SOUTHERN MEDICAL JOURNAL

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY AT BIRMINGHAM, ALABAMA

Volume XII

AUGUST 1919

Number 8

MEDICINE

INTERNAL DISEASES, PEDIATRICS, NEUROLOGY, DIAGNOSTIC METHODS, ETC.

DIAGNOSIS OF DISEASES OF THE PANCREAS*

By THOMAS R. BROWN, M.D.,
Baltimore, Md.

There is probably no organ of such importance in the human body the organic and functional diseases of which are less frequently and less correctly diagnosed than the pancreas.

In regard to its internal secretion, closely associated with the islands of Langerhans, and its role in the metabolism of the carbohydrates, a fairly clear conception is held, but the study of its external secretions in health and in disease is so difficult and so complex that the aid derived therefrom is comparatively slight in the diagnosis of pancreatic disease, although it is highly probable that many, if not most, of the organic diseases of this organ are associated with variations—quantitative or qualitative—in these secretions, and it seems obvious that an organ with such a large and varied secretory function and complex nervous supply, and one of such fundamental importance in the elaboration of practically all types of food stuffs, must show marked functional disturbances could we but unravel them. It seems, therefore, wise in this paper first to sketch very briefly the salient points in the anatomy and physiology of this organ, then to take up seriatim the various means of diagnosis at our command, and last of

all to review the various diseases of the pancreas in the light of their diagnostic methods, and, with a real knowledge of the organ's physiology, see if by the help of the newer modes of study we can get a step nearer to the correct diagnosis of its various pathological entities.

The names of some of the greatest physiologists and anatomists are linked with our knowledge of the anatomy and physiology of the pancreas. Claude Bernard studied the role of the pancreatic enzymes in the digestion of fats, proteids and starches. Heidenhain demonstrated the gross and microscopic changes in this organ during digestion. Langerhans described the islands bearing his name, and which subsequently were shown to be of such paramount importance in the combustion of the sugars. In recent years our knowledge has been immensely enriched by the work of Pawlow and his pupils and Bayliss and Starling, while with the clinical and surgical sides the names of Friedreich, Fetz, Oser, Moynihan, Mayo-Robson, Von Mikuliez, Boseman and Gussenbauer are closely allied.

ANATOMY

In regard to the anatomy of the pancreas, it is well to remember that this organ is subject to great variations in size; that it is very difficult to palpate through the abdominal wall, and, in fact, even when the abdomen is opened surgically; that its head lies in the concavity of the duodenum, and that head, body or tail lies in close juxtaposition to stomach, liver, gall-bladder or transverse colon as well; that it is

*Read before American Gastro-Euterological Association, Atlantic City, June, 1919.

subject to anomalies such as anular pancreas or accessory glands, which are not uncommon—which may be in the gastric or duodenal wall, or below the pancreas even as far down as the ileum.

The character of the ducts, however, is by far the most important point, anatomically considered, which we must remember relative to the etiology and diagnosis of pancreatic disease; the lower, that of Wirsung, is larger in about four-fifths of the cases; the upper, that of Santorini, usually anastomoses with the former and is larger in only about one-fifth of the cases. In the vast majority of instances the common duct, which in three-eighths of the cases lies in a groove on the surface of the gland, and in five-eighths passes through the head of the pancreas, joins with the duct of Wirsung to form the diverticulum of Vater—a short conical cavity represented in the duodenum by the papilla of Vater—recognized by a small elevation of the duodenal mucous membrane, and it is this—the usual though not the universal formation (for occasionally common duct and duct of Wirsung open separately)—which is the fundamental cause of determining the intimate connection between pancreatic and gall-bladder disease, especially in cases of stone in the common duct or in the diverticulum of Vater.

PHYSIOLOGY

In regard to the physiology of the pancreas it is only necessary to mention the fundamental role played by secretin, in calling forth the secretion of the gland, derived from the duodenal prosecretin by the action of acids, though peptones, salt, lipoids, fats and soaps can also activate the pancreas. We believe with Pawlow, however, that there is a nervous, as well as a hormonal control of pancreatic secretion, and we feel that our quantitative ferment studies of the pancreatic secretions in achylia gastrica strongly support this view—a view which Erhmann also holds from somewhat similar studies, using a different method. As regards the pancreatic ferments called forth by either mechanism, all, of course, admit the presence of diastase, or amyllopsin, lipase or steapsin, and trypsin zymogen or trypsinogen to be subsequently activated by the duodenal

enterokinase, but there is still much discussion as to the possible presence of other ferments or pro-ferments such as rennin, a hemolysin zymogen, nuclease and a lactase in children. We have shown by dog-experiments the primary stimulating and secondary inhibiting effect of bile upon pancreatic secretion, of considerable clinical importance in the case of pancreatic disease associated with jaundice, while Wohlgemuth lays especial stress upon the opposing effect of adrenal and pancreas, and Eppinger, Falta and Rudinger the intimate relationship between thyroid, adrenal and pancreas, of peculiar interest in connection with the study of the internal pancreatic secretion, apparently originating in the islands of Langerhans.

Disturbance of this internal secretion, either spontaneous or as an alimentary glycosuria after the administration of a large sugar meal, may be of considerable help in the diagnosis of diseases of the pancreas, although it is very striking how extensive changes may occur in the islands of Langerhans with no disturbance of the external secretion, and vice versa.

In discussing the means of diagnosing pancreatic diseases, let us in the first place call attention to the fact that an absolute diagnosis is possible only in a comparatively few cases, such as certain examples of pancreatic cyst and certain types of carcinoma of the head of the pancreas and possibly acute pancreatitis—in most cases the diagnosis must be only presumptive; in the second place to note that, however definite the evidences that we are able to demonstrate of functional disturbances, these furnish no proof of organic disease of this organ, although combined with other signs and symptoms these variations may be of inestimable value.

Let us take up in order the functional diagnosis, the etiological factors involved, and the signs and symptoms derived from the usual methods employed in studying disease—following these with a few words as to their application in the diagnosis of the various recognized pathological lesions.

The functional diagnosis may have to do with the study of the external secretion or of the internal secretion—the former, in our experience, of far more significance in the vast majority of cases.

As regards metabolic studies, determinations of the unabsorbed protein, fat and carbohydrate are all of value, though obviously of far less significance if associated with diarrhea with its marked diminution of the time of the transit of the food stuffs through the intestinal tract. An azotorrhea is certainly not so significant as the corresponding disturbances of fat absorption, due to the other accessory mechanisms for the digestion of the proteins, the pepsin and hydrochloric acid and erepsin for example, and the definitely noted fact that even with marked disease of the pancreas there may be very little waste of nitrogen.

The finding of bits of striped muscle or of thymus or other tissue rich in nuclei is, however, of more significance than data obtained from the pure metabolic studies of nitrogen loss, especially if associated with a fatty stool and in the absence of diarrhea, as of all the proteins these, perhaps, are more in need of pancreatic juice for complete digestion, although few agree with Schmidt's dictum that the nuclease of the pancreas is the sole ferment capable of digesting nuclei, most believing that they can be digested by the stomach and intestinal juices, or even possibly by the ferments from bacteria without the aid of the pancreatic secretion. In other words, it is not due to a specific nuclease.

In our experience the various older methods of showing deficient tryptic digestion, such as the glutoid capsule or gelodurat capsule test, are open to the same criticism, while direct methods of demonstrating trypsin quantitatively in the stool by the use of serum agar plates or by the casein method are not of great value again because erepsin or bacterial ferments may produce almost the same reactions, and the attempt at studying the gastric contents after an oil meal with its subsequent effect in producing a regurgitation of duodenal contents is open to considerable technical difficulty. Recently, however, the study of the duodenal contents for all three ferments, obtained by direct aspiration through an Einhorn or similar tube is of unquestionable qualitative though more doubtful quantitative value.

Unquestionably data of great value may be derived from the study of the fat in the

stools, especially in the absence of jaundice. Whether shown as a fatty diarrhea or a butter stool, whether by metabolic studies we find that 50 to 70 % of the fat is not absorbed, or whether by chemical investigation we show that of this unused fat 50 to 60 % is in the form of neutral fat, possibly with an associated increase in lecithin, it is an undoubted fact that such marked disturbances of fat digestion—macroscopic, microscopic or chemical are of extreme significance in the diagnosis of pancreatic disease.

As regards the other important ferment of the pancreas, diastase, we have always felt that it offered a singularly attractive field for study in this connection. In the first place if we eliminate the salivary diastase, a very simple problem technically, the only other sources of this ferment are Brunner's gland and possibly the liver where, however, they are present in almost negligible amounts. In the second place the myriad ferments met with in the small intestine have very little influence on this ferment. And in the third place, diastase is so much more stable than lipase that it lends itself peculiarly well to quantitative determination, in our opinion of fundamental importance in pancreatic diagnosis.

Of course, many methods have been suggested, but it has seemed to us that most of these were not sufficiently rigorous as regards technique to make their figures absolutely reliable.

By a method described by us a few years ago by which we believe that we have reduced error to a minimum, we determined that the readings of fifteen normal cases varied from 600 to 2,400 units—and as we firmly believe in a quantitative as well as a qualitative response on the part of the pancreas to a definite food-stimulus, we feel that these figures furnish a valuable criterion. At the same time we determined the normal amount of the diastase in the urine in 44 cases, and here we found the limits from 15 to 120 units, but in our experience, except for the enormous increase in pancreatic calculus, of which we have seen one case and studied the urine, the estimation of the diastase in the urine is of more value in determining renal function than as an aid in the diagnosis of pancreatic disease. Certainly, in our opin-

ion, the quantitative estimation of the diastase in the stool is the easiest technically, has the most clean-cut end-reaction and is less open to criticism than any other method attempting to estimate quantitatively pancreatic function.

The various tests for the internal secretion of the pancreas, the adrenalin, mydriasis, the permanent or transitory appearance of sugar in the urine and the alimentary glycosuria test may furnish data of interest and value, although, as we have said before, there is a singular lack of co-ordination between glycolytic function and extent of damage to the purely glandular portion of the pancreas. In our experience the Camidge reading is found in far too many other diseases and is too often absent in extensive pancreatic lesions to be of value.

ETIOLOGY

And now a word about etiological factors before discussing general and special symptoms—important because in many cases of pancreatic disease, the history of certain factors in the patient's past history or the finding of certain diseases elsewhere furnish us with data of real value in suggesting possible secondary pancreatic involvement. The etiological factors—of varying degrees of importance—are catarrhal inflammation of the stomach and intestines with its possibility of ascending infection of the pancreatic ducts by various bacteria, notably the *Bacillus coli* and certain cocci, or by the products of decomposition or inflammation—and of ever-greater import (catarrhal) inflammation of gall-bladder or gall ducts, or gall-stones—these two, especially disease of the biliary system being by far the most important etiological factors—easily understood if we remember the anatomy of biliary and pancreatic ducts. Other etiological factors—all of considerably less importance—are trauma, which possibly plays a role in the so-called pancreatic apoplexy and in cysts of the pancreas, arteriosclerosis, of special interest in the development of the various cirrhotic conditions, syphilis—in which gumma of the pancreas may be found though it apparently plays a very slight role in chronic pancreatitis; alcohol a possible factor in pancreatitis, and obviously various inflam-

mations or neoplasms of the contiguous organs which may involve the pancreas by extension or by metastasis.

SYMPTOMS

As regards the symptoms of pancreatic disease, they are, as a rule, very vague, very blurred, as in the main they are those common to all digestive diseases if chronic, such as fullness, pressure, gas, pyrosis, sometimes nausea and vomiting, loss of appetite, etc., while they practically always simulate those of certain other acute abdominal conditions, if acute. Certain symptoms should be especially mentioned—sialorrhea is often considered an important symptom, but in our experience more frequently met with in diseases of the duodenum; pain is somewhat suggestive when present, as it is often uncommonly violent, sudden and colicky, and it has been the first striking symptom in a few of our cases of carcinoma, sometimes associated with local sensitiveness; constipation is the rule though diarrhea is sometimes found; loss of weight and strength is often a striking symptom, especially in comparison with the paucity of other findings, and, of course, is peculiarly striking in the obese in whom pancreatic disease is more common; jaundice is present, is very important, and a persistent, usually in the main, painless jaundice in persons who have passed middle life is very suggestive of carcinoma of the head of the pancreas, or much less frequently of cirrhosis of the pancreas; a palpable tumor that is definitely shown to be pancreatic is very difficult to demonstrate, because of the consistency of the pancreas and the character of the overlying organs, and is rarely determined in abscess or carcinoma, much oftener in cyst—its situation is usually median, just above the umbilicus, occasionally to right or left, and its location may sometimes be determined better by inflation of stomach or colon; a diffuse shotty condition of the body fat, especially that of the abdomen, has seemed to Dr. Finney and to myself as somewhat significant of pancreatic disease as verified by subsequent operation.

These signs and symptoms, in the main not clear cut, are, with the functional tests already mentioned, and possibly with the aid of other laboratory tests, such as the

lessening of indica or of ethereal sulphates or the presence of fat or maltose in the urine. Our only means of making a diagnosis—and thus, obviously even with considerable experience, medical and surgical, correct diagnosis is the exception rather than the rule, with, of course, certain exceptions, notably certain types of pancreatic cancer, cyst, and possibly acute hemorrhagic pancreatitis. The picture of acute pancreatitis with its three stages—the hemorrhagic, gangrenous and suppurative—is not one of infection or inflammation, but one of toxemia or shock, and high intestinal obstruction, and with its profound prostration, thready pulse, lack of fever and absence of leucocytosis, sensitive epigastrium without muscle spasm, and the frequent previous history of gall-bladder or duodenal disease, especially the former, should make us suspect this condition more frequently than we usually do, while in cases with this history, not ending fatally and not operated upon, we should always be on the lookout for the symptoms of abscess or gangrene as late sequelæ. At operation, of course, the finding of evidences of fat necrosis is of extreme significance. As regards pancreatic calculus, a very rare condition, the symptoms are suggestive of biliary colic without jaundice, but if careful stool and urine studies are made a marked lessening of diastase in the former and enormous increase in the latter can be noted, as we have done in one case. Here the x-ray may be helpful.

In cases of chronic pancreatitis or cirrhosis of the pancreas, the history of the usual etiological factors, the vagueness of the symptoms with their intractability to the usual methods of treatment, the increasing weakness of the patient without demonstrable cause, sometimes the deficiency of digestion of the various food-stuffs, notably the fats, as shown by stool studies after a Schmidt diet, should make us suspicious, and in our experience a quantitative stool study often demonstrates—not the absence but a marked diminution of the diastase—as for example, in six cases so studied our figures read from 33 to 120 units in comparison with our normal readings of from 600 to 2,400 units. In cases of chronic pancreatitis as-

sociated with jaundice, the differentiation from carcinomas is often very difficult. In cirrhosis of the pancreas alimentary glycosuria is quite common as might be suspected.

Cancer of the pancreas is usually of the scirrhus type, most often confined to the head of the organ, and if associated with jaundice produces a rather characteristic picture—usually progressive jaundice often tending to a mahogany brown color of the patient, with loss of weight and strength, often fatty stool, often alimentary glycosuria, usually distended gall-bladder, a point of real importance in differentiating it from obstructive jaundice due to gall-stone, often a previous history of gall-bladder disease, while in our experience there is in almost all cases a practically complete disappearance of diastase from the stool—in five cases there being always less than twelve units, below which we have not tested, as we regard this as the limit of error.

In the case of the types of pancreatic carcinoma without jaundice the latent and those with marked loss of weight and strength, with no apparent cause, we can only suspect the diagnosis by the course of the disease and its lack of response to any treatment, and stool studies, especially quantitative estimations of the ferment should prove helpful. In our experience the only other condition showing a complete absence of the pancreatic ferment in the stool is sprue and here the differential diagnosis should not be difficult.

We have seen a few cases of pancreatic carcinoma in which the diastase is not absent, but is present in reduced or even in normal amounts, but the complete absence of diastatic ferment is the more probable finding. Thus, while presence of diastatic ferment does not rule out carcinoma, absence of diastatic ferment is extremely significant, in our opinion, in making this diagnosis.

Tuberculosis and syphilis of the pancreas are comparatively rare and offer no characteristic symptom-complex, as in the case of visceral lues gummata are occasionally found in the pancreas, but whether syphilis plays an important role in the production of diffuse indurative or cirrhotic processes is open to much doubt.

Fat necrosis is of singular interest from the pathological standpoint as an evidence of the effect of aberrant pancreatic secretion upon the fat of the body, notably, of course, that of the abdomen in the neighborhood of the pancreas; clinically its especial significance is, if found at operation, to suggest the presence of pancreatic disease, especially the various forms of pancreatitis.

Cysts of the pancreas have obviously been given special attention diagnostically speaking, because of their greater ease of diagnosis and their obvious surgical therapy; local pain of a colicky nature, a round or oval mass usually in the middle line about the umbilicus, small, sometimes fluctuating, more often tense, with occasionally slight and rarely marked spontaneous changes in size, sometimes if situated in the head of the organ (a rather uncommon finding) associated with jaundice, occasionally diagnosed by puncture and finding the ferments or proferments, are the points of especial diagnostic interest.

As to functional disturbances we have always felt that an organ of such complexity must show marked functional variation due to nervous and other influences, but at the present writing, no definite facts are available. Gross believed that the diarrhea met with in achylia gastrica was due to a functional pancreatic achylia, but our quantitative stool studies disproved this, at least in our series of cases. Nevertheless we feel that this offers a very fertile field for future study, and we are now carrying on certain investigations along these lines.

This, I take it, is practically the present status of our knowledge as regards diagnosis of diseases of the pancreas—not a very satisfactory showing if we are to judge by the percentage of correct diagnoses made of diseases of this organ as subsequently demonstrated by the results of surgery or by the findings at autopsy—but yet so pregnant with possibilities, so crammed full of suggestive fields of intensive study—mainly, of course, along more intensive clinical lines on the one hand, and on the other chemical, seriological or enzymic routes that I feel sure that within the next decade by the improvement of the

methods described in this paper, and by the elaboration of newer, more accurate and more refined means of study, we will make enormous strides in the diagnosis of both functional and organic diseases of this organ.

DIARRHEA*

BY H. GRAY, M.D., (Boston)

and

A. B. BROWER, M.D. (Dayton, O.)
Lieutenants, Medical Corps, U. S. Army,
American Expeditionary Forces,
France.

SYNOPSIS

Material
Etiology
Present Illness
Physical Examination
Diagnosis
Treatment
Course and Prognosis
Summary

MATERIAL

Place: Base Hospital 76, Amer. E. F.,
Vichy, Allier, France.

Period: approximately the month of
November, 1918.

Total Patients: medical ("disease") and
surgical ("injury"), 2,064.

Medical Patients: 1,002, i. e. 49 % of
total.

Diarrheas Studied: 227, i. e. 22 % of
the medical or 11 % of the total cases.
Other diarrhea cases have been left out
of consideration: 23 on whom the record
was incomplete, and an unknown number
who passed under treatment prior to the
keeping of this special record.

Handicaps: The figures presented are
thought of interest on a subject so little
understood, although they admit only gen-
eral conclusions owing to the following
drawbacks:

1. Rapidity of work under pressure of
"evacuation."
2. Inability satisfactorily to exclude
hemorrhoids.
3. Inability to control objectively the
character of the stools, owing to shortage
of wardmen and bedpans. Simulation

*Approved for publication by Surgeon-General.