



# The Annenberg Academy for Team-Based Care

## Interprofessional Care of Patients with Hereditary Transthyretin Amyloidosis

### MANAGING PATIENTS WITH OBESITY: KEY CONCEPTS

Transthyretin amyloidosis (ATTR) is one of the most common forms of amyloidosis, a group of systemic conditions resulting from misfolded proteins within the body, impacting organ function.<sup>1</sup> ATTR results when transthyretin tetramers become unstable, dissociate into monomers, and then re-polymerize into amyloid fibrils that deposit into tissues extracellularly, where they cannot be degraded, resulting in organ damage.<sup>2</sup> ATTR is generally classified based on the primary clinical presentation as ATTR with polyneuropathy (ATTR-PN) or ATTR with cardiomyopathy (ATTR-CM).<sup>1</sup> The significant physical, mental, and financial burden imposed by ATTR necessitates the involvement of an interprofessional and multidisciplinary care team, including cardiology, neurology, nephrology, physical therapy, pharmacy, and genetics.<sup>3-5</sup>

Key concepts to keep in mind when managing patients with transthyretin amyloidosis are:

- Disease recognition is a common barrier to patient management, which has led to the development of a list of 'red flags' involving the neurological, musculoskeletal, autonomic, cardiac, ocular, renal, and gastrointestinal systems.<sup>1,2,6-10</sup>
- While no single manifestation is specific to ATTRv, a combination of them indicating multisystem organ involvement, particularly in the setting of unexplained and progressive polyneuropathy or cardiomyopathy, should raise suspicion.
- *TTR* gene sequencing is a common first step in diagnosis, but alone is unable to confirm a diagnosis.<sup>9</sup>
- Tissue biopsy is recommended to confirm amyloid deposition; however, sensitivity is variable given the patchy nature of the disease.<sup>9,11</sup>
- Liver transplantation has been the only disease-modifying treatment available, but deposition of wild-type *TTR* can continue post-transplant.<sup>12</sup>
- Medications approved for ATTR encompass two different mechanisms:
  - *TTR* stabilizers (acoramidis and tafamidis)-approved for ATTR-cardiomyopathy
    - Acoramidis and tafamidis are orally administered
  - *TTR* silencers, including the small-interfering ribonucleic acids [siRNA] patisiran and vutrisiran and antisense oligonucleotide [ASO] eplontersen.<sup>13-17</sup>-approved for ATTR-cardiomyopathy
    - Patisiran and vutrisiran require parenteral administration by a healthcare professional, while eplontersen can be self-administered.
- The lack of head-to-head comparative data precludes recommending one disease-modifying medication over another.<sup>18</sup> Combination therapy is common,<sup>19</sup> although not supported by sufficient evidence of benefit.<sup>20</sup>
- Treatment selection is largely guided by ATTR type (wild-type vs hereditary), phenotypical presentation (polyneuropathy vs cardiomyopathy vs mixed), and patient-related factors (e.g., preference, cost, administration route, comorbidities).
- Beyond disease-modifying therapy, patients require symptomatic and supportive care according to their disease manifestations.<sup>11</sup>
- Interprofessional, multidisciplinary care, ideally within an amyloidosis center, is essential for ongoing management and monitoring of patients with ATTRv<sup>3,5</sup> as it allows for appropriate symptom management, advanced care planning, provision of emotional/psychological support, access to patient advocacy and support groups, and participation in clinical trials.<sup>10</sup>
- Monitoring using validated measures is recommended at least every 6 to 12 months
  - Polyneuropathy: Neuropathy Impairment Score, Rasch-Built Overall Disability Scale, Composite Autonomic Symptom Score, prealbumin level, neurofilament light chain level.<sup>21,22</sup>
  - Cardiomyopathy: 6-Minute Walk Test, NT-proBNP, high-sensitivity cardiac troponin T, estimated glomerular filtration rate, Kansas City Cardiomyopathy Questionnaire.<sup>23,24</sup>

### INTERPROFESSIONAL COLLABORATION: PRINCIPLES

For the evolution in treatment to be of optimal benefit to patients, comprehensive strategies for choosing, delivering, monitoring, and modifying therapy have become especially important. As a consequence, care is typically provided by an interprofessional, multidisciplinary care team that extends beyond physicians to include nurses, nurse practitioners, pharmacists, physician associates, social workers, and others, often involving collaboration between providers in community and academic settings.



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To that end, the following reflects a conversation among 3 healthcare professionals about interprofessional care and how collaborative practices and teams can strengthen our health systems.

**Christopher Flores, MD:** In medical school, I was taught that the patient-doctor relationship was the most critical and important dynamic in healthcare. But after 30-plus years in clinical care, I can attest that healthcare is a team sport and we deliver care in teams of individuals with different training, different skills, different talents. And we teach each other, we learn from each other, we brainstorm and solve problems to meet the needs of the patient.

I want to make a point that interprofessional refers to clinicians in different professions, such as nurses, nurse practitioners, pharmacists, physicians, and physician associates. Multidisciplinary refers to clinicians in different specialties or sub-specialties, such as cardiology, dermatology, and oncology. LaTosha, do you want to talk about interprofessional collaboration?

**LaTosha Mollette, DNP:** The World Health Organization defines interprofessional collaboration as when multiple healthcare workers from various backgrounds work together with patients, families, and communities to provide the best healthcare possible.<sup>25</sup> This is exactly what teamwork should look like, but it is important to remember that healthcare teams can vary from patient to patient.

I work in a rural setting, working together with various healthcare professionals to improve access to needed healthcare services, which helps to prevent unnecessary delays in care and treatment. Ultimately, working together as a team helps to meet the needs of others to improve health outcomes, patient care, and safety.

**Christopher Flores, MD:** I think all of us in healthcare are trying to figure out how to do things better, make life easier for ourselves, and make everybody happier, patients, our staff, and ourselves, to make things more sustainable. Interprofessional collaboration can accomplish this. There's a growing body of literature that shows that interprofessional collaboration can improve patient outcomes, acceptance of treatment, and satisfaction.<sup>26-29</sup> It can decrease costs, improve efficiency, reduce disparities, improve health equity, and make things more sustainable for providers.<sup>26,30-37</sup>

The Interprofessional Education Collaborative has identified 4 behavioral competencies for effective interprofessional collaboration: 1) roles and responsibilities; 2) values and ethics; 3) communication; and 4) teams and teamwork.<sup>38</sup> Michael, do you want to talk a little bit about the roles and responsibilities?

**Michael Smith, PharmD:** Certainly, it's one of these things that we don't often think about, but it's important for 2 reasons. One, understanding our own responsibility and roles that we have within our team and what our teammates can expect from us in terms of what we can deliver to them and deliver to patients.<sup>38</sup> The other is understanding what your team can do for you as well, so that you understand their educational background and you can help them practice at the top of their license by utilizing their skillset to the fullest extent.

It is increasingly common for clinicians, even those within a profession, to take different educational and practice paths leading to clinical practice. As an example, there are various differences in training a pharmacist. Nowadays, all pharmacists graduate with a Doctor of Pharmacy degree (PharmD), but some of us have done 1 or 2 years of residency training or postdoc fellowships. So, getting to know your teammates and what you can expect from them and what they can expect from you can really help your team function at a high level.

**Christopher Flores, MD:** We talk about values and ethics as well.<sup>38</sup> In medicine, we're constantly required to make very difficult and complicated treatment decisions for our patients. We really are missing a great opportunity if we don't involve the opinions of all the members of our team. What does the nurse think about this plan or what does the social worker who has talked to the family members think about this plan? Or what does the physical therapist think, who has been working with the patient for the last 3 days? LaTosha, what do you think about communication?

**LaTosha Mollette, DNP:** Communication is essential in everything we do, and it's how we're able to effectively achieve goals, as well as improve relationships and interactions with others.<sup>38</sup> The healthcare system is often described as being fragmented with little communication and collaboration, but when healthcare professionals communicate responsibly and respectfully, this allows them to overcome differences and work together to accomplish a shared goal, including learning from each other, to better improve patient outcomes and safety.<sup>31,39-41</sup>



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**Christopher Flores, MD:** We're talking a lot about teams and teamwork. Michael, do you have any other points you want to make about teamwork?

**Michael Smith, PharmD:** Most of us are members of various teams during the course of a typical day. Think about the team members that you work with to take care of patients, but also think about a team from a networking standpoint. Do you have a network of like colleagues? As an example, other pharmacists in our healthcare system may reach out to me for advice about a patient with pain, whether or not I'm actually seeing the patient. We can make our team small, we can make them big, but we should be making our teams in ways that everybody's functioning at a high level and putting the patient at the center of the team.

**Christopher Flores, MD:** Michael, LaTosha talked about the fragmented healthcare system and how interprofessional collaboration can help with that. Do you have any examples from your experience?

**Michael Smith, PharmD:** Think about the patient's experience through our healthcare system. Even if a patient receives all of their healthcare within 1 system, they often have to travel to many different places just to access care. From a primary care clinic to a hospital, to a specialty clinic, to a pharmacy. We can fill these gaps by using our interprofessional framework, our education, and allowing our collaborative practice teammates to step in and fill that.

**Christopher Flores, MD:** In conclusion, I just want to summarize that medicine is a team sport and that there is a growing body of evidence that supports the various benefits of interprofessional collaboration. LaTosha, Michael, do you have any final thoughts?

**LaTosha Mollette, DNP:** I think just being willing to change is crucial. I think sometimes we have become complacent in clinical practice, but our healthcare system is ever evolving. So, learning how to be a team player always benefits everyone involved.

**Michael Smith, PharmD:** I've learned a great deal from my interprofessional colleagues, and I hope that I've helped them learn as well, with the ultimate goal of really improving patient care.

### INTERPROFESSIONAL CARE OF PATIENTS WITH TRANSTHYRETIN AMYLOIDOSIS

Interprofessional, multidisciplinary care, ideally within an amyloidosis center, is essential for ongoing management and monitoring of patients with ATTRv<sup>3,5</sup> as it allows for appropriate symptom management, advanced care planning, provision of emotional/psychological support, access to patient advocacy and support groups, and participation in clinical trials.<sup>10</sup> One recent retrospective analysis found that cardiac and extra-cardiac red flag signs and symptoms were common, with three-quarters of patients exhibiting a mixed phenotype, highlighting the importance of early referral and close collaboration to ensure timely recognition and management.<sup>42</sup> Education aimed at improving multidisciplinary care between cardiology and neurology teams has been shown to improve screening and referral.<sup>43</sup>

The American College of Cardiology recently published *Transthyretin Cardiac Amyloidosis Evaluation and Management: 2025 ACC Concise Clinical Guidance* to offer updated strategies to clinicians, reflecting the expanding therapeutic landscape, and reinforcing best practices for the diagnosis and management of patients with ATTR-CM, focusing on disease-modifying therapies.<sup>20</sup> The *Concise Clinical Guidance* followed the previous report *2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis*.<sup>5</sup> Beyond the scope of this activity, the 2023 report emphasized the need for an interprofessional, multidisciplinary care approach to ATTR-CM and described the roles and collaboration strategies among cardiologists, amyloid specialists, genetics clinicians, neurologists, gastroenterologists, nephrologists, hematologists, and others.

A recent study assessed the holistic management of patients with hereditary ATTR as viewed by an international group of clinicians and patients with ATTR.<sup>44</sup> Using a Delphi survey, participants (N=122) were asked to react to recommendations developed by a 14-member joint patient advocate-clinician panel. The 50 recommendations related to 7 core goals on: 1) early diagnosis and access to treatment; 2) disease monitoring and organization of care; 3) maintenance of physical and mental health and quality of life; 4) family-centered care and caregiver support; 5) patient-clinician dialog and shared decision-making; 6) access to community and social support; and 7) spiritual support and social networking. There was moderate agreement among



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all survey participants that at a minimum, the (interprofessional) multidisciplinary care team should be comprised of a neurologist and cardiologist, a genetic counselor, a specialist nurse, and an ophthalmologist. Other clinicians with expertise in gastroenterology, nutrition, psychology, physical therapy, occupational therapy, nursing, nephrology, urology, and primary care should be consulted as needed. Eight recommendations were rated ( $\geq 66\%$  agreement) by clinicians as a core part of care; all emphasizing the key importance of care provided by an interprofessional, multidisciplinary care team.

- It should be mandatory to offer genetic testing (with genetic counseling) to confirm the diagnosis of symptomatic ATTRv amyloidosis
- If a *TTR* variant is identified, follow-up genetic counseling is recommended to discuss the implications for the patient and their family and to support presymptomatic genetic testing of at-risk family members, as well as provide advice on prenatal testing

- Comprehensive baseline assessments (eg, neurological, cardiac, ophthalmic) should be mandatory shortly after diagnosis to identify disease burden and guide decisions on pharmacological and non-pharmacological treatment
- Treatment decisions should be informed by the latest evidence, discussion within the multidisciplinary team (as needed) and made jointly with the needs and wishes of the patient
- Where available, disease-modifying treatments should be initiated immediately after diagnosis in all eligible patients
- Timely and regular multidisciplinary monitoring of asymptomatic gene carriers should be undertaken to identify and treat the first signs of disease
- Multidisciplinary follow up should be tailored for each patient according to their signs and symptoms and expected disease course (consistent with their genotype)
- Patients should be managed at centers with the facilities and expertise to provide multidisciplinary care with coordinated access to other specialist services as needed

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