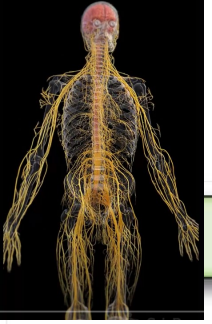
NEUROENDOCRINE CANCERS

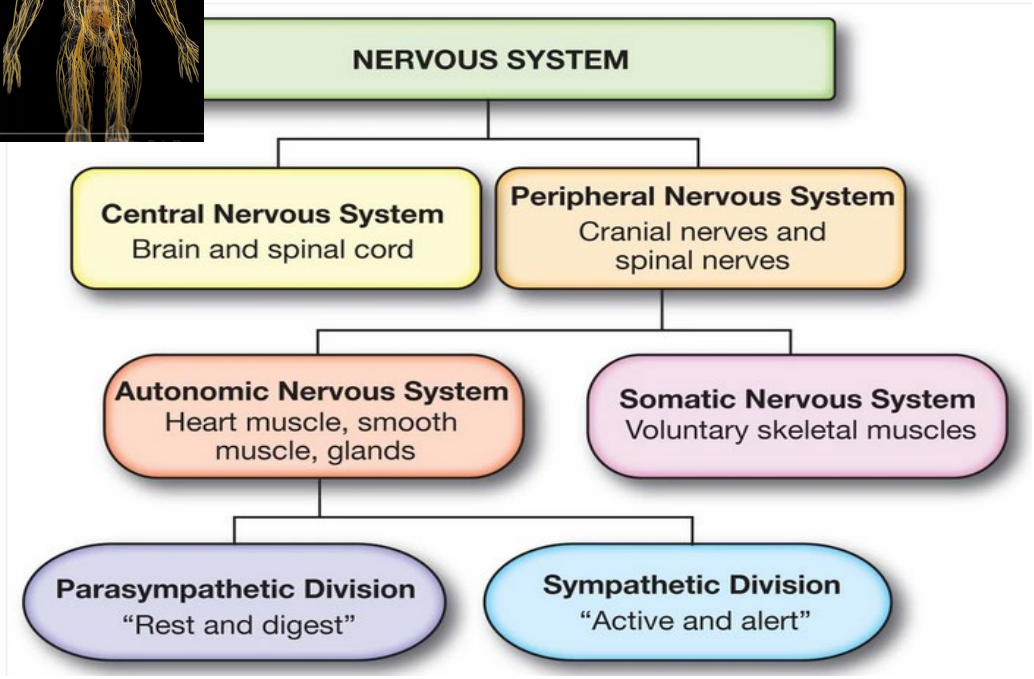
BETTY MALANOWSKI

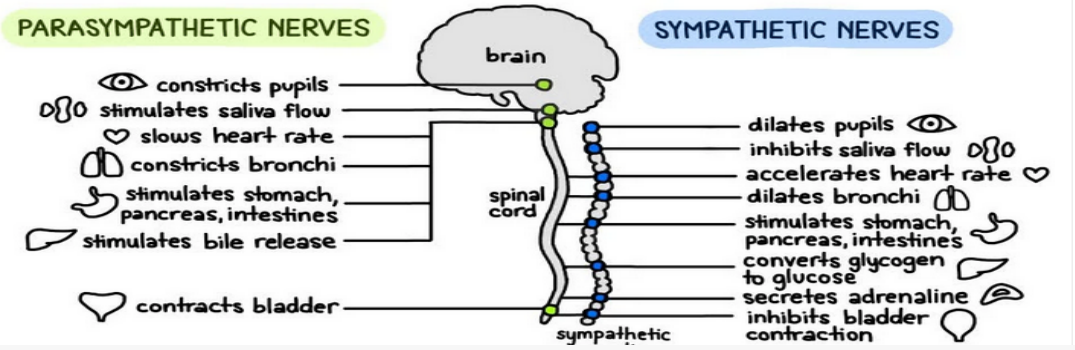
Oct 29, 2025



NEUROENDOCRINE

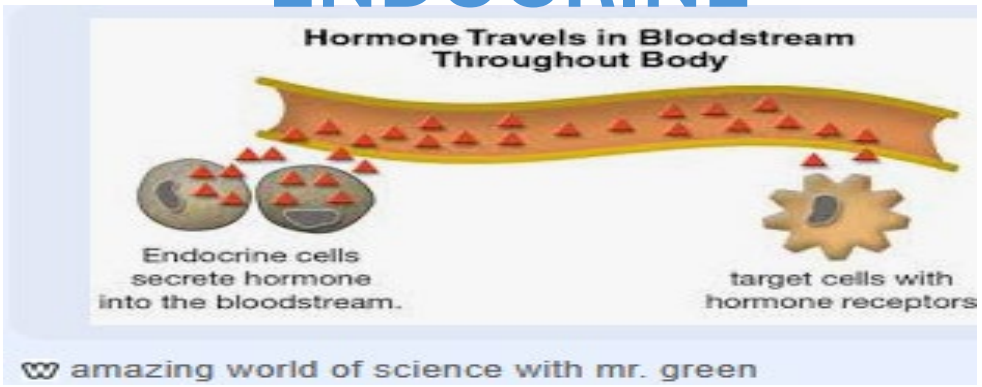
BETTY MALANOWSKI
Oct - 2025





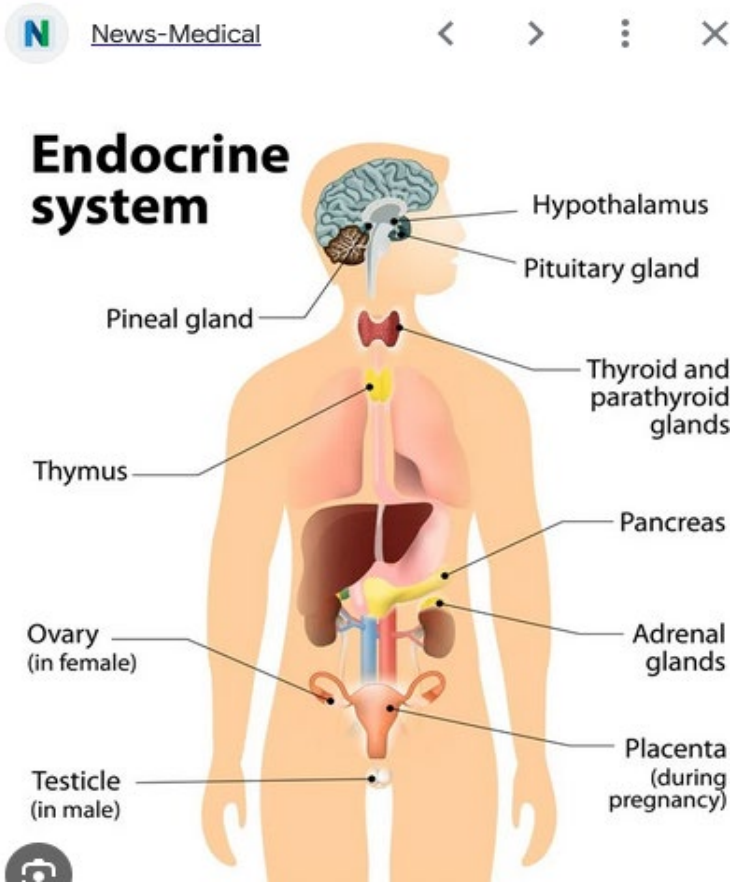
Neuroendocrine tumors (NETs) are rare neoplasms predominantly arising in the gastrointestinal-tract or the lungs of adults. To date, only ten cases of primary central nervous system (CNS) NETs have been reported, with just three of them describing a neuroendocrine carcinoma (NECA) and none occurring in a child. We report on a previously healthy 5-year-old

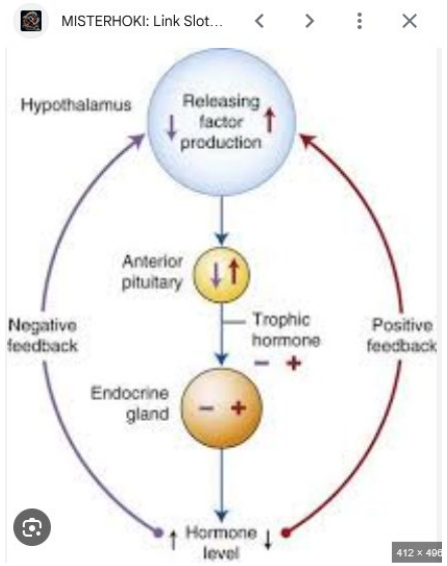
ENDOCRINE



DIFFERENCE between ENDOCRINE system and **NEURO**ENDOCRINE system

The endocrine system is made up of **glands**, while the neuroendocrine system is made up of **nerves** and **glands**.





The endocrine system is **SLOW** and LONG **LASTING**. Responsible for long-term bodily functions like growth, metabolism, and reproduction.

•A system of nerves and gland cells that produce and release hormones

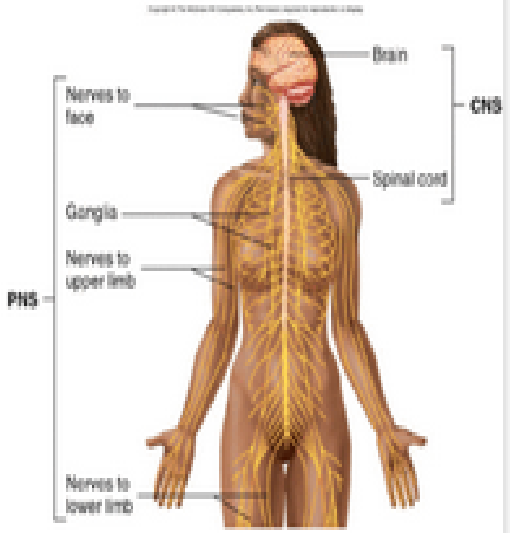
The Neuroendocrine System

(homeostasis control)

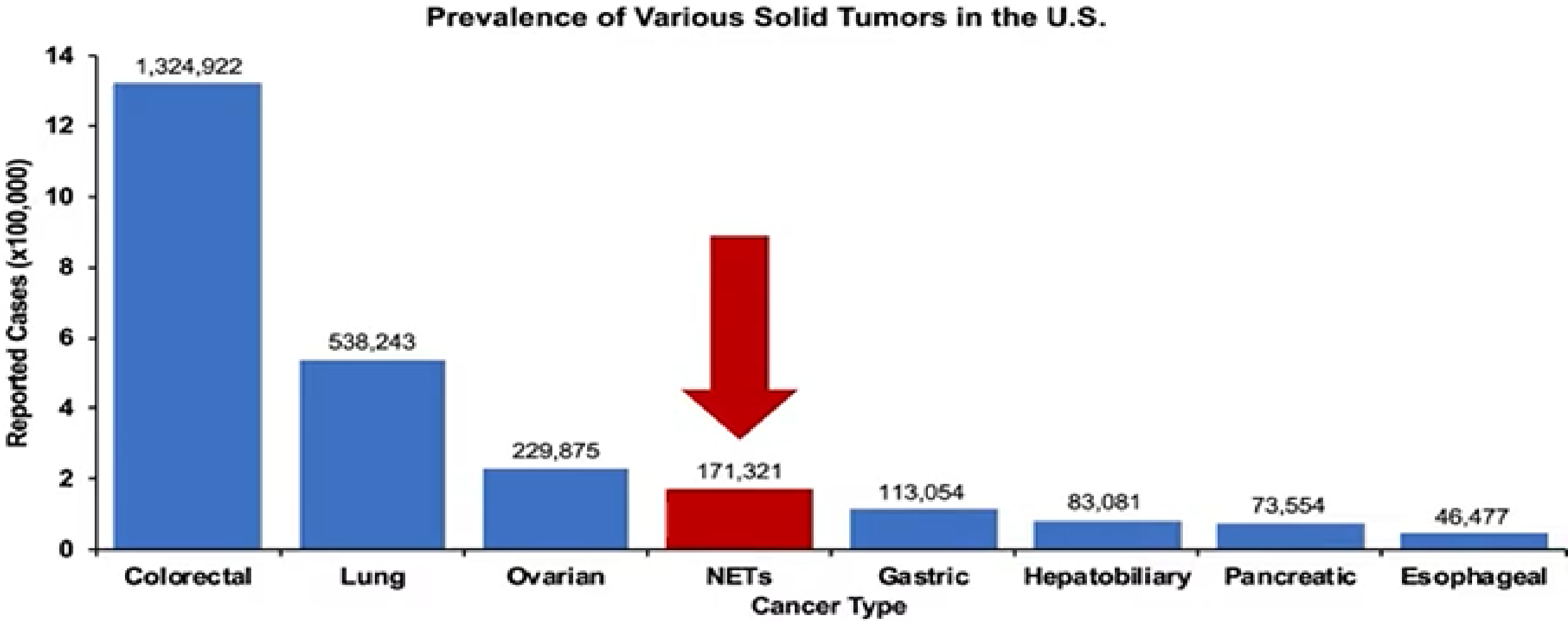
Nervous system (rapid & transient)

- Central
- Peripheral
  - Somatic: voluntary
  - Autonomic: involuntary

Endocrine system (slow & long lasting)

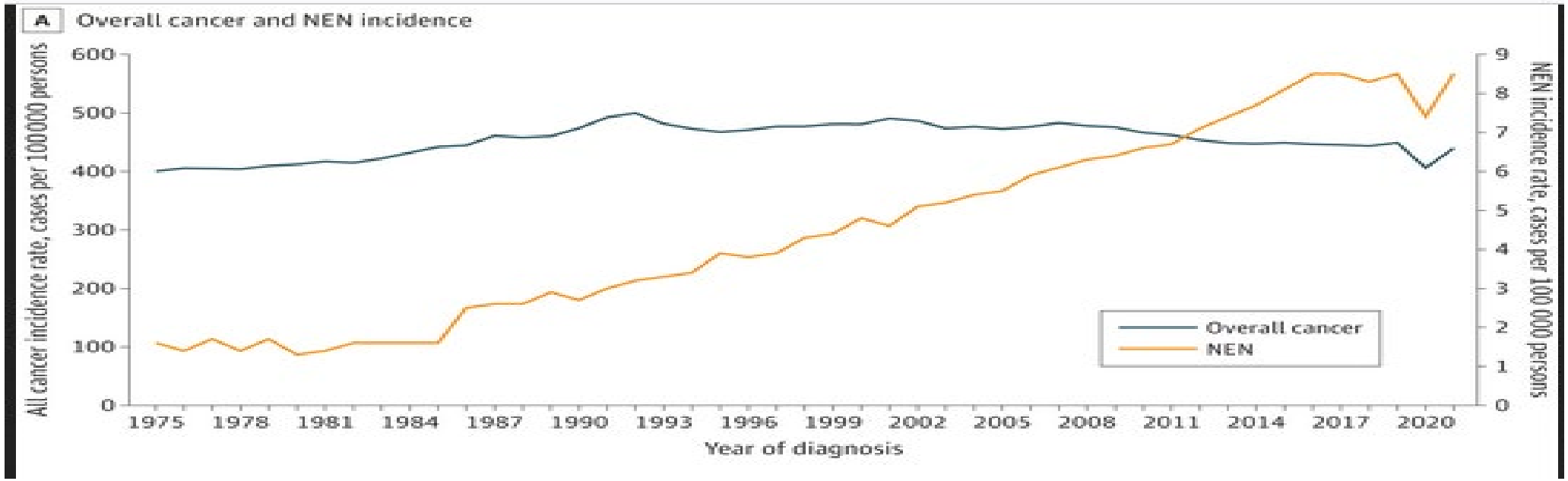


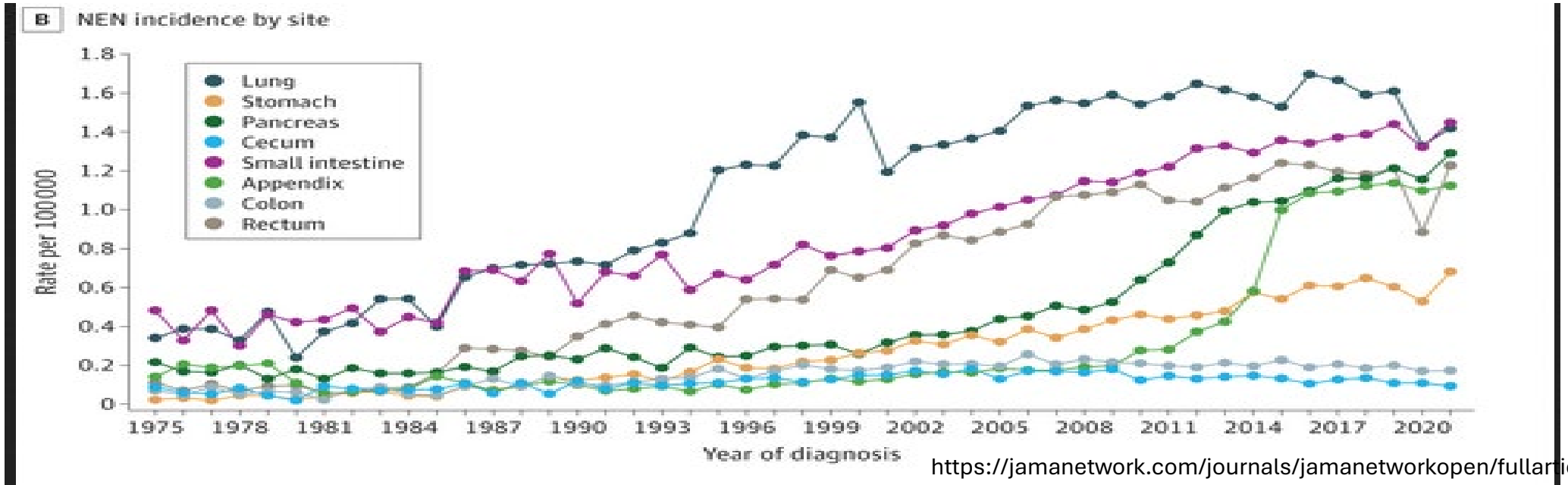
The neuroendocrine system receives messages from the nervous system and responds by releasing hormones.



Chauhan et. Al JAMA Onc 2019

NEN (Neuroendocrine Neoplasms in the USA)



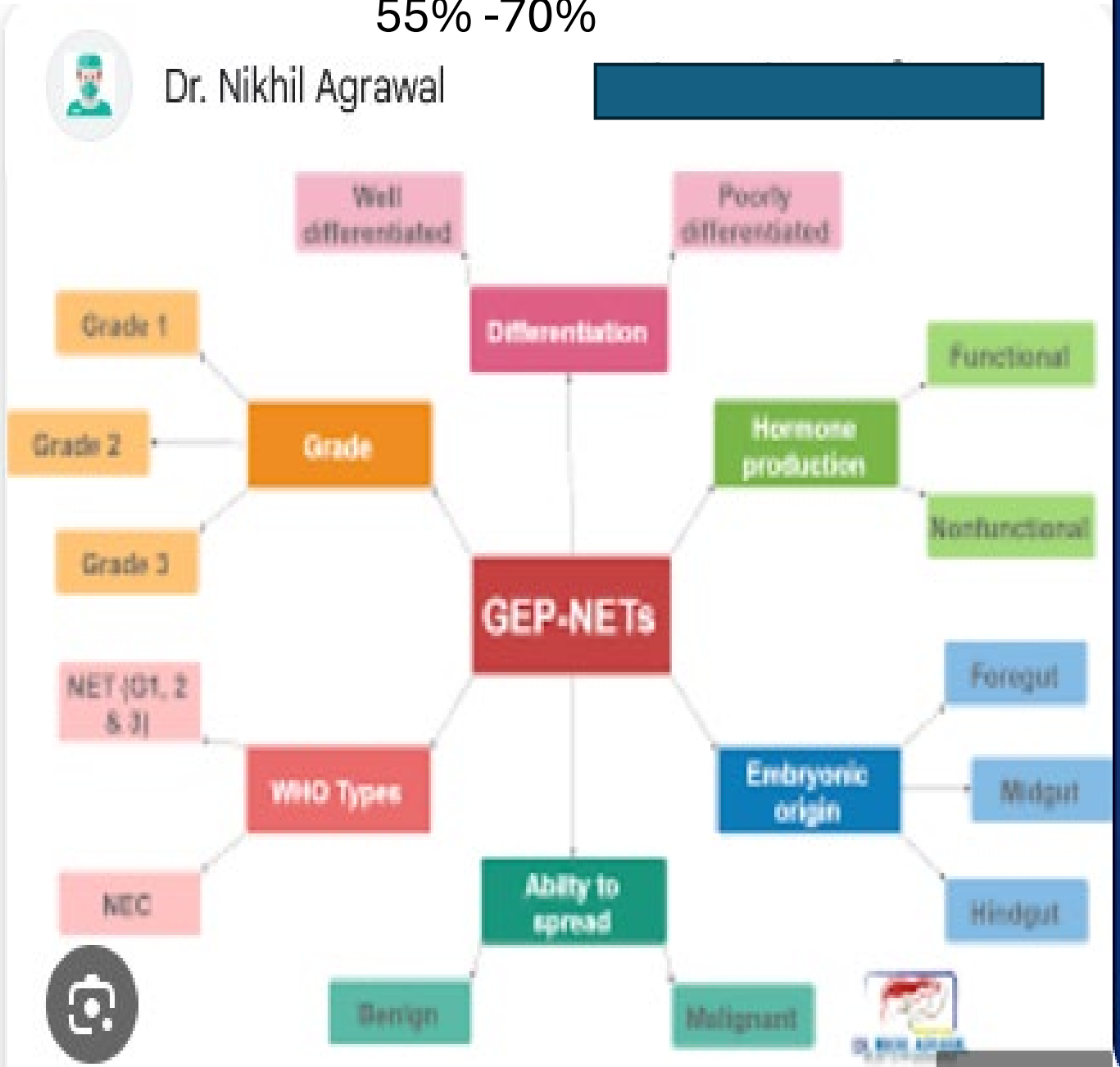


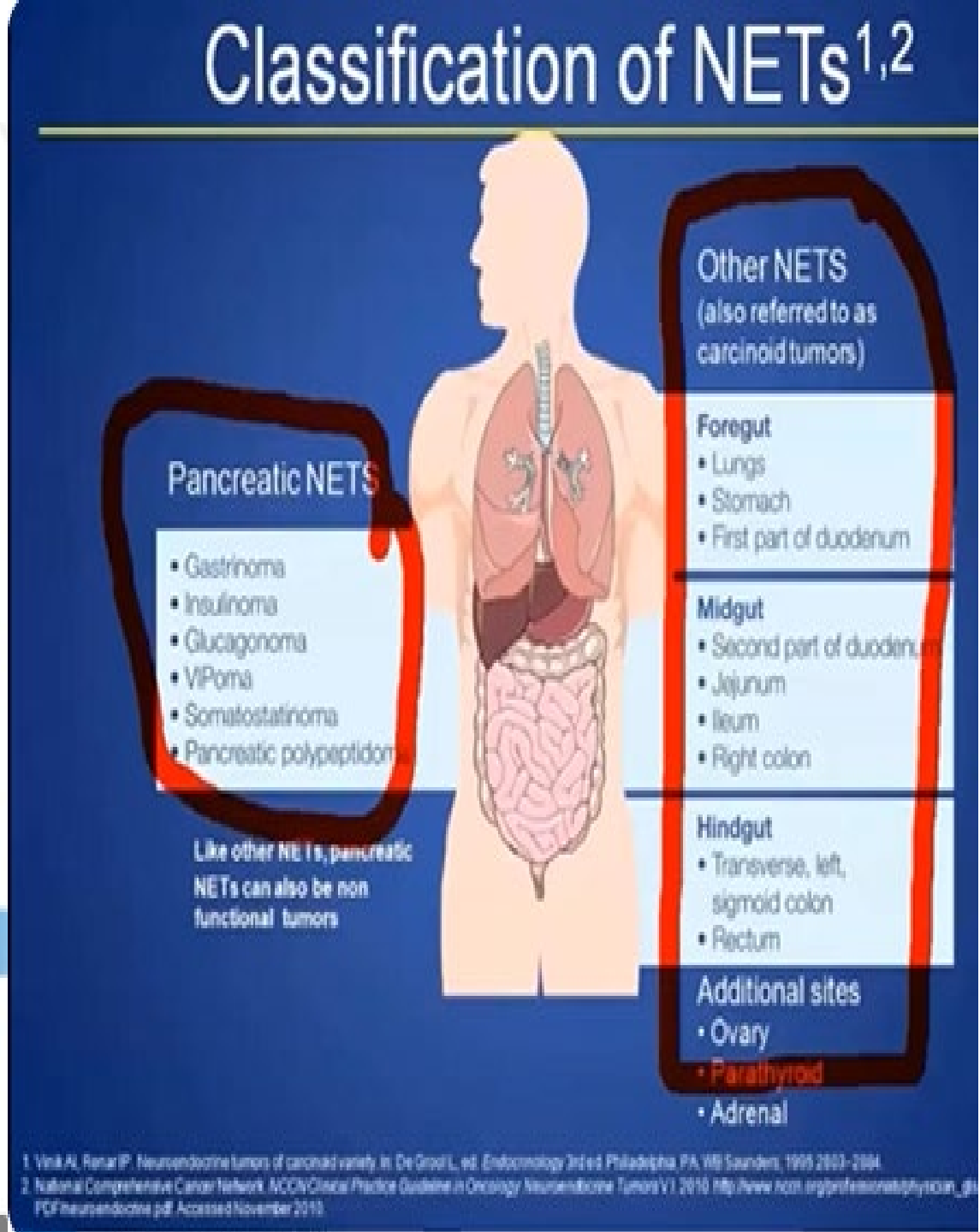
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2835520

Gastroenteropancreatic NETs

55% -70%

Dr. Nikhil Agrawal





classification, staging criteria, patient outcomes, diagnostics, and therapeutic drug

The new (Version 9) American Joint

Neuroendocrine Neoplasms (NEN)

Neuroendocrine Tumor (NET)

Well Differentiated

Grade 1	Grade 2	Grade 3
Ki 67 <3%	Ki 67 3-20%	Ki 67 >20%
MR <2 mitoses/2mm^2	MR 2-20 mitoses/2mm^2	MR >20 mitoses/2mm^2

Neuroendocrine Carcinoma (NEC)

Poorly Differentiated
Small Cell
Large Cell

Grade 3
Ki 67 >20%
MR >20 mitoses/2mm^2

*MR = mitotic rate

https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21840

Neuroendocrine system and NENs sites

Composed of:

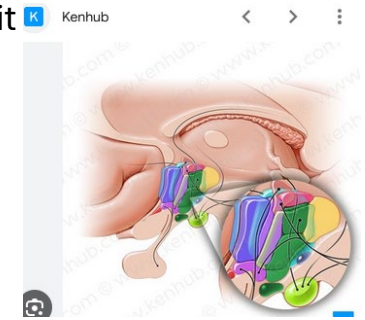
-CENTRAL COMPONENTS

- Hypothalamus
- Pituitary
- Adrenal glands

The HYPOTHALAMUS is the **neural control center** for all the **endocrine AND NEUROENDOCRINE** system. It is also considered a major endocrine organ because it produces several hormones.

The hypothalamus regulates temperature, water balance and thirst, sex drive , aggression…

The Pituitary gland is the MASTER gland



-DISPERSED NEUROENDOCRINE CELLS found in most glands throughout the body

- HEAD AND NECK (Salivary Glands…)
- GASTROINTESTINAL (Esophagus, Stomach, Small Intestine (Duodenum, Jejunum and Ileum), Ampulla of Vater, Appendix, Anus, Colon and Rectum
- Other sites: Pancreas, Breast, Lung, Thyroid, Thymus TESTIS, Ovaries (LCNEC), Pineal, Parathyroid, Skin, Bladder…

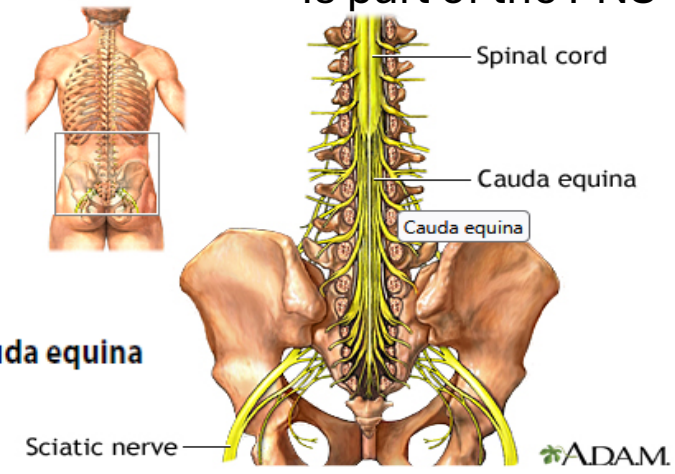
Malignant CNS and Peripher
C470-C479, C700, C701, C709, C
(Excludes lymphoma and leukemi

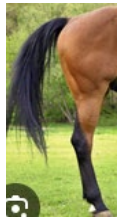
Table 3: Specific Histo

Specific and NOS Histology Codes	Synonyms
Anaplastic ganglioglioma 9505	
Astroblastoma 9430	Astroblastoma, M
Astrocytoma NOS 9400	Astrocytoma, IDH Diffuse astrocytom Diffuse astrocytom Diffuse astrocytom
Cauda equina neuroendocrine tumor 8693/3 *Note:* This neoplasm is coded with /3 behavior even though it is a WHO Grade 1.	

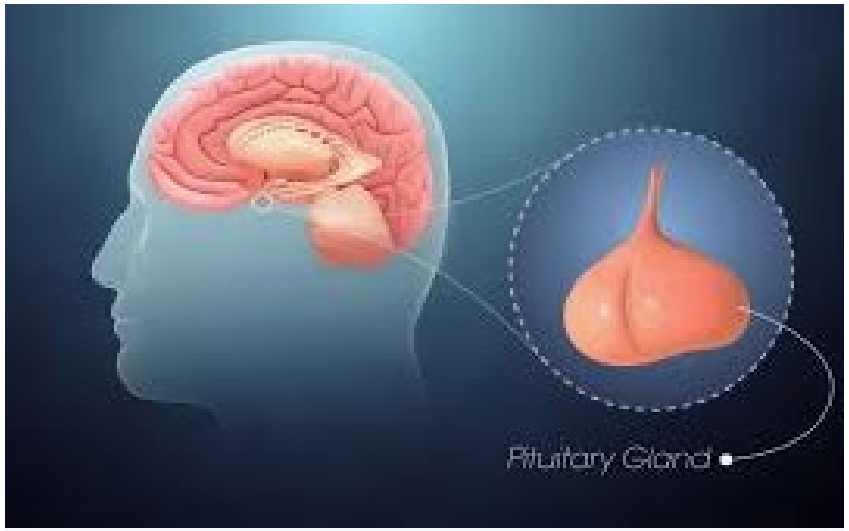
Cauda equina

Is part of the PNS





PitNET



Scientific Animations

2. From Adenoma to Pituitary Neuroendocrine Tumor (PitNET): Evolution Not Revolution

A classification of the pituitary tumor has been changed to neuroendocrine tumors, rather than organ-specific classification [4]. In the WHO Classification of Central Nervous System Tumors, 5th edition released in 2021, "pituitary adenoma" was incorporated under the same entry as "PitNET." In the WHO Classification of Endocrine and Neuroendocrine Tumors 5th edition released in 2022, it is listed as "PitNET/pituitary adenoma." The adenohypophysis is composed of at least six

morbidity in patients. "Invasive adenoma" is therefore an oxymoron. A panel of experts of the WHO/IARC also proposed to include pituitary tumors in "neuroendocrine neoplasms" (NEN), which divided into the neuroendocrine carcinomas (NEC) for aggressive, poorly differentiated tumors and the neuroendocrine tumors (NET) for the well differentiated, and generally low-grade neoplasms [6]. Although a large majority of PitNETs will behave as well differentiated, benign neoplasms, we believe that this terminology can only impact positively on clinical practice as it reflects more closely the variability of behavior of pituitary tumor (invasiveness linked to a higher risk of recurrence) and may open up new

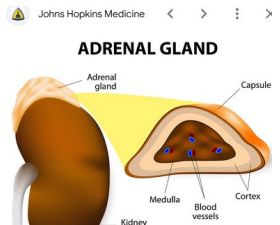
https://pmc.ncbi.nlm.nih.gov/articles/PMC7072139/

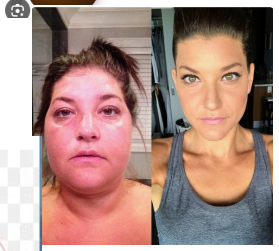
Pituitary adenoma/pituitary neuroendocrine tumor 8272/3	PitNET

Table 1: 2023 ICD-O-3.2 Update (Numerical)

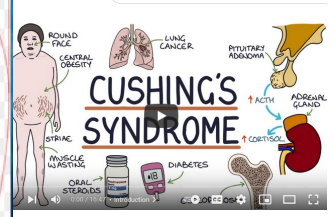
8272/3	Pituitary adenoma/pituitary neuroendocrine tumor (PitNET) **(C75.1)**	Y	Y	Y	Y	New term. Per WHO, both terms may be used in the diagnosis or pituitary neuroendocrine tumor, or PitNET. All are coded 8272/3. Pituitary adenoma, NOS is coded 8272/0

Pituitary Tumor

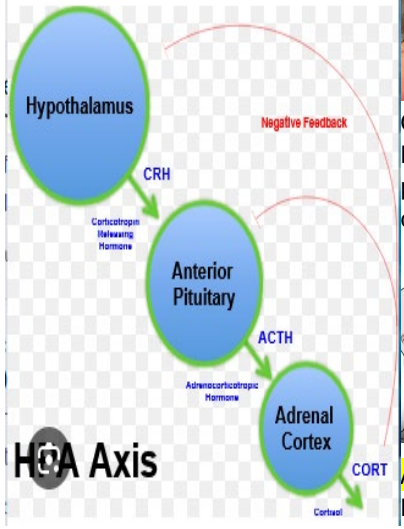




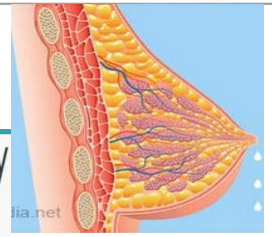
Cushing disease: Pituitary adenoma producing excess of Cortisol



Aldosterone producing Adenomas: Hypertension and low potassium .



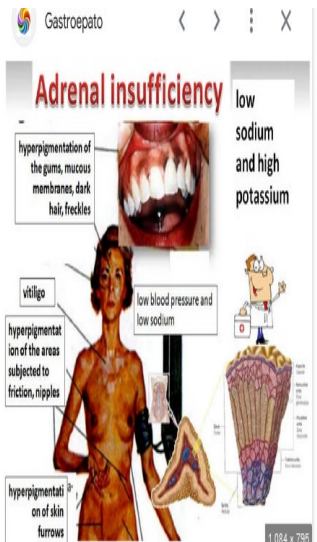
HYPERTHYROIDISM
Thyroid tumor
Accelerated metabolism:
-Tachycardia
-Diarrhea
-Heat intolerance
-Weight loss...



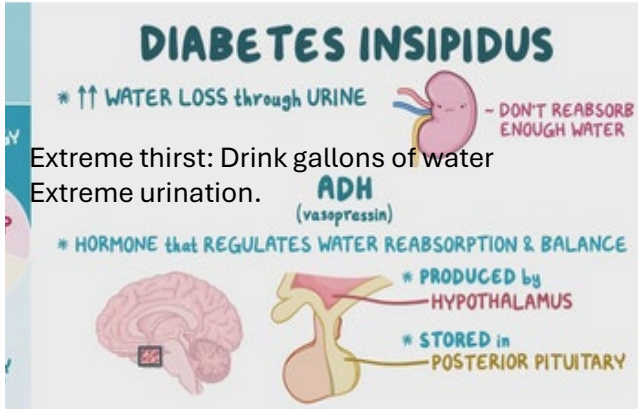
- Milky Nipple

Galactorrhea

More **ACTH** leads to increased production of **MSH Melanocyte stimulating hormone**.
Hyperpigmentation of skin in Adrenal Insufficiency in some adrenal tumors,
Always craving salt bc sodium is low



Oxytocin stimulates contractions for sperm transport.



Extreme thirst: Drink gallons of water
Extreme urination.

SKIN Neuroendocrine: Merkel cell carcinoma

Merkel cell carcinoma is a cutaneous neuroendocrine CARCINOMA

Merkel cells are localized in the EPIDERMIS. And they have characteristics of both nerve cells and endocrine cells.

Merkel cells are mechanoreceptors for touch and pressure .They are located in the **basal** layer of the **epidermis**. They produce Norepinephrine which communicate with sensory neurons. Also, produce Serotonin, VIP, and Neuropeptide (calcitonin gene related peptide, substance P) .

Merkel cell carcinoma is aggressive and it

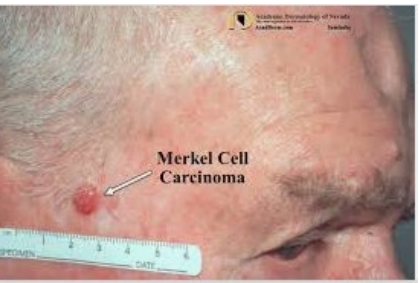
can metastasize to LNs, lung, bones, brain.

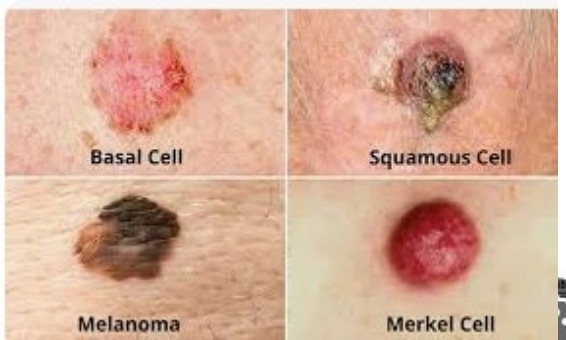
Early detection is important!

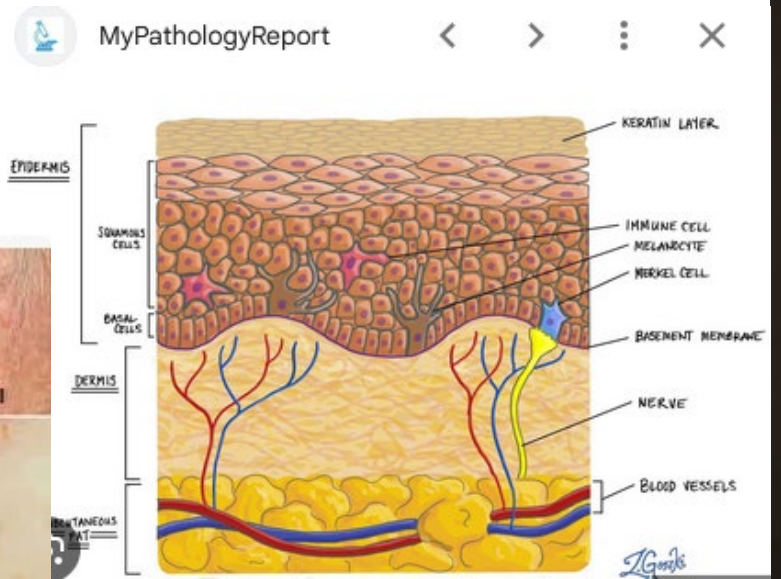
a type of skin cancer, but it's not common. About 3,000 people are diagnosed with Merkel cell carcinoma in the United States each year.

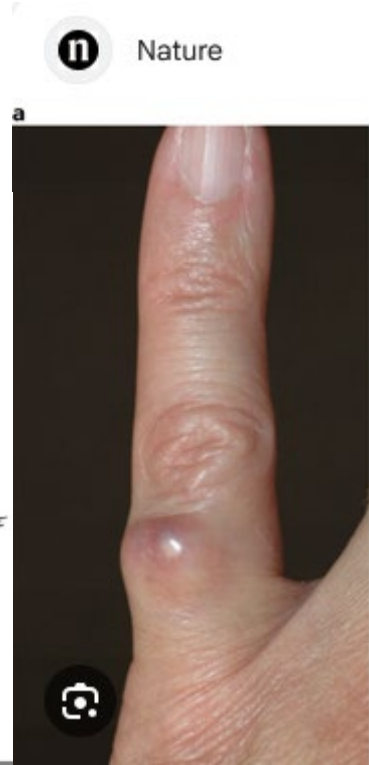
The number of people diagnosed with Merkel cell carcinoma each year has been rising quickly over the past few decades. This is in part because of an increased awareness of this cancer, but it might also be due to an increase in risk factors. For instance, people are living longer, and more people are living with weakened immune systems (from previous treatment for cancer or other medical conditions).

- Most Americans diagnosed with Merkel cell carcinoma are older than age 70.
- Men are more likely to have MCC than women.
- More than 9 out of 10 Americans diagnosed with Merkel cell carcinoma are White people.



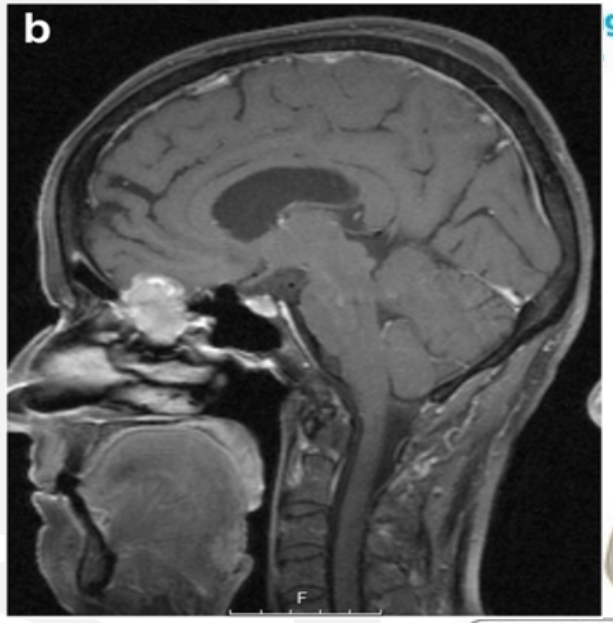


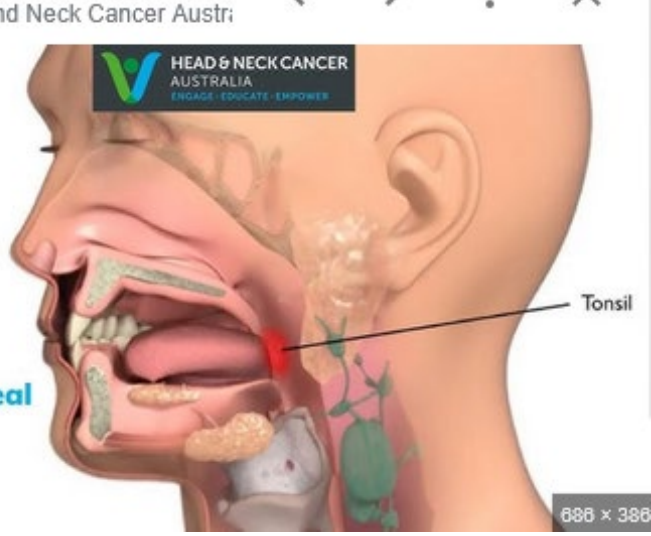




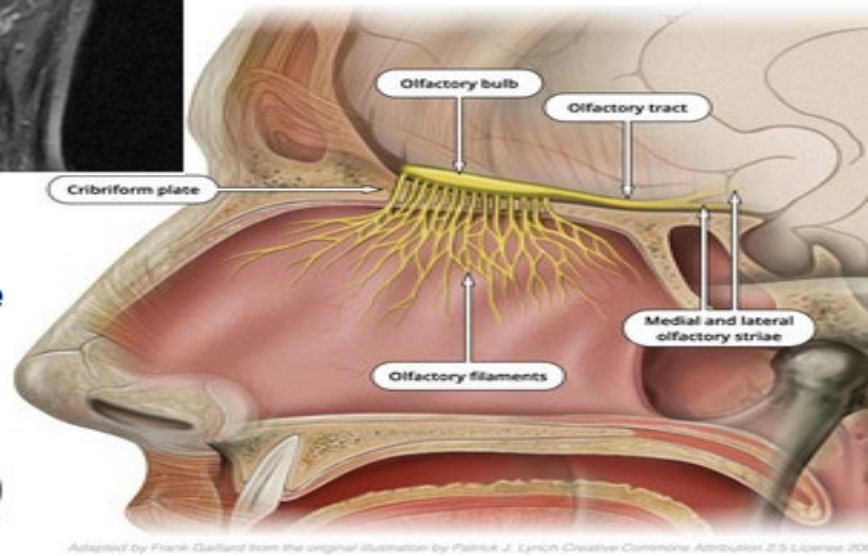
HEAD AND NECK NEUROENDOCRINE CA

- Small percentage: **0.3%** of all H&N Cancers.
- Neuroendocrine cancers from other sites may metastasize to H&N
- Some types:
  - EPITHELIAL (WD Carcinoids, MD Atypical Carcinoids, PD Small Cell C, SCNEC)
  - NEURAL (**Paragangliomas** and Olfactory Neuroblastomas)
  - MERKEL CELL
  - MIXED NEC
- Prompt Treatment as **airway obstruction** is life-threatening not to mention the aggressiveness
- Usually very aggressive with poor prognosis





geal



C72.2 Olfactory nerve

Olfactory neuroblastoma 9522/3	Esthesioneuroblastoma Olfactory placode tumor ONB	Esthesioneurocytoma 9521/3 Esthesioneuroepithelioma/Olfactory neuroepithelioma 9523/3

Olfactory neuroblastoma | Radiology

HEAD AND NECK (**SALIVARY GLANDS**)

- Neuroendocrine carcinomas are uncommon in salivary glands.
- Aggressive Nature with a poor prognosis. Treatment usually chemo-radiation.
- Most frequent types:
  - **small** cell neuroendocrine carcinomas (SC**NEC**)
  - **large** cell neuroendocrine carcinomas (LC**NEC**).
- Diagnosis: A definitive diagnosis is only possible with a histopathological examination and immunohistochemistry to confirm neuroendocrine differentiation using markers like CD56, synaptophysin, and chromogranin.

- Location: The **majority** of these primary **NECs arise in the parotid gland**, with a smaller proportion in the submandibular gland.

- Merkel cell carcinoma of the **submandibular** **salivary gland** (not just from skin origin). Although MCC can also arise in the parotid gland.

Salivary gland Neuroendocrine cancers

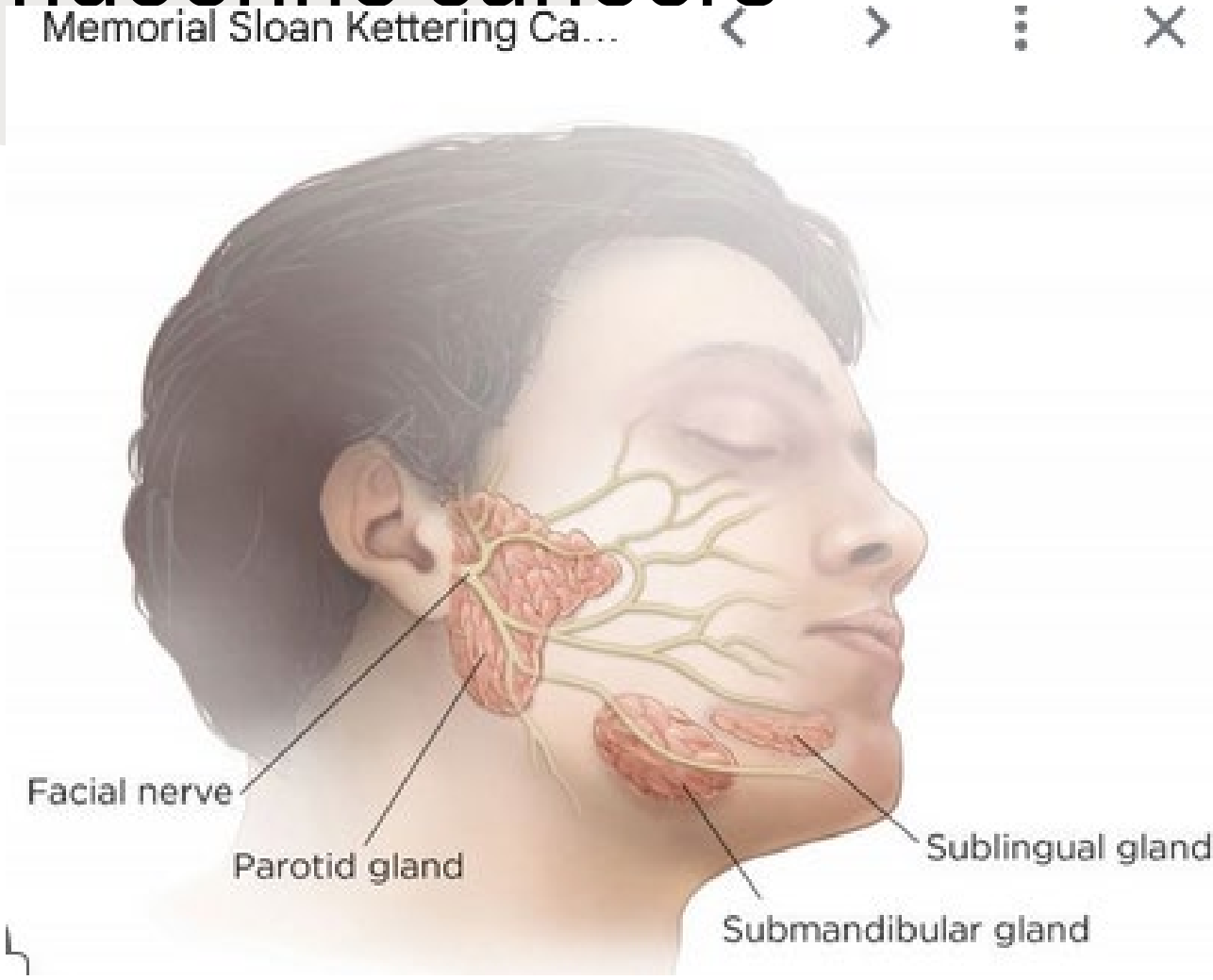
PRIMARY NECs (**N**euro**e**ndocrine **C**arcinomas) are rare 1-3% or less of major salivary gland malignancies.

- arise mainly in the PAROTID gland (3/4)
- others in the SUBMANDIBULAR gland.

Initially painless palpable mass or lump, then pain, facial weakness or numbness.

They are aggressive!

Tx: Surgery, chemotherapy, Radiation.



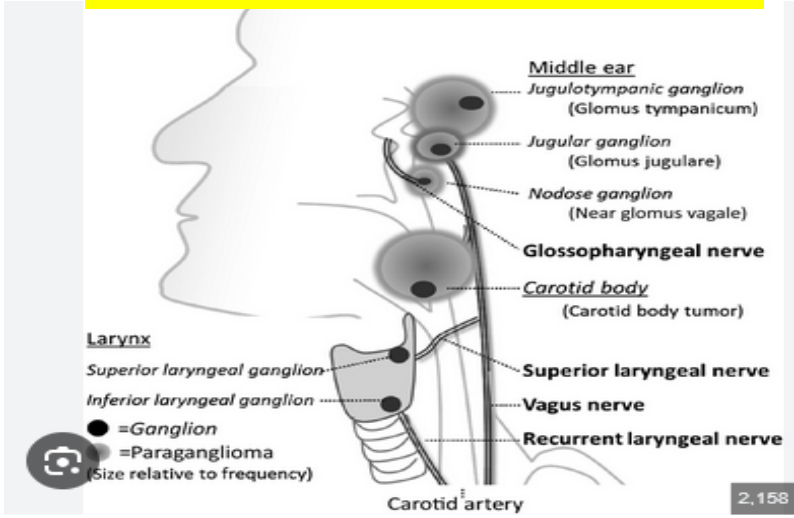
-Merkel cell carcinoma
-Small cell neuroendocrine carcinoma
-Large cell neuroendocrine carcinoma

H&N Paragangliomas

Head and Neck Equivalent Terms and Definitions
C000-C148, C300-C339, C410, C411, C479, C754, C755
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Table 9: Paraganglioma of Carotid Body, Extra-adrenal, Larynx, Middle Ear, Vagal Nerve

Specific or NOS Term and Code	ICD-O Code DX prior to 1/1/2021 *Must be stated to be malignant*	ICD-O Code DX 1/1/2021 forward *"Malignant" no longer required to assign /3*	Synonyms (Per ICD-O-3.2)
Aortic body paraganglioma (C75.5)	8691/3	8691/3	Aortic body tumor Aorticopulmonary paraganglioma
Carotid body paraganglioma (C75.4)	8692/3	8692/3	Carotid body tumor
Extra-Adrenal paraganglioma, NOS	8693/3	8693/3	Nonchromaffin paraganglioma, NOS Chemodectoma Composite paraganglioma
Laryngeal paraganglioma	8690/3	8693/3	
Middle ear paraganglioma (C75.5)	8690/3	8690/3	Glomus jugulare tumor Jugular Jugulotympanic paraganglioma
Paraganglioma, NOS	8680/3	8680/3	
Parasympathetic paraganglioma	8682/3	8682/3	
Sympathetic paraganglioma	8681/3	8681/3	
Vagal paraganglioma *Note:* Vagal paraganglioma has the same histology code as laryngeal paraganglioma. Extra-adrenal, laryngeal and vagal are in separate rows to emphasize primary site.	8690/3	8693/3	

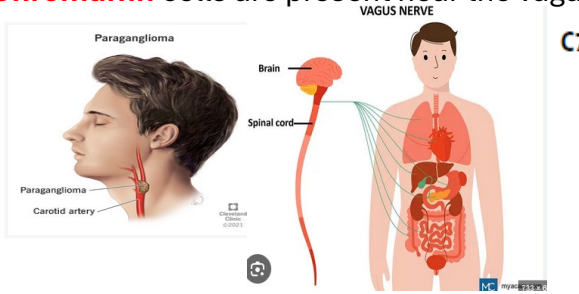


CHROMAFFIN cells are NEUROENDOCRINE **FUNCTIONAL** cells in close proximity with SYMPATHETIC GANGLIA, and they communicate to release catecholamines (Adrenaline, Noradrenaline) Hypertension, tachycardia, headaches, sweating.

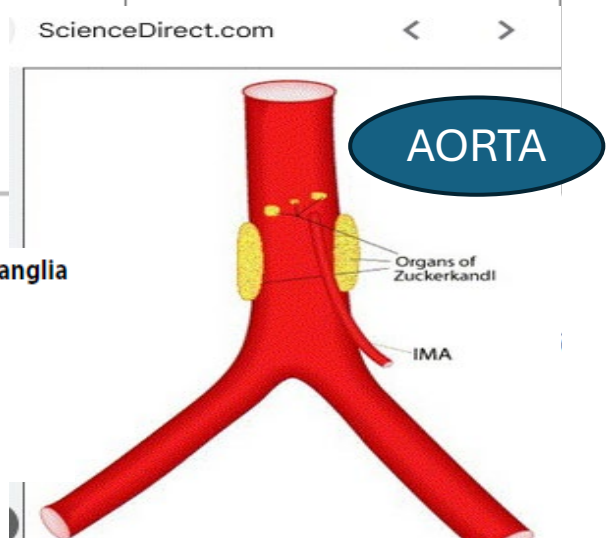
Chromaffin cells migrate to the area adjacent to the sympathetic ganglia (hence paraganglia), and to the ADRENAL MEDULLA.

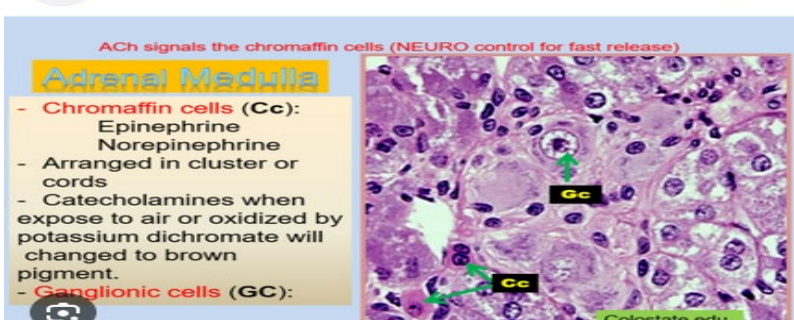
NONCHROMAFFIN NON-FUNCTIONAL paragangliomas from parasympathetic paraganglia and do not secrete hormones.

Chromaffin cells are present near the vagus nerve and carotid arteries.



C75.5 Aortic body and other paraganglia
Coccygeal body
Coccygeal glomus
Glomus jugulare
Para-aortic body
Organ of Zuckerkandl
Paraganglion





1/1/2021 Before and After

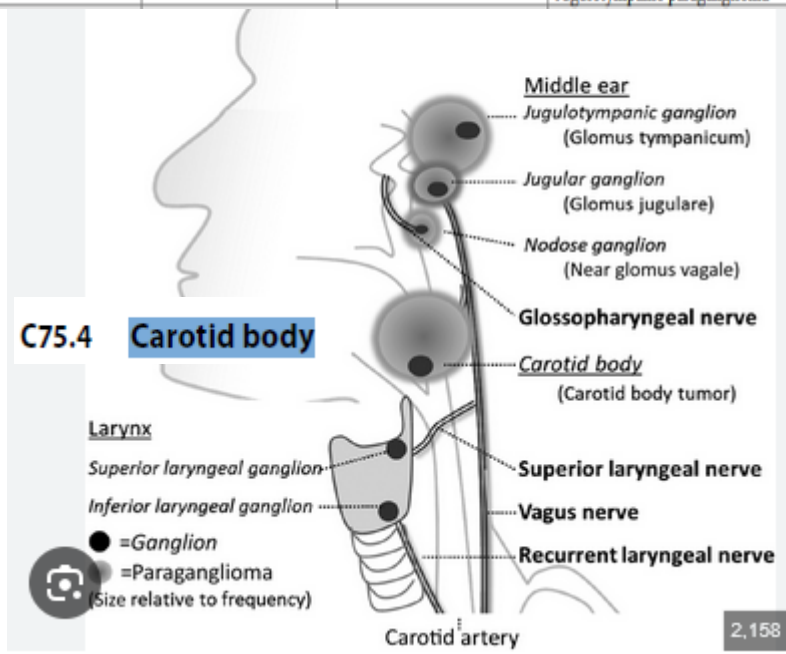
Middle ear paraganglioma (C75.5)	8690/3	8690/3	Glomus jugulare tumor Jugular Jugulotympanic paraganglioma

Table 9: Paraganglioma of Carotid Body, Extra-adrenal, Larynx, Middle Ear, Vagal Nerve

Table 9 lists codes for paragangliomas diagnosed prior to 1/1/2021 and new codes for cases diagnosed 1/1/2021 forward. Table 9 does not list all paragangliomas, only those common to head and neck sites.

Cases diagnosed prior to 1/1/2021:
Only report these neoplasms when the pathology/tissue specifies malignant (/3) behavior. Change the behavior using ICD-O-3 Rule F Matrix Concept.

Cases diagnosed 1/1/2021 forward:
The term "malignant" is no longer required to assign malignant (/3) behavior. Paragangliomas diagnosed 1/1/2021 or after are malignant unless otherwise stated by the pathologist.



2026

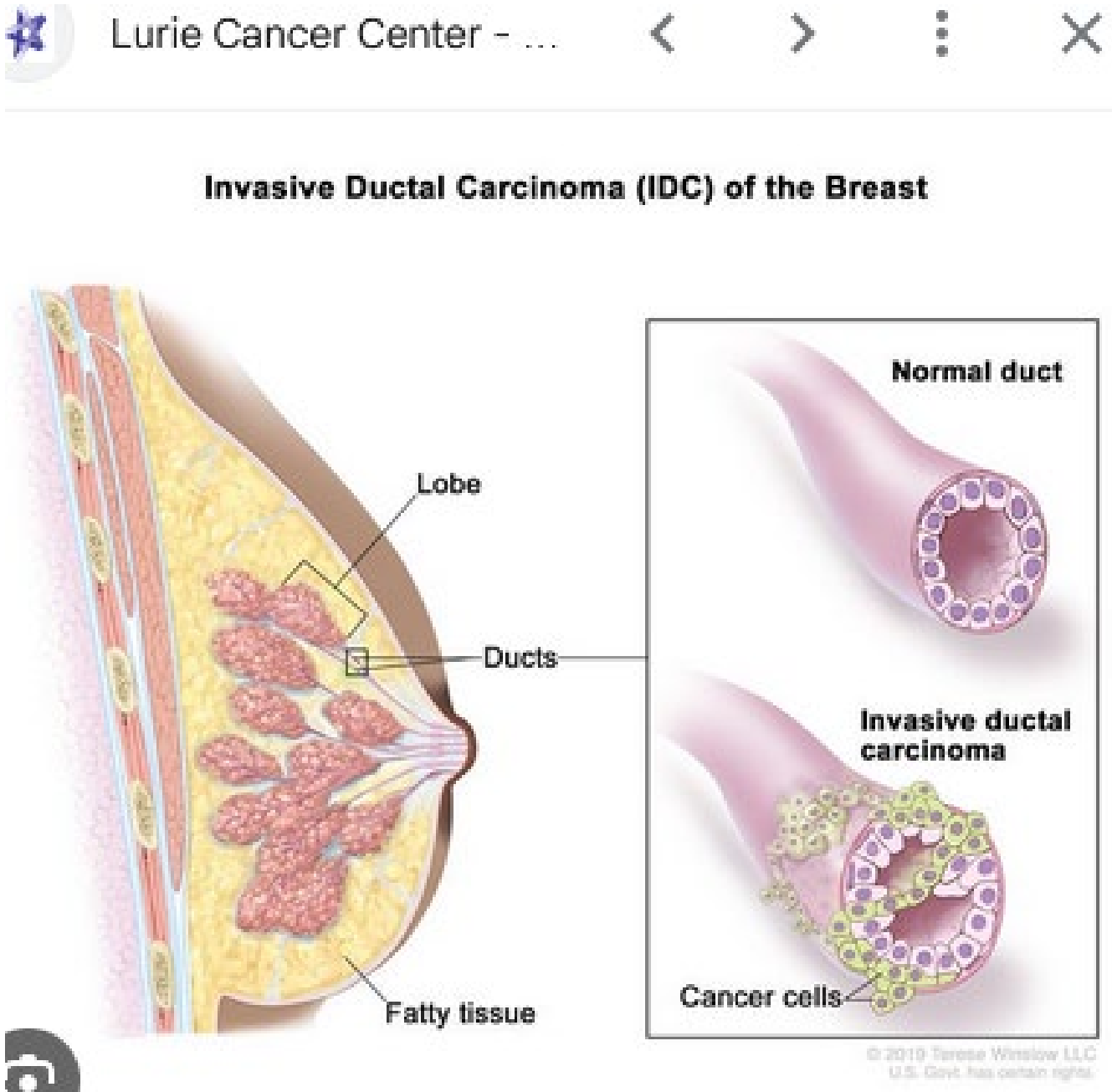
Table 1: 2026 ICD-O-3.2 Update (Numerical)f

- Codes/terms listed numerically
- Only new terminology to existing ICD-O-3.2 codes are included in the 2026 ICD-O Implementation guidelines and documentation. Terms are those listed in WHO Blue Books
- Update based on 5th Ed Classification of Head and Neck Tumors and 5th Ed Hematolymphoid Tumors

ICD-O Code	Term	Req SEER	Req NPCR	Req CoC	Req CCCR	Remarks
8240/3	Middle ear neuroendocrine tumor	Y	Y	Y	Y	New related term

8231/3	Preferred	Carcinoma simplex
8240/3	Preferred	Neuroendocrine tumor, NOS
8240/3	Synonym	Carcinoid tumor, NOS
8240/3	Synonym	Carcinoid, NOS
8240/3	Related	Bronchial adenoma, carcinoid
8240/3	Synonym	Neuroendocrine carcinoma, low grade
8240/3	Synonym	Neuroendocrine carcinoma, well differentiated
8240/3	Related	Neuroendocrine tumor, grade 1
8240/3	Synonym	Typical carcinoid
8241/3	Preferred	Enterochromaffin cell carcinoid

Breast


Lurie Cancer Center - ...
Invasive Ductal Carcinoma (IDC) of the Breast
Lobe
Ducts
Fatty tissue
Normal duct
Invasive ductal carcinoma
Cancer cells

8246/3
Neuroendocrine
CARCINOMA

8240/3
Neuroendocrine
TUMOR

Neuroendocrine carcinoma NOS 8246/3	Poorly differentiated neuroendocrine carcinoma	Carcinoma with neuroendocrine differentiation **8574/3** Large cell neuroendocrine carcinoma/large cell carcinoma **8013/3** Small cell neuroendocrine carcinoma/small cell carcinoma **8041/3**

https://seer.cancer.gov/tools/solidtumor/current/STM_Combined.pdf

Specific and NOS/NST Terms and Code	Synonyms	Subtypes/Variants
Neuroendocrine tumor NOS 8240/3	Carcinoid of breast Neuroendocrine carcinoma, low grade/neuroendocrine carcinoma, well differentiated Neuroendocrine tumor, grade 1	Neuroendocrine tumor, grade 2 **8249/3**

BREAST NEC vs NET

- **NET** For years this group of cancers was identified as a specific disease called **carcinoid**. This term is slowly being replaced in medical literature by the term **NETs**.
- Used interchangeably **CARCINOID, NET**, Neuroendocrine tumor.

BREAST Case

Total bilateral mastectomy. R Breast excised tumor 4 cm invasive with Neuroendocrine carcinoma and 95% Carcinoma with neuroendocrine differentiation.

How would you code it?

a)Neuroendocrine carcinoma 8246/3

b)Neuroendocrine tumor 8240/3

c)Carcinoma with neuroendocrine differentiation 8574/3

d)Mixed ductal-neuroendocrine carcinoma 8154/3

c)Carcinoma with neuroendocrine differentiation 8574/3

Breast Histology Rules
C500-C506, C508-C509
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Rule H19 Code the **subtype/variant** (specific histology) **ONLY** when there is a NOS/NST and a subtype/variant **AND** the subtype/variant is documented to be **greater than 90%** of the tumor.

Neuroendocrine carcinoma NOS 8246/3	Poorly differentiated neuroendocrine carcinoma	Carcinoma with neuroendocrine differentiation 8574/3 Large cell neuroendocrine carcinoma/large cell carcinoma 8013/3 Small cell neuroendocrine carcinoma/small cell carcinoma 8041/3

BREAST Case

How do you code **Small** cell carcinoma/**Small** cell neuroendocrine carcinoma?

A) 8246/3 WHY?

B) 8041/3

B) 8041/3

Because for Breast, **small** cell carcinoma/**small** cell **neuroendocrine** carcinoma is 8041/3

Neuroendocrine carcinoma NOS 8246/3	Poorly differentiated neuroendocrine carcinoma	Carcinoma with neuroendocrine differentiation **8574/3** Large cell neuroendocrine carcinoma/large cell carcinoma **8013/3** Small cell neuroendocrine carcinoma/small cell carcinoma **8041/3**

8041/3 STR 2025

Kidney : Small cell neuroendocrine carcinoma 8041/3

Bladder/urinary: Small cell neuroendocrine carcinoma 8041/3

Prostate: Small cell neuroendocrine carcinoma 8041/3

Esophagus: Small cell neuroendocrine carcinoma 8041/3

Stomach: Small cell neuroendocrine carcinoma 8041/3

Small intestine and Ampulla of Vater: Small cell neuroendocrine carcinoma 8041/3

Anus: Small cell neuroendocrine carcinoma 8041/3

Vagina/Cervix/Uterus: Small cell neuroendocrine carcinoma 8041/3

Thymus: SMALL CELL CARCINOMA 8041/3

BREAST AND HEAD AND NECK:

Small cell carcinoma/**Small** cell neuroendocrine carcinoma 8041/3 "Do NOT Code to 8246/3"

8246/3	Preferred	Neuroendocrine carcinoma, NOS
8240/3	Preferred	Neuroendocrine tumor, NOS

ICD-0-3.2

Code the **subtype/variant** and NOT the NOS.

They need the specific code to differentiate LARGE cell from SMALL cell or another variant.

Reminder: STR For **2024** new rows were added as shown below:

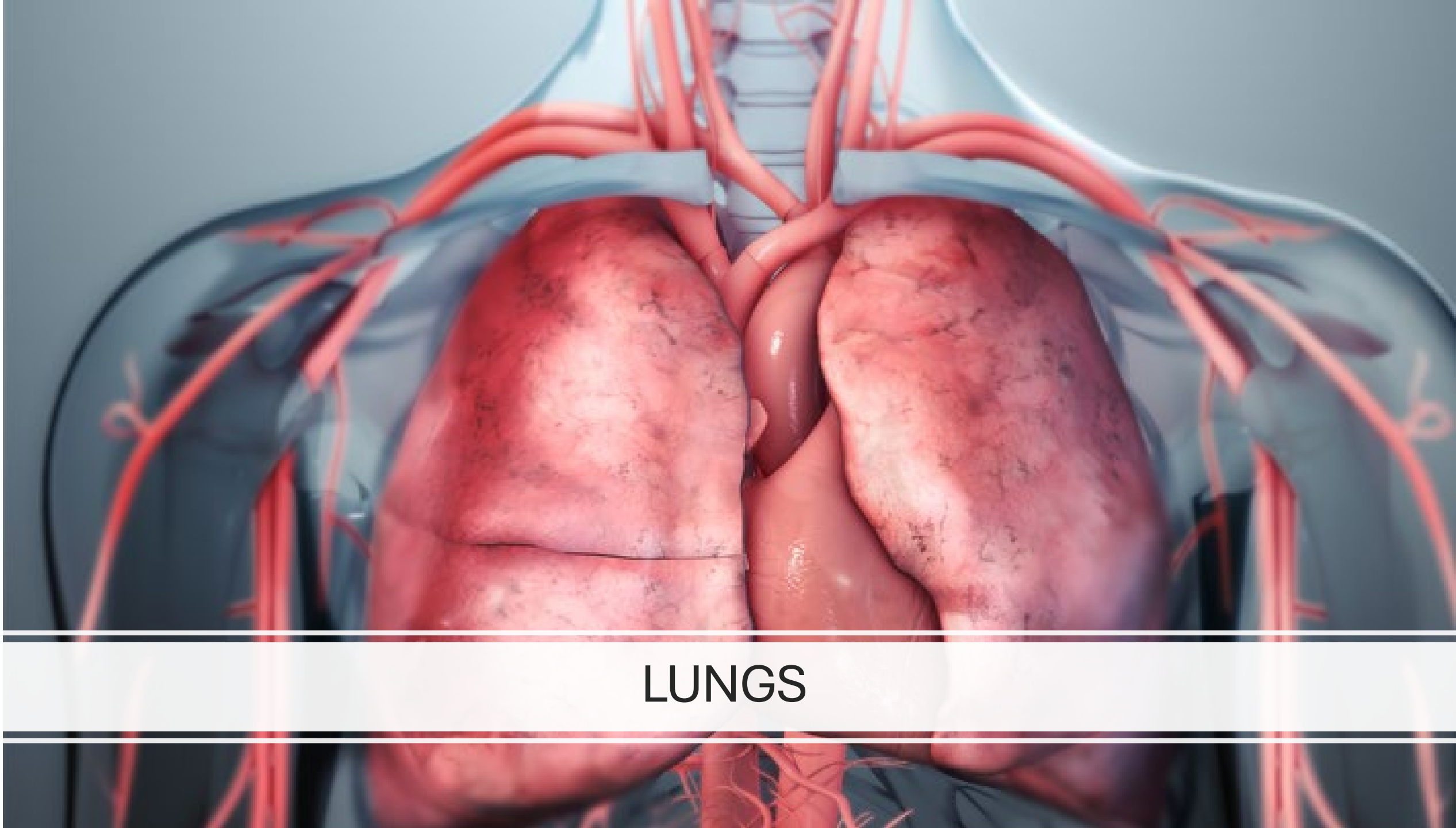
Head and Neck Equivalent Terms and Definitions
C000-C148, C300-C339, C410, C411, C479, C754, C755

Neuroendocrine tumor, NOS 8240/3	Carcinoid Neuroendocrine carcinoma grade 1 Well-differentiated neuroendocrine carcinoma	Large cell neuroendocrine carcinoma/LCNEC 8013/3 Neuroendocrine carcinoma grade 2/moderately-differentiated neuroendocrine carcinoma/atypical carcinoid 8249/3 Small cell neuroendocrine carcinoma/small cell carcinoma/SmCC 8041/3

Breast Equivalent Terms and Definitions
C500-C506, C508-C509
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Table 3: Specific Histologies, NOS/NST, and Subtypes/Variants

Specific and NOS/NST Terms and Code	Synonyms	Subtypes/Variants
Neuroendocrine carcinoma NOS 8246/3	Poorly differentiated neuroendocrine carcinoma	Carcinoma with neuroendocrine differentiation 8574/3 Large cell neuroendocrine carcinoma/large cell carcinoma 8013/3 Small cell neuroendocrine carcinoma/small cell carcinoma 8041/3



LUNGS

LU-NETS LUNG

The 4 major categories of **neuroendocrine tumors** of the lung are:

- Small cell carcinoma (SCLC)
  HG poorly differentiated with a very poor prognosis. Typical treatment is chemo/radiation
- Large cell neuroendocrine carcinoma (LCNEC)
  HG poorly differentiated with a POOR prognosis. Typical treatment is chemo/radiation
- Typical carcinoid of lung (TC)
  Low Grade and good prognosis. Usually cured with surgery alone
- Atypical carcinoid of lung (AC)
  Intermediate grade tumors, more aggressive than typical carcinoids. But better prognosis than Small and Large cell.

2015 WHO classification

IMPORTANT NOTE 2: The small cell neuroendocrine carcinoma row was deleted in the 2024 update and replaced with new rows for neuroendocrine carcinoma (NEC) and neuroendocrine tumor (NET). This change is based on the 5th Ed WHO Classification of Lung tumors book and current concepts.

Specific or NOS Histology Term and Code	Synonym of Specific or NOS	Subtype/variant of NOS and Code
Neuroendocrine tumor, NOS (NET) 8240	Bronchial adenoma, carcinoid Carcinoid, NOS Carcinoid tumor, NOS Neuroendocrine tumor, grade 1 Neuroendocrine tumor, low grade Neuroendocrine carcinoma, well differentiated Typical carcinoid	Atypical carcinoid/Neuroendocrine tumor, grade 2/ Neuroendocrine tumor, grade 3/Neuroendocrine carcinoma, moderately differentiated 8249

LU-NETS LU

Neuroendocrine carcinoma (NEC) 8246		Combined small cell carcinoma 8045 Small cell carcinoma/small cell neuroendocrine carcinoma 8041
Large cell neuroendocrine carcinoma 8013 *Note:* Per WHO, both large cell neuroendocrine carcinoma, NOS and combined large cell neuroendocrine carcinoma are coded 8013. See Table 2 for histologies included in combined large cell neuroendocrine carcinoma	Combined large cell neuroendocrine carcinoma	

STR 2025

Required Terms	Combination Histologies and Code
Large cell neuroendocrine carcinoma **AND** Adenocarcinoma NOS **OR** Squamous cell carcinoma NOS **OR** Spindle cell carcinoma **OR** Giant cell carcinoma	Combined large cell neuroendocrine carcinoma 8013

LUNG Case

60-year-old white non-Hispanic smoker male presents to the hospital with shortness of breath.

Imaging reveals a 12 mass in the right upper lobe compressing the trachea.

Biopsy of RUL**: Invasive Large cell carcinoma with Neuroendocrine differentiation.**

What is the correct code:

a) Large cell neuroendocrine carcinoma 8013/3

b) Large cell carcinoma 8012/3

c) Neuroendocrine carcinoma (NEC) 8246/3

b) Large cell carcinoma 8012/3

Remember for LUNG:

- **LARGE cell carcinoma with NEUROENDOCRINE differentiation** should be coded as LARGE CELL CARCINOMA **8012/3** and **NOT** large cell neuroendocrine carcinoma (8013/3) because it lacks Neuroendocrine morphology.

- 2025 Table 3-

Note 3: Large cell carcinoma with **neuroendocrine (NE) differentiation** lacks NE morphology and is coded as **large cell** carcinoma, **not large cell neuroendocrine** carcinoma.

LUNGS

- NSCLC (Non-Small Cell Lung Carcinoma)
  - ADENOCARCINOMA 8140
  - SQUAMOUS CELL CARCINOMA
  - LARGE CELL CARCINOMA **8012**

- Small cell Neuroendocrine carcinoma deleted in 2024 and replaced with
  - NEC and
  - NET (in 2025 STR)

Note 3: Large cell carcinoma with neuroendocrine (NE) differentiation lacks NE morphology and is coded as large cell carcinoma, not large cell neuroendocrine carcinoma.

2025

IMPORTANT NOTE 1: Non-small cell lung carcinoma (NSCLC) is a broad group of cancers which includes all carcinoma types in Table 3 with the exception of:

- Neuroendocrine tumors (NET), Neuroendocrine carcinoma (NEC)
- Large cell neuroendocrine carcinoma/combined large cell neuroendocrine carcinoma
- Sarcoma NOS 8800 (not a carcinoma) and all subtypes of sarcoma NOS

NSCLC is usually adenocarcinoma, squamous cell carcinoma, or large-cell carcinoma. See the instructions for coding histology when NSCLC is the diagnosis.

IMPORTANT NOTE 2: The small cell neuroendocrine carcinoma row was deleted in the 2024 update and replaced with new rows for neuroendocrine carcinoma (NEC) and neuroendocrine tumor (NET). This change is based on the 5th Ed WHO Classification of Lung tumors book and current concepts.

Neuroendocrine carcinoma (NEC) 8246		Combined small cell carcinoma **8045** Small cell carcinoma/small cell neuroendocrine carcinoma **8041**

Specific or NOS Histology Term and Code	Synonym of Specific or NOS	Subtype/variant of NOS and Code
Neuroendocrine tumor, NOS (NET) 8240	Bronchial adenoma, carcinoid Carcinoid, NOS Carcinoid tumor, NOS Neuroendocrine tumor, grade 1 Neuroendocrine tumor, low grade Neuroendocrine carcinoma, well differentiated Typical carcinoid	Atypical carcinoid/Neuroendocrine tumor, grade 2/ Neuroendocrine tumor, grade 3/Neuroendocrine carcinoma, moderately differentiated **8249**

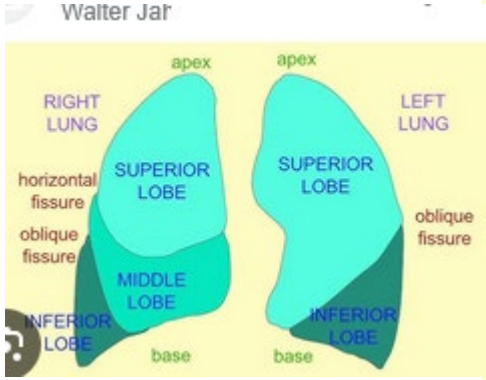
Large cell neuroendocrine carcinoma 8013 *Note:* Per WHO, both large cell neuroendocrine carcinoma, NOS and combined large cell neuroendocrine carcinoma are coded 8013. See Table 2 for histologies included in combined large cell neuroendocrine carcinoma	Combined large cell neuroendocrine carcinoma	

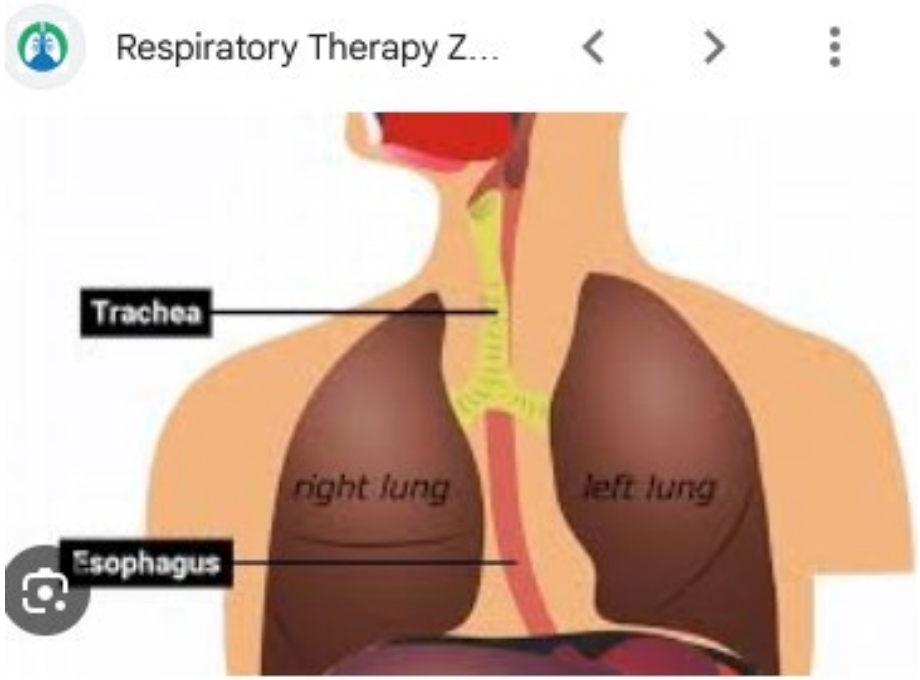
LUNGS

Seer Summary Stage 2 REGIONAL when:

- Compression of esophagus or trachea not specified as direct extension.
- Separate tumor nodule(s) **IN THE SAME LOBE** as the primary.

Regional by direct extension only
- Atelectasis/obstructive pneumonitis
  + Extends to hilar region, involving part or all of lung
- Blood vessel(s) (major)
  + Aorta
  + Azygos vein
  + Pulmonary artery or vein
  + Superior vena cava (SVC syndrome)
- Brachial plexus
- Carina from lung
- Chest wall (thoracic wall)
- Compression of esophagus or trachea not specified as direct extension
- Diaphragm (separate lesion-see code 7)
- Esophagus
- Mediastinum, extrapulmonary or NOS
- Nerve(s)
  + Cervical sympathetic (Horner's syndrome)
  + Recurrent laryngeal (vocal cord paralysis)
  + Vagus
- Pancoast tumor (superior sulcus syndrome), NOS
- Parietal pericardium
- Parietal pleura (PL3)
- Pericardium, NOS
- Phrenic nerve
- Pleura, NOS
- Pulmonary ligament
- Separate tumor nodule(s) in the same lobe as the primary
- Visceral pleura invasion (PL1, PL2, or NOS)
- Trachea





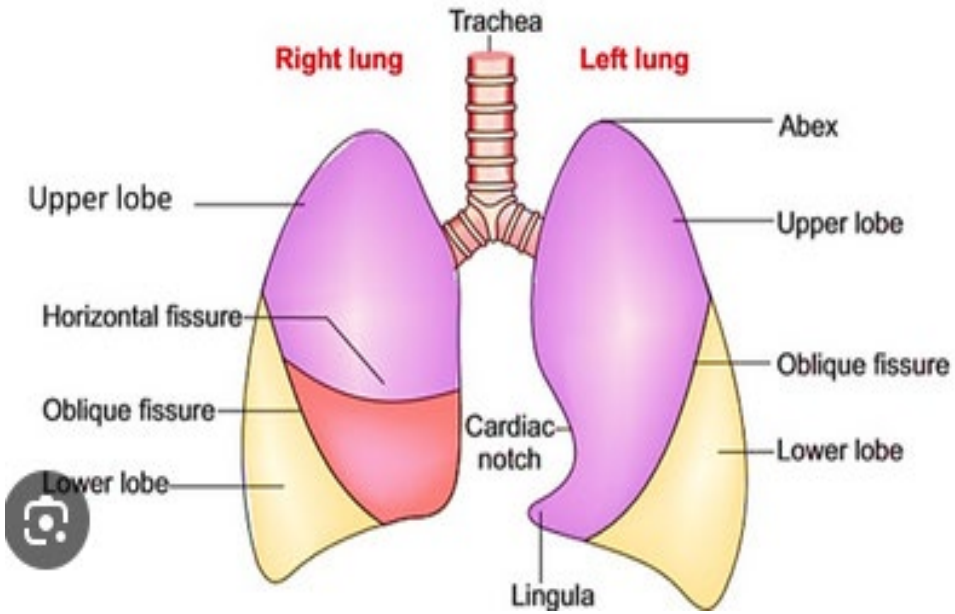
Seer Summary Stage 7 DISTANT when:

Distant site(s)/lymph node(s) involved
- Distant site(s) (including further contiguous extension)
  + Abdominal organs
  + Adjacent rib
  + Contralateral lung/main stem bronchus
  + Heart
  + Inferior vena cava
  + Neural foramina
  + Pericardial nodules or pleural effusion (malignant) (ipsilateral, contralateral, bilateral, NOS)
  + Pleural tumor foci or nodules on ipsilateral lung (separate from direct extension) or contralateral lung
  + Rib
  + Separate tumor nodule(s) in contralateral lung
  + Separate tumor nodule(s) in a different ipsilateral lobe
  + Skeletal muscle
  + Skin of chest
  + Sternum
  + Vertebra(e) (vertebral body)
  + Visceral pericardium
- Distant lymph node(s), NOS
  + IPSILATERAL or CONTRALATERAL
    * Low cervical
    * Proximal root
    * Scalene (inferior deep cervical)
    * Sternal notch
    * Supraclavicular (transverse cervical)
  + CONTRALATERAL/BILATERAL nodes
    * Bronchial
      - Peri/parabronchial
    * Carinal
    * Hilar (bronchopulmonary) (proximal lobar) (pulmonary root)
      - Intrapulmonary
        - Interlobar
        - Lobar
        - Segmental
        - Subsegmental
      - Superior mediastinal
        + Paratracheal (left, right, upper, low, NOS)
          - Azygos (lower paratracheal)

- Distant metastasis, NOS
  + Carcinomatosis
  + Distant metastasis WITH or WITHOUT distant lymph node(s)

LUNGS

Anatomy QA



-Remember the **lingula** is only on the **left lung** (there is NO Lingula on the right lung).

-For a Lung Primary, AXILLARY LYMPH NODE would be Distant, Seer Summary Stage 7

LUNG

· Pathology Report

DE/ TYAGI, ASHOK) SR24: 1245- RIGHT MIDDLE LOBE, LUNG MASS, CT-GUIDED NEEDLE CORE BIOPSY: SMALL CELL (NEUROENDOCRINE) CARCINOMA.

Primary Site C342 Histology 8246 Behavior 3 - Malignant

Discriminator1 Label

Schema 00360 Lung [8th: 2018-2024]

Description SS 9th Edition Schema: 00360 - Lung [8th: 2018-2
Florida Required SSDIs:
No SSDI data required by FCDS

Laterality 1 - Right

Text-Primary Site LUNG, RML

Text-Histology SMALL CELL (NEUROENDOCRINE) CARCINOMA, UNK GR

Small cell Neuroendocrine carcinoma is coded to 8041/3

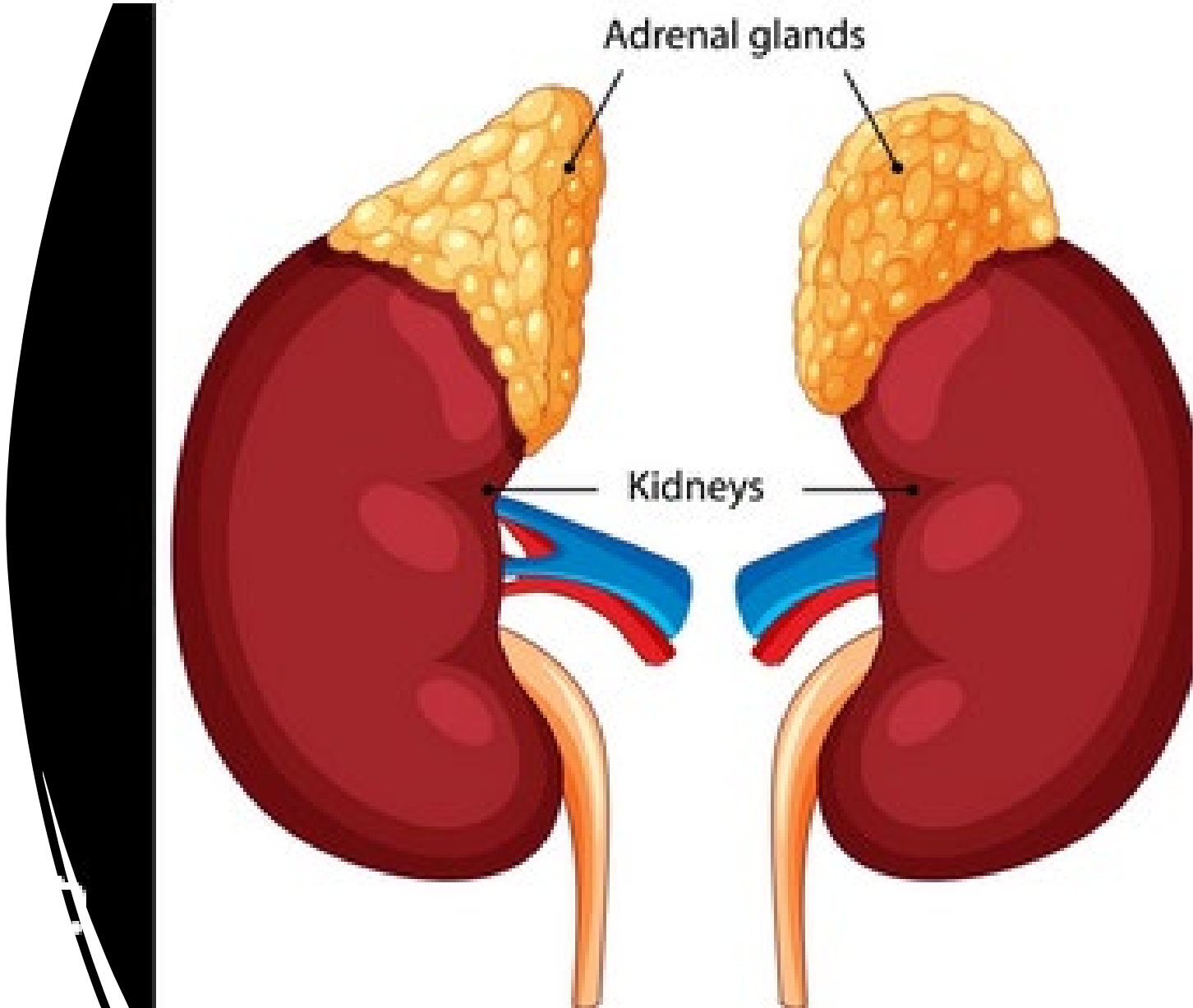
Small cell carcinoma 8041/3 *Note 1:* This row applies to neuroendocrine tumors (NET). *Note 2:* Large cell carcinoma with neuroendocrine differentiation lacks NE morphology and is coded as large cell carcinoma, not large cell neuroendocrine carcinoma.	Reserve cell carcinoma Round cell carcinoma SCLC Small cell carcinoma NOS Small cell neuroendocrine carcinoma	Atypical carcinoid 8249/3 Combined small cell carcinoma 8045/3 Typical carcinoid 8240/3 Neuroendocrine carcinoma, NOS Well-differentiated neuroendocrine carcinoma

STR 2021

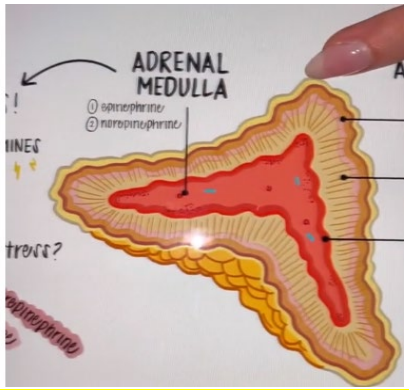
Neuroendocrine carcinoma (NEC) 8246		Combined small cell carcinoma 8045 Small cell carcinoma/small cell neuroendocrine carcinoma 8041

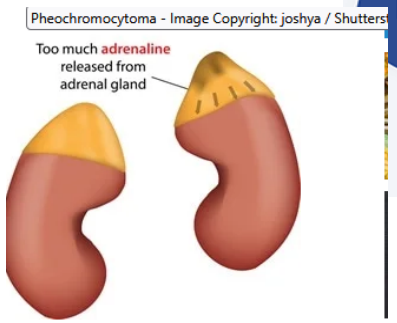
STR 2025

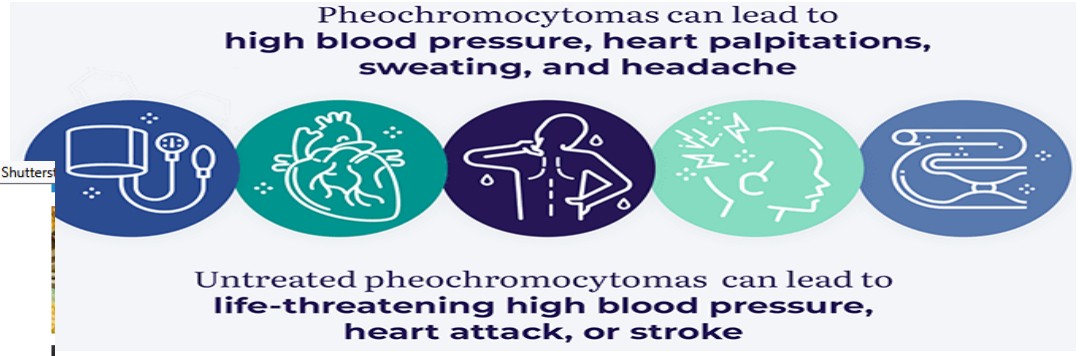
ADRENAL GLANDS/ Extra-adrenal sites



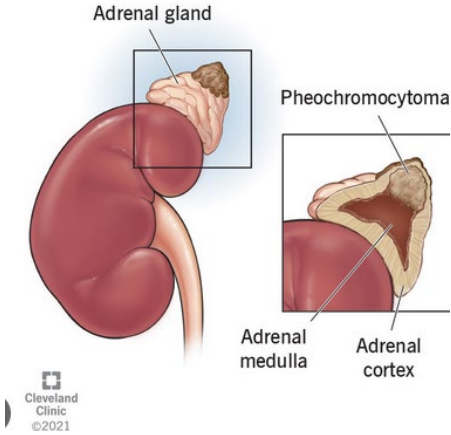
ADRENAL







Paragangliomas may produce high blood pressure if they produce catecholamines (norepinephrine, epinephrine aka adrenaline, and sometimes may produce dopamine.)



Extra-adrenal pheochromocytomas are also called PARAGANGLIOMAS (15-20% of all pheochromocytomas are extra-adrenal).

Pheochromocytomas and paragangliomas are rare: 2-8 per million

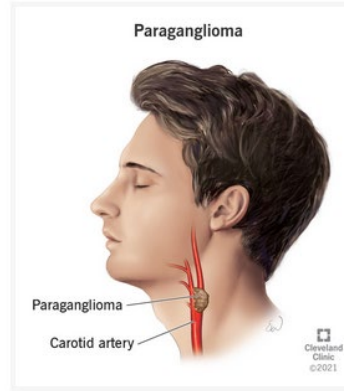
Incidence M=F Age range 30-50 years 10% occur in children 6 - 14 years old.

Most **paragangliomas** are **H&N** paragangliomas, but they can be in thorax, abdomen or pelvis

3-4 % of Head & Neck paragangliomas are FUNCTIONAL (secrete catecholamines).

Most common symptom is **hypertension**. Also, panic attack type symptoms, anxiety, **tachycardia**, diaphoresis.. Symptoms may be episodic or constant.

Most are sporadic. 35% of cases have a genetic component. Association with MEN IIA IIB, Von Hippel-Lindau Syndrome, Neurofibromatosis type 1



Extra -ADRENAL

Text - Dx Procedures - Physical Exam - PE

10 YR OLD WHITE, NON-HISPANIC FEMALE WHO HAS HX OF HLHS, AORTIC VALVE ATRESIA, CONGENITAL MITRAL STENOSIS, S/P SURGERIES BETWEEN 2014 AND 2023. IN DECEMBER 2024 SHE HAD US WHICH SHOWED AN ADRENAL MASS. CT FOLLOWED WHICH SHOWED HER TO HAVE A PHEOCHROMOCYTOMA AFTER EVAL FOR HTN AND TACHYCARDIA. SHE WAS RECOMMENDED RESECTION OF THE MASS WHICH CONFIRMED PHEOCHROMOCYTOMA. NO FURTHER TREATMENT RECOMMENDED.

Date of DX 2024-

Primary Site C741 Histology 8700 Behavior 3 - Malignant

Discriminator1 Label

Schema 00770 NET Adrenal Gland

Description SS 9th Edition Schema: 00770 - NET Adrenal G
Florida Required SSDIs:
No SSDI data required by FCDS

Laterality 2 - Left

Text-Primary Site ADRENAL GLAND

Text-Histology PARAGANGLIOMA (PHEOCHROMOCYTOMA)

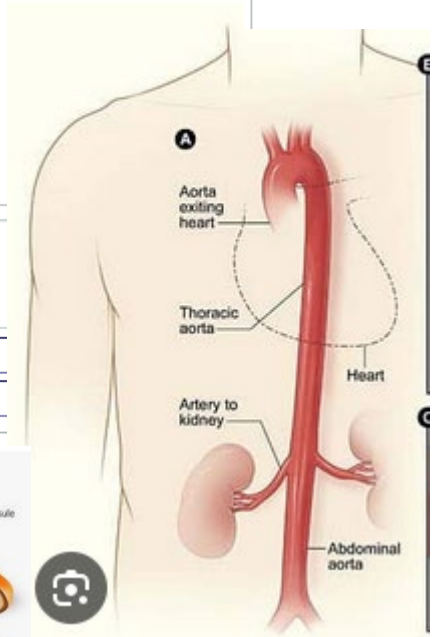
Text - Dx Procedures - X-ray/Scans

12/16/24 US PORTABLE DOPPLER AORTA (NICKLAUS) - A HETEROGENEOUS SOLID MASS CONTAINING INTERNAL VASCULARITY IS SEEN AT THE AORTIC BIFURCATION; 12/17/24 CT ABD PELVIS (NICKLAUS) - A HYPOENHANCING MASS (31 MM) IS SEEN AT THE AORTIC BIFURCATION, WHICH DEMONSTRATES EARLY HYPERENHANCEMENT WITH DELAYED FILLING ON PORTAL VENOUS IMAGING AND MEASURES 3.1 X 2.2 X 2.5 CM (SERIES 6, IMAGE 291, SERIES 5, IMAGE 271 AND SERIES 13, IMAGE 39). A SMALL AMOUNT OF FREE FLUID IS NOTED WITHIN THE PELVIS. A HYPERENHANCING NODULE IS SEEN ALONG THE LEFT LATERAL ABDOMINAL WALL, NEAR THE SPLEEN, MEASURING 9 X 9 X 7 MM; 12/20/24 WHOLE BODY (NICKLAUS) - MIBG AVID TUMOR IN THE MIDLINE/LEFT PARA MIDLINE ABDOMEN. NO EVIDENCE FOR METASTATIC DISEASE.

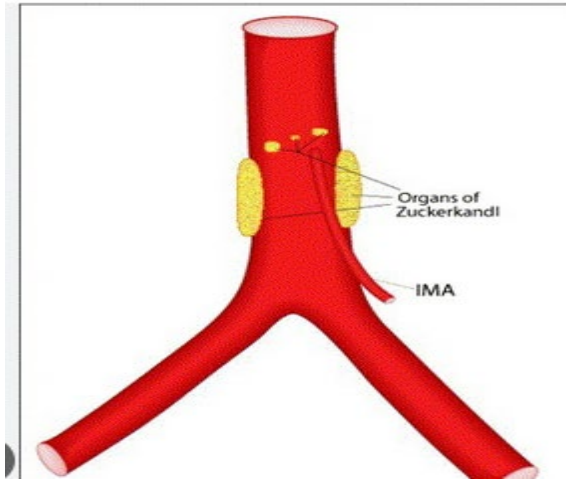
Text - Dx Procedures - Pathology Report

2/27/25 SP25-0000925: INTRAABDOMINAL MASS EXCISION - PARAGANGLIOMA (PHEOCHROMOCYTOMA). FOCI SUSPICIOUS FOR VASCULAR INVASION ARE PRESENT.

Teac...



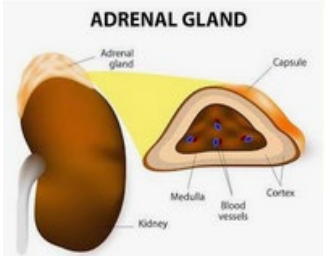
ScienceDirect.com



C75.5 Aortic body and other paraganglia

Coccygeal body
Coccygeal glomus
Glomus jugulare
Para-aortic body
Organ of Zuckerkandl
Paraganglion

9	8700/3	Preferred	Pheochromocytoma, NOS
0	8700/3	Synonym	Adrenal medullary paraganglioma
1	8700/3	Synonym	Chromaffin paraganglioma
2	8700/3	Synonym	Chromaffin tumor
3	8700/3	Synonym	Chromaffinoma
4	8700/3	Related	Composite pheochromocytoma
5	8700/3	Synonym	Pheochromoblastoma

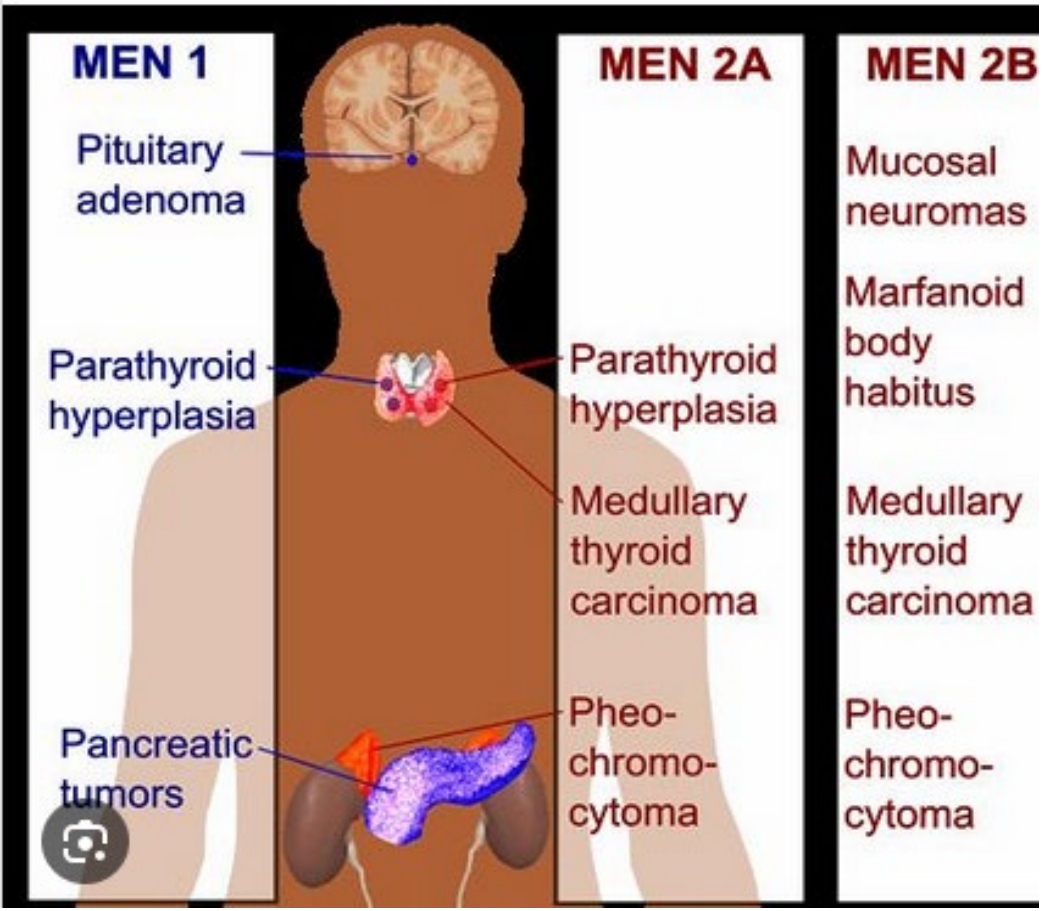


Aortic bifurcation: The point where the abdominal aorta splits into the **left** and **right** common **iliac arteries.**

Pheochromocytomas may be part or MEN Syndromes
-Even in children-

Medbullets Step 1

10 YR OLD WHITE, NON-HISPANIC FEMALE WHO HAS HX OF HLHS, AORTIC VALVE ATRESIA, CONGENITAL MITRAL STENOSIS, S/P SURGERIES BETWEEN 2014 AND 2023. IN DECEMBER 2024 SHE HAD US WHICH SHOWED AN ADRENAL MASS. CT FOLLOWED WHICH SHOWED HER TO HAVE A PHEOCHROMOCYTOMA AFTER EVAL FOR HTN AND TACHYCARDIA. SHE WAS RECOMMENDED RESECTION OF THE MASS WHICH CONFIRMED PHEOCHROMOCYTOMA. NO FURTHER TREATMENT RECOMMENDED.



Other Genetic conditions may increase risk:

-Von Hippel-Lindau disease

-Neurofibromatosis

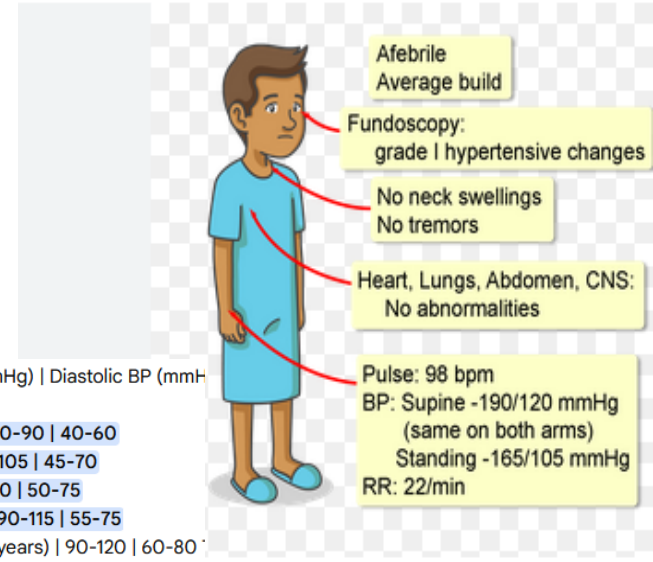
-Tuberous sclerosis

-Sturge-Weber Syndrome

-Ataxia-telangiectasia

Approximately 10% of NEN cases are associated with genetic syndromes.

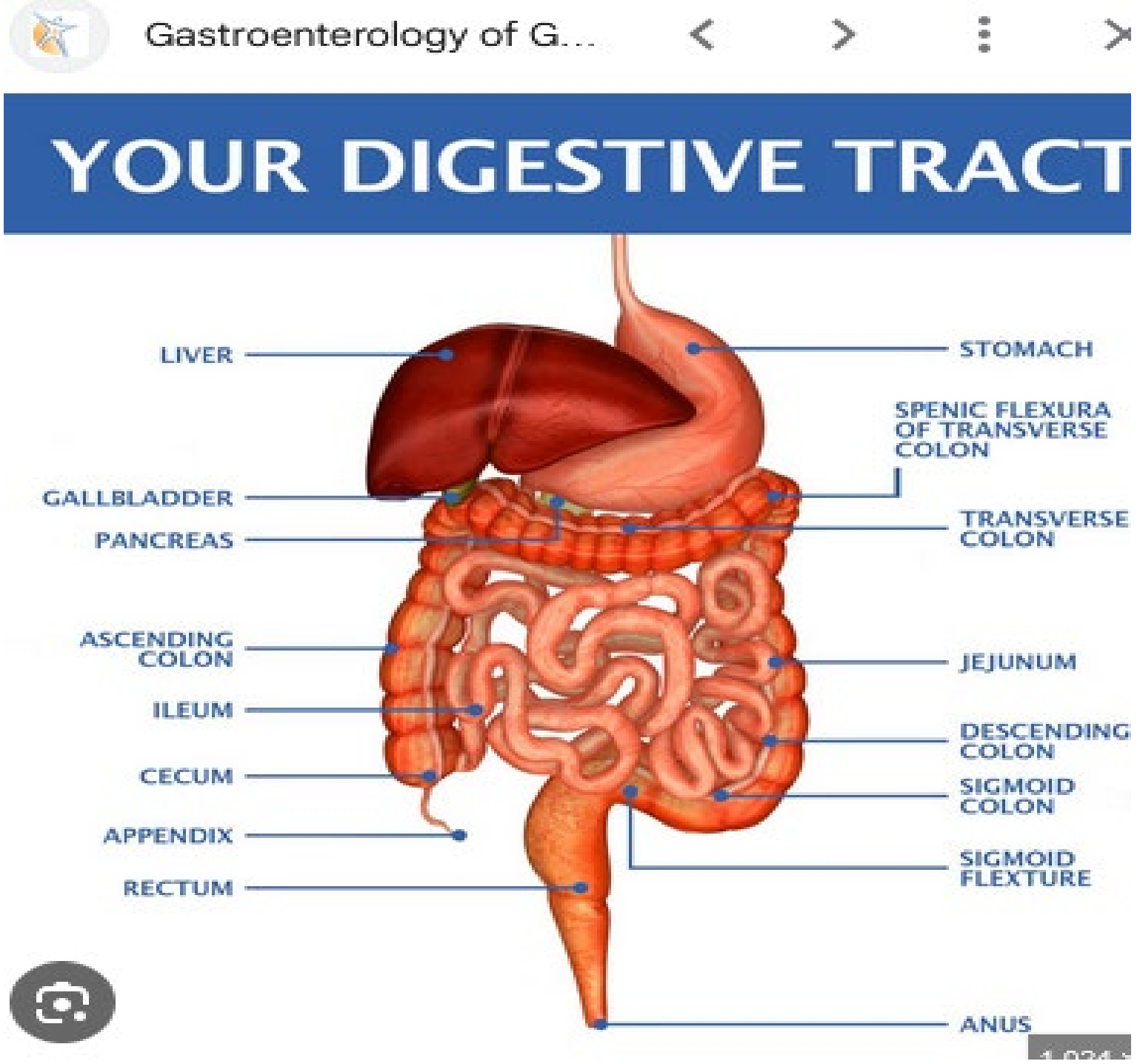
Clinical Odyssey



Age Group	Systolic BP (mmHg)	Diastolic BP (mmH
Newborns (0-3 months)	60-90	40-60
Infants (4-12 months)	70-105	45-70
Toddlers (1-3 years)	80-110	50-75
Preschoolers (4-5 years)	90-115	55-75
School-aged children (6-12 years)	90-120	60-80

Pheochromocytoma - Interactive

Gastrointestinal tract



8153/3	8153	3	Preferred	Gastrinoma, NOS
8153/3	8153	3	Synonym	G cell tumor, NOS
8153/3	8153	3	Synonym	Gastrin cell tumor

GASTRINOMA (Pancreas, Duodenum, Stomach)

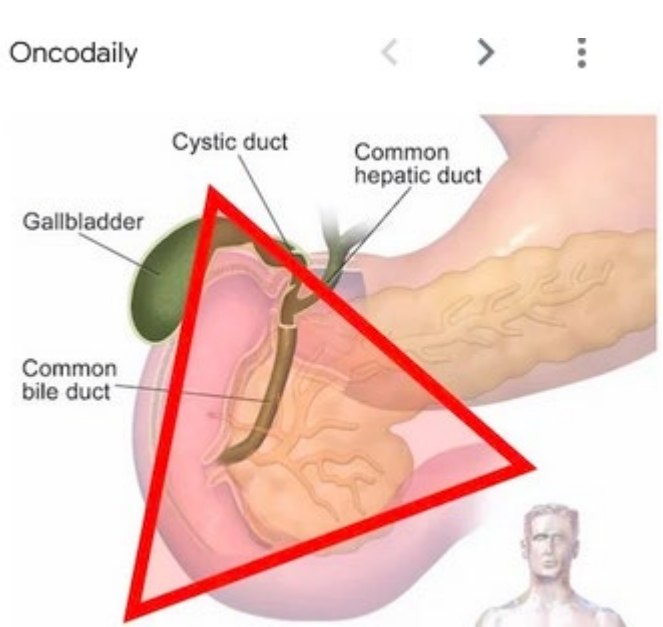
GASTRINOMAS: Endocrine or Neuroendocrine tumor that produces excess of the hormone GASTRIN which elevates gastric acid. Excessive gastrin production causes excessive HCl and promotes the formation of ulcers.

G-cells are endocrine cells in the stomach and duodenum that secrete the hormone Gastrin. Gastrin stimulates the release of hydrochloric acid (HCl).

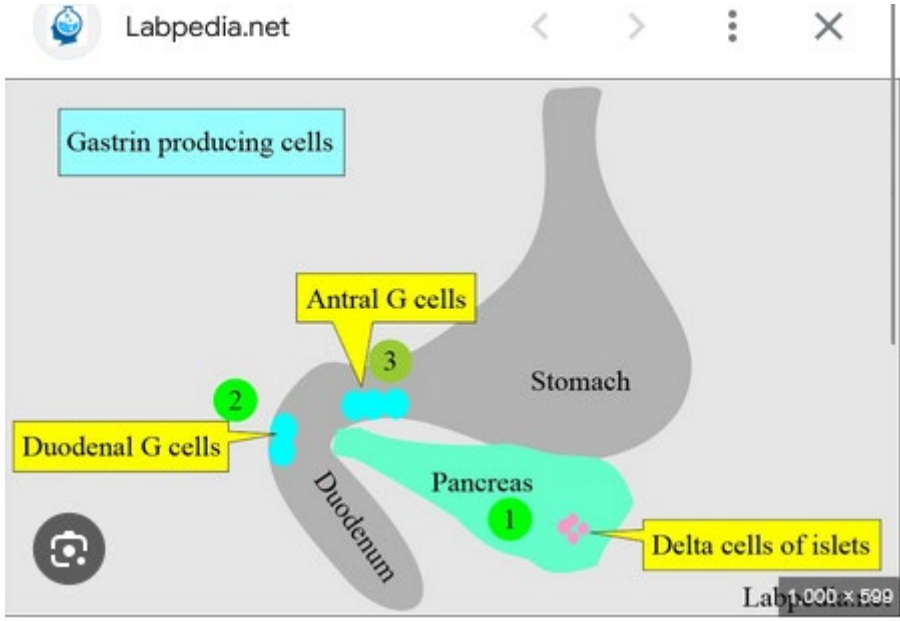
Normally, the **Delta cells** of the **pancreas** secrete **somatostatin**, a hormone that **inhibits acid** production.

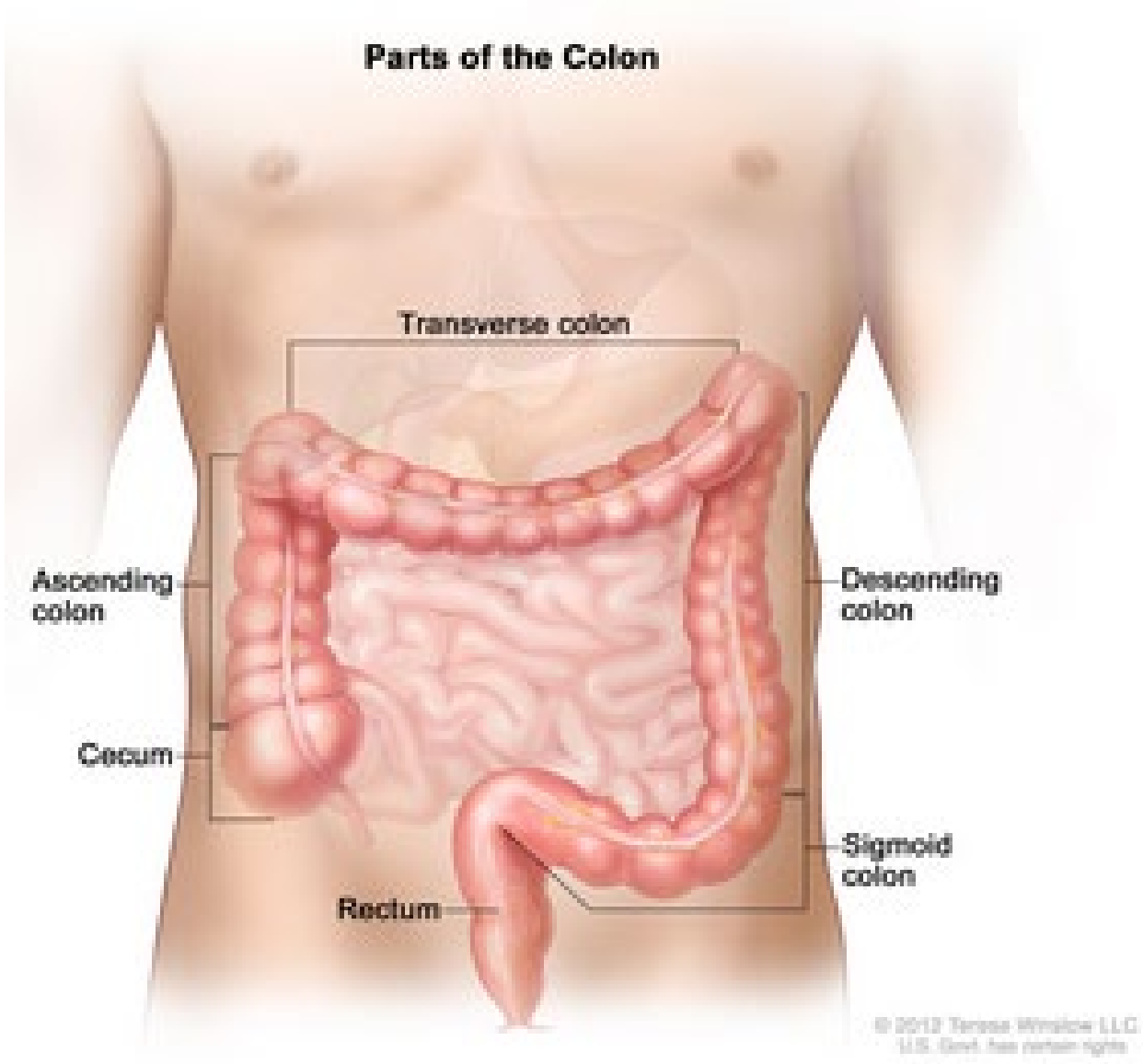
However, when there is a **Gastrinoma** present in the pancreas, these delta cells transform into malignant cells and start secreting **Gastrin instead**, leading to excess of HCL

Complications: Stomach or duodenal ulcers, GI bleeding, ulcer perforation…



The Gastrinoma triangle is an **anatomical region where a majority of gastrinomas are found.** It's roughly defined by the confluence of the cystic and common bile ducts superiorly, the second and third portions of the duodenum inferiorly, and the neck of the pancreas medially. About **80% to 90% of gastrinomas are located within this area.**




Parts of the Colon
Transverse colon
Ascending colon
Descending colon
Cecum
Sigmoid colon
Rectum

COLON

Colon, Rectosigmoid, and Rectum Equivalent Terms and Definitions
C180-C189, C199, C209
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Table 1: Specific Histologies, NOS, and Subtypes/Variants

Specific and NOS Term and Code	Synonyms for Specific or NOS Term	Subtypes/Variants
Neuroendocrine carcinoma 8246	NEC	Large cell NEC 8013 Small cell NEC 8041
Neuroendocrine tumor Grade 1 (G1) 8240 *Note*: When the diagnosis is exactly "carcinoid" it may be a Grade 1 or Grade 2 NET. Default is coding NET Grade 1 8240.	Carcinoid NOS Low-grade neuroendocrine tumor NET Grade 1 (G1) Well differentiated neuroendocrine tumor	EC cell serotonin-producing NET/enterochromaffin cell carcinoid 8241 Neuroendocrine tumor (NET) Grade 2 (G2) 8249 Somatostatin-producing NET 8156

We have the NE**C** (carcinomas) and the NE**T** (tumors) again.

- For the NEC we need to differentiate if it is
  - Large cell NEC 8013
  - Small cell Nec **8041**
- For the **NETs** that are the **CARCINOIDS** with grade 1 the default is 8240
  - and for Grade 2 is **8249**
  - we have other subtypes 8156, 8241

COLON, RECTOSIGMOID, RECTUM

62-year-old female has a screening colonoscopy with a partially obstructing single mass in the descending colon. Biopsies were sent to pathology which showed an invasive mixed neuroendocrine carcinoma with a minority of goblet cell adenocarcinoma.

What histology do you code:

a) 8244/3 Mixed Neuroendocrine carcinoma

b) 8243/3 Goblet Cell Adenocarcinoma

c) 8154/3 Mixed Neuroendocrine non-neuroendocrine

d) 8246/3 Neuroendocrine carcinoma

b) 8243/3 Goblet Cell Carcinoid

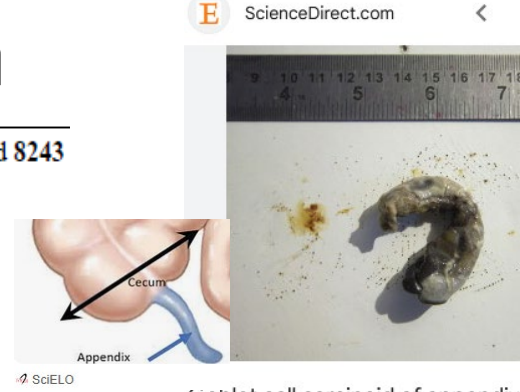
Code the subtype regardless of whether it is described as the majority or the minority component. -STR-

1. **Code the most specific** histology or **subtype/type/variant, regardless of whether it is described as:**
   A. The majority or predominant part of tumor
   B. The minority of tumor
   C. A component

Mixed adenoneuroendocrine carcinoma 8244	Adenocarcinoma ex-goblet cell Adenocarcinoma mixed with high-grade large cell neuroendocrine carcinoma Adenocarcinoma mixed with high-grade small cell neuroendocrine carcinoma MANEC Mixed neuroendocrine carcinoma	Goblet cell adenocarcinoma/Goblet cell carcinoid 8243
Mixed neuroendocrine non-neuroendocrine neoplasm 8154	MiNEN	

APPENDIX Goblet vs Ex-goblet Cell Adenocarcinoma

Mixed adenoneuroendocrine carcinoma 8244	Adenocarcinoma ex-goblet cell Adenocarcinoma mixed with high-grade large cell neuroendocrine carcinoma Adenocarcinoma mixed with high-grade small cell neuroendocrine carcinoma MANEC Mixed neuroendocrine carcinoma	Goblet cell adenocarcinoma/Goblet cell carcinoid 8243

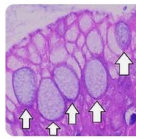


Goblet cell carcinoid of appendix

Goblet cells: Produce mucin which is a component of mucus (protection, barrier, traps damaging particles and bacteria).

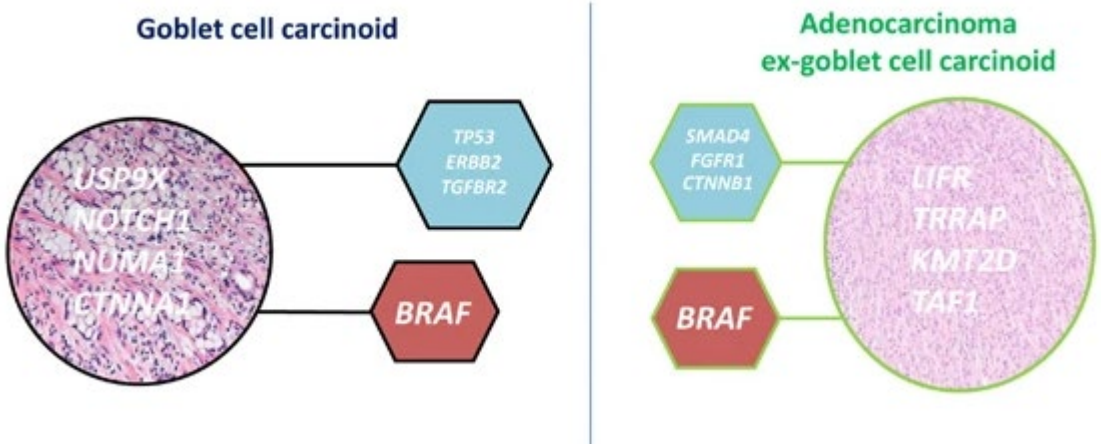
Comparison of GCA grades

Feature	Goblet Cell Adenocarcinoma (Low-grade) (ICD-O 8243/3)	Adenocarcinoma ex Goblet Cell (High-grade) (ICD-O 8244/3)
Microscopic appearance	Small, round, uniform clusters of goblet-like and neuroendocrine cells that resemble intestinal crypts. There is minimal nuclear atypia.	Higher-grade morphology with marked nuclear atypia. May present in various aggressive patterns, such as poorly cohesive cells, signet-ring cells, solid sheets, or conventional-type adenocarcinoma.
Differentiation	Displays features of both epithelial (goblet cells) and neuroendocrine cells. The neuroendocrine component is minor.	The tumor has undergone a process of dedifferentiation, where the adenocarcinoma component has become more prominent and poorly organized compared to the low-grade form.
Biological behavior	Behaves in an indolent (less aggressive) fashion.	Highly aggressive with a high propensity for peritoneal and intra-abdominal spread. It is often transmural at diagnosis.
Prognosis	Better prognosis than the high-grade form.	Worse prognosis, with a significantly greater malignant potential.
Clinical management	May require more aggressive surgery than a simple appendectomy, but still less aggressive management than the high-grade form.	Requires aggressive treatment similar to appendiceal or colorectal adenocarcinoma, including aggressive surgery and chemotherapy. These cases are managed based on protocols for adenocarcinomas, not neuroendocrine tumors.



Primary location: APPENDIX

Usually outside of the appendix are metastasis. But there are exceptions.



Pancreas

C25.4 Islets of Langerhans
Islands of Langerhans
Endocrine pancreas

Neuroendocrine tumor NOS 8240 *Note:* Pancreatic neuroendocrine tumor, non-functioning has the following synonyms (they are not subtype/variants): • Clear cell neuroendocrine tumor, non-functioning pancreatic • Cystic neuroendocrine tumor, non-functioning pancreatic • Oncocytic neuroendocrine tumor, non-functioning pancreatic • Pleomorphic neuroendocrine tumor, non-functioning pancreatic	Neuroendocrine tumor, grade 1 PanNET	ACTH-producing tumor 8158 Enterochromaffin-cell carcinoid / Serotonin-producing tumor 8241 Gastrinoma 8153 Glucagonoma 8152 Insulinoma 8151 Neuroendocrine tumor grade 2 / neuroendocrine tumor grade 3 8249 Pancreatic neuroendocrine tumor, non-functioning 8150 (see note for synonyms) Somatostatinoma 8156 VIPoma 8155

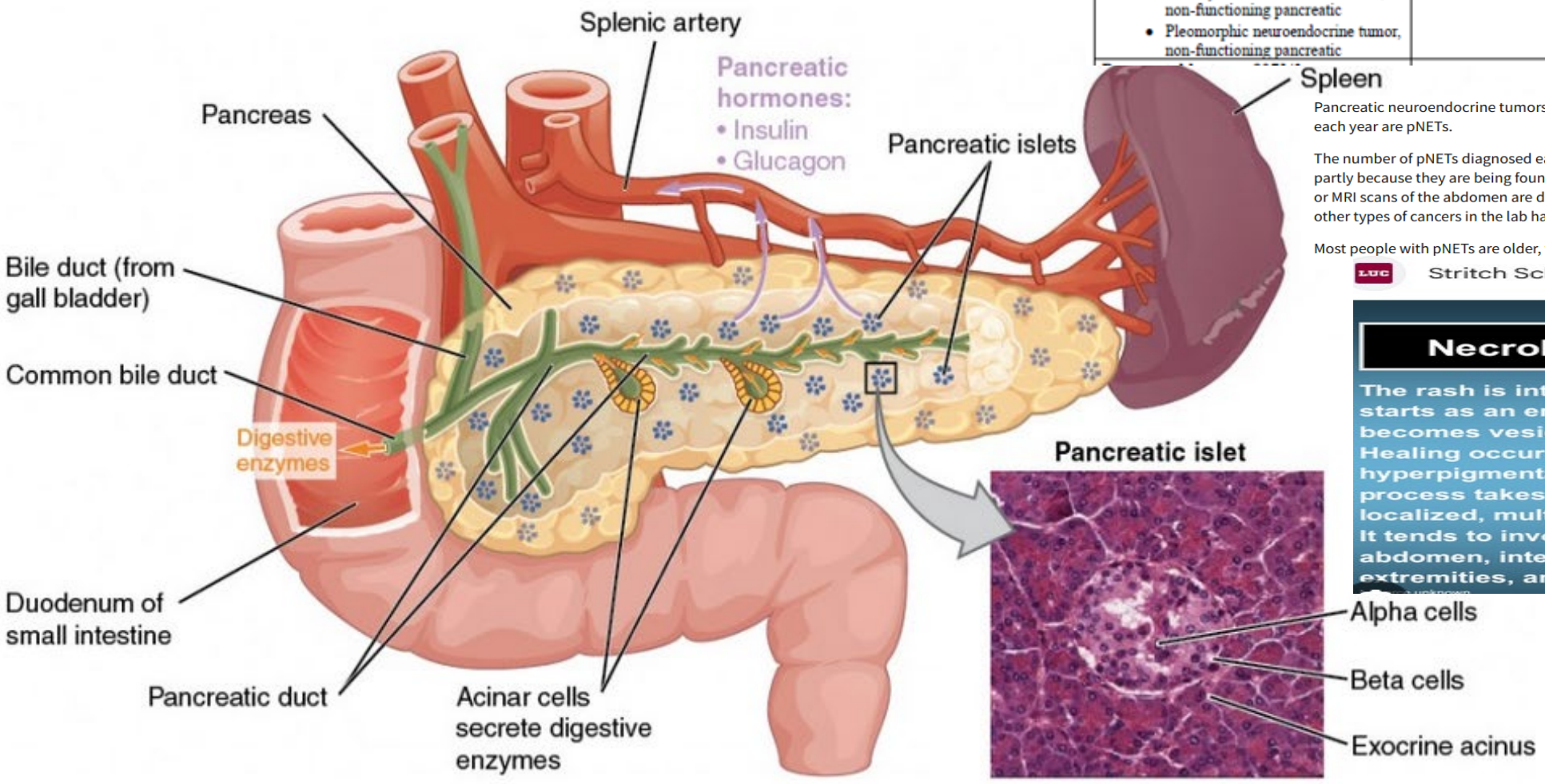


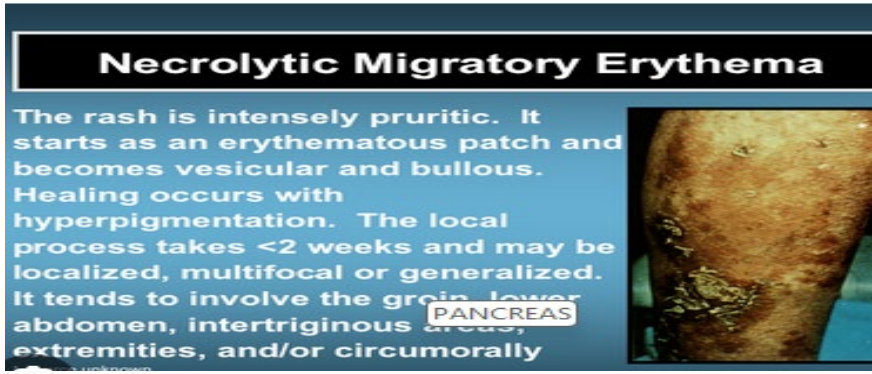
Figure 1. The pancreatic exocrine function involves the acinar cells secreting digestive enzymes that are transported into the small intestine by the pancreatic duct. Its endocrine function involves the secretion of insulin (produced by beta cells) and glucagon (produced by alpha cells) within the pancreatic islets. These two hormones regulate the rate of glucose metabolism in the body. The micrograph reveals pancreatic islets. LM × 760. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Pancreatic neuroendocrine tumors (pNETs) are rare. Less than 2% of all cancers found in the pancreas each year are pNETs.

The number of pNETs diagnosed each year; however, has been rising over time. This is thought to be partly because they are being found more often incidentally (by accident), when imaging tests such as CT or MRI scans of the abdomen are done for other reasons. The ability to distinguish these tumors from other types of cancers in the lab has also improved, leading to more of them being diagnosed.

Most people with pNETs are older, with the average age at diagnosis being 60.

Stritch School of Medi...



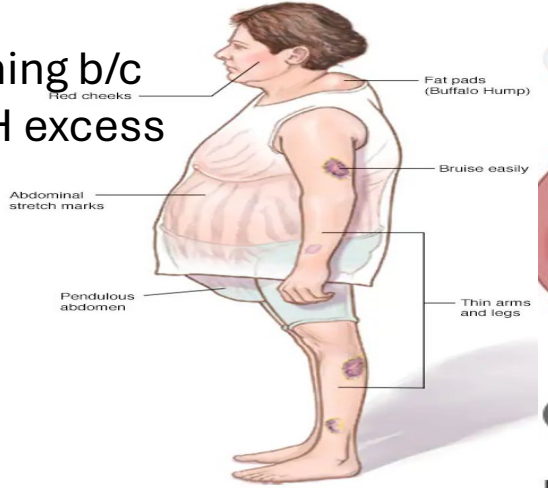
Glucagon. **Glucagonoma**

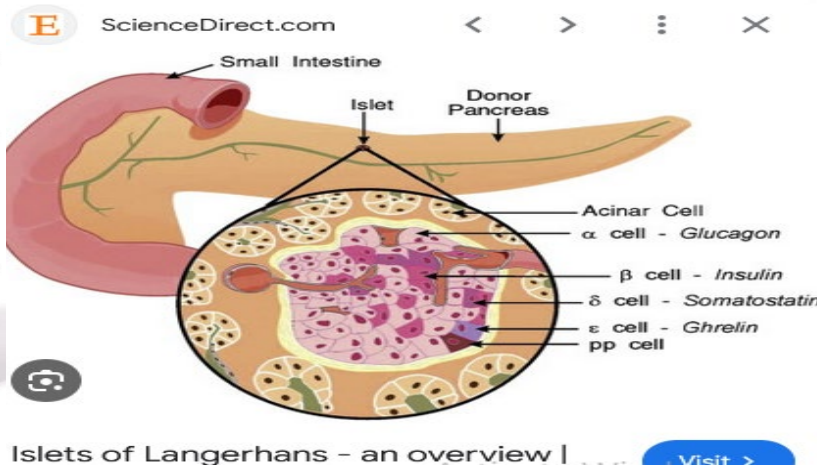
Insulin. **Insulinoma**

Glucagonoma gives HYPERGLYCEMIA/ Diabetes Mellitus, Necrolytic Migratory Erythema, Thromboembolic disease...

PANCREAS

Cushing b/c ACTH excess





Solid Tumor Rules
2025 Update

Table 11: Pancreas Histologies

Specific and NOS Terms and Code	Synonyms	Subtypes/Variants
Neuroendocrine carcinoma NOS 8246	PanNEC	Large cell neuroendocrine carcinoma 8013 Small cell neuroendocrine carcinoma 8041
Neuroendocrine tumor NOS 8240 *Note:* Pancreatic neuroendocrine tumor, non-functioning has the following synonyms (they are not subtype/variants): • Clear cell neuroendocrine tumor, non-functioning pancreatic • Cystic neuroendocrine tumor, non-functioning pancreatic • Oncocytic neuroendocrine tumor, non-functioning pancreatic • Pleomorphic neuroendocrine tumor, non-functioning pancreatic	Neuroendocrine tumor, grade 1 PanNET	ACTH-producing tumor 8158 Enterochromaffin-cell carcinoid / Serotonin-producing tumor 8241 Gastrinoma 8153 Glucagonoma 8152 Insulinoma 8151 Neuroendocrine tumor grade 2 / neuroendocrine tumor grade 3 8249 Pancreatic neuroendocrine tumor, non-functioning 8150 (see note for synonyms) Somatostatinoma 8156 VIPoma 8155

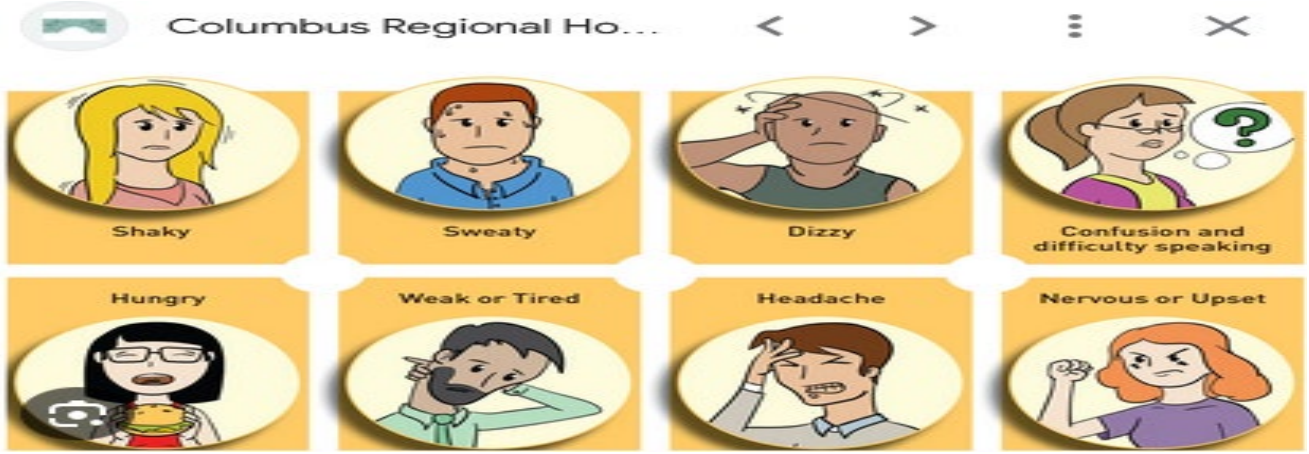
Somatostatin analogs NOT useful.

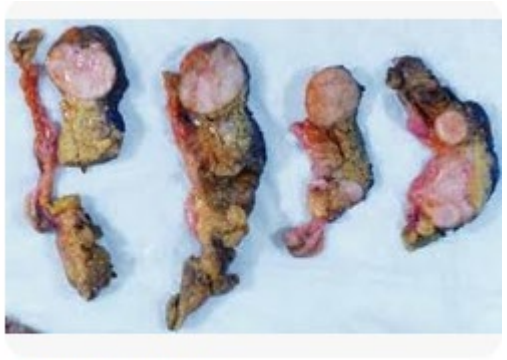
Somatostatin analogs are used as treatment (octreotide, Lanreotide) in NETs (CARCINOIDs) but NOT in NECs.

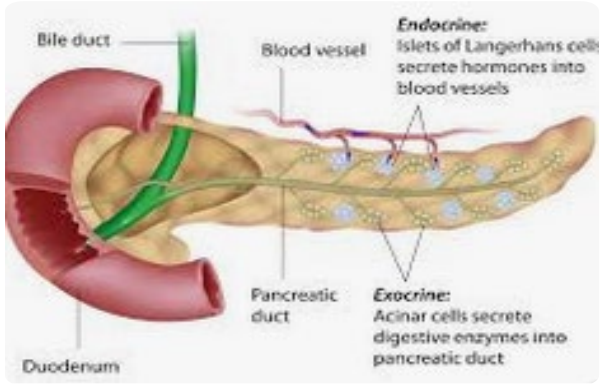
Table 1. Common gastrointestinal neuroendocrine tumors with their dominant hormone symptoms

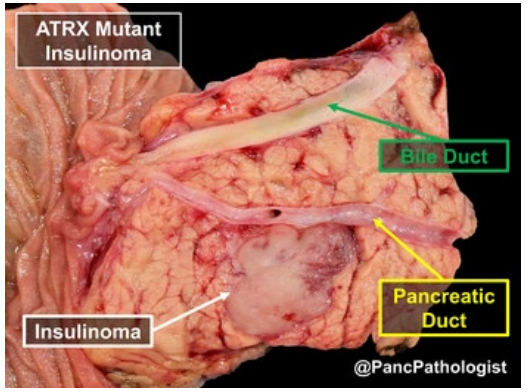
Tumor type	Percentage of cases	Dominant hormone	Classic symptoms
Carcinoid	56	Serotonin	Flushing, diarrhea, wheezing
Insulinoma	17	Insulin	Symptomatic hypoglycemia
Pancreatic polypeptidoma (PPoma)	15	Pancreatic polypeptide	Clinically silent
Gastrinoma	9	Gastrin	Peptic ulcer disease diarrhea
Vasoactive intestinal peptide-producing tumor (VIPoma)	2	Vasoactive intestinal polypeptide	Secretory diarrhea
Glucagonoma	1	Glucagon	Characteristic rash, glucose intolerance
Somatostatinoma	1	Somatostatin	Gallstones, diabetes diarrhea

INSULINOMA



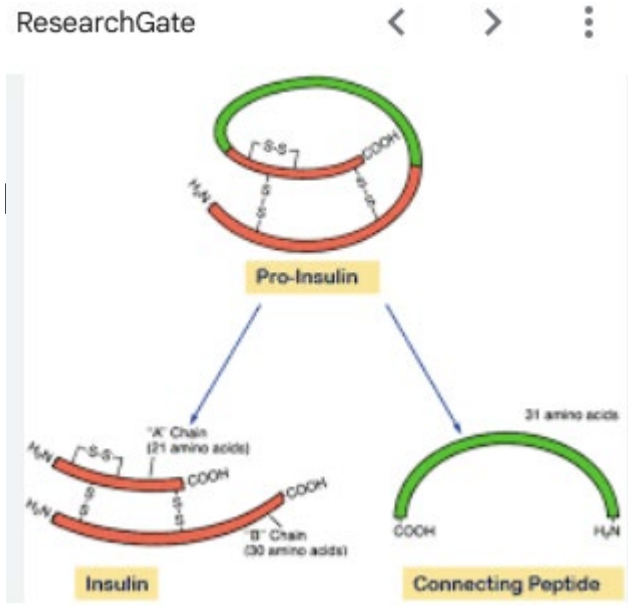






Produces **excessive insulin** which lowers glucose excessively

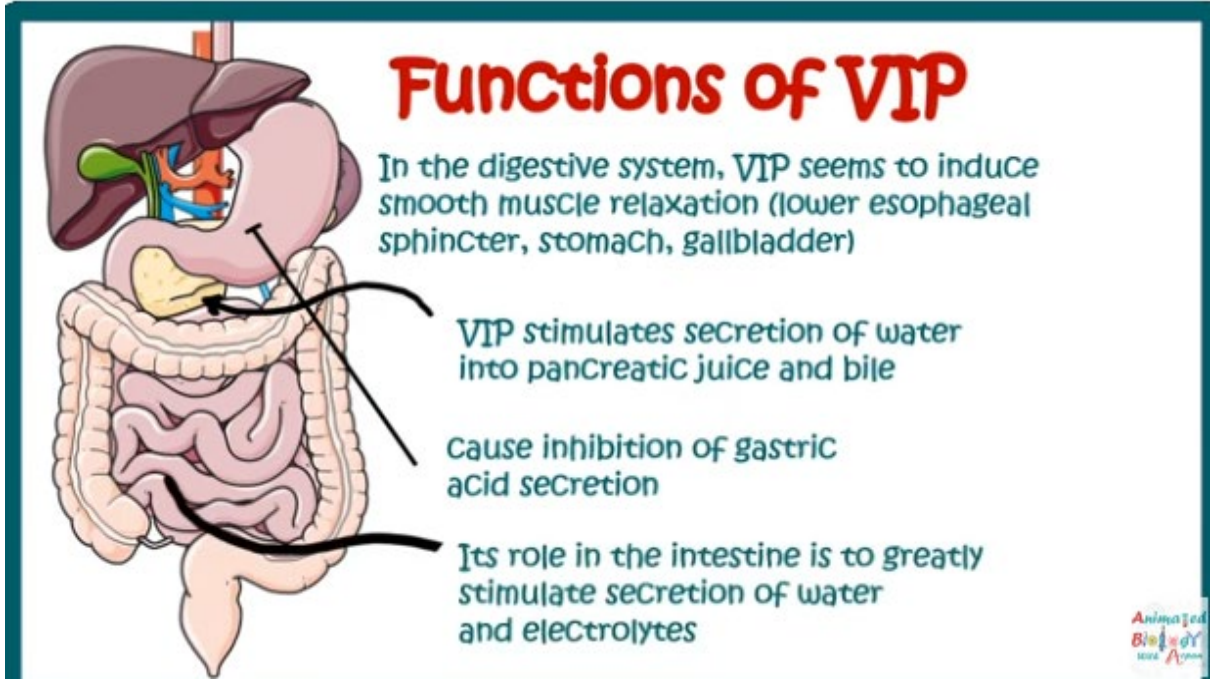
- Verified ⬇ Low glucose
- hypoglycemic symptoms (sweating, tremors, palpitations, confusio seizures, coma...) Glucose below 50 mg/dL is life-threatening
- Relief of symptoms with normalization of glucose



-Needs to rule out injecting too much external insulin:

Order levels of Insulin, **C- peptide**, and **proinsulin**.

Pancreatic VIPomas



- Excessive secretion of VIP (Vasoactive Intestinal Peptides)
- >50% malignant
- Verner-Morrison Syndrome
  - Chronic **watery diarrhea** (leading to dehydration and bicarbonate loss)
  - Hypokalemia (**Low Potassium**)
  - **Achlorhydria**

Also, flushing (red face and skin), muscle weakness or **paralysis** due to low K+

-Metabolic acidosis is possible-

Diagnosis serum VIP levels greater than 250 pg/mL), Imaging (CT scan, MRI, somatostatin receptor scintigraphy)

A somatostatin receptor scintigraphy (SRS), also called an octreotide scan, is a medical imaging test that uses a radioactive substance to find and visualize tumors, especially neuroendocrine tumors, which have receptors for somatostatin. During

- Responds well to Octreotide (blocks the action of VIP), **Surgical resection** when possible.

5 SOMATOSTATIN Receptors

Somatostatin Analogs:

octreotide systemic (Pro)

Brand names: Sandostatin LAR Depot, Sandostatin, Bynfezia Pen, Mycapssa

lanreotide systemic (Pro)

Brand name: Somatuline Depot

pasireotide systemic (Pro)

Brand names: Signifor, Signifor LAR

Somatostatin

Brain and pituitary	Eye	Gastrointestinal tract	Pancreas	Adrenals
				
SSTR 1-5	**SSTR1-3**	**SSTR1-5**	**SSTR1,2,3 and 5**	**SSTR 3 and 5**
Inhibition of NE, DA, CRH, TRH, TSH and GH	Inhibition of VEGF	Reduces the secretion of gastrin, secretin, gastric acid, motilin, CCK, enteroglucagon, VIP, pepsin, GIP, neurotensin, intrinsic factor, and bile	Reduces the secretion of glucagon, insulin, and PP	Inhibits the secretion of medullary catecholamine and aldosterone

SST is considered a universal endocrine molecule and peptide hormone in the CNS, PNS and ENS.[iii] SST is classified as a broad inhibitory neuropeptide. SST inhibits the secretion of several other hormones, including growth hormone, gastrin, glucagon, thyroid stimulating hormone, cholecystokinin, secretin, insulin, pancreatic polypeptide, vasoactive intestinal peptide (VIP), 5-Hydroxytryptamine (5-HT) and some anterior pituitary hormones.[iv] Due to its effect on growth hormone, it is also referred to as growth hormone inhibiting hormone (GHIH).

Pasireotide

Search Database

Name
Pasireotide

Alternate Names
SOM230

Abbreviations
None

Category
Hormones and hormonal mechanisms

Subcategory
Hormone

NSC Number
None

Primary Site
Carcinoids

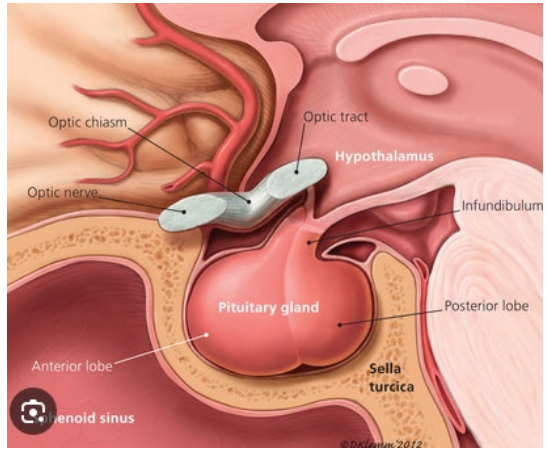
Histology
None

Remarks
Novartis. Inhibits hormone secretion.

Coding
This drug should be coded

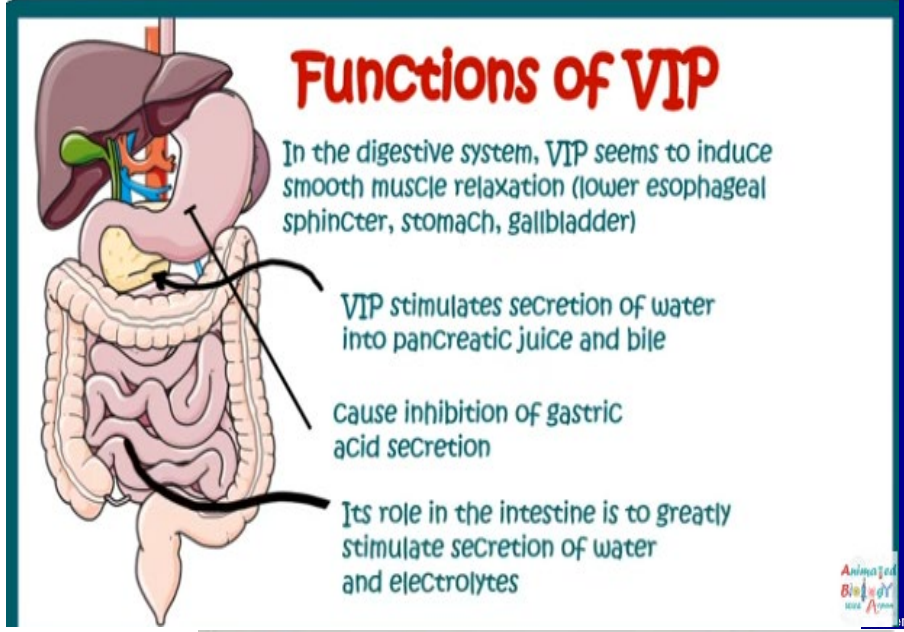
Sandostatin (OCTREOTIDE) Blocks the hormone secretions IN MOST of the **NETs**

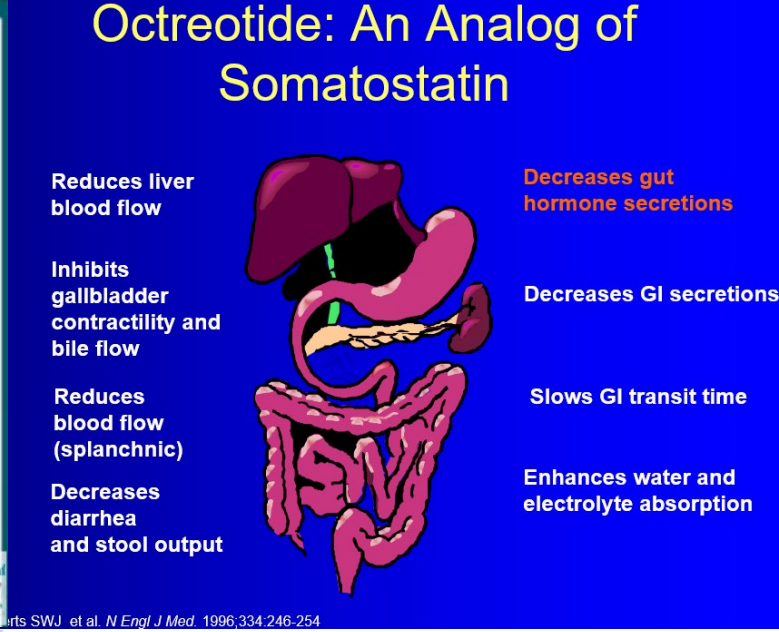
OCTREOTIDE

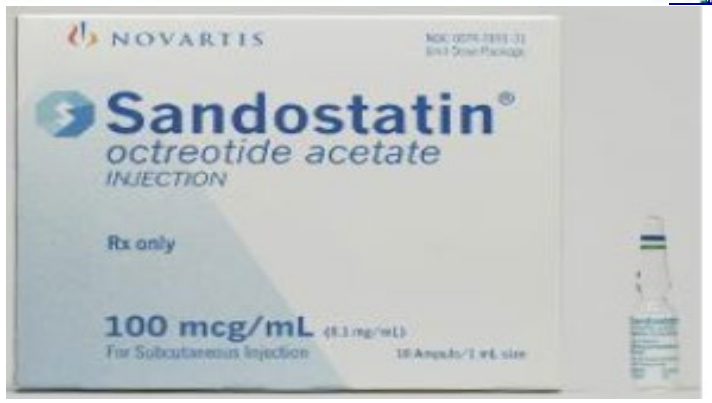


ACROMEGALY: Excess of GH in adults. Enlargement of hands, feet, and face (nose, lips, jaw), tongue. Deepening of the voice.

Studies have shown Sandostatin (OCTREOTIDE) can cause significant, and often predictable, **TUMOR SHRINKAGE** in more than half of patients with **ACROMEGALY (Growth Hormone or SOMATOTROPH ADENOMA IN THE PITUITARY)**







Remarks

Remark added 11/18/2015: *Sandostatin* us usually prescribed to treat side-effects/symptoms from TSH-secreting pituitary adenomas. Studies show this may also shrink tumors or inhibit further growth. If the physician states this agent is being prescribed to shrink or prohibit growth of the tumor, then code as hormone treatment.

Please note: not all drugs classified as hormone treat malignant neoplasms.

Coding

Please see remarks for additional information

https://seer.cancer.gov/seertools/seerrx/rx/53c44b10102c1290262dd2d8/?drug_direction=UP&regimen_direction=UP&rx_type=drug&drug_field=score&regimen_field=score&drug_offset=0&regimen_offset=0&limit=25&search_mode=&q=SANDOSTATIN&mode=

Name

Lanreotide Acetate

Alternate Names

BIM 23104
BIM-23014
BIM23014
Somatuline

LANREOTIDE

It is a Long-acting SOMATOSTATIN Analog similar to Octreotide (short acting).

Remarks

This drug is usually considered ancillary treatment for neuroendocrine tumors as it relieves symptoms of neuroendocrine tumors but does not kill the tumor cells. HOWEVER, as of June 1, 2019, Somatuline Depot is the 1st and only FDA-approved treatment for adults both to slow the growth of gastrointestinal and pancreatic neuroendocrine tumors (GEP NETs) that have spread or cannot be removed by surgery. It also treats carcinoid syndrome to reduce the need for the use of short-acting somatostatin medicine.

How to code: IF given to treat carcinoid syndrome, do not code. If give or stated to be prescribed to treat the tumor, then code as hormone

This drug is indicated for the treatment of acromegaly when the circulating levels of growth hormone remain abnormal after surgery and/or radiotherapy, but also used for the treatment of thyrotrophic adenomas when the circulating level of thyroid stimulating hormone remains inappropriately high after surgery and/or radiotherapy. It may be used to treat pituitary tumors. If so, code as hormonal treatment.

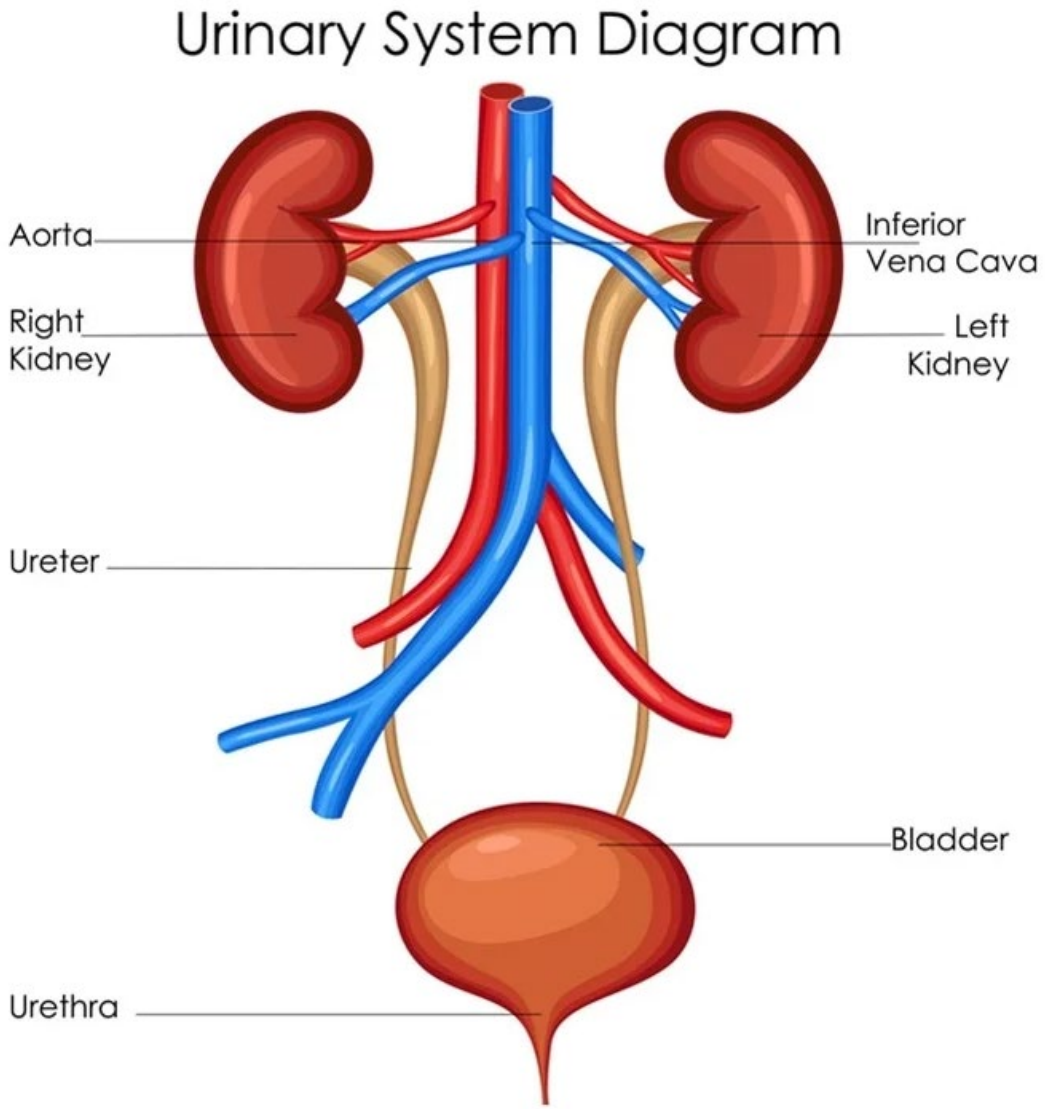
Coding

Please see remarks for additional information

Carcinoid syndrome: A set of symptoms tied to carcinoid tumors and the release of serotonin. Flushing, diarrhea, shortness of breath, wheezing, palpitations....

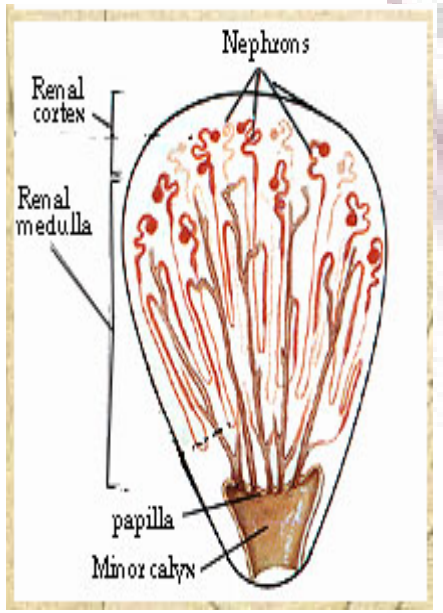
https://seer.cancer.gov/seertools/seerrx/rx/53c44af8102c1290262dc1bc/?drug_direction=UP&regimen_direction=UP&rx_type=drug&drug_field=score&regimen_field=score&drug_offset=0&regimen_offset=0&limit=25&search_mode=&q=Lanreotide+&mode=

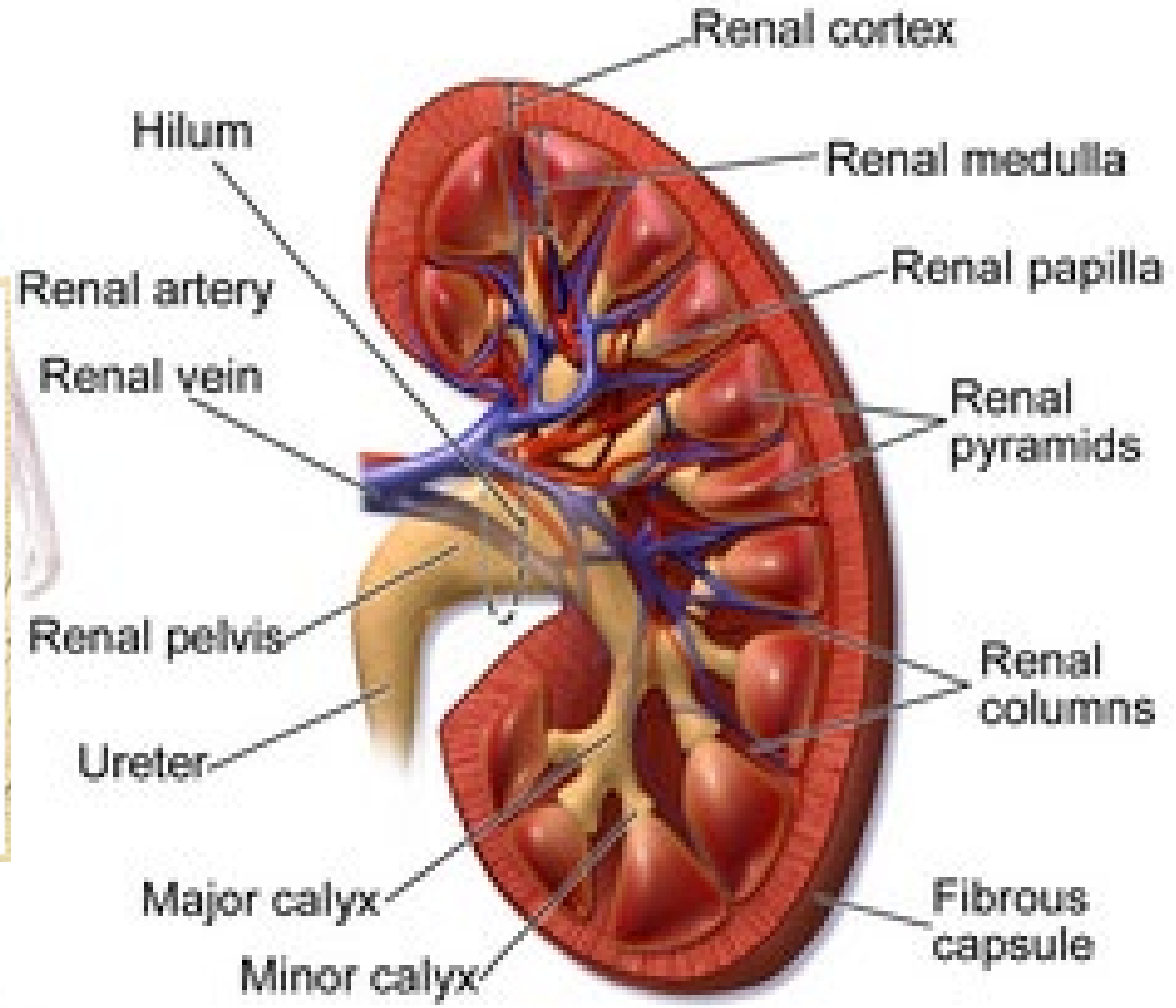
URINARY SYSTEM



Urinary System Diagram. Image Credit: Vecton / Shutterstock

KIDNEY ANATOMY



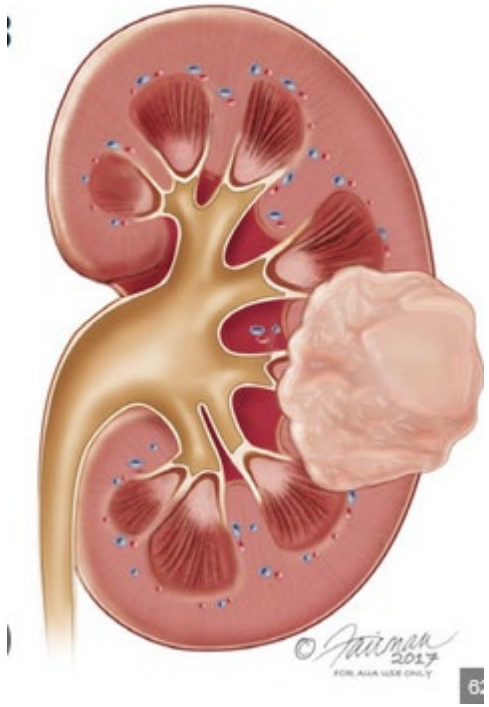


CORTEX: Outer layer
MEDULLA: Inner layer composed of **PYRAMIDS** apex is the **papilla**. The base of the pyramid is adjacent to the cortex.

CALYX: Is a cup-shaped structure which collects urine directly from the renal **papillae**. From the **minor calyces**, the urine passes to the **major calyces** and then drain into the renal pelvis and into the ureter. The renal calyx is covered by **urothelium.**

Site Term and code	Synonyms
Bladder, ureteric orifice C676	Just above ureteric orifice
Overlapping lesion of urinary organs C688	-
Paraurethral gland C681	-
Renal pelvis C659	Pelvis of kidney Pelviureteric junction Renal calyces Renal calyx

KIDNEY



Path report from kidney parenchyma biopsy: Single invasive neuroendocrine tumor with **<u>minority</u>** of tumor being large cell neuroendocrine carcinoma.

Code to:

a) 8240/3 Neuroendocrine tumor (NET)

b) 8246/3 Neuroendocrine carcinoma

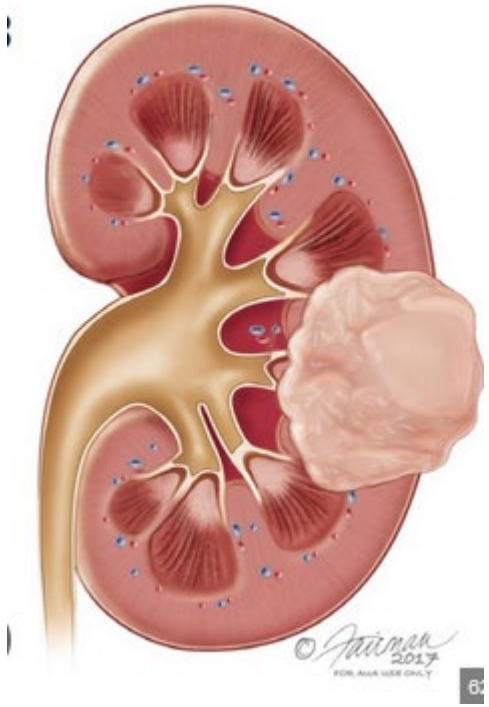
c) 8013/3 Large cell neuroendocrine carcinoma

c) 8013/3 Large cell neuroendocrine carcinoma

KIDNEY

NOS/Specific Histology Term and Code	Synonyms	Subtypes/Variants
Neuroendocrine tumor (NET) **8240/3** *Note*: Extra-adrenal paraganglioma, NOS reportable for cases diagnosed 1/1/2024 forward	Carcinoid [OBS] Well-differentiated neuroendocrine tumor	Extra-adrenal paraganglioma **8693/3*** Large cell neuroendocrine carcinoma/tumor **8013/3** Small cell neuroendocrine carcinoma **8041/3**
Paraganglioma **8700/3** *Note*: Reportable for kidney C64.9 beginning 1/1/2024	Extra-adrenal pheochromocytoma	

*** These new codes were approved by the IARC/WHO Committee for ICD-O.**



-Single invasive **neuroendocrine tumor** with **<u>minority</u>** of tumor being **large cell neuroendocrine** carcinoma-

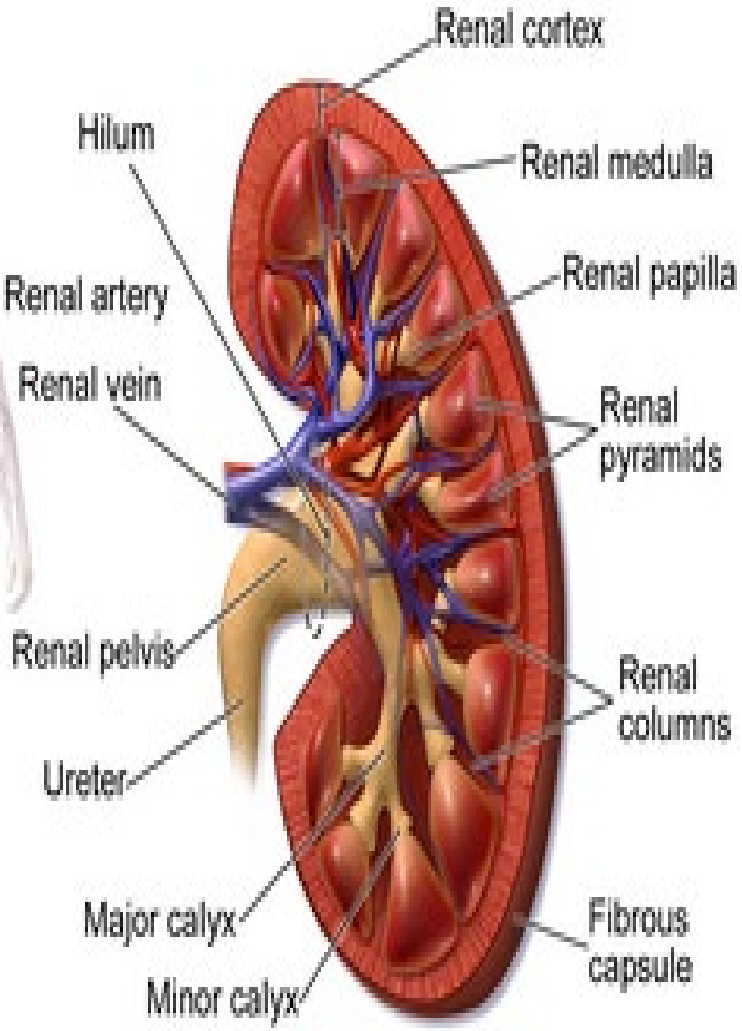
Code the most specific histology or subtype, regardless of whether it is described as:

-The majority or predominant part

-The **minority**

-A component STR 2025

kidney



Rule M11 Abstract a **single primary**[1] when there are **urothelial carcinomas** in multiple urinary organs.

Note 1: This rule is **ONLY** for urothelial carcinoma **8120** and all subtypes/variants of urothelial carcinoma (with the exception of micropapillary). This rule does not apply to any other carcinomas or sarcomas.

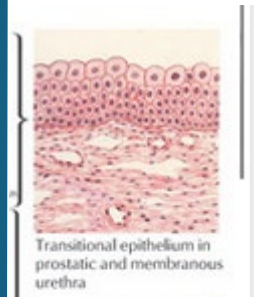
Note 2: Behavior is irrelevant.

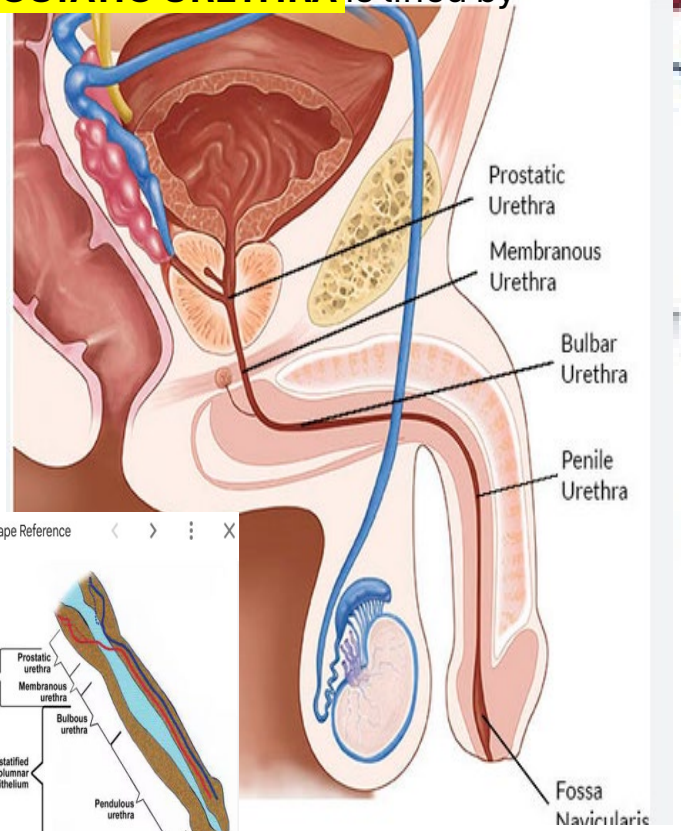
Note 3: This rule applies to multifocal/multicentric carcinoma which involves two or more of the following urinary sites:

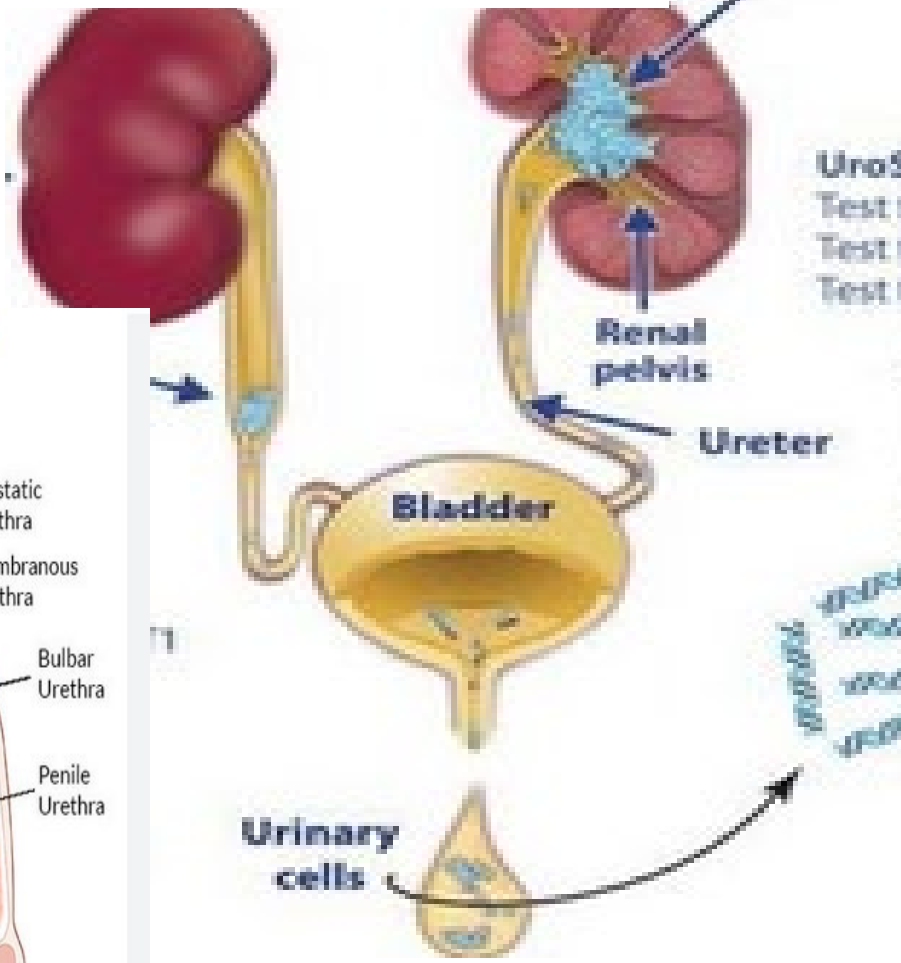
- Renal pelvis
- Ureter
- Bladder
- Urethra

Renal Pelvis, Ureter, Bladder, and Other Urinary

Urothelium or Transitional Epithelium is the specialized epithelial lining of the urinary tract, which includes 2/3 of the lining of the urethra. The **PROSTATIC URETHRA** is lined by UROTHELIUM.





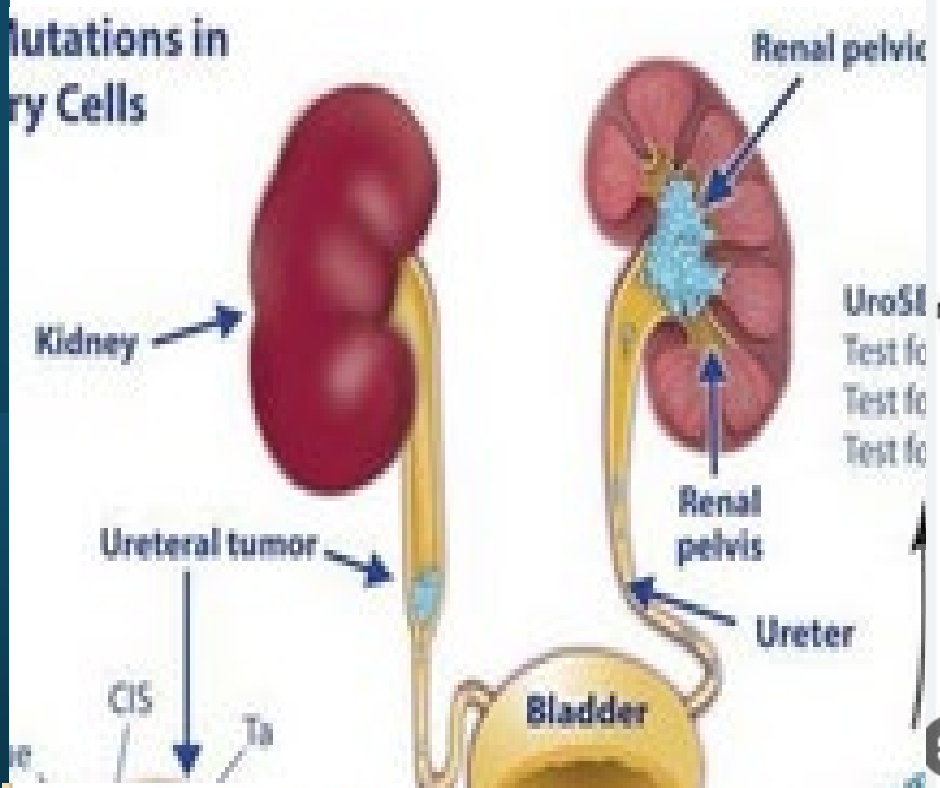


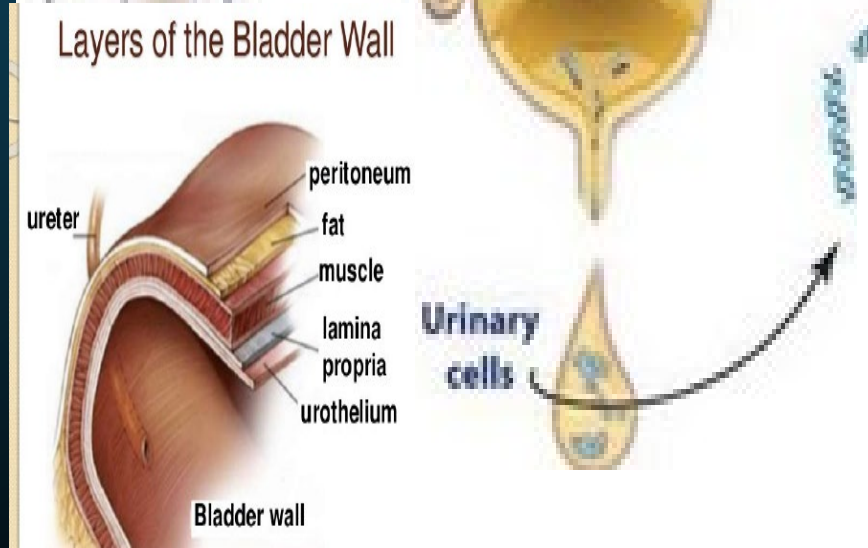
Urothelium is the specialized epithelial lining of the urinary tract, which includes 2/3 of the lining of the urethra. The **PROSTATIC URETHRA** is lined by UROTHELIUM.

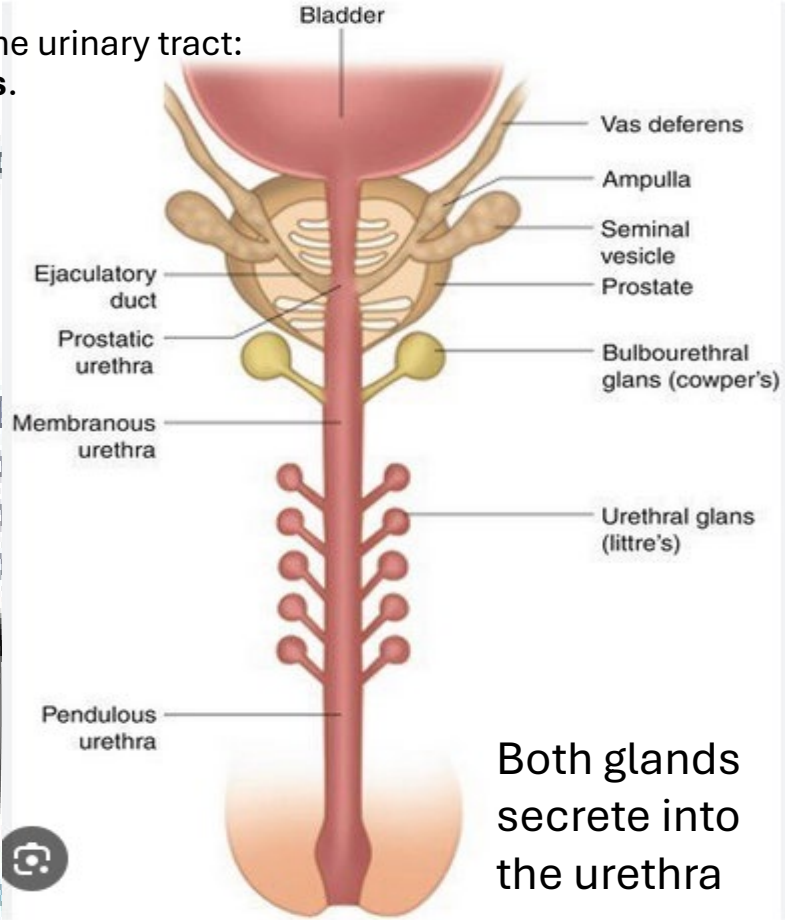
INGUINAL lymph node is Summary Stage 7 Distant for PROSTATE.

Renal pelvis, Ureter, Bladder and others

Urothelium or transitional epithelium is located lining the urinary tract: **Bladder**, proximal part of **urethra**, **ureters**, **renal pelvis**.







Both glands secrete into the urethra

Site Term and code	Synonyms
Bladder, ureteric orifice C676	Just above ureteric orifice
Overlapping lesion of urinary organs C688	-
Paraurethral gland C681	-
Renal pelvis C659	Pelvis of kidney Pelviureteric junction Renal calyces Renal calyx
Ureter C669	-
Urethra C680	Cowper gland Littre glands Prostatic utricle Urethral gland
Urinary system NOS C689	-

Vesico**ureteric** (**Ureteroves**ical) junction

Definition: Site where the lower distal end of the ureter connects to the urinary bladder.

Primary Site C 659 Histology 8120 Behavior 3 - Malign

Discriminator1

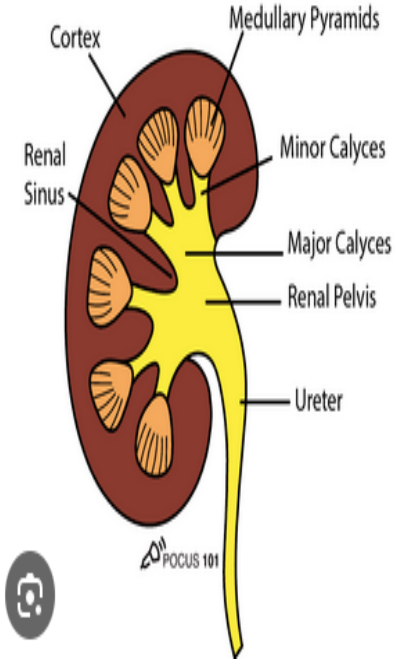
Schema 00610 Kidney Renal Pelvis

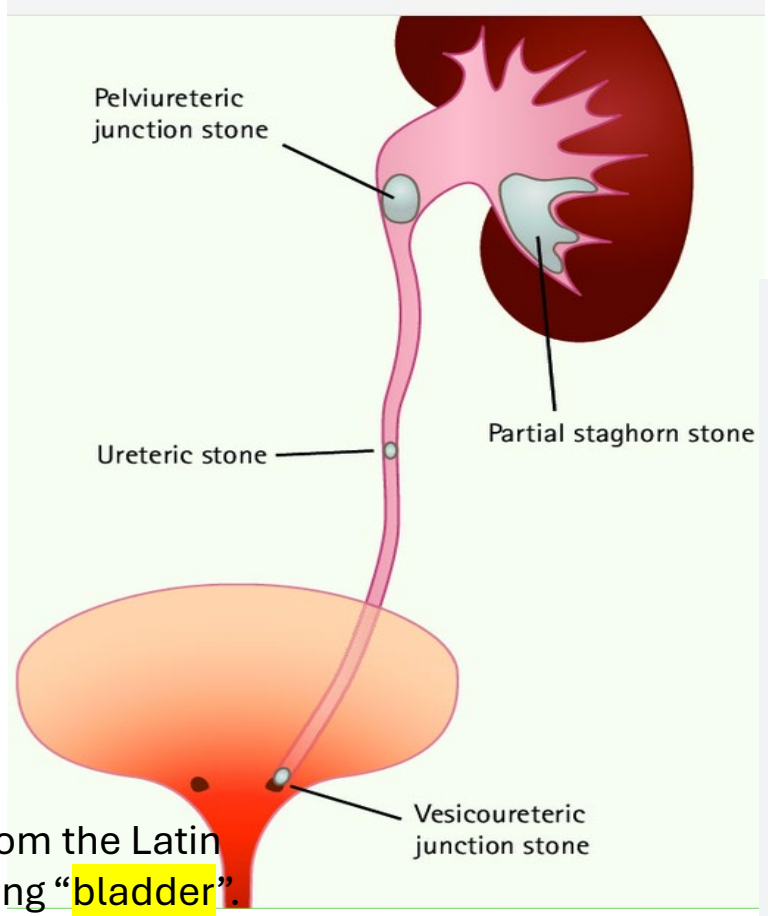
Description SS 9th Edition Schema: 00610 - Kidney
Florida Required SSDIs:
No SSDI data required by FCDS

Laterality 2 - Left

Text-Primary Site VESICOURETERIC JUNCTION

Text-Histology HIGH GRADE UROTHELIAL CARCINOMA

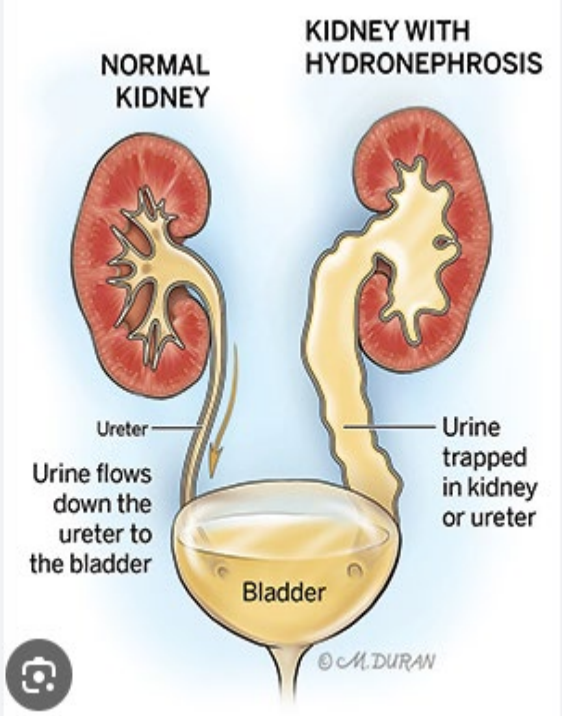




C65 RENAL PELVIS

C65.9 Renal pelvis
Pelvis of kidney
Renal calyces
Renal calyx
Pelviureteric junction

VESICO-: Comes from the Latin word VESICA meaning "bladder".



1. Code overlapping lesion of urinary bladder C678 when:
   A. A single tumor of any histology overlaps subsites of the bladder
   B. A single tumor or non-contiguous tumors which are:
      - Urothelial carcinoma in situ 8120/2 AND
      - Involves only bladder and one or both ureters (no other urinary sites involved)

Note: Overlapping non-invasive tumors of the bladder and ureter almost always originate in the bladder. They extend/overlap into the ureter by spreading along the mucosa. It is important to code these primaries to bladder C678, NOT to overlapping lesion of urinary organs C688

Text - Dx Procedures - X-ray/Scans

10/28/2024 AH FISH: CT A/P UROGRAMMARGINAL INCREASE IN SIZE OF 4.2 MASS LESION AT VESICOURETERIC JUNCTION W/PERIVESICAL STRANDING CONCERNING FOR TUMORAL EXTENSION INTO PERIVESICAL FAT. ADDITIONAL 2.1 CM LESION ANT AND INF TO LT SIDED VESICOURETERIC JUNCTION.LT HYDROURETERONEPHROSIS.INDETERMINATE ENLARGED LT EXTERNAL AND RT INTERNAL ILIAC NODES CONCERNING FOR NEOPLASTIC/METS.

Renal Pelvis, Ureter, **Bladder**, and Other Urinary

Diagnosis from TURB is invasive **Urothelial carcinoma** and Large cell Neuroendocrine carcinoma

a) 2 Abstracts: 1 for urothelial carcinoma **8120** and other for Large Cell Neuroendocrine carcinoma **8013**
b) 1 Abstract for Large Cell Neuroendocrine carcinoma **8013**
c) 1 Abstract for Mixed Neuroendocrine-Non-neuroendocrine carcinoma **8154**

b) 1 Abstract for Large Cell Neuroendocrine carcinoma 8013/3

Neuroendocrine carcinoma NOS 8246/3		Large cell neuroendocrine tumor/combined large cell neuroendocrine carcinoma 8013/3 Small cell neuroendocrine carcinoma 8041/3

Rule H5 Code combined large cell carcinoma **8013** when the final diagnosis is large cell neuroendocrine carcinoma and any other type of carcinoma (does not apply to sarcoma).

Renal Pelvis, Ureter, **Bladder**, Urethra…

- If the urethra biopsy pathology is invasive urothelial carcinoma and SMALL cell neuroendocrine carcinoma:
  - Code Mixed SMALL cell carcinoma 8045/3

8045/3	Preferred	Combined small cell carcinoma
8045/3	Synonym	Mixed small cell carcinoma
8045/3	Related	Combined small cell-adenocarcinoma
8045/3	Related	Combined small cell-large cell carcinoma
8045/3	Related	Combined small cell-squamous cell carcinoma

Rule H4 Code mixed small cell carcinoma 8045 when the final diagnosis small cell neuroendocrine mixed with any other type of carcinoma (does not apply to sarcoma).

- If the TURB is urothelial carcinoma and LARGE cell neuroendocrine carcinoma:
  - Code Combined LARGE cell carcinoma 8013/3

Rule H5 Code combined large cell carcinoma 8013 when the final diagnosis is large cell neuroendocrine carcinoma and any other type of carcinoma (does not apply to sarcoma).

Neuroendocrine carcinoma NOS 8246/3		Large cell neuroendocrine tumor/combined large cell neuroendocrine carcinoma 8013/3 Small cell neuroendocrine carcinoma 8041/3

Bladder

Bladder. Anterior wall with HG **urothelial** carcinoma. **Small cell neuroendocrine** carcinoma is found in the bladder dome.

How many abstracts you do? 1 or 2?

What code(s)?

a)Mixed neuroendocrine/non-neuroendocrine carcinoma **8154/3**

b)Neuroendocrine carcinoma NOS **8246/3**

d)Neuroendocrine tumor NOS **8240/3** AND Urothelial **8120/3**

c)Small cell neuroendocrine carcinoma **8041/3** and **8120/3** Urothelial

d) Mixed adenocarcinoma **8323/3**

c) 2 ABSTRACTS

-Small cell neuroendocrine carcinoma **8041/3** and

- **8120/3** Urothelial carcinoma

RULE M13

Rule M13 Abstract **multiple primaries**[ii] when separate/non-contiguous tumors are on **different** rows in Table 2 in the Equivalent Terms and Definitions. Timing is irrelevant.

Note: Each row in the table is a **distinctly different** histology.

Renal Pelvis, Ureter, Bladder, and Other Urinary Equivalent Terms and Definitions
C659, C669, C670-C679, C680-C689
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Table 2: Specific Histologies, NOS, and Subtypes/Variants

Mixed neuroendocrine-non-neuroendocrine carcinoma 8154/3		
Neuroendocrine carcinoma NOS 8246/3		Large cell neuroendocrine tumor/combined large cell neuroendocrine carcinoma **8013/3** Small cell neuroendocrine carcinoma **8041/3**
Neuroendocrine tumor NOS 8240/3	Neuroendocrine tumor, grade 1 Well differentiated neuroendocrine carcinoma Neuroendocrine carcinoma, low grade	Neuroendocrine tumor, grade 2 **8249/3**
Paraganglioma 8693/3 *Note*: Reportable for cases diagnosed 1/1/2021 forward	Extra-adrenal paraganglioma	

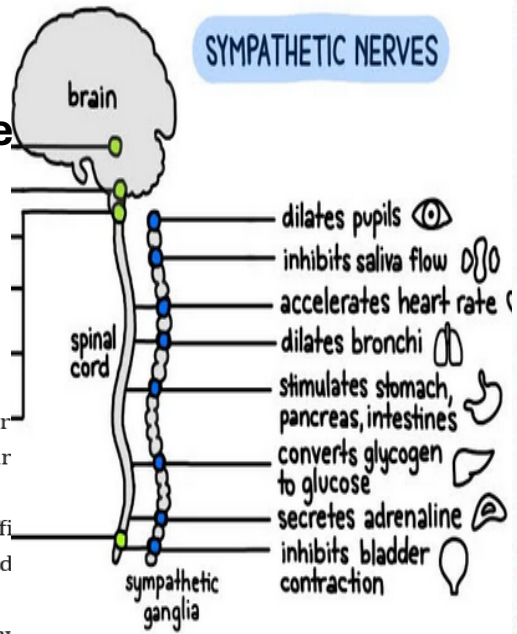
Paragangliomas of the bladder can also arise from parasympathetic paraganglia, though this is a less common origin.

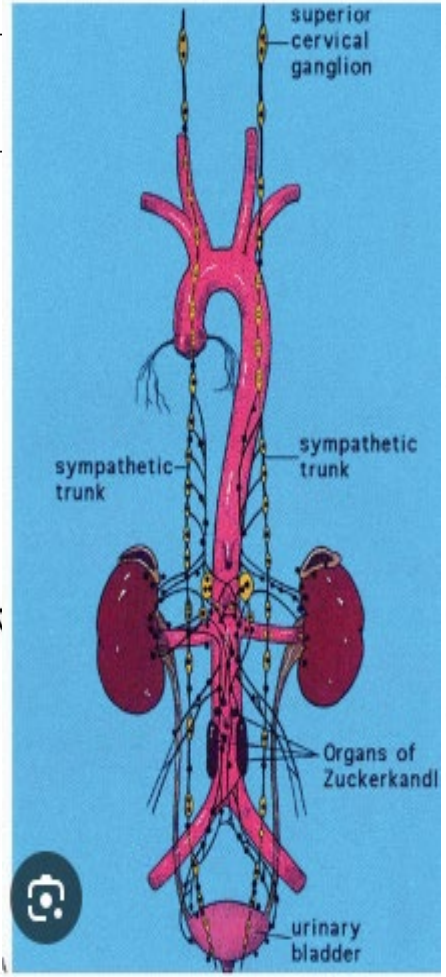
Tumors of chromaffin cells, derived from the embryonic neural crest, usually originate from the adrenal medulla and are designated as pheochromocytomas. However, 10% of these tumors occur at extra-adrenal sites and are known as paragangliomas.[1]

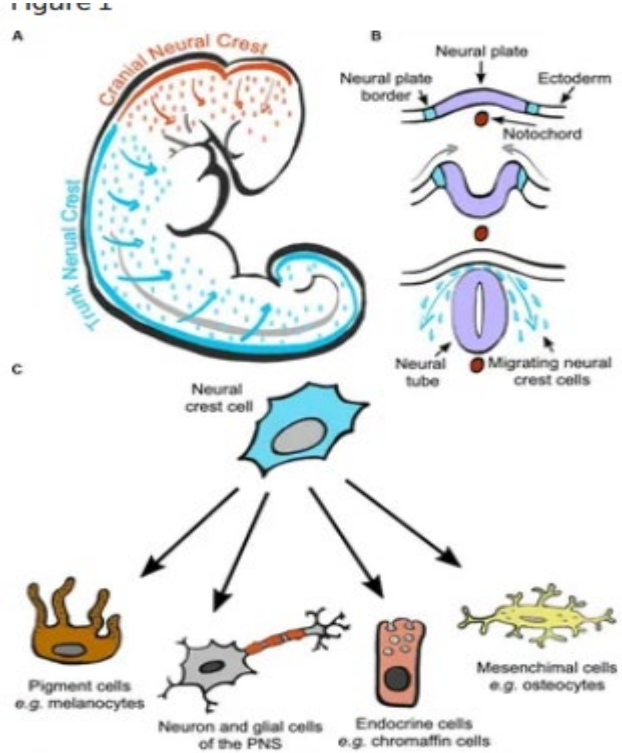
Basicmedical Key

Paraganglioma of the urinary bladder

Paragangliomas: tumors that develop from Chromaffin cells, which are specialized nerve cells that control functions like **blood pressure** because of the release of Epinephrine (Adrenaline), and Norepinephrine.
Ganglia: Bunches of nerve cells.
-**Para**: Alongside, beside, parallel.







CHROMAFFIN cells migrate to the area adjacent to the sympathetic ganglia (hence paraganglia), and to the ADRENAL MEDULLA. release catecholamines (Norepinephrine and epinephrine aka adrenaline).

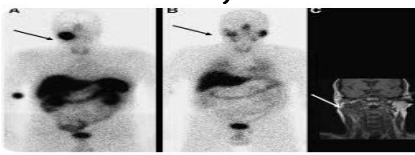
Paraganglioma of the urinary bladder is very rare and account for 0.06% of all bladder tumors and 6% of extra-adrenal pheochromocytomas.[1] However, in the genitourinar tract, the urinary bladder is the most common site (79.2%), followed by the urethra (12.7%), pelvis (4.9%), and ureter (3.2%).[3,4] These tumors originate from chromaffi tissue of the sympathetic nervous system associated with the urinary bladder wall and most commonly situated at the dome or the trigone of the bladder and may be nonfunctional or functional.[2,5] They remain usually benign, but 15–20% tumors may

https://pmc.ncbi.nlm.nih.gov/articles/PMC4518387/

Bladder Paragangliomas

Women > Men -Third decade of life -Rare: 0.06% of all bladder tumors and 6% of extra-adrenal pheochromocytomas

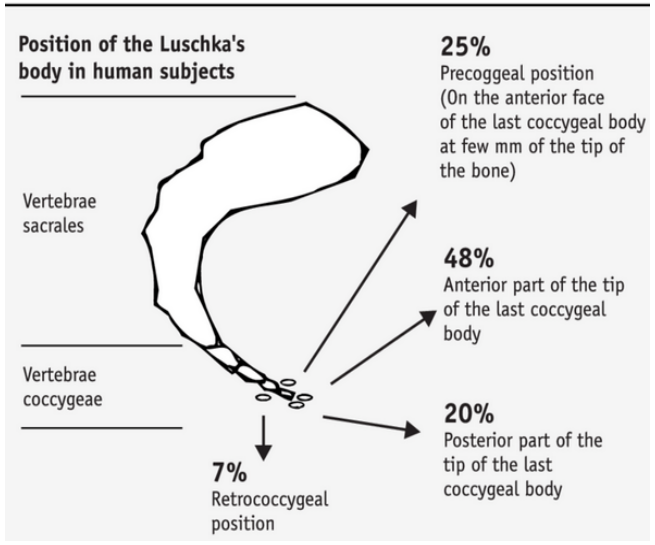
- Genitourinary tract sites: bladder (79.2%), urethra (12.7%), ureter (3.2%)
- Can be Functional or NON-Functional
- Presentation:
  - -Asymptomatic (Incidental finding)
  - -Symptomatic: Hypertensive crises with headaches, palpitations, hot flushes, diaphoresis or profuse sweating. Postmicturition hypotension and syncope. Painless Hematuria.
- Triggers:
  - Micturition, overdistention of the bladder, defecation, sexual activity, ejaculation, or bladder instrumentation, tumor manipulation.
- Localization and detection:
  - -Catecholamine levels and metabolites in plasma and urine
  - -CT scan, MRI, Scanning with 123 I-MIBG scintiscan
- Treatment:
  - -SURGERY: under **previous alpha-adrenergic blockade** (**phenoxybenzamine or prazosin**) to avoid a potentially lethal transient hypertension. Pre-treat for biopsy too!
  - -CHEMO-resistant and Radioresistant. Although they have been used.
  - -131 Iodine metaiodobenzylguanidine (MIBG) therapeutic
- Tendency to metastasize
- Lifelong follow-up due to High recurrence rate. Tools: Annual measurement of catecholamine levels, cystoscopy, CT scan, 123 I-MIBG scintiscan

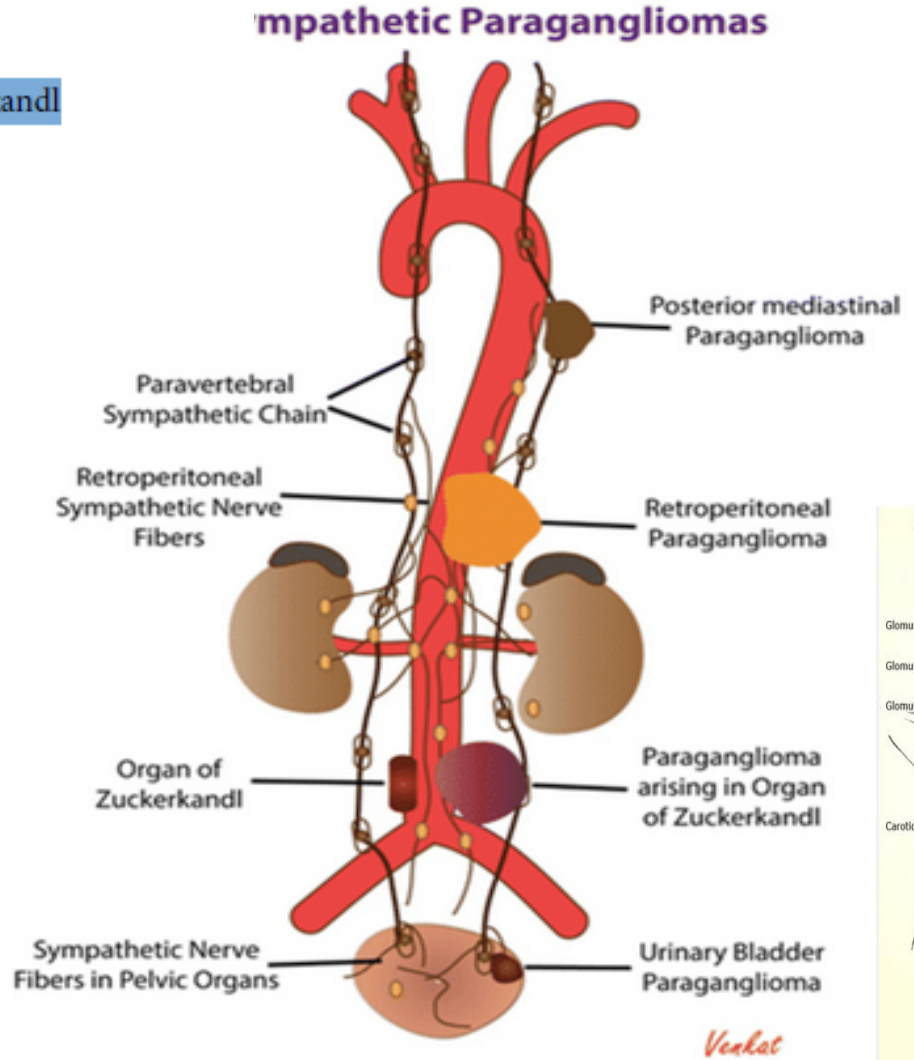


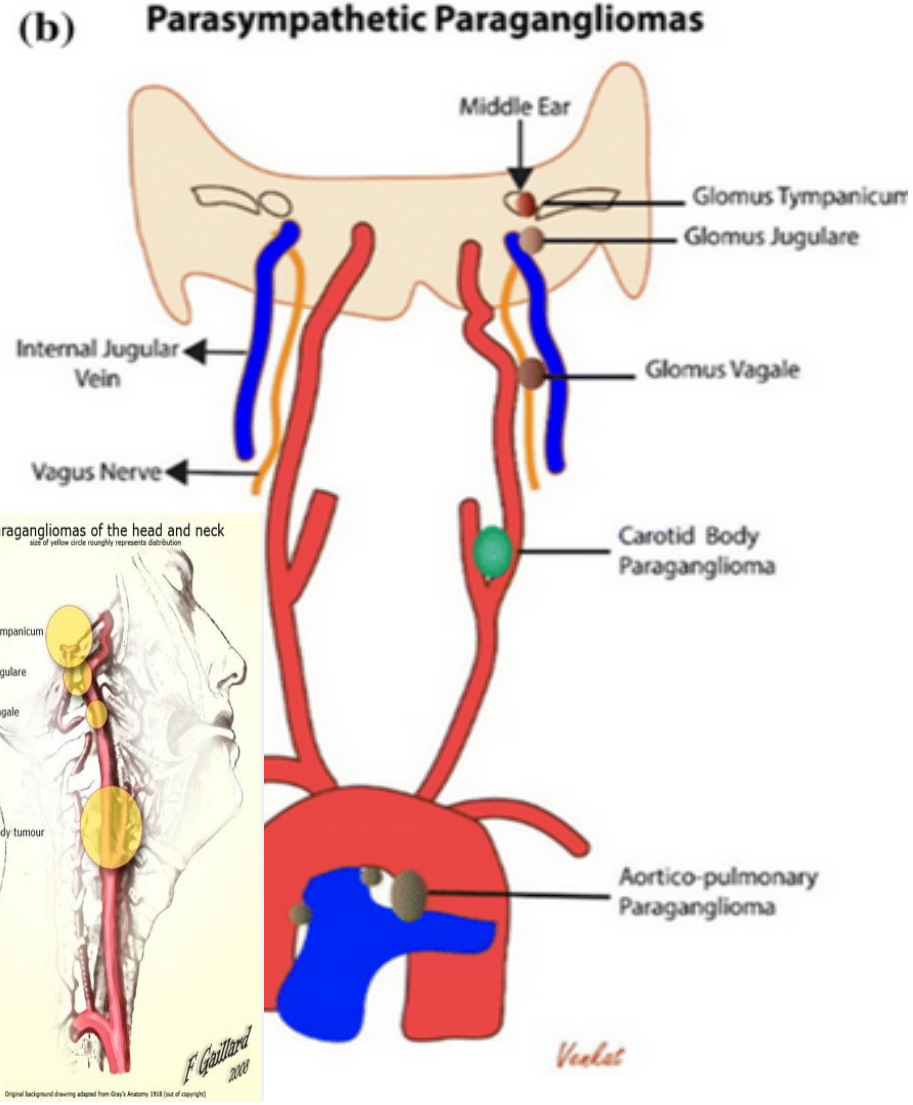
PARAGANGLIOMAS

C75.5 Aortic body and other paraganglia

Coccygeal body
Coccygeal glomus
Glomus jugulare
Para-aortic body
Organ of Zuckerkandl
Paraganglion



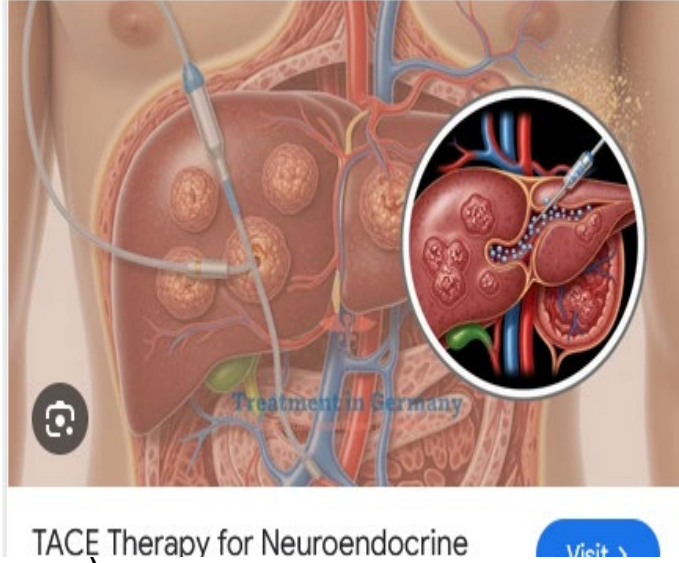




Sympathetic and parasympathetic paragangliomas. a Drawing of sympathetic paragangliomas originating from the organ of Zuckerkandl, paravertebral sympathetic chain, and sympathetic nerve fibers in the pelvic and retroperitoneal organs. b Drawing of parasympathetic paragangliomas originating from carotid body and along the cervical and thoracic branches of the vagus and glossopharyngeal nerves

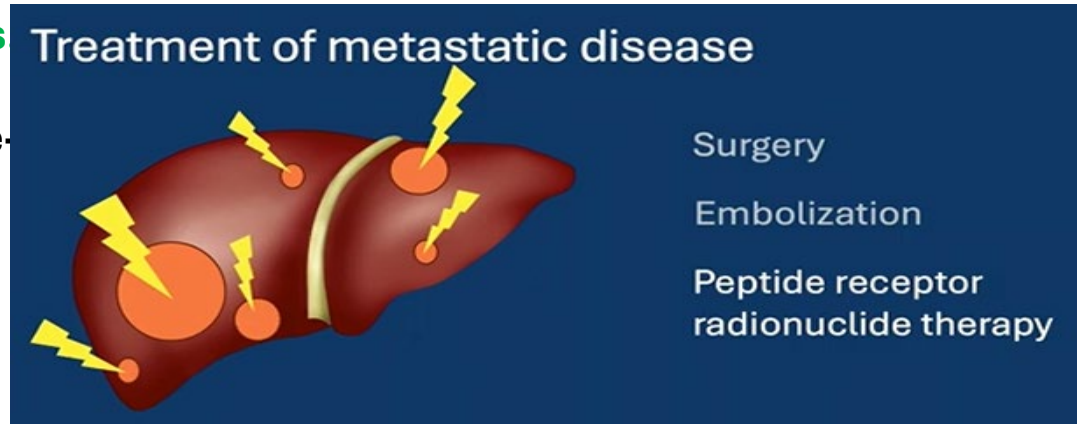
https://www.researchgate.net/figure/Sympathetic-and-parasympathetic-paragangliomas-a-Drawing-of-sympathetic-paragangliomas_fig1_332948703

Treatment options for NETs/NECs



- MEDICATIONS (Including **targeted therapy**)
  - First line of therapy: SSAs (Somatostatin analogs) Octreotide, **Lanreotide**
  - Tyrosine kinase inhibitors: Sunitinib, Cabozantinib…
  - **Angiogenesis** inhibitors including Anti-VEGF antibodies (Bevacizumab…),
  - mTOR inhibitors (block cancer growth): **Everolimus**, Temsirolimus
- Surgery, Chemotherapy, Radiation
- Embolization
  - BLAND Embolization (Tiny particles are injected to block the blood vessels feeding the tumor).
  - CHEMOEmbolization (TACE –Transarterial Chemoembolization-) Particles loaded with chemo drugs are injected (Doxorubicin, Mitomycin C, Streptozocin, Vinblastine, Gemcitabine, Fluorouracil). Cuts off blood supply and delivers a high concentration of chemo directly to the tumor, minimizing systemic side effects. Preferred for smaller tumors and pts with good liver function.
  - RADIOEmbolization (TARE –Transarterial (THROUGH **femoral artery** to **hepatic artery**) Radioembolization-) Tiny beads are injected containing radioactive material like **YTTRIUM-90**. Cuts off blood supply and delivers a high concentration of chemo directly to the tumor, minimizing systemic side effects. Preferred for larger tumors and pts with compromised liver function.

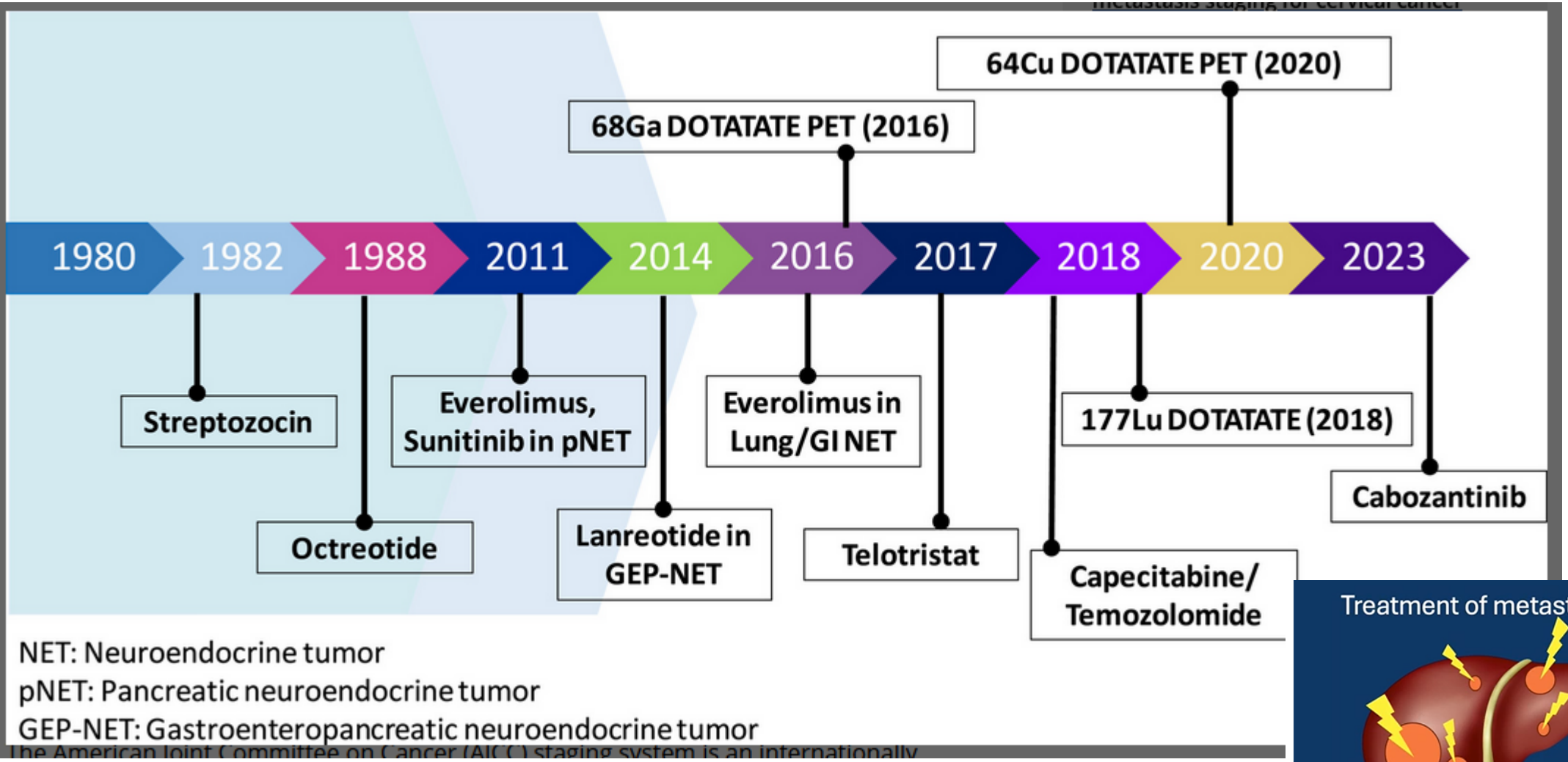
Despite not being curative, hepatic arterial embolization should be used in the management of NETs with liver metastasis.
It prolongs survival and improves symptoms!
-NETs metastasize most often to liver, peritoneal cavity and bone-

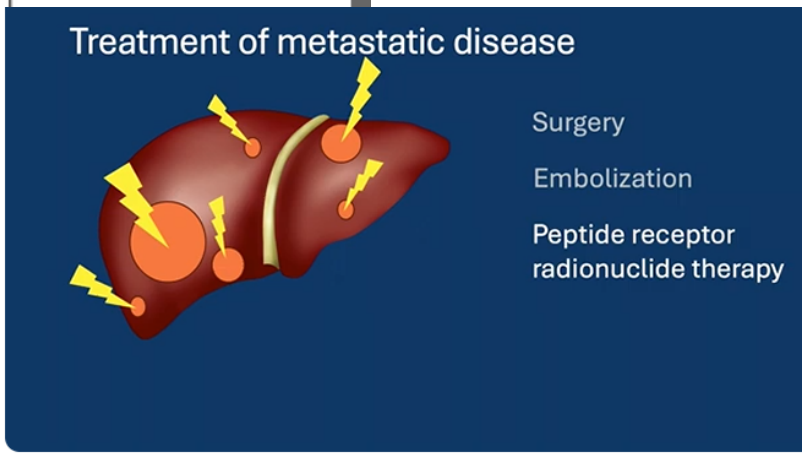


- Evaluate for PRRT (Peptide Receptor Radionuclide Therapy)

https://www.youtube.com/watch?v=XI84CMa5PyU

Neuroendocrine Treatment

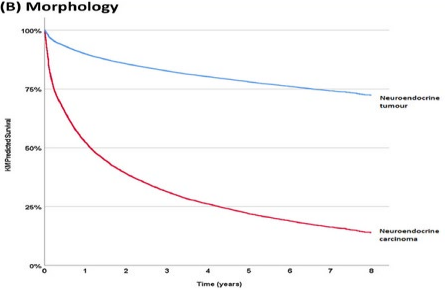




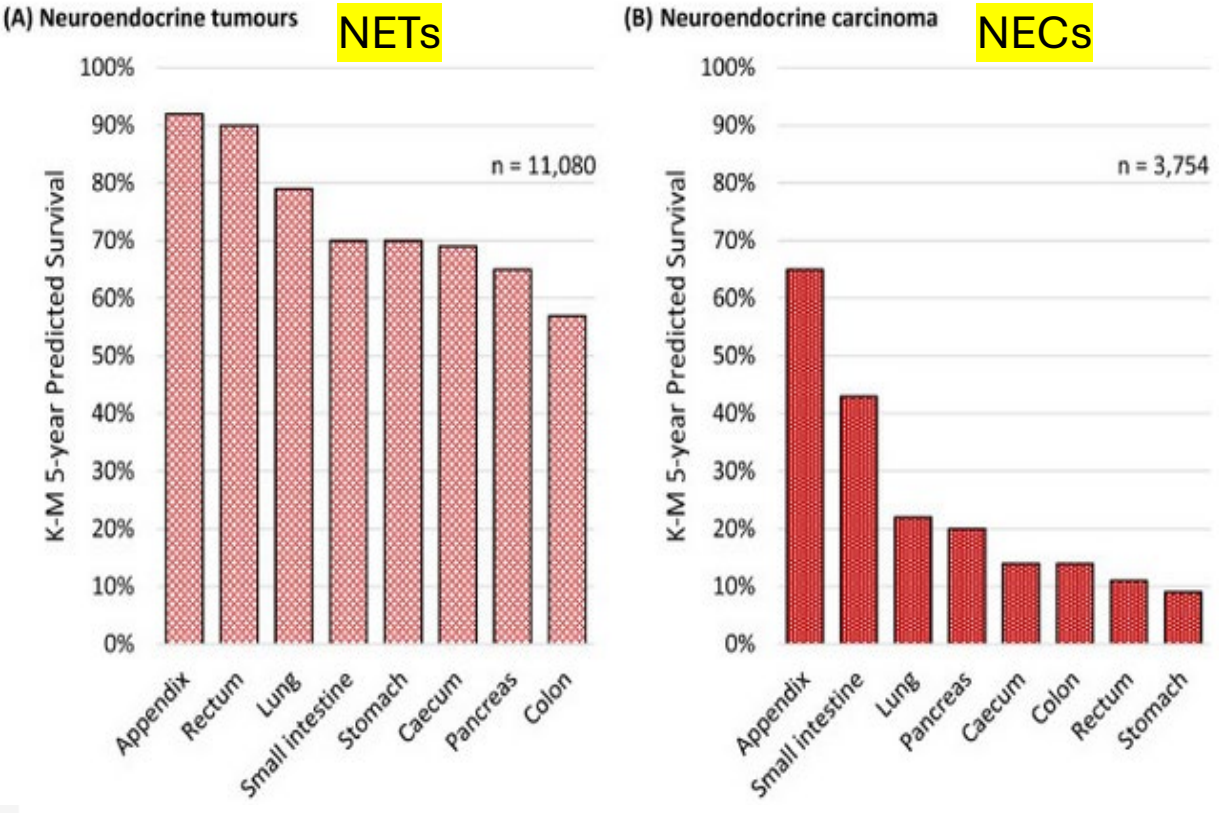
NCAN NET Patient Conference - New Orleans - Kristen Limbach MD - Pancreatic Neuroendocrine Tumors

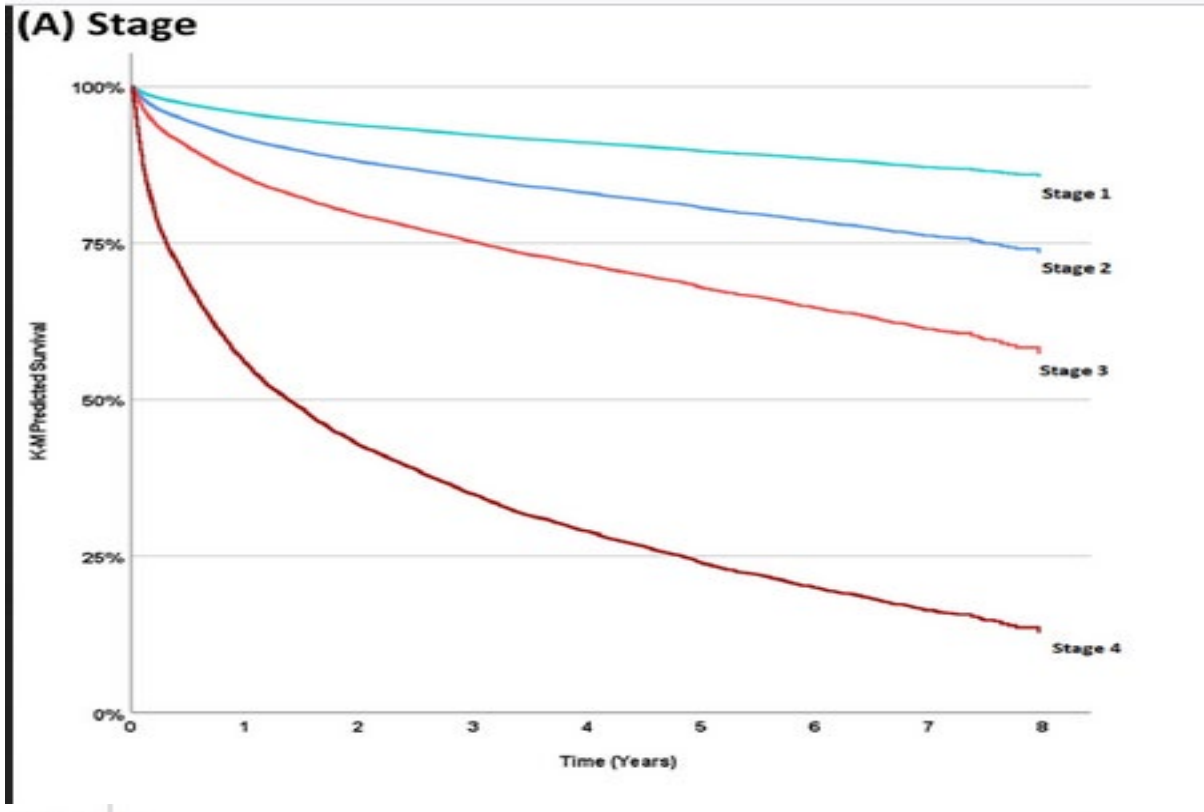
PRRT for **NETs** with Somatostatin Receptors

https://www.youtube.com/watch?v=XI84CMa5PyU



NENs Survival





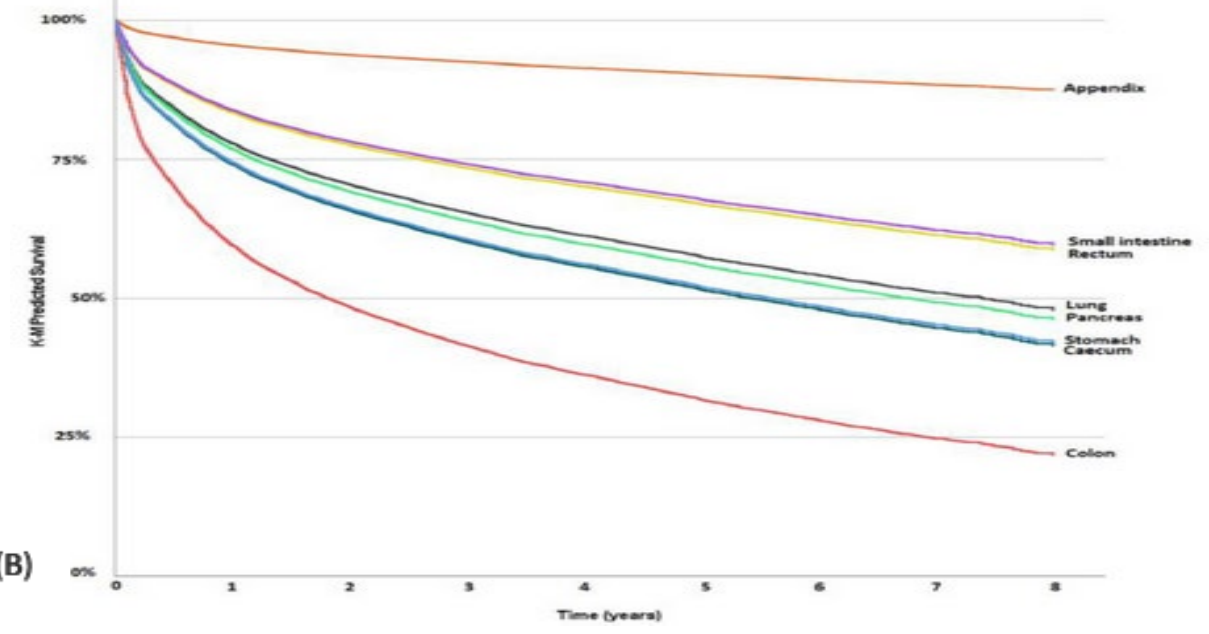


Figure 2 Kaplan–Meier predicted 5–year survival of (A) 11,080 neuroendocrine tumours and (B) 3,754 neuroendocrine carcinomas between 2012 and 2018 in England. Source data: NCRAS.

EXTRAS

CODING GRADE

GRADE Coding guidelines for solid tumors.

1. PREFERRED GRADING SYSTEM
2. GENERIC GRADE if allowed

When PREFERRED GRADING SYSTEM is not provided

Sometimes we can use the GENERIC grade system A,B,C,D in some sites

Other times we CANNOT use the GENERIC grade system, and we have to code 9

Prior to 2018	Description	2018 and forward
1	Well differentiated	A
2	Moderately differentiated	B
3	Poorly differentiated	C
4	Undifferentiated, anaplastic	D
9	Unknown	9

When using the PREFERRED GRADE for the specific site: we can put the same clinical grade in the path grade.

All Grade Tables (1-26, 98,99) except 88 (Hematopoietic and Lymphoid Neoplasms)have this Note in Pathology Grade

Grade Clinical 2

Grade Pathological 2

Note 6: Use the grade from the **clinical work up** from the primary tumor in different scenarios based on behavior or surgical resection

- **Behavior:**
  - Tumor behavior for the clinical and the pathological diagnoses are the same AND the clinical grade is the highest grade
  - Tumor behavior for clinical diagnosis is invasive, and the tumor behavior for the pathological diagnosis is in situ
- **Surgical Resection**
  - Surgical resection is done of the primary tumor and there is no grade documented from the surgical resection
  - Surgical resection is done of the primary tumor and there is no residual cancer
  -
- **No Surgical Resection**
  - Surgical resection of the primary tumor has not been done, but there is positive microscopic confirmation of distant metastases during the clinical time frame

Grade 88

Grade ID 88-Grade Clinical Instructions

Schema ID#	Schema ID Name	Active years
00790	Lymphoma	2018+
00795	Lymphoma-CLL/SLL	2018+
00811	Mycosis Fungoides	2018+
00812	Primary Cutaneous Lymphomas (excluding Mycosis Fungoides)	2018+
00821	Plasma Cell Myeloma	2018+
00822	Plasma Cell Disorders	2018+
00830	Hemeretic	2018+

Hematopoietic and Lymphoid Neoplasms: No grade fields included in the following schemas since grade is no longer applicable:

Note: Grade (cell indicator) is no longer applicable for this hematopoietic neoplasm.

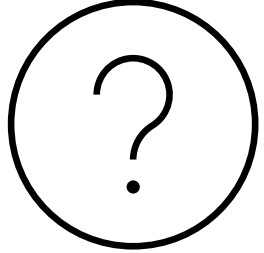
Code	Grade Description
8	Not applicable

Grade Clinical 2

Grade Pathological

Grade Pathological

9



NeuroEndocrine Tumors **Pathology grade** is different

Grade ID 07-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00290	NET Stomach	2018+
00301	NET Duodenum	2018+
00302	NET Ampulla of Vater	2018+
00310	NET Jejunum and Ileum	2018+
00320	NET Appendix	2018+
00330	NET Colon and Rectum	2018+
00340	NET Pancreas	2018+

Note 1: Grade Pathological must not be blank.

GENERIC grade A-D in NETs

Note 2: There is a preferred grading system for this schema. If the clinical grade given uses the preferred grading system and the pathological grade does not use the preferred grading system, do not record the Grade Clinical in the Grade Pathological field. Assign Grade Pathological using the applicable generic grade codes (A-D).

Grade ID 05-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00190	Appendix	2018-2022
09190	Appendix	2023+

Note 1: Grade Pathological must not be blank.

Note 2: There is a preferred grading system for this schema. If the clinical grade given uses the preferred grading system and the pathological grade does not use the preferred grading system, do not record the Grade Clinical in the Grade Pathological field. Assign Grade Pathological 9.

Grade ID 02-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00111	Oropharynx (p16-)	2018+
00112	Hypopharynx	2018+
00150	Cutaneous Carcinoma of Head and Neck	2018+
00180	Small Intestine	2018+
00200	Colon and Rectum	2018+
00220	Liver	2018+
00360	Lung	2018+
00370	Pleural Mesothelioma	2018+
00640	Skin Eyelid	2018+
00650	Conjunctiva	2018+

Note 1: Grade Pathological must not be blank.

Note 2: There is a preferred grading system for this schema. If the clinical grade given uses the preferred grading system and the pathological grade does not use the preferred grading system, do not record the Grade Clinical in the Grade Pathological field. Assign Grade Pathological 9.

Grade ID 04-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00170	Stomach	2018+

Note 1: Grade Pathological must not be blank.

Note 2: There is a preferred grading system for this schema. If the clinical grade given uses the preferred grading system and the pathological grade does not use the preferred grading system, do not record the Grade Clinical in the Grade Pathological field. Assign Grade Pathological 9.

00270	Ampulla of Vater	2018+
00280	Pancreas	2018+
00500	Vulva	2018+
00510	Vagina	2018+
00520	Cervix	2018-2020
09520	Cervix	2021+

Note 1: Grade Pathological must not be blank.

Note 2: There is a preferred grading system for this schema. If the clinical grade given uses the preferred grading system and the pathological grade does not use the preferred grading system, do not record the Grade Clinical in the Grade Pathological field. Assign Grade Pathological 9.

General grade (A-D)system DOES NOT apply!

Only the preferred grading system in Grade Path and yp. If no preferred grading system, then code 9.

Grade ID 01-Grade Pathological Instructions

Schema ID#	Schema ID Name	
00071	Lip	
00072	Tongue Anterior	
00073	Gum	
00074	Floor of Mouth	
00075	Palate Hard	
00076	Buccal Mucosa	
00077	Mouth Other	
00121	Maxillary Sinus	2018+
00122	Nasal Cavity and Ethmoid Sinus	2018+
00130	Larynx Other	2018+
00131	Larynx SupraGlottic	2018+
00132	Larynx Glottic	2018+
00133	Larynx SubGlottic	2018+
00230	Bile Ducts Intrahepatic	2018+
00241	Gallbladder	2018+
00242	Cystic Duct	2018+
00250	Bile Ducts Perihilar	2018+
00260	Bile Ducts Distal	2018+
00270	Ampulla of Vater	2018+
00280	Pancreas	2018+
00500	Vulva	2018+
00510	Vagina	2018+
00520	Cervix	2018-2020
09520	Cervix	2021+

Grade ID 02-Grade Pathological Instructions

Schema ID#	Schema ID Name
00111	Oropharynx (p16-)
00112	Hypopharynx
00150	Cutaneous Carcinoma of Head and Neck
00180	Small Intestine
00200	Colon and Rectum
00220	Liver
00360	Lung
00370	Pleural Mesothelioma
00640	Skin Eyelid
00650	Conjunctiva

Grade ID 03- Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00161	Esophagus (including GE junction) Squamous	2018+
00169	Esophagus (including GE junction) (excluding Squamous)	2018+

Grade ID 04-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00170	Stomach	2018+

Grade ID 05-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00190	Appendix	2018-2022
09190	Appendix	2023+

Schema ID#	Schema ID Name	Active years
00710	Lymphoma Ocular Adnexa	2018+

Grade ID 13-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00528	Cervix Sarcoma	2021+
00530	Corpus Carcinoma and Carcinosarcoma	2018+
00541	Corpus Sarcoma	2018+

Grade ID 16-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00570	Penis	2018+

Grade ID 22-Grade Pathological Instructions

Schema ID#	Schema ID Name	Active years
00690	Lacrimal Gland	2018+

GRADE PATH 9

When NO preferred grading system coding

The following table provides mapping from terms that may be used to describe one of the generic 4-grade system A-D categories to an appropriate code for 2018 and later cases.

Note 1: *Only use the table below when the appropriate grade table for a cancer uses the generic categories with alphabetic codes A-D, OR for a cancer site which includes codes A-D for when the priority grade system was not used/documented. In addition, do not use the table below for a cancer that uses the generic categories but assigns numeric codes. The latter condition means that the site uses nuclear grading for which the alphabetic codes are not appropriate.*

Note 2: *Do not use this table to code any priority AJCC recommended grade system terms.*

Description	Assigned Grade Code
Differentiated, NOS	A
Well differentiated	A
Only stated as 'Grade I'	A
Nuclear Grade 1	A
Fairly well differentiated	B
Intermediate differentiation	B
Low grade	B
Mid differentiated	B
Moderately differentiated	B
Moderately well differentiated	B
Partially differentiated	B
Partially well differentiated	B
Relatively or generally well differentiated	B

Description	2018 and forward
Well differentiated	A
Moderately differentiated	B
Poorly differentiated	C
Undifferentiated, anaplastic	D
Unknown	9

Coding Guidelines for Generic Grade

Description	Assigned Grade Code
Only stated as 'Grade II'	B
Nuclear Grade 2	B
Medium grade, intermediate grade	C
Moderately poorly differentiated	C
Moderately undifferentiated	C
Poorly differentiated	C
Relatively poorly differentiated	C
Relatively undifferentiated	C
Slightly differentiated	C
Dedifferentiated	C
Only stated as 'Grade III'	C
Nuclear Grade 3	C
High grade	D
Undifferentiated, anaplastic, not differentiated	D
Only stated as 'Grade IV'	D
Non-high grade	9
Nuclear Grade 4	D

Thank you!

Send your questions or inquires

betty.malanowski@med.miami.edu

•https://www.youtube.com/watch?v=nOhlcpbfgqI
•https://www.news-medical.net/health/Pheochromocytoma-Tumor-of-Adrenal-Gland-Tissue.aspx
•Pheochromocytoma: National Cancer Institute. National Cancer Institute. Published February 12, 2020. Accessed September 28, 2022.
•https://en.wikipedia.org/wiki/Chromaffin_cell
•https://pmc.ncbi.nlm.nih.gov/articles/PMC3830426/
•https://en.wikipedia.org/wiki/Chromaffin_cell
•https://cdn.jamanetwork.com/ama/content_public/journal/jamanetworkopen/939624/zoi250502f1_1749749052.08832.png?Expires=1759934419&Signature=gogonFDb~oaVwhUDfTp2fZKrnZ4pC5ASTThjo--ipQt-S4N2nTsvB3p1bTkMyiai0J7xqsDKaq~S3E21rDyYwDfmoa4pCN2e0WOq2HsND1NAzk-QE4C56egbDAWOo3Ezc5Xl5mZD9S6PFz9QTR2mdWNHIsVB2SYra4Ic4LR1FZEaMNVKaTRBvt95ue5G9QXFbQJK7jIUh~4NRQft60PmK2bMB1pMjrZsWTB~-aPvzO38Oy6iWengqePue4HnhUzE70s2tVINfzg0fnroWmpjzVeejPj-0upgo8ApUkQyD5zUWmc-B5UUH0VeqdvNG5shiLkvqE3HuoXQHqAXT84JXw__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA
•https://pmc.ncbi.nlm.nih.gov/articles/PMC5873497/
•https://pmc.ncbi.nlm.nih.gov/articles/PMC9520175/
•https://pmc.ncbi.nlm.nih.gov/articles/PMC8514330/
•https://pmc.ncbi.nlm.nih.gov/articles/PMC10409618/
•https://seer.cancer.gov/tools/solidtumor/current/STM_Combined.pdf
•https://www.cancerresearchuk.org/about-cancer/neuroendocrine-tumours-nets/types/pancreatic-nets/glucagonoma
•**NCAN NET Patient Conference - New Orleans - Kristen Limbach MD - Pancreatic Neuroendocrine Tumors**
•Planning for the future when diagnosed with neuroendocrine cancer - Dr Philip Lodge
•https://netcancerawareness.org/what-is-net-cancer/
•Lippincot
•Animated biology with arpan
•https://www.endocrinologyadvisor.com/ddi/pheochromocytoma/
•NIC National Institutes of Health
•https://www.sciencedirect.com/topics/medicine-and-dentistry/apudoma#:~:text=Cutaneous%20flushing%2C%20persistent%20diarrhea%2C%20and,the%20time%20of%20definitive%20diagnosis.
•https://meridian.allenpress.com/aplm/article/146/11/1402/477701/Appendiceal-Goblet-Cell-Adenocarcinoma-A
•https://pmc.ncbi.nlm.nih.gov/articles/PMC6499718/
•https://www.xiahepublishing.com/2771-165X/JCTP-2022-00018
•https://www.nature.com/articles/modpathol2017184
•https://www.tiktok.com/@sciepro/video/7402616968194297120
•https://pmc.ncbi.nlm.nih.gov/articles/PMC5653522/
•https://www.aafp.org/pubs/afp/issues/2013/0901/p319.html
•Pancreatic Cancer Action Network
•https://x.com/histocasino/status/1149118063050182657
•https://physioweb.org/excretory/kidney.html

•https://www.youtube.com/watch?v=nOhlcpbfgqI
https://pmc.ncbi.nlm.nih.gov/articles/PMC6239108/figure/f2-cmar-10-5629/
https://www.cancer.org/cancer/types/lung-carcinoid-tumor/detection-diagnosis-staging/survival-rates.html
https://www.cancer.org/cancer/types/merkel-cell-skin-cancer/about/key-statistics.html
https://www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/treating/targeted-therapy-for-gastrointestinal-neuroendocrine-tumors.html
https://www.cancer.org/cancer/types/thymus-cancer/about/what-is-thymus-cancer.html
https://www.researchgate.net/figure/Areas-of-the-kidney-ureter-and-bladder-where-stones-are-likely-to-occur-They-are_fig1_264219261
Gkand Linna
SOLID TUMOR RULES
GRADE MANUAL
ICD-0-3.2
https://pubmed.ncbi.nlm.nih.gov/22538258/
https://pmc.ncbi.nlm.nih.gov/articles/PMC3272914/
https://www.simplypsychology.org/peripheral-nervous-system.html
https://www.frontiersin.org/journals/ecology-and-evolution/articles/10.3389/fevo.2020.00278/full
https://www.frontiersin.org/journals/ecology-and-evolution/articles/10.3389/fevo.2020.00278/full
https://www.scientificanimations.com/lungs-functions-related-diseases/uncategorized/
https://pmc.ncbi.nlm.nih.gov/articles/PMC5697503/
https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2022.810645/full
https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21840
https://www.thelancet.com/cms/10.1016/j.lanepe.2022.100510/asset/4b9d4f84-2a0d-42a0-8d85-e7c21246b7fe/main.assets/gr3_lrg.jpg
https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2024.1424839/full
https://www.researchgate.net/figure/Preoperative-MRI-of-a-patient-with-olfactory-neuroblastoma-stage-T4bN0M0-a-coronal_fig1_328784413
https://www.researchgate.net/figure/Preoperative-MRI-of-a-patient-with-olfactory-neuroblastoma-stage-T4bN0M0-a-coronal_fig1_328784413