

AMYLOID TRANSTHYRETIN (ATTR) AMYLOIDOSIS: SIGNS, SYMPTOMS, AND DIAGNOSTIC WORKUP

TWO MAIN TYPES OF ATTR AMYLOIDOSIS

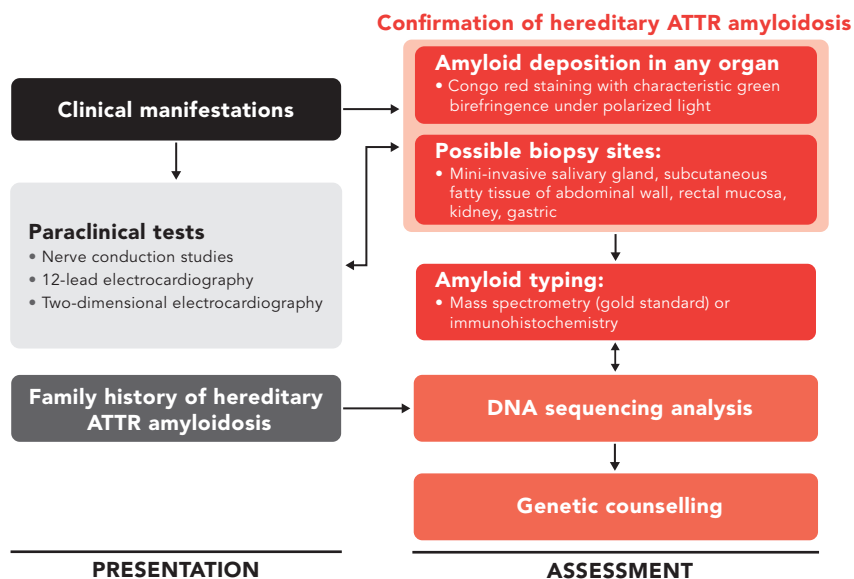
- Hereditary ATTR amyloidosis—affects multiple organs and body systems (eg, heart, nervous system, gastrointestinal tract, and kidney)¹⁻³
- Wild-type ATTR amyloidosis—primarily affects the heart¹⁻²

	Manifestations, Signs, and Symptoms ^a	“Red-flags”
NEUROPATHY⁴	<ul style="list-style-type: none"> • Peripheral sensory-motor neuropathy 	<ul style="list-style-type: none"> • Progressive symmetric sensory-motor neuropathy (plus ≥1 other “red flag” manifestation is suggestive of hereditary ATTR amyloidosis-polyneuropathy)
BILATERAL CARPAL TUNNEL SYNDROME^{4,7,8}	<ul style="list-style-type: none"> • Bilateral carpal tunnel syndrome 	<ul style="list-style-type: none"> • Bilateral carpal tunnel syndrome (especially if family history)
AUTONOMIC NEUROPATHY⁴	<ul style="list-style-type: none"> • Orthostatic hypotension • Recurrent urinary tract infection (due to urinary retention) • Sexual dysfunction • Sweating abnormalities 	<ul style="list-style-type: none"> • Orthostatic hypotension (early “red flag”)
CARDIOVASCULAR MANIFESTATIONS^{4-6,9-11}	<ul style="list-style-type: none"> • Irregular heart beat • Conduction blocks • Congestive heart failure (including shortness of breath, generalized fatigue, peripheral edema) • Ventricular wall thickening with preserved ejection fraction and absence of left ventricular dilation • Cardiomyopathy • Mild regurgitation 	<ul style="list-style-type: none"> • Irregular heart beat (atrial fibrillation most common) • Conduction blocks (fascicular and bundle branch block) • Increased ventricular wall thickness
GASTROINTESTINAL MANIFESTATIONS⁴	<ul style="list-style-type: none"> • Nausea and vomiting • Early satiety • Diarrhea • Severe constipation • Diarrhea/constipation • Unintentional weight loss 	<ul style="list-style-type: none"> • Chronic diarrhea • Constipation • Diarrhea/constipation • Unexplained weight loss
NEPHROPATHY⁴	<ul style="list-style-type: none"> • Protein in urine • Renal failure 	<ul style="list-style-type: none"> • Protein in urine • Mild azotemia
OCULAR MANIFESTATIONS⁴	<ul style="list-style-type: none"> • Dark floaters • Glaucoma • Abnormal blood vessels in eye • Pupillary abnormalities 	<ul style="list-style-type: none"> • Dark floaters
OTHER^{7,12}	<ul style="list-style-type: none"> • Lumbar spinal stenosis • Spontaneous biceps tendon rupture 	<ul style="list-style-type: none"> • Lumbar spinal stenosis • Spontaneous biceps tendon rupture

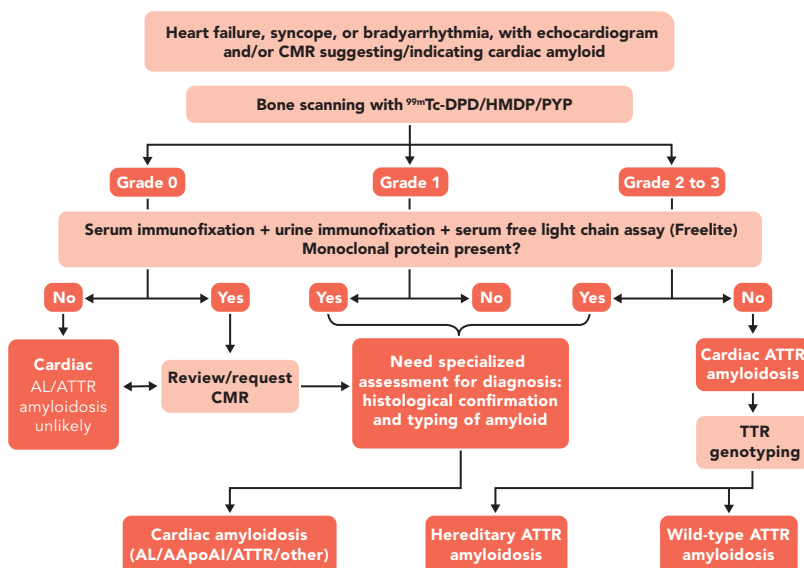
^aCNS symptoms can occur with certain TTR mutations but are not a common manifestation.

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DIAGNOSTIC WORKUP: POLYNEUROPATHY^a



DIAGNOSTIC WORKUP: CARDIAC^b



^{99m}Tc-DPD, ^{99m}technetium-labeled 3-diphosphono-1,2-propanodicarboxylic acid; AApoAI, apolipoprotein AI-derived amyloidosis; AL, amyloid light chain; ATTR, amyloid transthyretin; CMR, cardiac magnetic resonance imaging; DNA, deoxyribonucleic acid; HMDP, hydroxymethylene diphosphonate; PYP, pyrophosphate; TTR, transthyretin. ^aFigure modified with permission from Carvalho A, et al.¹¹; ^bFigure reproduced with permission from Gillmore JD, et al.¹⁰

REFERENCES

- Coelho T, et al. *Curr Med Res Opin.* 2013;29(1):63-76; 2. Ando Y, et al. *Orphanet J Rare Dis.* 2013;8:31; 3. Hawkins PN, et al. *Ann Med.* 2015;47(8):625-38; 4. Conceição I, et al. *J Peripher Nerv Syst.* 2016;21(1):5-9; 5. Castano A, et al. *J Nucl Cardiol.* 2016;23(6):1355-63; 6. Ruberg FL, Berk JL. *Circulation.* 2012;126(10):1286-300; 7. Donnelly JP, Hanna M. *Cleve Clin J Med.* 2017;84(12 suppl 3):12-26; 8. Ikram A, et al. *J Card Fail.* 2017;23(8):511-52 (P021); 9. Coelho T, et al. A physician's guide to transthyretin amyloidosis. Research Gate Amyloidosis Foundation, 2008; 10. Gertz MA. *Am J Manag Care.* 2017;23(7 suppl):S107-S12; 11. Galat A, et al. *Eur Heart J.* 2016;37(47):3525-31; 12. Geller HI, et al. *JAMA.* 2017;318(10):962-3; 13. Gillmore JD, et al. *Circulation.* 2016;133:2404-12; 14. Carvalho A, Rocha A, Lobato L. *Liver Transpl.* 2015;21(3):282-92.