OPEN ACCESS TEXTBOOK OF GENERAL SURGERY

# ACUTE AND CHRONIC PANCREATITIS

S Burmeister
PC Bornman
JEJ Krige

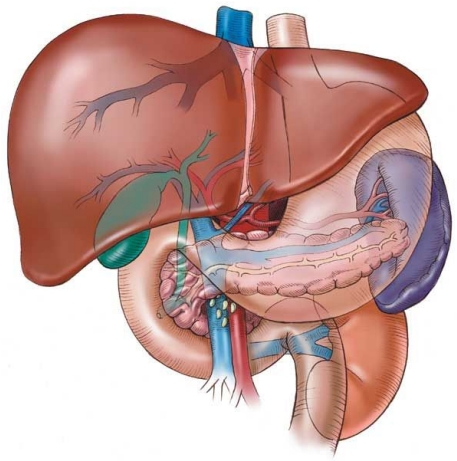
## ANATOMY AND PHYSIOLOGY OF THE PANCREAS

The pancreas lies in the epigastrium and left hypochondrium, crossing the midline at the level of L1 to L3. It is an elongated organ lying in the retroperitoneum, posterior to the stomach and anterior, from right to left, to the inferior Vena Cava; superior mesenteric, portal and splenic veins; the vertebral column; the aorta and splenic artery and the left kidney. It is comprised of a head, neck, body and tail with the head lying in the C-loop of the duodenum and the tail lying within the hilum of the spleen. A small prolongation, the uncinate process, extends from the head medially, posterior to the superior mesenteric vein. The neck is that part of the pancreas overlying the superior mesenteric and portal veins as they course towards the liver. The common bile duct lies in a groove on the postero-superior surface of pancreatic head, sometimes being embedded within it. Typically the pancreas is drained by 2 ducts, the main and accessory ducts. The main duct runs through the entire gland receiving tributaries from it and exits into the duodenum via the ampulla of Vater where it is in close relationship with the common bile duct. The accessory duct drains the head and has a separate opening into the duodenum.

The pancreas has both an exocrine and endocrine function. Digestive enzymes are secreted by acinar cells into the pancreatic ducts which then drain into the intestinal lumen to facilitate digestion and absorption. Pancreatic juice is alkaline and has a high $HCO3^-$ content; this together with bile and intestinal juice which are also neutral or alkaline neutralise gastric acid. Approximately 1500 ml of pancreatic juice is produced per day, under the influence of secretin and cholecystokinin.

Pancreatic juice contains trypsinogen which is converted to trypsin by the brush border enzyme enterokinase when pancreatic juice enters the duodenum. Trypsin converts pro-enzymes in pancreatic juice into active enzymes as well as further trypsinogen into trypsin in an autocatalytic chain reaction. Thus the release into the pancreas of even a small amount of trypsin results in a chain reaction that produces active enzymes that can digest the pancreas. Trypsin also activates phospholipase A2 which forms lysolecithin from lecithin, a normal constituent of bile. Lysolecithin damages cell membranes causing disruption of pancreatic tissue and necrosis of surrounding fat.

Various hormones are produced and secreted by the islets of Langerhans in the pancreas, including insulin, glucagon, somatostatin, pancreatic polypeptide and others. The first 2 are particularly important in glucose metabolism and homeostasis. Insulin is anabolic, increasing the storage of glucose, fatty acids and amino acids; deficiency results in the development of diabetes mellitus. Glucagon mobilises glucose, fatty acids and amino acids into the bloodstream. The 2 hormones are thus reciprocal in action and reciprocally secreted. Somatostatin regulates islet cell secretion while pancreatic polypeptide regulates GI function.



## ACUTE PANCREATITIS

## DEFINITION

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ systems.

## PATHOLOGY (INCLUDING AETIOLOGY) AND PATHOPHYSIOLOGY

Alcohol and gallstones make up about 70% of the causes of AP. Of these alcohol is the predominant cause in the Western Cape while the reverse is true for other countries such as the United Kingdom.

**Table 1 Aetiology of Pancreatitis**

Alcohol } 70%
Gallstones }
Idiopathic – 10%
Miscellaneous – 20%

- Obstructive
  - Post – ERCP
  - Ascariasis (children)
  - Pancreatic Carcinoma
  - Congenital abnormalities
    - choledochal cyst
    - pancreas divisum
- Metabolic
  - hyperparathyroidism
  - hyperlipidaemia
  - Aminoaciduria
  - Porphyria
- Drugs
  - Anti-tuberculous
  - Anti-biotics
  - Anti-retrovirals
  - Thiazide diuretics
- Trauma
  - Blunt
  - Post operative
- Viral infections (mumps / HIV)
- pregnancy (mostly associated with gallstones)
- Collagen disease

The pathogenesis of AP is caused by an inappropriate activation of **trypsinogen to trypsin** in the pancreatic cells (normally this only occurs when trypsinogen is secreted into the duodenum).Once activated these enzymes are responsible for autodigestion of pancreatic tissues which result in necrosis and in severe cases stimulate the production of inflammatory cytokines which in turn triggers an inflammatory cascade causing a **systemic inflammatory response syndrome (SIRS).** SIRS may develop into an acute respiratory stress syndrome (ARDS), multi-organ dysfunction syndrome (MODS) or organ failure.

The mechanism by which trypsin is activated in the pancreatic acini remains uncertain. Although it is known that in gallstone pancreatitis the trigger results from a gallbladder stone passing into the bile duct causing temporary obstruction at the sphincter of Oddi, it remains uncertain whether activation of pancreatic enzymes is the result of increased pancreatic duct pressure or due to bile reflux into the pancreatic duct. The mechanisms in alcohol induced and other causes of pancreatitis are even less clear but, in principle, intracellular protective mechanisms to prevent trypsinogen activation or reduce trypsin activity are overwhelmed. Genetic predisposition, such as mutation of the cationic

trypsinogen gene may promote AP in the presence of alcohol.

Two distinct pathological entities are recognised:

1. ***Acute interstitial oedematous pancreatitis (IOP)*** where there is diffuse or localised enlargement of the pancreas due to interstitial oedema together with peripancreatic inflammation and fluid. This type usually presents with a mild attack.
2. ***Acute necrotising pancreatitis (NP)*** where there is necrosis of the parenchyma, peripancreatic tissue or both. This type represents the more severe form of the disease. The natural history of the necrotic tissue is variable, as it may remain solid or liquefy, remain sterile or become infected and persist or disappear over time.

An attack of pancreatitis may become complicated as a result of the development of either local or systemic complications.

**Local complications** include the development of:

**A. <u>Collections</u>**

1. **An acute peripancreatic fluid collection** (associated with **IOP**)
   - Defined as peripancreatic fluid associated with IOP without necrosis and < 4 weeks after the onset of IOP, without a defined wall. Tend to resolve spontaneously unless there is persistent pancreatic duct disruption.

2. **A pancreatic pseudocyst** (**IOP**)
   - Encapsulated collection of fluid with a well-defined inflammatory wall, outside the pancreas with little or no necrosis. Usually >4 weeks from the onset of IOP and associated with duct disruption.

3. **An acute necrotic collection** (associated with **NP**)
   - Collection containing fluid and necrotic tissue, associated with NP involving the pancreas or peri-pancreatic tissue. There is no definable encapsulating wall. Peripancreatic necrosis may extend into the mesentery of small and large bowel, retro-peritoneal space, peri-renal tissues and as far as the pelvis or thorax. With time the necrotic process become liquefied and walled off, the so-called "walled-off" necrosis.

4. **Walled off necrosis** (**NP**)
   - Encapsulated collection of pancreatic / peripancreatic necrosis encapsulated by a well-defined inflammatory wall. Usually occurs >4 weeks after onset after NP.

Pancreatic or peripancreatic fluid collections or necrosis may be **sterile** or **infected**, however the development of the latter is particularly important as it is associated with increased morbidity and mortality and invariably requires intervention.

**B. <u>Other organ complications</u>**

- **Gastric outlet dysfunction**
- **Splenic / portal vein thrombosis**
- **Intestinal necrosis**

**Systemic complications** relate to either the development of new **organ failure** or exacerbation of pre-existing **co-morbid disease**.

**CLINICAL PRESENTATION AND COURSE (SYMPTOMS, SIGNS, GRADING)**

The diagnosis of pancreatitis requires 2 of the following:

1. **Abdominal pain** consistent with acute pancreatitis (acute onset, epigastric, severe, often radiating to the back).
2. Serum **lipase** or **amylase** ≥3x normal
3. Characteristic findings on **CT** or **MRI** scan

Nausea and vomiting are common. There is also a subgroup of patients where the onset is insidious, presenting with cardio-respiratory failure and non-specific abdominal signs such as unexplained ileus. This is seen after major surgery (eg, cardiac) or in immune compromised patients. Physical examination varies according to the severity of the attack; in mild cases there will be minimal signs while in severe cases, marked abdominal tenderness, distension and an ileus may be present. Ecchymosis in the flanks (Grey Turner's sign) or in the peri-umbilical region (Cullen's sign) occur in about 3% of patients and are considered signs of severe disease.

It is important to identify the **underlying cause** of acute pancreatitis during the patient's acute admission. With alcohol induced pancreatitis, a history of heavy alcohol intake of 5-10 years is usually obtained. The attack comes on typically the "afternoon after the night before". Gallstones or carcinoma of the pancreas should be considered in the middle aged or elderly patient, particularly when there is little or no alcohol history. With gallstones, the attack typically comes on after a large meal which stimulates gallbladder contraction (by the release of cholecystokinin). This causes migration of gallstone into the bile duct with temporary obstruction at the Ampulla of Vater. Trauma must always be kept in mind in the alcoholic group as the history is often unreliable in these patients. In young patients and children conditions such as ascariasis or more rarely congenital abnormalities should be considered.

Acute pancreatitis is a dynamic disease process which has 2 distinct phases with corresponding peaks in mortality.
The **early phase** lasts 1-2 weeks and is characterised by the host's response to pancreatic injury. Inflammatory cascades are activated which manifest clinically as the **systemic inflammatory response syndrome (SIRS**). SIRS is defined by the presence of 2 or more of the following criteria:

- Heart rate > 90 beats per minute
- Core temperature <36°C or >38°C
- White blood cell count < 4000 or >12000/mm³
- Respirations >20/min or PCO2 <32mmHg

When SIRS is persistent there is an increased risk of developing **organ failure**, which may be **transient** or **persistent** depending on whether it lasts less than or longer than 48 hours. The presence and duration of organ failure determines the **severity** of acute pancreatitis during the early phase.

The organ failure is secondary to the host's systemic inflammatory response caused by tissue injury/cytokine response. Hypovolaemic shock due to third space fluid sequestration (not bleeding), and ARDS are most commonly seen early on followed by renal failure and DIC. Renal failure is caused by a combination of factors which include shock and the development of an abdominal compartmental syndrome.

**Organ failure** is defined by the modified **Marshall scoring system** for organ dysfunction.

| Organ system | Score | | | | |
|---|---|---|---|---|---|
| | **0** | **1** | **2** | **3** | **4** |
| Respiratory (PaO2/ FiO2) | >400 | 301-400 | 201- 300 | 101-200 | ≤101 |
| Renal (creatinine umol/L) | ≤134 | 134-169 | 170-310 | 311-439 | >439 |
| CVS (systolic BP) | >90 | <90, response to fluid | <90, no response to fluid | <90, pH <7.3 | <90, pH <7.2 |

Organ failure is defined as a score of 2 or more for 1 of the organ systems. If organ failure affects more than 1 organ, it is termed multiple organ failure.

The **late phase** of pancreatitis is characterised by the **persistence of systemic signs of inflammation** or the presence of **local complications** which evolve during the late phase. **Persistent organ failure** is the result of the necrotising process and secondary infections. The morphological characteristics of local complications are assessed by radiological imaging, typically CT scan.

The onset of acute pancreatitis is defined as the time of onset of abdominal pain. Once the diagnosis of pancreatitis has been made and an estimation made as to the time of onset, it is important to **grade** the **severity** of the attack in order to identify those who require transfer to specialist care and aggressive early treatment. Three degrees of severity are defined:

1. **Mild acute pancreatitis - MAP** (80% of patients)
   a. No organ failure
   b. No local or systemic complications
2. **Moderately severe acute pancreatitis - MSAP**
   a. Transient organ failure that resolves within 48 hours
   b. Local / systemic complications without persistent organ failure
3. **Severe acute pancreatitis - SAP**
   a. Persistent single / multiple organ failure lasting >48 hours

The more severe forms of pancreatitis, in particular when associated with persistent organ failure, are associated with higher mortality rates. The addition of sepsis increases these rates further.

## MANAGEMENT INCLUDING INVESTIGATION AND TREATMENT

### Special investigations

1. **Serum Amylase & Lipase:** Although not specific for pancreatitis, levels of more than three times normal, is usually diagnostic. High levels can also be found in conditions such as perforated peptic ulcer and small bowel infarction but seldom reach 2-3 times the normal value. The serum amylase levels reduce or normalise within the first 24-48 hours. Amylase levels may be normal in severe pancreatitis and are unreliable in patients with acute on chronic pancreatitis when there is impaired pancreatic function. Raised urine amylase levels remain high for longer periods. Serum lipase levels have a slightly higher sensitivity and specificity than amylase. Newer tests, such as urine trypsinogen activation peptide (TAP) are more specific but this is currently not widely available.
2. **Blood investigations** to identify other aetological causes include serum calcium and a lipid profile. Blood gases and a full biochemistry are required in patients with suspected severe pancreatitis.
3. **Chest and abdominal x-rays** are useful to exclude other conditions

but the findings in pancreatitis are often non specific. Pleural effusion, typically on the L-side, and ileus with the so-called sentinel loop and/or colon cut off sign, may be seen. Pancreatic calcifications may also point to a diagnosis of acute on chronic pancreatitis.

4. **Ultrasound** is currently the most useful non-invasive tests to detect gallstones, while a **CT scan** can differentiate severe pancreatitis from other emergency abdominal conditions and monitor the development/progression of local complications.
5. **ERCP** is contra-indicated in the acute setting unless used as a therapeutic procedure in patients with gallstone pancreatitis associated with jaundice and cholangitis.

**General Treatment**

In **mild pancreatitis** hospitalisation with **supportive measures** such as bed rest, nil per mouth, intravenous fluids and analgesics usually suffice. Not all patients require nasogastric suction which is only indicated when pain is severe or in the presence of an ileus. Before discharge, it is important to identify the aetiological factor. In case of alcohol, the patient needs to understand that only complete abstinence will prevent recurrent attacks. An ultrasound will usually identify gallstones. Hypertriglyceridemia and very rarely hypercalcaemia need to be excluded as these require urgent correction.

**Gallstone pancreatitis** is best treated by initial conservative treatment as the majority of patients will settle spontaneously with the passage of the offending calculus into the bowel. Elective cholecystectomy 1-4 weeks after the acute attack is strongly recommended to pre-empt a possible second attack. Earlier intervention is sometimes required in the small group of patients with progressive jaundice with or without associated cholangitis. In this situation an ERCP/ papillotomy is indicated. In elderly patients and those with co-morbid diseases, a papillotomy will suffice to prevent recurrent attacks of pancreatitis.

Early recognition of the **severe** forms of **pancreatitis** is important and supportive therapy should be commenced without delay, preferably in a high care unit. Early and easily recognised **parameters indicating** the **development of severe pancreatitis** are:

1. Haemodynamic instability.
2. Hypoxic confusion.
3. Pleural effusion and pulmonary infiltrates on chest X rays.
4. SIRS response (2 or more criteria).

The **management of SAP** is complex and requires ICU management. Hypovolaemic **shock** must be **treated vigorously** with volume replacement. Inotrope support is often required. The early recognition and appropriate **management of respiratory failure** is of great importance and many patients will require ventilation. Other metabolic parameters requiring close observation and treatment are; **hyperglycaemia, hypocalcaemia** and **renal failure**. Prophylactic antibiotic therapy in the setting of sterile necrosis has been controversial however there remains scant evidence that it reduces the risk of pancreatic sepsis or mortality. There are as yet no drugs available which are effective in stopping the progression of SAP, nor reducing the mortality. Patient **nutrition** must not be neglected, with preference given to the enteral route if possible. This can be given via a naso-gastric tube however if gastroparesis or outlet obstruction is present a naso-jejunal tube may be necessary.

There is no place for surgery during the early phases of severe pancreatitis, unless there is ischaemic

large bowel necrosis which occurs rarely during this phase.

Numerous prognostic factors and scoring systems have been devised for severe pancreatitis. These include CRP, Ranson's and Imrie criteria, APACHE II and Marshall scoring systems, the latter two being used mainly in the ICU setting. From a practical point of view obesity (BMI>30), age over 60 years and multiple organ failure are more commonly associated with a poor prognosis.

**Treatment of local complications**
The diagnosis and characterisation of acute peri-pancreatic fluid collections and necrosis has been simplified by modern imaging including ultra-sound, endoscopic ultrasound, CT scanning and MRI/MRCP. **Interventional procedures** (**percutaneous radiological, endoscopic** or **surgica**l), in particular drainage of symptomatic collections or infected necrosis, may be required for local complications. Such interventions are typically only required after two weeks of the onset of severe pancreatitis. As a general rule, interventions are reserved for patients where there is **persistent organ failure** particularly in the presence of **sepsis**. But the therapeutic effects of interventions are often limited by, unliquefied necrosis and as such requires repeated procedures. The tendency today is to follow a **step up approach** and start with percutaneous drainage and to follow this up with minimal access percutaneous necrosectomy using a variety of scope instruments. Surgical necrosectomy is now reserved for cases where minimal access procedures fail.

Well circumscribed and encapsulated pure pancreatic fluid collections (**pseudocysts**) are easier to manage and intervention should be considered when these persist after 4-6 weeks, particularly when they are large and symptomatic. Other indications include obstruction (bowel or biliary) and secondary infection. Depending on the location and cyst content, these may be drained:

- percutaneously (generally not favoured)
- endoscopically
  - using endoscopic ultrasound, stents are placed between the stomach/duodenum to allow drainage
- surgery
  - at laparotomy, a communication is created between the cyst and enteral lumen (cyst-gastrostomy, cyst-duodenostomy, cyst-jejunostomy)

**Bleeding** from a false aneurysm associated with pancreatic fluid collections is managed mostly by selective angiographic embolisation.

## CHRONIC PANCREATITIS

### DEFINITION

Chronic pancreatitis (CP) is defined as a continuing inflammatory disease of the pancreas characterized by irreversible morphologic changes, often associated with pain and with the loss of exocrine and/or endocrine function which may be clinically relevant. The disease involves both the parenchyma and the ductal system of the pancreas.

### PATHOLOGY (INCLUDING AETIOLOGY) AND PATHOPHYSIOLOGY

The aetiological factors in chronic pancreatitis vary geographically, however globally alcohol remains by far the most common cause. Tropical pancreatitis is commonly seen in Asian, African and South American countries situated within 15º of the Equator.

| Table 2 Aetiology of Chronic Pancreatitis |
|---|
| Alcohol |
| Nutritional (tropical Africa & Asia) |
| Cystic fibrosis |
| Hereditary |
| Idiopathic (10-30%) |
| Autoimmune |
| Obstructive<br>• Pancreas Divisum<br>• Duct Obstruction (eg. Carcinaoma |

While the inflammatory process usually involves the entire pancreas, some parts may be more severely affected. A predominant inflammatory mass in the head of the pancreas occurs in about 30% of cases. During acute exacerbations there is increased interstitial oedema, necrosis and inflammatory infiltration. Intraductal calcification is seen in advanced disease and is more common in alcohol induced and tropical pancreatitis.

Although the pathophysiology of chronic pancreatitis is complex and poorly understood, in alcohol induced chronic pancreatitis the most widely accepted hypothesis is the so-called **necrosis-inflammation-fibrosis sequence**, mediated by the formation of fatty acid ethanol esters (FAEEs). This sequence, once established may be self-perpetuating. Smoking is an important co-factor in the pathological processes precipitated by alcohol. In addition there is formation of calcified stones believed to be the result of decreased bicarbonate and water secretion on the one hand and increased protein and calcium secretion on the other, resulting in precipitation of intraductal protein plugs which subsequently calcify.

Pain is the most predominant symptom in chronic pancreatitis. Understanding of the **mechanisms leading to** the development of **pain** remain equally poorly understood but are likely multi-factorial and may vary during the course of the disease. The most predominant theories include:

- Inflammatory processes and calcified ductal protein plugs lead to parenchymal fibrosis and ductal epithelial damage with morphological ductal changes resulting in strictures and obstruction with consequent ductal and tissue hypertension. Ductal dilatation eventually occurs.
- Interaction between the products of inflammation and damaged neural structures.
- Toxin metabolism and the generation of excessive oxygen derived free radicals which exceed normal protective mechanisms.
- Parenchymal fibrosis leads to a form of compartment syndrome with microvascular ischaemia and pain

**Complications** may develop in the setting of prolonged and persistent disease. Pancreatic destruction with **endocrine** and/or **exocrine insufficiency** are particularly clinically relevant and result in the development of diabetes mellitus and fat malabsorption, leading to significant morbidity and even mortality. Inflammation, necrosis and ductal hypertension may also lead to ductal disruption with the development of pancreatic fluid collections (**pseudocysts**) and **pancreatic ascites**. Other complications include the development of a **false aneurysm** with subsequent haemorrhage in relation to a pseudocyst; **splenic vein thrombosis** leading to segmental portal hypertension and **biliary** or **duodenal stenosis** with obstruction.

Although a causal relationship has not been demonstrated it is believed that there is a higher incidence of **pancreatic cancer** in patients with chronic pancreatitis. To this end, any patient known with chronic pancreatitis

who deteriorates clinically should be actively investigated to have malignancy excluded. Patients with hereditary pancreatitis are known to be at increased risk for cancer.

## CLINICAL PRESENTATION (SYMPTOMS AND SIGNS)

The first attack of alcohol induced pancreatitis is usually preceded by a long period (±10 years) of excessive alcohol intake. This first attack may be either in the form of a severe or mild attack. The attacks are usually induced by binge drinking and present on "the afternoon after the night before". **Two clinical patterns** subsequently emerge; a form where **intermittent attacks** remain **mild** and the disease may even "burn out" and a second more severe group, where the disease follows a **more progressive course** with severe and persistent pain with or without the development of complications. This pattern is also seen in the idiopathic form. Once established, pain may persist despite the patient being abstinent. Metabolic complications such as diabetes and steatorrhoea usually develop after 10-15 years.

**Pain** is the most incapacitating part of the disease. The pain is typically located in the epigastrium with radiation to the back and is frequently worse after meals and may be relieved by sitting upright or leaning forward. It is often associated with nausea and vomiting. Persistent pain is often linked with cyst formation or continued alcohol abuse. Patients seek relief by lying on their side in a jack-knife position. Hot water bottles are often used to relieve the pain which frequently leads to skin burn marks (erythema ab igne). Patients may also present with a palpable mass due to a pseudocyst, ascites, obstructive jaundice due to compression of the bile duct and gastrointestinal bleeding from a false aneurysm communicating with the pancreatic duct (haemosuccus pancreaticus) or gastric varices related to segmental portal hypertension.

Most patients who develop ***diabetes mellitus*** require insulin which often creates problems with sugar control due to a lack of endogenous glucagon. This contributes to a greater sensitivity to insulin which together with poor compliance, increase the risk of hypoglycaemic complications. Exocrine insufficiency with consequent **fat malabsortion** may result in ***steatorrhoea***, which when clinically overt, presents with bulky, pale and offensive stools. In severe cases uncontrolled passage of oil poses a major social problem for the patient and his family. Gross fat malabsorption may lead to severe weight loss and vitamin deficiencies. Most patients with alcohol induced pancreatitis are tobacco smokers and are therefore at risk of developing lung and throat cancers as well as cardiovascular diseases.

## MANAGEMENT INCLUDING INVESTIGATION AND TREATMENT

### Special investigations

1. **Blood investigations**
   **Serum amylase / lipase** may be raised, especially during acute exacerbations, however peak levels may be limited by reduced production due to long term pancreatic destruction. **HBA1C** and **random** or **fasting blood glucose** levels are accurate screening tools for the development of diabetes mellitus. Where doubt remains, oral glucose tolerance testing may be performed. A low **albumen** value may be a clue to malabsorption and nutritional deficiency. Elevated **liver function tests** (bilirubin, ALP, GGT) may indicate impending or established biliary obstruction.

2. **Pancreatic fuction tests**
   These may be either direct or indirect; direct tests are quite

cumbersome and have largely fallen out of favour. Many of the indirect tests are easier to perform but to a large degree lack sensitivity and specificity. **Faecal acid steatocrit** and **elastase** are reasonably accurate measurements of the stool fat content and are inexpensive and easy to perform, however they are limited in detecting mild to moderate disease.

3. **Imaging**
   This plays a crucial role in the diagnosis and characterisation of chronic pancreatitis. **CT** scanning, **MRI/MRCP** and **endoscopic ultrasound** are the diagnostic modalities of choice. **ERCP** has a more limited role in diagnosis but has the benefit of offering therapeutic options in select circumstances.

**Treatment**

**Pain control**

Patients with established chronic pancreatitis do not necessarily follow an intractable course and as such a majority can be **managed conservatively** for prolonged periods and in some indefinitely. In the group of patients with mild disease, recurrent episodes of acute exacerbations can be managed by hospitalisation to help the patient over the acute phase and to provide the patient with a pain control medication regime avoiding opiates as far as possible.

A **"step up" regime** is generally employed, utilising the following:

- Abstinence with a low fat diet
- Non-narcotic analgesia (paracetomol or non-steroidal anti-inflammatory drugs)
- Trial of high dose pancreatic enzymes together with acid suppression
- Narcotic analgesics, progressing in potency as necessary
- Consideration of anti-depressant medication to alleviate co-existent depression, ameliorate pain and potentiate opiates.

When opiates are required, it is advisable to avoid those which are highly addictive such as pethidine. To this end, morphine in one form or another remains the best opiate for long-term pain management. Anti-oxidant supplementation has also been evaluated in the management of pain in chronic pancreatitis and although there is some data in favour of this as a potential treatment, the evidence should probably still be considered insufficient to recommend this routinely.

Referral to a multidisciplinary pain clinic is advisable once control of pain becomes problematic. In alcohol induced pancreatitis, patients should be encouraged to enter a rehabilitation programme with support from a social worker, particularly when there are problems with employment. Patients should also be encouraged to stop smoking as there is evidence that this is an important contributing factor in the progression of the disease. In addition, complications or alternative diagnoses which may contribute to the development of pain should be excluded; these include pseudocyst formation, biliary / duodenal obstruction, malignancy and peptic ulcer disease.

There is a group of patients who continue to suffer intractable pain, despite giving up alcohol, maximal medical management and in the absence of complications such as pseudocysts. A percutaneous ***coeliac plexus block*** or division of the thoracic afferent sensory nerves with a ***thoracoscopic splanchnicectomy*** may provide temporary relief but most of these patients will eventually require some form of surgical intervention. The risk of opoid addiction in prolonged conservative management must be weighed against the operative risks, in particular that of compromised pancreatic function.

Various operations have been recommended in patients with intractable pain. These can be broadly divided into drainage and resectional procedures. The choice of surgery is largely governed by the morphological changes in the pancreas (in particular whether the pancreatic duct is suitable for a drainage procedure) and whether there is a suspicion of malignancy.

**Drainage procedures**: A pancreatic duct drainage procedure only ***(pancreatico-jejunostomy)*** is usually performed when there is isolated dilatation of the pancreatic duct. When there is an associated inflammatory mass in the head, the drainage procedure is extended further, into the head of the pancreas ***(Frey procedure)***.

**Resection procedures**: these are performed when there is concern about a malignancy or when a drainage procedure is not feasible. If a resection of the head is required, a ***pylorus preserving pancreatico-duodenectomy*** *or* ***duodenal preserving pancreatectomy*** is recommended to minimise nutritional disturbances. A ***distal pancreatectomy*** is performed when there is an inflammatory mass in the tail with or without an associated pseudocyst. Worsening of pancreatic endocrine and exocrine functions are common after these resectional operations thus drainage procedures are preferred where possible.

**Endoscopic treatment** by stenting with or without ***extracorporeal lithotripsy (ESWL)*** is seldom indicated in the treatment of pain in uncomplicated chronic pancreatitis and is limited in the main to localised and dominant strictures/stones near the Ampulla of Vater

**Treatment of complications**

**Diabetes mellitus** requires careful control with the emphasis on keeping the blood sugar above normoglycaemic levels to avoid hypoglycaemic complications. Insulin is invariably required for these patients but must be carefully monitored to avoid the aforementioned hypoglycaemic complications.

**Malapsorption and Steatorrhoea** can usually be controlled by pancreatic enzyme replacement therapy in the form of extracts from porcine pancreas taken with meals. Under optimal conditions approximately 25 - 40 000 IU of lipase is required per meal. Enteric coated preparations are preferred in order to protect the lipase from inactivation by gastric acid. Patients who remain symptomatic may benefit from acid suppressing medication.

**Pseudocysts** in chronic pancreatits should be treated only once they become symptomatic, either causing pain or obstruction. Size alone is not an indication to intervene. In suitable cases endoscopic treatment is the preferred treatment, the scope of which has increased when performed under endoscopic ultrasound guidance. Surgery is reserved for cases unsuitable for endoscopic drainage and failures with recurrence of pain with or without recurrence of the pseudocyst. Surgical drainage may include ***cyst-gastrostomy, cyst-duodenostomy*** and ***cyst-jejunostomy.*** Haemorrhage from false aneurysms related to a pseudocyst is best controlled by selective angiographic embolisation.

Patients with **pancreatic ascites** and/or pleural effusions may be effectively treated by decompression of the pancreatic duct by means of a pancreatic ductal stent placed at ERCP.

Patients with asymptomatic **bile duct strictures** should be treated conservatively with regular follow-up. Endoscopic interventions and stenting should be discouraged, as this may cause secondary infection particularly

when the stents occlude. Patients who present with jaundice should initially be treated conservatively, unless there is associated cholangitis when a temporary stent should be placed. If the jaundice resolves, no further intervention is required but patients will require follow-up. If jaundice persists or where a biliary stent has been placed to manage cholangitis, a biliary bypass procedure in the form of a ***hepatico-jejunostomy*** is indicated.

In the setting of **duodenal obstruction**, surgical relief of the obstruction is invariably required. This may involve simple mobilisation of the duodenum or a bypass type procedure such as a ***gastro-jejunostomy***, ***duodeno-duodenostomy*** or a ***duodeno-jejunostomy.***