WHAT’S WRONG WITH MY PANCREAS?

CANCER OF PANCREAS
This is a patient information booklet detailing practical information about pancreas in general & specific information about pancreatic cancer. Its aim is to provide the patient & his or her family with useful information on this particular pancreatic problem, the procedures and tests you may need to undergo, various treatment approaches available with risks involved and helpful advice on coping successfully with the problem. If you require any further information or advice or are unsure about anything, Dr. D. R. Kulkarni or your own doctor will be able to help.
WHAT IS PANCREAS?

The pancreas is a solid gland attached in the back of the abdominal cavity behind the stomach. The pancreas is divided into 5 parts - the head, the uncinate process, the neck, the body and the tail. The head of the gland is closely attached to the duodenum, which is the first part of the small intestine into which the stomach empties liquids and partially digested food. The head of the gland
is situated just to the right of the midline of the abdomen and below the right ribcage. The uncinate process is an extension of the lower part of the head of the gland, which surrounds important blood vessels. The body and tail of the pancreas lie at an angle so that the tail of the pancreas is situated beneath the extreme edge of the left rib cage. The tail of the gland is closely attached to the central part of the spleen & splenic blood vessels.

Running behind the neck and uncinate process are many important blood vessels which supply the liver, the rest of the gut organs and the kidneys, including the aorta (an artery) which takes all the blood to the lower abdomen and legs, and the inferior vena cava (a vein) which returns blood from these areas. The **spleenic vein** runs immediately under the tail and body of the pancreas and joins with the **portal vein** that runs immediately under the neck of the pancreas.

In short, pancreas is a centrally located and very precariousely connected to or is in very close contact with most of the important structures in the abdomen. Hence diseases affecting pancreas can inadvertently involve any one or more of these structures. Hence patients with pancreatic problems may not necessarily have pancreatic complaints, but can present with unrelated complaints.
Running along the length of the pancreas within its center is the **main pancreatic duct**, which empties pancreatic juice into the duodenum. Also running through the middle of the head of the pancreas is the **main bile duct, which** also empties into the duodenum. (The main bile duct carries bile from the liver where it is made and also from the **gallbladder** where it is stored). In most people the pancreatic duct and bile duct join together just before they open into the duodenum through a large fleshy nipple called the **ampulla of Vater** (after the person who described this).

Surrounding the openings of each of these ducts are small muscles that control the release of pancreatic juice and bile and thus act as valves (also called sphincters). There is also a valve that regulates the pancreatic juice and bile together and this sits in the ampulla. This common valve is called the **sphincter of Oddi**, also named after the man who described this.

About one in ten people have two separate pancreatic ducts, one that opens as normal through the ampulla of Vater and the other through a smaller nipple (called as papilla). For this reason the ampulla of Vater is sometimes called the major papilla and the other smaller opening is called the minor papilla. The pancreatic duct that opens through the minor papilla is called the **accessory pancreatic duct**
(normally this joins the main pancreatic duct rather than opening separately into the duodenum).

**WHAT DOES THE PANCREAS DO?**

The pancreas does two important things:

- It makes enzymes, which are necessary to digest food in the intestines. Food consists of carbohydrates (e.g. glucose), proteins (e.g. meat) and fat (e.g. butter). Pancreas secretes different enzymes, which are responsible for breaking down clumps of different types of food into small particles for absorption. (Process of digestion) The main enzymes include amylase for digesting carbohydrates, trypsin for digesting proteins and lipase for digesting fats. These enzymes are collected from the small glands in the pancreas into small ducts and finally into the main pancreatic duct to be released into the duodenum. The enzymes when they are first made in the acini are not active (otherwise they would digest the pancreas as well!). When they pass into the duodenum however, they are made active by the juice of the duodenum.

If there are not enough pancreatic enzymes, fat is not digested and the stools (bowel motions) become pale and greasy. These greasy stools may become difficult to flush away from the toilet and
may give off a strong offensive smell. Doctors call this **steatorrhoea** (fatty stool.)

**The digestion of fat is very special.** Fat needs to be dispersed before the pancreatic enzymes can properly break it down. This dispersion of fats is made by bile acids, which are present in bile produced by the liver and stored in the gall bladder. **Bile acids** act in exactly the same way as detergents, which are used to wash up greasy dishes. Therefore, both bile acids and pancreatic enzymes are needed for fat digestion. If the main bile duct becomes blocked, then the bile cannot get into the duodenum & fat cannot be properly digested.

When this common opening is blocked, the bile made by the liver cannot go into the bowel it goes into the blood and out through the kidneys into the urine. This results in the eyes and skin becoming yellow and is known as jaundice. As the bile is in the urine this now becomes dark in color. Because the flow of bile is blocked (or obstructed), doctors call this condition **obstructive jaundice.** As the bile duct goes through the head of the pancreas, jaundice can be caused by disease of the pancreas (such as pancreatitis or cancer).
• It produces insulin to enable every part of the body to use glucose (sugar).

Insulin is a hormone made in special groups of cells called **islets of Langerhans**, which are dispersed throughout the pancreatic gland. It helps the cells of the body to use glucose as a source of energy in order to maintain their different functions. In absence of insulin, sugar instead of entering the cells of the body, stays in the blood leading to harmfully high concentrations. (Diabetes mellitus)

A large proportion of the islets (pronounced 'eyelets') are in the tail of the gland. Most of the pancreas can be removed but there are usually enough islets remaining to make insulin sufficient to prevent sugar diabetes from occurring.

As you are probably aware, diabetes can be treated by taking regular injections of insulin, which can be taken from the pancreas of animals (e.g. pork insulin) or made by genetic engineering (so called 'human' insulin).

**WHAT HAPPENS TO PANCREATIC FUNCTION IN PANCREATIC DISEASES?**

If pancreatic duct outflow is blocked due to any reason, gradually pancreatic duct enlarges in any size due to backpressure. Eventually the increased pressure within the duct starts taking
toll on the pancreatic enzyme secretion, which drops and affects the digestion of food and absorption of nutrients, thereby affecting a person's weight and overall health. The insulin production is not immediately affected but over a period it will also drop thereby causing sugar diabetes in the patient.

Enzyme production and insulin production are independent. Because digestive enzymes and insulin are made by different parts of the pancreas, a problem with enzyme production does not mean necessarily that there will be a problem with insulin production. Similarly, if there is a problem with insulin production, this does not mean necessarily that there will be a problem with enzyme production.

Assuming that the pancreas was normal to begin with, increasing loss of the pancreas gland (by disease or surgery) usually results in more loss of enzyme production before there is obvious loss of insulin production. Another way of saying this is that the insulin 'reserve' is much more than the enzyme 'reserve' of the pancreas.

**WHICH ARE COMMON DISEASES OF PANCREAS?**

- Acute Pancreatitis
- Chronic Pancreatitis
- Pseudo cyst of pancreas
Cancer of pancreas
Cystic tumors
Neuroendocrine tumors

WHAT SPECIAL INVESTIGATIONS ARE DONE WHEN A PROBLEM IS SUSPECTED WITH THE PANCREAS?

You may need to do some tests to find out more about your particular problem. Perhaps you’ve already undergone one or more of them.

You may be advised to have certain blood tests like complete blood count, blood urea, creatinine, liver function tests (bilirubin, liver enzymes like SGOT, SGPT, Alkaline phosphatase, gamma GT, albumin), amylase, lipase, calcium, and parathormone. In case of acute pancreatic problems you will be advised to get admitted and all these tests will then be done in-house.

Similarly diagnosis of pancreatic problems requires radiological imaging studies of abdomen like Ultrasonography, CT scan, MRI or further interventions like gastrointestinal endoscopy, ERCP, PTHC or EUS. It quite often so happens that patient is advised these investigations in a sequential manner and not at one go. This does take time but considering the cost of these investigations it is always better to ask for the next investigation only if it is absolutely necessary. Unfortunately in a small group of
patients one cannot reach a diagnosis in spite of all this effort.

CANCER OF THE PANCREAS

WHAT IS CANCER?

Cancer can arise in any part of the body when particular cells begin to multiply more than normally and spread into other tissues. Cancer arises because of defects within the genes of cancer cells, although the reason for these defects arising in the first place is not known in most cases. If left untreated, cancers cause harmful effects by invading vital tissues.

HOW IS CANCER TREATED?

Many cancers can be cured by surgery, which is called ‘curative surgery’. In some cases, even though the cancer cannot be removed or can be removed only partly, surgery is still very helpful in relieving symptoms, in which case it is called ‘palliative surgery’.

Even if a patient has had ‘curative surgery’ the cancer cells may have already spread in blood vessels to other organs but cannot be seen or felt or diagnosed by investigations. Because of this it is often necessary to recommend additional treatment after curative surgery in the form of
chemotherapy (giving drugs which kill cancer cells). This type of additional treatment is called ‘adjuvant therapy’ and helps to increase the chances of being cured properly.

If the cancer cannot be removed by surgery it is often useful to give chemotherapy, radiotherapy or a combination of these to slow down the growth of the cancer. This type of treatment is known as ‘palliative therapy’.

There have been big advances in the use of chemotherapy and radiotherapy so that many of the serious side effects that used to be seen with these treatments do not occur frequently. The use of chemotherapy and radiotherapy for many cancers is being improved all the time by asking patients to participate in ‘clinical trials’. This means that the doctor treating the patient is not sure which type of treatment is best and so will allocate one or other treatment with the patient’s permission.

Inevitably some patients will die from cancer. It is important from the outset that the patient and relatives are both aware of what the situation is and are encouraged to talk freely about this between themselves and with friends. Most patients will be able to lead a normal life right up to the last few days or weeks. Pain and vomiting is a feature of some cancers but there are now
very effective drugs to deal with both. No patient should suffer from unbearable pain.

Hospices are specialized hospitals dealing with the needs of patients with advanced cancer. Patients may be attached to a hospice as an outpatient as well as being an inpatient. The most important doctor coordinating cancer care will be the General Practitioner. Many patients choose to spend their last days at home. In some cases, depending on the home circumstances and the patient’s particular problem, this is not possible so the hospice or even the hospital may be the best place.

It is always important to be open about the problem. Doctors involved with patients and their relatives will always be keen to discuss the issues and answer all their questions. Remember that even if it is not possible to guarantee a cure, treatment can prolong life and give patients an excellent quality of life. Also, remember that cancer can be cured!

**WHAT IS THE CAUSE OF CANCER OF THE PANCREAS?**

The cause of pancreatic cancer is largely not known, although in the case of ductal-type cancer (see below) there is an association with smoking tobacco. There is also an increased risk in patients with chronic pancreatitis and Hereditary
Pancreatitis. Pancreatic cancer also occurs in certain familial cancer syndromes such as Peutz-Jeghers Syndrome, Breast and Ovarian cancer Syndromes, Familial Atypical Mole and Melanoma Syndrome and Familial Adenomatous Polyposis. Rarely there are families with Familial Pancreatic Cancer.

ARE THERE DIFFERENT TYPES OF PANCREATIC TUMORS?

Pancreatic tumors can be solid tumors or those containing fluid (cystic). The solid tumors are usually adenocarcinomas even though rarely they can be of other types. There is also a special type of pancreatic tumor called neuroendocrine tumor (PNET). The type of tumor decides the long-term outcome and at times even the treatment.

**Cystic Tumors** may be benign or malignant & may be confused with pancreatic pseudo cysts (pronounced ‘Sue-doe-cyst’) that occur because of inflammation of the pancreas called pancreatitis. Hence it is important to confirm the nature of content of the cyst. The content of the cyst can be rather watery and this type of cystic tumor is called serous cyst adenoma. It is non-malignant and has very little cancer potential.

The fluid of the cyst can be filled with mucin and this type of cystic tumor can be a mucinous cyst adenoma or cyst adenocarcinoma or intraductal
papillary mucinous tumor. These are cancerous or have potential to become cancerous. These are the common varieties of cystic tumors. There are some uncommon ones too. The success rate of treatment of cystic tumors is better than the results of treatment of common pancreatic cancer.

WHAT IS A NET & PNET?

NET stands for neuroendocrine tumor. Neuroendocrine cells are special types of cells commonly located in the linings of gastrointestinal tract (esophagus to rectum), bronchus (airway) and pancreas. They are located elsewhere too. Tumor arising from these cells is called a neuroendocrine tumor or NET. The neuroendocrine cells secrete various hormones depending on their location. However not all NETs secrete tumors. Those that secrete hormones present due to the various effects of these hormones

PNETs short for pancreatic neuroendocrine tumors. These tumors may arise from the endocrine cells in the islets of Langerhans in the pancreas (islet cell tumors) or so called neuroendocrine cells either in the pancreas or ampulla of Vater (carcinoid tumors) or the duodenum (gastrinomas). The success rate of treatment of these PNETs is much better than the
results of treatment of other types of pancreatic cancer.

PNETs can secrete one of six or more different hormones causing different types of illness (or syndrome) and are called functioning neuroendocrine tumors. Also neuroendocrine tumors may not secret any hormones and are then called non-functioning neuroendocrine tumors. Endocrine tumors can affect individuals at any age and they can even arise in small babies.

Tumors that release excess insulin are called insulinoma. These tumors are nearly always benign, meaning non-malignant and non-cancerous. Tumors that release excess gastrin are called gastrinoma and occur in the pancreas and in the duodenum. These tumors are mostly cancerous. Other types of functioning neuroendocrine tumors are called glucagonomas, VIPomas, somatostatinomas & PPomas and are usually malignant or cancerous.

PNETs may be inherited and the two main types of hereditary pancreatic neuroendocrine tumors are found in multiple endocrine neoplasia type 1 (MEN-1) & von Hippel-Lindau disease (VHL), but also in the rare disorders of neurofibromatosis type 1 and tuberous sclerosis.
WHAT ARE THE EFFECTS OF PANCREATIC CANCER?

Most commonly cancers of the pancreas arise in the head of the gland. This has two effects. First, the cancer blocks the bile duct leading to jaundice, dark urine and pale stools. There is sometimes itching of the skin due to jaundice, which rapidly disappears once the blockage is cleared or bypassed.

Second, the cancer blocks the pancreatic duct leading to poor digestion, loose motions and weight loss. This can be relieved by clearing the blockage or by giving pancreatic enzyme tablets. Rarely it causes acute pancreatitis. Diabetes may already be present in a number of patients prior to developing the cancer or become apparent soon after it is diagnosed or following surgery.

Similarly blockage of the pancreatic duct can cause pain. Pain can be due to infiltration of nerves surrounding pancreas too.

WHAT ARE THE SYMPTOMS & SIGNS OF PANCREATIC CANCER?

The commonest type of pancreatic cancer is that arising from the small ducts of the pancreas (ductal-type adenocarcinoma). Most often it arises in the head of the gland and a principle
feature is the development of obstructive jaundice. This type of cancer often occurs in individuals aged 60 years or older but it can affect younger people as well. Typical early symptoms are jaundice, dark urine, pale stools, itching, feeling of sickness (nausea), weight loss & unexpected development of diabetes.

Tumors in the body and tail of pancreas are more difficult to pick up early because they do not cause obstructive jaundice earlier on. Therefore they remain undiagnosed for long time & spread by the time are diagnosed.

Typical symptoms for body and tail of pancreas tumors are vague abdominal pain, dyspepsia, stomach ulcer-like pain, intermittent diarrhea, feeling of sickness (nausea), weight loss, unexpected development of diabetes, back pain that does not go away & unexplained blood clots (venous thrombosis).

**Tumors of the Ampulla of Vater, Intra-pancreatic Bile Duct Cancer** (bile duct as it travels through the pancreas) & **Duodenal Cancer** can also cause similar complaints as the **cancer of head of pancreas**. Tumors from the ampulla & duodenum may cause bleeding & present as bloody vomiting or blood in stools (black stools) or only anemia. It is important to know that these cancers have better long-term outcome than pancreatic cancer.
Cystic tumors are relatively uncommon and are more frequent in females. They present with abdominal pain, back pain, vomiting, nausea, weight loss, an attack of acute pancreatitis & rarely gastrointestinal bleeding. If the cyst presses on the bile duct then this will cause obstructive jaundice. However it is often picked up while investigating the abdomen for relatively minor or unrelated complaints or during a routine health check up.

**HOW IS Pancreatic CANCER DIAGNOSED OR CONFIRMED?**

A patient with symptoms & signs of a pancreatic tumor may be 1st seen by family physician, internist, and general surgeon or directly by gastroenterologist. Specialist pancreatic surgeon is usually the last ring in the chain unfortunately and hence patients quite often come with a stent in the biliary system, which could be avoided.

Apart from a routine complete blood count investigations like liver function tests & abdominal USG are asked for as a rule. Once USG confirms suspicion then rest of the investigations like CT scan or MRI scan of abdomen and often a EUS are asked.

Remember that an abdominal US scan is likely to miss an early pancreas cancer. Therefore if
clinical picture & LFTs are in favor of pancreatic cancer (e.g. obstructive jaundice) patient will be sent for a pancreas specific CT scan which is fast & accurate. An MRI of abdomen is also equally useful & can be done.

Sometimes both are necessary when the tumor is cystic & nature of tumor (\textit{? cancer}) is uncertain. A EUS is most useful in doubtful cases and a EUS guided biopsy or aspiration of cyst fluid for analysis will be done whenever possible.

There are not many blood tests to diagnose any form of pancreatic cancer. Levels of a tumor marker CA 19.9 in the blood are measured and if they are significantly high, it raises a strong suspicion of biliary or pancreatic cancer. However it can rise even with noncancerous obstruction of bile duct.

In case of cystic tumor, estimation of levels of CarcinoEmbryonicAntigen or CEA & mucin in the cyst fluid aspirated during an EUS is useful to diagnose mucinous tumors

\textbf{ARE THERE SPECIAL INVESTIGATIONS FOR PNETs?}

Whenever a PNET is suspected on clinical picture & imaging studies, certain special tests will be asked. These include serum levels of gastrin, insulin, proinsulin, c-peptide levels and
Sometimes tests for uncommon tumors; nuclear scan called octreoscan or SRS (somatostatin receptor scintigraphy) scan, EUS guided aspiration cytology or biopsy. Rarely invasive tests are required to reach a diagnosis.

**SPECIAL TESTS AND OPERATIONS FOR PANCREATIC NEUROENDOCRINE TUMOURS**

Patients with pancreatic neuroendocrine tumors need to undergo some special tests that may be extra to those already described above.

**Hormone profile**

In order to find out whether your tumor is secreting hormones and which hormones are involved you will need to give several blood samples. You may also need to give a sample of urine or urine collected for a complete 24-hour period. If doctors are worried that you have an insulinoma you may need to be fasted for up to 72 hours. The endocrine team will help to advice and co-ordinate the collection of samples. The samples are sent to special labs (or laboratories). Because the tests are difficult to perform, the results may take several weeks to be completed. And unfortunately sometimes they have to be repeated.
Octreotide scan

Most pancreatic neuroendocrine tumors have what are called type-2 receptors (doctors say somatostatin type-2 receptors) on the outer surface of each cell of the tumor. By attaching a radioactive chemical to a particle that attaches to the receptor it is possible to see where the tumor is. This test is performed in the Nuclear Medicine Department and you are asked to lie on a special couch under a special camera called a gamma camera. It involves giving a small harmless intravenous injection of the radioactive chemical. Where and how many tumors there are can now be seen by the gamma camera.

MIBG scan

Because not all pancreatic neuroendocrine tumors (NET) can be seen by the octreotide scan we use another type of scan. MIBG is a special chemical that is taken up by the pancreatic NET cells and is concentrated inside the tumor cells. By attaching a radioactive chemical to the MIBG it is possible to see where the tumor is. This test is also performed in the Nuclear Medicine Department. Again you are asked to lie on a special couch under a special camera called a gamma camera. It involves giving a small harmless intravenous injection of the radioactive MIBG. Where and how many tumors there are can now be seen by the gamma camera.
Selective arteriography

Despite all the many tests already performed to locate where a pancreatic neuroendocrine tumor is, further tests may still be required. It might be possible to find the tumor because it has a special blood supply. Selective arteriography is performed in the X-ray department.

You will be placed on an X-ray table, the skin cleansed with antiseptic and covered with sterile gowns. Under local anesthetic a tube will be inserted into the artery in either the left or right groin (called an arterial catheter). ‘Dye’ (or contrast) is then injected into the catheter to see where it goes using an X-ray television screen. The catheter can be guided to the different small arteries that supply the pancreas. More ‘dye’ (or contrast) is then injected into each artery and using X-rays the tumor blood supply can be seen on a television screen and pictures are then taken.

Selective venous sampling

If selective arteriography has not been successful then this sampling technique can be used either in the same or separate sitting. Blood samples are taken from different positions in the veins that drain away from the pancreas. The procedure is also performed in the X-ray department.
You will be placed on an X-ray table, the skin cleansed with antiseptic and covered with sterile gowns. Usually using local anesthetic a wire is pushed through the skin and into one of the branches of the hepatic portal vein within the liver. A tube (or catheter) is pushed over the guidewire and the guidewire is removed. The tube is then advanced into the different veins that drain the pancreas and small samples of blood are then taken. The blood samples are then sent for special tests to see if there are any hormones and what the concentration is. Usually there is one area with a very high concentration. This tells the surgeon where about in the pancreas the tumor will be at operation.

**WHAT IS THE TREATMENT OF PANCREATIC CANCER?**

The best treatment for pancreatic cancers of above-mentioned types and peripancreatic cancers (ampulla, lower bile duct & duodenum) is surgery to remove the cancer (resection) by a specialist pancreatic surgeon. However this is possible only when the cancer is not spread to other tissues like liver, lungs, and bone etcetera.

Similarly the tumor should be free from surrounding important blood vessels. If this local involvement of vessels is limited to portal vein, a portion of this vein can be removed and reconstructed with a graft. The patient can have a
good life after this. But it is not true if the artery supplying the intestines is involved. The process involving assessment of surrounding & distant organ involvement is called staging of tumor.

Not all patients are lucky enough to undergo a surgery for various reasons and these patients undergo various palliative therapies. (Treatments that palliate or reduce complaints but don’t cure the patient)

**HOW IS STAGING OF TUMOUR DONE?**

In all patients it is important to determine whether an operation is feasible (‘staging’). This requires the use of a special CT scan. The specialist may request this investigation even if this has already been performed by the referring hospital. Another ‘staging’ procedure is to perform laparoscopy and/or laparoscopic ultrasound. This is a short operation under general anesthetic. Using ‘key hole’ surgery a telescope is inserted into the abdomen to examine the organs. A special ultrasound ‘probe’ may be used to look at deeper tissues. Some centers may also use a PET scan.

**WILL I WITHSTAND A SURGERY?**
It is necessary to ensure that you are fit enough to survive the major surgery. In order to determine this there will be some extra investigations.

An ECG (electro-cardio-gram) records the electrical heart activity and may be done on the ward or in the cardiology (meaning heart) department. A cardiac echo (doctors say echocardiogram or just echo) uses ultrasound waves to look at how the chambers of the heart are working. An echo is performed either in the cardiology department or the X-ray department. In selected cases you may be asked to undertake some exercise on a treadmill before and after the ECG or the echo.

PFTs (or pulmonary function tests) look at how well your lungs are functioning. This is usually performed in a special department and involves breathing into a tube attached to a machine.

After these tests a specialist anesthetist, who will tell you what the risks are of undergoing the surgery, will examine you. In addition, a heart specialist may assess you.

Only patients with good cardiac, lung and renal function are suggested major surgeries. Other patients may also undergo a major surgery but with added risk. Patients with highly compromised organ functions are advised against a surgery and sent for other treatment options.
WHAT IS THE NATURE OF SURGERY?

Depending on the location (head of pancreas or body-tail), size of the tumor and surrounding organ involvement, extent of surgery is decided. The commonest operation performed for cancer in and around head pancreas is called WHIPPLE’S SURGERY. It involves removing part of the stomach, the gallbladder and the bile duct, the duodenum and the head of the pancreas. For other locations a distal pancreatectomy is performed, wherein the body and tail of pancreas with or without the spleen are removed. In some cases, especially if there is a large cystic tumor or an endocrine tumor the whole pancreas is removed and may combine the Whipple and left pancreatectomy procedures.

Operations on pancreatic neuroendocrine tumors

The operations performed on PNETs are very similar to those performed on pancreatic cancers in general (see above). The choice of operation depends on the number and position of the tumors. In the case of insulinoma, usually only a very small procedure needs to be done on the pancreas. This simply involves removing the tumor only but not removing any of the pancreas. This operation is called enucleation. This is still classed, as a major operation however as a big
abdominal incision is still needed and major surgery is needed to find the pancreas. Also you will still need to be monitored closely after surgery to check on the blood sugar levels.

**DOES SURGERY INVOLVE ANY COMPLICATIONS?**

These operations are complex, have their own sets of minor and major complications, even a small percentage of death (2%) Removal of a pancreatic cancer by resection is a major procedure and will only be done by a specialist. Even so the complication rate is 40%. The minor complications include wound infection & pleural effusion.

The major complications include improper healing of stitched tissues (anastomosis) leading to leakages from pancreas, bile duct or intestine; intraabdominal infections due to leaks or preinserted biliary and pancreatic stents, pneumonia, septicemia, invasive fungal infections due to prolonged antibiotics, poor nutrition and underlying diabetes if present; gastrointestinal or intraabdominal bleeding.

Management of these problems involve insertion of tubes under CT scan guidance to drain infected fluid collections, insertion of tubes to divert bile, heavy antibiotics, endoscopic or radiological intervention guided control of bleeding
nutritional support, ICU monitoring, & care. An attempt is always made to continue oral & enteral feeding whenever possible. Rarely a second surgery is required for intraabdominal infections.

It is important to remember that rate of complications is always more in patients with biliary stents due to resistant infections. Although these complications can be dealt with, about 5% of patients will not be able to leave hospital. Thus the success rate is about 95% but is better in younger, fitter patients. Thus selecting patients for resection is very important.

**HOW LONG WILL THE PATIENT STAY IN THE HOSPITAL?**

Usually surgery like Whipple’s procedure involve stay of 10-12 days in the hospital. However patients with major complications may stay for 4-6 weeks. At times patients are sent home with drainage tubes.

**WHAT WILL BE THE EXPENSE?**

The expenses depend upon the hospital where it is done, the concerned consultant & operating team, stay, whether there are postoperative complications, medications required and many more things. Hence it is possible to give an idea about an uneventful surgery, which you should discuss with your consultant in person. Still it
will suffice to say that it involves significant expense.

**WILL I NEED CHEMOTHERAPY?**

It is now standard treatment to give chemotherapy if you have the common ductal type pancreas cancer once you recover from the resection surgery. This is called adjuvant chemotherapy. Chemotherapy is also given if the final histopathological report shows incomplete removal in spite of an apparently successful surgery. This can happen in a small percentage of patients. Chemotherapy is not recommended for other peripancreatic cancers (ampulla, bile duct & duodenum) unless tumor has spread to nearby lymph glands or is incompletely removed.

**HOW LONG WILL IT GO ON?**

Chemotherapy will only be started once you have fully recovered from your operation and have gotten over any post-operative complications. Usually six treatments (or cycles) are given by a local medical oncologist (cancer doctor). This period of treatment usually last six months.

**WILL I TOLERATE CHEMOTHERAPY?**

Immediately after your surgery you will feel quite weak and wonder whether you will ever get back to normal strength. In fact you will get back
to normal, although this may take 6-12 month. Even if you are feeling ‘rough’ you can still have the adjuvant chemotherapy and it will not interfere with your rate of recovery. We use adjuvant chemotherapy because it prolongs survival. In particular it is important to appreciate that modern chemotherapy is usually not associated with major side effects.

WHAT IS THE FOLLOW UP SCHEDULE AFTER A SUCCESSFUL SURGERY?

You will be asked to follow up once in three months with fresh reports of liver function tests, CA19.9 & ultrasonography of abdomen. If the reports show any abnormality then a CT scan of abdomen will be asked. If the reports are normal, three monthly follow up continues for 2 years. A CT scan is performed once a year during these 2 years. After 2 years the follow up is reduced to once in 6 months for next 3 years.

WHAT TREATMENT CAN BE GIVEN IF A PATIENT CANNOT BE OPERATED OR IS BEYOND CURE ON INITIAL ASSESSMENT?

This is called PALLIATIVE TREATMENT. If surgical removal of the cancer is not possible there are many treatments that will be given to help a patient.

PALLIATIVE SURGERY
This type of surgery is performed if the cancer cannot be removed.

**DEBULKING OF TUMOR**

This implies partial removal of the tumor to whatever extent possible with safety. This is never done for the common ductal type of pancreatic cancer. It is done in selected cases of cystic tumors and on many occasions for PNET. Patient should discuss the possibility in an individual case with his treating physician. Debulking reduces tumor volume allowing resolution of some complaints and also allows other form of therapies like chemotherapy or TACE or DOTATATE & DOTATOC work more effectively.

**BILIARY BYPASS**

This operation is performed for obstructive jaundice. Obstruction of the bile duct in pancreatic cancer is common. This happens because the cancer in the head of the pancreas can press on the bile duct and cause it to become partly blocked. This causes obstructive jaundice (see above). The narrowing (or stricture) is ‘bypassed’ using a special small bowel channel. This operation is called hepato-jejunostomy or choledocho-jejunostomy. Choleodocho’ is two words (from Greek and Latin) meaning bile (chole) and duct (docho), whilst ‘hepato’ refers to
the bile duct as it leaves the liver. This operation will be done either as a planned operation (rare with availability of stent) or sometimes as a last minute decision when patient has been taken up for surgery and found inoperable on opening the abdomen (common).

GASTRIC BYPASS

This procedure is undertaken if there is vomiting due to obstruction of the stomach or duodenum by a tumor. Obstruction of the duodenum is quite common. This happens because a cancer in the head of the pancreas can press or invade the duodenum and cause it to become partly blocked. This causes a feeling of sickness (nausea) and vomiting after food. This will obviously contribute to weight loss. The narrowing (or stricture) is ‘bypassed’ connecting the small bowel to the stomach. This operation is called a gastro-jejunostomy or gastric-bypass. In fact this may be done during the same time as biliary bypass to avoid the problems of duodenal obstruction at a later date.

BILIARY STENTING

Older patients may not be suitable for surgery. The jaundice can still be relieved by inserting a tube (stent) through the tumor during ERCP. If it is not possible to do this by ERCP, then an alternative is by PTHC or a combination of ERCP and PTHC and is called a combined
procedure or rendezvous procedure. A metallic stent, which is a permanent fixture, is inserted. It is better than a plastic stent as it doesn’t get blocked easily. But it is expensive.

Stenting should be done only if patient is having symptoms due to jaundice like severe itching. Stenting is not without complications because stent can get blocked and can cause infection and severe sepsis. At times a repeat stenting will be required.

**ENDOSCOPIC DUODENAL STENTING**

Obstruction to the duodenum usually needs surgery. An alternative in older or unfit patients is to insert a tube through the duodenum. In the X-ray department a flexible telescope or endoscope is passed into the mouth. This is then eased down the gullet and into the stomach and then into the duodenum. A small guidewire is then pushed through the tiniest gap left by the tumor. The special tube or stent is then pushed over the guidewire. This stent is metallic and expands on its own in next 48 hours. You lie on an X-ray table to enable pictures of the procedure to be taken as it is being performed.

It is essential that you do not eat or drink anything for at least 8 hours before the procedure is performed. Usually a plastic tube is put into a vein of the right forearm or the back of the hand
before you go to the X-ray department. You may need a drip of intravenous fluids. You will be asked to sign a consent form agreeing to this procedure because it is complicated.

Normally you are taken on a trolley to the X-ray department and, after being checked by a nurse, asked to move onto the X-ray table. You will be asked to lie on your left side with your left arm behind your back and be given a throat spray of local anesthetic. This tastes awful but the feeling quickly goes and it will stop any coughing during the procedure. A strong sedative is now given by injection. This is enough to make most patients very sleepy but not fully unconscious. It is very important that you are as relaxed as possible before and during the procedure. The telescope is easily passed into the mouth and stomach. There is then a strange sensation as air is introduced into the stomach. Belching should be avoided as the air helps the endoscopist to pass the tip of the telescope into the duodenum. Most patients usually do not remember anything of the procedure.

The special tube or stent is permanent and is a metal mesh. This gradually expands over a few days after it has been inserted, so the relief from nausea may not be immediate.

CHEMOTHERAPY
This is also advised for patients with a cancer that cannot be removed as this makes you feel better (doctors say ‘improves symptoms’) as well as increasing the length of time that you have to live. Because doctors have still to work out the best type of chemotherapy there are many clinical trials that compare the best available treatment with a new treatment. We have a trial because we do not know if the new treatment is actually better. Patients usually benefit by being in a trial so patients are recommended to consider joining an approved trial. Else one opts for a reasonably proven & efficacious protocol.

DO ALL CYSTIC TUMORS NEED TREATMENT?

All mucin containing tumors (because of their cancerous potential), tumors with evidence of cancer, all rapidly enlarging cystic (serous or otherwise) tumors, all tumors causing complaints, all cystic PNETS and tumors whose nature cannot be confirmed; all of them should ideally be subjected to surgical treatment and excision. However small sized serous cystic tumors do not need surgery if confirmed beyond doubt and are only observed by routine imaging like CT scan. If they grow in size or cause complaints only then a surgery is performed.
However some patients are not fit for surgery because of age, spread or medical illnesses and they are treated only for their prominent symptoms like pain (medicines), jaundice (stent), vomiting (medicines or stent or surgery if there is obstruction of stomach or intestine).

Chemotherapy is not very useful in patients with cystic tumors.

ARE THERE SPECIAL TREATMENT OPTIONS FOR PATIENTS WITH PANCREATIC NEUROENDOCRINE TUMOURS APART FROM SURGERY?

The symptoms of some patients with certain types of pancreatic neuroendocrine tumor are because their tumors are secreting a hormone or it’s a functioning tumor. An insulin secreting tumor reduces blood sugar and can cause repeated giddiness or fainting episodes, gastrin secreting tumor causes hyperacidity leading to gastric ulcers, others can cause watery diarrhea weakness, so on and so fourth.

These complaints can be greatly relieved by special drugs (such as octreotide) by blocking the secretion of the hormone from the tumor. However this does not stop the growth or spread of the tumor. Similarly the effect is limited if tumor load is very high. The exception is insulinoma, which should always be treated by surgical removal.
Some patients will also benefit from chemotherapy and also from a special drug called interferon–alpha (mainly for patients with carcinoid tumors).

Special radiotherapy treatment may be given using chemicals that are tagged with radioactive agents (DOTATOC & DOTATATE). These selectively go to the tumor, and destroy it. This is conditional on the tumor being positive for the octreotide scan.

There are other treatments also available if the tumor has spread to the liver such as chemo-embolization (TACE) or radiofrequency ablation (RFA). These are quite new treatments and your doctor will give you more specific information about these if they apply to you.

It is important to know that PNETS have a better outcome compared to other pancreatic cancers because they are slow growing, spread is late & multiple treatment options are there even when tumor has spread.

**HOW IS THE PAIN CONTROLLED IN INOPERABLE PATIENT?**

There may be severe pain from pancreatic cancer if the cancer cannot be removed. You will be seen by a specialist pain team, which will help to
find the best combination of medication for you. This frequently involves the use of morphine tablets of one kind or another. These kinds of tablet cause two particular problems. One is a feeling of sickness (called nausea), so you will need to take anti-sickness tablets. The other problem is constipation so you will need to take some form of stool loosening medicine or laxatives. Sometimes medicated skin patches are given which deliver the drug through skin avoiding certain side effects.

Most patients manage very well on this type of medication but sometimes it is necessary to resort to special pain killing measures. This involves paralyzing or cutting the pain nerves that go between the brain (where the pain is felt) and the pancreas.

COELIAC PLEXUS NERVE BLOCK

The nerves from the pancreas collect just behind the pancreas in a thick bundle called the coeliac plexus (coeliac is pronounced ‘see-lee-ack’). These nerves can be injected using a long needle and local anesthetic in the X-ray department or using a needle with the endoscope during EUS (see above). If a local anesthetic is used this may reduce the pain, but usually this only lasts for a few weeks. It is also possible to block the nerves permanently using special chemicals (called sclerosants) such as concentrated alcohol.
BILATERAL THORACOSCOPIC SYMPATHECTOMY (BITS)

The BITS procedure involves cutting the pain nerves from the pancreas as they travel through the chest towards the spinal cord in the spinal canal. The operation is done using fine instruments and telescopes using general anesthetic and is surprisingly simple and safe to perform. This is so called ‘keyhole’ surgery.

DOES PANCREATIC CANCER RUN IN FAMILIES?

In general, the answer is NO. Nevertheless in rare cases there are families in which pancreatic cancer can run in families. These include the following.
· Families with familial cancer syndromes including Peutz-Jeghers Syndrome, Breast and Ovarian Cancer Syndromes, Familial Atypical Mole and Melanoma Syndrome and Familial Adenomatous Polyposis.
· Hereditary Pancreatitis.
· Familial Pancreatic Cancer.
· Hereditary Pancreatic Neuroendocrine Tumors including multiple endocrine neoplasia type 1 (MEN-1) and von Hippel-Lindau disease, neurofibromatosis type1 and tuberous sclerosis.
Inherited pancreas cancer happens because there is an altered gene that predisposes to cancer and is passed on from one generation to the other.

WHAT ARE GENES?

Each person has exactly the same number of genes as every other person. The total number of genes is 30,000. Genes are in the nucleus of each cell of the body. Genes are like the blueprints in a factory. These blueprints (or genes) enable the cell to make proteins which then organize the two other types of basic molecule (carbohydrates and fats) to create particular types of cell and hence the different organs (such as liver, arms and legs and so on).

In the cells of different organs only some of the 30,000 genes in the nucleus are selected for use. This number varies from 6,000 to 10,000 genes in any particular cell. The different combination of genes used as blueprints for making proteins is how the human body can be organized in such a complicated way (compared to a simple worm that has only 900 genes).

Genes are always in pairs, so that one set comes from the mother and one set comes from the father. There are tiny variations in each gene. These tiny variations are essential to make every person an individual. Occasionally a tiny
variation in a gene can give rise to a disease condition.

WHAT IS MUTATION?

An alteration in a gene that gives rise to a disease is often referred to as a mutation (this is a Latin word that simply means ‘changed’). Patients and their families with inherited pancreatitis require the care of a specialist surgeon, pediatrician or gastroenterologist and genetic counseling.

WHICH GENES ARE INVOLVED IN PANCREAS CANCERS?

The main genes involved in all of the major familial cancer syndromes are known. The names of the genes sound quite strange so we only tend to use the short version name of each gene. The gene for Peutz-Jeghers Syndrome is the STK11 gene, the genes for Breast and Ovarian Cancer Syndromes are BRCA1 and BRCA2, the gene for Familial Atypical Mole and Melanoma Syndrome is the p16 gene and the gene for Familial Adenomatous Polyposis is the APC gene.

The main gene for Hereditary Pancreatitis is the PRSS1 gene. The main gene for Familial Pancreatic Cancer is not known, although 10-20% of families have a BRCA2 gene mutation.
The gene for multiple endocrine neoplasia type 1 is the MEN-1 gene. The gene for von Hippel-Lindau disease is the VHL gene. The gene for neurofibromatosis type 1 is NF-1. The genes for tuberous sclerosis are the TSC-1 and TSC-2 genes.

**MULTIPLE ENDOCRINE NEOPLASIA TYPE1 (MEN-1)**

This is an autosomal dominant familial cancer syndrome (passed on by the mother or the father) with tumors in small glands in the neck (called parathyroid), a small gland attached to the brain (called the anterior pituitary) as well as the pancreas. The neuroendocrine tumors in the pancreas are usually multiple.

**VON HIPPEL-LINDAU (VHL)**

Von Hippel-Lindau disease is another type of rare autosomal dominant familial cancer syndrome (passed on by the mother or the father). This condition causes a multiplication of small blood vessels in the brain, spinal chord and back of the eyes and also cancers of the kidney and the small gland next to the kidney called the adrenal gland. About two thirds of patients with VHL also have a problem with the pancreas, but this is usually in the form of simple harmless cysts. About one in ten people with VHL however will also have one or more pancreatic neuroendocrine tumors (these are usually non-functioning).
DO PATIENTS WITH AN INHERITED PANCREAS CANCER RISK REQUIRE SPECIAL FOLLOW UP?

Patients from families with familial cancer syndromes (including Peutz- Jeghers Syndrome, Breast and Ovarian Cancer Syndromes and Familial Adenomatous Polyposis), Hereditary Pancreatitis and Familial Pancreatic Cancer will need to undergo regular screening for cancer.

The International Association of Pancreatology recommends that all patients be seen at a specialized pancreas center. There is no standard set of methods at the present time and the following are only suggestions based on current practice in major pancreas cancer screening centers.

- In principle screening should start at the age of 40 years or ten years earlier than the youngest affected family member.
- All patients should have a baseline EUS and CT scan along with a tumor marker (such as CA 19-9). MRI is an alternative to a CT scan but an abdominal ultrasound scan is not acceptable.
- After this, the EUS and blood tests should be repeated every year.
- The CT scan or MRI scan can be repeated every three years, depending on EUS appearances.
- In the case of Hereditary Pancreatitis the pancreas may be so damaged as to invalidate the
EUS, in which case CT or MRI are recommended annually.
  · If possible participate in a research program and provide pancreatic juice samples for experimental molecular testing every 1-3 year.

GENETIC TESTING IN FAMILIAL PANCREATIC CANCER

  · These families should undergo general screening for cancer as above.
  · A proportion of families with Familial Pancreatic Cancer will have a mutation of the BRAC2 gene. Individuals from these families must be referred for genetic counseling and BRCA2 gene testing.

SCREENING IN PATIENTS WITH MEN-1

Surveillance of carriers of the MEN-1 gene should begin in early childhood with blood tests every year and imaging every 3 years. Consensus guidelines have recommended screening from the age of 5 years for anterior pituitary tumors with blood tests (called prolactin and Insulin like growth factor-1) and MRI and for insulinoma also MRI along with blood tests (called fasting glucose and insulin). Screening for parathyroid tumors should begin from the age of 8 years with blood tests
(Called calcium and parathyroid hormone) and for chest and abdominal tumors from the age of 20 years by CT.

Other neuroendocrine tumors should also be screened from the age of 20 years using other blood tests (called chromogranin A, glucagon and proinsulin) and MRI, CT or octreotide scan. There should also be endoscopy for gastric tumors (carcinoids) and EUS for duodenal and pancreatic tumors.

SCREENING IN PATIENTS WITH VHL

Surveillance of carriers of the VHL gene should begin at the age of 10yrs initially with abdominal ultrasound repeated annually looking to find tumors in the kidneys, adrenal glands and pancreas gland as well as the pelvis. From the age of 20yrs there should be 1-2 yearly abdominal CT or MRI scans. For the pancreas again EUS examinations are to be preferred.

CAN I DRINK ALCOHOL?

Alcohol is not recommended for any patient with pancreatic problem.

For Information
A unit of alcohol is 100mls of 10% alcohol (by volume) equivalent to a half-pint of regular beer or lager, a regular glass of table wine, or a single
measure of spirit. The **recommended intake for healthy adults** should be no more than 21 units per week for women and no more than 28 units per week for men.

**LIVING WITHOUT A PANCREAS**

There are some patients who have had either their pancreas removed or who still have pancreatic tissue but which is not functioning at all. Both types of patient are perfectly able to lead a normal life provided they take regular enzyme supplements and insulin injections.

**PANCREATIC ENZYME SUPPLEMENTS**

There are many preparations available. These preparations differ considerably in their effectiveness of action. The better preparations consist of capsules containing scores of small granules.

The enzyme preparations can be regular and high dose. The capsules need to be taken during each meal and with any snack. Requirements vary enormously from patient to patient: typically 20-30 high-dose capsules per day are required but this can be lower or much higher. The requirements vary greatly from patient to patient partly because of the different level of secretion by any functioning pancreas and partly because there are still some enzymes secreted by the
salivary glands, tongue, stomach and small intestines but which also varies greatly from person-to-person. Once patients are accustomed to taking enzyme supplements, they are usually allowed to adjust the number they take themselves to suit their own individual needs.

**INSULIN**

There are many types of insulin available including human insulin obtained by genetic engineering. Precise dosing and frequency of injections is an individual matter. Being under the care of a diabetic specialist is obviously important in the first instance.

**GASTRIC ACID SUPPRESSING TABLETS**

Medication of this sort is often prescribed to be taken once or twice a day. Pancreatic juice normally counters the acid of the stomach. In the absence of the pancreas, there may be excess acid, which can cause dyspepsia. There is also some evidence that taking this type of medication helps the action of pancreatic enzyme supplements, which means that fewer capsules are required each day.

**LIVING WITHOUT A SPLEEN**

Pancreatic surgery sometimes necessitates removal of the spleen. This is much more of a
problem in children than in adults. Without the spleen there is a small but real risk of developing a serious infection caused by certain bacteria especially pneumococcus. All children and adults without a spleen therefore require regular pneumococcal vaccination. All patients should also receive **vaccination for meningococcus groups A and B**, and **children less than 4 years old require Haemophilus influenza type b** vaccination. Children will also need to take a daily antibiotic. The risk is much less in adults, but nevertheless daily antibiotics are usually prescribed. Nevertheless if any infection develops, then appropriate antibiotics (such as **penicillin or erythromycin**) must be taken over-and above any other types of antibiotic that are required.

Removal of the spleen sometimes causes the number of platelets in the blood to increase. This increases the risk of developing unwanted blood clots. Regular blood tests are therefore needed. If the number of platelets in the blood rises excessively, it is common practice to prescribe **low dose aspirin, which** reduces the risk of undesirable clotting.
Above information will help you to make an informed decision but it cannot replace the professional advice and expertise of a doctor who is familiar with your condition. You may have questions that are not covered; you should discuss these with your surgeon. You must remember every individual is different.

DOCTORS DEALING WITH PANCREATIC DISEASE THAT YOU MAY MEET

**Dietician:** This is a specialist who is not a doctor but is an expert in advising on various types of diet.

**Endocrinologist:** A physician who is highly specialized in glandular problems including sugar diabetes.

**Endoscopist:** This may be a gastroenterologist or a surgeon who is able to undertake endoscopy (examination of the stomach or bowel using a flexible telescope). A few endoscopists can also perform ERCP and EUS, which are specialist forms of endoscopy that examine the biliary and pancreatic ducts and the pancreas.

**Gastroenterologist:** A physician who is highly specialized in ‘gut’ problems and is also usually an ‘endoscopist’.

**General physician:** A consultant medical doctor who works in a hospital and who is broadly specialized including ‘gut’ problems.
**General surgeon:** A consultant surgeon who works in a hospital and who is broadly specialized including ‘gut’ problems.

**Geneticist:** A consultant who specializes in diseases which may be inherited and may be able to provide additional help to that normally given by your other specialist doctors.

**Nutrition team:** A team of specialist doctors and nurses involved in providing specialist nutritional support, including the insertion of venous access lines and special stomach tubes to help patients who are unable to eat properly.

**Pediatrician:** A consultant who specializes in the care of children and who may be called to investigate a pancreatic problem in young children or teenagers.

**Pain team:** A team of specialist doctors who specialize in providing special treatment measures and support for patients who are experiencing difficulties in pain control.

**Radiologist:** A consultant who specializes in taking X-rays and scans of various sorts at the request of other specialists.

**Specialist surgeon:** A general surgeon who is highly specialized – a so-called PB-specialist is a pancreato-biliary surgeon.