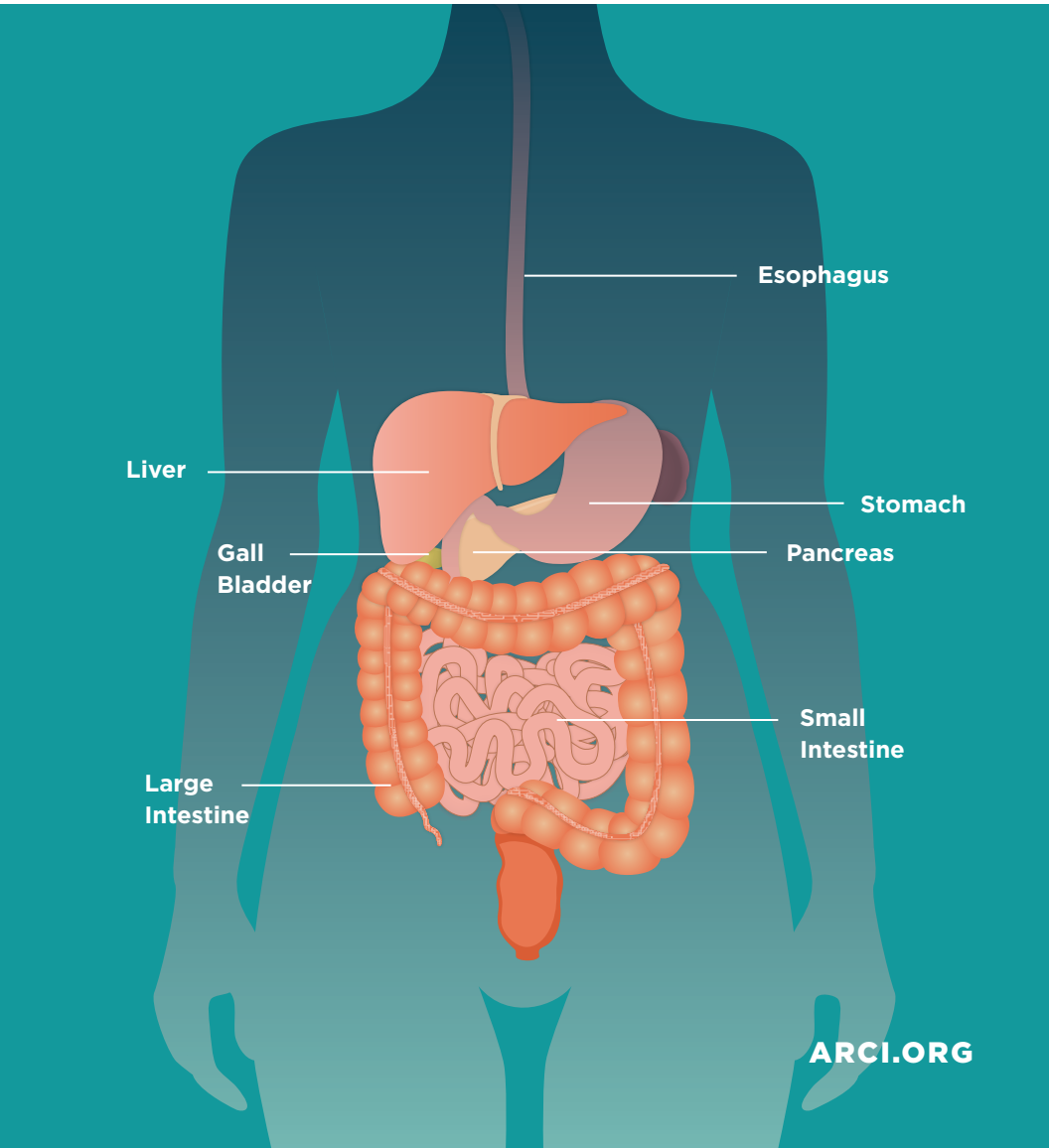
Amyloidosis Research Consortium

GASTROINTESTINAL INVOLVEMENT IN AMYLOIDOSIS

SYMPTOMS AND MANAGEMENT



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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.

Amyloidosis Research Consortium

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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

Many types of **amyloidosis** can affect patients' gastrointestinal (GI) tract, causing painful, annoying, or even debilitating symptoms. It is common for patients with **amyloidosis** to experience GI involvement and in fact, some patients may have GI-related symptoms as their most predominant sign or chief complaint.

This booklet discusses the various impacts that **amyloidosis** may have on a patient's gastrointestinal (GI) tract, the symptoms associated with GI involvement, and potential management techniques. We encourage you to contact your health care provider if you have specific questions about your diagnosis of **amyloidosis** and the gastrointestinal 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.

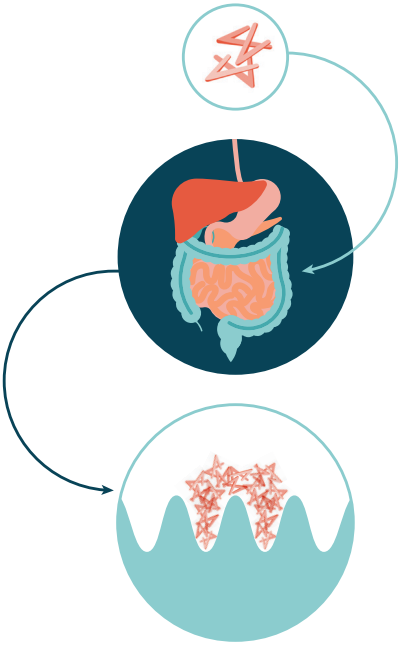
AMYLOIDOSIS

WHAT IS AMYLOIDOSIS?

Amyloidosis is a group of diseases caused when misfolded proteins, called amyloid, build up and form **fibrils** that deposit in the body's organs and tissues, affecting their ability to function. Amyloid **fibrils** typically accumulate in the heart, kidney, 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 protein has different associated symptoms and treatments and is linked with a unique sub-type of amyloidosis. Each sub-type is referred to by 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 is caused by abnormal transthyretin (TTR) protein. Treatment is determined by the type of amyloid and which organs and tissues are affected.



Amyloid fibrils can infiltrate the mucosal lining of the GI tract, the muscles, or nerves along the GI tract, or arteries that supply the GI tract.

WHY ARE PROTEINS SO IMPORTANT?

Many thousands of proteins do essential work inside our cells. Each has a specific job to keep us healthy. DNA instructions control the shape and structure of proteins. Normal proteins form (fold) into a specific shape, do their tasks, and are then recycled or removed from the body.

In amyloidosis, mutated proteins form incorrectly (misfold), which makes them unable to do their tasks and difficult for the body to remove. These misfolded proteins then accumulate in the body and form fibrils, known as amyloid, in organs and tissues, such as the heart, kidney, or nerves. As they accumulate over time, they impact the function of organs, causing symptoms to flare, which tells us something is wrong.

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 amyloid.

SYMPTOMS

Tongue and esophagus

Amyloidosis can impact the digestive system at the tongue and esophagus by causing **dysphagia** (difficuly swallowing), **food impaction**, where the food because stuck in the esophagus, and reflex

The stomach

Amyloidosis can impact the stomach by causing abdominal pain, nausea, vomiting, and bloating and abdominal swelling (distention).

The small intestines and colon

Amyloid deposits in the digestive system or gastrointestinal (GI) tract can cause chronic diarrhea, constipation, **malabsorption**, weight loss, **psuedo-obstruction** (symptoms that mimic an intestinal bloackage), fecal incontinence and bleeding.

When evaluating your GI symptoms, it is important to remember that many symptoms can be non-specific and could be caused by factors other than amyloidosis. For example, roughly 13% of adults in the US have Irritable Bowel Syndrome (IBS), and up to 20% experience symptoms of acid reflux at least once a week. If you are experiencing digestive symptoms that are bothering you, be sure to discuss your symptoms with your health care team.

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

Patients with **amyloidosis** may experience a wide variety of gastrointestinal (GI) symptoms. These GI symptoms can include weight loss, diarrhea, constipation, **reflux** or heartburn, abdominal pain and bloating, nausea, difficulty swallowing, **early satiety** (feeling full quickly), 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.

DIAGNOSING GI INVOLVEMENT IN AMYLOIDOSIS

There are several different reasons that **amyloidosis** may cause gastrointestinal 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. As part of your **amyloidosis** evaluation tests will be done to see which organs are impacted by **amyloidosis** and how.

The symptoms you are experiencing are important to discuss with your doctor. This information will help your doctor identify which tests are appropriate to evaluate the level of gastrointestinal impairment. Some examples include:

Endoscopy or colonoscopy: A thin, flexible tube is inserted into the GI tract 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 samples of tissue may be collected by taking biopsies during the procedure for further testing. This procedure can also allow for specialized treatment, such as dilation (stretching) or bleeding control, if it is needed. Biopsies through endoscopy and colonoscopy can provide valuable information about **amyloidosis**, as well as other conditions.

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. There are many different types of manometry including esophageal manometry, small bowel manometry, colonic manometry, and anorectal manometry. The type of manometry will depend on your symptoms and after discussion with your health care provider.

Wireless motility capsule: The patient swallows an oral capsule that can measure various aspects of GI health, such as pH level, pressure, temperature, and gut transit time. Your health care provider might recommend a wireless motility capsule to evaluate symptoms that may suggest slow passage of contents of the digestive tract such as nausea, vomiting, **early satiety** or constipation.

Sitz marker study: the patient swallows a small capsule containing very small radiopaque markers which disperse throughout the GI tract during digestion. An x-ray is taken 5 days after the capsule is swallowed (some health care providers might recommend more than one x-ray). Most markers should be naturally expelled from the body after 5 days. If there are still a lot of markers left, this can indicate that slow colon transit may contribute to constipation, providing important information to help guide treatment options.

Breath tests: Analyzing gas production in a patient's breath can help clinicians evaluate absorption and gut bacteria. 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 and diarrhea as these can indicate malabsorption or bacterial overgrowth 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?

There are two main approaches to treating **amyloidosis**:

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 the production of amyloid, thereby reducing 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, but this process can take many months, or even years. For this reason, where treatments are available, treating **amyloidosis** may not be enough to control gastrointestinal symptoms, and therefore, direct symptom management should be considered.

Symptom management may include over-the-counter (OTC) medications, dietary modifications, prescription medications, alternative therapies, and more.

ARC can help you find clinicians that specialize in the treatment of gastrointestinal (GI) symptoms from amyloidosis. Visit www.arci.org or call us at (617) 467-5170.

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 medications and dietary modifications.

OVERVIEW OF SYMPTOM MANAGEMENT APPROACHES

Esophagus Involvement: Symptoms include acid **reflux** and **dysphagia** (difficulty swallowing)

Acid Reflux and Heartburn:

- **Dietary modifications**: If specific foods tend to cause **reflux** more frequently for a patient, these foods should be minimized or avoided. If a patient is overweight, weight loss can help reduce symptoms. Avoiding late meals and staying upright after eating can also help reduce symptoms as it typically takes the stomach at least 3-4 hours to process the most of its contents.
- **Antacids:** Antacids are a common first line approach to relieving heartburn. Medications such as TUMS (calcium carbonate), fall under this category and work by neutralizing stomach acidity. Antacids are generally inexpensive, available over-the-counter without a prescription, and are easy to find in most drugstores. Antacids usually relieve symptoms within seconds; however, their effect is usually short lived.
- **Histamine receptor blockers:** Pepcid (famotidine) is an example of a histamine receptor blocker and works to reduce the amount of acid that is produced by the cells in the lining of the stomach. These blockers work for about 6-10 hours, and are preferred for occasional use for managing heartburn.
- **Proton pump inhibitors:** Proton pump inhibitors also work to reduce the amount of acid that is produced in the stomach and are generally used in cases of more severe or frequent heartburn. Nexium (esomeprazole) and Prilosec (omeprazole) are two examples of proton pump inhibitors but there are

many others available. In lower doses, they are available over the counter, and higher doses usually require a prescription. If you are considering taking a proton pump inhibitor, discuss this as an option with your health care provider before starting.

- **Endoscopic/surgical options:** These options are more invasive and may be considered in carefully selected patients. There are a variety of endoscopic and surgical management options, and these may be utilized in patients who have not had success or relief with other symptom management approaches or who may have additional medical conditions. It is very important to communicate with your clinicians if your current treatment options are ineffective.

Dysphagia (difficulty swallowing):

- **Dietary modification:** Patients that have difficulty swallowing food may consider making softer food options or adding liquid to food to make it more lubricated. Soups, smoothies, and shakes are also good options for individuals with **dysphagia**.
- **Dilation:** Dilation is a procedure that can be done if there is narrowing of the patient's esophagus. The procedure stretches part of the esophagus during an endoscopy.
- **Botox:** Some patients experience spasming of muscles around the esophagus. If this is the case, Botox injection may be considered as an option.

Stomach Involvement: Symptoms include abdominal pain, nausea, vomiting, and stomach distention or bloating. These symptoms may be caused by the stomach's inability to empty properly. Management techniques include the following:

- **Dietary modifications:** Switching to smaller, low-fat meals or smoothies and shakes which are more easily digested may help. Minimizing foods that have insoluble fiber can also be helpful as these are more challenging for the stomach to digest. Avoiding alcohol may be another approach to consider, as it can also slow down digestion.
- **Prokinetics:** These medications speed digestion and may be helpful for some patients. Currently, the only FDA-approved medication for gastroparesis (delayed stomach emptying) is Reglan® (metoclopramide). As with any medication, your

healthcare provider can help discuss the pros and cons, including potential side effects, and help you decide which option is best based on your symptoms and medical history.

- **Agents to help stomach expansion:** Herbs, such as peppermint and caraway, may relieve digestive symptoms such as nausea, indigestion, stomach cramps, bloating, and gas. Peppermint and caraway are thought to relax the muscles in the digestive tract. There are over-the-counter options available for these herbal remedies in capsule form.
- **Neuromodulators:** These medications can help reduce or relieve pain. Some medications in this category include Lyrica® (gabapentin/pregabalin), Neurontin® (gabapentin), Remeron® (mirtazapine), and Elavil® (amitriptyline).
- **Anti-emetics:** These medications are used to treat nausea and vomiting. There are quite a few options in this category, such as Zofran® (ondansetron) and Phenergan® (promethazine), which are commonly prescribed.
- **Endoscopic options:** There are procedures to stretch the portion of the stomach that empties into the small intestine, or as an alternative, Botox injections may be used to reduce spasms in the stomach, depending on your symptoms and the results from diagnostic testing.

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

- **Dietary modifications:** If you find that bloating and gassiness are bothersome, eliminating gas-producing foods such as beans, brussels sprouts, carbonated beverages and the like may help reduce symptoms. Consider working with a registered dietician or nutritionist if this support is available to you, particularly if you find that certain foods seem to trigger symptoms.

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.

- **Prokinetics:** These increase the speed of intestinal movement which may sound counter-intuitive for patients with diarrhea, but increasing contractions of the bowels can move bacteria out of the gut, and therefore improve absorption.
- **Antibiotics:** If there is an excess of bacteria in the gut (known as small intestinal bacterial overgrowth, or SIBO), antibiotics may be prescribed to remove some of the excess bacteria and return the gut to a more neutral state. Testing for SIBO can be done with a certain type of breath test.
- **Bile salt binding agents:** Medications such as Questran® (cholestyramine) contain agents that 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.
- **Anti-diarrheal medications:** There are a handful of medications, both over-the-counter (OTC) and by prescription, that can be used to prevent diarrhea. Imodium® (loperamide) is a common OTC product available at most drugstores. Lomotil® (diphenoxylate and atropine) is an example of a prescription anti-diarrheal that your clinician may prescribe. A tincture of opium can also be very effective at decreasing the number and frequency of bowel movements, although many doctors prescribe this sparingly, as it is in the same class of medicines as narcotic pain relievers.
- **Parenteral nutrition:** In rare cases, nutrition from intravenous infusions may be considered if a patient cannot tolerate eating by mouth, has severe absorption issues, and associated weight loss.

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

- **Dietary modifications:** Fiber supplementation should be evaluated on a case-by-case basis. An increase in fiber in the diet can help some patients, whereas in other patients, an increase in fiber may cause more bloating and gas. Hydration, drinking water and other fluids, is also important. Prunes can be effective as a natural remedy for constipation.

- **Laxatives:** These substances can loosen stool and increase bowel movements. Some laxatives are available over the counter (OTC), such as Miralax, Senna, and magnesium-based solutions.
- **Prescriptions:** There are also prescription medications to treat constipation, such as Motegrity® (prucalopride), Trulance® (plecanatide), Linzess® (linaclotide), and Amitiza® (lubiprostone). Talk to your health care provider to determine if a prescription therapy for constipation would be appropriate for you.

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 nad support. Please see the companion booklet in our Library under Patient Resources at www.arci.org.

MAP | My Amyloidosis Pathfinder

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

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

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.

Fibril. 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.

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 actually due to nerve or muscle issues in the GI tract that affect the movement of food, fluids, and air.

Reflux. Or acid reflux, 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.

ARC gratefully acknowledges Monica Nandwani, DNP, RN, FNP-BC Manager of Advanced Practice and Gastroenterology Nurse Practitioner at Stanford Health Care for her contributions to the development of this booklet.

This booklet is supported by grants from:

» *Alexion, AstraZeneca Rare Disease*
» *Alnylam Pharmaceuticals*
» *AstraZeneca*
» *BridgeBio*
» *Centogene*
» *Chip Miller Amyloidosis Foundation*
» *Immix Biopharma*
» *Intellia Therapeutics*
» *Ionis Pharmaceuticals*
» *Pfizer*
» *Protego Biopharma*
» *Prothena Biosciences*
» *Ultromics*

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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