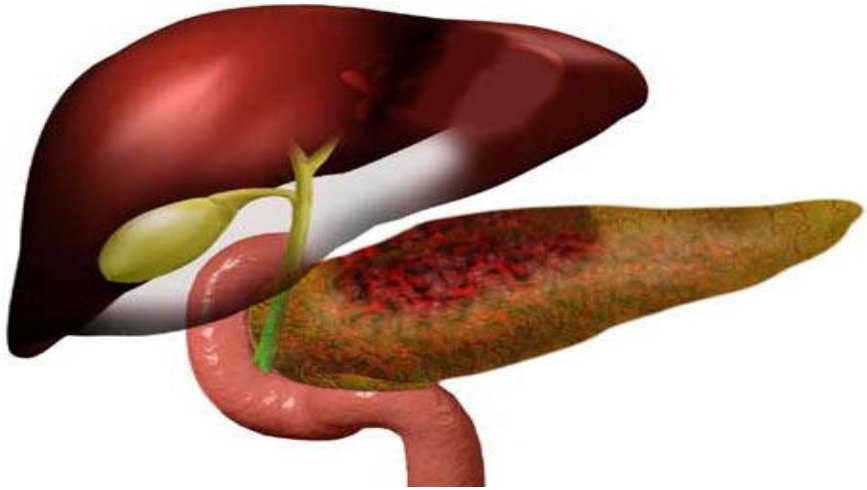
DISEASES OF THE PANCREAS

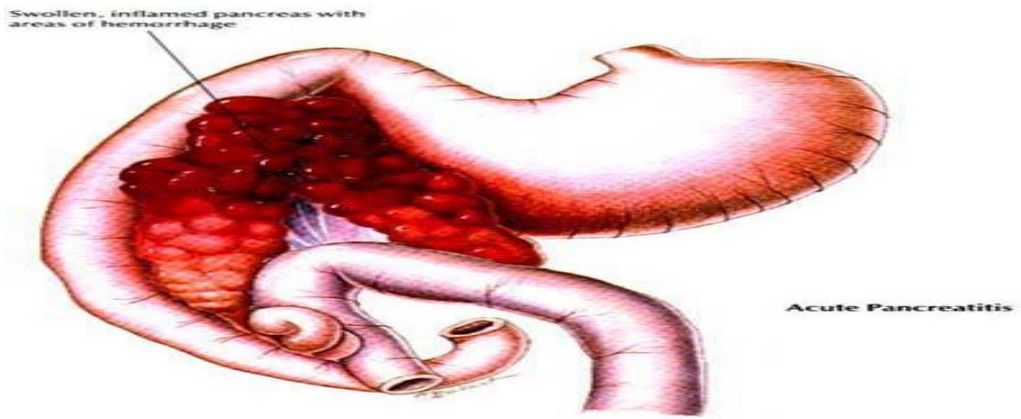
Acute pancreatitis

- () Acute pancreatitis accounts for 3% of all cases of abdominal pain admitted to hospital.
- () It affects 2-28 per 100 000 of the population and may be increasing in incidence.
- () mortality rate 10%.
- () One-third of death occur within the first week, usually from multi-organ failure. After this time the majority of deaths result from sepsis.
- () At admission it is possible to predict patients at risk of these complications:



Adverse prognostic factors in acute pancreatitis (Glasgow criteria)*

- Age > 55 years
- PO_2 < 8 kPa (60 mmHg)
- White blood cell count (WBC) > 15×10^9/L
- Albumin < 32 g/L
- Serum calcium < 2 mmol/L (8 mg/dL) (corrected)
- Glucose > 10 mmol/L (180 mg/dL)
- Urea > 16 mmol/L (45 mg/dL) (after rehydration)
- Alanine aminotransferase (ALT) > 200 U/L
- Lactate dehydrogenase (LDH) > 600 U/L



Factors that may predict severe pancreatitis within 48 hours of admission

Initial assessment:

- Clinical impression of severity
- Body mass index > 30
- Pleural effusion on chest X-ray
- APACHE II score > 8

24 hrs after admission:

- Clinical impression of severity
- APACHE II score > 8
- Glasgow score ≥ 3
- Persisting organ failure, especially if multiple
- CRP > 150 mg/L

48 hrs after admission:

- Clinical impression of severity
- Glasgow score ≥ 3
- CRP > 150 mg/L
- Persisting organ failure for 48 hrs
- Multiple or progressive organ failure

Pathophysiology

- () Acute pancreatitis occurs as a consequence of premature activation of proteolytic enzymes, releasing proteases which digest the pancreas and surrounding tissue.
- () Acute pancreatitis is often self-limiting.
- () In some patients, however, it is severe, with local complications such as necrosis, pseudocyst or abscess, and systemic complications leading to multi-organ failure.

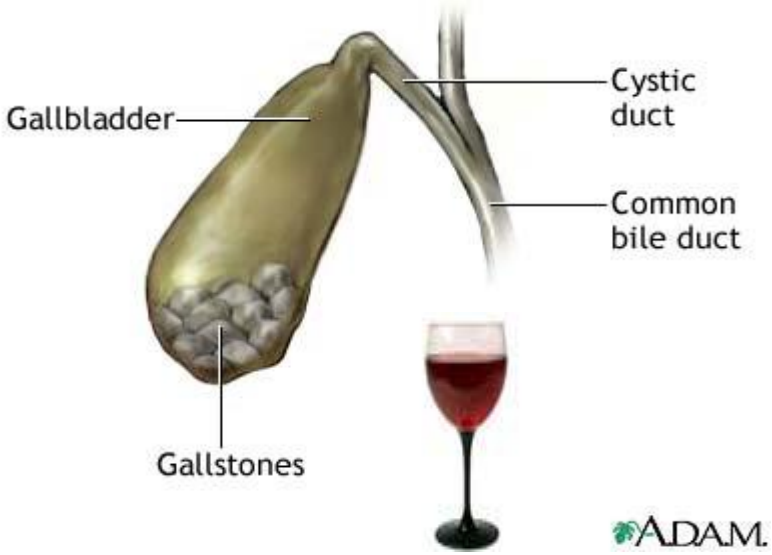
Causes of acute pancreatitis

Common (90% of cases)

- Gallstones
- Idiopathic
- Alcohol
- Post-ERCP

Rare:

- Post-surgical (abdominal, cardiopulmonary bypass)
- Trauma
- Drugs (azathioprine, thiazide diuretics, sodium valproate)
- Metabolic (hypercalcaemia, hypertriglyceridaemia)
- Pancreas divisum
- Sphincter of Oddi dysfunction
- Infection (mumps, Coxsackie virus)
- Hereditary
- Renal failure
- Organ transplantation (kidney, liver)
- Severe hypothermia
- Petrochemical exposure



Clinical features

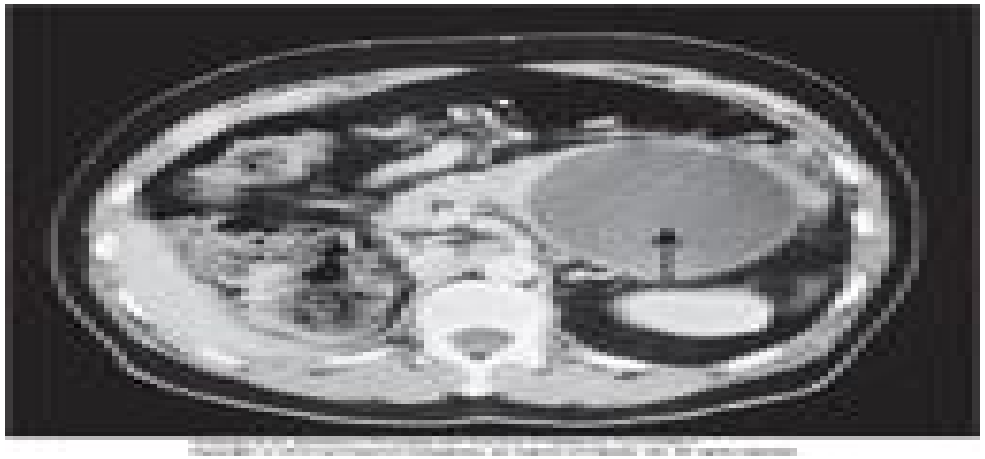
- () Severe, constant upper abdominal pain which radiates to the back in 65% of cases builds up over 15-60 minutes.
- () Nausea and vomiting are common.
- () There is marked epigastric tenderness, but in the early stages guarding and rebound tenderness are absent because the inflammation is principally retroperitoneal.
- () Bowel sounds become quiet or absent as paralytic ileus develops.
- () In severe cases the patient becomes hypoxic and develops hypovolaemic shock with oliguria.

- () Discoloration of the flanks (Grey Turner's sign) or the periumbilical region (Cullen's sign) is a feature of severe pancreatitis with haemorrhage.
- () An acute pancreatic pseudocyst is a localised peripancreatic collection of pancreatic juice and debris which usually develops in the lesser sac following inflammatory rupture of the pancreatic duct. The pseudocyst is initially contained within a poorly defined, fragile wall of granulation tissue which matures over a 6-week period to form a fibrous capsule
- () Small intrapancreatic cysts and pseudocysts are common and resolve as the pancreatitis recovers, but those greater than 6 cm seldom disappear spontaneously and can cause abdominal pain and may compress or erode surrounding structures including blood vessels to form pseudoaneurysms.
- () Pancreatic ascites occurs when fluid leaks from a disrupted pancreatic duct into the peritoneal cavity. Leakage into the thoracic cavity can result in a pleural effusion or a pleuro-pancreatic fistula.

Complications of acute pancreatitis

Systemic

- Systemic inflammatory response syndrome (SIRS): Increased vascular permeability from cytokine, platelet aggregating factor and kinin release
- Hypoxia: Acute respiratory distress syndrome (ARDS) due to microthrombi in pulmonary vessels
- Hyperglycaemia: Disruption of islets of Langerhans with altered insulin/glucagon release
- Hypocalcaemia: Sequestration of calcium in fat necrosis, fall in ionised calcium
- Reduced serum albumin concentration: Increased capillary permeability



Pancreatic

- Necrosis: Non-viable pancreatic tissue and peripancreatic tissue death; frequently infected
- Abscess: Circumscribed collection of pus close to the pancreas and containing little or no pancreatic necrotic tissue
- Pseudocyst: Disruption of pancreatic ducts
- Pancreatic ascites or pleural effusion: Disruption of pancreatic ducts

Gastrointestinal

- Upper gastrointestinal bleeding: Gastric or duodenal erosions
- Variceal haemorrhage: Splenic or portal vein thrombosis
- Erosion into colon
- Duodenal obstruction: Compression by pancreatic mass
- Obstructive jaundice: Compression of common bile duct

Investigations

() The diagnosis of acute pancreatitis is based upon finding raised serum amylase or lipase concentrations and ultrasound or CT evidence of pancreatic swelling.

() Plain X-rays are taken to exclude other diagnoses such as perforation or obstruction and to identify pulmonary complications.

()serum amylase:

1- Amylase is elevated within 24-48 hours after the onset of pancreatitis.

2- elevated urinary amylase:creatinine ratio.

3- A persistently elevated serum amylase concentration suggests pseudocyst formation.

4- Peritoneal amylase concentrations are massively elevated in pancreatic ascites.

5- Serum amylase concentrations are also elevated in intestinal ischaemia, perforated peptic ulcer and ruptured ovarian cyst,

6- It is worth noting that the serum amylase concentration has no prognostic value

() serum lipase measurements are preferable to amylase as they have greater diagnostic accuracy for acute pancreatitis.

() Ultrasound scanning :confirms the diagnosis, it may show gallstones, biliary obstruction or pseudocyst formation.

() Contrast-enhanced pancreatic CT :

6-10 days after admission is used to define the viability of the pancreas , it may indicate pancreatic necrosis.

The presence of gas within necrotic material suggests infection and impending abscess formation. Involvement of the colon, blood vessels and other adjacent structures by the inflammatory process is best seen by CT.

- () serial assessment of C-reactive protein (CRP) is a useful indicator of progress. A peak CRP > 210 mg/L in the first 4 days predicts severe acute pancreatitis with 80% accuracy.

Management

() All severe cases should be managed in intensive care unit. A central venous line or Swan-Ganz catheter and urinary catheter are used to monitor patients with shock.

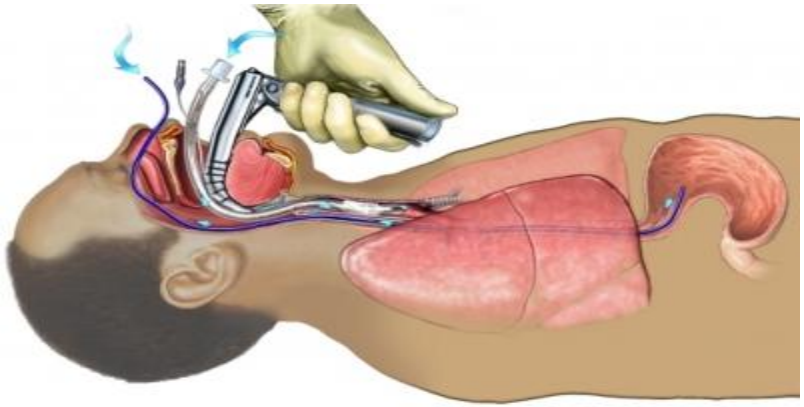
() analgesia using pethidine

() correction of hypovolaemia using normal saline and/or colloids.

() Hypoxic patients need oxygen and patients who develop acute respiratory distress syndrome (ARDS) may require ventilatory support.

() Hyperglycaemia is corrected using insulin, but it is not necessary to correct hypocalcaemia by intravenous calcium injection unless tetany occurs.

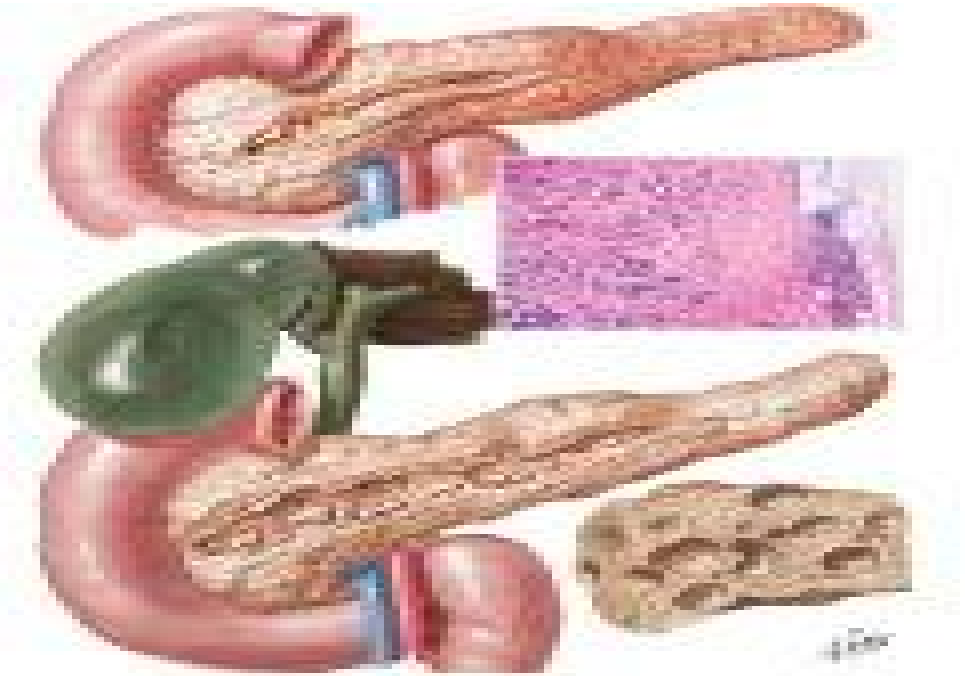
- () Nasogastric aspiration is only necessary if paralytic ileus is present.
- () Enteral feeding should be started at an early stage in patients with severe pancreatitis because they are in a severely catabolic state and need nutritional support. In addition enteral feeding decreases endotoxaemia and thereby may reduce systemic complications.
- () Prophylaxis of thromboembolism with low-dose subcutaneous heparin.
- () The use of prophylactic, broad-spectrum intravenous antibiotics such as imipenem or cefuroxime to prevent infection of pancreatic necrosis is controversial but they are often given.



- () Patients who present with cholangitis or jaundice in association with severe acute pancreatitis should undergo urgent ERCP to diagnose and treat choledocholithiasis.
- () If the liver function tests return to normal and ultrasound has not demonstrated a dilated biliary tree, laparoscopic cholecystectomy .
- () Cholecystectomy should be undertaken within 2 weeks following resolution of pancreatitis-and preferably during the same admission-to prevent further potentially fatal attacks of pancreatitis.
- () Patients who have developed necrotising pancreatitis or pancreatic abscess require urgent endoscopic or surgical necrosectomy to débride all cavities of necrotic material.
- () Pancreatic pseudocysts are treated by drainage into the stomach, duodenum or jejunum (Roux en Y). This is usually performed after an interval of at least 6 weeks, once a pseudocapsule has matured, using open surgery or endoscopic methods.

Chronic pancreatitis

- it is a chronic inflammatory disease characterised by fibrosis and destruction of exocrine pancreatic tissue.
- Diabetes mellitus occurs in advanced cases because the islets of Langerhans are involved.



Causes of chronic pancreatitis ('TIGAR-O')

1- Toxic-metabolic:

- Alcohol Tobacco
- Hypercalcaemia Chronic renal failure

2- Idiopathic:

- Tropical

3- Genetic:

- Hereditary pancreatitis Cystic fbrosis

4- Autoimmune:

- Isolated or as part of multi-organ problem

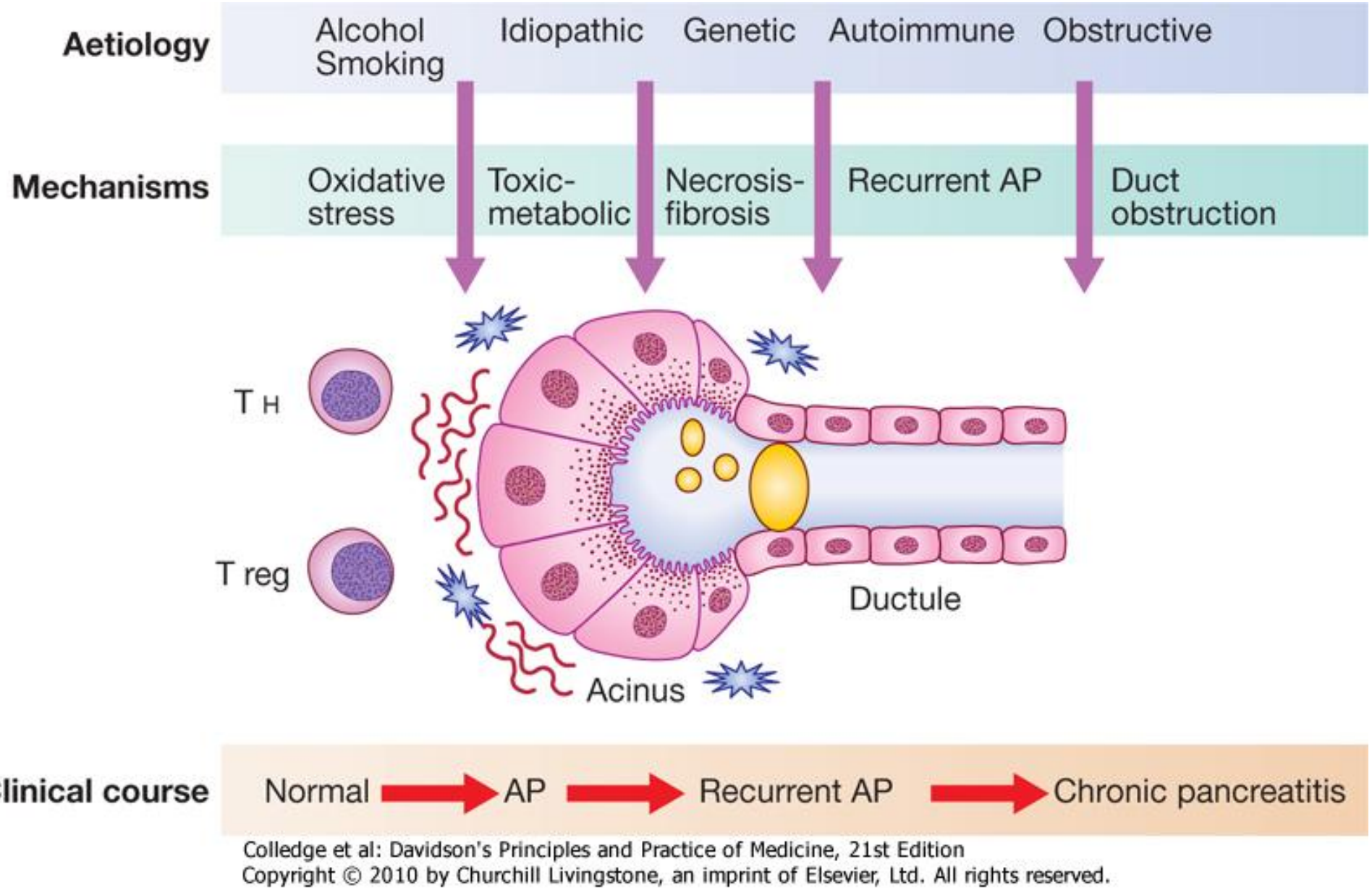
5- Recurrent and severe acute pancreatitis:

- Post-necrotic Recurrent acute pancreatitis

6- Obstructive:

- Ductal adenocarcinoma
- Intraductal papillary mucinous neoplasia
- Pancreas divisum
- Sphincter of Oddi stenosis

Pathophysiology



Colledge et al: Davidson's Principles and Practice of Medicine, 21st Edition

Clinical features

- () Its affects middle-aged alcoholic men.
- () Almost all present with abdominal pain. In 50% this occurs as episodes of 'acute pancreatitis', slowly progressive chronic pain without acute exacerbations affects 35% of patients, whilst the remainder have no pain but present with diarrhoea.
- () 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.
- () Pain may be relieved by leaning forwards or by drinking alcohol.
- () 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.
- () Physical examination 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).

Investigations

()Tests to establish the diagnosis:

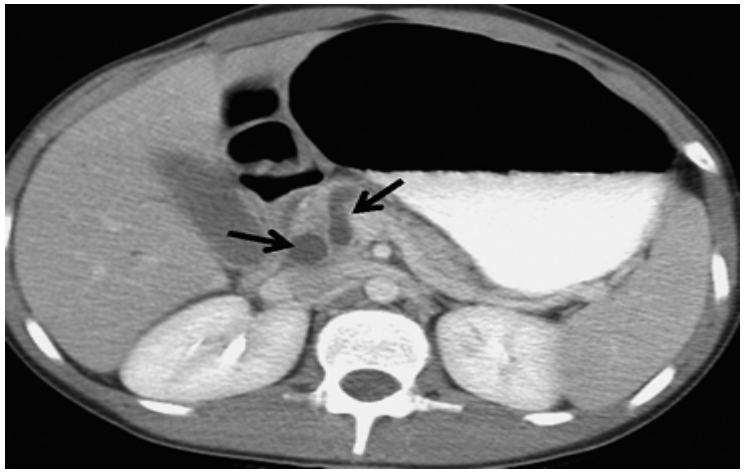
- Ultrasound
- CT (may show atrophy, calcification or ductal dilatation)
- Abdominal X-ray (may show calcification)
- MRCP
- Endoscopic ultrasound

() Tests of pancreatic function:

- Collection of pure pancreatic juice after secretin injection (gold standard but invasive and seldom used)
- Pancreolauryl test
- Faecal pancreatic elastase

() Tests of anatomy prior to surgery:

- MRCP



Complications of chronic pancreatitis

- 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

Management

- () Alcohol avoidance is crucial in halting the progression of the disease and reducing pain.
- () A range of analgesic drugs, particularly NSAIDs, opiate use with the risk of addiction.
- () Oral pancreatic enzyme supplements suppress pancreatic secretion and their regular use reduces analgesic consumption in some patients.
- () Coeliac plexus neurolysis or minimally invasive thoracoscopic splanchnicectomy sometimes produces long-lasting pain relief, although relapse eventually occurs in the majority of cases.

- *Malabsorption :* This is treated by dietary fat restriction (with supplementary medium-chain triglyceride therapy in malnourished patients) and oral pancreatic enzyme supplements. A PPI is added to optimise duodenal pH for pancreatic enzyme activity.
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Surgical intervention

() Endoscopic therapy:

- Dilatation or stenting of pancreatic duct strictures
- Removal of calculi (mechanical or shock-wave lithotripsy)
- Drainage of pseudocysts

() Surgical methods:

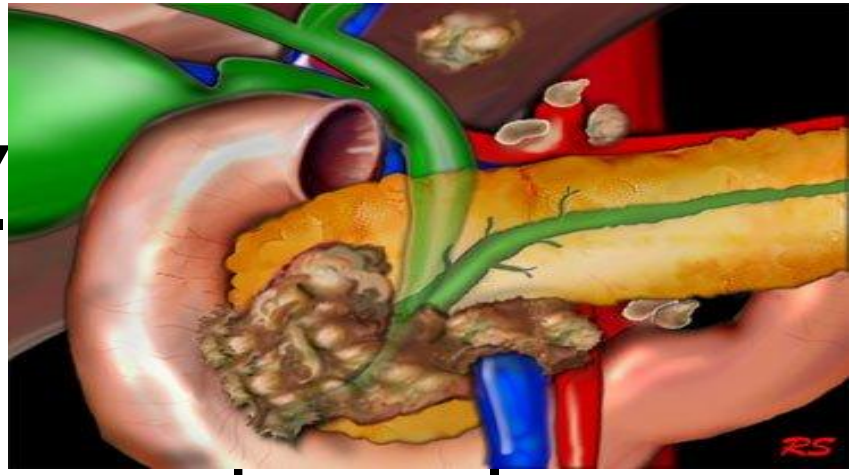
- Partial pancreatic resection, preserving the duodenum
- Pancreatico-jejunostomy

Tumours of the pancreas

- () Pancreatic carcinoma affects 10-15 per 100 000 in Western populations, rising to 100 per 100 000 in those over the age of 70.
- () Men are affected twice as often as women.
- () The disease is associated with increasing age, smoking and chronic pancreatitis, 5 and 10% of patients have a genetic predisposition (hereditary pancreatitis, MEN, hereditary non-polyposis colon cancer (HNPCC) and familial atypical mole multiple melanoma syndrome (FAMMM)).
- () Overall survival is only 3-5% with median survival of 6-10 months for those with locally advanced disease and 3-5 months if metastases are present.

Patrick Swayze

Pathophysiology

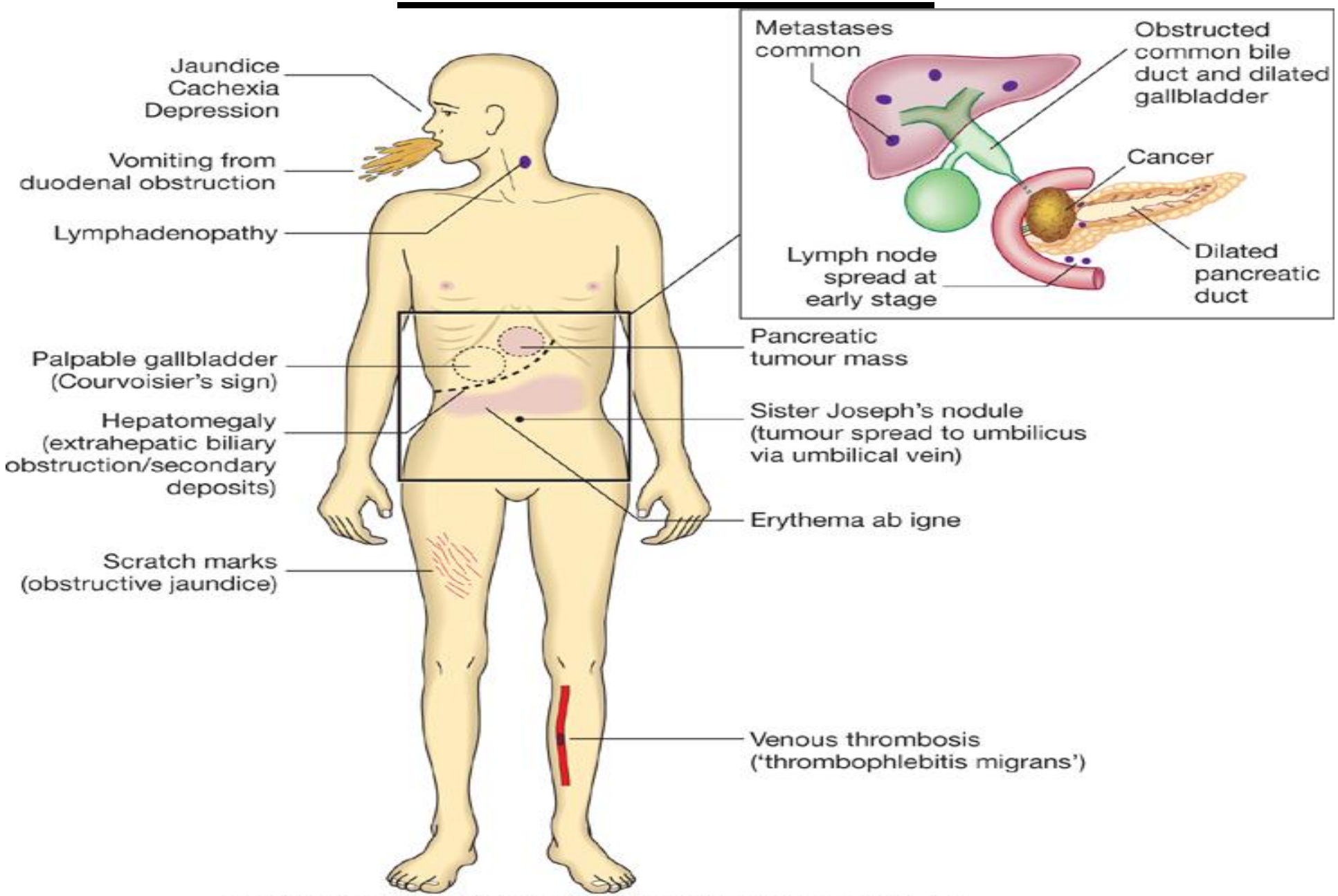


() Approximately 90% of pancreatic neoplasms are adenocarcinomas which arise from the pancreatic ducts.

() These tumours involve local structures and metastasise to regional lymph nodes at an early stage.

() The majority of patients have advanced disease at the time of presentation.

Clinical features



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Clinical features

() pain, weight loss and obstructive jaundice .

() The pain results from invasion of the coeliac plexus . It often radiates from the upper abdomen through to the back and may be eased a little by bending forwards.

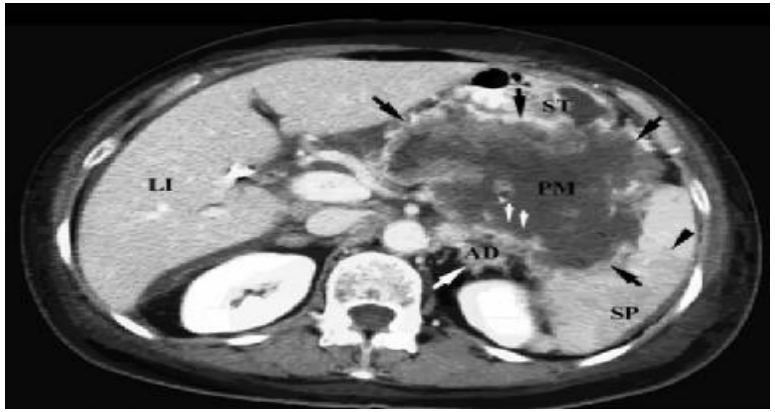
() Almost all patients lose weight and many are cachectic.

() Around 60% of tumours arise from the head of the pancreas, and involvement of the common bile duct results in the development of obstructive jaundice, often with severe pruritus.

() A few patients present with diarrhoea, vomiting from duodenal obstruction, diabetes mellitus, recurrent venous thrombosis, acute pancreatitis or depression.

() Physical examination reveals clear evidence of weight loss. An abdominal mass due to the tumour itself, a palpable gallbladder or hepatic metastasis is commonly found. A palpable gallbladder in a jaundiced patient is usually the consequence of distal biliary obstruction by a pancreatic cancer (Courvoisier's sign).

Investigations



- When a patient presents with biochemically confirmed obstructive jaundice, the diagnosis is usually made by ultrasound and contrast-enhanced CT .
- EUS or laparoscopy with laparoscopic ultrasound will define tumour size, involvement of blood vessels and metastatic spread. In patients unsuitable for surgery because of advanced disease, frailty or comorbidity, endoscopic ultrasound (EUS) or CT-guided cytology or biopsy may be used to confirm the diagnosis.
- MRCP and ERCP are sensitive methods of diagnosing pancreatic cancer and are valuable when the diagnosis is in doubt, although differentiation between cancer and localised chronic pancreatitis can be difficult.

management

- () Surgical resection is the only method of effecting cure, and 5-year survival in patients undergoing a complete resection is around 12%. Recent trials have demonstrated improved survival (21-29%) with adjuvant chemotherapy using 5-fluorouracil and folinic acid or gemcitabine.
- () Unfortunately, a mere 10-15% of tumours are amenable to curative resection since most neoplasms are locally advanced at the time of diagnosis.
- () Jaundice is relieved by choledochojejunostomy in fit patients; percutaneous or endoscopic stenting is used in the elderly or in patients who have very advanced disease.
- () Ampullary or periampullary adenocarcinomas are rare neoplasms which arise from the ampulla of Vater or adjacent duodenum. undergoing resection of ampullary or periampullary tumours survive for 5 years in contrast to patients with pancreatic ductal cancer.