

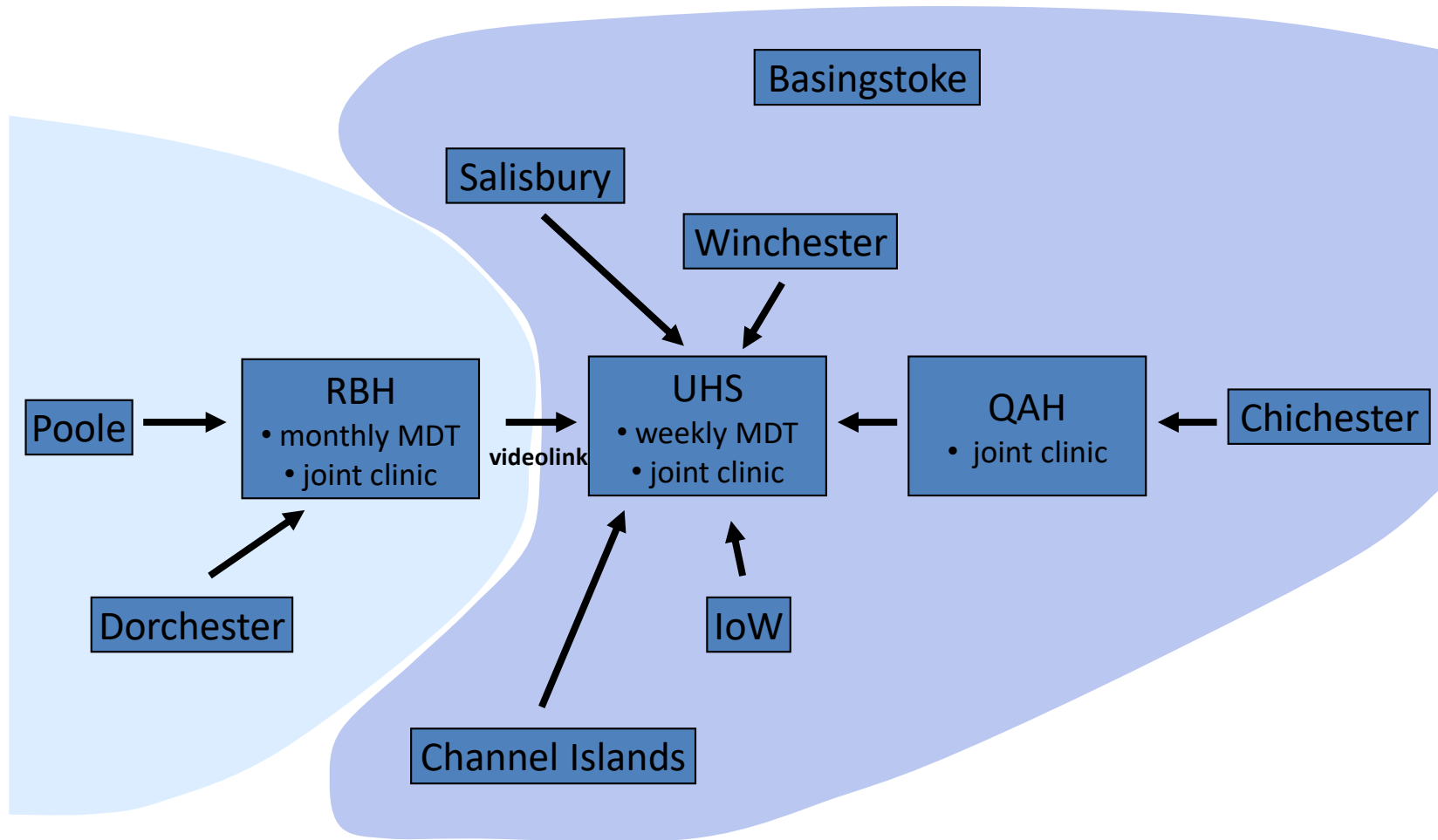
# What are Neuroendocrine Tumours ? (and a bit about surgery)

Tom Armstrong PhD FRCSEd  
Hepatobiliary Surgeon  
University Hospitals Southampton

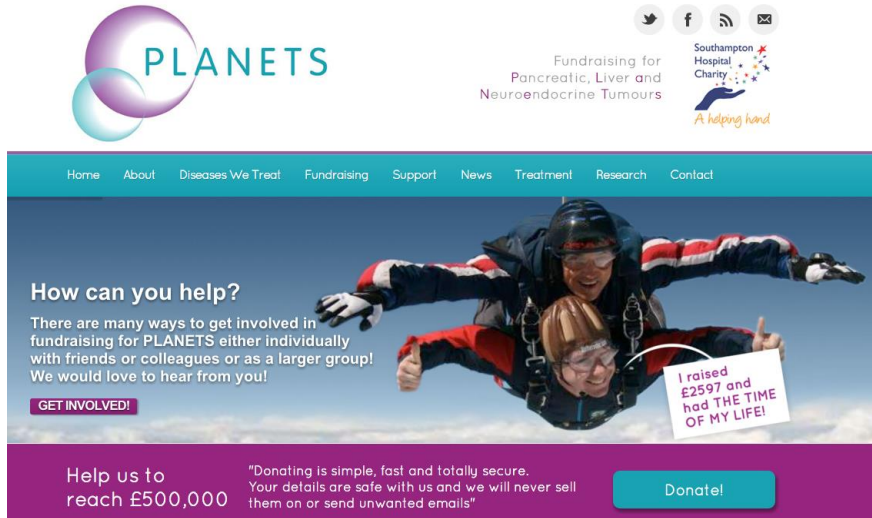


PLANETS NET Conference, Southampton 2018

# What is the Wessex NET Group?

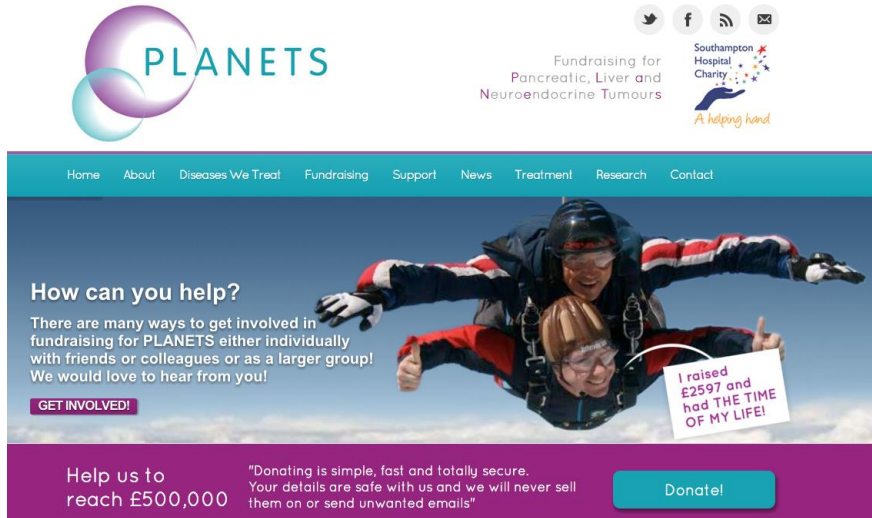


# What is the Wessex NET Group?



The screenshot shows the PLANETS website homepage. At the top left is the PLANETS logo, consisting of two overlapping circles (one purple, one blue) and the word "PLANETS" in teal. To the right are social media icons for Twitter, Facebook, RSS, and Email. Below these is the text "Fundraising for Pancreatic, Liver and Neuroendocrine Tumours" and the Southampton Hospital Charity logo with the tagline "A helping hand". A teal navigation bar contains links for Home, About, Diseases We Treat, Fundraising, Support, News, Treatment, Research, and Contact. The main content area features a background image of two skydivers. On the left, the text reads "How can you help? There are many ways to get involved in fundraising for PLANETS either individually with friends or colleagues or as a larger group! We would love to hear from you!" Below this is a purple button labeled "GET INVOLVED!". On the right, a skydiver holds a sign that says "I raised £2597 and had THE TIME OF MY LIFE!". At the bottom, a purple banner contains the text "Help us to reach £500,000" on the left, a quote "Donating is simple, fast and totally secure. Your details are safe with us and we will never sell them on or send unwanted emails" in the center, and a teal "Donate!" button on the right.

# What is the Wessex NET Group?



.... a partnership that has led to the recognition of the Wessex NET Group

European Centre of Excellence

# Nervism



1883 Ivan Pavlov

- recognised that dogs salivate when given food
- realised the dogs salivate when they think that they were going to be given food

First realisation that nervous system (brain) plays a dominant role in bodily functions

# More to it than just nervism: there is endocrinism too!

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- What does endocrine mean?

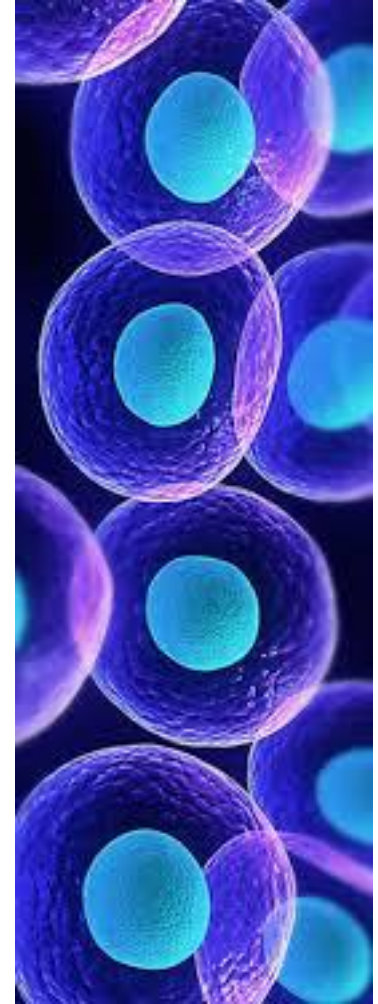
# More to it than just nervism: there is endocrinism too!

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- What does endocrine mean?
- Refers to a gland which secretes hormones directly into blood stream

# More to it than just nervism: there is endocrinism too!

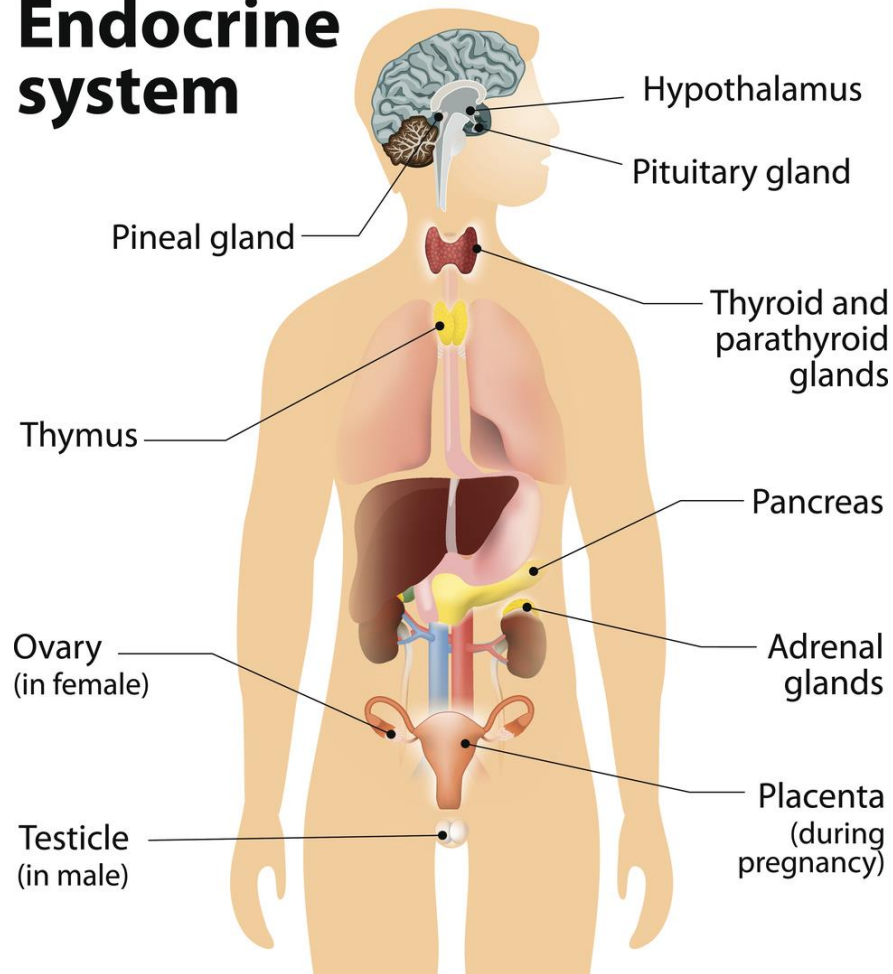
- Hormone=chemical messenger sent from one cell to another in blood stream





# Endocrine system in humans

## Endocrine system

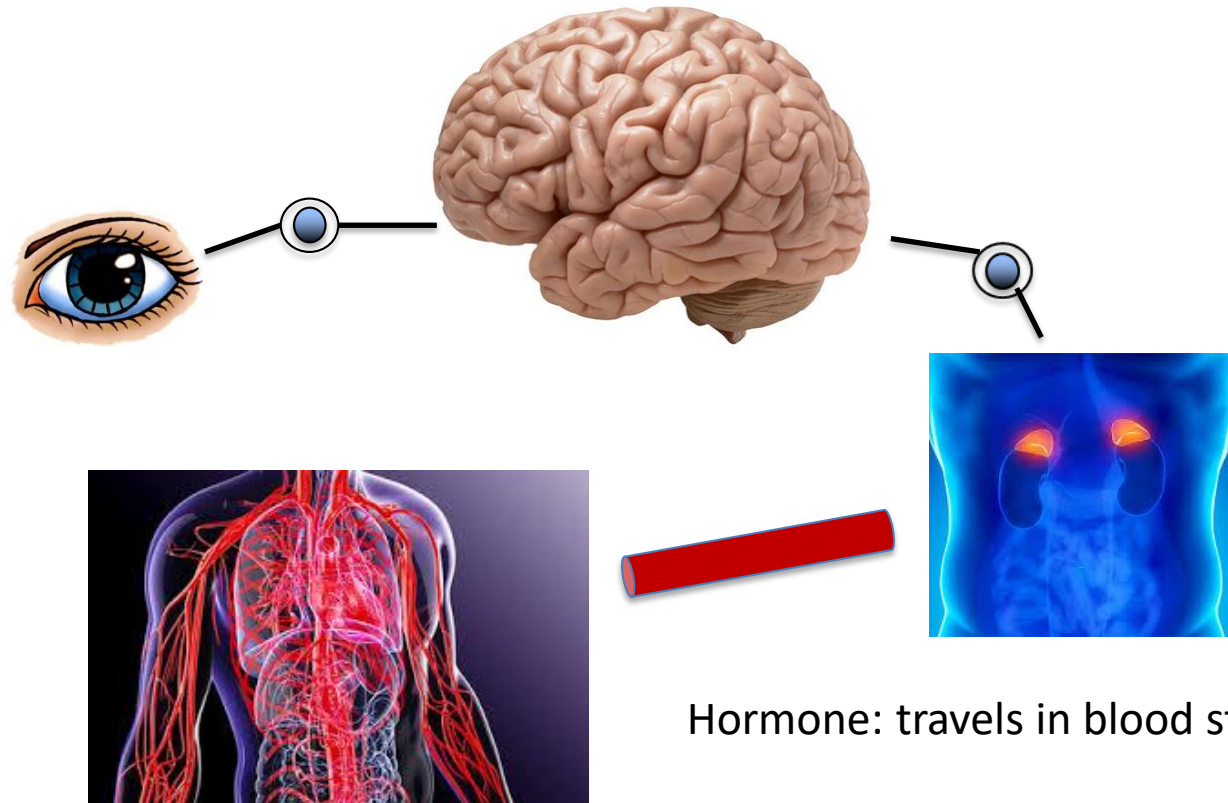


# How do nerves and endocrine system interact?

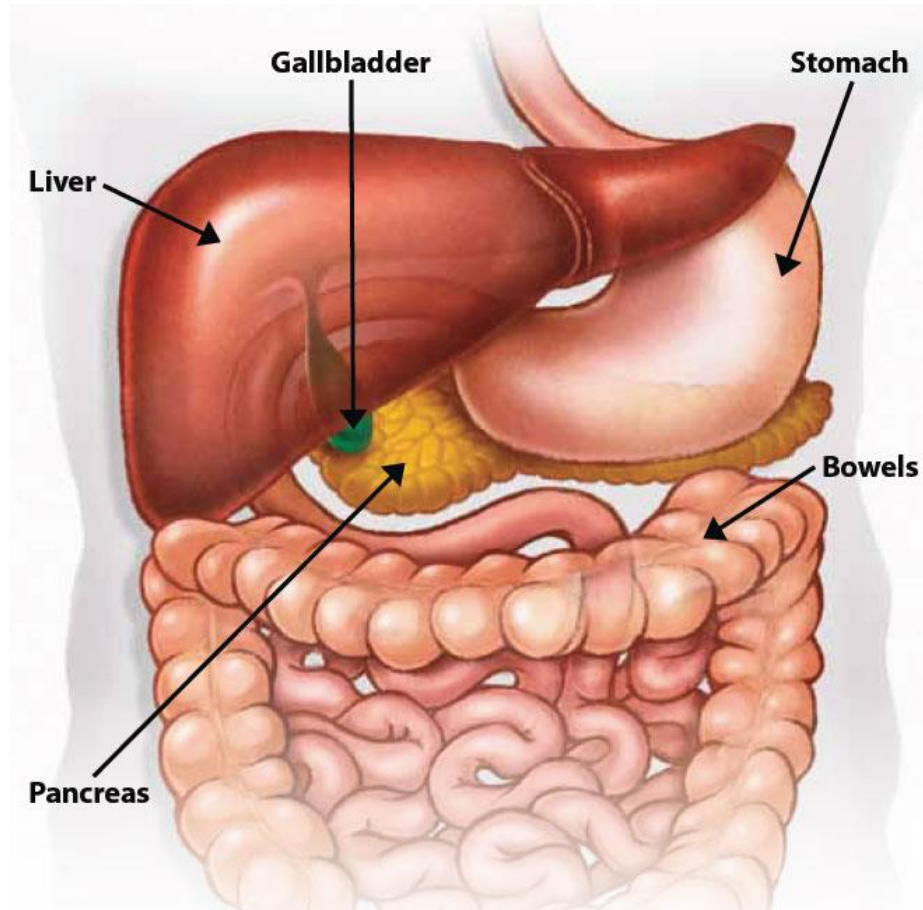
- 1867 Islands of cells in pancreas
  - Langerhans
- 1870 Glands within the intestines (EC cells)
  - Heidenhain
- 1902 Realisation that hormones regulated gut function
  - Bayliss and Starling
- 1938 EC cells made gut hormones and that these interacted with neurones
  - Feyter

# Neuroendocrine System in action

- Paradigm shift in understanding

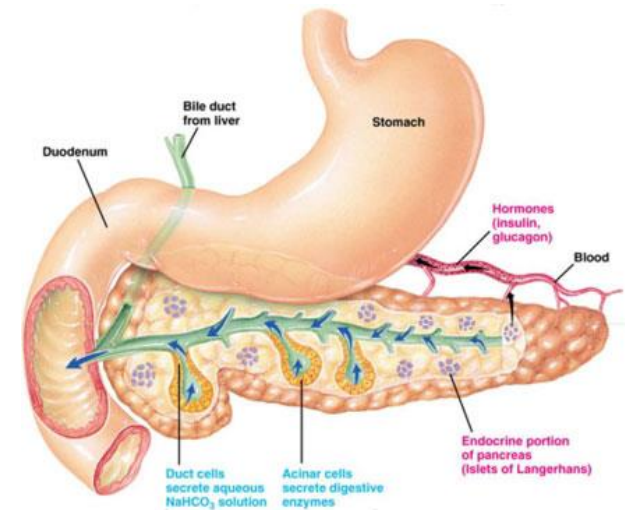


# Anatomy and Function of Gastrointestinal Tract

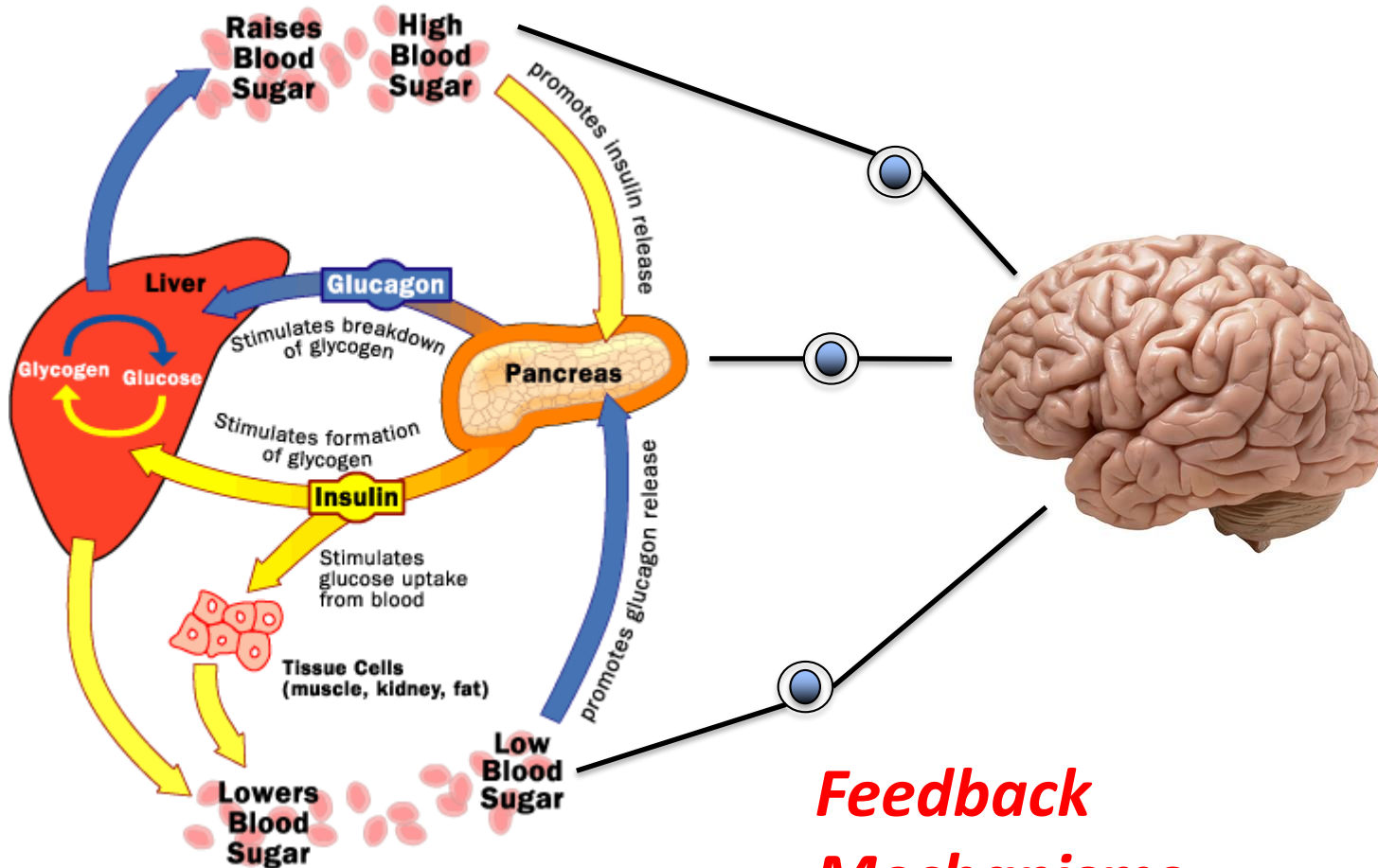


# Neuroendocrine Pancreatic Function

- Systemic Hormones
  - Insulin: drives sugars into cells
  - Glucagon: releases sugars from liver
- Gut Hormones
  - Gastrin: production of acid in stomach
  - VIP: encourages GI secretions
  - Somatostatin: suppresses release of other hormones
  - PPP: reduces appetite and slows release of digestive juices



# Neuroendocrine Pancreatic Function



**Feedback  
Mechanisms**

# Neuroendocrine Gut Function

- Gut Hormones

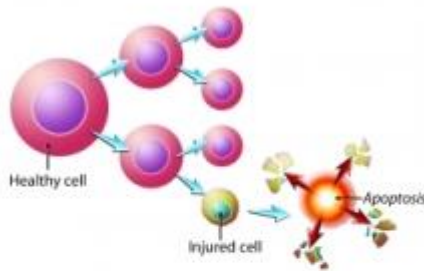
- Serotonin: gut function
  - (mood, sleep, healing)
- Bradykinin: gut contraction/motility
  - (dilate blood vessels, causes low blood pressure)
- Histamine: immune function
  - (too much causes wheezing and swelling)



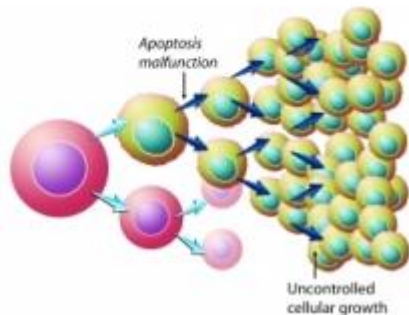


# Why do tumours form?

Normal Cell Division



Cancer Cell Division



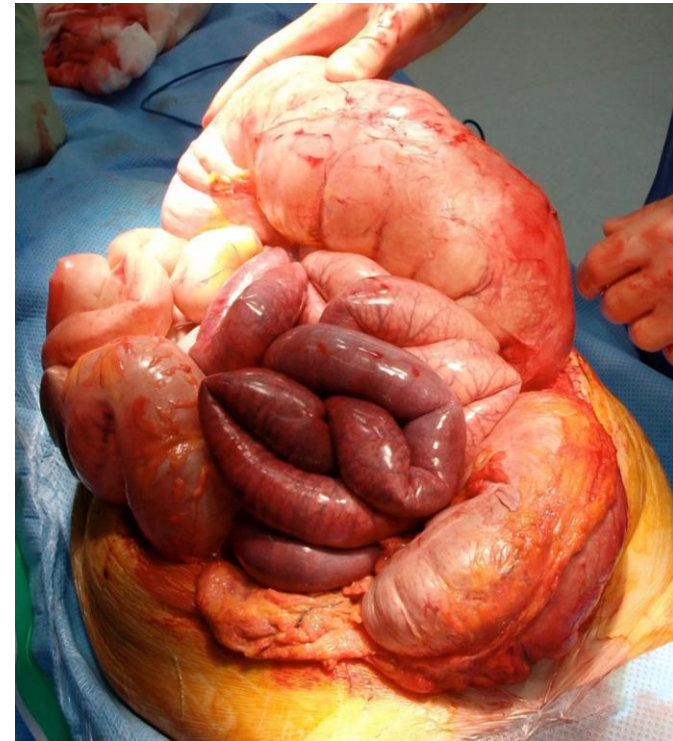
- Environmental Factors
  - Smoking, alcohol
- Chronic Inflammation
  - Inflammatory bowel disease
- Genetic Factors
  - MEN syndromes

***Normal Feedback Mechanisms Fail***



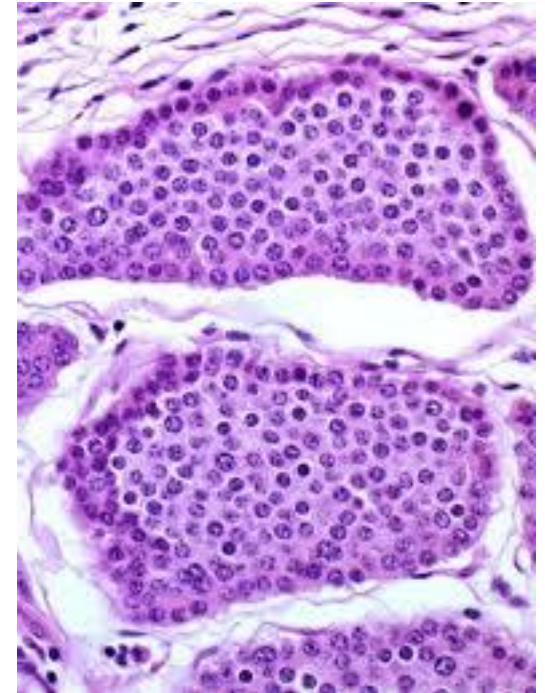
# Why do tumours cause disease?

- Block anatomical tracts (pipes)
  - eg jaundice, vomiting, pain
- Stop normal function of organs
  - eg liver
- Secrete excessive hormones
  - eg insulin, thyroxin
  - syndrome

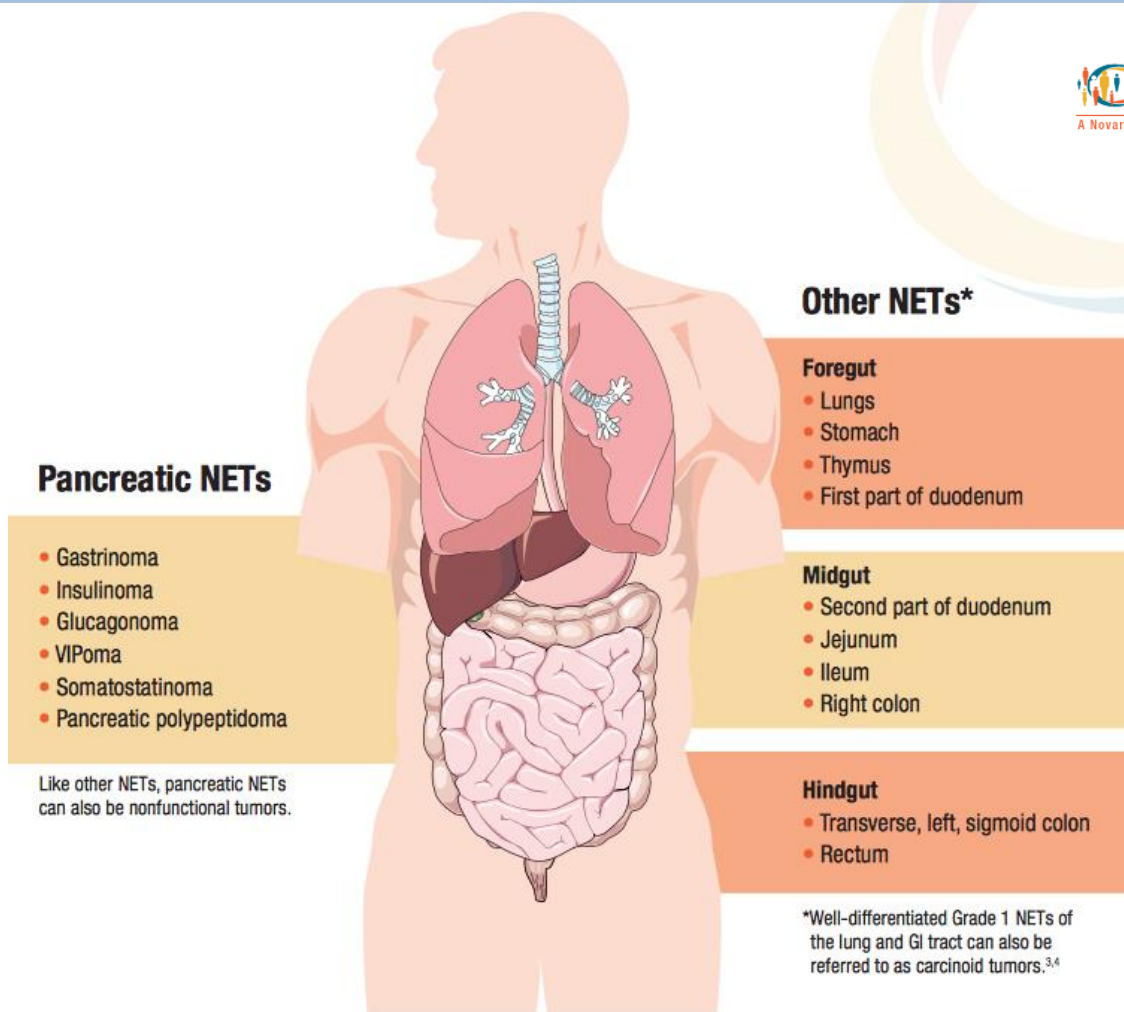


# NETS

- 1890 Case report in Lancet
  - Woman in 50's
  - Egg sized lumps in intestine
  - Diarrhoea
  - Flushing after eating
- 1907 Carcinoma like (Carcinoid)
  - Oberndorfer

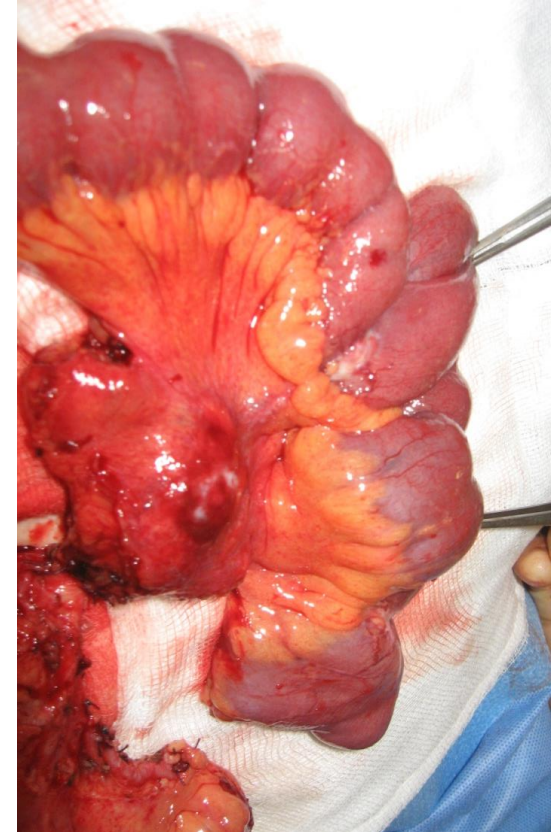


# NETS: anatomic distribution



# Functioning vs. Non-Functioning NETs

- Functioning
  - Hormonally active, cause syndromes which lead to investigation
- Non-functioning
  - Usually found incidentally or at a more advanced stage



# Presentation of Non-Functioning NETs

- Chance
- Jaundice
- Bowel Obstruction
- Cough
- Irritable bowel
- Anaemia



# Presentation of functioning NETs: Insulinoma

## Low Blood Sugar

- headache
- lethargy
- dizziness
- blurred vision



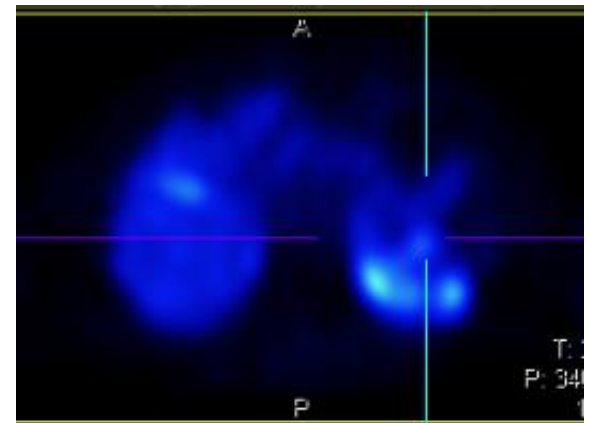
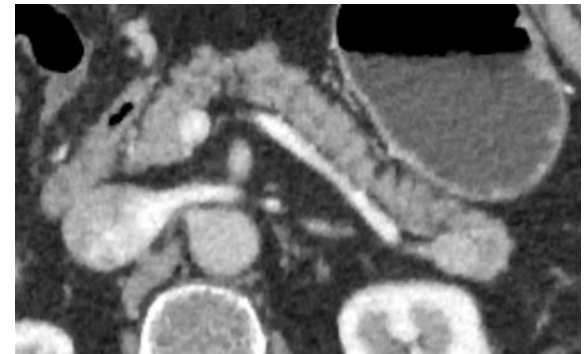
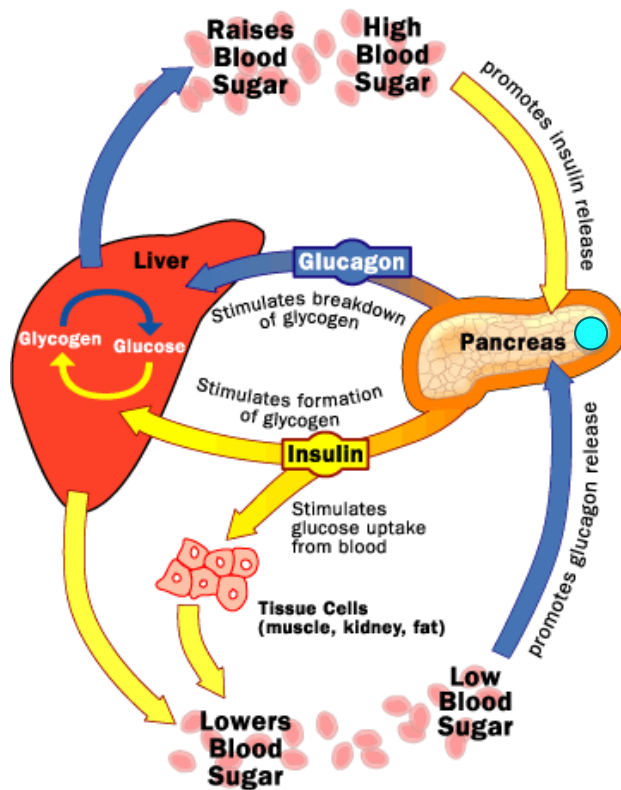
## Stress Response

- anxiety
- tremor
- nausea
- sweating



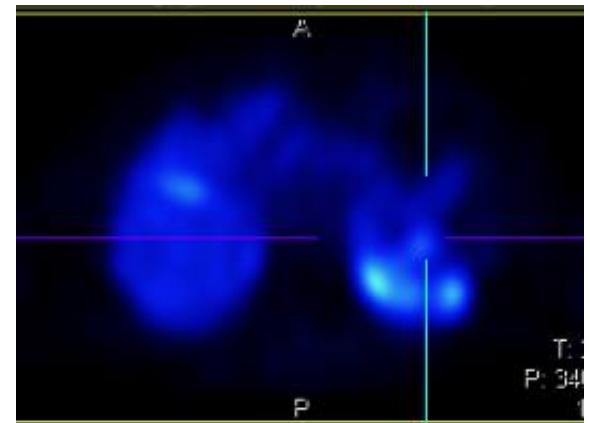
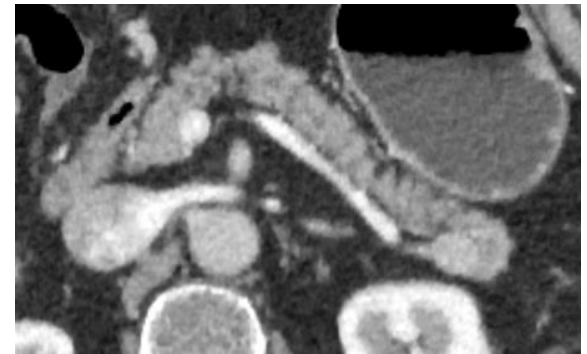
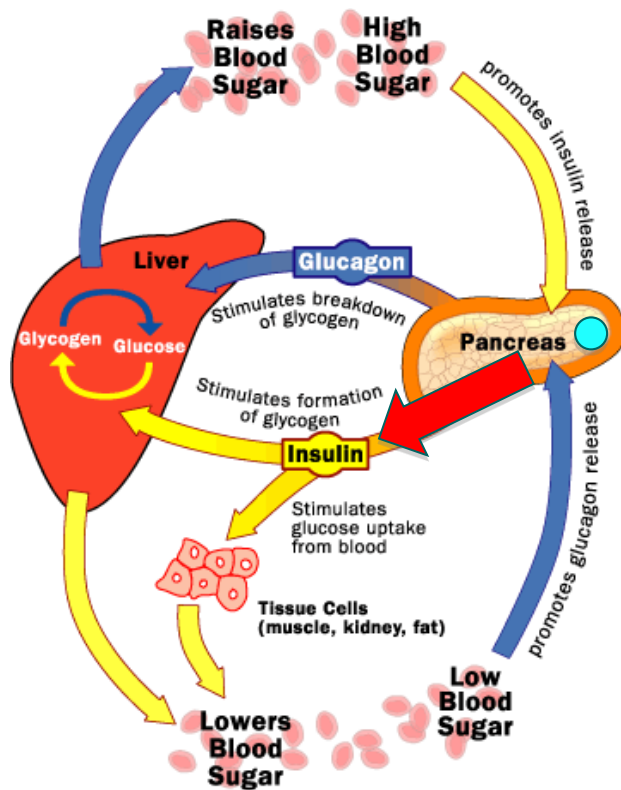
# Insulinoma

Insulinoma: failure of negative feedback



# Insulinoma

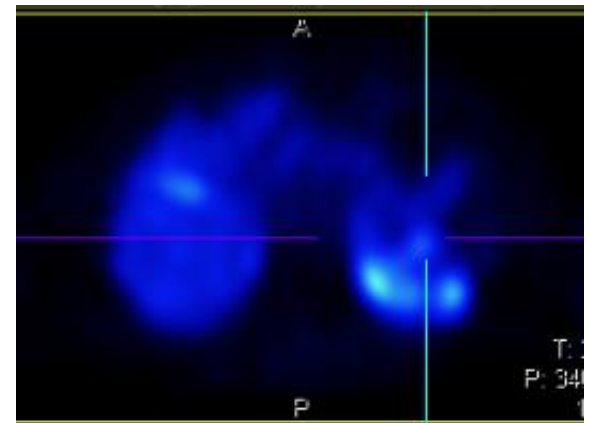
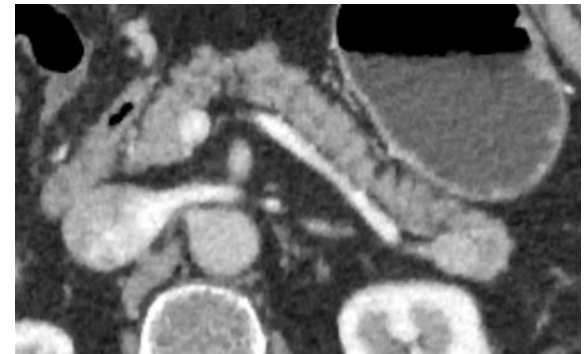
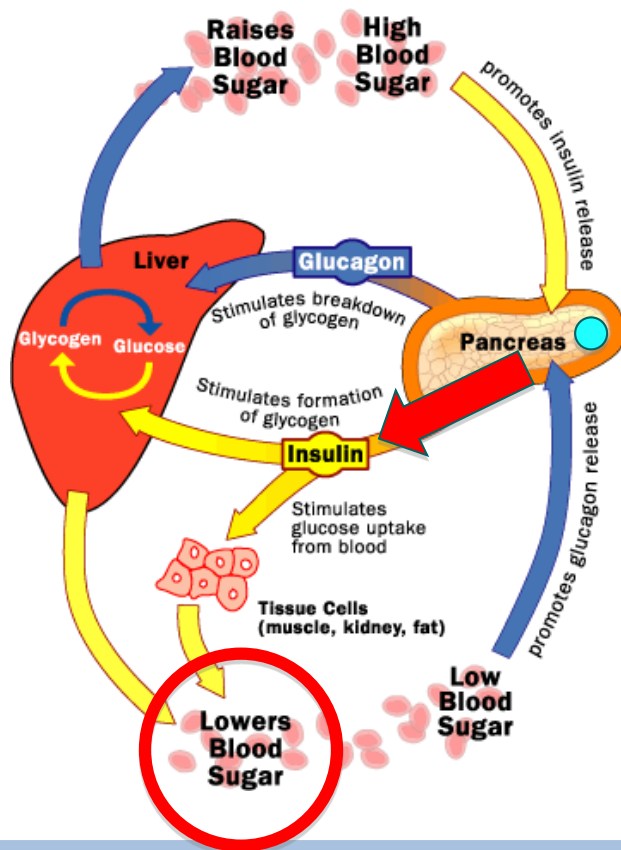
Insulinoma: failure of negative feedback





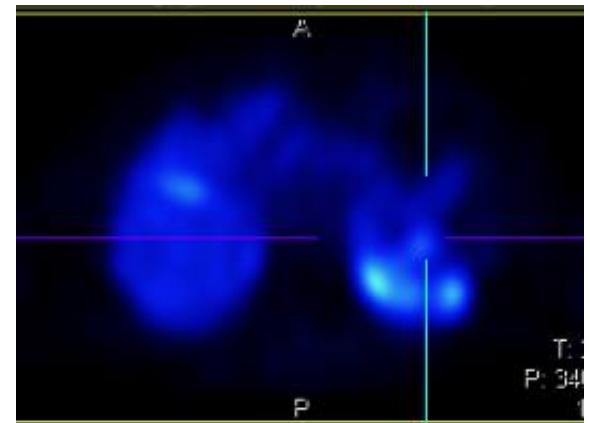
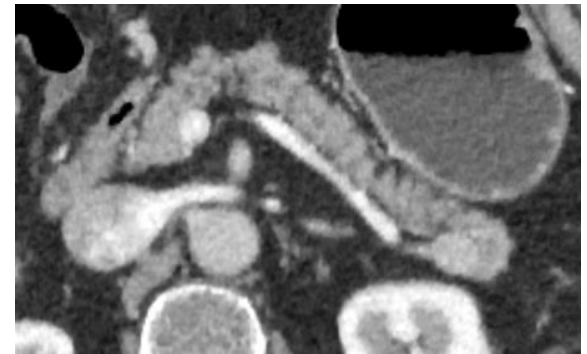
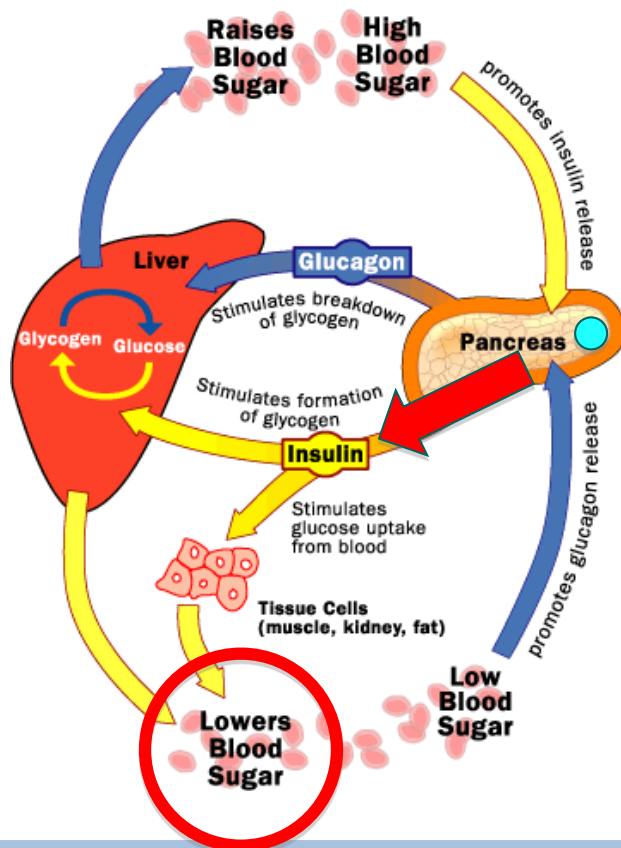
# Insulinoma

Insulinoma: failure of negative feedback



# Insulinoma

Insulinoma: failure of negative feedback

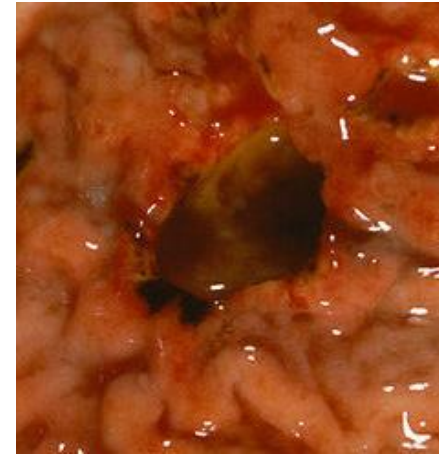
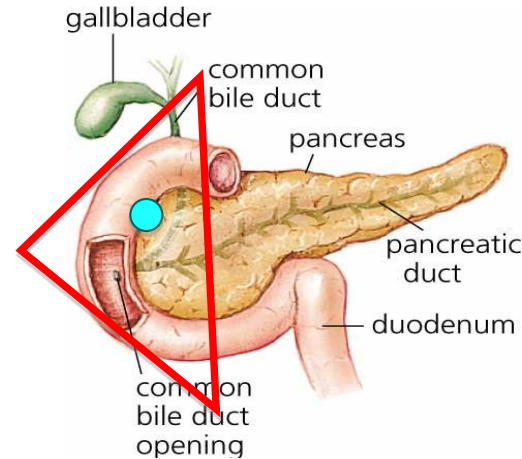


# Insulinoma

- Comprise 75% of functioning pancreatic NET
- Still rare
- Usually present in 50s
- 90% < 2cm
- 10% multiple
- 10% malignant: if metastasis
- 10% MEN-1

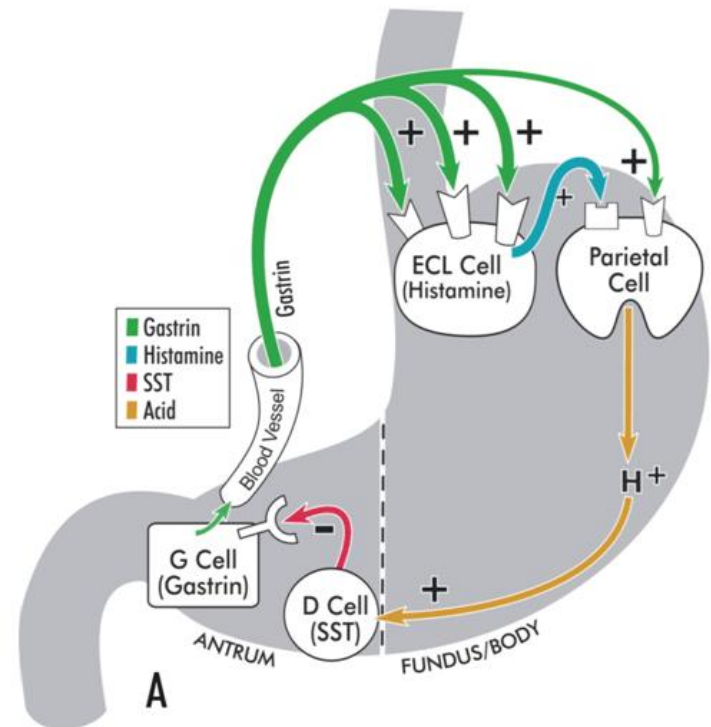
# Presentation of functioning NETs: Gastrinoma

- Excess stomach acid
- Ulceration
  - Stomach
  - Duodenum
- Pain, weight loss
- Doesn't respond to treatment



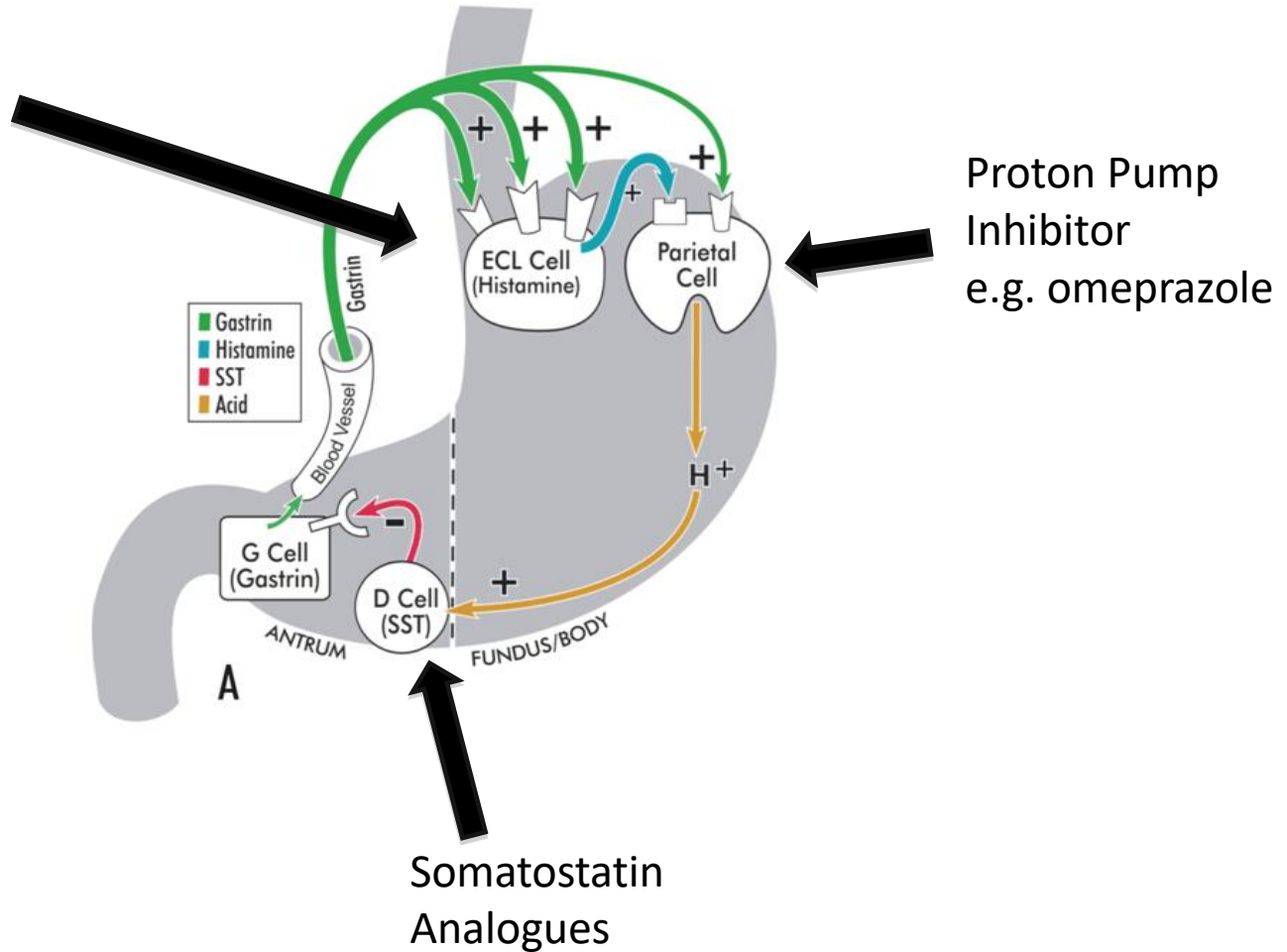
# Gastrinoma

- Zollinger-Ellison Syndrome



# Gastrinoma

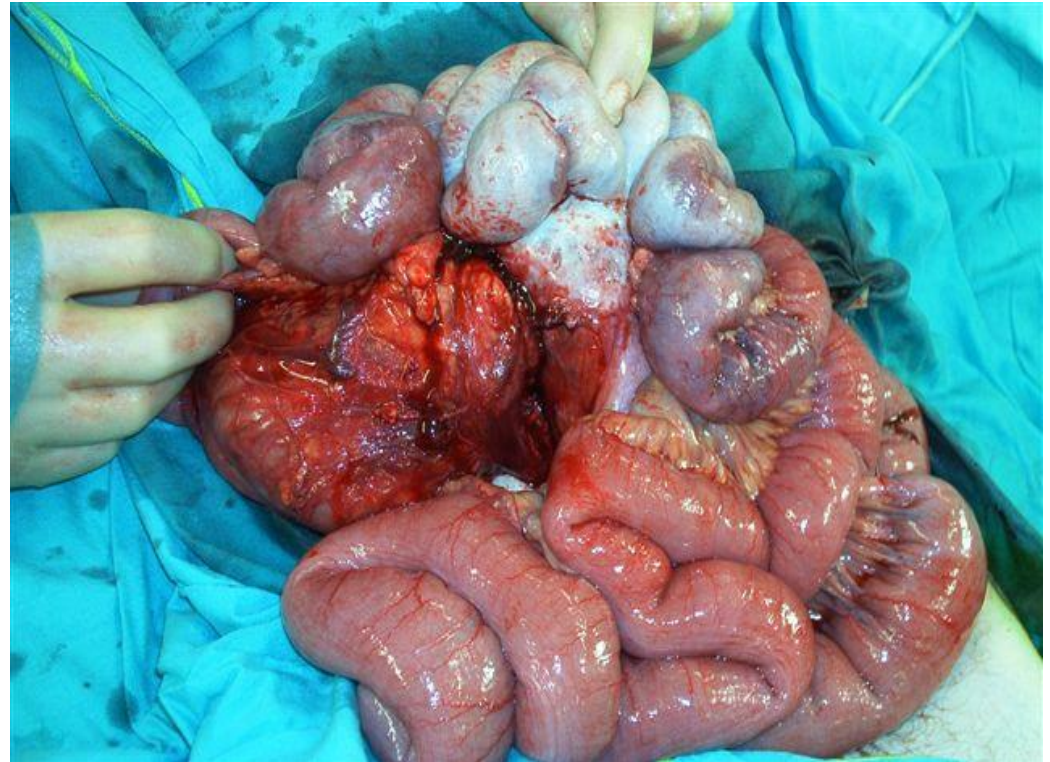
H<sub>2</sub> Blocker  
e.g. ranitidine





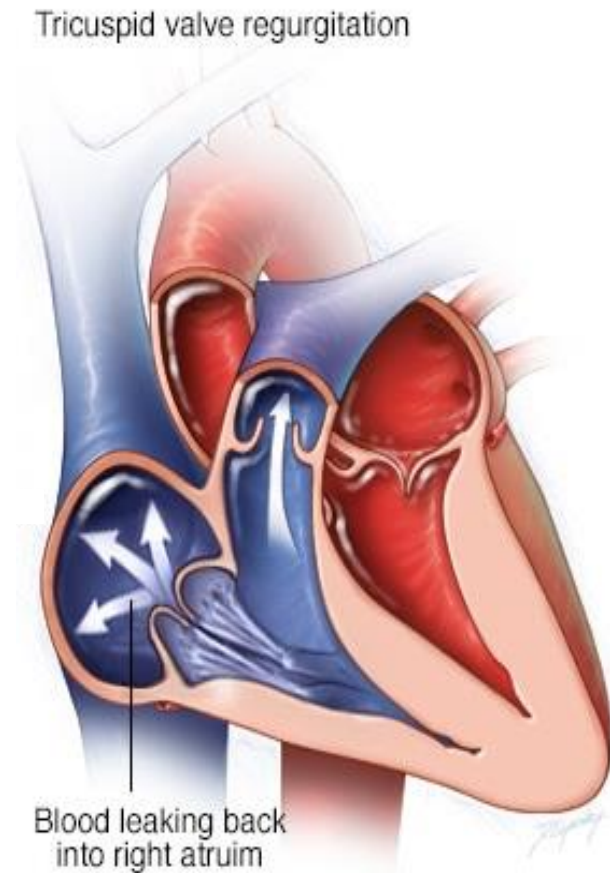
# Presentation of functioning NETs: Carcinoid (midgut NETs)

- Diarrhoea
- Abdominal pain
- Weight loss
- Flushing
- Heart failure



# Presentation of functioning NETs: Carcinoid (midgut NETs)

- Diarrhoea
- Abdominal pain
- Weight loss
- Flushing
- Heart failure
  - serotonin



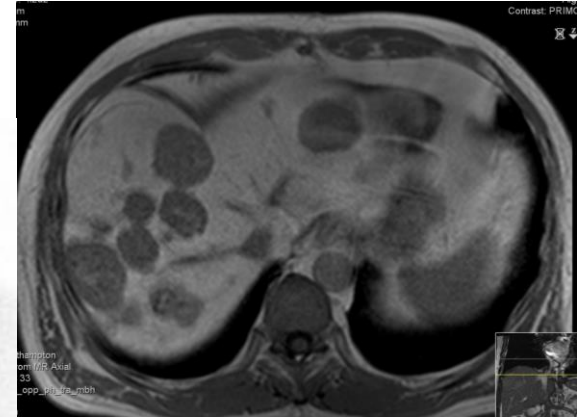
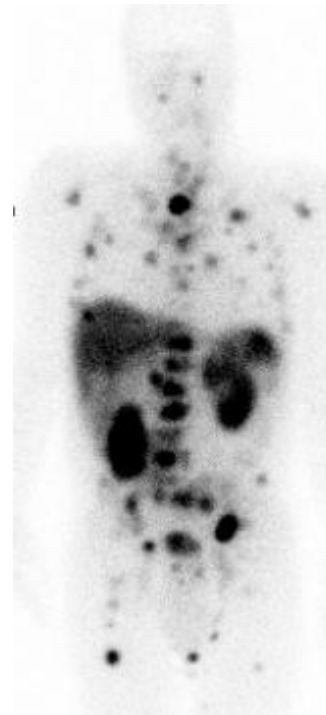


# Staging NETs

- TNM system
  - Tumour= size/site of primary tumour
    - +/- invasion of primary into adjacent organ
  - Node= spread of primary tumour to lymph nodes
    - via lymphatic channels
  - Metastasis= spread of primary tumour to other organs
    - via blood stream

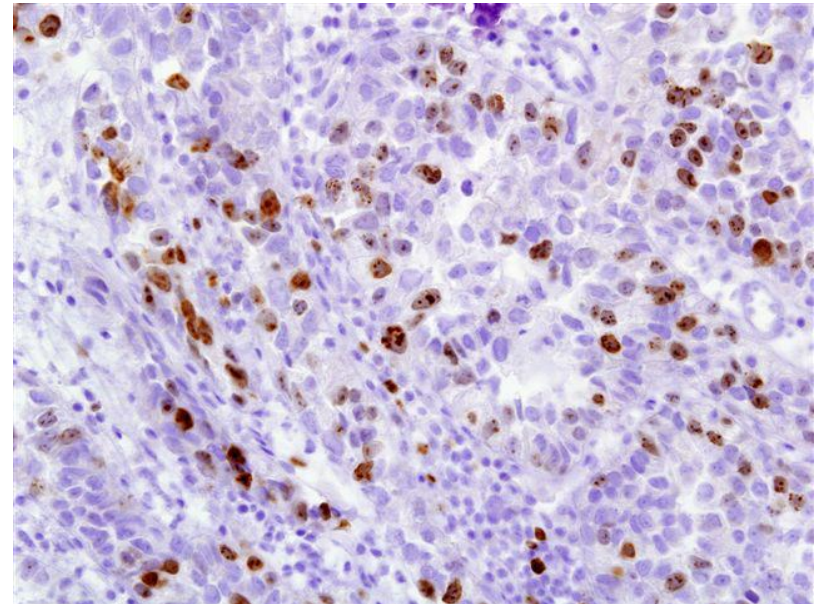
# Staging NETs

- Scans
  - CT
  - MRI
  - Octrotide
  - Gallium PET
- Endoscopy
  - Gastroscopy
  - Colonoscopy
  - Capsule
  - Endoscopic ultrasound



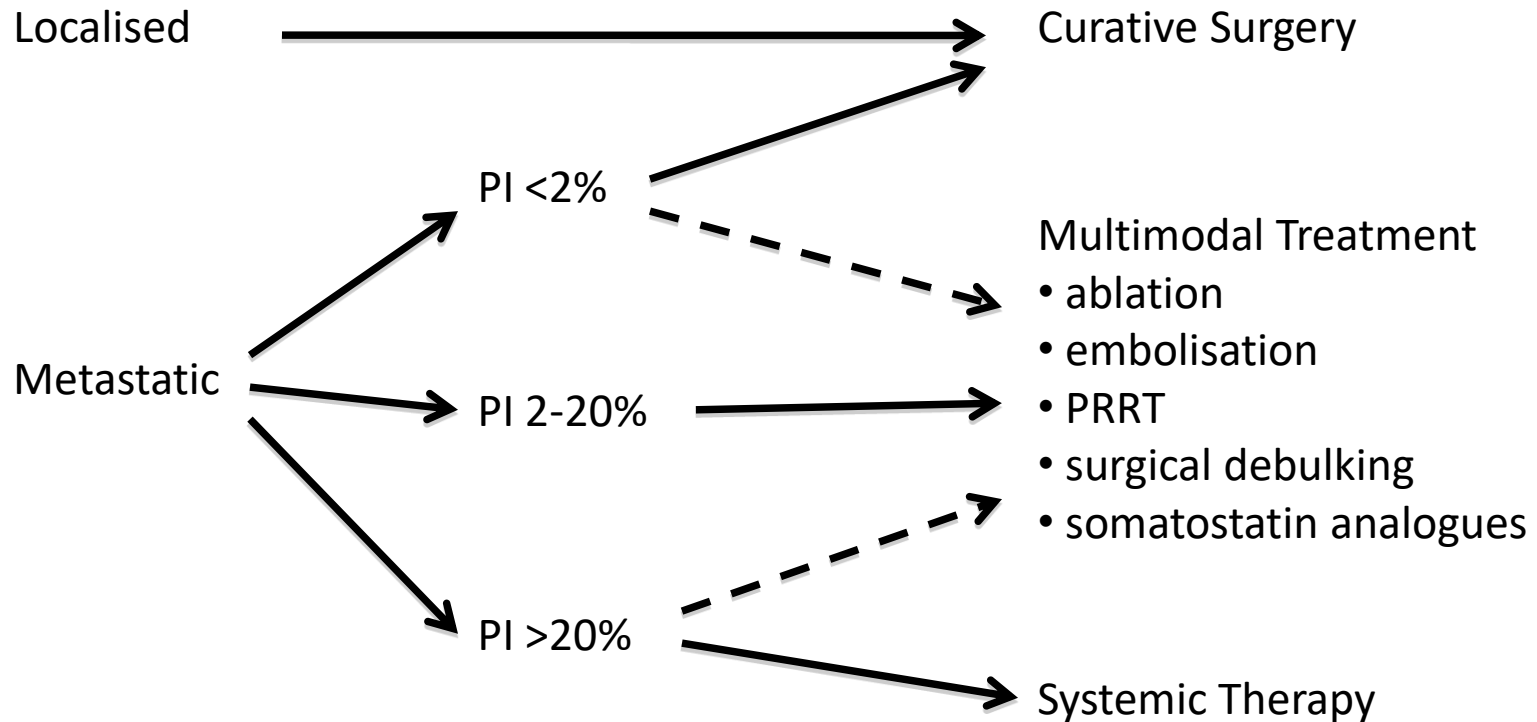
# Grading NETs

- Need biopsy
  - Primary
    - Endoscopy
  - Secondary/Metastasis
    - Liver



	Grade 1 NET	Grade 2 NET	Grade 3 NET	Grade 3 NEC
Proliferation index (Ki67)	<2%	3-19%	20-49%	>50%

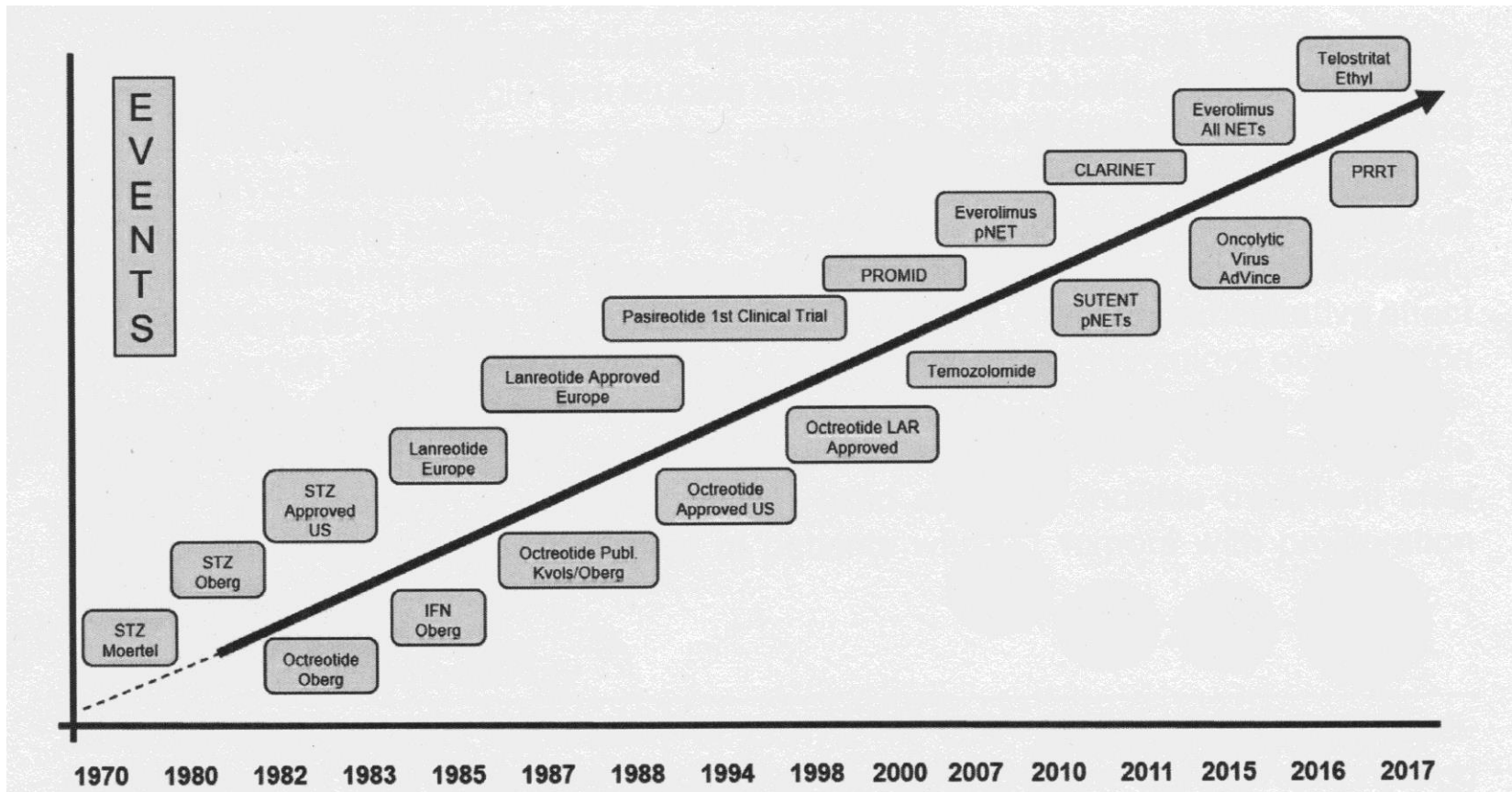
# Managing NETs



# Understanding Treatment Terminology

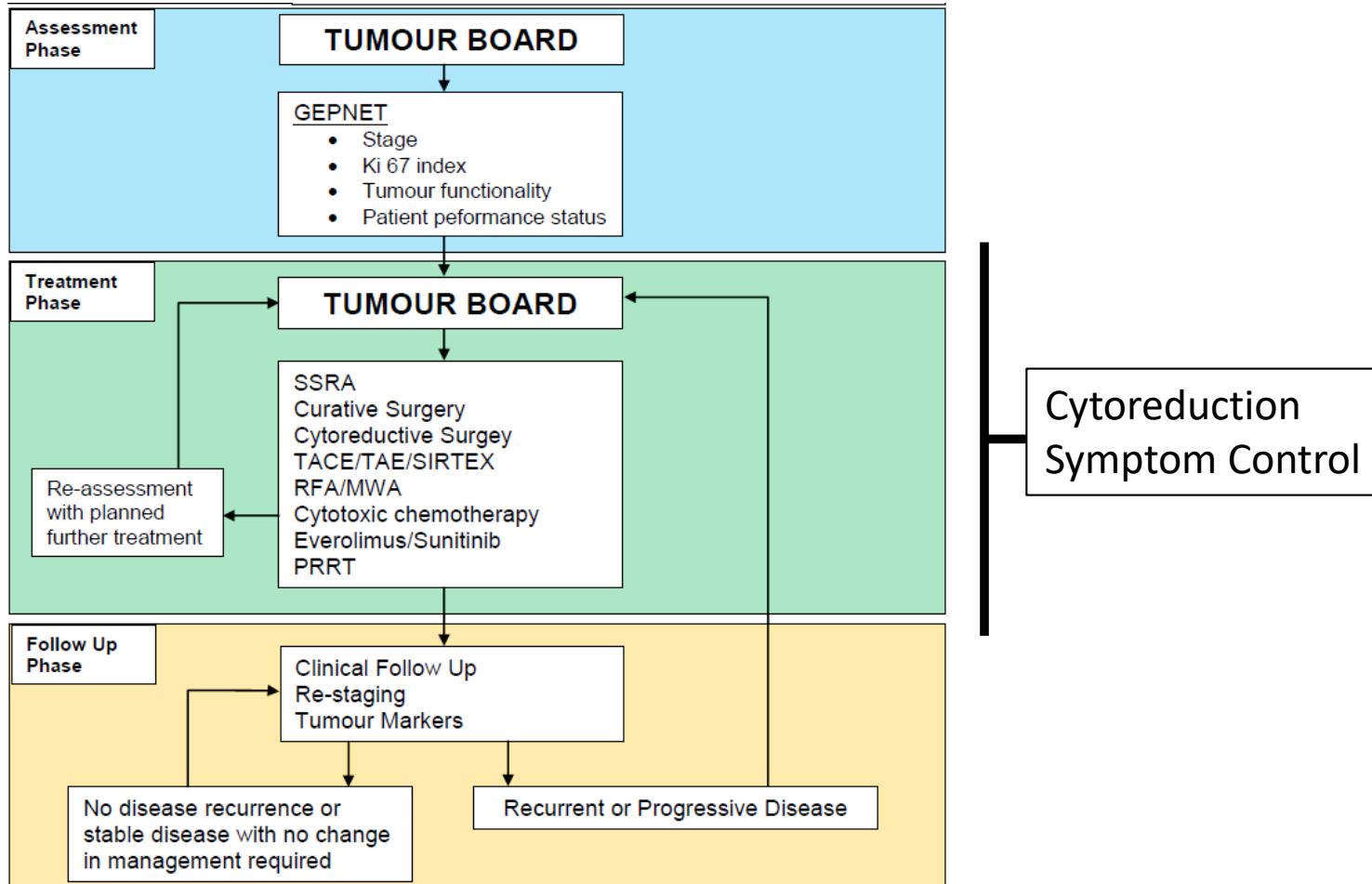
- Systemic:
  - a treatment that treats any NET cell in the body
    - Lanreotide/Octreotide
    - Chemotherapy
    - PRRT
- Locoregional:
  - a treatment aimed at one specific area of body or an organ
    - Surgery
    - TACE or SIRT
- Cytoreductive/Debulking:
  - surgery to remove bulk of disease
- Multimodal:
  - A combination of treatments

# Evolution of NET Treatment



Oberg K Endocrinol Metab Clin N Am 2018; 47: 711-31

# Wessex NET Group Management Algorithm



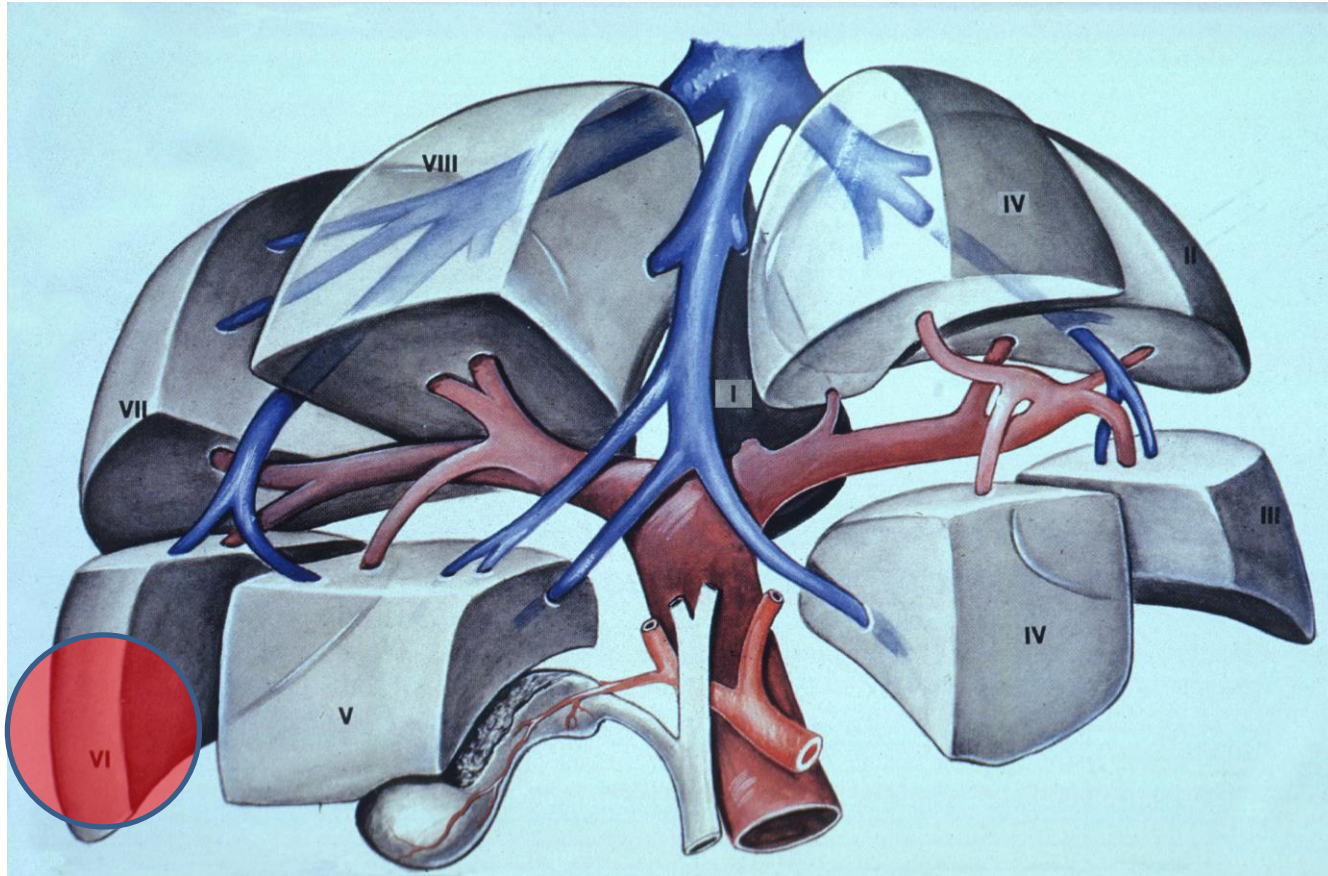


# Surgery for NETs

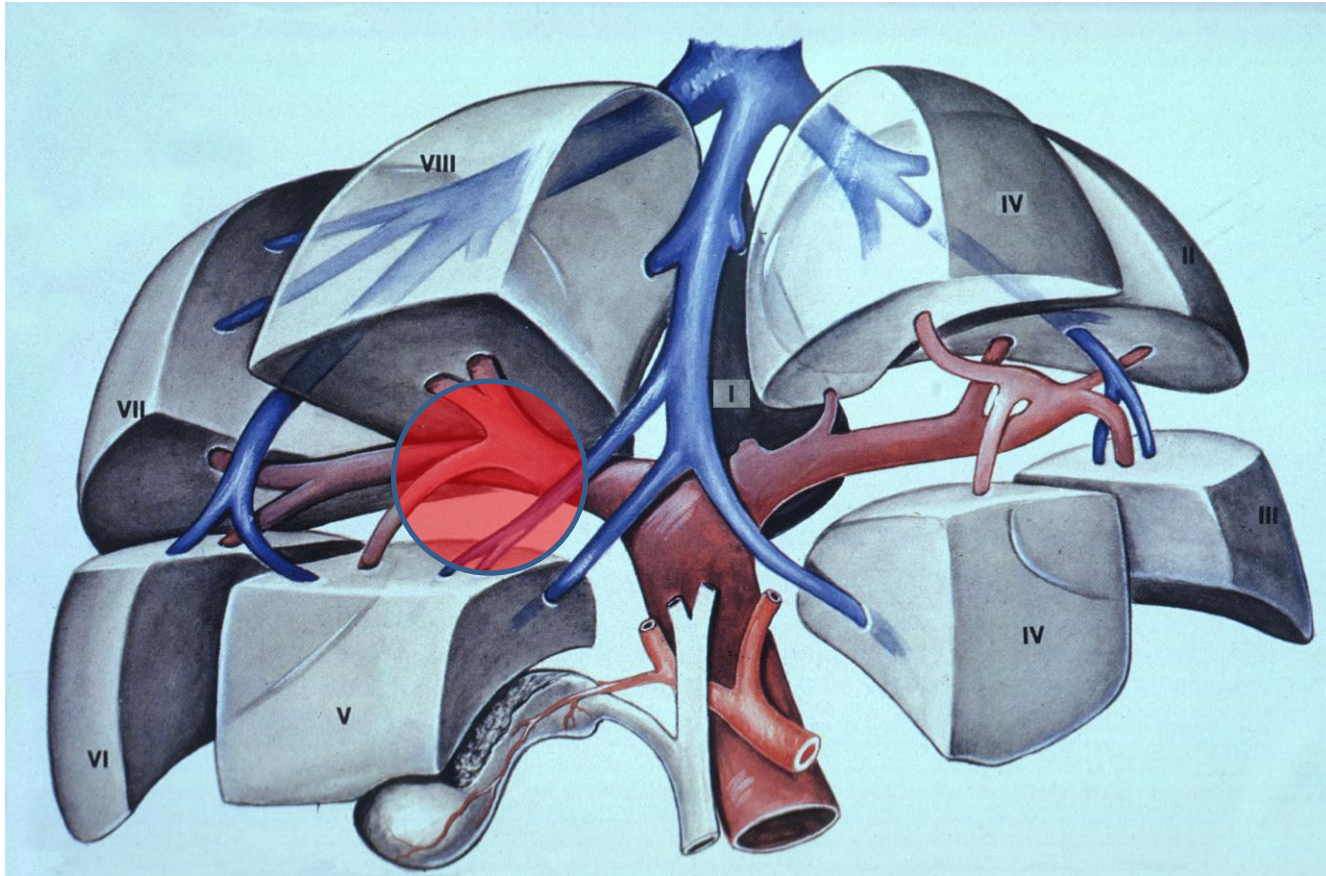




# Surgical Procedures: liver

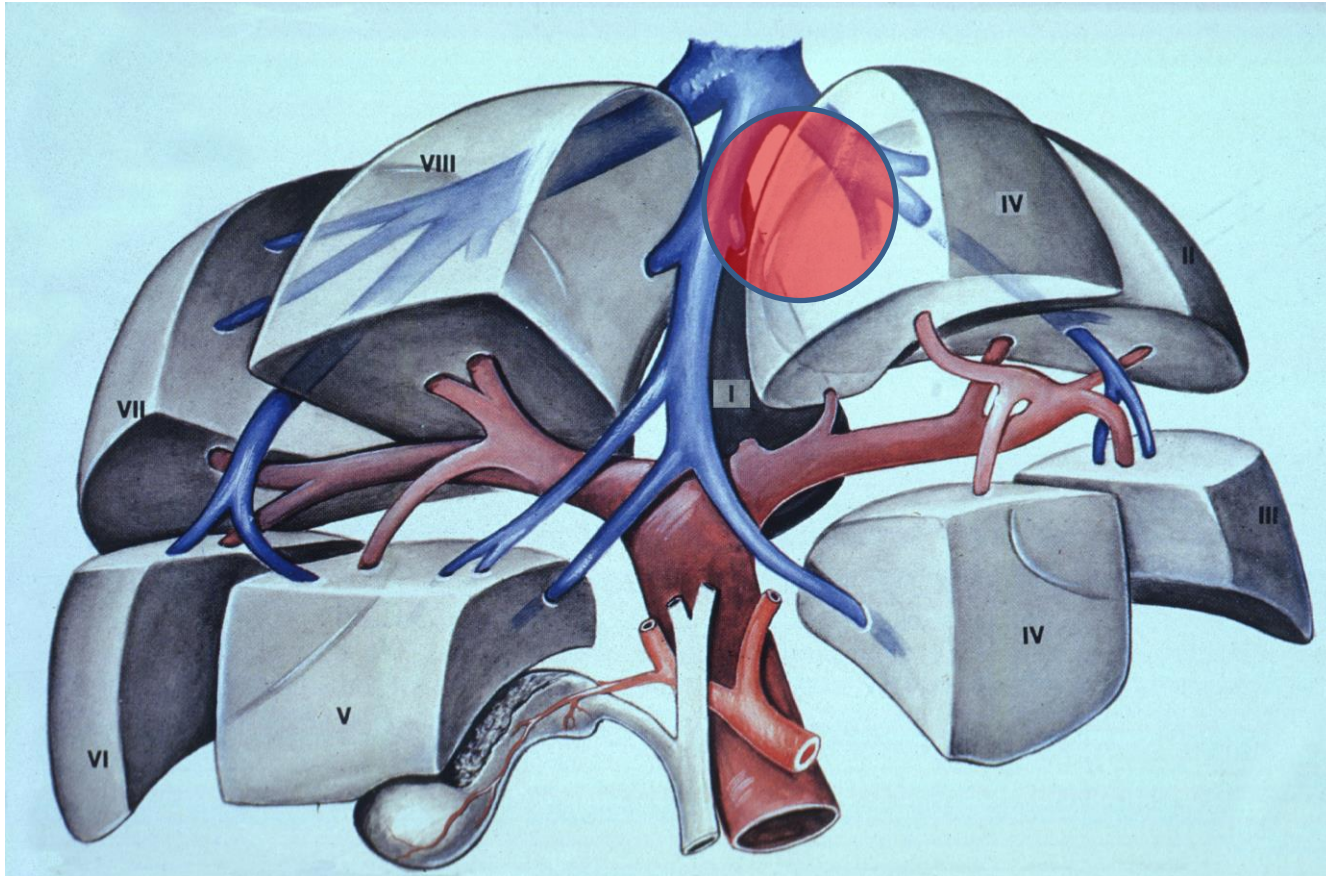


# Surgical Procedures: liver

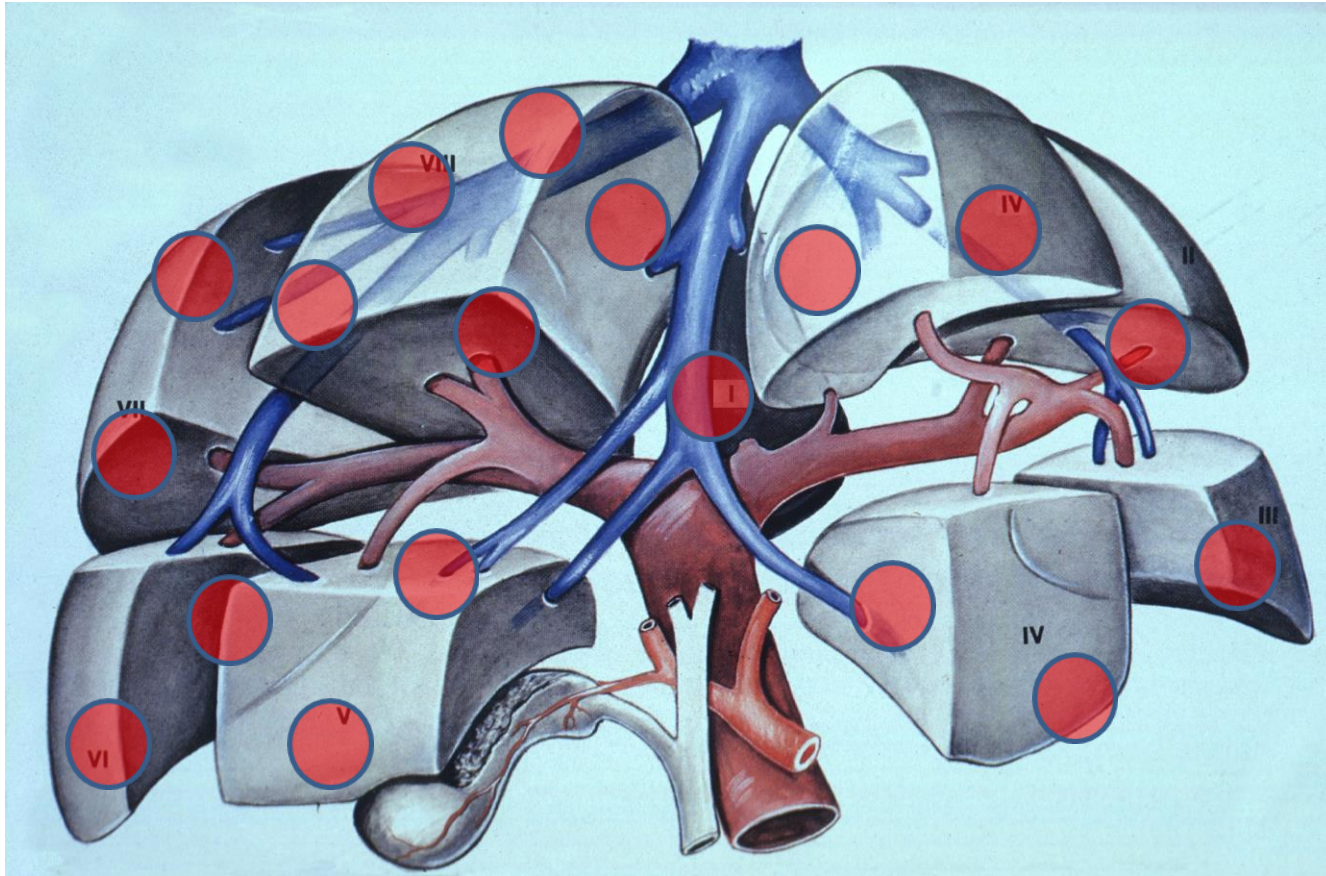




# Surgical Procedures: liver

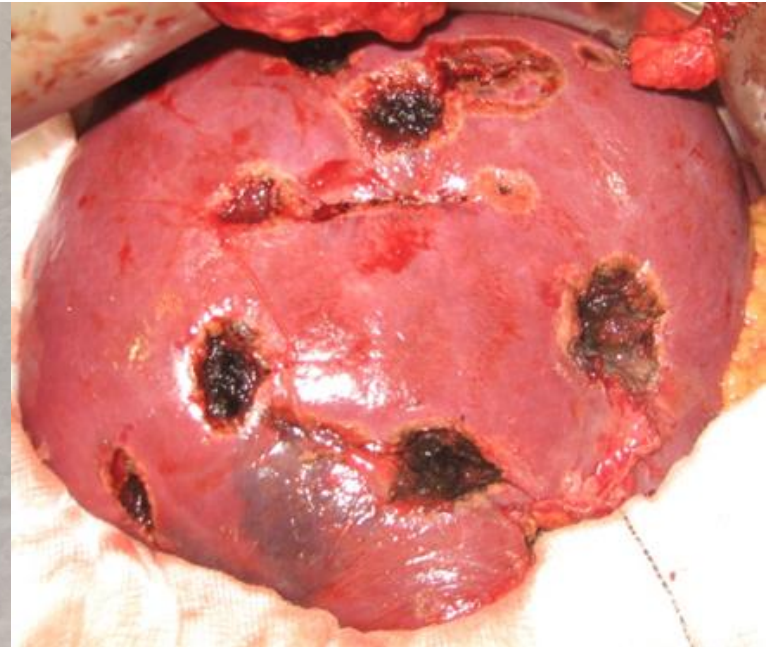


# Surgical Procedures: liver



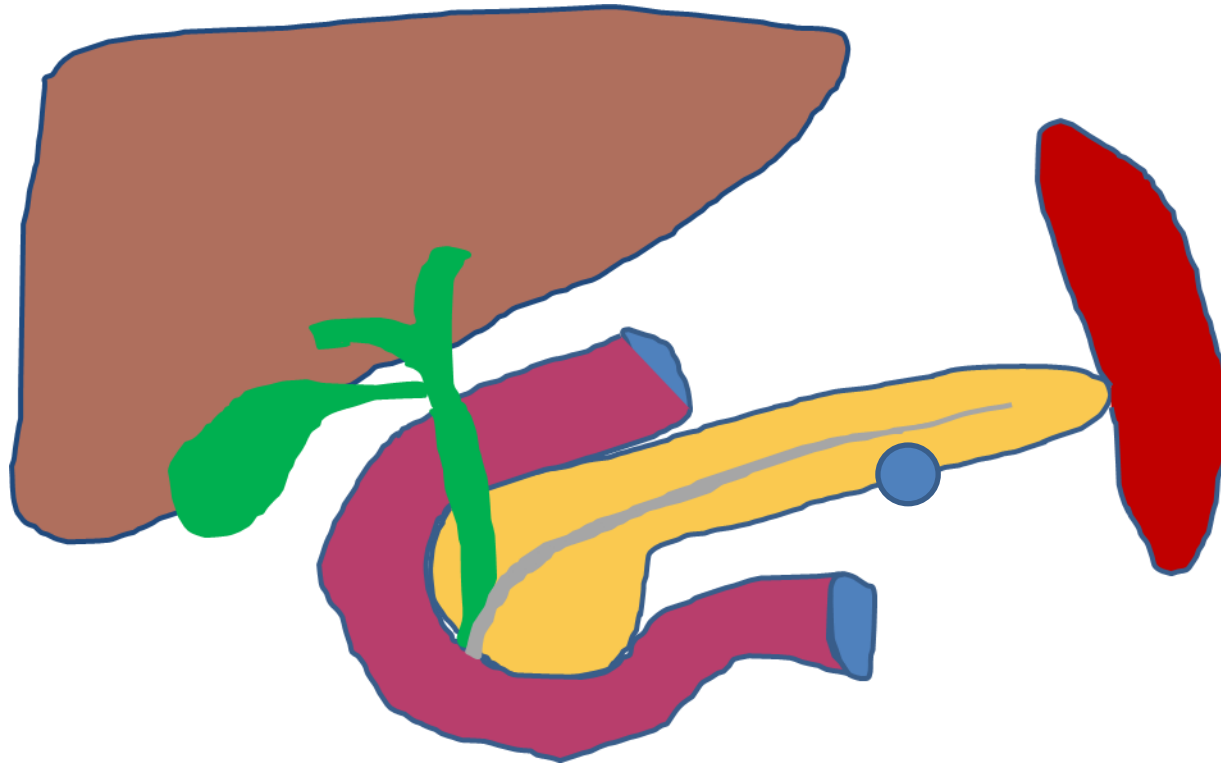


# Surgical Procedures: liver



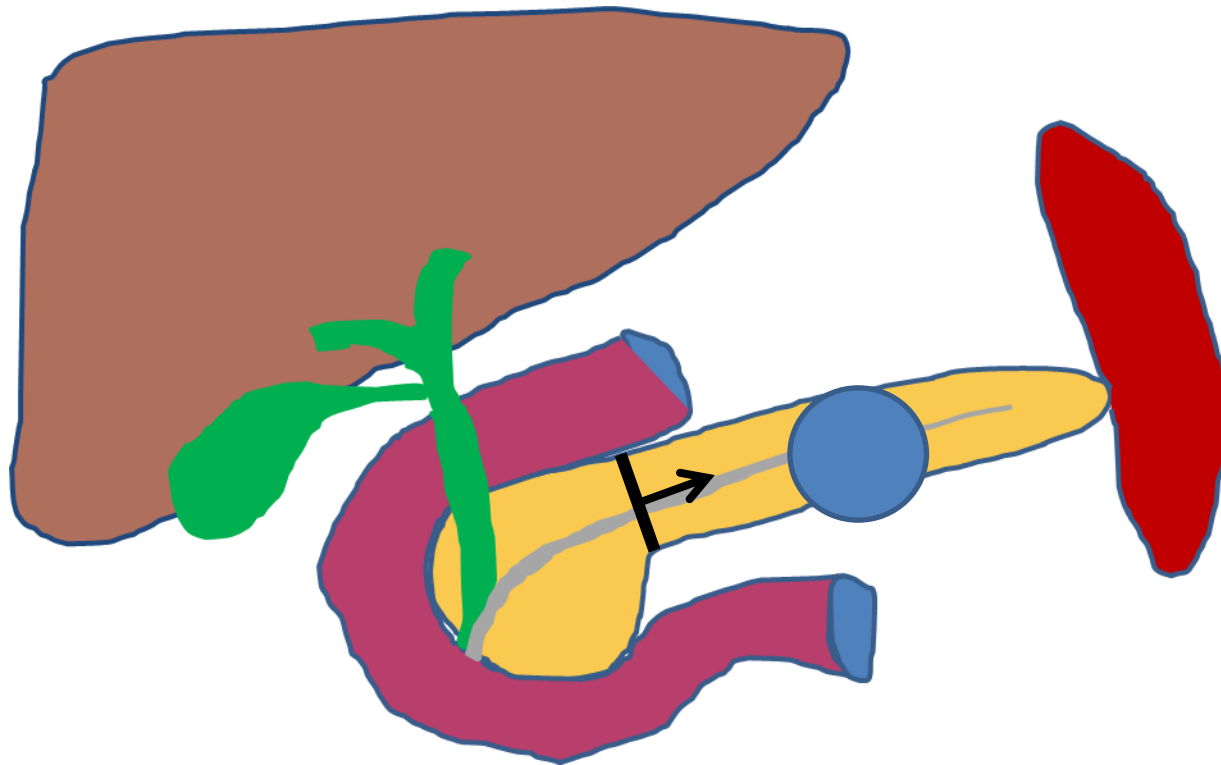
# Surgical Procedures: pancreas

Enucleation of small PNETs



# Surgical Procedures: pancreas

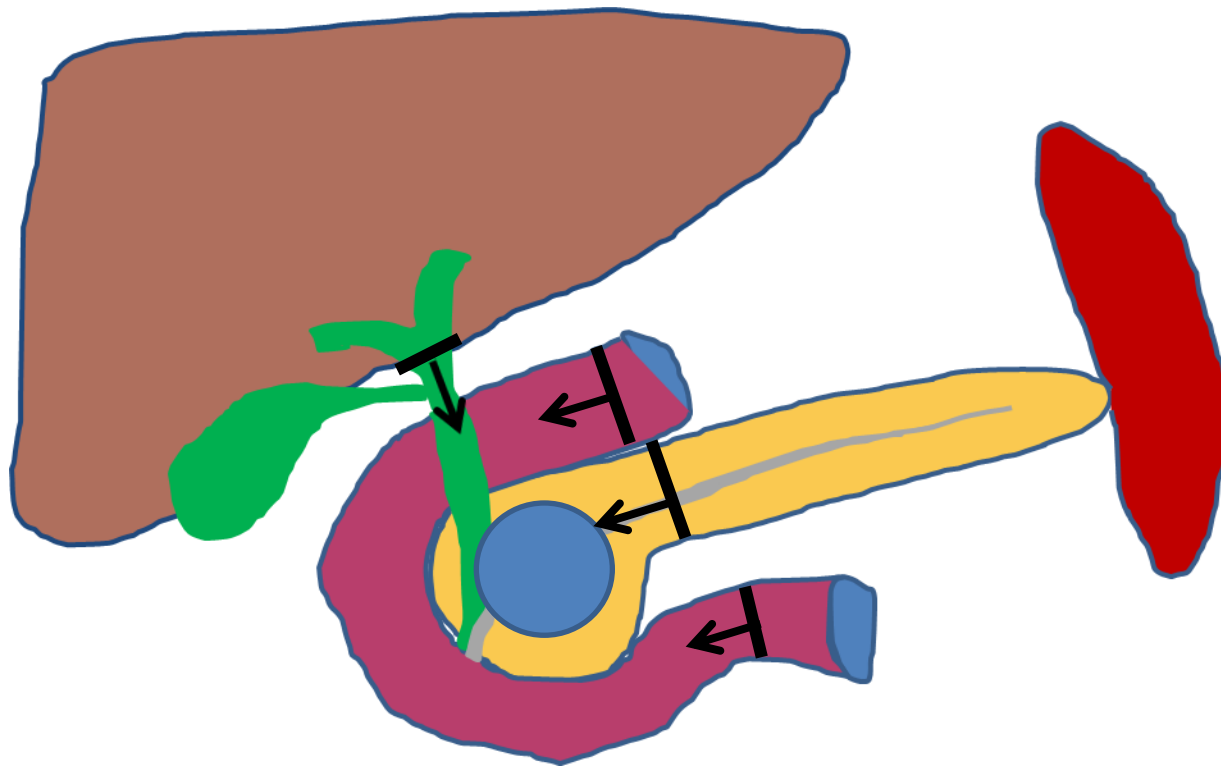
Distal pancreatectomy +/- splenectomy



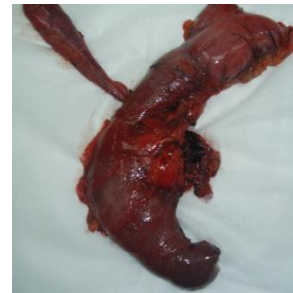
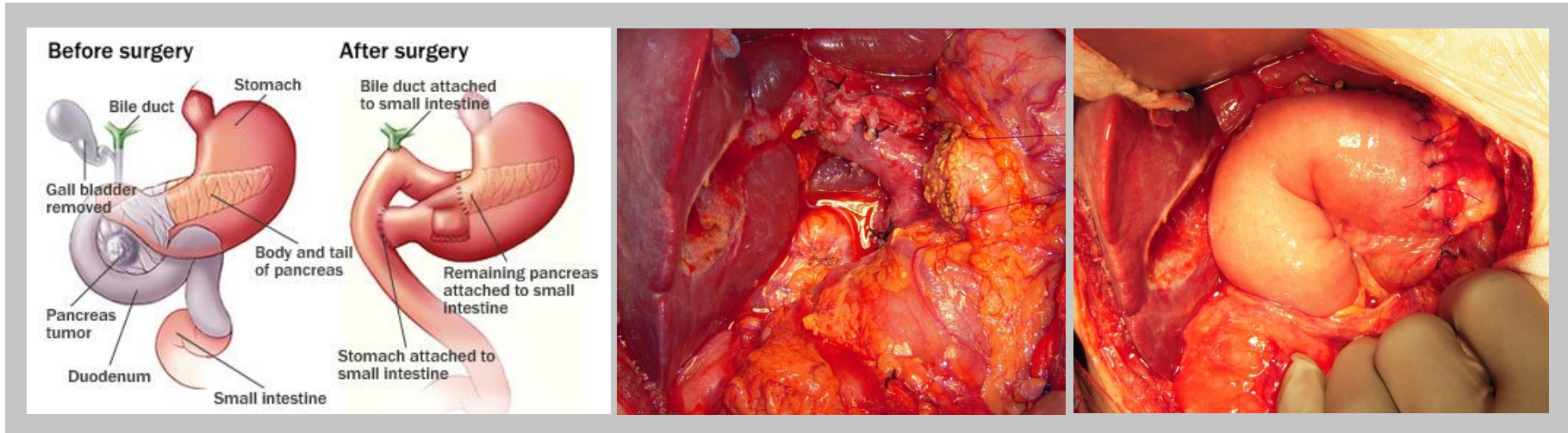


# Surgical Procedures: pancreas

Pancreaticoduodenectomy (Whipples)



# Whipple's Procedure

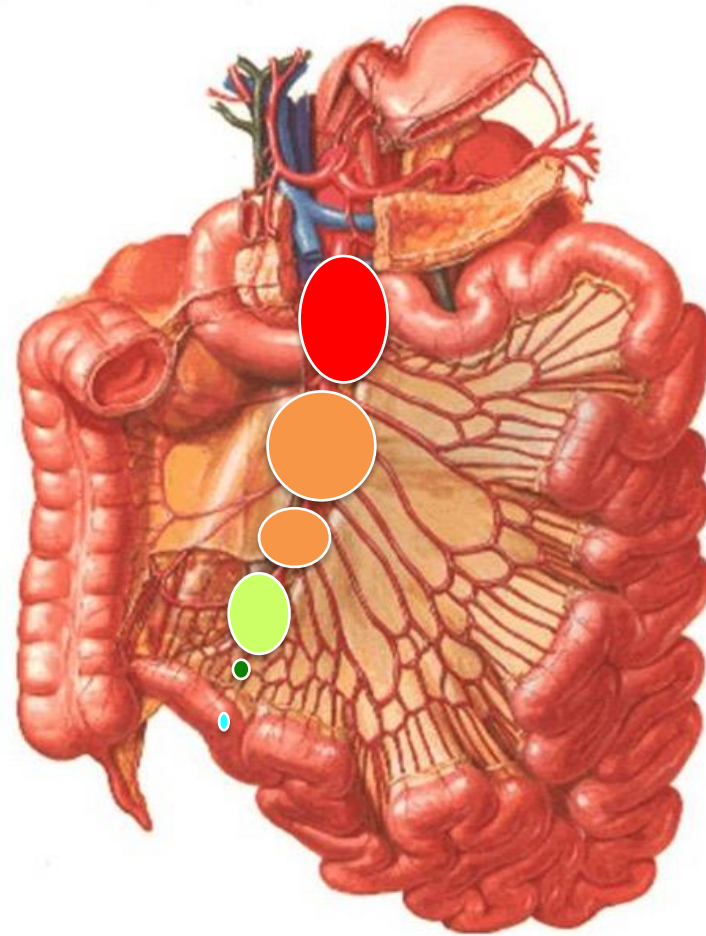


# Surgical Procedures: bowel



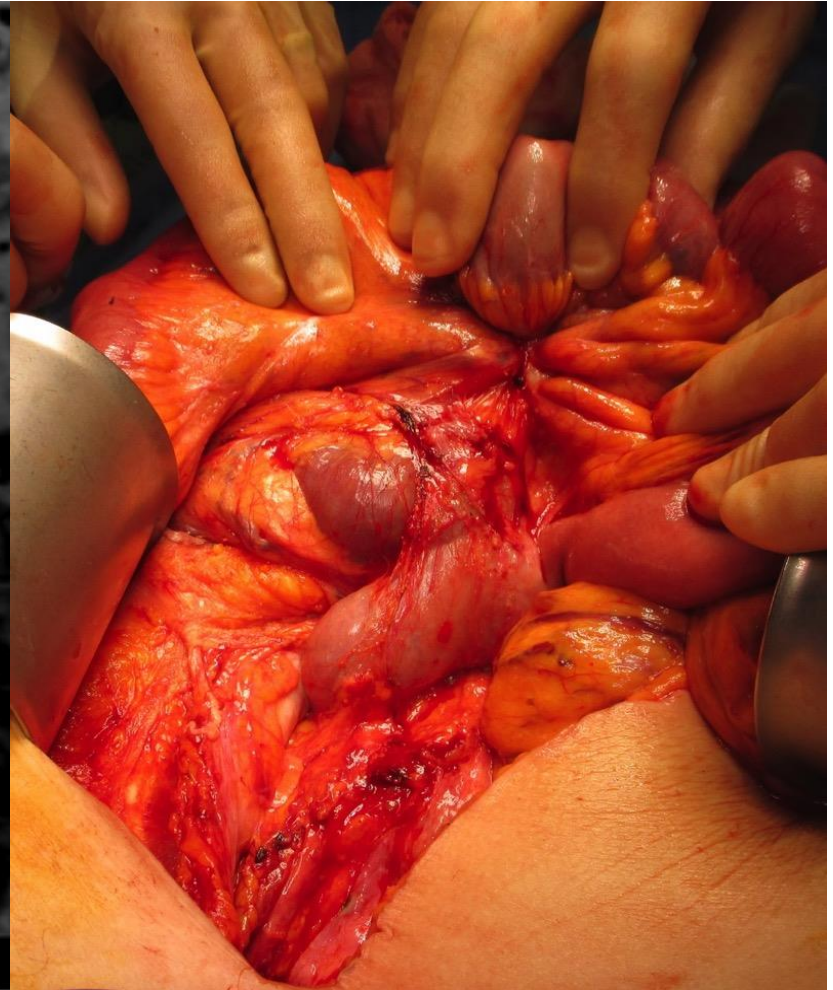
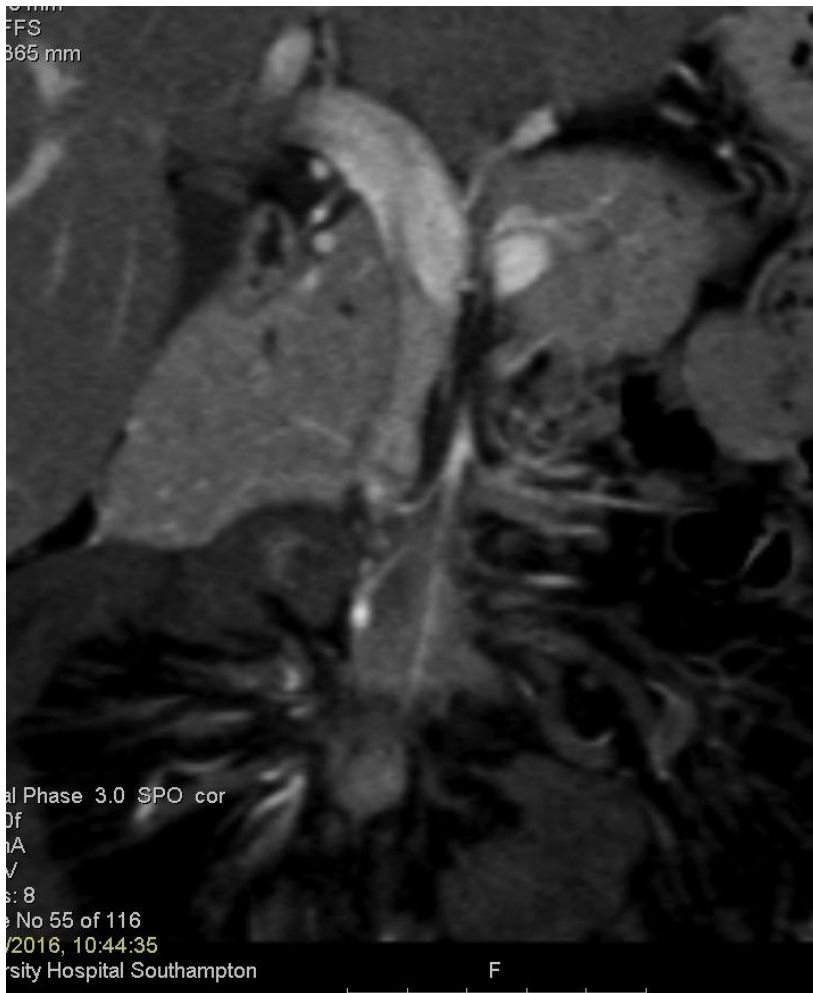
# Surgical Procedures: bowel

Lymph Node Stage
4
3
2
1
0





# Surgical Procedures: bowel



# Summary

- NETs are slow growing a slow growing type of cancer that form in the GI neuroendocrine system
- We do not know what causes them
- NETs can be described as functioning or non-functioning depending on whether they produce hormones
- There are many effective treatment modalities for NETs

