

# New Considerations in Use of Jejunioileal Bypass in Patients with Morbid Obesity

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**I**N THE LAST FIVE YEARS we have used jejunioileal bypass in surgical treatment of over 70 patients with massive obesity. These patients were selected for operation after in-hospital appraisal of their clinical, endocrinologic, metabolic, psychiatric, and body compositional status according to the following criteria:

- 1) Obesity of massive degree (weights two or three times ideal levels) of at least 5 years' duration.
- 2) Evidence from attending physician indicating failure of dietary efforts to correct obesity over a period of years.
- 3) Evidence from patient's history and evaluation indicating patient's apparent incapability to adhere to prescribed dietary regimen and/or exercise programs.
- 4) Absence of any correctable endocrinopathy (such as hypothyroidism or Cushing's syndrome) which might be the cause of obesity.
- 5) Absence of any other unrelated significant disease which might increase operative risk.
- 6) Presence of certain complications such as Pickwickian syndrome, hyperlipidemia, adult onset of diabetes, and hypertension which might be alleviated by significant weight reduction with intestinal bypass.
- 7) Assurance of patient's cooperation in conduct of pre- and postoperative metabolic and body compositional studies and prolonged follow-up evaluation.

The end-to-side jejunioileal shunt described by Payne and DeWind<sup>2</sup> was used in the first 11 patients. Because of dissatisfaction with some of the results in our experience with Payne's procedure we have used a different principle of jejunioileal bypass in the subsequent 62

patients: following the new principle the jejunum was divided a few inches from the ligament of Treitz and its proximal end anastomosed to the distal end of transected ileum a few inches proximal to the ileocecal valve. The long length of bypassed jejunioileum was drained by anastomosis of its ileal end to transverse colon or sigmoid.<sup>3,4</sup>

Although the optimal dimensions involved in surgical reduction of intestinal absorptive functions are uncertain, empiric experience has shown that extremely large amounts of jejunal and ileal mucosal surface areas must be taken out of contact with the very large amount of food ingested by morbidly obese subjects if excess body fat is to be effectively reduced. This study reports preliminary efforts to determine the optimal dimensions of jejunioileal bypass in surgical treatment of massive obesity.

## Clinical Appraisal of Patients

Sixty-two massively obese patients who were selected by the above criteria after careful study were submitted to the end-to-end jejunioileal bypass procedure during the period July, 1970 through November, 1972.

Ages ranged from 16 to 63 years (average 36 years). There were 36 women and 24 men. There was a long history (5 to 10 years or more) of massive obesity refractory to dietary control in each instance. Maximal weights prior to operation ranged from 280 to 600 pounds. Immediately before operation weights ranged from 240 to 486 pounds. One patient had been submit-

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ted to the Payne operation 3½ years previously but had failed to drop her weight below 260 pounds.

Each patient was admitted to the hospital for study prior to operation. Baseline studies were carried out with especial attention directed toward detecting possible endocrine causes of obesity, evaluation of cardiopulmonary status, baseline absorptive and metabolic studies, psychiatric and psychologic evaluation and body composition studies. Endocrine studies included evaluation of thyroid function by determination of serum protein bound iodine, basal metabolic rate or T<sub>3</sub> and T<sub>4</sub> measurements. Studies of adrenal function included plasma F determinations and 24-hour urine collections for measurements of 17 hydroxycorticosteroids and 17 ketosteroids. Pulmonary studies included measurement of arterial Po<sub>2</sub>, Pco<sub>2</sub> and pH in addition to spirometry for determination of respiratory rate, tidal volume, inspiratory capacity, inspiratory reserve volume, forced vital capacity and other aspects of pulmonary function. Cardiovascular appraisal included roentgenograms of

the chest, electrocardiograms, determination of serum lipids including cholesterol, triglycerides, phospholipids and lipoprotein electrophoretic patterns.

In addition to an extensive dietary history, gastroenterologic studies included X-ray examinations of the stomach, small bowel and colon with measurement of small intestinal transit time. Twelve-hour nocturnal collections of gastric juice or 2-hour basal measurements of gastric acid secretion were made. Intestinal absorption was evaluated by d-xylose tolerance tests, glucose tolerance tests and in some patients vitamin A tolerance tests and the cobalt 60 vitamin B<sub>12</sub> absorption tests (Schilling). Preoperative measurements of serum calcium, potassium, magnesium and other electrolytes as well as vitamins A, B<sub>12</sub>, C, E, and folic acid were carried out. Dietary intakes were calculated and recorded and serial 3-day collections of stool with daily collections of urine were obtained in a majority of patients. These were analyzed for electrolytes and nitrogen and stools were also analyzed for fat.

Studies of body composition included measurements of total body potassium by <sup>40</sup>K whole body counting; total body and extracellular water, red cell and plasma volumes were measured by isotope dilution methods.<sup>1</sup>

Psychologic evaluation of each patient involved the use of standard psychologic tests, including the Minnesota Multiphasic Personality Inventory, as well as interviews with the staff psychiatrists.

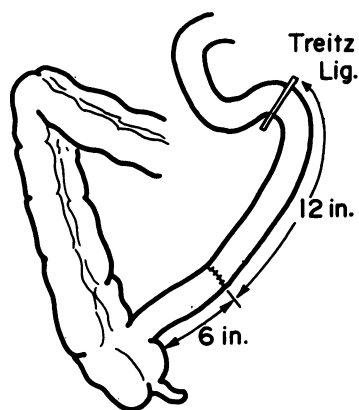
#### Plan of Study

In an effort to determine the optimal dimensions of the end-to-end jejunioileal bypass procedure the following plan has been followed in these patients. In the first 12 patients 12 to 18 inches of proximal jejunum were joined by end-to-end anastomosis to the distal 12 inches of ileum. In ten of this group 12 inches of proximal jejunum were used. In the subsequent 50 patients the proximal 12 inches of jejunum were joined end-to-end to the ileum 6 to 8 inches from the ileocecal valve. In the first 21 patients of the latter group the jejunum was joined to ileum 6 inches proximal to the ileocecal valve and in the subsequent group of patients the anastomosis has usually been made 8 inches from the ileocecal valve. In this report we shall compare the results of the group of ten patients who had 12 inches of jejunum joined to 12 inches of ileum (12 to 12) with those of the group who had 12 inches of jejunum joined to 6 inches of ileum (12 to 6) (Fig. 1).

#### Operative Procedure

Preoperative preparation included a 3 to 5-day bowel cleansing regimen involving liquid diet, castor oil, cleansing enemas and oral kanamycin. Anesthesia in almost all patients consisted of endotracheal fluothane

#### JEJUNOILEAL BYPASS FOR OBESITY (12 to 6)



#### JEJUNOILEAL BYPASS FOR OBESITY (12 to 12)

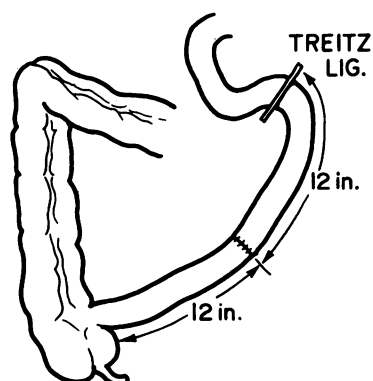


FIG. 1. Schematic diagrams of dimensions used in bypass procedures.

with bag assistance and succinyl choline intravenously as a muscle relaxant. For the larger patients the standard operating table was inadequate in width and a delivery table was substituted. A 15 to 20-minute scrub of the large redundant expanse of skin of the abdomen, chest, perineum and upper thighs was carried out in each instance with an iodine containing soap solution.

A long transverse supraumbilical incision was used in most patients. The redundant fatty apron was excised by transverse elliptical incision in a few. Rectus muscles were divided transversely and after entering the peritoneum a plastic wound protector was inserted. The use of large retractors coupled with liberal administration of muscle relaxants facilitated exposure of the coelomic cavity. A biopsy of the liver was done as a routine procedure.

The proximal jejunum was identified, placed on the stretch and carefully measured along its mesenteric border to a point 12 inches from the ligament of Treitz. At this point the jejunum was transected. The distal end was closed in two layers with nonabsorbable sutures and anchored to the root of the transverse mesocolon to prevent postoperative intussusception. The terminal ileum was then identified, placed on the stretch, measured along its mesenteric border and transected in the first group of patients (12 to 12) 12 inches proximal to the ileocecal valve. In the second group of patients (12 to 6) the ileum was transected 6 inches proximal to the ileocecal valve. Proximal jejunum was then anastomosed to the end of the terminal ileum. In eight of the 12 to 12 group of patients, the anastomosis between proximal jejunum and terminal ileum was made beneath the root of the mesentery. In these individuals the proximal end of the transected ileum was then anastomosed to the side of the transverse colon as a means of draining the bypassed segment of jejunol-

eum. In two other patients in this group and in all of the patients in the 12 to 6 group the anastomosis between proximal jejunum and terminal ileum was made superior to the root of the mesentery and, for drainage of bypassed jejunoleum, the proximal end of ileum was anastomosed to the side of the sigmoid colon. Mesenteric defects were then carefully closed with interrupted nonabsorbable sutures. The appendix was removed routinely. Additional procedures included cholecystectomy in four patients, repair of recurrent umbilical hernia in one patient, resection of malignant carcinoid of ileum in one patient, excision of ovarian cyst in one patient, and tubal ligation in another.

Prior to closure of the abdominal incision, gowns, gloves, instruments and drapes were changed and copious saline lavage of the coelomic cavity and wound was used. The transverse incisions were closed with interrupted 0 dacron sutures to the peritoneum and posterior sheath and interrupted 0 dacron sutures to the anterior rectus fascia and external oblique aponeurosis. Stay sutures were not used. Catheters were placed beneath the subcutaneous layer and exteriorized through stab wounds for postoperative suction drainage. The thick fatty layer was closed with interrupted 3-0 chromic catgut sutures and the skin edges were approximated by vertical mattress sutures of fine dacron. Figure 2 shows the steps in the operative procedure.

### Results

Preoperative clinical evaluation of the 31 patients in this study showed a variety of abnormalities in addition to massive obesity.

A family history of massive obesity in individual parents, grandparents or siblings was elicited in about half of the patients. Four patients had asymptomatic gallstones and one young woman was found to have

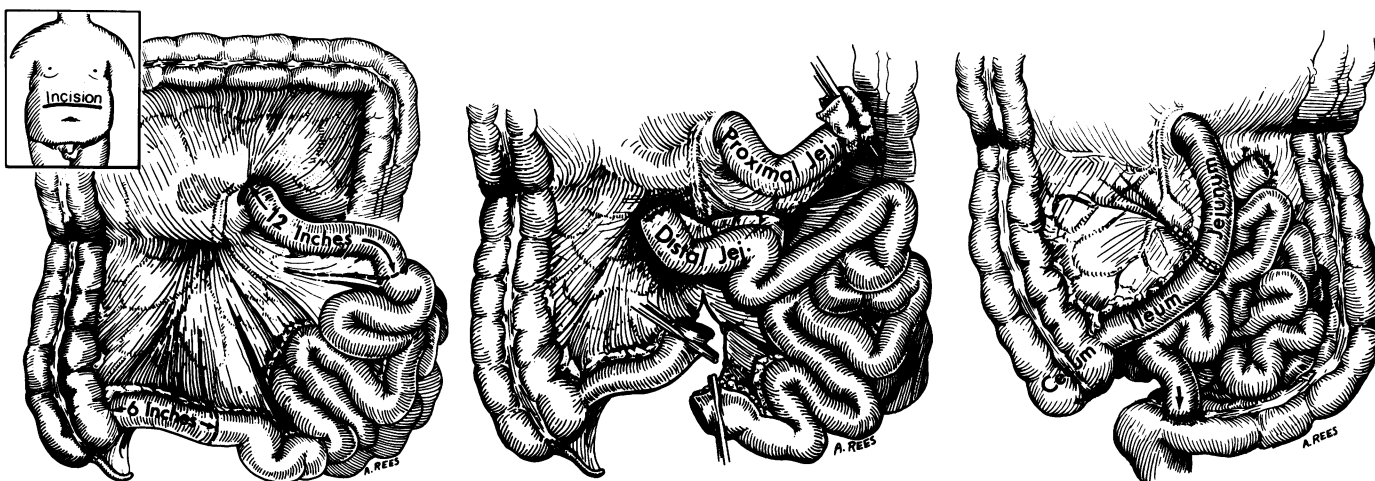


FIG. 2. Operative technic of 12 to 6 modification of jejunoleal bypass procedure.

fibroadenoma of the breast. Ten patients had glycosuria and diabetic glucose tolerance tests. Endocrine status was otherwise normal in each of the 31 patients prior to operation.

Cardiac evaluation before operation showed elevated diastolic pressures in the range of 100 to 130 mm. Hg in ten of the 31 patients. Roentgenograms of the chest showed no cardiac deformity in any patient. Electrocardiograms were within normal limits in 27 subjects; two patients had left axis deviation; two others had changes suggesting old healed myocardial infarction. Serum cholesterols were in the normal range in all but four subjects. Lipoprotein electrophoretic patterns showed these four individuals to have Fredrickson Type II hyperlipoproteinemia. In 12 other patients who had consistently elevated triglycerides, lipoprotein electrophoretogram patterns were indicative of Fredrickson Type IV.

Preoperative appraisal of intestinal fat, carbohydrate and nitrogen absorption was normal in each patient prior to operation except in one woman who had had a previous Payne procedure with attendant elevation in fecal fat losses. Measurements of serum vitamin levels, electrolytes and hematologic functions prior to operation in these obese patients showed no significant abnormalities.

One patient had had repeated episodes of unexplained gastrointestinal bleeding. In his case and in that of all the other patients, except the individual who had had the previous Payne operation, radiologic studies of the gastrointestinal tract before operation showed no abnormalities. Small intestinal transit times as measured with liquid barium ranged from 1½ to 4 hours.

Preoperative psychiatric evaluation consisted of interviews directed at evaluating the patient's life history, psychosocial factors related to obesity, typical defensive maneuvers for handling emotional conflict, response to other methods for treating obesity, expectations of the operation, attitudes toward weight loss, body image distortions, and a mental status examination. In general no specific psychopathology was elicited except for underlying conflicts of orality, aggression and dependency. The obese patients were also administered the Minnesota Multiphasic Personality Inventory preoperatively in order to ascertain their degree of psychopathology. A comparison group of 33 non-psychotic psychiatric outpatients was also assembled. From the data it appears that the massively obese patient is not routinely even moderately psychiatrically disturbed. At most, these obese patients can be said to be somewhat emotionally immature and unhappy.

Liver biopsies were taken at operation in 30 of the 31 obese patients. Abnormal accumulations of fat, ranging from minimal to severe degree, were present in all but

three patients. In addition, two patients had early microscopic evidence of periportal cellular infiltration and lobular fibrosis.

After operation each patient was maintained in the Surgical Intensive Care Unit with special attention paid to respiratory support and pulmonary toilet. Ventilatory assistance was rarely needed. Low grade fever which was possibly pulmonary in origin occurred in most of the patients for the first few days after operation, but no significant incidence of atelectasis or pneumonitis occurred.

Nasogastric suction was discontinued 3 to 5 days after operation and oral liquids, usually restricted to 1500 ml. daily, were started. In the first few days after institution of oral liquids multiple watery stools occurred. Low fat diet, restriction of fluids with meals and diphenoxylate hydrochloride in a dosage of 5 mg. three to four times a day or codeine 15 to 30 mg. three to four times a day usually resulted in control of the diarrhea during the early postoperative period.

There was one postoperative fatality in this series of patients. This occurred in the largest patient in the group under study. This 486-pound man had had multiple episodes of unexplained gastrointestinal bleeding before operation. At laparotomy he was found to have a malignant carcinoid tumor of his mid-ileum with metastases to nodes at the root of the mesentery. Resection of involved ileum with the mesentery and nodes was done along with jejunoileal bypass. Unfortunately, postoperative venous thrombosis in the mesentery resulted in infarction of a segment of bypassed ileum with the development of peritonitis, sepsis and fatal endotoxemia.

In the majority of patients the recovery from operation was uneventful. However, problems with wound healing occurred in almost a third of the group. Usually these were trivial, uninfected areas of fat necrosis and seroma, requiring local removal of sutures and a few days of superficial packing to promote healing. Frank wound infections occurred in three patients, requiring wide opening of the skin and fatty layers of the wound down to the fascia and a delay in convalescence.

Two patients who had otherwise uncomplicated postoperative courses developed hepatitis in the period immediately after discharge from the hospital. Symptoms of anorexia, nausea, weakness and malaise began about 7 to 8 days after operation and jaundice appeared several days later. In one patient these symptoms were mild and cleared with 2 weeks of bedrest at home. In the other the hepatitis was much more severe and required rehospitalization and many weeks of supportive therapy for recovery. Australia antigen was negative in each instance. Retrospective review of possible hepatotoxic factors in treatment has suggested to us that

the fluothane which each received as an anesthetic might be responsible for the hepatitis. Postoperative complications of jejunioleal bypass in this group of patients are summarized in Table 1.

After discharge from the hospital each patient has been followed in conjunction with the family physician and in our clinic. An effort has been made to have the patients return for both outpatient and inpatient studies of their clinical result, metabolic and body compositional status, psychiatric state and degree of rehabilitation.

Periods of follow-up in the groups under study range from 20 to 28 months in the 12 to 12 group and 6 to 19 months in the 12 to 6 group. The chronology of weight loss after jejunioleal bypass in the two groups is illustrated in graphic form in Figure 3. After the precipitant fall in weight induced by the operative procedure and the catabolic effects of the immediate postoperative period a majority of patients have lost weight on a gradual and steady basis during the period of follow-up. In the 12 to 12 group the maximal weight loss occurred in the first 12 months after operation. Weights appeared to stabilize thereafter in most patients. Five patients at 20 to 24 months had dropped their weights to 200 pounds or less while five others were still above this level. After losing 80 pounds, one patient has stabilized at 250 pounds. In contrast the rate of weight loss has been more rapid in the 12 to 6 group. By 6 to 12 months after operation the weights of eight of this group have fallen below 200 pounds and by 12 to 18 months several patients have achieved their ideal weight.

During the brief periods of follow-up in these patients the voracious appetites and large caloric intake which they had before operation have largely continued unchanged. In a few patients after 12 to 18 months the large appetite has gradually subsided. An exception occurred in one patient who became anorectic, most likely as a result of emotional disturbances, and lost over 100 pounds in the first 6 months after operation. Progressive weakness, malaise and persistent diarrhea combined with difficult domestic problems resulted in his request for discontinuance of the jejunioleal bypass. This was done in another institution 7 months after the bypass procedure.

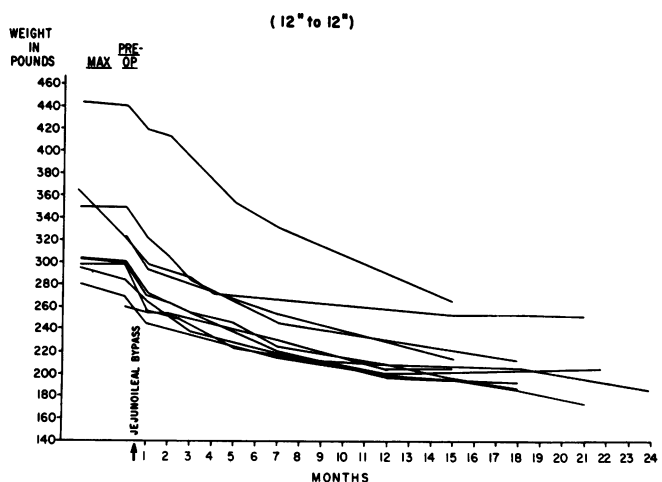
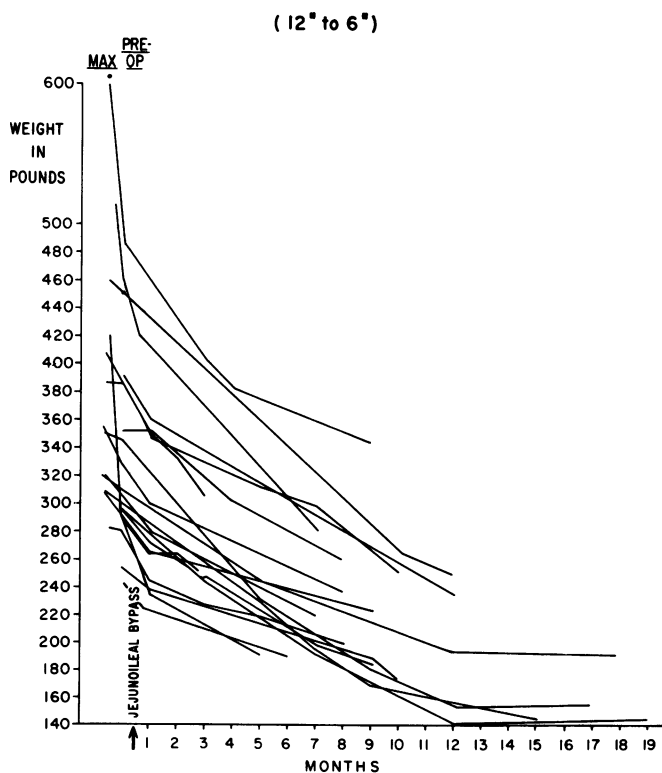


FIG. 3. Chronology of weight loss after jejunioleal bypass.

TABLE 1. *Non-fatal Postoperative Complications of Jejunioleal Bypass (30 Patients)*

Wound Infection	3
Subcutaneous Seroma and/or Fat Necrosis with Drainage	6
Hepatitis (? Fluothane)	2
Early Postoperative Partial Small Bowel Obstruction	1
Thrombophlebitis	1

In the 12 to 12 group the diarrhea of the first few weeks after operation has gradually ceased. No patient in the group has required regular medication for control of diarrhea after the first 1 to 3 months. These patients who are now 20 to 28 months postoperative have one to four formed to semi-formed stools per day unless they indulge in excessive liquid or fat intake. Their experience has taught them that excessive liquid intake and excessive fat intake will induce diarrhea.

In the 12 to 6 group the postoperative diarrhea has persisted for a slightly longer period in most of the patients. In four patients, including the patient who

was submitted to restoration of alimentary continuity, persistent diarrhea has required medication for its control for periods of 6 to 17 months. However, in the majority of this group diarrhea has ceased to be a problem after 4 or 5 months and medication for its control has not been required.

Except for three patients in the 12 to 6 group, all patients in both groups have returned to the occupations of the preoperative period and unrestricted activity. Twenty-four patients are currently engaged in full time work and three individuals are students. Among the three patients in whom rehabilitation has not been achieved are the patient who had the jejunioleal shunt taken down, another patient who is recuperating from halothane hepatitis and a third patient whose emotional problems have permitted only a return to part time employment.

Metabolic parameters which were assessed prior to operation have been studied in the period of follow-up. Reduction in carbohydrate absorption is indicated by impairment in d-xylose tolerance in the patients in whom this has been measured after operation and by the flattening of oral glucose tolerance curves in the postoperative period (Fig. 4). In seven of the ten patients with preoperative diabetic glucose tolerance curves in whom the test has been repeated after operation the curves have flattened into normal range. The data also indicate greater malabsorption of d-xylose in the patients of the 12 to 6 group.

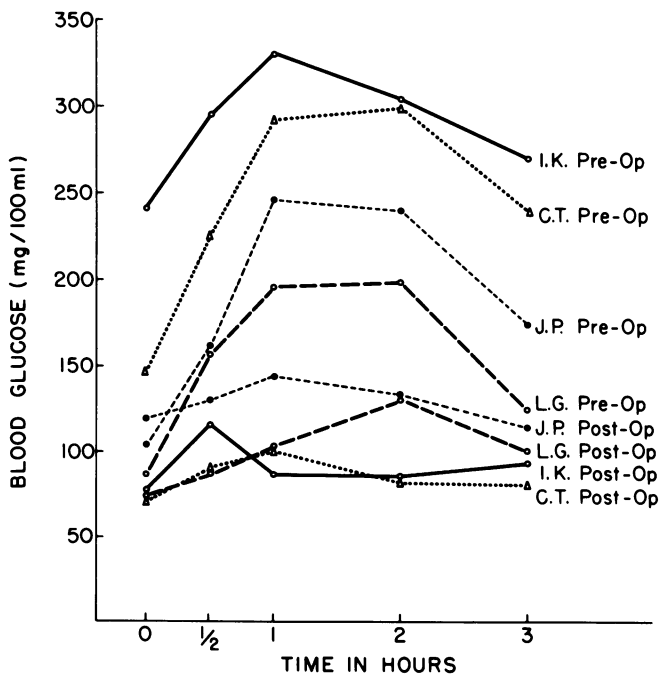


FIG. 4A. Oral glucose tolerance tests in diabetic subjects before and after jejunioleal bypass.

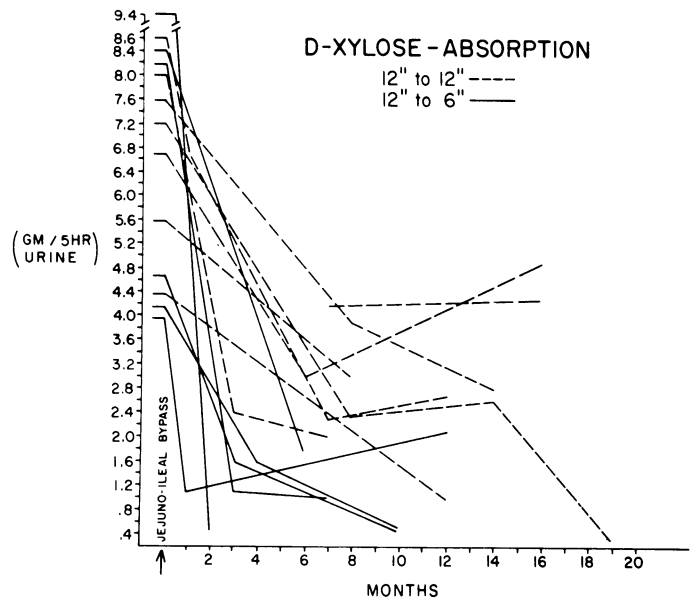


FIG. 4B. D-xylose absorption after 12 to 12 and 12 to 6 bypass procedures.

A large increase in fecal fat loss has occurred in each patient in whom it has been possible to measure this in the period after jejunioleal bypass. Malabsorption of fat by interference with enterohepatic cycles of cholesterol and bile acids has been accompanied by an impressive and sustained fall in serum cholesterol and triglyceride levels in both groups of patients. In Figure 5 serum cholesterol and triglyceride levels are plotted against time in the two groups of patients. As can be discerned from the figure, irrespective of baseline levels, there has been an impressive fall in both serum cholesterol and serum triglyceride concentrations after jejunioleal bypass in each group. These reductions have been maintained below 160 mg./100 ml. throughout the periods of follow-up. After jejunioleal bypass lipoprotein electrophoretograms have reverted to normal in each of the patients with Fredrickson Type II patterns and in ten of the 12 with Fredrickson Type IV abnormalities.

In Figure 6 serum levels of the various vitamins before and 6 to 24 months after jejunioleal bypass are compared in the two groups. Serum carotene levels are consistently low in both groups and the fat soluble vitamins A and E show a trend toward reduction in the follow-up period. The absorption of vitamin K as reflected by prothrombin times has shown a trend toward reduction in several patients in the early postoperative period but prothrombin times have been maintained in normal range in the follow-up period. Vitamin C levels have been consistently normal in the 12 to 12 group. A trend toward reduction in serum levels of this vitamin is evident in the 12 to 6 group. Although reduced levels

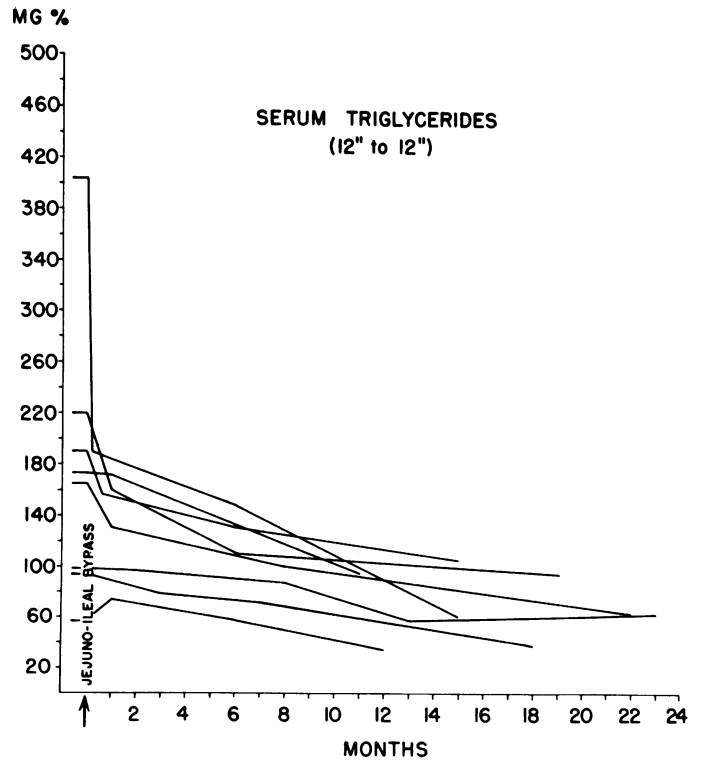
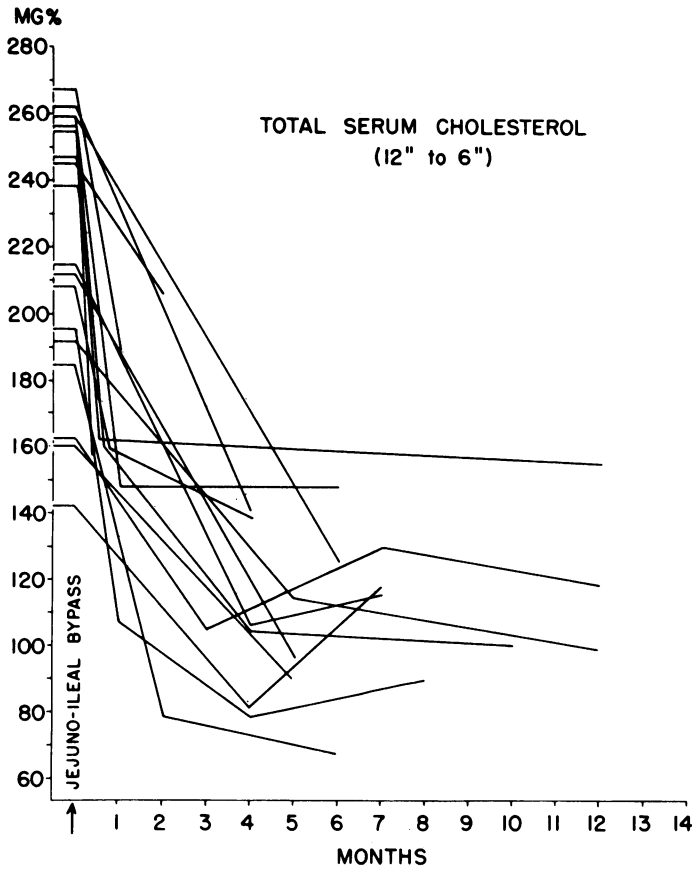


FIG. 5C. See legend for Figure 5A.

FIG. 5A. Changes in serum cholesterol and triglycerides after 12 to 12 and 12 to 6 bypass procedures.

of serum folate have appeared in both groups in follow-up, serum vitamin B<sub>12</sub> levels have remained in the normal range in all patients studied. Except for transitory reductions in a few patients in the early post-operative period, hematocrits have been maintained in the normal range.

Despite the steatorrhea induced by the operation, serum calcium, magnesium and potassium levels have

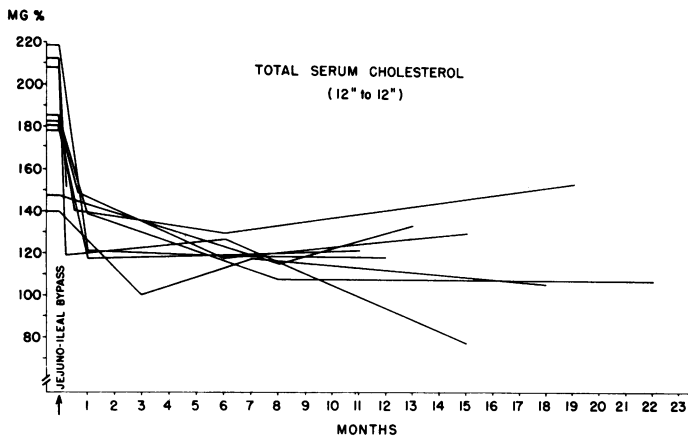


FIG. 5B. See legend for Figure 5A.

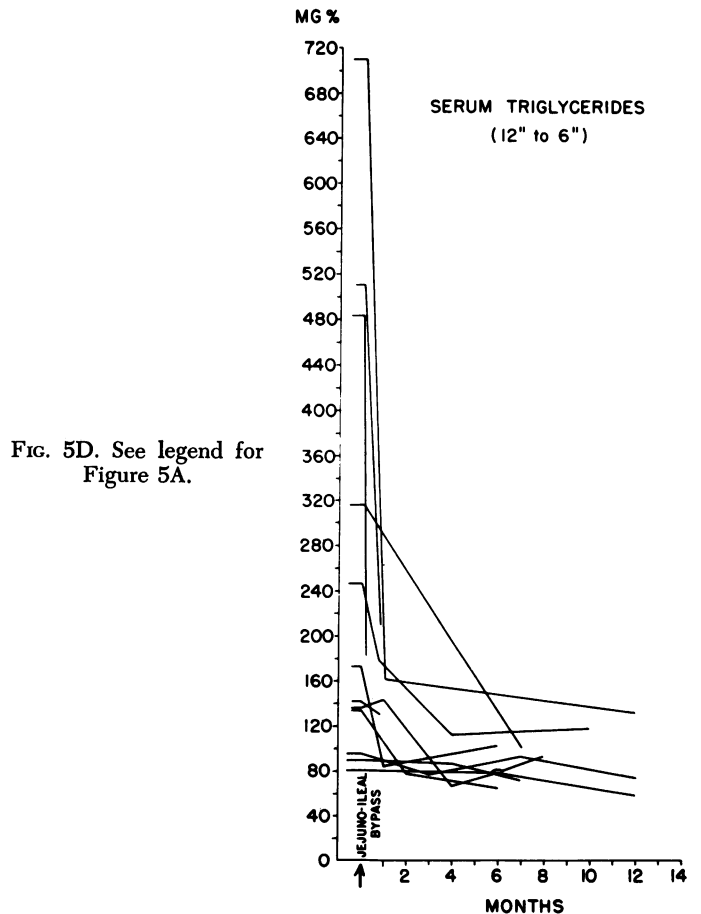


FIG. 5D. See legend for Figure 5A.

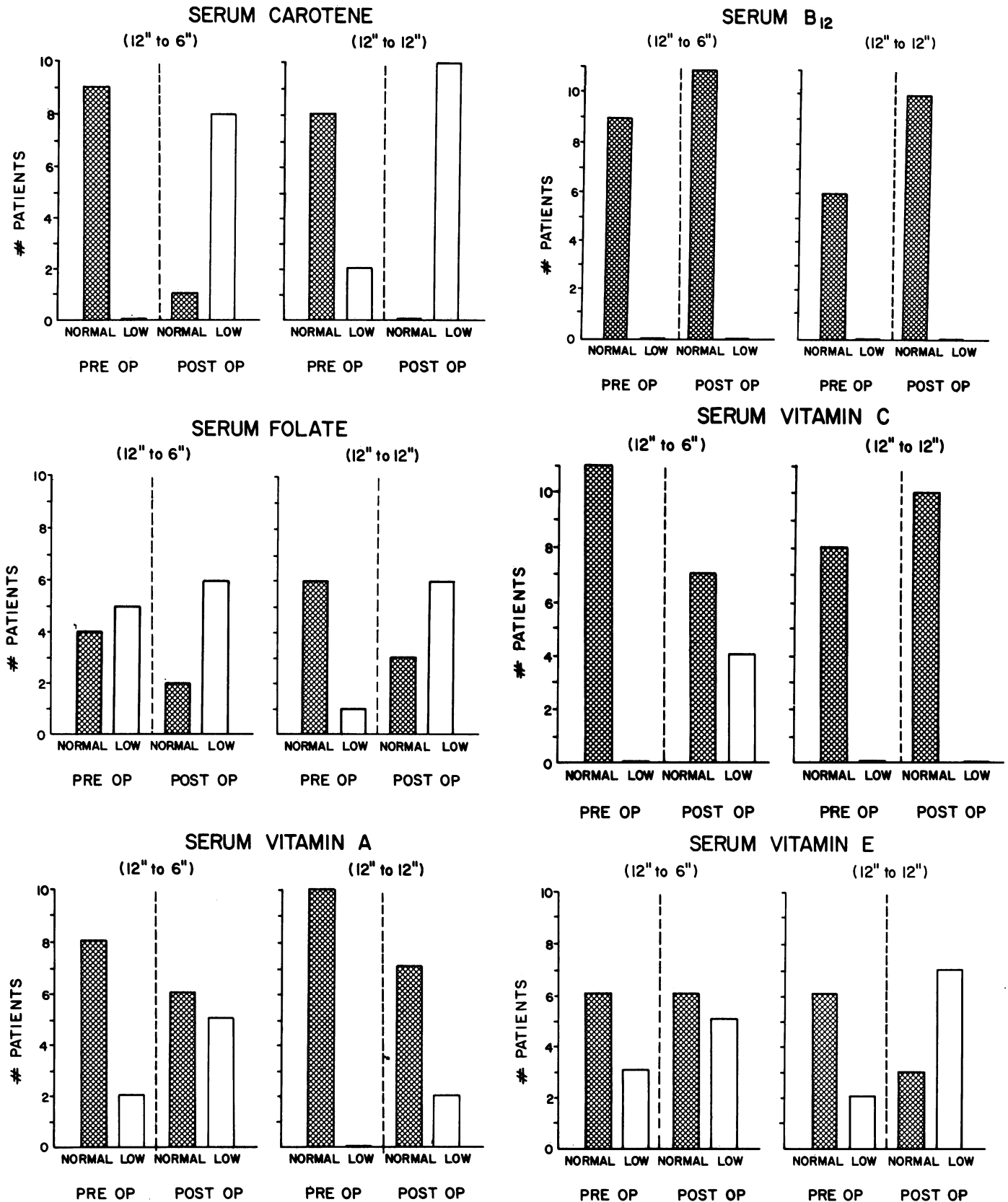


FIG. 6. Serum levels of Carotene, Folate, Vitamins A, B<sub>12</sub>, C and E.



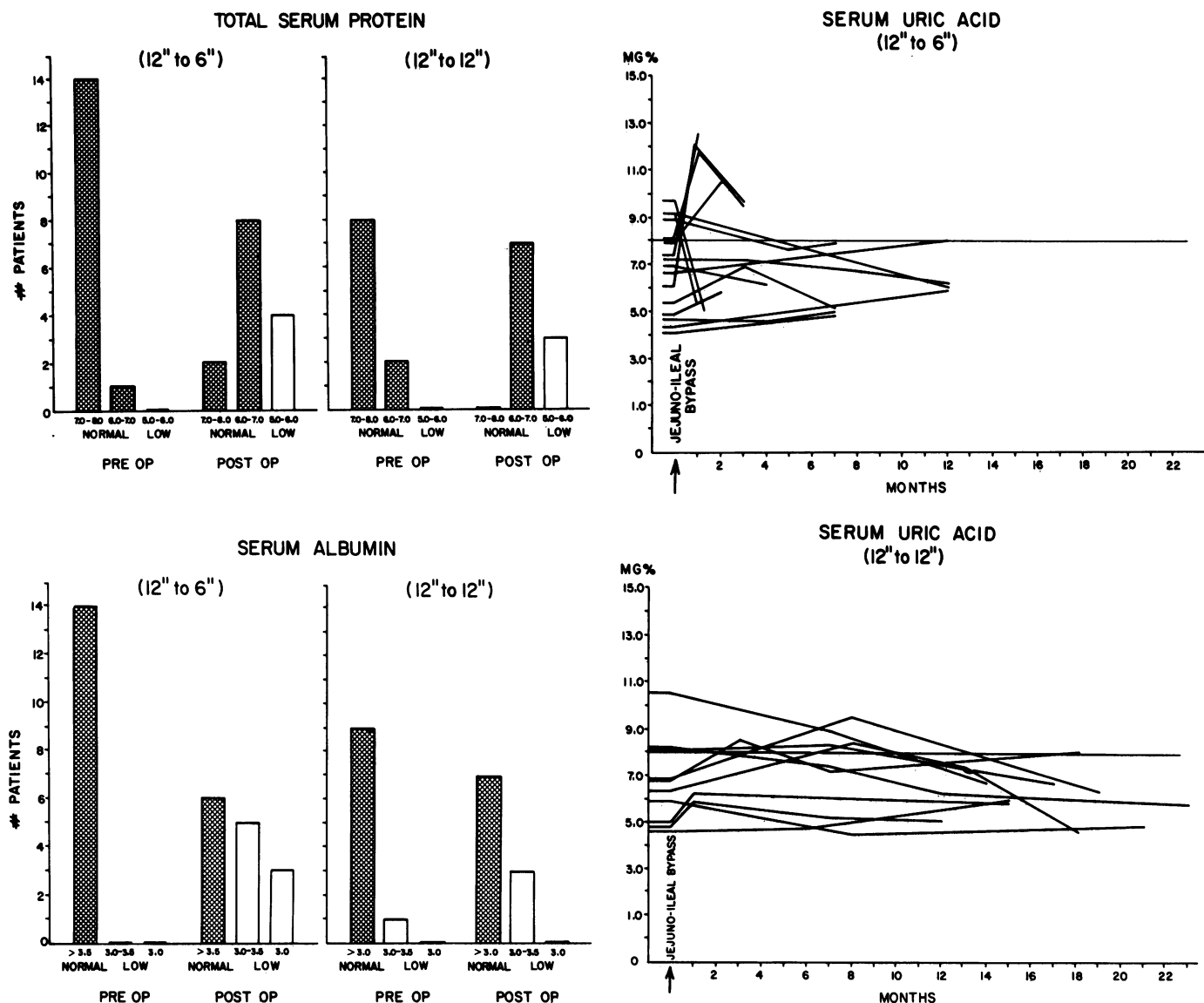


FIG. 7. Serum proteins, albumin and uric acid.

remained normal during the period of follow-up and no supplementation has been necessary in the patients of the 12 to 12 group. In three patients of the 12 to 6 group, each of whom has had a problem with persistent diarrhea, prolonged supplementation with oral cations was required.

Figure 7 summarizes comparative data on total serum protein, serum albumin and uric acid during the follow-up periods in the two groups. Total serum proteins have been well maintained in the majority of patients of both groups. In the 12 to 6 group hypoalbuminemia was present in eight of 14 patients in whom long range studies are available. The serum uric acid data reflect a trend toward hyperuricemia in many of the massively obese subjects, several of whom have been treated for "gout" prior to operation. Except for early

postoperative elevations in serum uric acid in several of the patients of the 12 to 6 group these data show little change from the baseline throughout the follow-up periods.

The studies of body composition after jejunoileal bypass will be reported separately. The data indicate that the patients lose both fat and lean tissue in the early postoperative months. The losses of lean body mass and body fat are greater in the 12 to 6 group. In both groups, however, after 4 to 6 months potassium homeostasis is achieved and with subsequent weight loss more fat is lost than lean tissue.

Follow-up studies of liver function have included the tests summarized in Figure 8. In the 12 to 12 group alkaline phosphatase and bilirubin have remained normal in all but two patients. SGOT was elevated in four

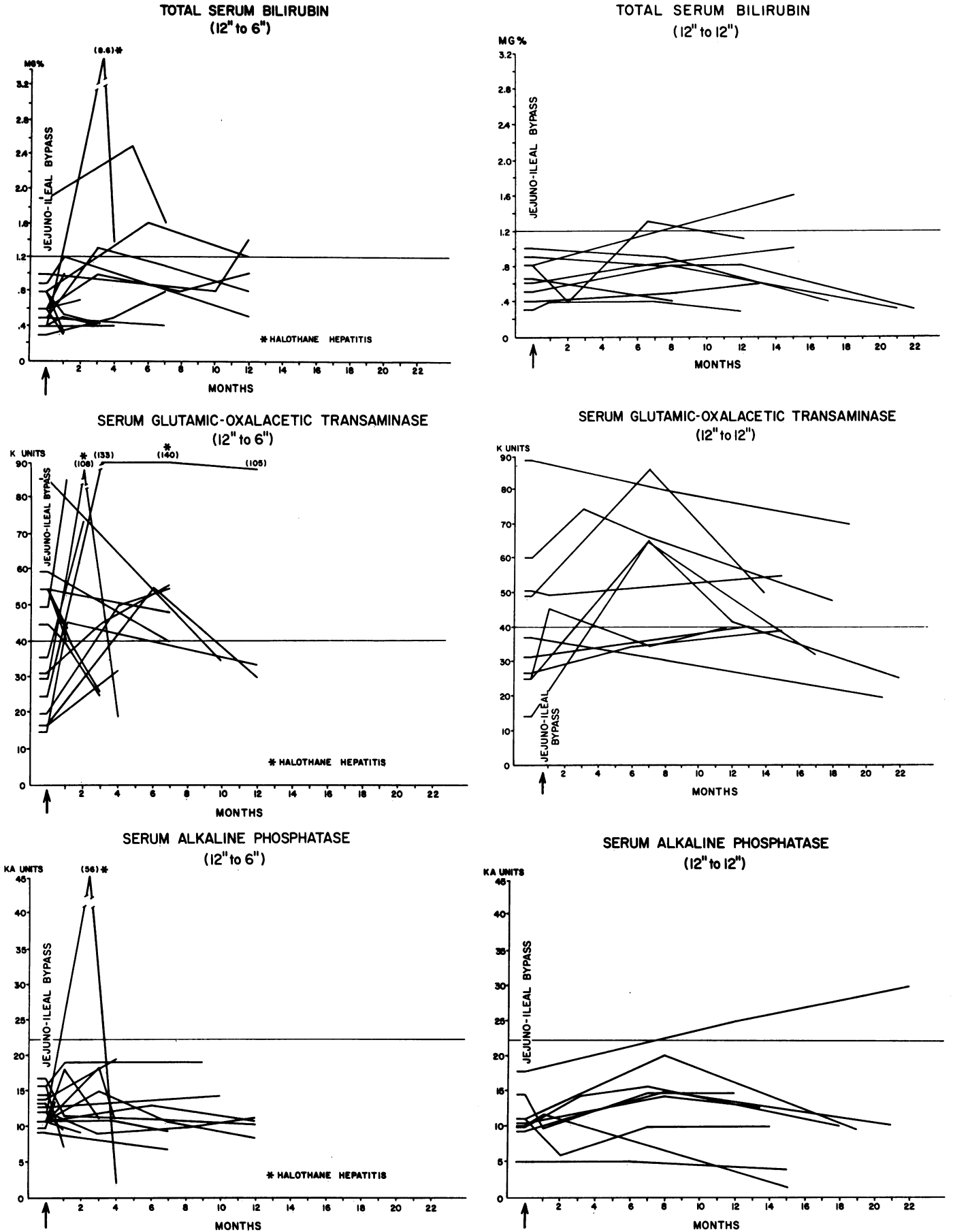


FIG. 8. Liver function tests.

patients before operation and two others had transitory postoperative elevation. All have shown a tendency to decline during the months of follow-up.

In the 12 to 6 group early postoperative elevations in serum bilirubin, alkaline phosphatase and SGOT occurred in the two patients with halothane hepatitis. One of these, who is currently clinically well, has a persistently elevated transaminase. One other individual in this group had an unexplained elevation of serum bilirubin to 1.9 mg./100 ml. before operation with a transitory rise in the postoperative period. There has been no hepatomegaly or clinical evidence of hepatic malfunction in any patient of either group during the period of follow-up.

Follow-up psychiatric evaluation of these patients revealed that depression was common in the early postoperative phase and continued for some months after discharge from the hospital. More severe psychiatric disturbances have been observed in two patients. After a year's follow-up most patients appeared to be grateful for the procedure and pleased with the result.

#### Comment and Summary

The objective of the jejunoileal bypass procedure is to induce malabsorption of fat and carbohydrate in massively obese patients who are clear cut failures of dietary management. The continuation of excessive caloric intake by massively obese patients after the bowel shortening procedure dictates that a severe degree of bowel shortening must be used if the procedure is to achieve its objective. Payne's<sup>2</sup> extensive experience with his technic of jejunoileal bypass in which the proximal 14 inches of jejunum are united to the side of the ileum 4 inches from the ileocecal valve has laid the empiric basis for the dimensional considerations selected by us for use in the present study. It has seemed desirable to us to maintain the active transport capability of both jejunal and terminal ileal mucosa in alimentary continuity and the highly important impedance of the ileocecal valve.

This study compares the responses of a carefully selected group of massively obese subjects to two operative variations of extensive small intestinal bypass with anastomosis of proximal jejunum to distal ileum. The

results of the group of ten patients who had the 12 to 12 procedure are good as regards bowel function, satisfactory nutritional and metabolic adaptation with minimal side effects, but less than good in achieving return to ideal weight status. In the 12 to 6 group, the results appear to be better in achieving ideal weight status but complications of the procedure and its side effects are increased. Although the patient's adaptive responses to the surgically induced short bowel syndrome compensate for many of the side effects after a period of months, the degree of bowel shortening in the 12 to 6 procedure may be too severe for some patients.

Accordingly in the use of jejunoileal bypass in a more recent group of obese patients, the 12 to 6 procedure has been restricted to patients who weigh over 350 pounds. In massively obese subjects who weighed less than 350 pounds we have more recently left 20 inches of small bowel (12 to 8) in alimentary continuity. This compromise, although seemingly trivial, may not be insignificant when one considers the transport capability of the millions of intestinal absorptive cells involved.

The degree of rehabilitation achieved by the majority of patients in this study has been impressive to us. The large reduction in serum lipid concentrations as well as the large reductions in body fat which result from jejunoileal bypass in obese patients should be of value in halting the progress of atherosclerosis and its accompanying cardiovascular manifestations. We believe that the results to date warrant continuation of this study with mandatory long range metabolic and nutritional follow-up.

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#### DISCUSSION

DR. GEORGE B. SANDERS (Louisville): I am sure you are all aware that Dr. Scott's very fine paper was a model of scientific precision, meticulous study, especially in the patients before and after the shunts were done.

I have done relatively few of these, and I am certainly not prepared to discuss Dr. Scott's paper in anything but a rather curious frame of mind. I thought it might occur to some of you

who are not familiar with these operations to wonder why, once the mechanism is set in motion for weight loss, the patient should stop losing weight at a certain place and time, and why he should level off.

Obviously, homeostatic mechanisms are at play, but precisely what is the mechanism, and how is it mediated? I think that probably the very first operation I did of this kind revealed accidentally to me what might be the mechanism. The operation, done about 4 years ago, was a prototype—an early prototype—of