Just Diagnosed With Neuroendocrine Cancers: What to Know And Understand

Osama M. MoSalem, MD

Saint Luke's Cancer Institute, Saint Luke's Hospital of Kansas City

University of Missouri-Kansas City

Kansas City, Missouri

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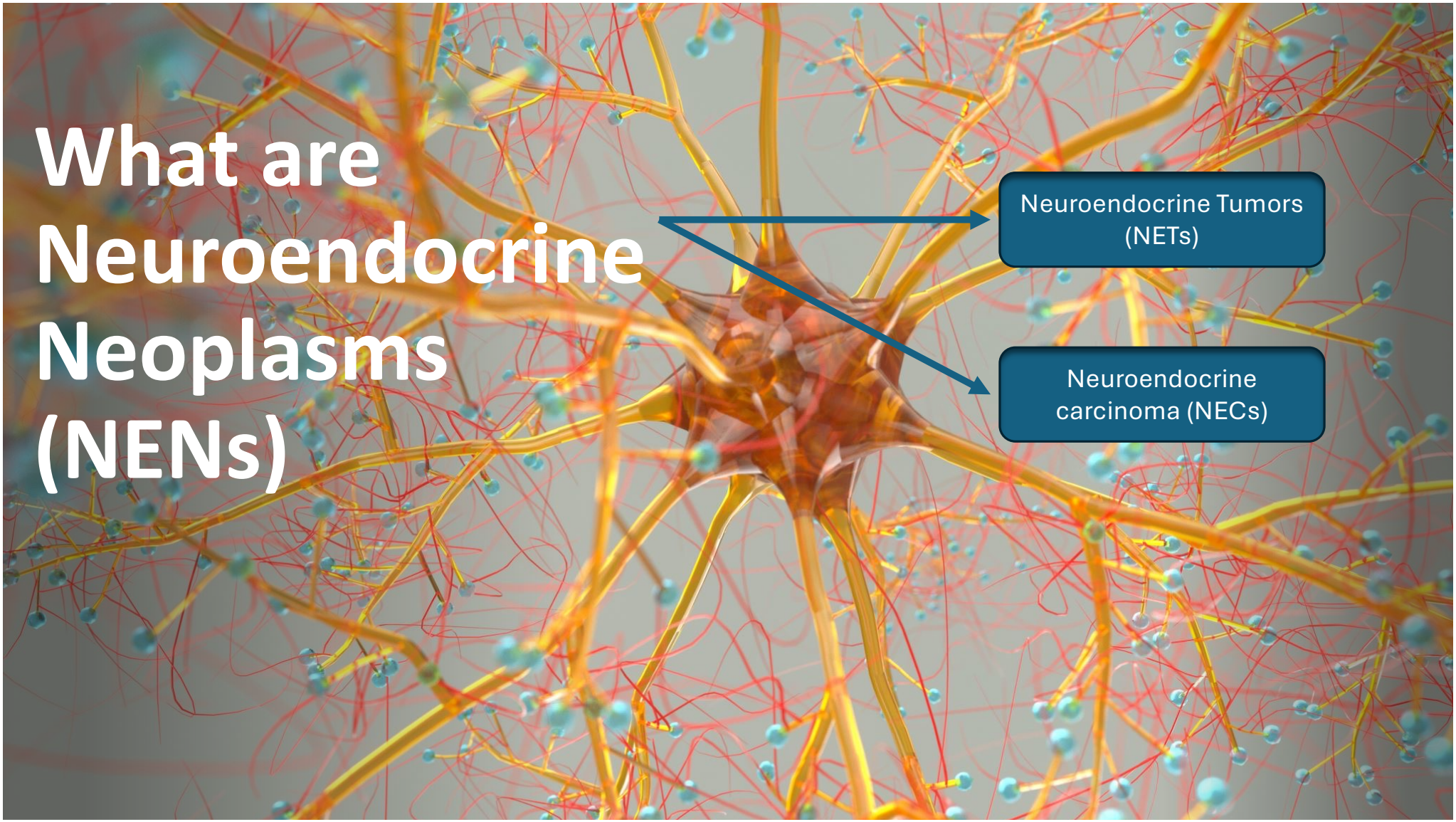
Objectives

- What are neuroendocrine cancers/ Neoplasms.
- Sites of NENs.
- Incidence and prognosis of NENs.
- How we diagnose and stage NENs.
- Treatment of NENs.
- Is neuroendocrine tumors (NETs) different from neuroendocrine carcinomas (NECs).
- How to live well with NETs.
- Common questions.


What are Neuroendocrine Neoplasms (NENs)
Neuroendocrine Tumors (NETs)
Neuroendocrine carcinoma (NECs)

Incidence and Epidemiology

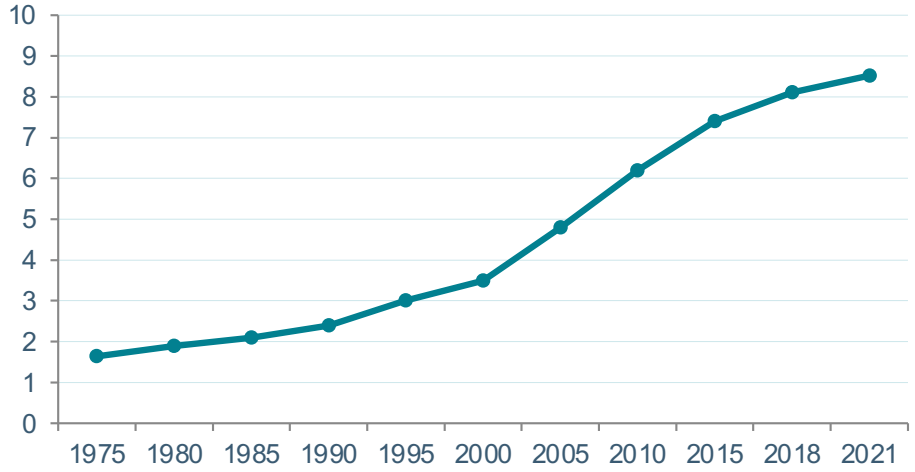
5.2×
increase in incidence
1975 → 2021

8.52
per 100,000 (2021)
Age-adjusted rate

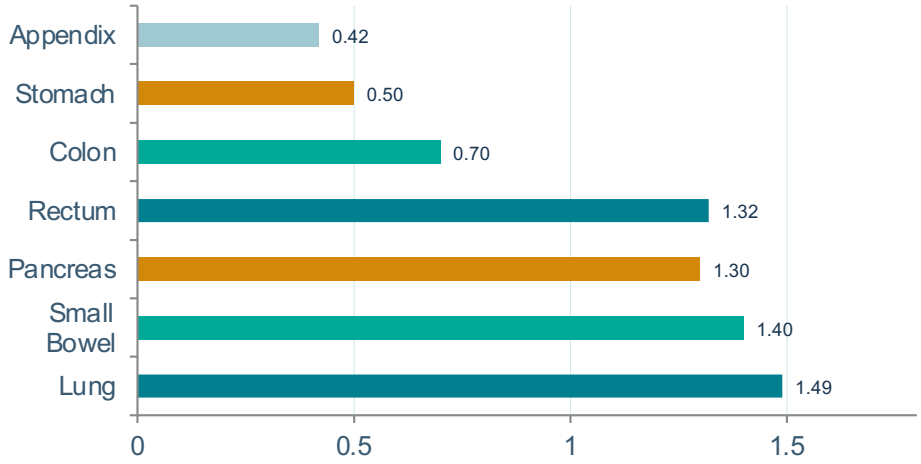
248,546
prevalent cases (US)
20-year limited duration, Jan 2021

11.8 yrs
median overall survival
All NENs combined

Age-Adjusted Incidence Rate (per 100,000) • 1975–2021



Incidence by Primary Site (per 100,000) — SEER 17, 2000–2021



Arvind Dasari et al. JAMA Network Open. 2025

Common Sites of NETs

Gastrointestinal (GI) NETs

Small intestine, stomach, colon, rectum. The most common location overall.

Pancreatic NETs (pNETs)

Include insulinomas, gastrinomas, and non-functional tumors. May cause hormonal symptoms.

Lung (Pulmonary) NETs

Includes typical and atypical carcinoids. Often found incidentally on imaging.

Paraganglioma / Pheochromocytoma

Arise from adrenal glands or nearby tissue. May cause high blood pressure, sweating, or headaches.

Unknown Primary

In some cases, the tumor is found in a lymph node or liver before the original site is identified.

Disease Biology

Ki-67:

What is it?

- Protein marker showing **how many cells are growing**

How is it measured?

- % of tumor cells staining positive

What it tells us

- Higher % = faster tumor growth

Typical ranges

- **<3%** → Low (Grade 1)-A
- **3–20%** → Intermediate (Grade 2)-- B
- **>20%** → High (Grade 3)- C

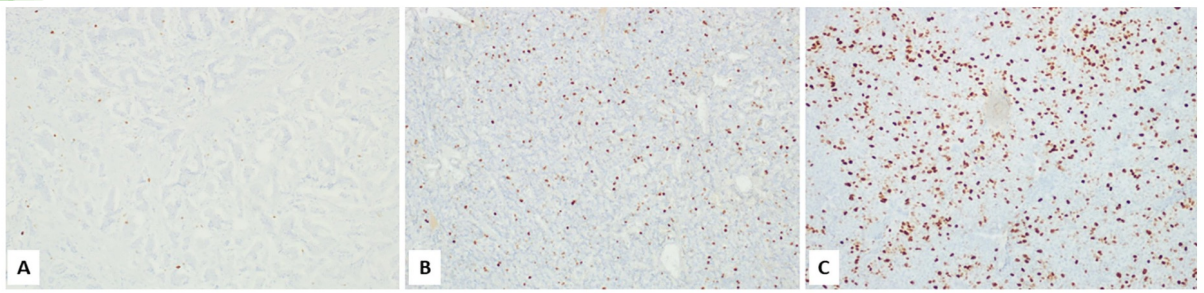


Photo source: La Rosa et al. Endocrine pathology. 2023

Disease Biology

Mitotic Rate:

What is it?

- Counts cells **actively dividing**

How is it measured?

- Number of mitoses per **10 high-power fields (HPF)**

What it tells us

- More mitoses = more aggressive tumor

Typical ranges

- **<2** → Low (Grade 1)
- **2–20** → Intermediate (Grade 2)
- **>20** → High (Grade 3)

Disease Biology

Tumor differentiation

How similar the tumor cells appear compared to normal neuroendocrine cells.

Well-differentiated (NET) vs Poorly differentiated (NEC)

Symptoms & Signs of NETs

Many NETs are found incidentally on imaging before causing symptoms. When symptoms occur, they vary by tumor location and whether the tumor releases hormones. The tumor is classified as functional or nonfunctional based on the presence or absence of hormonal symptoms.

Facial flushing

Sudden redness or warmth in face/neck (carcinoid syndrome)

Diarrhea

Frequent, watery stools — often related to hormone secretion

Wheezing / Breathlessness

Asthma-like symptoms, especially in pulmonary NETs

Abdominal pain or mass

Cramping, bloating, or a palpable mass in the belly

Low blood sugar (hypoglycemia)

Sweating, shakiness, confusion (insulinoma)

Peptic ulcers

Recurrent ulcers that don't respond to usual treatment (gastrinoma)

Unintended weight loss

May occur with advanced disease

No symptoms at all

Many NETs are found incidentally on CT scans or colonoscopy

How NETs Are Diagnosed: Labs

- **Chromogranin A (CgA):** low utility, PPI among others interferes with CgA and causes false elevation
- **5-HIAA (plasma or 24-hour urine):** Plasma 5HIAA could be very reliable. Certain foods can interfere with 24-hour urine 5HIAA.
- In **Pancreatic NETs**, check hormone levels for Insulin, C-peptide, vasoactive intestinal peptide (VIP), Glucagon and Gastrin levels.
- **Gastrin for duodenal NETs** (gastric ulcers).
- **Cortisol and ACTH** in Cushing syndrome.

💡 Hormonal workup should be guided by symptoms and routine screening is not routinely recommended.

How NETs Are Diagnosed: Imaging

- **CT scan** (preferably triphasic to assess liver).
- **MRI**: Could be helpful especially to evaluate liver metastases.
- **PET scan (Copper-61 or Gallium-68 DOTATATE PET):** Detects somatostatin receptor positive tumors. Can help with staging and confirm if eligible to PRRT in advanced/metastatic disease.
- **FDG-PET (Fluorodeoxyglucose PET):** best for poorly differentiated or high-grade neuroendocrine carcinoma (NEC). Low sensitivity for well differentiated NETs.

How NETs Are Diagnosed: Biopsy & Pathology

- Tissue sample confirms diagnosis, and tumor grade.
- Tumor grade (G1/G2/G3), differentiation (well differentiated or poorly differentiated) Ki-67 proliferation index determined.

💡 Ask your doctor: What stage is my tumor? What is my Ki-67 index? Has the tumor spread to lymph nodes or other organs? Is my tumor functional or nonfunctional ?

Treatment Options for NETs

Treatment depends on tumor type, grade, location, stage, and your overall health.

Surgery

Removal of the tumor is the primary treatment when possible. Even in advanced disease, surgery may be used to reduce tumor burden.

Somatostatin Analogs (SSAs)

Octreotide or lanreotide — slow tumor growth and control hormone-related symptoms.

PRRT

Peptide Receptor Radionuclide Therapy (Lutathera)-targeted radiation delivered directly to tumor cells expressing somatostatin receptors.

Systemic Therapy

Capecitabine, Temozolomide (CAPTEM), everolimus, cabozantinib, sunitinib or belzutifan (pheo/ para) are FDA approved. Used depending on the tumor site and disease stage.

Liver-Directed Therapy

Embolization, ablation, or radioembolization (Y-90) to treat liver metastases and reduce tumor burden and control hormone overproduction.

Clinical Trials

Access to cutting-edge treatments. Ask your team if a clinical trial may be right for you.

- Alpha PRRT.
- DLL3 inhibitors in NECs.

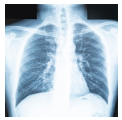
Carcinoid Syndrome

What Is It?

Carcinoid syndrome occurs when a functional NET releases serotonin and other substances directly into the bloodstream — most often when cancer has spread to the liver.

Flushing: Sudden redness of face, neck, and upper chest

Diarrhea: Frequent, watery stools; may be severe



Wheezing: Asthma-like bronchospasm

Carcinoid Heart Disease: Valve damage from chronic serotonin exposure

Abdominal cramping: Associated with diarrhea and gut motility changes

Carcinoid Syndrome

How It's Managed

- Somatostatin analogs (SSAs) are the cornerstone of symptom control — given as monthly injections.
- Avoid triggers: alcohol, stress, strenuous exercise, and certain foods (tyramine-rich foods).
- Telotristat (Xermelo) is an oral medication approved to reduce diarrhea when SSAs aren't enough.
- Regular echocardiograms are recommended to monitor heart valve function.
- 5-HIAA and CgA levels are monitored to track hormone output over time.

Monitoring & Follow-Up

NETs are often managed over many years. Regular follow-up allows early detection of changes and ensures your treatment stays optimized.

Lab Tests

- Chromogranin A (CgA) — overall tumor marker
- 5-HIAA (Urine or plasma)— serotonin byproduct
- Hormone levels specific to your tumor type
- Routine metabolic panel and liver function

Imaging Scans

- CT or MRI every 3–12 months (based on tumor behavior) and tumor stage.
- Gallium-68 Dotatate PET scan (somatostatin receptor imaging)
- FDG-PET for higher-grade tumors (NECs).
- Echocardiogram if carcinoid heart disease is a concern

Clinic Visits

- Multidisciplinary team (oncologist, surgeon, radiologist)
- Symptom review and quality of life assessment
- Medication adjustments (SSA dosing, etc.)
- Nutrition and lifestyle counseling as needed

Neuroendocrine Tumors vs. Neuroendocrine Carcinoma

These terms are related but refer to biologically distinct diseases with very different behaviors and treatment approaches.

Neuroendocrine Tumor (NET)

Well-Differentiated | Grade 1–2 (sometimes G3)**

Cell appearance:	Resemble normal neuroendocrine cells; organized structure
Growth rate:	Slow to moderate; Ki-67 typically < 20%
Hormones:	Can be functional — flushing, diarrhea, hypoglycemia
Prognosis:	Often years to decades; many patients live well long-term
Key treatments:	SSAs, PRRT (Lutathera), surgery, everolimus, sunitinib, cabozantinib, CAPTEM

VS

Neuroendocrine Carcinoma (NEC)

Poorly-Differentiated | Grade 3 (high-grade)

Cell appearance:	Poorly organized; small cell or large cell morphology
Growth rate:	Aggressive and rapid; Ki-67 typically > 55%
Hormones:	Non functional; symptoms driven by tumor mass
Prognosis:	More limited; often measured in months without treatment
Key treatments:	Platinum-based chemo (cisplatin/etoposide); immunotherapy

Living Well With NETs

Nutrition

- Eat small, frequent meals
- Limit high-tyramine foods (aged cheeses, cured meats) if symptomatic/ carcinoid syndrome.
- Stay hydrated; replace electrolytes if diarrhea is frequent
- Consider referral to a registered dietitian

Exercise & Activity

- Light to moderate exercise is generally encouraged
- Avoid intense exertion if it triggers flushing
- Consult your team before starting a new program
- Gentle yoga and walking are widely well-tolerated

Living Well With NETs

Mental Health

- A cancer diagnosis causes significant emotional stress
- Anxiety and depression are common — ask for support
- Individual counseling, peer support groups available.

Sexual Health

- Functional NETs can produce hormones that could impact sexual function and libido.
- SSAs can impact libido in both men and women.
- Avoid pregnancy with PRRT >7 months in females and > 4 months in males after completion of treatment.
- Pregnancy is possible with NETs but requires co-management between your OB and Medical Oncologist.

NET and their treatment can impact sexual and mental health. Your concerns are valid, and common, so please speak openly to your physician.

NENs are highly heterogenous

Neuroendocrine tumors (NETs)	Neuroendocrine carcinomas (NECs)
Well differentiated	Poorly differentiated
Can be Functional	Non-Functional

What do you need to know about your new diagnosis ?

- Location of the tumor: GI tract/ Lung/ Pancreas, etc.
- Differentiation: Is it well differentiated NET or poorly differentiated NEC.
- If well differentiated, then what is the tumor grade based on the Ki-67 and mitotic rate.
- Is the tumor functional or not (symptoms and lab workup).
-  What is the stage of my disease (I, II, III or IV).

Common Questions:

Is this hereditary ?

- Majority of NETs are sporadic but about 10-20% can occur in the setting of hereditary cancer syndrome (MEN1 & 2, VHL syndrome, etc.) [1, 2]

Can I still work and travel ?

- Most of the time for patients with well controlled NETs, travel and work is manageable.

Is this cancer ?

- Yes, however, NETs are a form of cancer that could behave differently from other types of cancers.

If its in my pancreas is this pancreatic cancer

- No, Pancreatic NET is biologically different from pancreatic cancer.

If its in the liver, is this liver cancer?

- No, NETs in the liver are metastatic not primary liver cancer and usually treated the same way as NETs.

1- Crona J. et al. Eur J Endocrinol. 2016
2- Papadopoulou-Marketou N et al. Cancers (Basel) 2024

You Are Not Alone in This Journey

A NET diagnosis can feel overwhelming — but many people live well with this condition for years, even decades. With the right care team and support, you can too.

Thank you

Osama MoSalem, MD
Twitter/X: OsamaMoSalemMD

NEUROENDOCRINE CANCER FOUNDATION

BJC Health Saint Luke's

References:

- NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. V3.2025.
- The NANETS Consensus Guidelines for Management of Neuroendocrine Tumors (NETS)-2024.