

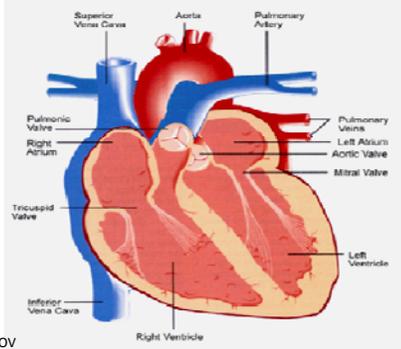


TTR Amyloid: Cardiac Symptoms and Issues

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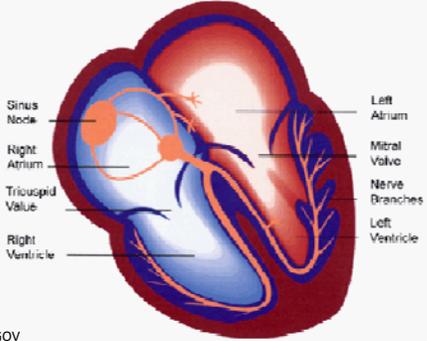


Introduction



NIAAA.NIH.GOV

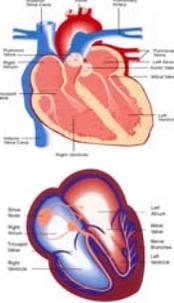
Heart's electrical system:



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Heart Problems with ATTR:

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



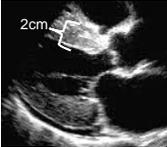
Cardiomyopathy

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



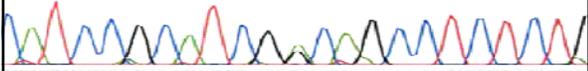
Amyloid Cardiomyopathy

- 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.

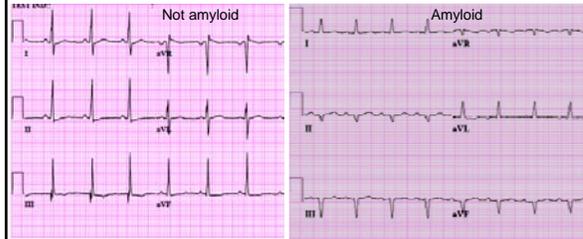
Symptoms of arrhythmia

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



Tests to find amyloid in the heart

Discord between EKG:

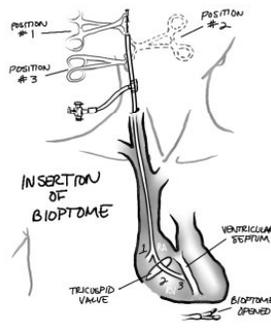


And echocardiogram: 2 cm wall thickness for both

Tests to find amyloid in the heart

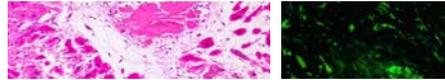
- Discord between EKG and echo
- Cardiac MRI may suggest it
- Heart biopsy, → which is far less painful than a biopsy of a nerve.

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.

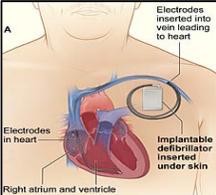


Atrial fibrillation - treatment

- 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. Fozard², and Jeffrey W. Kelly^{1*}

The Journal of Biological Chemistry VOL. 280, No. 12, Issue of February 14, pp. 2002-2005, 2005
Printed in U.S.A.

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





Other therapies...

CardioShen
 Journal of the American College of Cardiology
 © 2002 by the American College of Cardiology Foundation
 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



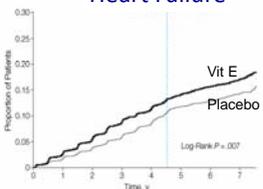


What about vitamins?

JAMA 2005

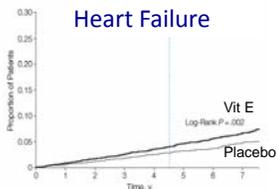
Effects of Long-term Vitamin E Supplementation on Cardiovascular Events

Heart Failure



Log-Rank P = .007

Hospitalized for Heart Failure



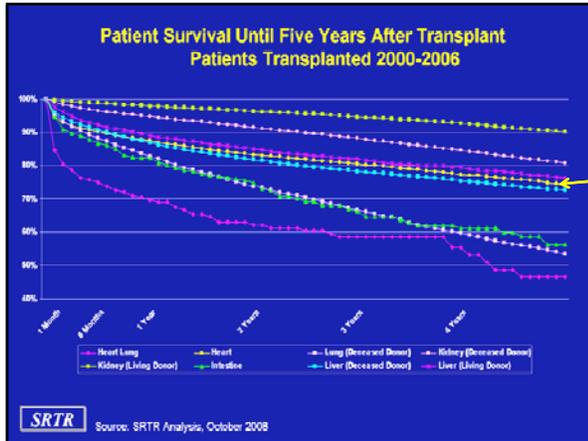
Log-Rank P = .002

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.

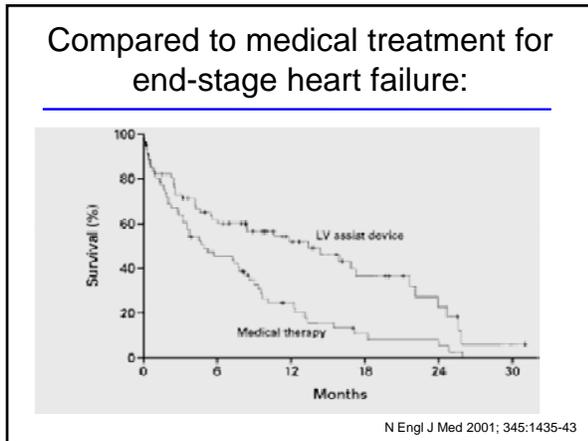
Cheney has heart pump surgically installed; former VP's latest cardiac issue

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:

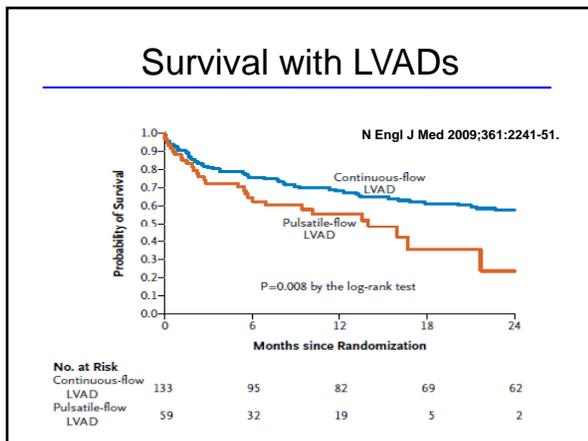
PF LVAD

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, AbiCor)



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.