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. Cancers sometimes produce harmful substances which can lead to poor appetite and weight loss.

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 (such as loss of hair) 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 are a feature of some cancers but there are now very effective drugs to deal wit both. No patient should suffer from unbearable pain.

There are now very good cancer services around the country. Macmillan Nurses are specially trained to deal with patients with cancer, who can visit the patient at home on a regular basis. Hospices are specialised 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 co-ordinating cancer care will be the General Practitioner. Many patients choose to spend their last days at home and health support services usually will be provided to make this possible. 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 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 .

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. 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.

There are many types of cancer of the pancreas.

Common 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 (see above). This type of cancer often occurs in individuals aged 60 years or older but it can affect younger people as well. Resection of the cancer followed by adjuvant chemotherapy is the standard treatment. If this is not possible it may be possible to obtain good palliative results with chemotherapy. Patients are strongly advised to join a clinical trial, which will normally always be available at their regional centre.

Typical early symptoms are:

- jaundice,
- dark urine,
- pale stools,
- itching,
- feeling of sickness (nausea),
- slight weight loss
- unexpected development of diabetes (in someone over 50 years old who is not obese).

Tumours in the body and tail of pancreas. These tumours are more difficult to pick up early because they do not cause obstructive jaundice.

Typical symptoms for body and tail of pancreas tumours are:

- vague abdominal pain,
- dyspepsia,
- stomach ulcer-like pain,
- intermittent diarrhoea,
- feeling of sickness (nausea),

- weight loss,
- unexpected development of diabetes (in someone over 50 years old who is not obese),
- back pain that does not go away,
- unexplained blood clots (venous thrombosis).

Remember that an abdominal US scan is likely to miss an early pancreas cancer. Therefore you must insist on a pancreas specific CT scan - this is fast (takes only a few minutes), highly accurate and not so expensive compared to the US scan.

Tumours of the Ampulla of Vater

Tumours may arise from the ampulla of Vater. They also cause obstructive jaundice (see above) and they tend to affect older patients. The best treatment is resection . The role of adjuvant chemotherapy is uncertain and therefore you should join a clinical trial if possible. The success rate of treatment of these 'ampullary' tumours is much, much better than the results of treatment of common pancreatic cancer.

Intra-pancreatic Bile Duct Cancer

A cancer may arise in the bile duct as it travels through the pancreas. They also cause obstructive jaundice (see above) and are usually confused with the common pancreatic cancer. In fact the only way of knowing this is for the pathologist to examine the resected specimen under the microscope. The best treatment is resection . The role of adjuvant chemotherapy is uncertain and therefore you should join a clinical trial if possible. The success rate of treatment of these bile duct cancers is much better than the results of treatment of common pancreatic cancer.

Duodenal Cancer

Tumours may arise from the duodenum and may cause anaemia bleeding or vomiting but sometimes they also cause obstructive jaundice (see above) . The best treatment is resection . The role of adjuvant chemotherapy is uncertain and therefore you should join a clinical trial if possible. The success rate of treatment of these duodenal tumours is much better than the results of treatment of common pancreatic cancer.

IPMT (Intraductal Pancreatic Mucinous Tumour)

These are cancers that arise from lining of the main pancreatic duct. These tumours secrete a large amount of mucous (much more than usual) and so the pancreatic duct dilates. The tumours may be benign or malignant . The tumours may occur in only a small part of the main pancreatic duct or affect the whole length of the pancreatic duct. Small swellings may develop from the sides of the main pancreatic duct full of mucous to give the appearance of cysts. If the mucous enters the bile duct then this will cause obstructive jaundice (see above) . Usually the best treatment of IPMTs is resection. The success rate of treatment of IPMTs is much, much better than the results of treatment of common pancreatic cancer.

Cystic Tumours

Tumours in the pancreas can develop as cysts. The tumours may be benign or malignant . In non-specialist centre they may be confused with pancreatic pseudocysts (pronounced 'Sue-doe-cyst') that occur because of inflammation of the pancreas called pancreatitis.

The content of the cyst can be rather watery and this type of cystic tumour is called serous cystadenoma. This type of tumour is benign, meaning non-malignant and non-cancerous.

The content of the cyst can be filled with mucin and this type of cystic tumour is called a mucinous cystadenocarcinoma. This type of tumour is malignant, meaning cancerous. If the cyst presses on the bile duct then this will cause obstructive jaundice (see above) . The best treatment is resection . The success rate depends on whether all of the cancer could be properly removed.

Neuroendocrine Tumours (PNETs)

These are also called PNETs, short for pancreatic neuroendocrine tumours. These tumours may arise from the endocrine cells in the islets of Langerhans in the pancreas (islet cell tumours) or so called neuroendocrine cells either in the pancreas or ampulla of Vater (carcinoid tumours) 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 tumours . Also neuroendocrine tumours may not secret any hormones and are then called non-functioning neuroendocrine tumours . Endocrine tumours can affect individuals at any age and they can even arise in small babies.

Tumours that release excess insulin are called insulinoma. These tumours are nearly always benign, meaning non-malignant and non-cancerous. Tumours that release excess gastrin are called gastrinoma a nd occur in the pancreas and in the duodenum. These tumours are mostly malignant, meaning cancerous. Other types of functioning neuroendocrine tumours are called glucagonomas, VIPomas, somatostatinomas and PPomas and are usually malignant, meaning cancerous. PNETs may be inherited and the two main types of hereditary pancreatic neuroendocrine tumours are found in multiple endocrine neoplasia type 1 (MEN-1) and von Hippel-Lindau disease (VHL), but also in the rarer disorders of neurofibromatosis type 1 and tuberous sclerosis.

TREATMENT OF PANCREATIC CANCER

CURATIVE TREATMENT

Pancreatic Cancer Resection

The best treatment for pancreatic cancer is surgery to remove the cancer (resection) but this can be quite difficult and is not always very successful. The best results are achieved in regional pancreas cancer centres that cover populations of at least two million people. So it is important that you are referred by your doctor or local hospital to your nearest regional centre.

Adjuvant 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. This 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. The medical oncologist will answer all your questions. In particular it is important to appreciate that modern chemotherapy is usually not associated with major side effects (such as hair loss). Because we are not sure which adjuvant chemotherapy is the best you may be asked to participate in an approved clinical trial .

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 months. We know that 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.

PALLIATIVE TREATMENT

If resection of the cancer is not possible there are many treatments that will be given to help you.

Biliary Stenting

Older patients may not suitable for surgery. The jaundice can still be relieved by inserting a tube (stent) through the tumour during ERCP (biliary stent, see above). 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 (see above).

Endoscopic Duodenal Stenting

Obstruction to the duodenum usually needs surgery. An alternative in older 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 trough the tumour. The special tube or stent is then pushed over the guidewire and through the tumour. 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 anaesthetic. 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.

Special Treatments For Patients With Pancreatic Neuroendocrine Tumours

The symptoms of some patients with certain types of pancreatic neuroendocrine tumour can be greatly relieved by special drugs (such as octreotide). The exception is insulinoma, which should always be treated by surgical removed. Some patients will also benefit from chemotherapy and also from a special drug called interferon-alpha (mainly for patients with carcinoid tumours). Special radiotherapy treatment may be given using chemicals that are tagged with radioactive agents that selectively go to the tumour. This is conditional on the tumour being positive for either the octreotide scan or the MIBG scan (see below). There are other treatments also available if the tumour has spread to the liver such as chemo-embolisation or radiofrequency ablation . These are quite new treatments and your doctor will give you more specific information about these if they apply to you.

OPERATIONS FOR CANCER

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%. 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 and requires several steps.

Staging of the tumour

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 anaesthetic. 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 centres may also use a PET scan (see above).

Are you fit for major surgery?

It is also necessary to ensure that all patients will be fit enough to survive the major surgery. In order to this there will be some extra investigations and may include one or more of the following.

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 case you may be asked to undertake some exercise on a treadmill before and after the ECG or the echo.

A MUGA scan looks at how well the chambers of the heart work. 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 a radioactive chemical. How well the heart works can now be seen by the gamma camera.

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 machine.

After these test you will always be examined by a specialist anaesthetist who will tell you what the risks are of undergoing the surgery. In addition you may be assessed by a heart specialist.

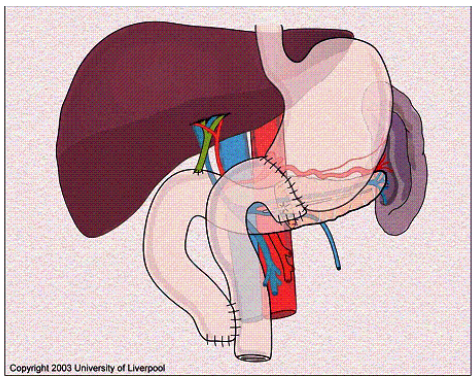
MY OPERATION

Your specialist will give you the details of which procedure is intended before you sign the consent form for operation. The common operations are outlined below.

CURATIVE SURGERY

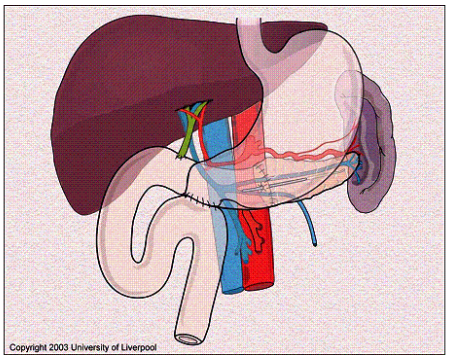
These operations aim to remove all of the tumour or cancerous tissue.

Kausch-Whipple Operation



This operation is often just called a 'Whipple's'. It involves removing part of the stomach, the gallbladder and the bile duct, the duodenum and the head of the pancreas.

Pylorus-Preserving Kausch-Whipple's Operation



In the procedure, the stomach and pylorus are preserved.

Left Pancreatectomy

This is also called a 'distal' pancreatectomy. It is performed if the tumour is in the body or tail of the pancreas a is.

Total Pancreatectomy

In some cases, especially if there is a large cystic tumour or an endocrine tumour the whole pancreas is removed and combines the Whipple and left pancreatectomy procedures.

Splenectomy

In a left or total pancreatectomy the spleen will be removed.

Pancreas Preserving Duodenectomy

In patients with many polyps of the duodenum that are considered a risk of developing into cancer (such as Familial Adenomatous Polyposis, or FAP) it is not necessary to remove the pancreas. In this operation the duodenum is separated from the pancreas and removed. The small bowel is then advanced and joined to the pylorus, the bile duct and pancreatic duct. In effect this creates a 'new duodenum'.

PALLIATIVE SURGERY

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

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 be come partly blocked. This causes obstructive jaundice (see above) . The narrowing (or stricture) is 'bypassed' using a special small bowel channel. This operation is called a Roux-en-Y hepato-jejunostomy or Roux-en-Y choledocho-jejunostomy . Sometimes a very simple bypass is created by joining the bile duct directly onto the duodenum and is called a choledocho-duodenostomy. 'Choledodocho' 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.

Gastric Bypass

This procedure is undertaken if there is vomiting due to obstruction by tumour of the duodenum,. Obstruction of the duodenum is quite common. This happens because a cancer in the head of the pancreas can press on the duodenum and cause it to be come partly blocked. This causes a feeling of sickness (nausea) and vomiting after a 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.

AFTER MY OPERATION

Following the operation it is common practice for you to be cared for on a special ward that has a high ratio of nurses to patients, has provision for expert anaesthetic care and has good monitoring facilities. The type of units and their names may vary from hospital to hospital. Typically you will be cared for in a Post-Operative Critical Care unit or POCCU for intensive monitoring for the first 24 hours. Following this you will be transferred to a High Dependency Unit (HDU) for several days until your condition has improved sufficiently for you to be returned to the regular ward . If there are serious complications you may need to be transferred to the Intensive Therapy Unit (ITU) but this is usually not necessary as most complications can be dealt with on the HDU or just the regular ward.

In some hospitals the POCCU facility is placed in the ITU or a special HDU. In these situations you may be routinely observed on the ITU and then HDU, or just the special HDU before going back to the regular ward.

For the first few days you will only be able to drink fluids but the amount will increase from day to day to day. After six or seven days you will gradually a light diet will gradually be introduced.

In the absence of any major complications you would expect to be in hospital for two to three weeks.

You will feel quite weak after the surgery. Your strength will gradually improve although this is likely to take 6-12 months before you feel one hundred percent. It may be necessary for you to take some pancreas enzyme tablets to help your digestion during the recovery period (see below). You will feel and look quite normal. Unless you have had a total pancreatectomy you will not become diabetic. You will be able to drink and eat all the foods that you normally would.

SPECIAL TESTS AND OPERATIONS FOR PANCREATIC NEUROENDOCRINE TUMOURS

Patients with pancreatic neuroendocrine tumours need to undergo some special test that may be extra to those already describe above.

Hormone profile

In order to find out whether your tumour 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 advise and co-ordinate the collection of samples. The samples are sent to special labs (or laboratories) around the country called reference labs. 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 tumours have what are called type-2 receptors (doctors says omatostatin type-2 receptors) on the outer surface of each cell of the tumour. By attaching a radioactive chemical to a particle that attaches to the receptor it is possible to see where the tumour 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 tumours there are can now be seen by the gamma camera.

MIBG scan

Because not all pancreatic neuroendocrine tumours 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 neuroendocrine tumours cells and is concentrated inside the tumour cells. By attaching a radioactive chemical to the MIBG it is possible to see where the tumour 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 tumours 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 tumour is, further tests may still be required. It might be possible to find the tumour because it has a special blood supply. Selective arteriography is performed in the X-ray department. You will then be placed on an X-ray table, the skin cleansed with antiseptic and covered with sterile

gowns. Under local anaesthetic 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 tumour blood supply can be seen on a television screen and pictures are the 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 anaesthetic 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 advance 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 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 tumour will be at operation.

Operations on pancreatic neuroendocrine tumours

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 tumours. In the case of insulinoma, usually only a very small procedure needs to be done on the pancreas. This simply involves removing the tumour 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.

CONTROL OF PAIN

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

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 . Most patients manage very well on this type of medication but sometimes it is necessary to resort to special pain killing measures. This involves paralysing 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 anaesthetic in the X-ray department or using a needle with the endoscope during EUS (see above) . If a local anaesthetic 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 anaesthetic and is surprisingly simple and safe to perform. This is so called 'keyhole' surgery. The operation lasts only 30 minutes and may be performed as an outpatient.

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 Tumours including multiple endocrine neoplasia type 1 (MEN-1) and von Hippel-Lindau disease (VHL), neurofibromatosis type 1 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 organise 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 organised 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. 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 an inherited cancer risk require the care of a specialist surgeon, paediatrician or gastroenterologist and genetic counselling.

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 Type 1 (MEN-1) This is an autosomal dominant familial cancer syndrome (passed on by the mother or the father) with tumours in small glands in the neck (called parathyroids), a small gland attached to the brain (called the anterior pituitary) as well as the pancreas. The neuroendocrine tumours 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 tumours (these are usually non-functioning).

SPECIAL FOLLOW UP OF PATIENTS WITH AN INHERITED PANCREAS CANCER RISK

General Screening For Cancer

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. Screening for cancer in high risk individuals is known as secondary cancer screening. The International Association of Pancreatology recommends that all patients be seen at a special pancreas centre. 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 centres.

• 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 tumour 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 programme such as EUROPAC and provide pancreatic juice samples for experimental molecular testing every 1-3 years (see below for contact details).

Genetic Testing in Familial pancreatic Cancer

• These families should undergo general secondary 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 counselling and BRCA2 gene testing.

• The families should also be invited to join the European programme searching for the main Familial Pancreatic Cancer gene (includes EUROPAC, see below for contact details).

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 tumours 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 tumours should begin from the age of 8

years with blood tests (called calcium and parathyroid hormone) and for chest and abdominal tumours from the age of 20 years by CT. Other neuroendocrine tumours 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 tumours (carcinoids) and EUS for duodenal and pancreatic tumours.

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 tumours 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?

You may drink alcohol if you wish. Indeed certain drinks such as English beer or stout are a good source of calories, iron and vitamins. Alcohol is not recommended for patients who have chronic pancreatitis or hereditary pancreatitis . If you are unsure about alcohol whilst you are having chemotherapy, you may check this with your medical oncologist.

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.

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 also be divided into two types depending upon their strength of action: 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.

In a few cases of children and adults with cystic fibrosis, a serious problem with the large bowel (colon) has been reported. This condition is called fibrosing colonopathy and causes narrowing of the bowel. It seems to be related to the use of a particular acid-resistant coating of the enzyme preparations (called methacrylic copolymer). The problem does not arise with preparations without this covering. The latter preparations are therefore recommended. The ingredients are always listed on the pack leaflet or label. 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

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 influenzae 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.

DOCTORS DEALING WITH PANCREATIC DISEASE THAT YOU MAY MEET

All surgeons are called 'Mr' and other medically qualified doctors are called 'Dr'. Either may be called 'Professor' if they work for a University. Senior doctors are called 'consultants' and the junior doctors are called house officers, senior house officer and registrar. In University departments, they are also called 'lecturer' (registrar) and 'senior lecturer' or 'reader' (consultants).

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 specialised in glandular problems including sugar diabetes.

Endoscopist

This may be a gastroenterologist, radiologist 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 specialised in 'gut' problems and is also usually an 'endoscopist'.

General physician

A consultant medical doctor who works in a hospital and who is broadly specialised including 'gut' problems.

General surgeon

A consultant surgeon who works in a hospital and who is broadly specialised including 'gut' problems.

Geneticist

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

Medical Oncologist

A special medical doctor who gives drugs and other treatment for cancer.

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.

Paediatrician

A consultant who specialises 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 specialise in providing special treatment measures and support for patients who are experiencing difficulties in pain control.

Pathologist

This is a specialist doctor who examines tissue under the microscope. The pathologist is extremely important as it is only they who can definitely say if you have cancer or not. The pathologist is also very important in saying what type of cancer you have as this will determine the best type of treatment and outcome.

Radiotherapist

A specialist medical doctor who gives X-ray treatment for cancer. Some radiotherapists are also expert medical oncologists.

Radiologist

A consultant who specialises in taking X-rays and scans of various sorts at the request of other specialists.

Specialist surgeon

A general surgeon who is highly specialised - a so called PB-specialist is a pancreato-biliary surgeon.

USEFUL ORGANISATIONS

Pancreatic Society of Great Britain and Ireland

This is a professional organisation of specialist doctors involved in the care of patients with pancreatic disease. The Society is allied to the European Pancreatic Club and the International Association of Pancreatology.

http://e-p-c.org/pancreatic-society-of-great-britain-and-ireland

Pancreas Research Fund

Specifically supports basic and clinical research of all diseases of the pancreas.

Write to:

Professor JP Neoptolemos,
Royal Liverpool University Hospital,
Daulby Street,
Liverpool, L69 3QA.
Tel: 0151 706 4175
j.p.neoptolemos@liv.ac.uk

Digestive Disorders Foundation Supports research into digestive diseases.

Write to: 3, St Andrew's Place,
London, NW1 4LB.
Tel : 0207 486 0341
http://www.digestivedisorders.org.uk

EUROPAC

European Register for Familial Pancreas Cancer and Hereditary Pancreatitis. The principal register in Europe providing advice and research in inherited pancreatic disorders.

Write to: EUROPAC Co-ordinator,
Department of Surgery,
Royal Liverpool University Hospital,
Daulby Street,
Liverpool, L69 3QA.
europac@liv.ac.uk

Pancreatic Cancer Research Fund

PCRF is a registered charity dedicated to raising new funds for pancreatic cancer research and to lobbying the major cancer research funding organisations to give pancreatic cancer the attention it deserves.

Write to: Pancreatic Cancer Research Fund
PO Box 47432
London N21 1XP
http://www.pcrf.org.uk

CancerHelp UK

CancerHelp UK is a free information service about cancer and cancer care for people with cancer and their families and is brought to you by Cancer Research UK . The information about cancer is freely available to all and written in a way that people can easily understand.

The specific pancreas cancer web page is:

http://www.cancerhelp.org.uk/help/default.asp?page=2795