LEC. 61

MEDICINE

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Lec. 8

PANCREATITIS

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مكتب آشور للاستنساخ

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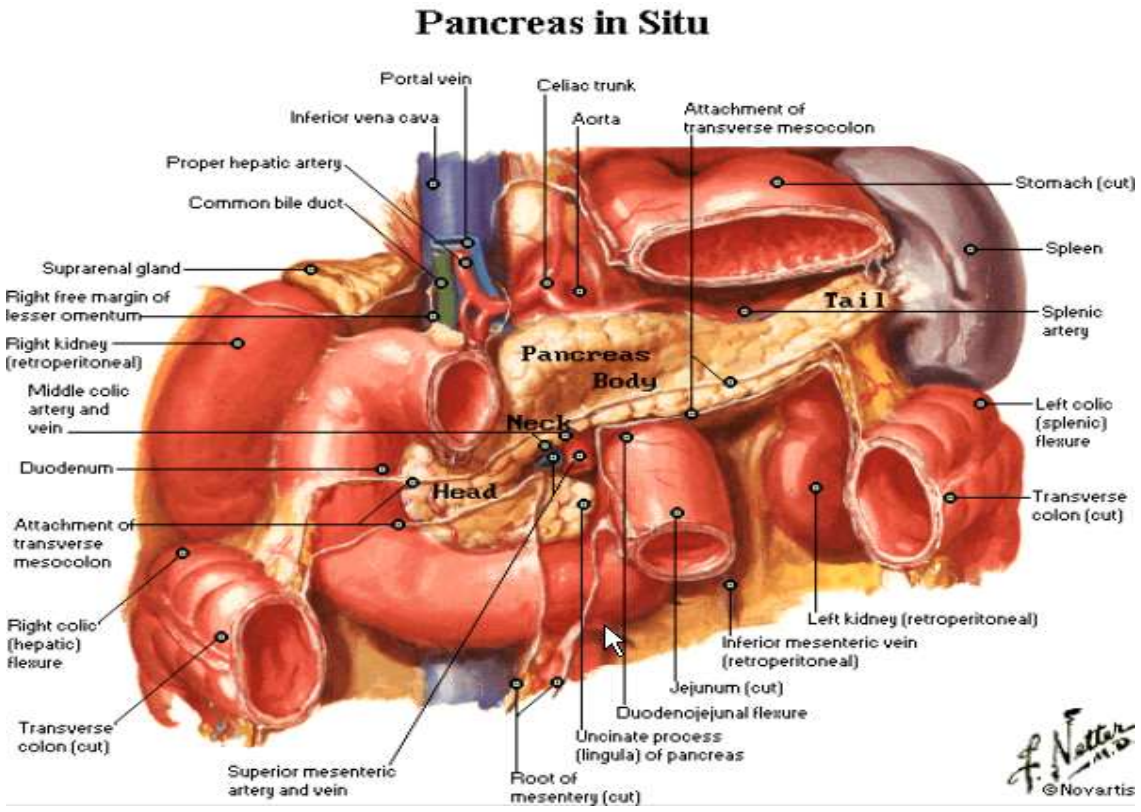
PANCREATITIS

THE PANCREATIC STRUCTURE AND FUNCTION

- *Extends retroperitoneally across the posterior abdominal wall from the second part of the duodenum to the spleen.*
- *The head is encircled by the duodenum; the body, which forms the main bulk of the organ, ends in a tail that lies in contact with the spleen.*
- *The pancreas consists of exocrine and endocrine cells making up 98% of the human pancreas.*
- *The pancreatic acinar cells are grouped into lobules forming the ductal system which eventually joins into the main pancreatic duct.*
- *The main pancreatic duct has many tributary ductules and gradually tapers towards the tail of the pancreas.*
- *The main pancreatic duct itself usually joins the common bile duct to enter the duodenum as a short single duct at the ampulla of Vater.*

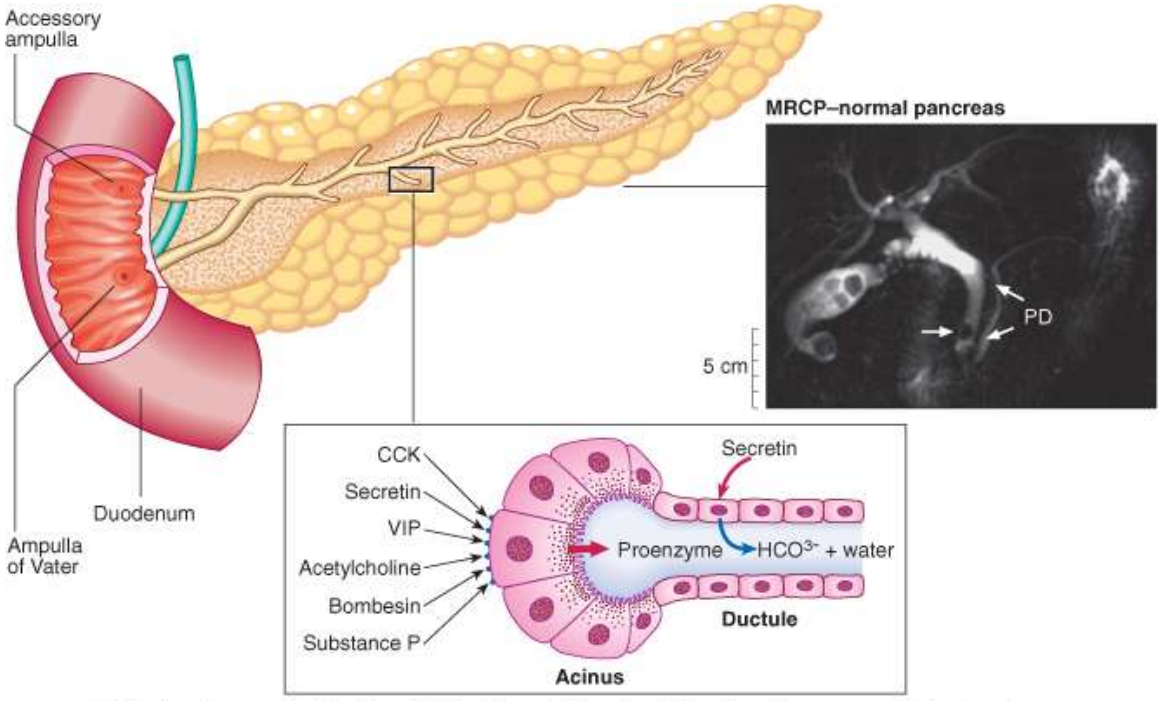


PANCREATIC DIGESTIVE ENZYMES

- *Pancreatic secretion contains multiple enzymes for digesting all of the three major types of food: proteins, carbohydrates, and fats.*
- *It also contains large quantities of bicarbonate ions, which play an important role in neutralizing the acidity of the chyme emptied from the stomach into the duodenum.*
- *The most important of the pancreatic enzymes for digesting proteins are trypsin, chymotrypsin, and carboxypolypeptidase. By far the most abundant of these is trypsin.*
- *Trypsin and chymotrypsin split whole and partially digested proteins into peptides of various sizes but do not cause release of individual amino acids. However, carboxypolypeptidase does split some peptides into individual amino acids, thus completing digestion of some proteins all the way to the amino acid state.*
- *The pancreatic enzyme for digesting carbohydrates is pancreatic amylase, which hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few trisaccharides.*
- *The main enzymes for fat digestion are (1) pancreatic lipase, which is capable of hydrolyzing neutral fat into fatty acids and monoglycerides; (2) cholesterol esterase, which causes hydrolysis of cholesterol esters; and (3) phospholipase, which splits fatty acids from phospholipids.*

THE ENDOCRINE PANCREAS

- *This consists of hormone-producing cells arranged in nests or islets (islets of Langerhans).*
- *The hormones produced are secreted directly into the circulation and there is no access to the pancreatic ductular system.*
- *There are **five main types of islet cells** corresponding to different secretory components.*
  - *The beta-cells for insulin production.*
  - *The alpha-cells produce glucagon.*
  - *The D cells produce somatostatin.*
  - *PP-cells produce pancreatic polypeptide.*
  - *Enterochromaffin cells produce serotonin.*
- *A number of other hormones have been identified within the endocrine pancreas including gastrin-releasing peptide, neuropeptide Y, and galanin. These are believed to be neurotransmitters active in the neuro-gastrointestinal axis*



Pancreatic structure and function

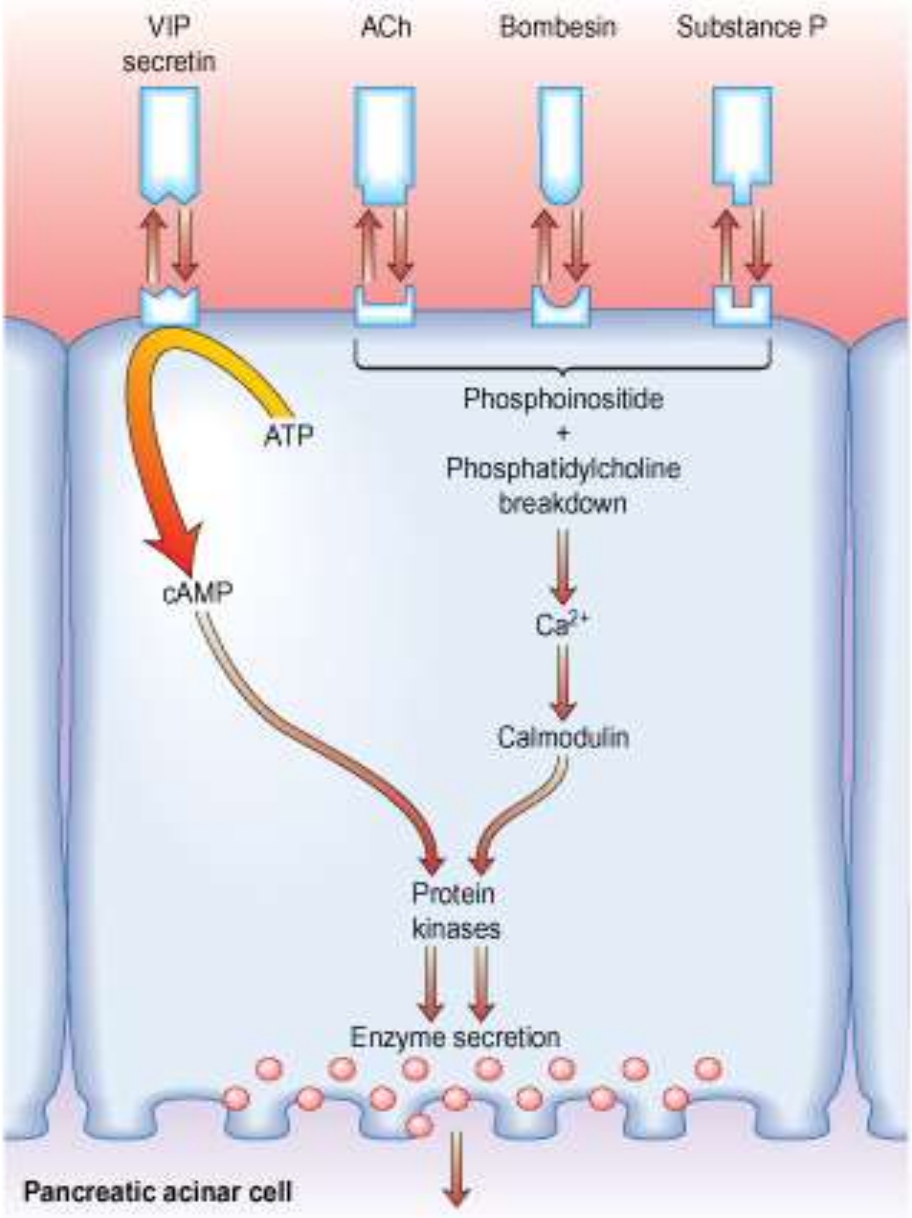


Diagram showing stimulus-secretion coupling of pancreatic cell protein secretion. There is no CCK receptor in humans; stimulation is probably via neural fibres. VIP, vasoactive intestinal polypeptide; CCK, cholecystokinin; ACh, acetylcholine

PANCREATITS DEFINITION AND CLASSIFICATION

Pancreatitis is divided into:-

1- *Acute pancreatitis.*

2- *Chronic pancreatitis.*

Acute pancreatitis: *an acute inflammatory process of the pancreas that may also involve peripancreatic tissues and remote organ systems.*

Pathologically*, two morphologic classifications of acute pancreatitis are recognized:-*

1- *Acute interstitial pancreatitis.*

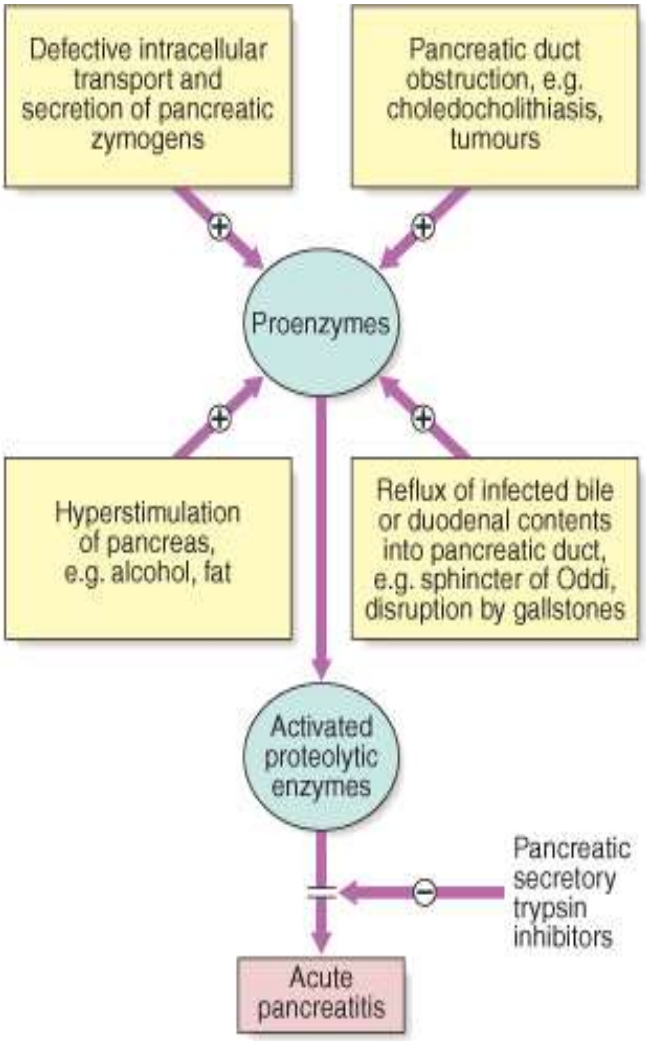
2- *Acute hemorrhagic necrotizing pancreatitis.*

EPIDEMIOLOGY

- *2-28/100,000 of population.*
- *79.8/100,000 per year in US.*
- *5.4/100,000 per year in England.*
- *3% of all cases of abdominal pain admitted to hospital.*
- *80% of cases are mild with mortality less than 5%.*
- *98% of deaths occur in the 20% of severe cases:*
  - *One third occurs within first week → multi-organ failure.*
  - *After that → sepsis.*

PATHOPHYSIOLOGY

- *Acute pancreatitis occurs as a consequence of premature activation of zymogen granules, releasing proteases which digest the pancreas and surrounding tissue.*
- *The severity of acute pancreatitis is dependent upon the **balance** between activity of released proteolytic enzymes and antiproteolytic factors.*
- *Acute pancreatitis is usually mild and self-limiting, with minimal organ dysfunction and uneventful recovery. In some patients, however, it is severe, with local complications such as necrosis, pseudocyst or abscess, and systemic complications leading to multi-organ failure.*



Pathophysiology of acute pancreatitis

ETIOLOGY

Obstructive causes

1- *Gallstones (including microlithiasis).*
2- *Tumors: ampullary or pancreatic tumors.*
3- *Development anomalies: pancreas divisum, choledochocele, annular pancreas.*
4- *Periampullary duodenal diverticula.*
5- *Hypertensive sphincter of Oddi.*
6- *Afferent duodenal loop obstruction.*

Toxins

1- *Ethyl alcohol.*
2- *Methyl alcohol.*
3- *Scorpion venom.*
4- *Organophosphorus insecticides.*

Drugs

Azathioprine, 6-mercaptopurine, sulfonamides, estrogens, tetracycline, valproic acid, metronidazole, furosemide, methyldopa, cimetidine.

Metabolic causes

Hypertriglyceridemia, hypercalcemia, end stage renal disease.

Trauma

1- *Accidental: (especially blunt abdominal trauma).*
2- *Iatrogenic: postoperative, ERCP.*

Infectious

1- *Parasitic: ascariasis, clonorchiasis.*
2- *Viral: mumps, coxsackievirus B, cytomegalovirus, echovirus.*
3- *Bacterial: mycoplasma, tuberculosis, legionella species.*

Vascular

1- *Ischemic: hypoperfusion (such as post cardiac surgery).*
2- *Vasculitis: SLE, polyarteritis nodosa.*

Idiopathic

Miscellaneous

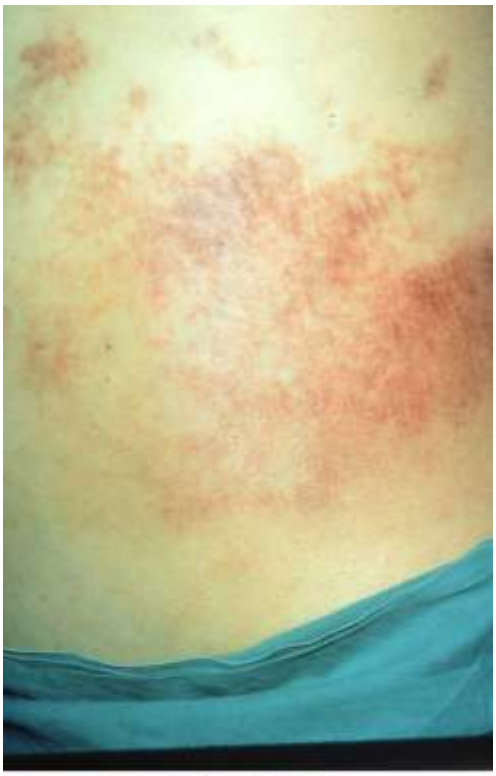
1- *Penetrating PU.*
2- *Crohn disease of the duodenum.*
3- *Pregnancy associated.*
4- *Pediatric association: Reye syndrome , cystic fibrosis.*

CLINICAL FEATURES

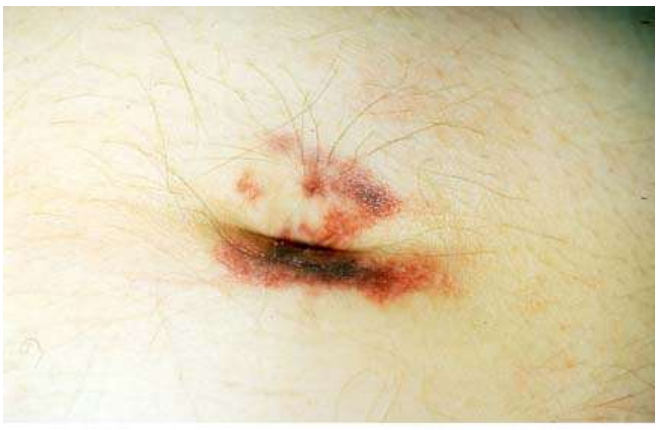
1- *Severe, constant upper abdominal pain (usually begins in the epigastrium), involvement of the retroperitoneum lead to radiation of pain to the midback in **65%** of cases, builds up over **15-60** minutes. The pain typically last for hours to days and not relieved by vomiting.*
2- *Nausea and vomiting are common.*
3- *Marked epigastric tenderness, but in early stages guarding and rebound tenderness are absent.*
4- *Bowel sounds become quiet or absent (paralytic ileus).*
5- *Hypoxic, hypovolemia shock, oliguria in severe cases.*
6- *Discoloration of the flanks (Grey Turner's sign) ,or periumbilical region (Cullen's sign) is a feature of severe pancreatitis with haemorrhage.*

7- *In patients with a gallstone aetiology the clinical picture may also include the features of jaundice or cholangitis.*

8- *Fever usually less than 38.5 C.*



Grey-Turner's sign



Cullen's sign

DIAGNOSIS

Blood tests

1- **S.Amylase:** *extremely sensitive test if it's 3 times the upper limit of normal when measured within 24 hours of the onset of pain. It falls back gradually towards normal over the next 3-5 days.*

Elevation of serum amylase unrelated to pancreatitis:

I. *Leakage of upper gastrointestinal contents into the peritoneum:*

- *Upper gastrointestinal perforation.*
- *Biliary peritonitis.*
- *Intestinal infarction.*

II. *Inherited abnormalities of amylase:*

- *Macroamylasaemia.*

2- ***Urinary amylase**: may be diagnostic as remain elevated over a **longer** period of time.*

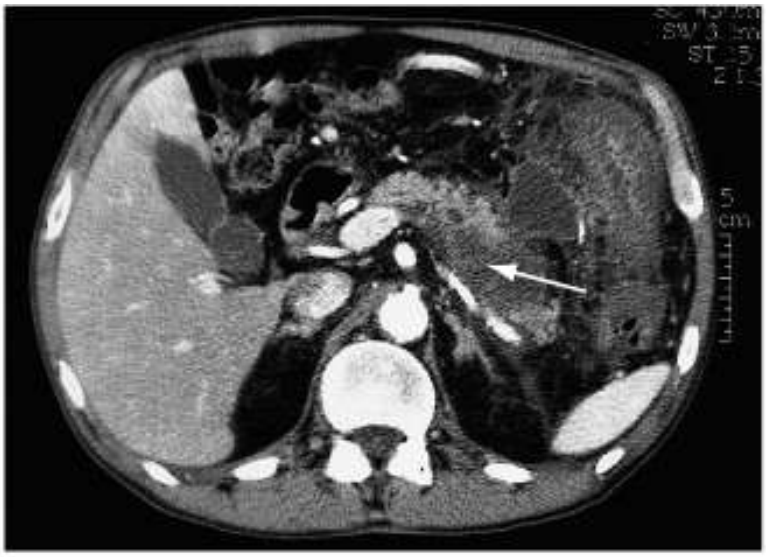
3- ***Serum lipase**: remains elevated for a longer period of time than those of amylase but accuracy is not greater than amylase and technically difficult.*

4- ***C reactive protein**: useful in assessment and prognosis.*

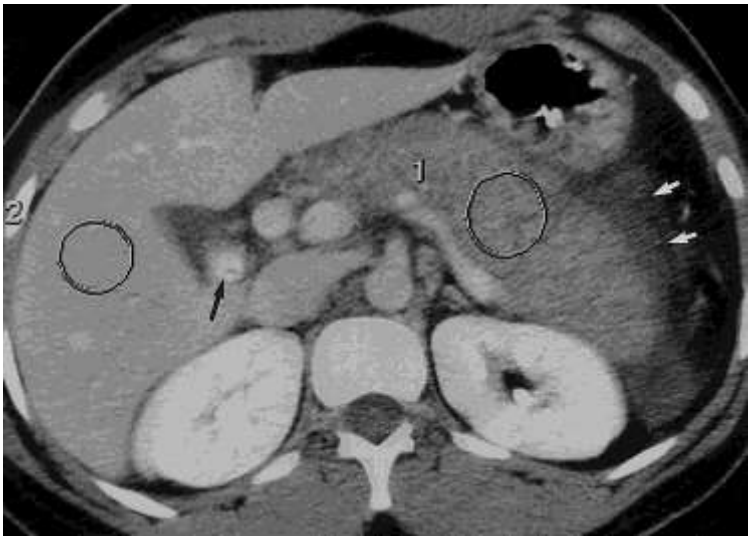
5- ***Full blood count, urea, electrolytes, blood glucose, liver biochemistry, plasma calcium, and arterial blood gases**, used for assessment.*

Radiology

1. ***An erect chest X-ray*** *is mandatory to exclude gastroduodenal perforation, which also raises the serum amylase. A supine abdominal film may show gallstones or pancreatic calcification.*
2. ***An abdominal ultrasound scan*** *is used as a screening test to identify a possible biliary (gallstone) cause of pancreatitis. Gallstones are difficult to detect in the distal common bile duct but dilated intrahepatic ducts may be present in the presence of bile duct obstruction. Stones within the gall bladder are not sufficient to justify a diagnosis of gallstone-related pancreatitis. The ultrasound may also demonstrate pancreatic swelling and necrosis as well as peripancreatic fluid collections if present. In severe pancreatitis the pancreas may be difficult to visualize because of gas-filled loops of bowel.*
3. ***Contrast-enhanced spiral CT scanning*** *is essential in all but the mildest attacks of pancreatitis. Carried out within 2-3 days of presentation, it allows the extent of pancreatic necrosis to be assessed. This provides very valuable prognostic information. Later in the course of the disease, repeated CT scans may be used to detect other complications including fluid collections, abscess formation, and pseudocyst development.*
4. ***MRI (MRCP)*** *can assess the degree of pancreatic damage and identify gallstones within the biliary tree. MRI is particularly useful to differentiate between fluid and solid inflammatory masses.*
5. ***ERCP*** *is used as a treatment measure to remove bile duct stones in the presence of gallstone-related pancreatitis.*

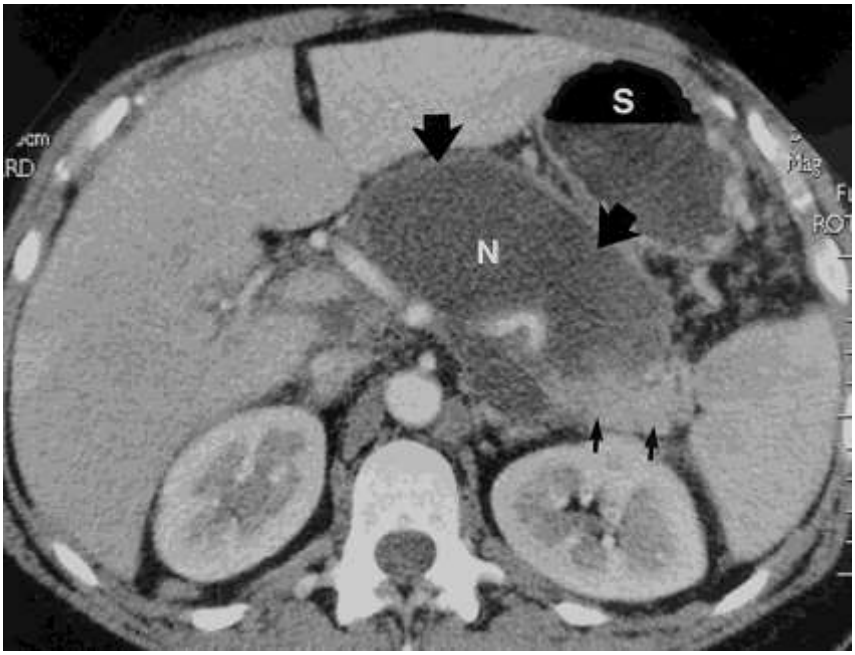


CT scan in patient with acute pancreatitis *showing necrosis of the pancreatic parenchyma (arrow) and a fluid collection extending outside the gland with inflammatory thickening of the colon.*



Gallstone-induced pancreatitis in 27 year-old woman

Transverse CT scan obtained with intravenous and oral contrast material reveals a large, edematous, homogeneously attenuating (73-HU) pancreas (1) and peripancreatic inflammatory changes (white arrows). Although the attenuation values are low, there is no pancreatic necrosis. Calcified gallstones are seen in gallbladder (black arrow). 2 = liver (140 HU).



50 year-old woman with acute pancreatitis (1st view)

(a, b) *Transverse CT scans obtained with intravenous and oral contrast material reveal an encapsulated fluid collection associated with liquefied necrosis (large straight arrows) in the body of the pancreas. The head, part of the body, and the tail of the pancreas are still enhancing (small straight arrows). N = liquefied gland necrosis, S = stomach.*

ASSESSMENT OF DISEASE SEVERITY

- *The majority of cases of acute pancreatitis are mild, but approximately 25% run a more complicated course which may result in haemodynamic instability and multiple organ failure. The early prediction of such a severe attack allows appropriate monitoring and intensive care to be in place.*
- *Factors during the first 48 hours that indicate severe pancreatitis & a poor prognosis (three or more factors present predict a severe episode): -*
  - *Age> 55 years, WBC> 15 ×109/L, Blood glucose> 10 mmol/L, Serum urea> 16 mmol/L, Serum albumin< 30 g/L, Serum aminotransferase> 200 U/L, Serum calcium< 2 mmol/L, Serum LDH> 600 U/L, Pao2< 8.0 kPa (60 mmHg).*

- *The Ranson and Glasgow scoring systems are based on such parameters and have been shown to have an 80% sensitivity for predicting a severe attack .*

THE APACHE II SCORING SYSTEM PARAMETERS

Physiological

- *Temperature.*
- *Heart rate.*
- *Respiratory rate.*
- *Mean arterial pressure.*
- *Glasgow Coma Scale.*

Laboratory

- *Oxygenation (Pao2).*
- *Arterial pH.*
- *Serum: sodium, potassium, creatinin levels.*
- *Haematocrit.*
- *White blood cells count.*

RANSON'S CRITERIA

Ranson's criteria on admission:

- *Age greater than 55 years.*
- *A white blood cell count of > 16,000/µL.*
- *Blood glucose > 11 mmol/L (>200 mg/dL).*
- *Serum LDH > 350 IU/L.*
- *Serum AST >250 IU/L.*

Score 0-2: 2% mortality
Score 3-4: 15% mortality
Score 5-6: 40% mortality
Score 7-8: 100% mortality

Ranson's criteria after 48 hours of admission:

- *Fall in hematocrit by more than 10 percent.*
- *Fluid sequestration of > 6 L.*
- *Hypocalcemia (serum calcium < 2.0 mmol/L (<8.0 mg/dL)).*
- *Hypoxemia (PO2 < 60 mmHg).*
- *Increase in BUN to >1.98 mmol/L (>5 mg/dL) after IV fluid hydration.*
- *Base deficit of >4 mmol/L.*

COMPLICATIONS

Local complications:

1. *Fluid collections.*
2. *Pancreatic necrosis.*
3. *Acute pseudocyst.*
4. *Pancreatic abscess.*

Systemic complications:

1. *Systemic inflammatory response syndrome (SIRS).*
2. *Respiratory complications: most frequent systemic complications. Hypoxemia occurs within first 48 hr.*
3. *Hyperglycemia.*
4. *Hypocalcaemia.*
5. *Reduced serum albumin concentration.*
6. *GI bleeding (gastric or duodenal erosions).*
7. *Renal failure.*
8. *Pancreatic encephalopathy.*
9. *Subcutaneous fat necrosis and bone abnormalities.*

DIFFERENTIAL DIAGNOSIS

1. *Biliary colic.*
2. *Perforated hollow viscus.*
3. *Mesenteric ischemia.*
4. *Closed-loop intestinal obstruction.*
5. *Inferior wall MI.*
6. *Dissecting aneurysm.*
7. *Ectopic pregnancy.*

TREATMENT

- ***The initial management of acute pancreatitis is similar, whatever the cause.***
- *A multiple factor scoring system (ideally APACHE II with a modification for obesity) should be carried out at the end of the first 24 hours after presentation to allow identification of the 25% of patients with a predicted severe attack. This should be repeated at 48 hours to identify a further subgroup who appear to be moving into the severe category.*
- *Early fluid losses in acute pancreatitis may be large, requiring well-maintained intravenous access as well as a central line and urinary catheter to monitor circulating volume and renal function.*
- *Naso-gastric suction: prevents abdominal distension and vomitus and hence the risk of aspiration pneumonia.*
- *Baseline arterial blood gases determine the need for continuous oxygen administration.*
- *Prophylactic antibiotics are not indicated unless there are infective complications (broad-spectrum antibiotics).*
- *Analgesia requirements: pethidine and tramadol are the drugs of choice. The morphine derivatives should be avoided because they can cause sphincter of Oddi contraction.*
- *Feeding: nn patients with a severe episode there is a little likelihood of oral nutrition for a number of weeks. Total parenteral nutrition has been associated with a high risk of infection and has been replaced by enteral nutrition. This is administered via a naso-jejunal tube, which is well tolerated and can maintain adequate nutritional input.*
- *In a small proportion of patients, multiorgan failure will develop in the first few days after presentation reflecting the extent of pancreatic necrosis. Such patients will require positive-pressure ventilation and often renal support.*

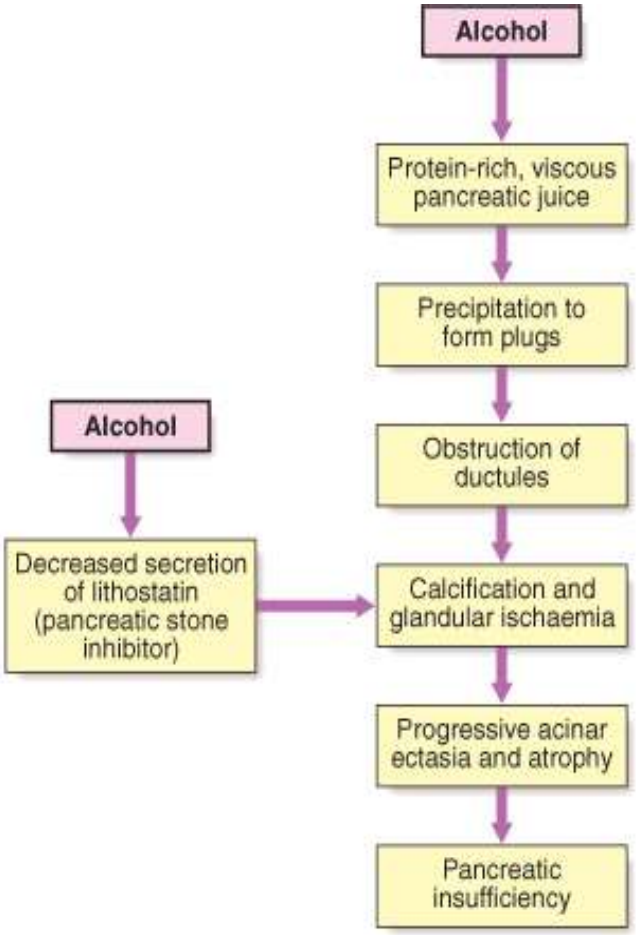
- ⇨ *Prophylaxis of thromboembolism with low-dose subcutaneous heparin is advisable.*
- ⇨ *Gallstone-related pancreatitis and associated cholangitis, endoscopic intervention with sphincterotomy and stone extraction is of proven benefit and is the treatment of choice.*

CHRONIC PANCREATITIS

- *It is a chronic inflammatory condition characterized by fibrosis, destruction of exocrine tissue and eventually destruction of exocrine and endocrine tissue.*
- *Chronic pancreatitis predominantly affects middle-aged alcoholic men.*

AETIOLOGY

1. *In developed countries the most common cause is alcohol in 60-80% of cases.*
2. *In developing countries malnutrition – induced (tropical) is the most prevalent.*
3. *In a small group of patients chronic pancreatitis has been shown to be hereditary.*
4. *Almost all patients with cystic fibrosis have established chronic pancreatitis, usually from birth.*
5. *Obstruction of the pancreatic duct because of either a benign or malignant process may result in chronic pancreatitis.*
6. *Congenital abnormalities of the pancreatic duct, in particular pancreas divisum.*
7. *20% of cases are idiopathic.*
8. *Trauma or prolonged metabolic disturbance.*
9. *Autoimune pancretitis – IGg4*



Pathophysiology of chronic pancreatitis

CLINICAL FEATURES

- *Almost all present with abdominal pain. Usually epigastric and often radiates through into the back. Pain is due to a combination of increased pressure within the pancreatic ducts and direct involvement of pancreatic and peripancreatic nerves by the inflammatory process. Approximately one-fifth of patients chronically consume opiate analgesics.*
- *Weight loss is common and results from a combination of anorexia, avoidance of food because of post - prandial pain, malabsorption and/or diabetes.*
- *Steatorrhoea occurs when more than 90% of the exocrine tissue has been destroyed; protein malabsorption only develops in the most advanced cases.*

- *Overall, 30% of patients are diabetic, but this figure rises to 70% in those with chronic calcific pancreatitis.*
- *O/E: reveals a thin, malnourished patient with epigastric tenderness. Skin pigmentation over the abdomen and back is common and results from chronic use of a hot water bottle (erythema ab igne). Many patients have features of other alcohol- and smoking-related diseases*

INVESTIGATIONS

Tests to establish the diagnosis

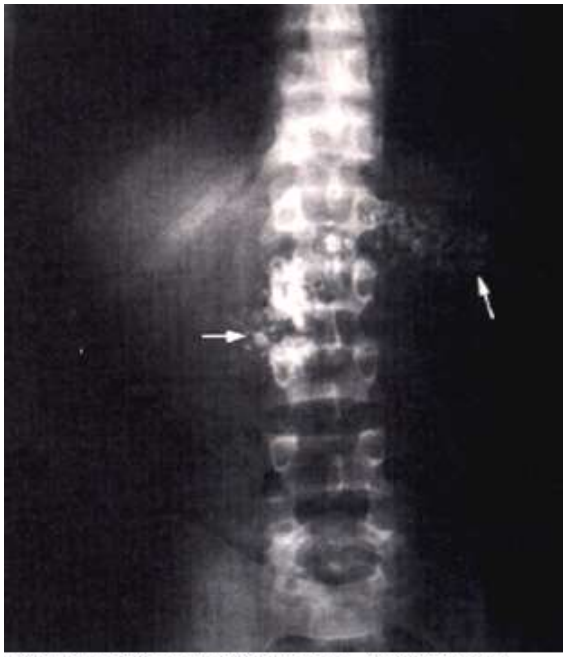
- *Ultrasound.*
- *CT (may show atrophy, calcification or ductal dilatation).*
- *Abdominal X-ray (may show calcification).*
- *MRCP.*
- *Endoscopic ultrasound.*

Tests of pancreatic function

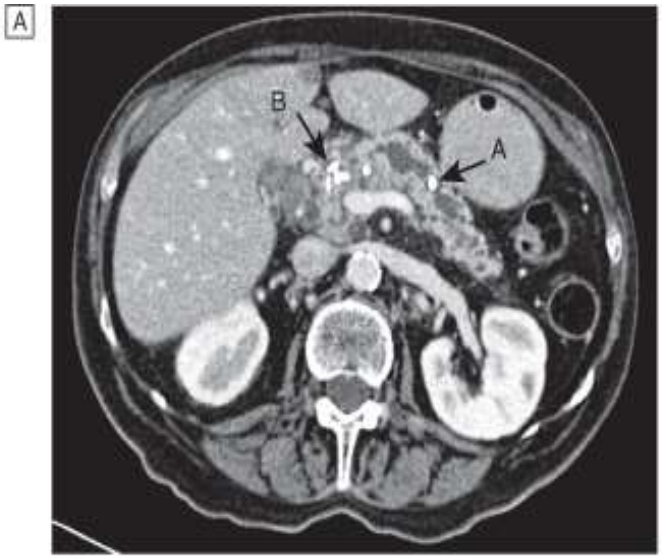
- *Collection of pure pancreatic juice after secretin injection (gold standard but invasive and seldom used).*
- *Faecal pancreatic chymotrypsin or elastase.*
- *Oral glucose tolerance test.*

Tests of anatomy prior to surgery

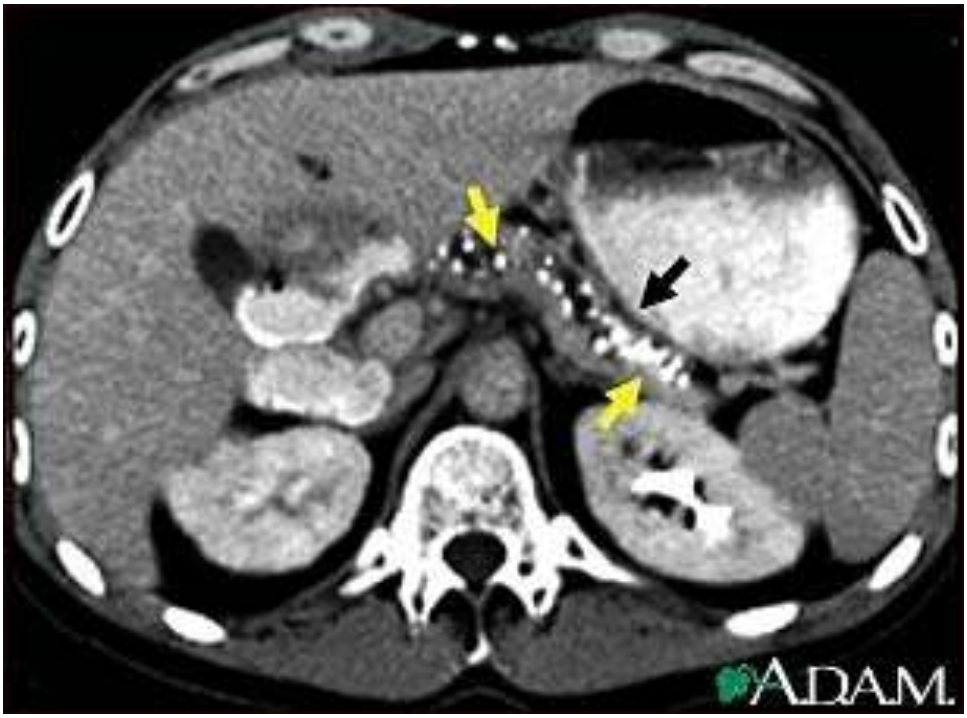
- *MRCP.*



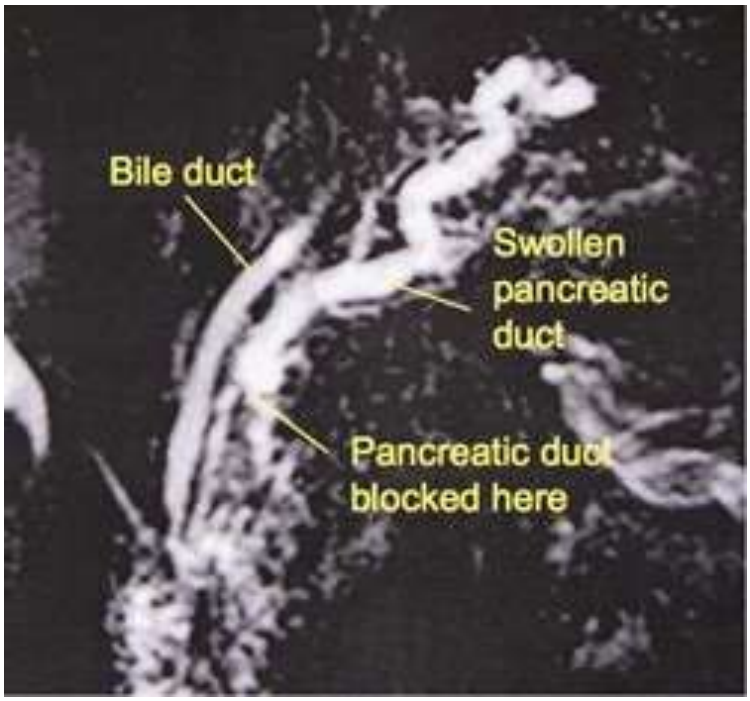
Pancreatic calcifications Plain film of the abdomen shows pancreatic calcifications (arrows) in a patient with chronic pancreatitis. (With permission from Steer, ML, Waxman, I, Freedman, SD, N Engl J Med 1995; 332:1482.)



Imaging in chronic pancreatitis. CT scan showing a grossly dilated and irregular duct with a calcified stone (arrow A). Note the calcification in the head of the gland (arrow B). MRCP of the same patient showing marked ductal dilatation with abnormal dilated side branches (arrows A). A small cyst is also present (arrow B).



CT scan of the upper abdomen showing multiple white-colored calcifications. These occur in chronic pancreatitis



This MRCP picture shows chronic pancreatitis causing a narrowing of the pancreatic duct, with a swollen tortuous duct visible upstream

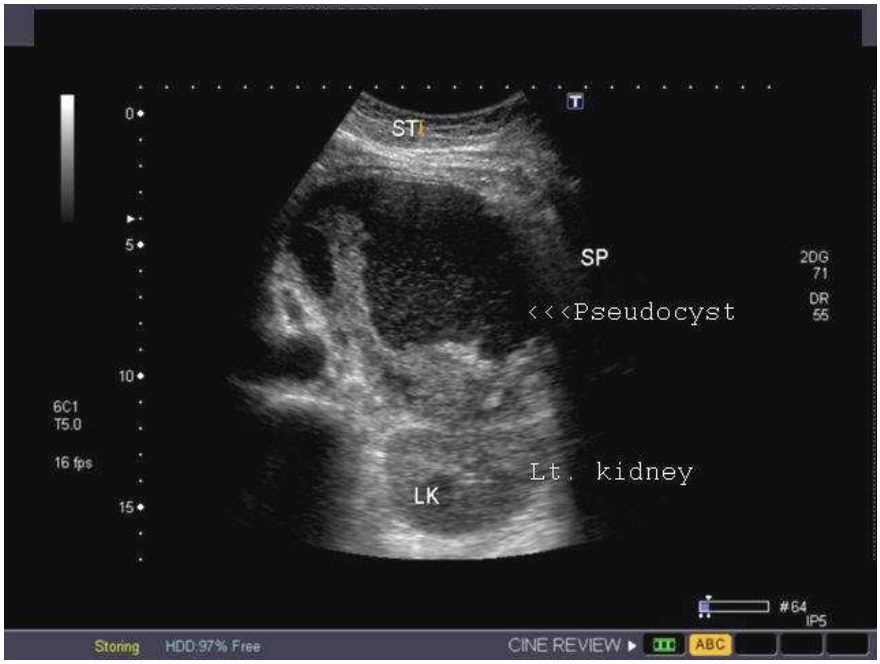
COMPLICATIONS

- *Pseudocysts and pancreatic ascites, which occur in both acute and chronic pancreatitis.*
- *Extrahepatic obstructive jaundice due to a benign stricture of the common bile duct as it passes through the diseased pancreas.*
- *Duodenal stenosis.*
- *Portal or splenic vein thrombosis leading to segmental portal hypertension and gastric varices.*
- *Peptic ulcer.*

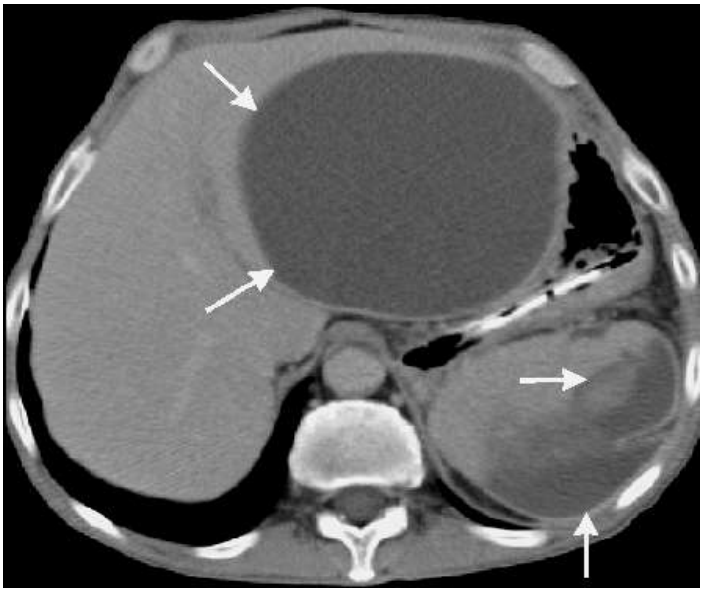
PANCREATIC PSEUDOCYST

- *It's the most common structural complication of chronic pancreatitis.*
- *It's a fluid collection surrounded by granulation tissue.*
- *Intra- or retroperitoneal rupture, bleeding or cyst infection occurs.*
- *The larger cysts may occlude nearby structures including the duodenum and the bile duct.*
- *In pseudocysts, less than 6 cm in diameter, spontaneous resolution can be anticipated.*
- *In larger cysts that have been present for a period in excess of 6 weeks, resolution is uncommon and a long-term complication rate of approximately 30% can be anticipated.*
- *Many pseudocysts are closely opposed to the posterior wall of the stomach or duodenum and can be successfully drained endoscopically using endoscopic ultrasound to identify the optimum drainage site. A direct fistula is created between the pseudocyst lumen and the gastric or duodenal lumen which is then kept patent by the insertion of plastic stents. This approach will be successful in approximately 75% of cases.*

- *Surgical drainage is required for failures of endoscopic therapy or in circumstances in which the pseudocyst anatomy does not allow endoscopic access*



Pancreatic pseudocyst



CT examination: A giant, sharp-contoured, hypodense lesion is depicted (arrows). Is pancreatic pseudocyst in the omental bursa

MANAGEMENT

- *Alcohol avoidance is crucial in halting the progression of the disease and reducing pain. Unfortunately, the majority of patients continue to drink alcohol.*
- *Pain relief: for short-term flare-ups of pain a combination of a non-steroidal anti-inflammatory drug and an opiate (tramadol) is usually sufficient for symptomatic relief, but the severe and unremitting nature of the pain often leads to opiate use with the risk of addiction.*
- *Tricyclic antidepressants are used for chronic pain and reduce the need for opiates.*
- *Oral pancreatic enzyme supplements suppress pancreatic secretion (by a negative-feedback mechanism) and their regular use reduces analgesic consumption in some patients.*
- *Patients who are abstinent from alcohol and who have severe chronic pain which is resistant to conservative measures are considered for surgical or endoscopic pancreatic therapy. Coeliac plexus nerve block or minimally invasive thoracoscopic splanchnicectomy sometimes produces long-lasting pain relief although relapse eventually occurs in the majority of cases.*
- *Steatorrhoea associated with pancreatic insufficiency may be high, with up to 30 mmol of fat lost per 24 hours. This will usually improve with pancreatic enzymes supplements and a low fat diet.*
- *Current preparations are presented in the form of microspheres which reduce the problems of acid degradation in the stomach. An acid suppressor (H2-receptor antagonist PPI) is also given.*

... END ...