



NeuroEndocrine
Cancer Australia

Neuroendocrine tumours:

A guide for
healthcare professionals

neuroendocrine.org.au

Neuroendocrine tumours: A guide for patients

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Introduction

This book has been developed for healthcare professionals to improve understanding and knowledge about neuroendocrine tumours (NETs). It contains information to help you understand diagnosis and treatment options.

This booklet may also help when explaining this complex diagnosis to patients' family and friends.

For more information, and to make sure you stay up to date with the latest developments in NETs, subscribe to NeuroEndocrine Cancer Australia's enews by visiting www.neuroendocrine.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.

Neuroendocrine tumours were first described over 100 years ago by the German pathologist, Siegfried Oberndorfer (1876–1944), who was the first to characterise the nature of the tumours and refer to them as 'benign carcinomas'. He named them 'karzinoide' ('carcinoma-like'), emphasising in particular their benign features. Oberndorfer later amended his classification to include the possibility that these small bowel tumours could be malignant and also metastasise.

Unfortunately, for more than 50 years there have been many medical misconceptions and much misunderstanding about NETs. Fortunately, over the last 10 years, there has been significant improvement in the diagnosis, management and understanding of NETs.

Brain

Thyroid

Skin

Lungs

Breast

Liver, Spleen

Gallbladder, Stomach

Kidney, Pancreas

Small Bowel

Large Bowel

Appendix, Ovary

Rectum, Prostate, Anus

Testicular

About NETs



What are NETs?

NETs are a complex group of tumours that develop predominantly in the digestive or respiratory tracts, but can occur in other areas of the body. These tumours arise from neuroendocrine cells. The main function of neuroendocrine cells in the body is to create, store and secrete a variety of peptides (little proteins) and hormones for normal bodily functions.

Like all cancers, NETs develop when these neuroendocrine cells undergo changes, causing them to divide uncontrollably and grow into a tumour (an abnormal tissue mass).

Neuroendocrine tumours can be indolent (very slow-growing) or can be more aggressive. In 1907, when neuroendocrine tumours were first classified, they were named ‘carcinoid’ (meaning ‘cancer-like’) as they seemed to grow slowly and were therefore not thought to be truly cancerous. The use of ‘carcinoid’ is being phased out in medical literature, as we now know that these tumours can be malignant.

Current terminology is simply neuroendocrine tumours (or NETs) or with the primary location of the tumour added: for example, lung NET, bowel NET or pancreatic NET.

Over the last two decades there has been a significant increase in the incidence of NETs, with most of them being sporadic (not related to another disease or inherited). However, in patients with genetic conditions such as multiple endocrine neoplasia (MEN), Von Hippel–Lindau (VHL) disease and neurofibromatosis (NF), there is an increased risk of developing these tumours.

Other neuroendocrine tumours are found outside the gastrointestinal or respiratory system, such as:

- in the adrenal glands—pheochromocytoma and adrenocortical carcinoma
- in the nervous system—paragangliomas
- in the skin—Merkel cell tumours
- in the thymus—thymic NET
- in the testes and ovaries
- in the thyroid gland—medullary thyroid cancer
- prostate
- neuroblastoma (a neuroendocrine cancer in children).

Although NETs share common cellular features, their behaviour is highly dependent on the cells that make up the tumour (as seen under the microscope). The cells can be classified into well-differentiated (low and intermediate grade) or poorly differentiated (high grade), which characterises their growth pattern (slow growing to aggressive) and gives an indication of prognosis and the appropriate treatments (see later in this booklet for grading systems).

Epidemiology

Neuroendocrine tumours have been a rare group of tumours with malignant potential however are now being classified when grouped together as a common cancer, not rare or less common. The incidence of NETs varies worldwide, and has doubled from 2,123 cases in 2000 to 4,693 cases in 2020 and tends to be greater in those over 65 years of age. The aetiology of NETs is currently not clear. Most of them are considered to be of sporadic origin, though a small familial risk has also been observed.

Based on an annual incidence of 21.1 per 100,000 people, and a current population of 27 million, Australia will see estimated 5,755 people diagnosed with NETs in 2024. Prevalence is much higher than incidence due to five-year survival rates of approximately 50–60%. The 39 year prevalence rate gives us 29,351 people in Australia living with NETs (2024).

The prevalence of gastroenteropancreatic NETs (GEPNET) is second only to colorectal cancers and is higher than most other gastrointestinal cancers, including pancreatic, gastric, oesophageal and hepato-biliary carcinomas.

Gastroenteropancreatic NETs (GEP-NETs)

Traditionally, these NETs were classified by the site of origin as:

- foregut—stomach, duodenum, pancreas, bronchus (lung)
- midgut—small bowel and beginning of large bowel, including
- hindgut—most of large bowel, rectum and genitourinary system

Now, the term gastroenteropancreatic (GEP-NET) is used.

Gastric NETs

Gastric NETs represent less than 1% of all gastric cancers; however, their detection has increased due to the increased use of gastroscopy.

There are four types of gastric NET:

- **Type I** is the most common and represents about 70–80% of all gastric NETs. These are associated with atrophic gastritis and an overproduction of gastrin (hypergastrinaemia). Typically, these are small polyps (less than 1–2 cm) and 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. There is a potential association with hypergastrinaemia induced by long-term use of proton pump inhibitors (antacid medications) used to control gastric reflux or dyspepsia.
- **Type II** accounts for around 5% of gastric NETs. These 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 quite small and can be managed conservatively with regular monitoring including endoscopic ultrasound.
- **Type III** accounts for 15–20% of gastric NETs. These tumours are often larger (>2 cm) and can metastasise. They are not related to over-production of gastrin and need to be surgically removed.
- **Type IV** is a very rare type of gastric NET and is the most difficult to manage. Tumours are often large and metastatic at diagnosis.

Small bowel NETs

- Jejunum and ileum NETs are often asymptomatic, slow-growing and small, which makes diagnosis in the early stages difficult. Often, when the diagnosis is made, the tumour is larger and may have metastasised—at which time the patient may present with abdominal pain, carcinoid syndrome or a bowel obstruction.
- There are many different types of duodenal NETs. These NETs produce many hormones and peptides such as serotonin, calcitonin and gastrin somatostatin. Patients may present with carcinoid syndrome (see later in this booklet), abdominal pain or fatigue due to anaemia.

Large bowel NETs

- Appendiceal NETs are usually discovered incidentally—quite often during surgery for a suspected appendicitis. If the tumours are less than 1 cm in size, further surgery is often not required.
- Another group of tumours that arise from the are the goblet cell carcinomas, so named because they have ‘goblet’ shaped cells when viewed under a microscope. Patients often present late with acute appendicitis, abdominal pain or abdominal mass and a significant proportion of females also have metastases on the ovary at the time of diagnosis.
- Colon NETs are rare and can be large, aggressive, have the potential to spread and may present with bowel obstruction and bleeding. If the NET has already metastasised to the liver, other symptoms classic of carcinoid syndrome—e.g. wheezing, facial flushing, watery diarrhoea—may also be present.

Rectal NETs

These account for about 27% of all NETs in the gastrointestinal tract and 16% of all NETs. In around half of the cases, the tumour is discovered incidentally. Patients may present with symptoms such as rectal bleeding or change in bowel habit, but often they are asymptomatic. Patients may present with metastatic disease due to a lack of symptoms.

Pancreatic NETs (pNETs): functioning and non-functioning

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

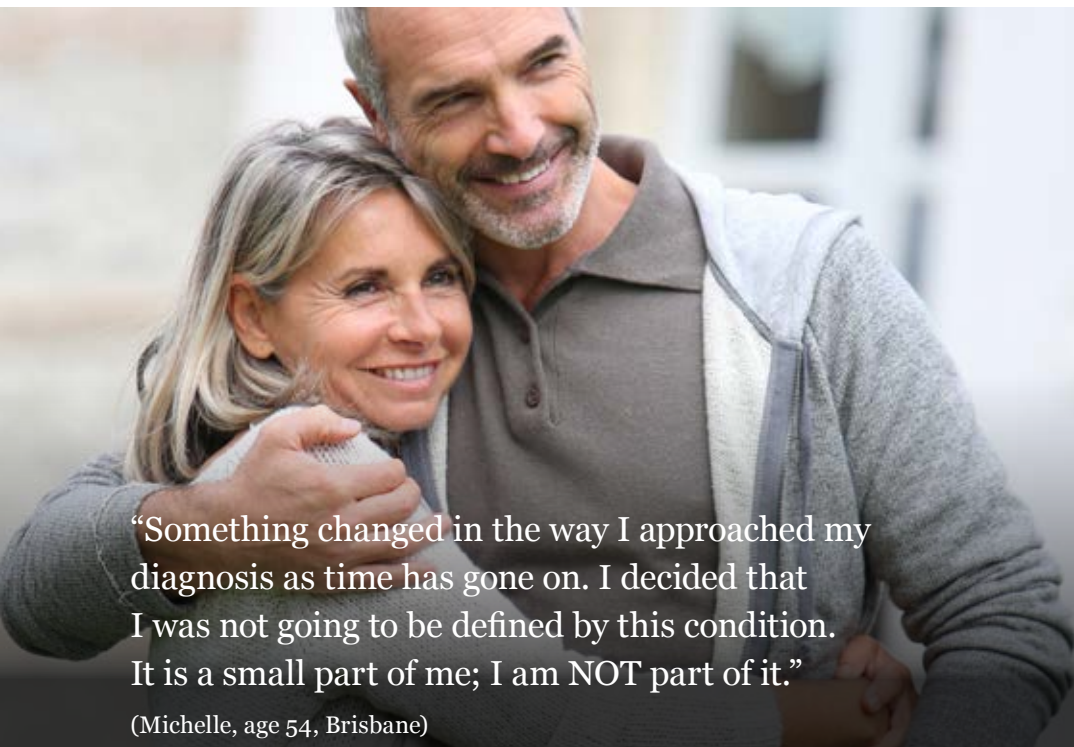
Functioning pNETs produce symptoms due to excessive hormone production by the tumours:

- **Insulinoma** - these 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 can cause stomach pain, diarrhoea, indigestion or heartburn, bloating, vomiting, nausea, bleeding, weight loss and poor appetite. Calcium levels should be checked, if a family history of gastrinoma or if excessive stomach acid which doesn't improve with treatment.
- **Glucagonoma** are tumours that secrete glucagon that can raise blood sugar (hyperglycaemia) causing fatigue, frequent urination, dry mouth, nausea, blurred vision, weight loss, anaemia and depression. Characteristic of this tumour is a red rash (migratory erythema) localised in the groin.

- **Somatostatinoma** are tumours that secrete somatostatin, which causes symptoms of diabetes, diarrhoea, steatorrhea (fatty pale stools) and weight loss.
- **VIPoma** are tumours that secrete vasoactive intestinal peptide, which causes severe watery diarrhoea, which leads to electrolyte imbalances in the blood such as low potassium (hypokalaemia) and low chloride (hypochlorhydria), weakness and fatigue.

The **non-functioning pNETs** still produce hormones and peptides but with no carcinoid syndrome and often present late due to local symptoms (abdominal pain, back pain) due to a growing mass.

Nonfunctioning NETs are not associated with a distinct hormonal syndrome so are more difficult to detect than functioning NETs; owing to this, patients generally present late with large primary tumours and advanced disease. However, nonfunctioning NETs may secrete bioactive hormones or amines at subclinical levels, or secrete compounds that lead to other, still under-recognized hormonal syndromes. They can also cause nonspecific symptoms related to increased tumour mass and/or metastases such as weight loss, bleeding or abdominal pain.



“Something changed in the way I approached my 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)

Bronchopulmonary (lung) NETs

The lung is the primary site for about 25% of NETs, which 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:

1. Typical carcinoid (TC)
2. Atypical carcinoid (AC)
3. Large cell neuroendocrine carcinoma (LCNEC)
4. Small cell lung cancer (SCLC)

Around 70% of patients will have the atypical type. Atypical bronchial NETs behave more aggressively than typical ones, although metastases develop in up to 20% of patients with typical bronchial NETs. NETs of the lung can occur at all ages.

A small proportion of bronchial NETs produce various symptoms related to hormone overproduction: carcinoid syndrome (serotonin), Cushing syndrome (ACTH) and acromegaly (growth hormone).

One other presentation is diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH). This is a rare disorder and information on DIPNECH is limited, especially with regard to its management and prognosis. It has generally become

accepted that DIPNECH is a precursor lesion to lung NETs.

Thymic NETs

NETs of the thymus are uncommon, accounting for 5% of all thymic tumours. Most are asymptomatic until they have grown to a size that causes local compression of structures in the chest (trachea, large veins). Thymic NETs can be aggressive and treatment options include surgical removal and chemotherapy. Two to five per cent of patients with MEN1 develop thymic NETs.

Ovarian and endometrial NETs

NETs of the ovary and endometrium are rare. Unfortunately most are diagnosed late and have metastasised. Patients can present with symptoms related to carcinoid syndrome and carcinoid heart disease.

Testicular NETs

Testicular NETs are rare tumours and are responsible for 1% of all testicular cancers. They can be primary or a metastasis and all patients must be investigated for NETs elsewhere in the body. They present as a painless scrotal mass and do not commonly produce symptoms of 'carcinoid syndrome'. Surgical removal (orchidectomy) is the treatment of choice, and long-term follow-up is indicated because of the potential for metastases.

Prostate NETs

Primary Prostate NETs are also rare and accounts for less than 5% of prostate cancers. More frequently, small sections of neuroendocrine carcinoma occur within the far more common adenocarcinoma form. Treatment options for prostate cancer are active surveillance; Radical prostatectomy, External beam radiotherapy, Brachytherapy (internal radiotherapy); and Hormonal therapy.

Multiple endocrine neoplasia (MEN syndrome)

Multiple endocrine neoplasia (MEN) is characterised by the occurrence of tumours involving two or more of the endocrine glands. There are four major forms of MEN and these may be inherited (autosomal dominant) or sporadic.

- **MEN 1:** Ninety-five per cent of patients develop parathyroid tumours (hyperparathyroidism), which is the most common feature of MEN 1; 40% develop pNETs; and 30% develop anterior pituitary tumours. Other tumours associated with MEN 1 are adrenocortical tumours, thymic NETs and gastric NETs. Patients and families need to have genetic testing (MEN1 gene) and should be managed by an expert multidisciplinary team.
- **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 pheochromocytomas 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.

Pheochromocytoma

Pheochromocytomas (PH) are rare neuroendocrine tumours with an incidence of one to four new cases per million/year.

They arise from the adrenal (adrenal medulla) glands, which lie atop the kidneys.

Sixty per cent of these tumours produce excessive amounts of catecholamines (adrenaline and noradrenaline), which produce symptoms such as:

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

Forty per cent do not secrete these hormones and are asymptomatic, remaining undiagnosed for many years.

Pheochromocytomas affect men and women equally with a peak age at diagnosis between 40–50 years, but 20% of all pheochromocytomas are found in children and adolescents.

Paraganglioma

Paraganglia are groups of cells that are 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 located in the head and neck, usually do not secrete hormones and rarely metastasise. Sympathetic paraganglioma are found in the thorax, abdomen and pelvis, secrete hormones such as adrenaline or noradrenaline, and metastasise in 20% of cases. Over the last 10 years the understanding of paragangliomas has improved. More than a third of patients with paraganglioma have a hereditary predisposition for the disease. The main treatment modalities are surgery, embolization, radiation therapy and stereotactic radiosurgery. People with these NETs may also be offered 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. When there is no family history of the disease and MTC occurs as an isolated case, it is called sporadic MTC. In 25% of all cases, MTC occurs as part of the inherited multiple endocrine neoplasia type 2 (MEN2) syndrome.

Adrenocortical carcinoma (ACC)

Adrenocortical cancer (ACC) is often known simply as adrenal cancer and affects one to two people per million per year, making it a rare form of cancer. ACC occurs in the outer part (cortex) of the adrenal gland. In adults, it most commonly occurs in the fourth or fifth decades of life. In children, the disease may be less aggressive and so treatment differs from that of adults.

Neuroblastoma

Neuroblastoma is the most common solid tumour of childhood. It is a neuroendocrine tumour, arising from any neural crest element of the sympathetic nervous system. It most frequently originates in one of the adrenal glands, but can also develop in nerve tissues in the neck, chest, abdomen or pelvis. It is almost exclusively a childhood cancer occurring most commonly up to the age of five years.

Merkel cell carcinoma (neuroendocrine tumour of the skin)

Merkel cell carcinoma (MCC) is a rare but aggressive skin cancer and presents as a solid purplish coloured 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 presence of Merkel cell polyoma virus. Surgical resection and local radiotherapy are the mainstays of current treatment.

the patient's hormonal receptor status. Small tumours with no axillary involvement and positive hormonal receptors have a better prognosis.

Neuroendocrine Breast Cancer (NEBC)

NEBC is a rare type of breast cancer that accounts for about 2–3% of all breast cancers. It's more common in older women and is characterized by:

- **Markers:** At least 50% of tumour cells express neuroendocrine markers, such as chromogranin, synaptophysin, or neuron-specific enolase
- **Hormone receptors:** Most cases are positive for hormone receptors and negative for HER2
- **Growth:** NEBC is a low-grade, slow-growing cancer

NEBC is treated like invasive breast carcinoma because of its rarity and limited evidence to guide treatment. The prognosis depends on several factors, including the size of the tumour, whether it has spread, and



Associated conditions

Von Hippel–Lindau syndrome (VHL)

Von Hippel–Lindau syndrome (VHL) is an inherited cancer syndrome caused by mutations of the VHL gene on chromosome 3p25. It affects both sexes equally and has an incidence of 1/30,000–40,000 people.

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 (NF1 tumour suppressor gene) disorder that affects 1/3000 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 lead to impaired function of these organs.

There is evidence that these patients may be at risk of developing insulinomas—a neuroendocrine tumour of the pancreas.

Succinate dehydrogenase gene complex (SDHA/B/C/D) mutations

Individuals with an inherited mutation to the succinate dehydrogenase (SDH) enzyme complex, have an increased risk of pheochromocytomas, paragangliomas, stomach gastrointestinal stromal tumours (GIST), kidney cancers and PitNETs.

A photograph of a male doctor and an older male patient. The doctor, on the left, is wearing a checkered shirt and a stethoscope, looking down at a clipboard. The patient, on the right, is wearing a light-colored button-down shirt and is also looking at the clipboard. The doctor is holding a pen over the clipboard. The entire image has a blue tint.

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 produce no symptoms.

The symptoms can be vague and non-specific (e.g. lethargy) or similar to those of other, more common conditions such as irritable bowel syndrome, Crohn disease, peptic ulcer disease, other gastrointestinal/digestive disorders, asthma and facial flushing associated with menopause.

The majority of doctors are unfamiliar with NETs and therefore less likely to suspect a NET cancer in their initial investigations.

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 metastasise, the most common site for metastatic tumours ('secondaries') is the liver. Other areas of spread can include the bones, the lungs and the lymphatic system.

Many GEP-NETs have an associated syndrome caused when the neuroendocrine cells over-produce hormones. The most common is **carcinoid syndrome**, which can occur in up to 35% of patients and is caused when an excess of hormones such as serotonin, histamine, somatostatin and chromogranin A are produced.

The symptoms of carcinoid syndrome vary and can often be highly individual. 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.
- Faecal Urgency.
- Wheezing: can occur in up to 20% of patients with carcinoid syndrome and may be associated with facial flushing. Unlike asthma, wheezing of carcinoid syndrome may not be triggered by colds/flu, 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: 10–20% of 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 a rash, dark pigmentation on skin, swollen mouth and bright red tongue, vomiting and diarrhoea, headache, fatigue, depression, disorientation or confusion, memory loss.

Not everyone with NETs will have this collection of symptoms, even if their disease has spread.

Carcinoid crisis

Sometimes patients may suffer a particularly bad episode of carcinoid syndrome triggered by stress, general anaesthetic or certain treatments. Symptoms include intense flushing, diarrhoea, abdominal pain, wheezing, palpitations, low or high blood pressure, altered mental state and, in extreme cases, coma.

Without treatment the complications can be life-threatening, but if the patient is having any procedures the NET specialist will ensure that the patient is monitored and may give an infusion of a somatostatin (octreotide) analogue as a preventative measure.

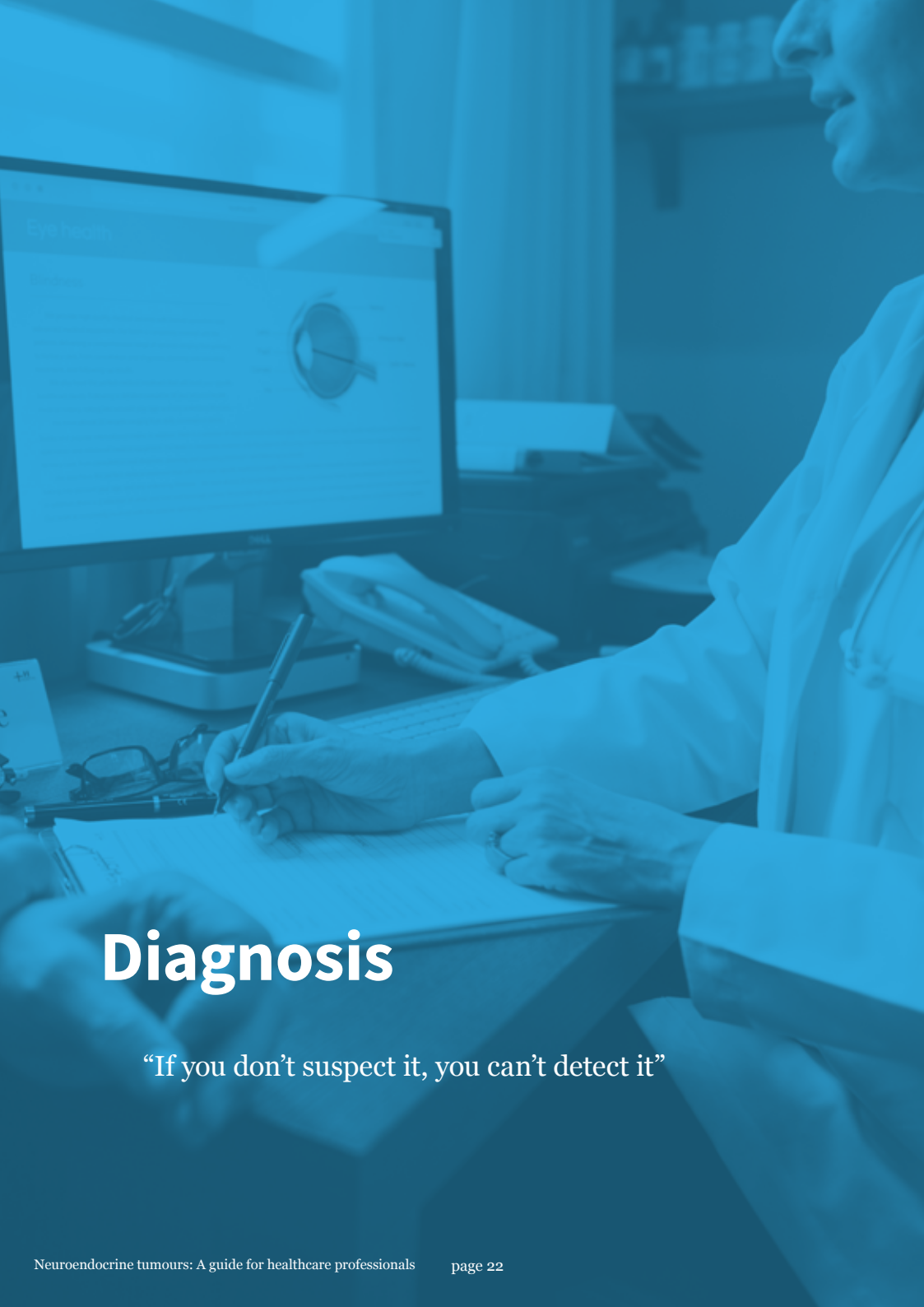
The NET specialist will also liaise with any other team, for example a surgical team, and pass on the guidelines that are available as a preventative measure for patients at risk.

NeuroEndocrine Cancer Australia also provides a wallet card for patients, which gives advice on treatment in the event of Carcinoid Crisis - [download here](#).

Carcinoid heart disease

The hormones released by the NETs into the bloodstream (serotonin) can affect the heart by causing thick 'plaques' within the heart muscle. The heart valves (tricuspid and pulmonary) 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 20% of patients with carcinoid syndrome present with carcinoid heart disease and without treatment can develop right heart failure. With somatostatin analogues, the progression of carcinoid heart disease is significantly slowed and other symptoms of heart failure can be managed with diuretics. Some patients with carcinoid heart disease may be suitable for cardiac surgery to replace the leaking valves.

ECG and chest x-ray may provide clues to the diagnosis of carcinoid heart disease but the most sensitive test is echocardiography of the heart. Echocardiography should be performed regularly to monitor the function of the heart in patients with neuroendocrine tumours.



Diagnosis

“If you don’t suspect it, you can’t detect it”

Neuroendocrine tumours 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 correct 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.

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

Please refer to The Optimal Care Pathway for People with Neuroendocrine Tumours for additional information on incorporating both the technical aspects of care and the delivery of such care.

neuroendocrine-tumours-1st-edition

<https://www.cancer.org.au/assets/pdf/neuroendocrine-tumours-1st-edition>

Specific Investigations for the NET Location

Gastroenteropancreatic NET	Lung NET	Paraganglioma / Pheochromocytoma
Full blood count LFTs Renal function Calcium/vitamin D CRP B12 and serum iron Ultrasound CXR CT Endoscopy/colonoscopy Chromogranin A (optional ascan have fals positives as stated above	Full blood count LFTs Renal function Calcium/vitamin D CRP Ultrasound CXR CT Bronchoscopy Chromogranin A (optional ascan have fals positives as stated above	Full blood count LFTs Renal function Calcium/vitamin D Plasma metanephrine, normetanephrine and 3-methoxytyramine or Urinary metanephrine/ normetanephrines (catecholamines) CT MRI

Tests

Tests include:

- **Biopsy**
- **Blood tests** (NET biomarkers particularly chromogranin A (CgA) and for evidence of a rise in certain peptides and hormones in the blood)
- **Full blood count**
 - 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.
- **Chromogranin A (CgA):** A glycoprotein that is produced and released into the bloodstream by neuroendocrine cells. It is a sensitive and specific marker, with blood levels of chromogranin A more than twice the reference range usually indicating the presence of a NET. Chromogranin A blood levels can correlate with tumour burden and activity and are often used for monitoring the disease or response to treatments. It is important to use the same laboratory so that changes in the levels can be interpreted correctly. Certain conditions can cause a false elevation in the blood chromogranin A levels, especially:
 - antacid medication especially the proton-pump inhibitors (omeprazole, esomeprazole, pantoprazole)
 - kidney and liver diseases
 - prostate cancer
 - atrophic gastritis
- **Plasma Metanephrines**

Testing for plasma metanephrines is to diagnose or rule out a rare adrenal tumour called a pheochromocytoma or a rare similar tumour located elsewhere in the body called a paraganglioma; these tumors produce excess hormones called catecholamines, which are broken down to metanephrines.

[Refer to NeuroEndocrine Cancer Australia Fact Sheet](#) for the procedure for this test. Studies have shown that plasma testing is more sensitive than the more traditional 24-hour urine catecholamines testing. Refer to FACT Sheet on NeCA Website for procedure instructions
- **Urine tests:** for 5-HIAA (5-hydroxyindole-3-acetic acid), which is excreted into the urine. Patients should be advised to avoid foods very high in serotonin/tryptophan (chocolate, olives, bananas, pineapple, all tomato products, plums, eggplant, avocado, kiwi fruit, walnuts, brazil nuts, cashew nuts, tea, coffee and alcohol), and certain cough, cold and flu remedies 3 to 7 days before the test.

- **Endoscopic procedures:**
 - Gastroscopy and colonoscopy
 - Wireless capsule endoscopy
 - Endoscopic ultrasound
 - Bronchoscopy
- **CT:** 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**
- **Ultrasound:** Remember that good ultrasound examinations are dependent on the skill of the sonographer.
- **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 routinely performed during the initial assessment stage of any NET patient, and as a part of the ongoing follow-up and management.
- **PET (Positron Emission Tomography):** Increasingly, PET scans are being combined with CT scans to provide more detailed images.
- **Gallium-68 (Ga68) PET:** This test can help reveal the site of NET tumours. Most NETs have somatostatin receptors on their cell surfaces. Gallium-68 is a radiotracer which, when combined with a peptide (DOTATATE), binds to these somatostatin receptors on NET tumours. This PET scan, when combined with CT—known as Ga68 PET/CT—is highly sensitive (90%) and specific (82%) for determining the location and biological activity of NETs. This test is **essential** in the assessment of any patient with a NET.
- **18F-FDG PET ([18 fluorine] fluoro-D-glucose):** 18F-FDG is a glucose analogue with the attached radiotracer 18fluorine. This compound is taken up by cells that rapidly metabolise glucose, which occurs in many different types of cancer including types of NETs. Patients are required to fast beforehand to minimise the natural blood glucose and insulin levels and after injection of the 18F-FDG they must remain quiet and still so that the tracer is taken up preferentially by the cancer cells rather than normal tissues like muscle. 18F-FDG PET/CT is often combined with the Gallium-68

PET/CT for staging of NET disease.

- **Octreotide scan:** The Octreoscan® uses octreotide combined with radiotracer Indium-111 (Indium111) and then injected via a vein in the arm, it binds to the somatostatin receptors on the tumour surface. The tumours are then detected using a gamma camera, 'lighting up' on the screen as radioactive 'hot spots'. In Australia, the more sensitive Gallium-68 PET/CT scan combined with an 18F-FDG PET/CT is the 'gold standard' for detecting NET primaries or metastases and should replace the octreotide scan.
- **MIBG:** This is another nuclear medical scan in which the radiotracer iodine-123-meta-iodobenzylguanidine (MIBG) is injected into the vein and then the whole body is scanned using a 'gamma camera'. This scan is used to detect pheochromocytoma, neuroblastomas and NETs. It is important for patients to stop taking certain medications a few days before this test, and often iodine tablets are prescribed to help protect the thyroid gland from taking up too much of the radiotracer. This investigation usually involves taking separate scans over 2 consecutive days and most patients are allowed home in between.
- **Bone scan:** A bone scan is an imaging test used to help diagnose problems with bones. It safely uses a very small amount of a radioactive drug called a radiopharmaceutical. Specifically, a bone scan is done to reveal problems with bone metabolism.

Genetic Testing

The majority of neuroendocrine cancers occur sporadically, this means there is no known underlying genetic cause. However, it is important to understand there are some neuroendocrine cancers that occur due to genetic disorders or inherited conditions.

Genetic conditions known to be associated with NETs

- Multiple Endocrine Neoplasia (MEN)
- Familial Pheochromocytoma and Paraganglioma Syndrome
- Von Hippel Lindau Disease (VHL)
- Succinate Dehydrogenase (SDH) Complex
- Neurofibromatosis Type 1
- Tuberous sclerosis

Knowledge that a patient or family member carries a genetic risk of neuroendocrine cancer can empower them to undergo counselling, screening tests and monitoring. This can lead to earlier diagnosis and treatment of neuroendocrine cancer should it occur.

Classification, staging and grades of NETs

The European Neuroendocrine Tumour Society (ENETS) and the World Health Organisation (WHO) divide NETs into four grades: low (G1), intermediate (G2) and high (G3) and Neuroendocrine Carcinoma (NEC). The grade represents the aggressiveness of the tumour.

Well Differentiated Neuroendocrine Neoplasms ¹	Ki67 ²	Mitotic ³	Biologic aggressiveness of the tumor
Low Grade (NET) G1	≤ 2%	< 2	Relatively indolent
Intermediate (NET) G2	3 - 20%	2 - 20	Moderately aggressive; less predictable
High Grade (NET) G3	> 20%	> 20	Extremely aggressive
Poorly Differentiated Neuroendocrine Neoplasms ¹			
Neuroendocrine Carcinomas (NEC) G3 <ul style="list-style-type: none">• Small cell type• large cell type	> 20%	> 20	Extremely aggressive

- 1. ENETs and UICC Differentiation
- 2. Proliferation rate by Ki-67 index (%)
- 3. Proliferation rate by mitotic rate (per 10/HPF)

To determine the grades of the NET cells, an experienced pathologist reviews the slides under a microscope to see how many cells are dividing (mitotic figures) in a number of high power fields (HPF = 2mm²). The tissues are also stained for neuroendocrine markers (e.g. chromogranin, synaptophysin) and particularly the MIB antibody that is used for the Ki-67 index.

A blue-tinted background image showing several hands in a clinical setting. One hand in the foreground is pointing towards the right, while other hands are visible in the background, some with fingers spread. The overall scene suggests a medical consultation or a group discussion.

Clinical Management

Patients should ideally be treated within a specialist multidisciplinary team (MDT).

Each patient will have an individualised treatment plan. There are a number of treatment options available, depending on the type and location of the tumour, and the general wellbeing of the patient

The role of NET multidisciplinary teams (NET MDT)

The care of NETs can be complex, and for the patient the journey can encompass 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 there has to be a collaboration between all key healthcare professional groups involved in recommending treatment for individual patients. This collaboration has been termed a 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 and disciplined MDT is a very important aspect for care when striving to achieve the best quality of life and the best outcome for NET patients. With a 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.

Studies have shown that NET patients who are managed by a NET MDT have better outcomes and quality of life compared to patients who do not have access to such groups.

Members of a NET MDT may include:

- Medical Oncologist
- Radiation Oncologist
- Pain team
- Gastroenterologist
- Respiratory Physician
- Counselling staff
- Surgeon
- General practitioner/Practice nurse
- Clinic staff
- Intervention Radiologist
- Endocrinologist
- Nurse specialist
- Nuclear medicine specialist
- Cardiologist
- Dietitian
- Clinical Trials staff
- Palliative care team
- Pathologist
- Genetic specialist (as needed)

Surgical Management

Patients with NETs often undergo surgical procedures to remove the tumours. The goal of surgery depends on the type of NET cancer, its location and size and whether there is spread distant from the primary site.

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

Most planned surgery for NET cancers should be carried out 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 is potentially curative 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 may be at risk of ‘carcinoid crisis’ in the perioperative period or during surgery. The NET specialist should discuss this with the anaesthetist before surgery.

Medical management

Somatostatin analogues

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

Somatostatin analogues are synthetic 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 now evidence that these injections also slow the rate of growth of tumours. Somatostatin analogues are the mainstay of medical treatment for most NETs.

Short acting Octreotide may be given several times a day to control symptoms for 2 to 3 days until a correct dose of long lasting SSA can be prescribed. Sometimes the short acting SSA may be included to reduce symptoms despite the use of the long acting SSA until a treatment regime can be ordered.

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

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

Chemotherapy

This may be an option, especially for NET patients with pancreatic, bronchial or high-grade (G2/G3) NETs. Not all NETs respond equally to chemotherapy, therefore careful selection of patients is imperative so as to improve the chance of response and avoid unnecessary side effects and toxicity.

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

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

Some of the current chemotherapeutic drugs used in the treatment of NETs include streptozotocin, 5-fluorouracil, etoposide, carboplatin, cisplatin, temozolamide and capecitabine.

Chemotherapy may sometimes be recommended after surgery (adjuvant therapy). Patients may be asked to be involved with current clinical trials looking into the different combinations of chemotherapy agents that are most appropriate 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. Recent trials have proven the efficacy of Everolimus for Lung and GI NETs (Radiant 4). Currently this is not on the Pharmaceutical Benefits Scheme (PBS) for these indications.

Peptide receptor radionuclide therapy (PRRT)

Peptide receptor radionuclide therapy (PRRT) uses radiolabelled somatostatin analogues linked to peptides which target and bind to somatostatin receptors on the tumour cells.

The radionuclides commonly used in PRRT for neuroendocrine tumours are indium -111(111In), lutetium-177 (177Lu) and yttrium-90 (90Y). As the radionuclides 'decay' they emit radiation (high-energy particles) that cause disruption to the DNA of the tumour cells. The damage caused by these radionuclides is targeted to the tumour cells (within millimetres) and spare normal tissues that do not have the somatostatin receptor on their cell surface.

PRRT can be considered in both non-functioning and functioning NETs with positive somatostatin receptor (seen on Gallium-68 PET) status, irrespective of the primary tumour site.

The basis for patient selection for PRRT is the evidence of somatostatin receptors seen with Gallium-68 PET scan.

PRRT is an outpatient therapy. Patients attend the clinic and may be given a course of chemotherapy which prepares or sensitises the tumour cells for the radionuclide. They are also given an infusion of amino acids which help protect the kidney function and antiemetic medication to reduce the risk of nausea and vomiting.

Depending on the treatment regime, PRRT is given as an induction course of four treatments separated by 6 to 8 weeks. Further doses of PRRT may be administered if disease grows again after the induction course, but the NET specialist, and the NET MDT determine this.

The side effects of PRRT are mild and usually limited to nausea, fatigue and minor changes in the production of blood. Occasionally patients can get a flare of symptoms which are associated with Carcinoid Syndrome. The patient should be instructed to contact the treating teams if this does occur.

Liver directed therapies

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

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

For this procedure, an experienced interventional radiologist using local anaesthetic (and sedation) accesses an artery in the groin and then directs 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. 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 is also combined with the injection of chemotherapy or the use of microspheres that contain chemotherapy; in this setting the therapy is called transcatheter arterial chemoembolisation (TACE).

For this procedure, patients are usually admitted to hospital overnight. The side effects 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.

In a process similar to hepatic artery embolisation, the interventional radiologist inserts a catheter into the hepatic artery supplying blood to the NET tumours and tiny beads (SIR-spheres) containing the radioactive substance yttrium- 90 (90Y) are injected. These SIR-spheres emits radiation (high energy particles), interfering with the tumour cell DNA and slowing tumour growth.

Radiofrequency ablation (RFA)

This is a treatment for metastatic or primary NET and is performed by an interventional 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 (Xermelo)

The trials conducted with Telotristat have concluded and results have been published. Effective 2018 Telotristat has been approved by the TGA <https://www.tga.gov.au/bookpage/120-telotristat-ethyl>

Telotristat is not available in Australia on the PBS.

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).

In some circumstances, poor general health or complications secondary to treatments may also make further NET treatment inadvisable.

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. They are heavily regulated to ensure that results are meaningful and reliable. For further information refer to

<https://www.tga.gov.au/community-qa/clinical-trials-information-consumers> or
<https://www.australianclinicaltrials.gov.au/consumers>

www.neuroendocrine.org.au

www.clinicaltrials.gov





The experience of having a NET



The experience of living with an uncommon cancer, such as a neuroendocrine cancer, 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 distinct chapters.

First chapter: Something feels wrong

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

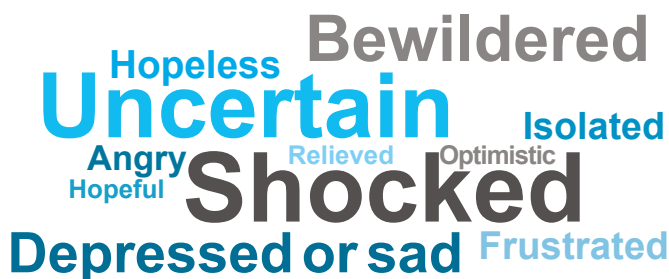
On average, NET patients see four to six different doctors (including specialists) over 4 to 7 years before the correct diagnosis is made.

Because of repeated misdiagnoses, patients may 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'.

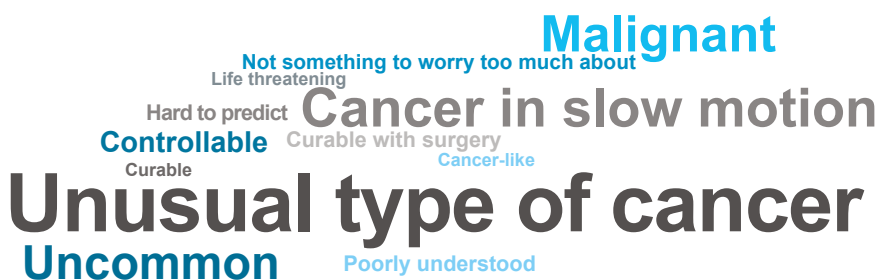
Second chapter: Diagnosis

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
- 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 below) captures many of the ways the medical community currently views NETs.



This period is very difficult for many NET patients. 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 each patient’s NET requires assessment and review of all the patient’s 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 NET multidisciplinary team (NET 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.

Many NET patients feel uncomfortable asking their 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.

To help Australian patients find a NET Specialist, NeuroEndocrine Cancer Australia has developed a register of NET specialists and NET MDTs to which patients can be referred - www.neuroendocrine.org.au

Third chapter: Transition

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

This can be an extremely difficult and stressful period of adjustment. They may face untold emotional and physical challenges in ‘coming to grips’ with their 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.

They can get support and comfort during this time from **NeuroEndocrine Cancer Australia** whose services includes NET nurse support, telephone support service and a private Facebook community where many patients converse in a safe, supportive and non-threatening forum. Other services, such as the **Cancer Council 13 11 20 Service**, can give general advice and support which includes legal and financial assistance.

Fourth chapter: Living with a NET

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

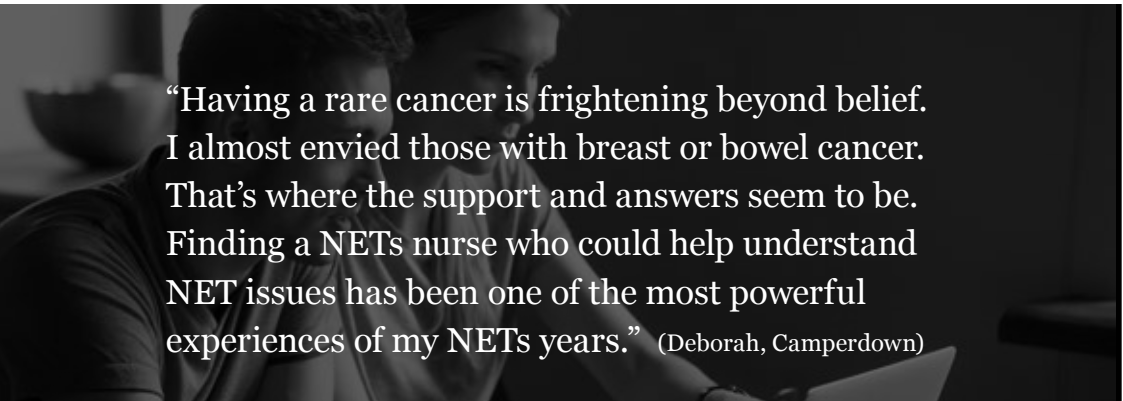
Living with a NET is challenging and can have a significant impact on activities of daily life, and many NET patients need to make significant adjustments. There are so many things to think about that it can be overwhelming. Even though the NET specialist and team will be focused on managing the disease and patient physical wellbeing, it is important to recognise and manage the patient's emotional and social wellbeing.

Unlike the more common cancers, such as breast, bowel, prostate, skin and lung cancer, the journey is less well defined for NETs. 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 to look well, they are struggling with many of these symptoms and need to be supported during such times.

It is important for patients to develop a 'working' relationship with their NET specialist, allowing them to guide their 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 their NET Specialist and allow them to share this burden, which will free up time for the patient to pursue things in life that empower and give joy, such as family, hobbies and holidays.



“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 NETs nurse who could help understand NET issues has been one of the most powerful experiences of my NETs years.” (Deborah, Camperdown)

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.

For patients to get the most out of their time with their doctor, the following tips may be helpful:

- 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. [The NeuroEndocrine Cancer Australia website has a Treatment and Wellness Plan which can be downloaded to assist in keeping a comprehensive record of the type of NET, tests, treatments, management and care.](#)
- 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 guest 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 (or as little) 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

Encourage patients to ask questions of their healthcare professionals, such as the following

General Neuroendocrine Cancer questions

- What type of NET do I have?
- Where in the body is the NET located? Has it spread to other parts of the body? If it has spread, where has it spread to?
- What are the risk factors for NETs?
- Are you a NET Specialist? How many NET patients do you treat a year?
- Are you able to discuss my case with or refer me to a NET Specialist?
- Are you involved with or have access to a NET Multidisciplinary team?

Diagnosis, tests, and investigations

- What can the biopsy/surgery histopathology report
- (the description of neuroendocrine cancer as it looks under a microscope) tell us?
- Did an experienced pathologist who understands NETs review the tumour?
- What tests do I need to have? Refer to the optimal care pathway for people with NETs for specific investigations related to the NET location.

<https://www.cancer.org.au/assets/pdf/neuroendocrine-tumours-1st-edition>

Grading and staging

- What is the grade of my NET (the description of the NET when looked at under a microscope)? What does this mean?
- What is the stage of my NET? What does this mean?
- Based on my grade and stage, what is my likely prognosis?
- What is Ki 67 % and what does it mean?

Treatment and management of NETs

- What are my treatment options?
- What is the treatment called and how does it work?
- Why is this treatment recommended?
- What is the goal of treatment? Is it to remove the cancer completely, to control the cancer, to manage the cancer symptoms?
- How soon do I need to commence treatment; urgently, semi urgently, non-urgent?

- How often do I need this treatment? (Treatment schedule)
- Will the treatment reduce my NET symptoms?
- Can I have written information about my treatment?
- Is there a home support program for this treatment, so I can have this at (or closer to) home?
- Where will I have my treatment? How long will it take (short appointment, day stay, overnight)?
- 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?
- Can I have a holiday while on treatment? Can I travel internationally while on treatment?

Patient support

NeuroEndocrine Cancer Australia operates face-to-face NET support group meetings in most Australian capital cities six times per year. Online support groups are also held monthly to ensure we reach everyone right across Australia and carers support group which is held quarterly. NET patients and carers can also access a 'closed' forum on Facebook as well as obtain information and support with our specialist NET nurse on **1300 287 363** or **netnurse@neuroendocrine.org.au**

NeuroEndocrine Cancer Australia also provides appointments with our Counsellor and NET Dietitian – appointments can be made with our NET Nurses.

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

“I have used the service that 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”

(Dorothy, Sydney)

Clinical trials

You can find out more about current NET trials at:

- Australian and New Zealand Clinical Trials Registry - www.anzctr.org.au
- Cancer Australia - 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
- Current Australian NET Clinical Trials - www.neuroendocrine.org.au

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 or tests?

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 that patients tell their NET specialist and pharmacist about any 'natural' medicines or complementary therapies as they can potentially have a negative impact on the disease or interact with other NET treatments.

Resources

Websites

www.netpatientfoundation.org.au

www.incalliance.org

www.cancer.org.au

www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs

<https://www.cancer.org.au/assets/pdf/neuroendocrine-tumours-1st-edition>

www.neuroendocrine.org.au

www.prostate.org.au

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- Medicare Local Foundation Ranges and North Western Melbourne
- NeuroEndocrine Cancer Australia Consumer Advisory Group Members

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Management of Neuroendocrine Tumors: Current and Future Therapies

Kjell E Öberg

Expert Rev Endocrinol Metab. 2011;6(1):49-62

Notes

Dotted lines for note-taking.

Notes

Handwriting practice area with 20 horizontal dotted lines.

About Neuroendocrine Cancer Australia

NeuroEndocrine Cancer Australia was formed in 2009 by Dr John Leyden and Simone Leyden 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 NeuroEndocrine Cancer Australia 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 NeuroEndocrine Cancer Australia or get involved please visit our website www.neuroendocrine.org.au or email info@neuroendocrine.org.au. All donations are most welcomed as we continue our work to improve the outcomes of NET patients.



NeuroEndocrine
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