with those following pancreaticoduodenectomy that the former procedure should not be performed unless the functional capacity of the entire gland has been severely involved in the destructive process.

## BIBLIOGRAPHY

- Barker, W. F., K. E. Rogers and F. D. Moore: Effect of Pancreatectomy on Phospholipid Synthesis in the Dog. Arch. Surg., 61: 1151, 1950.
- Catell, R. B. and K. W. Warren: Surgery of the Pancreas. Philadelphia, W. B. Saunders Co., 1953.
- Chapman, H. S.: Surgery of Pancreas. West. J. Surg., 58: 178, 1950.
- Nardi, G. L.: Metabolic Studies Following Total Pancreatectomy for Retroperitoneal Leiomyosarcoma. New England J. M., 247: 548, 1952.
- Owens, F. M., Jr.: Problem of Peptic Ulcer Following Pancreatectomy. Ann. Surg., 128: 15, 1948.

DISCUSSION.-DR. JOHN M. WAUGH, Rochester, Minnesota: Drs. Longmire, Jordan and Briggs have rightfully emphasized the value of resection in selected cases of relapsing pancreatitis. I brought some slides along, but I have decided to dispense with them because I was afraid Henry Harkins might measure them. (Laughter)

We have felt that the less radical procedures, such as sphincterotomy, and sphincterotomy has been done transduodenally, coupled with T tube drainage and cholecystectomy, even in the face of a normal-appearing and normal-feeling gallbladder, have been advisable, and we have also tried retrograde drainage of the tail of the pancreas. I used this latter procedure three times about two years ago, and two of those patients maintain that they have obtained benefit from it. The third is very questionable. However, these two less radical procedures have seemed to us to be advisable before undertaking the resection, bcause our early experience with total pancreatectomy was not entirely satisfactory.

We have had very poor results with the nerve severing procedures, both unilateral and bilateral. In general, we have used resection under the following circumstances:

First, when there is a localized abscess in the tail or adjacent body of the pancreas. This abscess can be very small—as small as 1 to 2 cm—and still give considerable pain. I resected one of these in 1942, thinking it was probably a very small

- Priestly, J. R., M. W. Comfort and J. Radcliffe, Jr.: Total Pancreatectomy for Hyperinsulinism Due to Islet Cell Adenoma; Survival and Cure at 16 Months After Operation; Presentation of Metabolic Studies. Ann. Surg., 119: 211, 1944.
- 7. Priestly, J. F.: Personnal communication.
- Rhoads, J. E., J. M. Howard and N. H. Moss: Clinical Experiences with Surgical Lesions of the Pancreas. S. Clin. North America, 29: 1801, 1949.
- Waugh, J. M., C. F. Dixon, O. T. Claggett, J. L. Bollman, R. G. Sprague and N. W. Comfort: Total Pancreatectomy: A Symposium Presenting 4 Successful Cases and a Report on Metabolic Observations. Proc. Staff Meet., Mayo Clin., 21: 25, 1946.
- Whipple, A. O.: Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas. Am. J. Surg., 40: 260, 1938.
- --: Radical Surgery for Certain Cases of Pancreatic Fibrosis Associated with Calcareous Deposits. Ann. Surg., 124: 991, 1946.
- 12. Zinninger, N. N.: Quoted by Whipple, reference no. 10.

carcinoma causing the pain, and when it was opened it was actually a small, well-encapsulated abscess. Dr. Priestley just recently removed a very similar one.

Second, there are large inflammatory masses that are due to resolving abscess or pseudocyst that will overlie the pancreas and will cause quite a bit of destruction of the pancreas, and I think it is better to remove that rather degenerating pancreatic tissue rather than leave it in the tail and adjacent body.

Third, there are cutaneous fistulae that result from both inflammation and trauma. Rather than do an anastomosis if that fistula arises in the tail or body, I would advise you to resect that portion of the pancreas and the portion distal to it.

Fourth, localized calcification in the head of the pancreas with severe pain, I feel, is a definite indication for resection if the less radical procedures fail. Certainly failure of the conservative procedures mentioned at the beginning would be an indication to think of resection.

As far as results are concerned, I have the impression that when we have used sphincterotomy and other procedures, we have not gone over those definitely because they are of too short duration, but I have the impression that sphincterotomy has not helped more than 60 to 65 per cent of our patients.

Dr. Longmire has well shown the advantages for proper fat digestion in leaving a portion of the pancreas even when it may appear quite fibrotic. I would like to caution you concerning the technical hazards of this procedure. In the burnedout, calcified stage it is not difficult. If the inflammatory process is still active, resection can be difficult, tedious and hazardous not only for the patient but for the surgeon's coronary vessels.

Immediate results in the relief of pain have been good. However, in two total pancreatectomies done by Dr. Clagett and myself, with diffuse pancreatitis, both of them have gotten into difficulties about 12 to 18 months later from management of their diabetes, and both expired.

Two other patients, one already cited by Dr. Longmire, operated on by Dr. Priestley, and one by me, have now gone approximately ten years without difficulty. They were both resected with total pancreatectomy for islet cell tumor. We had occasion to explore the patient on whom I operated about a year ago, and there was no evidence of fatty infiltration of the liver.

Partial pancreatectomy has given better late results, as you would expect, but one patient developed an acute fatal bowel obstruction secondary to impacted undigested fat in the lower small intestine.

DR. RALPH F. BOWERS, Memphis, Tennessee: I greatly enjoyed Dr. Longmire's paper; as usual, it is splendid and his work is excellent.

However, I am somewhat at a loss to understand why he has not obtained better results with indirect procedures, because in well-selected cases in the early phases of the disease, these simpler procedures have been beneficial. It is concerning that aspect of the subject about which I wish to make a few remarks.

Our plan involves the use of biliary tract surgery first if there is evidence of disease in that system after the attack of acute pancreatitis has subsided. If the patient experiences recurring attacks after the indicated biliary tract surgery has failed, then choledochojejunostomy en Roux Y is employed. Dr. Longmire has sparingly used this procedure which, in well-selected cases during the phase of recurring acute attacks, has yielded 80 per cent control in hands.

Sixteen of 17 patients have had their pancreatic attacks controlled and well controlled by this operation. The one failure occurred in a patient who has received great benefit and who works three-fourths of the time during the year.

Since our last report before this Association in 1955, I have had an interesting experience with two cases of persistent acute pancreatitis, one with persistent ascites and elevated amylase readings and the other with bilateral pleural effusion, pericardial effusion and an abscess attached to the wall of the stomach. They had been extremely ill, almost cadaveric for four months and five and onehalf months respectively.

Choledochojejunostomy was planned in the first case, but the peritonitis was so extensive that cholecystectomy, dilatation of the sphincter and T tube drainage were used. Ascites promptly disappeared and he gained 27 pounds in five months. There was no demonstrable biliary tract disease. When the T tube would be clamped, a mild pancreatic attack would often appear. Choledochojejunostomy will therefore probably be necessary later.

In the second case, a sleeve-type gastric resection was first performed, reasoning that the pancreatic infection may exist in aberrant pancreatic tissue located in the stomach wall, because the real pancreas appeared to be only mildly involved. He did not improve and in spite of what seemed to be a perfectly hopeless situation, choledochojejunostomy was deliberately performed three weeks later. The pleural fluid amylase was 6000 units and other serum amylase 1400 units before the second operation. Two days after the choledochojejunostomy the pleural fluid amylase was zero and the serum amylase fell to a near normal of 200 units!

One must agree that in the type of cases described by Dr. Longmire, it is tempting to employ resection. His cases approach the "burning out" or "burned out" phase which do not respond well to indirect procedures.

I have performed pancreaticoduodenectomy for pancreatitis only once when the infection was mistakenly thought to be malignant. The patient recovered nicely from the operation, but is mentally ill with signs and symptoms that do not ordinarily suggest pancreatitis. The result is not good, but all observers believe the mental illness is responsible for the symptoms.

I am very pleased to learn that pancreatic resection is a useful procedure when the patient's infection reaches this "burned out" stage. As Dr. Longmire pointed out, the pain of the recurrent acute attacks is severe, but it becomes less severe as the phase of pancreatic insufficiency arrives. This is manifested by malnutrition, cachexia, mild diabetes and vague and milder pain.

His work also suggests the reasons for the good results obtained by the indirect operation, choledochojejunostomy. This operation, as we have employed it, has been used when the chronicity of the infection manifests itself by recurring acute attacks.

DR. JOHN H. MUHOLLAND, New York, New York: I am sure everyone interested in this subject is concentrating on these difficult problems where the inception of the disease is acute pancreatitis but which has advanced to a complicated stage. Furthermore, the procedures of value in early pancreatitis fail in this group.

Dr. Henry Doubilet, my colleague, has devised a technique for catheterizing the pancreatic duct in such patients. He is enabled thus to sample pancreatic juice and measure resistance to flow. From his studies it has been shown that pain is due to distention of the pancreatic ducts and that the pain can be reproduced precisely by distending the ducts with saline solution. It can also be demonstrated by a diodrast injection into the catheter that the ducts are always distended. Although Dr. Longmire described the pain as "constant," there are sharp exacerbations when the pancreas is stimulated to secretion by food. This must result from an attempt on the part of the pancreas to function, and to be expected when one appreciates the great potential and actual regenerative power of the pancreas.

It seems somewhat defeatist to extirpate the gland as treatment for its attempts to regenerate. I believe some other measures, short of removal, should be tried.

We have observed relief of pain in patients of this type after sphincterotomy or after a decompressing procedure such as proposed by Dr. Duval. Others with partial obstruction to flow of pancreatic juice are benefited by removal of calcium carbonate stones from the distended duct. In some the implantation of a small T tube into the dilated pancreatic duct with drainage into the intestine, has relieved pain.

If the problem is considered as being one of removing the partially obstructing mechanism and promoting regeneration a salvageable organ can be preserved. Extirpation involves the production of two other diseases, sprue and diabetes. In only rare instances is this a fair exchange for some relief of pain. Thank you.

DR. RICHARD B. CATTELL, Boston, Massachusetts: Dr. Longmire has just made an important contribution relative to the treatment of a carefully selected group of patients with chronic relapsing pancreatitis. He has utilized resection of the pancreas in those patients in whom the process is advanced with sclerotic changes and with obstruction of the pancreatic ducts not relievable by lesser operative procedures.

Whenever the treatment of chronic relapsing pancreatitis is discussed one hears conflicting points of view, but this is usually due to the fact that cases of varying degrees of pancreatitis are being considered. Those of us particularly interested in this problem recognize that obstruction of the pancreatic duct is the most important factor in the production of symptoms and in the continuation of the inflammatory process. Obstruction can be relieved in some patients by sphincterotomy, by drainage of the pancreatic duct, by lithotomy of the duct or by the anastomosis of the duct to the gastro-intestinal tract. When multiple points of obstruction are present, however, and the pancreas has become fibrotic, usually with associated pancreatolithiasis, resection becomes necessary.

Dr. Kenneth W. Warren and I have recently reviewed the records of 104 patients operated upon for chronic relapsing pancreatitis in its various stages. Thirty-five had transduodenal exploration, ten of whom had sphincterotomy only. In twenty five, sphincterotomy was combined with dilatation of the main pancreatic duct. This permitted the removal of calcareous deposits causing obstruction of the duct. Fifteen patients with pancreatitis largely confined to the tail and body had distal pancreatectomy, removing the entire portion of the pancreas distal to the neck. This permitted retrograde probing of the pancreatic duct in the head. Twenty additional patients required pancreatoduodenal resection with anastomosis of the pancreatic duct to the jejunum, and one patient had total pancreatectomy.

We agree with Dr. Longmire that it is advisable to save some pancreatic tissue whenever possible even though that portion may be involved, since some pancreatic function will be preserved after the obstruction is relieved.

Based on our experience with 104 patients in whom the diagnosis of chronic relapsing pancreatitis has been verified by operation, we found that approximately one-third of all patients require resection of some portion of the pancreas to provide relief. Of the 20 patients submitted to pancreatoduodenal resection, 15 had a satisfactory result, with five having some continuing symptoms. Since no other relief is available for these severely handicapped patients, resection certainly is justified.

DR. I. RIDGEWAY TRIMBLE, Baltimore, Maryland: This very interesting and thoughtful paper by Dr. Longmire I know is appreciated by all of us. A disturbing feature in this whole problem, of course, is that the etiology, and therefore the treatment of this condition, remain controversial.

I was very interested today in trying to determine just how much the symptom of pain played in the cases described by those who have spoken here, because, as you know, pain is usually the presenting feature in these cases. Indeed, many of the patients are hopeless addicts when they come to us. The question resolves now as to whether or not one can relieve these patients of their pain and other symptoms indirectly by doing something to remove the chief cause of pancreatitis as we know it today, or whether you must attack the organ affected directly. Many of us believe that the chief cause of pancreatitis is an increased pressure in the biliary system, and that the essential treatment is to relieve that pressure. I will simply recite one case. I have had two cases of "burned out" pancreas with calcification diffusely through the pancreas on whom I have done a transplantation of the common duct with great success. This was a young man, not an alcoholic, who had severe pancreatitis with disabling pain. At operation he had a very dilated common duct. He was not jaundiced. At operation I cut the sphincter of Oddi and dilated the pancreatic portion of the common duct through an opening in the common duct. Then I put in a T tube and did no more. I think I made a mistake, because the disease was in the pancreatic portion of the common duct and cutting the sphincter would not relieve it. At any rate, all pain stopped immediately after the T tube was put in place.

Volume 144 Number 4

It is my experience that if you relieve the pressure in the biliary system you will stop the pain. This young man continued to drain bile in great quantities from the common duct. For the next three months he had no pain. Then I had to do what Warren Cole and Petersen described in 1945 and what Bowers has described now. I transplanted the common duct into the jejunum. The patient has remained well for three-and-one-half years. He has some steatorrhea which he had before we operated on him, but no pain. He has gained weight and is back at work.

I believe in pancreaticoduodenectomy; in fact, in April, 1940 I performed what I thought was the first one-stage operation for resection of the head of the pancreas by doing it. Later I learned that Dr. Allen Whipple had done it two weeks previously as a one-stage operation. I think, however, that I was the first to recommend putting the common duct and not the gallbladder into the jejunum in these cases of carcinoma so as to prevent serious biliary fistula as happens when the common duct is ligated and, also, I believe I was the first to stress the importance of a one-stage operation.

The operation which Dr. Longmire describes may be a satisfactory one in a very limited number of cases and in his hands. However, as the Indian said, for the ordinary surgeon that is "strong medicine" to resect the pancreas for inflammatory disease alone.

My plan at the present time in cases with recurring pancreatitis is that if the common duct is not dilated and the disease to my mind has not therefore greatly progressed, I do the sphincterotomy. However, if the common duct is greatly dilated and the disease is demonstrated as being in the pancreatic portion of the common duct, in those cases I will do this transplantation of the common duct into the jejunum in a Roux-Y procedure. Thank you.

DR. JONATHAN E. RHOADS, Philadelphia, Pennsylvania: I want particularly to congratulate Dr. Longmire on his operative mortality. To do eight pancreatic resections without any operative mortality is a great triumph, particularly when chronic relapsing pancreatitis is present.

We did a total pancreatectomy in one of the "burned-out" type of case who had already developed some diabetes in 1948. The patient was a man of 62. He is still living at the age of 70, and is getting along reasonably well, despite various intercurrent accidents and illnesses.

I think one has to pick the patients carefully for total pancreatectomy, because even if you get them through the operation, the patient has to keep himself alive, and if you do not have a fairly intelligent subject the chances are very great that the patient will lose his life after total pancreatectomy through mismanagement of his diabetes.

Our case, while it turned out well, was accompanied by such difficulties that we have been reluctant to employ the method. The patient had

a very stormy course. While the process was presumably somewhat burned out, it was not totally so, and the tissue surrounding the pancreas was exceedingly adherent and difficult to dissect. Therefore, this procedure has been avoided as far as possible in chronic pancreatitis since then. For a considerable time, the nerve-cutting operations were employed. Follow up of eight of these patients revealed that 50 per cent of them had had satisfactory relief from sympathectomy and splanchnicectomy. One patient was satisfied after a unilateral procedure. Of the other, one had gone elsewhere and had had a total pancreatectomy by the late Dr. Edward McLaughlin, with a satisfactory result. Another had had a sphincterotomy and had subsequently gone downhill and died. All of this left us with the impression, which others have had, that the nerve-cutting procedures are not as satisfactory as one would like, but that, nevertheless, a fair number of patients have gotten sufficient relief to be quite satisfied, and over periods of time ranging up to six years.

Again, I want to congratulate Dr. Longmire because if the procedures that he has used can be carried on with as little mortality as he has had, they certainly deserve much wider use.

DR. MERLIN K. DUVAL, JR., Brooklyn, New York: We don't have the competence nor the type of patient in Brooklyn who will withstand total pancreatectomy. Therefore, we have been making a plea, among our resident staff especially, to try to select these patients for a decompressing operation via the tail of the pancreas. However, I believe that even if this operation is used simply because one has made a diagnosis of pancreatitis, one can expect quite a few failures.

In our three years' experience we have found that there are two criteria which we think will predict a successful result. One is the presence of weight loss. We will not operate on a patient intending to decompress his pancreatic duct if he has not lost weight. The other criterion is a dilated pancreatic duct. Paradoxically, the more "burned out" the pancreas, the more eager we are to do this procedure. Of the nineteen patients we have done in this period of time, two had neither weight loss nor a dilated duct. Both have failed. Neither one, by microscopy, has very much in the way of pancreatitis. Apparently, the pathologists are not sure they even have the disease.

As nearly as I can honestly judge, being a partial observer, the other seventeen have thus far been highly satisfactory, and the patients very satisfied.

DR. ALFRED BLALOCK, Baltimore, Maryland: What does leaving the residual stump do other than in diabetes? Are you postulating an internal secretion of another sort?

DR. ALEXANDER BRUNSCHWIG, New York, New York: I think this series which Dr. Longmire and

associates have reported is certainly of interest, and touches off a great deal of thought. It leads us to wonder how complex the subject of pancreatitis really is. In those cases I have seen it was usually a question of cancer of the pancreas. But those who had chronic pancreatitis with severe pain and calcification were almost always severe alcoholics and narcotic addicts, with marked personality changes and great emotional instability. These are very sick individuals, and almost any form of excisional treatment to relieve the severe pain and thus permit rehabilitation would seem. justified. Certainly medical management has not gotten us very far in the very ill patient.

There is one other group of cases that has always interested me; the group which have no symptoms referrable to the pancreas but who have roentgenograms of the abdomen taken for other reasons and exhibit various degrees of pancreatic calcification. This calcification may be very extensive and be quite comparable to those patients who have the severe symptom complex. This raises the question of the significance of the extent of calcification relative to the severity of the symptoms.

Not long ago I saw a roentgenogram of a patient studied for something else, who had the whole pancreas outlined by very dense calcification, and yet repeated inquiry failed to elicit any history attributable to pancreatitis. Those cases, of course, we leave alone; but that suggests that the calcification phenomenon in the pancreas might sometime be something apart from that which we call pancreatitis accompanied by severe symptoms.

Finally, the question often raised is this: How do you tell the difference between pancreatitis limited to the head, and a deep-seated carcinoma? The implication is that if it is carcinoma, one would do a pancreatoduodenectomy, and if it is pancreatitis one may not do this operation but a short circuiting operation only.

DR. PAUL H. JORDAN, JR., Los Angeles, California: We would like to thank Drs. Waugh, Bowers, Mulholland, Cattell, Trimbull, Rhoads, Duval, Blalock and Brunschwig for their contributions to this paper. In answer to Dr. Waugh's admonition about the difficulty with diabetes in totally depancreatectomized patients, we can only add to that caution.

As Dr. Rhoads pointed out, the intelligence of these patients is quite important in considering whether or not one can do this procedure. The one death that we had was in a patient who was not intelligent enough to manage his diabetes. Incidentally, in the patient who died, total pancreatectomy was done under very extenuating circumstances following a caudal pancreatectomy and not as a primary procedure.

The interesting thing about that particular patient was the fact that his insulin requirement ranged from 60 to 80 units per day. That was two to three times the amount of insulin required by our other two totally depanceatectomized patients. The reason for the high insulin requirement in this patient was unknown to us, but because of the marked degree of inflammation present at the secondary procedure it was conceivable that a small remnant of pancreas was left, and that the problem encountered with this particular patient was similar to the experience reported by Dr. Dragstedt, wherein removal of all but a small portion of the pancreas in a dog created a diabetic state more difficult to control than that created by total pancreatectomy.

In answer to Dr. Bowers' question, we would like to emphasize the fact that pancreatectomy of any type should be utilized with great caution and that we do not undertake the procedures lightly. We feel that our experience with the more indirect surgical procedures has been unfavorable partly because we have not utilized them earlier in the progression of pancreatitis. Our results with choledochojejunostomy and sphincterotomy might be considerably improved if they were employed early in the course of the disease. We certainly want to see if we can improve our results with these procedures so that it will not be necessary to take recourse to radical pancreatectomy after the pancreas has gone on to marked destruction.

Dr. Cattell pointed out that he thinks it is very important to retain the tail of the pancreas. We heartily agree with that.

In answer to Dr. Blalock's question, namely, what is the purpose of retaining the tail of the pancreas, I would like to show two slides which summarize some preliminary data on the ability of patients who have undergone pancreatectomy to absorb fat and protein from the gastro-intestinal tract. To study this, we have used a method employing radioactive fat and protein in a manner similar to that which Dr. Shingleton reported to us yesterday.

(Slide) For a source of protein we have used 100 microcuries of iodinated serum albumen and have made daily stool collections on each of four successive days. These figures represent the per cent of the administered dose of protein excreted in the stool on each of the four days in a normal individual. The normal patient in this case excreted 2.7 per cent of the administered dose. Thus far we have not studied a partially depancreatectomized patient, but in the case of a completely depancreatectomized patient a total of 21.6 per cent of the administered dose of protein was excreted during the four-day period while the patient was on pancreatic substitution replacement therapy.

I should also point out that we collected blood two, four, and six hours after the administered dose. These figures, when multiplied by  $10^{-4}$ , represent the percentage of administered protein in 1 ml of blood. You can see that the results in the case of the normal and totally depancreatized patient were so similar that determination of the radioactivity in the blood could not be used as a quantitative index of absorption.

(Slide) For a source of fat we have used 100 microcuries of iodinated triolene. Again these figures represent the per cent of the administered dose excreted in the stool on each of four successive days. The normal individual excreted 0.60 per cent of the administered dose, the subtotal pancreatectomized patient excreted 1.5 per cent of the administered dose, while 28.7 per cent of the administered dose appeared in the stool of a totally depancreatectomized patient during the first two days. Unfortunately, in this latter patient we were unable to collect the stool during the third and fourth days of the study. In another patient, however, who also had had a total pancreatectomy, the pattern of excretion of fat during the four-day period amounted to 64 per cent of the administered dose. Therefore, the absence of diabetes and the greater efficiency in the absorption of nutrients from the gastro-intestinal tract in a partially depancreatectomized patient compared with a total depancreatectomized patient are the reasons we feel that it is so important to leave the tail of the pancreas unless there is incontrovertible evidence that its functional capacity has been lost by virtue of the pathologic process.

Dr. Brunschwig pointed out that these patients are frequently unstable, that they are alcoholics and narcotic addicts. That is frequently true, and we have that problem. We try to take that into consideration in choosing our patients.

In conclusion, I would like to express my appreciation to this Association for being permitted to attend this excellent meeting and for the privilege of closing this discussion.