a compensatory hyperplasia of the mucosa to occur as well. The dilatation of the colon in Mr. J. is difficult to explain. The animal preparations did not show this dilatation. Two possibilities present themselves. The first is a mechanical obstruction in the rectum to account for the colonic dilatation, and a narrowed stoma to account for the dilatation of the duodenum. However, the stoma was large and adequate, and no rectal stricture was present. It seems likely, therefore, that the dilatation of the duodenum and colon was due to an actual compensatory attempt on the part of the organism to provide a larger receptacle for the ingested food. There was no evidence of mucosal change visible in the colon due to the post-mortem autolysis; however, the dilated colon no doubt provided a large area for the absorption of water.

SUMMARY

It was intended to study the effects of a massive resection of the small intestine in the dog with particular reference to any alteration in the electrolyte metabolism, and to correlate these studies with the observations of a human surviving a massive resection of the entire small intestine, for 10 months.

No gross alteration in the fluid and electrolyte balance was observed in an animal after the loss of 66 2/3 % of the small intestine or in two animals after the loss of about 95% of the small intestine. These negative findings were also found in the human patient, except for a temporary mild potassium deficiency and a persistently mild calcium deficiency.

A review of the literature concerning the reported cases of massive intestinal resection in human beings and in the dog is presented and discussed. The difficulties attending the study of nitrogen and electrolyte balances after massive resection are discussed.

Compensatory dilatation and hyperplasia were observed in two animals and in the human subject.

CONCLUSIONS

1. Four adult male dogs were used in an experimental study into the effects of a massive resection of the small intestine.

2. One animal recovered completely in six months after resection of the proximal two-thirds of the small intestine.

3. One animal died in 135 days from severe inanition after the resection of about 95% of the small intestine.

4. One animal died in 85 days from severe inanition after the resection of about 95% of the small intestine.

5. One animal died in the immediate post-operative period from dehydration after the resection of about 95% of the small intestine.

6. A man, 43 years old, survived ten months after a resection of the entire small intestine, the third and fourth stages of the duodenum and the right colon.

7. It would appear that in the dog, compensatory hyperplasia of the remaining intestine after a resection of two-thirds of the small intestine will allow for a normal state of health and activity.

8. If less than six inches of jejunum remain after resection in the dog, no such survival can be expected.

9. Slightly less remaining intestine in the human being may be compatible with life for a prolonged time.

10. A severe hypochromic anemia is characteristic of

all massive intestinal resections.

11. No gross alteration in the acid-base balance or in the fluid and electrolyte balance is encountered after massive resection, except as a terminal event when dehydration is severe.

12. An initial severe loss of weight occurs and is then followed by a long period of relative stability of weight, during which time protein absorption just equals protein breakdown.

13. With nearly total small intestine resections, the organism is in a constant precarious state where sudden changes in environment may suddenly upset the metabolism and end in death.

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Part B

EFFECTS OF SPINAL ANESTHESIA

AND

DIFFERENT GRADES OF OPERATIVE TRAUMA

UPON

FLUID AND ELECTROLYTE BALANCE

by

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INTRODUCTION

It was originally proposed to study the changes in fluid and electrolyte balance resulting from spinal anesthesia and operative trauma, in patients at the Royal Victoria Hospital.

It was apparent that the division of anesthesia from operative trauma would be difficult to arrange and, therefore, the patients studied were undergoing both at about the same time.

Coller (18) was one of the first to draw attention to the acute temporary changes in renal function associated with major surgery. Pringle (74) observed the suppression of urine formation and urinary nitrogen output following ether anesthesia and an operative procedure. Moyer (6) briefly referred to the effect of spinal anesthesia alone, without operation, in producing temporary aberrations of renal function.

It was intended to conduct fluid and electrolyte balance studies on random public patients admitted to the general surgical services for elective operations under spinal anesthesia.

In addition to the study of fluid and electrolyte balances, observations on protein metabolism and the hematopoietic system were made.

It was hoped that, with a more detailed knowledge of alterations in the water and electrolyte balance likely to occur during spinal anesthesia, parenteral fluid therapy (during the pre-operative, operative, and post-operative periods) might be improved to maintain as normal relationships as possible.

A patient with a severe burn is included in the group herein reported. Admittedly, this was a deviation from the original problem, but a thermal burn represents an ideal example of severe trauma in which alterations in the fluid and electrolyte balance may be studied.

REVIEW OF THE LITERATURE

(A) GENERAL

Before any attempt was made to review the literature concerning the specific effect of anesthesia and trauma upon fluid, electrolyte and nitrogen balance, it became necessary to review the general field of fluid and electrolyte balance and protein metabolism. Excellent papers have been written by Moore (59), Darrow (25), Gamble (40), Maddock (55), Moyer (63), (64), Randall (78), (79), Peters (71), Scribner (87), Raudin (80), and Cole (16). Two charts (A, B) were made, summarizing much of the pertinent information necessary for the proper management of a problem in fluid and electrolytes.

A review of potassium metabolism was also necessary. Many excellent articles have appeared in the recent literature, notably the following: (7), (12), (17), (29), (31), (32), (36), (43), (48), (56), (57), (77), (86), (90), (94).

A knowledge of renal function and its abnormalities was gained from the following: (5), (6), (19), (20), (34), (38), (68), (98).

Protein metabolism has received much attention in the recent literature. The subject has been discussed in the writings of Albright (1), Allen et al (3), Chassin (15), and others, (33), (39(, (44), (51), (54), (72), (82), (92), (103).

		G.I. LOSSES Meq/L			SEMIQUANTITATIVE REPLACEMENT				
		NA	K	CL		T/W	T/S	M/6 NA lactate	0.75% nh4cl
GASTRIC fasting	AVE	59	9	89	AVE	33	67		
	RANGE	6-157	1-65	13-167	ULCER	20	30		50
					LOW AC	67	33		
SMALL BOWEL millerabbott	AVE	105	5	99		20	70	10	
	RANGE	20-157	1-11	43-156					
ILEOSTOMY recent or COPIOUS DIARRHEA	AVE	130	16	109		10	75	15	
	RANGE	92-146	4-98	66-136					
CECOSTOMY	AVE	80	20	48		50	30	20	
	RANGE	45-135	4-47	18-89					
BILE	AVE	145	5	100			67	33	
	RANGE	122-161	3-9	77-127					
PANCREAS	AVE	141	5	76			50	50	
	RANGE	113-151	2-7	54-95					

FLUID REGIME PER DAY

BASELINE
WATER 1600-2500
NA 76 Meq, CL 76 Meq } 500 NACL 0.9%
K 30-40 Meq (2-3 gm KCL)
CALORIE GLUCOSE 100 gm.
VITAMINS B. C. K.

DYNAMIC LOSS
G. I. TRACT- volume for volume - plus K 10 Meq/L
OPEN WOUNDS
SWEATING- hot & humid 2000-4000
NA, CL } 30-70 Meq/L

STATIC DEFICITS

	ELECTROLYTE CONTENT Meq/L			
	NA	K	CL	EFFECTIVE HCO_3
NACL 0.9%	154	0	154	0
M/6 NA LACT.	167	0	0	167
$NAHCO_3$ 1.2%	143	0	0	143
NH_4CL 0.75%	0	0	140	0
HARTMANN*	136	53	112	33
DARROW	120	35	103	50
MUDGE	110	30	140	0

* ca. 3.6 Meq.

EARLY BURN THERAPY

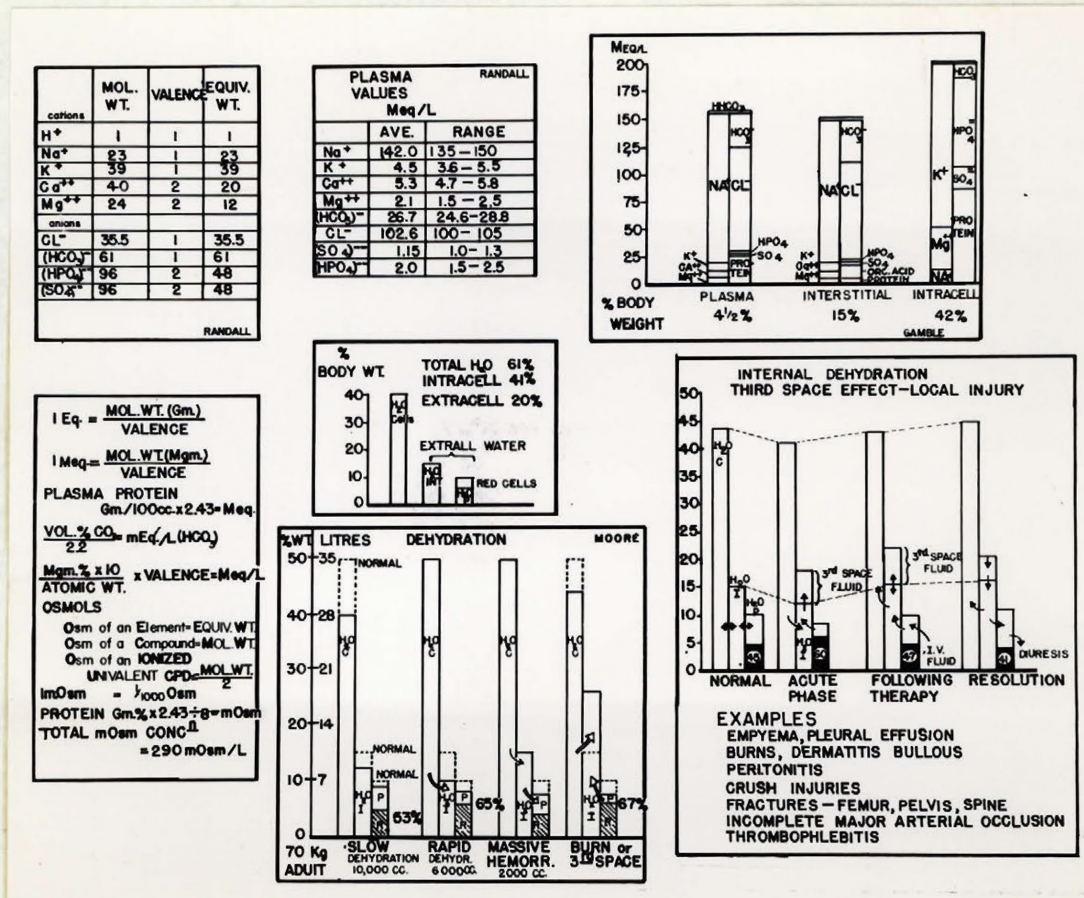
1st 24 hours
COLLOID 1cc/kg/%
1/2 PLASMA, 1/2 BLOOD } IF OVER 20%
ELECTROLYTE 1cc/kg/%
NACL 0.9%
WATER 2000 G/W

2nd 24 hours
COLLOID 1/2 cc/kg/%
1/4 PLASMA, 1/4 BLOOD } IF OVER 20%
ELECTROLYTE 1/2 cc/kg/%
WATER 2000 G/W

TREATMENT DEHYDRATION

1. SLOW { WATER, K, HPO_4, FOR I-C MAINLY; NACL, HCO_3 FOR E-C, LESS AMT.
2. RAPID
- NO VOMITING—EXPAND E C.
  1. HARTMANN OR
  2. 2/3 NACL & 1/3 NA { LACT. or BICARB
- VOMITING—EXPAND E-C.
  1. NACL 0.9%

Chart A



MOL. WT.
VALENCE
EQUIV. WT.
cations
H+ 1 1 1
Na+ 23 1 23
K+ 39 1 39
Ca++ 40 2 20
Mg++ 24 2 12
anions
CL- 35.5 1 35.5
(HCO3)- 61 1 61
(HPO4)= 96 2 48
(SO4)= 96 2 48
RANDALL
PLASMA VALUES Meq/L
RANDALL
AVE. RANGE
Na+ 142.0 135-150
K+ 4.5 3.6-5.5
Ca++ 5.3 4.7-5.8
Mg++ 2.1 1.5-2.5
(HCO3)- 26.7 24.6-28.8
CL- 102.6 100-105
SO4 1.15 1.0-1.3
HPO4 2.0 1.5-2.5
MEQ/L
PLASMA
INTERSTITIAL
INTRACELL
% BODY WEIGHT
4½%
15%
42%
GAMBLE
1 Eq. = MOL. WT. (Gm.) / VALENCE
1 Meq = MOL. WT. (Mgm.) / VALENCE
PLASMA PROTEIN Gm./100cc. x 2.43 = Meq.
VOL. % CO2 / 2.2 = mEq/L (HCO3)
Mgm.% x 10 / ATOMIC WT. x VALENCE = Meq/L
OSMOLS
Osm of an Element = EQUIV. WT.
Osm of a Compound = MOL. WT.
Osm of an IONIZED UNIVALENT CPD = MOL. WT. / 2
1mOsm = 1/1000 Osm
PROTEIN Gm.% x 2.43 ÷ 8 = mOsm
TOTAL mOsm CONC = 290 mOsm/L
% BODY WT.
TOTAL H2O 61%
INTRACELL 41%
EXTRACELL 20%
EXTRALL WATER
RED CELLS
%WT LITRES DEHYDRATION MOORE
NORMAL
63%
65%
67%
70 Kg ADULT
SLOW DEHYDRATION 10,000 CC.
RAPID DEHYDR. 6000 CC.
MASSIVE HEMORR. 2000 CC.
BURN or 3rd SPACE
INTERNAL DEHYDRATION
THIRD SPACE EFFECT-LOCAL INJURY
3rd SPACE FLUID
I.V. FLUID
DIURESIS
NORMAL
ACUTE PHASE
FOLLOWING THERAPY
RESOLUTION
EXAMPLES
EMPYEMA, PLEURAL EFFUSION
BURNS, DERMATITIS BULLOUS
PERITONITIS
CRUSH INJURIES
FRACTURES - FEMUR, PELVIS, SPINE
INCOMPLETE MAJOR ARTERIAL OCCLUSION
THROMBOPHLEBITIS

Chart B.

(B) SPINAL ANESTHESIA

Lassen (53) demonstrated the correlation between filtration pressure of the kidney and the level of blood pressure following spinal anesthesia. If the fall in blood pressure was marked, then the renal plasma flow, the glomerular filtration rate and pressure were decreased, and the tubular reabsorption of water was increased. The latter fact was probably due to a slower passage of filtrate through the tubules. The net renal result was an oliguria persisting only so long as the hypotension effect of the spinal anesthesia persisted. If peripheral vasoconstrictor drugs were administered to prevent the fall in blood pressure, then the previously observed changes in renal function did not occur. Hardy (46) summarized experimental and clinical work on the relation between anesthesia and renal function. He could find no consistent effect of spinal anesthesia on renal excretory efficiency or renal blood flow, if the level of blood pressure was maintained. Cyclopropane and ether anesthesia have been known to cause temporary suppression of urine formation; it has been suggested by Coller (17) (18) that extra-renal factors arising out of anesthesia (both spinal and general) might be at work, leading to the postoperative retention of salt and water. Another suggestion to explain this phenomenon arises from the fact that liver function may be temporarily impaired after anesthesia and/or operation, thereby reducing the organism's efficiency for inactivation of adrenal cortical and posterior pituitary hormones.

(C) POST-OPERATIVE RETENTION OF SALT AND WATER

Pringle (74) first observed a suppression of urine formation during ether anesthesia and an operative procedure. Stewart and O'Rourke (95) later proved that this was not due to dehydration because the effect was obtained even though large amounts of glucose in water were administered in infusions. As mentioned previously, Coller demonstrated this urine suppression occurring with spinal anesthesia. Moyer (61) described the acute temporary changes in renal function associated with major surgery, as consisting of a suppression of the pH regulatory action of the kidney; normall, the kidney will excrete chloride in excess of sodium following an infusion of 0.9% NA Cl to maintain acid base equilibrium, since the concentration ratio of sodium concentration exceeds the chloride concentration. In the immediate post-operative period, he found that chloride is not excreted in excess of sodium following an infusion of normal saline; he warned against the dangers of producing a dilutional acidosis due to this post-operative salt intolerance. Together with this retention of salt, there is also a marked retention of administered water. Ariel (4) reported on the effects of a water load administered to patients in the immediate post-operative period. As a result of trauma and/or anesthesia, post-operative oliguria may ensue, water given to these patients may be retained in part; if an excessive water load is administered, a hypotonic syndrome may result. Ariel (6) noted wide fluctuations in renal plasma flow and glomerular filtration rate in a series of twelve patients studied in the immediate post-operative period after abdominal surgery: in some, there was a marked decrease, whereas in others, no decrease occurred. It is probable that a hormonal imbalance, caused by surgery and reflected in kidney clearance tests, contributes to certain post-operative phenomena (oliguria, salt retention, water retention). The degree of alteration varies in different patients. Coller (18) found an average retention of 53% of sodium, 46% of chloride, and 19% of water, following an infusion of normal saline in the post-operative period. This effect persisted 30 hours. The retention was much less following hypotonic saline infusions. The human kidney does not guard a physiological saline solution in the immediate post-operative period, and should there be a need for saline in this period, then hypotonic saline is preferable. Moyer (62) found that the excretion rates of a positive load of sodium chloride and water are very small in the immediate post-operative period. He was unable to obtain these same effects with ether anesthesia alone. He drew attention to the finding of acute temporary alterations in renal function post-operatively, i.e., salt and water retention presumably due to increased tubular reabsorption and/or decreased glomerular filtration.

(D) ADRENAL CORTEX

There is increasing evidence that the regulation of water and electrolyte metabolism is, to a considerable extent, mediated through the hormones of the pituitary and adrenal cortex.

1. Adaptation Syndrome: Selye (89) defines this as the result of some stressor agent (operation, trauma, etc.) acting on the body to produce a change of two kinds. First, there is damage or shock and second, a defence reaction. In the first instance, exposure to stress results in an "alarm reaction". In the second stage or defence reaction, a resistance to the same stress develops. If this goes on to a third stage, there is death of the organism. The stressor stimulates the anterior lobe of the pituitary with the resultant discharge of adrenocorticotrophic hormone; this then acts on the adrenal cortex with the release of cortical hormones. Selye's original theory to explain the mechanism by which the stressor agent "fires" the pituitary gland, was based on the stressor damaging the target organ and thereby using up cortical hormone, whose relative deficiency then stimulated the pituitary. Another theory attributes the stressor agent firing the adrenal medulla as the cause: the discharge of adrenalin then acting on the pituitary. It is perhaps academic to dwell any further on theories because it is known that all stressors enter a final common pathway for stimulation of the pituitary gland.

The adrenal cortex secretes three main groups of steroid hormones. One group is the sex hormones; another is the glucocorticoids (so named because of their action on carbohydrate metabolism and gluconeogenesis); the third group is the mineral corticoids (so named because of their action on fluid and electrolyte metabolism). Desoxycorticosterone acetate is a good example of a mineral corticoid and cortisone, of a glucocorticoid. None of the group exists separately and all possess some actions of the others. The glucocorticoids tend to inhibit inflammation and the mineral corticoids tend to stimulate inflammation. ACTH has been shown to stimulate the production of glucocorticoids. Selye suggests that that the somatotrophic (STH), or growth hormone of the anterior pituitary, may be responsible for the stimulation of the mineral corticoids. ACTH and glucocorticoids are thought to dissolve inflammation at the target organ following stress to it, whereas STH and mineral corticoids stimulate formation of a granuloma with encapsulation of the focus of irritation, e.g., bacteria. In rheumatoid arthritis, the pathology is essentially a group of granulomas rather than a septicaemia. Selye suggests that in the future, when all four compounds are available, they may be juggled about to obtain an anti-phlogistic or pro-phlogistic effect in the treatment of disease. The synergism between ACTH and STH does not occur between the pituitary and adrenal, but at the target organ.

2. Adrenal Cortex in Relation to Water and Electrolyte Metabolism: The adrenal corticoids may produce water retention or water loss by virtue of two effects: they cause sodium retention

and water diuresis comparable to that of the antidiuretic hormone of the posterior lobe of the pituitary. An injection of Dexosy-cortico sterone acetate produces a retention of sodium and chloride with very low urine excretion of these substances, but a high potassium excretion. The mineral corticoids probably exert their effect of salt and water retention by acting on the renal tubular cell, facilitating sodium reabsorption and increasing potassium excretion by inhibiting its reabsorption. The salt and water hormone of the adrenal cortex may also increase urine volume, depending on the pre-existing state of the individual. In an adrenalectomized animal, DCA may augment thirst by producing sodium retention and it may also inhibit water reabsorption in the tubules. Rapid water excretion is never possible if both the antidiuretic hormone of the pituitary and the mineral corticoid of the adrenal cortex are absent.

According to the adaptation syndrome, the "shock" phase may last 24 hours, during which time water retention occurs; water diuresis follows in the counter-shock phase.

In summary, it may be said that the effects of the adrenal cortex in water metabolism are mediated in three ways: - 1) a direct action on the renal mechanism, independent of the electrolyte metabolism which stimulates the rate and extent of water excretion; 2) the renal retention of sodium, the osmotic consequence of which is water retention. The balance between the first and second depends on the physiological conditions existing at the time. In the excretion of salt and water, the adrenal cortex influence is opposite to that of the posterior pituitary; 3) vaguely defined extra-renal means by which cortical hormones affect internal fluid distribution. The normal diuretic response to water given by means depends upon the action of cortical hormones (42). When the cortical hormone level is normal, and the antidiuretic hormone is lacking, polyuria (diabetes insipidus) results due to the unopposed action of the cortical hormones.

Hardy (47) reported pre-operative and post-operative studies of the eosinophile count, the urine volume, and the electrolyte concentration of urine. He found that the retention of salt and water and increased excretion of potassium were most intense on the operation day. This corresponded with the expected time of maximal adrenal cortical secretion and the eosinophile counts were lowest at this time also. There was some variation in the rapidity of the return to normal of these observed changes, and he thought this was related in some way to the vitality of the patient pre-operatively. It is known that a debilitated, chronically ill individual may not show a maximal "alarm reaction" and furthermore may return to normal much more slowly after an attenuated "alarm reaction".

PATHOLOGICAL PHYSIOLOGY OF THE BURN

Wounds created by thermal traums, both heat and frostbite, swell rapidly with edema fluid, at the expense of circulating plasma: a crippled circulation may be the result. Thermal trauma damages the capillaries and their permeability, allowing a protein rich plasma filtrate to flow out into the wound area. Thermal trauma also abolishes the vasoconstriction reflex, allowing an unbridled arterial inflow into the damaged capillary area, with the result that further filtration out into the burn area occurs. The only restraining influence on the extent of edema formation is the resistance of the integument and the interstitial tissue tension. A severely coagulated burn area may be inelastic and force filtered fluid into unburned areas and lymphatics. Increased lymph flow occurs in the area of the burn.

The rate of edema formation is most rapid at first, then it tapers off. It may be accelerated if only non-colloid repair solutions are used in therapy. Edema formation reaches its peak in 36 to 42 hours: by this time, the less damaged capillaries, at the periphery or in the depths of the burn wound, have healed, and filtration no longer exceeds absorption. After 48 hours, further capillary healing leads to increase of absorption via the vascular and lymphatic systems. The extent of absorption may be so rapid as to equal the rate of its initial formation. During this phase of absorption, the kidney is faced with excreting the additional load of any administered fluid.

The electrolyte content of the wound fluid parallels that of plasma or extracellular fluid; the protein content is never as high as plasma; in severe burns, the protein content may reach 4.5 grams per 100 cc. As absorption progresses, the protein concentration decreases in the wound edema fluid. Early in the burn shock period, the plasma protein concentration may be high, owing to a decrease in volume of the extracellular fluid, and this exerts an increased colloid osmotic pressure which is of itself more dehydrating to the cells. With absorption of the edema fluid, the plasma protein concentration falls. The initial increased colloid osmotic pressure of the plasma cannot exert an absorption effect because of the damaged capillaries. If the extracellular volume expands beyond 50%, then the extreme dehydration of cells that occurs, together with the loss of intracellular electrolyte (potassium and phosphate), may lead to death with the immediate cause being anoxia of renal parenchyma due to a decreased blood volume.

With survival, the wound edema fluid is absorbed and the redistribution of fluid dilutes the plasma, normal protein concentration of plasma is regained and the cells regain their normal complement of water and electrolyte. Normal renal function returns.

In therapy, if only plasma or blood (colloid) are given, kidney function is maintained butthe body cells tend to remain dehydrated. If only electrolyte solutions (crystalloid) are given, then the wound edema increases, the plasma protein concentration and the colloid osmotic pressure of plasma decreases, and the fluid distributes itself in all compartments leading to generalized edema.

BERKOV SCALE OF SURFACE AREA

Head & Neck		6 %
Trunk		38 %
Anterior Trunk & Genitals	20.0	
Posterior Trunk	18.0	
Upper Extremities		18 %
Hands	4.5	
Arms	13.5	
Lower Extremities		38 %
Feet	6.3	
Legs	12.6	
Thighs & Buttocks	19.0	
		100 %

FLUID THERAPY OF THE BURNED PATIENT (23)

A) Surface area formula for adults:

1st 24 hours	- 75 cc of colloid per each % burn area
	75 cc of electrolyte " " " "
	2000 cc water ot maintain urine output

One half of this fluid is given in the first 8 hours and one half in the next 16 hours. These fluids are given to fill the expanding spaces and replace wound seepage. Since transudation into the wound usually ceases in 36 to 48 hours, the fluid requirements for the second day are one half of that in the first 24 hours.

The water loss from the burn surface may reach 50 cc. for each 1% of body surface area. If the extracellular space expands beyond 50%, the chance of survival is poor, because the body's disposal mechanisms will be inadequate when the absorption phase occurs. Inadequate treatment in the first 36 to 48 hours after the burn may result in renal and visceral failure. Overzealous therapy may exaggerate the extracellular volume expansion. External fluid loss is minor compared with the edema fluid pooling in the burned area, yet it must be taken into account. Absorption of edema has usually started about the 45th to 50th hour. It may be rapid and overwhelming if fluid and electrolyte therapy is not promptly curtailed.

The shortcomings of fluid therapy based on the surface area formula are: 1) it does not take into consideration the variations in the volume of edema which depend on the site and the depth of the burn; 2) it omits the relocation of edema from burned to unburned areas; 3) it omits the probability that many small burn areas located strategically may overload lymphatics and lead to a disproportionate volume of edema; 4) it omits respiratory tract injuries; 5) it omits the size of the patient as a factor; 6) it leaves a tendency to overestimate the area burned and so leads to overzealous therapy.

B) Formula based on the Anticipated Interstitial Space Expansion (23)

This is applicable to a burn area of over 30%. It replaces the losses of wound edema, wound seepage (protein 4%, electrolyte concentration of plasma), urine, and insensible water.

1st 48 hours

(1) Wound edema - Volume: 10% body weight
(2) External loss: 25 - 35 % burn = 1000 cc
35 - 60 % burn = 2000 cc
over 60 % burn = 3000 cc

Add (1) and (2) and then administer two thirds of the combined volume as a colloid solution and one third as an isotonic electrolyte solution.

48 hour ration for wound edema and seepage:

2 parts in the 1st 12 hours
1 part in the 2nd 12 hours
1 part in the 2nd 24 hours

(3) Urine - 1500 cc for each 24 hour period
750 cc isotonic saline
750 cc glucose in water (can be given orally)

(4) Insensible loss:
1500 cc for each 24 hour period
1500 cc glucose in water (can be given orally)

RENAL OUTPUT AS AN ADJUNCT TO THE PLAN OF THERAPY

Hourly urine volume recorded by means of a retention catheter is mandatory. An adequate range of urine volume is 50 to 200 cc/hour. If the output remains below 30 cc/ hour, then the treatment is inadequate or some renal disease is present; they can be differentiated by the use of a water tolerance test in which 1000 to 1500 cc of 5% glucose in water is rapidly administered over a period of one hour. If the hourly urine volume rises, then the treatment was inadequate. If the urine volume does not rise, then there is some renal disease present, and further fluid administration must be cautious.

After 48 hours, the volume and nature of the fluid administration should parallel that given during the 2nd 24 hour period and should be continued until diuresis occurs. In deeper burns the diuresis is usually more delayed.

Additional care of the burned patient includes a high caloric and vitamin intake, a high nitrogen intake, red blood cell replacement, sedation, tracheostomy if necessary for upper respiratory burn, and chemotherapy.

Oliver Cope summarized the pathological physiology of the burn wound in an excellent paper delivered in November 1950 (22). The guiding principle in therapy is to replace in the unburned part of the body what is being lost into the burn wound. Like a leech, the burn area wound sucks water, protein, and electrolytes from the plasma circulating through its depth and it swells with edema. If adequate replacement is not given, cell life fails and the circulation is depleted. The thermal trauma increases capillary permeability in the burn area and also destroys the reflex vasoconstrictor mechanism, allowing arteriolar dilatation and greater blood flow into the damaged capillaries, permitting further loss to the burn area. It is limited only by the elasticity of the skin. The rate of edema formation is greatest initially, then it tapers off as the wound edema tension rises. It reaches a peak in 36 to 48 hours. The edema fluid is similar to plasma and extracellular fluid in electrolyte concentration, but the protein content is lower than that of plasma. Initially, the plasma colloid osmotic pressure is high but it cannot overcome the capillary damage to absorb edema fluid. During the absorption phase, the plasma becomes diluted.

BURN THERAPY REGIME OF PARNELL & EVANS (75)

They noted a high incidence of pulmonary edema occurring in burned patients between the 3rd and 6th day. They devised a new formula for the therapy of burns.

(1) 1 cc of blood or blood substitute per kilogram of body weight for each per cent of burn area in the 1st 24 hours. One half of the colloid solution is given as blood and one half as plasma.

(2) 1 cc of isotonic electrolyte solution per kilogram for each per cent of burn area in the 1st 24 hours.

(3) water - 2000 cc should be given for a patient weighing over 70 Kg. during the 1st 24 hours.

In the second 24 hour period, one half the colloid solution and one half the electrolyte solution are aeministered together with the same volume of water (2000 cc).

If the face and buttocks are burned, slightly more fluid should be given. The danger of over-expanding the extracellular space should be realized and not more than 3500 cc of colloid, 3500 cc of electrolyte solution, and 2000 cc of water should be administered in the 1st 24 hours, and not more than one half this amount in the 2nd 24 hours.

METHODS

Studies of fluid, electrolyte, and nitrogen balance, as well as hematologic changes, in five patients, were carried out. The first patient was studied on a trial basis and the observations were inadequate to report: this patient is included only in chart #5 as Mrs. J.M. The remaining four patients were studied from the metabolic balance standpoint (fluid, sodium, potassium, chloride, and nitrogen). In addition, haematologic observations were made. The urine concentrations of electrolytes were determined. Attempts were made to have these studies extend over a minimal pre-operative period of two days: the operative day in more detail, and a postoperative period of at least five days.

(1) Patient W.D. : male, 20 years old. Femoral herniorrhaphy under pontocaine spinal anesthesia up to throacic 8 segment.

(2) Patient A.M. : male, 26 years old. Incision and drainage of left inguinal abscess, under pontocaine spinal anesthesia up to thoracic 9 segment.

(3) Patient H.B. : male, 46 years old. Subtotal gastrectomy for peptic ulcer under pontocaine spinal anesthesia up to thoracic 4 segment.

(4) Patient H.M. : female, 43 years old. A severe body burn involving a surface area of 55% to 60% with most of the burn being of 2nd and 3rd degree depth.

These four patients were studied in a side room off the main ward, so that collections of urine and drainages could be very carefully carried out.

The prerequisites of a patient for this study were seven in number:

(1) good nutritional s tate;
(2) normal renal function;
(3) age between 15 and 65 years;
(4) no cardiac decompensation;
(5) ability to cooperate;
(6) normal fluid and electrolyte balance preoperatively;
(7) forty-eight hours of observation in hospital before operation

It is clear that patient # 4, a victim of severe burn, did not fulfill all the pre-requisites but considerable interest in observing this patient developed and the resulting observations seemed interesting enough to include them in this report.

DIET

Some patients were given a fluid diet only. Others received some additional solid food. In patients # 3 and # 4, much of the intake was parenteral. The potassium and sodium content of the solid food used was obtained from the date reported by Bills (8), which was obtained from aliquot analysis of food lots, using the flame photometer. The milkshake was analysed for its sodium, chloride, potassium and nitrogen content in the Donner Laboratory; the other fluids administered orally were calculated on the basis of food-tables alone. The chloride content of food ingested was mainly assumed from the sodium content because the food tables contained very little data on the former. It was realized from the beginning, that any balance data in which the intake is based on food tables and not on daily aliquot analysis, will be necessarily lacking in accuracy. However, since the majority of the reports in the literature quote intake date on the basis of food tables, we felt that this method was justified. Considerable difficulty and expense would attend the carrying out of daily aliquot analyses, and, furthermore, the dietetic and laboratory facilities it would entail were not available to us. The fluid diet and the simple solid additions were used because of their relative freedom from variation in electrolyte content. Unfortunately, this diet often provoked diarrhea, which would interrupt a study period.

SURGICAL RESEARCH FLUID DIET
(2201 Calories)

			Prot.	Fat	C.H.O.	Na.	mg.	K.	mg.
	Milkshake	1000	60	55	75	828		2113	
8. A.M.	(Fr. Orange Juice	200	-	-	20		6	340	
	(Glucose #	20	-	-	20				
10. A.M.	(Grapefruit Juice	200	-	-	20	1		400	
	(Corn Syrup #	50	-	-	37	84		2	
2. P.M.	(Glucose	18	-	-	18				
	(Gingerale #	100	-	-	8	8		6	
	(Grape Juice	100	-	-	18	1		160	
5. P.M.	(Apple Juice	200	-	-	26	8		200	
	(Glucose #	10	-	-	10				
7. P.M.	(Glucose	18	-	-	18				
	(Gingerale #	100	-	-	8	8			6
	(Grape Juice	100	-	-	18	1		120	
9. P.M.	(Glucose	12	-	-	12				
	(Milk	200	6	8	10	100		280	
	(Chocolate Malted	25	3	2	17	110		180	
			69	65	335	1149.6		3761.6	

200 cc. Milkshake given.

SOFT ADDITIONS TO FLUID DIET

		AMT. GM.	P.	F.	C.H.O.	NA.	K.
1.	Puffed Wheat	20	2	-	14	1	68
	Milk	200	6	8	10	100	280
	Sugar	12	-	-	12	-	-
2.	Egg Soft cooked	1	7	5	- -	40	50
	Ry-Krisp	20	2	-	14	300	120
3.	Canned pears	150	-	-	24	12	108
	Graham Wafers	20	2	2	14	192	86
4.	Sliced Banana	150	1	-	30	.7	630
	Sugar	12	-	-	12	-	-
	Milk	200	6	8	10	100	280
5.	Chicken Leg Meat	50	10	3	-	22	50
	Raw Tomato	100	1	-	4	3	230
	Graham Wafers	20	2	2	14	192	86
6.	Cornflakes	20	2	-	16	132	32
	Milk	200	6	8	10	100	280
	Sugar	12	-	-	12	-	-

No salt and pepper.

COLLECTION OF SPECIMENS

(1) Urine: 24 hour periods were arbitrarily chosen, extending from 7 a.m. to 7 a.m. A Retention Foley Catheter was inserted pre-operatively and several specimens obtained on the operation day. This catheter was left in place as long as the patient would tolerate it.

(2) Drainages and abnormal losses: Gastric suction was used in patient # 3, the volume recorded, and an analysis performed. Vomitus was collected and analysed. Diarrhea volume was measured and analysed.

(3) Blood: A venapuncture was done every morning, preferably before the patient's breakfast, and 25 cc of blood withdrawn. On the day of operation, hourly blood and urine samples were obtained following the onset of anesthesia for about three to four hours.

On the day of operation, multiple determinations of blood and urine samples were made in an effort to demonstrate changes which might occur during the period of anesthesia and operative procedure.

DETERMINATIONS

(1) Food and Fluid Intake:

a) Fluid volume.
b) Sodium, potassium, nitrogen, chloride, and caloric content

(2) Urine:

a) Volume.
b) Routine urinalysis.
c) Sodium, chloride, potassium and nitrogen content.

(3) Whole Blood:

a) Hemoglobin.
b) Hematocrit.
c) Red blood cell count.
d) Eosinophile count.
e) White blood cell count.

(4) Blood Serum:

a) Sodium, potassium, chloride, bicarbonate.
b) Non protein nitrogen.
c) Total proteins, albumin, globulin.
d) Blood sugar.

(5) Body Weight Record.

(6) Blood Pressure & Temperature Record in patient # 4.

LABORATORY METHODS

(A) Donner Building Experimental Surgery Laboratory

Sodium	-	flame photometer
Potassium	-	" "
Bicarbonate	-	Manometric Van Slyke
N. P. N.	-	Nesslerization
Total Nitrogen	-	Semi micro-Kjedahl
Chloride	-	1) Van Slyke and Heller modification of Sendroy's Iodometric method 2) Fantus test
Blood Sugar	-	Folin Wu Method

(B) Royal Victoria Hospital Laboratory

Serum Protein	-	Phenol method
Eosinophile Count		

Graphic recording of the values on charts, according to the method of Albright and Reinfenstein (1), was used for Balance data.

RESULTS AND OBSERVATIONS

(1) Patient # 1: Mr. W.D., 20 years old. This patient was studied for three days pre-operatively and for five days post-operatively. Graphic recording is on charts # 1 and 2.

Fluid Balance: The urine volume remained high pre-operatively (2000 cc/day) due to the intake of fluids alone. Post-operatively, the urine volume remained comparatively low for four days, then rose sharply on the fifth day, even in the presence of a lowered intake. The urine specific gravity was highest on the day of operation. Following administration of the spinal anesthetic and the beginning of the operation, the urine volume remained small throughout the day.

Electrolyte Balance:

(A) Sodium - This balance was negative pre-operatively to a considerable degree. Following the anesthetic and for the next three days, the balance was in equilibrium but the intake and output of sodium were both very small. There was a marked excretion of sodium ion on the fourth and fifth post-operative days, which rendered the balance greatly negative, even in the presence of an increased sodium intake on these days. The serum sodium values remained within normal limits, except for a slight fall below normal (135 meq/L) on the third post-operative day.

(B) Chloride - This balance behaved similarly to that of sodium with a retention of chloride following anesthesia and operation and with a diuresis of chloride on the fourth and fifth post-operative day.

The serum chloride concentration remained normal.

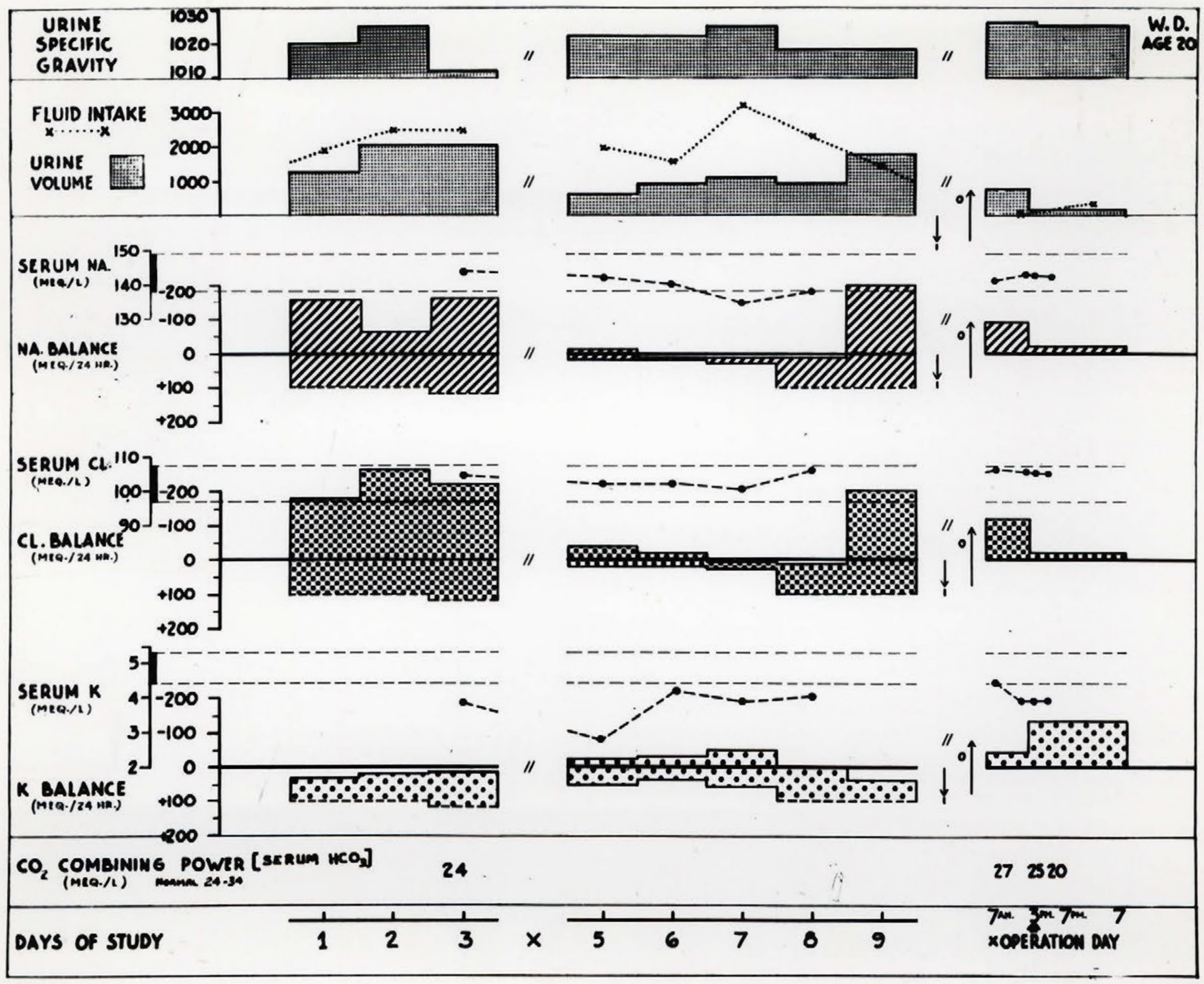


CHART # 1 PATIENT MR. W.D.

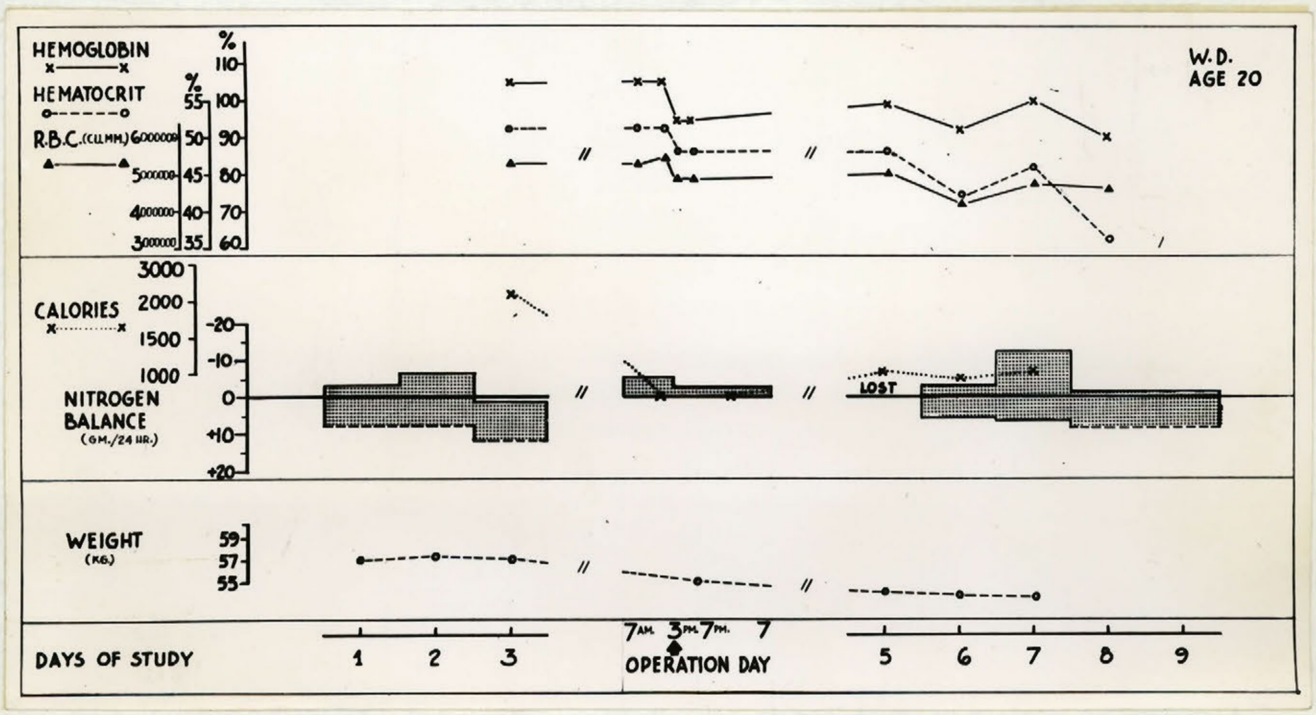


CHART # 2 PATIENT MR. W.D.

(C) Potassium - The balance was in equilibrium pre-operatively, but a large excretion of potassium occurred immediately following anesthesia and operation, turning the balance negative. Post-operatively, the balance remained slightly negative until the fourth post-operative day. The serum potassium concentration was at the lower limits of normal, except for one value on the first post-operative day when it was 3.0 meq/L. There were no symptoms of potassium deficiency at this time.

(D) Bicarbonate - The serum bicarbonate was low (20 meq/L) one hour following operation.

Nitrogen Balance:

The balance was negative on the day of operation and for three days post-operatively. During this period, the intake of nitrogen on the fluid diet was not very high, averaging 5 to 6 grams of nitrogen per day. Post-operatively, the caloric content of the diet was also deficient. The patient lost 2.5 kilograms of weight during the study.

Haematological Data:

There was an abrupt fall in the hemoglobin, red cell count and hematocrit in the hour following anesthesia and operation. This did not return to normal during the remaining period of observation. The operation was considered a bloodless one.

(2) Patient # 2: A.M., 26 years old. Incision and drainage of an inguinal abscess. This patient was studied for two days pre-operatively and for two days post-operatively. He developed diarrhea on the third post-operative day, which terminated the study. Graphic recording of the results are seen in charts # 3 and # 4 on pages 33 and 34.

Fluid Balance:

A suppression of urine output was noted, following the anesthesia and operation, but it lasted only one day. The urine specific gravity was highest on the day of operation.

Electrolyte Balance:

A) Sodium - The balance was negative pre-operatively, due to a relatively low intake of sodium (30 meq/day). Following the operation, there was marked sodium retention, with the balance positive. The serum sodium concentration remained within normal limits, except for a slightly low value on the first post-operative day (136 meq/L).

B) Chloride - There was a similar retention of chloride post-operatively, but a negative balance is shown on the chart because of the unknown intake. The serum chloride concentration was lowest (101 meq/L) on the first post-operative day.

C) Potassium - A positive balance was observed on the first post-operative day. The serum concentration remained within normal limits, but abruptly fell from 5.0 meq/L to 4.1 meq/l one hour after the anesthesia and operation.

D) Bicarbonate - The serum concentration remained within a normal range, except for the first hour after anesthesia and operation (22 meq/L).

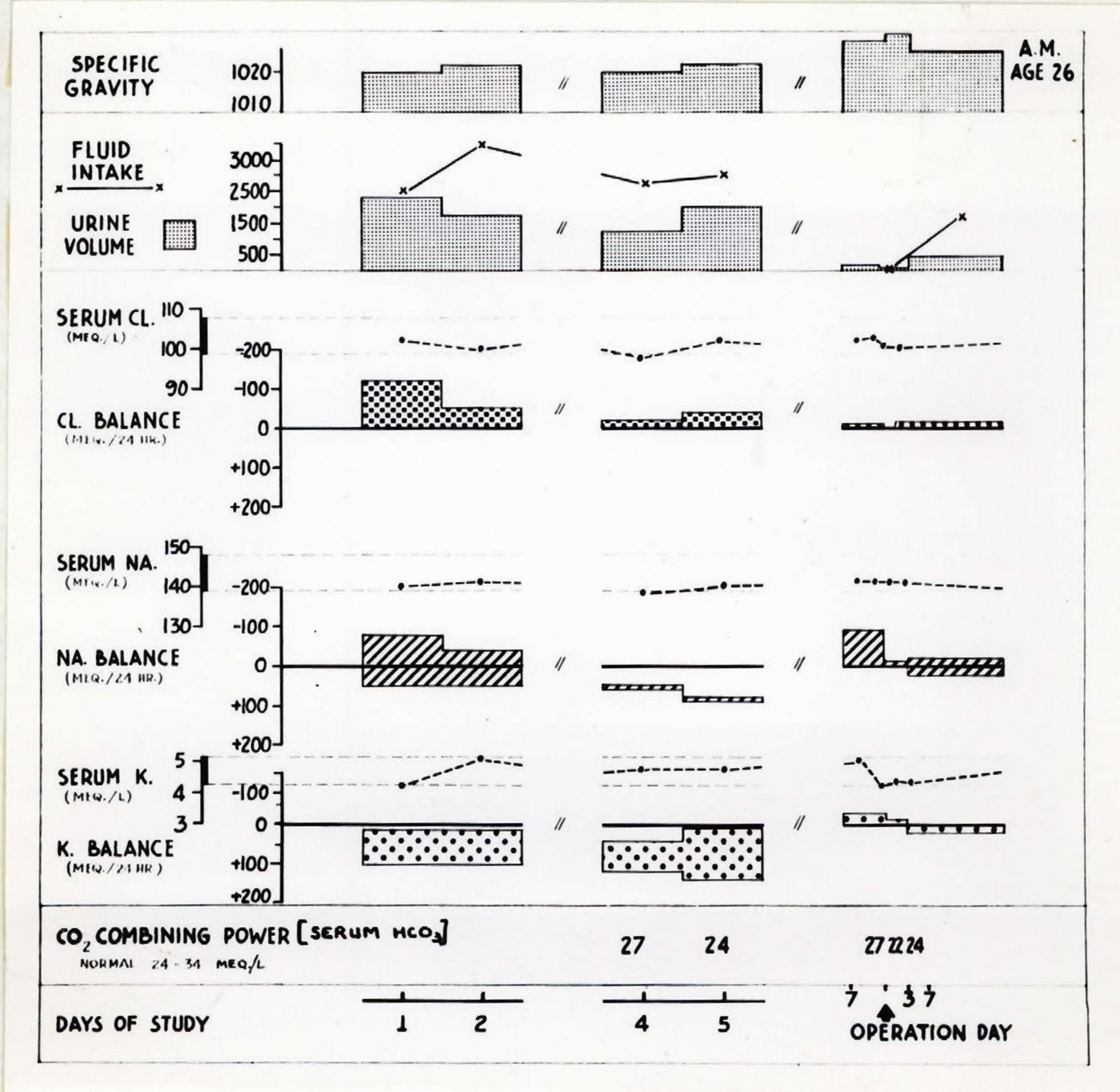


Chart #3 PATIENT Mr. A.M.

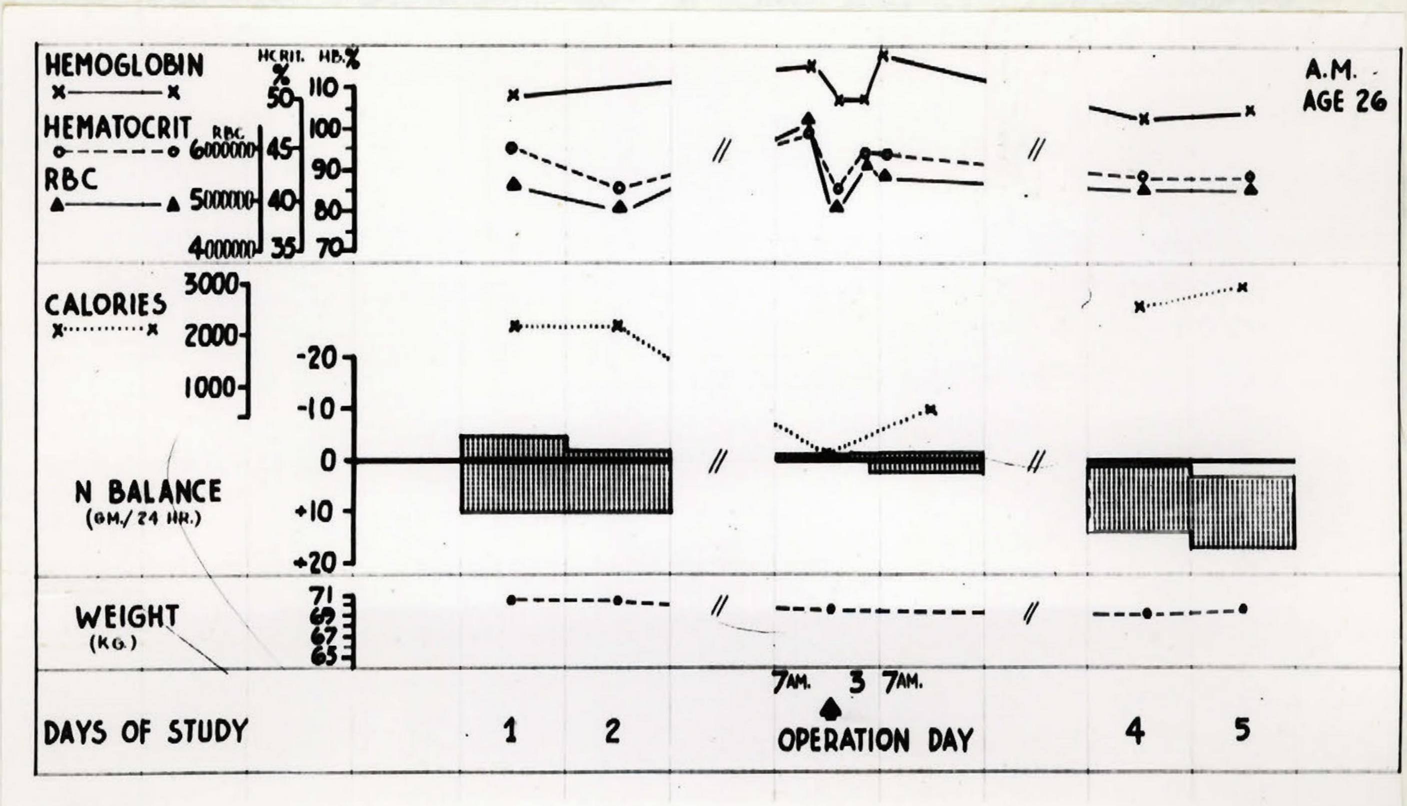


Chart #4 PATIENT Mr. A.M.

Nitrogen Balance:

This balance was negative pre-operatively when the intake was 10 grams of nitrogen per day and 2200 calories. Post-operatively, equilibrium existed, except for the second day, when the balance became positive. His weight remained essentially unchanged.

Haematological Data:

An abrupt fall in the hemoglobin concentration, red cell count, and hematocrit was noted one hour after the onset of anesthesia and operation. This change then rectified itself in the next hour.

URINE CONCENTRATION OF ELECTROLYTES

In Chart # 5, the concentrations of sodium, chloride and potassium are charted over the urine volumes for the first three patients studied. This chart includes patient J.M., who was a 52 year old woman requiring a hemorrhoidectomy under spinal anesthesia, as well as patients W.D. and A.M. Patient J.M., as previously mentioned, was not completely studied and this is the only reliable finding that has been charted. The arrows depict the time of onset of anesthesia and the operation. A marked rise in the concentration of potassium in the urine was noted following the administration of anesthesia and the beginning of operation. Coincident with this rise in potassium, there was a marked fall in the sodium and chloride concentration, almost to nothing. A marked rise in the sodium and chloride concentration occurred on the fourth and the fifth post-operative day in patient W.D., but this was not observed in patient A.M. (who was studied for only two days after operation). Patient J.M. showed an increase in sodium and chloride excretion on the last (i.e., the third post-operative day) day of her observation period. The potassium concentration gradually dropped to normal levels in the post-operative period after its initial rise. The suppression of urine formation in the immediate post-operative period is also evident.

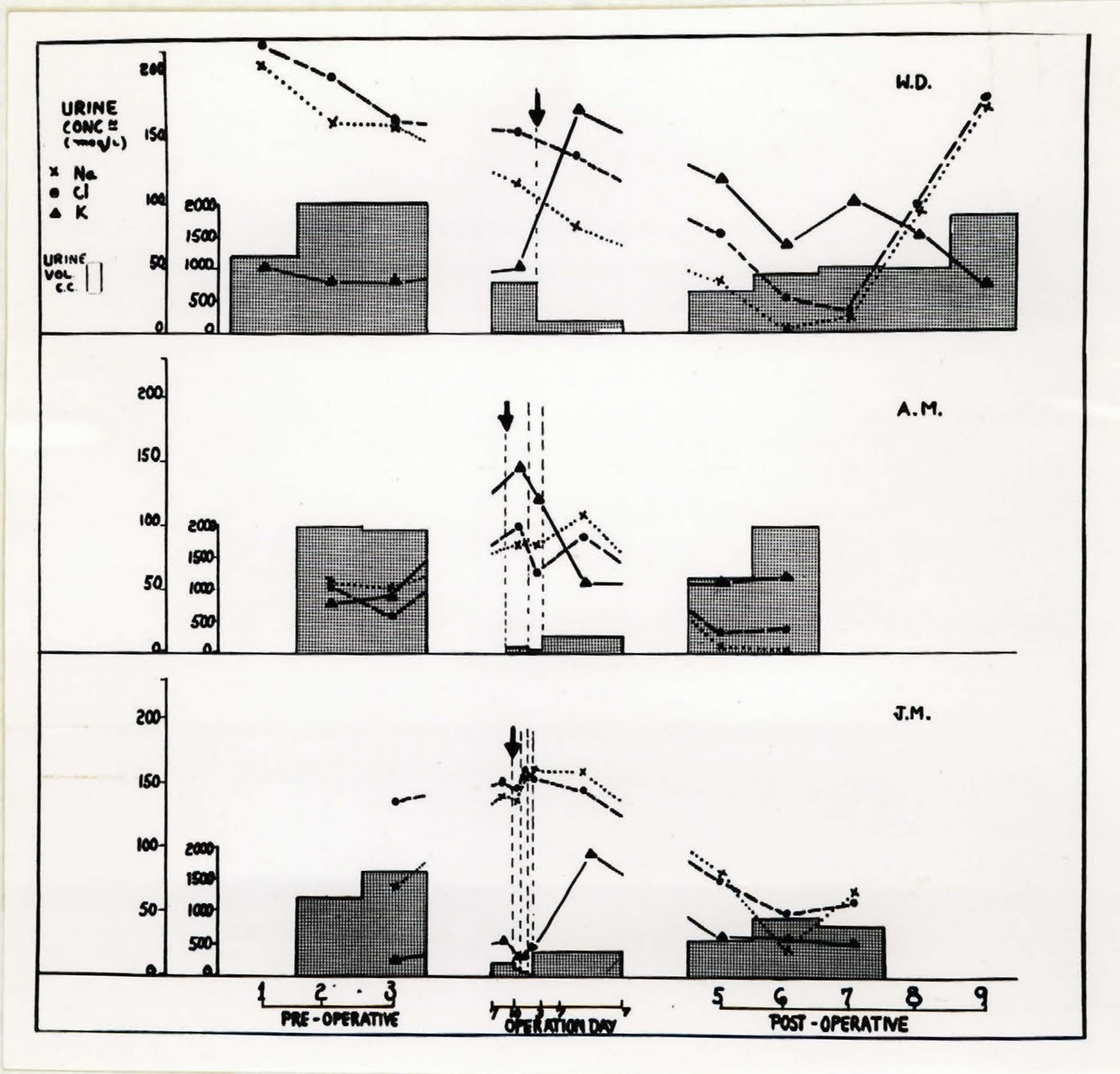


Chart #5 PATIENT Mr. W.D.

Mr. A.M.

Mrs. J.M.

(3) Patient H.B.: 46 years old. This man appeared to be in relatively good health pre-operatively. He had suffered peptic ulcer symptoms for several years. He underwent a sub-total gastrectomy and was free from post-operative complications until the eighth day, when a wound separation occurred and he was returned to the operating room for secondary closure of the abdominal incision. He was studied for four days pre-operatively and eight days post-operatively. No evidence which might indicate the cause of his wound disruption could be deduced from the data to be presented. It should be noted that he did develop diarrhea on the fifth post-operative day, but this was not severe; the diarrhea was probably a result of the controlled fluid diet.

A more detailed observation was carried out on this man on the operative day and these results are separately reported in chart # 8. The pre and post-operative observations are recorded on charts # 6 and # 7.

Fluid Balance:

The patient ingested an enormous amount of fluid pre-operatively and the expected large urine volume, with low specific gravity, was noted. Post-operatively, the fluid intake was more normal and the urine output less. The post-operative suppression of urine formation was less marked than that observed in patient A.M. and patient W.D. The specific gravity of the urine increased to a range of 1020 - 1025 in the post-operative period.

Electrolyte Balance:

A) Sodium - This balance was slightly positive for three days post-operatively, indicating sodium retention, and then became negative for the last four days. The lack of any sodium ingestion on the operative date accounts for the negative balance on this day. The serum sodium concentration decreased to 132 meq/L during the post-operative period and remained there until the seventh day.

B) Chloride - The chloride balance behaved in manner similar to the sodium balance. The serum chloride concentration was also below the normal range in the early post-operative period.

C) Potassium - A markedly negative balance occurred on the day of operation and for the following three days. The serum potassium concentration dropped to 3.5 meq/ Litre on the third post-operative day in the presence of a moderate potassium excretion and an intake of 20 meq. per day. The serum level did not return to a normal range until the seventh day, when the balance became positive.

D) Bicarbonate - The serum concentration remained within the normal range.

Haematological Data:

There was no great change in the hemoglobin concentration, the red cell count, or the hematocrit. At the time of the wound disruption, the hemoglobin concentration was 98%, the red cell count 4,600,000 per cu. mm., and the hematocrit 43%.

Nitrogen Balance:

A markedly negative nitrogen balance occurred from the

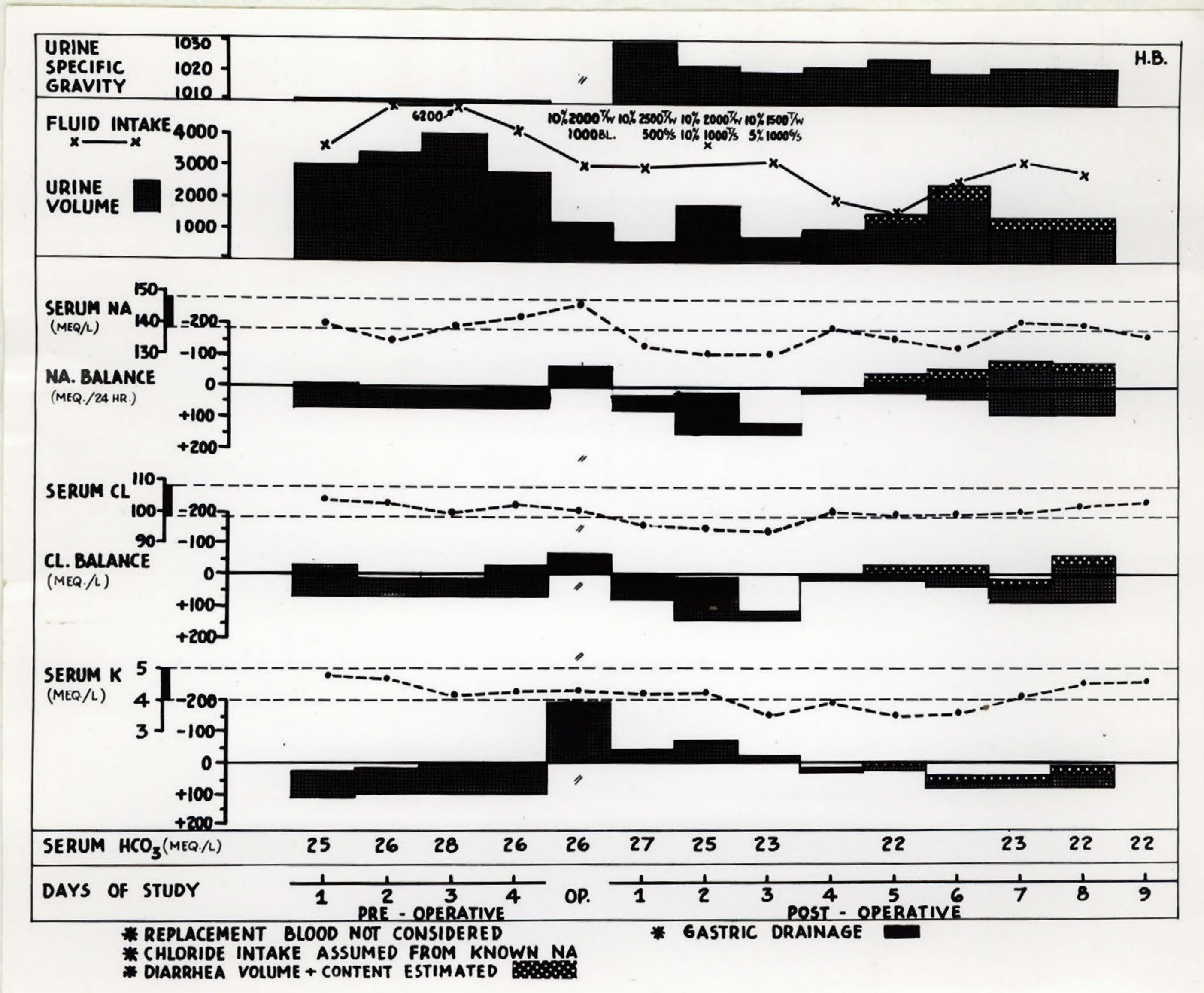

H.B.
URINE SPECIFIC GRAVITY
1030
1020
1010
FLUID INTAKE x——x
URINE VOLUME
4000
3000
2000
1000
6200
10% 2000 D/W 10% 2500 D/W 10% 2000 D/W 10% 1500 D/W
1000 BL. 500 D/S 10% 1000 D/S 5% 1000 D/S
SERUM NA (MEQ/L)
150
140
130
NA. BALANCE (MEQ./24 HR.)
-200
-100
0
+100
+200
SERUM CL
110
100
90
CL. BALANCE (MEQ./L)
SERUM K (MEQ/L)
5
4
3
SERUM HCO3 (MEQ/L)
25 26 28 26 26 27 25 23 22 23 22 22
DAYS OF STUDY
1 2 3 4 OP. 1 2 3 4 5 6 7 8 9
PRE - OPERATIVE
POST - OPERATIVE
* REPLACEMENT BLOOD NOT CONSIDERED
* CHLORIDE INTAKE ASSUMED FROM KNOWN NA
* DIARRHEA VOLUME + CONTENT ESTIMATED
* GASTRIC DRAINAGE

CHART # 6 MR. H.B.

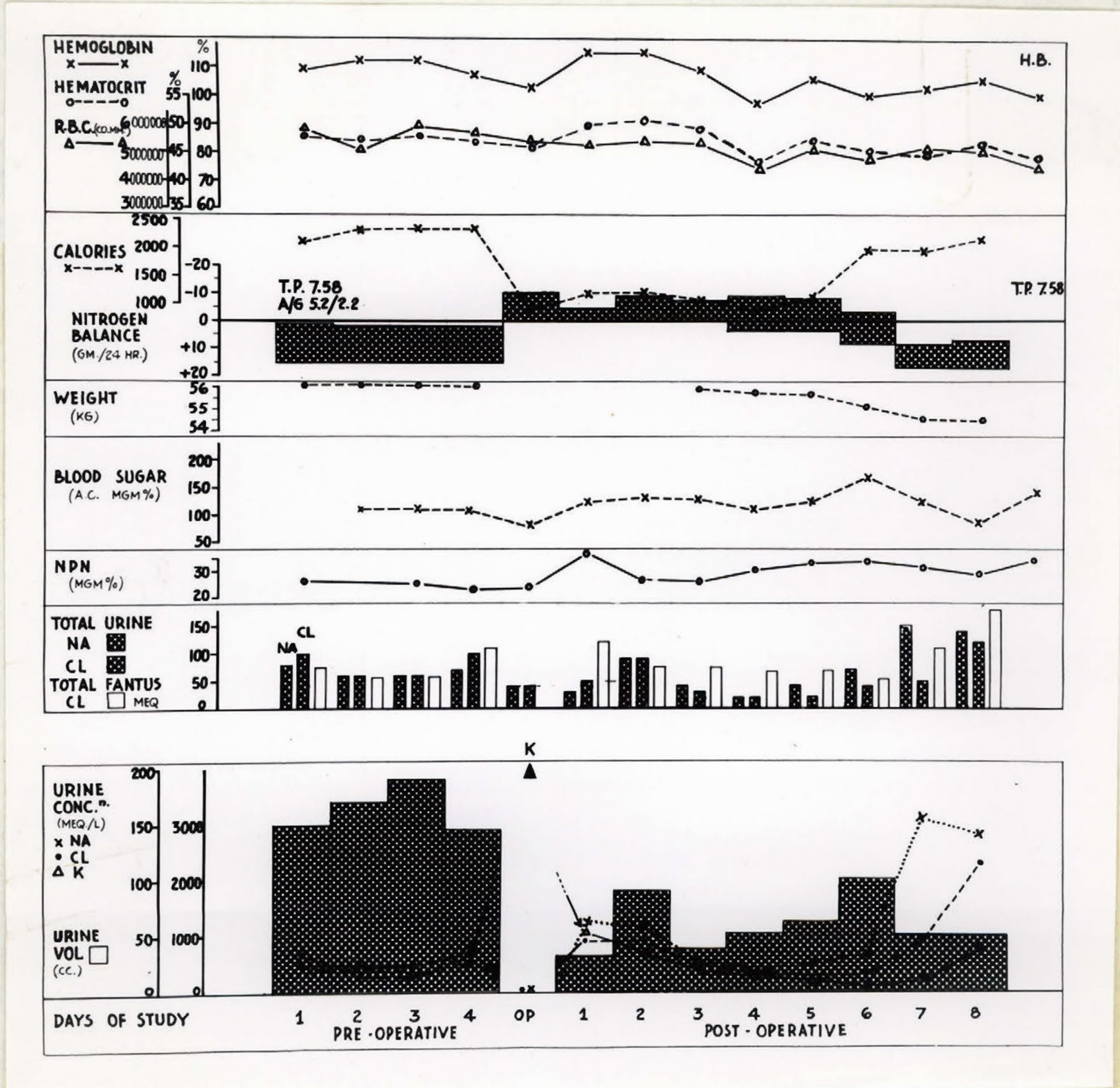


CHART # 7 PATIENT MR. H.B.

day of operation until the sixth post-operative day. This occurred with an intake nitrogen of 2 - 6 grams of nitrogen day (sub-normal amount) and in the presence of a low caloric diet (1000 cals./day). The caloric and nitrogen content of the diet increased from the sixth to the ninth day and at this time, the balance became positive. The total serum protein value pre-operatively, was 7.58 gms% with the albumin fraction 5.2 gms% and the globulin, 2.2 gms%. The weight loss was 3 kilograms.

Urine Electrolyte Concentration:

A marked rise in the potassium concentration occurred on the day of operation, then it gradually fell to reach its pre-operative level by the fifth post-operative day. The sodium and chloride concentration were almost zero on the day of operation and remained low until the sixth post-operative day, when a marked rise occurred.

Miscellaneous:

The validity of the Fantus test for urinary chloride as an index of the concentration of sodium in the urine unreliable. On a few occasions it even failed to indicate accurately the chloride concentration.

The blood sugar and non-protein nitrogen levels in the blood were not abnormal.

Operation Day - Chart # 8

1) Electrolyte Concentration of the Urine: The sodium, potassium, and chloride concentrations increased within the hour after

P. 17. Hanow & Shenvin
18 greater part are, retained
21 Crooshank
31. The a.a, from which amines have been produced have a basic polar group situated at the end of the molecule; removed from the COOH group attached.
39 sulfhydral.
quercetin
54 challanged
56 force fed.

Whatever histamine content of persons
Absence of macrophage
Dietary deficiency may be a cause of high histamine

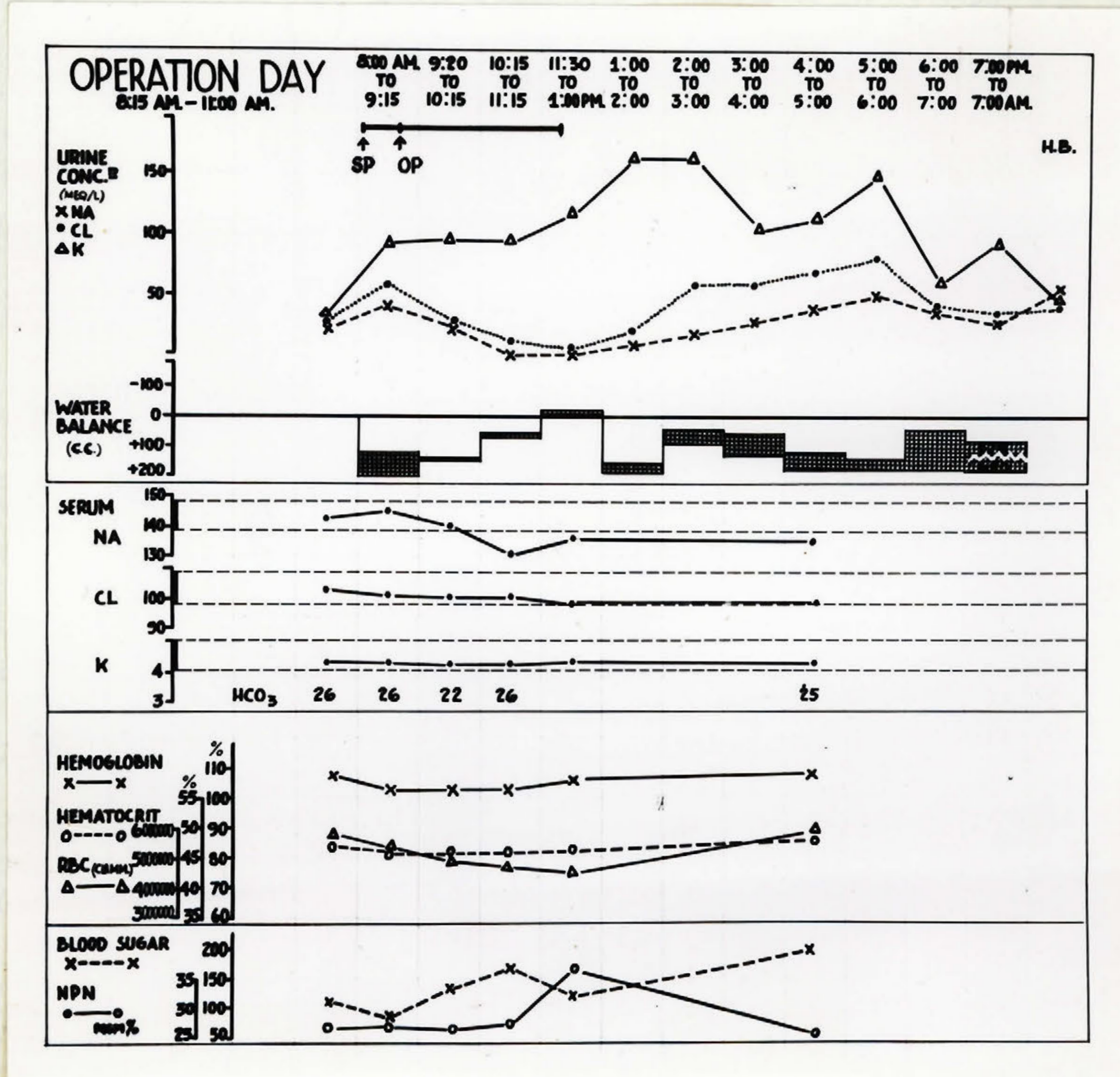


CHART # 8 PATIENT MR. H.B.

anesthesia was administered and before the beginning of the operation. Following the operation, the potassium concentration increased further in the hourly urine specimens, returning to the pre-anesthetic value in 24 hours. After the onset of the operation, the sodium and chloride concentrations decreased for four hours, then gradually returned to their pre-operative level.

2) Fluid Balance: A marked suppression of urine is evident from the markedly positive water balance which persisted throughout the operative day, even in the presence of an intake of 100 - 200 cc per hour.

3) Serum Electrolyte Concentration:

a) The serum sodium value decreased to 132 meq/litre, 2 hours after the beginning of the operation.

b) The serum chloride concentration remained normal.

c) The serum potassium concentration remained normal.

d) The serum bicarbonate concentration remained within the normal range.

4) Haematological Data: The hemoglobin concentration, the red cell count, and the hematocrit decreased slightly after the spinal anesthetic, and returned to their pre-operative levels in eight hours. The N.P.N. rose to 38 mgm% four hours after the operation, then returned to the pre-operative level.

(4) Patient Mrs. H.M: 43 years old. This patient suffered a severe body burn involving the face, neck, anterior and posterior trunk, buttocks, and the upper extremities. The estimated surface area burned was 55 - 60 %. About one-half was third degree, and the remainder, first and second degree. The patient arrived in hospital six hours after the burn. She died about five weeks later, from a combination of septicemia and possible electrolyte imbalance. There was no data obtained on the latter, apart from a serum potassium concentration of 2.6 meq/L three days prior to death. The study period herein reported extends from the date of admission to hospital until the 19th day thereafter. The patient weighed 50 kg. The patient's course in hospital was not conducted under our direction. We collected specimens and made the data available to those concerned with her management. See Charts # 9.

Fluid Balance:

The character and amount of fluids administered intravenously are shown. The fluid intake ranged from 3000 to 4000 cc per day, except for the first three days, when it was much higher. The urine output was less than 1000 cc per day until the fourth day, when it increased to 2000 cc, coincident with the onset of absorption of the edema fluid.

Electrolyte Balance:

A) Sodium: The balance was positive during the first three days of intensive intravenous therapy. The excretion of sodium at this time was very low. On the day that absorption of the edema fluid began, an enormous intake of oral sodium was inadvertently given, in addition to intravenous sodium. This intake measured 800 meq on the fourth day and 900 meq on the fifth day. This high sodium content was present in some chicken broth and baby meat food which was given through a stomach tube in the hope of supplying the patient with fluid and protein. The sodium contents was not analysed until after the serum concentration of sodium was found to be so elevated. Sodium intake was then restricted for the following seven days, during which time the balance became negative. The serum sodium concentration began to rise on the fourth day and reached a very high level on the eighth day (162 meq/L). At this time a cation exchange resin (Resodec) was given orally (35 grams/day) in an attempt to remove extra sodium from the gastrointestinal tract, even the sodium intake was being drastically restricted to a minimum of less than 100 meq per day. The serum value of sodium began to fall gradually to a normal level by the thirteenth day.

B) Chloride: The chloride balance behaved in fashion similar to that of the sodium. The serum chloride concentration increased to a maximum of 125 meq/L on the ninth day and then gradually decreased to a normal level by the thirteenth day. The intake of chloride was also enormous (832 meq/day) on the fourth and fifth day, at the time of absorption of edema.

C) Potassium: The balance remained in equilibrium, except for a negative balance of 75 meq on the third day and a negative balance of 100 meq. on the 6th day. The serum potassium concentration

concentration fell abruptly on the fourth day to a value of 3.0 meq/Litre. At this time oral potassium chloride was administered in a dosage of 35 meq/day until the twelfth day. The serum potassium value returned to a normal level at this time.

Nitrogen Balance:

The balance was computed from the third day. At this time it was negative by 7 grams. For the next four days, the balance became positive, during which time the intake average was 20 to 30 grams of nitrogen/day. The caloric intake remained between 3000 and 4000 calories per day from the fifth day until the end of the study period. The total serum protein remained below normal, ranging from 5.2 gms% to 5.4 gms%. The albumin-globulin ratio became reversed on the seventh day remained that day.

Haematological Data:

The hemoglobin concentration was high in the early burn period, but returned to a normal range by the sixth day. The eosinophile count was very low early in the study period and only increased to a limited degree by the ninth day. A less marked fall in the eosinophile count then followed during the remainder of the study period. The serum N.P.N. was above normal on the first day (55 mgm%) and again on the 19th day (60 mgm).

URINE CONCENTRATION OF ELECTROLYTES
AND HOURLY URINE VOLUME

Chart # 10

The concentration of urine sodium and chloride remained

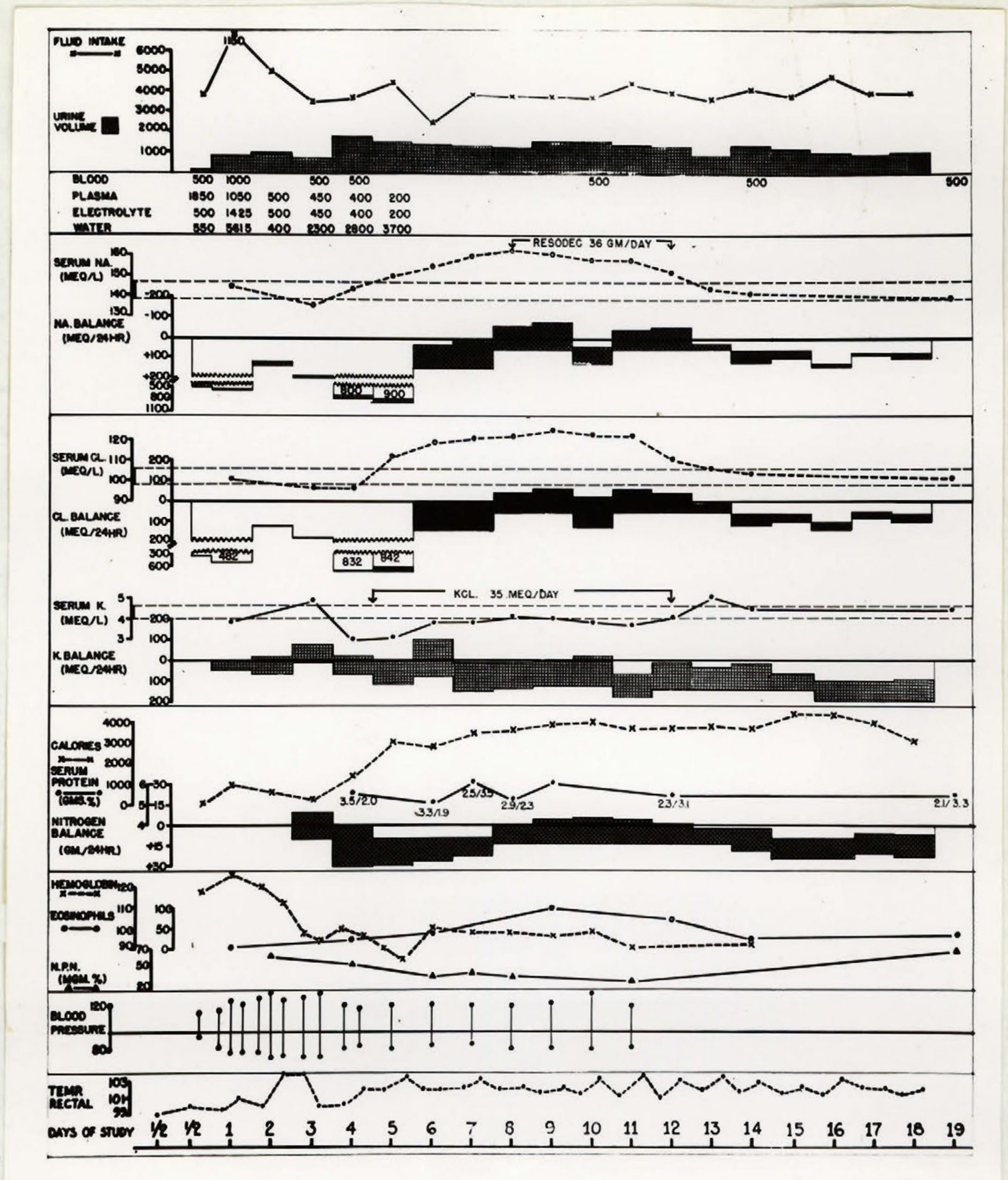


CHART # 9 PATIENT MRS. H.M.

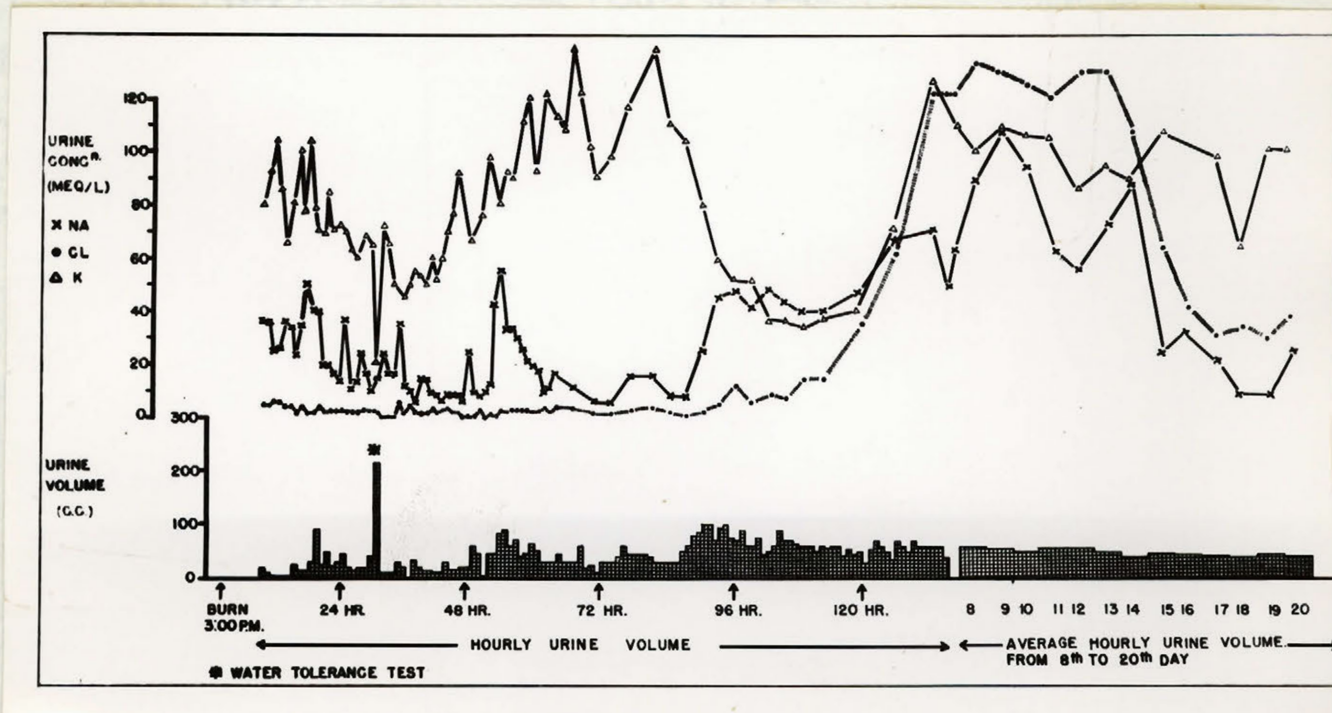


CHART # 10 PATIENT MRS. H.M.

very low, until the fifth day, when a marked increase occurred. Then it decreased to a low level by the 17th day. The potassium concentration was high at three periods: 1) the first 16 hours following the burn; 2) from the 48th hour to the 90th hour; 3) from the seventh to the ninth day. The hourly urine volume ranged from 30 to 75 cc during the first 48 hours, then increased to an average range of 100 to 125 cc per hour for the remainder of the study period. A water tolerance test at the 35th hour, indicated well functioning kidneys and thus an inadequate intake as the responsible factor for the low hourly urine volume in the first 36 hours.

The blood pressure was very labile during the first four days. The rectal temperature ranged between 101° and 103° F. throughout the study period. The patient was frequently irrational and restless, especially when the serum sodium and chloride levels were very high.

DISCUSSION OF RESULTS AND SUMMARY.

1. Fluid Balance

Those patients who had a spinal anesthetic and an operation, manifested a suppression of urine formation following the operation. In some this relative oliguria persisted for several days; in others it lasted only one day. In every patient it was followed by a moderate diuresis, lasting one or two days and producing a negative water balance. The day of operation was not unlike the first few post-operative days; here, also, a positive fluid balance was encountered due to the low urine output. In the burn patient a marked oliguria persisted for almost 72 hours and was then followed by a good urine output.

It is illogical to incriminate either the spinal anesthetic or the operative trauma as the agent responsible for the above fluid balance changes. It is certain that both evoke an alarm reaction in the organism leading to a sudden discharge of the adrenal cortex hormones. This in turn leads to the suppression of urine formation in a manner as yet unknown; probably by a direct action to increase tubular absorption in the kidney. In the burn patient the trauma is quite severe but there are other fluid shifts also occurring which lead to a decreased circulating blood volume. The response to trauma varies in individuals depending on homeostatic mechanisms operating at the time. Certain it is that when the discharge of cortical hormone ceases so does the oliguria revert to a diuresis. A burn is not so clearly explained since we have the repair of damaged capillaries promoting a return of fluid from the traumatized area added to the endocrinological kidney alteration. The variation in intensity of the alarm reaction among our patients may account for the variation in the length of time that the relative oliguria persists.

II Electrolyte Balance

A marked suppression of sodium and chloride excretion in the urine was found immediately following trauma, either by operation and spinal anesthetic or by a burn. Coincident with this there occurred a great increase in the excretion of potassium. These alterations persisted for different lengths of time in the patients studied but they were followed by a diuresis of sodium and chloride and a retention of potassium occurring together. The above phenomena occur in time with the observed alterations in fluid balance, i.e., the sodium and chloride retention are most evident when the urine formation is lowest (while the potassium excretion is high) and the reverse situation among the electrolytes obtains when the post-operative water diuresis begins. This observed electrolyte pattern is repeated in all the patients studied and is very likely associated with a high mineral corticoid discharge from the adrenal cortex during the alarm reaction to trauma. The exact mechanism by which the above acts on the kidney is not clearly understood. The sodium and chloride retention may be due to a direct tubular effect by mineral corticoids of increasing absorption of these ions while decreasing the absorption of potassium. It is also possible that water and ion exchange occurs between the intracellular and extracellular compartments producing these observed electrolyte excretion and retention patterns. The serum electrolyte concentrations are not noticeably altered by these abnormalities. This would indicate and support the idea that the post-operative salt and water retention and potassium excretion are physiological changes serving some good purpose. Failure to recognize these changes in the post-operative management of surgical patients can lead to great difficulties. This is exemplified by the last patient studied, Mrs. H.M., who suffered a severe burn. Large amounts of sodium and chloride were inadvertently administered on the third and fourth day with the result that the serum concentrations of sodium and chloride increased to dangerous levels. At the same time the serum potassium level fell to a clinically deficient level. Severe restriction of sodium and chloride intake was instituted promptly. Potassium therapy was begun. At this time it was decided to supplement this management with the use of an oral cation resin (Resodec) in the hope that extra sodium could be extracted from the body. The drug was given in doses of 1.f grams/hour by stomach tube for four days. Coincident with the onset of this therapy, the serum sodium level gradually returned to normal. The serum chloride level fell more precipitously to normal. The serum potassium level returned to normal. It is only speculation to assume that the cation resin played a part in the correction of the hypernatremia.

III Nitrogen Balance

In the three post-operative cases studied, Mr. A.M., Mr. W.D., and Mr. H.B., the nitrogen balance became negative after operation. It was also shown that the caloric intake during this negative period was very low. No special attempt was made to increase this caloric intake. The patients were given the usual post-operative parenteral fluids and diet that all surgical patients receive. It is known that this parenteral intake is inadequate in calories but until intravenous fat preparations become available, no remedy for the situation is possible. The length of time that the nitrogen balance remained negative varied among the patients, but none were followed for a sufficiently long enough period to observe the expected swing back into positive nitrogen balance.

In the burn patient, an expected positive nitrogen balance was encountered in the first week due to the numerous blood and protein containing infusions. The following week revealed an equilibrated nitrogen balance and the third week, a further positive nitrogen balance. This data cannot be considered significant because measurements of the wound seepage were not kept. This latter avenue of nitrogen loss must have been considerable because the serum protein concentration fell throughout the observation period and the albumin globulin ration became reversed.

IV Haematological Data

An abrupt fall in the levels for the hemoglobin concentration, red blood cell count, and the hematocrit were observed in patients A.M., W.D., and H.B., immediately following the spinal anesthetic. These levels returned to normal several hours after the operation. It is possible that a degree of peripheral vasodilatation may occur following the spinal anesthetic leading to a localized pooling of blood at the expense of the remainder of the circulation accounting for the sudden fall in hemoglobin concentration and red blood cell count. The burn patient exhibited a marked hemo-concentration for the first 36 hours.

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