DISEASE OVERVIEW

LIGHT CHAIN AMYLOIDOSIS (AL AMYLOIDOSIS)

Dan has AL amyloidosis.

Amyloidosis Research Consortium

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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.

Amyloidosis Research Consortium

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INTRODUCTION

A diagnosis of light chain amyloidosis (AL amyloidosis) can be confusing and stressful, bringing up many feelings and questions. It is important to learn as much as possible about the disease, its treatment, and how it might affect you.

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.

Amyloid is a starch-like substance caused by the misfolding of proteins. Amyloid binds together into rigid, linear structures (fibrils) that accumulate in tissues and organs.

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** cause various types of amyloidosis. Each is referred to by an "A" for **amyloid** followed by an abbreviation for the abnormal protein (for example, AL for amyloidosis caused by abnormal **immunoglobulin light chains** or ATTR for transthyretin amyloidosis). Treatment is determined by the type of **amyloid** and which organs and tissues are affected.

Major therapeutic advances have been discovered in the last decade. Current treatments can put AL amyloidosis into prolonged remission and extend life.

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, telling 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**.

In AL amyloidosis, proteins produced by abnormal plasma cells misfold into amyloid fibrils that build up in the body, causing organ damage.

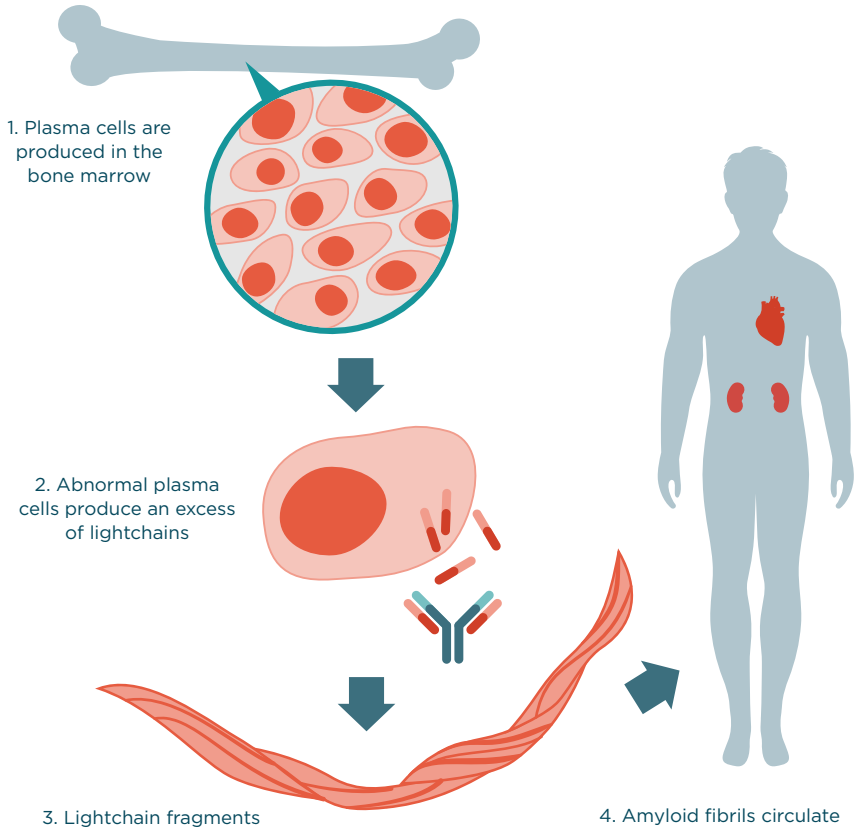
WHAT IS AL AMYLOIDOSIS?

Light chain amyloidosis (**AL amyloidosis**) is a rare, systemic disease caused by abnormal plasma (blood) cells located in the **bone marrow**. The function of our normal **plasma cells** is to form **immunoglobulins** (**free light chains)**, also known as **antibodies**, that target and neutralize bacteria and viruses. In **AL amyloidosis**, abnormal **plasma cells** produce abnormal light chain **proteins**, these **proteins** then misfold and form into **amyloid fibers (fibrils)**. Normal **light chains** are excreted by the kidneys. Abnormal (misfolded) **proteins** are not excreted, causing them to build up in the blood. As they build up and accumulate, these **fibrils** are deposited in organs, tissues, and nerves, causing damage.

Most **AL amyloidosis** patients are diagnosed after the age of 50, though some adult patients have been diagnosed as early as their 20s. **AL amyloidosis** affects both men and women, although there is a slight predominance in males. The pattern of **amyloid** build-up is different for each patient and often affects more than one organ. Early diagnosis and treatment are essential to prevent or slow disease progression.

Untreated, **AL amyloidosis** is progressive, and ultimately, fatal. Early diagnosis and treatment are essential for improved outcomes. Major therapeutic advances have been discovered over the last decade. These can put AL amyloidosis into prolonged remission and extend life.

LIGHT CHAIN (AL) AMYLOIDOSIS DISEASE PROCESS

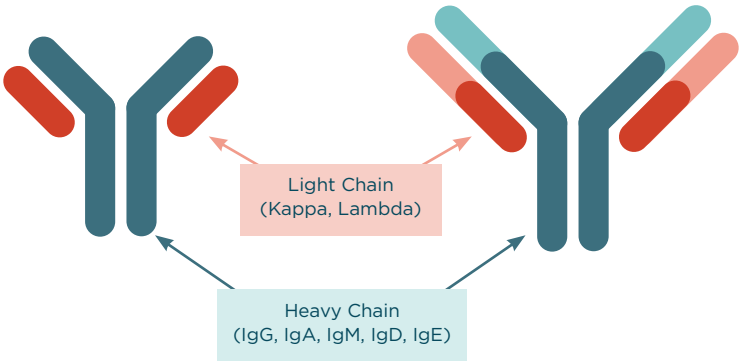


AN OVERVIEW OF PLASMA CELLS AND FREE LIGHT CHAINS

Blood cells are produced in **bone marrow,** a specialized tissue in the hollow center of bones. The main types of blood cells are red, white (including **plasma cells**), and **platelets**. Each plays a specialized role in your body's immune system.

Plasma cells produce **immunoglobulins**, a class of **antibodies** that fight infections. **Antibodies** are made up of two kinds of **protein** chains, heavy & light. In **AL amyloidosis**, there are too many **plasma cells** that produce an excess of **light chains.** These can either be Kappa and/or lambda light chain fragments. Your care team may also refer to these **free light chains** as "FLCs" or as "clones."

ANTIBODY STRUCTURE



As abnormal **plasma cells** multiply, they produce **light chain** fragments that aggregate and form **amyloid fibrils** and enter the blood stream. The goal of treatment is to reduce or eliminate the abnormal cells, decreasing or halting the accumulation of **amyloid** deposits and preserving organ function.

The ratio between the kappa and lambda light chains indicates a potential overproduction of one light chain over the other. The ratio is used to track disease progression or remission.

FREQUENTLY ASKED QUESTIONS ABOUT AL AMYLOIDOSIS

WHAT CAUSES AL AMYLOIDOSIS?

AL amyloidosis is not inherited or contagious. Its cause is still unknown, but research suggests a link between environmental exposure and eventual onset. For example, some Veterans exposed to Agent Orange have been treated for **AL amyloidosis**. There is also suspicion that **AL amyloidosis** is linked to inflammatory conditions in the body, but more research is needed to confirm this.

HOW COMMON IS AL AMYLOIDOSIS?

Although once considered to be a very rare disease, with the education of health care professionals and better diagnostic tools, it is now considered more common than previously thought. Previously known as "primary amyloidosis". In the United States, about 4,500 patients are diagnosed with **AL amyloidosis** each year. **AL amyloidosis** is more common in males than in females, though the cause of this is still not understood.

Although once considered to be a very rare disease, with the education of health care professionals and better diagnostic tools, it is now considered more common than previously thought.

IS AL AMYLOIDOSIS RELATED TO MULTIPLE MYELOMA?

AL amyloidosis is not a cancer although it is sometimes diagnosed with multiple myeloma, which is a type of **bone marrow** cancer. Both diseases are plasma cell disorders. **Plasma cells** create **antibodies** that fight infections and kill germs. Metastasized **plasma cells** like multiple myeloma crowd healthy blood cells, preventing the immune system from functioning properly. **AL amyloidosis** is caused by misfolded light chain **proteins** produced by **plasma cells**. Some 10% to 15% of patients with **AL amyloidosis** also have active multiple myeloma, known as

myeloma-associated **AL amyloidosis**. Both **AL amyloidosis** and multiple myeloma are treatable diseases. Some myeloma drugs are used "off label" to treat **AL amyloidosis**. Autologous stem cell transplants may also be used in treating each of these diseases

AL Amyloidosis patients are sometimes also diagnosed with multiple myeloma. Though the diseases are different, both are treatable with combinations of multiple myeloma treatment protocols.

SYMPTOMS

HOW DOES AL AMYLOIDOSIS AFFECT THE BODY?

AL amyloidosis is a progressive, systemic disease that can affect multiple organs, tissues, and nerves. The most common symptoms are weight loss, fatigue, swelling of the legs (edema), and breathlessness (dyspnea) with exertion.

The most frequently affected organs are the heart and kidneys. Others include the gastrointestinal (GI) tract, nervous system, and liver. Amyloid deposits in soft tissue, such as the skin or tongue, can also occur and are important signs of the disease. In some patients, only one organ is involved. In others, multiple organs are affected.

AL amyloidosis can affect many parts of the body. Symptoms vary for each patient, with some people having more than others.

Hand and arm symptoms

- Carpal tunnel syndrome
- Numbness, burning, pain, and/or tingling (peripheral neuropathy)
- Weak fingernails, or other nailbed changes

Leg symptoms

- Swelling of the feet or legs
- Muscle weakness
- Weak/brittle toenails
- Peripheral neuropathy

Head and neck symptoms

- Lightheadedness or dizziness when standing up quickly (orthostatic hypotension)
- Purple color on the eyelids and/or around the eyes (periorbital purpura)
- Enlarged tongue/scalloped tongue
- Problems with breathing, talking, swallowing, or chewing
- Jaw pain

Heart and lung symptoms

- Shortness of breath (dyspnea)
- Palpitations (arrhythmia)
- Chest pain
- Fatigue
- Swelling in the legs (edema)
- Arrhythmia (abnormal heartbeat)
- Syncope (fainting)

Stomach or intestinal (GI Tract) symptoms

- Poor appetite
- Feeling full after eating small amounts of food (early satiety)
- Nausea and vomiting
- Unintentional and significant weight loss
- Bloating
- Diarrhea and/or constipation
- Gastrointestinal bleeding
- Heartburn

Kidney symptoms

- Foamy urine
- Less frequent urination
- Getting up in the night to urinate
- Swelling in the lower legs, stomach, arms (edema)
- Kidney (renal) failure requiring dialysis

Other signs or symptoms

- Obstructive sleep apnea
- Skin changes, such as thickening or easy bruising
- Hoarseness
- Enlarged shoulder pad (on the back)
- Purple color in skinfolds
- Bruising or bleeding easily
- Blood clotting abnormalities

WHAT ARE OTHER NONSPECIFIC SYMPTOMS?

Nonspecific symptoms are those that can be caused by a wide range of illnesses. Examples may include fatigue, fever, general malaise, weight loss, difficulty concentrating, or stiffness. Because **AL amyloidosis** is a rare disease, physicians tend to attribute these symptoms to other, more common disorders. Misdiagnoses can lead to treatment for unrelated disorders that are potentially harmful to an amyloidosis patient, and delayed access to appropriate therapeutic options.

WHAT SHOULD I TELL MY DOCTOR?

It is important to tell your doctor about all symptoms and if they have worsened over time. Certain symptoms, or clusters of them, can indicate **AL amyloidosis**.

SHOULD I SEE AN AL AMYLOIDOSIS SPECIALIST?

Ask your healthcare provider for a referral to a clinic or center that specializes in the diagnosis and management of **AL amyloidosis.** To develop the best treatment plan, your primary care doctor and other specialists should coordinate care with experts at these centers. ARC has tools to help you locate and access these resources.

DIAGNOSIS

OVERVIEW

Early and accurate diagnosis of **AL amyloidosis** is essential for effective and timely treatment, but the disease can be difficult to diagnose. Symptoms often mimic those of more common disorders, and no single imaging, blood, or urine test is sufficient to make an accurate diagnosis.

Some cardiologists trained in amyloidosis are successful in identifying amyloidosis in cardiac imaging. However, a definitive diagnosis requires the identification of amyloid **fibrils** in cells or tissue samples taken from suspected affected organs or proxy sites. These small **biopsy** samples are stained with a dye called **Congo red** and viewed under a microscope with polarized light. Stained amyloid has a characteristic apple-green color or **birefringence** that identifies it under polarized light.

Many tests can be used to identify specific types of amyloid **proteins**. Some are performed once to confirm a diagnosis of **AL amyloidosis**; others are repeated many times to track disease progression and response to therapy.

WHAT DIAGNOSTIC TESTS WILL I NEED?

Your complete examination will include blood and urine tests, biopsies (small samples of cells or tissue), and imaging. Blood and/or urine tests can identify amyloid **protein**, but only **bone marrow** tests or other small **biopsy** samples of tissues or organs can confirm a diagnosis of **AL amyloidosis.**

TESTING PROTOCOLS

Initially, lab tests will look for abnormal **plasma cells** and an excess of either kappa or lambda **free light chains** in the blood and urine. These tests include serum **free light chain** levels, antibodies (**immunoglobulins**), and serum and **immunofixation** tests for excess **proteins**. These tests may confirm the presence and level of the lambda or kappa light chain fragments in your blood or urine.

A positive test for light chain fragments in your blood or urine may lead to additional testing to determine which organs or tissues may be affected. These tests may include blood tests for kidney, liver, and heart functions and a 24-hour urine test performed at home to evaluate the level of kidney involvement.

After the blood and urine tests, you may need imaging of certain organs to evaluate if amyloid is affecting them. These often include a chest X-ray to look for nodules in the lungs, an echocardiogram or cardiac MRI to evaluate the heart, and possibly a **CT scan** or **ultrasound** of the liver, kidneys, or lymph nodes. Patients with neurological symptoms may need additional testing of their muscles and nerves. These include electromyography and **nerve conduction studies**.

Your symptoms and your test results may indicate the need for a **biopsy**. Most patients require a **biopsy** of the **bone marrow** because it is the primary source of abnormal **plasma cells**. During the **biopsy**, a clinician will take a small sample of the bone and marrow, often from the hip area, to determine the concentration of **plasma cells**. These biopsies are also used to determine the results and the success of treatments. Your physician may also require an additional **biopsy** of an affected organ, but not all patients require these.

SHOULD I SEEK A SECOND OPINION?

Although amyloidosis is a rare disease, clinical expertise has developed and expanded into amyloidosis treatment centers around the U.S. and other parts of the world. Patients seeking a second opinion before starting treatment will find amyloidosis expertise in these treatment centers. Check with your insurance company about coverage of a second opinion.

Patients seeking a second opinion at another medical facility may need to repeat all or some of their previously performed tests. Ask your physician about your ability to transfer test results between sites.

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 see the companion booklet in the AL series, **Treatment Overview for Light Chain (AL) Amyloidosis**, for more information on AL, or check out our free online tool, My Amyloidosis Pathfinder, to learn about treatment centers and set up personalized notifications for clinical trials.

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

GLOSSARY

The language of diagnostics can be confusing or overwhelming. Don't let unfamiliar words or abbreviations get in the way of your understanding of **AL amyloidosis** and how it's diagnosed. Below is a brief checklist of medical abbreviations and terms you are likely to encounter. These and other terms are more fully defined in the Glossary below.

ABBREVIATIONS

SPEP – serum protein electrophoresis
IF – immunofixation electrophoresis
sFLC – serum free light chains
LFT – liver function tests
ECHO – echocardiogram or heart ultrasound
MRI – magnetic resonance imaging
IEM - Immunoelectron microscopy

TERMS

AL amyloidosis. A progressive form of systemic amyloidosis caused by abnormal plasma cells that produce light chain proteins; these misfold into amyloid and circulate in the blood, building up deposits in multiple organs and tissues.

Amyloid. An abnormal protein composed of peptides or peptide fragments with a β-pleated sheet shape at the molecular level.

Antibodies. Proteins in the blood produced by specialized white blood cells (plasma cells) that fight infection and disease; also called immunoglobulin.

Birefringence. The phenomenon shown by certain materials in which a ray of light is split into two rays (double refraction).

Bone marrow. Soft spongy tissue found in the center of many bones; the site of blood cell production.

Biopsy. A small piece of tissue that is removed and examined under a microscope.

Carpal tunnel syndrome. A common condition that causes pain, numbness, and tingling in the hand and arm; caused when one of the major nerves to the hand, the median nerve, is squeezed or compressed as it travels through the wrist.

Clinical trial. A research study of the safety and effectiveness of new or existing treatments in patients who have provided informed consent and understand potential risks and benefits. Trials are carried out after positive results in laboratory experiments, with the goal of finding better ways to prevent, detect, diagnose, or treat a disease.

Congo red. A histological staining technique that is the gold standard technique for the diagnosis of amyloidosis.

CT Scan. Computerized tomography is the use of computers and rotating X-ray machines to create cross-sectional images (slices) of the bones, blood vessels, and soft tissues inside your body; provides more-detailed information than standard X-rays.

Electrophoresis. A laboratory test used to measure the levels of protein in blood or urine; an electrical current is used to sort proteins by their charge.

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

Free light chain (FLC). Part of an immunoglobulin (antibody) that circulates freely in the bloodstream.

Immunofixation electrophoresis. A laboratory technique that allows the detection and typing of monoclonal antibodies or immunoglobulins in serum or urine; also called protein electrophoresis.

Immunoglobulin (Ig). A protein that helps protect the body from infection; also called an antibody.

Light chains. The shorter of two protein chains that make up an antibody, known as kappa or lambda.

Nerve conduction studies. Diagnostic tests used to evaluate the function, especially the ability to conduct electrical signals, of the motor and sensory nerves of the human body.

Peripheral neuropathy. Damage to or disease affecting nerves; may impair sensation, movement, gland or organ function, or other aspects of health.

Plasma cell. An antibody-secreting immune cell that develops in bone marrow; in AL amyloidosis, these cells produce toxic light chain fragments that misfold into circulating amyloid.

Platelets. Small cell fragments in the blood that enable it to clot.

Proteins. Large, complex molecules coded by our genes that play a central role in biological processes. The work they do in cells is required to maintain the structure, function, and regulation of tissues and organs.

Ultrasound. A medical test that uses high-frequency sound waves to capture live images from the inside of your body; also known as sonography.

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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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