SPOTLIGHT ON
NEUROENDOCRINE
CANCER

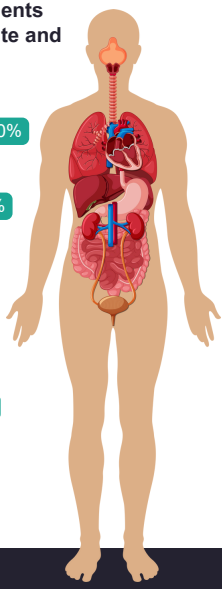
Neuroendocrine Cancer UK
Incorporating The Ann Edgar Trust

NEUROENDOCRINE CANCER

An overview for Surgeons

KEY FACTS

- **The incidence of neuroendocrine cancer has increased 371% (1995-2018) and it is now the 10th most prevalent cancer in England, and the second most prevalent GI cancer** (1).
- **With the rising incidence and the presentation of complications from advanced small bowel NENs such as obstruction, ischaemia, perforation and bleeding, these patients will be encountered by every general and sub-specialty surgeon undertaking acute and emergency surgery** (2).
- **Neuroendocrine cancer is challenging to diagnose** as it can occur almost anywhere in the body, can be asymptomatic and early symptoms can mimic more common pathologies such as IBS, asthma, menopause and /or anxiety (3).
- More than 50% of all cases will have advanced disease (Stage III & IV) at time of diagnosis (4).
- **CT and/or MR imaging can assist in detecting NENs in symptomatic patients where a diagnosis has not been established by endoscopic or other means** (5).
- **The diagnosis of a neuroendocrine cancer can result in a significant and negative impact on quality of life for patients (and their families).** This is due to multiple factors including the impact of a new cancer diagnosis, potential tumour-associated hormonal symptoms, information and diagnostic barriers and delays, alongside an often incurable and uncertain prognosis. (4)
- **Diagnosing patients earlier is life-changing because there are treatments that can improve the prognosis as well as symptoms even in the presence of metastatic disease.**



Neuroendocrine cancers may develop almost anywhere in the body, most commonly within the respiratory or digestive tracts (GI tract /pancreas).

The likely locations of Neuroendocrine Cancer shown above. (6)

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DEFINITION

DEFINITION OF NEUROENDOCRINE CANCER

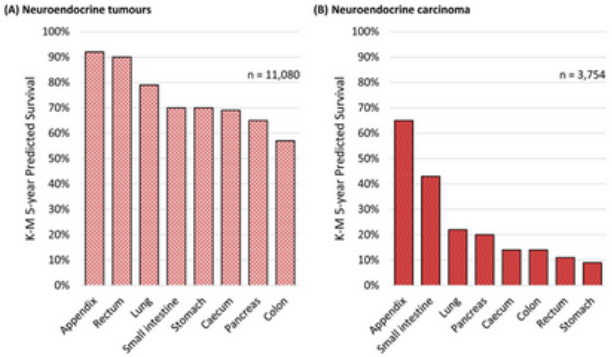
Neuroendocrine neoplasms (NENs) are a heterogeneous group of cancers, which arise in the neuroendocrine cells. The WHO has defined two principal subtypes – neuroendocrine tumours (NETs) and neuroendocrine carcinomas (NECs):

Neuroendocrine Tumours (NETs) and Neuroendocrine Carcinomas (NECs).
Both subtypes are considered as malignant tumours.

Neuroendocrine tumours (NETs)	Neuroendocrine carcinomas (NECs)
• Two-thirds of NENs are NETs ~70% • Well-differentiated • Slow to rapid growth - Graded 1-3 • Relatively good prognosis • May present/develop site- associated hormone syndrome	• One-third of NENs are NECs ~30% • Poorly differentiated • Rapid growth - Grade 3 • Poor prognosis • May present/develop paraneoplastic syndrome

- NENs are complex with aspects of both a cancer and a chronic disease and may develop almost anywhere in the body, most commonly within the respiratory or digestive tracts (GI tract /pancreas).
- Neuroendocrine neoplasms arising from the digestive tract are referred to as gastro-entero-pancreatic NENs (GEP-NENs), and these account for over 60% of NENs (7). The respiratory system represents the site of disease in 20-30% of patients, and less commonly affected sites include skin, thymus, and reproductive system structures, such as the ovaries.

Determining whether patients have NETs or NECs is of vital importance, as this can have a significant impact on prognosis as well as treatment planning (8)**. There are significant differences in 5-year survival of NETs and NECs** (9)**.**



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PRESENTATION

CLINICAL PRESENTATION

- **Diagnosing NENs is challenging with data and patient experience reports indicating an average time to diagnosis of 3 years** (3).
    - Routine tests may not raise suspicion or diagnosis of NENs, e.g., small bowel NENs may have negative endoscopy and normal FBC and CEA, despite bowel symptoms.
    - Symptoms may be tumour and/or hormone excess related. However, many may be asymptomatic at early stages, found incidentally through screening or other tests.
- Those with functioning tumours can have specific symptoms for example, those with carcinoid syndrome may present with the classical triad of diarrhoea, flushing and/or wheeze.
- In contrast to most other GI cancers, some patients who have widespread stage 4 NETs have a relatively good prognosis, especially when the tumour is grade 1.

SURGICAL MANAGEMENT OF GASTROENTEROPANCREATIC NENS

NENs usually require consultative, multidisciplinary management at specialized centres.

Gastric NENs: Consideration of tumour type is paramount in treatment planning. Type I can be managed non-operatively and/or endoscopically, Type 2 are managed within parameters of neuroendocrine syndromes in which they arise whilst Type 3 are managed akin to gastric adenocarcinoma (11).

Small bowel NENs: Up to one quarter of these present acutely, many present as an incidental finding, and most present with metastatic stage IV disease. **With the rising incidence and the presentation of complications from advanced disease such as obstruction, ischaemia, perforation and bleeding, these patients will be encountered by every general and sub-specialty surgeon undertaking acute and emergency surgery** (2)**.**

Appendix NENs: The majority are diagnosed following appendicectomy for acute appendicitis or after laparotomies for other pathologies (12)**.** Tumour size is the most important criterion to determine further management.

Pancreas NENs: Non-functioning pancreas NENs < 2cm show a relatively indolent behaviour with a limited risk of progression. Therefore, a surveillance strategy has generally been advocated. Localised functional pancreas NENs generally require surgical resection (13).

Colorectal NENs: Most rectal NENs are small is size and can be treated by adequate endoscopic resection techniques.

Refer patients with a confirmed or highly suspected diagnosis of NENs on to your local expert MDT clinic or Centre of Excellence.

USEFUL INVESTIGATIONS FOR DIAGNOSING NEUROENDOCRINE NEOPLASMS

- For people with persistent, troublesome, particularly watery diarrhoea for whom the standard tests have not confirmed a diagnosis, consider a functional NET and arrange a Gut Hormone Profile and measurement of plasma/urinary 5-HIAA (10).
- Chromogranin A is the most useful general biomarker for NENs but is not completely sensitive or specific. It is helpful for patients with confirmed NEN but shouldn't be used as a screening test.
- Unusual looking polyps in the stomach, duodenum or rectum that could potentially be NENs should initially be biopsied rather than being removed at the time of the initial endoscopy. If a NEN is histologically confirmed, full tumour characterisation and staging is required to determine the optimal treatment plan.
- CT and MR imaging are useful for patients with persistent abdominal pain and diarrhoea and will often detect previously undiagnosed NENs. However, they will not necessarily demonstrate the full extent of disease.
- Nuclear medicine scans (e.g. 68Ga DOTATATE PET/CT and FDG-PET/CT), whilst not available in every hospital, can be very useful for determining the full extent of the disease, risk stratification and optimising treatment plans. DOTATAE PET/CT is useful for defining the extent of well differentiated, low grade disease, whereas FDG-PET/CT can help identify high grade components in complex or progressive disease states and are almost mutually exclusive.
- Endoscopic Ultrasound can be a valuable tool in staging, locating and allows for FNA biopsy/cytology, and for immunohistochemical staining of hormones for culprit lesions.

SPOTLIGHT ON NEUROENDOCRINE CANCER IS A COLLABORATION BETWEEN UKINETS & NEUROENDOCRINE CANCER UK

UKI NETS

Clinical guidelines are available - alongside expert advice from any one of 14 UK accredited European Centres for Neuroendocrine Cancer - should NENs be suspected/diagnosed: UKINETs: www.ukinets.org ENETs: www.enets.org

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Patient-facing and HCP information, education and support is available from Neuroendocrine Cancer UK Office: 01926 883487 I Helpline: 0800 434 6476 Registered charity number: 1092386

THE LACK OF A NATIONAL PATHWAY AND NON-INCLUSION IN NG12 DIFFERENTIALS HAMPERED THE DIAGNOSIS OF NENS, HOWEVER, A COLLABORATIVE MULTI-STAKEHOLDER WORKING GROUP – INCLUDING NHS EARLY DIAGNOSTIC LEADS – HAS ADDRESSED THIS DISPARITY. THE **NEUROENDOCRINE CANCER PATIENT CARE PATHWAY** WAS LAUNCHED MAY 2023. VISIT WWW.NEUROENDOCRINECANCER.ORG.UK FOR FURTHER INFORMATION.

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