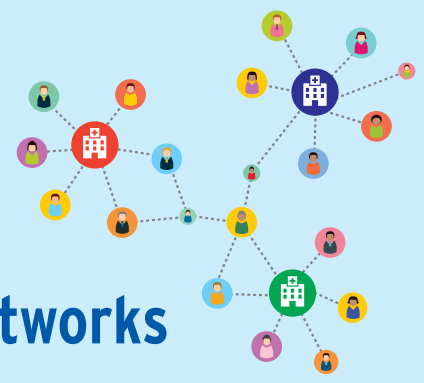


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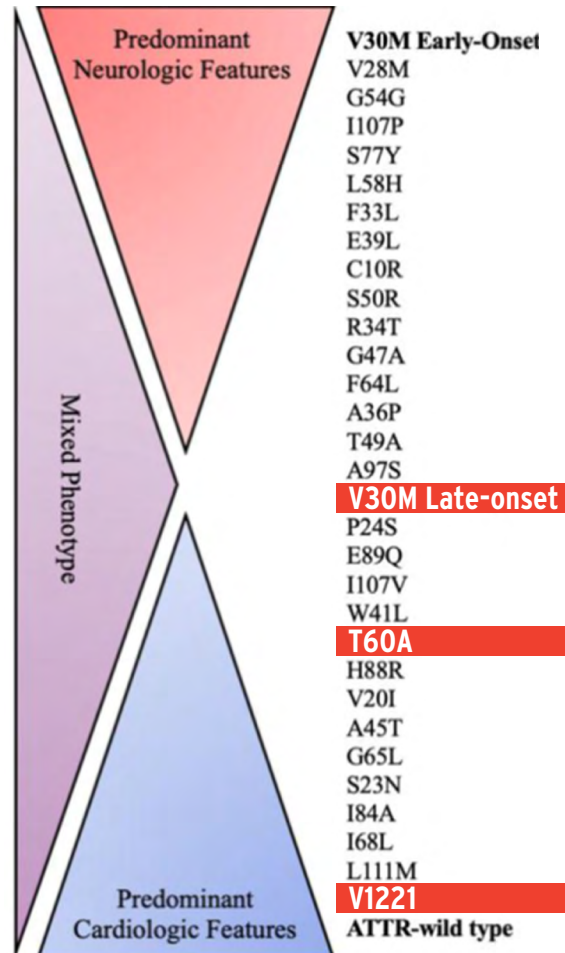
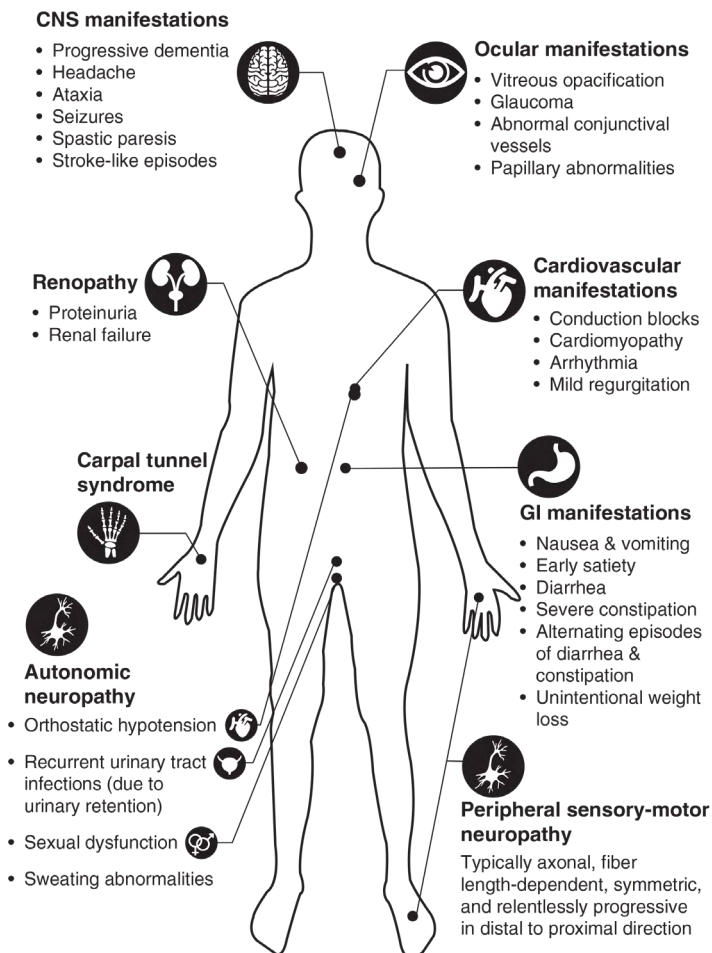
## ATTR-PN: Management and Treatment

### Overview of ATTR-PN Clinical Features<sup>1,2</sup>

- Amyloid transthyretin with polyneuropathy (ATTR-PN) is a multisystemic disease with predominant involvement of the central nervous system (see figure below)
- It may be caused by wildtype (ATTRwt) or mutated variants (ATTRv) of the *TTR* gene
- More than 120 pathogenic *TTR* variants are known and associated with ATTR cardiomyopathy (ATTR-CM) or ATTR-PN (see figure below). The most common variants in the US are V30M (late onset), T60A, and V122I.

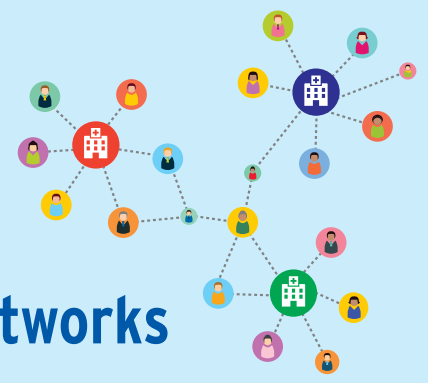
### Clinical Manifestations of ATTR-PN<sup>3</sup>

### Genotype-phenotype Correlation in ATTR Amyloidosis<sup>2</sup>



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## ATTR-PN: Management and Treatment

### Expert Consensus Recommendations for Diagnosis<sup>1</sup>

- Misdiagnosis, leading to delays in diagnosis, is common. The most common misdiagnoses are chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), idiopathic polyneuropathy, and lumbar spinal stenosis
- ATTR-PN should be considered in patients with neuropathy plus one of the red flag symptoms suggestive of multisystem involvement:

**Idiopathic rapidly progressive sensory motor axonal neuropathy**  
or  
**Atypical CIDP**



#### At least one of the following:

- Positive family history
- Bilateral carpal tunnel syndrome
- Autonomic dysfunction
- Gait disorder
- Unexplained weight loss > 10 lbs
- Cardiac hypertrophy/heart rhythm abnormalities
- Vitreous opacities
- Renal abnormalities

- Confirmatory tests include electromyography/nerve conduction studies, genetic testing, skin biopsy, and mass spectrometry amyloid typing

### Management and Treatment<sup>4</sup>

- Care of ATTR-PN includes disease-directed therapy (approved for ATTRv-PN) and the management of symptoms/assessment tools to assess neuropathy

Disease-directed Therapy	Symptom Management		
	Autonomic Dysfunction	Sensory Neuropathy	Motor Dysfunction
Patisiran, Vutrisiran, Eplontersen <i>FDA-approved for ATTRv-PN</i>	<ul style="list-style-type: none"> <li>• Compression stockings, abdominal binders</li> <li>• Increased salt/fluid intake</li> <li>• Salt tablets</li> <li>• Fludrocortisone</li> <li>• Midodrine</li> <li>• Droxidopa</li> <li>• Pyridostigmine</li> </ul>	<ul style="list-style-type: none"> <li>• Pregabalin</li> <li>• Gabapentin</li> <li>• Duloxetine</li> <li>• Tricyclic antidepressants</li> <li>• Topicals: lidocaine, capsaicin</li> </ul>	<ul style="list-style-type: none"> <li>• Ankle foot orthoses</li> <li>• Assistive devices (cane, walker, wheelchair)</li> </ul>

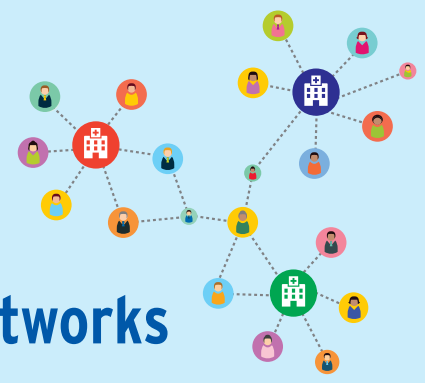
- Therapies in development include nucsiran (NCT07223203) and nexiguran ziclumeran (NCT06672237) for ATTRv-PN and acoramidis (NCT06563895) for asymptomatic carriers of pathogenic TTR variants
- Longitudinal care and follow-up are necessary for asymptomatic carriers and symptomatic patients; use standard assessment tools to assess neuropathy

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## ATTR-PN: Management and Treatment

### Key Takeaways

- Because amyloid neuropathy can progress rapidly, early recognition and treatment initiation are necessary
- Evaluate patients with progressive sensory motor axonal neuropathy and one or more red flag symptoms for ATTR-PN
- Consider evaluating patients with carpal tunnel syndrome for ATTR amyloidosis
- Use ATTRv-PN specific therapies and symptom management for holistic care
- Red flag symptoms include
  - Autonomic dysfunction
  - Gastrointestinal symptoms
  - Cardiomyopathy
  - Rapid progression of neuropathy
  - Failure of response to prior therapies
- Refer patients to neurologist or Gold Center as appropriate
- Monitor patients and asymptomatic carriers using multidisciplinary teams and assessment tools

### References

1. Adams D, et al. *J Neurol.* 2021;268(6):2109-2122.
2. Poli L, et al. *Front Neurol.* 2023;14:1242815.
3. Conceição I, et al. *J Peripher Nerv Syst.* 2016;21(1):5-9.
4. Writing Committee, et al. *J Am Coll Cardiol.* 2023;81(11):1076-1126.