Understanding neuroendocrine tumours: information for you and your family

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This booklet proudly produced by Ipsen with valuable input from members of the CNSA.

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The Cancer Nurses Society of Australia supports access to quality information for patients and carers, and commends Ipsen for the production of this booklet.

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Introduction

This booklet is designed to provide you with some basic, easy-to-understand information about neuroendocrine tumours (NETs). If you require information and support additional to what is provided here, please refer to the 'Support network' section at the end of this booklet, where some useful contacts and websites are listed.

We encourage you to discuss any information you find on the internet with your healthcare team. They can answer any questions that you may have and provide you with further information.

What are neuroendocrine tumours (NETs)?

NETs are rare tumours that grow specifically in the neuroendocrine system. The neuroendocrine system is a network of glands that are present throughout the body. Cells of the neuroendocrine system are responsible for producing and secreting a variety of hormones or hormone-like substances. These substances act on different parts of the body, keeping it in balance.

NETs commonly occur in the gut, but they can also arise in other parts of the body where neuroendocrine cells are present – for example, in the lungs and the pancreas. The first place where a NET develops in the body is known as the 'primary' site. NETs can also spread to other parts of the body, such as the liver. When this happens, the tumours are called 'secondary' tumours or 'metastases'.

NETs are generally slow growing and can be cancerous (malignant) or non-cancerous (benign). Some NETs can cause the over-production of certain hormones. The symptoms experienced by a person with a NET depend on the type of NET, its location in the body and the type of hormone it produces.

Since NETs are generally slow growing, and because not all NETs cause an over-production of hormones, there may not be any signs or symptoms of disease for some months or years.

What causes NETs?

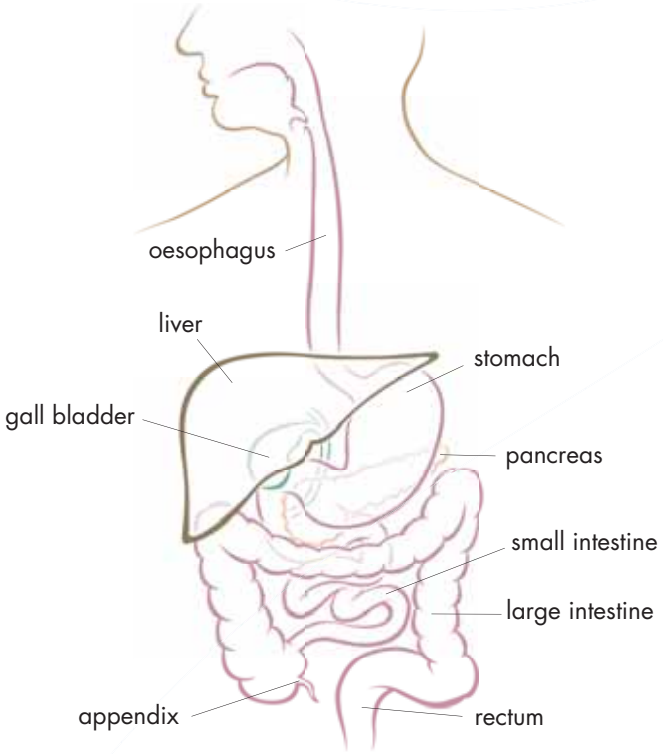
It is not fully understood what causes NETs. The reason for this is that it is unclear what triggers the process of abnormal growth of neuroendocrine cells. In most cases it is not an inherited disease. However, people with some rare family conditions have an increased chance of developing a NET.

Are there different types of NETs?

There are a number of different types of NETs, known also as gastroenteropancreatic NETs (GEP-NETs). They can be functioning (hormone-secreting) and non-functioning (non-hormone-secreting).

Depending on where they are found in the body, GEP-NETs are known as carcinoid NETs or pancreatic NETs. Carcinoid tumours are the most common type, making up about 55% of all NETs that are diagnosed. Carcinoid tumours, or 'carcinoids', arise from a type of neuroendocrine cell called the 'enterochromaffin cell'. They most commonly occur in the appendix and in the small intestine. They can also develop in the lung, kidney, colon and pancreas.

Pancreatic NETs develop from the abnormal growth of neuroendocrine cells present in the pancreas. The different types of pancreatic NETs are named according to the specific hormone they over secrete. Some examples include insulinomas, gastrinomas, VIPomas and somatostatinomas. About half of all pancreatic NETs do not secrete any hormones. They are the non-functioning type.



The digestive system

This diagram is not an exact reproduction of the human anatomy and is intended for orientation only.

What are the signs and symptoms of NETs?

Different NETs affect people in different ways. Symptoms may depend on a number of factors, including:

- the type of NET the person has
- where it is located in the body
- whether or not it has spread to other parts of the body
- whether or not it is functioning (secreting hormones)
- the type of hormone it secretes and how the hormone affects the body.

Generally, NETs do not cause any symptoms in their early stages as they are small and are not necessarily secreting hormones into the body (non-functioning). This makes early detection difficult. Diagnosis usually occurs when non-functioning NETs increase in size or when functioning NETs cause a clinical syndrome.

The specific symptoms of carcinoid tumours and pancreatic NETs are explained in the following sections.

What are the symptoms of carcinoid tumours?

Non-functioning carcinoid tumours have very few symptoms. For example, a carcinoid in the appendix may cause pain when it becomes large. A carcinoid in the lung can cause wheezing and chest pain, while a carcinoid in the stomach may result in weight loss and pain.

Functioning carcinoid tumours secrete various types of hormones. Most functioning carcinoid tumours produce a hormone called 'serotonin'. Many of the symptoms of carcinoid tumours are due to increased amounts of serotonin in the blood. Normally, serotonin causes blood vessels to open (dilate) and close (constrict). Too much serotonin can cause diarrhoea, abdominal cramps and skin flushing.

Both functioning and non-functioning tumours often first present as an obstruction of the bowel.

What is carcinoid syndrome?

Carcinoid syndrome is the name given to a group of symptoms that occur when large amounts of serotonin and other hormone-like substances are released directly into the blood. Not all people with carcinoid tumours will develop the syndrome. It generally occurs when a carcinoid tumour has spread to the liver.

Common symptoms include flushing of the skin, sweating, abdominal cramping and diarrhoea. Other symptoms include wheezing, weight loss and changes in heart rate and in blood pressure. Less common symptoms are telangiectasia (reddish marks on the skin, often spidery in appearance), pellagra (a skin rash) and diarrhoea due to lack of niacin (part of the vitamin B complex).

What are the symptoms of pancreatic NETs?

Approximately half of pancreatic NETs are non-functioning and the person usually presents with symptoms associated with the location and size of the tumour, such as obstruction, bleeding and pain.

The symptoms caused by functioning pancreatic NETs depend on the type of cells affected and the specific hormones being produced. Symptoms of some of these tumours are listed below.

Gastrinoma

Gastrinomas, representing 15% of all pancreatic NETs, produce excessive amounts of the hormone 'gastrin'. This may result in ulcers in the oesophagus (gullet), stomach and small bowel. Symptoms can include abdominal pain, reflux, vomiting, bleeding from the ulcer into the stomach, diarrhoea and steatorrhoea (pale, offensive-odour, fatty loose stools).

Insulinoma

Insulinomas originate from specialised cells in the pancreas, called 'islet cells', that produce insulin. Insulin lowers the level of sugar in the blood. An excessive production of insulin from insulinomas results in a drop in blood sugar levels, a condition known as 'hypoglycaemia'. Hypoglycaemia can lead to symptoms such as sweating, headache, trembling or shaking, pounding of the heart, anxiety, weakness, dizziness, hunger and confusion. Symptoms tend to occur at night or early in the morning.

Glucagonoma

Glucagonomas occur in the pancreas and usually cause excessive release of glucagon, which increases the level of sugar in the blood. The condition in which there is too much sugar in the blood is known as 'hyperglycaemia'. If uncontrolled, this may lead to diabetes mellitus.

Glucagonomas may cause symptoms such as excessive thirst, frequent passing of large volumes of urine, tiredness or weakness, unexplained weight loss and blurred vision. Other symptoms of glucagonomas include diarrhoea, blood clots, anaemia and a characteristic skin rash.

Somatostatinoma

Somatostatinomas occur in the pancreas and small intestine, and secrete somatostatin. Somatostatin is a hormone that helps control the release of other hormones throughout the body. Symptoms of a somatostatinoma can include diabetes mellitus, anaemia, weight loss, diarrhoea and steatorrhoea (pale, offensive-odour, fatty loose stools).

VIPoma

VIPomas over-secrete a hormone-like substance called 'vasoactive intestinal polypeptide' (VIP). Symptoms include nausea, vomiting and large amounts of very watery diarrhoea. These symptoms can result in low potassium levels in the blood, weakness and tiredness.

How are NETs diagnosed?

Besides a physical examination, various tests may be performed to diagnose a NET. The most appropriate testing will depend on the particular circumstances of each person and their history.

The types of tests that are used to diagnose a NET include:

- blood and urine tests
- various types of scans and X-rays
- endoscopy
- biopsy.

Most tests follow specific procedures. Healthcare professionals will give guidance about what is involved before the tests are performed.

Blood tests

Various general and specific blood tests are used to help diagnose and to monitor NETs. Blood samples are taken to detect certain hormone levels and tumour markers. The most common tumour marker for NETs is chromogranin A (CgA). The presence of CgA confirms the diagnosis of a NET but does not identify the type of NET present. Through other blood tests, it is possible to measure specific hormones or hormone-like substances (such as insulin or gastrin) in the blood to identify the type of NET.

Urine tests

A 24-hour urine sample may be collected to test for levels of certain hormones or for by-products of hormones. For carcinoid tumours, urine can be tested for 5-HIAA, which is a breakdown product of the hormone serotonin.

Scans

A number of scans and X-rays may be used to confirm the position of the NET and to check whether it has spread to other parts of the body. Your doctor will discuss the available options with you.

CT (Computerised Tomography)[1]

A CT scan creates an X-ray picture of the inside of the body.

MRI (Magnetic Resonance Imaging)[1]

MRI uses magnetism rather than X-rays to produce detailed pictures of the body.

PET (Positron Emission Tomography)[2]

Radioactive sugar is used to show the chemical function or 'activity' of tissue. A small amount of the radioactive sugar solution is injected into the arm. The solution is absorbed by the cells in the body and the PET scan detects the radiation released by the sugar in the cells. As cancer cells absorb sugar more rapidly than normal cells, the cancer cells will appear brighter in the scan pictures.

1. Tests performed usually in the Radiology Department
2. Tests performed usually in the Nuclear Medicine Department

SRS (Somatostatin Receptor Scintigraphy)/ Octreoscan®[1]

SRS is very accurate in detecting the location of tumour cells in the body. It is a very sensitive scan commonly used for detecting and diagnosing NETs. About 90% of NETs have receptors for the hormone somatostatin. Radioactive octreotide (a drug similar to somatostatin) is injected into the vein. It travels in the body via the blood and attaches itself to the somatostatin receptors of the NET. The SRS is taken about 24 hours after the injection.

^{131}MIBG[1]

This scan uses a low-dose radioactive drug called ^{131}MIBG, which is injected into the arm. About 60% of NETs will absorb the drug. You may be asked to take some potassium tablets on the day of the scan and for a couple of days afterwards. This test takes 1–3 days to conduct. ^{131}MIBG can also be used as a treatment for NETs.

Endoscopy[2]

For this test, a flexible fibre-optic tube called an 'endoscope' is inserted into the digestive tract. It can be inserted either down the oesophagus or into the rectum/back passage (a colonoscopy). It enables the doctor to examine the digestive tract more closely. If anything suspicious is identified, the doctor may perform a biopsy – take a small sample of the tissue – to help find out what type of tumour is present.

1. Tests performed usually in the Nuclear Medicine Department
2. Tests performed usually in the Endoscopy Unit

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Endoscopic ultrasound[1]

An ultrasound is attached to the endoscope (as described above) to obtain clear ultrasound images of tumours in the digestive tract. Such images are particularly helpful for identifying small pancreatic NETs and stomach carcinoid tumours.

How are NETs treated?

This is a guide only. Please consult your healthcare professional about your specific management.

Treatment of NETs varies according to:

- the type and size of the NET
- the stage of the NET and how quickly it is growing
- where it is located in the body
- whether it has spread to other parts of the body
- whether it is secreting excessive amounts of hormone (functioning tumour)
- the aim or goal of treatment (either to cure, to reduce the size of the tumour or to control symptoms)
- the person's general wellbeing.

There are many types of treatment available. The results of all the diagnostic tests will help decide the best treatment plan.

1. Tests performed usually in the Endoscopy Unit

The various treatments for NETs include:

- surgery
- cryotherapy, radiofrequency ablation and liver embolisation
- interferon treatment and chemotherapy
- radiation therapy
- SIR-Spheres®
- medications for the management of the symptoms associated with carcinoid syndrome.

Your doctor will discuss the appropriate therapy with you.

Surgery

Curative

Surgery can be used to remove a primary tumour completely – if the tumour is small in size and contained in one area. In some cases, if surgery is successful, no other treatment is required.

Non-curative

If the tumour has spread to the liver, sections of the liver may be removed surgically.

In people with a larger tumour, or tumours that have spread to other parts of the body, surgery can be used to remove as much of the tumour as possible. This is called 'tumour debulking'.

In non-functioning tumours, tumour debulking may provide relief of symptoms such as small intestinal

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blockage or pain. In functioning tumours, reducing the size of the tumour may reduce the symptoms associated with the overproduction of hormones.

Cryotherapy, radiofrequency ablation and liver embolisation

Cryotherapy, radiofrequency ablation (RFA) and liver embolisation are different techniques that can be used to debulk tumours, mainly when NETs have spread to the liver. These techniques require a surgical procedure.

Cryotherapy

A probe containing liquid nitrogen is placed into the tumour in the liver. The liquid nitrogen makes the probe extremely cold so that it freezes the tumour. Freezing the tumour destroys the cells.

Radiofrequency ablation (RFA)

RFA uses high-frequency electrical energy to create heat. A needle is placed into the liver, and radio waves or laser beams are passed through the needle to heat the tumour. Heating the tumour destroys the cells.

Liver embolisation

Embolisation involves the injection of small particles and/or a chemical into the blood vessels supplying the tumour in the liver. This cuts off the blood supply to the tumour, causing the tumour cells to die. A similar procedure can be performed by injecting cancer-destroying chemicals (chemotherapy) or radioactive substances into the blood vessels that supply blood to tumours in the liver. This procedure needs to be carried out under X-ray guidance.

Chemotherapy

Chemotherapy is the use of anti-cancer medications to kill or slow the growth of tumour cells. It can be used alone or in combination with other therapies to treat NETs. It is mostly used for pancreatic NETs and can sometimes be used for carcinoid tumours that have spread to other organs. Chemotherapy is generally given by intravenous drip.

Interferon treatment

Interferon treatment is a biological drug therapy. Interferon is a protein that occurs naturally in the body and stimulates the body's natural defence system, 'the immune system'. It works by directing the immune system to block the growth of tumours. Interferon can be used alone or in combination with other medications to treat NETs. The therapy is given via an intravenous drip. Flu-like symptoms may be experienced.

Radiotherapy

Radiotherapy involves the use of X-ray beams to destroy cancer cells. Radiotherapy is most commonly used to treat pain, which may occur if the tumour has spread to the bones.

Peptide receptor radionuclide therapy

This is a recently developed treatment and is available only at a few centres in Australia. Peptide receptor radionuclide therapy delivers radioactive compounds directly to tumours. This therapy is particularly effective for NETs that have a lot of somatostatin receptors. The receptors act as targets for radioactive compounds.

The neuroendocrine cells absorb the radiation, which kills the cells, shrinks the tumour and reduces symptoms.

^{131}MIBG

A drug called ^{131}MIBG is used to deliver radiation to NET cells. The cells absorb the drug and the radiation kills the cells. It can be used to shrink the tumour and to reduce symptoms.

SIR-Spheres

SIR-Spheres are a treatment combining radioactive isotopes with tiny particles. These particles are lodged into the small vessels of the liver, especially inside the tumour, where the isotope delivers radiotherapy to kill the cancer cells.

How is carcinoid syndrome treated?

The most effective way to treat carcinoid syndrome is to reduce the symptoms caused by excess hormone production. Somatostatin is a naturally occurring hormone in the body that inhibits the release of hormones from enterochromaffin cells in carcinoid tumours. Man-made versions (or analogues) of somatostatin, such as lanreotide and octreotide, are available to help control the symptoms of flushing, diarrhoea and cramping associated with carcinoid syndrome.

Lanreotide and octreotide are available as long-acting injections. Octreotide is also available as a short-acting injection.

Other medications, such as antihistamines and drugs to stop diarrhoea, may also be used to help reduce symptoms of carcinoid syndrome. Patients are advised to avoid stress, and the consumption of alcohol, caffeine and large meals, as these may bring on some of the symptoms of the syndrome.

Living with a NET

If you or someone close to you has been diagnosed with a NET, you are likely to experience many different emotions. You may be feeling scared, confused or angry. This is a normal reaction.

Everyone has their own ways of coping with difficult situations. Some people find it helpful to gather as much information as possible. Some are comforted by speaking to friends or family about how they are feeling, while others prefer to seek help from their treatment team or from health professionals such as counsellors and psychologists. Remember, help and support are available.

You may wish to contact the Cancer Council helpline. Nurse counsellors can provide you with information and support as well as connect you with a local cancer support group in your area. Contact details are available on pages 18 and 19 of this booklet. The helpline number for all states is 13 11 20.

If you have been diagnosed with NETs then you need to continue on surveillance as instructed by your treating physician.

Support network

The Cancer Council in each state can be contacted for online cancer information or telephone support and to help you find a local cancer support group. The helpline number is 13 11 20.

The Cancer Council ACT

5 Richmond Avenue, Fairbairn, ACT 2609
Tel: (02) 6257 9999 Fax: (02) 6257 5055
Email: reception@actcancer.org
www.actcancer.org

The Cancer Council Northern Territory

Units 2 & 3/25, Casi House, Vanderlin Drive,
Casuarina Wanguri, NT 0811
Tel: (08) 8927 4888 Fax: (08) 8927 4990
Email: admin@cancernt.org.au
www.cancercouncilnt.com.au

The Cancer Council South Australia

202 Greenhill Road, Eastwood, SA 5063
Tel: (08) 8291 4111 Fax: (08) 8291 4122
Email: cc@cancersa.org.au
www.cancersa.org.au

The Cancer Council Victoria

1 Rathdowne Street, Carlton, VIC 3053
Tel: (03) 9635 5000 Fax: (03) 9635 5270
Email: enquiries@cancervic.org.au
www.cancervic.org.au

The Cancer Council NSW

153 Dowling Street, Woolloomooloo, NSW 2011
Tel: (02) 9334 1900 Fax: (02) 9358 1452
Email: feedback@nswcc.org.au
www.cancercouncil.com.au

The Cancer Council Queensland

553 Gregory Terrace, Fortitude Valley, QLD 4006
Tel: (07) 3258 2200 Fax: (07) 3257 1306
Email: info@cancerqld.org.au
www.cancerqld.org.au

The Cancer Council Tasmania

180–184 Collins Street, Hobart, TAS 7000
Tel: (03) 6233 2030 Fax: (03) 6233 2123
Email: infotas@cancer.org.au
www.cancertas.org.au

The Cancer Council Western Australia

46 Ventnor Avenue, West Perth, WA 6005
Tel: (08) 9212 4333 Fax: (08) 9212 4334
Email: inquiries@cancerwa.asn.au
www.cancerwa.asn.au

Useful websites

Cancer Backup (UK)

Europe's leading cancer information charity with up-to-date cancer information.
www.cancerbackup.org.uk

The Carcinoid Cancer Foundation (US)

A not-for-profit organisation that encourages and supports research and education on NETs.
www.carcinoid.org

National Cancer Institute (US)

A comprehensive cancer website with patient and health-professional information concerning a wide range of cancers.
It also covers relationships, sexuality and coping.
www.cancer.gov

Cancer Information Network (US)

Provides health professionals and patients with access to up-to-date cancer information and the results of current research.
www.cancernetwork.com

Virtual Cancer Centre (Australia)

One of Australia's leading medical information websites – delivers the latest cancer information.
www.virtualcancercentre.com

The Caring for Carcinoid Foundation (US)

A leading not-for-profit organisation dedicated to discovering a cure for carcinoid cancer. The site provides a wealth of information about carcinoid and related NETs to support patients and families.

www.caringforcarcinoid.org

The NET Patient Foundation

A charity dedicated to providing support and information to patients with NETs.

www.netpatientfoundation.com

Glossary

Benign a tumour that is not cancerous and does not spread.

Biopsy the removal and examination of a sample of tissue from a tumour in order to aid diagnosis.

Carcinoid syndrome a pattern of symptoms (usually diarrhoea, skin flushing and stomach pain) particularly associated with serotonin-secreting carcinoid tumours.

Carcinoid tumour the most common form of NET. Usually found in the gastrointestinal tract (digestive system) or lungs.

Chemotherapy a form of anti-cancer treatment that uses prescribed medicines (drugs) to kill cancer cells.

Cryotherapy the use of cold in the treatment of diseases. The freezing of certain tumours can reduce their size.

CT or CAT scan a type of X-ray of the inside of the body. CT stands for Computerised Tomography. The test may also be called a CAT (Computerised Axial Tomography) scan. The scan displays detailed pictures of the body's internal organs on a computer screen. The pictures are cross-sections (slices) of the body.

Diabetes mellitus a condition resulting in high blood sugar levels.

Endoscopy the use of a tube called an 'endoscope' to inspect the inside of the body (e.g. the colon, bladder or stomach).

Enterochromaffin cells a type of neuroendocrine cell that produces the hormone serotonin.

Gastrinoma a pancreatic tumour, usually malignant, that results in over-production of gastric acid.

Glucagonoma occurs in the pancreas and usually causes excessive release of glucagon, a hormone that controls the levels of sugar in the blood.

Hyperglycaemia a condition in which there is too much sugar in the blood.

Hypoglycaemia a condition in which blood sugar levels drop below normal.

Insulinoma a pancreatic tumour, usually malignant, that results in over-production of insulin, causing low blood sugar levels.

Interferon treatment an injected treatment that helps fight cancer by stimulating the body's natural defence system – the immune system.

Liver embolisation the injection of small particles or a chemical into the blood vessels supplying a tumour in the liver, cutting off the blood supply to the tumour.

Magnetic Resonance Imaging (MRI) an imaging method that uses a magnetic field, radio waves and a computer to form a picture that is used to identify normal and diseased tissue.

Malignant cancerous, tending to spread (metastasise).

Metastasis the spread of cancer from one body site to another.

MRI scan *see 'Magnetic Resonance Imaging'.*

Neuroendocrine cells specific cells usually located in the gut, lung and pancreas that release a hormone into the blood.

Neuroendocrine system a system of glands that secrete hormones or other substances directly into the blood to regulate bodily activities in response to neural stimuli.

Neuroendocrine tumours (NETs) rare tumours that grow specifically in the neuroendocrine system, a network of glands throughout the body.

Octreoscan a very sensitive scan commonly used for diagnosing NETs and detecting the location of tumour cells in the body.

Pancreas a large gland behind the stomach that secretes digestive enzymes (helping to break down food) into the small intestine. Embedded into the pancreas are the 'islets of Langerhans', which are responsible for producing and secreting the hormones insulin and glucagon.

Pancreatic NETs NETs originating in the pancreas, such as insulinomas, gastrinomas and VIPomas.

Pellagra a vitamin-deficiency disease caused by dietary lack of niacin (vitamin B_3), which can cause symptoms such as skin rash and diarrhoea.

Radiotherapy the use of radiation to kill cancer cells. The treatment is administered either externally (outside the body) via a beam of radiation or internally (inside the body) via a targeted injection or implants.

Secondary tumour a malignant tumour that spreads (metastasises) into another part of the body.

Serotonin a hormone, secreted by some NETs, that causes large blood vessels to constrict and small blood vessels to dilate. This can lead to skin flushing. Serotonin is also known as 5-hydroxy tryptamine (5-HT).

Somatostatin a naturally occurring hormone produced by the hypothalamus (a part of the brain). It inhibits the release of hormones and other body chemicals.

Somatostatin analogues synthetic (man-made) medicines that are very similar to somatostatin; they are used to treat the symptoms experienced by people with NETs.

Steatorrhoea pale, offensive-odour, fatty loose stools.

Telangiectasia small red spidery clusters on the skin caused by the dilation of small blood vessels near the surface of the skin.

Tumour an abnormal growth of cells, generally described as being 'benign' (non-cancerous) or 'malignant' (cancerous).

VIPoma pancreatic tumour, usually malignant, that produces a substance called 'vasoactive intestinal polypeptide' (VIP).

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WMP IPS21096 07/09

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