

Amyloidosis & the GI Tract

John O. Clarke, M.D.
Director, Esophageal Program
Clinical Associate Professor of Medicine
Stanford University
john.clarke@stanford.edu

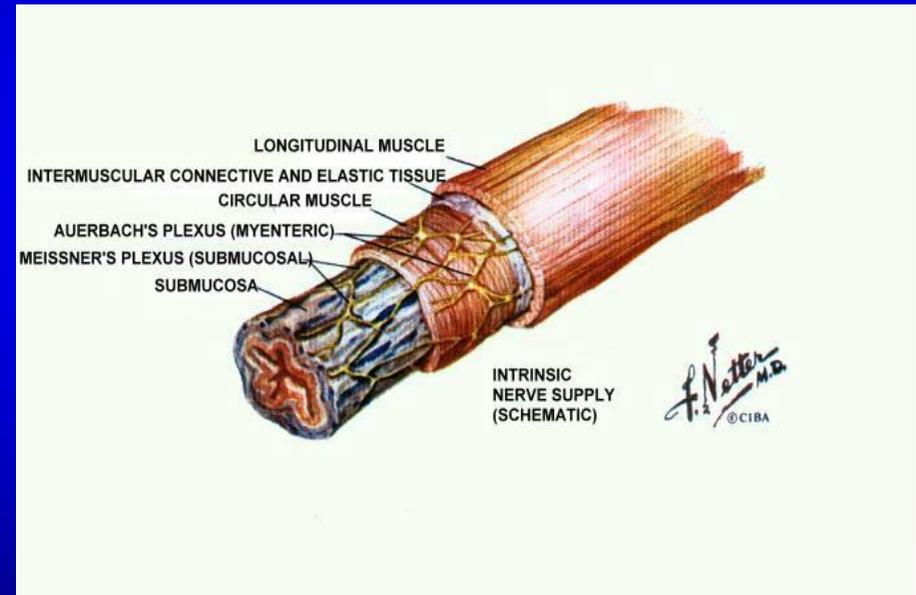
2017

Topics to cover

- 1) Patterns of GI amyloid involvement
- 2) Symptoms associated with amyloidosis
- 3) Diagnostic tests at our disposal
- 4) Treatment options
- 5) Epidemiology & data regarding variants

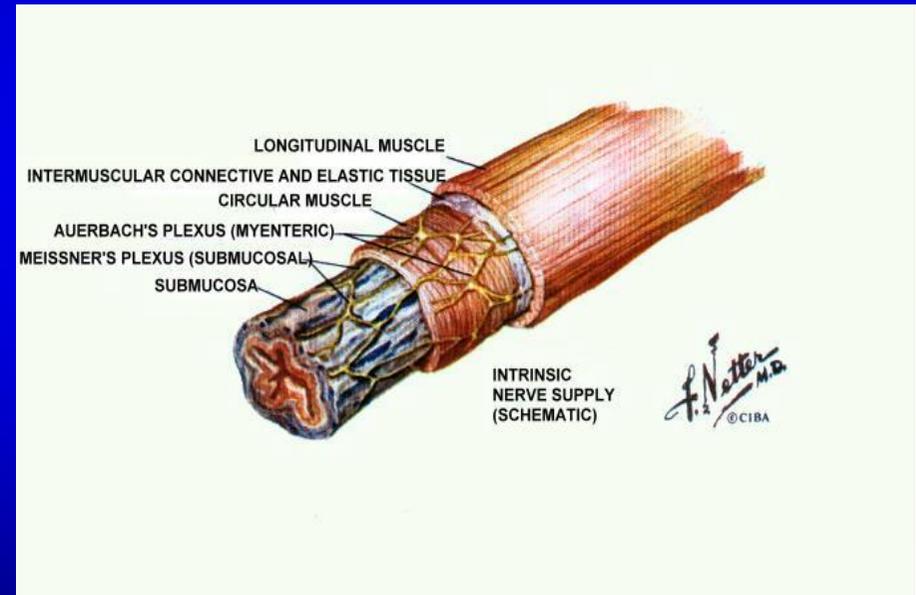
Patterns of GI amyloid

- Amyloid can deposit anywhere in the GI tract or nerves that regulate it
- Luminal GI Patterns:
 - Mucosal infiltration
 - Muscle infiltration
 - Neuropathy
 - Vascular



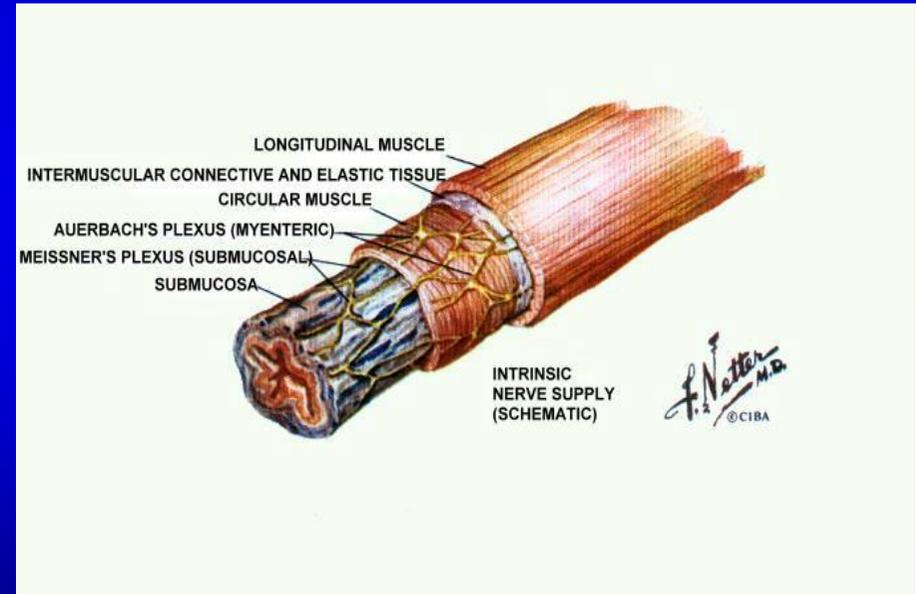
Patterns of GI amyloid

- Mucosal involvement
 - Role: site of absorption
 - Symptoms
 - Diarrhea
 - Malabsorption
 - Diagnosis
 - Endoscopic biopsy



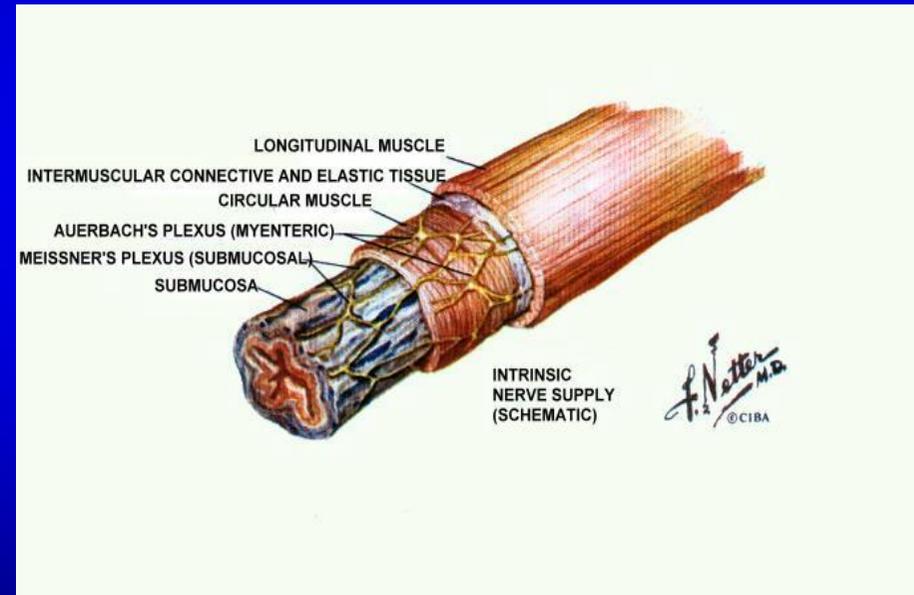
Patterns of GI amyloid

- Muscular infiltration
 - Role: site of contraction & motility
 - Symptoms
 - Decreased motility/stasis
 - Small intestinal bacterial overgrowth
 - » Diarrhea
 - » Malabsorption
 - Constipation
 - Pseudo-obstruction
 - Nausea/vomiting/abdominal pain
 - Diagnosis
 - Imaging studies
 - Transit studies
 - Manometry



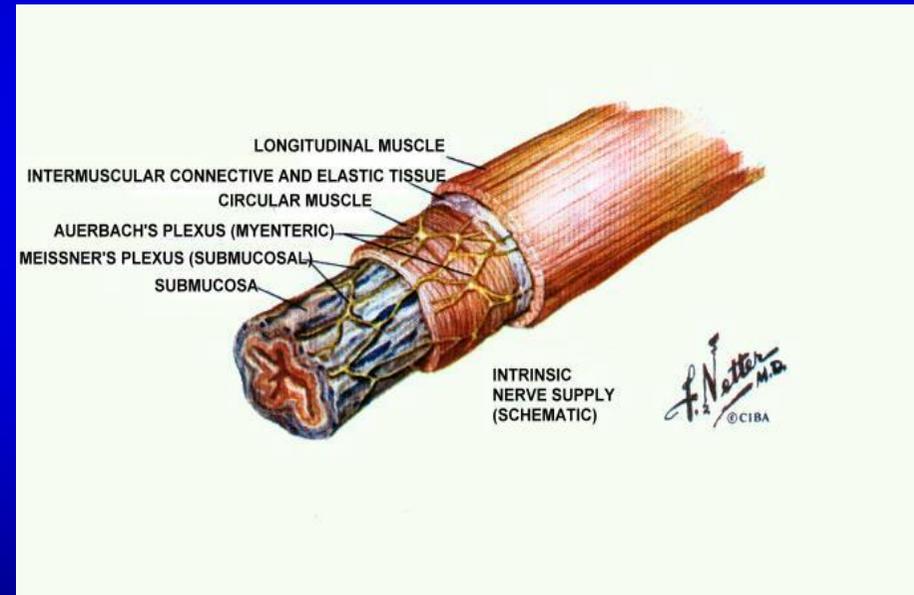
Patterns of GI amyloid

- Neuropathy
 - Role: coordination of GI motility & neuroendocrine secretion
 - Symptoms
 - Dysmotility
 - Nausea/vomiting/pain
 - Diarrhea
 - Constipation
 - Increased sensation
 - Diagnosis
 - Manometry



Patterns of GI amyloid

- Vascular
 - Role: delivery of blood flow to gut
 - Symptoms
 - GI Bleeding
 - Ischemia (pain/diarrhea)
 - Diagnosis
 - Endoscopy



Non-luminal GI patterns

- Liver involvement
 - Liver enlargement
 - Elevated liver tests (alkaline phosphatase)
 - Clinical manifestations usually mild but a marker of widespread systemic deposition
- Cholangitis
- Pancreas
- Peritonitis

Symptoms

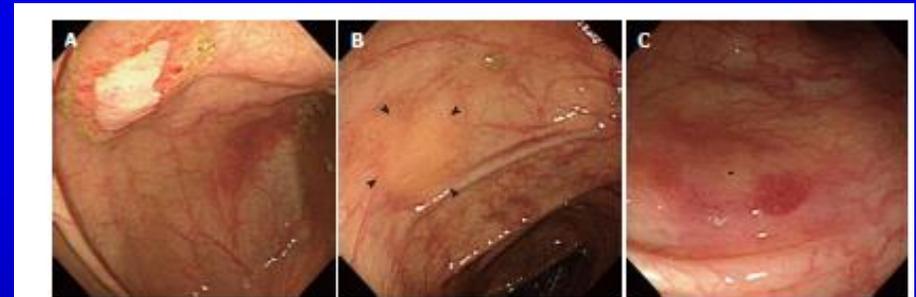
- Symptoms are linked to area of involvement & are often non-specific
 - Esophagus:
 - Reflux
 - Dysphagia
 - Food impaction
 - Stomach
 - Abdominal pain
 - Nausea
 - Vomiting
 - Distention
- Small intestine
 - Diarrhea
 - Malabsorption
 - Weight loss
 - Pseudo-obstruction
- Colon
 - Diarrhea
 - Constipation
 - Fecal incontinence

Symptoms Caveat

- When evaluating symptoms in amyloid, it is important to remember that most symptoms are nonspecific and can also be seen outside of amyloid
 - Reflux: 20% adults
 - Dysphagia: 4% adults
 - Functional dyspepsia: 20-30% adults
 - IBS: 13% adults
 - Constipation: 15% adults
 - Fecal incontinence: 6% adults
- Just because someone has amyloid, doesn't mean they can't have other GI conditions
 - Inflammatory bowel disease
 - Celiac disease
 - Eosinophilic esophagitis
 - Cancers
- Symptoms can also relate to medication adverse effects
 - GI symptoms most common adverse effects listed for most medications
 - > 80% of people who take 5 or more medications will have at least one adverse effect

Diagnostic tests

- Endoscopy & colonoscopy are usually the first tests performed
 - Allows option to take biopsies for diagnosis
 - Can also allow treatment
 - Bleeding control
 - Dilation
 - Findings can be nonspecific
 - Will only pick up mucosal GI involvement
 - Rectum commonly chosen as yield high (> 75%) and easy to get to
 - Highest yield in GI tract is in duodenum



Diagnostic tests

- Other tests to consider
 - Imaging studies
 - CT
 - MRI
 - Barium
 - Motility studies
 - Scintigraphy
 - Manometry
 - Wireless motility capsule
 - Sitz marker study
 - Breath tests



Treatment options

- Treatment should be tailored to symptoms & GI involvement

Treatment options

- Esophagus
 - Reflux treatment options
 - Dietary modification
 - Antacids
 - Histamine receptor blockers
 - Proton pump inhibitors
 - Endoscopic/surgical options in carefully selected patients
 - Dysphagia treatment options
 - Dietary modification
 - Dilatation
 - Botox

Treatment options

- Stomach
 - Dietary modification
 - Prokinetics
 - Metoclopramide (Reglan)
 - Erythromycin/azithromycin
 - Domperidone (not FDA-approved)
 - Prucalopride (not FDA-approved)
 - Bethanechol
 - Pyridostigmine
 - Agents to help stomach expansion
 - Herbal therapies (peppermint/caraway)
 - Buspirone
 - Neuromodulators
 - Tricyclics (amitriptyline)
 - Mirtazapine (Remeron)
 - Gabapentin/pregabalin (Lyrica)
 - Anti-emetics
 - Endoscopic options: Botox

Treatment options

- Small bowel
 - Dietary modifications
 - Prokinetics
 - Antibiotics (focused on small intestinal bacterial overgrowth)
 - Octreotide
 - Steroids
 - Anti-diarrheals
 - Imodium
 - Lomotil
 - Tincture of opium
 - Parenteral nutrition (rare cases)

Treatment options

- Colon
 - Dietary modifications
 - Laxatives
 - Over the counter
 - Miralax
 - Senna
 - Prescription
 - Lubiprostone (Amitiza)
 - Linaclotide (Linzess)
 - Plecanatide (Trulance)
 - Prokinetics

Epidemiology

- GI involvement in amyloid as a whole is (to me at least) reported to be surprisingly low:
 - 2013: In retrospective study of 2334 patients with amyloidosis, only 76 (3%) had amyloid on GI biopsies
 - 2015: In Korean study, only 24 of 155 symptomatic; all with amyloid on biopsy (15%)
 - 2017: In retrospective study of 583 amyloid patients, only 96 reported GI symptoms; 82 underwent endoscopy with biopsies; only 45% had amyloid on biopsies (16% symptomatic; 6% amyloid on biopsies)

Cowan AJ. Haematologica 2013

Young Lim A. Korean J Intern Med 2015

Yen T. Neurogastroenterol Motil 2017

Data regarding variants

- Extremely limited
 - I could find not data on GI manifestations of TTR variants
 - All GI series published on amyloid are > 80% AL/AA
 - Weight loss reported to be in 30% range, but multifactorial
 - Frequent diarrhea/constipation mentioned in TTR articles in other fields (cardiac mostly)
- My subjective impression
 - Perhaps more neuropathy than AL/AA
 - All distribution patterns seen
- Needs a good study

Thank you



john.clarke@stanford.edu

Cell: 443-798-5042