Pancreatic & Duodenal NENs

Nikie Jervis
Director of Support Services & Policy (RN, PGDip)
Neuroendocrine Cancer UK

www.neuroendocrinecancer.org.uk

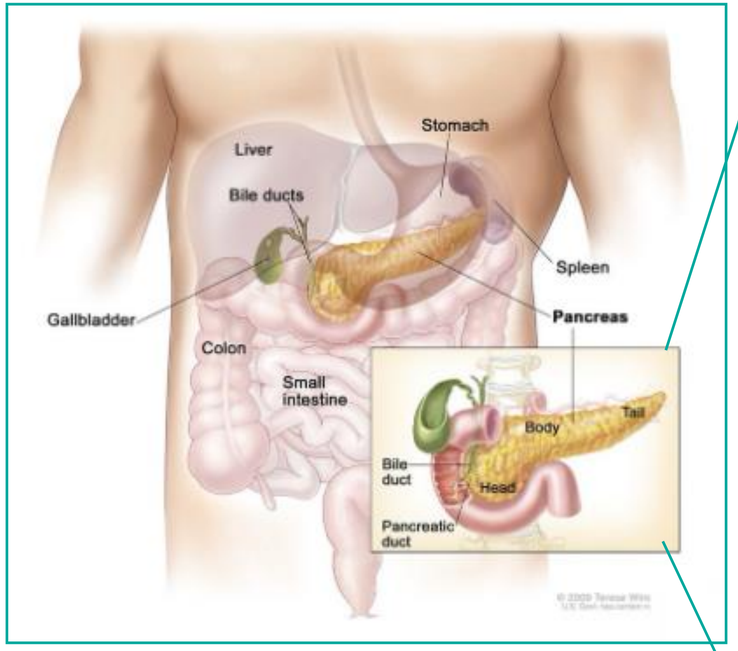
Pancreatic & Duodenal NENs

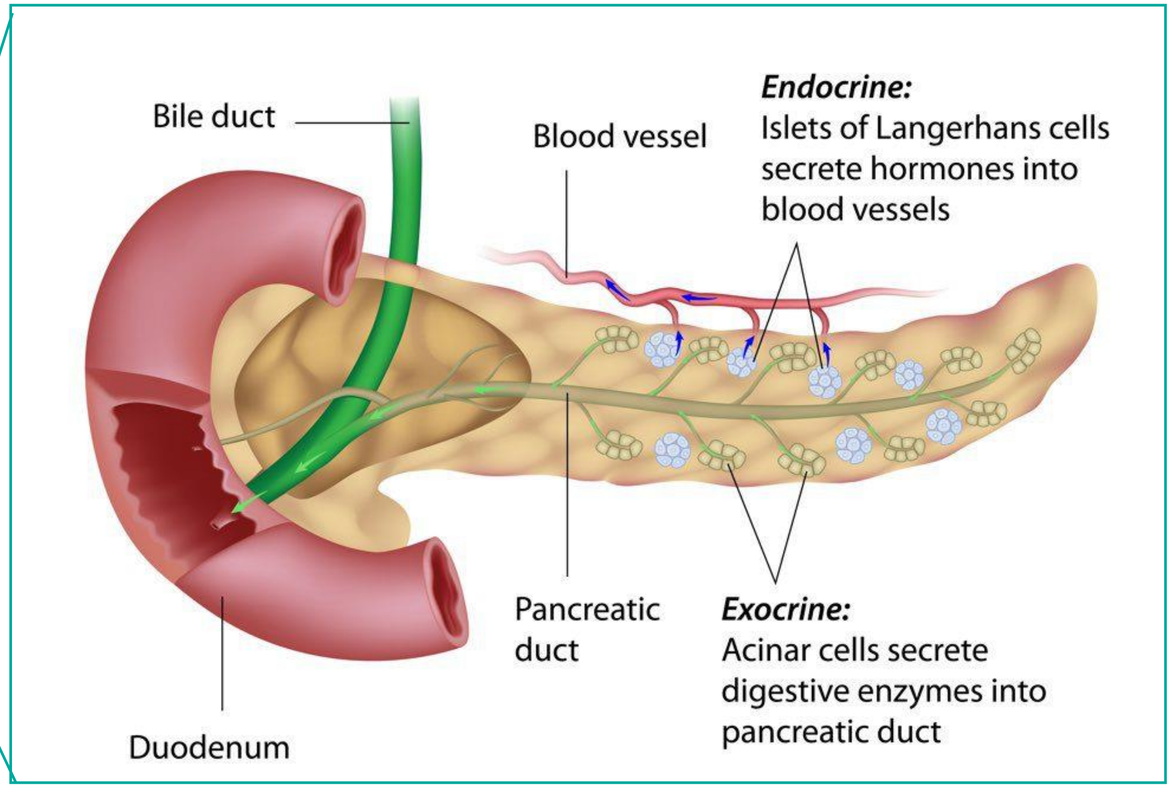
- The Pancreas & Duodenum
- What do we mean by NENs?
- Diagnosis
- Treatment incl trials, diabetes and support
- Q&A

Pancreatic & Duodenal NENs

The Pancreas

& Duodenum

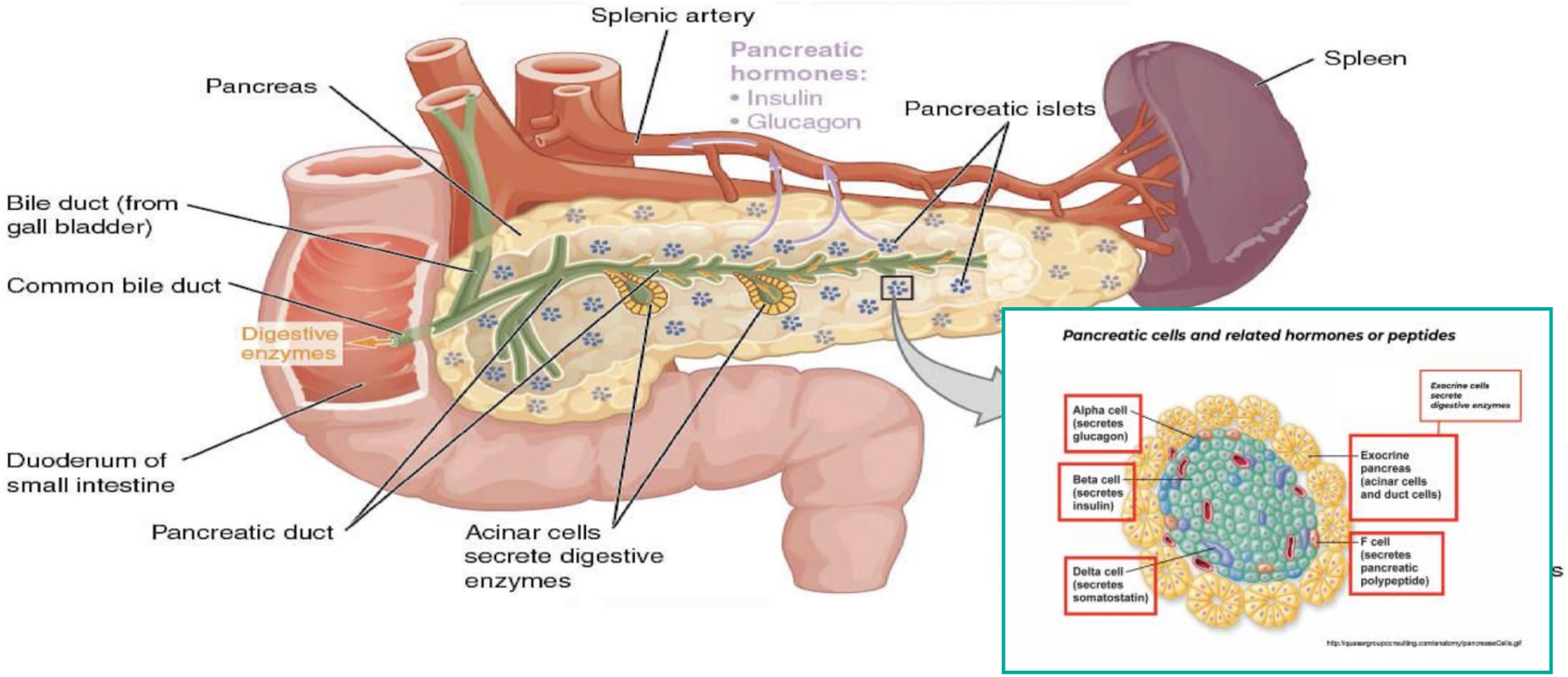




Duodenal NENs account for around 3% of all duodenal cancers: most (~80%) are NETs

Pancreatic NENs account for up to 3% of all pancreatic cancers: 70% are NETs, 30% are NECs

Pancreatic & Duodenal NENs



The Pancreas & Duodenum

Both play a role in digestion

Duodenum: connects the stomach with the small bowel, releases some gut hormones and plays a role in neutralising stomach acid and absorbing nutrients: iron, calcium, phosphorus, magnesium, copper, selenium, and several vitamins, including the fat-soluble vitamins A, D, E, and K.

Pancreas: Produces gut hormones, digestive enzymes (which help break down sugars, fats and starches) and bicarbonate (to help neutralise stomach acid)

Pancreatic & Duodenal NENs

Neuroendocrine (NE) cells are specialised cells that respond to signals from the nervous system to produce and releases hormones and other bioactive substances to maintain normal bodily functions.

What are NENs?

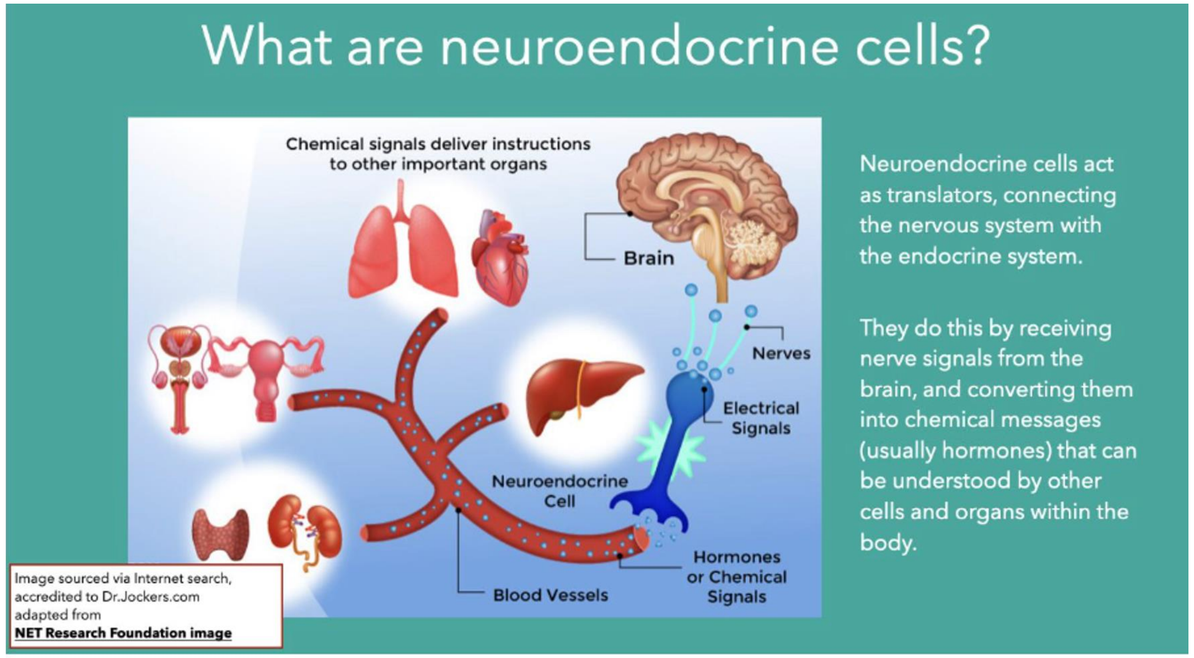
NEN = neuroendocrine neoplasm*

Umbrella term that includes both:

NET: neuroendocrine tumour

NEC: neuroendocrine carcinoma

*neoplasm = new growth, a term often used to mean cancer.



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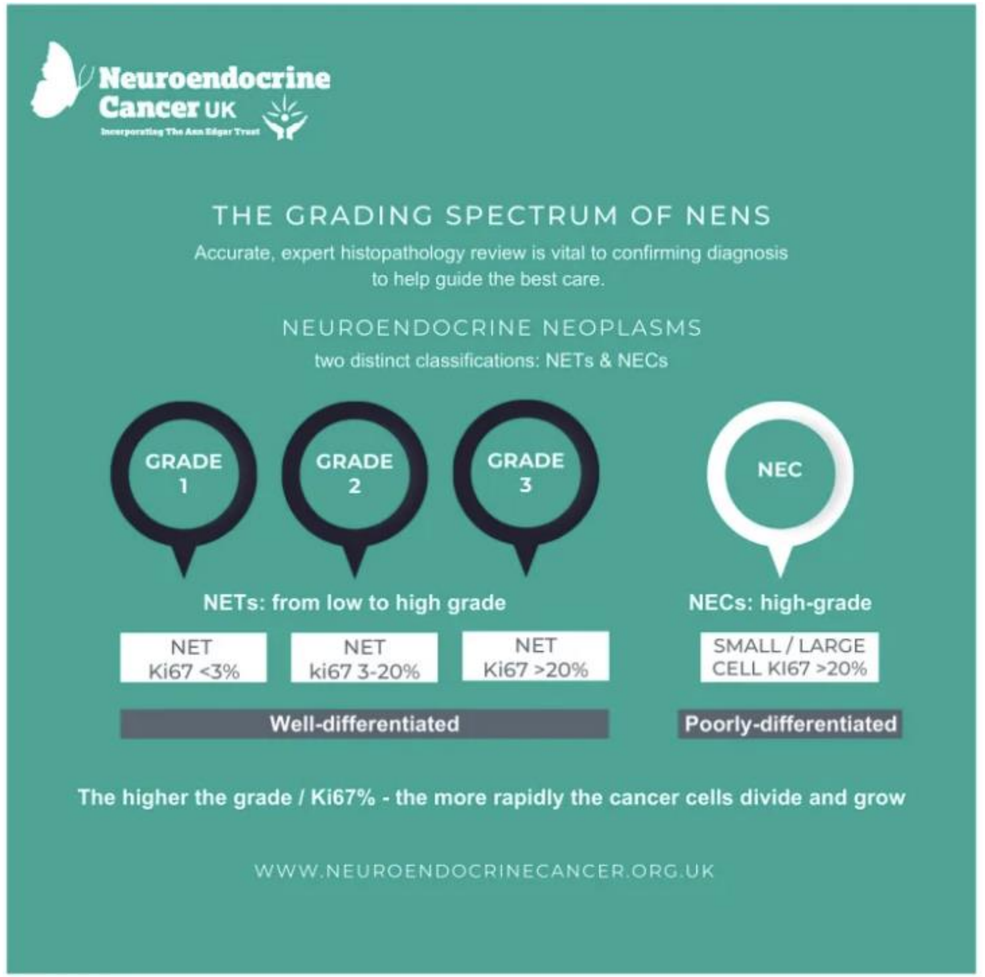
Grading

Incl differentiation

How slow/fast



Differentiation

Refers to the cell appearance and the differences cancer has made to the normal cell.
Well-differentiated cancer cells look more like normal cells and tend to grow and spread more slowly than poorly differentiated cancer cells, which look and behave . . .very differently!

Ki67%

is a protein that is present during all of the active stages of the cell cycle.
It is a valuable marker of proliferation (cell division and growth), often expressed as a percentage (%).
The higher the %, the more active the division and growth rate is.

NETs are well-differentiated: graded 1-3
NECs are poorly differentiated: all high grade

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Staging

Where

Stage 1 — Early Stage:

- A small, invasive mass or tumour has been found
- No spread to lymph nodes or other tissues
- Sometime called early-stage or "localised" cancer

Stage 2 — Localised:

- Cancer has started to affect nearby tissue
- Mass may have grown in size
- Spread to lymph nodes near the mass

Stage 3 — Regional Spread:

- Cancer affects more surrounding tissue
- Mass may have grown in size
- Spread to distant lymph nodes away from the mass

Stage 4 — Advanced Stage:

- Cancer has spread to other tissues or organs beyond the region where it originated
- Sometimes called advanced or "metastatic" cancer

TNM STAGING SYSTEM

T — Tumor

TX:
Primary tumor cannot be measured.

T0:
Primary tumor cannot be found.

T1, T2, T3 or T4:
Primary tumor has been measured.
Higher numbers indicate the tumor is larger or has expanded further into nearby tissue.

N — Lymph Nodes

NX:
There is no information about the lymph nodes.

N0:
Nearby lymph nodes do not contain cancer.

N1, N2 or N3:
Cancer is present in the lymph nodes.
A higher number indicates the cancer has been found in more lymph nodes.

M — Metastasis

MX:
Spread cannot be measured.

M0:
Cancer has not spread to other parts of the body.

M1:
Cancer has spread to other parts of the body.

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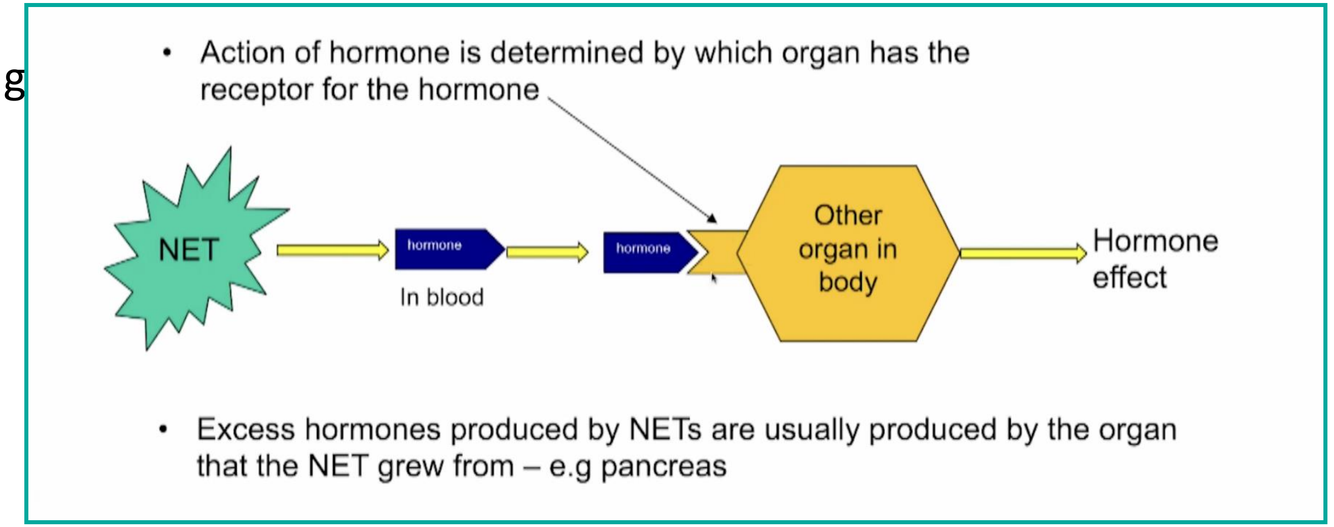
Neuroendocrine cells produce/release hormones.

What is a hormone?

A hormone is a chemical message or signal that has 2 communications:

1. Influences other (neuro)endocrine cells or glands
2. Influences a target organ e.g



Functional

Associated with hormone hyper-secretion

Non-Functional

No associated hormone hyper-secretion

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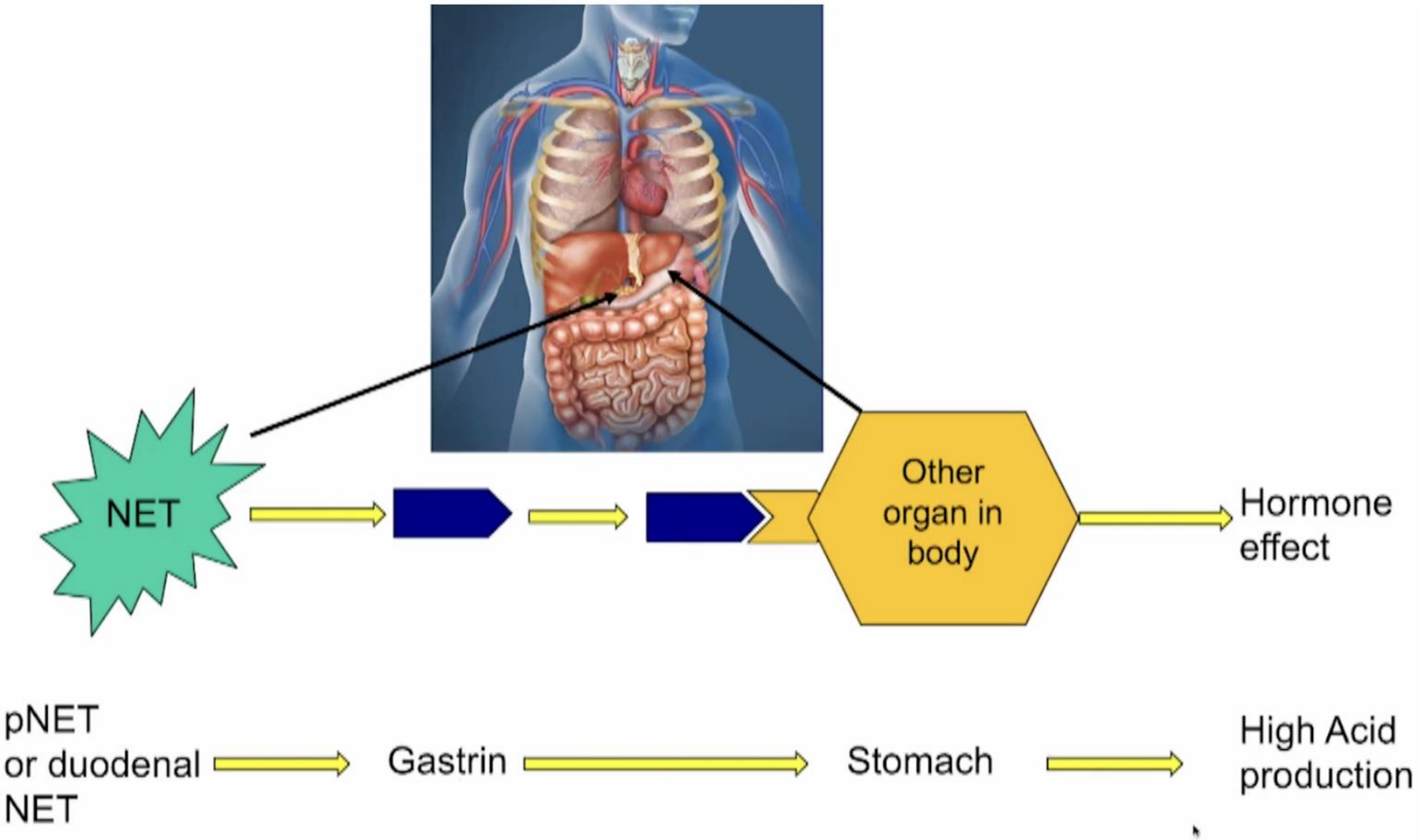
Gastrinoma



Symptoms include: ZES syndrome, peptic ulceration, dyspepsia, diarrhoea respondent to PPI

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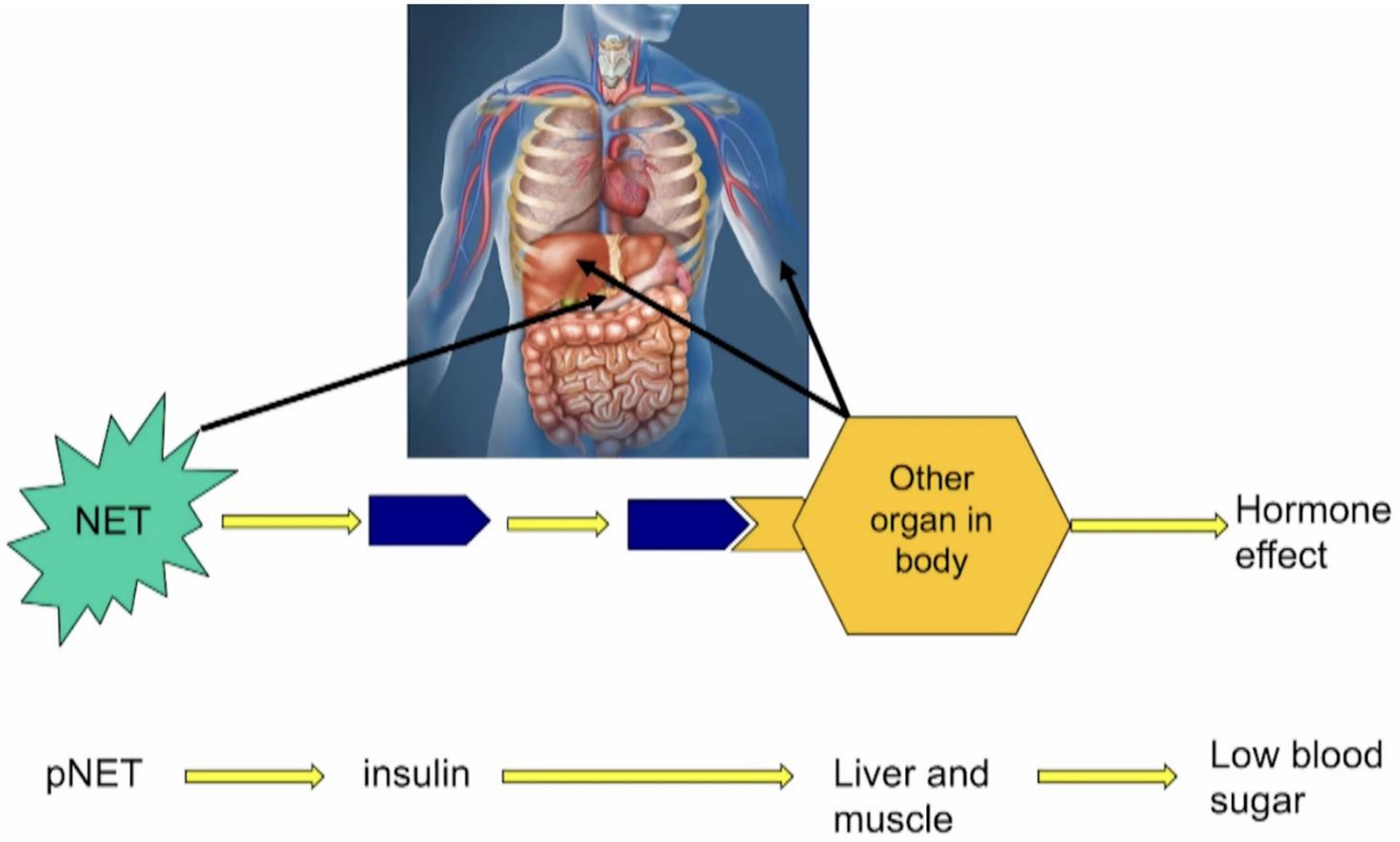
Insulinoma



Symptoms include: hypoglycaemia, weight gain

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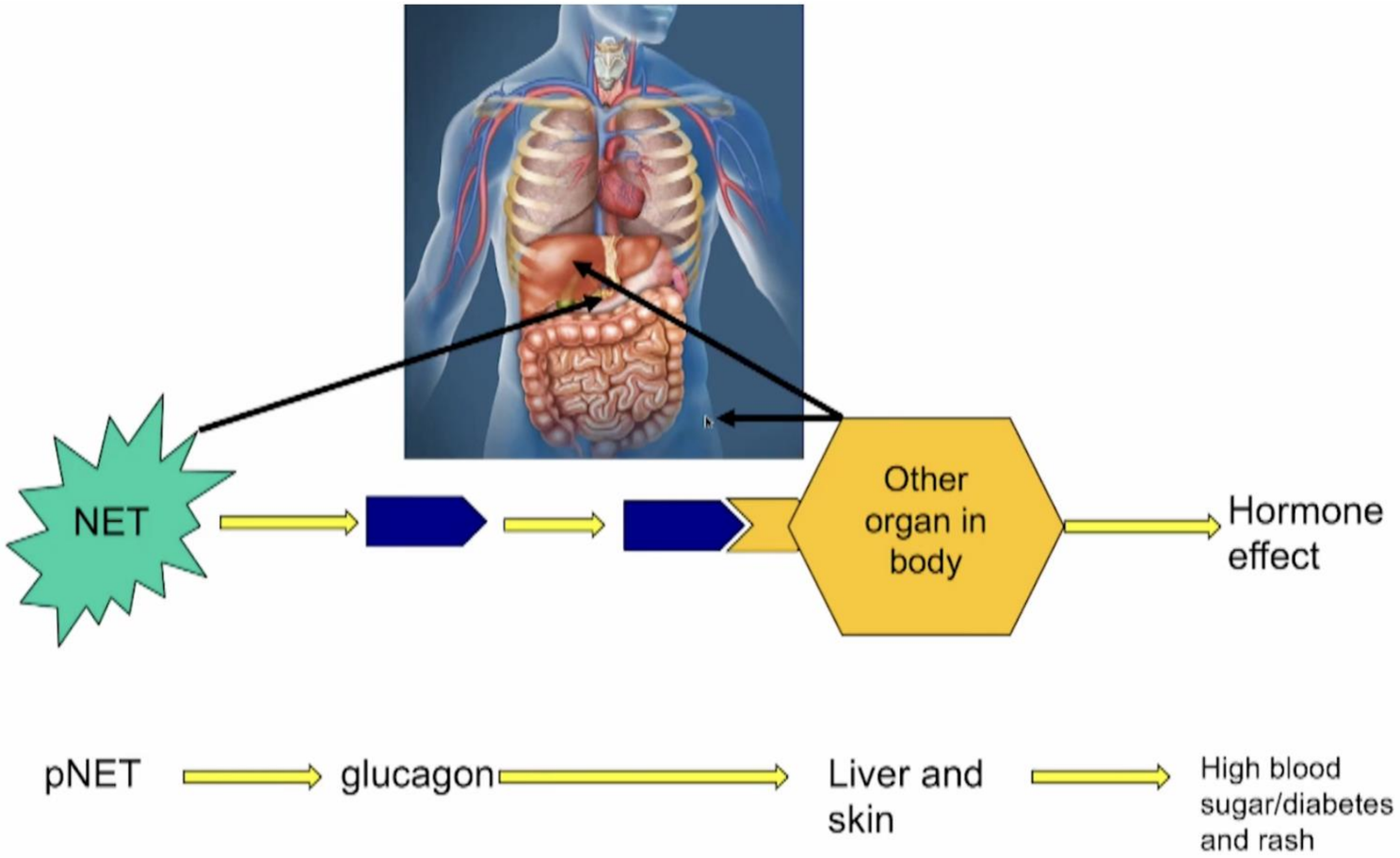
Glucagonoma



Symptoms include: hyperglycaemia, weight loss, N.M.E.

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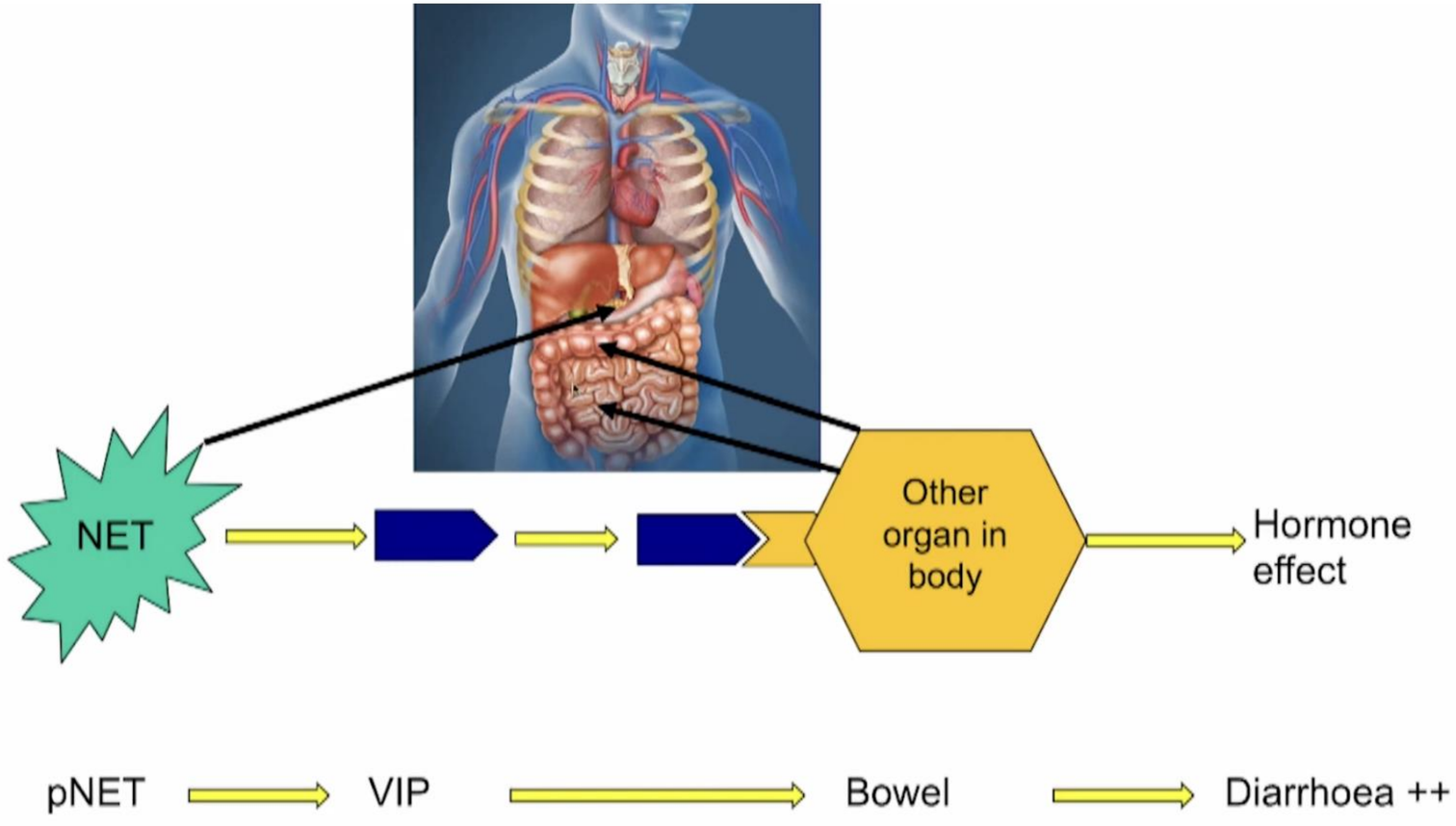
VIPoma



Symptoms include: severe diarrhoea, dehydration +/- electrolyte imbalances

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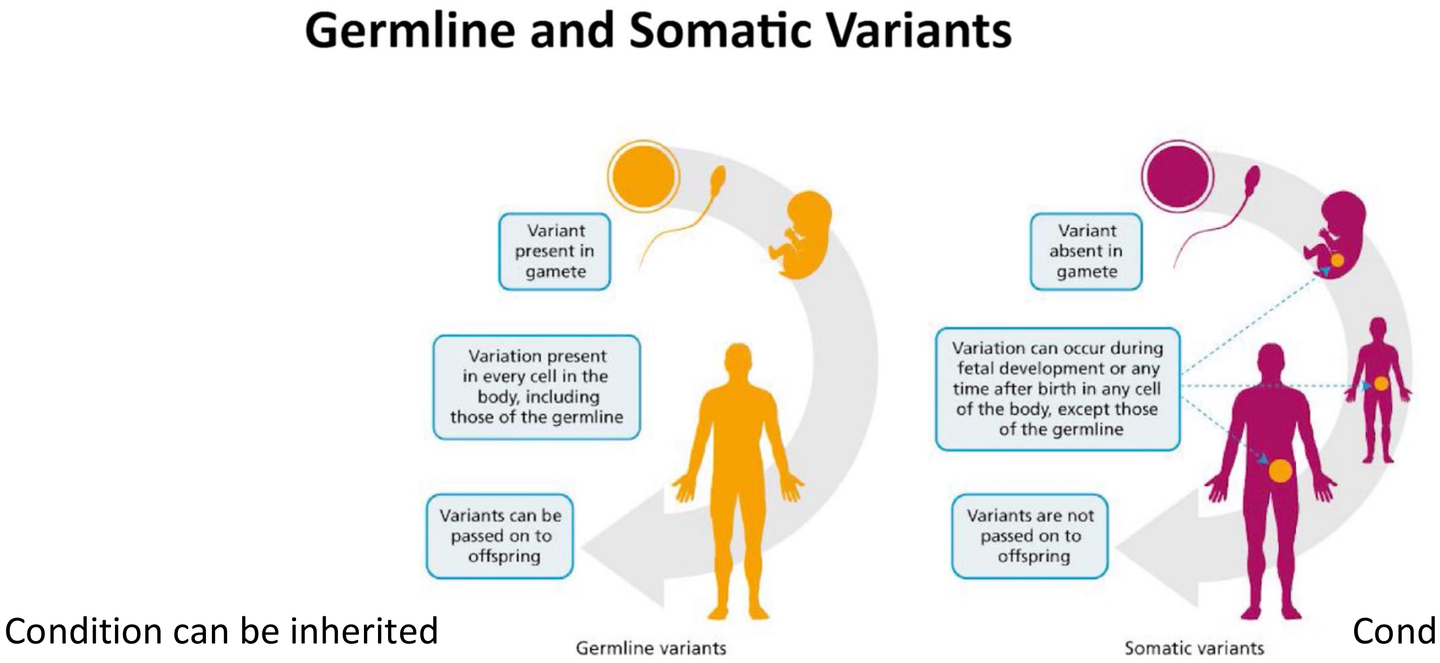
Sporadic (Somatic)

Familial (Germline)



Condition can be inherited

Condition is not inherited

There are a number of underlying germline mutations (inherited disorders) that are associated with an increased risk of developing a NEN: these include MEN1*, VHL, TSC, NF1

Up to 30% of all pancreatic NETs develop on background of one of these conditions

Primarily MEN1

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There are 4 key types of symptoms associated with neuroendocrine tumours of the duodenum, These may occur before and/or after diagnosis - and include:

1. those due to the size, site and position of the cancer.
2. those due to the abnormal release of hormones from neuroendocrine cancer cells.
3. those due to the body's immune response to the presence of cancer (paraneoplastic syndromes).
4. those due to the effects or side-effects of treatment(s).

Most UK NHS hospitals now have Acute Oncology Teams: who provide out-of-hours assistance for cancer-related emergencies.
Your hospital switchboard and/or Emergency Department will have their contact details.

Not everyone with a neuroendocrine cancer will experience symptoms - especially in the early stages of disease - the possible exception being those with a 'functional' tumour.

- Functioning neuroendocrine tumours produce and release abnormal levels of hormone (usually higher levels than normal).
- Non-functioning neuroendocrine tumours maintain the usual level of hormone production and release.

Approximately 4 in 10 people with a neuroendocrine tumour will have a functional tumour.

These can caused a single symptom or a syndrome (a group of signs and symptoms that occur together and characterise a particular disease, disorder or health condition),

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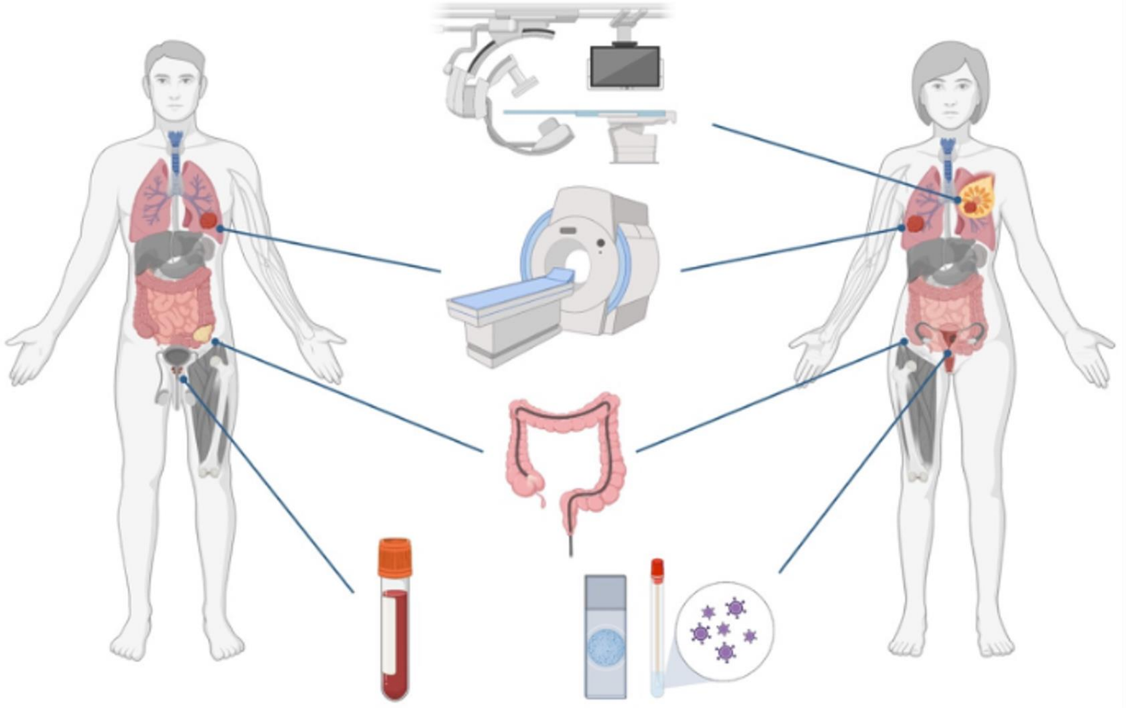
Diagnosis

Physical examination is vital: many people with a NEN look well

But may have physical / clinical signs e.g. ‘guarding’, rash, muscle tone loss, . . .



Blood and / or urine:
Full blood count
Liver and kidney function
B12/Iron/Ferritin/Folate
Chromogranin A
Urinary or serum 5HiAA (serotonin).
Site-specific tumour markers
+/- Gut Hormone Profile
+/- proInsulin + C-peptide
+/- Vitamin & mineral panel

Scans:
Bi/tri-phasic contrast CT TAP
MRI
Octreotide (SPECT) or Gallium-Dotatate PET/CT
FDG-PET

Endoscopy:
OGD / EUS
ERCP (if jaundiced)

Histopathology

+ ideally : a full dietetic / nutritional assessment

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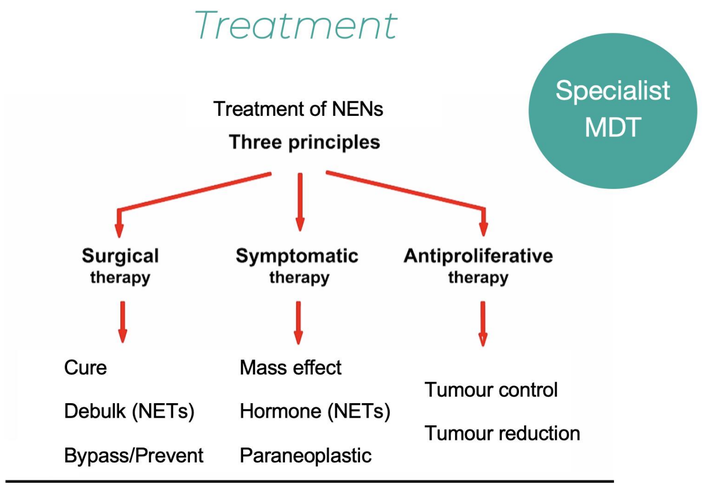
The primary goal of treatment is to provide you with the best possible care and quality of life. This includes access to appropriate treatments, symptom management, and addressing your individual priorities. Treatment decisions are tailored to your specific neuroendocrine cancer type.

Treatment

Personalised Treatment

Even if your diagnosis sounds similar to another patient's, your treatment plan may differ significantly. Your care team will discuss treatment options, ensuring you receive written and verbal information to make informed choices.



Factors Influencing Treatment

- The specific type of neuroendocrine cancer you have: tumour (NET) or carcinoma (NEC).
- Tumour Location and Size: Where the tumour is located in the body and its dimensions.
- Spread of the Disease: Whether and /or how far the cancer has spread (metastasised).
- Other Health Concerns or Illnesses: Any additional medical conditions you may have
- Your Overall Health and Fitness: your general health and potential ability to tolerate treatment(s)
- Your personal wishes and consent to treatment(s)

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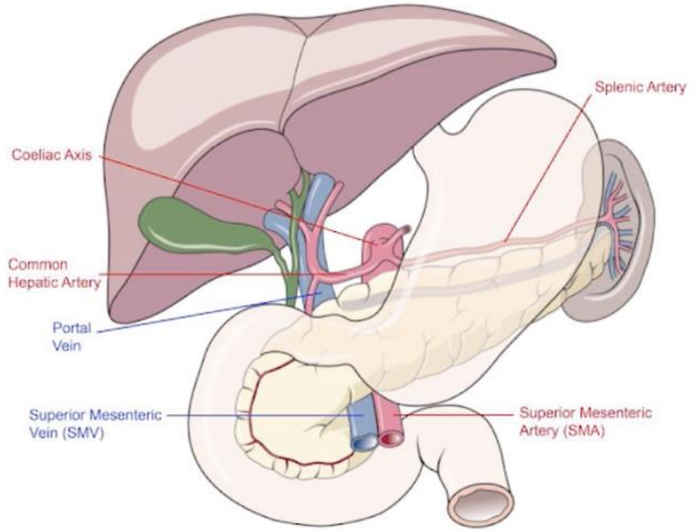
Surgical considerations

Close to major vessels



Surgical Complications

- Bleeding
- Post operative pancreatic fistula
- Intraabdominal/wound/chest infection
- Delayed gastric emptying
- Type 3 diabetes
- Pancreatic exocrine insufficiency
- DVT/PE
- Mortality

Mr Ryan Baron, Consultant Surgeon: https://youtu.be/4g3JfjEzOt0?si=wwae3eLNp6GF1Xus

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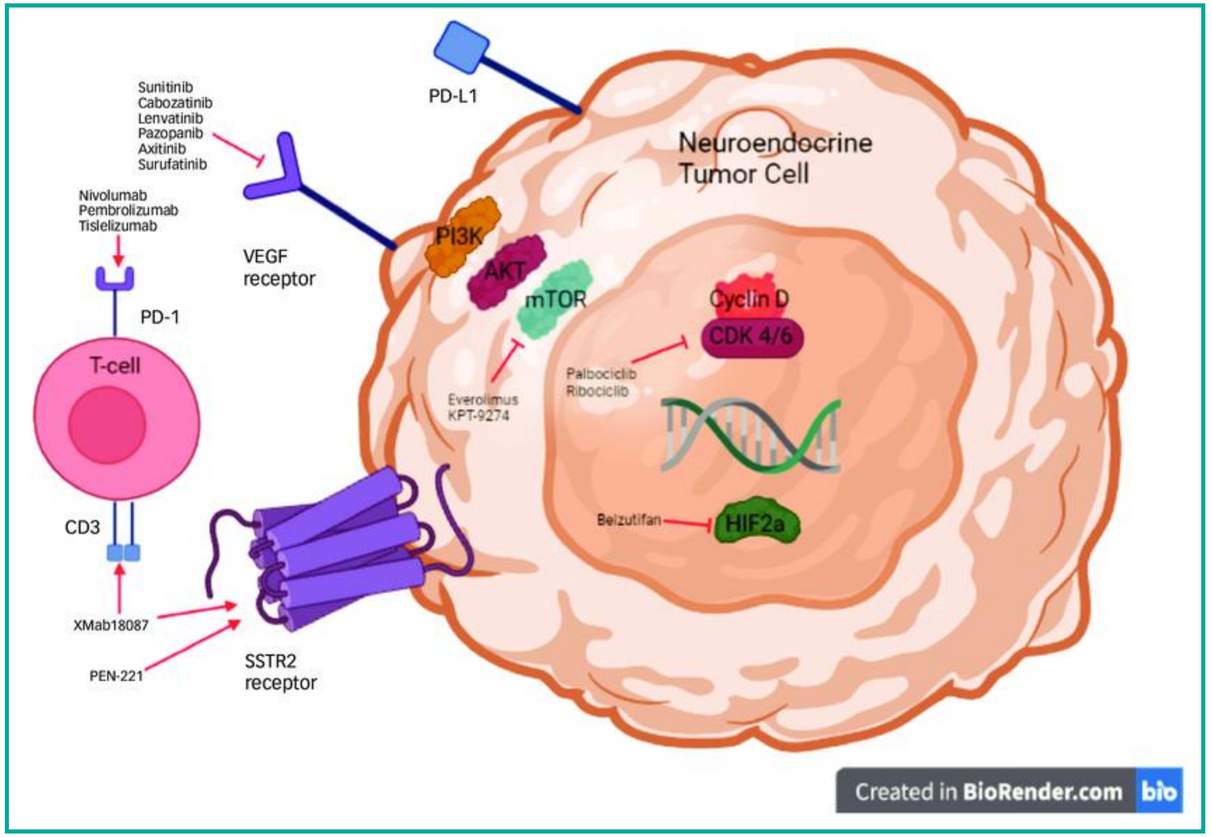
Non-Surgical

Symptom alleviation

Tumour control

while maintaining QoL



NCUK YouTube channel: https://www.youtube.com/@neuroendocrinecanceruk/videos

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Non-Surgical

Symptom control incl other medicines and therapies

includes any treatment that may ease or reduce symptoms - this may be medical , dietary and/or psychological intervention - for example mindfulness to help reduce pain, fatigue and/or anxiety.

- High dose **PPI's** (proton pump inhibitors) such as esomeprazole, can help reduce excess gastrin secretion for those with a gastrinoma. Lower doses can be effective to treat heartburn/indigestion symptoms in those with other p or dNET types.
- **Diazoxide** may be prescribed in advanced insulinomas: alongside specific dietary advice about carbohydrate intake.
- **PERT** (Pancreatic Enzyme Replacement Therapy) for example Creon®, Nutrizym® and Pancrex® can help to manage pancreatic enzyme insufficiency: which may occur due to tumour presence, surgery, SSA treatment and/or other causes.
- **Vitamin** supplementation - while a multivitamin may be prescribed to accompany PERT, specific vitamin supplementation is best considered in response to prevent or treat specific deficiencies. CAUTION: there is a NICE recommendation regarding Vitamin D supplementation during winter months for the general UK population - and an awareness that those with a NET may have a higher risk of Vitamin D deficiency: however, for those who may experience or be at risk of hypercalcaemia (high calcium) advice should be sought from your specialist team before starting or stopping vitamin D supplementation.

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Source: UKINETs (April 2025) BePart of Research (April 2025)

- COMPOSE NCT04919226: Lutetium 177Lu-Edotreotide Versus Best Standard of Care (TMTs/chemo) in WD G2-3 GEP-NETs (Ki67 <55%)
- LANtana NCT 05178693: Lutathera and ASTX727 in WD G1-3 NETs (Ki67 <55%)
- NELMAS NCT05987176: Comparison of Adjuvant Treatment With 177Lu-DOTATATE to Best Supportive Care in Patients After Resection of Neuroendocrine Liver Metastases. WD G1-2 GEP-NETs (Ki67 <20%)
- *RFH study looking at RLT in unlicensed groups: eg re-treat GEP-NETs, Lung, PGL, . .*

Clinical Trials

RareCan. Together we Can

https://rarecan.com/

Pancreatic & Duodenal NENs

Clinical Trials

Source: UKINETs (April 2025) BePart of Research (April 2025)

- PELICAN ISRCTN12812346: Study of etoposide carboplatin chemotherapy in combination with pembrolizumab and lenvatinib: PD NEC (Ki67 >20%) excl Lung/MCC
- DAREON-5 NCT05882058: use of BI 764532 in People With Small Cell Lung Cancer or Other Neuroendocrine Cancers: PD NEC excl MCC, MTC and NEPC.
- Belzutifan/MK-6482 NCT04924075: in advanced/metastatic PPGL, pNETs, VHL associated tumours, wild-type GIST or Solid Tumors With HIF-2α Related Genetic Alterations
- TARGET National: A study looking at the genetics of advanced solid cancers and matching people to early stage targeted treatment trials
- Genomic Analyses of Endocrine and Neuroendocrine tumours: 18-80 years of age with a diagnosis of an endocrine or neuroendocrine tumour.

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Diabetes:

Type I

Type II

Type III

Type III Diabetes : 5 subcategories: Type IIIa-IIIe

- Type IIIa & b: relate to genetic influences separate to NEN
- Type IIIc: damage to the pancreas eg pancreatitis, CF, tumour, surgery
- Type IIId: hormonal abnormalities eg functional pNETs, Cushings, acromegaly
- Type IIIe: drug-induced eg SSAs, some anti-tumour medications, steroids, statins

Symptoms: weight loss, increasing fatigue, wind, diarrhoea, PEI, hypoglycaemia

Clinically:

Type II (Age: adult onset): hyperglycaemia (mild), hypoglycaemia (**rare**), Insulin/PP **raised**, Glucagon N or raised.

Type III (Age: any): hyperglycaemia (mild) hypoglycaemia (**common**), Insulin/PP/Glucagon **low**.

Peripheral insulin sensitivity (how well cells respond to insulin) is low in Type II, but high in Type III. Hepatic insulin sensitivity (how well the liver responds) is normal or low Type II, and low in Type III

Pancreatic & Duodenal NENs

Diabetes:

Type I
Type II
Type III

Management

- Avoid skipping meals - eat little and often
- Avoid simple sugars/carbohydrates - include complex carbohydrates
- Medications: Metformin and/or Insulin
- Weight and dietary management - where available NET dietitian support.
- Where possible remove tumour

Simple sugars / carbohydrates: are found in a variety of natural food sources including fruit, vegetables and milk, and give food a sweet taste: they can raise blood glucose levels quickly. May be used to avoid or treat a hypo.
Complex sugars / carbohydrates: are found in a variety of food sources including bread, pasta, cakes, pastries, vegetables and grains: they have a slower release, so are less likely to cause spikes in blood sugar.

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Support & Information

Neuroendocrine Cancer UK Helpline : 0800 434 6476

Open Tuesdays to Thursdays, 10am - 4pm

Peer Support Groups

All scheduled group meetings can be found on our website Calendar

Counselling & Psychotherapy Services

This can be on a one-to-one basis - or through attendance at one of our group therapy programmes.

Also our 8 week Mindfulness course - run twice a year

Information Resources

Explore a wealth of patient-centered information and resources by visiting our **website** and **YouTube channel** - where you will also find shared patient and family experiences, podcasts, videos and blogs.

You can also keep up to date by checking out our News page and/or subscribing to our newsletter.

If English is not your first language - you may find it helpful to visit the **INCA website** -

where you will find the NETInfo Packs - that we helped to develop (11 languages).

AMEND

For those with MEN1 and other NEN-associated genetic conditions

www.amend.org.uk