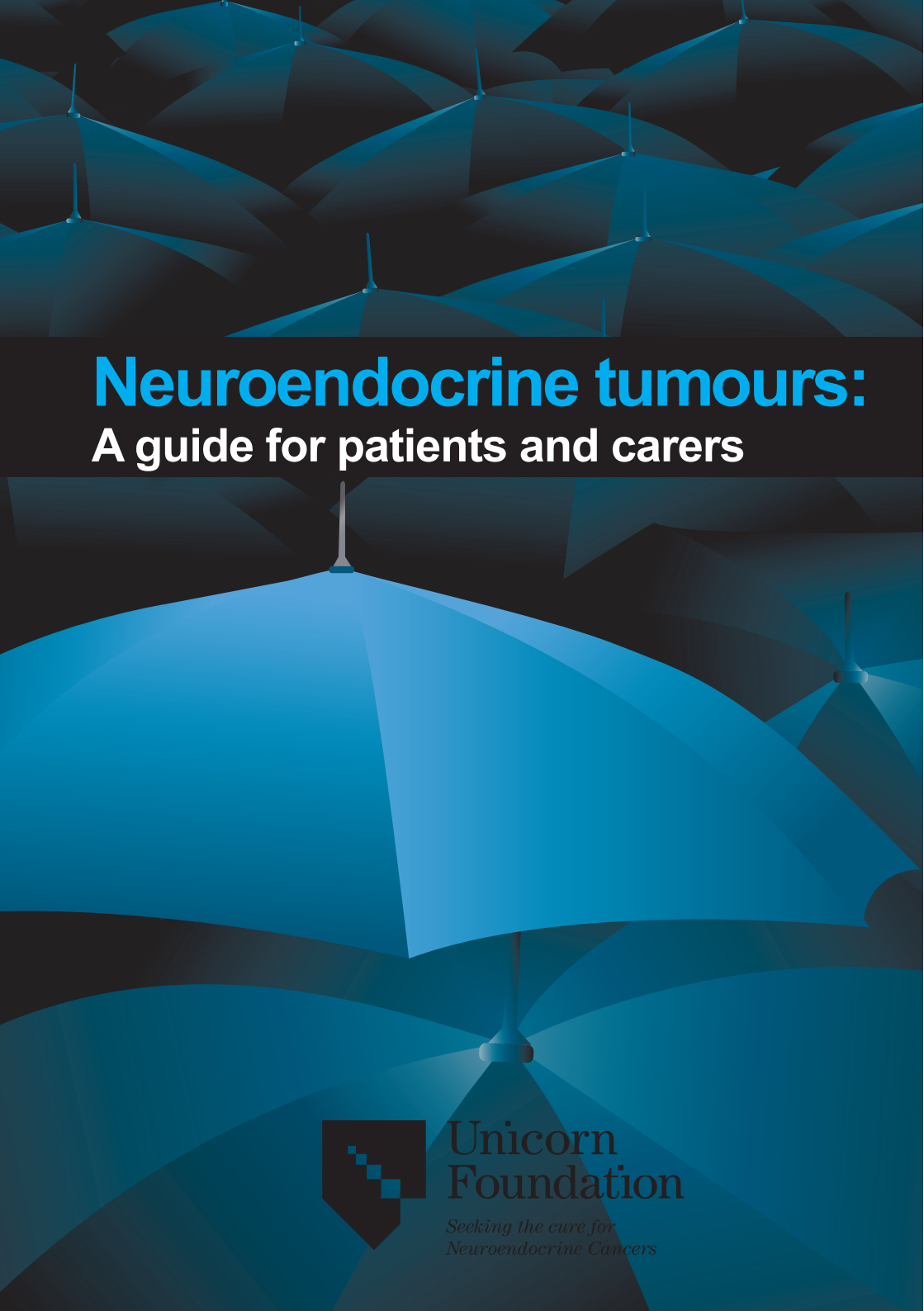

Neuroendocrine tumours:
A guide for patients and carers

Unicorn Foundation

Seeking the cure for Neuroendocrine Cancers

Neuroendocrine tumours:
A guide for patients and carers

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Disclaimer

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Contents

"Having a rare cancer is frightening beyond belief. I almost envied those with breast or bowel cancer – that's where the support and answers seem to be. Finding a NET nurse who could help understand NET issues has been one of the most powerful experiences since my NET diagnosis."

(Deborah Burdett, Sydney)

Introduction

This book has been developed for people with neuroendocrine tumours (NET). It contains information to help you understand diagnosis and treatment options.

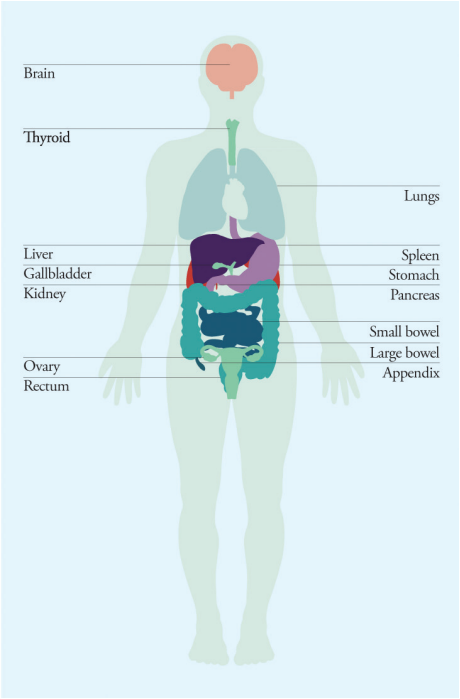
This booklet may also help when talking about NETs with family and friends. Everyone's journey is different; therefore, this information may be helpful now or in the future. Its purpose is as a guide to help you understand what is available to you and for you to use this information to help you make choices.

For more information, and to make sure you stay up to date with the latest developments in NETs, subscribe to the Unicorn Foundation's enews by visiting www.unicornfoundation.org.au.

This booklet was developed by medical professionals with input from NET patients. New treatments and technologies are continually being developed, so this information may change in the future. If you hear of anything not listed in these pages, please ask your healthcare professional for more information.

About NETs

What are NETs?



NETs are tumours that usually develop in the digestive or respiratory tracts, but can occur in other areas of the body. These tumours arise from cells called neuroendocrine cells. Neuroendocrine cells create, store and secrete proteins called peptides and hormones for normal body functions.

NETs develop when these neuroendocrine cells undergo changes, causing them to divide uncontrollably and grow into a mass (called a tumour).

Neuroendocrine tumours can be very slow-growing or can be more aggressive. While they were once thought to be non-cancerous (benign), we now know that these tumours can be cancerous.

These tumours are called neuroendocrine tumours (or NETs). The location of the tumour may be added to the name: for example, lung NET, bowel NET or pancreatic NET.

People with genetic conditions such as multiple endocrine neoplasia (MEN), Von Hippel–Lindau (VHL) disease and neurofibromatosis (NF) have an increased risk of developing NETs.

How common are NETs?

Previously considered to be rare, NETs are increasing in incidence in Australia (three to four people per 100,000). This is about the same as testicular cancer, cervical cancer, multiple myeloma, Hodgkin lymphoma and cancers of the central nervous system.

Gastroenteropancreatic NETs (GEP-NETs)

Gastric NETs

These are NETs of the stomach. There are four types of gastric NET:

- **Type I** is the most common. These are associated with atrophic gastritis and an overproduction of gastrin (hypergastrinaemia). These are small polyps (less than 1–2 cm) that are found during a gastroscopy. These polyps may not be cancerous, but they may recur. They can be removed and a regular follow-up plan put in place. Long-term use of proton pump inhibitors (anti-acid medications) for gastric reflux or dyspepsia may increase risk of this type of NETs.
- **Type II**: These are uncommon and occur as part of an inherited condition known as multiple endocrine neoplasia type 1 (MEN 1): when excessive secretion of the hormone gastrin by a tumour (gastrinoma) causes over-production of stomach acid. This is known as Zollinger–Ellison syndrome. • The tumours in the stomach are often small and are often simply monitored with endoscopic ultrasound.
- **Type III**: These uncommon tumours are often larger (>2 cm) and can spread to other parts of the body (metastasise). They need to be surgically removed.
- **Type IV** is a very rare type of gastric NET and is the most difficult to treat. Tumours are often large and have spread (metastasised) at diagnosis.

Small bowel NETs

- **Duodenal NETs** produce many hormones and peptides such as serotonin, calcitonin and gastrin somatostatin. Patients may present with ‘carcinoid syndrome’ (see later in this booklet), pain in the abdomen or fatigue due to anaemia.
- **Jejunum and ileum NETs** are often slow-growing and small and cause no symptoms, which makes diagnosis in the early stages difficult. Often, when the diagnosis is made, the tumour is larger and may have metastasised. The person may have pain in the abdomen, carcinoid syndrome or a bowel obstruction.

Large bowel NETs

- **Appendiceal NETs** are often found during surgery for appendicitis. If the tumours are less than 1 cm in size, surgery may be all that is needed to cure the cancer.
- **Goblet cell carcinomas** have ‘goblet’ shaped cells when viewed under a microscope. They may be found when the person seeks treatment for acute appendicitis, pain in the abdomen or a mass in the abdomen. Women with this type of NETs may also have metastases on the ovary.
- **Colon NETs** are rare and can be large, aggressive, have the potential to spread and may cause bowel obstruction and bleeding. If the NET has spread to the liver, the person may have symptoms like wheezing, facial flushing and watery diarrhoea.

Rectal NETs

These NETs are often found 'by accident' such as during an endoscopy. Patients may present with symptoms such as rectal bleeding or change in bowel habit, but often have no symptoms. Because it doesn't cause symptoms, the cancer may spread before it is found.

Pancreatic NETs (pNETs): functioning and non-functioning

Pancreatic NETs are divided into two groups: functioning and non-functioning.

Functioning pNETs produce symptoms due to excessive hormone production by the tumours:

- **Insulinoma** are tumours that secrete insulin causing low blood sugar and symptoms such as disorientation, confusion, sweating, trembling and heart palpitations.
- **Gastrinoma** are tumours that secrete gastrin, which stimulates the stomach to produce too much acid, causing symptoms such as dyspepsia, stomach ulcers, nausea, diarrhoea and weight loss.
- **Glucagonoma** are tumours that secrete glucagon, which can raise blood sugar (hyperglycaemia) causing fatigue, frequent urination, dry mouth, nausea, blurred vision, weight loss, anaemia and depression. This tumour can cause a red rash (migratory erythema) in the groin.
- **Somatostatinoma** are tumours that secrete somatostatin, which causes symptoms of diabetes, diarrhoea, steatorrhoea (fatty pale stools) and weight loss.
- **VIPoma** are tumours that secrete vasoactive intestinal peptide, which causes severe watery diarrhoea, which leads to imbalances such as low potassium (hypokalaemia) and low chloride (hypochorhydria), weakness and fatigue.

The **non-functioning pNETs** also produce hormones and peptides and often present late due to symptoms such as abdomen or back pain due to the growing tumour.

> *"Googling tumours on the pancreas and liver was not at all what anyone wants to read about, so I didn't."* (Katie, age 41, Sydney)

Bronchopulmonary (lung) NETs

About one in four NETs start in the lung. This can cause recurrent pneumonia from airway obstruction, chest pain on breathing, coughing blood (haemoptysis) and shortness of breath or wheezing.

Patients with MEN1 have an increased risk of developing bronchial NETS.
There are four types of NETs of the lungs:

i) Typical carcinoid (TC)
ii) Atypical carcinoid (AC)
iii) Small cell lung cancer (SCLC)
iv) Large cell neuroendocrine carcinoma (LCNEC).

The atypical types are the most common. These NETs can be more aggressive (grow more quickly). Lung NETs can affect people of all ages.

Some bronchial NETs produce symptoms related to hormone overproduction: carcinoid syndrome (serotonin), Cushing syndrome (ACTH) and acromegaly (growth hormone).

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare disorder and can occur before lung NETs.

Thymic NETs

NETs of the thymus are uncommon. Most don't cause symptoms until they have grown big enough to press on structures in the chest (trachea, large veins). Thymic NETs can be aggressive. Treatment includes surgical removal and chemotherapy. A very small number of patients with MEN1 develop thymic NETs.

Testicular NETs

Testicular NETs are rare. There may be a painless mass in the scrotum. The NETs do not usually produce symptoms of carcinoid syndrome. Removal with surgery (orchidectomy) is currently considered the best treatment. People with testicular NETs need long-term follow-up because there is a chance of the cancer having spread before surgery.

Ovarian and endometrial NETs

NETs of the ovary and endometrium are rare. Most are found late, after they have spread. Patients can present with symptoms related to carcinoid syndrome and carcinoid heart disease (see later in this booklet).

"Something changed in the way I approached my MEN 1 diagnosis as time has gone on. I decided that I was not going to be defined by this condition. It is a small part of me; I am NOT part of it." (Michelle, age 54, Brisbane)

Multiple endocrine neoplasias (MEN syndrome)

In multiple endocrine neoplasia (MEN) there are tumours in two or more of the endocrine glands. There are four major forms of MEN. They may be inherited (autosomal dominant) or sporadic.

- **MEN 1**: Most people with MEN 1 develop parathyroid tumours (hyperparathyroidism); others develop pNETs or tumours in the pituitary gland. Other MEN 1 tumours include adrenocortical tumours, thymic NETs and gastric NETs. Patients and their families are advised to have genetic testing (MEN1 gene).
- **MEN 2** is a rare genetic (RET gene) syndrome that has three categories: 2A, MEN2B and medullary thyroid carcinoma (MTC).
    - **MEN2A** is characterised by the development of medullary thyroid carcinoma (MTC), pheochromocytoma and parathyroid adenomas.
    - **MEN 2B** patients develop MTC earlier in life, develop pheochromoctyomas and neuromas of the skin and intestine. It is an aggressive form of MEN.
    - **Familial medullary thyroid carcinoma (MTC)** does not have the other tumours that are associated with MEN 2.

"What I am trying to say is that this tumour can be in your body and you have no idea about it. It can be hereditary and it has deadly consequences. If you experience headaches, excessive sweating and increased heart rate and high blood pressure then I encourage you to see your doctor because it may save your life." (Glenn, age 43, Brisbane)

Pheochromocytoma

Pheochromocytomas (PH) are rare NETs. They start in the adrenal glands on top of the kidneys.

Six in ten people with these tumours have symptoms cause by excessive hormone secretion such as:

- high blood pressure and rapid heart rate (palpitations)
- sweating
- severe headaches
- anxiety and feelings of rapid heart rate
- loss of weight.

The remaining four in ten have no symptoms and are often undiagnosed for many years. They mostly affect adults but can also affect children and adolescents.

Paraganglioma

Paraganglia are groups of cells found near nerve cell bundles called ganglia. These ganglia are located in the head, neck, thorax, abdomen or pelvis and are classified as either parasympathetic or sympathetic. A tumour involving the paraganglia is known as a paraganglioma.

- Parasympathetic paragangliomas are mainly found in the head and neck, usually do not secrete hormones and rarely spread.
- Sympathetic paraganglioma are found in the thorax, abdomen and pelvis, secrete hormones such as adrenaline or noradrenaline, and metastasise in one in five cases.

More than a third of patients with paraganglioma inherit a chance of getting this disease.

Surgery is the only curative treatment, but people with these NETs may also have chemotherapy and peptide receptor radionuclide therapy (PRRT).

Medullary thyroid carcinoma

Medullary thyroid cancer (MTC) is a rare form of cancer of the thyroid gland in the neck.

Adrenocortical carcinoma (ACC)

Often known simply as adrenal cancer, this NET affects one to two people per million per year, which means it is very rare. ACC occurs in the outer part (cortex) of the adrenal gland. In adults, it most commonly occurs in middle age.

The disease may be less aggressive in children, who have different treatment from adults.

Merkel cell carcinoma (neuroendocrine tumour of the skin)

Merkel cell carcinoma (MCC) is a rare but aggressive skin cancer. The first symptom may be a solid purple nodule in the skin, especially in sun-exposed skin areas (e.g. head and neck). Risk factors for the disease are sun exposure, old age, previous cancers and the Merkel cell polyoma virus.

Surgery and radiotherapy are commonly used to treat these NETs.

Neuroblastoma

Neuroblastoma starts in one of the adrenal glands, but can also develop in nerve tissues in the neck, chest, abdomen or pelvis. It mostly affects children, usually under the age of five.

Associated conditions

Von Hippel–Lindau syndrome (VHL)

Von Hippel Lindau (VHL) is an inherited cancer syndrome caused by mutations of the VHL gene. It affects both sexes equally, About one in every 30,000 to 40,000 people get this syndrome.

VHL causes retinal (eye) haemangiomas, cerebellar and spinal cord haemangioblastomas, renal cell carcinomas (RCC) and pheochromocytomas.

Cystic masses in the pancreas are common and 10–15% of VHL patients develop islet cell neuroendocrine tumours.

Neurofibromatosis type 1

Neurofibromatosis type 1 is a relatively common inherited disorder that affects 1 in every 3000 people.

Patients usually have skin pigmentation (‘café au lait spots’), neurofibromas (nodules on the skin) and bone deformities, including scoliosis of the spine, and are at risk of bone fractures due to osteoporosis.

Patients with neurofibromatosis type 1 are prone to developing benign and malignant tumours in the body. These tumours include:

- brain and eye tumours (glioma)
- tumours of the nerves
- gastrointestinal stromal tumours (GIST)
- pheochromocytoma
- small bowel (duodenal) NET
- breast cancer, leukaemia, sarcomas.

Tuberous sclerosis

Tuberous sclerosis (TS) is an inherited condition characterised by benign growths in the skin, brain, kidneys, lungs and heart, which can affect how these organs function.

People with TS may be at risk of developing insulinomas—a neuroendocrine tumour of the pancreas.

Symptoms and signs (Clinical presentation)

NETs are often small and slow-growing. Depending on where they are in the body, they can produce a variety of symptoms or in some cases no symptoms.

The symptoms can be vague (e.g. extreme tiredness) or similar to those of conditions such as irritable bowel syndrome, Crohn's disease, peptic ulcer disease, stomach/digestive disorders, asthma and facial flushing associated with menopause.

Most doctors are unfamiliar with NETs. They are therefore less likely to suspect a NET when they first see a patient with NET.

Quick guide to symptoms of GEP-NETs and bronchial NETs

Intestinal NETs	Watery diarrhoea Cramping, intermittent abdominal pain Flushing; asthma-like wheezing Bowel obstruction
Pancreatic NETs	Epigastric or back pain Peptic ulcer disease Diarrhoea Intermittent hypoglycemic episodes (low blood sugars) Diabetes Rash
Bronchial NETs	Wheezing Cough Bloody sputum Recurrent chest infections/pneumonia

Carcinoid syndrome

When GEP-NETs spread (metastasise), the most common site for secondary tumours to grow is in the liver. They can also spread to the bones, the lungs and the lymphatic system.

Many GEP-NETs have an associated syndrome (a collection of symptoms related to a disease or disorder). The most common is carcinoid syndrome, which can occur in up to one in three patients. It is caused when an excess of hormones such as serotonin, histamine, somatostatin and chromogranin A are produced due to the NETs.

The symptoms of carcinoid syndrome vary between people with NETs. Typical symptoms include:

- **Flushing**: usually a red/purple flush of the face, neck and upper chest, which may be related to triggers such as alcohol, certain foods, exercise and emotions.
- **Diarrhoea**: usually presents as watery diarrhoea occurring without warning, which includes night-time episodes. It usually does not respond to anti-diarrhoea medications or other treatments prescribed for irritable bowel syndrome.
- **Wheezing**: affects about one in five patients with carcinoid syndrome and may be associated with facial flushing. Unlike asthma, wheezing of carcinoid syndrome may not be triggered by colds/flus, exercise, allergens or cold air.
- **Abdominal pain**: often colicky (intermittent) and cramping. It is often not relieved by going to the toilet.
- **Carcinoid heart disease**: up to one in five NET patients have carcinoid heart disease at diagnosis. The right side of the heart is mostly affected with leaking of the tricuspid and pulmonary valves causing shortness of breath and swelling (oedema) of the legs.
- **Fatigue**.
- **Skin changes**: a small number of patients have skin changes such as telangiectasia (red/purple spots of face, neck and chest).
- Rarely, some patients with NETs develop a condition known as **pellagra (niacin deficiency)**, which presents as brown patches on the skin, beefy red tongue and mental changes.

Not everyone with NETs will have carcinoid syndrome, even if their disease has spread.

Carcinoid crisis

Sometimes people with NETs have a particularly bad episode of carcinoid syndrome triggered by stress, general anaesthetic or certain treatments. This is called 'carcinoid crisis'.

Symptoms include intense flushing, diarrhoea, abdominal pain, wheezing, palpitations, low or high blood pressure, altered mental state and, in extreme cases, coma.

Your NET specialist will ensure you are monitored and may give you medication to prevent such a crisis occurring (e.g. an infusion of a somatostatin (octreotide) analogue).

Your NET specialist will also liaise with your other healthcare professionals and provide guidelines for preventing carcinoid crisis.

Carcinoid heart disease

The hormones released by the NET tumours into the bloodstream (serotonin) can affect the heart by causing thick 'plaques' within the heart muscle. The valves on the right side of the heart are also affected and become 'leaky', causing symptoms such as breathlessness, fatigue, enlarged liver and swollen ankles.

Up to one in five patients with carcinoid syndrome have carcinoid heart disease and without treatment can develop right heart failure. Medication can be prescribed to manage symptoms and slow the progression of carcinoid heart disease. Some patients with carcinoid heart disease may be advised to have heart surgery to replace the leaking valves.

Echocardiography should be done regularly to monitor the function of the heart in patients with NETs.

Diagnosis

"If you don't suspect it, you can't detect it."

NETs are difficult to detect for a number of reasons:

- They are often very small.
- They can occur almost anywhere in the body.
- Symptoms can vary widely and some patients have no symptoms at all.
- There are many types of NETs and the diagnosis requires a series of tests, which may include blood tests, imaging (CT/MRI), endoscopy, nuclear medicine scans (PET scans) and biopsies to prove the diagnosis.

Patients who are diagnosed with a NET have often seen many different doctors (general practitioners and specialists) over many years and had many tests before the diagnosis is made.

On average it takes 4 to 7 years for this diagnosis. This is because NETs often present with similar symptoms to other common conditions. There is also a widespread lack of awareness of the disease among doctors.

You will be advised to have a number tests and scans that will tell your doctor about your disease, its spread and the rate of growth.

Tests

Some of the tests you might have are listed below.

Biopsy

This involves taking a piece of tissue from the suspect tumour and having it analysed in the laboratory by a medical specialist called a pathologist.

Tissue biopsies are usually taken during medical tests (e.g. an endoscopy) or during operations. The biopsy sample is sent to the laboratory and the cells are examined under a microscope to see if they are normal or cancer cells. NET cells look quite different to normal cells. Doctors can sometimes tell from biopsies where in the body a cancer has started.

Biopsies are very important in medicine. It is impossible to diagnose some types of cancer any other way. Often, the only way to be sure of the diagnosis is to look for cancer cells under the microscope and by special tests performed on the tissue.

It is essential to have your biopsies or tissues assessed by a pathologist who has experience in NETs. The pathologist's report is critical for oncologists to decide on the treatments that will manage your NET best.

Blood tests

You will be asked to have a fasting gut hormone blood test, and blood will also be collected for a range of other tests.

Doctors will be looking for NET biomarkers, particularly chromogranin A (CgA) and for evidence of a rise in certain peptides and hormones in the blood.

Full blood count

This will include:

- kidney function test (urea and electrolytes)
- liver function tests
- thyroid function tests
- pituitary hormone screen (e.g. adrenocorticotrophic hormone (ACTH), prolactin, growth hormones and cortisol)
- serum calcium, parathyroid hormone levels (as a simple screening test for MEN-1 syndrome)
- hormone assays,

You may also be asked to give an extra blood sample for use in research studies. You should always be informed of this and asked to sign a consent form.

Chromogranin A (CgA)

Chromogranin A is produced and released into the bloodstream by neuroendocrine cells. It is a 'marker', or indicator that there is a NET in the body.

Chromogranin A blood levels can relate to the activity of the tumour in your body. They are often used for monitoring the disease or response to treatments.

Different laboratories use different methods (test kits or assays) to measure chromogranin A. It important to go to the same laboratory so that changes in the levels can be interpreted correctly.

Certain conditions can cause higher chromogranin A levels, especially:

- anti-acid medication especially the proton-pump inhibitors (omeprazole, esomoprazole, pantoprazole).
- kidney and liver diseases.
- prostate cancer.
- atrophic gastritis.

Urine tests

When serotonin breaks down in the body it produces 5-HIAA (5-hydroxyindole-3-acetic acid), which is excreted into the urine.

To test for 5-HIAA in the urine, you will be asked to provide urine samples over a 24-hour period. Keep the urine sample in the refrigerator during the collection period.

Higher than normal levels of serotonin, produced by NET tumours, show up as raised levels of 5-HIAA in urine. Some foods are very high in serotonin/tryptophan

and you will be asked to avoid them before and during the test: including chocolate, olives, bananas, pineapple, all tomato products, plums, eggplant, avocado, kiwi fruit, walnuts, brazil nuts, cashew nuts, tea, coffee and alcohol. You will also be asked to avoid certain cough, cold and flu remedies 3 to 7 days before the test.

Endoscopy

Gastroscopy and colonoscopy

This is a way of examining parts of the gut using a flexible fibre-optic tube called an **endoscope**. The tube can either be inserted down the back of the throat and into the stomach (gastroscopy) or into the colon via the rectum (colonoscopy). During the endoscopy, suspicious lesions in the large bowel and rectum, oesophagus and stomach can be biopsied.

You would usually have these procedures under sedation as a hospital outpatient.

Wireless capsule endoscopy

This involves swallowing a small capsule (the size of a large vitamin pill), which contains a colour camera, battery, light source and transmitter. The camera takes two pictures every second for eight hours, transmitting images to a data recorder about the size of a portable CD player that patients wear around the waist. This system allows your doctor to see the small bowel but is unable to take biopsies.

Endoscopic ultrasound

This is usually done under sedation and involves looking at the digestive tract with a flexible camera with ultrasound capabilities. This test is sensitive for detection NETs in the stomach, duodenum, pancreas and rectum. Ultrasound guided biopsies can also be performed. The test can help pick up small tumours that might not be clearly visible on other scans.

Bronchoscopy

If you have a suspected lung NET, the doctor may suggest a bronchoscopy. This test looks at the inside of the airways. Your doctor puts a narrow, flexible tube called a bronchoscope down your throat and into the airway to see the trachea and bronchus and also take biopsies.

You can have this procedure under sedation as a hospital outpatient.

Radiological imaging

CT scans

A multi-slice spiral (CT) scan can rapidly take fine slice (millimetres thick) images of the body with computer reconstruction providing a three-dimensional picture of the inside of the body.

The scan usually takes about 5 minutes. Depending on the scan, you need to arrive earlier in order to drink about a litre of oral contrast material (which outlines the bowel). Sometimes the radiologist will also put a drip in a vein so you can have intravenous contrast. These help produce good images so your doctor can see the tumours or other abnormalities.

You may be advised to have a blood test prior to the scan to ensure normal kidney function.

When looking at the liver images, a multi-phase liver scan must be requested (non-contrast- arterial phase, portal venous and delayed). If this is not requested, often it is difficult to detect NETs in the liver.

MRI scans

The magnetic resonance imaging (MRI) scans use magnetic fields to create a signal that is processed into an image. MRI scans are safe; however, there if you have any metal parts in your body (e.g. a pacemaker), you cannot have an MRI.

MRI scans take longer to perform and are noisy (you can use ear plugs). Some people can feel claustrophobic when in the MRI tunnel and may require some sedation to tolerate the scan.

MRI can add further information to the results of CT scans.

Ultrasound scans

Ultrasound imaging (sonography) involves high-frequency sound waves to produce pictures of the inside of the body. Ultrasound scans are non-invasive and the images are captured in ‘real time’. They can show the structure and movement of your body’s internal organs, as well as blood flowing through blood vessels.

Nuclear imaging (functional imaging)

Nuclear imaging techniques use radiolabelled compounds (small radioactive particles connected to small proteins or peptides) that are injected into the blood stream. These compounds are then taken up by the tumour cells or bind to receptors (somatostatin receptors) on the surface of the tumour, which are then detected by monitors (cameras). Nuclear imaging techniques are very sensitive and specific in detecting NETs and their metastases.

It is important for these scans to be done during the initial assessment stage of any NET patient, and as a part of the ongoing follow-up and management.

PET (positron emission tomography) scan

A PET scan can show how body tissues are working, as well as what they look like. PET scanners are very expensive and only a few hospitals have one. This means that you may have to travel to another hospital for your scan. Increasingly, PET scans are being combined with CT scans to provide more detailed images. These types of scanners are known as PET/CT scanners.

With a PET scan, you first have an injection of a small amount of a radioactive drug (radiotracer). The amount of radiation is no more than you have during a normal X-ray, and it only stays in the body for a few hours.

PET scans usually take a few hours and are perform as an outpatient procedure.

Gallium-68 (Ga^{68}) PET scan

This test can help reveal the site of NET tumours. This test is essential for any patient with a NET.

^{18}F-FDG PET ([18 fluorine] fluoro-D-glucose)

^{18}F-FDG is a glucose analogue with the attached radiotracer ^{18}florine. This compound is taken up by cells that rapidly metabolise glucose, which occurs in many different types of cancer including types of NETs.

This test can help to show whether there are cells, like cancer cells, that rapidly take up glucose in the body.

You will need to fast beforehand and remain still before the test.

MIBG scan

This scan can help find NETs in the body.

Your doctor may ask you to stop taking certain medications a few days before this test. Your doctor may suggest taking iodine tablets to help protect the thyroid gland during the test. This investigation usually involves taking separate scans over two consecutive days and most patients are allowed home in between.

"Because of the length of time before being diagnosed, my small intestine NETs metastasised to the liver. A bad case of menopause was the common answer from the range of specialists that I saw." (Kathy , Adelaide)

PET/CT Scanner (Siemens)

Bone scan

You may have a bone scan to see if cancer cells have spread to bone in your body. You will have a small injection of radioactive tracer into the vein and images taken by the camera 2 to 4 hours later. There are very few side effects or risks involved with nuclear medicine bone scans and you can usually have it as an outpatient or day-only procedure.

‘Grading’ the NET

NETs, like all cancer, are ‘graded’ into low (G1), intermediate (G2) or high (G3). The grade represents the aggressiveness of the tumour—the higher the grade, the faster growing it is. Grading the tumour help your doctors work out the best treatment for you.

Treatment

Being diagnosed with cancer can be a confusing and frightening time for you and your loved ones. Although your healthcare team will do their best to support you, medical appointments can be stressful and it is worth finding ways to get the most out of each appointment. The information in this section will help you work out what questions you want to ask your doctors.

Each person with NETs should have an individualised treatment plan. This is because there are a number of treatment options available, depending on the type and location of the tumour, your general health and what you want.

Multidisciplinary teams

The care of NETs can be complex. Your journey may involve not only a whole host of emotions, but also a whole range of investigations, treatments and healthcare professionals.

The fact that there is often not just one treatment option at diagnosis and throughout the patient journey means that healthcare professionals involved in your care need to consult with each other to work out the best treatment for you. This is called an MDT (multidisciplinary team). MDTs are used across the world in the care of cancer patients and are particularly important for a complex cancer such as NET.

A coordinated MDT is a very important aspect of NET care. With an MDT, patients can feel more confident that all aspects of their care have been discussed and that the best possible treatment plan will be formulated.

Members of a NET MDT may include:

Oncologist	Radiologist	Pain Team
Gastroenterologist	Physician	Counselling Staff
Surgeon	General Practitioner/ Practice Nurse	Clinic Staff
Endocrinologist	Nurse Specialist	Palliative Care Team
Nuclear Medicine	Dietitian	Pathologist

Surgery

People with NETs often have surgery to remove the tumours. The goal of surgery depends on the type of NET cancer, its location in the body and size and whether it has spread from where it began.

Different surgeons may be involved with NETs depending on their expertise and training (e.g. endocrine, colorectal, hepatobiliary and pancreatic, and cardiothoracic surgeons).

Most surgery for NETs should be done in specialist units where the surgeons work as part of a team including anaesthetists, oncologists, gastroenterologists, nurses, radiologists and other doctors with expertise in NET cancers.

Curative surgery

This is surgery used when the cancer has not metastasised (spread outside the organ or area where it started). If the tumour can be removed whole and intact with a surrounding margin of clear, healthy tissue, then the surgery will potentially cure the cancer and no other treatment may be necessary.

A follow-up plan will be needed after surgery.

Palliative surgery

When the tumour or tumours have spread or become too large to remove completely, then surgery may be considered to 'de-bulk' the tumour. This will relieve symptoms caused if the tumour is affecting other organs or producing excessive amounts of hormones.

Cardiac and thoracic surgery

Thoracic surgery may be indicated for patients with pulmonary NETs and cardiac surgery for patients with carcinoid heart disease who may need cardiac valve replacement.

Perioperative and anaesthetic management of NET patients

Patients with NET are at risk of 'carcinoid crisis' in the perioperative period or during surgery. The specialist should discuss this with the anaesthetist before surgery.

Medical management

Somatostatin analogues

Daily or monthly injections of somatostatin analogues (Sandostatin, Lanreotide) are available to control some symptoms caused by NETs.

Somatostatin analogues are versions of the naturally occurring somatostatin, which is a hormone produced in the brain and digestive tract. Somatostatin regulates the release of several other hormones and chemicals from our internal organs.

Injections of these analogues can stop the overproduction of hormones (e.g. serotonin) that cause symptoms such as flushing and diarrhoea. There is evidence that these injections also slow down rate of growth of tumours.

Sandostatin LAR® (depot preparation of Octreotide)

Octreotide may be used instead of somatostatin because it is more potent, lasts longer in the body and is usually given as a monthly injection. Sandostatin LAR® blocks the somatostatin receptors and can slow the tumour growth and treat the symptoms of NETs

Somatuline® Autogel (depot preparation of Lanreotide)

Lanreotide may be used instead of somatostatin because it is more potent, lasts longer in the body and is given as a monthly injection. Somatuline® Autogel blocks the somatostatin receptors and can slow the NET tumour growth and treat the symptoms of NETs.

Chemotherapy

Chemotherapy may be an option, especially for NET patients with pancreatic, bronchial or high-grade (G2/G3) NETs. Not all NETs respond equally to chemotherapy, so your doctor may or may not recommend it as part of your treatment.

Many chemotherapy treatments involve intravenous drugs that are given in hospital as a day procedure; however, there are also oral chemotherapy agents—your NET doctor will discuss the best option with you.

The histology of the tumour (i.e. how it looks under the microscope after biopsy or operation) may help determine the type of treatment you receive.

Chemotherapy may sometimes be recommended after surgery (adjuvant therapy). You may be asked if you would like to join a clinical trial researching chemotherapy for different types of NET cancer.

Targeted molecular therapies

Sunitinib (Sutent) is a medication that comes in capsule form. It is mainly used in patients with pancreatic neuroendocrine tumours. It works mainly by blocking a process called angiogenesis. Angiogenesis is the process of making new blood vessels. Tumours need a good blood supply to grow and Sutent helps stop that process. The drug comes under an umbrella group of drugs known as tyrosine kinase inhibitors.

Everolimus (Affinitor®) is another medication for patients with pancreatic neuroendocrine tumours. It also comes in a capsule form and is a type of drug that interferes with the mTOR enzyme in cells that regulates growth and metabolism. Blocking the action of this enzyme has been shown to slow the growth of neuroendocrine tumour cells in patients with progressive disease.

Peptide receptor radionuclide therapy (PRRT)

PRRT is an outpatient therapy. You will probably have a dose of chemotherapy to prepare or sensitise the tumour cells for the PRRT. You will also have an infusion of amino acids to help protect your kidneys.

Depending on the treatment regime, PRRT is given as an induction course of four treatments separated by 6 to 8 weeks. You may have more PRRT later your doctor will advise you about this.

You may have nausea, fatigue and minor changes in the production of blood as side effects of this treatment.

Liver directed therapies

Hepatic artery embolization (HAE)/transcatheter arterial chemoembolisation (TACE)

If the NET tumour has spread to the liver, you may be offered hepatic artery embolisation (HAE), which will aim to block the blood supply to the tumours in the liver.

You will have local anaesthetic (and sedation). The radiologist will access an artery in the groin and then direct a catheter, with the help of x-ray imaging, into the main supply of the liver (hepatic artery) and into the artery that supplies blood to the NET tumours in the liver. Tiny particles called microspheres are then injected through the catheter into the artery. These particles block the blood supply to the tumour, which can cause the tumour to shrink or even die.

This procedure may be combined with the injection of chemotherapy or the use of microspheres that contain chemotherapy. This is called transcatheter arterial chemoembolisation (TACE). For this procedure, you will probably be admitted to hospital overnight. The side effects can include fatigue, nausea, vomiting and pain especially around the liver.

Selective internal radiation therapy (SIRT)

This is a new way of using radiotherapy to treat liver metastases that cannot be removed with surgery.

It is similar to hepatic artery embolisation. An experienced interventional radiologist will insert a catheter into the hepatic artery supplying blood to the NET tumours and tiny beads containing a radioactive substance will be injected. These interfere with the tumour cell DNA and slow tumour growth.

Radiofrequency ablation (RFA)

This is a treatment for metastatic or primary NET and is done by a radiologist. Using ultrasound or CT guidance, a needle (under local anaesthetic and sedation) is inserted through the abdominal wall and into the liver tumour. Once the needle is localised within the tumour, a generator is used to deliver a rapidly alternating current (radiofrequency energy) producing high temperatures (heat) that destroy the cancer cells (necrosis).

Symptom control

Telotristat etipirate (Telestar®)

Telotristat is a new oral drug undergoing trials. Its action blocks as enzyme that is responsible for the production of serotonin. Excessive blood levels of serotonin cause carcinoid syndrome (diarrhoea, flushing, abdominal pain); therefore, decreasing its production should minimise these symptoms. This drug does not act on the tumours to control their growth.

No treatment

No treatment, or watchful waiting, may be suitable for some NET patients especially if the NET is not causing symptoms or problems, the disease is stable, or the tumour is low grade (G1).

For some people, poor general health or complications secondary to treatments may also make further NET treatment risky.

Clinical trials

Clinical trials are medical research trials involving patients. They are done to try to find new and better treatments. Clinical trials are the only sure way to find out if a new approach to cancer care is better than the standard treatment currently available.

Living with a NET

The experience of living with an uncommon cancer, such as a NET, is not fully appreciated by most people in the medical and general community. For many patients it is an emotional journey.

For most patients with NETs, their story can be divided into four chapters.

First chapter: Something feels wrong

For patients this is the phase of knowing, or feeling, that something is wrong with their health. You may have periods of feeling well punctuated with episodes of symptoms or have symptoms that become more frequent. You visit your general practitioner many times with the vague symptoms of fatigue or 'feeling just not right'. Your doctor may discuss irritable bowel; flushing/rashes or asthma, which mimic common conditions but actually are due to NET.

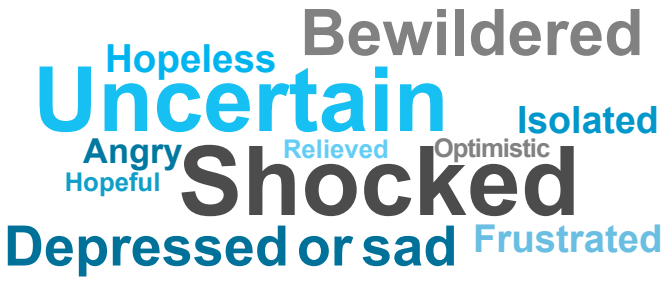
On average, NET patients see four to six different doctors (including specialists) over 4 to 7 years before the correct diagnosis is made.

Because of repeated misdiagnoses, patients feel frustrated, confused, and at times depressed. Some lose faith in the medical system altogether. You may have spent considerable time and money seeking the correct diagnosis. Tragically, because NET patients visit their doctors on so many occasions, some are labelled as being mentally unstable or 'hypochondriacs'.

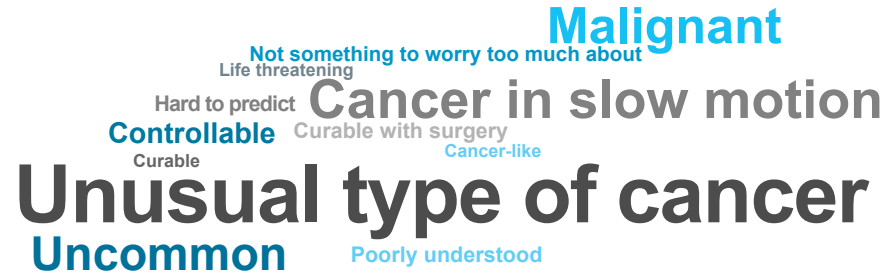
Second chapter: Diagnosis

This is when a diagnosis of NET is finally made. Patients experience a range of emotions at this point.

- **relief** that the correct diagnosis has been finally made and they have not been malingering or crazy
- **anger** at the medical community for the delays and misunderstanding in the diagnosis
- **confusion**
- **fear and hopelessness** about what the future holds.



The treating doctors can present a confusing picture of NETs to patients. The word cloud (see image) captures many of the ways many in the medical community currently view NETs.



This time can be very difficult. Despite the fact that they have a diagnosis, many patients are inadequately treated, mismanaged and given incorrect information by doctors who do not understand NETs. This is understandable given that NETs are an uncommon cancer and many doctors would not have seen a patient with NET in their practice before and may not know where or who are the 'experts' in treating this uncommon cancer.

Because of the different types of NETs—functioning or non-functioning, their location and grade (e.g. slow growing or aggressive), the hormones that they may secrete and whether they have spread—the medical and surgical options for managing each patient's NET are specific to that patient.

A treatment plan that is clinically suitable for your NET requires assessment and review of your medical history by a NET specialist with access to a NET multidisciplinary team.

Many clinical studies demonstrate that NET patient care and long-term outcomes are improved when managed by a specialised neuroendocrine multidisciplinary team (MDT). It is critical for NET patients to have access to such people and teams to ensure that they are being managed appropriately and receiving the best available treatments.

You may feel uncomfortable asking your doctors for a 'second opinion' to be provided by a NET specialist; however, doctors are usually agreeable to this

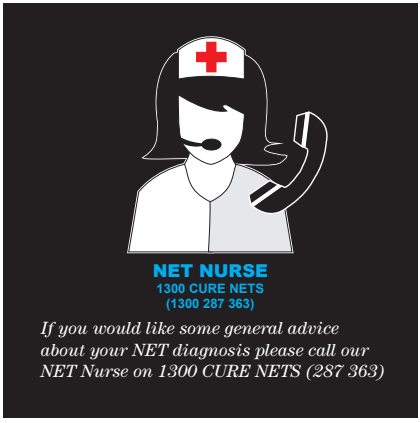
because they appreciate the fact that making an effective treatment choice can be very challenging. If getting a second opinion through your treating doctor is not possible, you can get a referral from any doctor, including your general practitioner. To help Australian patients find a NET Specialist, the Unicorn Foundation has developed a register of NET specialists and NET MDTs to which patients can be referred (www.unicornfoundation.org.au).

Third chapter: Transition

During this time, many patients are commenced on treatments and/or receive surgery for their NET.

This is an extremely difficult and stressful period of adjustment. You may face untold emotional and physical challenges in 'coming to grips' with your situation and this can be compounded and magnified by the reactions of loved ones, family and friends, who are trying to help but may not understand the cancer.

You can get support and comfort during this time from the Unicorn Foundation. This includes NET nurse support, telephone support service and our private Facebook community where many patients converse in a safe, supportive and non-threatening forum. Other services, such as the Cancer Council helplines, can give general advice and support but often do not have expertise in NETs.



"Having a rare cancer is frightening beyond belief. I almost envied those with breast or bowel cancer. That's where the support and answers seem to be. Finding a NET nurse who could help understand NET issues has been one of the most powerful experiences of my NET years." (Deborah, Camperdown)

"I have used the service the NET nurse provides on many occasions. Just recently I had my first treatment of Lutate and she was very helpful to me during this time explaining that my reaction to it was a good sign. Explaining that it was a sign that the tumours had been hit hard by the treatment. She calls me back after I have a concern and has been a great support to me as a country patient." (Dorothy, NSW)

Fourth chapter: Living with a NET

This is the adjustment period, when, after years of misdiagnosis and the shock of being told you have a cancer, you receive expert treatment and advice and begin to comprehend the notion of 'living with a NET'.

Living with a NET is challenging and can have a significant impact on activities of daily life, and many NET patients need to make significant adjustments. There are so many things to think about that it can be overwhelming.

Questions about what will happen 'next' are at the forefront of every patient's thoughts and actions and for many people the impact on their physical, mental and emotional health is significant.

Generally, most people with NETs describe themselves as having 'good health' but that often hides the reality of symptoms of fatigue, muscle weakness, intermittent abdominal pain, diarrhoea, skin rashes, headaches, anxiety and depression. It is important for caregivers, family, friends and work associates to understand that although the NET patient appears well, they are struggling with many of these symptoms and need to be supported during such times.

It is important for you to develop a 'working' relationship with your NET specialist, allowing them to guide your treatment.

Many NET patients describe feeling that their identity has been 'stolen' and replaced by an overwhelming focus on their disease. Therefore, it is vital to develop trust in your NET specialist and allow them to share this burden, which will free up time for you to pursue things in life that empower and give joy, such as family, hobbies and holidays.

The NET specialist

NET patients see their NET specialist and many other members of the NET team, including their general practitioner, on a regular basis. These appointments are stressful as there are often many issues to discuss, questions to ask, and explanations to be given within a limited time in the consultation room or outpatient clinic.

It is vital to prepare for these consultations in order to get the most out of the time spent with your doctor.

- Take all recent pathology (blood tests) and radiology results to the appointment.
- Regularly take notes on how you are feeling and take these notes to the appointment.
- Write down questions that you want to ask before the consultation. If you do not understand the answers, don't be embarrassed to ask for the answer to be repeated or rephrased.
- Keep a diary of all your symptoms, even if they seem minor or unrelated to your NET, including triggers for the symptoms, their frequency and severity, and factors that may relieve the symptoms.
- Take a trusted friend or family member with you to the appointment. If you are feeling anxious, you may not hear everything that is said, or ask all the questions you wanted to. It helps to have additional ears there to listen, and your companion may help to make sure your concerns are raised.

Deciding on a treatment strategy can be difficult, so choosing to get a second opinion is quite common.

Patients should be assured that they have the right to know as much about their prognosis as they wish and have the right to know the overall treatment strategy, including what options are available if initial treatments are not successful in stabilising the disease.

Patients have the right to make decisions for themselves, even if the decision is against having medical treatment or to end medical treatment.

Questions to ask during the consultation

General

- What type of NET do I have?
- Where is the NET located? Has it spread to other parts of my body?
- What are the risk factors for NETs?
- Is my NET likely to be caused by genetic factors? Are any other members of my family at risk of developing a NET?
- Are you a NET specialist? How many NET patients do you treat a year?
- Are you able to consult with or refer me to a NET specialist?
- Are you involved with or have access to a NET multidisciplinary team?
- Where can I find out more information about my NET?

Tests

- What type of histology is my NET (the description of the NET as it looks under the microscope)? Did an experienced NET pathologist review the tumour?
- What other tests do I need to have? (Refer to the diagnosis section. Tests may include blood tests such as chromogranin A (CgA); 24-hour urine tests (5-HIAA); functional nuclear medicine scans (Gallium-68 PET scan, FDG scan, PET-CT scan); triple phase CT of the liver; MRI; and echocardiography of the heart.

Staging

- What is the grade and staging of my NET? What does this mean?
- Based on my grade and staging, what is my prognosis?

Management

- What are my management options?
- What is the expected timeline for my management plan? Do I need to be treated immediately?
- Which treatments, or combination of treatments, do you recommend? Why?
- What is the goal of the treatment you are recommending?

Treatments

- What will be done during the treatment and how will it affect me?
- How often do I need this treatment? (Treatment schedule)
- Will I need to be hospitalised for a treatment, or is this treatment done as an outpatient?
- What are the side effects or risks (short term and long term) of this treatment?
- How can I best prepare myself for this treatment?
- What should I avoid or not do while having this treatment?
- How will this treatment affect my daily life? Will I be able to work, exercise and do my usual activities?
- Does this treatment treat my symptoms of NET?
- What are the costs for my NET treatments? Are my treatments covered by Medicare, Pharmaceutical Benefits scheme (PBS) or my insurance?

Clinical trials

- What are clinical trials?
- Are there any relevant clinical trials for my NET?
- What are the benefits and risks of participating in a clinical trial?
- How will I be monitored while participating in a clinical trial?
- What are my responsibilities during a clinical trial?
- Are there any costs associated with being in the clinical trial?
- Where can I learn more about clinical trials for NET?

Support

- What supports are available to me? To my family?
- Who should I call with questions or concerns out of hours?
- May I contact you or the nurse to talk about additional information I find?
- Do you know of any support groups or resources for NET patients?
- I am concerned about managing the costs related to my NET care: who can help me with these concerns?
- Am I eligible for any benefits if I cannot work?

Patient support

The Unicorn Foundation operates face-to-face NET support group meetings in most Australian capital cities six times per year. NET patients and carers can also access a 'closed' forum on Facebook as well as deal directly with our specialist NET nurse on 1300 287 363 or netnurse@unicornfoundation.org.au.

It is very important for all Australian NET patients to contact the Unicorn Foundation (unicornfoundation.org.au) or join the mailing list to remain updated on current issues related to NET in Australia.

Clinical trials

You can find out more about current NET trials at:

- Australian and New Zealand Clinical Trials Registry www.anzctr.org.au
- Australian Cancer Trials www.australiancancertrials.gov.au
- Australian National Health and Medical Research Council www.australianclinicaltrials.gov.au
- United States National Health Institutes Clinical Trials (includes international and Australian trials) www.clinicaltrials.gov

Complementary (alternative) therapies

Complementary therapies are also known as natural or traditional therapies and can be divided into three main categories:

- **'natural' therapies**: herbal and naturopathic compounds, Chinese medicines, homeopathy, etc.
- **mind-body (mindfulness) techniques**: meditation, relaxation, support groups, counselling, music or art therapy, hypnotherapy, aromatherapy, etc.
- **physical therapies**: massage, yoga, tai chi, acupuncture, reflexology, Pilates, Alexander technique, etc.

Studies have shown that more than 50% of patients with cancer have used some form of complementary therapies in addition to their conventional medical treatments. For many NET patients, taking a 'holistic' approach to their health improves their quality of life by addressing their dietary, physical, emotional and spiritual needs.

Before starting any complementary medicines or therapies it is important to understand:

- How the therapy works.
- Will the therapy cause harm, have side effects or interact with other medications?

Currently there is no conclusive scientific evidence for the use of natural therapies to treat cancers; however, there is anecdotal evidence for mind-body techniques and physical therapies to assist in improving pain management, sleep, stress relief, depression, anxiety and general quality of life.

It is vitally important to tell your NET specialist about any 'natural' medicines or complementary therapies as they can potentially have a negative impact on the disease or interact with other NET treatments.

Diet

Why diet is important

There are a number of reasons why focusing on diet and healthy eating is important for NETs patients.

Eating well can:

- Help you cope better with treatment.
- Assist in healing. This is important after surgery, chemotherapy, radiotherapy or other medical treatment.
- Improve your body's immune system, its natural defence.
- Help you maintain your weight and feel better in yourself. This is important even if you are not having treatment.

For those people who are not losing weight, have symptoms controlled well and are otherwise well on no other prescribed diet, their focus should be to follow a healthy eating diet. This should be high in foods such as fruit, vegetables and wholegrains but low in nutrients such as salt, saturated fat and added sugars. Choose from a range of natural colours: at least three vegetable and two fruit portions a day.

Some NET patients may need to seek advice about the right foods. Patients with pancreatic NETs in particular may have more complex needs and should seek guidance from an experienced nutritionist.

Carcinoid trigger foods

For some patients, certain foods and drinks can 'trigger' symptoms such as abdominal pain, diarrhoea and flushing. The types of foods/drinks that cause this reaction vary. The most reliable method of identifying them is with a food and symptom diary. The diary is completed over a 2–4 week period and includes foods eaten, medications and any symptoms experienced afterwards.
If you identify a 'trigger food', try reducing the portion size. If this does not help, you may need to exclude it completely from your diet. Possible common triggers include:

- size of the meal
- fat content
- spice and alcohol
- meals moderate to high in amines
  (e.g. aged cheese, alcohol, smoked/salted fish and meat).

Common issues and strategies

Weight loss

It is important not to ignore loss of weight. Progressive loss of weight may be as a result of a number of problems, so you should discuss this with your doctor, nurse specialist and dietitian.

General tips to boost your intake:

- Eat 'little and often'.
- Small, frequent meals and snacks may be easier for you to manage rather than the traditional three meals per day.
- Have snacks in between your meals.
- Eat when you feel hungry.
- Use convenience foods (ready meals, canned foods, frozen foods) if you are too tired to prepare meals.

Tips to increase your protein and energy intake:

- Foods rich in protein: meat, poultry, fish, eggs, dairy products (milk, yoghurt, cheese), pulses and nuts.
- Foods rich in energy: oils, nuts, butter, margarine, and any other foods high in fat and sugar. Use full-fat dairy products (e.g. whole milk, full fat cheese, full cream yoghurts, double cream).
- Fortified milk: add 3–4 tablespoons of skimmed milk powder to 1 pint of milk. Use in the same way that you would use ordinary milk.
- Breakfast cereals: use fortified milk or neutral flavoured supplement drinks. Try adding dried fruit, nuts, sugar, honey, yoghurt, evaporated milk or cream.
- Stews or casseroles: add noodles, lentils or beans. Stir in cream or sour cream.
- Soups or sauces: make with fortified milk or add grated cheese, double cream, butter or oil.
- Desserts: add ice cream, cream, evaporated milk, condensed milk, jam, honey, golden syrup, lemon curd, dried fruit, nuts or chocolate.
- Use fortified milk to make milky deserts (e.g. custard).
- Sandwiches, toast, plain biscuits or jacket potatoes: add butter, margarine, mayonnaise, cheese, peanut butter, olives or avocado.
- Vegetables: add grated cheese, oil, butter or margarine.
- Salads: use oil, mayonnaise, salad cream, salad dressing, Greek yoghurt, nuts or seeds.
- Try using fortified milk in hot chocolate, smoothies or other high energy drinks.
- If necessary, your dietitian may advise you to get a prescription of supplement drinks.

"Regular exercise such as walking has been shown to reduce muscle wasting and fatigue, as well as nausea and vomiting, and can help some people sleep better."

(Net Specialist)

Diarrhoea

Diarrhoea may be a result of many things in NETs including the tumour-secreting hormones, treatment, intolerance to foods or an infection. Here are some things to try:

- If you have diarrhoea and you have not started a new treatment, see your doctor as you may have an infection.
- Eat little and often.
- Reduce insoluble fibre (e.g. bran, wheat germ) but increase soluble fibre in diet (oats, apricots, high fruit jams).
- Cook and peel fruit and vegetables.
- Juices 'without bits' rather than whole products/smoothies.
- Non-dairy, multi-strain probiotics (check with your doctor if you are on chemotherapy).

Wind and bloating

This problem can accompany diarrhoea and constipation. Here are some tips to help:

- Avoid gas-forming foods (e.g. onions, garlic, cabbage, pulses, cauliflower, broccoli, nuts and spicy foods).
- Trial a low-fibre diet.
- Avoid fizzy drinks and chewing/bubble gum.
- Skipping meals is more likely to cause wind, therefore eat regular meals.
- Chew your food well to reduce the amount of air swallowed.
- Monitor your bowel movements and speak to your doctor or nurse if the problem persists.

Nausea and vomiting

You may feel nauseous or vomit for several reasons. Please tell your treatment team so they can investigate possible causes.

- Eat small, frequent meals throughout the day to avoid feeling full.
- Take little sips of nutritious drinks between meals rather than with them.
- Avoid cooking smells if possible.
- Cold food and drinks usually have less smell than hot cooked foods.
- Seek out tart flavours (e.g. citrus juices, sorbets and lemon curd) and salty and minty flavours.
- Eat plain biscuits, crackers or dry toast.
- Avoid greasy or fatty foods.
- Try ginger extract in foods or drinks (e.g. crystallised stem and fresh ginger in stir fries / juices / grated onto salads).

When to ask for help

It is important to note that this is only a very basic guide. It is important to discuss your needs with your treatment team, particularly if you have weight loss, diarrhoea or any other prolonged symptoms.

This chapter was adapted from: Whyand, T., Davies, P. and Caplin, M. (2014), Food and Neuroendocrine Tumours (NETs), Royal Free Hospital Neuroendocrine Tumour Unit, European Neuroendocrine Tumour Society Centre of Excellence, Royal Free London, NHS Foundation Trust, London.

Resources

Websites

www.netcancerday.org
www.netpatientfoundation.org.au
www.incalliance.org

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- Novartis Australia
- Pfizer Australia
- IPSEN Australia
- The Wilson HTM Foundation
- Medicare Local Foundation Ranges and North Western Melbourne.

About the Unicorn Foundation

The Unicorn Foundation was formed in 2009 by Dr John Leyden (Chair and co-founder) and Simone Leyden (CEO and co-founder) due to the experience they had with their sister Kate's diagnosis with pancreatic neuroendocrine cancer.

The Foundation is an independent medical not-for-profit charity directed towards improving the outcomes of patients with NETs.
The mission of the Unicorn Foundation is:

- to assist and support patients and carers, through support groups and access to networks of expertise
- to lobby for access to new and appropriate investigations and treatments
- to raise awareness and knowledge of neuroendocrine cancers within the medical community and general public
- to encourage and support Australian based research in the area of neuroendocrine cancers.

If you would like to know more about the Unicorn Foundation or get involved please visit our website www.unicornfoundation.org.au or email info@unicornfoundation.org.au. All donations are most welcomed as we continue our work to improve the outcomes of NET patients.

"I will never forget the complete and utter shock, fear and sadness that engulfed me when I was told I had NET cancer."

(Jamie, age 37, Adelaide)

Glossary

What does that word mean?

Use this glossary to find the meanings of important terms that are highlighted in this brochure.

Adrenal gland: A gland near the top of the kidney that creates hormones, like adrenaline and cortisol. Your body has 2 adrenal glands.

Aggressive: A term used to describe the speed or extent to which a tumour grows and spreads.

Atrophic gastritis: Chronic inflammation of the stomach, especially the fundus, characterised by atrophic mucosa, decreased acid secretion, increased gastrin levels and hyperplasia of enterochromaffin-like cells resulting in increased CgA levels and histamine production.

Biopsy: A procedure where a small amount of tissue is removed from the body and examined under a microscope or using other tests to find out if there is a tumour.

Calcitonin: A 32-amino acid peptide hormone produced by thyroid C cells that modulates blood calcium levels by opposing the effects of parathyroid hormone, which causes release of calcium from the bone. Calcitonin functions to lower blood calcium levels by inhibiting osteoclast limiting bone cell activity and reducing absorption and reabsorption of calcium in the intestine and kidney, respectively. Calcitonin is also secreted by medullary carcinomas of the thyroid and occasionally by other neuroendocrine tumours.

Carcinoid: Has the same meaning as NET or GEP-NET (see below). The words may be used in place of one another.

Carcinoid crisis: A potentially life-threatening heart-lung collapse caused by sudden release into the systemic circulation of vasoactive amines and peptides from a NET. It may occur as a result of an event (e.g food, alcohol, exercise, or a drug administration) or during a diagnostic provocative study such as a pentagastrin or certain tests. Hepatic embolisation may engender this event subsequent to massive tumour infarction. An intravenous somatostatin analogue and appropriate heart and blood support is often needed to address dangerous changes in heart and blood function.

Carcinoid syndrome: A set of symptoms that occur when a functioning NET releases the hormone serotonin. The symptoms may be sudden or severe.

Carcinoma: Cancer that starts in the skin or in tissues that line or cover internal organs.

Catestatin: A bioactive peptide fragment of chromogranin A (amino acids 352-2372) that inhibits catecholamine release from adrenal chromaffin cells and stimulates histamine release from mast cells, thereby regulating blood pressure.

Chemotherapy: The use of drugs to destroy cancer cells, usually by affecting their ability to grow.

Chromogranin A (CgA): Detection of elevated plasma levels of CgA has be shown to be a sensitive biomarker for neuroendocrine tumours.

Chronic atrophic gastritis type A: Chronic inflammation of the stomach usually caused by an autoimmune response associated with loss of parietal cells of foci of endocrine cell (ECL) hyperplasia.

Cushing syndrome: Hypersecretion of cortisol from the adrenal cortex, which may be secondary to hypersecretion of ACTH from the pituitary, resulting in rapid weight gain, particularly of the trunk and face with sparing of the limbs (central obesity), growth of fat pads along the collar bone and back of the neck (buffalo hump) and a round face often referred to as a `moon face'. Other symptoms include excess sweating, thinning of the skin and bruising, fatigue, osteoporosis, and diabetes. Cushing was a pioneer in the management of pituitary tumours.

Differentiation/differentiated cells: In tumour cells, differentiation refers to how developed the cells are. Differentiated tumour cells look like normal cells. Undifferentiated or poorly differentiated tumour cells don't have the structure of normal cells, and don't work the way normal cells do. Poorly differentiated tumour cells usually have a greater chance of being malignant.

Duodenum: The first part of the small intestine, connected to the stomach. The duodenum gets enzymes from the pancreas and chemicals from the liver and the gallbladder to help with digestion.

Endocrine system: A group of glands and organs that control different body functions by producing and releasing hormones.

Functional NET: A NET that releases hormones and may cause many different symptoms. Also causes a secretory NET.

Gastrin: A hormone released by the pancreas that tells the stomach to produce digestive acids and enzymes.

Gastrinoma: A G-cell derived neuroendocrine tumour, mainly (60%) occurring the duodenum, that overproduces and secretes gastrin, thereby giving rise to the respective gastrinoma. The typical symptoms of a gastrinoma are related to peptic ulceration and excessive acid production (e.g. dyspepsia, acid reflux symptoms, abdominal pain, gastrointestinal bleeding, and duodenal perforation). Secretory diarrhoea is also caused due to high gastric output in the duodenum that neutralises the pancreatic enzymes.

Gastroenteropancreatic NET (GEP-NET): A NET that most often starts in the gastrointestinal tract or pancreas

Gastrointestinal (GI) tract: Another name for the digestive system. It includes the mouth, throat, oesophagus, stomach, small intestine, large intestine, rectum and anus.

Glucagon: A hormone released by the pancreas that raises glucose (sugar) levels in the blood.

Glucagonoma: A pancreatic NET derived predominantly from alpha cells of the pancreas that secrete glucagon. The inappropriate glucagon secretion by the tumour cells can cause diabetes, mellitus, cachexia, anaemia, venous thrombosis, migratory necrolytic erythema, diarrhoea, and neuropsychiatric symptoms.

Grade: A system of classifying tumour cells. The cells are graded based on how they look under a microscope and how quickly the tumour is likely to grow and spread. Low-grade tumours (grades 1 and 2) look like the tissue around them. They are less aggressive. High-grade tumours (grades 3 and 4) do not look like the tissue around them. They are more aggressive.

Growth hormone-releasing factor (GRF): A chemical released by the brain that tells the pituitary gland to produce growth hormone.

Hormone: A substance, usually a protein, that is released and travels through the bloodstream to different organs. Hormones help control how some of the organs in the body work.

Hyperglycaemia: Having high levels of glucose (sugar) in the blood. Symptoms include dry mouth, thirst, frequent urination (including at night) blurry vision, and dry, itchy skin.

Hypoclorydria: Having low levels of hydrochloric acid in the stomach. Symptoms include halitosis (bad breath), heartburn, bloating or belching, gas right after eating, and indigestion.

Hypoglycaemia: Low levels of glucose (sugar) in the blood. Symptoms include dizziness, headache, tiredness and confusion.

Hypokalemia: Low levels of potassium (salt) in your blood. It may be caused by diarrhoea.

Insulin: A hormone released by the pancreas that lowers glucose (sugar) levels in the blood.

Insulinoma: A pancreatic NET derived predominantly from beta cells of the pancreas that is benign in 90% of cases. The tumour oversecretes insulin, causing intermittent symptoms of hypoglycaemia (I.e., visual disturbance, irritability, bizarre behaviour, sweating, headache, tachycardia, anxiety, somnolence, paraesthesia, etc.). In more severe cases, seizures, stupor, coma and even permanent brain damage may occur.

Lesions: Areas of abnormal tissue that may or may not be cancerous.

Metastasise: To spread from one part of the body to another. The words `localised', `regional', and `distant' are sometimes used to describe how much a NET has spread.

Multiple Endocrine Neoplasia syndrome type 1: An inherited genetic disorder caused by germ-line mutations in the MEN-1 gene. It (menin) is on chromosome 11q13 that is associated with an increased risk of developing multiple cancerous and non-cancerous tumours in glands such as the parathyroid, pituitary, and pancreas. This disorder affects approximately 1 in 30000 people.

Non-functional NET: A NET that doesn't release hormones. This type of NET may only cause symptoms when it grows. Also called a non-secretory NET.

Pancreas: An organ that produces hormones and enzymes that help your body digest food.

Pellagra: A condition caused by low levels of niacin (a B vitamin) in the blood. Symptoms include diarrhoea, scaly skin rash, mental confusion, change in skin colour and inflamed mucus membranes.

Proteins: The basic building blocks of tissue and other structures in the body. An enzyme is a kind of protein that causes chemical changes in the body.

Radiation: A form of therapy used to kill cancer cells by damaging their DNA. Radiation can damage normal cells too, so treatment should be carefully planned to decrease side effects.

Radiology: The use of radiation to treat or diagnose disease.

Radiotherapy: The use of high-energy radiation to destroy cancer cells and shrink tumours. The radiation may come from a machine outside the body or from radioactive material that is placed in the body near cancer cells.

Serotonin: A hormone made by certain types of cells in the body, mostly in the gastrointestinal tract. Serotonin helps with various functions, including digestion.

Somatostatin: A hormone that stops the release of other hormones, including gastrin, insulin, glucagon, and serotonin (see definitions for these hormones in this glossary).

Somatostatin analogues: Synthetic analogues of the peptide hormone somatostatin that have a longer half-life in circulation and can be used for imaging or as therapeutic agents.

Specialised cells: Cells that have specific jobs in the body. They start as unspecialised cells, also known as stem cells, which are present in babies still in the womb. Unspecialised cells can turn into any kind of cell. The DNA in the cell determines the kind of cells they will become. The cells then grow and change shape, becoming specialised cells.

Syndrome: A set of symptoms that occur together. A syndrome may be a sign of a certain disease or it may mean there's an increased chance of developing the disease. For example hypoglycaemia syndrome may be caused by a type of NET called an insulinoma, and Zollinger Ellison syndrome may be caused by a type of NET called gastrinoma.

Thymus: An organ near the base of the neck that produces infection-fighting cells.

Thyroid: A small gland in the neck, just under the skin below the Adam's apple. It produces thyroid hormones which control metabolism.

Tumour: An abnormal growth or mass in the body caused when cells grow out of control or don't die when they are supposed to. A tumour may be non-cancerous (benign) or cancerous (malignant).

Tumour burden: The number of cancer cells, size of a tumour, or the amount of cancer in a person's body.

Ulcer: A round sore where the lining of the stomach or duodenum has been eaten away by stomach acid and digestive juices.

Unspecialised cells: Also known as stem cells. These cells are present in babies still in the womb. They can turn into any kind of cell. The DNA in the cell determines the kind of cells they will become. The cells then grow and change shape, becoming specialised cells with specific jobs in the body.

Vasoactive intestinal peptide (VIP): A substance released by the pancreas that causes watery diarrhoea.

Von Hippel-Lindau syndrome: An inherited genetic disorder associated with renal angioma, renal cell carcinoma and pheochromocytoma (a neuroendocrine tumour of the medulla of the adrenal glands). The disorder is caused by mutations of VHL tumour suppressor gene on the short arm of chromosome 3.

Wheezing: A whistling sound made during breathing that happens when airways become partially blocked. Some tumours can squeeze an airway and cause the blocking.

Zollinger Ellison Syndrome: A disorder caused by excess secretion of gastrin from a duodenal or pancreatic neuroendocrine tumour resulting in excessive secretory diarrhoea and intractable peptic ulcers.

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the Unicorn Foundation
I can honestly say I would be lost.
The support and friendship
I have received is priceless."

(Kay, Adelaide)

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