# Neuroendocrine Neoplasms Reference Handout

# NEN Diagnosis

**Heterogenous tumors can occur anywhere in NE system**

**Common Tumor Sites**
Gastrointestinal
Pancreatic
Thoracic
Adrenal

**Many NENs express somatostatin receptors**

**IHC Markers**
Chromogranin
Synaptophysin
CD56
INSM1

**Standard Imaging**
Endoscopy
CT
MRI
FDG-PET

**Somatostatin Receptor Scans**
Radionuclide PET Scans (Ga-68 or Cu-64 Dotate)
Octreotide Scintigraphy Scan

**Peripheral Blood Tests**

**Chromogranin A:**
Non-specific marker

**Small Intestine Tumors:**
Serotonin, 5HIAA (serum > urine)

**Pancreatic Tumors:**
Hypoglycemia: insulin, proinsulin, c-peptide
Hyperglycemia: glucagon, somatostatin
PUD: gastrin
Diarrhea: gastrin, VIP, somatostatin

**Thoracic Tumors:**
ACTH, cortisol

**Adrenal Tumors:**
ACTH, cortisol, renin, aldosterone, testosterone, DHEA, plasma/24-urine metanephrines

# Carcinoid Syndrome

**Neuroendocrine cells of GI tract secrete serotonin**
**Occurs in NENs of midgut origin**
(small intestine, appendix, ascending colon)
Often with hepatic metastases

**tryptophan → serotonin → 5HIAA**

**Symptoms**

**Watery Diarrhea**
**Flushing**
**Wheezing/Bronchospasm**
**Hypotension**
**Palpitations**
**Right-sided heart disease (TR, PS)**
**Retroperitoneal Fibrosis**

* Low niacin/B3 from tryptophan consumption can cause pellagra (dermatitis, diarrhea, dementia)

**Management**

**Telotristat**
Inhibits serotonin production

**Somatostatin Analogues**
Inhibits hormone secretion
* Octreotide HD IV or gtt if carcinoid crisis

**Cardiac Monitoring**
TTEs Q6-12 months

# NEN Grading

**Low Grade/Well-differentiated Cancers = Neuroendocrine Tumors (NETs)**

**High Grade/Poorly-differentiated Cancers = Neuroendocrine Carcinomas (NECs)**

| GI NENs | Differentiation | Mitotic Count (per 10 HPF) | Ki-67 Index |
|---|---|---|---|
| (G1) Low Grade | Well Differentiated | <2 | < 3% |
| (G2) Intermediate Grade | Well Differentiated | 2-20 | 3-20% |
| (G3) High Grade | Well Differentiated | >20 | > 20% |
| High Grade NEC | Poorly Differentiated | >20 | > 20% |
| High Grade NEC | Poorly Differentiated | >20 | > 20% |

| Thoracic NENs | Grade | Typical Characteristics | Mitotic Count (per 10 HPF) |
|---|---|---|---|
| Typical Carcinoid | (G1) Low Grade | Central | <2 |
| Atypical Carcinoid | (G2) Intermediate Grade | Peripheral<br>+ Smoking<br>+ Paraneoplastic | <2 – 10<br>(or necrosis) |
| Large Cell NEC | (G3) High Grade | Peripheral<br>+ Smoking | >10 |
| Small Cell NEC | (G3) High Grade | Hilar/Perihilar<br>+ Smoking<br>++ Paraneoplastic | >10 |

# Pancreatic NENs

| NEN | Secreted Product | Presentation |
|---|---|---|
| Insulinoma | Insulin | hypoglycemia (Whipple's Triad), hypokalemia |
| Gastrinoma | Gastrin | Zollinger-Ellison Syndrome:<br>Severe PUD |
| VIPoma | VIP<br>Vasoactive intestinal polypeptide | Verner-Morrison Syndrome:<br>watery diarrhea, hypokalemia, achlorhydria |
| Glucagonoma | Glucagon | DM, dermatitis, DVT, depression |
| Somatostatinoma | Somatostatin | cholelithiasis, hyperglycemia, steatorrhea |
| PPoma | PP<br>Pancreatic polypeptide | No syndrome |

# Adrenal NENs

**Adrenal NENs can be functional or non-functional**

## Cushing's Syndrome

**Labs:**
ACTH (low)
Cortisol (high)

**Presentation:**
Hypertension
Hypokalemia
Metabolic alkalosis
Hyperglycemia

## Conn's Syndrome

**Labs:**
Renin (low)
Aldosterone (high)

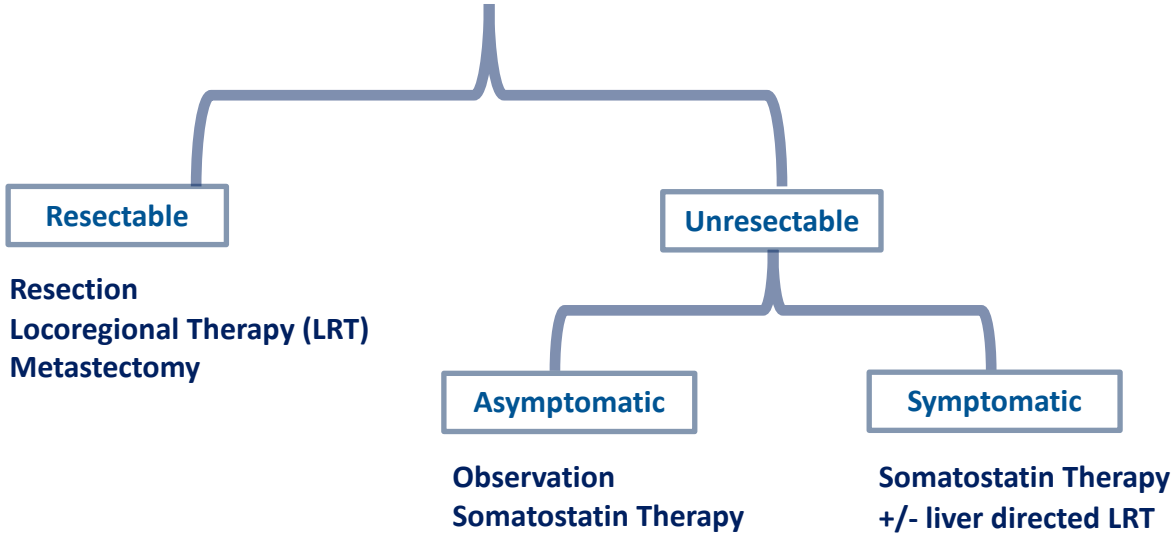
**Presentation:**
Hypertension
Hypokalemia

## Pheochromocytoma

**Labs:**
Serum metanephrines (high)
Urine metanephrines (high)

**Presentation:**
Hypertension
Headache
Sweating
Tachycardia

## Low/Intermediate Grade NEN Front-Line Treatment




**Resection**
**Locoregional Therapy (LRT)**
**Metastectomy**

**Observation**
**Somatostatin Therapy**

**Somatostatin Therapy**
**+/- liver directed LRT**

## Somatostatin Analogue Therapy

**Somatostatin analogues target the somatostatin receptor that is present on the majority of NENs**

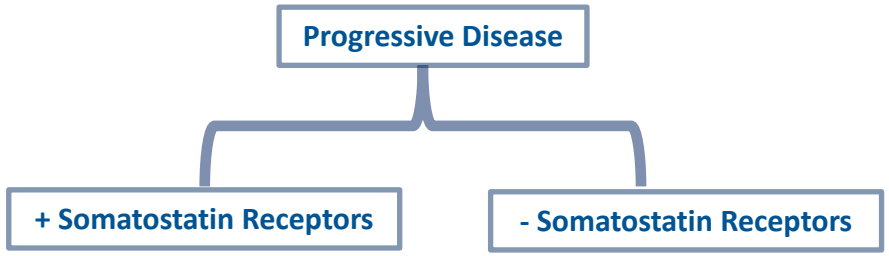
**Somatostatin Receptor Localization**
Radionuclide PET scans (Ga-63 or Cu-64) are required to confirm presence of somatostatin receptors

**Somatostatin Function**
(1) inhibits secretion of many hormones
(2) controls tumor growth

**Octreotide = intermediate-acting** (BID dosing)
**Lanreotide = long-acting** (monthly dosing)

**** Pre-surgery:*** *Consider octreotide pre/post surgery to prevent carcinoid crisis*

## Low/Intermediate Grade NEN Second-Line Treatment




**PRRT**
**Everolimus**
* Capecitabine/Temozolamide

**Everolimus**
* Capecitabine/Temozolamide

## High Grade NEN Treatment

**Chemotherapy**

**Carboplatin/Etoposide**

Capecitabine + Temozolamide
FOLFOX
FOLIRI

* Ki-67 < 55% are less responsive to chemo