Myeloma Patients Europe

# Question & Answer

MYELOMA PATIENTS EUROPE

## Diagnosis, treatment and monitoring of AL amyloidosis


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# Table of content

AL amyloidosis is commonly misdiagnosed or overlooked because its symptoms can mimic those of more common illnesses. It is important to diagnose AL amyloidosis as quickly as possible, because early treatment may prevent or mitigate further organ damage. See MPE's AL amyloidosis guide to learn more about AL amyloidosis.

This Q&A explains the following:

## How is AL amyloidosis diagnosed?

Diagnosing AL amyloidosis generally involves several tests, including blood tests, urine tests, imaging and biopsies. The following list outlines the most common tests that are performed to establish an AL amyloidosis diagnosis (see MPE's AL amyloidosis guide for more details about these tests):

### Blood and urine tests

These can be used to determine if there are abnormal proteins produced by the bone marrow and which organs are involved in the disease and to what extent. These tests can also help determine the best treatment response once the diagnosis has been established. Examples of such tests are:

- **Assessing proteinuria:** 24-hour urine collection to determine protein levels in your urine. Excess protein in the urine (proteinuria), composed of albumin, can indicate that the kidneys are affected by the disease, which can lead to damage to kidneys and, ultimately, kidney failure.

- **ALP (alkaline phosphatase) levels in blood:** The levels of the enzyme alkaline phosphatase in the blood may be assessed. ALP is an enzyme present throughout the body, which is needed for the breakdown of proteins, an important part of the healthy function of cells and tissues. Abnormal ALP levels most often indicate a liver involvement.

- **Cardiac biomarker assessment:** A biomarker is a biological feature of the body that can be measured by looking at the presence or absence - and rate - of a certain biomarker. The biomarkers of cardiac health may be looked at through the examination of blood samples to investigate whether the disease affects the heart, and if it does, to what extent. Standard biomarkers include troponin I and T (these proteins are also known to enter the bloodstream shortly after a heart attack and stay in the blood days after all other biomarkers return to normal levels), NT-proBNP (which stands for N-terminal pro-brain natriuretic peptide - high levels of this biomarker can indicate that the heart isn't pumping as much blood as the body requires, this can indicate heart failure) and BNP (brain natriuretic peptide - high levels of this may also signal heart failure). Those markers were described as diagnostic tools for cardiac involvement with high sensitivity and can detect early (non-symptomatic) disease.

- **Abnormal antibody** (immunoglobulin) testing in blood, such as the serum free light chain (FLC) test: this test allows the assessment of kappa and lambda light chain levels that will be very useful for monitoring of response under therapy.

- **Immunofixation and electrophoresis:** this test can be performed on blood or urine samples. It allows the measurement of abnormal monoclonal proteins (M proteins).

The collection of urine samples is a straightforward process, although somewhat cumbersome in the case of 24-hour urine samples. For a test performed from blood, the nurse will insert a needle into a vein on your arm and extract several vials of blood. The amount withdrawn depends on the laboratory technology and protocol applied: it is usually between 30ml and 50ml distributed across several vials.

### Tissue biopsies

Biopsies are necessary to establish the diagnosis of amyloidosis and determine what type of amyloidosis you have. A biopsy involves taking a small piece of tissue from you. This is often taken from the thin layer of fat under the skin of the abdomen area (abdominal fat biopsy) or from the salivary gland. Alternatively, a biopsy can also be taken from the organ affected by amyloid deposits. The tissue samples are then stained with a dye called "Congo red stain" and examined under a microscope. Congo red reacts with the amyloid proteins; hence, they can be visualised. The amount of amyloid protein is clearly visible to the doctor, who can establish an amyloidosis diagnosis. There are additional tests (performed by the pathologist) in order to know the type of amyloid, since AL is not the only type of amyloidosis.

Specialist centres can aid with the correct diagnosis of AL amyloidosis.

### Bone marrow tests

A bone marrow biopsy must be performed to find the cells producing the free light chains. Alternatively, a bone marrow aspirate may be taken, which means that a small amount of liquid bone marrow is collected. After sample collection, Congo red staining can only be performed on bone marrow biopsy samples to determine if amyloid is present.

### Echocardiogram and imaging

An echocardiogram (or "echo") is a type of ultrasound scan used to look at the heart and nearby blood vessels. Amyloid deposits in the heart cannot be visualised with an echocardiogram but it can detect thickened cardiac walls that do not relax as they should. Alternatively, magnetic resonance imaging (MRI) can be useful for visualising certain aspects that are very specific for amyloid deposits.

Another important imaging technique is referred to as the SAP scan. SAP stands for serum amyloid P component. During this test, the patient receives an injection of this component together with a labelling agent. The amyloid deposits can then be visualised with a scanning method, thus determining the size and location of the deposits. This test is only available in few countries such as the Netherlands and the UK, so it is not mandatory for a compete clinical assessment.

### Electrocardiogram (ECG)

An ECG is a test that checks and records your heart's rhythm, and electrical activity, using electrodes placed on the skin. ECG patterns can help differentiate between AL amyloidosis and TTR cardiac amyloidosis, another type of amyloidosis.

### Specialised testing of affected organs

Specialised testing of organs may be required to determine the extent of damage to the organs affected by the disease. If signs of organ involvement are detected throughout initial testing (for example by looking at blood and urine samples), doctors may decide to carry out biopsies taken from these organs or perform other diagnostic methods (such as an echocardiogram to investigate heart health) to determine the extent and severity of organ damage.

## Is AL amyloidosis contagious?

No, AL amyloidosis is not contagious. It is also not considered a hereditary disease. There are other types of amyloidosis that are hereditary.

## What is a biopsy, and what should I expect?

As mentioned above, a biopsy is necessary for diagnosing AL amyloidosis. Generally, the term biopsy refers to the removal of tissue from any part of the body, which is then examined in a laboratory for signs of disease. Abdominal fat biopsies are relatively easy and not particularly painful. During biopsies of internal organs, a long needle is inserted into the organ that needs to be examined, and a little bit of tissue is extracted for the test. This may be painful or uncomfortable. Bone marrow biopsies must be performed in a hospital setting, and a certain resting time (generally only 30 minutes) is needed after the examination. Although you most likely won't need to be hospitalised before or after the examination, you may experience some discomfort during the days following the procedure. A long needle is inserted into one of the larger bones, usually the pelvis and a small amount of bone marrow is obtained. Bone marrow biopsies can be painful and local anaesthesia will be given. In some hospitals you can be sedated for the duration of the test.

Alternatively, a bone marrow aspirate may be taken, which means that a small amount of liquid bone marrow is collected from you. This happens with the same method, i.e., by inserting a needle into the bone and extracting some liquid material from the marrow. It is quicker and less exerting; however, this is not advised in AL amyloidosis because an aspirate cannot be examined for amyloid presence.

## What symptoms are characteristic for AL amyloidosis?

### Heart:

- **Shortness of breath:** You may experience a tight sensation in the chest and feel the need to breathe more or quicker than usual, especially when exercising such as climbing stairs.
- **Palpitations (arrhythmias):** Palpitations are feelings or sensations that the heart is racing or pounding. You may experience an unpleasant awareness

of your own heartbeat, or feel like your heart skips a few beats, or feel a pounding sensation in the chest, throat, or neck.

- **Chest pain:** Pain can be experienced as dull, sharp, burning, aching, or a stabbing feeling.
- **Fatigue:** You may tire easily, even from day-to-day activities that normally would not tire you out.
- **Light-headedness:** You may feel dizzy, or have the feeling that you might faint, especially when standing up .

### Lungs:

- **Noisy, wheezing, troublesome or uncomfortable breathing.**
- **Cough.**

### Gastro-intestinal tract (mouth, oesophagus, stomach, small intestine, large intestine and anus):

- **Poor appetite:** You may experience a loss of appetite and struggle to consume enough food.
- **Bloating or excessive gas:** Symptoms of this include frequent burping and passing of gas, abdominal pain, pressure, or cramps. You may experience a feeling of fullness and a visible increase in the size of your abdomen.
- **Constipation or diarrhoea:** Your stools may become loose or your bowel movements may decrease.

### Nervous system:

- **Carpal tunnel syndrome (or median nerve compression):** This is a condition characterised by numbness, tingling, or weakness in the hand. It is caused by pressure on the median nerve, which innervates the arm, all the way to the hand, passing through the wrist inside the carpal tunnel.
- **Peripheral neuropathy:** This is experienced when damage occurs to the nerves located outside of the brain and spinal cord. It is usually felt as numbness, burning and/or tingling in the hands or feet.
- **Autonomous neuropathy:** You may experience low blood pressure when standing up, difficulty swallowing and difficulty urinating.
- **Muscle weakness:** Muscle weakness is especially common in the legs.

### Liver :

- **Enlarged liver (hepatomegaly):** This means that the liver is swollen to a larger size than usual.

- **Increased alkaline phosphatase (ALP) level:** ALP is an enzyme present throughout the body, which is needed for the breakdown of proteins. Elevated levels of it usually indicate an underlying medical condition, most commonly related to the liver, bones, or gallbladder. Elevated ALP predicts progressive liver involvement, which needs to be treated to prevent further organ damage.

### Kidney:

- **Excessive bubbles in the urine:** Your urine may become foamy, which can be the sign of excess protein in the urine, and can indicate kidney abnormalities. A small amount of protein in the urine is considered normal, however, too much can signal a problem.
- **Decreased urination:** You may urinate less than normal.
- **Nocturia:** You may feel the need to get up at night to urinate.

### Other symptoms:

- **Brittle nails:** Fingernails and toenails may become weaker and break more easily.
- **Oedema:** A visible swelling of the feet or legs may be present.
- Bruising or bleeding more easily than usual.
- Purple colour in folds of skin .
- **Periorbital purpura:** Purple colour on the eyelids and/or around the eyes.
- **Macroglossia:** Your tongue can become enlarged if the disease affects the oral tissues and you may experience painful joints.

## When should I see a doctor and what are the warning signs of AL amyloidosis?

You should see a doctor if you have any of the above symptoms and an M protein, or elevated free light chains in the blood. Early diagnosis of AL amyloidosis is vital in order to prevent irreversible organ damage.

## What is the prognosis of AL amyloidosis? How long will I live?

It is difficult to make a general statement about the prognosis of AL amyloidosis, because is highly dependent on which organs are affected by the disease and on the extent of organ damage present. Notably, the extent and severity of heart involvement is considered the most significant determinant of the prognosis of AL amyloidosis. When extensive damage to the heart is already present at the point

of diagnosis, patients generally have a poor prognostic outlook (with a high risk of death within a few months). Furthermore, response to treatment is an important determining factor in how long you may live. If you respond well to treatment, you may survive for 10 years or more.

## What treatment options exist for AL amyloidosis?

AL amyloidosis treatment is often highly individualised because the disease manifests differently from patient to patient. The treatment options available to you will largely depend on which of your organs are affected by your illness and to what degree. There is only one approved treatment for AL amyloidosis, and multiple myeloma treatments are often prescribed to AL amyloidosis patients. The approved combination of medications is the immunotherapy drug daratumumab together with the chemotherapy drugs cyclophosphamide and bortezomib with corticosteroid dexamethasone (Dara-CyBorD). Further effective combinations that your doctor may recommend are bortezomib, the chemotherapy drug melphalan and dexamethasone (BMDex), as well as cyclophosphamide, bortezomib and dexamethasone (CyBorD). Immunomodulatory drugs (such as lenalidomide or pomalidomide) can also be prescribed.

Another effective treatment approach is carrying out an autologous stem cell transplant (ASCT). An ASCT involves the use of your own blood stem cells to replace your bone marrow. This procedure is often effective because it leads to the eradication of the plasma cells producing amyloid proteins. ASCT can significantly prolong survival, however, only approximately 20% of patients qualify for this, as you need to be in otherwise good health to safely undergo the procedure.

Reversal of organ damage, as well as the removal of amyloid deposits that are already present in tissues is challenging. However, there are some novel drugs in clinical trials that are designed to enable the removal of amyloid deposits.

See MPE's factsheets on treatments here.

## How long does treatment usually last?

Treatment duration greatly varies and is determined by your overall health, the stage of your illness, which organs are affected by your disease, how you respond to therapy and how you tolerate it. An ASCT procedure lasts approximately four weeks, however, it might take several more months for you to recover fully and resume your normal day-to-day activities. In case of regimens like Dara-CyBorD, you may receive several treatment cycles. Normally, each cycle lasts around 28 days and six cycles are carried out followed by daratumumab maintenance therapy for a total of two years. The time without treatment between cycles may last 1-4 weeks.

## How effective are the existing treatment options?

Due to the large variations between the manifestation of AL amyloidosis, it is challenging to provide an overview on treatment efficacy. However, both ASCT and therapeutic combinations such as Dara-CyBorD can lead to a significant reduction in plasma cells and, consequently, the circulating free light chains. Therapy can significantly prolong survival, however, due to the damage that AL amyloidosis causes to the organs (e.g., kidneys, liver and heart), many therapeutic options may not be tolerated by patients.

## Can I choose my treatment?

Ideally, you should have regular, extensive consultations with your doctors and healthcare team about your disease, your treatment preferences and your overall health condition. Your doctor will suggest treatment options and advise you on which treatment would be most beneficial for you. The choice is always yours, but the options might be limited. You can always ask for a second opinion if you have any doubt about the care you are receiving. You can also inform yourself about treatment options, their efficacy and side effects. MPE has several resources that can support you with this, including our factsheets and AL amyloidosis guide.

## What are the most common side effects of treatment?

AL amyloidosis treatment, especially chemotherapy drugs, may produce side effects that can be challenging to cope with. However, it is important to keep in mind that side effects are almost always reversible and will go away after treatment is complete, and that there are several options to help minimise or prevent them. Furthermore, most patients will not experience all the side effects listed.

Some of the most common side effects include:

- Anaemia. (deficiency in the number or quality of red blood cells)
- Appetite loss.
- Constipation.
- Diarrhoea.
- Dysphagia. (difficulty swallowing)
- Oedema. (fluid retention that leads to swelling)
- Fatigue.
- Hair loss.

- Infertility. (this may or may not be reversible, depending on the treatment. If you are planning on having children in the future, make sure you discuss this with your doctor before starting treatment)
- Nausea and vomiting.
- Neutropoenia. (a lower level of neutrophils, a type of white blood cell, in the blood)
- Pain.
- Peripheral neuropathy. (damage to the peripheral nervous system (PNS), which includes all the nerves in the body except the brain and spinal cord)
- Skin conditions.
- Thrombocytopenia. (low level of blood platelets, an essential blood component necessary for blood clotting)
- Infections.

## How can treatment side effects be handled?

It is important to consult your doctor and healthcare team about any side effects you are experiencing, as they might be able to alleviate or minimise your discomfort, or offer you support. For some side effects, standard medications like anti emetics and antibiotics are prescribed to be used in combination with chemotherapy. For advice on coping with the treatment side effects listed above, have a look at MPE's AL amyloidosis guide.

## Do I need to be hospitalised? And for how long?

This depends on several factors, particularly how advanced your illness is, which organs it affects and to what extent. For example, a patient with AL amyloidosis with advanced heart involvement may have to be hospitalised to receive necessary emergency care. Certain diagnostic tests and several treatment options (for example, stem cell transplant) may involve extended hospital stays, sometimes for several weeks in a row. In most cases, however, hospitalisation is not needed.

## How will my illness be monitored?

You will have regular check-ups from the time of your diagnosis – the frequency may vary in different countries in Europe, but they are likely to be every few weeks to months, and will be set by your doctor. To monitor your disease, your healthcare team will generally use the same tests used to diagnose AL amyloidosis (these include blood tests, urine tests and imaging, see page 4). You will be monitored to determine if you are responding well to the treatment you

are receiving, or while in remission to determine if you need to start treatment again. If your disease seems to be progressing or worsening, or if you are suffering from treatment side effects, the doctor will most likely discuss new treatment options with you.

## Are there any warning signs after treatment that my health is worsening?

If your symptoms return, or you notice new symptoms, notify your doctor. The doctor will carry out tests to determine if your disease is progressing, in which case, you may need to start a new treatment, or your treatment regime might have to be revised. If you are currently receiving treatment, it is possible that you are experiencing side effects. Regardless, it is important to consult your healthcare provider as they may be able to offer medications that will lessen your discomfort, or they may decide to modify your dose, dosing schedule, or treatment regime.

## What can I do to preserve my health and wellbeing beyond available treatment options?

It is important to follow a healthy diet, if you are an AL amyloidosis patient. How much you drink a day and your salt and protein intake are crucial. It is advisable to consult a dietician.

Furthermore, taking up some form of exercise can be beneficial. Exercise may reduce fatigue, and feelings of anxiety and depression, and build muscle strength. Aerobic exercises (walking, cycling, using a cross trainer etc.) must be performed carefully especially by patients with heart involvement. If you are not used to regular physical activity, make sure you speak to your doctor in advance and then build up your routine gradually, while listening to your body and staying within your limits to avoid over-exerting yourself. You could consider seeing a physiotherapist, who can help to assemble an exercise routine that fits your needs and ability.

To preserve your mental health, try to maintain a positive frame of mind and give yourself sufficient time to rest and recuperate. Receiving a diagnosis of AL amyloidosis can be a stressful experience so, if you are finding it difficult to cope, please reach out to a mental health professional and/or a patient organisation. A patient organisation may be able to put you in touch with a peer helper. Discussing your struggles with someone who is living with the same disease may help relieve the negative feelings you may be experiencing.

Since fatigue is a major issue for many patients with this disease, getting plenty of sleep is also important.

## Where can I turn to for support and more information?

There are several useful resources available on the MPE website (for example, our AL amyloidosis guide and factsheets), and make sure you follow MPE on our social media channels (Facebook, Twitter and YouTube) for regular updates related to myeloma and AL amyloidosis. It may also be a good idea to join a local patient/advocacy group that represents amyloidosis patients, if one exists in your country, as it can be very helpful to form connections with others who are struggling with the same illness as you. Furthermore, you will gain access to valuable information about the disease and treatment options, which healthcare professionals to turn to, self-caring and career suggestions etc. The group might be hosting social events as well, and attending these can be a motivating, informative and positive experience.

Examples of such groups are:

- Austria: Leben mit Amyloidose. www.amyloidosis-austria.at
- France: Association Française contre l'Amylose. https://amylose.asso.fr
- Germany: Amyloidose Selbshilfegruppe. www.amyloidose-selbsthilfe.de
- Israel: Amyloidosis Israel. www.amyloidosis.org.il
- Italy: Associazione Italiana contro leucemi limfomi e mieloma (AIL). www.ail.it
- Macedonia: Association for help and support of patients and their caregivers with hematological diseases (HEMA). www.hema.org.mk
- Netherlands: Stichting Amyloïdose Nederland (SAN). www.amyloidose.nl
- Norway: Blodkreftforeningenn. www.blodkreftforeningen.no

- Slovakia: Slovak Myeloma Society (SMyS). www.myelom.sk
- Slovenia: Association of Patients with Blood Diseases Slovenia www.drustvo-bkb.si
- Spain: Asociación Española de Amiloidosis (AMILO). www.amilo.es
- United Kingdom: Myeloma UK. www.myeloma.org.uk

Alternatively, you may consider reaching out to an umbrella organisation (like MPE) or other non-profit organisations that represent AL amyloidosis patients for support and information. Examples of such organisations are:

- Amyloidosis Alliance. www.amyloidosisalliance.org
- Amyloidosis Foundation. www.amyloidosis.org
- Amyloidosis Research Consortium. www.arci.org

# Glossary

**Amyloid:** A type of wrongly assembled (misfolded) protein that forms insoluble aggregates, which deposit in tissues and organs.

**Antibodies:** proteins that help the body fight infection; these are made up of large (heavy chain) proteins and small (kappa and lambda) light chain proteins.

**Autologous stem cell transplant (ASCT):** the patient receives an infusion of stem cells that was derived from him/her.

**Biomarker:** a biological feature/characteristic that can be objectively measured and used to investigate the functioning of certain parts/processes within the body, as well as to monitor if treatments are effective.

**Biopsy:** the removal of a small quantity of tissue from any part of the body to examine it for disease.

**Bone marrow:** the spongy material inside some of the larger bones, which contains stem cells. These stem cells can develop into blood cells.

**Cell clones:** a group of identical cells that originate from the same cell.

**Diagnosis:** the process of finding out which disease or condition explains a person's symptoms.

**Fibrils:** a thread- /fibre-like structure made up of proteins.

**Incidence:** the occurrence of new cases of disease or injury in a population over a specified time period.

**Median:** middle value in a list of data/numbers.

**Plasma cells:** a type of white blood cell (an immune cell) that makes large amounts of a specific antibody. Plasma cells develop from B cells that have been activated.

**Prevalence:** the proportion of a population that has a specific characteristic (or a given disease) in a given time period.

**Proteins:** essential components of biological organisms. They are made up of amino acids and have to assemble into a correct form/shape (folding) to fulfil their biological purposes.

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MPE is a network of European myeloma patient organisations. It supports national patient organisations to improve treatment and access for patients in their countries, and helps inform and raise awareness on a European level through its educational programmes. Please note, this information does not replace the information provided by your doctor. If there is anything that is not clear to you, please always ask your clinical team.

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Q&A