

# Pancreas

## Investigations of pancreatic disease

It is possible to obtain information about:

- (1) Pancreatic damage by measuring levels of pancreatic enzymes in body fluids;
- (2) Pancreatic function by measuring bicarbonate and enzymes produced in the pancreatic juice; and
- (3) Morphological abnormality of the parenchyma and duct system by ultrasonography, computerised tomography (CT), magnetic resonance imaging (MRI) and endoscopic retrograde cholangiopancreatography (ERCP).

## Estimation of pancreatic enzymes in body fluids

When the pancreas is damaged, enzymes such as amylase, lipase, trypsin, elastase and chymotrypsin are released into the serum. A markedly elevated serum level is highly suspicious of acute pancreatitis. If confirmation of the diagnosis is required, CT of the pancreas is of greater value.

## Pancreatic function tests

Pancreatic secretion in response to a standardised stimulus can provide an assessment of the functional capacity of the gland. The tests can be divided into those where the stimulus to secretion is indirect — produced by the ingestion of a test meal — and those where secretion is directly stimulated by injection of a hormone. The more practical test is the nitroblue tetrazolium—para-aminobenzoic acid (NBT PABA) test in which the recovery in the urine of PABA is measured after oral administration. The para-aminobenzoic acid is liberated by pancreatic chymotrypsin and excreted in the urine after absorption and liver conjugation.

A simpler test now available is one which measures faecal elastase levels; absence indicates chronic pancreatitis and is specific.

## Imaging investigations of the pancreas

### Ultrasonography

- ✚ Can outline the pancreas with accuracy. However, in patients who are fat and those with much gas or fluid in the bowel, the images of the pancreas are poor.
- ✚ In the investigation of jaundice ultrasonography remains the initial preferred investigation. It determine whether or not the bile duct is dilated, and also define the presence or absence of a mass in the pancreas and the coexistence of gallstones or gross disease within the liver such as metastases.

### Computerised tomography

- ✚ Pancreatic carcinomas of 1—2 cm in size can usually be demonstrated whether in the head, body or tail of the pancreas. Prior to injection of contrast an unenhanced CT scan is essential to determine the presence of calcification within the pancreas and gall bladder. The stomach and duodenum should be outlined with water and distended to

define the duodenal loop. All significant pathologies within the pancreas can be diagnosed on high quality spiral CT scans.

- ✚ CT scanning is also of value in the therapeutic setting to drain cysts or abscesses, or to guide percutaneous biopsies.

### Magnetic resonance imaging

- ✚ With MRI the pancreas can be clearly displayed in a manner similar to the best CT image. In addition, clear images of the bile duct and the pancreatic duct, together with fluid collections, can be defined.
- ✚ Magnetic resonance pancreatography and cholangiography may well replace diagnostic ERCP.

### Endoscopic retrograde Cholangiopancreatography

By using this technique with a side-viewing fiberoptic duodenoscope the ampulla of Vater can be clearly seen. Images of contrast injected into the biliary and pancreatic ducts can display the anatomy and pathology of these ducts. Changes seen in **chronic pancreatitis** include pancreatic duct strictures, dilatation of the main pancreatic duct with stones, abnormalities of pancreatic duct side branches, communication of the pancreatic duct with cysts and bile-duct strictures. **In pancreatic carcinoma**, the main pancreatic duct may be narrowed or completely obstructed at the site of the tumour with dilatation upstream but with a normal duct system downstream.

**Collection of bile or pancreatic juice** at endoscopy and brushing of these ducts can yield cells which confirm the suspected diagnosis of carcinoma.

### Plain X-ray

**Chest X-ray** should never be forgotten as it may show a complication of pancreatic disease. Also plain abdominal X-ray before contrast studies is essential to delineate calcification.

### Cystic fibrosis

This is inherited as an autosomal recessive condition. It most frequently occurs amongst Caucasians, in whom it is the most commonly occurring inherited disorder (incidence one in 1800 live births). Heterozygous carriers of the gene are asymptomatic but can be identified by DNA analysis.

The disorder is the result of a generalised dysfunction of exocrine glands. Glandular secretions have abnormal physio-chemical properties resulting in **malabsorption** caused by pancreatic insufficiency, **chronic pulmonary disease** arising from plugging of bronchi and bronchioles, and elevated sodium and chloride ion concentrations in sweat.

Secretions precipitate in the lumen of the pancreatic duct causing blockage which results in duct ectasia and fatty replacement of exocrine acinar tissue. The islets of Langerhans usually appear normal, but diabetes mellitus can occur in older patients. **Steatorrhoea** is usually present from birth resulting in stools which are bulky, oily and offensive. At birth the meconium may set in a sticky mass and produce intestinal obstruction (meconium ileus). Although about 15 per cent of patients do not develop clinical steatorrhoea, most show complete exocrine insufficiency.

The earliest clinical signs of cystic fibrosis are poor growth, poor appetite, rancid فاسد greasy stools, abdominal distension, persistent cough,

emphysematous chest and finger clubbing. Later the liver may become cirrhotic as a result of bile-duct plugging and signs of portal hypertension may appear; corpulmonale may develop and the appearance of secondary sexual characteristics may be delayed. The mother may have noticed that the child is salty when kissed — levels of sodium and chloride ions in the sweat above 90 mmol/litre confirm the diagnosis.

Treatment is aimed at control of the secondary consequences of the disease. Malabsorption is treated by administration of pancreatic enzyme preparations, and pulmonary function preserved with aggressive physiotherapy and antibiotics. A suitable diet is low in fat but contains added salt to replace the high losses in the sweat. With optimal treatment 80 percent of the patients diagnosed early should survive to beyond their 19th year.

### **Iatrogenic injury to the pancreas**

#### ***This can occur in four ways.***

- ☒ Injury to the tail of the pancreas during splenectomy resulting in a pancreatic fistula.
- ☒ Injury to the accessory pancreatic duct (Santorini) which is the main duct in 7 per cent of patients during Billroth II gastrectomy. A pancreatogram performed by cannulating the duct at the time of discovery of such an injury will demonstrate whether it is safe to ligate and divide the duct. If no alternative drainage duct can be demonstrated then the duct should be reanastomosed to the duodenum.
- ☒ Attempts at enucleation of islet cell tumours of the pancreas can result in fistulae.
- ☒ Duodenal or ampullary bleeding following sphincterotomy. This injury may require duodenotomy to control the bleeding.

### **Pancreatic fistula**

This usually follows operative trauma to the gland, or may occur as a complication of acute or chronic pancreatitis. Management is to define the site of the fistula, the epithelial structure to which it communicates (e.g. external to skin or internal to bowel), and to correct metabolic and electrolyte disturbances. The danger of a pancreatic fistula is that there is digestion of surrounding structures by activated pancreatic enzymes causing local damage, perforation, bleeding and digestion of the skin.

Immediate control of the fistula can be obtained by a nil by mouth regime, the use of octreotide and adequate drainage of the fistula with protection of the skin. Investigation of the cause of the fistula is required and, usually, once the cause is determined appropriate remedies can be introduced. Frequently the cause is related to obstruction within the pancreatic duct which can be overcome by the insertion of a stent or catheter endoscopically into the pancreatic duct, and waiting for closure of the fistula while supporting the patient by a conservative regime with parenteral nutritional support and good nursing.

## Pancreatitis

Pancreatitis is primarily due to the intracellular activation of trypsinogen to trypsin by numerous stimuli which, as yet, have not been fully elucidated.

**Acute pancreatitis** is defined as an acute condition presenting with abdominal pain and usually associated with raised pancreatic enzyme levels in the blood or urine as a result of inflammatory disease of the pancreas.

Acute pancreatitis may recur.

**Chronic pancreatitis** is defined as a continuing inflammatory disease of the pancreas characterised by irreversible morphological change typically causing pain and/or permanent loss of function. Many patients with chronic pancreatitis have exacerbations, but the condition may be completely painless.

## Acute pancreatitis

Acute pancreatitis accounts for 3 per cent of all cases of abdominal pain. The disease may occur at any age, with a peak in the young male and the older female. About one-third of patients die in the early phase of an attack from multiple organ failure, while deaths occurring after the first week of onset are due to infective complications. Eighty per cent of patients will have a mild attack of pancreatitis in which the mortality is around 1 per cent, while in those who have a severe attack of pancreatitis the mortality varies from 20 to 50 per cent.

### Aetiology

The two major causes of acute pancreatitis are biliary calculi, which occurs in 50—70 per cent of patients, and alcohol, which occurs in 25 per cent. The remaining cases may be due to rare causes or be idiopathic.

Etiologies of Acute Pancreatitis
Alcohol
Biliary tract disease
Hyperlipidemia
Hereditary
Hypercalcemia
Trauma
<ul style="list-style-type: none"> <li>• External</li> </ul>
<ul style="list-style-type: none"> <li>• Surgical</li> </ul>
<ul style="list-style-type: none"> <li>• Endoscopic retrograde cholangiopancreatography</li> </ul>
Ischemia
<ul style="list-style-type: none"> <li>• Hypoperfusion</li> </ul>
<ul style="list-style-type: none"> <li>• Atheroembolic</li> </ul>

<ul style="list-style-type: none"> <li>• Vasculitis</li> </ul>
<b>Pancreatic duct obstruction</b>
<ul style="list-style-type: none"> <li>• Neoplasms</li> </ul>
<ul style="list-style-type: none"> <li>• Pancreas divisum</li> </ul>
<ul style="list-style-type: none"> <li>• Ampullary and duodenal lesions</li> </ul>
<b>Infections</b>
<b>Venom</b>
<b>Drugs</b>
<b>Idiopathic</b>

The importance of aetiology is that removal of the causative factor can avoid further episodes of pancreatitis. Thus, in a patient who has gallstone pancreatitis, the gallstones should be removed as soon as the patient is fit to undergo surgery and, preferably, before discharge from hospital.

### Clinical presentation

- ✚ Pain is usually the cardinal symptom. It characteristically develops quickly, reaching maximum intensity within minutes rather than hours, and persists for hours or even days. The pain is frequently severe or even agonising, it is refractory to the usual doses of analgesics, and constant in nature and intensity. Pain is usually experienced first in the epigastrium but may be localised to either upper quadrant or felt diffusely throughout the abdomen. There is radiation to the back in about 50 per cent of patients and some patients may gain relief by sitting or leaning forwards.

### ***Acute pancreatitis should be suspected in the patient who:***

- Develops marked abdominal pain, fever or unexplained shock following abdominal surgery;
- Presents with diabetic coma and shock;
- Has clinical features suggesting myocardial infarction with abdominal distension.

- ✚ Nausea, vomiting and retching are usually marked accompaniments. Vomiting is often frequent and persistent, and retching may persist despite the stomach being kept empty by nasogastric aspiration. Hiccoughs can be troublesome and may be due to gastric distension or irritation of the diaphragm.

- ✚ On examination the appearance may be that of a patient who is well or, at the other extreme, one who is gravely ill with profound shock, toxicity and confusion. Tachypnoea is common, tachycardia is usual and hypotension may be present. The body temperature is often normal or even subnormal, but frequently rises as inflammation develops. Mild icterus can be caused by biliary obstruction in gallstone pancreatitis, and an acute swinging pyrexia suggests cholangitis. Bleeding into the fascial planes can produce bluish discoloration of the flanks (Grey Turner sign) or umbilicus (Cullen's sign). Neither sign is

pathognomonic of acute pancreatitis. Subcutaneous fat necrosis may produce small red tender nodules on the skin of the legs. Abdominal examination may reveal distension due to ileus or, more rarely, ascites with shifting dullness. A mass can develop in the epigastrium due to inflammation. There is usually muscle guarding in the upper abdomen, although marked rigidity is unusual. A pleural effusion is present in 10—20 per cent of patients. Pulmonary oedema and pneumonitis are also described and may give rise to the differential diagnosis of pneumonia or myocardial infarction. The patient may be confused and exhibit the signs of metabolic derangement together with hypoxaemia.

### Investigations

- ✚ **A serum amylase** four times above normal is indicative of the disease.
- ✚ Plain abdominal X-ray findings include a generalised or local ileus (sentinel loop), a colon 'cut-off' sign and a renal 'halo' sign الهالة. Occasional helpful, but nondiagnostic, signs include calcified gallstones and pancreatic calcification.
- ✚ **A chest X-ray** may show a spectrum of changes depending on the disease severity. A pleural effusion is present in 20 per cent, and in severe cases a diffuse alveolar interstitial shadowing may suggest an acute respiratory distress syndrome.
- ✚ **Ultrasound scanning.** The swollen pancreas may be detected but the gland is poorly visualised in 25—50 per cent of cases. Ultrasound is valuable in detecting free peritoneal fluid, gallstones, dilatation of the common bile duct.
- ✚ If doubt remains a **CT scan** should be performed in order to determine the diagnosis.

### Management

First assess the severity of the disease using the Ranson's scoring system. After initial assessment a patient is considered to have a mild attack of pancreatitis, a conservative approach is indicated with nil by mouth, intravenous fluid administration and frequent, but noninvasive, observation. However, if the patient develops a severe attack of pancreatitis then a more aggressive approach is required with the patient being admitted to a high-dependency or an intensive care unit. The patient is monitored invasively to ensure homeostasis of the cardiovascular, respiratory and renal systems. In the mild attack, antibiotics are not indicated unless there is evidence of infection. The management of the severe attack involves full resuscitation, and strict asepsis should be observed in the placement of all monitoring lines. If there is evidence of cardiocirculatory compromise then a Swan—Ganz catheter should be inserted in order to measure pulmonary artery wedge pressure, cardiac output and systemic resistance. Regular arterial blood gas analysis is essential as the onset of hypoxia and acidosis may be detected late by clinical means alone. The patient should be made comfortable, appropriately sedated and adequate analgesics given. There is some evidence to support the use of prophylactic antibiotics in the prevention of local and other septic complications. Intravenous cefuroxime or imipenem is advised. If gallstones are the aetiology of severe pancreatitis, an urgent ERCP is indicated to exclude the presence of a stone stuck in the ampulla of

Vater if there is no improvement in the general condition of the patient within 48 hours. The presence of cholangitis with abnormal liver function tests is an indication for urgent endoscopic intervention.

<b>Ranson's Prognostic Signs of Pancreatitis</b>	
<b>At admission</b>	<b>During the initial 48 h</b>
Age >55 y	Hematocrit fall >10 points
WBC >16,000/mm <sup>3</sup>	BUN elevation >5 mg/dL
Blood glucose >180 mg/dL	Serum calcium <2 mmol per liter
Serum LDH >700 IU/L	Arterial PO <sub>2</sub> <60 mm Hg
Serum AST >250 sigma frankel %	Base deficit >4 mEq/L
	Estimated fluid sequestration >6 L

**AST** = aspartate transaminase; **BUN** = blood urea nitrogen; **LDH** = lactate dehydrogenase; **PO<sub>2</sub>** = partial pressure of oxygen; **WBC** = white blood cell count.

### Complications

#### ***Surgical intervention is indicated in:***

- 1) Patient who deteriorates following successful stabilisation.
- 2) Once the presence of infected necrosis is suspected and confirmed
- 3) The presence of cholangitis, in which case an endoscopic sphincterotomy should be performed.

#### ***General complications include:***

- + Cardiovascular as shock and arrhythmia
- + Pulmonary as ARDS
- + Renal failure
- + Metabolic as hypocalcaemia ,hyperglycaemia ,and hyperlipidemia
- + Haematological as DIC
- + Gastrointestinal as ileus
- + Neurological as visual disturbance ,confusion ,irritability ,and encephalopathy
- + Others as subcutaneous fat necrosis and arthralgia

#### ***Local complications***

Once the acute phase has been survived, usually by the end of the first week, and major organ failure is under control, then local complications become pre-eminent in the management of these patients.

**Acute fluid collection.** This is located in or near the pancreas. The wall encompassing the collection is ill defined.

**Acute pseudocyst.** A collection of pancreatic juice enclosed in a wall of fibrous or granulation tissue that arises following an attack of acute pancreatitis. Formation of a pseudocyst requires 4 weeks or more from the onset of acute pancreatitis.

**Pancreatic necrosis.** A diffuse or focal area of nonviable parenchyma which is typically associated with peri pancreatic fat necrosis. The onset of infection results in infected necrosis which is associated with increasing the mortality rate.

**Pancreatic abscess.** A circumscribed intra-abdominal collection of pus, usually in proximity to the pancreas containing little or no pancreatic necrosis.

**Pancreatic effusion.** An encapsulated collection of fluid arising as a consequence of acute pancreatitis, typically in the pleural cavity.

**Pancreatic ascites.** Chronic generalised peritoneal enzyme-rich effusion usually associated with pancreatic duct disruption.

**Pseudoaneurysm.** Pseudoaneurysm is a false aneurysm of a major peripancreatic vessel confined as a clot by the surrounding tissues and often associated with infection. Recurrent bleeding is common, often culminating in fatal haemorrhage.

### Nutritional support

During the early phase of disease parenteral nutrition is important and no advantage has yet been shown for early enteral nutrition. However, once the phase of paralytic ileus has been passed it is appropriate to commence nasojejunal feeding or feeding via a jejunostomy placed in those who have undergone laparotomy. This has the effect of reducing the risk of sepsis from parenteral feeding, and enteral feeding restores the gut mucosal barrier preventing bacterial translocation through the damaged mucosa.

### Chronic pancreatitis

Chronic pancreatitis is a chronic inflammatory disease in which there is irreversible progressive destruction of pancreatic tissue. Its clinical course is characterised by a dynamic progressive fibrosis of the pancreas. In the early stages of its evolution it is frequently complicated by attacks of acute pancreatitis that are responsible for recurrent pain which may be the only clinical symptom. The disease occurs more frequently in men (male to female ratio of 4:1) and the mean age of onset is about 40 years.

### Pathology and aetiology

- ✚ **At the onset** of the disease when symptoms have developed the pancreas may appear normal.
- ✚ **Later** the pancreas enlarges and becomes hard as a result of fibrosis.
- ✚ The ducts become distorted and dilated with areas both of **stricture formation and of ectasia**.
- ✚ **Calcified stones** may form within the ducts.
- ✚ The **ducts may become occluded** with a gelatinous proteinaceous fluid and debris-deformed cysts.
- ✚ Histologically, the lesions affect the lobules producing **ductular metaplasia and atrophy of acini, hyperplasia of duct epithelium and interlobular fibrosis**.

**Aetiology**

- ✚ The most frequent cause is a high alcohol consumption.
- ✚ Pancreatic duct obstruction resulting from stricture formation after trauma, acute pancreatitis or even occlusion of the duct by pancreatic cancer.
- ✚ Hereditary pancreatitis,
- ✚ Infantile malnutrition.
- ✚ Idiopathic.

**Clinical features**

- ❖ Pain is the outstanding symptom in the majority of patients. The site of pain depends to some extent on the main focus of the disease. If the disease is mainly in the head of the pancreas then epigastric and right subcostal pain is common, while if it is limited to the left side of the pancreas then left subcostal and back pain are the presenting manifestations. In some patients the back pain predominates, while in others the pain is more diffuse. Radiation to the shoulder, usually the left shoulder, occurs. The pain is dull and gnawing. The pain is both continuous and episodic, in that severe bouts of pain may occur superimposed on background discomfort.
- ❖ Nausea is common during attacks, and vomiting may occur.
- ❖ All of the complications of acute pancreatitis can occur with chronic pancreatitis.
- ❖ Because of the pain weight loss is common, in that the patient does not feel like eating. The pain prevents sleep and time off work is frequent.
- ❖ The number of hospital admissions for acute exacerbations is a pointer towards the severity of the disease. Analgesic use—abuse is frequent. This, too, gives an indication of the severity of the disability. The patient's lifestyle will gradually be destroyed by pain, analgesic dependence, weight loss and inability to work.
- ❖ Loss of exocrine function will occur leading to steatorrhoea which can be debilitating without supplementation.
- ❖ Loss of endocrine function and the development of diabetes are not uncommon, and the incidence increases as the disease progresses.

**Investigation**

- ☒ Rise in serum amylase only in the early stages of the disease.
- ☒ Pancreatic function tests merely confirm the presence of pancreatic insufficiency or that more than 70 per cent of the gland has been destroyed.
- ☒ Steatorrhoea affects more than 30 per cent of patients with chronic pancreatitis.
- ☒ The prime investigation is either an MRI scan or a CT scan which will show the outline of the gland, the main area of damage and the possibilities for surgical correction. An MR cholangiogram will show the presence of biliary obstruction, and an MR pancreatogram the state of the pancreatic duct. An ERCP can elucidate the anatomy of the duct and, in conjunction with the whole organ morphology, determine the type of operation required, if operative intervention is indicated.

### Treatment

- A diet low in fat and with no alcohol is advised.
- Pancreatic enzyme supplementation may reduce the frequency of painful crises.
- Attention must be paid to nutrition to ensure that the patient gains weight and takes an adequately varied and nutritionally appropriate diet.
- The role of surgery is in overcoming obstruction and removing mass lesions. Most patients have a mass in the head of the pancreas, for which a resection of the head of the pancreas either by a pancreatoduodenectomy or a Beget procedure. If the duct is markedly dilated, then a longitudinal pancreatojejunostomy or Frey procedure can be of value. The rare patient with disease limited to the tail will be cured by a distal pancreatectomy.

### Prognosis

Correctly chosen surgery will relieve symptoms in 75 per cent of patients provided that the aetiological factor is removed. Development of pancreatic cancer is a risk in those who have had the disease more than 20 years.

### Carcinoma of the exocrine pancreas

The disease is a disease of ageing, with the average age of death in men being 74 years and that in women 79 years. It affects men and women to the same degree. Predisposing factors are tobacco smoking and chronic pancreatitis.

### Pathology

More than 85 per cent of cases are duct cell adenocarcinomas.

### Clinical features

- ✚ The most frequent symptoms are nonspecific, namely epigastric discomfort, anorexia and weight loss.
- ✚ Jaundice is the commonest sign and symptom, which brings the patient to the attention of his or her physician. Some 85 per cent of patients present with this symptom. It is characteristically painless jaundice but may be associated with nausea and epigastric discomfort.
- ✚ Change of bowel habit is rare.
- ✚ On examination, there is frequently evidence of weight loss, a palpable liver, a palpable gall bladder (Courvoisier sign).
- ✚ Other signs are ascites and tumour deposits in the pelvis.

### Investigation

- If the patient is jaundiced, the usual **blood tests and ultrasound** scan should be performed. This will determine whether or not the bile duct is dilated. If it is dilated and there is a suspicion of a tumour in the head of the pancreas, the preferred test is now a **contrast enhanced spiral CT** scan specific for the pancreas.
- The next investigation is that of an **endoscopic examination** to determine whether the jaundice can be relieved endoscopically. If it can, a stent should be inserted through the stricture to relieve the jaundice.

- Attention should be paid to the **coagulation** to ensure that no bleeding occurs during this process.
- More accurate information can be obtained by **endoscopic ultrasound** giving good definition of the tumour and its extent.

### Management

At the time of presentation, 90—95 per cent of patients are unsuitable for resection. ***CT findings that indicate a tumor is unresectable include:***

1. Invasion of the hepatic or superior mesenteric artery,
2. enlarged lymph nodes outside the boundaries of resection,
3. Ascites,
4. Distant metastases (e.g., liver), and
5. Distant organ invasion (e.g., colon).

For those patients who are inoperable palliative treatment should be offered.

- **Jaundice** is relieved by stenting. If the patient is not a suitable candidate for endoscopic biliary stenting a percutaneous transhepatic stent can be placed.
- **Obstruction of the duodenum** occurs in approximately 15 per cent; if this occurs early in the course of the disease surgical bypass by gastrojejunostomy is appropriate, but if it is late in the course of the disease then the use of expanding metal stents inserted endoscopically is preferred.

In younger patients who may have a better prognosis a laparotomy to assess the tumour can be appropriate; if the tumour is proved inoperable a choledochoduodenostomy and gastrojejunostomy is the preferred approach. Any patient who has palliative treatment should have a biopsy performed to obtain histological verification. If operation is undertaken this can be done at the time of the operation, but if no operative procedure is undertaken a percutaneous tru-cut biopsy of the tumour should be performed.

Patients with duct cell cancers which are less than 4 cm in diameter, not involving the superior mesenteric or portal veins and with no evidence of multiple enlarged nodes or distant spread, should be considered for a resection. The appropriate resection is that of a pylorus-preserving pancreatoduodenectomy with a local lymphadenectomy.

### Neoplasms of the endocrine pancreas

#### Insulinoma

Insulinomas are the most common pancreatic endocrine neoplasms and present with a typical clinical syndrome known as Whipple triad. The triad consists of symptomatic fasting hypoglycemia, a documented serum glucose level less than 50 mg/dL, and relief of symptoms with the administration of glucose.

Patients often will present with a profound syncopal episode and will admit to similar less severe episodes in the recent past. They also may admit to palpitations, trembling, diaphoresis, confusion or obtundation, and seizure, and family members may report that the patient has undergone a personality change. Insulinomas usually are localized with CT scanning and endoscopic ultrasound (EUS).

Technical advances in EUS have led to preoperative identification of more than 90 percent of insulinomas. The majority (90 percent) of insulinomas are benign and solitary, with only 10 percent malignant. They are typically cured by simple enucleation. However, tumors located close to the main pancreatic duct and large (> 2 cm) tumors may require a distal pancreatectomy or pancreatico-duodenectomy.

Ninety percent of insulinomas are sporadic and 10 percent are associated with the MEN-1 syndrome. Insulinomas associated with the MEN-1 syndrome are more likely to be multifocal and have a higher rate of recurrence.

### **Gastrinoma**

Zollinger-Ellison syndrome (ZES) is caused by a gastrinoma, an endocrine tumor that secretes gastrin, leading to acid hypersecretion and peptic ulceration.

Many patients with ZES present with abdominal pain, peptic ulcer disease, and severe esophagitis. While most of the ulcers are solitary, multiple ulcers in atypical locations that fail to respond to antacids should raise suspicion for ZES and prompt a work-up. Twenty percent of patients with gastrinoma have diarrhoea at the time of diagnosis.

The diagnosis of ZES is made by measuring the serum gastrin level. It is important that patients stop taking proton pump inhibitors for this test. In most patients with gastrinomas, the level is greater than 1000 pg/mL. In equivocal cases, when the gastrin level is not markedly elevated, a secretin stimulation test is helpful.

In 70–90 percent of patients, the primary gastrinoma is found in the Passaro triangle, an area defined by a triangle with points located at the junction of the cystic duct and common bile duct, the second and third portion of the duodenum, and the neck and body of the pancreas. However, because gastrinomas can be found almost anywhere, whole-body imaging is required. The test of choice is somatostatin receptor (octreotide) scintigraphy in combination with CT. The octreotide scan is more sensitive than CT, locating about 85 percent of gastrinomas and detecting tumors smaller than 1 cm.

Multiple tumors are more common in patients with MEN-1 syndrome. Aggressive surgical treatment is justified in patients with sporadic gastrinomas.

If patients have MEN-1 syndrome, the parathyroid hyperplasia is addressed with total parathyroidectomy and implantation of parathyroid tissue in the forearm.

**Good luck**

**Muqdad fuad**