Treatments for Hereditary Transthyretin Amyloidosis With Polyneuropathy

By **Sarah Gleim**

Medically Reviewed by **Laura J. Martin, MD** on February 20, 2024

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What Is Hereditary Transthyretin Amyloidosis With Polyneuropathy?

Hereditary transthyretin amyloidosis with polyneuropathy (hATTR) is a rare disease caused by a gene mutation you inherit from one of your parents. This means the gene – in this case, the transthyretin (TTR) gene – is different from a normal one. The mutation causes your liver to produce an amyloid protein that clumps together and builds up in your tissues, organs, and nerves. The clumps damage your tissues and organs over time.

Symptoms depend on which of your organs are affected and how much. Hereditary transthyretin amyloidosis with polyneuropathy affects your nerves, so you might have:

- Tingling or numbness in your legs or feet
- A hard time walking
- Weakness or pain in your limbs
- Lightheadedness when you stand up
- Bladder or bowel problems
- Sexual problems like erectile dysfunction

hATTR is a progressive disease, which means it gets worse over time. There is no cure, but treatments continue to improve. Talk to your doctor, friends, and family about your options, and be sure you're getting the support you need.

SLIDESHOW

Tips for Daily Living with hATTR with Polyneuropathy

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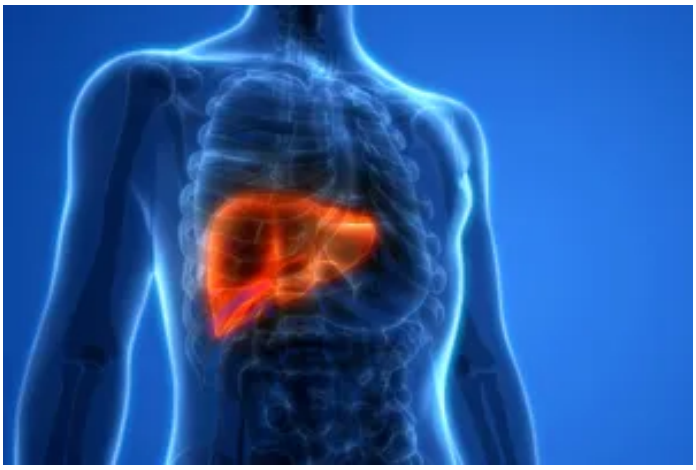

What Is HATTR?

Medically Reviewed by **Neha Pathak, MD** on February 07, 2024

Treatments for Hereditary Transthyretin Amyloidosis With Polyneuropathy

Liver transplant was once the only way to treat hereditary transthyretin amyloidosis with polyneuropathy. But there are many new FDA-approved medications and clinical trials testing new therapies.

Talk to your doctor about the best treatment options for you, and be sure they include ways to reduce your body's production of amyloid proteins and manage your symptoms.

Gene silencers

Gene silencers break down the TTR protein and stop your body from producing it. Eplontersen (Wainua), inotersen (Tegsedi), patisiran (Onpattro), and vutrisiran (Amvuttra) are approved by the FDA for gene silencing in adults. They work by targeting the protein at the mRNA level, so your liver stops creating it.

A large international study on inotersen found it reduced TTR by as much as 74% in some people. A separate clinical trial on patisiran also found people taking the drug after 18 months had improved

ared to those who had taken a placebo (a pill with no active ingredient).

Inotersen and patisiran could also benefit some people who've had liver transplants, but more long-term studies are needed to know how well gene silencers like these work.

Transthyretin stabilizers (TTR stabilizers)

TTR stabilizers maintain your TTR protein level and prevent it from mutating, especially when you can start them early.

Tafamidis (Vyndamax) and tafamidis meglumine (Vyndaqel) are FDA-approved to treat the hATTR-related heart problem called cardiomyopathy.

Liver transplant

Because your liver makes the faulty protein TTR, liver transplants can improve hATTR in some people.

While liver transplant was once the only treatment available for hATTR with polyneuropathy, today studies show it may not stop the protein clusters from building up in your organs because of something called amyloid seeding. If you're in the advanced stage of the disease, researchers think you may already have small bits of the TTR protein – seeds – in your tissues that will form into clumps, so even a new liver won't prevent them.

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hATTR Can Cause Complications In Your:

Nervous system

Cardiac system

Kidneys

Other Treatment Options and Clinical Trials Underway

Anti-seeding as a therapy

Ongoing research shows anti-seeding treatment might help people considering a transplant or those in the late stages of the disease. The therapy works by blocking the amyloid seeds from ever

depositing in your tissues. Studies done in labs suggest high doses of the peptide TabFH2 can stop seeding and might work together with tafamidis. But more research on anti-seeding therapy in people is needed. Researchers also need to look at how it works in the earliest stages of the disease.

Monoclonal antibody therapy

Using monoclonal antibodies, or antibodies from a single cell, is one of the newest therapies for hereditary transthyretin amyloidosis with polyneuropathy. Monoclonal antibodies target the mutated TTR protein and prevent it from turning into amyloid clusters. The antibodies also can remove the fibril deposits already in your body. In phase I of the clinical trial, all 21 people receiving monoclonal antibodies saw some improvement. Phase I research is expected to continue until August 2026.

CRISPR/Cas9 gene editing

CRISPR, a gene editing tool, shows promise for treating transthyretin amyloidosis. A clinical trial on mice had a knockdown of its TTR gene by more than 97%, which means production of the TTR protein was temporarily or reduced almost entirely. A clinical trial of people had encouraging results. All patients had reduced TTR protein between 52% and 87% with few bad side effects. The study is expected to run until August 2028.

Acoramidis (AG-10)

A large clinical trial on the TTR stabilizer acoramidis found patients with transthyretin amyloid cardiomyopathy who took the drug did much better than those who took a placebo. But we need more studies to know if acoramidis is better than other TTR stabilizers the FDA has already approved. Phase III of a separate clinical trial focuses on how people with transthyretin amyloid polyneuropathy respond to acroramidis and is estimated to be completed in October 2026.

Epigallocatechin-3-gallate (EGCG)

Epigallocatechin-3-gallate (EGCG), a substance in green tea, has been studied to see whether it can stabilize or reduce TTR deposits. Research on mice who were given ECGC for 6 weeks showed

ch areas. But studies on humans are limited.

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Dealing With Complications

Treatments for hereditary transthyretin amyloidosis (hATTR) with polyneuropathy were once limited, but there’s progress to slow the disease’s progression.

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