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What is Neuroendocrine Cancer of the Pancreas?

(also known as a pNET or pNEC)

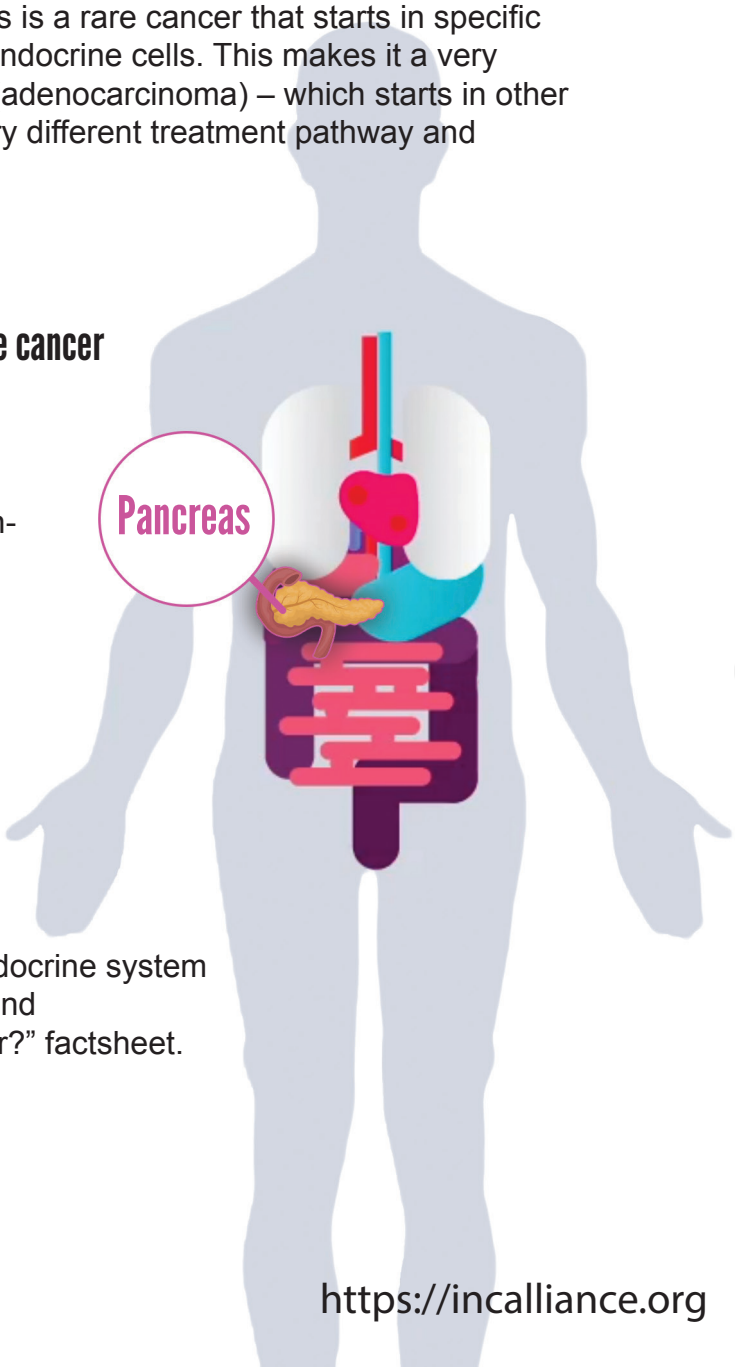
The pancreas is a large gland that is located behind the stomach and joins the digestive tract via the main pancreatic duct. It has a number of different types of cells that are responsible for producing substances (enzymes, peptides hormones) that play an essential role in converting the food we eat into fuel for the body's cells – as well as regulating our blood sugars.

Neuroendocrine cancer of the pancreas is a rare cancer that starts in specific cells within the pancreas called neuroendocrine cells. This makes it a very different disease to pancreatic cancer (adenocarcinoma) – which starts in other cells within the pancreas and has a very different treatment pathway and outcome.

There are two key types of neuroendocrine cancer that may be found in the pancreas:

1. NET (neuroendocrine tumor) is cancer starting within neuroendocrine cells that have abnormal changes that are called 'well-differentiated': pNET

2. NEC (neuroendocrine carcinoma) - these changes are called 'poorly differentiated': pNEC



Further information about the neuroendocrine system and neuroendocrine cancer can be found in our "What is Neuroendocrine Cancer?" factsheet.

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Symptoms and syndromes

A syndrome is where 2 or more symptoms occur together – often suggesting a particular illness or disease. In pancreatic neuroendocrine cancer – you may hear the terms “functioning” (meaning “with hormone related symptoms”) or “non-functioning” (meaning “without hormone related symptoms”).

Nb functioning or non-functioning may also be terms used to describe whether these cancers show up on nuclear medicine imaging* (see diagnostic tests).

The majority of neuroendocrine cancers of the pancreas are non-functioning, meaning that they do not over produce hormones. Symptoms, if/when they occur, tend to be related to the size and/or position of the cancer and can include back pain, jaundice, stomach pain and/or weight loss.

Functioning pancreatic neuroendocrine cancers produce syndromes – due to producing too much of specific pancreatic hormone. These include:

- **Insulinoma syndrome (insulin):** dizziness, light-headedness, sweating, hunger, confusion & irritability. Symptoms may get better by eating – so weight gain, rather than weight loss, may also be seen.
- **Gastrinoma (gastrin):** Zollinger-Ellison syndrome - acid reflux, heartburn, stomach/chest pain, diarrhoea, low haemoglobin causing tiredness.
- **VIPoma (vasoactive intestinal polypeptide):** Werner-Morrison syndrome – very watery, frequent and high-volume diarrhoea, with changes in potassium levels in the blood (low potassium) and low levels of acid in the stomach.
- **Glucagonoma (glucagon):** NMES – necrotising migratory erythema syndrome – a skin rash that can spread across the body: It may look like eczema. It may also cause symptoms of diabetes, like feeling tired, frequent urination, dry mouth, nausea, weight loss and a low haemoglobin. Diarrhoea, blood clots and changes to skin, nails and hair may also be seen.
- **Somatostatinoma (somatostatin):** can cause symptoms of diabetes - like feeling tired, frequent urination, dry mouth, nausea, weight loss. It may also cause anaemia (a low haemoglobin), diarrhoea and /or steatorrhea (fatty, pale, loose faeces that may be difficult to flush away).
- **PPoma (pancreatic polypeptide):** rarely produces a syndrome.

Others (rare and associated with 'ectopic' hormone excess – hormones not usually produced in the pancreas) may include

- Cushing's syndrome (ACTHoma),
- Hyperparathyroidism (PTHrPoma),
- Calcitoninoma (watery diarrhoea and facial flushing),
- Neurotensinomas (low blood pressure /hypotension, flushing, diarrhoea, unintended weight loss, and diabetes)
- and GRFoma (associated with acromegaly)

Causes and/or risk factors for pancreatic neuroendocrine cancer

There is no known causal factor – however it is important to follow advice in leading a healthy lifestyle: eat healthily, exercise and avoid smoking and too much alcohol.

Most occur without there being a family history of neuroendocrine and/or pancreatic cancer.

However, up to 30% occur on the background of a specific genetic syndrome / inherited condition. These include MEN1 (multiple endocrine neoplasia 1 – also known as Wermer's syndrome), VHL (Von-Hippel Landau), NF1 (neurofibromatosis 1) and tuberous sclerosis.

It is therefore vitally important that you are aware of and can tell your specialist team about not only your medical history, but also any family medical illnesses or conditions.

Further information on the genetic/inherited conditions mentioned here can be found in the multiple endocrine neoplasia factsheet.

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Common test that may or may not be used to help diagnosis

Blood/Urine Tests

NB screening for potential genetic conditions is advisable where it is suspected and/or family history unclear or not available.

Full blood count
(B12 + serum iron)
Liver and kidney function
Chromogranin A +/- B
Gut hormones (as baseline): e.g. insulin, glucagon, VIP, somatostatin, etc
Urinary 5-HIAA
Calcium, calcitonin

Endoscopy

Endoscopic ultrasound (EUS)

Scans

Contrast CT/MRI
PET-based somatostatin receptor imaging
(SPECT-based somatostatin receptor imaging if DOTA-octreotide PET n/a)
If available a FDG-PET – may be of benefit if high-grade / rapidly progressing disease
(if available a GLP-1 scan may be of benefit for insulinoma)

Pathology

Differentiation and cellular morphology
Synaptophysin
Chromogranin
Ki67
+/- gut hormone

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Treatment

The key aim of treatment, should be to help you have the best possible quality of life - by ensuring access to appropriate treatment, management of symptoms and addressing what's most important to you.

There is global consensus agreement that all neuroendocrine cancer patients should be reviewed by a specialist neuroendocrine cancer MDT to ensure best care.

Treatment options will depend on the type (grading, functionality, etc), position and size of your pancreatic neuroendocrine cancer – and whether (and to where) it has spread. It will also depend on whether you have any other health concerns and/or illnesses and your general health and fitness.

One or more of the approaches below may be suggested:

- Monitoring or surveillance
- Removal of all or part of your NET/ NEC
- Control of your disease, by slowing or stopping the growth of your NET/ NEC
- Palliation, or easing of, your symptoms

A big part of meeting with your doctors or specialist nurse/team, is to make sure you get the information you need to understand what's being discussed, so that you can make an informed choice about your care.

There may be variations in access to the treatments available depending on the country.

One or more of the approaches below may be suggested:

- Surveillance – can be used to assess how well treatment is working or in periods between treatments (which may be months/years)– Not everyone will need to be on treatment – surveillance can be used to check your cancer and general health for any signs of change that may mean that a treatment might need to be considered. All treatments have possible side effects, therefore, it is important to know when treatment may be helpful for you or not.
- Surgery to remove or partially remove or bypass the primary pancreatic neuroendocrine cancer and/or secondary sites of disease (metastases).

- Somatostatin analogues (SSAs) and/or other drugs can be used to help regulate the secretion of gut hormones if too much is being produced (e.g. high dose proton pump inhibitors to reduce too much acid – gastrinoma). SSAs may also be used to further slow down growth rate in low to moderate grade pancreatic neuroendocrine cancer (pNET) – whether they are 'functioning' or not.

- Chemotherapy can be given orally (in tablets) or IV (through a vein) to slow tumor growth or try to reduce tumor size – this may be the first line therapy in high-grade disease - particularly pNEC. Chemotherapy may also be used to increase tumor cell sensitivity to radiation therapies.

- Targeted molecular therapies – can be given orally (in tablets) or IV (through a vein) to slow tumor growth or try to reduce tumor size.

- Peptide Receptor Radionuclide Therapy (PRRT) may also be called radioligand therapy – uses targeted radiation to treat neuroendocrine cancer cells. This treatment can be used in some patients who have had a 'positive' somatostatin receptor-based scan.

- Interventional radiology –through techniques such as embolisation or ablation – to treat pNET that has spread to the liver.

- Irreversible electroporation (IRE also known as nanoknife) is a relatively novel therapy that uses a strong electric current to kill cancer cells. It may be particularly useful in treating primary or secondary disease when surgery, or other ablation techniques, are risky because tumors are located too close to structures such as major blood vessels.

- Clinical trial – clinical research and safe new treatment development is essential to provide best care for those with neuroendocrine cancer – we need to know that treatments not only work, but work safely. There are several phases of trial therapy – further information can be found in our "Clinical Trials" factsheet. Participation in a trial is voluntary.

NB: external beam radiotherapy to deliver radiation precisely to a tumor is rarely used except in specific circumstances.

Follow up – there are expert agreed guidelines regarding how and when follow up should occur, however, in practice this varies and often with good reason – follow up should be expert informed & evidence /research based, but also tailored to you and what is appropriate for your best care.

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Resources

- **Association for Multiple Endocrine Neoplasia Disorders**
  www.amend.org.uk
- **International Neuroendocrine Cancer Alliance (INCA)**
  www.incalliance.org
- **The Carcinoid Cancer Foundation**
  www.carcinoid.org
- **Neuroendocrine Tumor Research Foundation**
  www.netrf.org
- **NeuroEndocrine Cancer Australia**
  www.neuroendocrine.org.au
- **Neuroendocrine Cancer UK**
  www.neuroendocrinecancer.org.uk
- **Canadian Neuroendocrine Tumour Society (CNETS)**
  www.cnets.ca/

For the full list of INCA members: **https://incalliance.org/full-members/**

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