Classification of neuroendocrine tumors

There are a number of factors, including site of origin, clinical syndrome, grade and differentiation, staging, extent of disease, and imaging tests, that can help health care professionals classify neuroendocrine tumors (NET).[1,2]

Correct NET classification can facilitate accurate diagnosis and may lead to better patient outcomes[3]

Site of origin

Foregut[4,5]
- Lungs
- Stomach
- First part of duodenum
- Pancreas

Midgut[4]
- Second part of duodenum
- Jejunum
- Ileum
- Right colon

Hindgut[4]
- Transverse, left, and sigmoid colon
- Rectum

Additional sites[3,6]
- Ovary
- Adrenal gland
- Paraganglia
- Thymus
- Appendix

Clinical syndrome

NONFUNCTIONAL

- Tumors that do not secrete active hormones and do not produce hormone-related symptoms[1]
- Symptoms, if present, are related to tumor mass[1,7,8]
- Majority of NET[9]
- Tend to be more aggressive and often present after metastases[10]

FUNCTIONAL

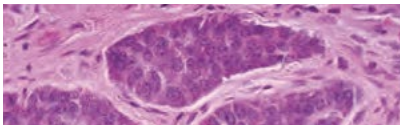
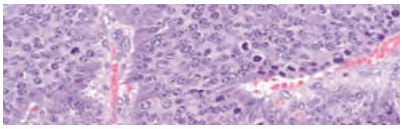
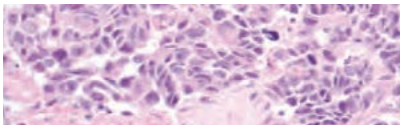
- Tumors that secrete active hormones and produce hormone-related symptoms[1]
- Symptoms are related to the excess production of hormones[1]
- Minority of NET[9]
- Tend to be slow growing[10]

NET can be functional (tumors that secrete hormones) or nonfunctional (tumors that do not secrete hormones)[1]

Pathology

NET can be well-differentiated, moderately differentiated, or poorly differentiated, and over half of NET originate in the GI tract. A complete GI NET pathology report can include site of origin, diagnosis, histological features, IHC staining, grade (proliferation, determined by mitotic rate or Ki-67), and other pathological components.[11]

A GI NET pathology report includes:

	Well-differentiated NET (Low grade, G1)[6]	**Well-differentiated NET** (Intermediate grade, G2)[6,12]	**Poorly differentiated NEC** (High grade, G3)[6]
			
Appearance[12]	Monomorphic population of small, round cells	*	Cellular pleomorphism
Prognosis[12]	Prolonged survival	Intermediate	Poor
Mitotic rate[6]	<2 mitoses/10 HPF	2-20 mitoses/10 HPF	>20 mitoses/10 HPF
Ki-67 index[6]	<3%	3%-20%	>20%

*Not well-defined in the medical literature.
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Staging[13,14]

TNM staging is a classification system based on 3 factors:

TUMOR (T):

Size and location of the primary tumor

NODE (N):

Whether cancer cells have spread to the lymph nodes located near the tumor

METASTASIS (M):

Whether the tumor has spread to other parts of the body

The definition of TNM may vary by primary tumor site, but staging relies predominantly on tumor size and extent of invasion into anatomical structures

Abbreviations: HPF, high-power field; IHC, immunohistochemical; NEC, neuroendocrine carcinoma.

Extent of disease[2]

- **Localized:** tumors contained within the organ of origin
- **Regional:** tumors that have spread through the organ wall to nearby tissues
- **Distant:** tumors that have spread beyond primary site to distant tissues and/or organs

Imaging tests[2,6,15,16]

Imaging tests can be helpful to detect and localize NET. Many NET are detected incidentally through routine imaging tests for unrelated problems.

- Computed tomography (CT)
- Magnetic resonance imaging (MRI)
- Somatostatin receptor scintigraphy (SRS) (Octreoscan™), as appropriate
- Ga 68 dotatate PET
- Endoscopic ultrasound (EUS)
- Endoscopy
- Colonoscopy
- Bronchoscopy
- Esophagogastroduodenoscopy (EGD)

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Abbreviation: PET, positron emission tomography.
Octreoscan is a trademark of Curium.

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