CONDITION

Cardiac amyloidosis

Learn how abnormal amyloid proteins can affect the heart, including symptoms, causes, testing, treatment options, complications, and follow-up care.

WHAT IT IS
Amyloid protein buildup that thickens and stiffens the heart

BODY SYSTEM
Heart and circulation

MAIN SYMPTOMS
Shortness of breath, swelling, fatigue, irregular heartbeat

WHAT CAUSES IT
Unstable transthyretin or abnormal plasma cells

HOW IT IS DIAGNOSED
Nuclear medicine scan or typed tissue biopsy

MAIN TREATMENT
Symptom control and amyloid-type-specific therapy

CAN IT BE CURED?
No, treatments can slow progression

IS IT AN EMERGENCY?
Sometimes, severe breathing trouble, fainting, persistent chest pain, or stroke signs

LONG-TERM OUTLOOK
Variable, with risk of worsening heart failure

Overview

Cardiac amyloidosis is a condition in which abnormal proteins called amyloid build up in the heart. These deposits make the heart muscle thick and stiff. Over time, the heart may have trouble filling with blood, pumping normally, or maintaining a steady rhythm.

Cardiac amyloidosis is not a single disease. The two main forms are transthyretin amyloid cardiomyopathy, called ATTR-CM, and light-chain cardiac amyloidosis, called AL amyloidosis. They have different causes and treatments, so identifying the exact amyloid protein is essential.

ATTR-CM develops when a protein made by the liver, transthyretin, becomes unstable and forms amyloid deposits. It may be related to aging or to an inherited gene change. AL amyloidosis develops when abnormal cells in the bone marrow produce parts of antibodies

called light chains. These light chains can form deposits and directly damage the heart and other organs.

Both types can cause heart failure, meaning the heart cannot meet the body's needs as well as it should. AL amyloidosis can progress quickly and usually requires prompt evaluation by a hematology team. Earlier recognition of either type may allow treatment to begin before advanced organ damage develops.

Symptoms

Symptoms vary according to the type and stage of disease. Early symptoms may be mild or mistaken for more common heart or lung conditions.

Possible heart-related symptoms include:

Amyloid may also affect nerves, tendons, kidneys, or the digestive system. Symptoms outside the heart can provide important clues. These may include numbness or burning in the hands and feet, dizziness when standing, diarrhea or constipation, unexplained weight loss, and foamy urine from protein loss through the kidneys.

Some people with ATTR-CM have a history of carpal tunnel syndrome in both wrists, narrowing around the lower spinal cord, or a biceps tendon rupture. These problems can appear years before heart symptoms.

Easy bruising around the eyes, an enlarged tongue, or significant protein in the urine may occur with AL amyloidosis, although not everyone has these findings.

Call the treating clinician promptly about increasing swelling, a sudden change in weight, worsening shortness of breath, new palpitations, or repeated dizziness. These symptoms may require an earlier appointment or adjustment to the management plan.

Seek emergency care for severe trouble breathing, fainting, chest pain that does not quickly improve, sudden weakness on one side, difficulty speaking, or other possible signs of a stroke or heart emergency.

- Shortness of breath during activity or while lying flat
- Swelling in the feet, ankles, legs, or abdomen
- Rapid weight gain caused by fluid buildup
- Fatigue, weakness, or reduced ability to exercise
- A fast, slow, or irregular heartbeat
- Lightheadedness or fainting

- Chest discomfort

Causes and risk factors

In wild-type ATTR-CM, normal transthyretin protein becomes unstable with age. This form is not caused by an inherited gene change and tends to affect older adults, particularly men.

Hereditary ATTR amyloidosis results from a change in the TTR gene. The specific gene change can influence whether the disease mainly affects the heart, nerves, or both. A person can inherit the gene change from one parent, but not everyone who carries it develops symptoms. The age at which symptoms begin also varies.

One TTR variant, historically called V122I and now usually called V142I, is more common among people with West African ancestry. Ancestry alone does not establish a diagnosis, and genetic testing is needed to identify a variant.

AL amyloidosis is caused by an abnormal group of plasma cells in the bone marrow. Plasma cells normally make antibodies that help fight infection. In AL amyloidosis, they produce abnormal light chains that can deposit in organs. AL amyloidosis may occur with a plasma cell disorder such as multiple myeloma, but many affected people do not have myeloma.

Most AL amyloidosis is not inherited. Other amyloid proteins can rarely affect the heart, but ATTR and AL account for most cases encountered in clinical practice.

Diagnosis

No single symptom or routine heart test can confirm cardiac amyloidosis. Evaluation usually combines blood and urine testing, heart imaging, and sometimes a biopsy.

An electrocardiogram records the heart's electrical activity. It may show rhythm or conduction problems, but a normal or nonspecific result does not exclude amyloidosis.

An echocardiogram uses ultrasound to examine the heart. It can show thickened walls, enlarged upper chambers, abnormal filling, or fluid around the heart. A measurement called strain evaluates how the heart muscle contracts. A characteristic strain pattern can raise suspicion, but it cannot identify the amyloid type by itself.

Cardiac magnetic resonance imaging, or cardiac MRI, provides detailed pictures of the heart muscle. It can show patterns of tissue injury and expansion that support the diagnosis.

Blood and urine tests are used to look for abnormal light chains. The recommended assessment generally includes serum free light chains plus immunofixation testing of both

blood and urine. Standard protein electrophoresis alone may miss a small abnormal protein.

If light-chain testing does not suggest AL amyloidosis, a nuclear medicine scan using a bone-seeking tracer may help diagnose ATTR-CM. Strong heart uptake on the scan, together with typical heart findings and no evidence of an abnormal light-chain protein, can sometimes establish ATTR-CM without a heart biopsy.

A positive scan should not automatically be assumed to mean ATTR when an abnormal light-chain protein is present. Older adults can have an unrelated abnormal blood protein, and AL amyloidosis can sometimes produce scan uptake. In this situation, a biopsy may be needed.

A biopsy removes a small tissue sample. It may be taken from abdominal fat, bone marrow, another affected organ, or the heart. The amyloid protein should be typed with a reliable laboratory method because treatment depends on the protein involved.

People with confirmed ATTR amyloidosis are generally offered genetic testing to distinguish hereditary disease from wild-type disease. Genetic counseling can help explain the result and what it may mean for relatives.

Treatment and management

Treatment has two goals: reduce symptoms caused by the heart condition and slow or stop production of the amyloid-forming protein. Care often involves cardiology, hematology, neurology, genetics, and other specialists.

Diuretics like furosemide or hydrochlorothiazide , sometimes called water pills, help the kidneys remove extra salt and water. They are central to controlling swelling and breathlessness. Finding the right fluid balance can be challenging because too much diuresis may cause low blood pressure, dizziness, or kidney problems.

People may be advised to monitor their weight and swelling. The care team may also recommend an individualized sodium or fluid plan. Major dietary restrictions should not be started without guidance, especially when poor appetite or weight loss is present.

Some medicines commonly used for other forms of heart failure may be poorly tolerated because cardiac amyloidosis can cause low blood pressure or a relatively fixed amount of blood pumped with each heartbeat. Treatment decisions must therefore be individualized. Medicines should not be stopped without speaking with the prescriber.

For ATTR-CM, disease-modifying medicines can stabilize transthyretin or reduce its production. Tafamidis and acoramidis are transthyretin stabilizers. Vutrisiran reduces transthyretin production in the liver. Eligibility depends on factors such as the type and stage of disease, other health conditions, local approval, and access. These medicines can slow

progression but do not immediately remove existing deposits.

AL amyloidosis is treated by targeting the abnormal plasma cells that make light chains. Treatment may include a combination built around medicines such as daratumumab, bortezomib, cyclophosphamide, and dexamethasone. Selected patients may be considered for an autologous stem cell transplant, which uses their own blood-forming stem cells. Because heart involvement affects treatment tolerance, an experienced amyloidosis team should guide therapy.

Atrial fibrillation is a common irregular rhythm in cardiac amyloidosis. It can increase the risk of blood clots and stroke. Clinicians may recommend an anticoagulant like warfarin or apixaban , commonly called a blood thinner, after assessing bleeding risk and other factors. Rhythm procedures, pacemakers, or implantable defibrillators may be appropriate in selected cases, but they do not treat the underlying amyloid deposits.

Heart transplantation may be considered for a small number of people with advanced disease. In AL amyloidosis, control of the plasma cell disorder is also necessary. In hereditary ATTR disease with major liver and heart involvement, transplant planning is especially specialized.

Complications

Cardiac amyloidosis can lead to worsening heart failure and repeated fluid buildup. Stiff heart chambers may create high pressure in the lungs and veins even when the heart's pumping percentage appears normal.

Electrical problems may cause atrial fibrillation, a very slow heartbeat, heart block, or dangerous ventricular rhythms. Blood clots can form inside the heart, creating a risk of stroke or blockage elsewhere in the body.

Low blood pressure can result from reduced heart output, medicines, dehydration, or amyloid-related nerve damage. Kidney dysfunction may develop from reduced circulation, congestion, AL amyloid deposits, or treatment effects.

Amyloid outside the heart may cause peripheral neuropathy, which is nerve damage in the hands or feet; autonomic neuropathy, which affects automatic functions such as blood pressure and digestion; or poor nutrition from digestive symptoms and loss of appetite.

The likely course differs greatly between ATTR and AL amyloidosis and from person to person. Amyloid type, heart function, involvement of other organs, and response to treatment all affect outlook.

Follow up

Follow-up should be coordinated with clinicians experienced in the specific amyloid type. Visits may include a symptom review, physical examination, electrocardiogram, blood tests, and assessment of kidney and liver function. Heart-related blood markers and repeat imaging may be used to follow the condition, although the schedule depends on the individual situation.

People receiving AL therapy need close monitoring of light-chain levels, blood counts, organ function, infections, and treatment side effects. Those taking an ATTR medicine need follow-up for symptoms, heart function, medication tolerance, and progression outside the heart.

At home, it may be useful to track weight, swelling, breathing, blood pressure if advised, and ability to complete usual activities. Contact the care team if symptoms steadily worsen rather than waiting for the next routine visit.

Relatives of a person with hereditary ATTR amyloidosis may be offered genetic counseling. Testing is a personal choice and is best performed with counseling about possible medical and family implications.

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