

CSGNA
25 September 2015, Moncton



The Moncton Hospital

Peter Lightfoot MD FRCPC

NETs

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Weir fishing, Grand Manan, N.B –

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Weir fishing, Grand Manan, N.B –
Like G.I.s, fish also are attracted to any orifice!

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NETs

**Notes on
Erotica and
Tumultuous
Sex**



NETs

Neuroendocrine Tumors

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25 September 2015, Moncton



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NETs

Historically:



NETs

Historically:

1897 Kulchitsky – enterochromaffin cell

1907 Oberndorfer – “karznoide” tumor



NETs

Historically:

- Cells with:
Neural connections



NETs

Historically:

- Cells with:

Neural connections

Production and secretion of chemicals

(“hormones”)

Amine precursor uptake and
decarboxylation (“APUDomas”)



NETs

- Neuroendocrine cells in almost all tissues



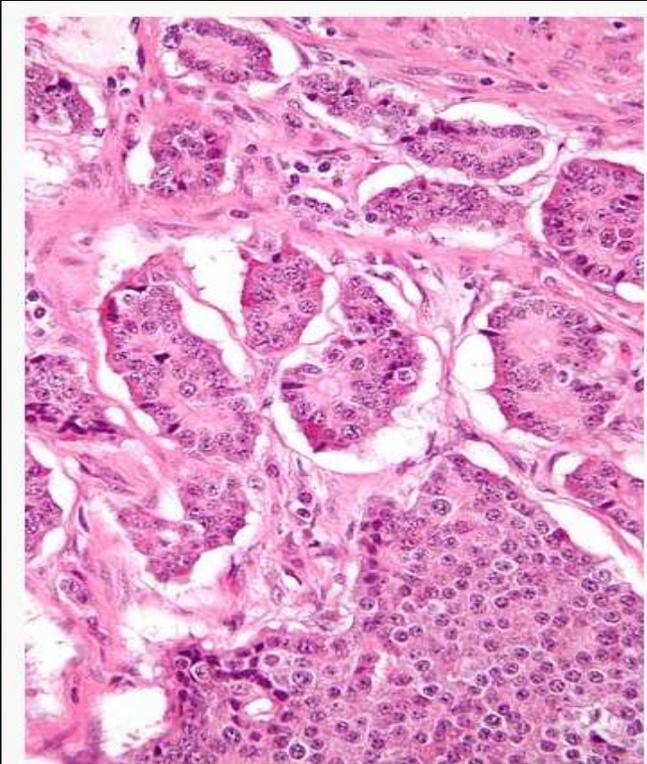
NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy



NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy

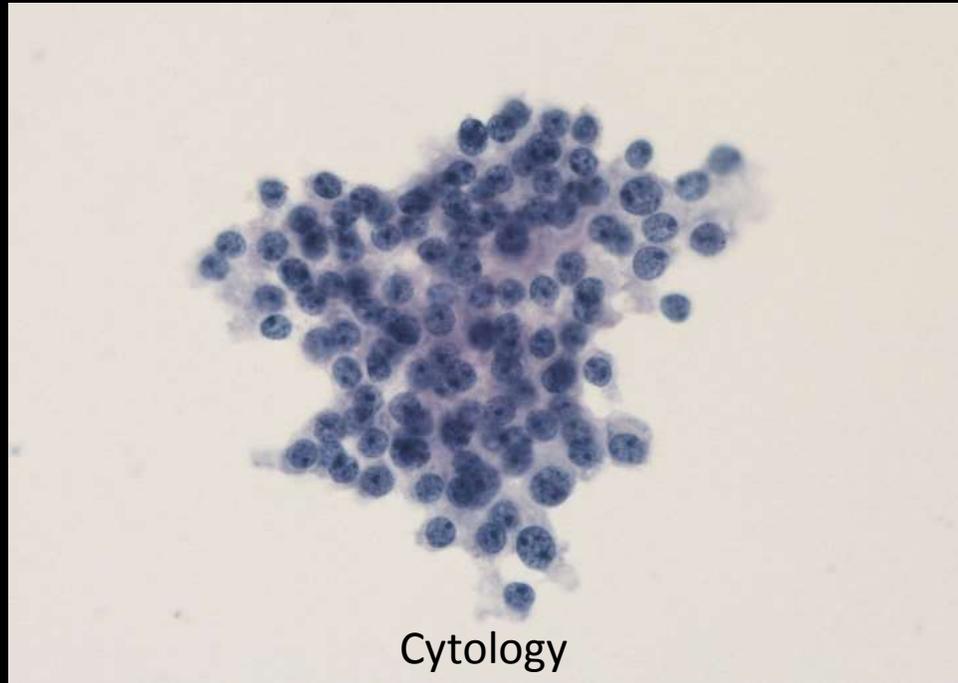


Micrograph of a neuroendocrine tumor. H&E stain.



NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy



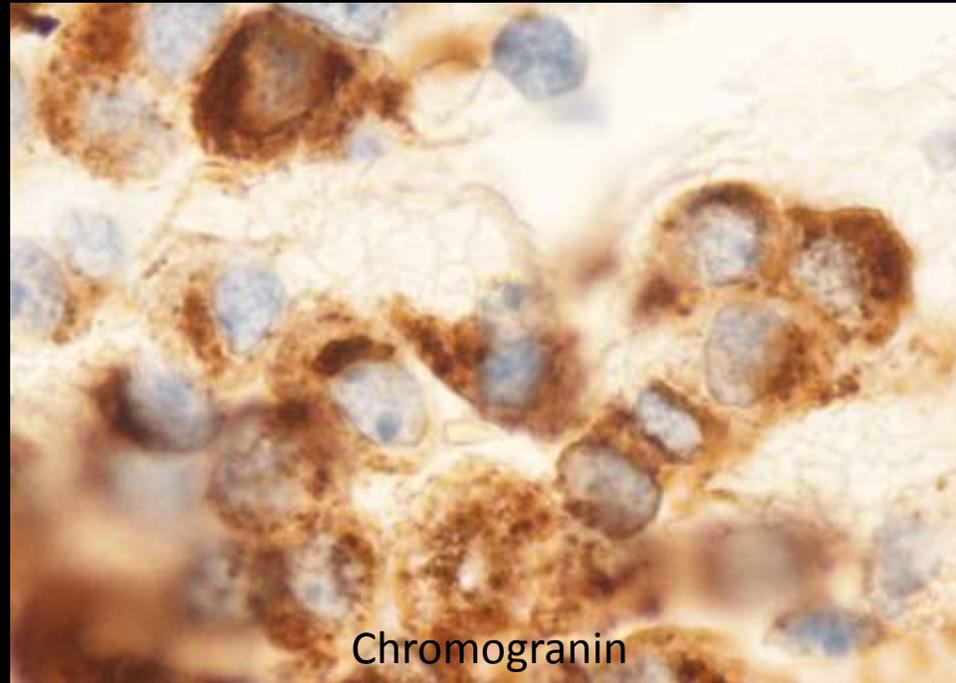
NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy



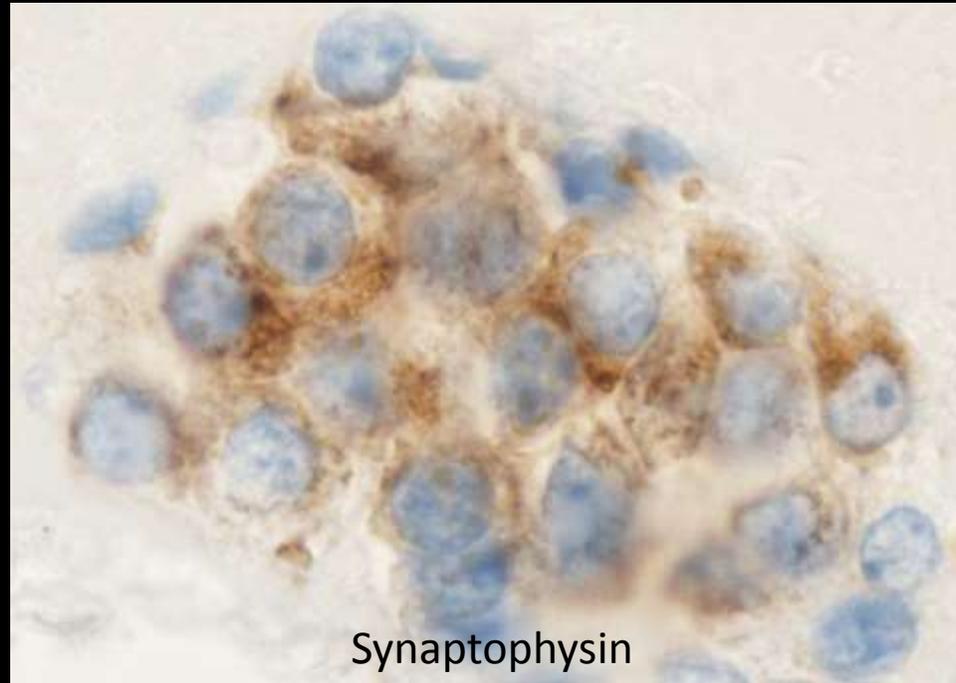
NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy



NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy



Synaptophysin



NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy
- Tumors from everywhere
 - skin (Merkel cell)
 - lung
 - thymus
 - endocrine glands



NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy
- Tumors from everywhere
 - skin (Merkel cell)
 - lung
 - thymus
 - endocrine glands, such as
 - GI tract:



NETs

- Neuroendocrine cells in almost all tissues
 - Now defined by characteristic microscopy
 - Tumors from everywhere
 - skin (Merkel cell)
 - lung
 - thymus
 - endocrine glands, such as
- GI tract: 14 endocrine types
33 amines



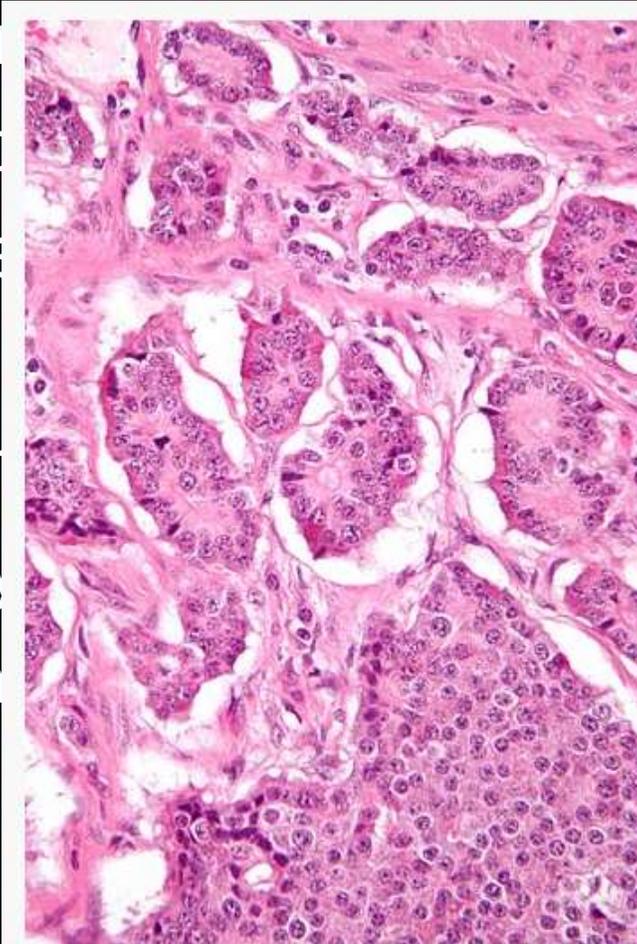
NETs

- Neuroendocrine cells in almost all tissues
- Now defined by characteristic microscopy
- Tumors from everywhere
 - skin (Merkel cell)
 - lung
 - thymus
 - endocrine glands, such as gastroenteropancreatic (GEP) NETs



NETs

- Neuroendocrine
- Now defined by
- Tumors from e
 - sk
 - lun
 - thy
 - en
 - ga



Micrograph of a neuroendocrine tumor. H&E stain.

tissues
scopy

(GEP) NETs



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

75% are carcinoids



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

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75% are carcinoids

non-carcinoid incidence $0.4-1.5/10^5$



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

75% are carcinoids

non-carcinoid incidence $0.4-1.5/10^5$

Increasing incidence:



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

75% are carcinoids

non-carcinoid incidence $0.4-1.5/10^5$

Increasing incidence:

$2.1 \rightarrow 9.3/10^5$ from 1973 to 2004



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

75% are carcinoids

non-carcinoid incidence $0.4-1.5/10^5$

Increasing incidence:

$2.1 \rightarrow 9.3/10^5$ from 1973 to 2004

? due to improved detection



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1: Werner’s syndrome

pituitary

parathyroid

pancreas



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN2: Sipple syndrome

thyroid

parathyroid

adrenal

pancreas



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:



Quasimodo - ?von Recklinghausen's disease (NF-1)



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau

CNS, hemangioblastomas

renal CA, pheo's, NETs



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau

Carney complex



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau

Carney complex

heart, lentiginosis, endocr.



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau

Carney complex

tuberous sclerosis



NETs

- Gastroenteropancreatic (GEP) NETs

“Rare”:

2% of all GI malignancies

10-15% are hereditary:

multiple endocrine neoplasia –

MEN1, MEN2

neurofibromatosis type 1

Von Hippel Lindau

Carney complex

tuberous sclerosis skin, NETs, etc



NETs

- Gastroenteropancreatic NETs
 - Non-functioning
 - Functioning



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”:
serotonin (carcinoids)
insulin



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)

insulin

gastrin



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)

insulin

gastrin

glucagon



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)

insulin

gastrin

glucagon

vasoactive intestinal peptide



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)

insulin

gastrin

glucagon

vasoactive intestinal peptide

somatostatin



NETs

- Gastroenteropancreatic NETs

Non-functioning >60% (no hormone effect)

Functioning “oma’s”: serotonin (carcinoids)

insulin

gastrin

glucagon

vasoactive intestinal peptide

somatostatin

others (ACTH, PTH, GRF,
neurotensin, calcitonin)



NETs

- Presentation:



NETs

- Presentation:
obstruction, bleeding, mass



NETs

- Presentation:
obstruction, bleeding, mass
metastases



NETs

- Presentation:
 - obstruction, bleeding, mass
 - metastases
 - syndromic (from hormones)



NETs

- Presentation:
 - obstruction, bleeding, mass
 - metastases
 - syndromic (from hormones)
 - incidental finding



NETs

- Diagnosis



NETs

- Diagnosis: scopes



NETs

- Diagnosis: scopes
capsule endoscopy



NETs

- Diagnosis: scopes
capsule endoscopy
CT



NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound



NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound
 - MRI



NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound
 - MRI
 - PET scan



NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound
 - MRI
 - PET scan
 - octreotide scan



NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound
 - MRI
 - PET scan
 - octreotide scan
 - EUS



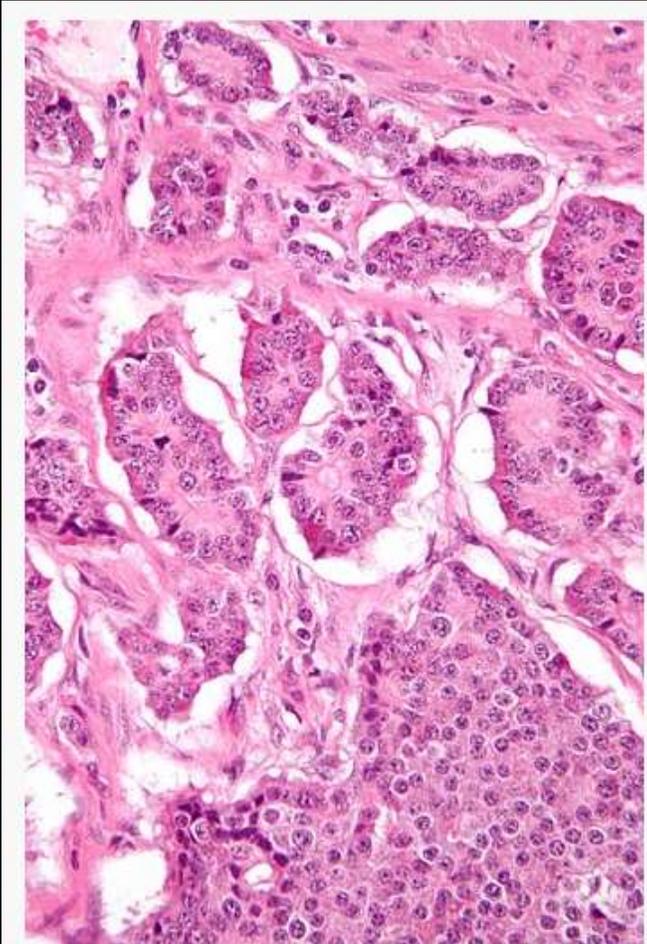
NETs

- Diagnosis:
 - scopes
 - capsule endoscopy
 - CT
 - ultrasound
 - MRI
 - PET scan
 - octreotide scan
 - EUS
 - biopsy



NETs

- Diagnosis:



Micrograph of a neuroendocrine tumor. H&E stain.



NETs

- Management



NETs

- Management
Early detection



NETs

- Management

Early detection (average delay 4-6 yr)



NETs

- Management

Early detection (average delay 4-6 yr)

Accurate classification



NETs

- Management

Early detection (average delay 4-6 yr)

Accurate classification

Multidisciplinary approach



NETs

- Management

 - Early detection (average delay 4-6 yr)

 - Accurate classification

 - Multidisciplinary approach

 - Aggressive treatment where appropriate



NETs

- Treatment



NETs

- Treatment
Observation only



NETs

- Treatment
 - Observation only
 - Surgery for cure



NETs

- Treatment

- Observation only

- Surgery for cure

- Surgery for symptom relief (incl. debulking)



NETs

- Treatment

- Observation only

- Surgery for cure

- Surgery for symptom relief (incl. debulking)

- Endovascular surgery, RFA, EtOH injection



NETs

- Treatment

- Observation only

- Surgery for cure

- Surgery for symptom relief (incl. debulking)

- Endovascular surgery, RFA, EtOH injection

- Block hormone - octreotide (may debulk)



NETs

- Treatment

- Observation only

- Surgery for cure

- Surgery for symptom relief (incl. debulking)

- Endovascular surgery, RFA, EtOH injection

- Block hormone - octreotide (may debulk)

- Block effect - diazoxide (insulin)

- proton pump inhibitor



NETs

- Treatment

Observation only

Surgery for cure

Surgery for symptom relief (incl. debulking)

Endovascular surgery, RFA, EtOH injection

Block hormone - octreotide (may debulk)

Block effect - diazoxide (insulin)

proton pump inhibitor

Chemotherapy



NETs

- Treatment

Observation only

Surgery for cure

Surgery for symptom relief (incl. debulking)

Endovascular surgery, RFA, EtOH injection

Block hormone - octreotide (may debulk)

Block effect - diazoxide (insulin)

proton pump inhibitor

Chemotherapy

Biological targeting



NETs

- Prognosis



NETs

- Prognosis
 - Tend to be slow growing



NETs

- Prognosis

Tend to be slow growing

JF

1975



NETs

- Prognosis

Tend to be slow growing

JF

?

1975



NETs

- Prognosis

Tend to be slow growing

JF

2005

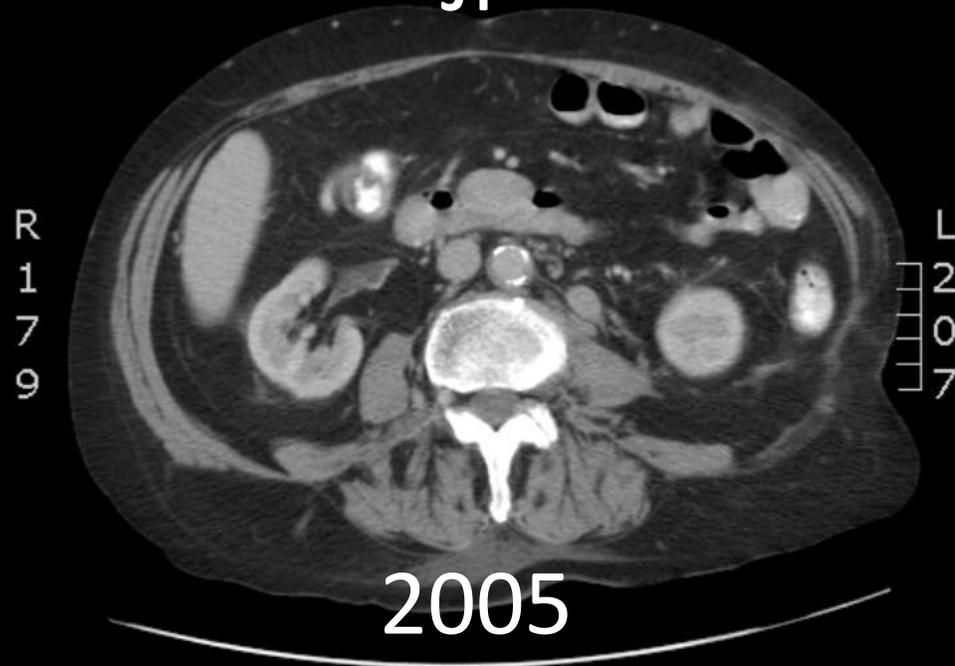


NETs

- Prognosis

Tend to be slow growing

JF

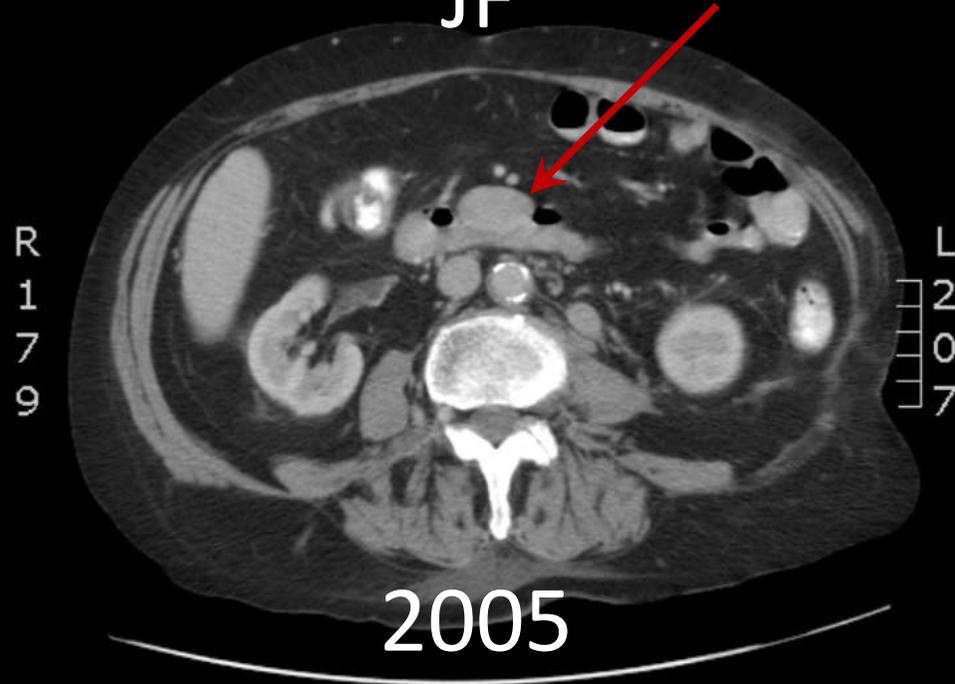


NETs

- Prognosis

Tend to be slow growing

JF

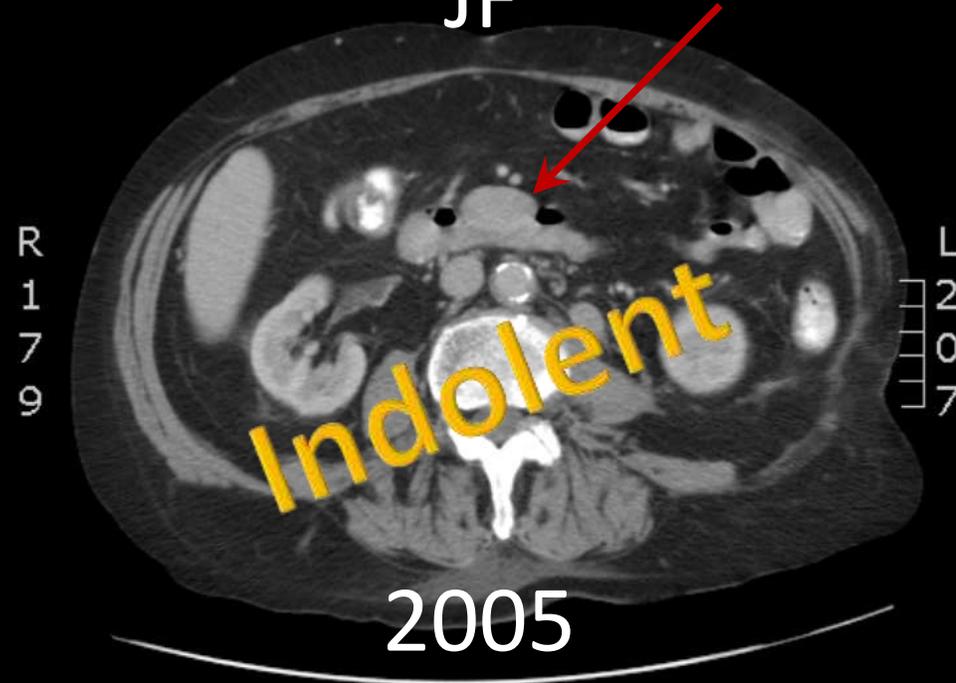


NETs

- Prognosis

Tend to be slow growing

JF



NETs

- Prognosis

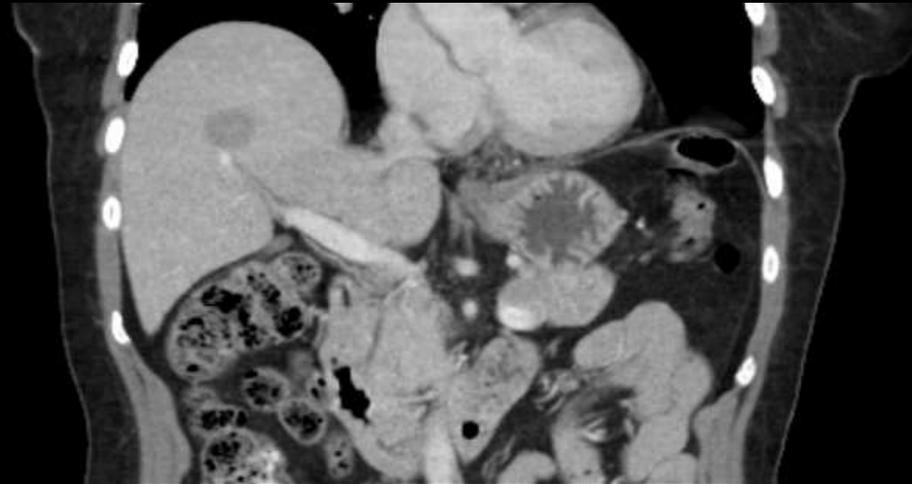
Tend (....) to be slow growing, but -



NETs

- Prognosis

Tend (....) to be slow growing, but -
EF



Oct 2013



NETs

- Prognosis

Tend (....) to be slow growing, but -
EF



Oct 2013



NETs

- Prognosis

Tend (....) to be slow growing, but -
EF

Mar 2014



NETs

- Prognosis

Tend (....) to be slow growing, but -
EF



Mar 2014



NETs

- Prognosis

Tend (....) to be slow growing, but -
EF



Mar 2014



NETs

- Prognosis

Tend (....) to be slow growing

but not all, therefore need -

Grading System

TABLE 4. Grading Systems for Neuroendocrine Tumors

Grade	Lung and Thymus	GEP-NETs	Lung and Thymus	Pancreas
	(WHO) ³⁴	(ENETS, WHO) ^{3,28,29}	(Moran et al) ²³	(Hochwald et al) ¹⁴
Low grade	<2 mitoses / 10 hpf AND no necrosis	<2 mitoses / 10 hpf AND <3% Ki67 index	≤3 mitoses / 10 hpf AND no necrosis	<2 mitoses / 50 hpf AND no necrosis
Intermediate grade	2–10 mitoses / 10 hpf OR foci of necrosis	2–20 mitoses / 10 hpf OR 3%–20% Ki67 index	4–10 mitoses / 10 hpf OR foci of necrosis	2–50 mitoses / 50 hpf OR foci of necrosis
High grade	>10 mitoses / 10 hpf	>20 mitoses / 10 hpf OR >20% Ki67 index	>10 mitoses / 10 hpf, Necrosis present	>50 mitoses / 50 hpf



NETs

- Prognosis

5 yr survival 1988 for pNET with mets 40%



NETs

- Prognosis

5 yr survival 1988 for pNET with mets 40%

“ “ 2002 “ “ “ “ 82%



NETs - summary



NETs - summary

- Characteristic cell types – need biopsy



NETs - summary

- Characteristic cell types – need biopsy
 - but may suspect a NET by:
 - clinical presentation
 - imaging features (round, localized, vascular)
 - serum markers (chromogranin A, hormones)



NETs - summary

- Characteristic cell types – need biopsy
- Uncommon but increasing occurrence
- Unusual “hormone” syndromes
- Most slow-growing
- Found incidentally
- Only cure is surgery, but “may outlive tumor”
- Exciting new advances



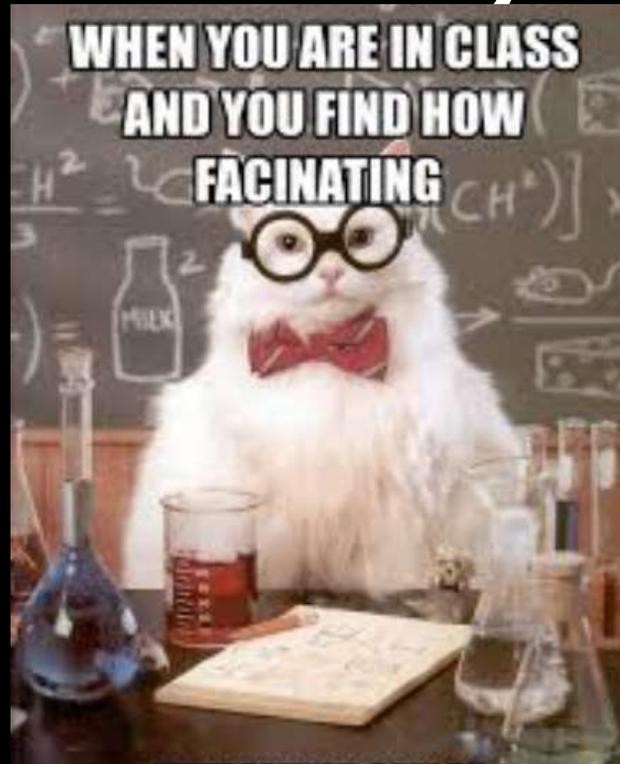
NETs - summary

Thank you



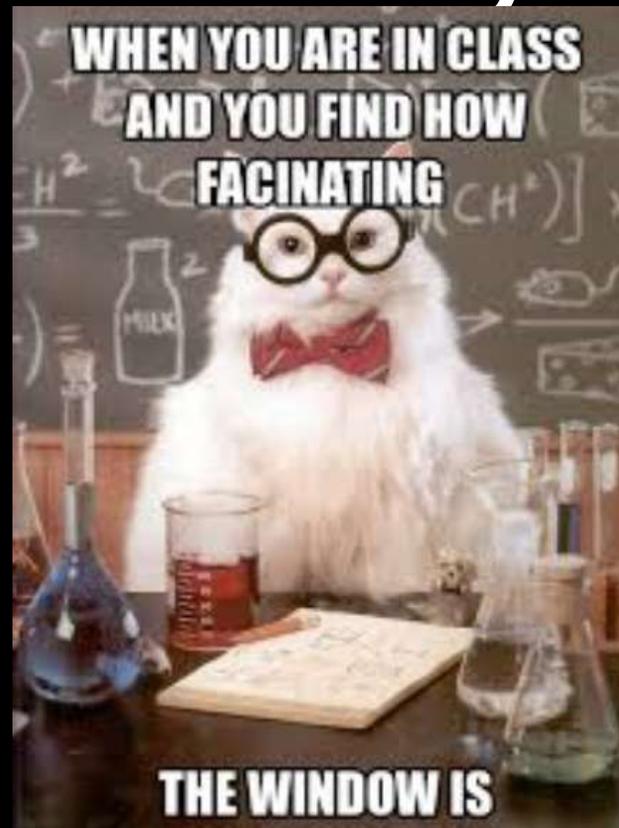
NETs - summary

Thank you



NETs - summary

Thank you



NETs - summary
Thank you
for staying awake



NETs - summary

**Thank you
for staying awake**

..... the quiz starts now



