THESIS SUBMITTED FOR THE PARTIAL FULFILMENT
OF THE M.D. DEGREE IN GENERAL SURGERY.

INCIDENCE OF PANCREATITIS IN ASSOCIATION WITH CHRONIC CALCULAR CHOLECYSTITIS.

PRESENTED BY

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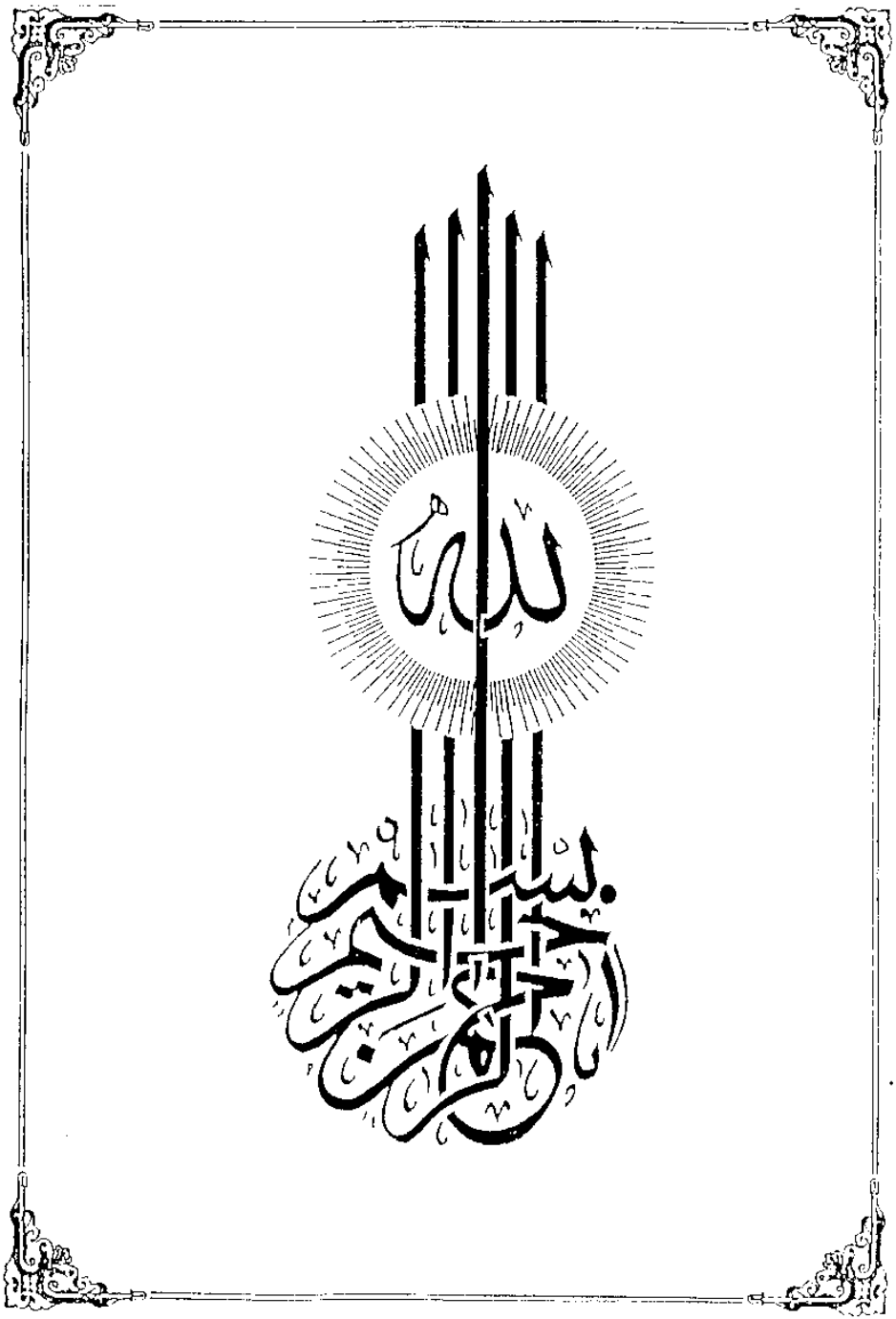
LIVES OF GREAT MEN ALL REMIND US,
WE CAN MAKE OUR LIVES SUBLIME,
ON DEPARTING, LEAVE BEHIND US,
FOOTPRINTS ON THE SANDS OF TIME.

WHITMAN



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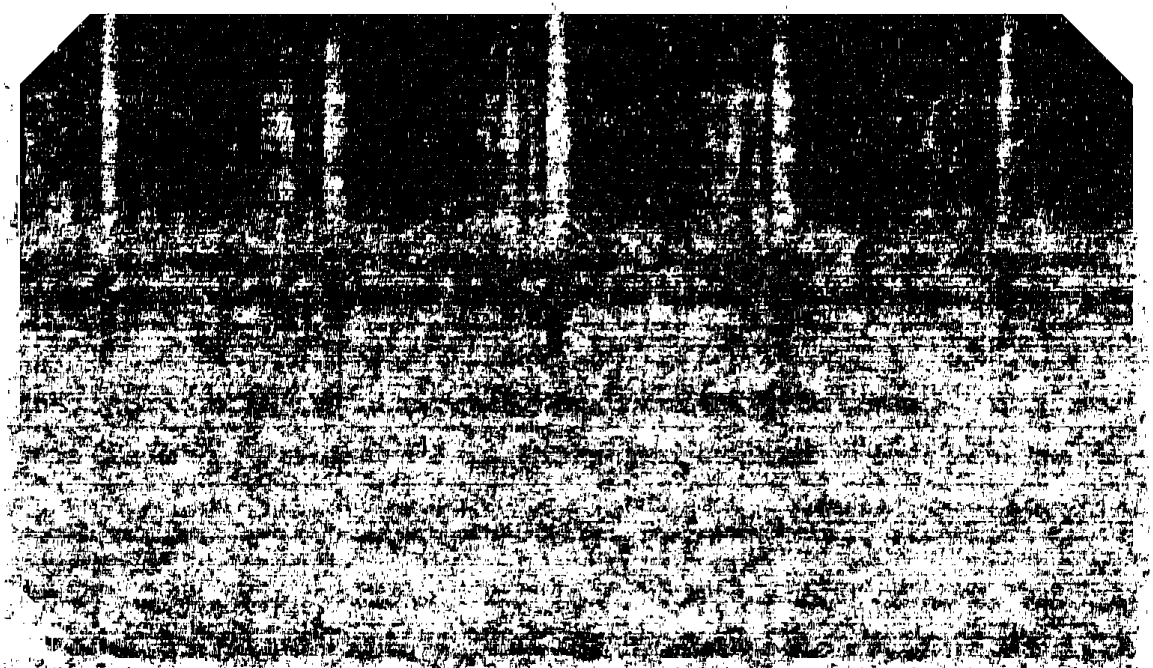


As expected, despite the excellent results from the operative treatment for gallstones, much attention has been directed to the small group of patients (about 10%) who continue to get symptoms after removal of their gallbladder.

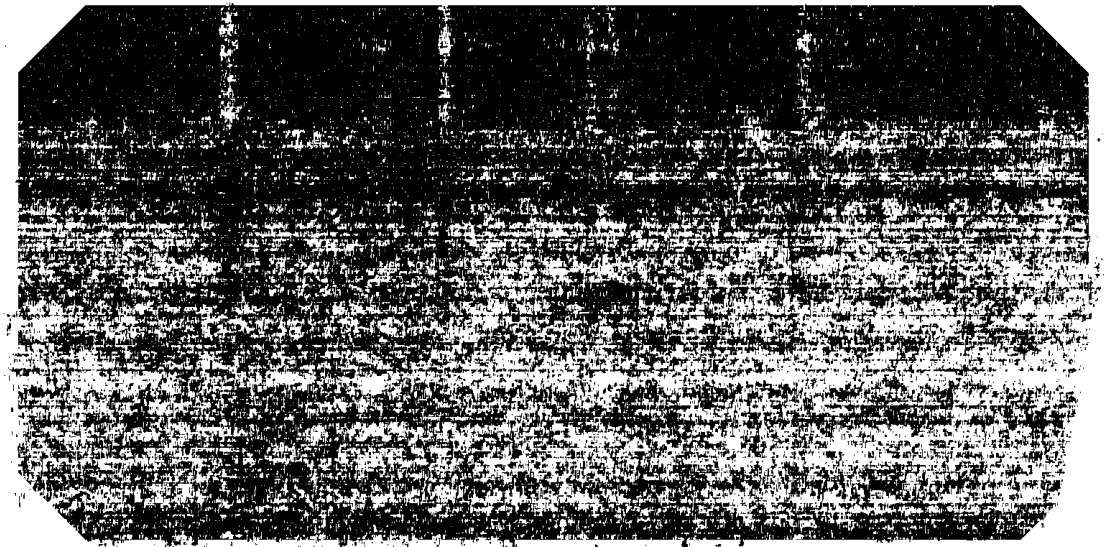
It is obvious that following removal of the gallbladder patients may develop abdominal symptoms due to some totally unrelated abdominal conditions. The problem of postcholecystectomy symptoms really centers around that small group of patients who, after operation, continue to experience the same symptoms as they have had before operation. In these patients, the symptoms may be caused by extrabiliary disorders. The most common of these conditions are chronic pancreatitis, reflux oesophagitis and peptic ulceration. (LE QUESNE and BOLTON, 1980).

Many clinicians feel that biliary tract disease is a much more direct and common cause of both acute and chronic pancreatitis. MAINGOT, (1980), stated that : " Cholecystitis, calculous cholecystitis, choledocholithiasis, stricture of the lower end of the choledochus, papillitis, dysfunction of the sphincter of Oddi, or benign or malignant growths of the ampulla of Vater or periampullary region are important factors, they are responsible for fully 50% of cases of acute and chronic relapsing pancreatitis. "

In a review of etiology of pancreatitis in over 1000 patients, CREUTZFELDT and SCHMIDT, (1970), found that in

approximately one third of their patients, the cause was biliary tract disease.

The mechanism by which biliary tract disease results in pancreatitis is still unknown. (BRADELY and ZEPPA, 1981).



Pancreatitis is a common non bacterial inflammatory disease caused by activation, interstitial liberation, and autodigestion of the pancreas by its own enzymes. The process may or may not be accompanied by permenant morphologic and functional changes in the gland.(REBER and WAY,1985).

Pancreatitis may assume one of several forms. These forms of pancreatitis often overlap.(WARREN,1980).

MODIFIED MARSIELLES CLASIFICATION OF PANCREATITIS:

1)ACUTE PANCREATITIS:

A single episode of pancreatitis in a previously normal gland.

2)ACUTE RELAPSING PANCREATITIS:

Reccurent attacks which do not lead to permenant functional damage, clinical and biological normalcy in intervals between attacks. (HARRISSON, 1982).

3)CHRONIC RELAPSING PANCREATITIS:

Progressive functional damage persisting between attacks, frequent pain free intervals.

4)CHRONIC PANCREATITIS:

Inexorable and irreversable destruction of pancreatic function, constant pain.(BRADELY and ZEPPA,1981).

Acute pancreatitis is by far the most common type. It may be oedemetous or haemorrhagic or a combination of both. It is commonly associated with cholecystitis and gallstones.

abdominal trauma, acute alcohol poisoning or systemic infections for example, mumps. Relapsing pancreatitis is associated with recurrent episodes of acute pancreatitis. It may be related to infections of the gallbladder, to choledocholithiasis, to sclerosing papillitis, or to stenosis of the sphincter of Oddi. The relationship of this form of pancreatitis to alcohol is controversial. Chronic pancreatitis, this progressive disorder leading to sclerosis of the gland and many distressing complications, is commonly associated with alcoholism and less frequently, hyperparathyroidism, familial hyperlipaemia, severe protein-deficiency states and metabolic disturbances.(WARREN, 1980).

The pathophsiology of pancreatitis is very poorly understood despite extensive clinical and experimental studies of this process. It is clear that clinical pancreatitis is associated with biliary tract disease, alcohol consumption, and disorders of lipid metabolism but it is not apparent how these associated processes lead to inflammation within the pancreas. Most students of pancreatitis have concluded that intrapancreatic activation of digestive enzymes synthesized by the pancreas itself occurs during early stages in the evolution of this pancreatitis and that the subsequent inflammatory and necrotic changes represent autodigestion.(STEER, 1984).

The concept that pancreatitis is due to enzymatic digestion of the gland is supported by the finding of proteolytic enzymes

in ascitic fluid and increased amounts of phospholipase A and lysolecithins in pancreatic tissue obtained from patients with acute pancreatitis. (REBER and WAY, 1985).

For many years, trypsin and other proteases were held to be the principal injurious agents, but recent evidence have emphasized phospholipase A, lipase and elastase as possibly of great importance. Trypsin ordinarily does not attack living cells, and even when trypsin is forced into the interstitial spaces, the resulting pancreatitis does not include coagulation necrosis, which is so prominant in human pancreatitis. Phospholipase A, in the presence of small amounts of bile salts attacks free phospholipids (e.g. lecithin) and those bound in cellular membranes to produce extremely potent lyso-compounds. Lysolecithin, which would result from the action of phospholipase A on biliary lecithin, or phospholipase A itself, plus bile salts, is capable of producing severe necrotising pancreatitis. Trypsin is important in this scheme, because small amounts are needed to activate phospholipase A from its inactive precursor. Elastase, which is both elastolytic and proteolytic, is secreted in an inactive form. Because it can digest the walls of blood vessels, elastase has been thought to be important in the pathogenesis of haemorrhagic pancreatitis.(REBER and WAY,1985).

If autodigestion is the final common pathway in pancreatitis, earlier steps must account for the presence of active enzymes and their products in the ducts and their escape into the

interstitium. The following are the most popular theories that attempt to link the known etiologic factors with autodigestion:

A)Obstruction-secretion:

In animals, ligation of the pancreatic duct generally produces a mild oedema of the pancreas that resolves within a week. Thereafter, atrophy of the secretory apparatus occurs. On the other hand, partial or intermittent ductal obstruction, which more closely mimics what seems to happen in humans, can produce frank pancreatitis if the gland is simultaneously stimulated to secrete. The major shortcoming of these experiments has been the difficulty encountered in attempting to cause severe pancreatitis in this way. However, since the human pancreas manufactures 10 times as much phospholipase A as does the dog or rat pancreas, the consequences of obstruction in humans conceivably could be more serious.(REBER and WAY, 1985).

B)Reflux of duodenal contents:

Experimental work suggested that if the intraduodenal pressure is elevated, reflux of the duodenal contents into the pancreatic duct occurs, and this may initiate pancreatitis.(BOUCHIER, 1980). In experimental animals, if the segment of the duodenum into which the pancreatic duct empties is surgically converted to a closed loop, reflux of duodenal juice initiates severe pancreatitis (Pfeffer loop). Pancreatitis associated with acute afferent loop obstruction after Billiroth II gastrectomy is probably the result of

similar factors. Other than in this spesific example, there is no direct evidence for duodenal reflux in the pathogenesis of pancreatitis in humans.(REBER and WAY, 1985).

C)Back diffusion across the pancreatic duct:

Just as the gastric mucosa must serve as a barrier to maintain high concentrations of acid, so must the epithelium of the pancreatic duct prevent diffusion of luminal enzymes into the pancreatic parenchyma. Experiments in cats have shown that the barrier function of the pancreatic duct is vulnerable to several injurious agents, including alcohol and bile acids. Furthermore, the effects of alcohol can occur even after oral ingestion, because alcohol is secreted in the pancreatic juice. Injury to the barrier renders the duct permeable to molecules as large as molocular weight 20000, and enzymes from the lumen may be able to enter the gland and produce pancreatitis. It must be admitted, however, that a coherent explanation of the pathogenesis of pancreatitis is not presently available. In biliary pancreatitis, transient obstruction of the ampulla of Vater by a gallstone is most likely the first event. Whether bile reflux follows is problamatic.(STEER, 1984)

In a review of the etiology of pancreatitis in over 1000 patients, CREUTZFELDT and SCHMIDT, (1970), found that in

approximately one-third of their patients the cause was biliary tract disease, in another one-third the cause was alcoholism, in the remainder, either no cause could be identified or the inflammation was caused by uncommon agents(CREUTZFELDT and SCHMIDT, 1970).

When taken together, biliary tract disease and alcohol are associated with 80 to 90 percent of cases of pancreatitis. Whereas pancreatitis associated with alcohol predominantly occurs in an underpriveleged population, pancreatitis associated with biliary tract disease is characteristically found in the general population.(BRADELY and ZEPPA, 1981).

The association between biliary tract disease and pancreatitis include acute cholecystitis, cholelithiasis, and choledocholithiasis.(BOUCHIER, 1980).

About 40 percent of cases of acute pancreatitis are associated with gallstones, which if untreated, usually give rise to additional acute attacks. For unknown reasons, even repeated attacks of acute biliary pancreatitis fail to produce chronic pancreatitis. Eradication of the biliary disease nearly always prevents recurrent pancreatitis.(REBER and WAY, 1985).

WARREN, (1980), found that cholelithiasis was associated with 28 percent of the patients operated for chronic relapsing pancreatitis. In some of these patients it was impossible to ascertain whether colelithiasis was present before or after the onset of chronic relapsing pancreatitis. In many of the