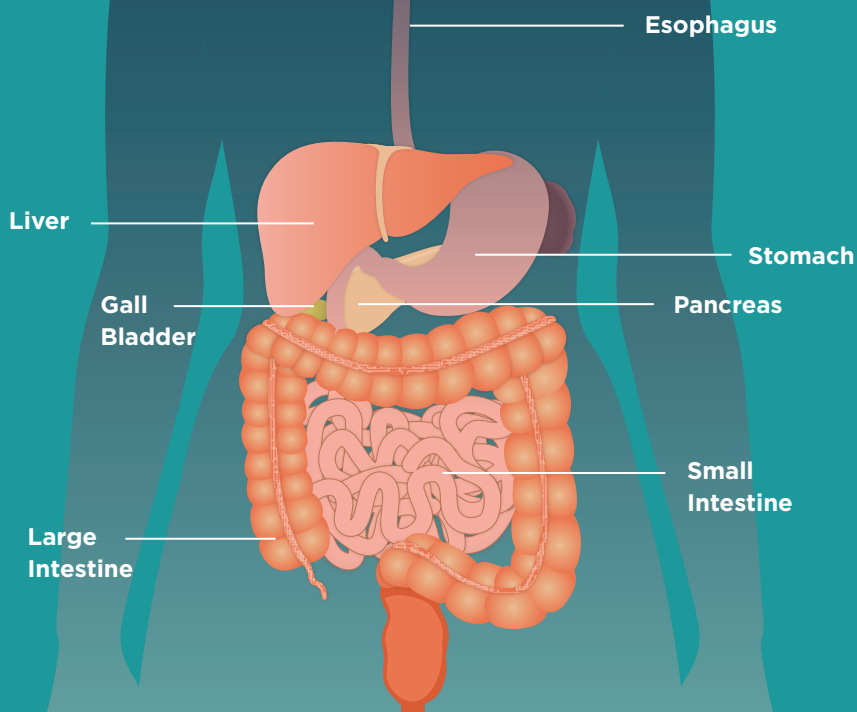


GASTROINTESTINAL INVOLVEMENT IN AMYLOIDOSIS

SYMPTOMS AND MANAGEMENT



KNOWLEDGE IS POWER

ABOUT THE AMYLOIDOSIS RESEARCH CONSORTIUM

The Amyloidosis Research Consortium (ARC) is a nonprofit organization dedicated to driving advances in awareness, science, and treatment of amyloid diseases. ARC's mission is to improve and extend the lives of those with amyloidosis. ARC is committed to collaborative efforts that accelerate the pace of discovery, expand patient access to the most effective care, and improve short- and long-term outcomes. Working with partners in industry, government, and academia, ARC seeks to spark innovation and to bring promising treatments from labs to clinics. Our outreach and educational efforts inform and empower patients, families, caregivers, physicians, and researchers.

To learn more about ARC, visit www.arci.org or call **(617) 467-5170**.

This booklet is not intended to provide medical advice. It is merely an educational tool. Patients should speak with their care team when making any treatment decisions.



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To learn more about specific types of amyloidosis, view ARC’s companion brochures at www.arci.org, or contact an ARC patient support specialist at (617) 467-5170.

INTRODUCTION

Amyloidosis can affect many parts of the body, including the gastrointestinal (GI) tract, which includes the esophagus, stomach, small intestine, pancreas, liver, colon, and related nerves. GI involvement can occur in several types of **amyloidosis**. In some patients, digestive symptoms may be among the earliest or most noticeable symptoms, while others may develop symptoms later. Severity of GI symptoms also varies from mild to significantly affecting quality of life.

This booklet discusses:

- How **amyloidosis** can affect gastrointestinal (GI) tract
- Common GI symptoms
- How GI involvement is diagnosed
- Ways to manage symptoms (available treatments and approaches)

We encourage you to contact your health care provider if you have specific questions about your diagnosis of **amyloidosis** and the GI symptoms you may be experiencing.

A well-informed patient is better able to be an active partner with their health care team in making decisions about treatment, managing their care, and advocating for their needs.

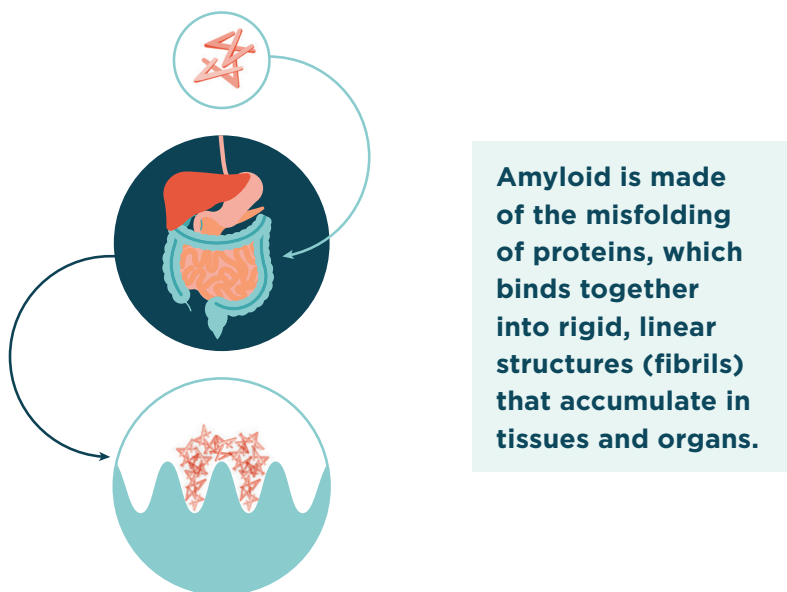
AMYLOIDOSIS

WHAT IS AMYLOIDOSIS?

Amyloidosis is a group of diseases caused when abnormal misfolded proteins, called **amyloids**, clump together and form **fibrils**, which are rigid fibers. Over time, amyloid **fibrils** deposit and build up in the organs and tissues, affecting their normal function. They typically accumulate in the heart, kidneys, gastrointestinal tract, and nerves, less often in the liver, spleen, and airway. These can impair multiple organs and nerves or be localized in one area of the body. Symptoms are often mistaken for more common conditions.

Over 30 different proteins can cause **amyloidosis**. Each

sub-type is named based on the protein involved with an “A” for amyloid followed by an abbreviation for the abnormal protein. For example, **AL amyloidosis** is caused by abnormal immunoglobulin Light chains, and **ATTR amyloidosis** is caused by abnormal transthyretin (**TTR**) protein. Treatment depends on the type of amyloid and which organs are involved.



WHY ARE PROTEINS SO IMPORTANT?

Proteins are complex molecules that serve as building blocks for our body. There are thousands of proteins with each formed or folded into a specific shape that carries out their tasks and are then recycled or removed from the body.

Many different proteins can misfold and lead to different types of **amyloidosis**, but they all share the same abnormal structure. Diagnostic tests can identify specific types of amyloids.

In some types of **amyloidosis**, proteins are genetically altered (hereditary form). In others, the proteins are normal but produced in excess or become unstable and fold incorrectly (misfold). Either type makes them unable to do their tasks and difficult for

the body to remove. These misfolded proteins form **fibrils**, known as amyloid. There are two main ways that amyloid affects organs: (1) direct infiltration from amyloid building up in tissues, such as those of the heart, kidney, or GI tract (2) nerve damage especially the **autonomic nerves** that control digestion. Amyloids are difficult for the body to remove. As they accumulate overtime, organs have difficulty carrying out their function, causing symptoms to worsen.

To learn more about specific types of amyloidosis, view ARC's companion brochures at www.arci.org,

WHAT ARE THE SYMPTOMS OF GASTROINTESTINAL (GI) INVOLVEMENT FROM AMYLOIDOSIS

Patients with **amyloidosis** may experience a wide variety of GI symptoms, based on the anatomic area of amyloid deposition, and the layer of the gut affected. These GI symptoms can include weight loss, diarrhea, constipation, reflux or heartburn, abdominal pain and bloating, nausea, **dysphagia** (difficulty swallowing), **early satiety** (feeling full quickly), **malabsorption** (difficulty absorbing nutrients), and bleeding. Many types of **amyloidosis** can cause GI symptoms which can range in severity from being mild and a slight annoyance to severe and debilitating.



Tongue and Esophagus

Amyloidosis can impact the digestive system at the tongue and esophagus by causing **dysphagia** or **food impaction**, where the food becomes stuck in the esophagus, and reflux.



Stomach

Amyloidosis can impact the stomach by causing delayed emptying with symptoms such as fullness, nausea, vomiting, bloating, and abdominal swelling (distention). Amyloid related inflammation can cause stomach ulcers and bleeding. Bleeding may occur because amyloids can weaken small blood vessels, making them fragile.



Small Intestine

This small intestine is the most frequently involved site in systemic **amyloidosis**. The small bowel is largely responsible for nutrient absorption, and thus symptoms may include malnutrition, bloating, weight loss pain, and diarrhea. This may be a source of disruption in the gut microbiome, called **small intestinal bacterial overgrowth (SIBO)**.



Colon and Rectum

Amyloid deposits in the colon may cause inflammation, bleeding and ulceration, or may contribute to motility issues. Amyloid can affect colon and rectal nervous systems, resulting in symptoms of bowel blockages (called **pseudo-obstruction**), diarrhea, constipation, difficulty evacuating stool, or bowel incontinence.

Not all digestive symptoms in someone with amyloidosis are caused by amyloid deposits. Many common GI conditions, such as acid reflux, irritable bowel syndrome (IBS), medication side effects, or diabetes-related nerve damage, can cause similar symptoms. Careful evaluation is important. If you are experiencing digestive symptoms that are bothering you, be sure to discuss your symptoms with your health care team.

Red Flag Symptoms – Seek Immediate Medical Care

Seek urgent medical attention if you experience the following symptoms:

- Severe abdominal pain
- Black or bloody stools
- Vomiting blood
- Inability to keep liquids down
- Rapid weight loss
- Dry mouth, dizziness, fainting (Signs of dehydration)

HOW IS GI INVOLVEMENT IN AMYLOIDOSIS DIAGNOSED?

There are several different reasons that **amyloidosis** may cause GI issues. Amyloid deposits can be:

- In the muscles along the GI tract
- In the mucosal lining of the GI tract
- In nerves along the GI tract
- In the arteries that supply the GI tract

Amyloid **fibrils** can also deposit in and around other organs that fall under the gastrointestinal “umbrella.” Problems with organs like the liver, pancreas, gallbladder, and others may also cause abdominal or digestive issues.

Your health care team may recommend testing based on your symptoms and the affected organs. Commonly used tests include:

Endoscopy or Colonoscopy: A thin, flexible tube with a camera is inserted through the mouth (endoscopy) or anus (colonoscopy) while the patient is sedated to stay comfortable. A small camera at the end of the tubing allows clinicians to visualize and capture images along the GI tract. Small tissue samples (biopsies) may be taken during the procedure. Identifying amyloid on biopsy samples requires using special stains, called as Congo red staining. Sometimes amyloid is found incidentally during evaluation of other symptoms. In other cases, biopsy may not show amyloid even if symptoms are present, especially if symptoms are caused by nerve involvement rather than visible amyloid deposits. This procedure can also allow for specialized treatment, such as dilation (stretching) or bleeding control, if it is needed.

Imaging: Imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) can show if there is any thickening or narrowing in the digestive tract that may be contributing to symptoms.

Manometry: A thin tube with pressure sensors is placed at a specific area in the GI tract to measure the strength and patterns

of the contractions. Common types of manometry tests include Esophageal Manometry to better understand swallowing related issues, and Anorectal Manometry to evaluate symptoms related to constipation, diarrhea, and stool incontinence.

Sitz Marker Study: The patient swallows a capsule containing very small radiopaque markers which disperse throughout the GI tract during digestion. A series of x-rays over the next several days track how quickly stool moves through the intestine and colon.

Gastric Emptying Study: this is an examination to assess the motility of your stomach by viewing how fast food leaves your stomach. A delay in gastric emptying is termed “**gastroparesis.**” You will be given a solid meal that has small amounts of harmless radioactive tracer. Pictures will be taken periodically of your stomach over the next several hours.

Breath tests: Analyzing gas production in a patient’s breath can help clinicians evaluate absorption and gut bacteria balance. There are different types of breath tests, and your clinician may recommend a certain type based on your symptoms. Breath testing may be considered if you are experiencing symptoms of bloating, diarrhea, or constipation as these can indicate **malabsorption** or **small intestinal bacterial overgrowth (SIBO)** in the gut.

These diagnostic tests can help your clinician understand how your GI tract is **functioning** and the **potential impact** of **amyloidosis**, providing important information on how best to help you manage your symptoms. It is important that you keep track of the digestive symptoms you experience as this can help your clinician make diagnostic testing recommendations.

DOES TREATMENT FOR MY DISEASE ALSO IMPROVE GI SYMPTOMS?

Treatment for **amyloidosis** can be broken down into two main approaches:

1. **Targeting** the underlying disease, **amyloidosis**
2. **Treating** the GI symptoms caused by **amyloidosis**

By targeting the underlying disease, treatments aim to **slow or stop** amyloid production. This approach reduces the amount of amyloid that is circulating through the body and depositing on tissues and organs. Studies show that the body can slowly break down existing amyloid deposits, resulting in the improvement of symptoms. However, improvement in organ function can take many months or even years. In some cases, symptoms may not fully reverse. Even when amyloid production is controlled, nerve-related symptoms may persist because nerve tissue heals slowly. At this time, treatment for GI symptoms related to **amyloidosis** are focused on treating both the underlying systemic disease, and symptom-directed supportive care.

MANAGEMENT OF GI SYMPTOMS

There are many different therapeutic options that GI specialists and other clinicians can recommend or prescribe to help you manage your symptoms. These tend to be most helpful for relieving painful or uncomfortable symptoms. Aside from prescription medications, this section will also cover over-the-counter (OTC) medications, dietary modifications, and alternative therapies.

Be sure to talk to your doctor before starting or stopping any medications and always keep your doctor informed of any new or worsening symptoms or side effects.

OVERVIEW OF SYMPTOM MANAGEMENT APPROACHES

Esophagus Involvement: Symptoms may include **acid reflux/heartburn** and **dysphagia** (difficulty swallowing).

Acid Reflux and Heartburn:

1. Dietary and lifestyle modifications:

- a. Minimize triggers. This may include alcohol, tobacco, acidic and spicy foods, peppermint, and caffeine.
- b. Maintain healthy weight

- c. Avoiding late meals
- d. Staying upright for at least 3-4 hours after eating

2. Medications: Lower doses available over the counter, higher doses require prescription. It is very important you discuss

with your doctors if your current treatments are safe or effective.

- a. Antacids (e.g. calcium carbonate/TUMS®)
 - Neutralize stomach acidity
 - Work quickly (within minutes)
 - Short-lasting relief
- b. Histamine receptor blockers (e.g. famotidine/Pepcid®)
 - Reduce stomach acid production
 - Helpful in mild or occasional symptoms
 - Lasts about 6-10 hours.
- c. Proton pump inhibitors (PPIs) (e.g. Pantoprazole/Protonix®, Omeprazole/Prilosec®, Esomeprazole/Nexium®)
 - Stronger stomach acid suppression
 - Used for more severe or frequent symptoms
 - These may also be prescribed to help with ulcer healing

3. Endoscopic or surgical options:

- a. More invasive and considered in selected patients if lifestyle changes or medications have been tried and are not effective.

Dysphagia (difficulty swallowing):

1. Dietary modification:

- a. Choose softer food options
- b. Add liquids or sauces to food for better lubrication
- c. Soups, smoothies, and shakes may be easier to swallow

2. Swallowing evaluation:

- a. Often done with a speech-language pathologist using x-ray
- a. Helps identify the reason for **dysphagia** and safe swallowing strategies

3. Procedures:

- a. Esophageal dilation for narrowing by stretching part of the esophagus during an endoscopy
- b. Botox injections if muscle spasms around the esophagus are present

Stomach Involvement: Symptoms may include nausea, vomiting, bloating, abdominal pain and **distension**, **early satiety**, and **gastroparesis** (delayed stomach emptying).

1. Dietary modifications:

- a. Smaller, frequent meals
- b. Low-fat, low insoluble fiber foods meals
- c. Liquid nutrition e.g. smoothies or shakes may be easier to digest
- d. Avoid alcohol (may slow down digestion)

2. Medications:

- a. Anti-nausea medications (e.g. ondansetron/Zofran®, promethazine/Phenergan®)
- b. Prokinetics (e.g. metoclopramide/Reglan®)
 - Speed up digestion and help with stomach emptying
 - Discuss potential side effects with your care team before starting
- c. Neuromodulators (e.g. mirtazapine/Remeron®, amitriptyline/Elavil®, Nortriptyline/Pamelor®, Desipramine/Norpramin®)
 - Modulate pain signaling between the gut and brain
 - May reduce pain sensitivity of the intestines
- d. Herbs (e.g. peppermint or caraway)
 - May relax certain GI muscles and help with cramps, but may worsen **acid reflux** in some patients

- Available over the counter in capsule form

3. Procedures:

- Endoscopic or surgical opening of part of the stomach that empties into the small intestine

Small intestine involvement: Symptoms may include bloating, gas, diarrhea, **malabsorption**, and weight loss.

1. Dietary modifications:

- Reduce or eliminate gas-producing foods (e.g. beans, brussels sprouts, raw cruciferous vegetables, carbonated beverages) for bloating and gas
- Talk to your care team for a referral to a registered dietitian or nutritionist if available

2. Medications:

- Prokinetics (e.g. Metoclopramide/Reglan®, Prucalopride/Motegrity®)
 - Stimulate muscle contractions in the intestines
 - Increase the speed of intestinal movement (reduce transit time)
 - Help food move more efficiently through the digestive tract
 - Prevent food from sitting too long in the gut (reduces stagnation)
 - Decreases risk of bacterial overgrowth
 - May indirectly improve bloating, diarrhea, and nutrient absorption
- Pancreatic enzyme supplements (e.g. Creon®, Zenpep®, or Pancreaze®)
 - Pancreatic enzyme insufficiency may contribute to diarrhea or weight loss in some patients, which can improve with pancreatic enzyme supplements
- Antibiotics (e.g. Rifaximin/Xifaxan®)
 - For excess bacteria in the gut called **small intestinal bacterial overgrowth (SIBO)** to help restore microbial balance

- May be used in combination with other antibiotics or herbal remedies
- d. Bile salt binding agents (e.g. Cholestyramine/Questran®)
 - Bind to bile acids in the GI tract and can help reduce diarrhea if bile acid **malabsorption** is thought to be a contributor to symptoms.
- e. Anti-diarrheal (e.g. OTC: Loperamide/Imodium®, Prescription: Diphenoxylate and Atropine/ Lomotil®)
 - Slow intestinal motility to reduce stool frequency
- f. Antispasmodics (e.g. Dicyclomine/Bentyl®, Hyoscyamine/Levsin®)
 - Work to treat digestive track muscle cramping
 - May help alleviate diarrhea

Colon involvement: Symptoms may include diarrhea, constipation, and fecal incontinence.

1. Dietary modifications:

- a. Fiber supplementation based on individual tolerance, as some may experience more bloating and gas
- b. Maintain adequate hydration
- c. Prunes, pears, kiwi and stone-fruits may all help with constipation

2. Medications:

- a. Laxatives (e.g. Miralax, Senna, and magnesium-based solutions)
 - Helpful for constipation
 - Loosen stools and increase bowel movements
 - Many available over the counter.
- b. Prescriptions (e.g. Prucalopride/Motegrity®, Linaclotide/Linzess®, Plecanatide/ Trulance®, Lubiprostone/Amitiza®)
 - Helpful for constipation
 - Speed up colonic contraction
 - Discuss options with your health care provider to determine what is appropriate for you

3. Pelvic floor physical therapy:

- a. Involves targeted exercises and retrains your brain and body to strengthen the muscles that control the gatekeeper, known as anal sphincter
- b. Improves your ability to sense when you need to go and prevents accidental leakage

NUTRITION SUPPORT

Working with a dietitian familiar with **amyloidosis** or digestive symptoms can be extremely helpful. Discuss with your care team for a dietitian referral. In cases of severe **malabsorption**, supplemental nutrition through oral, intestinal tubes or intravenous (called TPN) may be necessary.

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ARC PATIENT SUPPORT AND RESOURCES

The Amyloidosis Research Consortium (ARC) is a nonprofit organization with a mission to advance scientific discovery, improve access to state-of-the-art care, and empower patients with innovative educational tools and support. Please explore the companion booklets available in our Patient Resources library online at www.arci.org.



New trials are always in development to help expand treatment options and improve quality of life. Join MAP to receive notifications as new clinical trials and treatment centers are posted.



Treatment Center
Selector



Clinical Trial
Finder

www.myamyloidosispathfinder.org

GLOSSARY

Acid reflux. Or heartburn, a condition in which the sphincter at the lower end of the esophagus relaxes, allowing stomach acid to rise into the esophagus. This irritates the lining of the esophagus, causing heartburn, nausea, regurgitation, and belching. Symptoms typically worsen when lying down.

Amyloidosis. A disease caused by the accumulation of abnormally shaped proteins (amyloid proteins) in tissues and organs.

Autonomic nerves. Nerves that automatically control digestion, blood pressure, and heart rate.

Distension. Bloating and swelling of the abdomen.

Dysphagia. Difficulty swallowing.

Early satiety. Feeling full early on in a meal or after just a few bites of food.

Fibrils. Long strands of normally soluble proteins that clump together to form insoluble fibers resistant to degradation.

Food impaction. Occurs when food becomes stuck in a patient's esophagus.

Gastroparesis. Delayed emptying of the stomach.

Malabsorption. Difficulty absorbing nutrients from food.

Pseudo-obstruction. A rare condition in which a patient's symptoms might lead a clinician to believe that there is a blockage or obstruction in the intestines, however upon examination or imaging, no blockage is found. The symptoms are due to nerve or muscle issues in the GI tract that affect the movement of food, fluids, and air.

Small intestinal bacterial overgrowth (SIBO). A condition where excess bacteria grow in the small intestine, causing bloating and diarrhea

You are not alone — ARC is here to support you every step of the way.

To receive one-on-one guidance, learn more about ARC, or support our mission, contact us:

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Learn more at **ARCI.ORG**

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