Neuroendocrine Cancer UK

Incorporating The Ann Edgar Trust

NEUROENDOCRINE CANCER GUIDE

# SYNDROMES

2023

www.neuroendocrinecancer.org.uk

Neuroendocrine Cancer-related Syndromes occur due when Neuroendocrine Cancer causes changes to the cell resulting in the abnormal production and excess release of specific peptides and / or hormones by

Neuroendocrine Cancer cells.
These syndromes occur in approximately 40% of all Neuroendocrine Tumours, rarely occurring in Neuroendocrine Carcinomas.

In this guide we look at the following Neuroendocrine Cancer-related syndromes:

- Carcinoid Syndrome (Serotonin, Histamine & Kinins)
- Pheochromocytoma and Paraganglioma
- Zollinger-Ellison Syndrome
- Clinical Hypoglycaemia
- Werner-Morrison Syndrome
- Glucagonoma Syndrome.

Other syndromes include:

- GHoma
- PTHrPoma
- ACTHoma
- Calcitoninoma
- Neurotensinoma
- PPoma
- Somatostatinoma.

## Carcinoid Syndrome

Carcinoid Syndrome is primarily associated with Neuroendocrine Tumours (NETs) that form in the Small Bowel, but may also occur in about 10% of primary Lung or Gynaecological (uterus, cervix, ovary and vagina) NETs. It may not present in the early stages of disease, being a more common occurrence once a Neuroendocrine Tumour has spread to the liver (metastasised). This may be because of the way blood circulates around the body and the role the liver plays in normalising hormone balance.


*Click on the image above to order our free of charge, Carcinoid Crisis cards.*

## Carcinoid Syndrome

The blood flow to and through the mid or lower part of the body, flows through the liver on its way back to the heart and lungs. If a primary tumour occurs in this part of the body and is producing too much peptide or hormone, the levels within the circulating blood carry this excess to the liver. An important role of the liver is to keep healthy balance by regulating circulating amounts of peptide or hormone. As the blood flows through the liver, it is filtered to remove any excesses or abnormalities – reducing the potential for symptoms and / or harmful effects.
However, if the primary has spread to the liver and is producing too much peptide or hormone there, it may bypass the liver's ability to filter and remove it – making Carcinoid Syndrome more likely to be experienced.

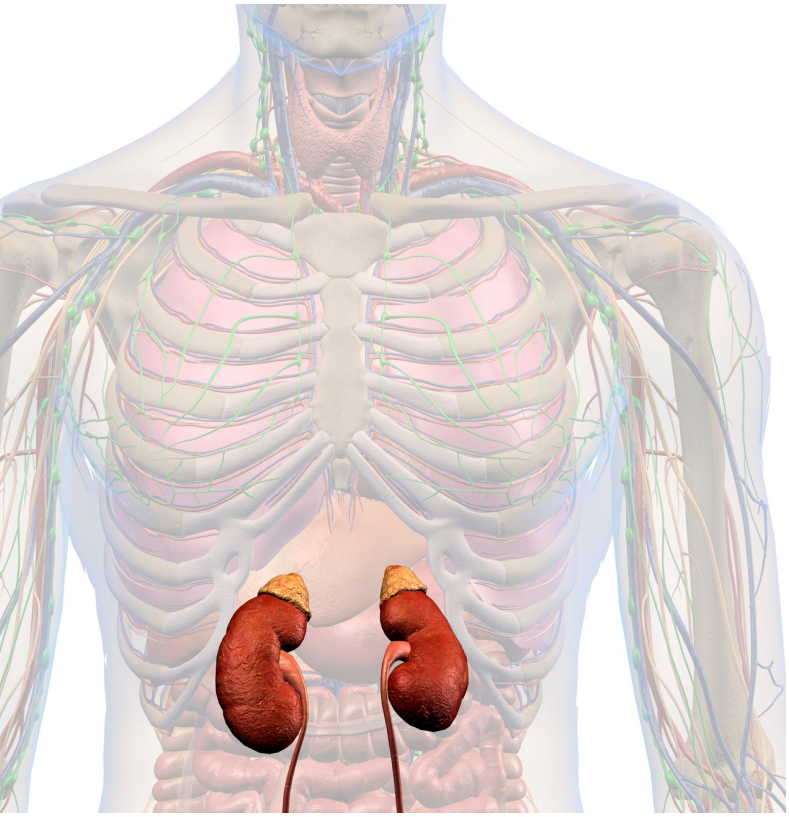
One exception is the lung, if a primary there is producing too much peptide or hormone, not all of the blood is filtered by the liver and therefore there is a higher potential for developing Carcinoid Syndrome before spread of disease occurs.

The hormones and peptides most commonly associated with Carcinoid Syndrome include Serotonin, Histamine and Kinnins. These help in several important ways such as keeping the bowel working properly, the immune response – and, by acting as messengers, they can carry signals around the body to maintain normal body functions – such as heart rate, blood pressure and breathing. Abnormal levels can result in diarrhoea, abdominal (tummy) cramping, flushing, palpitations and / or wheezing. A combination of 2 or more of these symptoms, due to too much serotonin, histamine and / or kinins, is called Carcinoid Syndrome. Approximately 40% of those with Carcinoid Syndrome may also be at risk of complications such as Carcinoid Heart Disease.

For those with diarrhoea:
Neuroendocrine Cancer UK supply wallet alert cards for those who may require quick access to toilet facilities. Toilet finder apps are available for both Apple and Android devices from the App Store or Google Play.

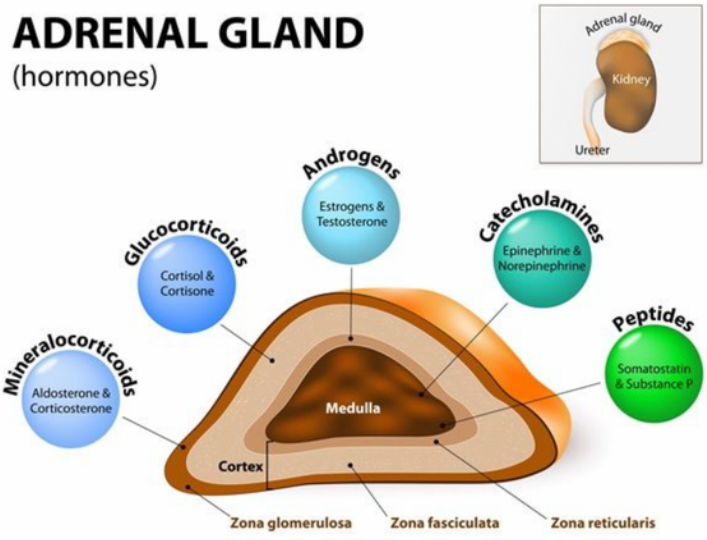
Radar Key: The National Key Scheme (NKS) offers independent access to locked public toilets around the country. Toilets fitted with National Key Scheme (NKS) locks can now be found in shopping centres, pubs, cafés, department stores, bus and train stations and many other locations in most parts of the country.


*Click on the image above to order our free of charge, Urgent Toilet cards.*



## Pheochromocytoma and Paraganglioma (PPGL).

Pheochromocytoma and Paraganglioma (PPGL) is associated with Neuroendocrine Tumours of the adrenal glands (Pheochromocytoma) and / or paraganglia (Paraganglioma).




The central part of an adrenal gland, the medulla, is responsible for producing catecholamines - which are hormones that include epinephrine and norepinephrine (adrenaline and noradrenaline) – our fight or flight hormones.

Paraganglia are cells or nerve-like structures that form part of the Neuroendocrine System, found close to blood vessels and nerves. Paraganglia sense certain balances in the body including carbon dioxide and oxygen concentrations in the blood and play a role in maintaining normal breathing and heart functions.

Pheochromocytoma and Paragangliomas can produce excess amounts of catecholamines, which in normal health are released when we are under physical or emotional stress. When catecholamine levels are too high this can result headaches, dizziness, facial paleness (pallor), excessive sweating, racing heart rate (palpitations), panic attacks/ sense of doom, anxiety, weight loss, heat intolerance, high (and rarely low) blood pressure (sustained or episodic), nausea (with or without vomiting), breathlessness, depression and / or lethargy.

In rare circumstances PPGL may have a familial link.

## Zollinger-Ellison Syndrome

is associated with Neuroendocrine Tumours (NETs) that form in your pancreas or the upper part of your small intestine (duodenum). These tumours, called Gastrinomas, secrete large amounts of the hormone gastrin, which causes your stomach to produce too much acid. The excess acid then leads to peptic ulcers, as well as to diarrhoea and other symptoms, including acid reflux, heartburn, stomach/chest pain, diarrhoea and low haemoglobin (anaemia) causing tiredness.

## Clinical Hypoglycaemia

is associated with Neuroendocrine Tumours (NETs) that form in your pancreas or the upper part of your small intestine (duodenum). These tumours, called Insulinomas, secrete large amounts of the hormone insulin, which causes your blood sugar levels to drop - sometimes quite severely. We need a certain blood sugar level to ensure our body (and all of it cells) has enough energy to function normally. When blood sugar levels drop too low, or too severely, this can lead to symptoms that may include dizziness, light-headedness, sweating, hunger, confusion & irritability. If the level drops too low or too severely this can even lead to coma / loss of consciousness. Symptoms often get better, are alleviated, by eating – so weight gain - sometimes to obese levels, rather than weight loss, can occur.

Clinical hypoglycaemia is proven through fasting blood tests, that are carried out in hospital, in order to be completed safely.

## Werner-Morrison Syndrome

is associated with Neuroendocrine Tumours (NETs) that form in your pancreas. These tumours, called VIPomas, secrete large amounts of Vasoactive Intestinal Peptide (VIP). This peptide helps regulate gastrin, it works to neutralise stomach acid when food leaves the stomach and enters the small bowel - which helps with nutrient uptake and promotes the secretion of water and electrolytes by the small and large intestines. It also works to ensure that food passes through the small and large intestines slowly enough for nutrients from food to be absorbed properly (a process known as transit time).

Too much VIP can result in reduced levels of acid in the stomach, very watery, frequent and high-volume diarrhoea (up to or in excess of 3 litres a day), and severe changes in potassium levels in the blood (low potassium) - that may affect heart rate. Hospital admission may be needed to deal with these symptoms - as severe symptoms can be life-threatening.

## Glucagonoma Syndrome

is associated with Neuroendocrine Tumours (NETs) that form in your pancreas or the upper part of your small intestine (duodenum). These tumours, called Glucagonomas, secrete large amounts of the hormone glucagon, which can cause your blood sugar levels to rise above normal.

Glucagon works along with the hormone insulin to control blood sugar levels and keep them within set levels. When glucagon levels rise too high, this can lead to Necrotising Migratory Erythema (NME) – a skin rash that can spread across the body that may look like eczema. Glucagonomas may also cause symptoms of diabetes, (like feeling tired, going pee a lot, dry mouth), nausea, weight loss and a low haemoglobin (anaemia). Diarrhoea, blood clots and other changes to skin, nails and hair may also occur.

Other syndromes may include:

- GHoma
  - Growth Hormone is usually produced and released from the pituitary gland and helps to regulate all cell growth. When growth hormone is over-produced, from any source, it can cause a condition called Acromegaly. Acromegaly usually affects middle-aged adults, though it can develop at any age. In children who are still growing, too much growth hormone can cause a condition called gigantism. Bones increase in size, including those of the hands, feet and face.

- PTHrPoma
  - ParaThyroid Hormone related Peptide - is usually associated with the parathyroid glands. Four small glands that sit close to the thyroid gland in the neck. They help to regulate normal calcium levels within the blood. Abnormal levels can cause symptoms of hyperparathyroidism - which can be mild, vague or severe - and include hypercalcaemia (high calcium levels), nausea, vomiting or loss of appetite, depression, confusion, agitation or forgetfulness, excessive urination, palpitations, abdominal pain, tiring easily or weakness and / or bone and joint pain.

- ACTHoma
  - AdrenoCorticoTropic Hormone plays a part in how the body responds to stress. ACTH is produced in the pituitary gland and stimulates the production and release of cortisol from the adrenal gland. In health, cortisol helps the body respond to stress by maintaining blood pressure and heart function, keeping the immune system in check and by converting fat, carbohydrates, and proteins into energy. Too much cortisol can lead a condition called Cushing's Syndrome - symptoms include muscle weakness, weight loss, hypertension (high blood pressure), excessive hair growth, and osteoporosis, hypokalaemia (low potassium levels) and hyperglycaemia (raised blood sugars).

- Calcitoninoma
  - Calcitonin is produced in the thyroid gland and is involved in helping to regulate levels of calcium and phosphate in the blood, balancing out the effects of parathyroid hormone.
  - Too much calcitonin can lead to watery diarrhoea and facial flushing, may also lead to Hypercalcaemia (raised calcium). nausea, vomiting or loss of appetite, depression, confusion, agitation or forgetfulness, excessive urination, palpitations, abdominal pain, tiring easily or weakness and / or bone and joint pain.

Other syndromes may include:

- Neurotensinoma
  - Neurotensin is produced in the lower end of the small bowel and helps to regulate how the small bowel works. It also plays a role in gastric acid production. There is no syndrome associated with neurotensin alone, but symptoms may occur if it is secreted alongside VIP and / or Gastrin - and may lead to symptoms that include low blood pressure /hypotension, flushing, diarrhoea, unintended weight loss, and diabetes.

- PPoma
  - Pancreatic Polypeptide - rarely produces syndrome. But may be secreted alongside VIP and / or Gastrin. It may play a role in smooth muscle contraction and is thought to be what causes the gallbladder to squeeze and release bile into the digestive system when we eat.

- Somatostatinomas
  - Somatostatin is a hormone that is produced in several parts of the body including the pancreas and gut (digestive system) - it helps to regulate the production and release of several other hormones. Given its effect on the digestive system and in particular gut hormones and peptides, too much can result in symptoms that may include diabetes mellitus, formation of gallstones, intolerance to fat in the diet and diarrhoea.
  - Note: Chemically similar equivalents of somatostatin (somatostatin analogues) are often used as a medical therapy to control excess hormone secretion in patients with Neuroendocrine Cancer-related Syndromes.

For information on Tests that help diagnose and monitor Neuroendocrine Cancer-related Syndromes click here – for information on Treatments click here.