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Acute pancreatitis (a general consideration)

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ACUTE PANCREATITIS

(A general consideration)

SENIOR THESIS

Presented by-

John N. Round
ACUTE PANCREATITIS
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ACUTE PANCREATITIS

INTRODUCTION

Acute pancreatitis has been called 'that terrible abdominal catastrophe.' (1).

It is a disease with a sudden incipience and rapid course, anatomically characterized by more or less extensive necrosis of the glandular tissue, sometimes very severe hemorrhages into the pancreatic and neighboring tissues, disseminated fatty necrosis of the nearer and farther surrounding and formation of a serosanguineous exudate in the abdominal cavity. The necrosis is due to autodigestion of the glandular tissue, but the "primum mobile" of this autodigestion has not yet been found. (2).

Some hesitation has been felt in the use of the title 'acute pancreatitis' for the term denotes inflammation and it may be further inferred that such inflammation must be of microbial origin. The immediate cause of the pancreatic lesions is in all probability a cytolysis of the gland tissue, not necessarily associated with bacterial activities. A continuation of this process, associated with the liberation of activated ferments, is responsible for the capillary hemorrhage, destruction, and fat necrosis, which are the outstanding features of this disease. The belief that the lesions are of biochemical as opposed to inflammatory origin has led several recent writers to choose the term 'acute pancreatic necrosis'
in their papers upon the subject. Provided it be clearly recognized that the necrosis is by no means constantly gross and macroscopic, this entitlement is to be commended. Nevertheless, the older term carries with it the sanction of long usage, and it has been thought well to retain it.

A quarter of a century ago, in a lecture before the congress of American Physicians and Surgeons on "The Present Status of Pancreatic Surgery with Especial Emphasis upon Injuries and Inflammations," the famous German surgeon von Meuli, designated pancreatic surgery as the least complete chapter in abdominal surgery. Even today there are numerous unsolved questions in practical as well as scientific pancreatic surgery. (3).

It has been stated (4) that acute pancreatitis is the most serious of the abdominal diseases with which the surgeons have to deal with. The symptoms are acute, the diagnosis obscure, the treatment radical, and the results are not satisfactory. Linder (5) says that the onset of a severe attack of acute pancreatitis is intensely dramatic, like a thunderbolt out of a clear sky, in a robust, obese and apparently healthy individual. Such statements as this and also the frequently stated fact that acute pancreatitis causes the worst abdominal pain known, one that is quite often unreleived by the administration of morphine, led me to inquire into the literature to see just what the nature of this abd-
ominal catastrophe could be.

This consideration of pancreatitis is not intended to be comprehensive. The mass of literature written on this subject makes this impossible. Neither has it been approached from a scientific research standpoint, time and facilities do not permit this. My intent is to review, in a general way, the subject 'Acute Pancreatitis' as it is known today.
ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The pancreas is situated not only functionally but anatomically at the centre of the abdominal cavity, lying transversely across the spinal column at the level of the first or second lumbar vertebrae. It has been compared in shape to a revolver (44). The head, representing the handle of the revolver, lies in the curve of the duodenum in front of the vena cavae and slightly in front of the aorta. The common bile duct descends behind the right portion of the head and is often embedded in a groove in its substance. The neck shows a deep groove posteriorly for the portal vein. The body extends to the left across the front of the left kidney and terminates in a tail which often passes in the lienorenal ligament as far as the spleen, occasionally it extends still further and lies between the layers of the gastro-splenic ligament.

The body is triangular on cross section and the transverse mesocolon is attached to its anterior border, so that the antero-superior surface is covered by the peritoneum of the lesser sac, while the inferior surface is covered by that of the greater sac. The pancreas is best exposed by opening the lesser sac, usually by tearing through the great omentum just below the stomach, or occasionally, if the stomach is low set, by passing through the lesser omentum above the stomach.

The arrangement of the ducts of the pancreas is of special interest in the consideration of the etiology of acute
pancreatitis. Developmentally, the pancreas is derived mainly from two sources, and this is illustrated by the scheme of the ducts. Originally, it comes from three anlagen, one dorsal and two ventral, budding out from the duodenal part of the fore-gut. The left ventral anlage soon disappears, perhaps forming the source of aberrant glands, often found in the gut wall. The right ventral is in close relationship to the common bile duct and forms the head of the pancreas. The dorsal rudiment forms the body and tail. The ducts of the two fuse together and then, curiously enough, the duct system of the smaller ventral portion develops into the most important duct, the duct of Wirsung, while the duct of the dorsal anlage becomes the slightly developed duct of Santorini.

The duct of Wirsung opens at the duodenal papilla either in common with, or alongside of, the common bile duct. The significance of the manner of termination will be referred to later. The smaller duct of Santorini opens into the duodenum about three-fourths inch higher up.

The lymphatic connections of the pancreas are of special importance in the consideration of infective conditions. Bartels has shown that there exists throughout the pancreas a perilobular net work of lymph vessels; these vessels anastomose with a similar net work of lymph vessels in the wall of the duodenum and with the lymphatics of other adjoining
structures, as those of the gallbladder and bile ducts (27). The efferent vessels are divided into four groups, a left, a right, superior and inferior group. The left group run from the tail of the pancreas to the pancreatico-splenic lymph glands and to the hilus of the spleen. The right vessels pass to anterior and posterior pancreatico-duodenal glands. The superior group pass to the glands along the upper border of the pancreas and to the glands at the porta hepatis. The inferior pass to the aortic, mesenteric, mesocolic, and inferior pancreatic glands.

Frankie has made a very important observation with regards to the relationship between the lymphatics of the gallbladder and bile ducts, and those of the pancreas. He has shown that it is possible to inject the lymphatics of the upper part of the head of the pancreas from the gallbladder.

From the physiological point of view, Sweet (28) describes the pancreas as a complete self contained laboratory of physiological chemistry. The mechanism of the process of secretion furnishes one of the most striking examples of the action of a hormone, or chemical messenger. Although, the pancreas, like the other abdominal organs, receives a nerve supply by two paths, the vagus and splanchnic, and also possesses numerous ganglia in its substance belonging to the autonomous system, yet the most potent stimulant of pancre-
atic activity is not nerve stimulation, but the action of a chemical stimulant, brought to the gland from its place of origin in the intestinal mucous. This substance, called "secretin" by its discoverers, Bayliss and Starling, is formed by the action of hydrochloric acid upon a substance called "prosecretin" contained in the cells of the duodenum and the entire jejunum. When the pylorus relaxes during digestion and allows small amounts of hydrochloric acid to enter the intestine, the Hcl. converts the prosecretin into secretin, this is carried to the pancreas by the blood stream, and pancreatic secretion at once begins, to complete the work of digestion begun by the ferments of the stomach. The amount of pancreatic juice secreted daily is estimated to amount in man to about 1,500 cubic cm.

The most important constituent of the pancreatic juice, are the ferments, or, better the proferments or zymogens. These ferments are the proteolytic trypsin, which breaks down the proteins to the amino-acids; a lipase or steapsin, which transforms neutral fats into fatty acids and glycerin, a rennin like ferment, a siastase or ptyalin, like that of the saliva, a maltose and a lactose. There is apparently also a nuclease, which dissolves the nucleins which have been precipitated in the stomach. The ferments of most interest are steapsin and trypsin.
Steapsin is of special interest in that it gives a positive, usually unfailing diagnostic sign of pancreatic disease. The conversion of neutral fats into fatty acids takes place normally, only within the intestine, but if the pancreatic juice escapes into the peritoneum or into the tissues, the steapsin acts on the fat of the body itself, forming characteristic round, dead white patches, which once seen, are never mistaken for any other condition. This fat splitting ferment is not contained in the pancreas as such but as azymogen, steapsinogen, which is transformed into the ferment steapsin by some constituent of the bile.

The proteolytic ferment of the pancreas, trypsin, is the product all important to the surgeon. Like steapsin it is contained in the pancreas as a proferment orzymogen, trypsinogen, which is quite inactive. The normal activating factor for trypsinogen, the agent which makes the harmless trypsinogen the powerful proteolytic ferment trypsin, is produced exclusively, under normal conditions by the cells of the mucosae of the small intestine, and is called enterokinase. This body is only secreted when trypsinogen enters the lumen of the intestine. The change occurs immediately.

Enterokinase appears to be the only substance normally present in the body which can change trypsinogen into trypsin. There is, however, some evidence to show that trypsinogen may
be activated by some constituent of the pancreas itself when the gland is injured in such a manner that disintegration of its cells take place.

An experiment by Sweet (28) has an important bearing on this question. A part of the pancreas of one dog, removed under strict asepsis, was placed, again under asepsis, into the peritoneal cavity of another dog. This procedure inevitably killed the animal in about twenty-four hours, showing that some powerful poison has been developed. This is either trypsin or the toxic products of tryptic digestion. But if fresh normal pancreatic juice was injected into the dog's peritoneal cavities nothing followed.

In addition to the glandular parenchyma the pancreas contains curious little groups of cells which differ in appearance from the rest of the gland—the Islands of Langerhans. These islets consist of small groups of epithelium-like cells, unfurnished with ducts, scattered throughout the glandular substance. They are supplied with a close network of large convoluted capillary vessels. Macleod, Banting and Best, proved that the islets produced a specific internal secretion, concerned in the metabolism of glucose.

This brief resume of the anatomical and physiological set-up of the pancreas will help, I hope, in the comprehension of the pancreas in disease.
HISTORY

A systematic clinical study of diseases of the pancreas was begun about thirty-five years ago. Prior to this our clinical knowledge of this organ was rather fragmentary and rudimentary, and was incommeasurable with its physiological importance. Isolated pathological data were limited to accidental post mortem or operative findings. Physically inaccessible to direct examination on account of its deep anatomical position and environment, functionally interdependent upon gastric, hepatic and duodenal digestion, it eluded the skill of the older clinicians as a factor in the production of disease.

When studying the subject of pancreatitis, in the light of modern pathological knowledge, it behoves us to bear in mind that the older pathologists had noticed and described the naked eye appearance of nearly all the conditions that are engaging so much of our attention at the present time (6). Tulpins, so far back as 1672 describes a diffuse pancreatic abscess of pyemic origin, and Mathew Baille, physician to St. George's Hospital, in a work on "Morbid Anatomy," published in 1799, describes what he calls a hard pancreas with the lobules distinct. He also figures in the same volume a case of pancreatic calculi most carefully dissected showing the relation of the bile
and pancreatic ducts.

Accurate information of the diseases that affect the pancreas is the result of investigations made first by Kawley in 1789 (7). He called attention to the co-existence of diabetes and pancreatic disease on account of finding multiple calculi in the pancreas of a patient suffering from diabetes but thought the lesions of the gland the result of and not the cause.

Portal in 1804 described a case of acute suppurative pancreatitis following an attack of gout in the feet, and Percival, in 1818, described a well marked case of pancreatic abscess associated with jaundice (6).

Until the time of Classen (1842) the evidence of acute inflammation of the pancreas was almost wholly theoretical, and was not controlled by any considerable number of anatomical observations (8). Mercury was known to produce salivation, and the watery diarrhea following its use was supposed to be due to irritation on the pancreas.

Influenced by this and other consideration, Schmackpfeffer, having found certain alterations of the pancreas in a syphilitic woman who had been liberally treated with mercury, attributed her symptoms to the pancreatic changes. The latter he regarded as anatomical evidence of acute inflammation. He describes these changes as follows: "The
pancreas was unusually dense, dry, and very much swollen, it was inflamed and red throughout, although more in the right than in the left side. The duct was very much dilated especially at its mouth."

Some years later Newmann stated that "death" might take place within a few hours from a fatal metastasis of the buccal salivation to the pancreas. Under such circumstances the pancreas is found decidedly swollen, although but slightly reddened (8).

Clasen knows of no confirmation of Newmanns' observations and doubts their truth. He collects, however, a half dozen cases, among them Schmackpfeffers', of what he regards as fatal pancreatic inflammation, and from them establishes the symptomatology of acute pancreatitis. The views thus obtained have essentially prevailed up to the time of Friedreichs' article in Ziemssen's "Cyclopedia" in 1875. The common symptoms were deep seated pain near the stomach, producing a peculiar anxiety, restlessness, perhaps frequent fainting. The pain bore no definite relation to the vomiting or other symptoms and was not increased in proportion to external pressure. The vomiting was forceful, more or less greenish material being expelled. The abdomen was moderately tense, there was slight fever and the appetite was but little disturbed and might be increased. There was moist tongue, thirst,
and constipation (8).

The effects of Glāssens treatment of the subject may be seen nearly thirty years later in the statements by Wardwell (Reynold's System of Medicine, 1871, v3, 414) that the paramount symptoms of acute pancreatitis are deep seated dull epigastric pain, distention, sickness, and vomiting of a clear, greenish, viscid fluid, thirst, faintness, moist tongue, constipation, and slight pyrexia.

The first step toward an essential modification of these views was made by Klebs, in 1870. He preferred to say nothing about inflammation of the pancreas, but described the various lesions which have been found in and around this gland, without attempting to show their possible relations to each other. He availed himself of the cases published up to that time and from his own experience came to recognize the possibility of a hemorrhagic inflammation of the pancreas. Klebs further recognized that this hemorrhagic inflammation might possibly result in a purulent peripancreatitis with partial sequestration of the gland.

Freidrich in 1875 present a more or less complete picture of acute pancreatitis suggesting two varieties (9). He undertook to present a complete picture of acute pancreatitis more in accordance with the anatomical treatment of Klebs than with that of Glāssen (8). He availed himself
of the cases used by Klebs in addition to one under his own observation. He suggested that acute pancreatitis was either primary or secondary. The former appeared to have a tendency to hemorrhage in the pancreas or in its vicinity, in which case a termination in gangrene and ichorous peripancreatitis might occur. If the acute pancreatitis became suppurative, multiple, minute abscesses were to be found, which tended to become confluent and produce resulting peritonitis. The secondary variety of acute pancreatitis was either the granular degeneration found in infective diseases or the circumscribed 'metastatic' abscess. The possibility of a metastatic pancreatitis in the course of a parotitis was not to be absolutely denied, especially in virtue of the case reported by Schmackpfeffer.

Since Friedrich's anatomical recognition of an acute pancreatitis was based upon the consideration of four cases he admitted his symptomatology of this affection to be neither precise nor complete. Furthermore he seemed to include under the head of pancreatic hemorrhage those cases where this lesion is associated with necrosis and gangrene, and others where hemorrhage into the pancreas appears to be the sole cause of death.

Klebs (10) had already (1863) recognized the existence of a suppurative peripancreatitis, and stated, presumably
from his own observation, that in most instances this proceeded from lymph glands. These were either the seat of metastatic abscesses or were primarily diseased by traumatic agencies or injurious food. In the light of the observations published up to the time of his article, Klebs regarded as doubtful existence any pancreatic lesion which did not arise from a peripancreatitis for from a suppurating cyst.

Casper says (11) that according to Max Bauman (Munich) "In 1866 Spiess for the first time reported the characteristics of pancreatitis." But this has not been corroborated.

The next communication of interest in connection with the subject of acute pancreatitis was by Baker. He calls attention to the presence of nodules and patches of necrotic fat tissue in the mesentery and in the contents of a cavity behind the mesentery. In the latter lay the pancreas, attached to the duodenum, with its lobules appearing as if macerated. A second case was reported by Baker, in which there were patches of necrosis of the abdominal fat associated with similar appearance of the pancreas (8).

However, Mayo Robson & Cammidge (6) and Schmeden and Sebening (3) give credit to Balzer in 1879 for being the first to describe acute pancreatitis with fat necrosis. Gussenbauer was the first to record a case of pancreatic surgery, his report being made in 1883. Halstead in 1898 described an
operative procedure for the cure of acute pancreatitis, and Köerte, in the same year, set forth his very comprehensive and fundamental work which seemed to cover all of the then current knowledge of pancreatitis.

However, little attention was attracted by the subject until Fitz in 1889 wrote his classical papers that the medical world really became aware of the inflammatory diseases of the pancreas (6). His exposition of this subject constitutes one of the classics of diagnosis contributed to American and world medical literature (10). His classification of acute pancreatitis into; acute hemorrhagic, acute gangrenous, and acute suppurative holds good today and cannot be improved upon (15). This publication of Fitz' excited tremendous interest in a subject that had, up until that time, been more or less disregarded as a cause of acute abdominal disease. Since that time there has been a tremendous amount of literature aggregated upon the subject, both clinical and experimental, including many case reports, and dispute over the etiology that has arisen.
ETIOLOGY

The etiological factors which cause this disease are still controversial and the methods of infection and portals of entry are open to debate. Innumerable researches have stressed either one or another mechanism, and, when all are considered, it is more than likely that each avenue of infection may be responsible for the individual cases.

The division of opinion occurs chiefly between those who follow the teaching of Maugeret, Deaver, and Mann, that the cellular and other products of lymph borne infection constitute the activating agents, and those others, the majority, who believe that the process is one in which some mechanical defect (blockage) or physiological error (spasm) at the biliary outlet brings about a reflux of bile into the pancreatic duct (12).

During the course of years numerous theories have been suggested. These have undergone various modifications until at present we are faced with three main possible explanations:

1. Blocking of the common duct with reflux of bile.
2. Inflammatory extension from neighboring organs by lymphatics.
3. Rugurgitation of duodenal contents.

Of these three theories the first two command the
greater attention of the literature. Both seek their explanation chiefly on the frequent association of biliary tract disease, and acute pancreatitis, therefore, I do not think that it would be amiss at this point to discuss this important relationship before going into the etiological discussion.

The consistent frequency with which gallstones or diseases of the gallbladder have been found in association with acute pancreatitis has served to confirm the belief that biliary infection predisposes to pancreatitis. Fitz (98) who recognized acute pancreatitis as a disease entity was cognizant of a probable causitive relationship between these two diseases. In 1907 Egdahl found that gallstones were present in forty-two percent. of one hundred seven reported cases (13), and seventy-five percent. of these complained of gallbladder symptomatology. In 1919, W.J. Mayo stated that infected gallbladders and usually stones were present in ninety percent. of all cases of acute and chronic disease of the pancreas in which operation was performed at the Mayo clinic. Fifty percent of Linders cases had associated gallbladder pathology (5). Abell reports ten cases and all but one occurred in the course of more or less prolonged cholecystitis. According to McWhorter, (14), Judd found twenty-six and eight tenths percent. of two hundred and
ninety cases of acute pancreatitis associated with gallbladder pathology, and Kovacs (15) reported seventy to eighty percent. In 1930 Colp (16) reported eighty-five percent of his series of fifty-four patients having pathological evidence of cholelithiasis and cholecystitis, while Schmieden and Sibening (3) found that gall stones were present in sixty-nine and eight-tenths percent of a series of one hundred seventy-eight cases of acute pancreatitis collected from one hundred fourteen German surgical clinics, from 1917 to 1927. It is significant, too, that sixty-five percent of the total number of instances of acute pancreatitis occurred in women. This observation is in agreement with the greater incidence of disease of the gallbladder in women.

Acute pancreatitis is not a primary disease, but rather a sequelae. Whether we favor one or the other hypothesis in its production we must face the fact that biliary disease is usually the precurseres. It is more than mere coincidence that Eg dall found biliary calculi in fifty percent of his cases and seventy-five percent complained of gallbladder symptomatology.

Wangensten, Leven, and Manson (13) agree that clinically, the common factor or denominator (at least far more frequent than any other factor) of acute pancreatitis is disease of the biliary tract.
I. The Bile Theory

This theory can be stated somewhat as follows: In the pancreas the digestive ferments are in the inactive form and are first activated in the intestine by the bile (17). If a gall stone in incarcerated in the papilla the bile no longer flows into the intestine but into the pancreatic duct, since the common bile duct and pancreatic duct are then united, the bile rises there and activates the ferments in the pancreas and the ferments digest and destroy the gland.

The acceptance of the reflux of bile as an etiological agent centers about the observation by Opie, in 1901, that a gall stone lodged at the ampulla of Vater may convert the choledochus and duct of Wirsung into a common channel and permit the retrojection of bile into the pancreatic duct. White states that the cause was quite obscure until Opie discovered this case (18).

The action played by bile in the production of acute pancreatitis was first demonstrated by Claude Bernard (14) in 1856, when he reported the production of acute hemorrhagic pancreatitis following the experimental injection of bile and sweet oil into the pancreatic duct with death in eighteen hours. (19, 20, 14) In 1899 Lancereaux suggested that gall stones lodged in the ampulla of vater might cause pancre-
atitis by obstructing the pancreatic duct (19) and this was followed by Opie's necropsy case. Other experimental causes found at this time were: Gastric juice, Hlava, 1890; weak solutions acid as hydrochloric and chronic and also alkalies, Flexnor, 1900; formalin, sweet oil, fatty acids, sodium soaps, and bile, Opie, 1901; duodenal contents, Polya, 1906; and pure bile salts, Flexner, 1906.

Bile has been known for years to be a factor in the production of acute pancreatitis. Bunting and Brown (14) found that measured small amounts of bile introduced into the pancreas resulted in acute pancreatitis. Others have found that small amounts of bile must be injected at the height of digestion about three hours after a meal. Opie found that it was necessary to inject considerable amounts of bile and Nordmann found that it was necessary to also introduce infection.

Since Opie's demonstration in 1901, this etiological method of production has probably been the most widely accepted. Flexner next showed that it was the bile salts that were the activating agents in the production of necrosis and that mucus greatly inhibited the action of the bile (21).

Archibald (22) next suggested in explanation of those cases in which no stones were found, that the mechanism by which the two ducts are converted into one may be the
sphincter of Oddi, due to failure of relaxation or spasm of the sphincter. He believed that there were three factors in acute pancreatitis; a change in the composition of the bile, an undue resistance, perhaps spasm of the common duct sphincter and an abnormal rise of pressure in the gallbladder or the bile ducts producing a reflux of bile into the pancreas.

However, Mann and Giordano (23) examined the condition of the common bile duct, and the pancreatic duct in two hundred consecutive cases and found that in only four and five-tenths percent was there the condition of the ampulla described by Opie. The conclusion was therefore that the occurrence of acute pancreatitis as a result of the injection of bile into the duct of the pancreas must be exceedingly small. But says Moynihan (20) an ardent supporter of the bile theory, may not the conclusion be drawn with greater likelihood that it is only those patients in whom the anatomical and physiological conditions are favorable, who suffer from acute pancreatitis?

A further difficulty lies in the fact that only in a minority of cases of pancreatitis is a stone found in the ampulla. A stone was found in eighteen percent of Schmieden and Sebening's cases and in four and five-tenths percent of the cases that they collected. Thirty percent of the cases
showed no signs of gall stones whatever (12). But by the same evidence it was shown that there was an associated cholelithiasis in seventy percent of cases and in a considerable proportion of the cases a stone was found in the common duct.

Linder (1) believes that bile frequently enters the pancreatic duct without much damage. To produce pancreatitis bile must be infected, the proportion of biliary salts increased or normal bile under considerable pressure. Nordmann purse stringed the ampulla but produced no pancreatic involvement. We may assume, therefore, to induce pancreatitis not only must bile be infected, but an increased biliary pressure must be counter balanced by unusual sphincter spasm.

(21). Abell (24) says that in order for acute pancreatitis to be produced the bile must be infected. Bacteria change the composition of the bile and in addition activate the trypsinogen of the pancreatic juice. They act through the chemical change that they produce and not by invading the pancreatic tissue. Cultures of the pancreas in acute pancreatitis are, however, usually rare. Mann and Giordano (23) were unable to produce pancreatitis by injecting sterile bile, however, a good many others have.

Obstruction at the ampulla in the absence of gall stones may be due to a spasm of the sphincter of Oddi, congestion,
inflammatory swelling, and obstruction by mucus and by intestinal parasites (14). The resistance of the common duct sphincter has been found to vary considerably. Local duodenal congestion and cattarrhal inflammation of the papilla may cause stasis and reflux of bile into the pancreas. Balo and Ballon (quoted by McWhorter 14) reported three cases of acute pancreatitis with obstruction of the papilla due to venous congestion resulting from a decompensated heart; others have noted these findings due to gastro duodenitis, following dietary indiscretion or accompanying cattarrhal jaundice.

Popper (25) believes that the pancreatic secretion is activated in the distal end of the common duct by the bile and not in the pancreas but by diffusion reaches the pancreas.

Characteristic of the criticism of the bile theory is that of Landon (26) who favors the lymphatic theory because: 1) Gall stones are found in only fifty percent of the cases. 2) Anatomically impossible for stones to become impacted in large percentage of cases. 3) Not sufficient force to inject bile into the pancreas as to cause damage to its cells. 4) Bacteriologic powers of pancreas are very great. 5) Infrequency by which glands are infected by excretory ducts. 6) Because of the peculiar and intimate relationship between the lymphatics and head of the pancreas.
II Inflammatory Extension by Lymphatics

Infection of the pancreas as propounded by Maugeret, Arnsperger, and Deaver is based on the contention that the pancreatic lymphatics bear a very intimate relation with those of the biliary tract, (21), secondly on the fact that enlarged lymph nodes are found about the head of the pancreas in acute inflammation of that gland; and, lastly, that anatomically regurgitation of bile into the duct of Wirsung can occur in but two of four varieties of papillae of Vater embryologically possible.

Serious consideration of the lymphatic factor as an etiological agent of acute pancreatitis dates from the experimental work of Maugeret in 1908 (13) after producing a chemical cholecystitis in a dog, Maugeret believed that the swelling and interstitial edema of the gland demonstrated that infection may be propagated to the pancreas from the biliary passages by the lymphatic route. This suggestion soon found corroboration in the clinical observations of Arnsperger. In this country Deaver in particular has championed the belief that acute pancreatitis results through the spread of infection from gallbladder to the pancreas by way of the lymphatics.

The lymphatics of the pancreas have been shown by numerous writers to anastomose freely with those of the
surrounding viscera, especially with those of the duodenum and gallbladder.

Deaver says (27) that an infective process seems to play the chief part, and the route by the lymphatics. "This, because in those cases of disease secondary to gallbladder disease, it is chiefly the head of the gland that is often involved. The fact that this is the portion furthest removed from the duct of Wirsung, together with the fact that the rest of the gland is apparently normal certainly detracts from the theory of duct borne infection. On the other hand not only are the lymphatics known to be carries par excellence of infection but the peculiar intimate relation existing between the lymphatics of the head of the pancreas and those of the surrounding areas lends support to our theory."

Sweet (28) another adherent states that 'injection of the triangle of pancreatic inflammation ' which lies between the duodenum and the converging ducts of Santorini and Wirsung, in so many pancreatic cases, the lymphatics of which according to Franke, can be injected from the gallbladder, is the most convincing argument.

Abel is in accordance by stating that the lymphatics draining the bile ducts are in intimate association with the lymphatics of the head of the pancreas before they join the aortic group. Infection following this path readily enters
the head of the pancreas where resultant inflammation and minute hemorrhage may readily activate the pancreatic ferment.

Deaver who has been one of the foremost in championing the cause of the lymphatic theory believes that twenty-five percent of the cases not secondary to biliary disease, may follow appendical or other intra abdominal infections by lymphatic extension and produce a peri-pancreatic lymphangitis. But even Deaver admits that the question like many other problems in surgical pathology is still a matter of opinion. (29)

The lymphogenous theory carries with it, however, the assumption that infection spreads against the stream and directly through the lymph nodes. Infection does not run up stream nor does it break the locks of the lymph nodes. (21). Colp (16) is quite emphatically opposed to the theory as shown by his remark that, "the lymphatic origin of pancreatitis while defended by some has never been satisfactorily proven experimentally and certainly the weight of anatomical, experimental, and clinical evidence speaks against it. Recently Kaufman (30) stated that no experimental or clinical proof exists for the origin of acute pancreatitis through the medium of lymphangitis extending from infection in the gall-bladder. Jones (9) says that the work of Kaufmann seems to successfully refute the opinion of Deaver and others as to the
lymphatic theory of acute pancreatitis. While Weeden (6) believes that the adherents of the lymphatic theory are talking in the main about chronic pancreatitis.

In their monograph on "Diseases of the Gallbladder and Bile Ducts" (1915) Graham and his associates stated that "We were probably in error in our former conclusion that we had demonstrated a lymphogenous origin of pancreatitis from a cholecystitis." The virtual abandonment in the genesis of a pancreatitis by Mann and Giordano (31) due to lymphatic spread has dealt a severe blow to this theory, while Schmeiden and Sebening (3) who collected the most extensive series of cases in recent literature state that infection through the lymphatics is still given as a cause -- though most probably a theoretical one.

III Regarding the Regurgitation of Duodenal Contents

Regurgitation of duodenal contents into the pancreatic ducts with or without infection, may produce necrosis of the pancreas. (14). This has been championed by Hess and by Williams and Busch (22). This modus operandi has been done experimentally. There are a number of factors in the duodenum that may produce pancreatitis including bile, gastric juice, enterokinase, intestinal secretions and bacteria.

In support of the duodenal origin of acute pancreatitis may be mentioned the large proportion of clinical cases in
which the bile tract was not inflamed, although, the condi-
tion of the sphincter was not often determined. The ac-
tual method of duodenal origin has rarely been demon-
strated clinically. It is possible that a regurgitation
might occur into the pancreatic duct in the presence of an
acute or chronic dilation of the duodenum or with a relaxed
or dilated sphincter (14).

Experimentally the injection of interokinase into the
duct of Wirsung produced pancreatitis. However, the proba-
ibility of this mechanism must be exceedingly rare, not with-
standing the work of Williams and Busch. These investigators
observed post mortem dilatation of the biliary orifice as
though it had been recently traversed by a stone. By dilating
the biliary orifice of dogs by the passage of glass tubes,
they produced pancreatitis. They concluded that regurgitation
of intestinal contents may also be responsible for the pro-
duction of pancreatic necrosis.

Schmieden and Sebing state that successful passing
of a stone through the papilla may stretch it and cause it to
gape so that the duodenal contents may invade the duct of
Wirsung and activate the pancreatic enzyme.

Colp (16) reports two cases in his series that were,
as demonstrated by autopsy, undoubtedly due to direct in-
fecion from the duodenum or the retrojection of the succus
interlicus, one via the duct of Wirsung opening separately and directly into the duodenum, and one by the way of the duct of Santorini.

It can be seen then that the duodenal theory has its followers to explain some of the cases that do not seem to fit into the lymph or bile theories, but that these cases must be quite few and far between.

Other Factors in Etiology.

The Role Played by Infection--

This is another of the etiological questions that is still controversial. Schneiden and Sebening (3) contend that bacteriology is purposely slighted because it is not possible to evaluate its significance, at present, in the development of acute pancreatitis. The following report from their statistical survey is given--

Bacteriological findings in Acute Pancreatitis as a result of two hundred and eighty-two examinations.--

<table>
<thead>
<tr>
<th>Sterile</th>
<th>Bacteria</th>
<th>Bacillus coli</th>
<th>Staphlococcus</th>
<th>Streptococcus</th>
<th>Frankel gas Bacillus</th>
<th>Paratyphoid and Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>84</td>
<td>103</td>
<td>24</td>
<td>34</td>
<td>37</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Sterile --------- 84  Bacteria --------- 103  Bacillus coli ------ 24  Staphlococcus ------ 34  Streptococcus ------ 37  Frankel gas Bacillus ---- 2  Paratyphoid and Mixed --- 1

Sterile ----------- 40  Bacteria --------- 54  Bacillus coli ---- 26  Staphlococcus ---- 10  Streptococcus ---- 10  Paratyphoid and Mixed --- 10
This table shows that bacteria are not always found and neither are they always absent. It is not known at the present time whether the bacteria, when they are cultured, are primary invaders or if they are secondary.

Waring and Griffiths (32) are of the belief that all cases of acute pancreatitis are due to infection, the infecting organism nearly always the Bacillus Coli comminus but occasionally streptococcus may also be found. "It is not unusual to find that the material removed at operation is sterile, probably because the activated pancreatic ferments have killed the bacteria." Which would, as one can readily see, put it back into the theoretical class as is suggested by Stillmann (33).

However, Barling and Wolfer (34) are of the opinion that infection, direct or indirect may be a cause in acute pancreatitis. They state that the bacteria most frequently found are the colon, pneumococcus and staphlococcus.

In a series of eighty careful bacteriological exams, Truhart (13) found bacteria in thirty-seven cases from the pancreas, the peritoneal fluid or from the foci of necrosis, and in forty-three instances no bacteria were found. However, Tower (35) showed that bacteria may be present in the normal liver, and pancreas.

Attention has been directed recently to the co-exist-
ence of pancreatitis in the course of certain infectious diseases as typhoid, influenzae and the association with mumps is well established, although the manner in which the complication is produced is not clear. (19,13).

The fact that bacteria are or are not present primarily or secondarily has not been settled, "But, says Abell (24), considering the pathology found at operation the leucocyte counts were not high. These blood findings are in harmony with the belief that the extensive destruction of the pancreatic tissue is due to an activation of the trypsinogen within the pancreas rather than to actual bacterial attack."

Ruppanner (2) considers the probability of passage of infection from the biliary system to the pancreas as entirely possible but he concludes that infection does not play an important part, since infection would lead to inflammatory suppuration, which, if it happens is usually later in the course of the disease and not to aseptic necrosis.

Hematogenous Role.

This is closely associated with the infective role. Acute pancreatitis infection by way of the blood stream is rare, although the occurrence of chronic pancreatitis secondary to constitutional disorders is much more frequent (19).

Etiological factors that may damage the pancreas be-
cause of an imperfect blood supply indicates that they may include nutrition of the gland due to impaired circulation secondary to spasm, thrombosis, embolism arteriosclerosis or lues. Post operative emboli, belongs to this category and may follow any operation in the peritoneal cavity. It may follow intoxication through the blood stream either in cases of severe poisoning lysol, oxalic acid, meat or sausage poison or as frequently happens after septic processes such as puerperal sepsis, typhus, measles, osteomyritis, or paroitis. But here, only certain individuals out of an entire group develop this complication. No explanation can be given (3). McKrae (36) adds that the hematogenous route of infection can produce acute pancreatitis by metastasis or by extension along the blood vessels, as thrombophlebitis, from the foci of infection (14).

McKrae (36) notes that abdominal upsets frequently occur during acute infectious diseases as endocarditis, septicemia, typhoid, diphtheria, scarlet fever, small pox, etc., and especially mumps. He thinks that this occurrence emphasizes the hematogenous conveyance to the organ and Jones (9) is in accordance and adds that the hematogenous route has not been enough emphasized.

Loewenthal (17) is an ardent supporter of the arterial pathogenesis of acute pancreatitis. He cites fifteen cases
that have come to autopsy, which, he maintains, can only be explained upon an arterial base.

That the hematogenous route plays a role in the genesis of acute pancreatitis cannot be doubted but indications are that it is a rather infrequent happening.

Etiology-- Predisposing Factors

Carleton (37) makes quite a long list of predisposing factors, amongst which we find:

Gall stones, infections of the gallbladder, obesity, alcoholism, pregnancy, obstruction at the ampulla of Vater by a stone or tumor, infection of neighboring viscera, colitis, gastric or duodenal ulcer or appendicitis, injuries to the pancreas, pyemia, acute infectious diseases, arteriosclerosis, pancreatic calculi and focal infections. McWhorter adds a primary increase in biliary pressure, intestinal parasites, and over acid contents of the duodenum.

The significance of gall bladder and biliary disease has already been touched upon.

Operative trauma is not an unusual cause (16,33,3). It has been known to follow operations upon the stomach, duodenum and gallbladder, partial excision of the pancreas and splenectomy.

Intestinal parasites have been identified as the cause of a goodly number of cases. Fifty cases caused by the
ascarides have been reported in the literature, it obstructs by invading the duct of Wirsung. Grant (38) says acute pancreatitis is produced because it carries in duodenal contents, and Andler (39) believes it to be due to trauma and toxic excretions.

Alcoholism was previously thought to be one of the main predisposing factors, as so many cases happened right after alcoholic debauches. However, this has not been mentioned in the literature so much recently.

Obesity is thought to be a predisposing factor. This may be associated with the greater incidence of acute pancreatitis in fat women with gallbladder history. McWhorter reports seventeen or twenty-six percent of his sixty-four cases as being definitely obese.

The occurrence of so many cases right after a heavy meal is noted in this literature survey. Casper (11) contends that improper diet, over eating, and lack of vitamins are predisposing factors, and he states that no doubt many cases of so called acute indigestion are in reality acute pancreatitis.

Pregnancy and acute pancreatitis are quite frequently associated. Bernnabio (40) found eighteen percent of nine hundred and sixty-seven cases in the literature associated with pregnancy concludes that pregnancy may be a predisposing
factor in that it favors cholelithiasis.

Incidence; Age and Sex.

No age is safe from acute pancreatitis. In McWhorter's series of sixty-four cases the age varied from nineteen to seventy years but was chiefly between thirty and sixty years. The average was forty-three and three tenths years. There was an equal number of men and women which is in variance with older reports. Eliason and North (42) report of authentic cases on record occurring at the ages of two and one half, three, four, and also as late as seventy-seven years, and they found an almost uniform distribution from the third to the sixth decades.

It used to be the opinion that more males than females were afflicted but the more recent literature is in favor of the larger percentage in females (14,3,42,43).

Locality.

Acute pancreatitis occurs much more frequently in Germany and England, much more rarely in America and France, is extremely rare in Italy and in Spain it is practically unknown. This is thought to be due to different climatic and alimentary conditions (2, 40).

During the past four years, forty-five proved cases have occurred in patients admitted to the Alfred Hospital, Melbourne, says Quick (1932). This represents one case in
ever five hundred seventy-eight admissions, medical as well as surgical. Quick mentions that during the same period of time there were admitted sixty-five patients with perforated gastric or duodenal ulcer for means of comparison and he is of the belief that the incidence is considerably higher than is generally believed.

The incidence according to Love (43) is about 1:5000 surgical cases and there is a considerable increase in the number of cases every year.

At the University Hospital, Omaha, Nebraska there has been one case of acute pancreatitis during the two year period, January 1932 to January 1934.
CLASSIFICATION AND PATHOLOGY

The classification of Fitz' (8) in 1899, of acute pancreatitis holds good today, and according to most authorities cannot be improved upon. He categories the cases into:

1) Acute hemorrhagic.
2) Gangrenous.
3) Suppurative.

Most authorities believe that these are one and the safe process only to a different degree (20), representing different phases of the same condition and are not distinct pathological entities.

Sir Mayo Robson uses a rather comprehensive classification of pancreatitis:

Pancreatitis

Acute

a) Hemorrhagic (1) Ultra acute, hemorrhage precedes inflammation.
   (2) Acute, inflammation precedes hemorrhage.

b) Gangrenous

c) Suppurative (diffuse)

Sub Acute

a) Abscess of the pancreas

Chronic interstitial

a) Interlobar
b) Intercinar.
But we find that few pathologists seem to have observed the changes which his classification would indicate.

In 1933 Elman (35) attempted to establish a new clinical pathological entity into the classification, i.e. Acute interstitial pancreatitis, characterized by edema, swelling and induration of the gland with absence of actual necrosis, suppuration and hemorrhage. This was originally suggested by Zoepffer in 1922, under the title of acute edema of the pancreas. Thirty-seven cases were analyzed and presented evidence of this type of pathology. Of this Ruppanner (2) stated that this type of acute pancreatitis has been recognized more recently to form any definite conclusions but he believes that edema without hemorrhage and necrosis may be the first incipient stage of acute pancreatitis.

Amongst other suggested classifications Brady and Ouster (45) divide acute pancreatitis into Inflammatory and Degenerative, dependent upon theoretical etiology and clinical manifestations. However, as the process is recognized to be an acute manifestation and we are considering only the acute, the classification of Fitz seems to suffice and is adhered to by most authorities, although as has been stated, they qualify his classification to be one of degrees, and each not a clinical-pathological entity in itself.
Pathology Considered.

The pathology of the pancreas has never been studied to the degree comparable to that of other organs (34). The reason for this is very apparent, according to Wolfer, because hardly ever, if ever, is there a section of the pancreas removed on the operating table for microscopic examination, although it has been demonstrated that this procedure carries but little danger. In the majority of laparotomies, the pancreas is not subjected to digital or visual exploration. After death there is a rapid digestion of the pancreas which so mars the histological picture that the pathologist fails to note any lesion which may be characteristic of ante-mortem changes.

The changes in the pancreas vary tremendously in type and degree and it is almost impossible to set up a pathological picture of each type that would not overlap that of another type. However, Fitz's description of his classification gives quite a vivid description of the pathology present: Acute Hemorrhagic Pancreatitis (8).

The pancreas in the severe forms of acute necrosis with hemorrhage is found at autopsy to be enlarged either uniformly, or at one end, usually at the head. It is dense, often friable and of diminished consistency. The surface is a varying shade of red and on section the color, depending on the extent of
the hemorrhage, may be dark red, reddish brown, violet or even black. It may have a uniform dark color or present a mottled appearance. There may be bands and spots of translucent yellow, which are formed of fat tissue, and opaque white specks and streaks due to fat necrosis (Fitz was the first to describe fat necrosis in association with acute pancreatitis). These areas of fat necrosis, although most common in and about the pancreas, are often found in the fat tissue at a distance, usually in the mesentery, omentum and parietal peritoneum. They have even been present in the subcutaneous fat and the pericardium. In size they vary from pinpoint to a pea. Their appearance is so striking and distinctive that once seen and recognized they cannot easily be mistaken afterwards for any other lesion. As they occur only in the cases of pancreatic disease their presence on opening the abdomen frequently reveals the existence of unsuspected pancreatitis.

Gangrenous Type:

The gangrenous type as first described by Fitz: The gland in the early stage is swollen, dark, red and soft, or it may be transformed into a dark slate colored mass. At the end of about ten days the pancreas is often dry, dark brown and firm. Throughout its substance areas of hemorrhage alternate with yellow spots of softening. At the end of the second
weak the organ may form a soft black mass, while the lesser omental cavity contains a large quantity of chocolate colored fluid containing bluish black dots.

Suppurative Form:

Two forms of suppuration of the pancreas are distinguished. The first and more important is the suppurative type of acute toxic necrosis, due to the growth of pyogenic bacteria in the necrotic tissue. This is the suppurative pancreatitis described by Fitz. The pancreas may also, like any other organ, be the seat of metastatic abscesses in pyemia. Clinically this type has little importance among diseases of the pancreas, as it is merely a local manifestation of a general blood condition.

Waring and Griffiths (32) give a very graphic description of the process of acute pancreatitis and I thought it best to incorporate this to give the reader a better idea of the sequence of pathological changes:

"In the first stage of acute pancreatitis the head of the gland becomes swollen and pink, and its peritoneal surface shiny and tense. The swelling rapidly spreads along the body of the organ until two-thirds or more may be involved. A little serous peritoneal exudate may be observed, but fat necrosis is not found at this stage. The next stages occur very rapidly. First, softening in the region of the head, and then sudden hemorrhage ploughing the gland tissue and
causing a large dark swelling. The blood may infiltrate between the layers of the transverse mesocolon into the root of the mesentery or into the retroperitoneal tissues of the posterior abdominal wall. In some cases the hemorrhage remains localized; in others it bursts through the serous covering into the lesser or greater sac, or both, producing the most acute symptoms of perforation of the pancreas. In the hemorrhagic stage fat necrosis is found. With the progress of the disease, pancreatic juice is mixed with the blood, producing alteration in the character of the exudate, which becomes chocolate colored and often fowl smelling from secondary infection. General peritonitis supervenes, and unless drainage is established death occurs."

"Large areas of the pancreas become necrosed and are extruded as putty like sloughs; occasionally the whole of the gland has been sequestrated as a slough, either through a drainage wound or the rectum. In cases where the hemorrhage remains confined in the preperitoneal capsule of the pancreas, (gangrenous pancreatitis), secondary infection occurs later, with the production of a localized abscess (suppurative pancreatitis). The disease then runs a much more chronic course."

In considering the individual pathological changes of chief import hemorrhage, being the most impressive phenomena (2), has long been believed to be the primary cause of the acute
syndrome, and also the cause of death. But Rupanner (2) is emphatic in declaring that hemorrhage is secondary to necrosis, and is due to erosion of the capillary walls by the tryptic ferment freed by the necrosis, or as others believe, to a nervous injury of the capillaries (primary capillary hemorrhage per diapedesin).

It is thought that necrosis is due to chemical decomposition of tissue, and in cases of suppuration and gangrene the question of secondary infection is always brought up. The necrosis is the inherent feature of the disease. It is due to autodigestion of the organ under the influence of the enzymes of the pancreatic juice. In the microscopical picture, the glandular cells are destroyed, their nuclei losing very soon their capacity of being stained. Then the intrapancreatic adipose tissue undergoes necrosis, and finally, the interstitial framework. The early appearance of reactive inflammatory symptoms is entirely consistent with the laws of general pathology (2).

The Role of Edema has been Considered.

Fat necrosis is important especially diagnostically. It is expressed by small stipplings and patches, varying in size from that of a lentil to that of a pin's head, roundish or oblong-oval, sometimes jagged, and of a characteristic opaque white color, reminiscent of lime splashes or stearin
drops. They are present in the pancreas itself and in the
direct peripancreatic adipose tissue, in the transverse colon,
in the gastrocolic and hepatogastric ligaments, in the greater
omentum, the mesenteric adipose tissue and in the retro-
peritoneal, perirenal, and even mediastinal, pericardiac and
subpleural adipose tissue. Also subcutaneous fatty necrosis,
often symmetrically arranged, have been observed. In brief,
the small foci of fatty necrosis spread, from the pancreas
as a center, slowly all over the adipose tissue of the ab-
dominal cavity and its neighborhood. It is due to ferme-
tative splitting of neutral fat into glycerin and free fatty
acid by a steapsin or lipase, secreted by the pancreas.
The question how the lipase reaches the abdominal fat, has
not yet been answered satisfactorily. Besides a direct con-
tact or diffusion effect, there must be embolic processes
and transportation of activated secretions by the lymphatics.

A hemorrhagic exudate in the abdominal cavity is
usually mentioned in acute pancreatitis. It is usually brown-
ish, and not infrequently bilious. Ruppanner says that this
has no toxic or fermentative properties but others disagree
with this and it is usually removed at operation. The
presence of fat necrosis and a hemorrhagic exudate on open-
ing the abdomen are the two factors giving a diagnosis.

Another finding mentioned only by Linder and Morse (5)
and later affirmed by Eliason and North (42) is that of a change in the consistency of the omentum, by the loss of its peculiar oily or fatty feel and the acquisition of a peculiar greenish tinged edema. It is noted only in the proximity of the pancreas.

The important operative pathological findings would be: 1) Odorless beef broth fluid; 2) Spots of fat necrosis on mesentery, omentum or pancreas; 3) Marked cyanosis of the small intestine; 4) A change in consistency of the omentum; 5) The pancreas usually is soft enlarged and thickened and on exposure shows areas of hemorrhagic fluid beneath its peritoneal covering.
SYMPTOMATOLOGY

Acute Hemorrhagic Pancreatitis

Acute hemorrhagic pancreatitis frequently occurs in persons who have suffered from previous attacks of biliary colic or indigestion (46, 8, 1). In these attacks in addition to the pain there is frequently nausea and vomiting. Ordinarily the attack begins with a sudden and violent pain, which is referred to the epigastrium and in some instances extends to the back or the loins. It may occur in intermittent paroxysms, but it is usually constant. In acute cases it may continue till death. The pain may be so violent as to suggest rupture of a gastric ulcer or gallbladder. Collapse is common, shock, rapid faint pulse, low blood pressure and cold extremities. Nausea and vomiting and hiccoughs are early manifestations and constipation is usually obstinate, although diarrhea (8) may follow. Fever is rarely noted, though a leucocytosis is common. Examination reveals extreme tenderness in the epigastrium above the umbilicus, not only in the mid line but spreading across the abdomen to both sides. Later there is rigidity. A tumor mass is rarely palpable before three or four days. Slate colored patches are often observed on the abdomen and limbs.

Acute Gangrenous Pancreatitis

If death does not occur as a result of the hemorrhagic
stage, manifestations of gangrenous pancreatitis supervene. The fulminating symptoms now subside. The pain tenderness and vomiting lessen, and the constipation is relieved. The onset is characterized by fever and the formation of a mass in the epigastrium within a week or two after the beginning of the hemorrhagic stage. It may begin with a chill, or chills may occur during the course of the fever. The temperature is usually irregular ranging from 103 degrees F. to 104 and higher. Only rarely is fever absent. Leucocytosis is the rule. The tumor in the epigastrium is ordinarily fairly definite, though it may vary in size, at times extending as far to the left as the spleen. At this stage the stools become soft, not infrequently, diarrheic, and jaundice may occur.

Acute Suppurative Pancreatitis.

In this form bacterial invasion is common, so that suppuration with abscess formation is frequent. The nature of the onset depends largely on its cause, whether it results from an antecedent acute hemorrhagic pancreatitis or is due to carcinoma or supplicative inflammation in the bile passage. It usually comes on suddenly with severe gastric pain which may radiate throughout the abdomen. There is epigastric tenderness, nausea and vomiting are early. Fever is irregular and chills are not uncommon. Constipation is
usual, and is sometimes followed by diarrhea. Abscesses occasionally rupture into the intestine and blood and pus are discharged in the stools. Jaundice is common and so is leucocytosis. Physical shows that the liver and spleen are enlarged, the epigastrium destended, and in a certain number of cases a tumor mass can be felt on palpation. The extension of the inflammation brings about a peritonitis as a complication of acute suppurative pancreatitis.

According to Thomas the most common symptoms in acute pancreatitis are pain, shock, hiccough and vomiting (1). When pancreatitis occurs in a severe form, there is a sudden onset of agonizing abdominal pain, which is most pronounced in the epigastric region. Pain is regarded as the outstanding symptom of acute pancreatitis, it is the first symptom to appear and is described as the most severe type of pain encountered, frequently being unrelieved by large doses of morphine(19). In many cases the acute onset of the pain follows some diet irregularity (8), and frequently radiates transversely to the left (21). The pain is at times exaggerated on inspiration with complaint "catching the breath" and Quick (12) says that it is impossible to place too much emphasis on the dorsal radiation of pain, to the lumbar region or to the left shoulder blade. This pain may be continuous, or attacks of increasing severity may recur
culminating in a final agon of colic, but Linders' experience is that it may, after twenty-four to forty-eight hours, abate. The cause of the pain has been ascribed to pressure upon and involvement of the celiac plexus, hemorrhage into the mesocolon, the shedding of enzymes into the peritoneal cavity and distention of the gland capsule.

Vomiting accompanies and follows pain and consists of stomach contents and later of bile, but it is not progressive, although usually quite persistent during the first twenty-four hours, and it may be a very distressing symptom. It is usually said to never be fecal but according to Schnitzler (47) fecal vomiting may be observed. Nausea usually accompanies the vomiting.

Hiccupping frequently accompanies the vomiting because of irritation of the diaphragm by the swollen and enlarged pancreas. The hiccupping tends to persist after the vomiting subsides (12).

Collapse and shock are usually present in the severe cases. Quick believes the shock due to pressure on the celiac plexus while Linder ascribes it to an allergic phenomenon. It is usually very prolonged, more so than in the case of a perforated viscus, and is usually followed by extreme prostration, weak and rapid pulse, cyanosis and marked systemic depression.
Jaundice is present in some cases, Bernabeo (40) says thirty-five percent of the cases, although the frequent association with disease of the biliary tract makes it of little diagnostic import. It is thought to be due to the pressure of the pancreas on the ductus choledochus and Linder says that it is never severe.

Temperature. Subnormal temperature is a significant finding, especially in the early stages, fever occurs later if peritonitis develops. Linder believes that the temperature is of little import but that the temperature pulse rate is highly significant as the pulse is out of all proportion to the temperature.

Slate blue patches of color which may appear on the abdomen or extremities are considered of great importance, especially diagnostically. While not always present its occurrence is of import because it does not occur in other abdominal conditions.

Physical examination reveals a tense and swollen abdomen, due to rapidly increasing distention, especially of the upper abdomen. This is marked in fifty percent of cases and is due to intestinal parisis (12). Abdominal tenderness in mid epigastrium is present, and is transverse in character. Rigidity is absent at the onset. An abdominal tumor never appears before the third day and then
it is felt as an indefinite mass, extremely tender, situated in the mid epigastrium above the navel and because of the overlying stomach and colon has a dull tympanitic note on percussion. Tenderness in the left costo-vertibral angle is of extreme importance and invariably means involvement of the tail of the pancrea (12, 21).
"When I get a telephone call, and hear that it is an acute abdomen, and the doctor says that he has given morphin and the pain is unrelieved, I say, 'Ha, acute pancreatitis!'" (48) While this statement by Bailey would not always be correct it emphasizes the fact that to think of acute pancreatitis in a goodly number of acute abdomens is to make the diagnosis.

The batting average of the medical profession in the diagnosis is not very high. In Schmieden and Sebenings' two thousand one hundred and thirty-seven cases collected from the literature a positive diagnosis was made in only twenty-one and eight tenths percent, and suspected in seventeen and five percent. So it was considered in little less than forty percent. The most common source of error in this series was cholecystitis which occurred in twenty-two and ninety-five one percent. The difficulty of diagnosis is due to various causes: First its comparative infrequency, second, the absence of a definite pathognomonic sign or symptom, third, its frequent association with other severe abdominal lesions, fourth, its deep situation in the abdomen making it usually inaccessible to palpation and lastly the desperate condition of the patient, which makes operation imperative without the formality of a
diagnosis (27).

The diagnosis should be considered from the symptomatology, physical findings, laboratory and differential diagnosis.

Symptomatology has been considered. In brief the history of previous upper abdominal disease is present in a great number of patients but the symptomatology and physical findings are of the greatest aid in making the diagnosis. An individual who is overly fat and has had previous attacks of biliary tract disease or of indigestion who is suddenly brought down with a severe pain in the epigastrium should be considered as a candidate. The pain is usually excruciating, unrelieved by morphine, and radiates across the abdomen. This pain is usually persistent at least for the first twenty-four to forty-eight hours and may then abate. It is usually accompanied by or followed by vomiting and hiccoughing, the hiccoughing tends to persist. In the severe cases collapse and shock quickly ensue and while this is usually present it is not necessary for diagnosis. Constipation or severe obstipation usually accompanies the onset and may turn into a diarrhea. Jaundice may be present but it is usually slight. The temperature is normal to sub-normal at first tending to rise later in the disease and the pulse is fast.
Physical Findings.

These depend upon the time at which the patient is seen and the severity of the disease. The patient usually assumes a physical position between the extreme writhing of biliary colic and the absolute quietude of a perforated gastric ulcer, and the general appearance is that of a great toxemia. On observation slate colored patches may be found over the abdomen and the extremities.

Tenderness usually follows the outline of the pancreas, that is transversely across the abdomen, being always, however, more decided above the umbilicus. Tenderness elicited over the left upper quadrant and left costovertebral angle should aid greatly in the confirmation of the diagnosis, and an attempt to elicit this sign should be made in all cases. Linder says that it is due to an involvement of the tail of the pancreas and Forbes (49) says that it is due to an effusion in the lesser sac.

Rigidity is usually absent in the early cases but may later assume a board-like rigidity especially above the umbilicus, and it does not necessarily indicate the extent of the disease. It can always be detected at some stage of the disease.(49).

Distention may occur early, when it is usually limited to the epigastric region. Fitz noted, "circumscribed epigastric swelling, tympanitic or resistant", and referred to
it as an epigastric peritonitis. General abdominal distention may develop.

A tumor mass may be palpated early in the epigastrium but this usually does not appear until later, on the third or fourth day, or when the hemorrhagic type becomes the gangrenous (46). It is felt as an indefinite mass, extremely tender, situated in the mid epigastrium above the navel and because of the overlying stomach and colon has a dull tympanic note on percussion (5).

Colp (21,16) states that abdominal puncture, which he employed several times, when positive, was of great aid in several of his cases. The intra peritoneal aspiration of a characteristic oily beef juice fluid is almost pathognomonic of acute pancreatitis. This diagnostic method was performed seven times by Neuhof and Cohn (50) and this was positive in six instances. This test as an aid in differential diagnosis has not been given the place it deserves, according to Colp.

Laboratory Findings.

In regards to the ordinary laboratory procedures as an aid to diagnosis, I find that the general concensus of opinion is that they are of very little value due mainly to the time element (53, 1, 43, 51, 52). However, as opinion is divided laboratory procedures will be considered.

The usual investigations available for the detection
of pancreatic inefficiency are those concerned with, (1) mydriasis, (2) changes in the feces, (3) changes in the urine and blood. Mushin (51) states that the results of most of the investigations recommended are notoriously inconstant, and many quite unfit for practical application to the condition of acute pancreatitis by virtue of the complicated technique and length of time involved in their execution, while Smith (52) says that the pancreas, as regards its external secretion, is still a subject that lies away behind the stomach, duodenum and the liver, both in the patients abdomen and in the purview of the diagnostician.

(1) Mydriatic Test.

This is known as Loewe's Mydriatic Test. It consists in the instillation of two drops of adrenalin hydrochloride (1:1000) into the eye, and repeating it in five minutes. Thirty minutes after the second instillation, any appearance of dilatation of the pupil of this eye is noted. A dilated and usually fixed pupil denotes a positive result (51). The mechanism is explained more or less theoretically. An inflamed pancreas by some means renders the whole of the sympathetic nervous system very sensitive, either by hormones via secretion of the Islets of Langerhans or by pressure of the swollen pancreas in the solar plexus. With this sensitization brought about, adrenalin in the conjunctival sac detonates the ocular sympathetic causing a dilatation of the pupil (54).
Bailey (48) states that it is a valuable scientific confirmatory sign. Waring and Griffiths (32) report the test positive in three out of four cases. Mushin (51) reports it positive in thirteen percent of his cases, and Palmer (54) cites three cases in which the mydriatic test was positive and concludes that it is a most practical aid. However, the test is far from infallible and while, no doubt, being of aid in certain cases, innumerable authors are of the opinion that it is of very little aid.

(2) Examination of the Stool.

The typical stool in disease of the pancreas is bulky, pale, soft, gaseous, offensive, high in fat content and may contain undigested muscle fibres (52). Deaver says that the appearance of large bulky fatty stools, while characteristic are inconstant.

Tests for the external secretion, that is, the presence and activity of the pancreatic ferments, may be indirect or direct. The indirect method consists of introducing certain substances into the digestive tract which, unaffected by the gastric juice, are acted upon by the pancreatic secretion and liberate certain substances which appear either in the urine or the stools. The two most popular tests of this kind are the glutoid capsule of Sahli and the gelodurat capsule of Muller and Schlecht (27). The direct method is not concerned
with the stool, but is accomplished by the use of an Einhorns' duodenal bucket. Of these tests Sweet (28) comments that the absence of trypsin in the feces is not essentially indicative of pancreatic disease and Deaver states that although the approximate normal amount of the principle pancreatic ferments is known, the problem of correlating deviations from this normal with pancreatic disease is still unsolved.

Shortage of diastase, the starch splitting ferment, to reach the intestine and feces is determined by the Wohlgemuth Method, but its value is inconclusive (28, 3)

Examination of the Urine and Blood.

A series of tests have been devised for the diagnosis of acute pancreatitis per the urine and blood stream in recent years. Wohlgemuth's diastase test occupies the most important place (55, 56). Diastase, secreted by the pancreas, is prevented from flowing into the duodenum and due to congestion enters the blood and appears in the urine in cases of pancreatitis. The opinions are divided concerning the question whether the test in the urine or in the blood is more reliable. (For method of determination we refer you to 51, index bibliography, page 134). Normal urine contains ten to twenty units of diastase. In disease of the pancreas, associated with pancreatic insufficiency, the diastase may amount to one hundred to two hundred units (4), while Mushin
reports a series of twenty-six cases in which the urinary diastase varied from fifty to four thousand one hundred units. Beigler and Marchs (56) reported fifteen cases of acute pancreatitis in which the diastatic reaction was always positive and it varied between three hundred twenty and two thousand units, and they found that during an attack the diastatic value was always increased. Mushin also found that the sooner after an attack of acute pancreatitis that the test was performed, the higher the figure obtained. Schnitzler (55) a strong advocate of the diastatic test says, "The positive proof of an increase of diastase has a certain diagnostic value but the greatest importance of the test lies in the fact that it gives suggestions regarding the indications for an operation." And, "The absence of an increase of diastase test is of value but even when it is carefully done, failures will run about twenty percent. There are those, too, who do not put much faith in the test as Love (43), Maertens (41) and others, but opinion of those who have used it most seems to be that it is of value when carefully carried out.

Glycosuria has been debated upon pro and con, but it seems that sugar is present in the urine in a small proportion of cases of acute pancreatitis, and it is of little diagnostic significance unless we know that glycosuria was not present previously.
Other urinary findings in nine hundred sixty-seven cases reviewed by Bernabeo (40) were: Albumin in fifteen percent; biliary pigments, in ten percent; acetone, in ten percent; and perfectly normal urine in thirty percent.

Schnitzler prefers the blood serum to urine for doing the diastase test. Beigler and Marcus sometimes run a serum lipolytic ferment test on the blood serum. It depends on the fact that the normal lipolytic ferments in the blood are different than those in pancreatitis, and so different reactions are received. They tried it on eight patients with acute pancreatitis and the test was positive in all eight. However, they are using it only as a control.

Leucocyte count in acute pancreatitis is usually low at first but tends to rise later if the disease goes on to suppuration. In Abell's ten cases the white count varied from five thousand three hundred to eighteen thousand and eight hundred. And he concludes that such findings are in harmony with the belief that the extensive destruction of pancreatic tissue is due to an activation of the trypsinogen within the pancreas rather than to actual bacterial attack.

Hulten, according to Thomas (1), made radiographical studies of fourteen patients suffering with acute pancreatitis and made interesting observations. These, however, were not considered practical enough to aid greatly in
diagnosis. Schnitzler (55) says that Brunner found certain roentgenological signs in acute pancreatitis. He concludes that the roentgenological changes mentioned are not characteristic for acute pancreatitis. So this procedure as an aid can, I believe, be dismissed at the present time.

Differential Diagnosis.

The differential diagnosis of acute pancreatitis is regarded as difficult, and the lesion most frequently is recognized first at the time of operation. The disease occurs less frequently than the conditions that closely simulate it, and because of the relative infrequency, its possibility is not born in mind as often as it should be. Moynihan (20) states that, "Acute pancreatitis should present little difficulty in making a differential diagnosis as no other catastrophe within the abdomen produces such unendurable agony and so profound collapse." However, Johnson (17) is not of the same opinion when he remarks that, "One can be sure of the diagnosis on this disease only by seeing and feeling the suspected organ."

The conditions from which acute pancreatitis must be differentiated are acute cholecystitis, acute intestinal obstruction, perforation of the stomach, duodenum and gallbladder, biliary colic, acute appendicitis, and rupture of an ectopic pregnancy. These are the chief offenders. Other conditions that must be considered at times, as suggested by Toland (4)
are; incarcerated epigastric hernia; acute gastric dilatation; ptomain or mineral poisoning; angina pectoris; spasm of the mesenteric arteries; mesenteric thrombosis; ruptured aneurysm of the abdominal aorta; acute hematogenous infection of the left kidney; and Foss's disease. We will consider the more important ones:

(I) Acute Cholecystitis: In Schmeiden and Sebenings' collection of two thousand one hundred and thirty-seven cases the most common source of error in diagnosis was acute cholecystitis which occurred in twenty-two and ninety-five one hundredths percent. Acute cholecystitis, particularly the suppurative variety, requires careful consideration. This is especially true where impending perforation and localized peritonitis may be present. Here is found a palpable mass which attaches itself to the lower border of the liver, pear shaped, globular this mass denotes a distended gallbladder. Irregularity or bogginess of the mass is usual. Thoracic breathing is the rule. Slight cyanosis of the face may be present. The above findings and a previous history of gallbladder trouble should suffice to differentiate. (21).

(2) Biliary Colic: The pain here is severe in character, but the patient is able to twist and toss about in an effort to find a position of ease, whereas in pancreatitis the patient is usually quiet. Radiation of the pain into the
back or towards the shoulder is quite common, and a history may be obtained of belching, qualitative food distress, the occurrence of previous attacks, which may or may not have been accompanied by jaundice. The presence of jaundice during the attack is very significant of either cholelithiasis or common duct obstruction. Nausea and vomiting may be distressing, but as a rule, the general condition of the patient is more favorable, and shock and cyanosis are absent. On examination of the abdomen, pain, tenderness, and rigidity are usually localized over the gallbladder if inflammation is present (19).

(3) Acute Intestinal Obstruction: The differentiation of this condition and acute pancreatitis is very confusing and extremely difficult and Sweet (28) goes so far as to say that they cannot be differentiated. In acute pancreatitis the patient is generally so prostrated and suffers such pain that a history cannot be elicited. The pain in obstruction is usually mild at first, increasing in intensity, but never becoming so severe as that of acute pancreatitis, which is agonizing even at the onset. Vomiting, quite frequent and distressing in both cases, is projectile in type, with little or no nausea, and may become fecal in character in obstruction, whereas in pancreatitis, nausea, retching, and hiccoughs frequently accompany vomiting which is never fecal
and which consists mostly of gastric and duodenal contents. Peristalsis is hyperactive and may be visible through the abdominal wall in obstruction, in pancreatitis it is either decreased or absent. On examination the physical signs are more marked in the upper abdomen in pancreatitis, while in intestinal obstruction they may be more pronounced in the lower abdomen. Difficulty in breathing and cyanosis are particularly indicative of pancreatitis. A palpable mass at the site of obstruction may aid in differentiation.

(4) Perforated Ulcer: The pain following perforation of an ulcer is almost as severe as in pancreatitis, and suffering may be so intense that the patient does not wish to be disturbed by an examination of the abdomen. When perforation of a gastric or duodenal ulcer occurs, if the history is available it may be of material aid in diagnosis for ulcer cases are preceded by pain, often relieved by alkalies, and extend over a long period of time. In the early stages there is a striking contrast between the profound circulatory collapse in pancreatitis and the slightly altered volume and rate of the pulse in perforation. If perforation is seen late, when peritonitis has developed, the pulse becomes rapid, and decreases in volume, so that there is little difference in the condition of the circulatory system in the two conditions. On examination, the abdomen is tender and the board
like rigidity of the muscles is generalized, constituting one of the most significant features of perforation. In pancreatitis, although the tenderness and rigidity may be quite marked in the epigastrium, rarely are they found as pronounced in the lower abdomen. In the group of chronic perforating ulcers, the symptoms and signs are more localized in the epigastrium, and the differentiation from mild pancreatitis in which circulatory collapse is not so marked, is quite difficult, although the history, if obtained, may be of assistance (19). Lividity of the face in pancreatitis as compared to pallor with sweating of the brow and temples in perforated viscus is an important sign according to Moynihan (20). Both Moynihan and Linder emphasize the lack of signs of circulatory collapse in perforated gastric ulcer.

(5) Acute Appendicitis: The pain in acute appendicitis is not so severe, it is more or less generalized in the early stage, but in most instances becomes localized in a short time to the right lower quadrant. Although the patient may suffer greatly, the circulatory collapse and shock found in acute pancreatitis are absent. Examination reveals tenderness and rigidity in the lower abdomen, most marked in the right lower quadrant. As a rule the differentiation should not be difficult, although appendicitis is sometimes mistaken
for pancreatitis, when this is mild in type, the frequency of the former being a misleading factor.

(6) Acute Renal Colic: Especially when on the left side is at times attended by pain and shock similar to that of pancreatitis. If there is absence of pain radiating down to the groin it is still more confusing. Pyuria aids greatly in the differential. A sudden torsion of a ptotic kidney with strangulation of the renal pedicle may also simulate acute pancreatitis. Here the history of ptosis in a patient who has lost considerable weight with a history of Dietl's crisis, and a sudden physical exertion may be the exciting cause. The kidney is easily palpated and found enlarged and tender.

It is interesting to note that the mortality, according to the statistics of Bernabeo (40), is twenty-eight percent, in the diagnosed cases, while in the non-diagnosed cases it is forty-one and nineteen one hundredths percent. This emphasizes the importance of correct diagnosis. However, Jones (9) speaks the minds of most authors in regards to diagnosis when he states, "The matter of most importance in diagnosis is not to differentiate before operation but to recognize when acute surgical abdomen exists and not to delay operation when it is known that a matter of hours may be of such tremendous importance in saving the life of the patient."
TREATMENT

The treatment of acute pancreatitis today, almost forty years after Fitz recognized and classified it as a disease entity, is problematical. There seems to be two chief schools of thought, that of early or of late intervention, and then there are those that believe that treatment is only one of 'watchful expectancy'. To show the gravity of the disease we quote Miller (10) who says, "Truly, gentlemen, Moynihan was right when he stated that acute pancreatitis is the most serious condition the abdominal surgeon is called upon to treat." The deep seated position of the gland, its complicated functions, the intimate relationship to other abdominal structures, and the difficulty of surgical approach, have prevented knowledge gained at the time of surgical intervention from being so precise as it is in the case of other less important abdominal organs. The danger of hemorrhage and escape of pancreatic secretion, perhaps somewhat over emphasized in the past, have acted as factors impeding surgical progress.

In 1898, Korte advocated delay in operation until the subacute stage developed, and in the same year Fitz said that, "It is evident that all treatment, at the outset, can be nothing but palliative." (57) However, Koert's point of view changed in 1907 and since that time he has advised early operation. (19).
The operative mortality in operations for acute pancreatitis has decreased in direct proportion to early diagnosis and prompt surgical treatment of the disease (19). In 1912 Korte reported the result of one hundred three operations for acute pancreatitis: forty-one recovered, sixty-two died a mortality of sixty and two tenths percent. At the same time he reported his own experience from 1899 to 1910, which comprised forty-four cases. Of these, there were six cases in which no operation was done and all died. In 1913 Deaver reported eleven operations for acute pancreatitis with five deaths, showing a mortality of forty-five percent, whereas in 1921 he reported twenty-four cases with nine deaths a mortality of thirty-seven and five tenths percent. Moynihan has collected the cases of acute pancreatitis seen in the Leeds General Infirmary during the years 1915-1924. In all, there were twenty-one cases with eight deaths a mortality of thirty-eight percent. Korte and Stephan (56) have shown that when the patients are operated upon early, the mortality ranges from forty-five and fifty-five percent. But when operation is performed two to three days after the onset of the disease the mortality is almost one hundred percent.

A strong argument in favor of early surgical interference lies in the fact that toxic substances and pancreatic secretions readily escape into the peritoneal cavity, and
extravasation of blood is rapid. Abell states in regards to early operation, "The earlier the operation the less the destruction of the pancreas, the less the absorption of the toxic protosis, the less the peritonitis and consequently the greater number of recoveries. While Colp (16) is of the opinion that many more cases have probably died from skillful neglect than from active intervention. He continues, "Acute pancreatitis cannot be considered as a medical disease and the expectant treatment has no more a place here than it would have in acuted appendicitis or perforated ulcers."

Those men advocating late surgical intervention refer mainly to the patient who is in extreme shock and whose physical condition is such as to nullify any interference at the time or in those cases seen later in the disease in whom they have hopes of the process becoming localized.

Of the expectant treatment in acute pancreatitis Deaver (27) says, "Recovery from acute pancreatitis without operation is not unknown, but it is safe to say that cases that recover by medical, that is, expectant treatment, would also recover by operative treatment; while some of those that die without operation might have been saved had they been submitted to operation."

Immediate Treatment:

For immediate relief in allaying the violent pain and
lessening shock, morphine in adequate doses is indicated, sometimes inhalations of chloroform may be used. For the vomiting gastric lavage has been found to give some relief and no food should be given per mouth. Strength should be maintained by glucose by proctoclysis, and normal salt and soda solution should be employed. Schmeiden and Sebening suggest using glucose and insulin intravenously to combat shock, and Deaver is of the opinion that shock can be controlled by infusions of salt solution, or adrenalin and pituitrin.

Grant says that the two drugs aspirin and hexamene, are secreted by the pancreas, and their administration, theoretically, might be supposed to have some action in disinfecting the gland, and would at least do no harm. He also says that the administration of atropine would be worth a trial on account of its inhibiting action on pancreatic secretion.

Going to the more radical, Schnitzler, says that paravertebral blocking of nerves in the area of D 8, 9, and 10 on the left side eliminated pains caused by pancreatitis.

Operative Treatment:

The general concensus of opinion at the present time is that operation is the treatment of choice, and that
operation should be early. As to the correct surgical procedure there is no classical operation but the method of approach is still one of opinion.

The indications at operation should be to remove the toxic protein products; to relieve pancreatic tension, and thereby lessen glandular necrosis; and if possible, to remove the cause of the pancreatitis.

Methods of approach to the gland are the transperitoneal and the extraperitoneal (37). The transperitoneal is accomplished by incising through the gastro hepatic omentum, the gastro colic omentum or through the transverse mesocolon. The extraperitoneal is by posterior lumbar drainage used in cases where it is evident that the tail of the pancreas is involved.

A symposium of the operative procedures that are in use will be given. Cullen and Friedenwald (46).

When operation has been decided upon, an upper median abdominal incision should be made, and the pancreas should be approached through the gastro hepatic omentum, gastro colic omentum or in rare instances through the transverse mesocolon, after reflection of the omentum. The pancreas should be cautiously isolated, packs being utilized with meticulous care in order to prevent the escape of the toxic pancreatic
fluid into the peritoneal cavity. Evacuation of the pancreatic fluid is accomplished by aspiration, followed by incision into the gland itself to release fluid, blood and pus. Finally, through drainage should be obtained by means of gauze surrounding a drainage tube passing through the anterior abdominal wall. Posterior drainage, in addition, is sometimes necessary. If the condition of the patient admits, gall stones, if present should be removed.

Colp (16).

Colp thinks that spinal anesthesia is the best anesthetic, provided the blood pressure is not too low. He had the lowest mortality where cholecystostomy plus drainage of the pancreas was done-- thirty-five percent, and where simple drainage of the pancreas was done the mortality was fifty-five percent.

Fiske Jones (58).

Finds that the best results followed drainage of the pancreas and the pancreatic fatty capsule alone.

Deaver (27).

Deaver believes that treatment of the gallbladder is prophylactic, but that the essential thing is draining the toxins away from the pancreas. He says that, "Free fluid in the peritoneal cavity must be removed as far as possible by gentle wiping, and also by means of a glass tube inserted
in the pelvis through a stab wound above the pubis, since
the pancreatic exudate itself contains sufficient toxic
material to cause death."
Archibald (22).

The absolute, essential thing is prolonged drainage,
according to Archibald. He also believes that rise of
pressure in the bile system should be prevented by cutting
the common duct sphincter. Cholecystectomy should be done
if the condition of the patient permits.
Henderson (59).

In more specific technique, snipps through peritoneum
on the anterior surface and pushes finger well down into the
middle of the swollen gland. Then works the finger from one
end to the other, allowing it to some extent to follow the
line of least resistance, so that there is a trench along
the anterior surface of the gland, extending from head to
tail and nearer the upper than the lower border of the gland,
so as to avoid injury to the duct of Wirsung. Short lateral
branches are made from this longitudinal trench by the finger.
The bleeding is free but easily stopped by packing. A wide
bore rubber tube is passed to the pancreas, the gastrocolic
omentum snugly adjusted around it, the upper part of the tube
wrapped with gauze to shut off the general peritoneal cavity.
The wound is dressed daily and the pancreas gently mopped
through the tube. The drainage is kept up for a week. This
method has been used successfully in three cases.

Love (43).

Believes in local drainage and does not believe in incision or stabbing the gland with blunt instruments. He reports the use of local drainage in eighteen cases with a mortality of twenty-eight percent. He believes that a large drain should be used and this should leave abdomen by a separate stab wound and not through the original incision, as this would predispose to hernia.

Schmieden and Sebening (3).

The operation of choice is cholecystectomy with choledochostome, cholecystectomy alone being unsatisfactory. They believe that the best time to operate is when the disease is just beginning, and that the surgical interference must be radical. They believe that it is necessary to guard against the characteristic downward seepage of pus which is associated with pancreatic pathology.

Occasionally in the primary operation it is necessary to provide counter drainage in the lumbar region. As stated with biliary pathology, cholecystectomy with drainage of the common duct is the choice, and the biliary operation is done last. They believe that operative mortality will be reduced only by earlier operation and diagnosis.

Quick (12)

Advocates, in the presence of biliary pathology, the
opening, exploring and drainage of the common duct. Turner (I).

Believes that incision into the gland should be made to relieve the tension. He says, "A large drain should be introduced to the diseased areas of the pancreas and brought out of the lower angle of the wound. This drain may be made up of one or more large rubber dam cigarette drains or a large rubber tube surrounded by a considerable thickness of gauze. Some surgeons will provide a separate opening for the tube because the pancreatic enzymes may dissolve the catgut and break down the wound tissues. Some surgeons provide an additional drainage opening through the posterior abdominal wall. "No particular difficulty was experienced by Turner from digestion or dissolution of the catgut or wound tissues by the pancreatic secretions escaping through the draining wound. Turner believes that long continued drainage seems to be very important.

Haynes (60).

Reports a series of six cases in which he successfully used a new surgical procedure. His method is to approach the pancreas per the transperitoneal route expose it lift it out of its bed, by careful blunt dissection and then establish posterior drainage of the gland.

It can be readily seen then that there is no conformity in the type of operation recommended by the different authors.
However, it seems generally agreed that the peritoneal exudate
should be eradicated by either, sponging, aspiration or by
drainage; there should be established a good system of drain-
age either down to the fatty capsule of the pancreas or into
the glandular substance according to the authority that one
would follow; and if there is associated biliary pathology
present it should be taken care of at the time of the opera-
tion by cholecystectomy, cholecystostomy, or choldeochostomy,
if the condition of the patient will permit.

Post Operative Treatment.

This consists of the usual post-operative treatment of
any severe abdominal operation. Fluids should be given per
rectum, subcutaneously, intravenously as the state of the
patient indicates. Nutrition can be kept up by the use of
glucose intravenously.

One of the most troublesome postoperative effects of
drainage in acute pancreatitis is the formation of sinuses.
The effect of the powerful pancreatic ferment on the tissues
can be seen in the intensely irritated skin over which the
discharge flows and in the sluggish manner of granulation.
For this reason the skin should be protected by a bland oint-
ment to prevent contact with the secretions (27). Waring
and Griffiths (32) suggest the use of an ointment of heavy
oil, and Bailey (48) suggests the use of an ointment con-
taining two percent hydrochloric acid which renders the ferments impotent.

The diet post operative should be low in fats and carbohydrates according to Schmeiden and Sebening and Linder and Deaver both recommend the use of a strict antidiabetic diet.

Speece and Klein (61) found that the postoperative use of iletin caused a marked clinical improvement. They think that iletin helped to tide over a critical period and was without doubt of great aid in reestablishing the patient's carbohydrate tolerance.
Possible sequelae, according to Schmeiden and Sebening, are: Hemorrhage, abscess formation, empyema, parotitis, liver abscess, chronic pancreatitis, recurrence, cyst formation, pancreatic fistula and adhesions, but they later state that the cases successfully operated upon usually remain permanently cured. To this list Eliason and North (42) add ventral hernia, and Bailey adds pancreatic asthenia.

Diabetes which would be expected to be an important complication in a disease with so wide spread destruction of pancreatic tissue does not, however, seem to play such an important role. Warfield (62) reports four cases in the literature of diabetes following acute pancreatitis. He seems to think that lesions in the tail predispose, as the Isle's of Langerhans are more numerous here.

An exceptional case of acute necrosis of the pancreas is reported in which almost the entire organ was spontaneously extruded through the drainage wound. Despite the great loss of pancreatic tissue and grave complications that arose (abscess formation and duodenal fistula followed by a jejunostomy), the carbohydrate metabolism and pancreatic digestion showed remarkably impairment, the patient ultimately making an excellent recovery (63).

Downie (64) reports eleven patients known to have suffered from acute pancreatitis who were investigated by
means of the glucose tolerance test. In eight cases the response to the test was normal. In one case after a period of impaired tolerance, a normal response was obtained and in another only a lowered renal threshold to sugar remained. Only in one case did a true diabetes mellitus apparently develop as a sequel to an acute pancreatitis eighteen months previously.

Diabetes and glycosuria can then be concluded to be the exception rather than the rule as a complication of acute pancreatitis (65).

Pancreatic asthenia as reported by Whipple (607) occurs during the second and ninth days after operation and lasts for a varying period of time. Seven of Whipple's forty cases followed acute pancreatitis. Weakness is the chief complaint. The asthenia in some cases approaches that of Addison's disease. There is a mask-like expression, a drawling voice, muscular relaxation, and a tendency to salivation. The only treatment of value is blood transfusion.

Hemorrhage as a complication is always a possibility because of the powerful digestive action of the liberated pancreatic juice. This has to be combated by packing or by actual suturing. Hohlen (68) reports a case of severe hemorrhage two weeks postoperative which he stopped with packs and two ounces of mercurochrome poured in the drains. This patient had a chill, the temperature went to 106.6 F. but went on to recovery.
PROGNOSIS

The influence of advanced pancreatic disease on the prognosis is indicated in the following table by Eliason and Norty (42), compiled from the literature.

Prognosis in advanced pancreatic disease.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Cases</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>None, except fat necrosis</td>
<td>4</td>
<td>25%</td>
</tr>
<tr>
<td>Pancreatic edema and fat necrosis</td>
<td>42</td>
<td>24%</td>
</tr>
<tr>
<td>Pancreatic hemorrhage or necrosis or both</td>
<td>61</td>
<td>65%</td>
</tr>
<tr>
<td>Gangrene</td>
<td>7</td>
<td>71%</td>
</tr>
<tr>
<td>Abscess</td>
<td>6</td>
<td>33%</td>
</tr>
</tbody>
</table>

Prognosis depends upon the amount of damage done, the intensity of the toxemia and the time at which operation is performed.

If the entire pancreas is involved there is very little hope for the patient unless immediate operation is done.

Once operated on for pancreatitis what is the possibility of a recurrence? Theoretically one would say that if the predisposing factors continue to operate, there is reason to believe that subsequent attacks may follow (69).

The prognosis in this acute condition of the abdomen will undoubtedly brighten when earlier diagnosis and earlier operation are carried out.
SUMMARY

This has been a general consideration of the disease acute pancreatitis. It has been more or less of a review of the work done so far on this dread disease, and was not a specific consideration of any of the various features of the disease.

A brief resumé of the anatomical setup and physiological activities of the pancreas was given. This served to acquaint one, anew, with the normal gland.

The consideration of the pancreas as a disease center was first mentioned around the middle of the nineteenth century. Historically, Fitz in 1889 established acute pancreatitis as a disease entity.

Etiological factors were reviewed. It was found that the three chief theoretical causitive factors were; regurgitation of bile, the spread of infection per the lymphatics, and by retrojection of duodenal contents. The relative importance of these theories was considered in length. Disease of the biliary tract was found to be the greatest of the predisposing factors.

The pathology of acute pancreatitis of today seems to be more or less different degrees of the same process as described and classified by Fitz in 1889. These are; acute hemorrhagic pancreatitis, acute gangrenous and acute suppurative.

Symptomatology was reviewed. There was found to be no
pathognomonic symptoms. Excruciating pain in the epigastrium vomiting, hiccoughing, shock and collapse seem to be the cardinal symptoms. In physical signs the absence of early marked rigidity in the upper abdomen was found to be important.

Diagnosis was taken up from symptomatology, physical finds, laboratory aids, and a consideration of the differential diagnosis, which is usually difficult and at times impossible, but the really important thing was found to be the early diagnosis of an acute abdomen.

Treatment as advocated by most is surgical and the earlier the intervention the better. Immediate treatment and the different surgical approaches were taken up. Drainage seems to be paramount and this of the pancreas or of the biliary system according to the pathology found.

Prognosis is generally considered to be poor. Over fifty percent of the patients affected with this disease die. It will improve only when the patients are seen earlier and when earlier surgical steps are taken.

Sequelae are found to be of less importance than one would anticipate. Diabetes as a complication, as would be expected, is quite rare.
CONCLUSIONS

The conclusions herewith stated are mostly those from men of authority and experience who have studied this subject both from clinical experience and from the literature. What conclusions that I have to draw are due to the trend of the literature read on this subject, acute pancreatitis.

(1) Acute pancreatitis is not an extreme rarity and is entitled to more serious consideration than is ordinarily accorded it.

(2) The etiology is not fully understood. Regurgitation of bile, due to mechanical or physiological block of the common duct, as the activating agent seems to enjoy the preference of most of the clinical and experimental work, although the lymphatic theory of origin has many adherents.

(2a) Diseases of the biliary tract, cholecystitis and cholelithiasis, seem to be the chief predisposing causes.

(3) The onset of an acute case of pancreatitis is one of the most dramatic and excruciating abdominal catastrophies known.

(4) There are no pathognomonic symptoms.

(5) Correct pre-operative diagnosis is not made in over fifty percent of the cases. Diagnosis is usually made at the time of operation or at autopsy.
(6) There is no distinct diagnostic laboratory aid at the present time.

(7) The really important thing is to recognize an acute abdomen and operate immediately.

(8) Treatment is surgical, by drainage of the pancreas or of the biliary system or both, and the earlier instituted the better.

(9) The mortality of all the collected cases is fifty-one percent (42)

(10) The prognosis in this disease will be brighter when the clinician begins to think of acute pancreatitis in his differential diagnosis and insists upon early surgical interference.
CASE REPORTS

CASE #1

From Hagyard (66)

Mrs. McK., seen in consultation with Dr. E.S. Reedy, September, 1922. A large, obese woman who had had much abdominal distress, sour stomach over a period of years. On the evening before admission, while in a picture show, she was taken with a very severe abdominal pain. She was taken home and Dr. Reedy called, who gave a quarter grain of morphine. Examination the following morning showed a very large woman, complaining constantly of intense pain in the epigastrium through to the back, with nausea and vomiting. There was marked collapse with moderate abdominal rigidity and tenderness. A diagnosis of perforated ulcer was made.

Operation revealed considerable peritoneal reaction with numerous areas of fat necrosis. There was considerable free brown fluid. The gallbladder was large with thick, opaque walls and marked local hepatitis. The pancreas on exposure was large, mahogany brown in color and surrounded by considerable edema. The capsule of the pancreas was split and the substance opened up and drained. After a serious fight the patient recovered. Postoperative diagnosis was acute pancreatitis and chronic cholecystitis.

Comment: This is a typical case of acute pancreatitis. The previous history of abdominal distress is significant.
The sudden onset and continuous distressing pain are typical. The rest of the history and physical findings should have given a hint as to the probable diagnosis, and one of the common errors was made in diagnosis. Although an acute abdomen was recognized and operated the importance of bringing acute pancreatitis into the mind in differential diagnosis is emphasized by this case, also the association of the cholecystitis.

CASE #2

From Opie.(70)

For several months the patient, a male aged forty-nine years, had suffered with pain in the epigastrium, and at times in the right hypochondrium. He had been jaundiced at one time. About sixteen hours before death he was suddenly attacked with vomiting and severe epigastric pain, followed by collapse. The gallbladder contained one small concretion of impissated bile; two others were lodged in the duodenal extremity of the common duct. The body and tail of the pancreas were enlarged and infiltrated with blood. In the neighborhood of the gland were foci of fat necrosis.

Comment: This is one of the early cases reported by Opie when he was contending the etiology due to a stone in the common duct causing regurgitation of bile. The sudden onset, symptomatology and sudden death show what a marked toxic process this disease must cause.
CASE #3

From Jones (9).

A patient affected with cholelithiasis. The patient, a female of twenty-four years, had had numerous attacks of typical gall stone colic. She had been pregnant and had gone through a normal confinement two weeks prior to her entrance to the hospital. She was suddenly taken with acute abdominal pain in the region of the gallbladder with vomiting, and obstinate constipation. On entering, she was in a state of shock, with rapid pulse and sub-normal temperature. The abdomen was distended and rigid. A diagnosis of cholelithiasis with perforation was made and immediate operation advised. On entering the abdomen a serous fluid was encountered and milky patches of fat necrosis noted in the omentum and peritoneum. The gallbladder was enlarged and contained from twenty to forty mulberry like stones.

Comment: This case again shows the association of cholelithiasis, and the possible etiological role played by pregnancy. The diagnosis, as in many cases, was made on opening the abdomen.

CASE #4

From Kappis (1).

A man, forty-nine years old, was referred with the diagnosis of incarcerated femoral hernia and accordingly
operated upon immediately. The hernia was not incarcerated, but the hernial sac contained, necrotic adipose tissue revealing pancreatitis. As there were no extreme abdominal symptoms, and the general condition was excellent, no laparotomy was performed. On the sixth day, symptoms of ileus appeared quite suddenly, and the laparotomy which was immediately performed could not prevent the patient's death on the following day. "The waiting!" says Kappis, 'had evidently been a mistake."

Comment: This is a patient in whom watchful waiting resulted disastrously, and emphasizes the fact that early surgical interference would most likely given a better prognosis.
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