

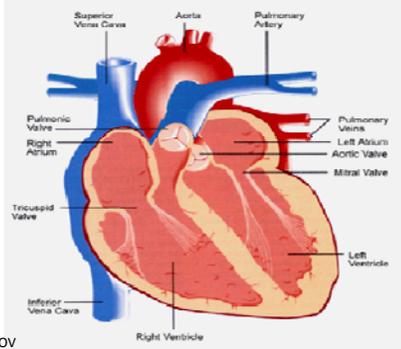


TTR Amyloid: Cardiac Symptoms and Issues

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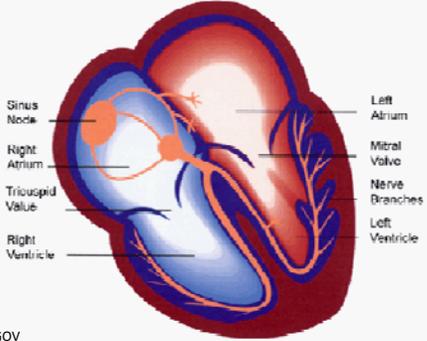


Introduction



NIAAA.NIH.GOV

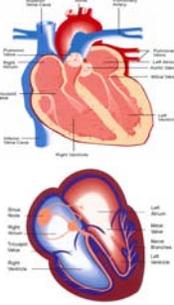
Heart's electrical system:



NIAAA.NIH.GOV

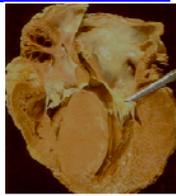
Heart Problems with ATTR:

- Cardiomyopathy
- Heart Failure
- Arrhythmia
 - Heart rate is too slow
 - Heart rate is too fast
 - Atrial fibrillation



Cardiomyopathy

- Greek derivation:
 - Kardia → heart
 - Mys → muscle
 - Pathos → suffering
- WHO: “diseases of the myocardium associated with ventricular dysfunction”



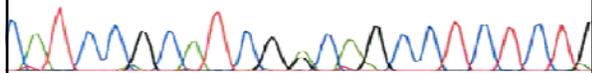
Amyloid Cardiomyopathy

- Heart becomes too thick due to amyloid
- Typically affects all portions of the heart, but the ventricles (bottom chambers) are the most important.
- Strength of the heart (ejection fraction) can be normal, high, or low.
- The heart gets very stiff.



TTR Amyloid Cardiomyopathy

- Cardiac involvement varies substantially among different *TTR* mutations.
- Val122Ile – prominent cardiac disease, typically recognized age 60 and later.
- Val30Met – cardiac problems tend to be less severe than neuropathy, but electrical heart problems (“heart block”) often occur despite transplant.



Other problems that make the heart too thick:

- Hypertrophic cardiomyopathy (HCM)
 - IHSS (idiopathic hypertrophic subaortic stenosis)
 - HOcm (hypertrophic obstructive cardiomyopathy)
 - ASH (asymmetric septal hypertrophy)
- Hypertension
- Aortic stenosis

Heart Failure

- The heart is not able to pump blood adequately to meet the demands from the rest of the body.
- Exercise / At rest
- It's a “clinical diagnosis,” meaning that it is determined by a blood test or echocardiogram.

Heart Failure Symptoms

- Shortness of breath (SOB)
- Fatigue
- Swelling (abdomen, ankles)
- Unable to lie down due to SOB
- Awakening during the night with SOB
- Wheezing
- Coughing
- Lack of appetite

Arrhythmia

- Heart goes too slowly (bradycardia).
 - Defined as less than 60 beats/minute, but not typically treated unless there are symptoms.
- Heart goes too quickly (tachycardia).
 - Defined as greater than 100 beats/minute.
 - Lots of different types (SVT, VT, sinus tach)
 - Usually treated
- Heart is out of rhythm (atrial fibrillation)
 - Top chambers (atria) have disorganized electrical activity.

Atrial fibrillation:

- Very common (>5% of people >age 65)
- Frequent in cardiac amyloid and in all forms of heart failure.
- Complications:
 - Worse heart failure
 - Heart goes too fast or too slowly
 - Blood clots in the atria, which can then cause a stroke or clotted blood vessels.

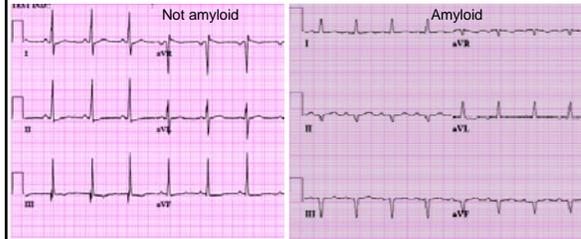
Symptoms of arrhythmia

- “Syncope” (fainting, passing out)
- Palpitations
- Lightheadedness
- Shortness of breath
- Fatigue



Tests to find amyloid in the heart

Discord between EKG:

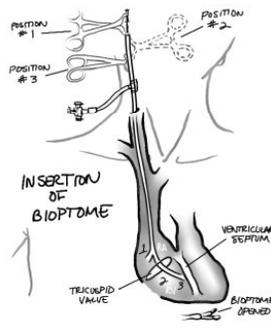


And echocardiogram: 2 cm wall thickness for both

Tests to find amyloid in the heart

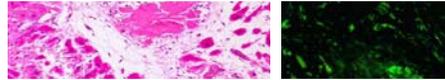
- Discord between EKG and echo
- Cardiac MRI may suggest it
- Heart biopsy, → which is far less painful than a biopsy of a nerve.

www.ctsnet.org



Risks of heart biopsy

- Infection (rare)
- Damage to a blood vessel (rare)
- Electrical problems:
 - Electrical delay in the heart (bundle branch block; rare)
 - Extra heart beats (common)
- Hole in the heart (~1:1000)



Useful blood tests for heart disease in *TTR* amyloid:

- Troponin – a protein that comes from the heart. Normally it is not detected in the blood. In amyloid, low levels are very common. This can look like a heart attack.
- BNP or ProBNP – another protein from the heart, usually with very low level in blood. Heart failure (among other things) can increase this level.

Treatments: Medications

Commonly used for HF:

- Beta blockers
- ACE-inhibitors
- Angiotensin receptor blockers
- Digoxin
- Diuretics

Cardiac Amyloid:

- Mechanisms for those medications to help are mostly not applicable in amyloid.
- Digoxin may be particularly harmful for people with amyloid.
- Diuretics are usually very helpful for symptoms.

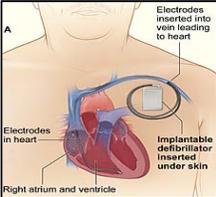


Atrial fibrillation - treatment

- Medications to help maintain normal rhythm
- Cardioversion (electrical shock to restore normal rhythm)
- Prevent heart from going too fast
- Blood thinners to help prevent strokes
 - Coumadin
 - Aspirin
 - Newer agents (Pradaxa, soon Apixaban)

Treatment of arrhythmias

- Pacemakers can be very helpful for slow heart rates or severe electrical heart block.
- Defibrillators:
 - Pacemaker-like devices that shock the heart if it goes too fast;
 - Likelihood of firing
 - Pros and cons
 - Personal decision



www.nhlbi.nih.gov

Natural remedies

- Both soy and curry have been shown (in massive amounts) to inhibit amyloid deposition, leading several people to ask me whether they should use these as treatment.

Genistein, a natural product from soy, is a potent inhibitor of transthyretin amyloidosis

Mura S. Green¹, Ted R. Fozz², and Jeffrey W. Kelly³



Curcumin Inhibits Formation of Amyloid β Oligomers and Fibrils, Binds Plaques, and Reduces Amyloid *in Vivo*

The Journal of Biological Chemistry, Vol. 283, No. 12, Second February 18, pp. 2022-2031, 2008. Printed in U.S.A.



Other therapies...

CardioShen
Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

REVIEW ARTICLE

Benefits, Adverse Effects and Drug Interactions of Herbal Therapies With Cardiovascular Effects

Georgianne Valli, MD, Elsa-Grace V. Giardina, MD, FACC
New York, New York

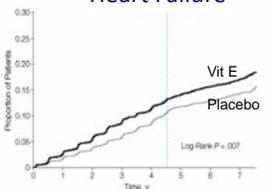


What about vitamins?

JAMA 2005

Effects of Long-term Vitamin E Supplementation on Cardiovascular Events

Heart Failure



Hospitalized for Heart Failure

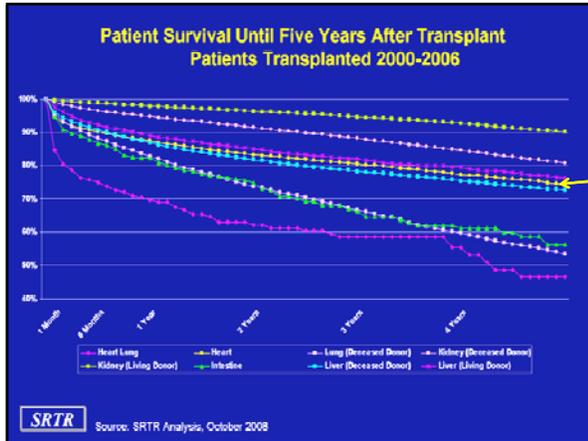


Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality

Edgar R. Miller III, MD, PhD; Roberto Pastor-Barriuso, PhD; Danhan Dalal, MD, MPH; Rudolph A. Riemersma, PhD, FRCP; Lawrence J. Appel, MD, MPH; and Eliseo Guallar, MD, DrPH

Cardiac transplantation

- About 1,600 performed yearly in the USA
- Number on waiting lists is far greater
- Eligibility depends on many factors; amyloid generally excludes consideration unless liver transplant is also done.
- Immunosuppression, rejection, infections, and blockage of blood vessels are long term problems after transplant.



Left Ventricular Assist Device

- Mechanical pump attached to the heart, assisting with circulation.

POSTPOLITICS New home. Still the best political coverage.

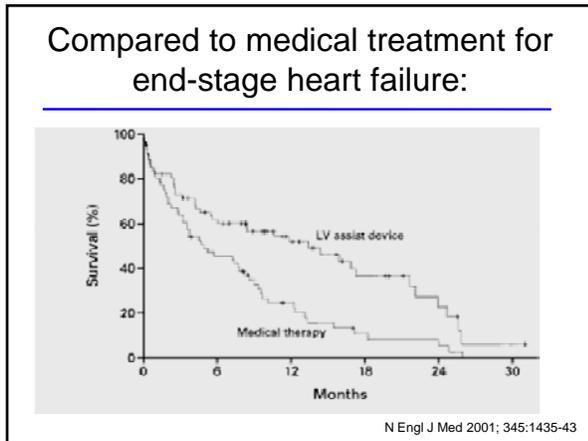
Cheney has heart pump surgically installed; former VP's latest cardiac issue

By Michael D. Shear and David Brown
Washington Post Staff Writers
Wednesday, July 14, 2010, 6:11 PM

Former vice president Richard Cheney long suffered with cardiac issues. He last week to have a pump implanted, announced Wednesday.

www.articles.cnn.com
www.washingtonpost.com

NEJM 2001;345:1435-43



Newer devices:

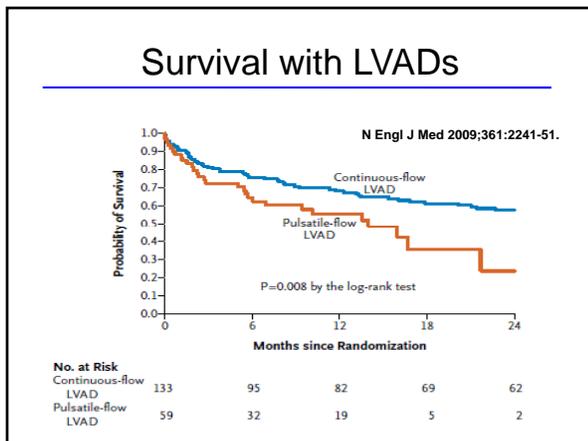
PF LVAD

CF LVAD

	PF LVAD	CF LVAD
Weight (gm)	1250	390
Volume (ml)	450	63
Noise	Audible	Silent
Moving parts	Many	One
Maximal flow (l/min)*	10	10
Clinical Durability (yr)	1.5	Est. > 5 yrs

CF LVAD with controller and batteries

Courtesy of Dr Stuart Russell, Johns Hopkins



Problems with LVADs

- Need for continuous external power
- Infections through skin opening to connect to power source
- Gastrointestinal bleeding.
- Only supports the left ventricle, not the right. Larger Bi-Ventricular Assist Devices are not portable.

What's next?

Total artificial heart (ie, Abioco^r)



Summary

- Heart problems commonly occur for people with *TTR* amyloid.
- The most effective treatment right now is to get rid of congestion (diuretics) and prevent the heart from going too fast or too slowly.
- Technological improvements in care for end-stage heart failure are making mechanical support more feasible.