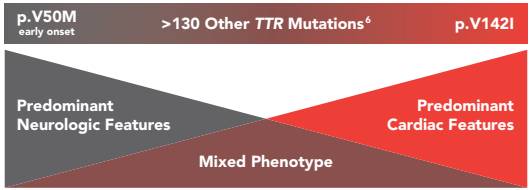
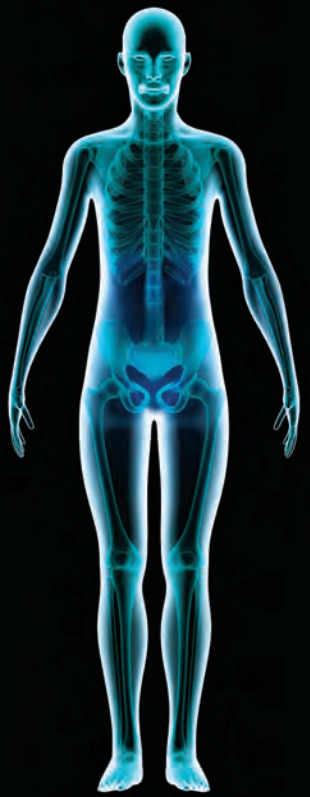
Hereditary ATTR amyloidosis is a systemic disease

that presents with a wide range of symptoms

Hereditary ATTR amyloidosis lies on a spectrum of neurologic and cardiac symptoms, depending on the *TTR* mutation[4,5]



- While primarily associated with neuropathy, 29% of patients with the early-onset p.V50M (previously V30M) mutation experience cardiac symptoms[2]
- The p.V142I (previously V122I) mutation presents primarily with cardiomyopathy, but 30%–60% of these patients experience neuropathy[7,8]
- **Coordination with neurologists or cardiologists is recommended for many patients with hereditary ATTR amyloidosis**



Hereditary ATTR amyloidosis is a progressive and fatal disease manifested by buildup of transthyretin amyloid causing[1-3]:

PERIPHERAL SENSORIMOTOR NEUROPATHY
- Numbness and tingling in the hands and feet
- Loss of balance
- Neuropathic pain
- Walking disability

AUTONOMIC NEUROPATHY
- Orthostatic hypotension
- Urinary retention and incontinence
- Erectile dysfunction

Including GI MANIFESTATIONS
- Alternating diarrhea and constipation
- Unexplained weight loss

BILATERAL CARPAL TUNNEL SYNDROME

NEPHROPATHY
- Protein in urine
- Mild azotemia

OCULAR MANIFESTATIONS
- Vitreous opacities

CARDIOVASCULAR MANIFESTATIONS
- Congestive heart failure
- Heart rhythm disorders
- Conduction blocks

When a patient presents with at least 2 red-flag signs, symptoms, or family history, suspect hereditary ATTR amyloidosis[1,3]

AL, amyloid light-chain; ATTR, amyloid transthyretin; GI, gastrointestinal; MGUS, monoclonal gammopathy of undetermined significance; ^{99m}Tc-PYP, technetium-99m pyrophosphate; TTR, transthyretin

In life-threatening hereditary ATTR amyloidosis, **early diagnosis is critical**

BIOPSY AND AMYLOID TYPING

- Possible biopsy sites: labial salivary gland, subcutaneous fatty tissue of abdominal wall, skin, kidney, nerve, gastrointestinal tract including submucosa[3]
- Congo red staining with characteristic green birefringence under polarized light[3]
- Amyloid fibril typing with immunohistochemistry or mass spectrometry is necessary to differentiate ATTR amyloidosis and other amyloid forms, including AL amyloidosis[9]

NUCLEAR SCINTIGRAPHY

- Nuclear scintigraphy with ^{99m}Tc-PYP can help assess for amyloid in the heart even in patients with hereditary ATTR with polyneuropathy[10]
- Must be combined with testing for serum or urine monoclonal protein to rule out other types of amyloidosis[10]

DNA SEQUENCING

- DNA sequencing of the *TTR* gene can support or exclude a diagnosis of hereditary ATTR amyloidosis[3]
- Presence of a heritable *TTR* mutation has important implications for a patient's family

45%–57% of patients with hereditary ATTR amyloidosis are misdiagnosed[12,13]

- Misdiagnoses can include: idiopathic polyneuropathy, carpal tunnel syndrome, congestive heart failure, AL amyloidosis, and more[3,13]

It is possible that those with presumed AL amyloidosis actually have hereditary ATTR amyloidosis[14]

- Protein typing to determine the precursor protein is important for choosing the right treatment
- 49% of hereditary ATTR (single study involving p.V142I mutation) patients can present with monoclonal gammopathy of undetermined significance (MGUS),[15] which can make differentiating AL and ATTR amyloidosis difficult

AL and ATTR amyloidosis have different natural histories and therapies[11,16]

- AL amyloidosis treatments include chemotherapy and stem cell transplantation, which can be harmful to patients with ATTR amyloidosis[11,14]

To learn more about hereditary ATTR amyloidosis, visit
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US-TTR-2000125 05/20