**The Pancreas**

The pancreas is 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. Exocrine function – enzyme production, released into ducts within the pancreas which then flow into the duodenum via the main pancreatic duct. Endocrine function – hormone production, such as insulin and glucagon, released directly into the bloodstream.

Most pNENs occur incidentally, that is without a family history, but up to 30% may occur on the background of a genetic syndrome/inherited condition e.g. MEN1, VHL, NF1 and Tuberous Sclerosis.

Signs and symptoms of functioning pNENs may be related to tumour position / size (1) and / or excess hormone production (2):

(1) Pain, nausea/vomiting +/- jaundice (yellowing of the skin and whites of the eyes).

(2) Insulinoma: dizziness, light-headedness, sweating, hunger, pallor, confusion & irritability. Symptoms may be alleviated by eating – weight gain may also be seen.

Gastrinoma: acid reflux, heartburn, stomach/chest pain, diarrhoea, anaemia

VIPoma: Werner-Morrison syndrome – very watery, frequent and high-volume diarrhea, with associated electrolyte disturbances (low potassium) and low levels of hydrochloric acid in the stomach.

Glucagonoma: NME – Necrotising Migratory Erythema – a skin rash that can spread across the body. It may mimic eczema.

Diabetic symptoms, diarrhoea, blood clots and changes to skin, nails and hair may be seen.
## Diagnosis for Pancreas - Functioning

### Blood / Urine Tests
- Full blood count
- (B12 + serum Iron)
- Liver and kidney function
- Biochemical:
  - Chromogranin A (and B)
  - Gut hormone profile incl gastrin, insulin, somatostatin, pancreatic polypeptide, VIP, GRH, ACTH, PTHRP
- Urinary 5-HIAA
- Calcium, Calcitonin, Prolactin
- Gastrinoma* suspected/known: Fasting gastrin, Gastric pH, +/- secretin test
- Evaluate other potential causes of raised gastrin: PPIs, H Pylori/infection, atrophic gastritis and pernicious anaemia
- Follow recommendations for PPIs - do not stop suddenly, especially if symptomatic +/- evidence of peptic ulceration
- Insulinoma* suspected/known: 48-72hr fast, C-peptide, Pro-Insulin and β-hydroxybutyrate
- Stimulation / secretion tests may also be undertaken

*If inherited disorder present/suspected: screen as per disorder e.g. MEN1, VHL, TS, NF1.

### Endoscopy
- Endoscopic Ultrasound (EUS).

### Scans
- Contrast CT / MRI
- *Gallium-Dotatate PET/CT (SRS SPECT/CT if Dotatate PET n/a)
- FDG-PET – if High Grade / rapidly progressing disease. nb if available GLP-1 scan may be of more benefit in Insulinoma.

### Pathology
- Differentiation and cellular morphology
- Synaptophysin
- Chromogranin
- Ki67
- Gut hormone
- p53, SSR and lymphovascular markers (optional).
For all patients, there are many things to consider in planning treatments. Your treatment will be personalised to you and the type of NEN you have.

Even if you have a diagnosis that sounds the same as another patient, your treatment and follow up plan may be different.

Your care team will discuss your treatment options with you - giving you both written and verbal information - to help you make an informed choice. Together you can agree on the most appropriate treatment for you.

Information about the treatments that are used in NET and NEC can be found in the NPF Handbook - Your Guide to Living with Neuroendocrine Cancer - www.netpatientfoundation.org

There is consensus agreement that all Neuroendocrine Cancer patients should be reviewed by a Specialist Neuroendocrine Cancer MDT.

Follow-up for Pancreas - Functioning

As per national and international guidelines nb local policy may differ

G1/G2: 3 - 9monthly intervals in first 2 years - then at intervals dependent on presence / absence of disease / functionality (see below) - min annual CT + bloods
- (EUS/functional 3 yearly unless recurrence suspected)

G3: 2-4monthly on treatment / potential for treatment

By type:
- Gastrinoma: Routine + B12, ionised calcium, PTH, Gastrin - with annual assessment for Cushing syndrome
- Insulinoma: Routine + Fasting glucose, Insulin, C-Peptide, Pro-Insulin, β-hydroxybutyrate
- Others e.g. VIPoma, PTHRPoma, etc.

If no metastatic disease: 3-6monthly then annual follow up with specific biomarkers, CT/MRI.
- (EUS/functional 3 yearly unless recurrence suspected).

If metastatic disease present: 3-6monthly on treatment/ potential for treatment : with specific biomarkers, CT/MRI.
- (EUS +/- re-biopsy and / or functional imaging in progressive disease)

If inherited disorder present/suspected: follow up as per disorder e.g. MEN1, VHL, TS, NF1.
Advanced disease: follow up as per guidelines – nb should be guided by prognosis, expected treatment efficacy and treatment related toxicity (performance status and clinical indication for active intervention).
A big part of meeting with your doctors, or specialist nurse, is to make sure you get the information you need to understand what’s happening, so that you can make an informed choice about your care. Asking questions can be difficult, especially if you’re feeling nervous, confused, frightened or struggling to understand what you are being told. You might want to know as much as possible straight away or prefer to take things in small amounts at your own pace.

**Suggestions that may help:**
- Prepare a list of questions that are important to you
- Ask for simple explanations - do not be worried about asking your nurse or doctor to repeat what they have said
- Take someone with you or ask if you can record the conversation. Many mobile phones have a record function or an app you can download
- Ask for a copy of any letters sent to your GP and/or other care team(s)
- If you have a nurse specialist - keep in touch. They can be a great source of information and support for you.

**Example questions:**
- Who can I call if I have any questions? Who is my main point of contact?
- Who will be involved in my care?
- What are the treatment options for me? How might they affect me?
- How often will I need to have scans and tests?
- Are there any flags or warning signs I need to look out for?

Further information about making the most of your consultations can be found in our handbook: www.netpatientfoundation.org

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**REFERENCES**

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