AN EXPERIMENTAL EVALUATION OF THE NUTRITIONAL IMPORTANCE OF PROXIMAL AND DISTAL SMALL INTESTINE*

ARNOLD J. KREMEN, M.D., JOHN H. LINNER, M.D. AND CHARLES H. NELSON, M.D.

MINNEAPOLIS, MINNESOTA

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA, THE UNIVERSITY SURGICAL SERVICE, MOUNT SINAI HOSPITAL, MINNEAPOLIS, MINN., AND THE EXPERIMENTAL SURGICAL LABORATORY OF THE MINNEAPOLIS VETERANS' HOSPITAL

ACCUMULATED CLINICAL experience has long suggested that man not uncommonly survives the sacrifice of large segments of small intestine.[2, 4, 6, 9, 11, 14] The results, however, are variable, and for every favorable case that finds its way into the literature, there are without question a considerable but unknown number of patients who do not survive such a catastrophe. Since in clinical practices, resections for the most part are performed under uncontrolled conditions, usually for extensive neoplastic disease or for infarcted gut, reliable data concerning essential functions of specific levels of the intestine cannot be gathered in this fashion.

Experimental studies in dogs reveal that animals also can, with reasonable assurance, be deprived of from 50 to 70 per cent of their small intestine and maintain a near normal nutritional status. However, more detailed information relating to the relative nutritional importance of the various levels of the small intestine is sparse and conflicting. Reports of Flint,[5] Althauser,[1] Weckesser,[15] Jensenius[7] and others[11] suggests that the principal deficiency following such procedures is a moderate to severe interference with absorption of fat; protein absorption is less severely affected, and carbohydrate remains relatively unaffected.

The present study was undertaken to define differences of nutritional adjustment after sacrifice of comparable segments of proximal and distal small intestine. As a result of these studies it is apparent that in the dog, the major discernible abnormality after loss of the distal small bowel is a marked diminution in efficiency of fat absorption associated with loss of weight. On the other hand, after sacrifice of comparable lengths of the proximal small intestine, the animal's weight is satisfactorily maintained near preoperative levels, and no great interference with fat absorption is observed.

METHOD OF PREPARATION

Dogs were operated upon under aseptic conditions. Measurements were made along the mesenteric border of the gut from the ligament of Treitz to the ileocecal valve. Fifty to 70 per cent of the mesenteric small bowel was then removed from the intestinal stream. The defunctionated bowel had its blood supply preserved and its proximal and distal ends were exteriorized as a cutaneous stoma. Intestinal continuity was re-established by end-to-end anastomosis except when the ileocecal valve was bypassed. On these occasions the intestinal-colic anastomosis was made end-to-side.

Five groups of animals with three animals per group were originally prepared. Figure 1 illustrates the various groups. Group I had the proximal 50 per cent of small bowel removed from intestinal continuity. In Group II the distal 50 per cent of small bowel was removed from 3 cm. proximal to the ileocecal valve extending the necessary measured

* This investigation was supported by U. S. P. H. S. grant No. C-1876.

Read before the American Surgical Association, Cleveland, Ohio, April 29, 1954.

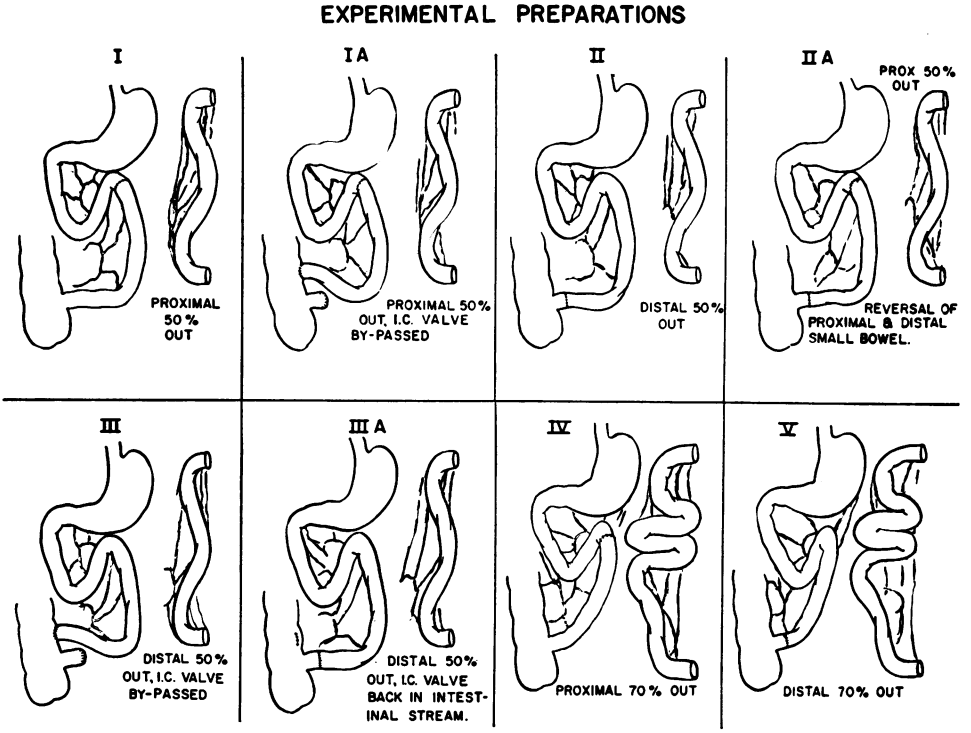

FIG. 1. Experimental animal preparations. (I) The proximal 50 per cent of small intestine removed from intestinal continuity as a Thiry-Vella fistula. Anastomosis at ligament of Treitz. (IA) Group I animals reoperated upon after 24 weeks with bypass of ileocecal valve. Distal two centimeters of ileum inverted and closed. (II) The distal 50 per cent of small intestine removed from intestinal continuity as a Thiry-Vella fistula. Anastomosis two to three centimeters proximal to ileocecal valve. (IIA) Group II animals reoperated upon after 24 weeks of observation. The previously excluded distal bowel replaced into the intestinal stream and the proximal 50 per cent of small bowel excluded as a Thiry-Vella fistula. (III) The distal 50 per cent of small intestine removed from intestinal continuity as a Thiry-Vella fistula. The terminal three centimeters of ileum closed and inverted. Anastomosis end-to-side to right colon. (IIIA) Group III animals reoperated upon after 24 weeks. The anastomosis to the right colon taken down with reanastomosis to the previously closed three-centimeter stump of terminal ileum. (IV) The proximal 70 per cent of small intestine removed from intestinal continuity as a Thiry-Vella fistula. Anastomosis at ligament of Treitz. (V) The distal 70 per cent of small intestine removed from intestinal continuity as a Thiry-Vella fistula. Anastomosis two to three centimeters proximal to ileocecal valve.

distance cephalad. Group III was similar to Group II, except that the ileocecal valve was bypassed. The terminal ileum was transected 3 cm. proximal to the ileocecal valve. The distal transected ileum was inverted and closed, and an anastomosis to restore intestinal continuity performed end-to-side onto the right colon, just distal to the ileocecal junction. Group IV was similar to Group I except that the proximal 70 per cent of small bowel was removed from continuity. Group V was similar to Group II except that the distal 70 per cent of small bowel was removed from intestinal continuity.

Group IA, IIA and IIIA were conversions of the original groups after a 24-week period of observation which served as a control for the further study. In Group I, in order to test further the effect of the ileocecal valve, at reoperation the original anastomosis at the terminal ileum three cm. proximal to the ileocecal valve was taken down. The remain-

ing stump of terminal ileum was closed and inverted. The residual small intestine was anastomosed end-to-side to the right colon. In Group II at reoperation, the proximal 50 per cent of small intestine was removed from its position in the intestinal stream and converted to a Thiry-Vella fistula. In its place the distal 50 per cent of small bowel, which previously had been out of intestinal continuity in the original preparation, was returned to the intestinal stream. One of the three dogs in this group died following reconversion, two survived in good health for further observation. In Group III at reoperation, the anastomosis of small intestine to right colon was taken down and intestinal continuity was re-established by reanastomosis to the previously closed 3 cm. stump of the residual terminal ileum. This group of dogs had lost the most weight and were in the poorest condition at the time of reoperation. One animal died of pneumonia, one died of postoperative obstruction, and one survived the reoperation without complication.

After a suitable time had elapsed following an intestinal preparation (usually in excess of four weeks), each dog participating in the balance study was fed 700 Gm. of a canned dog food (Pard) daily for three days. On the last two days the feedings were colored with carmine red and during this 48-hour period all carmine-colored stools were collected. Studies were also done using the canned dog food with added lard, thus increasing the fat content from approximately 5 per cent to 18 per cent. Each animal was studied for at least four periods during the time of observation.

The water, fat and nitrogen content of the carmine-colored food and stool was then determined. The water content was measured by weighing, dehydrating and reweighing an aliquot sample of food or stool. The nitrogen concentration of food and stool was determined by a standard Kjeldahl technic. The total fat content was determined by a

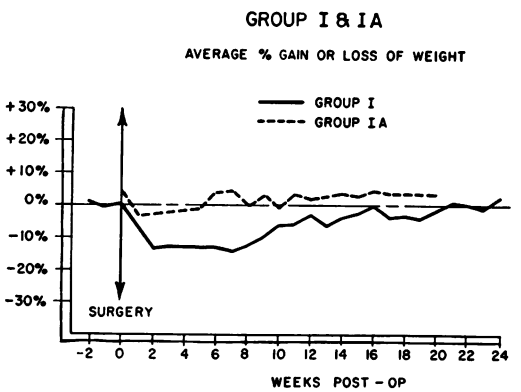

FIG. 2. Weight curve of Group I and IA animals charted as the percentage of gain or loss from initial normal weight before the first operation.

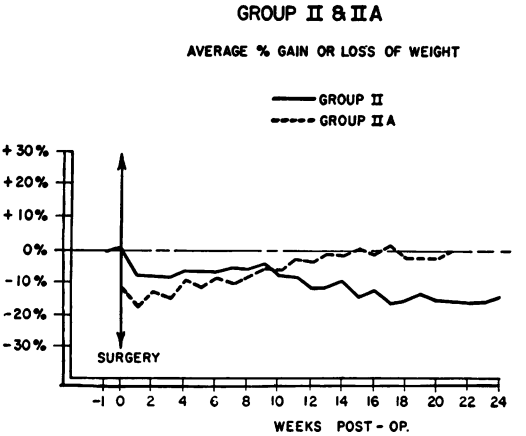

FIG. 3. Weight curve of Group II and IIA animals charted as the percentage of gain or loss from initial normal weight before the first operation.

wet method developed by Van de Kamer and his associates.[13] In brief, the method consists of first saponifying a weighed sample of the well-mixed stool (or dog food) with a concentrated alcoholic solution of KOH. The soaps thus formed are converted to fatty acids with HCL and the fatty acids then extracted with petroleum ether. After evaporation of the ether, the fatty acids are titrated against 0.1 N NaOH, using thymol blue as an indicator. The calculation is carried out assuming an average molecular weight of 284 for fatty acids. The method has a margin of error of less than two per cent.

RESULTS

Animals were carefully weighed at weekly intervals. Figures 2, 3, 4, 5 and 6 depict the average of the deviations from the preoperative normal weights of all animals in the group. Group I animals, with loss of the proximal 50 per cent of small bowel, lost 15 per cent of their preoperative weight by seven weeks, but by 24 weeks had regained their normal weight. When these animals were converted to Group IA, with bypass of the ileocecal valve, no change in their normal weight was observed.

Group II animals, with loss of the distal 50 per cent of small bowel, on the other hand, exhibited progressive weight loss equal to 15 per cent of their body weight by 15 weeks postoperatively, and then appeared to hold their weight stable to 24 weeks, but did not regain the weight they had lost. At this time they were reoperated upon and converted to Group IIA. The distal 50 per cent of small bowel which previously had been out of the intestinal stream was replaced and the proximal 50 per cent of small bowel was removed from intestinal continuity as a Thiry-Vella fistula. Following this procedure the animals steadily gained weight and in 14 weeks had regained their original normal weight, which they maintained to 22 weeks.

Group III animals, which were similar to Group II except for bypass of the ileocecal valve, lost weight steadily and progressively, and exhibited the most profound cachexia of all the groups. There did not appear to be any tendency in this group of animals toward compensation and stability of their weights. When these animals were reoperated upon and converted to Group IIIA by re-establishing intestinal flow through the ileocecal valve, two animals in the group died soon postoperatively from inanition and technical difficulties. However dog 147, which had suffered the most profound weight loss (50 per cent of its preoperative body weight), survived. It remains in good health, although still undernourished. Its progressive weight loss was halted, and it was able to regain the weight loss incident to its reoperation.

Group IV animals, which were similar to Group I except that 70 per cent instead of 50

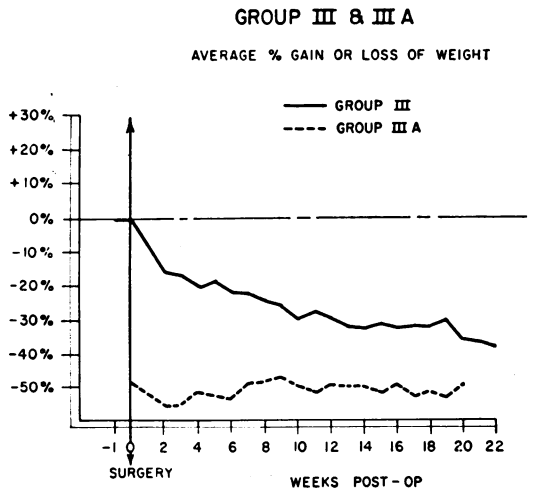

FIG. 4. Weight curve of Group III and IIIA animals charted as the percentage of gain or loss from initial normal weight before the first operation.

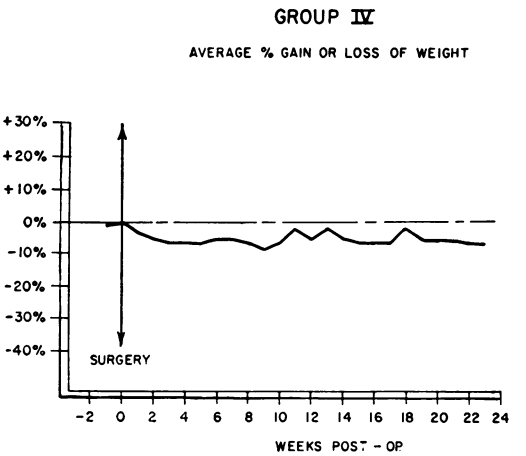

FIG. 5. Weight curve of Group IV animals charted as the percentage of gain or loss from initial normal weight before operation.

per cent of proximal small bowel was removed from intestinal continuity, lost about five per cent of their preoperative weight and then stabilized at about this level. Group V animals, which again were similar to Group II except that 70 per cent of the distal small bowel was removed from intestinal continuity, lost one-fifth of their preoperative weight, and then appeared to hold their weight at that level without any other apparent ill effects.

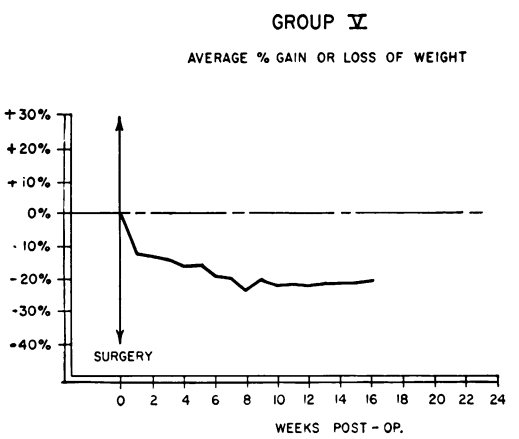

FIG. 6. Weight curve of Group V animals charted as the percentage of gain or loss from initial normal weight before operation.

BALANCE STUDIES

Pard dog food was selected for the test diet during study periods because of its ready availability and its standard consistency. Each batch was separately analyzed for nitrogen and fat during the study periods, with closely reproducible results. On this diet, normal control animals consistently exhibited a greater fecal nitrogen excretion than one would normally expect, averaging 28 per cent the ingested nitrogen in the food. This finding was observed on many animals on repeated occasions, and remained constant. When the method was checked on normal dogs on a horsemeat diet, expected normal values were consistently obtained, averaging six per cent of ingested nitrogen appearing in the stools. According to the manufacturer, over 50 per cent of the protein of Pard is of animal origin and the remainder (under 50 per cent) of the protein is from cereal, fiber and soya flour. It would appear that these vegetable proteins are more poorly digested and absorbed in the dog, accounting for the high values of nitrogen in the stools of the control dogs. Comparison of experimental animals to these control values are nevertheless reproducible and valid for the purposes of this study. Fat losses on the Pard diet, however, were uniformly within expected normal levels in all control animals tested.

Figure 7 presents in summary the averages of two or more balance studies of all animals in each group for both the low and high fat diet. The data are tabulated as the percentage of ingested fat and nitrogen appearing in the stools, the water content of the stools, and as the percentage of fat in dessicated stool.

In Groups II, III, IIIA and V, where the distal small bowel is out of the intestinal stream, there is a consistently high loss of fat in the stools. Whereas percentage of fat losses in the control animals on the Pard diet were 10 per cent of the intake, fecal losses in these animals varied from 80 to 90 per cent of fat intake. In Groups I, IA, IIA and IV, where the proximal small bowel is out of intestinal continuity and the distal small bowel is in place, the fecal fat losses were only slightly above control values.

On the high fat intake (18 per cent fat) studies, control animals showed an 8 per cent loss in the stool. This apparent decrease in percentage of ingested fat lost in the stools as the fat intake increased has been pointed out by Magnus-Levy[8] and Wollaeger and associates.[16] Even under starvation conditions, fats can be found in the stool as was observed by F. Mueller.[10] When the intake of fat is low, the percentage of loss of ingested fat appears to be higher, even though the actual output of fat is not in-

creased over the normal. In these studies the percentage of ingested fat appearing in the feces in all comparable experimental groups was quite similar in both the high and low fat intake periods, but averaged somewhat less on the high fat diet.

The percentage of fat of fecal solids on the low fat diet was not greatly increased when the distal small bowel was in the intestinal stream (Groups I, IA, IIA and IV), and was increased markedly when the distal small bowel was excluded (Groups II, III, IIIA and V). On the high fat diet, the percentage of fat in fecal solids was increased in all groups, but again exhibited similar patterns of distribution in the various groups of preparations. No striking changes in H_2O content of the stool was observed in any of the groups of animals studied.

Bypass of the ileocecal valve by conversion of Group I to IA in the proximal bowel exclusion group did not appear to alter the efficiency of fat absorption in any discernible way. Similarly, in Group III and IIIA, animals with the distal small bowel excluded, no significant effect of the ileocecal valve on fat absorption was observed, although there was a slight decrease in the percentage of fat in fecal solids when the ileocecal valve was in the intestinal stream.

Reoperation upon Group II animals, with conversion to Group IIA, produced the most striking changes in fat absorption. When the distal bowel was excluded from the intestinal stream the fat losses in the stool were 87.9 per cent on the low fat diet and 72.5 per cent on the high fat diet. After re-operation with substitution of the distal small intestine for the proximal small bowel, the fat losses in these animals fell to normal levels of 7 per cent on the low fat diet, and to 4.59 per cent on the high fat diet. Similar changes in percentage of fecal fat solids were observed, with a fall from 40 per cent to 7 per cent on the low fat diet, and from 65 per cent to 15 per cent on the high fat diet.

Nitrogen losses in the stool, although less striking and less marked, were observed to follow similar patterns to fat losses for the various groups of animals. No significant increases of fecal nitrogen loss over controls were observed when the proximal small bowel was defunctionated, whereas moderate but significant increases in fecal nitrogen excretion occurred on loss of the distal small bowel.

TRANSIT TIME

Efforts were made to determine transit time through the small intestine, to evaluate the effect of this item on nutritional adjustment, and to correlate, if possible, speed of intestinal transport to its various levels. It is notoriously difficult to obtain exact measurements, indeed to know exactly what the measurements mean. A number of factors appear to be important in this regard, namely gastric emptying time, speed of transit of material through the small bowel, and the time of complete emptying of the small bowel. These factors may or may not be interdependent, but any or all could have an effect on nutritional adjustment.

Measurements were made by taking serial roentgenograms after the ingestion of 75 cc. of a suspension of barium sulfate and cereal in water. The time from feeding to the first appearance of barium in the cecum was considered the transit time, and the time of apparent complete emptying of the small bowel of barium was also noted. Comparison of average results in various groups reveal a slightly shorter transit time in those groups of preparations where the distal small bowel was excluded. Interpretation of these findings were difficult, however, since variations of animals within each group on occasion exceeded intergroup variations. Under the conditions of these experiments the alterations in motility did not appear to reflect the more marked differences in absorptive capacity of the proximal and distal small bowel. In the preparations where the ileocecal valve was bypassed (Group IA and Group III), the transit time was considerably more rapid than it was in Groups I and IIIA. Similarly, Group III animals exhibited a more rapid transit time than did Group II.

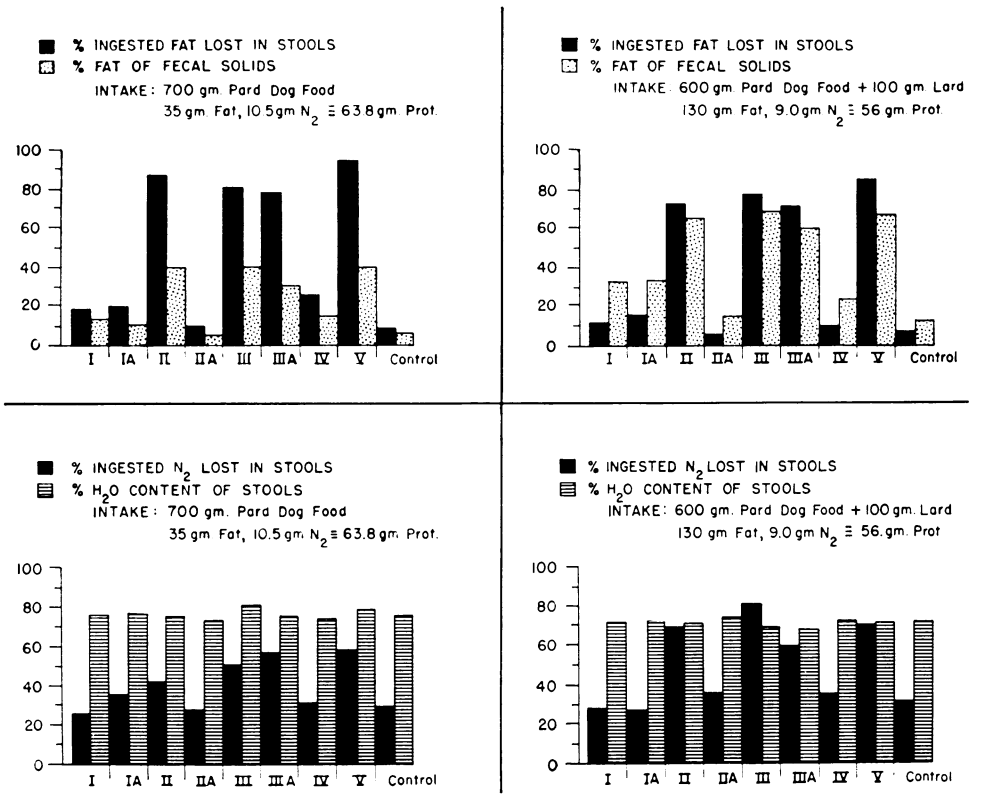

FIG. 7. Balance study data charting averages of all animals in each group of the percentage of ingested fat lost in the stools, the percentage of fat in fecal solids, the percentage of ingested nitrogen recovered in stools and the water content of stools on low and high fat diets.

DISCUSSION

The vast length of small intestine with its combined functions of digestion, transport, and absorption has received very little intensive scrutiny regarding essential functions of its various levels. Although considerable segments of the small bowel can be sacrificed, a portion of it is absolutely essential to life, in contradistinction to the stomach, duodenum or colon, which can be sacrificed *in toto*. In clinical practice, extensive resections of the small bowel are usually dictated by the exigency of the situation immediately at hand; most commonly, infarcted bowel or extensive neoplastic involvement, and the surgeon has little choice but to remove the area of involvement. However, even under these circumstances a certain latitude of judgment may be available to the surgeon, and it is of real importance to have factual data regarding important physiologic functions of the various levels of the gut. Another consideration, which to date has not received clinical trial, is the possibility of treating extreme cases of obesity by removing from intestinal continuity sufficient small bowel to produce weight loss without any other serious hazard or impairment. It is entirely possible that such an effect could be obtained by the sacrifice of most of the ileum with preservation of the ileocecal juncture. One such case has recently been treated in this fashion, and will be reported in a subsequent publication.

Trzebicky[12] in 1894 first studied the problem of comparative function of the small bowel experimentally, and concluded that

proximal resection produced more marked nutritional sequelae than did distal resections. Clatworthy *et al.*[3] more recently studied the effects of extensive intestinal resections on growth of newborn dogs. They observed no difference in subsequent growth, with sacrifice of comparable lengths of proximal, middle or distal small intestine. Similarly, Weckesser *et al.*[15] in 1951 reported that he was unable to observe any marked difference in nutritional adjustment between proximal and distal resections of the small bowel. In the proximal resections, two-thirds of the measured gut, beginning at the level of the ampula of Vater, was removed; and in the distal resections, two-thirds of the measured small bowel was removed from the ileocecal juncture upward. Vagotomy was also performed in an effort to increase the transit time and thereby improve the nutritional adjustment. However, although transient beneficial results were obtained thereby, there was no lasting benefit derived from the latter procedure.

Jensenius,[7] on the other hand, found a very definite difference in fat absorption between proximal and distal small bowel resections, noting increased loss of fat in the stools after ileal resections. Our own results corroborate the observations of Jensenius, showing the ileum to be the primary area of fat absorption in the dog. Markedly increased fat losses on all balance studies where the distal small bowel is out of intestinal continuity (Groups II, III, IIIA and V) was consistently observed, whereas relatively normal values were noted when only the proximal bowel was excluded from the intestinal stream. Moreover, the striking fall in fat loss to normal values associated with gain in weight when Group II animals were converted to Group IIA appears to justify this conclusion.

Protein absorption also appears to occur in considerable measure in the ileum, since fecal nitrogen losses were increased in all preparations where the ileum was removed. However, this may in part be due to the presence of higher concentrations of fat being lost from the intestinal stream under these circumstances. A further suggestion in this direction is the observation that greater fecal nitrogen losses occurred when these animals were on a high fat diet, resulting in greater concentrations of fat being lost in the stool.

CONCLUSIONS

The proximal 50 to 70 per cent of the small intestine of dogs can be removed with no apparent ill effects. Weight is maintained, and protein and fat absorption are not significantly altered.

Sacrifice of the distal 50 per cent of the small intestine produces a profound interference with fat absorption associated with loss of weight.

The ileocecal valve appears to have an important effect on the nutritional adjustment to sacrifice of the distal small bowel, but appears less important in sacrifice of the proximal small bowel.

BIBLIOGRAPHY

1. Althauser, T. L., K. Vyeyama, and R. G. Simpson: Digestion and Absorption after Massive Resection of the Small Intestine. Gastroenterol., **12:** 795, 1949.
2. Cattel, R. B.: Massive Resection of the Small Intestine. Lahey Clin. Bull., **4:** 167, 1945.
3. Clatworthy, H. W., Jr., R. Saleeby, and C. Lovingood: Extensive Small Bowel Resection in Young Dogs: Its effect on Growth and Development. An experimental study. Surgery, **32:** 341, 1952.
4. Doerfler, H.: Kann der Mensch ohne Dunndarm leben?, Zentralb. f. Chir., **50:** 1502, 1923.
5. Flint, J. M.: Effect of Extensive Resections of Small Intestine. Bull. Johns Hopkins Hosp., **23:** 127, 1912.
6. Haymond, H. E.: Massive Resection of the Small Intestine: An Analysis of 257 Collected Cases. Surg. Gynec. and Obst., **61:** 693, 1935.
7. Jensenius, Hans: Results of Experimental Resections of the Small Intestine on Dogs. Universitetsforlaget, NYT Nordisk Forlog, Copenhagen, Arnold Busck, 1945.
8. Magnus-Levy, Adolf: Vol. I, Von Noorden: Metabolism and practical medicine, Chicago, W. T. Keener and Co., 1907. Vol. I, pp. 54-57.

[9] Meyer, H. W.: Acute Superior Mesenteric Artery Thrombosis: Recovery Following Extensive Resection of the Large and Small Intestine. Arch. Surg., **53**: 298, 1946.

[10] Mueller, F.: Virchows Arch. f. Path. Anat. Suppl., **131**: 17, 64, 1893.

[11] Todd, W. R., M. Ditterbrandt, J. R. Montague, and E. I. West: Digestion and Absorption in a Man with all but Three Feet of Small Intestine Removed Surgically. Am. J. Digest. Dis., **7**: 295, 1940.

[12] Trzebicky, R.: Uber die Grenzen der Zulassigkeit der Dunndarm-resection. Arch. f. Klin. Chir., **48**: 54, 1894.

[13] Van de Kamer, J. H., Huinink, H. Ten Bokkel and H. A. Weyers: Rapid Method for the Determination of Fat in Feces. J. Biol. Chem., **177**: 347, 1949.

[14] Weckesser, E. C., A. B. Chinn, M. W. Scott and J. W. Price: Extensive Resection of the Small Intestine. Am. J. Surg., **78**: 706, 1949.

[15] Weckesser, E. C., J. L. Ankenny, A. F. Portman, J. W. Price and F. A. Cebul: Extensive Resection of the Small Intestine Followed by Vagotomy. Surgery, **30**: 465, 1951.

[16] Wollaeger, E. E., M. W. Comfort, J. F. Weir and A. E. Osterberg: The Total Solids, Fat and Nitrogen in the Feces. I. A Study of Normal Persons and of Patients with Duodenal Ulcer on a Test Diet Containing Large Amounts of Fat. Gastroenterology, **6**: 83, 1946.

DISCUSSION.—DR. HERBERT WILLY MEYER, New York, New York: I have been tremendously interested in this beautiful study by Dr. Kremen, and I would like to take just one minute to give a clinical report on a young soldier whom I had the opportunity of operating on during the Battle of the Bulge in Luxemburg.

He had had a minor shell fragment wound, and during his stay in the hospital developed acute thrombosis of the superior mesenteric artery just distal to the mid-colic artery. I had to resect all of the small intestine except the upper 18 inches of the jejunum, all of the cecum, ascending colon, and a portion of the transverse colon. I then performed a jejuno-transverse colostomy.

This soldier was evacuated to England and then brought to the United States to the Mayo General Hospital. Colonel John Gibbon, Jr., who was chief of surgery, was kind enough to study him. They found that he had very little digestion of carbohydrates and fats. He was later discharged. The interesting part of the story, and the only reason I speak about it is that it is now over nine years since that extensive resection. I know that many cases have appeared in the literature, but this follow-up of nine years is of interest because his original weight at the time of operation was 138 pounds. His low weight was 99 pounds and he now weighs 125 pounds. He is married and has two children and works daily.

He has three or four soft bowel movements, but they have found that he suffers from avitaminosis. He lives in Waterloo, Iowa, and has been studied at the Veterans Hospital at Des Moines and by a doctor in Waterloo. He also has developed some anemia, and has had to have liver injections.

I would like to show you two slides that were made in Waterloo.

(Slide) This is a postevacuation film after a barium clysma. You will note in the lower righthand corner the empty sigmoid colon. The large amount of barium that you see is in the distended jejunum —the residual 18 inches. You also will note that the barium clysma has partly outlined the duodenal cap, and a little of it has run into the stomach.

(Slide) This shows a photograph of the patient nine years after the removal of all of the small intestine and half of the large intestine. A report of this case appeared in the *Archives of Surgery*, **53**: 208, September, 1946.

DR. PHILIP SANDBLOM, Lund, Sweden: A Swedish surgeon, Dr. V. Henrikson of Gothenburg, tried to control obesity in a woman whose appetite was better than her character, by resection of an appropriate amount of the small intestine. He found that although the lady lost very much weight, it was difficult to keep her in balance. After this beautiful study by Dr. Kremen *et al*, this questionable method of controlling obesity will have the necessary experimental foundation.

DR. ARNOLD J. KREMEN, Minneapolis, Minnesota: I would like to thank Dr. Meyer for bringing us up-to-date on this remarkable case of his. I remember reading the original report in 1946. It is one of the few cases that I know of where such a remarkable convalescence has occurred after