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Seeking the cure for Neuroendocrine Cancer

Neuroendocrine Tumours (NETs)
An introduction

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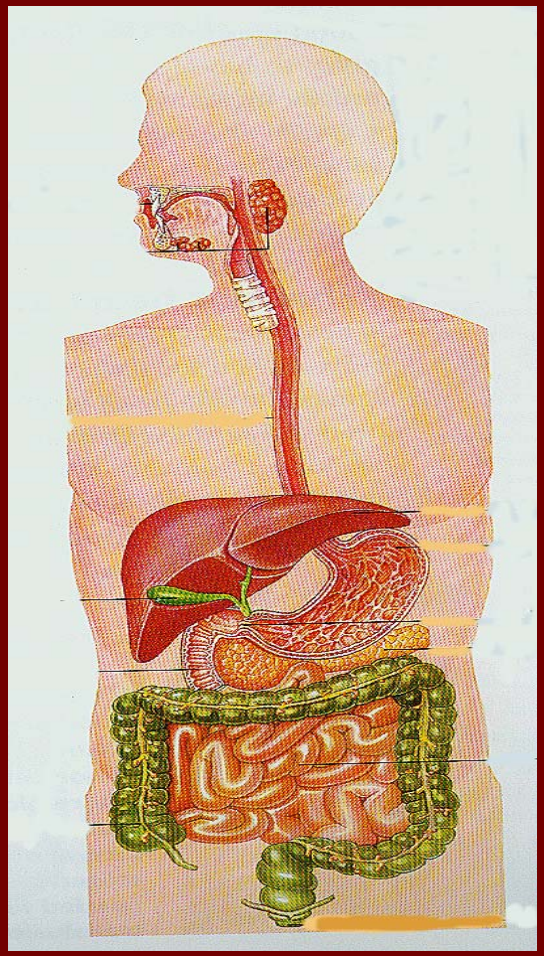
Neuroendocrine Tumours (NETs)

- Rare group of tumours derived from secretory cells (GIT, lung etc.)
- Most come from gastrointestinal tract (carcinoid)
- Incidence appears to be increasing 3-5/100,000 pa
- Unfortunately often misdiagnosed or overlooked in diagnosis
- 60% have spread at diagnosis



Foregut

Midgut

Hindgut

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Location of NETs

- **Gastric carcinoid**
  Zollinger – Ellison syndrome; ↑ gastrin level
  Peptic ulcer disease

- **Foregut carcinoid**
  Bronchus, stomach; 1st part of duodenum, pancreas and ovaries
  Can secrete a number of hormones (GH, ACTH)

- **Midgut carcinoid**
  2nd portion of the duodenum; jejenum; ileum; right colon
  Secretes serotonin, prostaglandins and substance P
  Classically produce carcinoid syndrome

- **Hindgut carcinoid**
  Transverse colon; left colon/sigmoid; rectum
  Rarely secrete hormones and hence clinically silent

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Associated Conditions

- Von Hippel Lindau
- Multiple endocrine neoplasia syndromes (MEN)
  - pheochromocytomas
  - carcinoma of thyroid
  - parathyroid disease
- Von Recklinghausen disease
- Neurofibromatosis
- Tuberous sclerosis

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- Diagnosis is complex – relying on a high index of suspicion by physician and many radiological and laboratory tests
- The treatment for metastatic disease is multi-modal – surgery; combination chemotherapy; hormonal manipulation (somatostatin analogues); radionuclide; interferon.
- Early diagnosis before tumour spread can allow for curative surgical resection of the primary.

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Characteristics of NETs

- Rare,
- Usually small <1cm
- Slow growing

- Usually metastasize to liver before becoming symptomatic; often when primary tumour is >2cm

- Episodic clinical symptoms; may be 'silent' for many years

- Often misdiagnosed as symptoms may mimic common conditions

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Carcinoid Tumours

- The most common of the gut endocrine tumours – account for 15-30% of small bowel tumours
- Can occur in the bronchus, pancreas, rectum, ovary, lung
- Derived from enterochromaffin cells which secrete serotonin (5-HT)

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Carcinoid Syndrome

- Occurs in less than 10% of patients with carcinoid. More common with tumours of small bowel (midgut)
- Vague abdominal pain (intermittent); diarrhoea; flushing; heart lesions; cramps; wheezing; arthropathy and myopathies.

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Biochemical Markers

- Chromogranin A
  - A protein released from the enterochromaffin cells with other hormones
  - Absolute levels not important but trend is
- Synaptophysin
- Ki-67; proliferative index; mitotic rate
- Serotonin breakdown products
  - 5-hydroxyindoleacetic acid (5-HIAA) in urine
- Gastrin, serotonin, pancreatic polypeptide

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Imaging Modalities

- Contrast CT
- MRI
- Angiography
- Ultrasound
- Invasive – ERCP; gastroscopy; colonoscopy

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Functional and Radioisotope Scanning

- ^{111}Indium labelled octreotide (Octreoscan) – binds to somatostatin receptors on NETs and taken up into cell → high affinity, responsive to somatostatin analogues
- Fluorodeoxyglucose PET (FDG-PET) – increased affinity for high Ki-67 lesions (inversely related to somatostatin affinity)
- ^{68}Gallium labelled octreotide PET/CT – new gold standard in nuclear medicine imaging for NETs

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Treatments

- Surgery
- Somatostatin analogues for octreotide-avid, slow growing asymptomatic tumours
- Chemotherapy – Streptozotocin +/- 5-FU; doxirubicin; cisplatin/carboplatin; temozolomide and other novel agents such as anti-vascular growth factor – Avastin
- Radiolabelled peptides – ^{111}Indium, ^{90}Yttrium, ^{177}Lutetium

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Where next?

- Support and be supported
- Unite with other sufferers to ensure the best delivery of care, hopefully with the assistance of the Unicorn Foundation as advocacy
- Don't settle for "I don't know…"