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THE SYMPTOMATOLOGY AND DIAGNOSIS OF DISEASES OF THE PANCREAS.*

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The consideration of the symptomatology and diagnosis of diseases of the pancreas may appropriately be introduced by referring to the memorable communication on this subject by Friedreich[1] nearly 30 years ago. According to this authority "no single symptom which may occur in diseases of the pancreas is pathognomonic, and the concurrence of several does not always result in a positive diagnosis. Fatty stools, mellituria, epigastric pains with the characteristics of the celiac neuralgia and a palpable tumor lead among the symptoms most useful in diagnosis," and (p. 223) the presence of undigested, striated muscle fibers in the feces "is worthy of every consideration, and may, perhaps, prove of diagnostic value."

For awhile no material additions were made to our knowledge of the clinical pathology of the pancreas, but in 1887 the investigations of Müller,[2] and especially those of v. Mering and Minkowski[3] in 1889, excited a renewal of interest in the matter. Since then physiologists and pathologists, physicians and surgeons in various parts of the world have made numerous contributions to the knowledge of the functions and lesions of the pancreas, and this gland has become recognized as of the greatest importance in maintaining and promoting a healthy state of the body. Within the past five years have appeared the notable treatises of Körte, Oser, and more recently that of Mayo Robson and Moynihan. These are the authors now to be consulted for classified knowledge of the questions under consideration. From them is to be learned in what respects the clinical characteristics of pancreatic diseases are now more sharply defined than in the days of Friedreich and his predecessors.

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It is generally agreed that the symptoms especially suggestive of pancreatic disease are dependent largely upon the resulting disturbances of its functions and upon the situation of the organ. The former include the various modifications in the composition of the urine and feces; the latter comprise the localized resistance, tenderness and pain, and the evidence of obstruction of the gastrointestinal and biliary tracts. Unfortunately for diagnostic purposes the functions of the pancreas are not the exclusive property of this gland, but are possessed to a greater or less extent by other structures and other agencies.

For more than a century it has been known that diabetes may be associated with disease of the pancreas. More than 80 years ago visible fecal fat was found to hold a like relation. Forty years later the presence of undigested muscle fibers in the feces first attracted attention. These observations have since been repeated with sufficient frequency to lead the physician to suspect, often to assert the presence of, disease of the pancreas when one or more of these conditions have been determined. The comparison, however, of the results of anatomic investigation with clinical observation makes it evident that diseases of the pancreas much more frequently occur without the recognition of glycosuria and fat and muscle in the feces than when these abnormalities are apparent.

The physician, therefore, wishes to know if one or more of these conditions are present in some diseases of the pancreas, why are they not present in all? If found in a certain instance of a single variety, why are they not present in all or in most of the cases of this particular affection. Morbid changes of the pancreas are found frequently after death without symptoms having been observed during life to indicate their presence. On the other hand, the diagnosis of probable pancreatic disease, perhaps of the gravest sort, has been made from the recognition of one or more of the symptoms or signs which, at times, have been found associated with alterations of the pancreas, and the patient has recovered or the gland when exposed has presented no abnormal appearance.

From the data collected by Oser it is evident that the symptoms attributable to disturbed pancreatic function are almost invariably connected with chronic lesions productive of extensive destruction of pancreatic tissue or with interference to the passage of its secretion into

the intestine. The pancreatic lesions usually associated with diabetes are those in which the common element of interstitial inflammation exists with a corresponding destruction of the parenchyma of the gland. This may occur in the form of the genuine, granular atrophy of Hausemann, in calculous pancreatitis, or in the sequence of chronic suppuration, cysts, and tumors.

Visible fecal fat and azotorrhea on the contrary are oftener associated with chronic conditions interfering with the flow of pancreatic juice into the intestine as obstruction of the ducts from calculi, stricture or tumors, than with those causing destruction of the secreting cells of the gland. Rarest of all is the presence of alterations which are associated with diabetes, and fat and numerous muscle fibers in the feces. The case reported by Fles[4] is almost unique in these respects. His diabetic patient ate much bacon and fat meat, and evacuated so much unabsorbed fat that it could be scooped by the ounce from the feces. The latter contained also large numbers of undigested, striated muscle fibers. The autopsy showed that the pancreas was represented only by fragments of the fibrous framework and scarcely recognizable traces of the gland substance. The duct could not be found. Nevertheless, it is evident from human pathology that extensive destruction of the pancreas may take place without observable modification of function. Franke[5] extirpated a cancerous pancreas, and although the patient lived five months after the operation, there was glycosuria merely for a few days, and the stools appeared normal. The patient of Trafoyer[6] was well 17 years after a pancreatic slough was discharged from the bowel.

The inference from such observations is that in extensive destruction of the pancreas without obvious disturbance of function enough of the gland is left intact, or an accessory pancreas or other organs or agencies are present to assume the pancreatic functions. Even when the pancreas presents an apparent integrity and fatal diabetes exist the researches of Ssoboleu[7] and Opie[8] make it evident that destruction of the islands of Langerhans may have taken place. Their investigations, and those of other observers directed to this possibility, add force to the suggestion that in the destruction of these islands may lie the important factor in explanation of diabetes in certain of the cases in which the gross appearances of the pancreas are normal. Hence with the recognition of various causes of glycosuria and diabetes, these

affections, in the light of our present knowledge, are attributable to disease of the pancreas only in those instances in which there is extensive degeneration or destruction either limited to these islands or affecting also the parenchyma of the gland.

If the diabetes is associated with long-continued bronzing of the skin and enlargement of the liver, in the absence of jaundice and the characteristic distribution of the pigment in Addison's disease, the suggestion is direct that chronic, fibrous pancreatitis is present. Since the original publication by Hanot and Chauffard[9] on this subject, the bronzed diabetes of French writers, Anschutz[10] has tabulated 24 cases of this combination. The view of us that the affection of the pancreas is the remote result of the deposition of the pigment in the hemochomatosis of v. Recklinghausen has repeatedly been favored by recent writers.[11]

Steatorrhea is next in importance to glycosuria and diabetes as evidence of disturbance of pancreatic functional, though the views concerning its significance are somewhat divergent.

The presence of oil readily attracted attention, but it soon became apparent that the fat might assume a solid as well as a liquid form. It was considered that the presence of visible fat represented an increase of this constituent, the absorption of which was interfered with in consequence of the disease of the pancreas. Müller,[12] however, called attention to the frequent concurrence of disturbance of biliary secretion in the cases reported. He emphasized the importance of a lack of bile in the intestine as interfering with the absorption of fat, and considered it doubtful if a lack of pancreatic juice could cause steatorrhea. He endeavored to show that a deficiency of split fat the proportion of total fecal fat being normal, was the chief feature when there was lack of the pancreatic juice, and that interference with the flow of bile was the main cause of pathologic steatorrhea. Müller reported but three cases of pancreatic disease in support of his views. Jaundice was present in one only. In another the actual condition of the pancreas and its duct was not to be determined, as the patient was seen after having been operated upon for "cyst" of the pancreas.

In order to obtain further clinical evidence on this point, a table has been prepared to show the relation between visible fecal fat, jaundice and pancreatic disease. Only those cases are included which give anatomic evi-

dence at an autopsy, a laparotomy or by the passage of a pancreatic calculus that there was actual disease of the gland.

Twenty-nine cases of steatorrhea are the basis of this table. Jaundice was present in 12 and absent in 17. Among those with jaundice, tumors, chiefly cancer, were present in 8. The lesions existing in the remaining 4 cases were a cyst in 1, and induration rarefaction and fatty transformation in 3, in which there was also either obstruction or obliteration of the duct. Of the 17 cases of steatorrhea without jaundice, in 7 the lesions were tumors, chiefly cancer; in 6 calculi were present; 2 were fatty and 2 were single examples of cyst and atrophy.

It was considered interesting to note also the relation of diabetes or glycosuria to the steatorrhea. Diabetes was present in 11 cases and absent in 18. The lesions present in the former series were tumors, chiefly cancer in 4, calculi in 4, a cyst in 2, and fatty degeneration in 1 instance. Among the 18 cases of steatorrhea without diabetes were 11 of tumors, chiefly cancer; 2 of calculi, 2 of fatty transformation, and 1 each of atrophy and induration. Visible fecal fat, jaundice and diabetes were present in 3 cases only, 2 of tumor and 1 of cyst. This table, therefore, does not support the view that jaundice is an important factor in the origin of the fatty stools connected with disease of the pancreas. It suggests that in about three-fifths of the cases of steatorrhea attributable to pancreatic disease there is neither diabetes nor jaundice, that in two-fifths there is either diabetes or jaundice, in about equal proportion, and in but few instances is there a combination of diabetes and jaundice.

Müller's researches were of value in another direction by calling attention to the clinical importance of a chemical analysis of fecal fat in cases of suspected disease of the pancreas. A table has been prepared showing the analyses given by him and others of fat extracted from the feces in health, catarrhal jaundice and in diseases of the pancreas with and without jaundice. The last mentioned include only those actually demonstrated either by the knife or by the passage of a typical calculus.

It is evident from this table that the feces of the healthy individual contain about 20% of unabsorbed fat and that in catarrhal jaundice this ratio may be doubled. In affections of the pancreas the percentage of unab-

RELATION OF FATTY STOOLS IN PANCREATIC DISEASE TO DIABETES OR GLYCOSURIA AND TO JAUNDICE.

Lesion.	Stools.	Diabetes or glycosuria.	Jaundice.	Authority.
Fibroadenoma.	Fatty.	Present.	Present.	Biondi: Oser, op. cit.
Cancer.	Fatty.	Absent.	Present.	Bowditch: Boston M. and S. J., 1872, lxxxvii, 65.
Cancer.	Like butter.	Absent.	Absent.	Bright: Med. Chir. Trans., 1833, xviii, 1.
Cancer.	Like butter.	Present.	Present.	Bright: Med. Chir. Trans., 1833, xviii, 1.
"Cyst."	Free fat.	Present.	Temporary.	Bull: N. Y. Med. Jour., 1887, 376.
Calculi.	Fatty.	Absent.	Absent.	Capparelli: Oser, op. cit.
Calculi.	Fatty.	Absent.	Absent.	Chopart: Oser, op. cit.
Calculus passed.	Fatty diarrhea.	Present.	Absent.	Cipriani: Therap. Monatsh., 1898, xii, 617.
Cancer.	Like butter.	Absent.	Absent.	Clark: Lancet, 1851, ii, 152.
Atrophy, cong. syphilis.	Like asbestos.	Absent.	Absent.	Demme: Oser, op. cit.
Calculus.	Oily at times like butter.	Present.	Absent.	Elliotson: Med. Chir. Trans., 1833, xviii, 77.
"Cyst," atrophy, fibrous tissue in head of pancreas.	Masses of fat crystals, once consistency of sweet oil.	Present.	Absent.	Goodman: Tr. Path. Soc., Phila., 1878, viii, 41.
Indurated pancreas, obliterated duct.	Fatty.	Absent.	Present.	Kuntzmann: Friedreich, op. cit.
Cancer.	Fatty.	Absent.	Absent.	Labadie-Lagrave: Oser, op cit.
Calculus, atrophy. Growth of fibrous and fat tissue.	Fatty before onset of diabetes.	Present.	Absent.	Lancereaux: Bull. Acad. de Méd., 1888, xix, 588.
Cancer.	Fatty.	Absent.	Absent.	Luithlen: Oser, op. cit.
Cancer.	Gray with white portions. Fat with microscope.	Absent.	Absent bronzed.	Mager: Wiener Med. Pr., 1899, xl, 15.
Cancer.	Fatty.	Absent.	Present.	Maragliano: Oser, op. cit.
Cancer.	Very fatty, tenacious, slimy.	Present.	Absent.	Marston: Am. Jour. Med. Sci., 1854, xxviii. 212.
Scirrhus of head, obliteration of duct.	Fatty diarrhea.	Present.	Absent.	Martsen: Oser, op. cit.
Cancer.	Fatty.	Absent.	Present.	Molander and Blix: Oser, op. cit.
Enlarged pancreas, marked fatty degeneration.	Fatty.	Absent.	Absent.	Notta: Union Méd., 1881, xxxi, 289.
Calculus, fibrous pancreas. Duct did not communicate with common duct or duodenum.	Gray, greasy, at times solid fat on cooling.	Present.	Absent.	Phillips: Lancet, 1900, ii, 104.
Cancer.	Fatty.	Absent.	Present.	Pott; Oser, op. cit.
Fatty degeneration.	Oily.	Present.	Absent.	Silver: Tr. Path. Soc., London, 1873, xxiv, 121.
Cancer.	Fatty.	Absent.	Present.	Roques: Bull. Soc. Anat., 1857, ii, 245.
Cancer, closed duct.	Silver gray, 25% fat.	Absent.	Present.	Ziehl: Deutsche med. Wochenschr., 1833, ix, 538.
Rarefied pancreas, obstructed pancreatic duct.	Silvery white, consistency of salve.	Absent.	Present.	Müller: Loc. cit.
Pancreas appeared like fat. Calculus in duct.	Free oil or fat.	Absent.	Present.	Walker: Med. Chir. Trans., 1889, lxxii, 257.

sorbed fat is generally not much increased, except when jaundice is an accompaniment, thus sustaining the position of Müller.

In health this extracted fat contains from 20% to 30% of neutral fat, and from 70% to 80% of split fats, namely, fat acids and soaps. In 10 cases of disease of the pancreas the neutral fat ranged from 17.50% to 91.6%. In but 2 of these was the percentage of neutral fat below normal, while in 9 of them it was largely or greatly increased. That of split fat, on the contrary, was decidedly diminished in 9 out of 11 patients. In the remaining 2 it was as high as in health. The table thus bears out the view of Müller, though not without exceptions, that in pancreatic disease there is less splitting of the fat and consequently an increase of the neutral fat, thus giving a satisfactory explanation of the oily stools of the older observers.

On the other hand, there is a sufficient lack of anatomic control to permit his conclusions to be accepted without question. Enough pancreatic juice may have been supplied to effect the results of chemical analysis in many of the cases of obstruction of the duct of Wirsung by a flow through the duct of Santorini. If both ducts were closed and the pancreas extensively diseased an accessory pancreas may have existed. Müller himself recognized the influence of intestinal bacteria and gastric contents[13] in splitting fat, although he regarded their importance as slight. It is obvious also, as stated by him, that the feces may contain an excess of fat not only in cases of jaundice, but also when there is a superabundance of fat in the food and when there is disease of the absorbents within or without the intestinal wall.

Steatorrhea, therefore, is to be regarded as evidence of disease of the pancreas only when other causes of its presence can be excluded, the most important of which is interference with the flow of bile into the intestine. Its recognition depends not merely on the presence of fat resembling oil, butter, lard or tallow, but in doubtful cases requires the skill and facilities of the chemist trained in physiologic methods.

The probability that steatorrhea is due to extensive disease of the pancreas and may exist for years without disturbance to the general health is suggested in the communication of Walker.[14] His patient, a physician, free from jaundice, passed for 20 years large colorless stools of a peculiar putrid odor, occasionally accompanied by free oil, or fat, liquid or solid. During this period he

was in perfect health and in the active pursuit of his profession. He died at the age of 90. There was no marked absence of fat. The pancreas was large, apparently composed of nearly purely fat. The duct was rendered almost absolutely impermeable within an inch of the duodenum by a very irregular calculus.

Despite the attention which has been given since the time of Friedreich to azotorrhea, as manifested by the presence of numerous undigested muscle fibers in the feces, but little clinical evidence has been offered that this sign is likely to prove of especial value in the diagnosis of diseases of the pancreas.

In the preparation of the accompanying table but 8 cases have been found which fulfil the demanded requirements. In 6 sugar was present in the urine; in 5 there was visible fecal fat, and jaundice was present in 2 instances. In Lichtheim's case the diabetic patient's diet was composed largely of meat, but diarrhea existed, a combination sufficiently explanatory of azotorrhea without the assumption of the presence of disease of the pancreas. The relative frequence of steatorrhea as compared with azotorrhea indicates that proteids are better digested than fats if the supply of pancreatic juice is notably diminished. Any significant increase of undigested muscle fibers in the stools would be expected only when there was extreme diminution of pancreatic juice in the bowel, gastric digestion was relatively normal, the diet contained no excess of meat, and there was no diarrhea.

Bulky stools are mentioned by Oser [15] as suggestive of disease of the pancreas. These are notably excessive in quantity as compared with that of the food taken, and are composed of unabsorbed muscle fibers, fat and carbohydrates. He has met this condition in a number of cases in which the suspicion of pancreatic disease was confirmed.

The various possible disturbances of function in pancreatic disease have usually been sought by inspection and microscopic examination, and by the use of the simplest chemical and physical methods. It must be recognized, however, that any considerable disturbance in the digestion and assimilation of fat, muscle, and carbohydrates from affections of the pancreas has almost invariably been connected with extensive and protracted lesions. It is obvious, therefore, that feeding with an increased quantity of one or the other of these constituents of diet in suspected cases of pancreatic disease

RELATION BETWEEN DIABETES OR GLYCOSURIA, STEATORRHEA, AZOTORRHEA AND JAUNDICE IN DISEASES OF THE PANCREAS.

Condition.	Diabetes or glycosuria.	Steatorrhea.	Azotorrhea.	Jaundice.	Authority.
Cancer secondary to cancer of stomach.	Maltosuria.	Absent.	Present.	Absent.	v. Ackeren: Berliner klin. Wochens., 1889, xxvi, 493.
Only traces of parenchyma. Duct not recognized.	Present.	Present.	Present.	Absent.	Fies: v. Friedreich, v. Ziemssen's Handb.
Abscess.	Present three weeks before death.	Present. Resembling cod-liver oil.	Present.	Absent.	Hartley: Tr. Path Soc. Lor., 1862, xiii, 118.
Calculus.	Present.	Fat crystals.	Present. Copious meat diet, diarrhea.	Absent.	Lichtheim: Berliner klin. Wochens., 1894, xxi, 185.
Cancer.	Absent.	Present.	Present.	Present.	Oser: Op. cit., 87.
"Cyst."	Traces of sugar.	Absent.	Present.	Absent.	Riegner: Berliner klin. Wochens., 1890, xxvii, 959.
Indurated, atrophied pancreas. Almost complete obliteration of lower part of common bile duct.	Present, but almost wholly disappeared after occurrence of jaundice, despite carbohydrates in diet.	Present.	Present.	Present.	Teleky: Wiener klin. Wochens., 1902, xv, 741.
Cyst.	Absent.	Absent.	Present.	Absent.	Müller: Loc. cit.

might be followed by appreciable changes in the secretions and excretions earlier than otherwise would have been the case. It is clear, also, that disturbances in the digestion of fats, starches and proteids, relieved by the addition of pancreas or its preparations to the diet, provided disease of the digestive glands could be eliminated, might furnish additional evidence in favor of the pancreatic source of the disturbance.

It has been repeatedly noted that the fecal fat has been observed when the patient was eating abundantly of fat. It is desirable, therefore, in possible cases of pancreatic disease to increase the quantity of fat in the diet nearly to the limit which is to be reached without producing steatorrhea in healthy persons or in patients not suffering from disease interfering with the absorption of fat. It is particularly desirable to determine the toleration of fat in those cases of diabetes in which the pancreas presents no abnormal conditions. These limits are not sufficiently known at present, especially as the thorough appreciation of this method of investigation demands the use of especial training and a properly equipped laboratory.

For the immediate future, however, observations are more important which can be made simply with the eye, at the most aided by the microscope. Hartsen[16] gave eight to ten teaspoonfuls of cod-liver oil to two diabetic patients, in each of whom extreme atrophy of the pancreas was found, but there was no unusual quantity of fat observed in the feces. Müller[17] despite an almost exclusive milk diet in his case of cyst of the pancreas, found only a trifling increase in the fat extracted from the feces, and but little variation in the split and neutral fats from that observed when a mixed diet was taken. Herter gave to Northrup's patient with probable cancer of the pancreas an exclusive milk diet. Although the feces probably were fatty before this test was applied, no chemical analysis of their condition was reported. While the milk diet was being taken (see table) there was a large excess of fat in the feces, although there was no considerable modification in the percentage of neutral fats. The especial change seems to have been an increase in the percentage of fat acids and a diminution in that of the soaps. The reported cases are few in which pancreatic disease has been found after death, and properly controlled dietetic tests with fat have been made during life. Important additions to our knowledge are likely to be made by further observations in this direction.

In like manner should be tested the capacity of the patient for digesting muscle in the intestine as compared with that of the normal individual or with one suffering from affections in which there is no reason for supposing that the pancreas or intestine is diseased. For this purpose it is important first to determine the condition of the gastric functions and then to introduce into the intestine the muscle fiber, as free as possible from the influence of gastric digestion. It may be that the glutoid capsules of Sahli, to be mentioned later, will suffice for the latter purpose, or that other more satisfactory means may be devised.

Müller found well preserved muscle fibers in his case of cyst of the pancreas when the patient was not eating more meat than a healthy adult could easily digest. A similar appearance was observed during several days while the patient was taking but little meat. The evidence furnished by this patient has only a relative value, since the nature of the lesion was determined by a surgical operation, and the condition of the pancreatic duct was known.

The possibility of testing the efficiency of the pancreas by attempting to produce an alimentary glycosuria also demands consideration. The researches of Wille[18] in this direction are especially significant. This observer gave at breakfast to each of 800 patients $\frac{1}{100}$ gr. of glucose in a half liter of tea or coffee. This quantity was selected with the view that the limit of physiologic glycosuria lay between doses of 150 and 250 gr. The urine of the patients was collected every two hours after the glucose was taken. In 15 of 77 patients who died glycosuria occurred, and the postmortem examination showed alterations of the pancreas. In certain instances the changes were slight, and ascertained only by microscopic examination. The test was positive in three out of four cases of cancer of the pancreas. Unfortunately, the ease with which a similar result is obtained with this test in a great variety of conditions in which there is no reason to suspect disease of the pancreas makes it of little value in diagnosis under present conditions.[19] The comparison of the quantities of glucose necessary and the percentages of sugar obtained may lead to further information.

The functions of the pancreas may be tested also by the use of agents which demand largely the action of the pancreatic juice to promote their absorption and elimination. Salol was first suggested for this purpose by Ewald and Sievers.[20] It had been stated by Nencki that

COMPARATIVE RESULTS OF ANALYSES OF FECAL FAT.

Condition.	Percentages of					Authority.
	Extracted fat.	Fat acids.	Soaps.	Split fat.	Neutral fat.	
Health, milk diet	21.0	51.3	20 9	72.2	27.88	Muller: Zeitschr. f. klin. Med., 1887, xii, 45.
Health, milk diet	.....	39.8	40.5	80.3	20.5	
Health, bread and milk	.....	25.3	49.7	75.	24.8	
Catarrhal jaundice	43.9	21.6	27.5	48.11	50.83	
Catarrhal jaundice	9.56	.....	.....	88.59	11.41	Katz: Wiener med. Wochen., 1899, xlix, 153.
Catarrhal jaundice	21.31	34.54	43.26	77.8	22.10	
Rarefied pancreas, obstructed pancreatic duct, jaundice	43.9	21.6	27.5	49.1	50.83	Muller: Loc. cit.
Necrosis of pancreas	33.3	.....	.....	29.5	76 1	v. Noorden: Berl. klin. Wochen., 1890, xxvii, 1022.
Calculus in pancreas, extensive atrophy, diabetes	29.04	17.08	5.33	22.41	77.57	Muller: Loc. cit.
Calculi, pancreatic, found in stools	.....	19.2	38.2	57.4	42.6	Kinnicutt and Herter: Am. J. M. Sci., 1902, cxxiv, 948.
"Cyst" of pancreas	28.7	30.9	16.8	47.7	52.	Muller: Loc. cit.
Cancer of pancreas	33.3	.....	.....	8.4	91.6	v. Noorden: Loc. cit.
Fibrous and fatty pancreas, glycosuria, jaundice	38.66	.....	.....	51.42	48.58	Teleky: Wiener klin. Wochen., 1902, xv, 741.
Cancer of pancreas, closure of common and pancreatic ducts	.....	73.3	7.1	80.4	19.6	Deucher: Cor. bl. f. Schw. Aerzte, 1898, xxviii, 321.
Cancer of pancreas	.....	52.1	9.5	61.6	38.4	
Large, hard pancreas, small hemorrhages, necroses, jaundice	34.22	.....	.....	13.93	86.07	
Thick, flat mass in pancreas, eventual jaundice	46 76	64.2	17.58	82 50	17.50	Northrup and Herter: Am. J. M. Sci., 1899, xvii, 131.

salol was split by pancreatic juice into salicylic acid and phenol, and that the former could readily be detected in the urine. It was recommended that the salol be given in capsule or in pills coated with keratin. A delay in the cleavage would suggest retention in the stomach or deficiency of pancreatic juice.

Sahli [21] has suggested the use of "glutoid" capsules containing iodoform to determine the presence of pancreatic secretion in the intestine. It is claimed that these capsules are sufficiently hardened in formaldehyd to withstand powerful gastric digestion for at least 12 hours, although rapidly digested in pancreatic juice. If there is normal motility of the stomach, the iodin reaction will appear in the saliva in from four to six hours after the capsule containing the iodoform is swallowed, provided there is a satisfactory pancreatic digestion and there is no interference with intestinal absorption. Sahli [22] reports a number of cases in which the reaction was delayed for 24 hours or more, and obstruction of the pancreatic duct from cancer of the gland was found.

The late reaction is evidence of defective pancreatic digestion only when there are normal gastric motility and intestinal absorption. If the latter is defective and there is diarrhea the undigested capsule may be found in the feces. Fromme [23] applied this test in a case proving to be one of inoperable sarcoma of the omentum. Visible fecal fat was present, but neither jaundice nor glycosuria. The reaction did not appear till the end of 27 hours. In a patient who was found to have a "cyst" of the pancreas the glutoid capsule test gave only a slightly delayed reaction, from seven and a half to nine hours. Although these cases were reported to illustrate the inaccuracy of the test, the evidence given is insufficient to exclude closure of the pancreatic duct in the first, and it is possible that the "cyst" of the pancreas was an omental bursitis, or, if of the pancreas, that there was no considerable interference with the passage of the pancreatic juice into the intestine.

The suggestion is obvious that if symptoms attributable to disturbed functions of the pancreas be present and other conditions, especially jaundice, be absent, the use of pancreatic preparations or of minced pancreas might favorably affect these disturbances and thus indirectly confirm the diagnosis of pancreatic disease. Fles [24] gave daily a calf's pancreas to his patient with atrophied pancreas and unrecognizable duct. The fat and muscle fibers disappeared from the feces, to return again when

the pancreas was omitted from the diet. Repeated instances of the disappearance of visible fat from the feces and of improvement in diabetics have followed the use of pancreas and its preparations, but they are not included in this consideration as lacking the control of anatomic investigation.

The examination of the urine for pentose has attracted attention since the statement by Hammarsten [25] that the pancreas contained a nucleoproteid, the cleavage of which produced pentose. Salkowski, who had discovered the condition pentosuria, recognized the identity of the pentosazon in the pancreas and that in the urine, and suggested that pentosuria might be regarded as an affection of the pancreas. Blumenthal [26] showed that the condition might be persistent during a period of five months. Pentose was usually sought with phenylhydrazin, acetic acid and heat. Mayo Robson [27] states that Cammidge obtained yellow crystals in sheaves and rosets from the urine of a patient with chronic pancreatins by boiling it for a short time with an oxidizing agent and adding phenylhydrazin. Urine from a case of catarrhal jaundice gave a negative result when similarly treated. It was suggested by him that this test might prove useful in diagnosis. If these crystals were an osazon it is possible to find them even in normal urine, and further evidence is needed before any diagnostic importance in connection with pancreatic disease is to be attached to their presence. Blumenthal,[28] moreover, was able to isolate nucleoproteids from various organs and find pentose in them, which obviously excludes the pancreas as the necessary place of their origin.

It is known that the putrefaction of the proteid contents of the intestine is caused by bacteria and that their action is enhanced by the presence of pancreatic juice. In consequence, the aromatic compounds—indol, skatol and phenol—are formed, and the quantities of indican and of ethereal sulfates in the urine give evidence of the extent of the proteid putrefaction and indirectly of the condition of the pancreas. Gerhardi [29] observed an absence of indican in the urine in a case of obstruction of the small intestine, in which condition, according to Jaffé, it should have been increased. After the patient's death acute hemorrhagic pancreatitis and an obstructed pancreatic duct were found. Gerhardi suggested that the absence of indican when the small intestine was obstructed might be regarded as evidence of disease of the pancreas. Two confirmatory and one contradictory

observations have been made. Oser, however, maintains that variations in the excretions of indican may have no direct relation to disease of the pancreas, hence be of no diagnostic value.

The quantity of ethereal sulfates eliminated seem to have a more constant relation to the extent of intestinal putrefaction and to the secretion of pancreatic juice. The clinical observations on these points, especially those sufficiently controlled, are few. Herter found increased indican and an increased ratio of ethereal to preformed sulfates in Northrup's case, in which disease of the pancreas, though not the condition of the duct, was ascertained. Edsall [30] concludes in his communication on this subject "if, with suspicion of pancreatic disease, factors which usually cause an increase of the ethereal sulfates be present and yet the values be found low, the test would at present appear to be of distinct practical importance in diagnosis. Constipation, gastric hypoacidity or anacidity, icterus, grave anemia, and cachexia are very likely to cause an increase in the relative or absolute values of the ethereal sulfates."

Finally, Opie [31] has suggested the possibility of discovering in the urine the fat-splitting ferment set free in acute pancreatitis. He endeavored to determine its presence in one case by following the method proposed by Cassell and Loevenhardt which is based upon the decomposition of ethyl butyrate by the ferment and the production of butyric acid. The urine neutralized with potassium hydroxid was divided into two portions, one of which was boiled for the purpose of destroying the ferment. Ethyl butyrate was added to each specimen. That unboiled after 24 hours gave an acid reaction, while the boiled specimen showed little if any change.

The symptoms which have proved most useful in diagnosis are those which call attention directly to the region of the pancreas. They are the epigastric pain, tenderness, tension and tumor, with or without obstructive jaundice, and evidence of mechanical interference with the motility of the stomach and duodenum.

Pain, when present, usually is manifested early in the course of the disease and may be the initial symptom. If often suggests gastric cramp or intestinal or biliary colic. It is occasional, paroxysmal or persistent, dull or sharp, squeezing, tearing or piercing, mild or severe, even agonizing and not infrequently is associated with signs of collapse. It may be clearly defined near the median line, midway between the ensiform cartilage

and the navel or may shoot laterally especially toward the left side. It occasionally is continued upward into the thorax or downward into the lower abdomen.

Tenderness is a frequent accompaniment, especially of persistent pain. It often is described as sensitiveness and although usually limited to the epigastrium, may be found in the region of the spleen or in the left groin. Ultimately tender spots may appear in remoter parts of the abdomen, especially when disseminated foci of fat necrosis accompany the pancreatic affection. Epigastric tension often is observed, and may be apparent at the outset or develop later in the course of the disease. When an early symptom it is followed soon by a circumscribed, tympanitic, epigastric swelling, evidently due to gaseous distention of the stomach.

The resistance found late in the course of pancreatic disease is due to the formation of a tumor. When the latter is the result of disease of the pancreas its characteristics depend largely upon the nature of the affection. Small, circumscribed, dense tumors result from chronic inflammation or neoplasms, usually of the head of the gland, while large, tense tumors of pancreatic origin in the left half of the epigastrium or symmetrically involving more or less of the upper abdomen are indicative generally of cysts of the pancreas or of collections of fluid in the omental bursa, more common than the former and generally confounded with them.

Jaundice, commonly slight and of short duration, is occasionally encountered in acute affections of the pancreas. Then it is oftener seen in the course of a few days after the onset of the attack than as an earlier symptom. Prolonged jaundice is a frequent accompaniment of chronic affections of the head of the pancreas, especially of fibrous inflammation and neoplasms. The association of the jaundice with distention of the gallbladder is sufficiently frequent as noted by Courvoisier and others to make this combination suggestive rather of disease of the pancreas than of affections of the biliary tract.

Motor disturbances of the stomach and intestine are among the usual symptoms associated with pancreatic disease. Vomiting, sometimes frequent or incessant and often distressing, is customary among the early symptoms of acute pancreatitis, and constipation, at times obstinate, is the rule. So constant are these motor disturbances that the frequent diagnosis in cases of acute pancreatitis is acute intestinal obstruction.

The prolonged motor insufficiency of the stomach mechanically induced by chronic affections of the pancreas, especially from enlargement of the head of the gland, not infrequently give rise to dilation of the stomach. In consequence frequent or persistent vomiting may take place late in the course of pancreatic disease.

Although the diagnosis of diseases of the pancreas in the light of our present knowledge practically depends more on the symptoms calling attention to the locality of the organ than upon the evidence of disturbances of its function it is reached eventually by the exclusion of other sources than the pancreas of the local symptoms.

The differential diagnosis lies first between acute and chronic affections and second between the several varieties of chronic pancreatic disease. The former include pancreatic hemorrhage and the hemorrhagic gangrenous and suppurative varieties of acute pancreatitis, all of which are characterized by similar symptoms and some of which presumably represent stages of the same affection. The latter include chronic pancreatitis with or without calculi, cysts and tumors.

Of acute pancreatitis it may be said now as in 1889[32]: "The symptoms are essentially those of a peritonitis beginning in the epigastrium and occurring suddenly, during ordinary health, without obvious cause. The diagnosis, therefore, is based on pain, tenderness and tympany limited to the region of the pancreas, and on the gradual development of a deepseated peritonitis in the same place."

DIFFERENTIAL DIAGNOSIS.

The differential diagnosis lies practically between an irritant poison, perforation of the digestive or biliary tracts, and acute intestinal obstruction. An irritant poison is excluded by the history of the case and by the examination of the vomit. Perforating ulcer of the stomach or duodenum is to be excluded by the absence of pain after eating, hemorrhages from the digestive canal and cachexia. Acute perforation of the transverse colon is rare, and the resulting peritonitis progresses more rapidly and is likely to be general. Perforation from gallstones is usually preceded by attacks of biliary colic and jaundice, while the seat of the pain is rather in

the region of the gallbladder than in that of the pancreas. Acute intestinal obstruction is most likely to give rise to doubt. It is to be eliminated by determining the patency and capacity of the large intestine, by the rarity in the epigastrium of an obstructed small intestine, by the immediate presence of localized tenderness and by the usual absence of conspicuous, general tympany or limited distention of intestinal coils.

In the cases of acute pancreatitis thus far reported no new evidence, unless that of Opie be confirmed, has been furnished which gives to the diagnosis more than a variable degree of probability. Certainty has been reached only by a laparotomy or a postmortem examination. The former has made clear the condition of the pancreas by the usual disclosure of multiple areas of disseminated fat necrosis, a condition occurring on an extensive scale only in the sequence of acute pancreatitis, or by the demonstration of the enlarged, hemorrhagic or necrotic pancreas as the focus of the surrounding peritonitic manifestations.

Fortunately the exploratory laparotomy in an increasing number of cases has proved the most satisfactory method of treatment, and, like most abdominal operations for the relief of acute symptoms, is the more helpful the earlier in the course of the disease it is performed.

The diagnosis of chronic pancreatic affections is based usually on the occurrence of localized pain and upon the presence of a tumor. The pain may exist without the tumor, but the latter is rarely present without the former at some time during its formation. The pain of chronic pancreatic affections is often a deep-seated discomfort; when severe it is likely to be paroxysmal, and then is suggestive of biliary colic, but is referred rather to the region of the pancreas than to that of the biliary tract. The tumor is of slow or rapid growth, large or small, perhaps distinctly palpable only in narcosis, fixed or slightly movable, with or without symptoms of pressure upon the surrounding parts. Its position behind the stomach and above or behind the colon is made apparent by inflation and percussion of these portions of the alimentary canal. Evidences of disturbance of pancreatic function are to be sought along the lines previously mentioned, but experience has shown that definite and convenient additions to our knowledge must be made before functional disturbances of the pancreas can be ascertained sufficiently early and with sufficient certainty to

render assured the pancreatic source of the disease. The discovery of sugar in the urine should lead to the examination of the feces for fat. The presence of the latter should suggest the search for undigested muscle fibers and for glycosuria, and alimentary and therapeutic tests should be applied to all suspected cases.

The differential diagnosis lies between chronic pancreatitis, with or without pancreatic calculi, cysts, and tumors.

The association of jaundice with tumor has led to the diagnosis of chronic pancreatitis and to its effective treatment by Mayo Robson and others. The relatively rapid formation of the tumor in the sequence of symptoms suggestive of gallstones may serve in certain instances to differentiate this condition from malignant neoplasms.

The discovery of characteristic calculi in the feces has made clear in a few instances the source of discomforting or severe symptoms without tumor in the region of the pancreas, and exploratory laparotomies have confirmed or suggested the diagnosis of neoplasms of this organ.

The various possibilities of a more accurate study of the symptomatology and diagnosis of diseases of the pancreas suggest an early advance in our knowledge of the subject. With the increase of clinical laboratories in our general hospitals and with the more frequent addition of biologic chemists to the force of pathologists the errors of the past are likely to be avoided and new lines of research are sure to be planned.

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