Cardiac Amyloidosis – What You Need To Know.

A Presentation for Patients, Families and Caregivers

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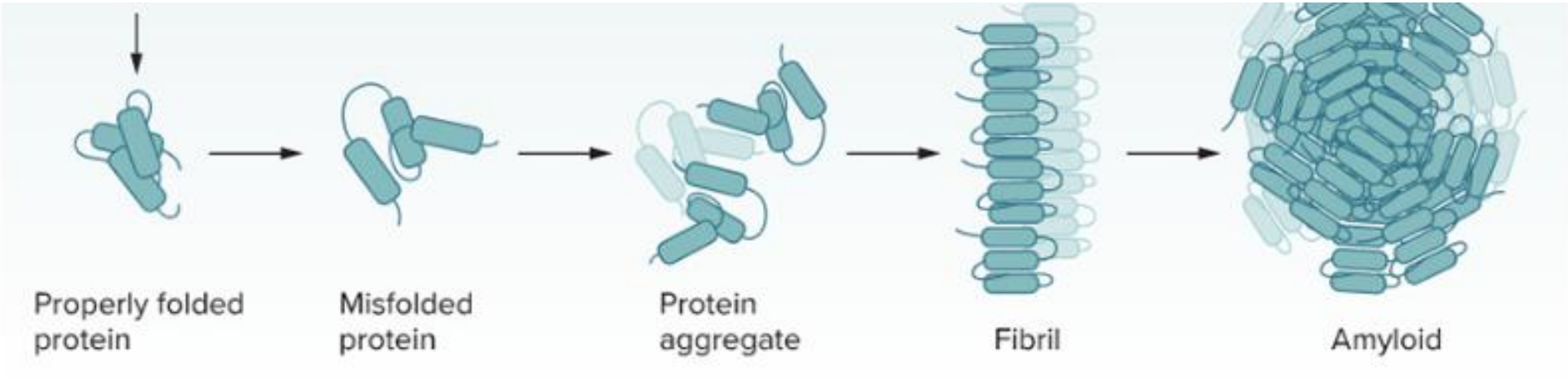
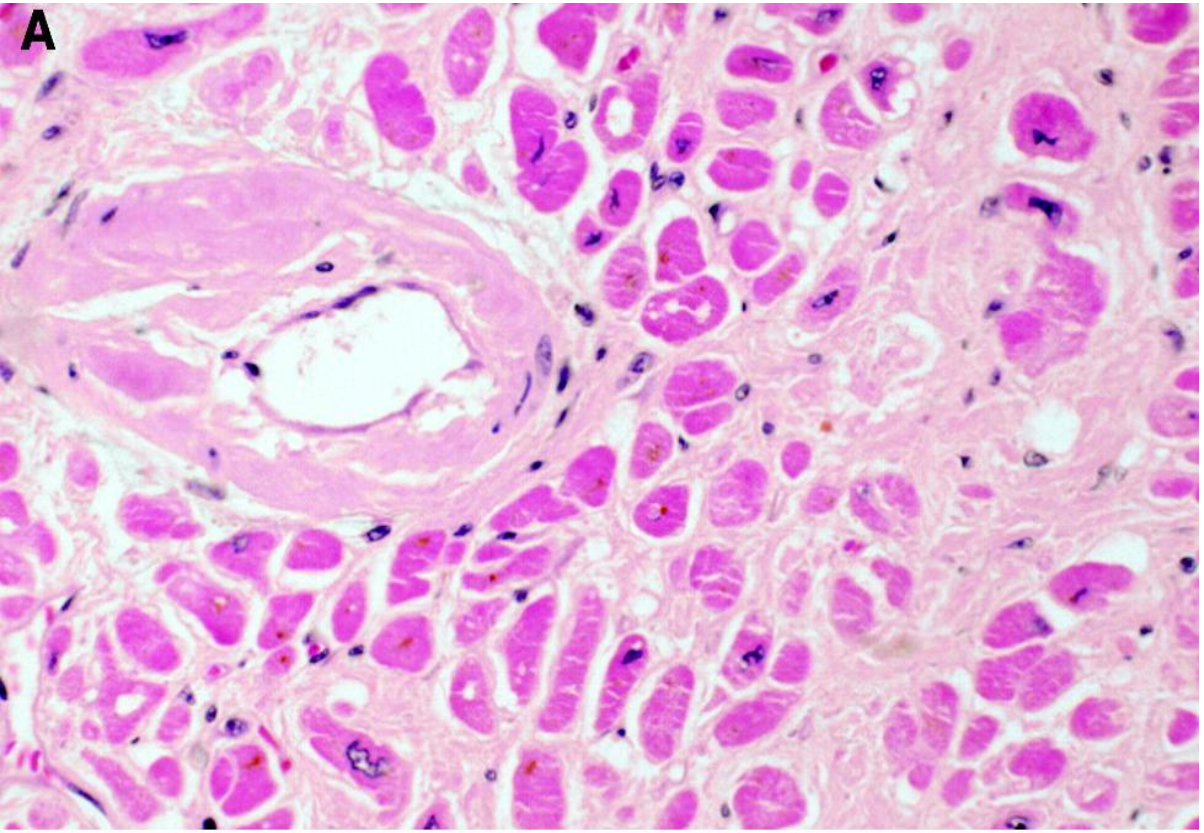
What we'll cover today

- What is amyloidosis? (The basics)
- How does it affect the heart?
- The two main types: AL and ATTR
- Warning signs and symptoms
- How doctors find it (diagnosis)
- Treatment options
- Heart transplantation
- Resources and support

WHAT IS AMYLOIDOSIS?

- Our bodies are made of thousands of proteins — tiny building blocks that do important jobs.
- Sometimes, a protein gets "misfolded“, which makes it “sticky”.
- These “sticky” proteins like to make long chains called fibrils.
- These fibrils clump together and are called **amyloid**. They build up in organs and get in the way of normal function.
- Amyloid can deposit in the heart, kidneys, nerves, and other organs.

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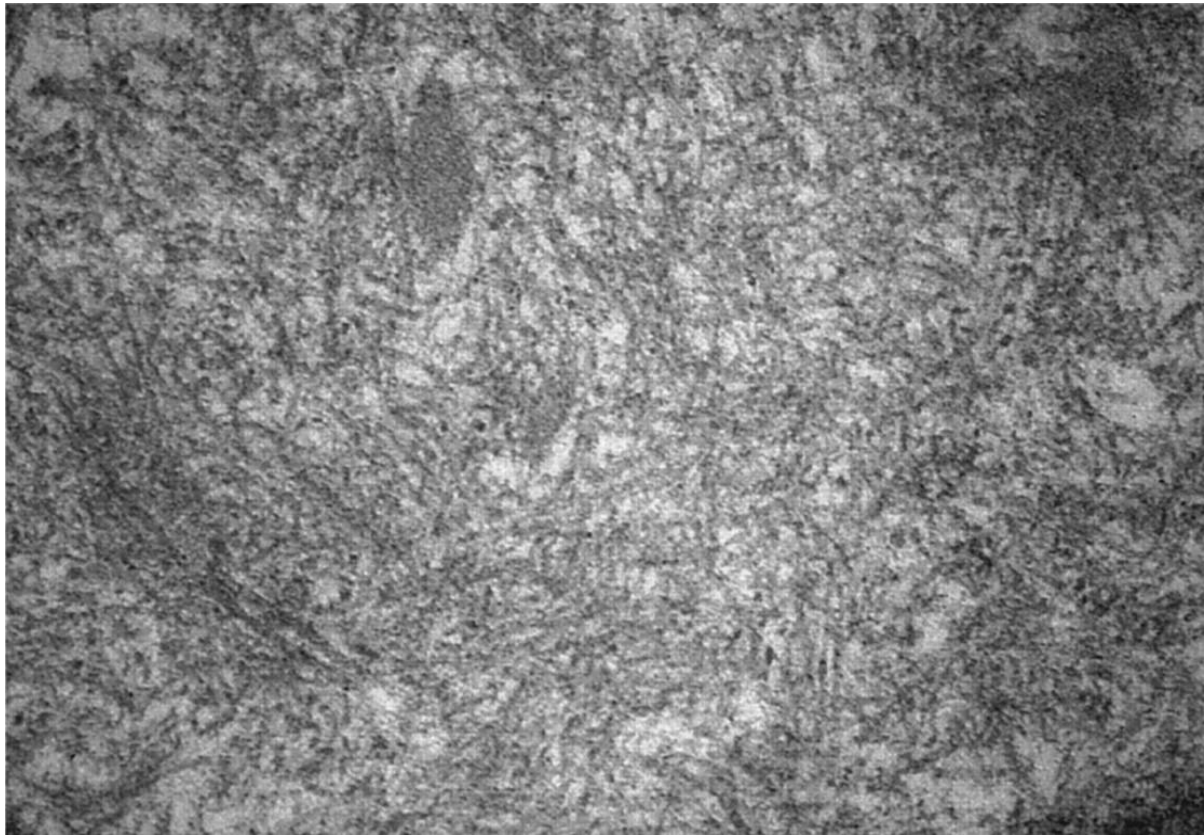
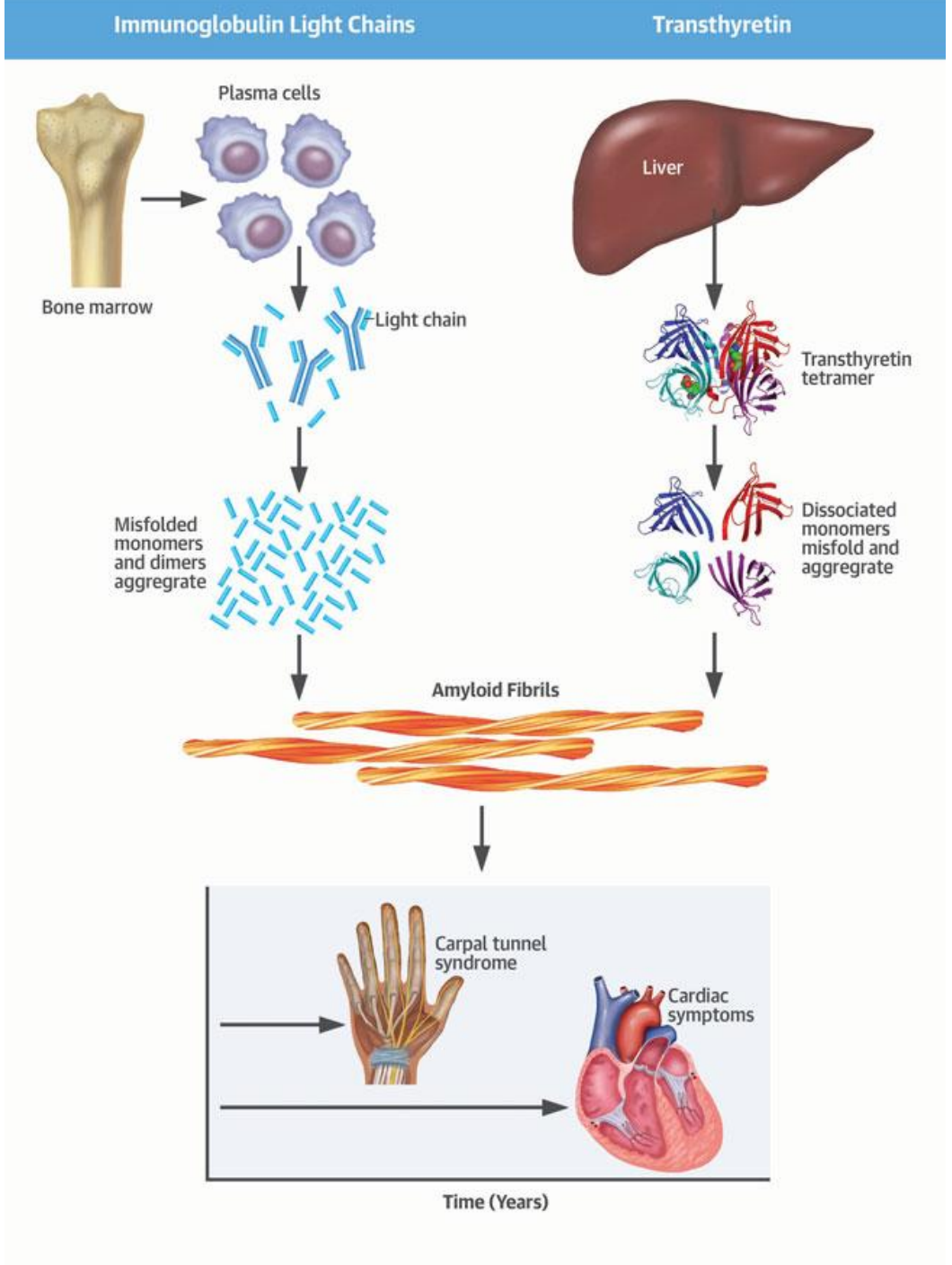


MAIN TYPES OF AMYLOID THAT AFFECT THE HEART

	AL Amyloidosis	ATTR Amyloidosis
What is the abnormal protein?	Light chains (made by bone marrow cells)	Transthyretin or "TTR" (made by the liver)
How does it become amyloid?	A small group of bone marrow cells makes too much of an abnormal protein	The TTR protein becomes unstable and misfolds
Is it genetic (passed down in families)?	No	One form is genetic (hereditary). Another (more common) form is not genetic.
Age/sex	Can occur at any age; slightly more common in men	Wild-type: mostly men over 65–70. Hereditary: varies by mutation
Progression	Can progress quickly	Usually progresses more slowly

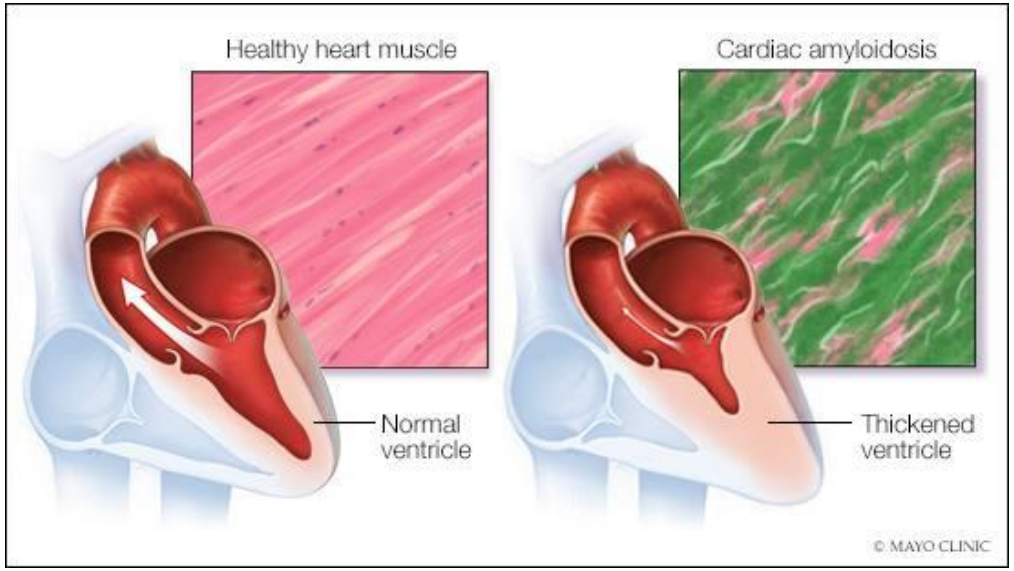
MAIN TYPES OF AMYLOID THAT AFFECT THE HEART



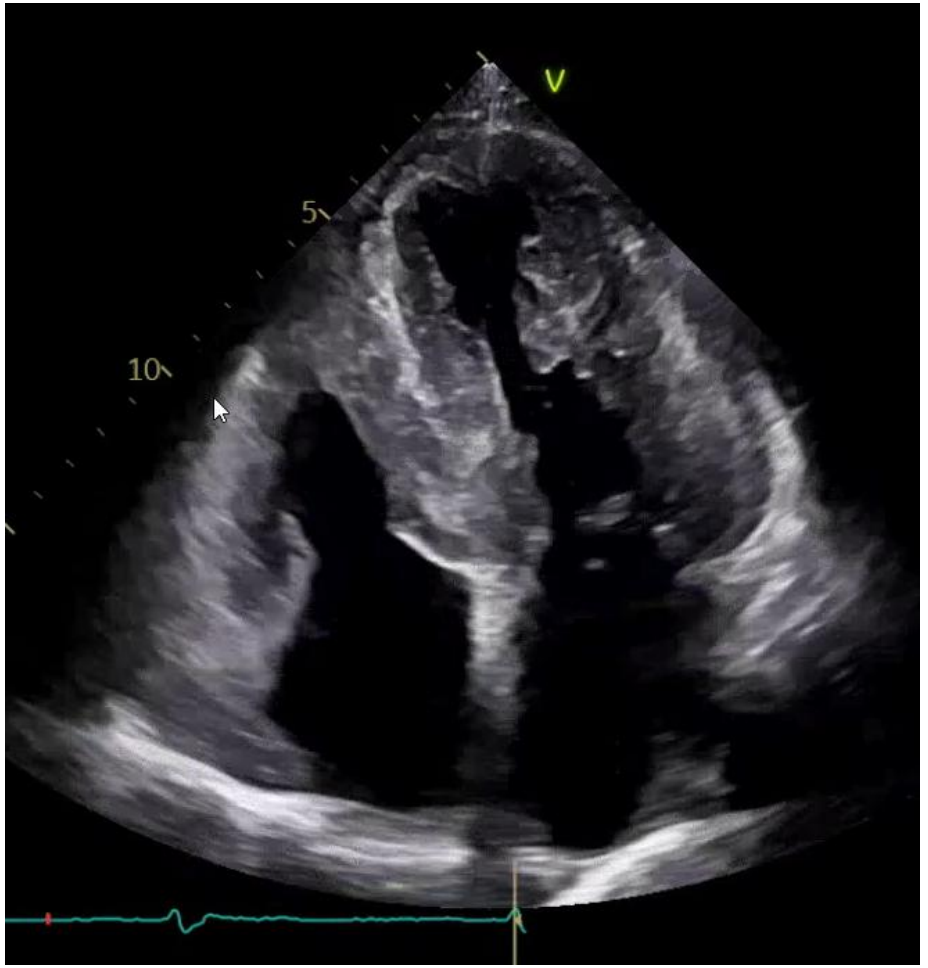
https://cardiacamyloid.ca/about-amyloidosis/

HOW AMYLOIDOSIS HURTS THE HEART

- Protein deposits build up in the spaces between heart muscle cells
- Heart walls become thick and stiff (like cardboard instead of rubber)
- Heart’s chambers become smaller
- Heart can't relax properly to fill with blood
- Eventually, heart can't pump enough blood to the body (heart failure)



Without amyloidosis



With amyloidosis

WARNING SIGNS AND SYMPTOMS

Key message: Many of these symptoms overlap with common conditions of aging, which is why amyloidosis is often missed or diagnosed late.

Back pain
Palpitations

HOW IS CARDIAC AMYLOIDOSIS DIAGNOSED?

Suspicion — Doctor notices warning signs

Heart imaging — Ultrasound (echocardiogram), sometimes MRI

Blood and urine tests — To check for abnormal light chain proteins

Nuclear bone scan — A special scan that lights up if TTR amyloid is in the heart

Biopsy — Sometimes a small tissue sample is needed

Genetic testing — To check for hereditary ATTR

TREATMENT OVERVIEW

Treatment depends on the ***type*** of amyloidosis

Type	AL Amyloidosis	ATTR Amyloidosis
Goal	Stop the bone marrow from making the bad protein	Stabilize or silence the TTR protein to stop new amyloid from forming
Treatment	Chemotherapy-like drugs targeting bone marrow cells; Stem cell transplant	Stabilizer pills or silencer injections
Heart Failure Management	Heart failure meds, diuretics, careful fluid management	Heart failure meds, diuretics, careful fluid management

TREATING AL CARDIAC AMYLOIDOSIS

The goal: Quickly stop the abnormal bone marrow cells from making toxic light chains.

Standard first-line treatment: Daratumumab + CyBorD

- **Daratumumab** — An antibody injection under the skin that targets/kills abnormal bone marrow cells
- **Cyclophosphamide** — A chemotherapy drug
- **Bortezomib** — A drug that blocks a protein recycling system in abnormal cells
- **Dexamethasone** — A steroid that helps the other drugs work better

This combination (called "Dara-CyBorD") was proven in a major study called ANDROMEDA to produce deep responses in about 78% of patients — meaning the harmful protein levels dropped dramatically.

Stem cell transplant:

- For a select group of patients (about 10–20%) who are healthy enough, high-dose chemotherapy followed by a stem cell transplant can produce very long-lasting remissions.

Key point: Speed matters in AL amyloidosis. The toxic light chains directly damage the heart, so getting them under control quickly is critical.

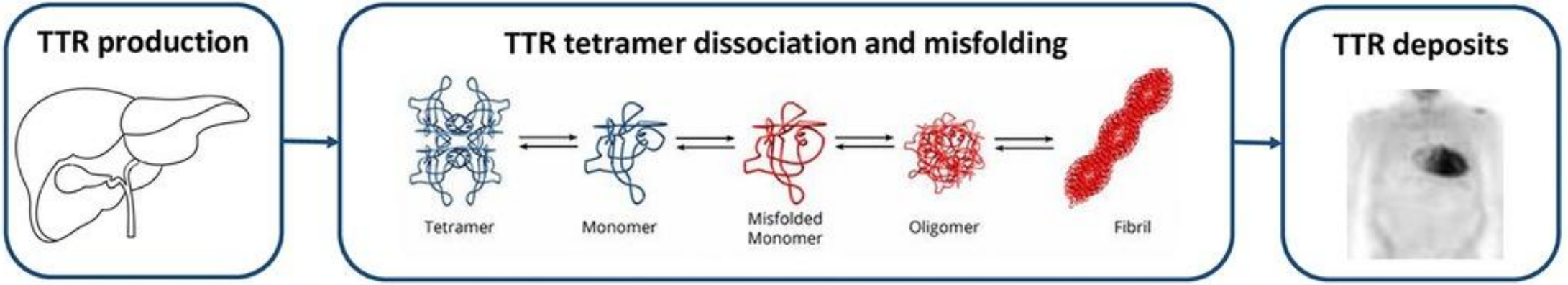
Having a strong oncology team is necessary for the treatment of AL amyloidosis

TREATING ATTR CARDIAC AMYLOIDOSIS

The goal: Stop new amyloid from forming. Current treatments slow or stop the disease but do not remove amyloid that has already built up.

FDA-approved treatments:

- **TTR Stabilizers** (pills) — Hold the TTR protein together so it doesn't fall apart and misfold
  - **Tafamidis (Vyndamax)** — Once daily pill. Approved since 2019.
  - **Acoramidis (Attruby)** — Twice daily pill. Approved in 2024.
- **TTR Silencer** (injection) — Tells the liver to stop making the TTR protein altogether
  - **Vutrisiran (Amvuttra)** — Injection under the skin every 3 months. Requires vitamin A supplements. Approved in 2025. Also approved for ATTRv neuropathy.
- **Important:** These treatments work best when started **early**, before the heart is severely damaged. They slow progression but generally do not reverse existing damage.



Inhibition of TTR synthesis

- **Liver transplantation**
- **RNA silencing**

siRNA:
- Patisiran
- Revusiran
- Vutrisiran

ASO
- Inotersen
- Eplontersen

- **Gene editing**

CRISPR–Cas9:
- NTLA-2001

TTR stabilization

Non-selective agents
- Diflusinal

Selective agents
- Tafamidis
- Acoramidis

TTR degradation

- Doxyciclin and (T)UDCA

Monclonal Ab
- PRX004
- NI006

Tomasoni D et al. Front. Cardiovasc. Med. 2023

MANAGING HEART FAILURE SYMPTOMS

Regardless of the type of amyloidosis, managing fluid and symptoms is essential:

- **Diuretics ("water pills")** — Help remove excess fluid to reduce swelling and shortness of breath. Careful dosing is important. (Furosemide, torsemide, bumetanide)
- **SGLT2i** – Help manage the stiffness of the heart muscle. (Farxiga and Jardiance)
- **MRA** – Also helps manage stiffness of the heart muscle. (Spironolactone, eplerenone, finerenone)
- **Fluid restriction** – Limiting intake to about 2L or 64 ounces of total fluid in a day
- **Low-salt diet** — Helps prevent fluid buildup.
- **Daily weight monitoring** — A sudden weight gain of 2–3 pounds in a day may mean fluid is building up.
- **Gentle exercise** — As tolerated; helps maintain strength and well-being.

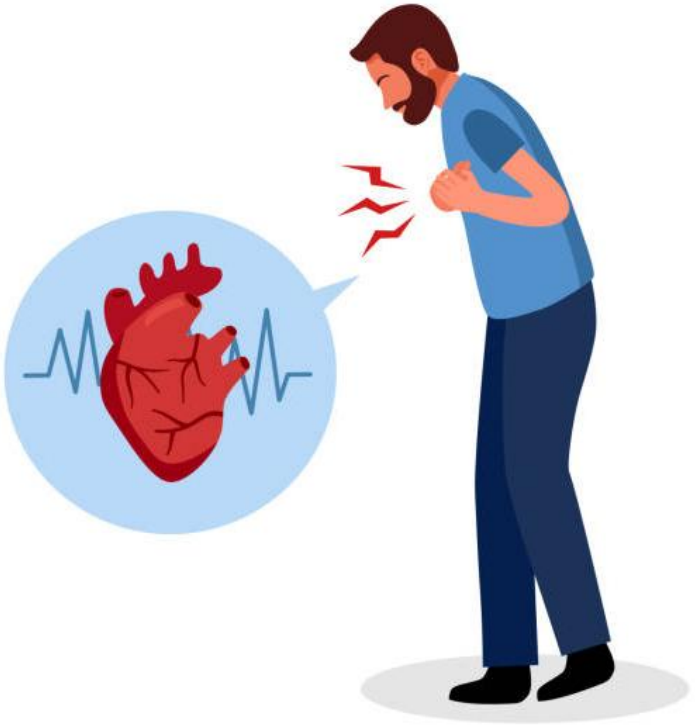
In extreme and rare cases where amyloid treatment and heart failure management do not stabilize the patient and they have worsening heart failure, **heart transplantation** may be considered.

Why Would Someone Need a Heart Transplant?

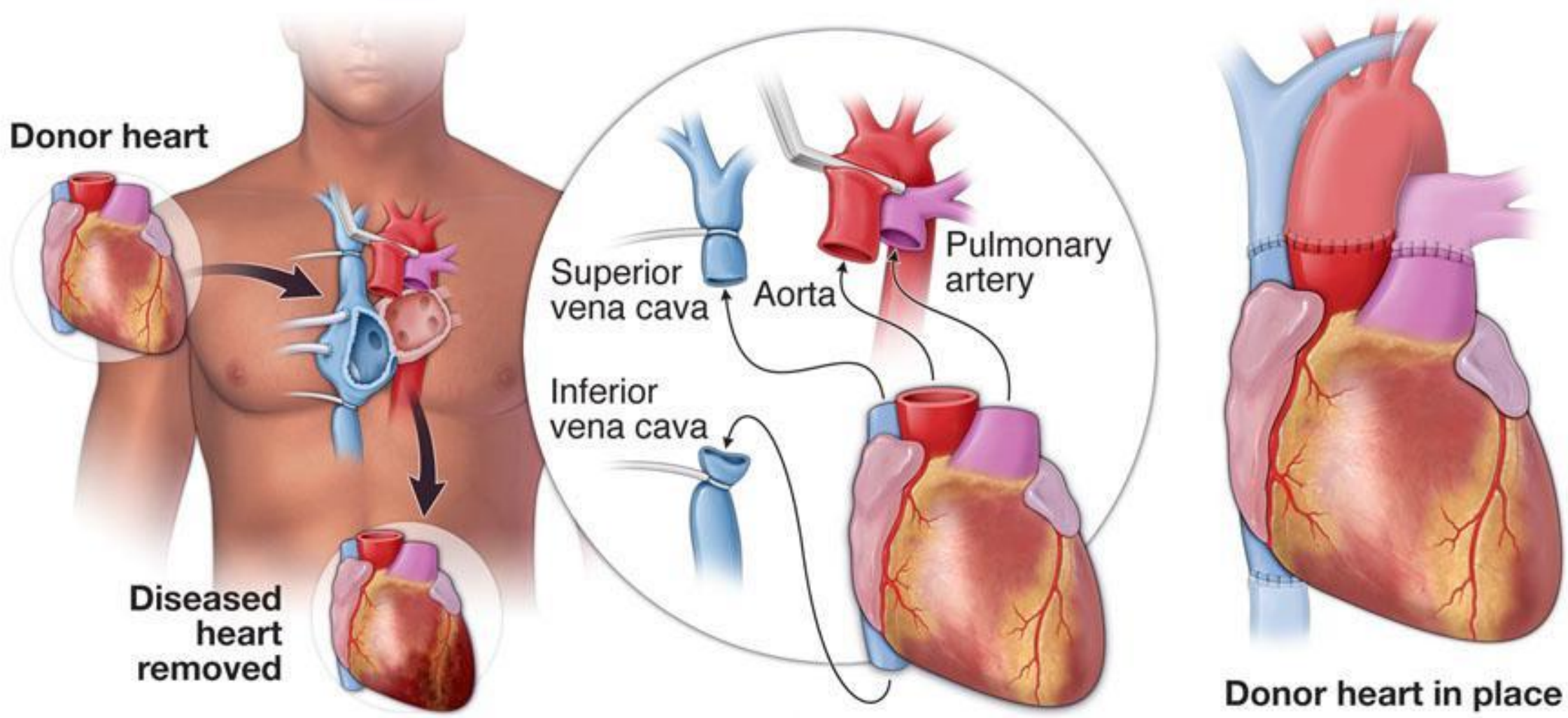
When the Heart Fails:

Despite medications and treatments, some patients develop **advanced heart failure**, meaning:

- Repeated hospital visits for heart problems
- Can't walk even one block without getting tired
- Need IV medications to help the heart pump
- Swelling that won't go away with pills
- Other organs (kidneys, liver) start failing because heart can't pump enough blood



Important: Not everyone with cardiac amyloidosis needs a transplant—only those with the most severe heart damage who haven't responded to other treatments.



https://www.templehealth.org/services/treatments/heart-transplant

Heart Transplantation in Cardiac Amyloidosis From "No Way" to "Yes, Carefully"

The Old Days (Before 2010):

- Doctors thought heart transplant for amyloidosis was too risky
- Survival rates were poor (only 20-30% alive at 5 years)
- Disease would come back in the new heart

The Modern Era (2010-Now):

- **Huge improvement!** 3-year survival now over 80%
- Number of transplants doubled from 2010 to 2020
- Better patient selection and new treatments made the difference
- Outcomes now similar to transplants for other heart diseases

What Changed? Better understanding of who is a good candidate + new medications to prevent disease from coming back

Who is a Candidate for Heart Transplantation?

Good Candidates:

✓ Severe heart failure from amyloidosis

✓ Otherwise healthy enough for major surgery

✓ No severe disease in other organs

✓ Strong support system at home

✓ Willing to take medications for life

Not Good Candidates:

✗ Too frail or weak for surgery

✗ Severe nerve damage affecting ability to walk

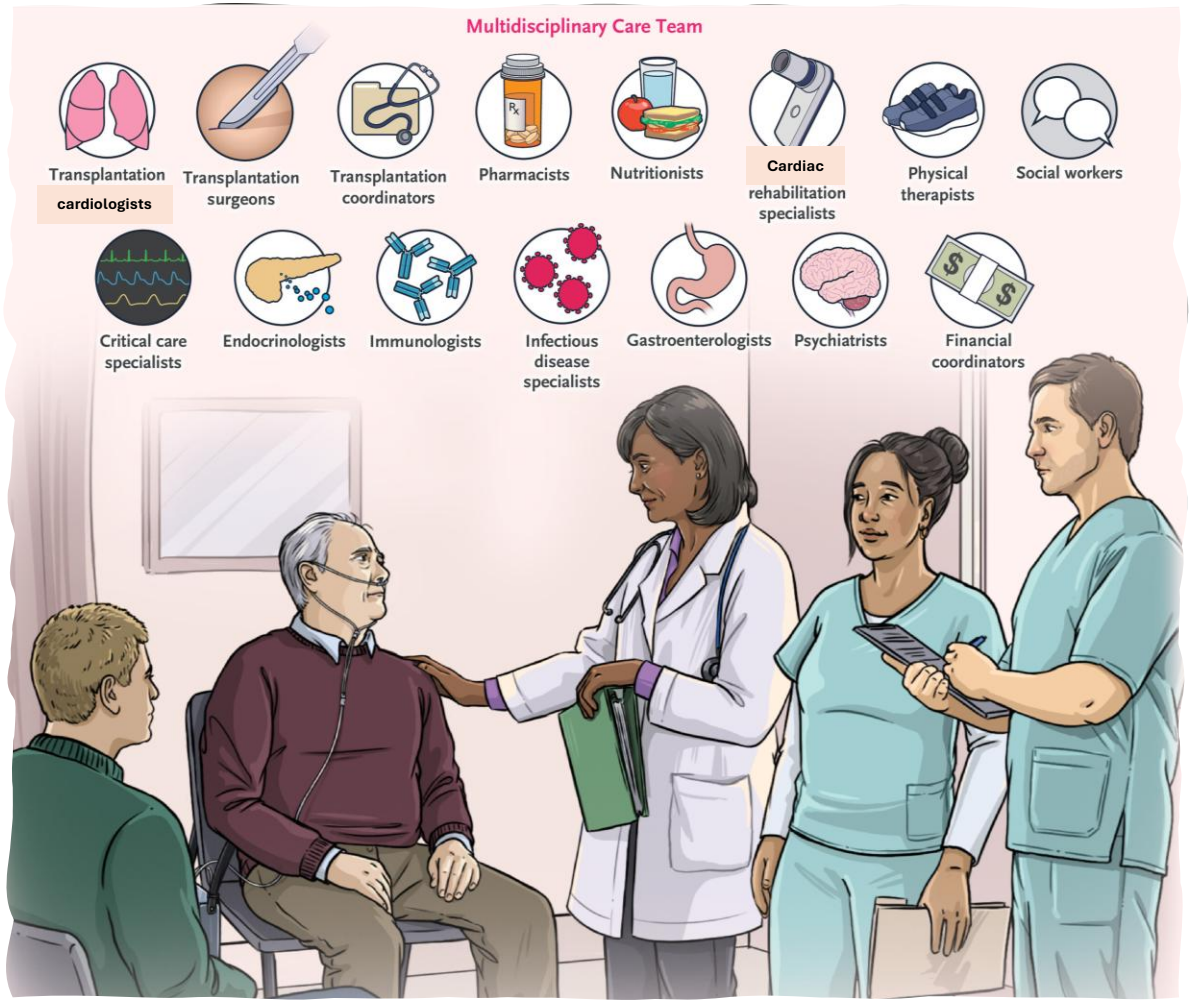
✗ Kidney failure requiring dialysis

✗ Active cancer or uncontrolled infections

✗ For AL: Bone marrow disease not responding to treatment

The Team Approach:

- Decisions made by team of specialists: cardiologists, transplant surgeons, hematologists (for AL), pharmacists, nutritionists, social workers and more!



10.1056/NEJMra2401039

Life after Heart Transplantation

The Good News:

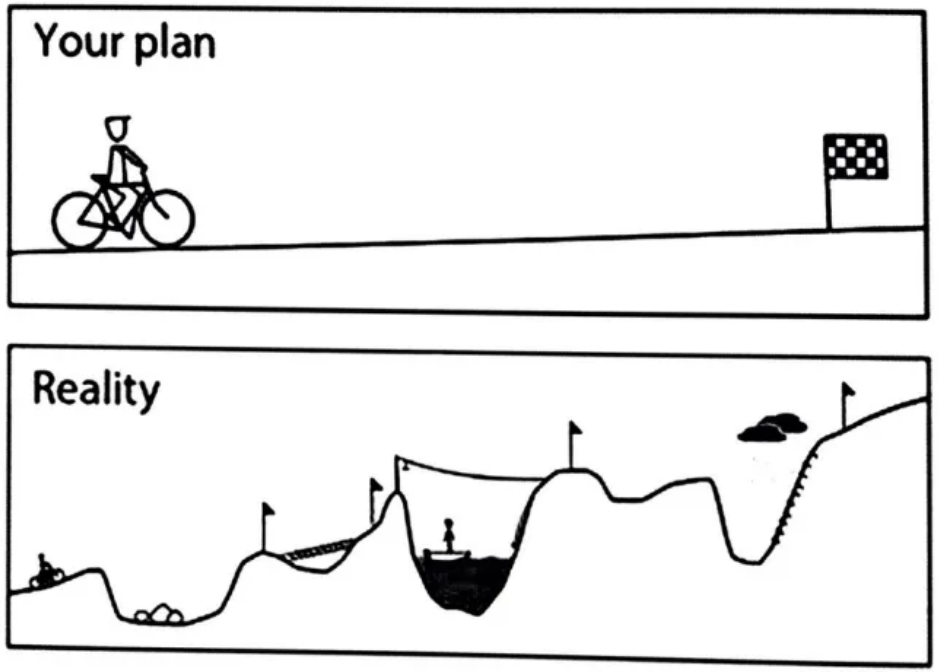
- Most patients feel dramatically better - can return to normal activities
- Survival rates similar to other transplant patients
- Disease rarely comes back in new heart (if properly managed)

The Challenges:

- Must take anti-rejection medications every day for life
- Regular heart biopsies to check for rejection
- Frequent doctor visits
- For AL patients: Ongoing chemotherapy to prevent recurrence
- For ATTR: Continue TTR therapies to prevent reaccumulation of protein

Complications:

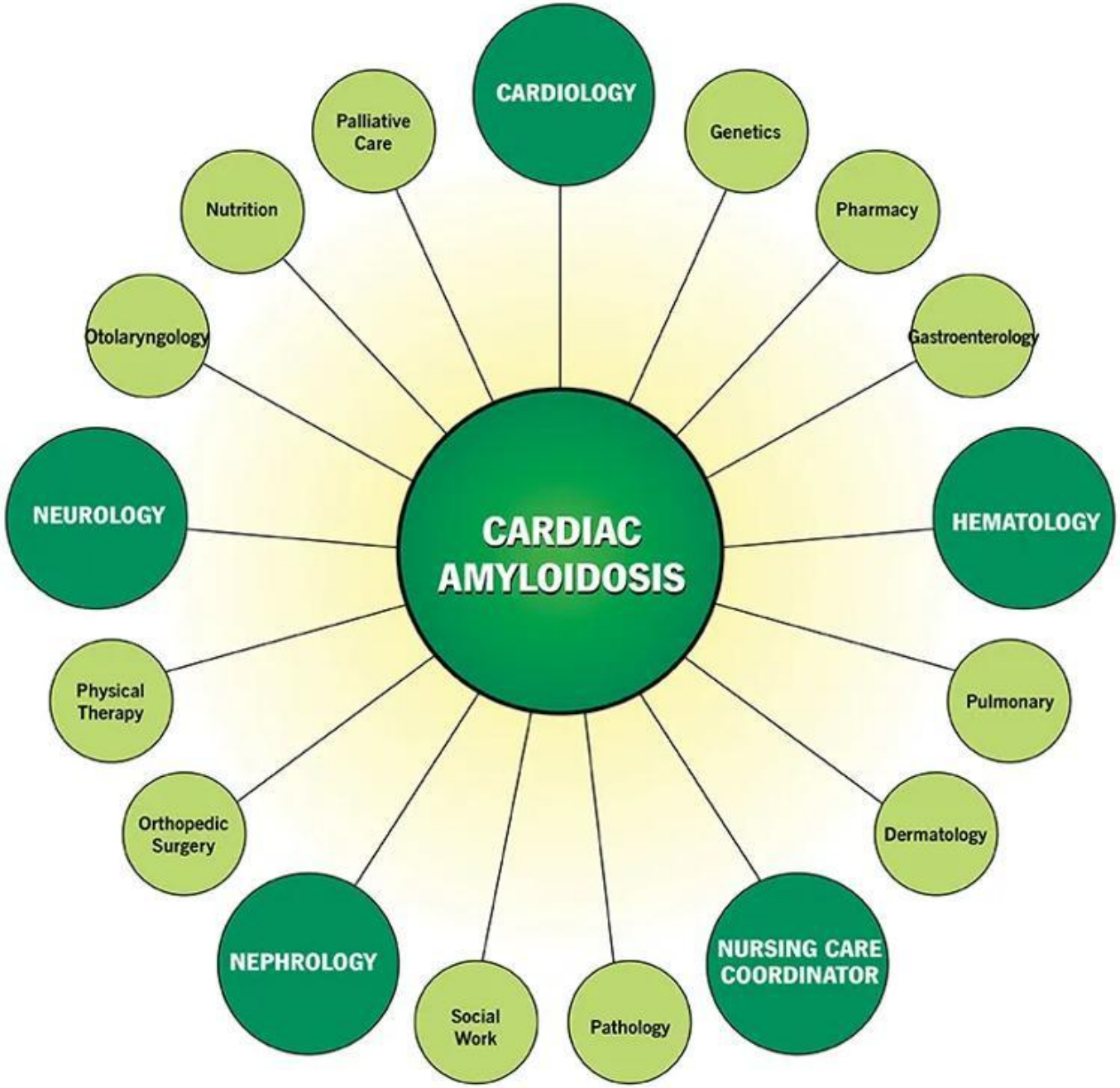
- Rejection episodes (body trying to attack new heart): Happens but usually treatable
- Infections (because immune system is suppressed)
- Side effects from medications



THE IMPORTANCE OF EARLY DIAGNOSIS

- Cardiac amyloidosis is **underdiagnosed** — many patients see multiple doctors over years before getting the right diagnosis.
- ATTR-CM may be present in up to **10–16% of older patients** with heart failure or severe aortic valve disease.
- Treatments work best when started **early**, before severe heart damage occurs.
- If you or a loved one has unexplained heart thickening, heart failure that doesn't respond to usual treatments, or a history of carpal tunnel syndrome in both hands — **ask about amyloidosis**.

THE BEST AMYLOIDOSIS CARE REQUIRES A MULTI-DISCIPLINARY TEAM!



KEY TAKEAWAYS

1. Cardiac amyloidosis is caused by misfolded proteins building up in the heart.
2. The two main types — **AL** and **ATTR** — have different causes and different treatments.
3. Diagnosis has gotten much easier with modern scans and blood tests.
4. Effective treatments now exist for both types, and more are on the way.
5. **Early diagnosis and early treatment** lead to the best outcomes.
6. Heart transplantation is an option for selected patients with advanced disease, and outcomes are improving.
7. A team approach to care is essential.

RESOURCES AND SUPPORT

- **Amyloidosis Foundation:** www.amyloidosis.org
- **Amyloidosis Research Consortium (ARC):** www.arci.org
- **Amyloidosis Support Groups (ASG):** www.amyloidosissupport.org
- **American Heart Association:** www.heart.org (search "cardiac amyloidosis")
- **ClinicalTrials.gov:** www.clinicaltrials.gov (search "cardiac amyloidosis" to find research studies)
- **You are not alone.** Connecting with others who understand this journey can make a real difference.

Thank you for being here today!

Your questions are welcome!