

## Tests and investigations to identify the initial signs and symptoms of hATTR

This protocol is intended to help you decide whether hATTR should be considered in your differential diagnosis. It is not intended to diagnose hATTR. A positive test for a TTR gene mutation and/or a positive TTR amyloid biopsy can confirm diagnosis of hATTR.

Potential signs and symptoms which may suggest initial onset of active hATTR	Routine tests and investigations which may reveal initial signs and symptoms
<p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>• Appearance or signs of autonomic dysfunction<sup>6</sup></li> <li>• Unexplained weight loss<sup>3</sup></li> </ul>	<p><b>Clinical examination</b></p> <ul style="list-style-type: none"> <li>• Family history<sup>5</sup></li> <li>• Autonomic function (especially GI changes, sexual function, postural BP)<sup>6</sup></li> <li>• Weight/mBMI<sup>3</sup></li> </ul>
<p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>• Symmetrical small fiber neuropathy<sup>4</sup></li> <li>• Bilateral discomfort in the feet, numbness<sup>4</sup></li> <li>• Decreased temperature sensation<sup>4</sup></li> <li>• Decreased pin-prick sensation<sup>4</sup></li> </ul>	<p><b>Neurophysiologic (vs. 'asymptomatic' baseline)</b></p> <ul style="list-style-type: none"> <li>• NIS-LL assessments (especially pin-prick, temperature and quantitative sensory testing)<sup>1,3</sup></li> <li>• Nerve conduction assessment<sup>2</sup></li> </ul>
<p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>• Decline in the renal function<sup>3</sup></li> </ul>	<p><b>Biochemical tests</b></p> <ul style="list-style-type: none"> <li>• Renal function<sup>3</sup></li> </ul>
<p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>• Intraventricular conduction delay and atrioventricular block<sup>10</sup></li> <li>• Low or normal QRS voltages despite left ventricle hypertrophy (discordant voltage: mass ratio)<sup>10</sup></li> <li>• Unexplained ventricular hypertrophy (e.g. in the absence of hypertension)<sup>10</sup></li> </ul>	<p><b>Cardiac tests and investigations</b></p> <ul style="list-style-type: none"> <li>• Cardiac testing: ECG, ECHO, cardiac MRI and scintigraphy<sup>7,11</sup></li> <li>• Heart Rate Response (HRR)/variability (HRV)<sup>8,9</sup></li> </ul>

## References

1. Conceição I, et al. *Muscle Nerve*. 2014;49(2):181-6.
2. Coelho T, et al. *Neurology*. 2012;79(8):785-92.
3. Planté-bordeneuve V. *Lancet Neurol*. 2011;10(12):1086-97.
4. Plante-bordeneuve V. *J Neurol*. 2014;261(6):1227-33
5. Graceffa A, et al. *Neuromuscul Disord*. 2009;19(1):44-8.
6. Sekijima Y, et al. In: *GeneReviews*® [Internet]. Seattle; 1993-2009
7. Conceição I, et al. *Clin Neurophysiol*. 2008;119(5):1082-7.
8. Suhr OB, et al. *Degener Neurol Neuromuscul Dis*. 2012;2:93-106.
9. Ando Y, et al. *Orphanet J Rare Dis*. 2013;8:31.
10. Rapezzi C, et al. *Circulation*. 2009;120(13):1203-12.
11. Ruberg FL, et al. *Circulation*. 2012;126(10):1286-300.

