

## CLINICAL DIAGNOSIS GUIDELINES FOR TRANSTHYRETIN AMYLOIDOSIS

Amyloidosis is a rare disease caused by a buildup of abnormal proteins in the body's organs and tissue.

Diagnosing amyloidosis can be difficult because symptoms often seem unrelated. In fact, an amyloidosis diagnosis is generally delayed three to four years.<sup>1</sup> The disease is also frequently misdiagnosed.

Delayed diagnosis or misdiagnosis means delayed treatment, allowing amyloidosis to progress and increasing the risk of premature death for patients.

Recent guidelines reflect global consensus on the clues that lead to a diagnosis of transthyretin amyloidosis, a specific type of the disease. This form of amyloidosis can be hereditary, where a genetic mutation spans multiple generations, or spontaneous, where no genetic mutation exists.

Guidelines simplify disease patterns and highlight commonly affected populations. By bridging the gap between the onset of symptoms and the beginning of treatment, the guidelines can help to improve patients' quality of life and slow disease progression as early as possible.



*Q: What symptoms should cause a health care provider to suspect amyloidosis?*

Common disease patterns provide important clues for diagnosis, the guidelines explain. Early indicators include:

- Neuropathy, a tingling or numbness in the limbs
- High blood pressure that resolves over time
- Gait disorders, marked by abnormal movement or positioning of the body
- Heart rhythm disorders
- Cardiac hypertrophy, enlargement or thickening of the heart muscle.

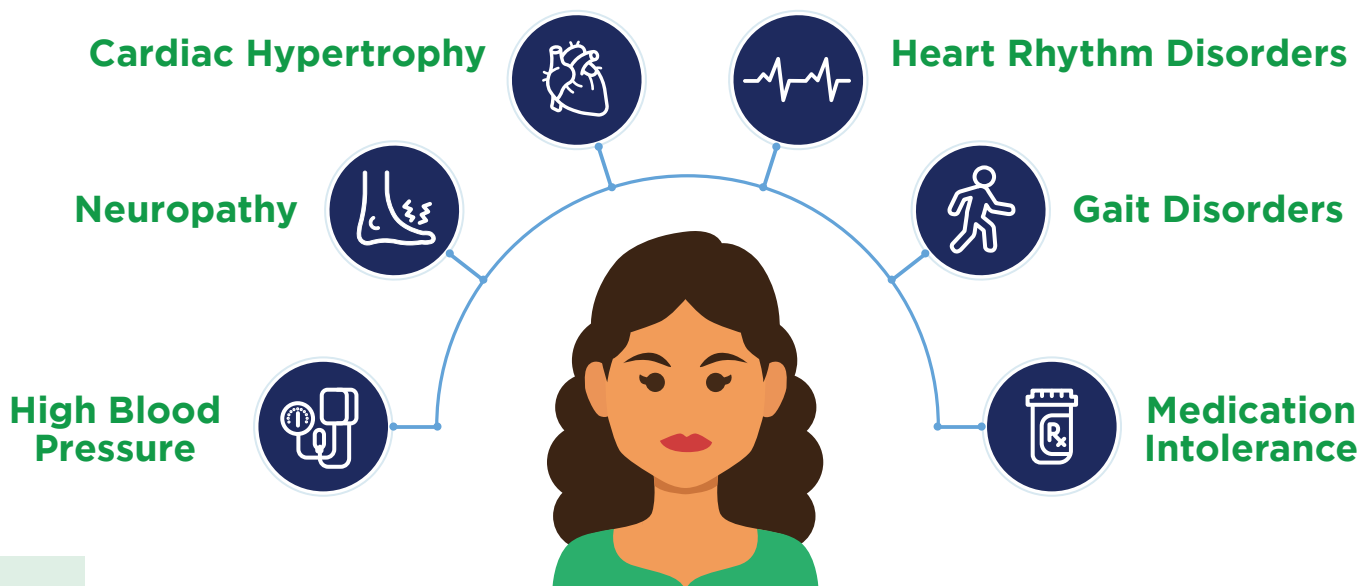
Another telltale sign may be intolerance of certain medications. For example, blood pressure medications like beta blockers and

calcium-channel blockers may be poorly tolerated by people with amyloidosis.

Patients and providers should also pay attention to what appear to be coincidental symptoms. These may include:

- Bilateral carpal tunnel syndrome
- A history of orthopedic procedures, especially those involving the lower spine
- Spontaneous ruptures to the biceps tendon
- Unexplained weight loss and eye disorders.

Together, these symptoms may signal amyloidosis, particularly in older patients or those with a family history of the disease. Even in the absence of symptoms, screening family members is important for patients with a family history of the disease.





## *Q: Why is early diagnosis important for amyloidosis?*

Amyloidosis is a debilitating, progressive disease. Without early intervention, patients may lose function that they might never regain. They also may have a poor life expectancy. Recent studies suggest a survival rate of only two-12 years after diagnosis.<sup>1-2</sup> Outcomes are particularly dire for those with cardiac involvement.

### **Early intervention can improve a patient's life significantly.**

Research indicates that treatment is more effective, and overall results are better, when providers can intervene at the onset of the disease.

## *Q: Are most health care providers aware of amyloidosis?*

Sometimes delays in diagnosis stem from providers' lack of awareness about amyloidosis. Though certain forms of amyloidosis are not as rare as once believed, the disease can be difficult to diagnose.<sup>3</sup> Given the complexity and variability of symptoms, generalists and even certain specialists may not recognize all the signs.

In addition, too few centers and specialists are dedicated to amyloidosis management. Because amyloidosis symptoms vary so widely, a given patient's case can become fragmented across different specialists and subspecialists.

Lastly, the medical community may overemphasize the disease's rarity and harbor a mistaken belief that amyloidosis is not treatable. This can discourage providers from focusing on the disease.

*Q: How can amyloidosis symptoms be misinterpreted?*

Misdiagnosis is a common challenge for people with rare diseases. When health care providers struggle to make an accurate diagnosis, patients are often treated for their individual symptoms rather than for the disease itself. Amyloidosis patients often face this challenge.

People with cardiac amyloidosis, for example, are commonly misdiagnosed with other cardiovascular conditions. Because these patients can experience shortness of breath, fatigue and swelling of the extremities, they may experience heart failure. But rather than identifying amyloidosis as the root cause, health care providers may mistakenly attribute the heart failure to hypertension or coronary artery disease.

Guidelines now urge health care providers to have a “high index of suspicion” about possible amyloidosis when patients exhibit clinical signs.<sup>3</sup>

Likewise, people with neurologic symptoms from amyloidosis may be misdiagnosed with other neurological conditions. Symptoms such as uncontrolled nerve pain and weight loss may lead to a misdiagnosis of diabetic neuropathy. Symptoms such as loss of balance and nerve pain may be diagnosed as lumbar spinal stenosis, where the spinal canal narrows and compresses nerves. Again, the diagnosis of lumbar spinal stenosis may be accurate, but the physician may not link the condition to amyloidosis.



## *Q: Does age complicate an amyloidosis diagnosis?*

Seniors are most frequently diagnosed with amyloidosis. Diagnosing patients at this stage of life presents unique challenges, as the guidelines explain. Older patients may already face preexisting conditions like hypertension, diabetes and heart disease. Symptoms from amyloidosis may be attributed to those pre-existing conditions, making diagnosis more complicated.

The symptoms of amyloidosis can cause a decline in neurologic function, which can resemble the natural aging process in an older person. Clinicians may need a higher degree of suspicion to identify amyloidosis in these patients. Sometimes this means more testing and specialist consultations. In cases of rapidly progressive decline out of proportion with normal aging, health care providers should consider the possibility of amyloidosis.

To simplify the process, the guidelines also suggest that practitioners consider

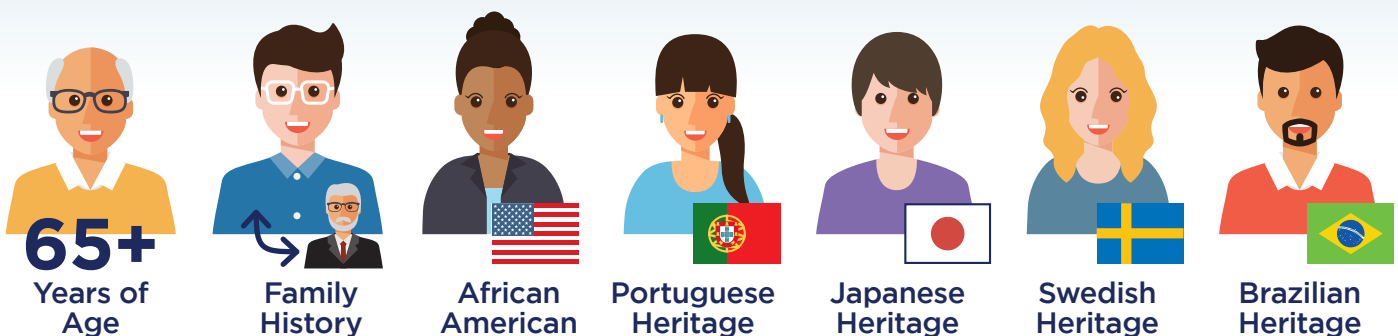
amyloidosis whenever an older patient experiences worsening neuropathy alongside GI or cardiac complications.

## *Q: Do genetics and country of origin predispose people to amyloidosis?*

Transthyretin amyloidosis can be genetic. People with a family history of the disease should take note if they begin to experience progressive nerve pain, numbness or tingling with an unknown cause or are diagnosed with the neurological disorder CIDP, which is a common misdiagnosis for hereditary amyloidosis. Genetic counseling can help if a close family member is diagnosed with hereditary amyloidosis.

The diagnosis of hereditary transthyretin amyloidosis should be considered, particularly for people with ancestors from Portugal, Japan, Sweden and Brazil, where amyloidosis is more common. African Americans are also at increased risk but typically have cardiac symptoms.

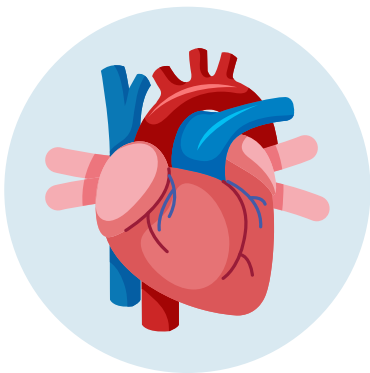
## *Who Is Predisposed to Amyloidosis?*



### *Q: How can diagnostic tools help?*

Multiple tools can help diagnose amyloidosis or monitor disease progression. As the new guidelines explain, clinicians should choose their tools and tests based upon the type of symptoms their patient experiences.

Testing for patients with **primarily cardiac symptoms** may include:



- **Electrocardiography**, which measures electrical activity in the heart. It can provide useful information on cardiac abnormalities related to the disease.
- **Echocardiography**, a test that uses sound waves to produce images of the heart. It is a low-cost, widely available tool that can identify heart abnormalities related to amyloidosis.
- **Cardiac magnetic resonance imaging**, which allows clinicians to analyze cardiac tissue and differentiate amyloidosis from nonamyloid disorders that cause thickening of the heart's walls.
- **Myocardial scintigraphy**, which traces the blood supply to the heart. This test can identify amyloid deposits early, which is important for early detection and halting disease progression.

Testing for patients with **neurological symptoms** may include:



- **DNA sequencing**, to look for the amyloidosis mutation, amyloid typing and biopsy of where the amyloid deposits may exist.
- **Bone scintigraphy**, which can be particularly helpful when biopsies come back negative but the clinician still suspects amyloidosis.
- **Nerve conduction studies**, which can identify the presence or location of nerve damage and gauge its impact.

The guidelines make clear that a holistic assessment approach includes testing, collaboration and consultation across multiple medical specialties.



## CONCLUSION

Diagnosing amyloidosis early gives patients and clinicians the best chance to take control of symptoms and to slow the progression of the disease. With the help of new guidelines, health care providers across disciplines can identify amyloidosis nearer to the onset of the disease, protecting patients' lives and quality of life by providing the most effective treatment as soon as possible.

## REFERENCES

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