MYELOMA CANADA
MAKING MYELOMA MATTER

InfoSheet

AMYLOID LIGHT CHAIN (AL) AMYLOIDOSIS*

What is AL amyloidosis?

In AL amyloidosis, amyloid protein fibre deposits build up in tissues and organs throughout the body (e.g., heart, kidneys, liver, soft tissues, nervous and digestive systems).

- Amyloid protein fibres gradually damage tissues and organs which can cause many different symptoms (See "What are the symptoms and complications of AL amyloidosis?");
- Amyloid protein fibres can affect more than one organ at the same time;
- All patients have a different amyloid protein fibre deposition pattern.

What causes AL amyloidosis? Is there a cure?

The exact cause of AL amyloidosis is unknown. The belief is that the disease is likely attributed to a combination of genetic and environmental factors. A cure for AL amyloidosis has not yet been found.

Are AL amyloidosis and myeloma related?

Both AL amyloidosis and myeloma result from abnormal plasma cells, a type of white blood cell produced in the bone marrow.

- People may have AL amyloidosis on its own or with myeloma.
- While some people with myeloma may also have, or develop, AL amyloidosis, it is rare for people with AL amyloidosis to develop myeloma.

What are the symptoms and complications of AL amyloidosis?

Symptoms may be hard to detect since they are similar to those of other diseases (e.g., heart/kidney disease), and so not all people living with AL amyloidosis will experience the same symptoms and complications. Over time, one or more symptoms can become dominant and result in complications which will depend on the organ(s) most affected by the amyloid protein fibre deposits.

The most common symptoms include:

- Shortness of breath, dizziness, fatigue
- Swollen legs/feet
- Bruising (e.g., around the eyes, known as raccoon eyes)
- Skin rash, nail changes
- Swollen tongue (macroglossia)
- Swelling of both shoulder joints
- Peripheral neuropathy: Pain, numbness, and tingling in the extremities
- Digestive problems: Diarrhea, nausea, weight loss
- Carpal tunnel syndrome: Wrist tingling/pain and/or pins/needles in the hands/fingers

The most common complications include:

- **Heart (cardiac) problems:** Amyloid protein fibre deposits in the heart can cause the heart to become stiff and enlarged, impairing its ability to efficiently pump blood through the body.

  > **Symptoms include:** Fluid retention (edema) causing swollen legs/feet/abdomen and rapid weight increase, shortness of breath, irregular heartbeat (arrhythmia), low blood pressure, and fatigue.

- **Kidney (renal) problems:** Amyloid protein fibre deposits in the kidneys can “clog” their filtering elements, damage them, and impair their ability to maintain a normal salt-to-water balance in the body.

  > **Symptoms include:** Fluid retention (edema) causing swollen legs/feet/abdomen and rapid weight increase, blood in urine, frothy urine, anemia, and loss of appetite.

*Other forms of amyloidosis are not discussed in this InfoSheet.

What tests are used to diagnose and monitor AL amyloidosis?

Prompt initial assessments are crucial for the diagnosis of AL amyloidosis. The most common tests used to diagnose the disease include:

- Blood tests:
  - **Serum free light chain assay** - measures normal and abnormal light chains
  - **Complete blood count** - measures red blood cells, white blood cells, and platelets
- 24-hour measurement of urine protein
- Bone marrow biopsy: Looks for and quantifies abnormal plasma cells
- Heart biomarkers (BNP, NT-proBNP), kidney function (creatinine clearance), and liver function tests
- Heart-specific tests (e.g., echocardiogram, electrocardiogram, heart MRI)
- Tissue biopsy: Removal and examination of some tissue from the affected organ(s). This is used to identify - or type - the amyloid protein affecting the tissues and/or organs. Results often take longer but are key to diagnosing the disease.

The same tests are used to monitor for disease relapse.

How is AL amyloidosis treated?

Treatments for AL amyloidosis are similar to those for multiple myeloma. Newly diagnosed AL amyloidosis patients may benefit from:

- treatment with a combination of drugs called CyBorD (cyclophosphamide, bortezomib [Velcade], dexamethasone);
- daratumumab (Darzalex) in combination with CyBorD (may not be available in all provinces/territories);
- high-dose therapy and autologous stem cell transplantation. (See Myeloma Canada's *High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide* on Myeloma Canada's website, myeloma.ca, under Resources.)

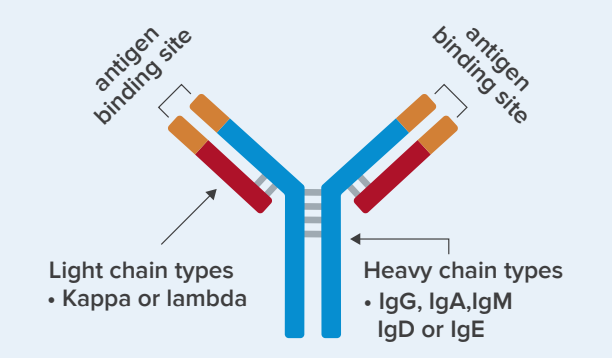
At relapse, new amyloid protein fibre deposits build-up in tissues and/or organs. Treatment should be individualized based on previous therapies and potential side effects. Relapsed AL amyloidosis may be treated with the same combination of drugs as before or a different combination of drugs.

Supportive care treatments can be given alongside AL amyloidosis treatment to control or alleviate the symptoms and complications of the disease, as well as any side effects that may result from the treatment itself.

Where do amyloid protein fibres come from?

Healthy plasma cells produce a variety of antibodies (proteins known as *immunoglobulins*) that circulate in the blood and are critical to the body's immune system function. (See Figure 1)

Figure 1. Structure of an antibody (immunoglobulin)



In AL amyloidosis, abnormal plasma cells:

- overproduce unstable immunoglobulin light chain fragments that circulate in the blood;
- produce abnormal immunoglobulins that have no useful function.

Unstable immunoglobulin light chain (e.g., kappa or lambda) fragments can misfold or "become sticky" and link together to form amyloid protein fibres.

Can amyloid protein fibre deposits be broken down by the body?

Amyloid protein fibre deposits, or protein fibres, are broken down extremely slowly (months to years) by the body.

Can amyloid protein fibre deposits be broken down by treatment?

Treatments for AL amyloidosis cannot effectively break down amyloid protein fibre deposits.

Treatment can:

- kill abnormal plasma cells to prevent new deposits from forming;
- allow for effective disease control, symptom reduction, and improved quality of life;
- result in periods of remission where the disease is not active or causing symptoms.

Over time, AL amyloidosis will likely become active again (disease relapse).

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