

# Neuroendocrine tumours (NETs) / Neuroendocrine neoplasm (NEN)

- NETs are not as rare as you may think
- NETs can arise throughout the GI tract and pancreas, but the most common sites are the small bowel, rectum, pancreas, stomach and appendix
- A recent epidemiological study reported a 6.4-fold increase in NET incidence between 1973 and 2012
- Incidence: 8.6 per 100000 persons
- Tumour site is a major determinant of prognosis. Tumour size is also an important prognostic factor for localised NETs at most sites.
- A crucial feature is the establishment of a tumour's grade (which is an indication of the proportion of NET cells that are proliferating at a particular time) by Ki- 67 immunohistochemistry or mitotic count.
- The complete evaluation of a patient who has a NET also involves determining whether the tumour is functional or non-functional NET.

**Table 1. Classification of neuroendocrine neoplasms according to pathological differentiation and grade according to Ki-67 proliferation index**

Differentiation	Ki-67 (%)	Grade	Classification of neuroendocrine neoplasm (NEN)
Well differentiated	<3	1 (G1)	NET
Well differentiated	3-20	2 (G2)	NET
Well differentiated	20, usually <55%	3 (G3)	NET
Poorly differentiated	Usually >55%	3 (G3)	NEC

NEC, neuroendocrine carcinoma; NET, neuroendocrine tumour.

## Clinical presentation:

- Clinical presentation can be variable, often patients are asymptomatic and NET was diagnosed incidentally, while some patients may present with chronic diarrhoea and flushing. The diagnosis of patients with NETs can therefore be very challenging. There are frequently considerable delays in diagnosing NETs, as symptoms may be similar to those found in other commoner conditions such as irritable bowel syndrome.

## General investigation

- Upper endoscopy – to exclude coeliac disease, upper GI pathology, including gastric and proximal small bowel NET
- Colonoscopy – to exclude neoplasm, microscopic colitis, and lower GI NET
- Images: CT, MRI, DOTATATE PET-CT
- Biochemical tests – very limited use:
  - chromogranin A: levels may be normal especially in small localised NETs and conditions such as renal failure, inflammatory bowel disease and proton pump inhibitor use can sometimes cause false positive elevations.
  - 24hours urinary concentration of 5-hydroxyindoleacetic acid (5-HIAA) can be helpful in evaluating a patient who potentially has a metastatic small bowel NET and/or suspected carcinoid syndrome

**Table 2. Gastric NET classification and features**

Characteristic	Type I	Type II	Type III
Associated disease	Chronic atrophic gastritis-A and pernicious anaemia	Zollinger Ellison syndrome and MEN-1	None NET
Proportion of tumours	80%	5%	15%
Site of tumour	Multiple	Multiple	Single
Size of tumour	<1 cm	<1 cm	2-5cm
Plasma gastrin concentration	High	High	Normal
Gastric acid output	Low	High	Normal
Prognosis	Good	Good	Poor

MEN, multiple endocrine neoplasia

## Treatment

In principle, if a NET is localised and resectable, it should usually be resected

- If a NET is functional, somatostatin analogue injections (lanreotide autogel or octreotide long-acting release which bind to somatostatin receptors) can be used to reduce the symptoms
- Somatostatin analogues are also the mainstay of treatment in the more common non-functional, unresectable, locally advanced or metastatic NETs of low/intermediate grade.
- Patient prognosis varies greatly, but can be excellent in some patients who have widespread metastatic disease.

## Reference

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## Dr Montri Gururatsakul

MD, PhD (Aus), FRACP (Aus)

**Gastroenterologist**

Cairns Gastroenterology  
Level 3, Suite 3  
120 Bunda Street  
Cairns QLD 4870

P: 07 4041 2877

F: 07 4041 6135

E: [reception@guthealth.net.au](mailto:reception@guthealth.net.au)  
[www.cairnsgastro.com.au](http://www.cairnsgastro.com.au)