1955

The Diagnosis and management of acute pancreatitis

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THE DIAGNOSIS AND MANAGEMENT OF ACUTE PANCREATITIS

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SENIOR THESIS

PRESENTED TO THE COLLEGE OF MEDICINE

UNIVERSITY OF NEBRASKA

OMAHA, NEBRASKA

1955

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I. INTRODUCTION

The diagnosis of disorders of pancreatic function and disease constitutes a real challenge to the physiologist and clinician. There is a great disparity between the importance of the pancreas functionally and our ability to discern evidence of abnormalities of its function, or to detect evidence of early disease. Therefore, it would appear obvious that the clinician constantly be aware of acute pancreatitis as a diagnosis whenever confronted by an acute abdomen or many cases of acute pancreatitis may be missed. It is the purpose of this paper to discuss the symptom complex, and the various laboratory aids which will aid in making the diagnosis of acute pancreatitis. And once the diagnosis is established, to discuss the modern medical management of the disease.

II. DIAGNOSIS

A. History, Symptoms and Signs.

Acute pancreatitis may affect all age groups.

However, the average age for males is about 40-45 and in women slightly older. It is also slightly more common in women than in men. A positive point in about 25% of cases will be the history of onset of symptoms following ingestion of a heavy meal. Repeated experiments have shown that pancreatic necrosis is more readily produced soon after ingestion of a heavy meal--presumably, when the pancreas is active producing digestive enzymes. The role of alcohol in the pathogenesis of acute pancreatitis has received some attention. In one large series of cases of proven acute pancreatitis 18% were admitted to the hospital intoxicated or recuperating from a recent alcoholic bout. The three predominating symptoms in the acute phase of the disease are (1) pain, (2)nausea, and (3) vomiting. In a large series of cases 94.5% had pain, 94.6% had nausea and 84.0% had vomiting. Paxton and Payne (1) divide the disease into 5 groups according to the clinical picture. In group I is the standard textbook description of acute pancreatitis--the elderly obese florid individual who has eaten a large meal preceded by several highballs. A few hours thereafter he is seized with excruciating

upper abdominal pain followed immediately by nausea and profuse vomiting. Generally he is in profound shock with cyanotic mottled skin and diffuse abdominal rigidity and tenderness. Later he may have ecchymoses of the flanks --Grey-Turner sign--or umbilicus--Cullen's sign. Death usually ensues within 24-36 hours after the onset with a terminal hyperpyrexia of 105-106 degrees Fahrenheit. The patient who simulates acute coronary occlusion is in this group. The patients in group II simulate acute cholecystitis. The onset is usually sudden with moderate severe epigastric or right upper quadrant pain. The pain often radiates through to the back and is followed at once by nausea and persistent vomiting. Group III imitates mechanical small bowel obstruction. The diagnosis of obstruction is usually characteristic but there is usually no apparent etiology--such as a hernia or abdominal scar--for the obstruction. Any patient who appears to have an intestinal obstruction with no apparent etiology should have a serum amylase and urinary diastase determinations before surgery is contemplated. Group IV resembles acute alcoholism with acute gastritis. Included in this

group are those patients who are thought to have perforated a peptic ulcer. These patients usually are admitted intoxicated or give a history of being on a recent alcoholic spree. Subsequently they develop abdominal pain, nausea and vomiting. However, these symptoms may be minimal and the slight degree of abdominal rigidity often leads to the mistaken diagnosis of a perforated peptic ulcer. In Group V are those patients who have a mass either in the epigastrium or the left lower quandrant of the abdomen. They give a history of having acute pancreatitis three-four weeks before admission and now present with a pseudocyst. Their initial symptoms may fall into any of the previous four groups described.

Other symptoms also include (1) massive gastrointestinal hemorrhage--manifested either by bloody diarrhea or hematemesis. This occurs in approximately 10% of cases of acute pancreatitis. The exact cause of the ulcerations found in the stomach, small intestine and colon at autopsy have not been determined. They may be related to the fact that trypsin can produce vascular necrosis

and hemorrhage in all tissues in the body.

Diarrhea mav be a misleading symptom. It is present in 5-10% of cases. It is probablv caused bv the initial increase in peristaltic movements produced bv the irritation of the autonomic nerve supplv of the intestine.

Hvpertension--about 20% of patients with acute pancreatitis have clinical hvpertension. This observation varies from the widespread belief that profound shock is generallv present. Actuallv onlv 11.7% of one large series were in shock while 78% had no clinical evidence of shock at all.

Shock--the degree of shock principallv depends on the pathologv present. In the earlv stages, this reduction in blood pressure represents a neurovascular reaction excited bv pain and tissue destruction. Later it merges into secondary shock without an interval of partial recovery and precedes death in a state of severe peripheral vascular collapse. This peripheral vascular collapse is the probable explanation for the peculiar cvanosis exhibited bv the patient. This is not to be confused with the brownish discoloration of the flanks (Grev-Turner's sign) (2), or the slate blue color of the umbilicus (Cullen's sign) (22). These

are infrequent and are produced by an entirely different mechanism. They are caused by a subcutaneous extravasation of blood and edema fluid secondary to the digestive action of trypsin and to a minor degree, lipase. With the patient lying on his back the pancreatic ferments spread along the retroperitoneal spaces laterally and cause a yellow-green and bluish discoloration from degenerating blood pigments. Another infrequent sign is Leowi's sign.(3) It depends on the response of the pupil to adrenalin which is placed in the conjunctival sac. When several drops of a 1:1000 solution are placed in the eye the pupil dilates and may become assymetrical. This does not occur in a normal person and probably represents a non-specific sign of shock.

B. Laboratory Tests.

1: Serum Amylase--this test is usually not considered pathognomic of acute pancreatitis except under certain conditions, i.e., if the elevation is greater than four times the normal level, and the decision to treat an acute abdomen conservatively because of an elevated serun amylase may be hazardous. Reports on the clinical significance of this test are

somewhat varied depending on whether the author favors conservative management or surgical diagnosis. Cole (4) pointed out in 1938 that the serum amylase is usually elevated during acute pancreatitis. Rothman (5) reported elevated serum amylase in 11 proven cases of acute pancreatitis. Caudel and Wheelock (6) found an elevated serum amylase in 96% of patients with mumps. Polowe (7) reported elevated serum amylase in pneumonia, perforated peptic ulcer, high intestinal obstruction, infection of the salivary glands, impaired renal function, splenic trauma, portal or mesenteric thrombosis. Even still he states that moderate to marked serum amylase elevation is almost always associated with disease of the pancreas. McCall and Reinhold (8) reported occasional high serum amylase levels in patients with gallstones or common duct stones. Domzalski and Wedge (9) found high serum amylase levels in 24% of chronic alcoholics and in only 10 of 50 controls. Comfort (10) reports a case of carcinoma of the head of the pancreas simulating an acute abdomen in which serum amylase levels of 3200-25600 units were found. Bennett and Burgess (11) report a serum amylase of 815 units in acute morphine poisoning. Despite all the foregoing,

Coffey (12) in May 1952, reported that the diagnosis of acute pancreatitis is confirmed by an elevated serum amylase test. Malinowski (13), reiterates the value of serum amylase in diagnosis of acute pancreatic disease. He points out the elevation of serum amylase reflects existance of a pancreatic lesion but does not reveal the nature of it. He also reports elevation of serum amylase in carcinoma of the pancreas, perforated peptic ulcer, mumps, azotemia, and diseases of the biliary tract. Wilson and Seabrook (14) report several cases with elevated serum amylase only three of which had acute pancreatitis. Five had cholelithiasis, two had peptic ulcers one of which had perforated. They also stated that "the importance of this test seems to be overemphasized and that the decision to treat an acute abdomen conservatively on the basis of an elevated serum amylase should not be made." Grollman (15) considers the diagnosis of acute pancreatitis positive when the serum amylase is elevated above 400 Somogyi units and demonstration at operation. Zollinger (16) reports that the serum amylase remains elevated longer in the peritoneal fluid than in the serum. Bockus (17) also reports on false positive serum amylase elevation in the

absence of acute pancreatic disease. He states that the serum amylase is elevated due to increased choledochal pressure due to spasm of the biliary musculature. Burke (18) reported the occurence of elevated serum amylase in three normal persons following injection of morphine. Gross (19) obtained elevations in serum amylase and lipase within four hours following the administration of two grains of codeine intramuscularly in five patients with biliary dyskinesia (post-cholecystectomy syndrome) and in one patient with duodenal ulcer penetrating into the head of the pancreas. Bogoch (20) used 36 normal people and found 25% of them had elevated serum amylase 2.5-5 hours after injections of morphine sulphate. Despite all these various reports of elevation of serum amylase in conditions other than pancreatic disease, Bockus states that very seldom does the serum amylase become elevated more than five times normal except in acute pancreatitis and that the serum amylase test is still the most valuable aid in diagnosis of acute pancreatitis.

Amylase may be determined also in fluid aspirated from the peritoneal cavity and from areas of discoloration in the flanks. (21) According to

Bower, the serum amylase on this fluid in a case of acute pancreatitis was 4210 units with a control of 177 units.

Although the serum amylase usually returns to normal within 24 hours after the onset of the disease (24), Olander states that in 5 of 86 cases of acute pancreatitis, the serum amylase remained elevated up to five days, indicating that this test might be of value even late in the disease. (25)

2. Serum Lipase: The serum lipase test is of more limited value in the diagnosis of this disease than is the serum amylase determination, consequently much less has been written on this test in the literature. However it does have certain advantages over the serum amylase, in that it will remain elevated for a longer period of time in the disease and therefore may be of diagnostic value if the patient is not seen in the first day or two of his disease. The height of the serum amylase and lipase cannot be correlated with the amount of inflammation or necrosis present. (23)

3. Antithrombin titer: The plasma antithrombin level is an intravascular response to blood trypsin. Innerfield states that in 97.3% of 304 cases diag-

nosed as acute surgical abdomens, the antithrombin titers were normal thereas in 50 of 55 patients with acute pancreatitis, a strongly elevated result was obtained. (26) In patients with acute pancreatitis, plasma antithrombin determination aids in exact diagnosis, clinical evaluation, and serves as a reliable prognostic index since its value closely parallels the course of the disease. This may be related to the hemorrhagic aspects of severe acute pancreatitis and also perhaps to the cause of venous thromboses occasionally seen as presenting manifestations of carcinoma of the pancreas. Shinowara also describes plasma coagulation factors in acute pancreatitis. (27) He reports elevated thromboplastic plasma component values of 5-22 times the normal mean in five patients with acute pancreatitis.

Comparison of serum amylase, lipase, and antithrombin; (28)

Factors	Antithrombin	Amylase	Lipase
Time required to perform test	10-25 min.	2 hours	24 hours
Period of illness during which test is diagnostic	throughout the acute phase	first 8-24 hours	after first 24 hours
Period of illness during which test may be performed	plasma can be refrigerated and reliable results had	must be done immediately	no result until 24 hrs. after beginning test
Chemical agents	simple, stable	complex	complex
Specificity	highly specific	not specific	not specific

4. Serum Electrolytes:

A. Calcium--the serum calcium is usually below 9 mg% at some time between the first and ninth day of the disease. (29) The lowest calcium level is usually between the second and fourth day of the disease. The usual explanation for the decreased calcium is the formation of soaps. However, there may be other mechanisms; the excretion of calcium in the bowel may occur with excess stimulation of the adrenals by ACTH. The low calcium may be of diagnostic value especially in cases where the serum amylase is not elevated.

B. Potassium--the level of serum potassium is usually diminished. The mechanism for this is not at all clear but maybe related to continuous gastric suction used in therapy. If potassium is elevated, it is usually of grave significance because it is probably due to the great amount of tissue breakdown with associated hemolysis of red blood cells in hemorrhagic pancreatitis and to renal failure due to shock, hemoglobinemia or other mechanisms. The elevation of serum potassium in this disease is always associated with a fatal outcome.

C. Magnesium--this is also decreased due to the formation of soaps. However whether this mechanism

alone is responsible is doubtful due to the large intracellular reserve of this ion.

4. X-Ray:

X-Ray has little diagnostic value except to establish the absence of disease in other organs. (30) Gas may be present in the small bowel but ileus and peritoneal reaction can also be caused by a number of other disorders. The paralytic ileus seen in acute pancreatitis is frequently of the segmental type. (31) According to Grollman (32) 50% of cases showed a single sentinel loop of distended small bowel--simulating an early mechanical obstruction. Contra and Santos (33) have reported an extensive experience with barium meal studies in acute pancreatitis. They mention the frequent occurence of antero-cephalad displacement of the stomach, straightening of the greater curvature of the stomach, atonic stasis in the duodenum and upper jejunum, widening of the duodenal loop and downward displacement and distention of duodenal-jejunal angle.

5. Electrocardiographic changes:

The EKG findings in acute pancreatitis are most usually confused with those of an acute coronary

thrombosis. Gottesman (34) reported EKG changes simulating coronary thrombosis in acute pancreatitis which returned to normal when the acute phase of the disease was over. These changes were chiefly a depression of ST in leads 2 and 3 and a diphasic T in leads 1,2, and 3. Bellet (35) states the main changes are an inversion of T in lead 1, in the other limb leads, and precordial leads accompanied by various degrees of ST segment depression. The changes are due to part to a shock like state and also to a potassium ion decrease. The potassium may be due to continuous gastric suction and also to diabetes associated with acute pancreatitis since administration of insulin and glucose may still lower the serum potassium further. (36)

III. MANAGEMENT

Although there are many dissenting opinions about the treatment of acute pancreatitis, the prevailing attitude today is one of conservatism. Except for suggestive differences in clinical severity and degree of chemical alteration, precise distinction between acute edematous or interstitial pancreatitis and acute hemorrhagic necrosis of the

pancreas is impossible. The eventual progress of the disease cannot be accurately foretold when the patient is first seen. Hence during the early phase of an acute attack, the seemingly mild case and the obviously severe one are treated basically the same.

Success or failure of the conservative management of acutepancreatitis depends to a large degree on the manner and care with which the various available therapeutic measures are selected and applied. Intelligent use of these measures requires constant awareness of the clinical situation and the physical and chemical changes taking place within the patient. It is of utmost importance, therefore, that the patient be observed carefully from the very onset of treatment. The initial appraisal of the clinical situation should include assessment of chemical and electrolyte status as shown by various laboratory tests. After this, the general appearance of the patient, his temperature, pulse, blood pressure, cardiovascular status, abdominal signs, renal output, fluid intake, blood cell count and concentration of serum electrolytes must be determined at frequent intervals. The information obtained from these observa-

tions serves to guide treatment and determines the choice of measures to be applied. Generally speaking, the conservative plan of management is aimed at attaining certain basic objectives that, if realized, will ultimately result in complete subsidence of the acute inflammatory process. These objectives and some of the measures used to attain them follow.

A. Relief of Pain:

1. Nitrites--nitrites are thought to diminish pain of acute pancreatitis by directly relaxing smooth muscle and thereby reducing duodenal and ductal spasm. They may also lessen pain by overcoming vasoconstriction. The duration of action of these drugs is extremely short and their influence on pain is generally negligable when used alone. Also, their hypotensive action is undesirable, particularly in acutely ill patients who may be in a shock-like state. When nitrites are used, they are usually given either as inhalations of a pearl of amyl nitrite or as 0.6 mg. tablets of glyceryl trinitrate (nitroglycerine) dissolved sublingually. (37)

2. Morphine sulfate--morphine sulfate and other opiates and synthetic analgesics have the

disadvantage of inducing duodenal and ductal spasm. Through this action they may aggravate the local situation in acute pancreatitis, even though they succeed, through their central effect, in temporarily relieving pain. For this reason the use of morphine is controversial. (38)(39) The spasmogenic effects of meperidine (demerol) hydrochloride seem to be less pronounced and less sustained than those of other members of this group of drugs. (40) For this reason it would appear to be the analgesic of choice. The usual therapeutic dose is 100 mg. given subcutaneously every four hours or even more frequently if necessary. The simultaneous administration of nitrite may partially counteract the spasm induced by demerol and other analgesics with related action.

3. Tetraethylammonium chloride--this drug may relieve pain so effectively in some cases of acute pancreatitis that narcotics are not required. The drug effectively blocks both the sympathetic and parasympathetic impulses at the ganglion synapse but does not block painful afferent stimuli from the gastrointestinal tract. Its pain relieving action in acute inflammation of the pancreas is probably principally due to reduction in pancreatic

secretory activity. The latter results directly from interuption of transmission of excitatory impulses to the pancreas and indirectly by depression of gastric secretion and thereby diminished secretin formation in the upper small intestine. Relief of pain may also be due in part to reduction in tone of the sphincter of Oddi as a result of vagal block. (41) Hypotension and other distressing side reactions following administration of this drug detract from its usefullness in patients acutely ill with pancreatitis. The initial dose of tetraethylammonium chloride (etamon) should not exceed 1.0 cc. If there is no untoward reaction, subsequent doses may be increased up to 5.0 cc. This dose, given intramuscularly, may be repeated as often as every four hours to control pain.

4. Methantheline bromide--methantheline bromide (Banthine) has also been reported to relieve pain remarkably in acute pancreatitis. (42) The beneficial effect of this drug is likewise probably chiefly due to the depression of pancreatic secretion.resulting from its anticholinergic action. (43). The vagal depressing action of Banthine may also help to diminish pain by overcoming spasm and

reducing hypertonicity of the sphincter of Oddi. For prompt and effective results, parenteral administration of Banthine is required in amounts of 50-100 mg. every 4-6 hours. Doses of this magnitude are almost invariable attended by side reactions, such as dryness of the mouth. These may become so intolerable so as to prohibit further use of the drug. Other cholinergic blocking agents, notably hexamethonium bromide (C-6) may prove to be as effective in some cases as Etamon and Banthine for essentially the same physiologic reasons. It is usually given in oral doses of 250 mg. a day for five days with continuous blood pressure recordings. (44)

5. Procaine hydrochloride--this drug administered intravenously has been used successfully to control pain in acute pancreatitis. (45) After the intravenous injection of procaine solution, pain may be controlled for hours and the general clinical situation improved. Among its properties, procaine is known to possess local anesthetic, analgesic and antihistaminic actions. Also it is known to cause vasodilatation and exert a spasmolytic effect on smooth muscle. Although these several actions, and possibly others, are

probably responsible for the observed beneficial effects of procaine, the precise mechanisms that bring them about are poorly understood. When procaine is given intravenously, it is quickly hydrolyzed and rapidly disappears from the plasma. This encourages the thought that one of the breakdown products of procaine hydrochloride, possible dimethylaminoethanol, which persists in a relatively high concentration, may actually be responsible for some of the actions of this drug. Intravenous injection of procaine is not without danger, however, and great caution must be exercised in its use. Tests for sensitivity to the drug and slow administration of a barbiturate would also appear wise precautions. During administration the blood pressure and pulse should be checked at intervals. The patient should also be watched for appearance of any toxic symptoms such as excitement, restlessness, dizziness, irritability, numbness, muscular twitching, skin reaction and dyspnea.
Despite the extensive use of procaine in treatment of arthritis and other painful conditions, the dose and method of administration of the drug are not standard. The use of a "procaine unit", consisting of 4 mg. of procaine hydrochloride per kilogram

of body weight given in 0.1% isotonic sodium chloride or in 5% dextrose in water over a period of twenty minutes has been shown to be relatively safe. Some, however, prefer to add 1 gram of procaine to 1000 cc. of isotonic saline and give this by slow infusion at a rate of twenty to seventy-five drops a minute. Still others prefer to use smaller quantities of a more concentrated solution given over a shorter period of time.

6. Nerve block--in cases of severe acute pancreatitis particularly those with pronounced pain resistant to or only partially relieved by drugs, nerve block may be used. The most commonly employed nerve-blocking procedures are paravertebral sympathetic block and splanchnic block. (46) The diminution in pain effected by these procedures probably results from interference with transmission of visceral afferent fibers originating in and about the pancreas. They may also influence pain by vasomotor and secretory changes that may by produced in the pancreas as a result of blocking the sympathetic nerve supply to this organ. The block is also thought to relax the sphincter of Oddi allowing drainage of dammed up secretions.

Paravertebral block is aimed at selected segments of the ganglionated sympathetic trunk; splanchnic block at the splanchnic nerves. Nerve block is not without danger however, in addition to being a painful procedure, should the anesthetic agent become widely diffused and some of the spinal nerves blocked, many somatic afferent fibers would be affected. The sixth-eleventh thoracic sympathetic ganglions are usually blocked on the side on which the pain is severest. The bilateral afferent innervation of the pancreas often requires block bilaterally. Even then pain is not always relieved. Furthermore, relief is only temporary, so that the block often has to be repeated. Also the extensive sympathetic interuption often causes a marked fall in blood pressure, an undesirable affect particularly in shock-like states associated with acute pancreatitis. Despite the foregoing, nerve block has been reported as being effective. Pepper (47) reported left paravertebral block T8-T10 with a therapeutic as well as diagnostic effect in four cases of acute pancreatitis. Mallet-Guy produced acute pancreatitis in dogs by electrical stimulation of the left splanchnic nerve. (48) Marion had good results in treatment of acute pancreatitis

by splanchnic block. (49) Gage, Floyd, and Gillespie report excellent results in thirty cases of acute pancreatitis in which splanchnic block was used. (50)(51) Berk (52), advocates the use of fractional epidural block. This consists of introducing a catheter in the interspace between the first and second lumbar vertebrae and then threading it until its tip lies at the level of the sixth thoracic vertebrae. Through the catheter is introduced ten-twenty cc. of 1% procaine and cobefrin initially and fractional instillations of ten cc. made at intervals required to relieve pain. The instillations are usually continued for four to five days. The catheter remains in place , which is an advantage over multiple injections required by other techniques. Despite its merits, nerve block is not invariably effective in relieving pain of severe acute pancreatitis. Moreover, it has been observed by some that the overall course of the disease is not significantly altered even when the pain is successfully relieved. It would seem logical then that nerve block be used in conjunction with other measures in the treatment of acute pancreatitis and should not be considered a substitute for them.

B. Combating shock and correcting fluid and electrolyte imbalances:

Plasma, blood and sodium chloride solutions are given in amounts required to restore fluid volume, sustain blood pressure and insure adequate urinary output. Glucose, either in distilled water or in isotonic saline solutions must be given cautiously to these patients, since carbohydrate metabolism may be seriously impaired by the diffuse inflammation of the gland. Determination of blood sugar should be made therefore before glucose is given and at intervals. In addition, ten units of regular insulin is usually given with each fifty grams of glucose. (53) Whenever insulin is used, it is well to bear in mind that hypoglycemia is a powerful vagal stimulus which should be avoided if at all possible.

At least two other electrolytes deserve special thought in acute pancreatitis. Surprisingly large amounts of calcium may be transferred from the serum to areas of fat necrosis so that soaps are formed from the hydrolyzed fats. Other mechanisms, such as excretion of calcium into the bowel may also contribute to the hypocalcemia. The hypocalcemia thus produced may cause neuromuscular

alterations and even cause myocardial abnormalities. The degree of hypocalcemia bears a close relationship to the severity of the disease and is of difinite prognostic importance. Lowering of serum calcium may be encountered at variable intervals after onset, usually from the second to the fifth day and may persist for two weeks or longer. It is important therefore to make frequent determinations of serum calsium. It is also equally important to replace the loss of calcium from the serum. For this purpose, 20 cc. of 10% calcium gluconate may be give intravenously.

Potassium is the other electrolyte meriting particular attention. Significant decrease in intracellular and serum potassium may result from tissue destruction and urinary loss, diminished intake during the phase of acute illness, the influence of increased secretion of 11-oxysteroids, withdrawal of fluids by nasogastric suction, and intravenous administration of glucose. Depletion of this electrolyte is much more frequent and important than formerly suspected and may be responsible for some of the asthenia, myocardial derangement, and other phenomena seen in patients with

acute pancreatitis. Inclusion of potassium salts in parenteral administered fluids is a basic need. Usually 3 gm. of KCl a day is sufficient, bearing in mind that impairment of renal function is common in acute pancreatitis. Hence potassium salts should not be given without control by frequent determinations of serum potassium levels and electrocardiographic tracings.

C. Reduction of Pancreatic Secretory Activity:

To reduce pancreatic secretion to a minimum it is essential to remove all stimuli known to provoke secretory activity. This requires keeping all foodstuffs out of the stomach and upper small intestine, removal of all gastric secretion to avoid elaboration of secretin by acid in the small intestine and depression to the fullest extent possible of all nervous influences capable of stimulating either the stomach or pancreas.

The first requirement is very simply assured by withholding all food and drink. The second requirement may be met by means of constant nasogastric suction. Care should be taken to place the tip of the tube as close to the pylorus as possible in order to minimize passage of gastric juice into

the duodenum. Suction may be interupted at intervals of about fifteen minutes every two hours, at which time an antacid may be introduced into the stomach. The third requirement may be fulfilled by relieving pain through use of measures previously described, general sedation of the patient, and use of drugs which depress vagal activity. Barbiturates not only reduce nervous excitation but also depress pancreatic secretion. Phenobarbital sodium, 120-180 mg., administered subcutaneously as often as every six hours is a suitable drug for this purpose. In order to interrupt vagal impulses, anticholinergic drugs may be used. Among these, atropine has been used the longest. It is usually given in doses of 0.6 mg. sub- cutaneously every 4-6 hours. Banthine has more recently been shown to diminish pancreatic secretion and , as mentioned earlier, to relieve pain in patients with acute pancreatitis when given in doses of 50-100 mg. every 4-6 hours.

Sympathomimetic drugs generally inhibit pancreatic secretion, perhaps by decreasing the blood flow through the gland. That effect and the vasoconstriction probably responsible for it are definite deterrents to the use of these drugs in

acute pancreatitis. Of this group ephedrine sulfate is the one used most often in doses of 25-50 mg. every 6 hours.

X-ray radiation has been given some consideration as a method of temporarily inhibiting pancreatic secretion. Morton and Widger in 1940 (54) were the first to report the use of X-ray as a method of treatment for acute pancreatitis. They reported three cases in which 250-450 roentgens were given with beneficial effect. Since then successful response has also been reported by others. (55)(56)(57)(58)(59)(60) The primary objective is the suppression of the pancreatic secretion which is largely responsible for the autodigestion of the gland. That this can be accomplished by deep X-ray has been demonstrated by Rauch and Stenstrom in dog experiments. (61) They found that secretion was depressed for days following total dose of 600 r given in 200 r doses on three consecutive days. Despite these encouraging observations, irradiation appears to have little to recommend it as a thera- adjuvant in acute pancreatitis. The secretory inhibiting action of X-rays seem to be variable and the dosage unsettled. It is entirely possible that X-ray may further damage an already injured organ.

D. Combating infection and peritonitis:

Observations in dogs with experimentally produced acute pancreatitis have conclusively demonstrated the lifesaving qualities of penicillin and aureomycin. Aureomycin and oxytetracycline would appear to be the antibiotics of choice because of their concentration in the bile and their greater effectiveness against the type of organisms commonly found in cases of peritonitis. The desirable route of administration of these drugs is orally because of their effect on the bacterial flora of the intestinal tract. Oral administration may be accomplished by introducing a suspension of 0.5 gm. of aureomycin or oxytetracycline through the suction tube every six hours. If this results in nausea, either drug may be given intravenously in amounts of 0.5 gm. every 12 hours.

E. Other measures:

In addition to the foregoing measures, two other means of approach deserve mention. There is reason to believe that abnormal tryptic activity is an important factor in lethal pancreatic necrosis. Trypsin inhibitor, derived from soybean, has been shown to control abnormal tryptic activity in dogs and promises to be of value in patients with acute

pancreatitis. ACTH has thus far also been given a limited trial in this disease. The current opinion based on observation is that even though fall in serum amylase and improvement in shock may follow administration of ACTH, progression of severe hemorrhagic pancreatitis is not prevented. Therefore it remains to be proven whether ACTH and cortisone are of value in the treatment of acute pancreatitis.

If, despite full use and application of the measures outlined above, the clinical situation fails to improve, or becomes more serious because of progressive and spreading peritonitis, unyielding obstructive jaundice, or the development of such complications as hematoma, acute cystic formation or localized suppuration, surgical intervention may become mandatory. What is done at operation is determined by the findings when the abdomen is explored. It is generally agreed, however, that the surgical procedures employed should be the least extensive ones feasible. Most surgeons are content to provide adequate drainage of the lesser peritoneal sac and to establish external biliary drainage. More definitive

corrective procedures directed at the pancreas or biliary tract are postponed until the acute phase of the pancreatitis has subsided.

On the other hand, if the clinical picture shows progressive improvement, conservative medical measures should be continued until the inflammatory process appears to have subsided. There are no fixed criteria determining when the nasogastric tube may be removed, mouth feedings begun, and the medications stopped. These are all determined individually and depend on the clinical status of the patient. As the situation improves, the rigidity with which these measures are applied is gradually relaxed. With subsidence of the clinical signs of pancreatic and peritoneal inflammation, food and fluids may cautiously be given by mouth. At the beginning, warm water and tea in 30cc. amounts may be given, and cereal gruels, strained fruit juices, clear non-fatty diluted broths, gelatin preparations and junket may then be progressively added. Eventually an adequate diet, low in fat and high in carbohydrate and protein is provided.

After complete subsidence, studies should be made to determine the presence of associated biliary

tract disease and the type and extent of residual pancreatic damage. Depending on the results of these studies, an interval operation may be performed to correct any demonstrated biliary tract disease, overcome persistent narrowing of the sphincter of Oddi, draining any pancreatic cyst or residual fluid collection in the lesser peritoneal sac or remove readily accessible pancreatic calculi.

Finally, prior to discharge, the patient should be made to realize that recurrences are possible and perhaps probable. Overeating and the use of alcoholic beverages, both of which appear to be precipitating factors or at least common precursors of acute attacks, should be rigidly avoided. Although none of these precautions guarantees that acute pancreatic inflammation will not recur, they should be observed with the hope of reducing the possiblilty of future attacks.

IV. SUMMARY

The diagnosis of acute pancreatitis, although difficult to make with surety, can be made in a majority of cases if the clinician is aware of it as a possibility in any acute abdomen. Of the physical signs and symptoms, three are outstanding.

Pain, nausea and vomiting are almost universally present in this disease.. Serum amylase elevation is pathognomonic of the disease if it is elevated four to five times the normal level. The antithrombin titer is most valuable in prognosis of the disease as its level closely parallels the course of acute pancreatitis. X-ray is of little value in confirmative diagnosis although several other differential diagnoses can be excluded by this means. EKG studies and serum electrolyte determinations are of little help in diagnosis of this disease.

The management of acute pancreatitis is exceedingly difficult. Relief of pain may be best accomplished by a combination of drugs. Of these, use of Banthine together with denerol and the nitrites would appear most effective. Nerve blocks may be of value in selected cases. Fluid imbalances and shock may be best combated by use of intravenous glucose along with calcium and potassium, watching the level of these ions by frequent determinations. Reduction of pancreatic secretion may be best accomplished by allowing no food by mouth, continuous nasogastric suction and by use of

one of the cholinergic blocking agents such as Banthine. Aureomycin and oxytetracycline are the drugs of choice in controlling infection. Other general supportive measures, diet and vitamins are of value after the acute phase has been controlled.

V. CONCLUSIONS

The many and varied clinical pictures of acute pancreatitis make the diagnosis of this disease very difficult, particularly if the clinician is not constantly aware of it as a possibility. However the diagnosis may be made by use of various laboratory enzyme tests, physical diagnosis and the total clinical picture as outlined in this paper. The prevailing attitude toward treatment of acute pancreatitis is one of conservatism. The major points to be considered in the treatment are: relief of pain, combating shock and correcting fluid and electrolyte imbalances, reduction of pancreatic secretory activity, and combating infections and peritonitis. The management of a case of acute pancreatitis should be a challenge to any physician.

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