deciphEHR™

connecting the dots of rare disease

Amyloidosis

Amyloidosis is a group of rare, heterogeneous, progressive diseases that can lead to organ dysfunction and eventual death[1]

- Amyloidosis is a treatable disease characterized by the misfolding of proteins that form **amyloid fibrils** that aggregate in tissues and/or organs, which can result in **organ failure**[1,2]
- Patients with amyloidosis present with a wide variety of **nonspecific symptoms** that often **mimic more common diseases,** which can complicate diagnosis and lead to **misdiagnosis and mistreatment**[2,3]
- Misdiagnosis and diagnostic delays are associated with a high risk for **morbidity and mortality** amongst patients[4,5] and a large **cost to healthcare organizations** (HCOs)[6,7]

The deciphEHR™ program provides educational resources on disease characteristics and diagnostic best practices to help healthcare providers, health systems, hospitals, and specialty practices to leverage their electronic health record (EHR) systems to triage suspect patients for further clinician evaluation leading to rapid, accurate diagnoses.

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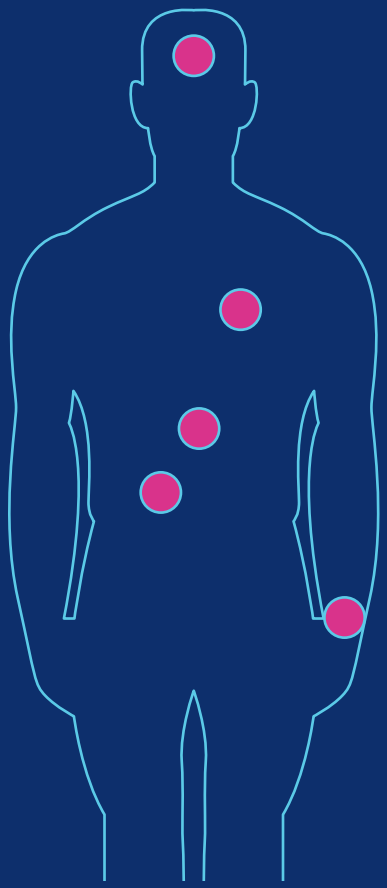
Two of the most common forms of amyloidosis are light-chain (AL) amyloidosis, derived from abnormal circulating light chains produced by plasma cell dyscrasia and transthyretin amyloidosis (ATTR), derived from wild type (wt) or mutant transthyretin (hereditary).[1,2] Within these subtypes are a **variety of phenotypes**, including hereditary ATTR polyneuropathy (hATTR-PN), hereditary and wild-type ATTR cardiomyopathy (hATTR-CM, ATTRwt-CM) and mixed phenotype ATTR (patients exhibit polyneuropathy and cardiomyopathy symptoms).[3] Within these phenotypes, presentation can vary widely. **Because of the wide array of nonspecific symptoms, disease recognition can be challenging.**[3]

Organ involvement can vary widely across patients, some can have ≥3 organs involved.[8]



Examples for system involvement[2-4]*:

Cardiovascular System†
Heart failure/congestive heart failure, arterial fibrillation, bradyarrhythmias/conduction abnormalities

Nervous System
Headache, ataxia, seizures, progressive dementia, stroke-like episodes, neuropathic pain

Renal System
Proteinuria, renal failure, edema

Musculoskeletal System‡
Carpal tunnel syndrome, back pain/lumbar spinal stenosis, ruptured distal biceps tendon

Gastrointestinal System
Nausea, vomiting, early satiety, diarrhea, unintentional weight loss

*Not an exhaustive list. Organ involvement can vary by sub-type (AL, hATTR, ATTRwt). Furthermore, organ involvement and symptoms in hATTR are largely dependent on mutation, which is associated with phenotype: CM, PN, or a mixed phenotype.[9]
†Cardiac involvement in AL worsens the prognosis[9], and AL patients with primary cardiac involvement were more likely to receive a delayed diagnosis than those with primary kidney involvement.[10]
‡Note that involvement in ATTRwt is commonly related to the presence of carpal tunnel syndrome (CTS), which is often the earliest presenting symptom and may precede cardiac symptoms by several years.[11]

Note: These data reflect results from multiple studies and may not be generalizable to the whole population.

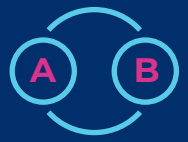
Missed diagnoses and diagnostic delays are common in patients with amyloidosis[3,10]

Diagnosing amyloidosis can be challenging for physicians in part due to the wide variety of **nonspecific symptoms** along with a general **lack of disease state awareness**.[3,4,8,10] Although there are gold standards for amyloidosis testing and typing, these tests may elicit **false negatives**[12] and there is **no one single test that can provide all the information needed** to diagnose and type amyloidosis.[13,14]

Up to **57%** of patients with ATTR-CM are misdiagnosed before receiving a correct diagnosis[15]

40-75% of patients with AL or ATTR see ≥3 physicians before receiving an accurate diagnosis[15-17]

Up to **25%** of persons older than 80 years may have ATTRwt, as seen in autopsy data, indicating ATTRwt may be widely underdiagnosed[18]



63% of healthcare providers who are already aware of amyloidosis are not confident differentiating between ATTR-CM and AL[19]

Note: These data reflect results from multiple studies and may not be generalizable to the whole population.

Definitive amyloid typing is critical in establishing a diagnosis and initiating appropriate therapy.[20*]

*It is possible to have a mixed phenotype of ATTR-CM and -PN—up to 80% of hereditary patients and ~30% of wt patients have a mixed CM and PN presentation.[13,14,21,22] Additionally, although rare, two different types of amyloidosis can occur in individual patients.[23]

~25% of patients die within 6–24 months[5*]; improvements in patient recognition can make a difference

Untreated ATTR can lead to confinement to a wheelchair, heart failure, and death, but timely diagnosis and treatment may help **improve survival**[1,2,24]

Misdiagnosis and subsequent mistreatment can lead to clinical worsening and early mortality in amyloidosis patients[17,25]; accurate diagnoses are needed to **prevent**

Shortened diagnostic timelines have been associated with a **decreased risk of death** in patients with AL[26]

Effective therapy exists and needs to be initiated as soon as possible to prevent further organ damage[5]

*Median survival from diagnosis of hATTR with predominantly neuropathic symptoms is 5–15 years and 2.5–6 years with predominantly cardiomyopathic symptoms; median survival from diagnosis of ATTRwt is 3–5 years; and median survival from diagnosis of AL is largely dependent on stage of disease at diagnosis with Stage I 10+ years, Stage II 4.5 years, Stage IIIa 2 years, and Stage IIIb 5 months (based on the 2013 European Modification of the 2004 Standard Mayo Clinic Staging).[13,24]

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Taking action is important; missed or delayed diagnoses of rare diseases may potentially increase morbidity and mortality, as well as increase healthcare costs.[6,7] Consult the **Amyloidosis deciphEHR™ Program Implementation Guide** or visit deciphEHRrare.com to get started.

Leveraging EHR data may help healthcare organizations rapidly triage patients for further clinical evaluation to diagnose amyloidosis[27]

The Problem

- Patients with amyloidosis face **delays in diagnosis**, which can result in **organ damage, morbidity, and mortality**
- Delays in diagnoses are driven in part by the **rarity** of disease, **heterogeneous** phenotypes, lack of physician **awareness, false negatives,** and **the absence of a single test** that can provide all the information needed to diagnose and type amyloidosis[1,12,14]

deciphEHR™ may be able to help

- **Your EHR system can work for you to help triage suspect amyloidosis patients.** AstraZeneca & Alexion provide resources for you to share with your EHR team
- The deciphEHR™ program identifies **clinical features** that may be used to build **suspect patient lists** in your EHR to triage patients for further clinical evaluation
- **Order Sets** and **Best Practice Alerts (BPAs)** can be utilized in your EHR system to support healthcare providers as they navigate the amyloidosis diagnostic process

The Benefits

- EHR systems can help triage patients based on existing data, prioritize resources, and provide more **coordinated care that may foster improved outcomes**[27]
- Automated Order Sets and BPAs can assist healthcare providers in timely access to diagnostic best practices and **reduce inefficiency** by decreasing manual efforts[28]

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AstraZeneca and Alexion provide educational resources to help you leverage your EHR, which may decrease the diagnostic timeline for many amyloidosis patients

- Many patients with amyloidosis face large diagnostic delays, misdiagnosis, and underdiagnosis[15-17]
- The nonspecific, heterogeneous presentation of amyloidosis combined with false negatives and the absence of a single test to diagnose and type amyloidosis makes a rapid diagnosis challenging[1,12-14]
- Misdiagnosis and subsequent mistreatment can lead to clinical worsening and early mortality in amyloidosis patients[17,25]
- Timely diagnosis and treatment may be associated with improved survival impairment[2,13,16]
- Improving the diagnostic and disease management process can decrease burden to the healthcare system[6,7]
- The data needed to shorten diagnostic delays may exist in your EHR
- The deciphEHR™ program has suggested EHR codes that may be used to build patient lists to flag suspect amyloidosis patients for further clinical evaluation

Visit deciphEHRrare.com or contact your AstraZeneca or Alexion representative to find out how utilizing your EHR system can help you triage patients who would benefit from further clinical evaluation for amyloidosis.

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