Amyloidosis is a group of rare, serious conditions caused by a build-up of an abnormal protein called amyloid in organs and tissues throughout the body. The build-up of amyloid proteins (deposits) can make it difficult for the organs and tissues to work properly.

Without treatment, this can lead to organ failure. Early diagnosis of amyloidosis is essential to minimise organ damage and improve prognosis.
AMYLOIDOSIS DIAGNOSIS PATHWAY

TYPES OF AMYLOIDOSIS

1. AL amyloidosis
   (light chain amyloidosis)
   This is the most common form, occurring when abnormal plasma cells in the bone marrow produce misfolded light chain proteins. These enter the blood stream and form amyloid deposits in the tissues and organs causing complications. AL amyloidosis can affect the kidneys, heart, skin, liver, spleen, nerves, tongue or digestive system (bowels). 60% of patients will present with 2 or more organs involved.

2. ATTR amyloidosis
   ATTR amyloidosis is caused by amyloid deposits from abnormal versions of a protein called transthyretin (TTR). There are two types:• Hereditary (familial) ATTR amyloidosis where people have an inherited mutation of the TTR gene and produce abnormal TTR proteins, which form amyloid deposits. These deposits usually affect the nerves and/or heart, although the digestive system and kidneys can be affected. • Wild-type ATTR amyloidosis is non-hereditary. It is like hereditary ATTR, except the deposited TTR protein is the normal, non-mutated TTR protein. It most commonly affects the heart and can cause carpal tunnel syndrome (this may be an early symptom). This mostly affects people over the age of 60.

3. AA amyloidosis
   AA amyloidosis is very rare and occurs as a reaction to another illness, e.g., chronic inflammatory disease (such as Crohn’s disease and rheumatoid arthritis), chronic or recurrent infections (such as tuberculosis) and some types of cancer (such as Hodgkin’s Lymphoma). In response to the infection or inflammation, the body produces serum Amyloid A (SAA) protein at high levels. Where this reaction is ongoing, the SAA can form amyloid fibrils and deposit in tissues. The organs most commonly affected are the kidneys. Complications can occur for some patients in the liver, spleen (which may be enlarged), thyroid, digestive tract, or heart. Heart involvement is very rare.

AMYLOIDOSIS SIGNS AND SYMPTOMS

If a patient presents with one, or particularly more, of the following unexplained symptoms, you should consider testing for amyloidosis:

- Severe weakness and fatigue, especially during exercise.
- Oedema (swelling in legs, abdomen or generalised swelling).
- Numbness or painful tingling in hands or feet (peripheral neuropathy).
- Numbness, tingling and pain in wrist, hand or fingers in both hands (carpal tunnel syndrome).
- Shortness of breath, especially during exercise.
- Foaming urine.
- Diarrhoea or constipation.
- Easy bruising.
- An enlarged tongue, which sometimes looks rippled around the edge (macroglossia).
- Difficulty swallowing or eating.
- Skin bleeding (purpura), especially spontaneous in the neck and face, and around the eyes ("racoon eyes").
- Low blood pressure, and dizziness when standing up.
- Abnormal heartbeat (I.e. symptoms of atrial fibrillation).

In most cases, the above-listed signs and symptoms are not due to amyloidosis. However, doctors treating a patient with these symptoms should carry out further investigations or refer the patient to secondary care, particularly if:

- The signs and symptoms listed above occur together without any apparent cause.
- The patient has unexpectedly presented at the GP with such symptoms, without any resolution.
- Initial tests show M-proteins or free light chains detected in the blood or urine.
- There is evidence of a longstanding inflammatory disease or infection.

AMYLOIDOSIS DIAGNOSIS PATHWAY

If you suspect a patient has amyloidosis, based on their symptoms and test results, you should contact or refer them to a specialist amyloidosis clinic, haematologist or other relevant specialist (e.g., cardiologist or nephrologist) for further tests and investigations.

FURTHER TESTS AND INVESTIGATIONS

- Bone marrow biopsy and aspirate, if M-protein is present.
- Tissue diagnosis and typing: biopsy of affected organ or abdominal fat pad, Congo red staining to identify amyloid fibrils, mass spectrometry (or other accepted method for amyloid deposits typing according to guidelines).
- Electrocardiogram.
- Echocardiogram.
- 99m-Tc-PYP/DPD/HMDP scan (particularly if a patient has cardiac symptoms).
- Cardiac Magnetic Resonance (CMR) or Magnetic Resonance Imaging (MRI) scans.
- Chest X-ray.
- Genetic testing (particularly where ATTR is indicated).

SPECIALIST AMYLOIDOSIS CENTRES

In some European countries, there are Amyloidosis Centres of Expertise which specialize in the diagnosis and treatment of AL amyloidosis and other types of amyloidosis. These are listed below:

- National Amyloidosis Centre, University College London, UK
- Amyloidosis Research and Treatment Centre, University of Pavia, Italy
- Amyloidosis Centre of Expertise, University Medical Centre, Groningen and Utrecht, The Netherlands
- National and Kapodistrian University of Athens, Greece
- National Reference Centre for Amyloidosis, CHU Limoges
- Amyloidosis Centre, Heidelberg University Hospital, Germany
- University of Uppsala, Sweden
- University Hospital of Salamanca-IBSAL, Salamanca, Spain
- Hospital Clinica de Barcelona, IDIBAPS, Barcelona, Spain
- University Hospital Puerta de Hierro Majadahonda, Madrid, Spain
ADDITIONAL RESOURCES


