

Core Lecture: Small Bowel Physiology and Motility Disorders

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Case Presentation

- 43 yr old female presented with multiple hospitalizations for nausea, abdominal distension, vomiting over past 8 years
- Can eat after discharge, but readmitted every month
- Weight loss of 90 lbs over several yrs
- Diarrhea 10-12 x /day

Case Presentation (cont.)

- PMH
 - Polymyositis, dermatomyositis, scleroderma
- Outside work-up
 - Normal EGD
 - Gastroparesis by GET
 - Abd CT no neoplasm
 - No SBO by UGI-SBFT
- Refractory to reglan, tegaserod, erythromycin
- J-tube placed for nutrition

Case Presentation (cont.)

- PE
 - Cachetic 85 lbs, telangectasia, percussion dullness on lung exam, abdominal distension
- NG suction 3.8 liters in 1 day
- Labs
 - Normal CBC
 - CPK 780, TSH 7.1, albumin 1.4, TP 4.3
 - Normal liver tests, PT, PTT, Cosyntropin test

Case Presentation (cont.)



Case Presentation (cont.)



Case Presentation (cont.)



Case Presentation (cont.)

- EGD
 - Loss of duodenal folds
 - Biopsy non-specific inflammation
 - Immunohistochemical stain negative
 - Congo red negative

Case Presentation (cont.)

- In hospital
 - Tolerated J-tube isosource 85cc/hr at night
 - Liquids only, no solid foods by mouth
 - Octreotide 200 µg sc bid
 - Reglan 10 mg liquids q6

Case Presentation (cont.)

- 6 weeks later
 - Diarrhea 6x/day
 - Gained 5 pounds
- To start
 - Cipro 500 mg bid x 21 days
 - Domperidone
 - ↑ Octerotide dose



Core Lecture:

Small Bowel Physiology and Motility Disorders

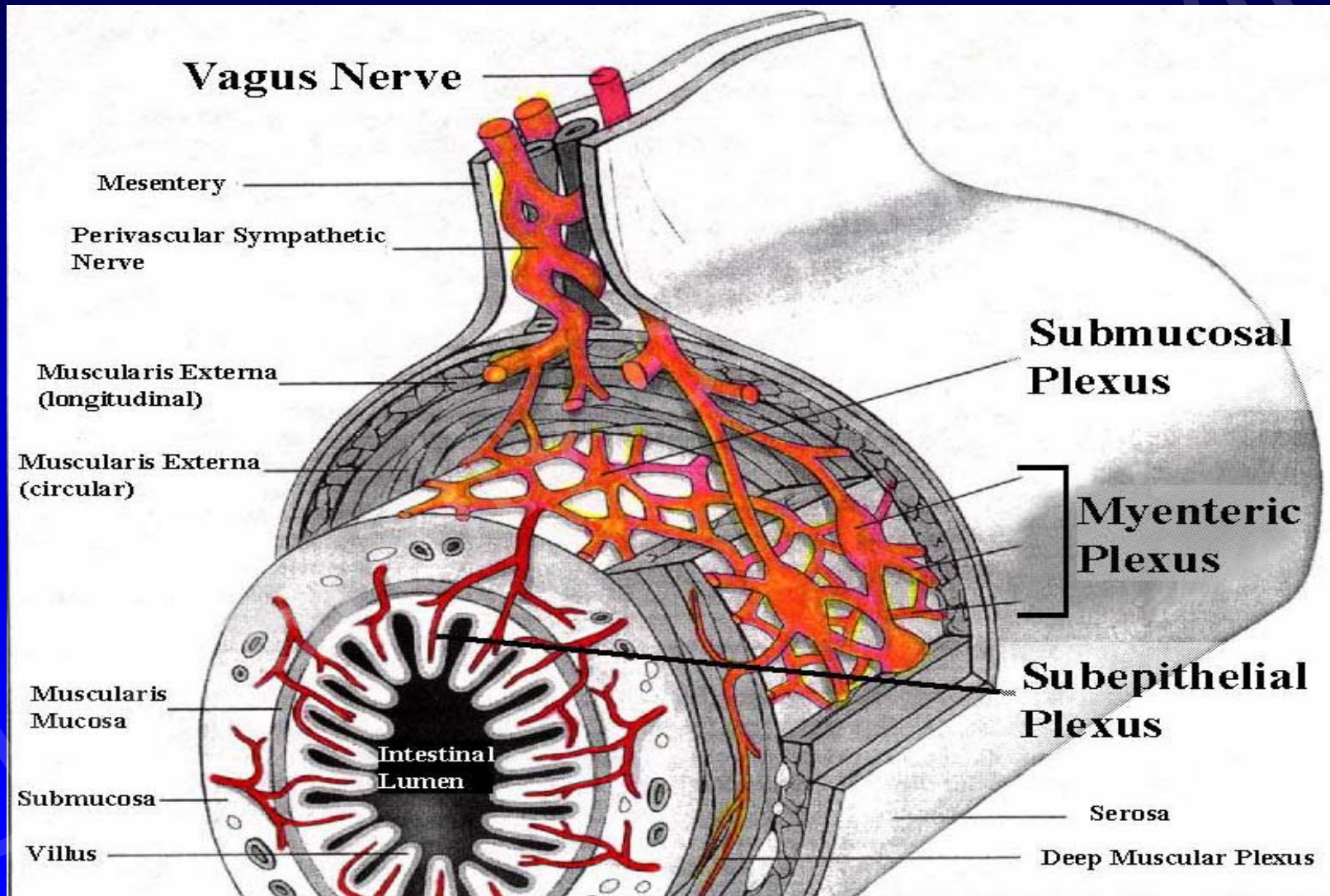
- Case presentation of chronic intestinal pseudo-obstruction
- Normal physiology
- Pathophysiology of small bowel motility disorders
- Clinical manifestation
- Diagnostic evaluation
- Treatment

Differences in the GI Tract

	Embryonic origin	ANS dependence	ENS dependence
Oropharynx to mid duod.	Foregut	+++	++
Small bowel to prox. colon	Midgut	++	+++
Colon to rectum	Hindgut	+	+++

ANS (autonomic nervous system); ENS (enteric nervous system)

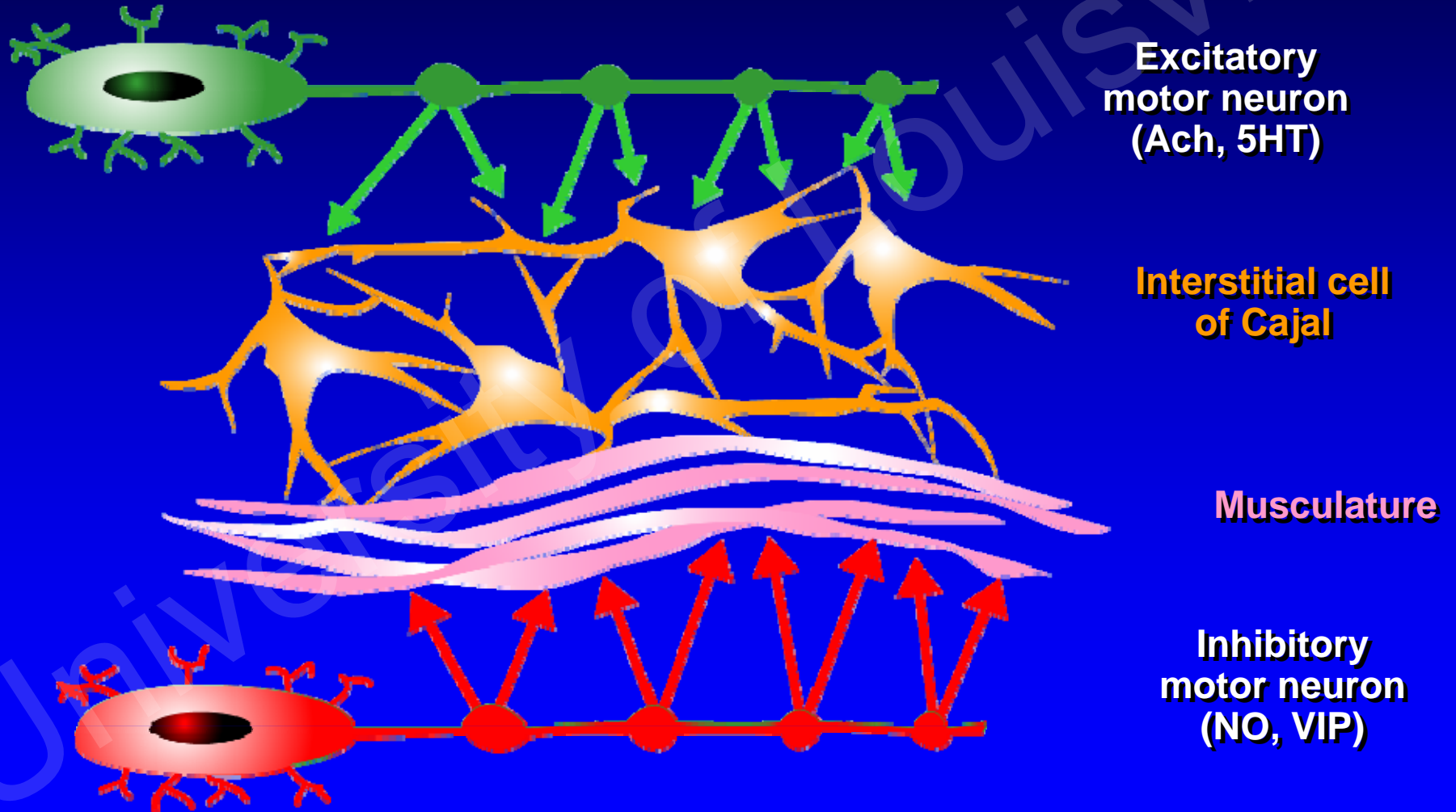
Enteric Nervous System



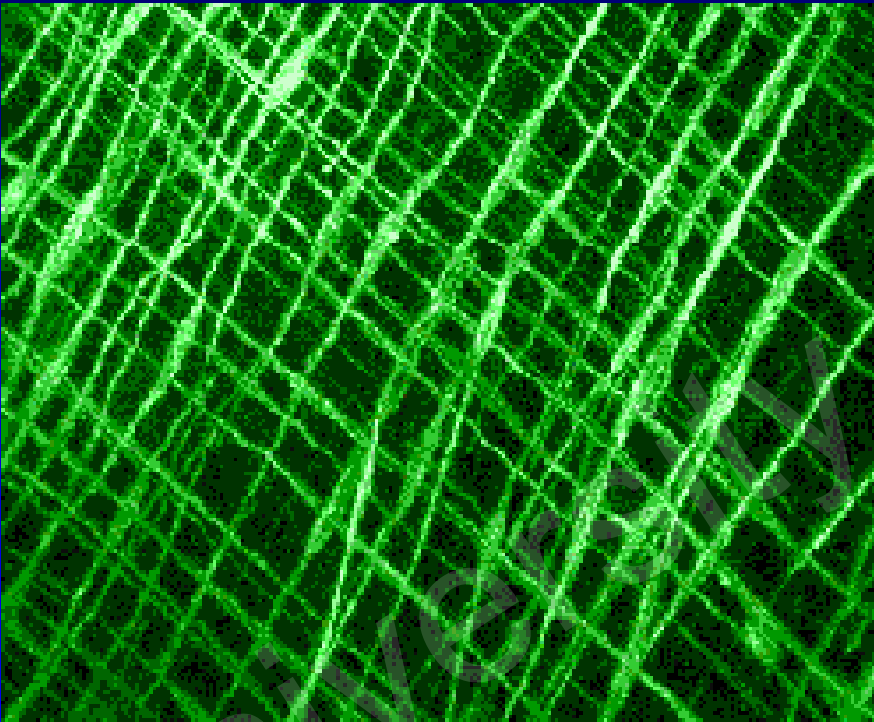
Enteric Nervous System

- Most important control in GI motility
- Provided frequency and direction of peristalsis
- Can function independently of CNS
- Output is modulated by CNS, autonomic system, peptides, glucose, etc.

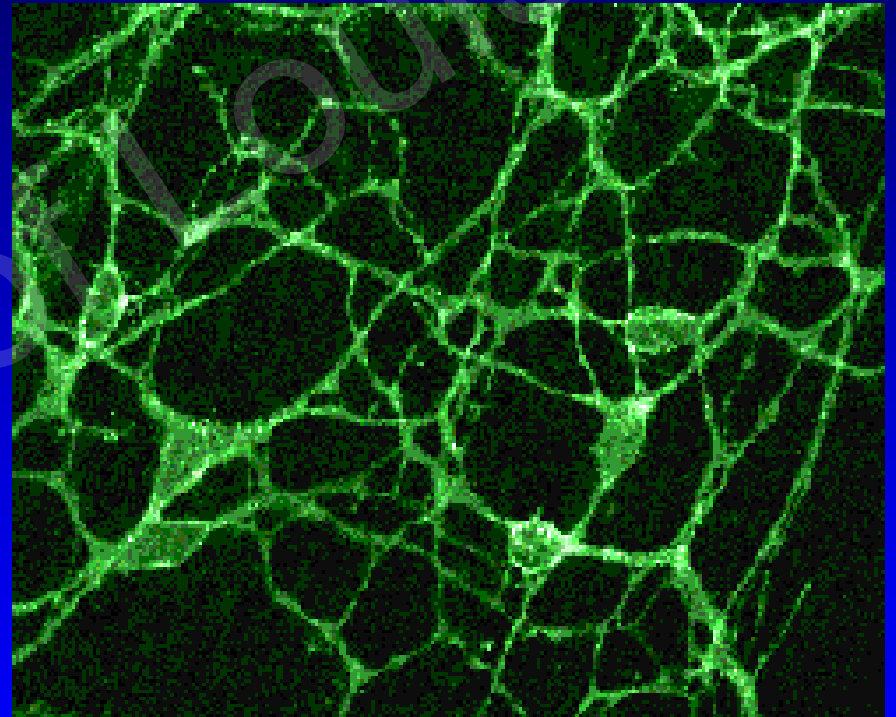
Enteric Nervous System



Interstitial Cells of Cajal

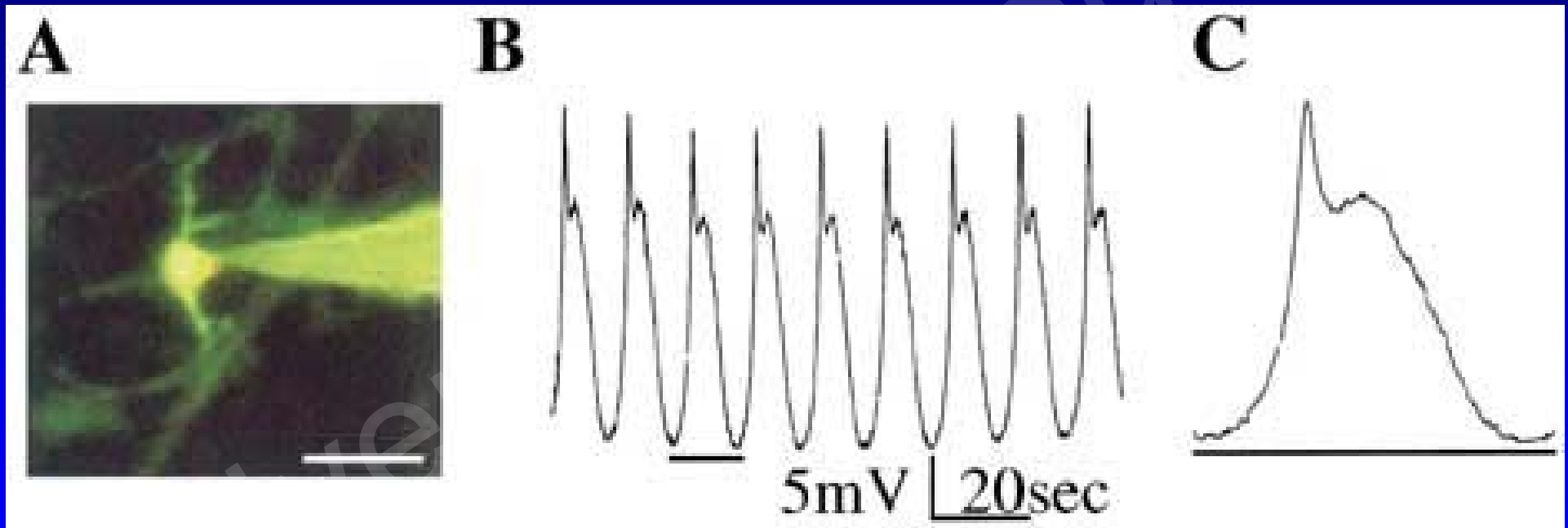


Gastric fundus



Small bowel

Slow Wave from Interstitial Cells of Cajal



Electromechanical Association

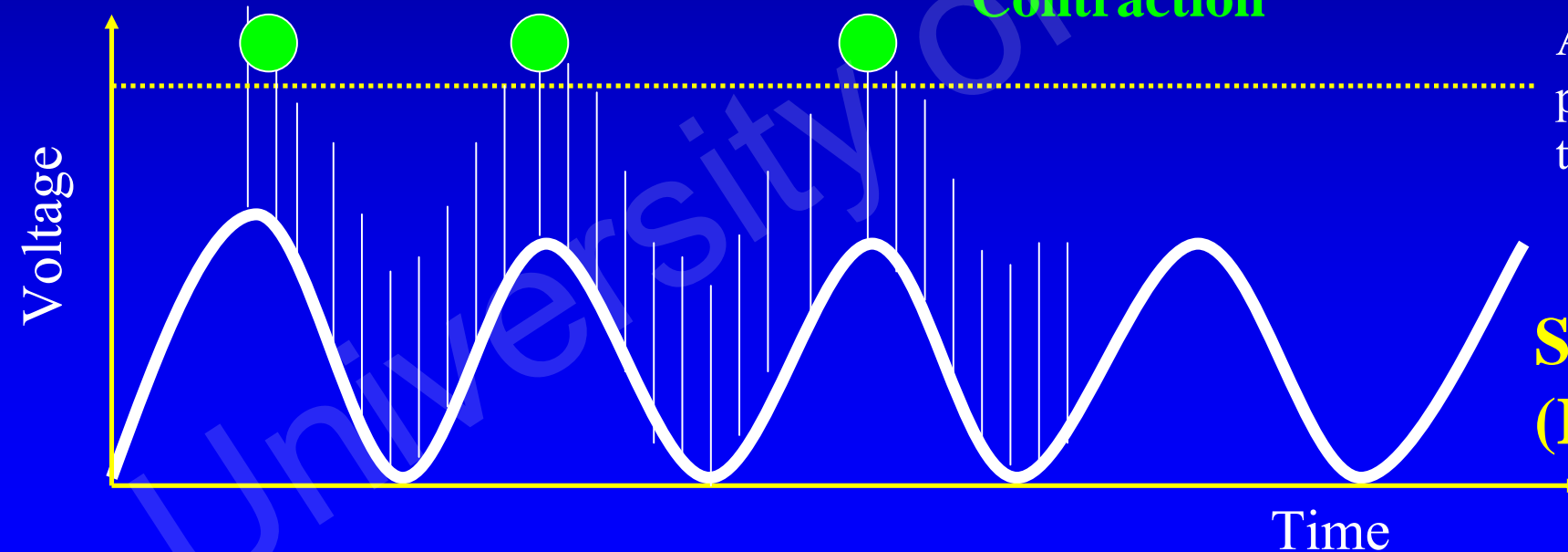
Food, vagal input, peptides, distension

Spike potentials

Contraction

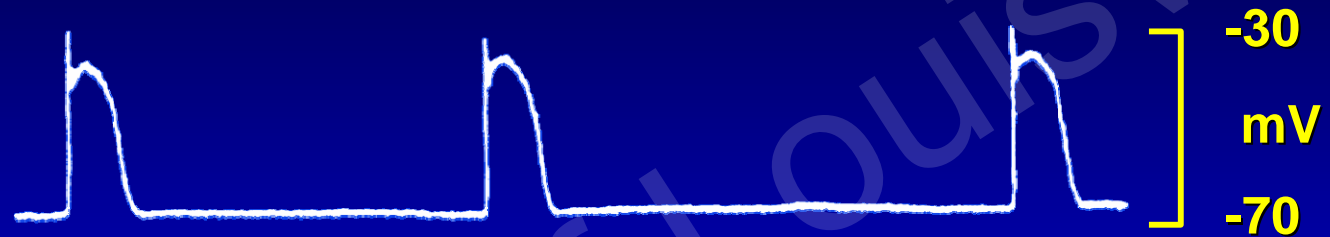
Action potential threshold

Slow Waves (ICC)

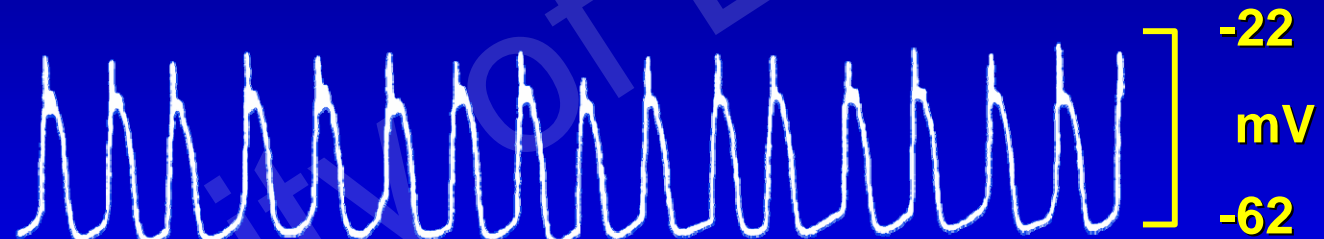


Enteric Nervous System Controls GI Electrical Rhythm

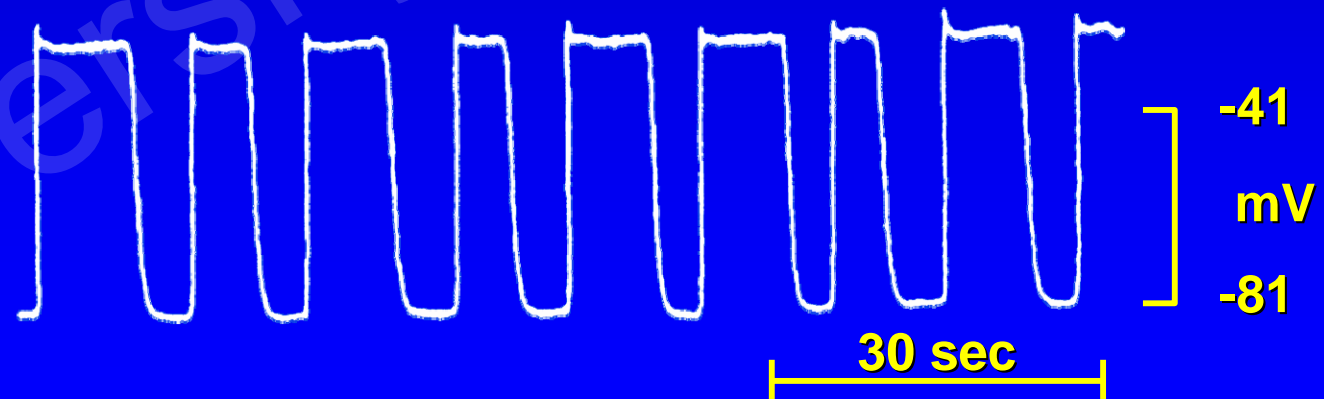
Stomach
(3/min)



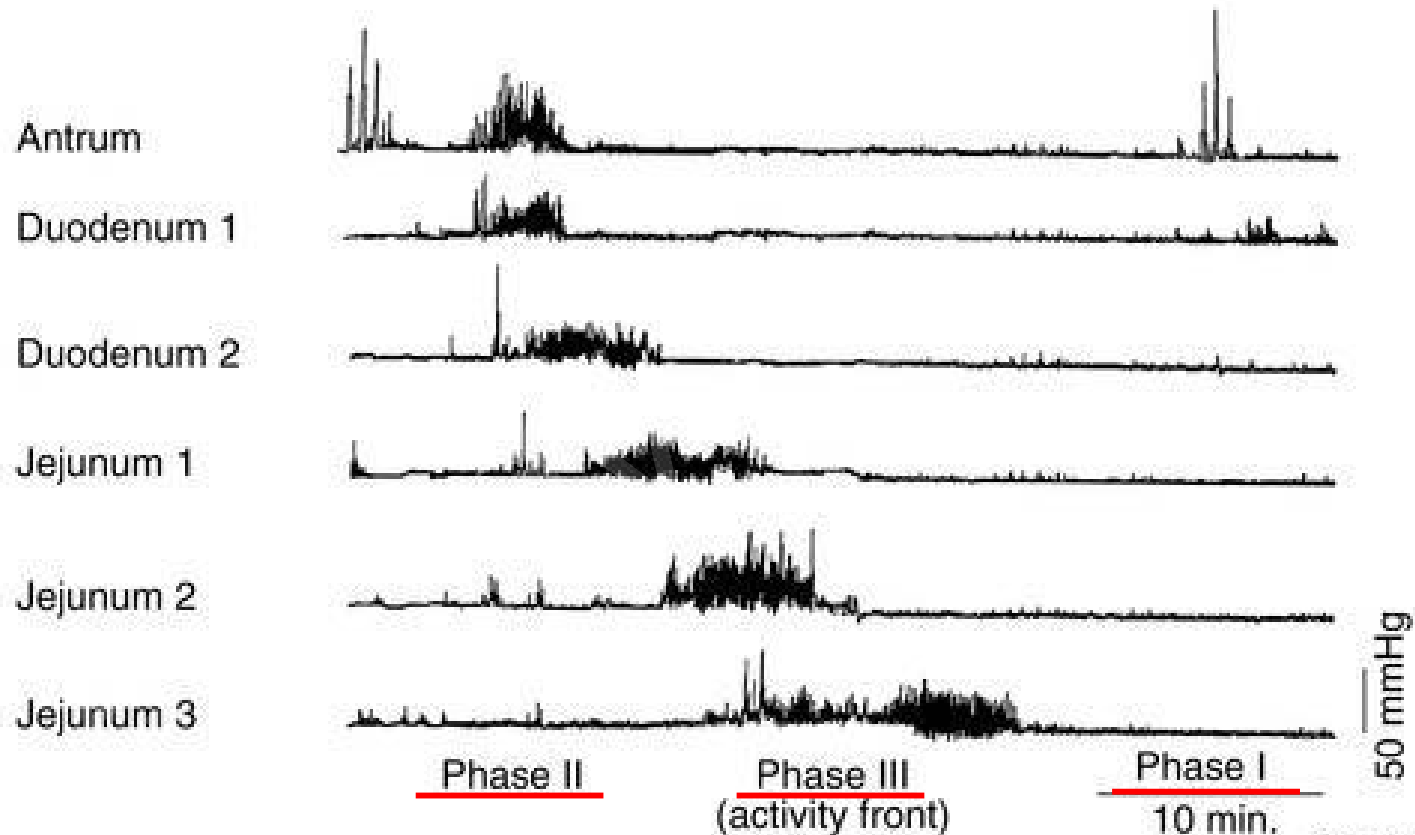
Small intestine
(8-12/min)



Colon
(3-6/min)



Normal Fasting Motor Patterns: Migratory Motor Complex



Irregular

Maximal propulsion

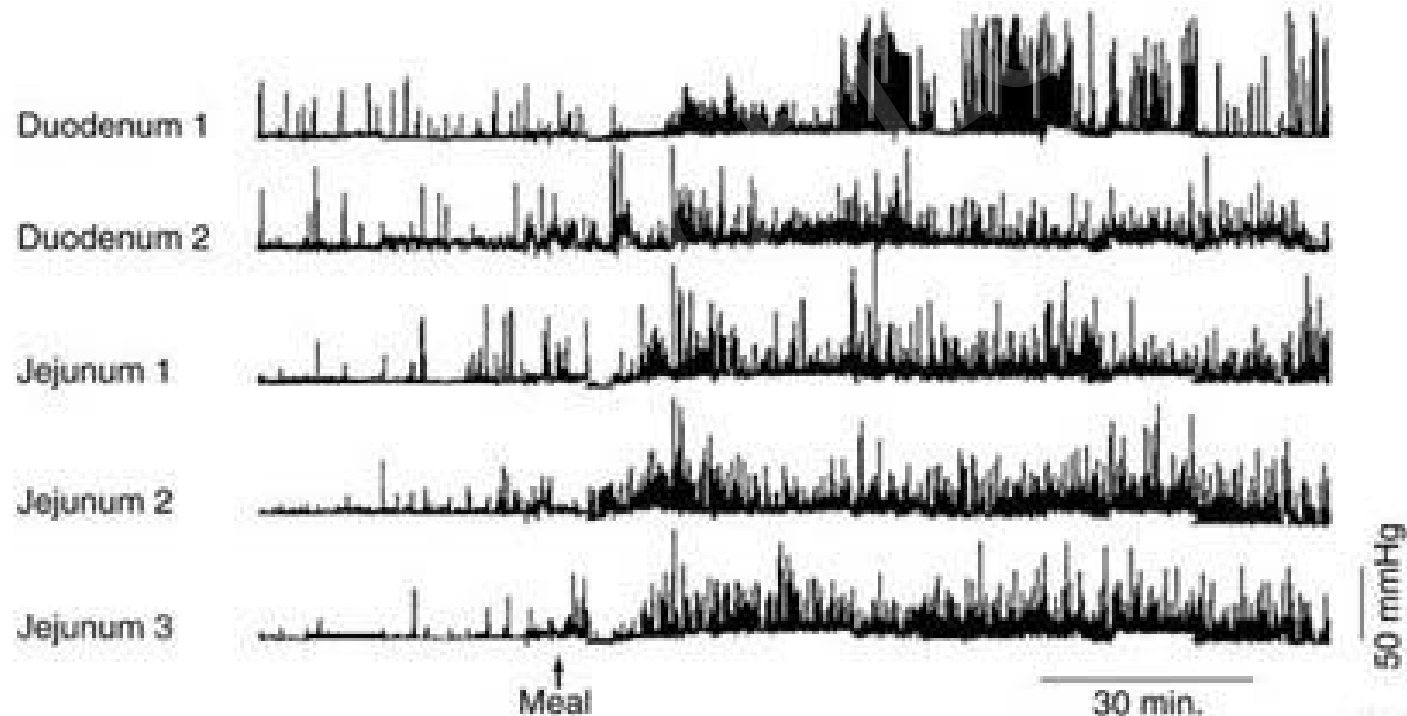
Quiescent

Fasting Migratory Motor Complex

“Intestinal Housekeeper”

- Most powerful propulsion
- Maximal electrical-mechanical association at phase 3
- Function of enteric nervous system
- Important for
 - Transit of indigestible solids
 - Prevention of bacterial overgrowth

Normal Postprandial Motor Patterns

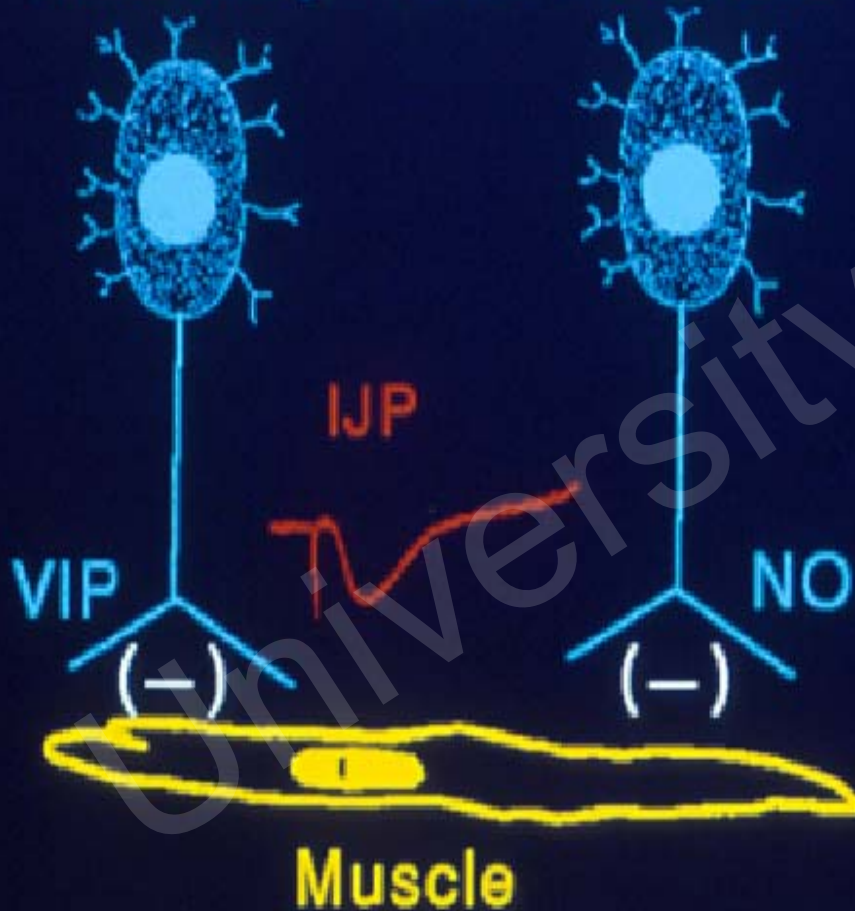


Postprandial Motor Patterns

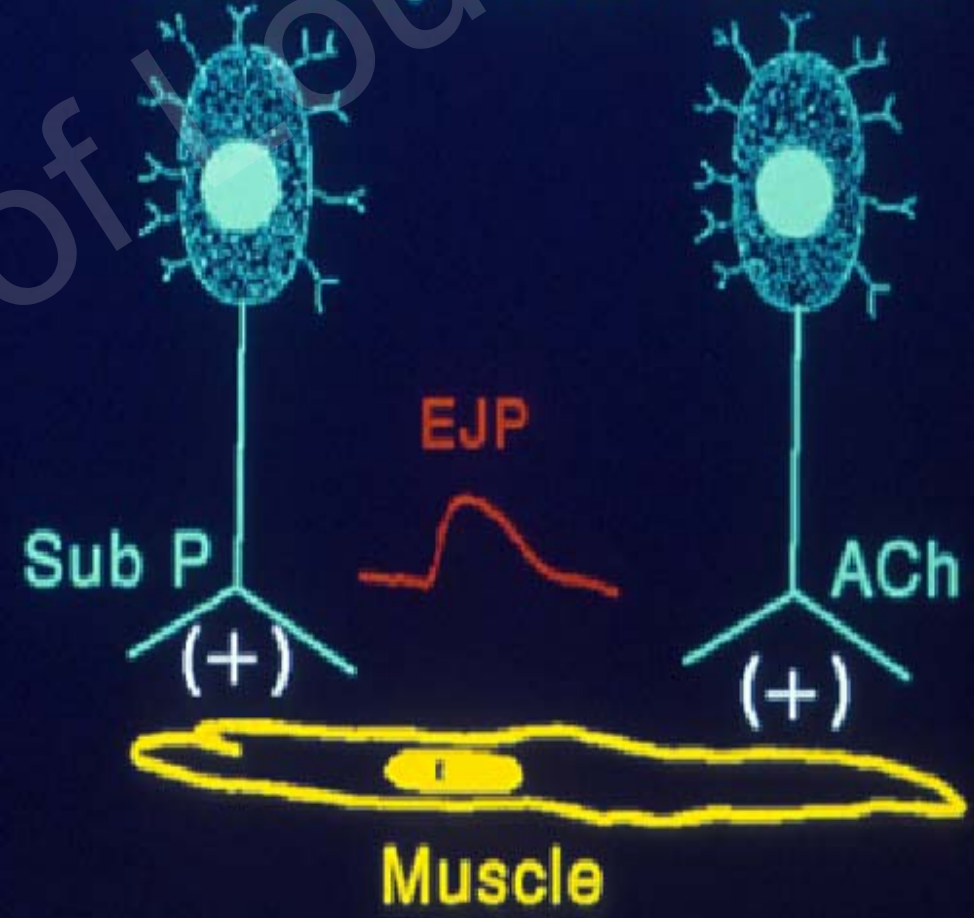
- Contractions of variable frequency, amplitude, propagation
- Depends on caloric content
- Initiated by vagal reflex
- Important for mixing

ENTERIC MOTOR NEURONS ARE FINAL PATHWAYS FROM THE ENTERIC NERVOUS SYSTEM TO THE GASTROINTESTINAL MUSCULATURE

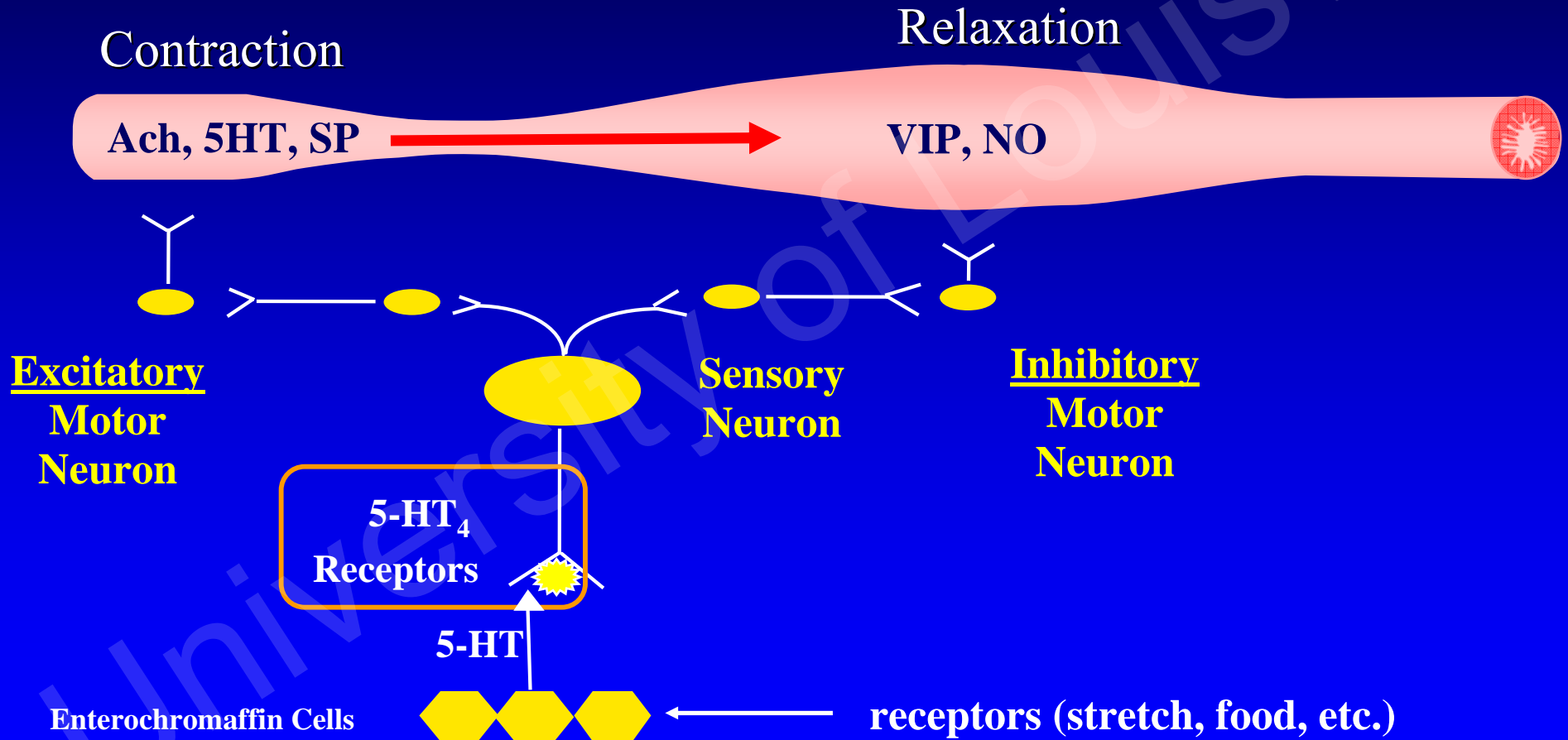
Inhibitory Motor Neurons



Excitatory Motor Neurons



Enteric Nervous System Controls GI Peristalsis



Diagnostic Testing for the Small Bowel Motility Disorders

	<u>TESTS</u>
Visualize lumen to exclude other diseases	Enteroscopy, UGI/SBFT, capsule endoscopy
Vasculature	CT-angiogram
Look for dilated small bowel	KUB, UGI/SBFT, CT scan
Small bowel transit	SBFT, small bowel scintigraphy, capsule endoscopy, smart pill
Bacterial overgrowth	H2 breath test, culture of small bowel aspirate
Motor patters	Antroduodenal or SB manometry
Neuromuscular structures	Full thickness biopsy

KUB



- Dilated small bowel
- Air-fluid levels may not be present

UGI/SBFT

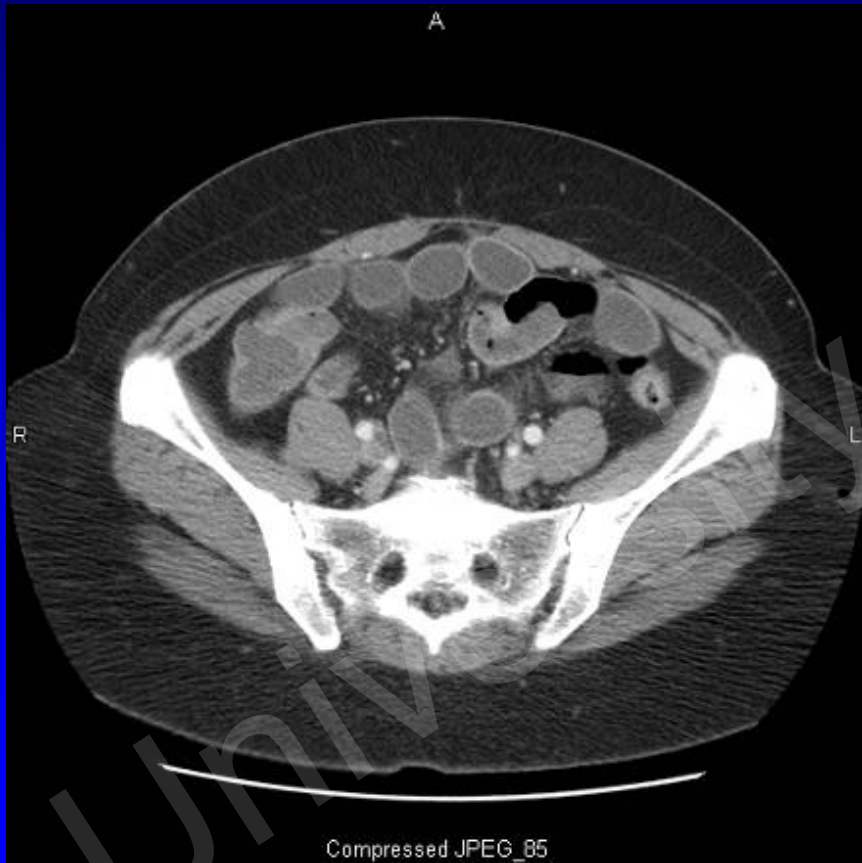


- Look for small bowel dilation and diverticulum
- Rule out obstruction
- Segmental involvement

UGI-SBFT (Incomplete Malrotation)



Abdominal CT



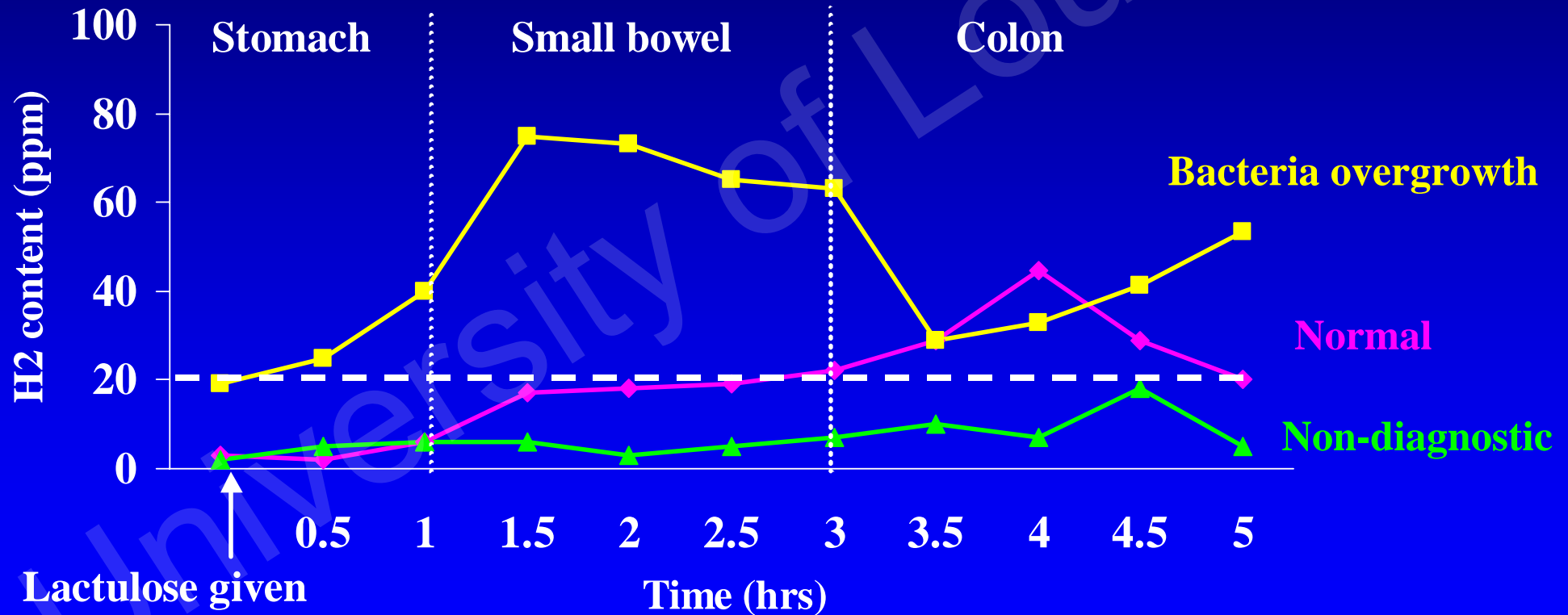
- Small bowel dilation
- Neoplasm

Patient with ovarian cancer and radiation

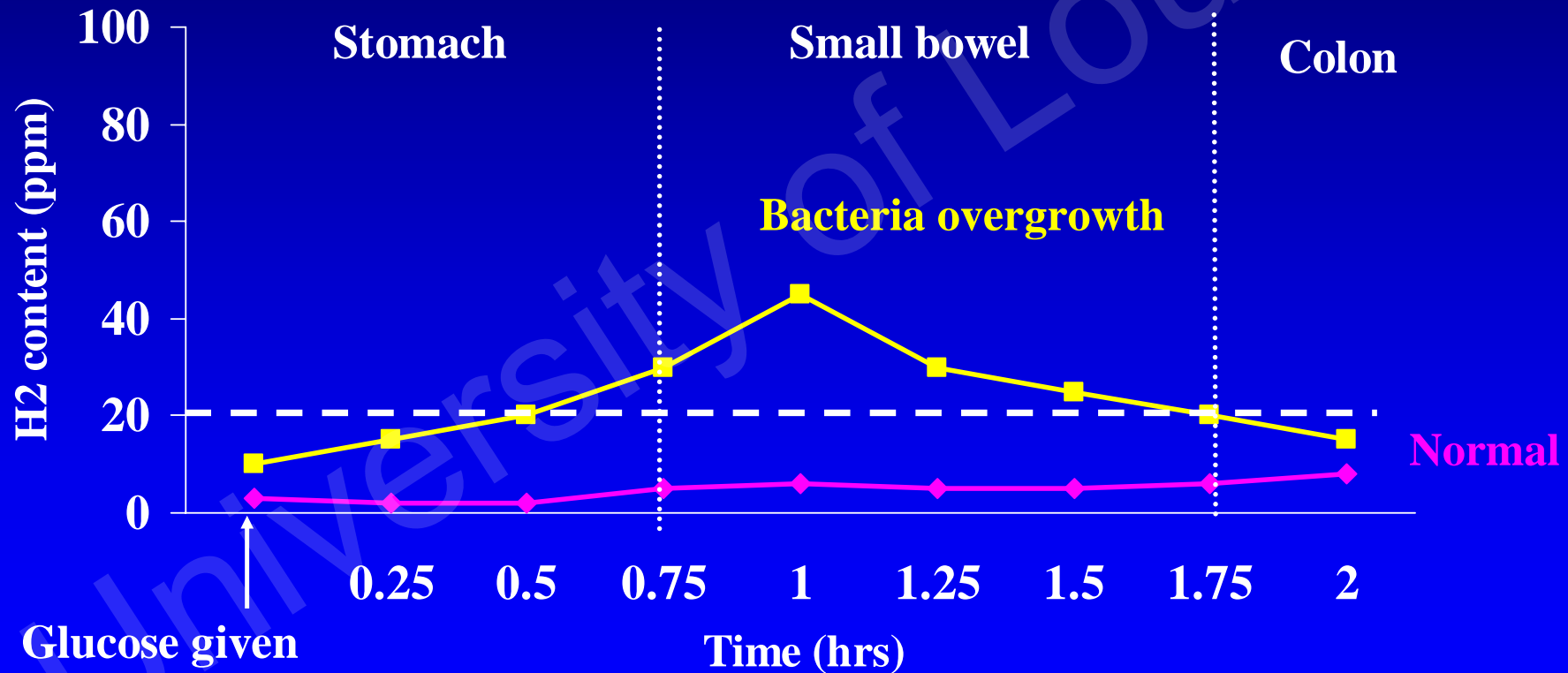
CT-Angiogram (Celiac Artery Stenosis – Median Arcuate Ligament Syndrome)



H₂ Breath Testing with Lactulose



H₂ Breath Testing with Glucose

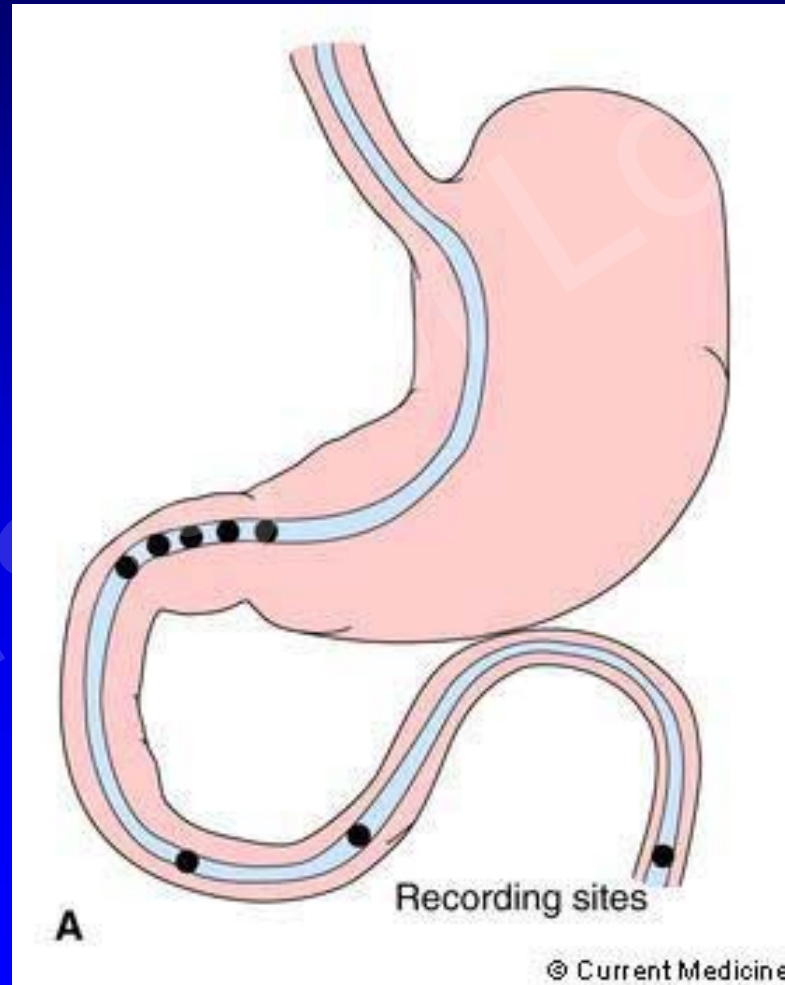


Accuracy of Tests for Small Intestinal Bacteria Overgrowth

Diagnostic test	Abnormal test	Sensitive*	Specificity*
Lactulose breath test	Double peaks of >20 ppm H ₂ above baseline	17 – 68%	70 – 100%
Glucose breath test	>12 ppm H ₂ above baseline	41 – 100%	67 – 98%

*Gold standard: $>10^5$ aerobes or anaerobes CFU/ml of jejunal aspirate

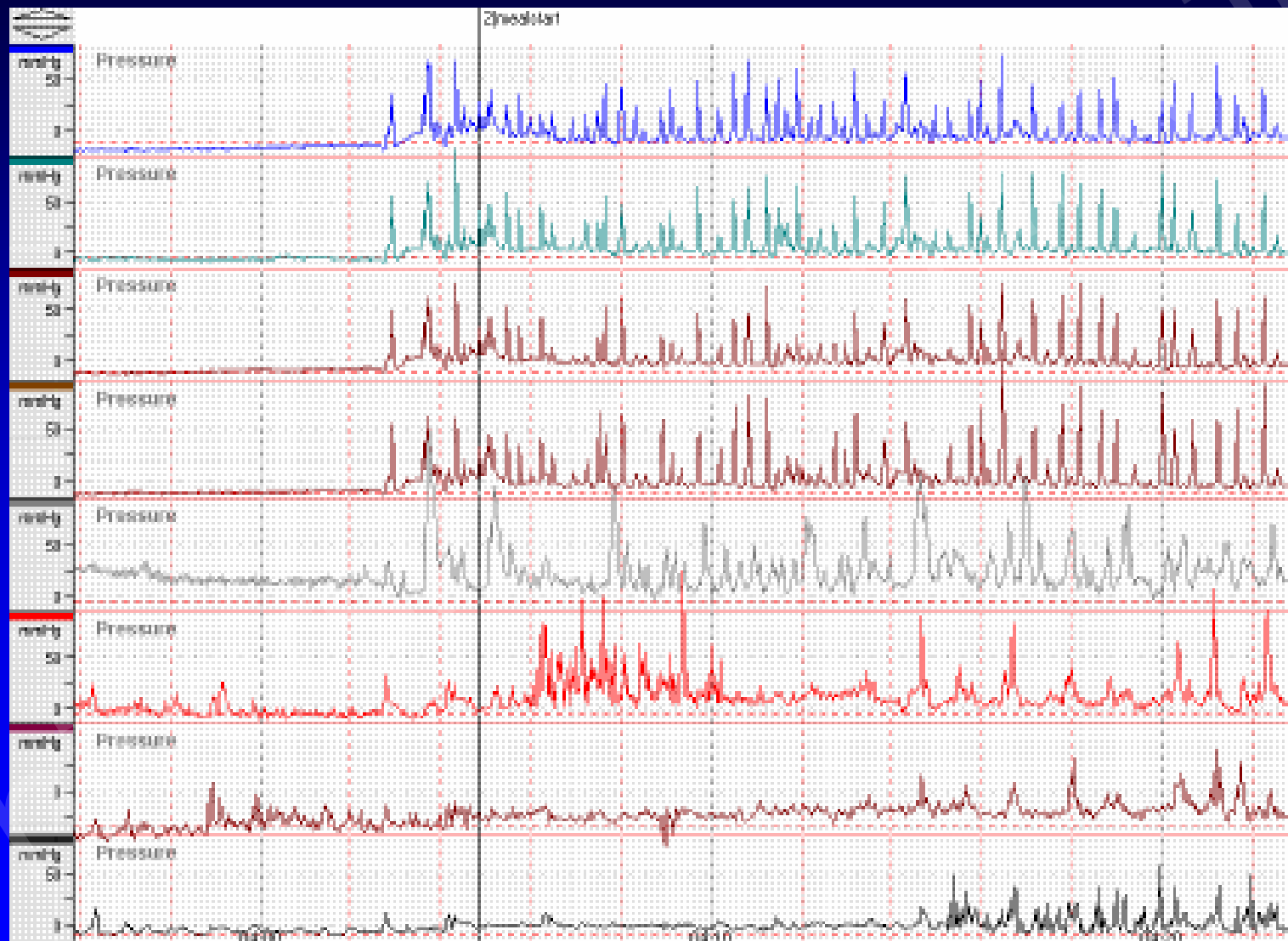
Antroduodenal Manometry



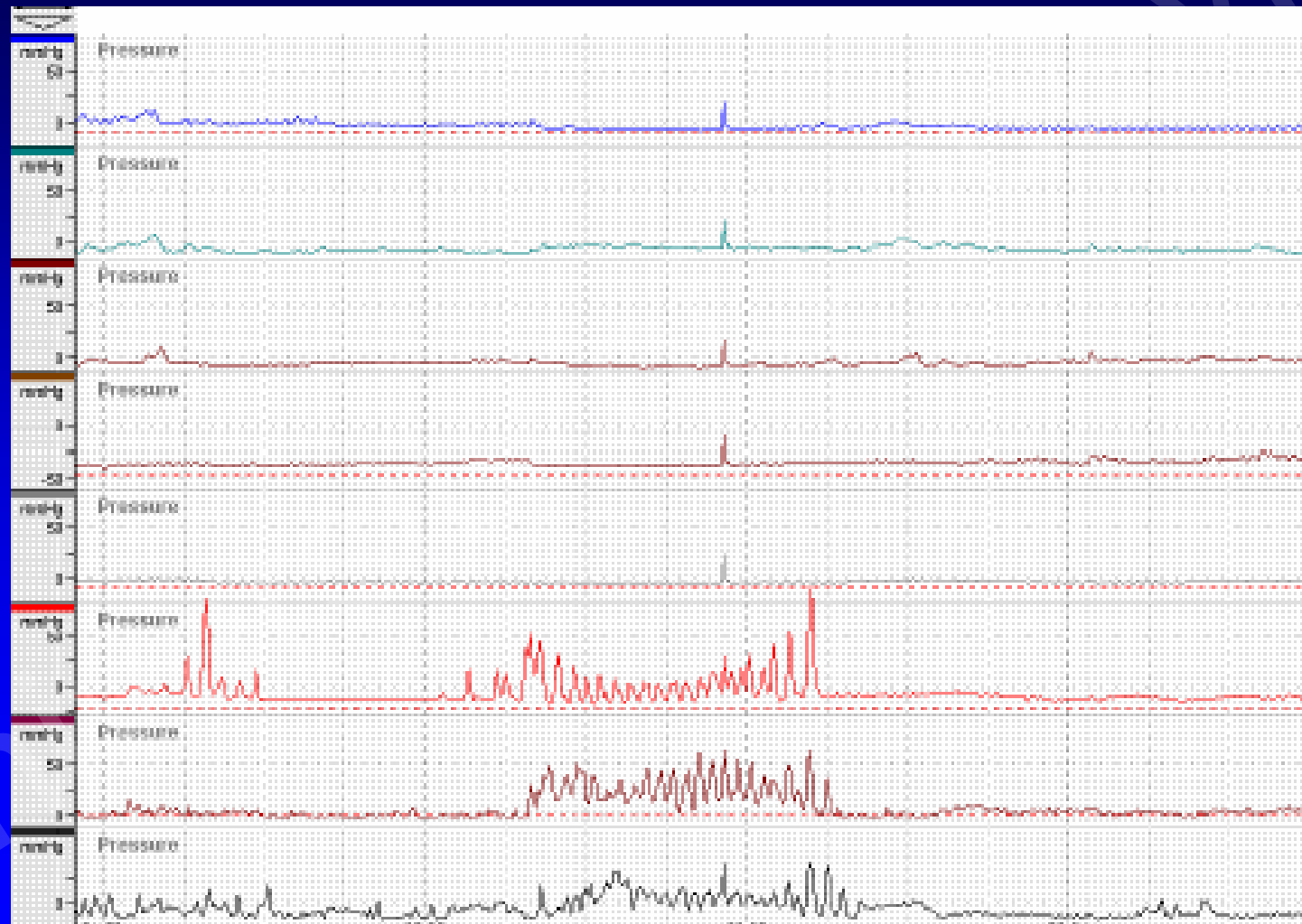
Indication for Small Bowel Manometry

- Refractory nausea and vomiting
- Unexplained nausea and vomiting
- Intolerance of jejunal feeding
- Considering colectomy for colonic inertia

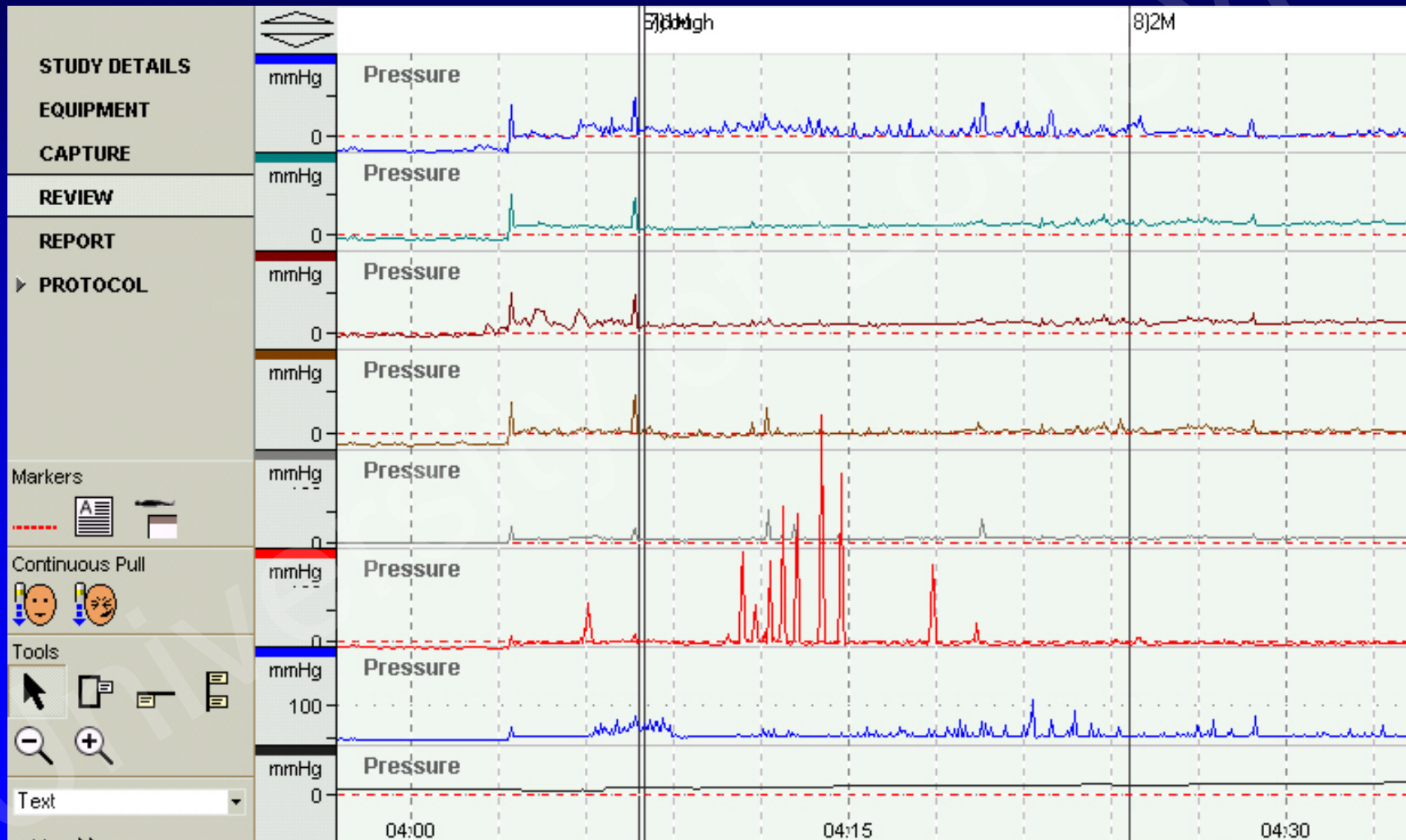
Normal Postprandial SBM



Abnormal Fasting SBM: Intrinsic (Enteric) Neuropathy



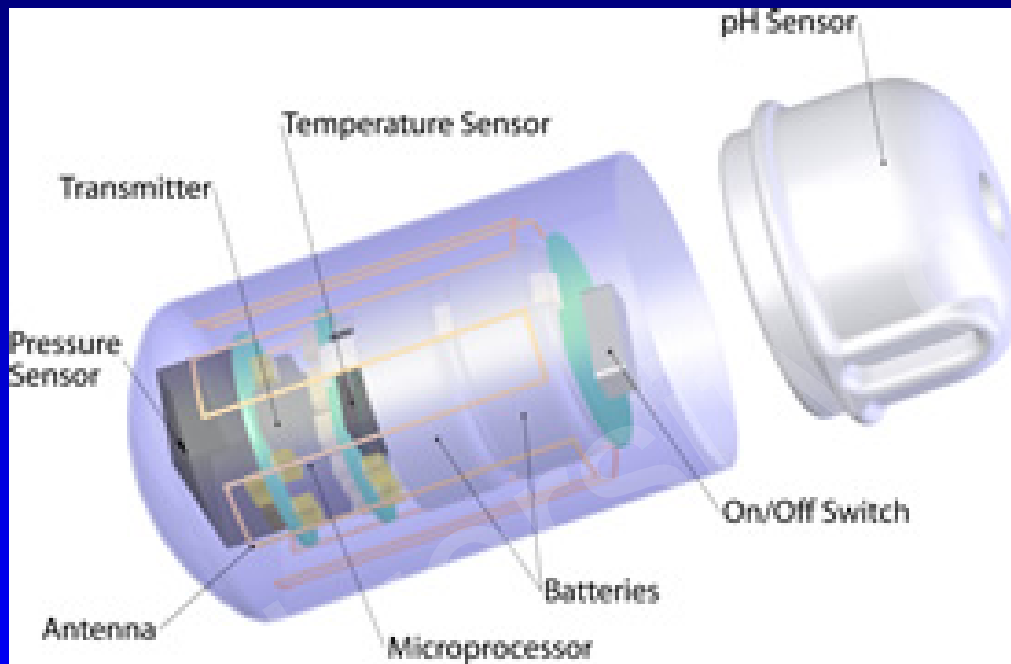
Abnormal Postprandial SBM: Extrinsic (Vagal) Neuropathy



Abnormalities Diagnosed by Small Bowel Manometry

- Intrinsic Neuropathy (enteric nervous system)
 - Fasting pattern: abnormal MMC
- Extrinsic Neuropathy (vagal neuropathy)
 - Fed pattern: impaired postprandial response
- Myopathy
 - Low contraction pressures

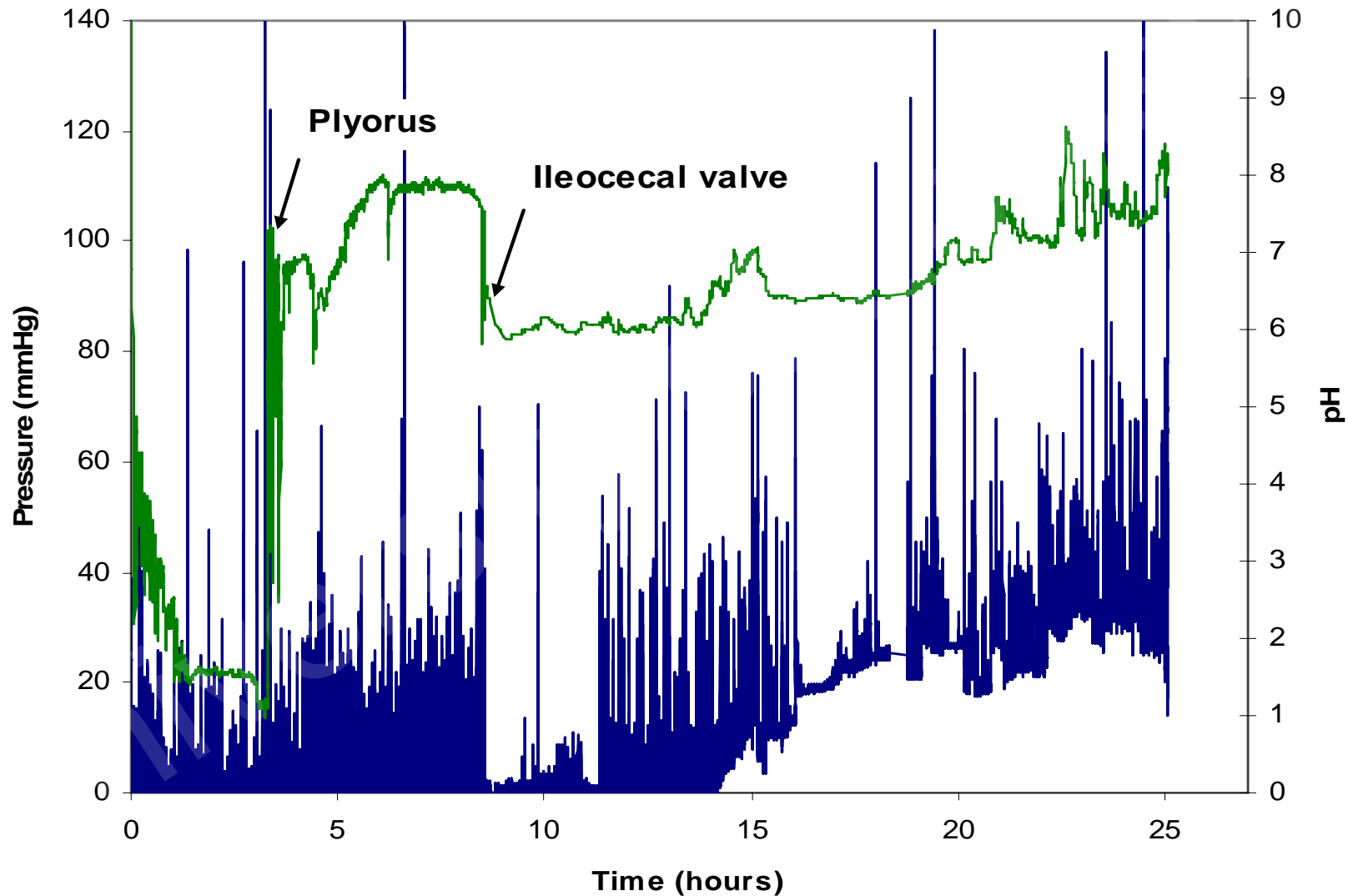
Smartpill® Wireless Diagnostics Capsule



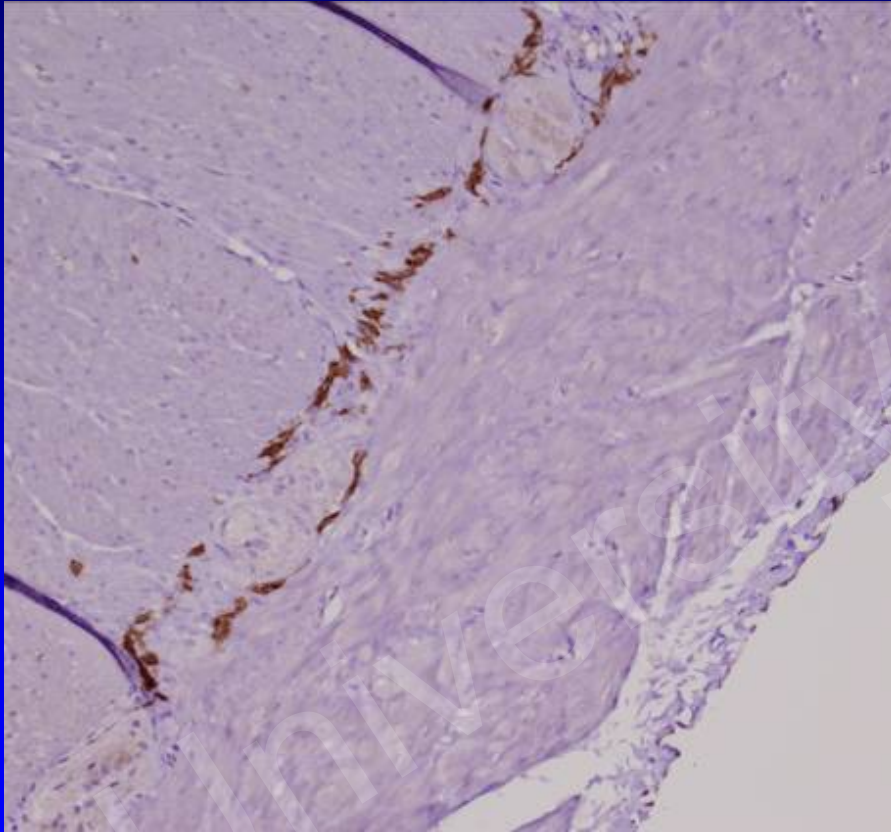
- Wireless measurements:
 - Pressure
 - pH
 - Temperature



Smartpill® Wireless Pressure and pH Tracing

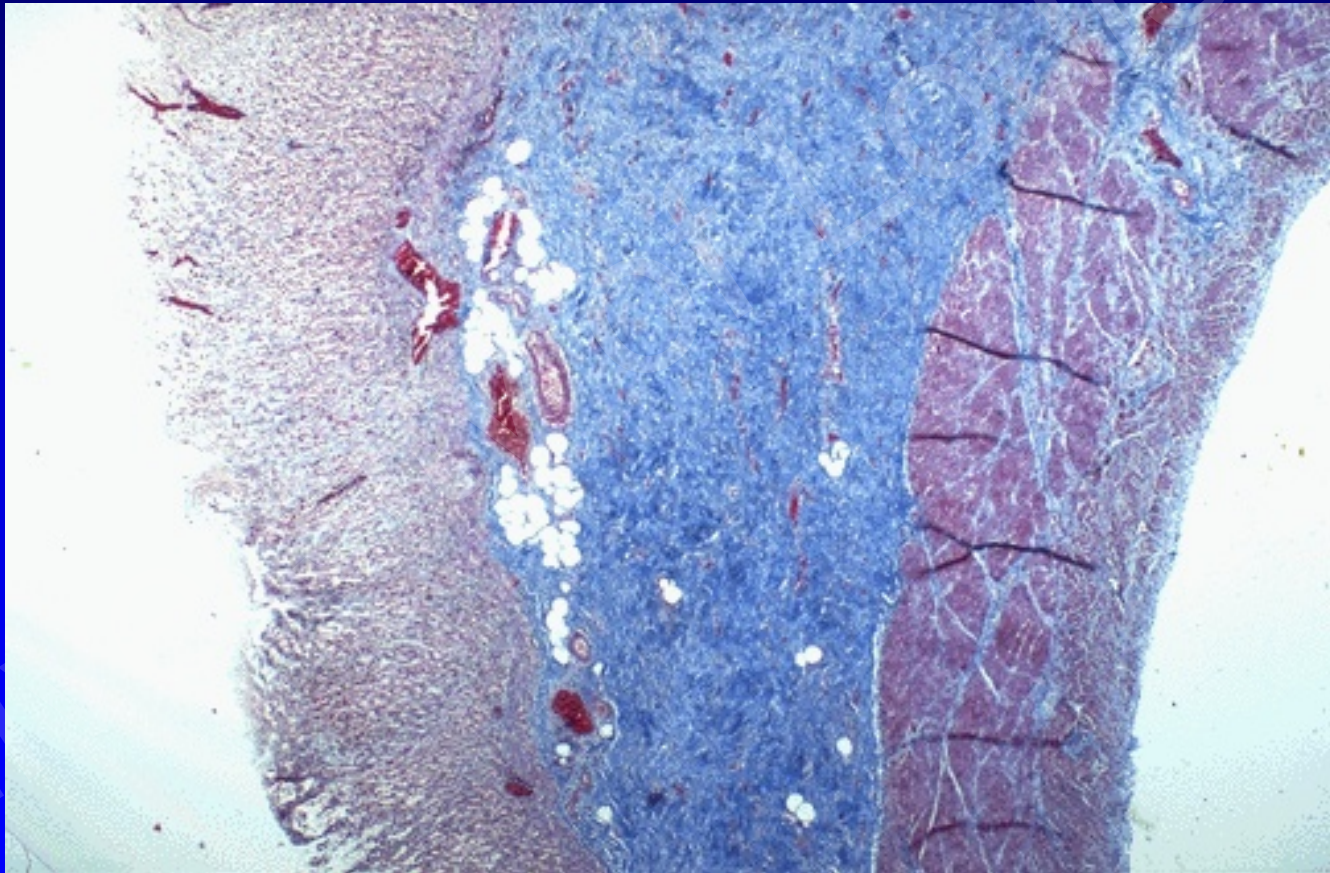


Full-Thickness Biopsy

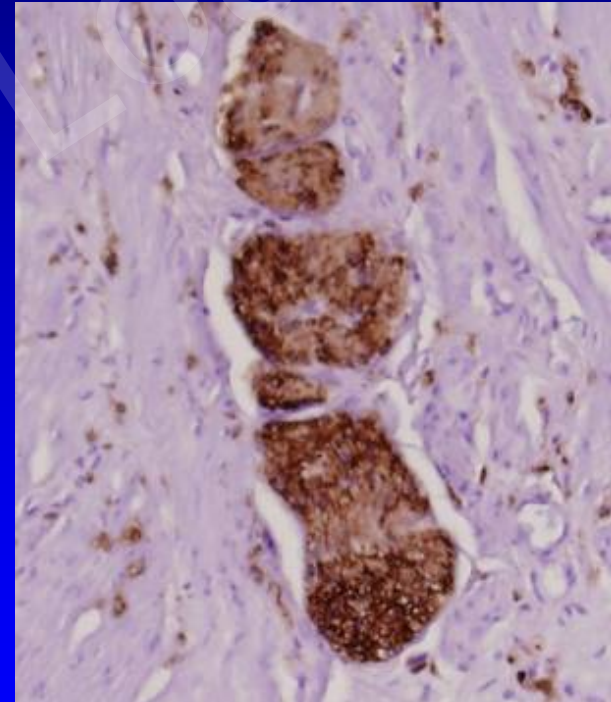
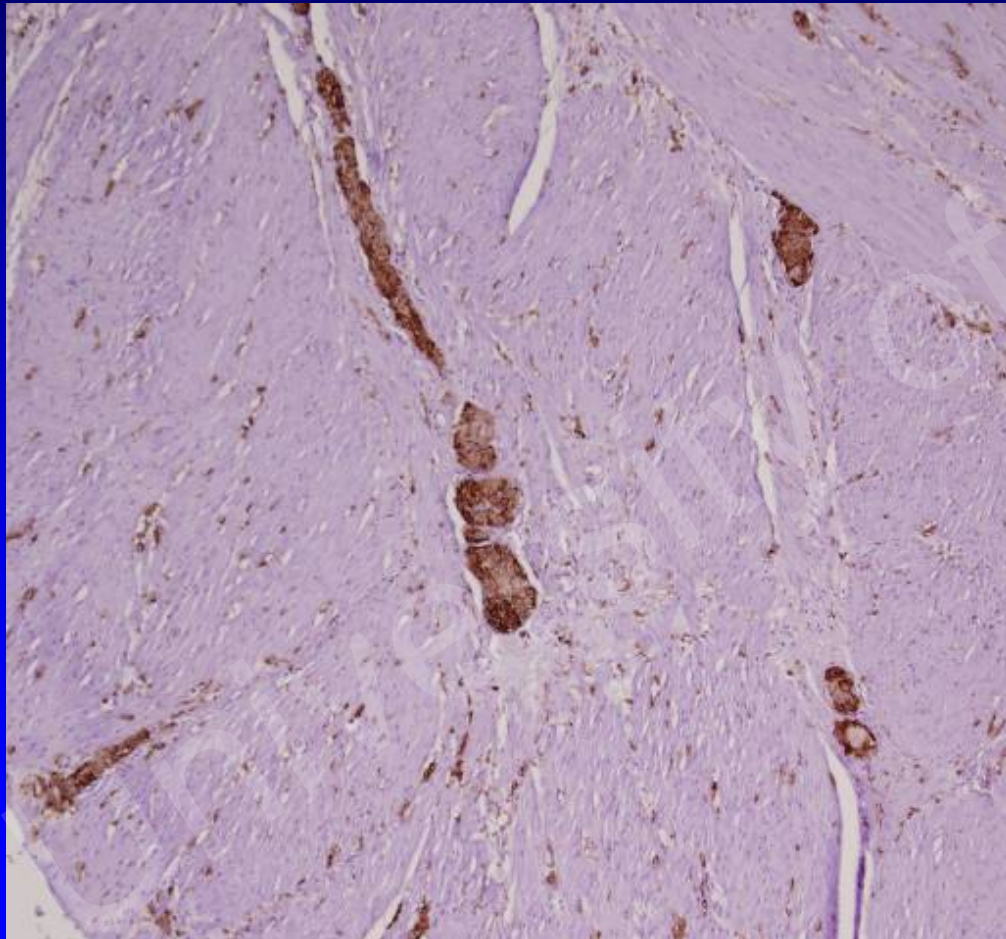


- H&E for inflammatory infiltrate
- Trichrome stain for fibrosis
- Congo red for amyloidosis
- Silver stain for enteric neurons
- C-kit immunochemical stain for interstitial cells of Cajal
- Viral culture

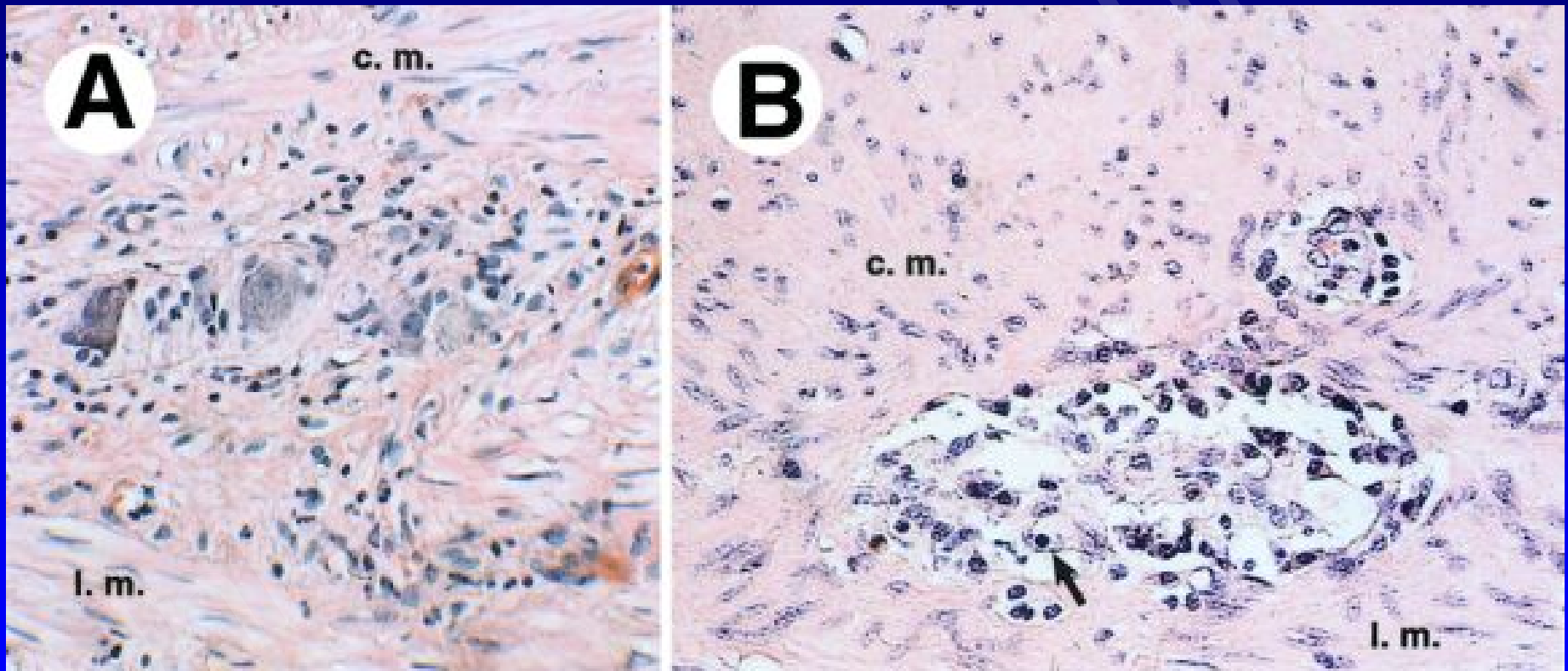
Scleroderma



Reactive Hyperganglionosis



Myenteric Neuritis of the Enteric Nervous System



Small Bowel Motility Disorders

- Slow transit
 - Chronic intestinal psuedo-obstruction
 - Bacterial overgrowth
 - Post-surgical dysmotility
- Fast transit
 - Dumping syndrome
 - Post-vagotomy diarrhea

Chronic Intestinal Pseudo-Obstruction (CIP)

- Rare in adults
- Symptoms and signs of intestinal obstruction
- No mechanical obstruction
- Primary disorder of small bowel, but can involve anywhere in the GI tract

Primary CIP

- Familial
 - Familial visceral myopathies
 - type 1 (AD) megaduodenum & urinary involvement
 - type 2 (AR) mitochondrial defect, ophthalmoplegia & peripheral neuropathy
 - type 3 (AR) diffuse GI involvement
 - Familial visceral neuropathies
- Sporadic
 - Visceral myopathies
 - Visceral neuropathies
 - Localized Hirschsprung's disease

Secondary (Acquired) CIP

- Connective tissue disorders
 - Scleroderma, MCTD, SLE, polymyositis, dermatomyositis
- Neuromuscular disorders
 - Paraneoplastic
 - Amyloidosis
 - Muscular dystrophies (myotonic, Duchenne, and oculopharyngeal muscular dystrophies)

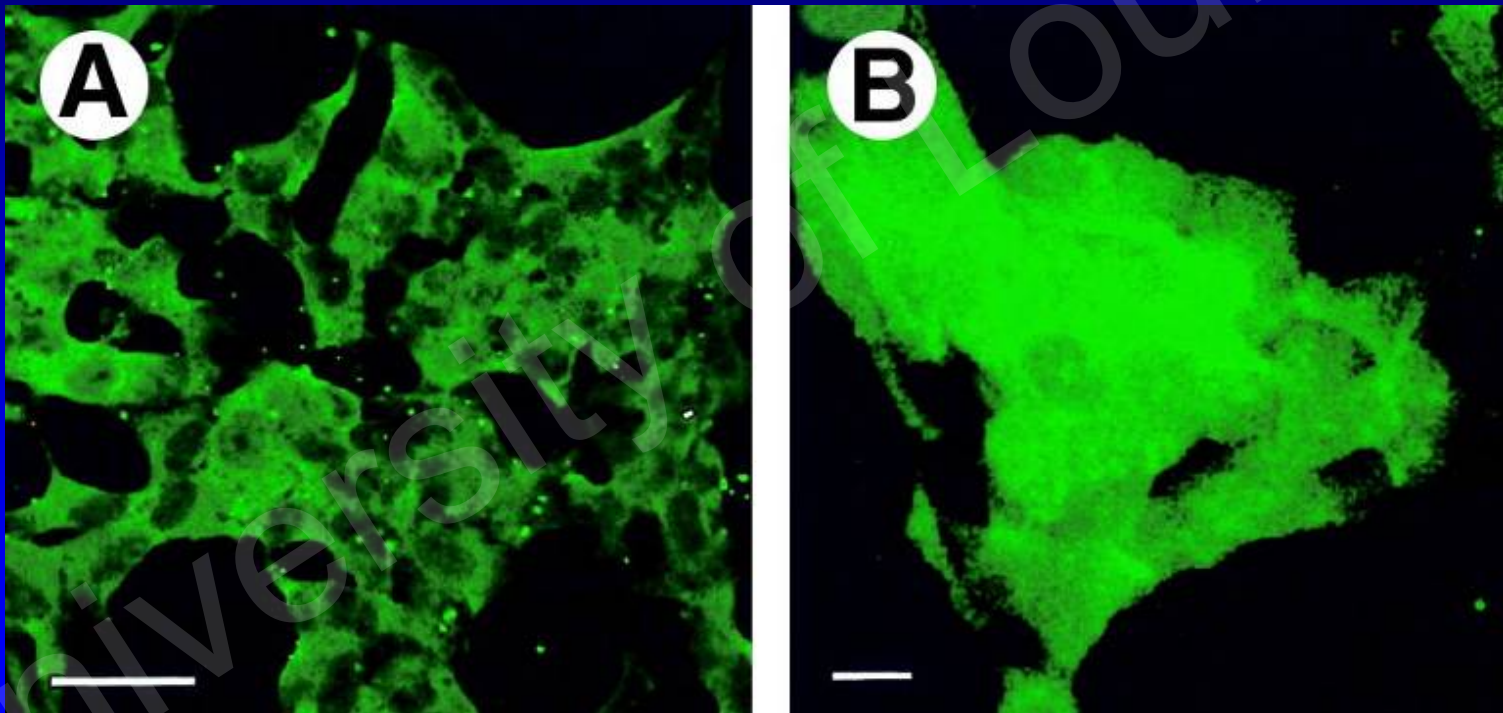
Secondary (Acquired) CIP

- Endocrine disorders
 - Hypothyroidism, hypoparathyroidism
- Infections
 - Trypanosoma cruzi, CMV, EBV
- Myenteric ganglionitis
- Radiation
- Paraneoplastic
- Miscellaneous
 - Medications (opiates, tricyclic antidepressants, antiparkinson medications, anticholinergics)

Paraneoplastic GI Motility Syndrome

- Cancer antigens mimicking neuronal tissues.
- Myenteric plexus infiltrated by lymphocytes and plasma cells.
- Cancers
 - Small cell lung cancer (80%), breast, ovarian, multiple myeloma, Hodgkin's lymphoma.
- GI symptoms can precede diagnosis of cancer.

Paraneoplastic GI Motility Syndrome: Anti-Hu Antibody* Against Enteric Neurons



*Antinuclear neuronal antibodies (ANNA)

Clinical Manifestations of CIP

Depends on Primary GI Involvement

- Small bowel: SBO, bacteria overgrowth
 - nausea, vomiting, high-output NG suction, abdominal distension, diarrhea, weight loss
- Stomach: gastroparesis
 - nausea and vomiting
- Esophagus: achalasia
 - dysphagia, regurgitation
- Colon: colonic inertia
 - constipation

Management Goals for CIP

- Confirm the diagnosis
- Identify the etiology
- Look for coexisting motility dysfunction
- Restore proper nutrition and fluid balance
- Relieve symptoms and improve motility

Diagnostic Criteria for CIP

- No uniform criteria in adult CIP
- Suggested criteria
 1. Recurrent symptoms of SBO
 2. Dilated small bowel
 3. No mechanical obstruction
- Diagnosis should not be based solely by manometry

Small Bowel Manometry

- Alternative test for vagal neuropathy
- Should not diagnose CIP solely by SBM

Treatment for CIP

- Nutrition
- Pharmacologic
- Surgical
- Intestinal transplant

Nutritional Support for CIP

- Similar to gastroparesis
- Behavior modification for aerophagia
- Enteral nutrition
 - Nasojejunal feeding before percutaneous
 - Isosmotic, low in fat, low in fiber
 - Nocturnal enteric feed
- Parenteral nutrition

Complications of TPN

- Line infections
- Selenium and chromium deficiencies
- Hepatotoxicity
 - Biliary sludge
 - Steatosis
 - Cholestasis
 - Cirrhosis

Pharmacologic Therapy for CIP

- Anti-emetic
- Prokinetics
 - Anti-dopaminergic (metoclopramide, domperidone)
 - Acetylcholine agents (bethanechol, and neostigmine)
 - Motilin agonists (erythromycin)
 - 5HT4 agonists (tegaserod)
- Antibiotics for bacteria overgrowth

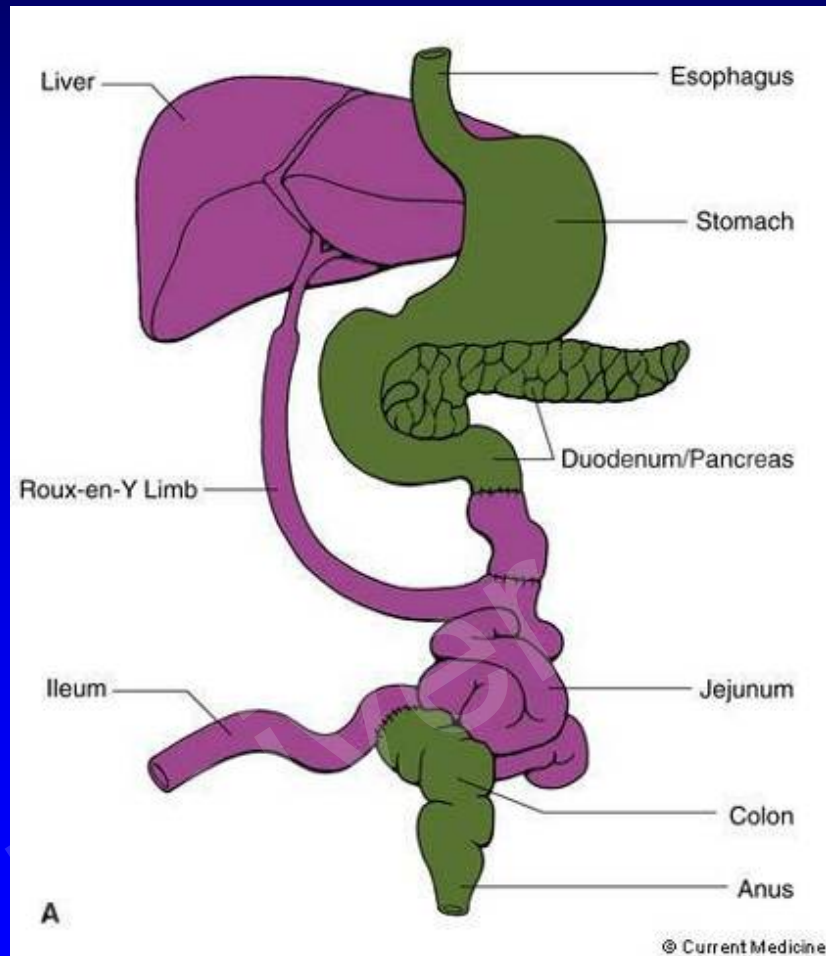
Octreotide for Scleroderma

- 6 normal subjects
 - Octreotide (10 µg sc) increased # of MMC from 1.5 to 4.1 over 3 hrs
- 5 patients with scleroderma + bacterial overgrowth
 - Octreotide (100 µg sc) increased # MMC from 0 to 3.6 over 3 hrs
 - Octreotide (50 µg sc qhs) improved bacteria overgrowth by H2 breath test
 - ↓ nausea, bloating, and abdominal pain

Surgical Intervention

- Full-thickness biopsy
- Enteral feeding tube
- Resection of dilated segments is controversial

Intestinal Transplantation



- Treatment of last resort
- Indications
 - TPN failure
 - Loss of vascular access
 - TPN associated hepatotoxicity
- 61% of transplant are <18 yrs old

Intestinal Transplantation

- Transplant organ
 - Isolated intestines (41%)
 - Intestines with other viscera, such as liver or pancreas (59%)
- At 3 yrs
 - Graft survival 71%
 - Patient survival 88%
 - Survival without TPN 81-96%

Conclusion for CIP

- Rare in adults
- Diagnostic criteria
 - Symptoms of SBO
 - Dilated small bowel
 - Exclude mechanical obstruction
- Look for etiology and coexisting dysmotility
- Management
 - Restore proper nutrition and fluid balance
 - Relieve symptoms
 - Improve motility
 - Treat complications