DIAGNOSING HEREDITARY AMYLOID TRANSTHYRETIN (ATTR) AMYLOIDOSIS WITH CARDIOMYOPATHY AND POLYNEUROPATHY

- Hereditary ATTR amyloidosis is an underrecognized cause of cardiomyopathy and polyneuropathy[1]
- Recognizing hereditary ATTR amyloidosis can be challenging because of the multisystem nature of the disease. Many patients experience a mixed phenotype, exhibiting both neuropathic and cardiac manifestations. Although specific genotypes have been traditionally associated with predominant cardiac features, most mutations result in clinical heterogeneity that include signs and symptoms of polyneuropathy[1,2]

DIAGNOSTIC ALGORITHM FOR HEREDITARY ATTR AMYLOIDOSIS*[3-7]

SUSPECT AMYLOIDOSIS

Based on red-flag symptoms and/or imaging data

At least one of:

- ☐ Cardiomyopathy
- ☐ HFpEF
- ☐ Atrial fibrillation

+

At least one of:

- ☐ Carpal tunnel syndrome
- ☐ Aortic stenosis
- ☐ Lumbar stenosis
- ☐ Polyneuropathy

DIFFERENTIATE ATTR FROM AL

Screen for the presence of monoclonal protein

- ☐ Serum kappa/lambda free light chain ratio (abnormal if ratio is <0.26 or >1.65)
- ☐ Serum or urine protein immunofixation (abnormal if monoclonal protein is detected)

If positive (Refer to hematology) Progress to biopsy and tissue typing	**If negative** Progress to ^{99m}Tc-PYP/DPD bone scintigraphy If PYP is not available, progress to biopsy and tissue typing

Positive PYP scan or cardiac biopsy

DIFFERENTIATE HEREDITARY FROM WILD-TYPE

- ☐ If ATTR, confirm hereditary with genetic testing

IN PATIENTS WITH HEREDITARY ATTR, ASSESS SIGNS AND SYMPTOMS OF POLYNEUROPATHY

- ☐ Assess for neurologic involvement, including signs and symptoms of autonomic neuropathy

AL, amyloid light chain; ATTR, amyloid transthyretin; HFpEF, heart failure with preserved ejection fraction; ^{99m}Tc, technetium-99m; PYP, pyrophosphate; DPD, 3,3-diphosphono-1,2 propanodicarboxylic acid.

*The above algorithm represents a pathway for diagnosis of polyneuropathy within ATTR cardiac amyloidosis, as outlined in the following publications.[3-7]

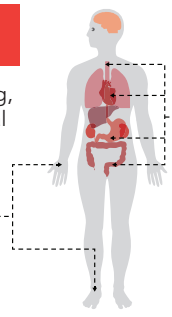
BECAUSE HEREDITARY ATTR AMYLOIDOSIS CAN HAVE MULTISYSTEM MANIFESTATIONS, IT IS IMPORTANT FOR CARDIOLOGISTS TO EVALUATE THEIR PATIENTS FOR MANIFESTATIONS OF POLYNEUROPATHY

POLYNEUROPATHY OF HEREDITARY ATTR AMYLOIDOSIS CAN AFFECT VARIOUS ORGANS, PROGRESSES RAPIDLY, AND LEADS TO SIGNIFICANT MORBIDITY

- Polyneuropathy contributes to the cardiovascular impact of the disease
  - Autonomic symptoms can affect the heart, leading to arrhythmias, and can play a critical role in poor outcomes[8,9]
  - Orthostatic hypotension from autonomic dysfunction is a common cause of syncope in patients with cardiac amyloidosis[9]
- Polyneuropathy can drastically reduce patients' quality of life
  - Quality of life declines rapidly, particularly early in the disease; over a matter of years, a patient can decline from walking without assistance to being wheelchair-bound[10,11]

Peripheral Sensorimotor Neuropathy[12-14]

- Numbness, tingling, swelling, burning, and other abnormal feelings in hands and feet
- Neuropathic pain
- Walking disability
- Loss of balance



Autonomic Neuropathy[12-14]

- Constipation and diarrhea that often alternate
- Nausea and vomiting
- Orthostatic hypotension
- Urinary incontinence retention
- Sweating abnormalities
- Sexual dysfunction

CONSIDER ASKING THE FOLLOWING QUESTIONS TO IDENTIFY SIGNS OF POLYNEUROPATHY IF YOU SUSPECT HEREDITARY ATTR AMYLOIDOSIS:

- ☐ Has anyone in your family ever been diagnosed with hereditary ATTR amyloidosis or any progressive form of neuropathy (eg, diabetic neuropathy, chronic inflammatory demyelinating polyneuropathy [CIDP], or idiopathic neuropathy)?
- ☐ Are you experiencing signs of peripheral neuropathy:
  - ☐ In your upper extremities such as tingling, loss of sensation, or neuropathic pain in your hands or arms?
  - ☐ In your lower extremities such as tingling, loss of sensation, neuropathic pain or motor weakness in your feet or legs, or difficulty walking?
- ☐ Are you experiencing any signs of autonomic dysfunction such as dizziness upon standing (orthostatic hypotension), severe diarrhea or constipation, unintentional weight loss or sexual dysfunction?

No-cost, confidential genetic testing and counseling is available through the hATTR Compass program to patients suspected of having or clinically diagnosed with hATTR amyloidosis with polyneuropathy.

Learn more at:
www.hATTRCompass.com

hATTR Compass™
Map Your Genetic Journey

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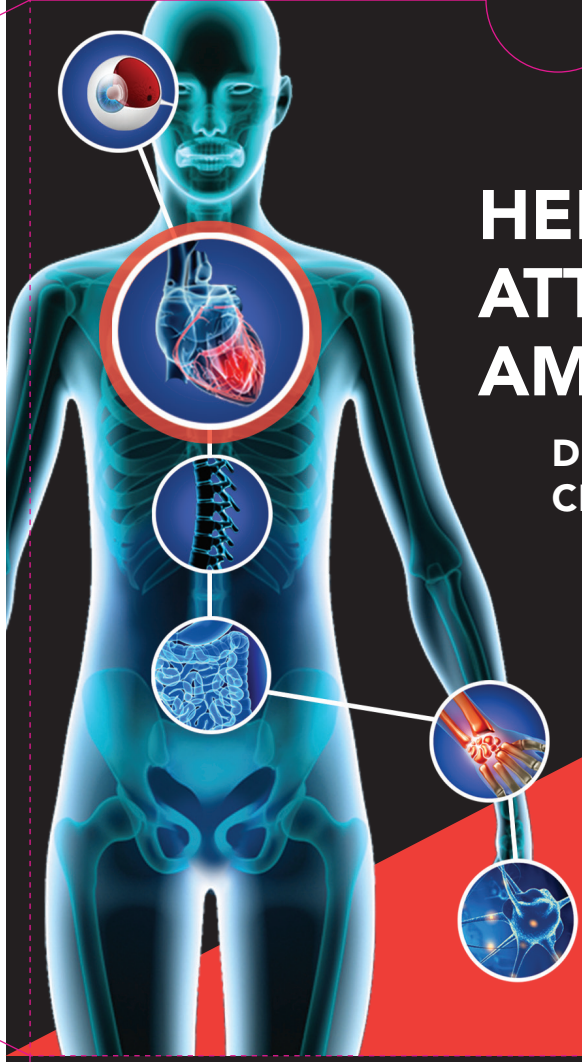

HEREDITARY ATTR AMYLOIDOSIS

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