Amyloidosis Research Consortium

When the Gut Speaks:

Centering Symptoms in Amyloid Care

Presented by: Melissa Hershman, M.D., B.S.N.

Wednesday, March 18, 2026 | 12:00pm – 1:00pm EST

Epidemiology of GI Amyloidosis

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- Gastrointestinal (GI) symptoms occur in **1 of 6 patients with amyloid**
- Only **3-15% will have + GI biopsies**
  - Even in patients with GI symptoms **less than ½** have + biopsies
  - Poor correlation between symptoms and degree of tissue infiltration
- Yet 40% have pathologic GI deposits at autopsy (ATTR)

Yen, T., et al. Neurogastoenterology & Motility (2018)

Clinical presentation is variable

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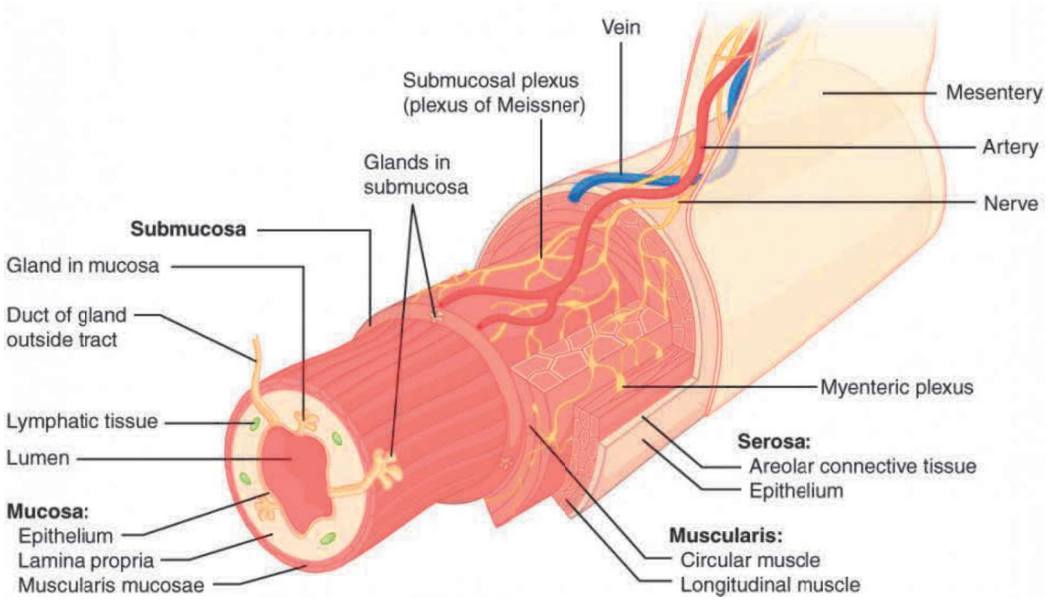
Depending on:

1. Anatomic location

2. Layer within Gastrointestinal (GI) lining



Common Amyloid Subtypes

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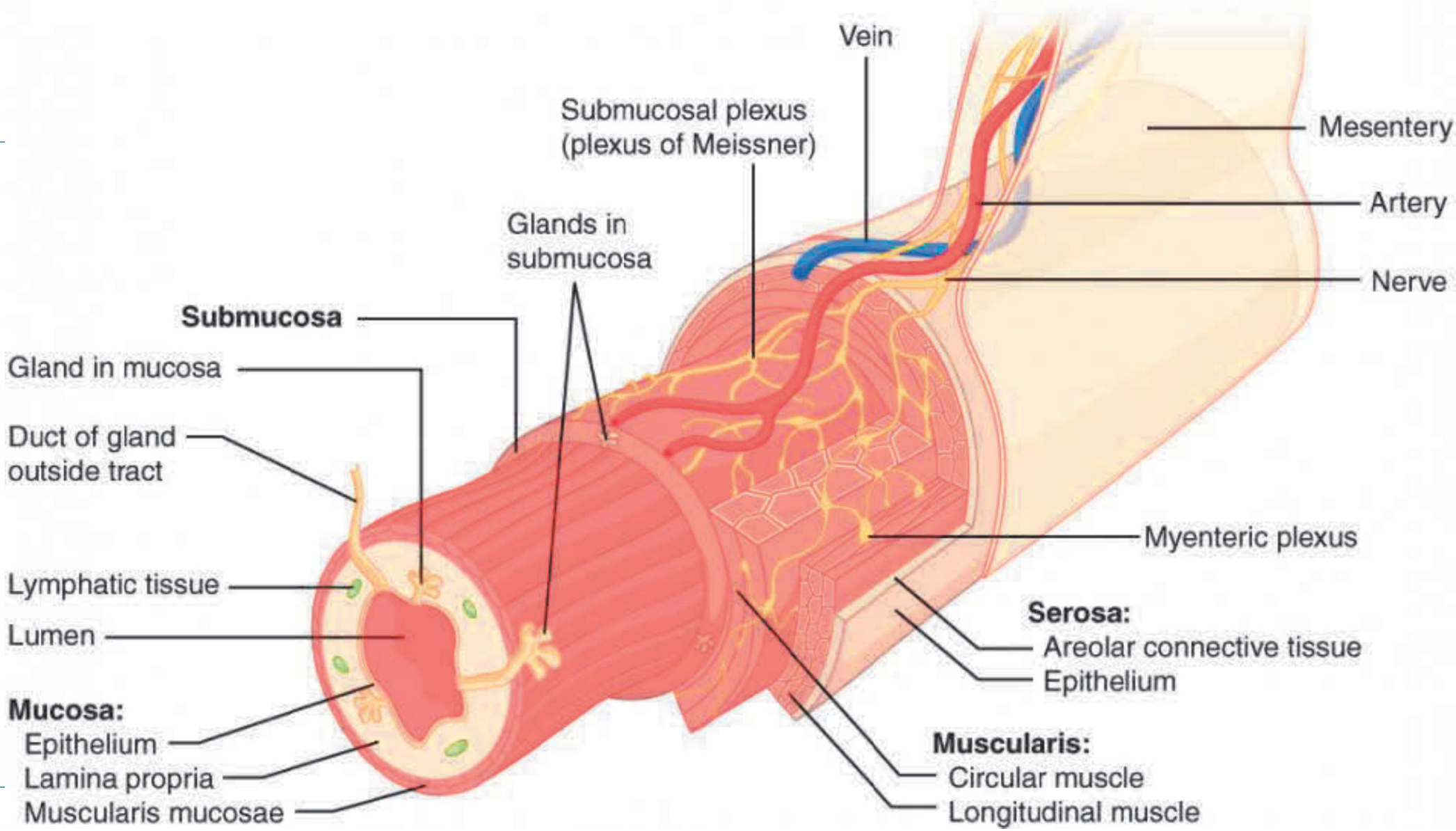
Subtype	Amyloidogenic protein fibril	Organs involved
AL amyloidosis (acquired)	Immunoglobulin light chain	All organs except CNS Most common: heart, kidneys
AA amyloidosis (acquired)	Serum amyloid A	All organs except CNS Most common: kidneys, liver
ATTRv amyloidosis (hereditary)	Transthyretin	Heart, PNS, ANS, eye, leptomeningeal
ATTRwt amyloidosis (wild-type; acquired)		Heart, ligaments, tenosynovium


Vein
Submucosal plexus
(plexus of Meissner)
Mesentery
Artery
Glands in
submucosa
Nerve
Submucosa
Gland in mucosa
Duct of gland
outside tract
Myenteric plexus
Lymphatic tissue
Lumen
Serosa:
Areolar connective tissue
Epithelium
Mucosa:
Epithelium
Lamina propria
Muscularis mucosae
Muscularis:
Circular muscle
Longitudinal muscle

Mucosal involvement

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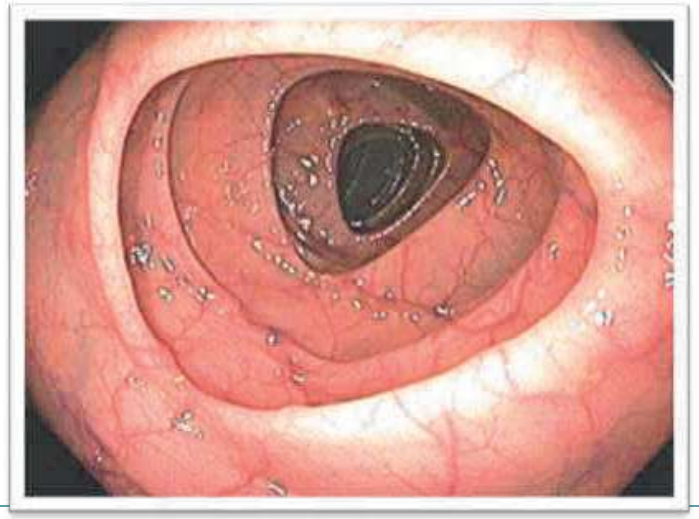
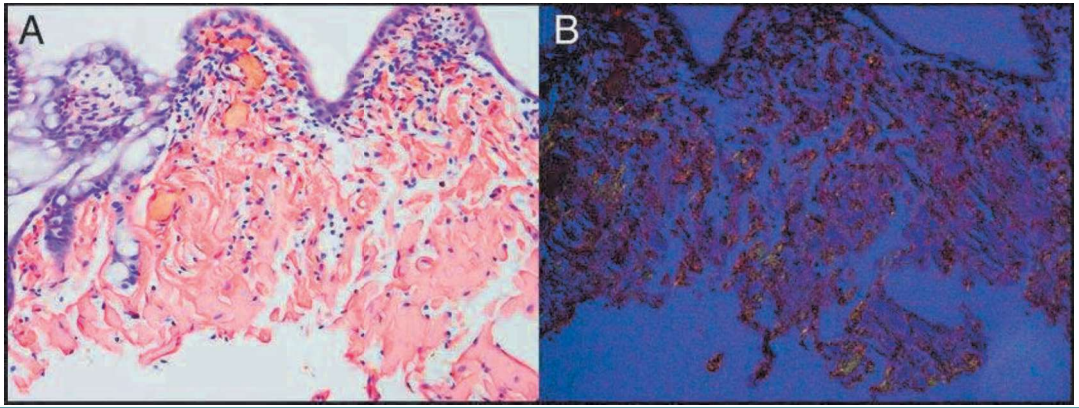
- Inner lining of the intestines, responsible for absorption
- This is the ONLY layer that can be sampled with routine GI biopsies via endoscopy/colonoscopy

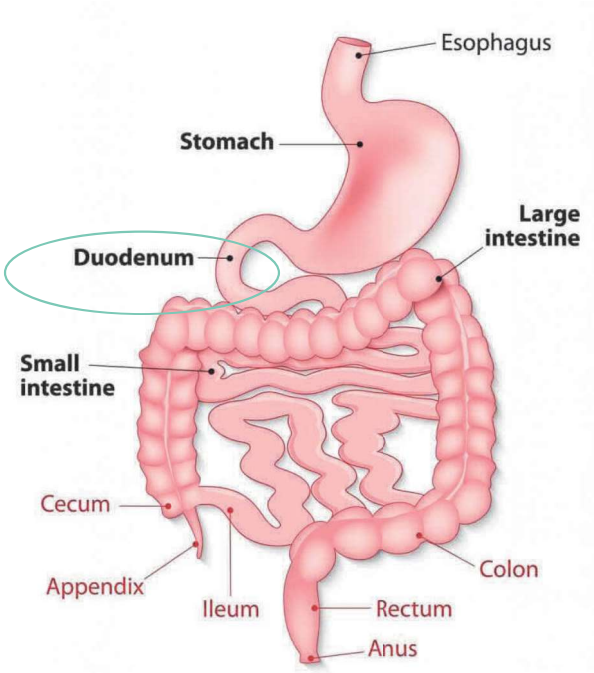




Lee, B., et al. ACG Case Reports Journal (2019)

Mucosal involvement symptoms

- Malabsorption:
  - Diarrhea
  - Weight loss
  - Loss of appetite
- Protein losing enteropathy
  - Severe protein losses resulting in edema (leg swelling) and ascites (fluid retention around the abdomen)
- Gastrointestinal bleeding:
  - Related to ulcerations or friable blood vessels



Vascular involvement

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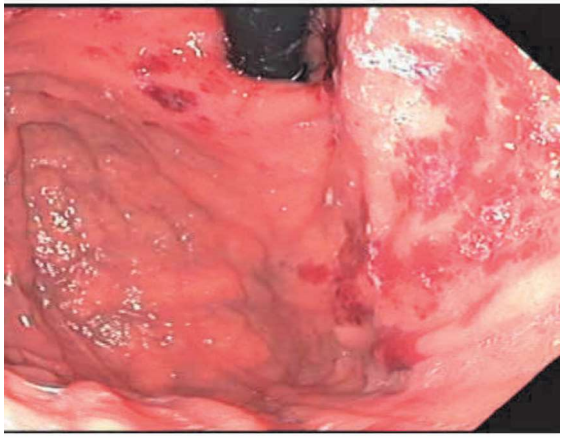
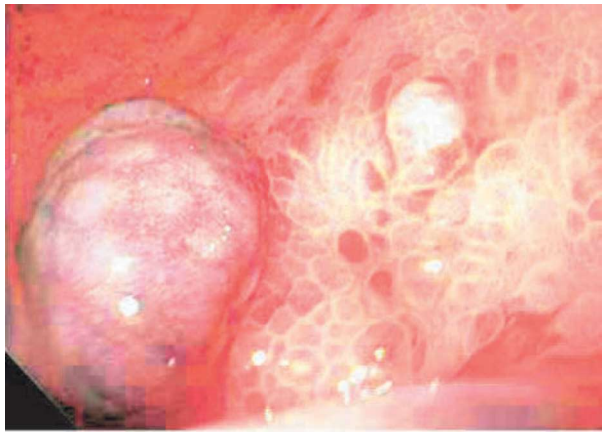
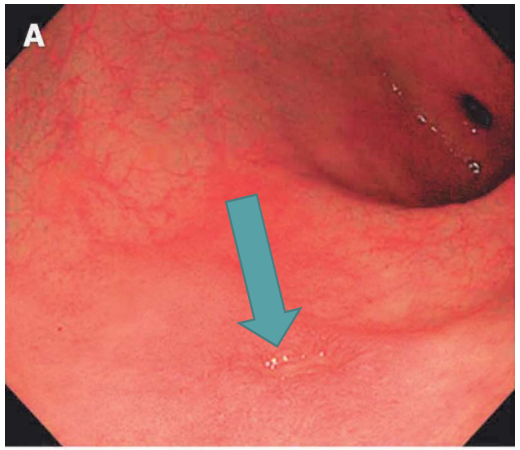
- Vascular system delivers blood and nutrients to the intestines
- Symptoms:
  - Bleeding: presenting symptom of GI involvement in 25-45%
  - Chronic ischemia (low blood flow state): pain after eating







 Hokama, A., et al. WJGE (2011); James, D.G., et al. CGH (2007); Kim, S.H., et al. Cardiovasc Intervent Radiol. (2009); Petre, S., et al. Aliment Pharmacol Ther. (2008)

Neuromuscular Infiltration

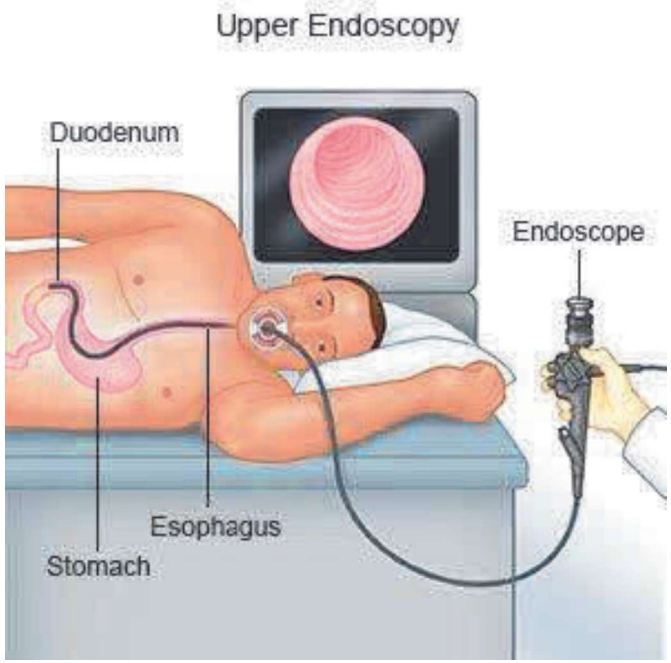
- Deposition of the amyloid proteins into the intrinsic **nerve plexus** and the muscularis externa (longitudinal and circular muscles)

- Together, the nerves and muscles of the intestines control coordination, motility, pain signaling

Dysmotility Symptoms

- Nausea/Vomiting
- Diarrhea
- Constipation
- Chronic intestinal pseudo-obstruction
- Bloating

Testing for GI Amyloid



- Endoscopy/Colonoscopy can:
  - Sample for mucosal disease
  - Looks for bleeding, potentially treat
  - Evaluate for other non-amyloid issues (ex: polyps, Barrett's, Celiac dx, Crohn's etc.)
  - Dilate/stretch some types of narrowing

Why is GI amyloid missed?

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- Nonspecific symptoms
- Endoscopy finding are subtle or absent
- Requires specific staining
- Symptom-type doesn't predict biopsy being +

Key Insight: Symptoms may result from autonomic neuropathy rather than direct amyloid deposition

Yen, T., et al. Neurogastoenterology & Motility (2018)

GI symptoms in amyloid are nonspecific

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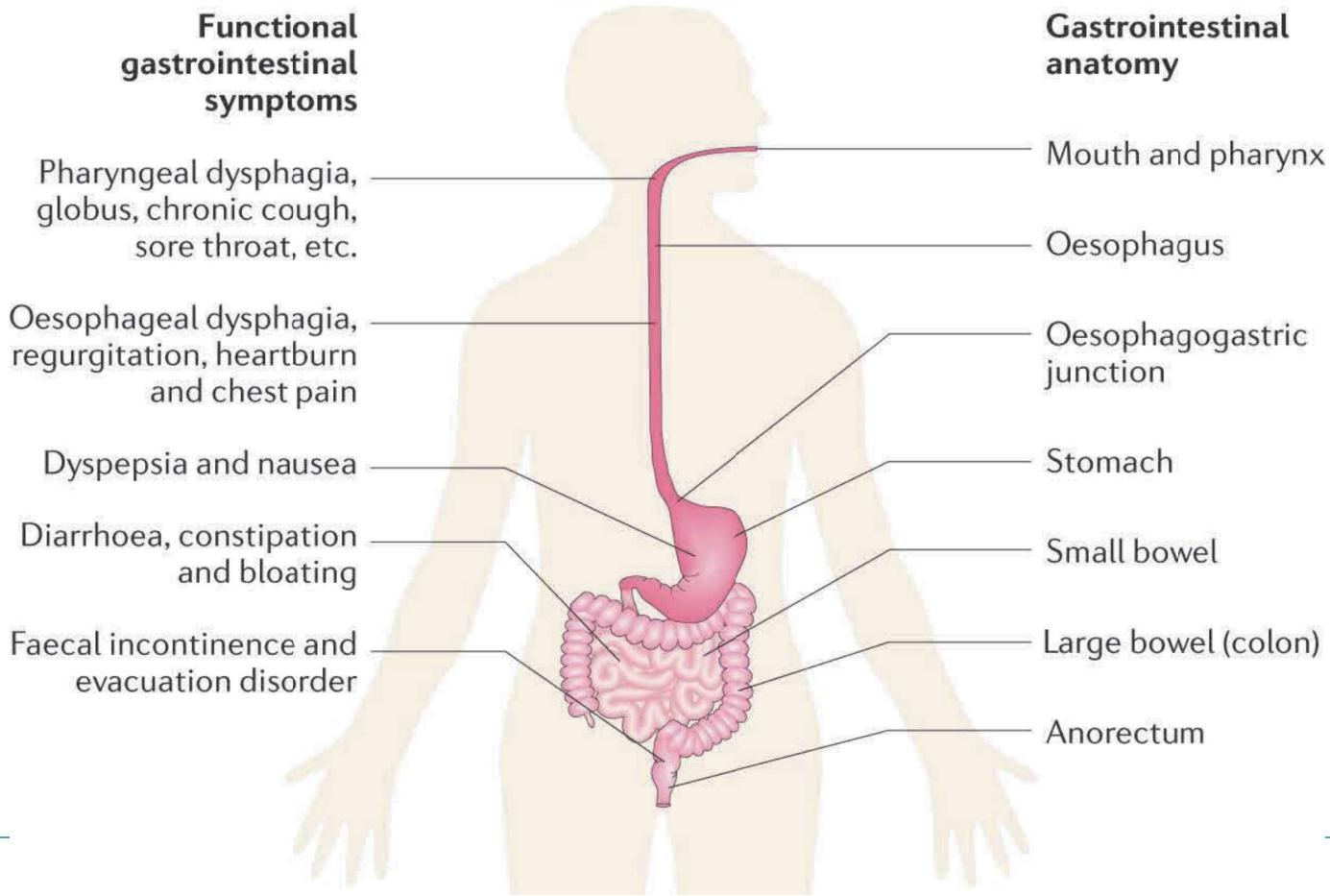
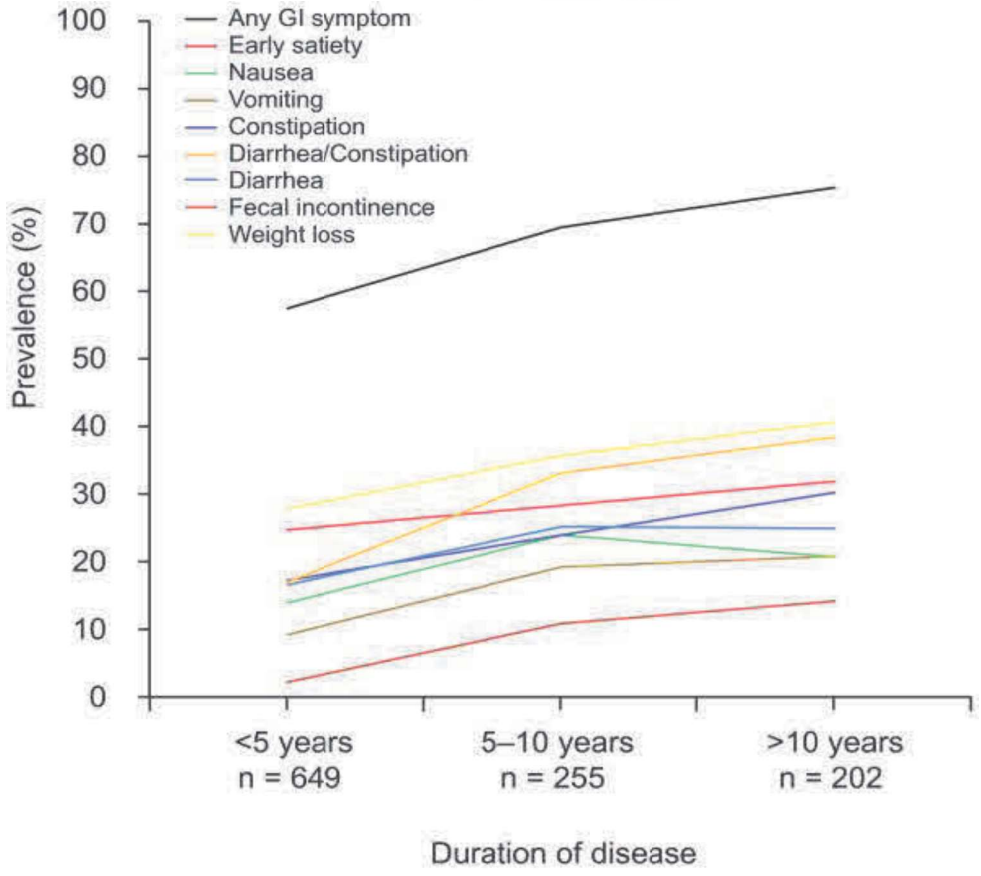
Up to 30% of adults also experience these



GI symptoms increase with disease duration



Wixner, J., et al. Orphanet J Rare Dis. (2014)

GI Involvement by Amyloid Subtype

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AL Amyloidosis

GI symptoms in up to 60%
Possible organ changes: hepatomegaly, macroglossia
Autonomic: early satiety, orthostatic hypotension

ATTR Amyloidosis

63% hereditary reported GI symmptoms (THAOS registry)
More common with neuropathic variants (ATTRv)
ATTRwt has rates similar to the general population

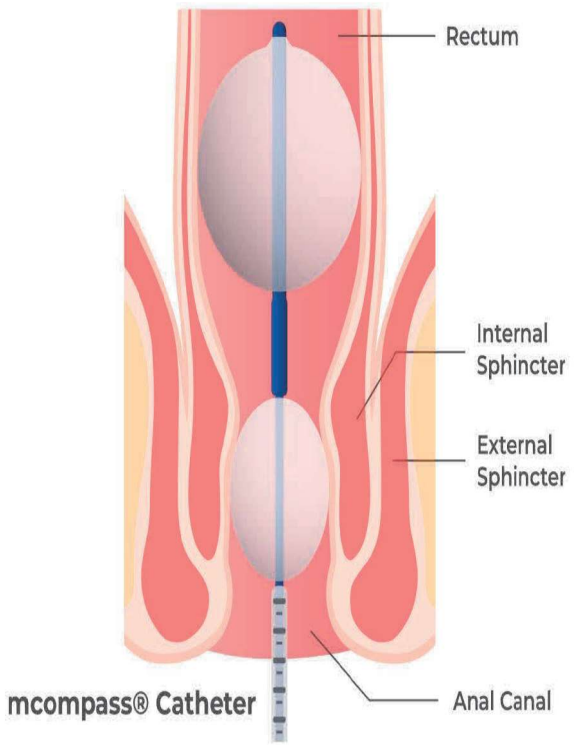
AA Amyloidosis

Diarrhea and malabsorption most prominent
Linked to chronic inflammatory disease

Wixner, J., et al. Orphanet J Rare Dis. (2014)

Additional testing to assess GI motility

- Esophagus:
  - Barium swallow / Esophagram
  - Esophageal Manometry
  - Acid tests: BRAVO, 24 hour pH impedance
  - Endoflip
- Stomach
  - Gastric emptying study
- Small Intestine
  - Upper GI Xray series
- Colon
  - SITZ marker study
- Rectum
  - Anorectal manometry



Small intestinal bacterial overgrowth (SIBO)

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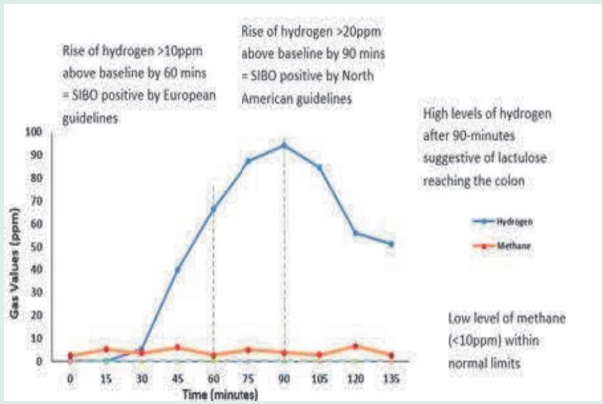
Symptoms:

- Bloating (delayed), flatulence, diarrhea, fatty stools, brain fog
- Nutritional deficiencies – Albumin, Iron, Carotene, Selenium, B12

Testing:



Treatment

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- Most GI amyloidosis (79%) occur as part of a systemic disease
  - Treatment is directed at systemic process
  - Management of GI symptoms is supportive and nonspecific
- Local GI Amyloid (21%) deposition does not require treatment

Treatment: GERD (reflux)

- Lifestyle interventions: bed elevation with wedge, no food 3 hr prior to reclining, small frequent meals, weight loss if needed, stop smoking
- Acid suppression
  - Antiacids (ex Tums)
  - H2 blockers (ex Pepcid/famotidine)
  - Proton Pump Inhibitors (ex Prilosec/omeprazole, Protonix/pantoprazole, etc)
  - PCABs (vonoprazan)
- Surgical interventions in select patients

Treatment: Gastroparesis & Nausea

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- 1st line treatment **small particle diet**
  - Vegetables: cooked only; remove skins and seeds; mashed, riced or puree forms
  - Fruit: puree, compote, smoothie, squeeze pouches
  - Proteins: hummus, Greek yogurt, baked egg, tofu
- **6 small frequent meals**
- **Avoid**: Fatty foods; roughage-based; insoluble fiber; acidic; carbonated beverages
- **Lifestyle**: avoid alcohol/smoking; Marijuana can alleviate nausea but ↓ gut motility

Camilleri, M., et al. AJG (2022)

Treatment: Gastroparesis & Nausea

- Medications:
  - Antiemetic: Zofran (Ondansetron), Phenergan, Compazine, Scopolamine patches
  - Prokinetics: Reglan (Metoclopramide), Domperidone, Erythromycin, Azithromycin, Prucalopride, Pyridostigmine
  - Adjunctive therapy: Acupuncture, Ginger, Vitamin B6, Cognitive Behavioral Therapy

Camilleri, M., et al. AJG (2022)

Treatment: Diarrhea – requires targeted approach

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1. Malabsorption:

- Direct mucosal infiltration
- Small intestinal involvement
- Steatorrhea, weight loss

2. Small Intestinal Bacterial Overgrowth (SIBO):

- Secondary to dysmotility
- Bloating, gas, watery diarrhea

3. Bile Salt Malabsorption:

- Terminal ileum involvement
- Watery diarrhea, often postprandial

4. Autonomic Neuropathy:

- Rapid transit
- Exaggerated gastrocolic reflex
- Uncontrollable bowel movements after eating

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LOW FODMAP DIET

FOOD	VEGETABLES	FRUITS	PROTEINS	FATS	STARCHES, CEREALS & GRAINS
EAT	 lettuce, carrot, cucumber	 strawberries, pineapples, grapes	 chicken, eggs, tofu	 oils, butter, peanuts	 potatoes, tortilla chips, popcorn
AVOID	 garlic, beans, onion	 blackberries, watermelon, peaches	 sausage, battered fish, breaded meats	 almonds, avocado, pistachio	 beans, gluten-based bread, muffins

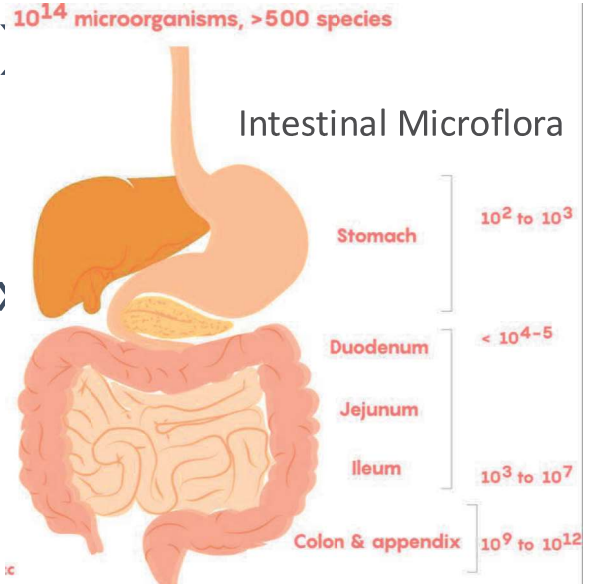
Treatment: Diarrhea

- Decrease gut bacteria (SIBO) with antibiotics
- Bile salt binding agents
  - Especially if history of cholecystectomy, surgery on ileocecal valve
- Antidiarrheals
  - Imodium
  - Lomotil
  - Tincture of Opium
- Rarely: octreotide, parenteral (IV) nutrition

SIBO treatment

- Hydrogen-type overgrowth (~ diarrhea predominant sxs)
  - Rifaximin (xifaxan) x 14 days*
- Methane-type overgrowth (~constipation predominant s
  - Rifaximin x 14 days PLUS neomycin x 10 days*

*Consider alternative antibiotics based on cost/availability



Pimentel, M., et al. AJG (2020)

Treatment may help improve symptoms

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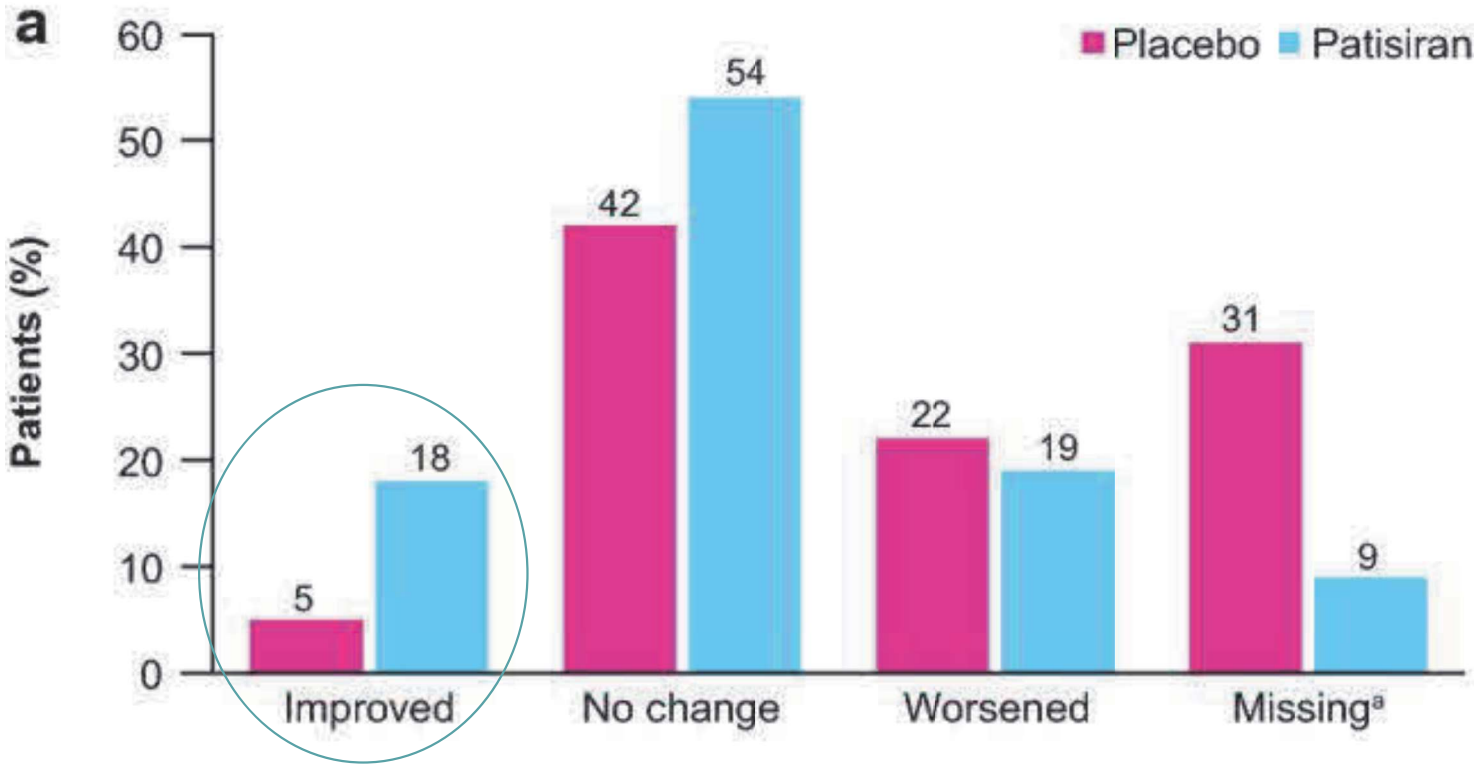


APOLLO Phase III trial: Diarrhea symptoms **Placebo** vs **Patisiran**

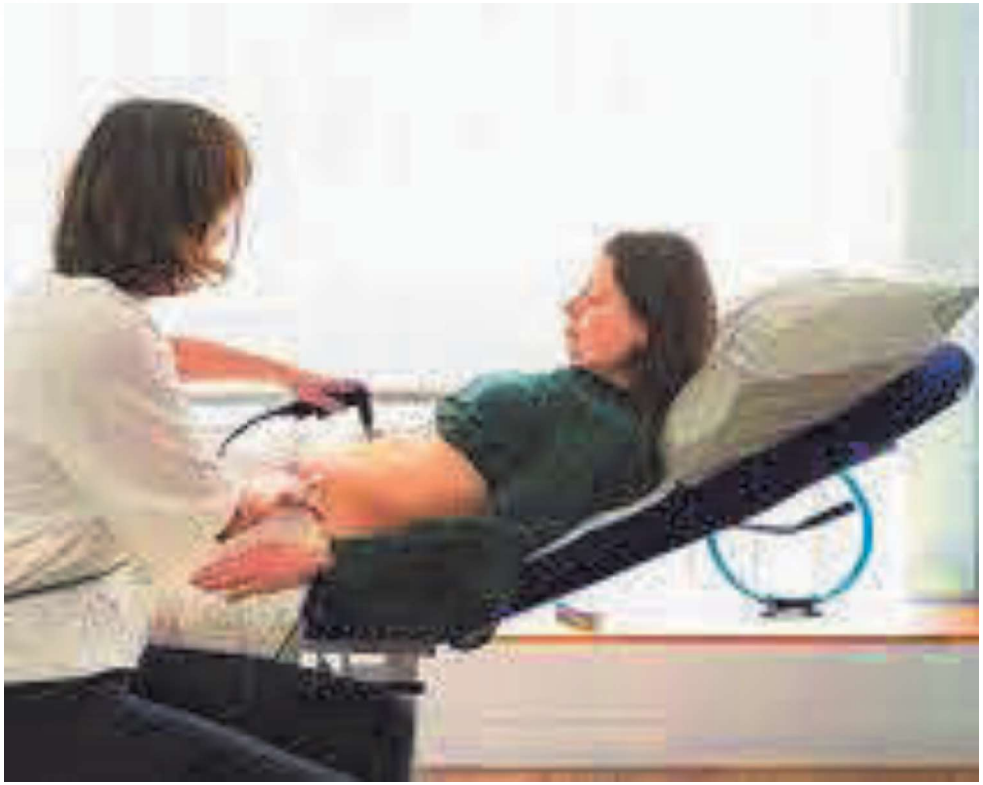
Gonzalez-Duarte, A., et al. J Neurol. (2020)

Treatment: Constipation

- Lifestyle changes: ↑↑↑ water intake, physical activity & dietary fiber
- Medications:
  - Over the counter:
    - Osmotic: **MIRALAX** (polyethylene glycol), Magnesium products, Lactulose
    - Lubricants: Mineral Oil
    - Stimulants: Senna, Dulcolax (bisacodyl)
    - Stool Softeners: Colace (docusate)
    - Bulk forming: Fiber supplements
  - Prescriptions: Linzess, Amitiza, Trulance, Motegrity, Zelnorm, Ibsrela Opiate antagonists (Naltrexone, Methylnaltrexone), Vibrant (vibrating capsules)

Treatment: Pelvic Floor Dysfunction

- Bulking agents: Fiber
- Digital stimulation maneuvers
- Suppository/enemas to empty the vault
- Pelvic floor PT
- Colorectal surgery eval for refractory cases/anatomic abnormalities



Treatment: Abdominal Cramping

- Evidence based non-pharmacologic:
  - Acupuncture, Yoga, Cognitive behavioral therapy
  - Diaphragmatic Breathing Exercises
  - Peppermint supplements
- Neuromodulators:
  - Amitriptyline, Nortriptyline, Desipramine, Imipramine, Mirtazapine
- Antispasmodics:
  - Hyoscyamine, Dicyclomine
- Others:
  - Lyrica, Gabapentin

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Thank you!