to the patient those foods which he should eat rather than to place emphasis, as has been done for generations, on those foods which he should not eat.

Dr. Jones raised the question of disturbance of the colon in relation to deficiency states. In two of our cases we found evidence of chronic ulcerative colitis. What the relationship may be between disease of the colon and deficiency states, in other words, which is primary and which is secondary, is impossible to state in many instances.

The Diarrhea of the Pancreatic Insufficiency*

By

J. ARNOLD BARGEN, M.D.,† JESSE L. BOLLMAN, M.D.‡

and

EDWIN J. KEPLER, M.D.§

ROCHESTER, MINNESOTA

THERE are innumerable causes of diarrhea. Many diseases and functional disturbances of the body are associated with this symptom. Often, the cause is some form of intestinal disease, but the cause of a diarrhea frequently is found at points distant from the intestine. In many cases no real cause of this symptom can be found. It is difficult, for instance, to account for the diarrhea which occurs during a thyroid crisis. Unfortunately, in the minds of many persons, the terms "diarrhea" and "colitis" have been considered synonymous. This is so common that the clinician often finds it difficult to disabuse the patients of the idea that all diarrhea originates in the colon. The diabetic who has diarrhea feels certain that his diarrhea indicates a disease of the intestine. Eventually, this type of diarrhea may be proved to be an entirely independent entity which has no relation to diabetes or to the mechanism responsible for it.

Steatorrhea is a form of diarrhea in which the loose stools contain an abundance of fat. There also are numerous causes of steatorrhea. The two which are probably most commonly encountered are pancreatic insufficiency and sprue. It is more than likely that the mechanism of production of the steatorrhea in these two conditions is different. In sprue, pancreatic enzymes are present in the duodenal contents and the steatorrhea probably results from a failure of proper absorption of fat by a damaged small intestine. In the steatorrhea of pancreatic insufficiency, pancreatic enzymes cannot be demonstrated in the intestinal contents of the duodenum. The steatorrhea in this case probably results from improper splitting of fats taken in.

In cases in which the diarrhea of pancreatic insufficiency is associated with steatorrhea, the stools are bulky, have an offensive odor, and contain excessive amounts of fat. Diabetes, if present, is mild most of the time, except during episodes of acute inflammatory changes in the pancreas, which may be characterized by severe abdominal pain and occasionally by chills and fever in cases in which the condition is severe. Roentgenographic evidence of diffuse calcareous changes in the pancreas may be present.

The treatment of steatorrhea which is the result of pancreatic insufficiency has been most unsatisfactory in the past. Symptomatic measures and the administration of commercial pancreatic preparations have either failed to produce relief or at best have produced only transient relief. Then, too, the diabetes usually becomes difficult to control because of the necessity for dietary changes and the difficulty in estimating the optimal dose of insulin.

In these cases one obviously would search for trouble in the pancreas. In the cases of steatorrhea, there is evidence of a disturbance of the external secretions of the pancreas. It has been suggested that in some of the diarrheas associated with diabetes, there may be a relative decrease in the flow of pancreatic juice and therefore an intestinal disturbance without steatorrhea. A careful analysis, however, of the two types of diarrhea impressed us with the fact that in cases of severe diabetes associated with watery diarrhea, pancreatic enzymes exist in the duodenal contents whereas in cases of steatorrhea, the enzymes might be absent.

It is a well known fact that in diabetes produced in animals by complete pancreatectomy, difficulty in their management has been encountered because of the occurrence of diarrhea. It also has been found that this diarrhea may be fairly well controlled by the addition of bone ash and raw pancreas to the diet. As soon as diets which do not contain pancreas are administered, diarrhea again becomes a serious complication. Various preparations made from pancreatic tissue have not proved satisfactory substitutes for raw pancreas nor has the feeding of pancreatic juice been of great benefit in these animals. On the other hand, the addition of precipitates containing some of the active enzymes of pancreatic juice has given better results. These facts suggested to us that the administration of pancreatic juice or its active substances would be worth a trial in the treatment of the diarrhea of pancreatic insufficiency which affects human beings.

Because of the enzymatic nature of the active substances of pancreatic juice, small quantities may act on a relatively large quantity of food in the intestine and may produce nearly complete digestion. The effectiveness of small amounts of pancreatic juice was demonstrated in the case of animals whose pancreatic ducts were almost completely occluded. Patency of one small duct prevented the development of all the signs of pancreatic insufficiency which are characteristic of complete pancreatic occlusion. The effectiveness of

*Read at the Annual Meeting of the American Gastro-Enterological Association, Atlantic City, June 5, 1937.

†Division of Medicine, The Mayo Clinic.
‡Division of Experimental Medicine, The Mayo Foundation.
§Division of Medicine, The Mayo Clinic.

small amounts of pancreatic juice was likewise shown by Elman and McCaughan in studies on animals which had pancreatic fistulas from which all secretions were drained. Such animals secreted great quantities of pancreatic juice, and symptoms and changes in the chemical composition of the blood which were similar to those found in cases of obstruction of the upper part of the intestine developed. Death occurred within the first week unless large amounts of physiologic saline solution were administered, but the administration of a few cubic centimeters of pancreatic juice greatly reduced the secretion of pancreatic juice and the subsequent occurrence of symptoms, and prolonged life more or less indefinitely.

METHOD OF PREPARATION AND ADMINISTRATION OF PANCREATIC JUICE

Pancreatic juice for administration to patients was prepared in the following manner: With an aseptic surgical technic, a cannula was tied in the major pancreatic duct and the minor pancreatic duct was ligated while the dogs were under ether anesthesia. A sterile rubber tube was passed through the skin to connect the cannula in the pancreatic duct to a sterile rubber bag placed in a small basket on the animal's side. The pancreatic juice then was removed from the bag once or twice daily. The animals maintained themselves well if a small amount of pancreatic juice was administered by mouth.

Administration of whole pancreatic juice by means of a duodenal tube proved efficacious in the treatment of patients with this type of diarrhea. Because of the inconveniences of this method and the bulk of whole pancreatic juice, we then tried administration of dried precipitates which represented less than 0.5 per cent of the whole pancreatic juice. The following types of precipitates have been found to be active: (1) material precipitated from pancreatic juice by the addition of five volumes of alcohol at a temperature of — 20° C.; this precipitate was dried with cold alcohol and ether; (2) material precipitated by the addition of picric acid; this precipitate was dried and the picric acid was removed with alcohol and ether, and (3) material precipitated by the addition of a 5 per cent solution of trichloracetic acid; this precipitate was dried and the trichloracetic acid was removed with alcohol, acetone and ether. At present, we are using the last preparation.

RESULTS OF TREATING STEATORRHEA WITH PANCREATIC JUICE

The following cases exemplify the results of substitution therapy in the treatment of steatorrhea which is the result of pancreatic insufficiency:

Case 1. An unmarried man, aged thirty-six years, came to the clinic March 9, 1935. For eight years he had had periodic attacks of pain in the upper part of the abdomen, which had been associated with chills, fever and sweats. Between attacks there had been constant soreness in the upper part of the abdomen. The attacks had lasted about four days, and had been initiated by anorexia and abdominal discomfort. The pain had been situated in the epigastrium and had extended to the right and left side and at times to the back, between the shoulders. It had been severe and hypodermic injections of morphine frequently had been required for relief. With the coming of an attack, the patient had felt restless and irritable. During the attack the abdomen had become tight and distended, but had not been sore to touch. Relief had been obtained by crouching or bending forward, or by sitting in a tub of hot water. Vomiting had occurred occasionally, but had produced relief. The chills and fever had continued for several days after the pain had gone. No food had been taken during the attack.

A year before the patient came to the clinic these attacks gradually had subsided, but they had recurred six weeks prior to his admission. An exploratory laparotomy had been performed a year after the onset of the attacks. The preoperative diagnosis had been peptic ulcer, but none had been found. The abdominal organs had been normal, except the pancreas, which had been inflamed. The attacks had continued to occur about eight to ten times each year after the operation. The patient had gone to a hospital for four or five days during most of the attacks. Six weeks before he came to the clinic diabetes had been discovered following one of the attacks of pain. A diet had been instituted and for a time 40 units of insulin had been given daily. The patient had noticed for a long time that his stools had appeared greasy and foamy and had floated on water; they had contained much undigested food but no blood. The diarrhea had been severe until six weeks before his admission to the clinic, when some improvement had occurred.

When the patient arrived at the clinic he seemed ill enough to be hospitalized at once. The value for the blood pressure, measured in millimeters of mercury, was 130 for the systolic and 80 for the diastolic, and his weight was 121½ pounds (55 kg.). The value for the hemoglobin was 13.3 gm. per 100 c.c. of blood; the erythrocytes numbered 4,100,000 and the leukocytes 7,900 per cubic millimeter of blood respectively. The differential blood count was approximately normal. The value for blood sugar was 163 mg. per 100 c.c. A serologic test for syphilis was negative. The urine contained a trace of a reducing substance. Subsequent urinalyses revealed from 1 to 2.4 per cent of sugar. The results of tests of liver function were normal and there was no retention of dye. The value for the bilirubin was 1 mg., that for the calcium was 9 mg., that for the phosphate was 4 mg. and that for the protein was 6.4 mg. per 100 c.c. of serum respectively. Roentgenologic studies revealed a normally functioning gall bladder and extensive pancreatic lithiasis. As a result of a strict diabetic program the urine became free of sugar but the distress in the upper part of the abdomen continued.

After a medical regimen had been employed for two weeks, an exploratory operation was performed (March 22, 1936). An operative diagnosis of chronic pancreatitis with calcification was made by the surgeon, who described the pancreas as being about three times the normal size and diffusely indurated throughout. The common bile duct was dilated to about twice its normal size. Choledochostomy and cholecystostomy were performed. No stones were demonstrated in the gall bladder or its ducts. The postoperative convalescence was satisfactory although somewhat prolonged. The expected improvement, however, did not result and the patient returned to the clinic July 15, complaining of nausea, vomiting and a heavy feeling in the right upper quadrant of his abdomen, but he thought the pains had decreased somewhat in severity. His urine had remained free of sugar. His bowels moved every two or three hours throughout the day and night, the stools being light brown, soft to liquid, frothy, bulky and fatty; they had an offensive odor.

The patient was then given the prepared pancreatic juice through a tube which was passed very cautiously into the duodenum. We began by giving 1 c.c. every hour; the maximal amount given at one time was 2 c.c. In twenty-four hours the number of stools had been reduced from twelve or fifteen to four, and this status was maintained by continued administration of a measured amount of pancreatic juice. In a few days, the stools became

nearly normal. The patient was then dismissed from the clinic and instructed to take minute capsules containing the concentrated pancreatic juice. The patient continued to improve so long as he took these capsules; if he stopped taking them the trouble recurred. It was ultimately found that a minimal quantity of the dried juice was necessary to maintain normal intestinal function.

Case 2. A man, aged sixty-five years, came to the clinic December 4, 1935, because of progressive loss of weight and diarrhea. Five years previously he had weighed 150 pounds (68 kg.). When he came to the clinic he weighed 100 pounds (45.4 kg.). He said that he formerly had been very energetic and had taken a good deal of physical exercise, but that he had gradually become weak, tired and had lacked energy. His stools had been soft or liquid and had contained a great deal of oil and fat. At the time of his admission he was having four to six large, oily stools every twenty-four hours. Sugar first had been found in his urine in 1931. At that time the value for the blood sugar had been 170 mg. per 100 c.c. He had been given an adequate diet and his urine had been free of sugar, but in spite of this he had gradually lost weight.

Examination at the clinic revealed that the diabetes was mild. The value for the blood sugar while the patient was fasting was only 101 mg. per 100 c.c., and the urine was free of sugar. He was constantly hungry and always ready to eat. He commented repeatedly on the fact that the fat he took was not digested. The value for the systolic blood pressure was 120 mm. of mercury and that for the diastolic pressure was 80 mm. The patient appeared exhausted and emaciated. Numerous stools were examined and all contained oil or fat in excess. Their gross appearance was that of an oily fatty mass. Meat fibers were present. Results of examination of a typical stool revealed 21.2 per cent of total fat, 13.8 per cent of which was fatty acid and 7.4 per cent of which was neutral fat. The value for cholesterol was 139, that for the cholesterol esters was 82, that for the total fat was 421, and that for fatty acids was 282 mg. per 100 c.c. of plasma respectively. The value for the serum protein was 5.4 mg. per 100 c.c. The duodenal contents did not contain amylase and trypsin. Proctoscopic examination revealed a normal rectal lining. Roentgenologic studies of the stomach, colon and small intestine did not disclose any intrinsic organic disease. The gall bladder was reported as normally functioning, but there were multiple stones in the pancreas.

We started treatment of this patient by giving a capsule containing the pancreatic extract every four hours. Improvement started on the second day, and by the fourth day, his stools had become nearly normal. We have been able to maintain the normal stools by administering two capsules daily, each of which contains a fifth of the amount of pancreatic extract given at one dose when treatment was started. The diabetes has been readily controlled.

You will recall that this patient was under our observation in December, 1935. For many months, capsules of the pancreatic juice were supplied him. Because of the difficulties of maintaining the supply, he was advised from time to time to try commercially prepared pancreatic enzymes. He has tried every available product. In March, 1937, he wrote that none of them had helped appreciably. After each trial of a new one and its failure, prompt and complete relief followed the use of the one capsule, as described, twice a day. Less than this would not produce striking or lasting results.

COMMENT

It should be emphasized that the results obtained have been gratifying only in the type of diarrhea associated with steatorrhea. One would expect the best results in cases in which there is marked interference or total inhibition of the external secretions of the pancreas. Such a condition exists when obstruction of the pancreatic ducts, as by a stone, occurs.

Fortunately, the association of diarrhea and diabetes is infrequent. With the exception of some of the serious organic causes of diarrhea, it represents one of the most distressing conditions confronting the present day practitioner. The diet advisable for the diabetic is so obviously not the kind one would offer an individual who has diarrhea. Hence, the dietetic problem becomes a real one. Furthermore, the problem of the evaluation of the amount of insulin necessary for control of the diabetes is intensified. Loss of weight may be great and its control is exceedingly difficult.

These experiments bid fair to offer help to at least one type of patient who suffers from steatorrhea. Intensive dietary studies on animals whose pancreatic ducts have been evulsed are under way and we hope these may offer further leads which will point to the control of other phases of this difficult problem.

REFERENCE

1. Elman, Robert and McCaughan, J. M.: On the collection of the entire external secretion of the pancreas under sterile conditions and the fatal effect of total loss of pancreatic juice. *Jour. Exper. Med.*, 45:561-570, March 1, 1927.

DISCUSSION

DR. J. PAUL QUIGLEY (Cleveland, Ohio): Dr. Bargen has called our attention to the fact that diarrhea may occur from some disturbance in the gastro-intestinal tract located higher than the colon. I want to go a step further. Dr. Einsel and I prepared a series of dogs from which the body and fundus of the stomach had been removed and the esophagus anastomosed to the pyloric antrum. The only striking appearance in these animals was the condition emphasized by Dr. Bargen, diarrhea and excessive fecal fat. Practically all the fat in the diet of the animals passed on through.

We haven't developed a complete explanation for this condition. The portion of the gastro-intestinal tract which produces the essential factors of gastric juice has been removed. However, the diarrhea and steatorrhea are not essentially the result of absence of hydrochloric acid and pepsin but are related to the deficient reservoir function of the stomach and the consequent excessively rapid propulsion of food through the intestine.

Our results emphasize the possibility of diarrhea and steatorrhea developing from a disturbance not primarily located in the colon or pancreas.

DR. A. C. IVY (Chicago, Ill.): Dr. Bargen's report implies that pancreatic juice, dried or extracted, is more potent or more favorably administered than pancreatin. I doubt the truth of that implication and, before I believe it, a lot of good experimental evidence will have to be supplied.

I know of nothing at present in pancreatic juice that is not present in properly prepared and potent pancreatin; as a matter of fact, there is something present in pancreatin that is not present in pancreatic juice, which we do know is of value to the organism, namely, lecithin, which contains choline.

Why have a number of physicians been disappointed with the results obtained on the administration of pancreatin to patients with suspected pancreatic achylia? The first reason is that the pancreatin given the patient has not been a potent preparation. At the drug stores in Chicago a year ago, I bought six different preparations of pancreatin. We found only three preparations out of the six worthy of presentation to a patient.

The second reason is that adequate quantities of pancreatin are not administered. Two, three, or four tablets

after a meal are usually given. In our animals in which we have been studying oral enzyme therapy, we have given 25 grams of pancreatin a day in the form of powder or enteric coated tablets, and we have shown that the enteric coating increases the effectiveness of the orally administered pancreatin.

When we give pancreatin to our patients, we must know that it is potent. We can't rely on the Council of Pharmacy and Chemistry for such potency, because they do not accept pancreatin or any other enzyme for oral administration, and the U.S.P. requirements in regard to pancreatin are not to be praised; so, if we are going to give pancreatin, we should know first, by having a competent chemist test it, that it is potent, and, when we give it, we must give it in adequate quantities.

We have two patients with pancreatic achylia and we have demonstrated that 25 grams of pancreatin, or 75 five-grain tablets, given per day, with and after meals, is effective. I say that on the basis of reliable evidence, and not on the basis of the patient's feelings or reports.

I was glad to see that Dr. Bargen showed the absence of enzymes from the duodenal drainage in his patients, but he did not say he had analyzed the stools chemically for fats, protein, and starch.

I think the only reason why the Council of Pharmacy and Chemistry of the American Medical Association does not accept pancreatin for oral administration is that there is very little good evidence in the literature showing that pancreatin is effective in man. There is plenty for the dog, which now demonstrates that it is effective. In many of the reports in which pancreatin has been used in man, analysis of duodenal drainage has not been done, to prove that a case of pancreatic insufficiency is actually being treated; and, secondly, the stools have not been examined chemically under dietary control before and after treatment with pancreatin.

The only way that one can establish scientifically that pancreatin is or is not effective in a particular patient, is to place the patient on a diet, collect the stools and analyze them for fat, nitrogen, and carbohydrate, and then repeat the analysis after pancreatin. When this is done on a sufficient number of patients, then we will have data which will establish, I believe, that oral enzyme therapy is effective in human subject suffering pancreatic insufficiency.

DR. WILLIAM C. BOECK (Los Angeles, Calif.): I have enjoyed hearing Dr. Bargen's paper which has brought the subject of steatorrhea before us again. I trust that the new method of treatment will be available to the rest of us who have such patients under our care.

I have the excuse of appearing before you simply to recount the history and treatment of another case in which steatorrhea was the prominent finding but which apparently was due to extrinsic factors outside of the organs of the gastro-intestinal system.

This case was that of a physician, 45 years of age whose illness lasted for one year. He had a persistent diarrhea which proved to be a steatorrhea, for the stools were made up mostly of fatty acid crystals. They were as plentiful as to appear like the sediment of a turbid specimen of urine.

He had abdominal distention and marked tenderness in the left upper hypochondrium. There was adenopathy of the axillary and inguinal glands. He had lost some twenty-five pounds in weight.

Physical examination and X-rays were negative for tuberculosis. Achlorhydria was present. The small intestine showed "laking" of barium in the jejunum and upper ileum suggestive of that described in cases of sprue. The blood picture was that of a moderate secondary anemia, with erthryocytes varying from 3,500,000 to 4,000,000, and hemoglobin from 75 to 85 per cent (Sahli) most of the time; a persistent leucopenia of 2,500 to 3,500 leucocytes was present all the time until one month before his death when it became normal.

Biopsy of an inguinal gland revealed a picture somewhat resembling tuberculosis, but no pathologist would agree that it was. Later, laparotomy was performed. The mesenteric glands were all enlarged, especially in the area of the jejunum and pancreas, but not in the region of the terminal ileum. A large mass of mesenteric glands was found at the origin of the mesentery near the pancreas. The small intestine and colon appeared to be normal.

The biopsy examination of one of the mesenteric glands showed almost complete disappearance of all lymphoid tissue with replacement by fat present in reticulocyte cells and deposits of cholesterol crystals. The microscopic preparations of this tissue were examined by several prominent pathologists throughout the country but no one made a definite diagnosis. It was thought that the condition was some form of lymphoma.

As to treatment, liver extract was used extensively, along with dilute hydrochloric acid, a fat-free diet, then later a normal diet, but no benefit occurred until the patient was given X-ray treatment. Then the diarrhea ceased almost entirely and also the steatorrhea. The adenopathy and abdominal distention disappeared. The patient gained 7 pounds in the next four months, but weakness persisted. One month before he died, his white cell count became normal and we were hopeful that his change portended a better prognosis. However one month later he suffered from acute cardiac decompensation and died a few days later.

Autopsy findings were those of cardiac dilatation. The pancreas, liver, adrenals, and mesenteric glands all appeared to be normal. There was no evidence of fat and cholesterol deposits in the glands, but some occurred in the walls of the small intestine with some mucosal atrophy.

Whether or not his case belongs in the category of those described as acute or chronic mesenteric adenitis or as some form of lymphoma I do not know but it illustrates the occurrence of steatorrhea from some disturbance extrinsic of the gastro-intestinal system, which vanished after X-ray treatment but the treatment did not cure the patient.

DR. J. ARNOLD BARGEN (Rochester, Minn.) (closing the discussion): I appreciate the discussion of Drs. Boeck, Ivy and Aaron. I tried to bring to your attention only one other method of aiding some of these very miserable people.

I believe, after hearing Drs. Aaron and Ivy, that in the past we have at times not used enough pancreatic extract. This very simple method came through Dr. Bollmann's work on animals and we were able to control the diarrhea of man. We were able to control it in one case by administering two small capsules of the powder daily. The patient had tried all kinds of drugs on the market, including very large amounts of pancreatic extract. Whole pancreas has been used sporadically but not enough to permit us to conclude how it would compare with this pancreatic juice. However the second patient received 75 to 100 grains daily of pancreatic extract of a preparation supposedly potent without effect, whereas two small capsules of the dried juice controlled his symptoms.
how it would compare with this pancreatic juice.

The pancreatic juice is not a cure-all. Some patients have not received adequate relief. A minister from the South received what we thought was an adequate quantity of these capsules but he was not particularly helped. All persons who have these types of diarrheas are thoroughly miserable and a certain number of them, I think most of them, will be helped when the pancreatic ducts have been occluded. Whether there are enough of them even to

warrant making such a preparation commercially, I do not know. In reply to Doctor Ivy's question about stool analysis, I should like to say that in all these individuals careful chemical analysis was made in all, as indicated in the second case.

Regarding the different causes of steatorrhea, Dr. Boeck mentioned an entirely different type. I think we must keep in mind that there is a steatorrhea which is probably due to a failure of the proper splitting of fats, and a steatorrhea which probably is due to failure of absorption. The latter may be associated with sprue. I saw a patient who had a definite clinical picture of sprue and tuberculosis of the abdominal lymph nodes. At necropsy there was marked atrophy of the intestinal mucous membrane. That patient presented a picture such as Dr. Boeck has described, but the course of the disease was not affected in the slightest by these capsules.

I hope this study may result in a stimulation to further study of this type of diarrhea and a trial of an adequate quantity and an adequate type of pancreatic product.

The Diagnosis and Treatment of Acute Non-Hemorrhagic Pancreatitis*

By

ROBERT ELMAN, M.D.
ST. LOUIS, MISSOURI

THE current conception of acute pancreatic disease is usually confined to the lesion often called pancreatic necrosis or acute hemorrhagic pancreatitis. The pathology of this remarkable condition is well known, its course is nearly always progressively downward and is associated with a high mortality even when an emergency operation is carried out. Acute pancreatic necrosis is, however, a relatively rare disease and in recent years has not evoked much interest in spite of the mystery which still surrounds its pathogenesis.

Acute pancreatitis which is not associated with necrosis, i.e., nonhemorrhagic pancreatitis, has from time to time been discussed in the literature as a mild type of pancreatitis which stopped short of actual destruction of the gland and subsided. In general, this group of patients comprises those operated upon with a diagnosis of pancreatic necrosis (or some other acute abdominal condition) but in whom at laparotomy the pancreas presented no hemorrhage or necrosis, but merely an edema or induration particularly of the head of the gland (1, 2). The possibility, however, that the pancreas is very often the site of acute inflammation which subsided has never been very widely held, in spite of the fact that surgeons, during the course of cholecystectomy, have frequently found the pancreas to be indurated and enlarged. This association of pancreatic with cholecystic disease has, of course, been repeatedly observed and may account for the fact that the lesion in the pancreas has consistently been afforded little consideration in favor of the more well known lesions in the gall bladder and liver. It has been my experience that this type of pancreatitis is relatively frequent but that it nearly always masquerades as another lesion; because of these considerations I have made a clinical study of a number of these cases. Review of the literature has been made in previous papers (1, 2, 3).

The present observations concern patients who suffered acute subsiding attacks of epigastric pain due undoubtedly to an acute process in the pancreas, most likely an inflammation, in most cases at least, but not of the hemorrhagic type and without evidence of necrosis. In most of these patients the original diagnosis did not refer to the pancreas; many were suspected of suffering from biliary colic, others of acute cholecystitis, perforated peptic ulcer, acute appendicitis, acute intestinal obstruction, and a few, coronary thrombosis. In the first cases observed the true diagnosis was revealed only at operation when the lesion in the pancreas was noted. Later it was possible to make a clinical diagnosis by studying the blood for its concentration of amylase. This determination when made at the height of the patient's symptoms and repeated as the clinical manifestations subsided, revealed a striking correlation with the course of the attack. In a few patients both objective evidences of pancreatitis were obtained, i.e., the rise and fall of the blood amylase and anatomical changes through biopsy of the pancreatic lesion.

As far as the clinical behavior itself is concerned the bed-side manifestations frequently gave only suggestive indications of the true nature of the disease. In all cases, the attacks were severe and disabling, the patient seeking bed rest at once. The pain was often cramp-like in character and nearly always accompanied by vomiting. While located in the mid epigastrium, the pain was often more severe to the right or to the left of the midline and occasionally was diffuse. A nearly constant feature was the reference of the pain to the small of the back, i.e., over the spines of the lumbar vertebrae. Occasionally the pain was referred to the mid-scapular region. Attacks varied in severity and duration, but rarely did they exceed four days before subsidence. Only occasionally were patients seen in their first attack; a history was fre-

*Read at the Annual Meeting of the American Gastro-Enterological Association, Atlantic City, June 7-8, 1937.
From the Department of Surgery, Washington University, School of Medicine, and Barnes and St. Louis City Hospitals, St. Louis.