

Lecture 19: Heart Failure

3.25.08

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Outline: Treatment of Heart Disease

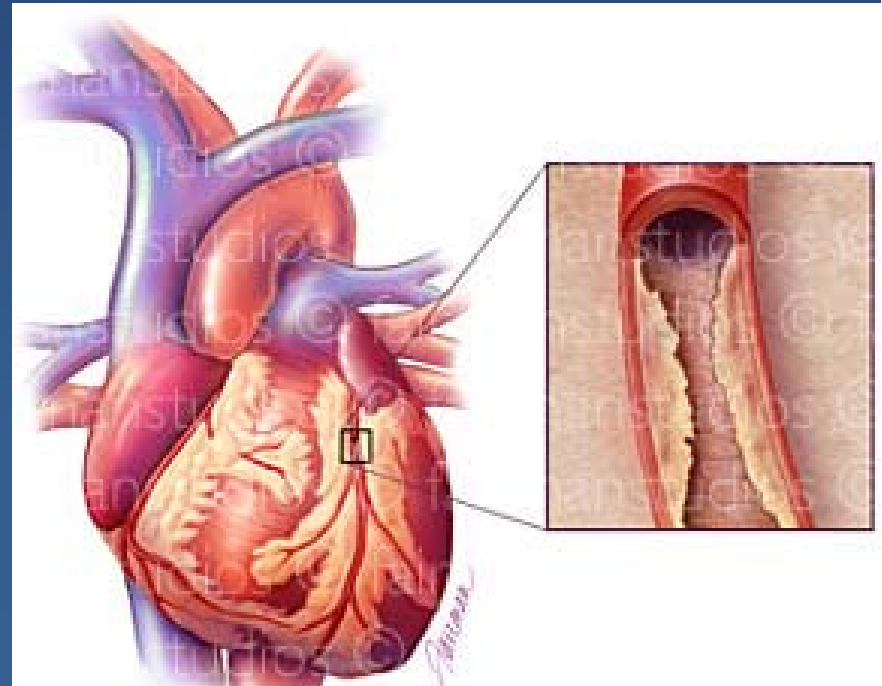
- Burden of cardiovascular disease (CVD)
- Cardiovascular system
- Measuring cardiovascular health
- Valve diseases
- Atherosclerosis/CAD and treatments
 - Stroke
 - Heart attack
- Heart failure and treatments

From Last Time

- Burden of cardiovascular disease (CVD)
- Cardiovascular system
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Review of Last Time

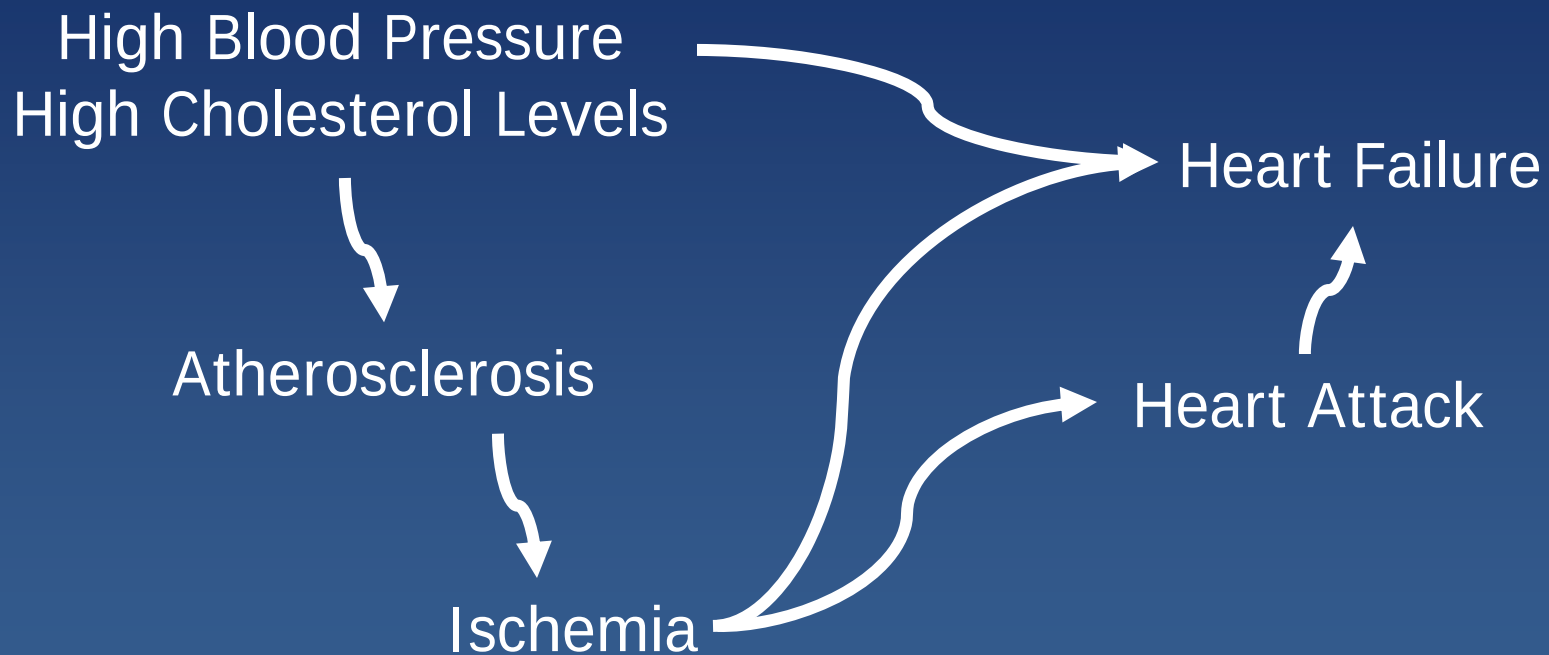
- How do we treat coronary artery disease?
 - Thrombolytic drugs
 - Only a small fraction of patients qualify
 - Percutaneous transluminal coronary angioplasty
 - PTCA
 - Stent
 - Coronary artery bypass graft
 - CABG
 - Prevention



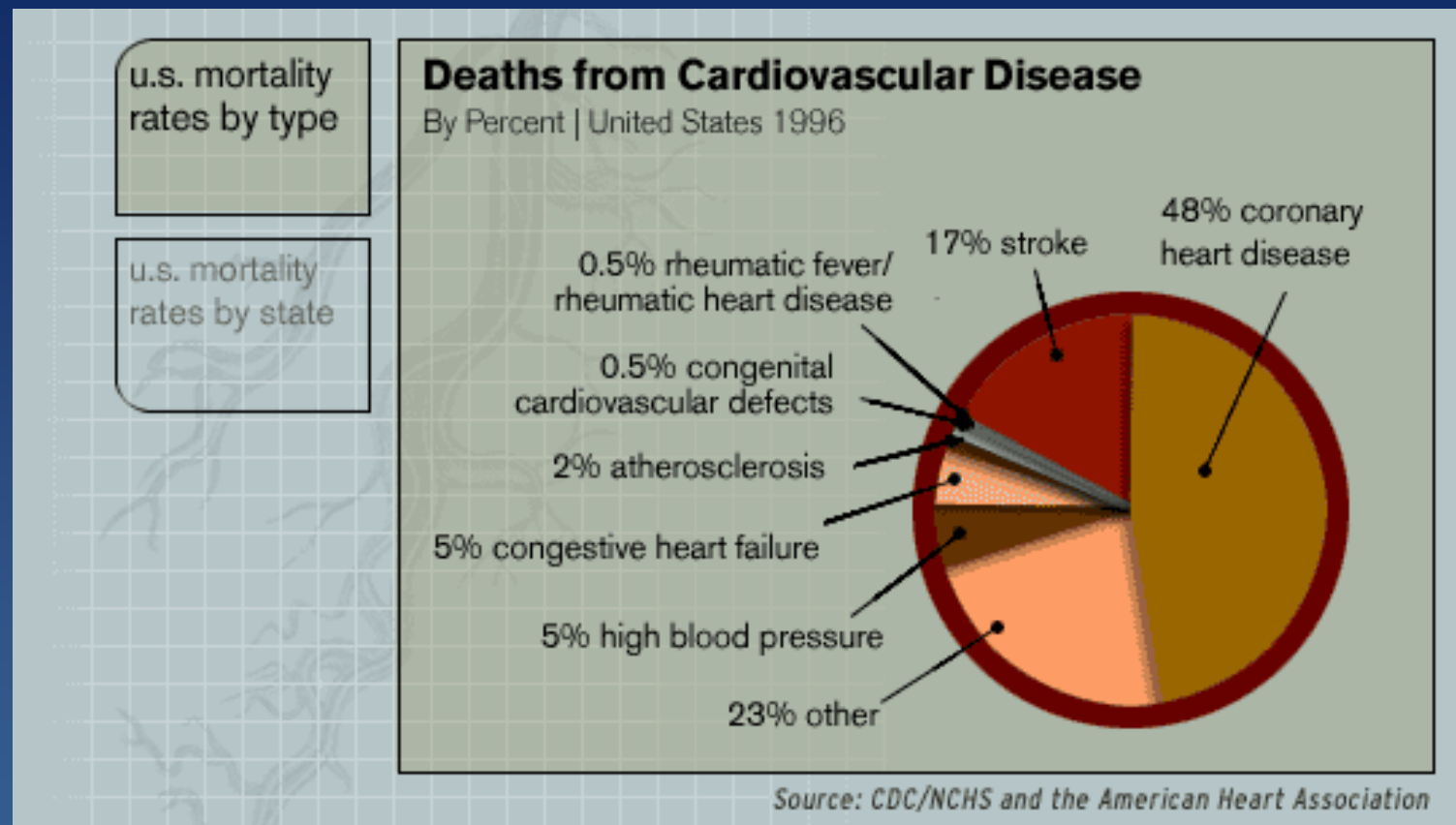
Prevention vs. Treatment

- Risk Factors for Heart Disease
 - Tobacco use
 - High blood pressure
 - Over 70% not under control
 - High cholesterol
 - Over 80% not under control
 - Inappropriate diet
 - Obesity
 - Low levels of physical activity
- Super Size Me

Progression of Heart Disease



Burden of CVD



<http://www.pbs.org/secondopinion/episodes/heartfailure/>

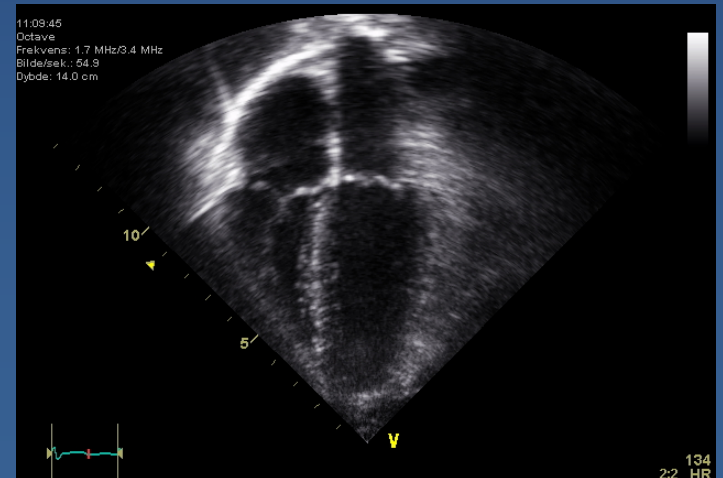
<http://www.pbs.org/wgbh/nova/heart/>

Heart Failure

- Heart failure:
 - Occurs when left or right ventricle loses the ability to keep up with amount of blood flow
 - Can involve the heart's left side, right side or both sides
 - Usually affects the left side first
- About 5 million Americans are living with heart failure
- 550,000 new cases diagnosed each year

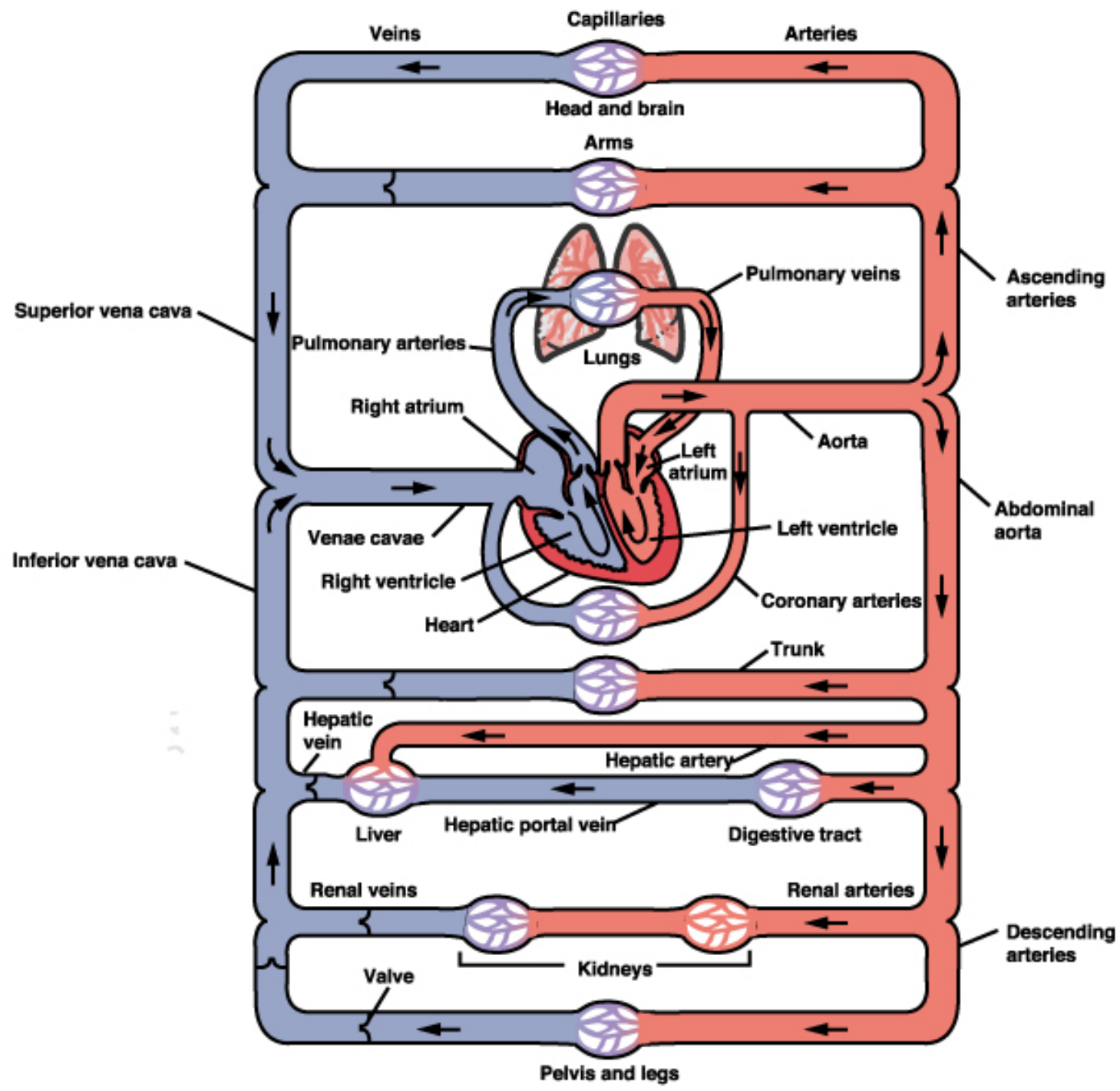
Quantifying Heart Performance

- Ejection Fraction (EF)
 - Fraction of blood pumped out of ventricle relative to total volume (at end diastole)
 - $EF = SV/EDV$
 - Normal value > 60%
 - Measured using echocardiography



Left Sided Heart Failure

- Involves left ventricle
- Systolic failure
 - Left ventricle loses ability to contract
 - Can't push enough blood into circulation
- Diastolic failure
 - Ventricle loses ability to relax; muscle has become stiff
 - Can't properly fill during resting period between beats
- Pulmonary edema
 - Blood coming into left chamber from lungs "backs up," causing fluid to leak into the lungs
 - As ability to pump decreases, blood flow slows, causing fluid to build up in tissues throughout body (edema)
- Congestive Heart Failure



Symptoms of Heart Failure

Symptom	Why It Happens	People May Experience:
<i>Shortness of breath (also called dyspnea)</i>	Blood "backs up" in pulmonary veins (the vessels that return blood from the lungs to the heart) because the heart can't keep up with the supply. Causes fluid to	Breathlessness during activity, at rest, or while sleeping, which may come on suddenly and wake them up. Often have difficulty breathing while lying flat; may need to prop up upper body and head on pillows
<i>Persistent coughing or wheezing</i>	leak into lungs Fluid builds up in lungs	Coughing that produces white or pink blood-tinged phlegm.
<i>Buildup of excess fluid in body tissues (edema)</i>	As flow out of heart slows, blood returning to heart through veins backs up, causing fluid build up in tissues.	Swelling in feet, ankles, legs or abdomen or weight gain. May find that shoes feel tight

Symptoms of Heart Failure

Symptom	Why It Happens	People May Experience:
<i>Increased heart rate</i>	To "make up for" loss in pumping capacity, heart beats faster	Heart palpitations, which feel like the heart is racing or throbbing.
<i>Confusion, impaired thinking</i>	Changing levels of blood substances, such as sodium, can cause confusion	Memory loss and feelings of disorientation.
<i>Lack of appetite, nausea</i>	Digestive system receives less blood, causing problems with digestion	Feeling of being full or sick to their stomach.
<i>Tiredness, fatigue</i>	Heart can't pump enough blood to meet needs of tissues. Body diverts blood away from less vital organs (limb muscles) and sends it to heart & brain.	Tired feeling all the time and difficulty with everyday activities, such as shopping, climbing stairs, carrying groceries or walking.

How Do We Treat Heart Failure?

- Diet modification
 - Weight loss
 - Salt intake
- Moderate exercise
- Medication
- Heart Transplant
- Cardiac Assist Devices
- Artificial Heart

<http://video.google.com/videoplay?docid=-7504680635958708617&q=heart+failure+duration%3Ashort&hl=en>

<http://www.cbsnews.com/htdocs/health/heart/framesource.html>

How Do We Treat Heart Failure?

- Balance a lot of issues
 - Prevent disease progress
 - Cause of heart failure
 - Can it be reversed?
 - Prognosis
 - Cost
- SC Heart Hospital's IT solution

<http://video.google.com/videoplay?docid=-6557199641577284256&q=heart+failure&hl=en>

Stages of Heart Failure

Stag	Description	Typical Therapies
A	No diagnosis or symptoms of heart failure, but the risk is high because of: hypertension; diabetes; CAD/MI; cardiotoxic drugs or alcohol abuse; rheumatic fever; family history of cardiomyopathy	Stop smoking; start exercise; treat hypertension and high cholesterol; stop use of alcohol and illicit drugs (ACE) inhibitors and/or beta blockers
B	Heart failure diagnosed by an EF < 40%, but no past or current symptoms	All therapies in Stage A plus: Surgical consultation for coronary artery revascularization and valve repair or replacement ACE inhibitor and beta blocker (unless contraindicated).

Stages of Heart Failure

Stag	Description	Typical Therapies
	Heart failure diagnosed, with past or current symptoms, including shortness of breath, fatigue, and reduced exercise tolerance	All therapies in Stage A plus ACE inhibitor and beta blocker + diuretic and digoxin Restrict salt intake, monitor weight, and restrict fluid intake Spironolactone when symptoms remain severe
<i>D</i>	Advanced symptoms of heart failure after receiving optimal medical care	All therapies in Stages A-C plus: Evaluation for other treatments: heart transplant, ventricular assist device, other surgeries, continuous IV infusion of inotropic drugs, and research therapies

<http://health.usnews.com/usnews/health/heart/chf/chf.manage.stages.htm>

12-29-06

How Do We Treat Heart Failure? Heart Transplant

Heart Transplant

- 1960s:
 - First heart transplants performed
 - Limited success
- 1980s:
 - Anti-rejection meds became available (Cyclosporine)
- Today:
 - About 80% of heart transplants are alive two years after the operation
 - 50% percent survive 5 years
- Need:
 - $\approx$ 2 million Americans have CHF
 - 4,000 patients are on the national patient waiting list for a heart transplant
 - Only about 2,500 donor hearts become available for transplantation each year

Surgical Procedure

<http://www.pbs.org/wgbh/nova/eheart/transplantwave.html>

Yes, it's a little cheesy!

Rejection

- Risk of rejection is highest right after surgery
 - In one study, first year after transplant:
 - 37% of patients had no rejection episodes
 - 40% had one episode
 - 23% had more than one episode
- Induction therapy:
 - Use of drugs to heavily suppress immune system right after transplant surgery
- Patients keep taking some anti-rejection drugs for the rest of their life

Connection to Lecture 17

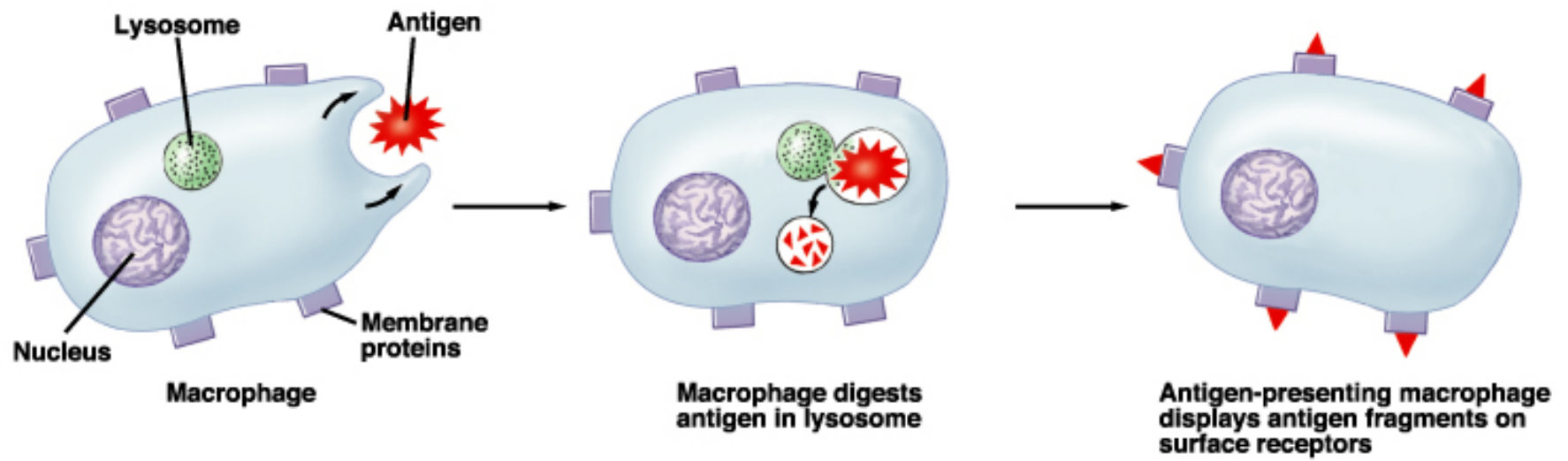
- Heart valve replacements
 - Xenografts
 - Allografts
 - Especially for children
- These carry similar risks and problems as heart transplant

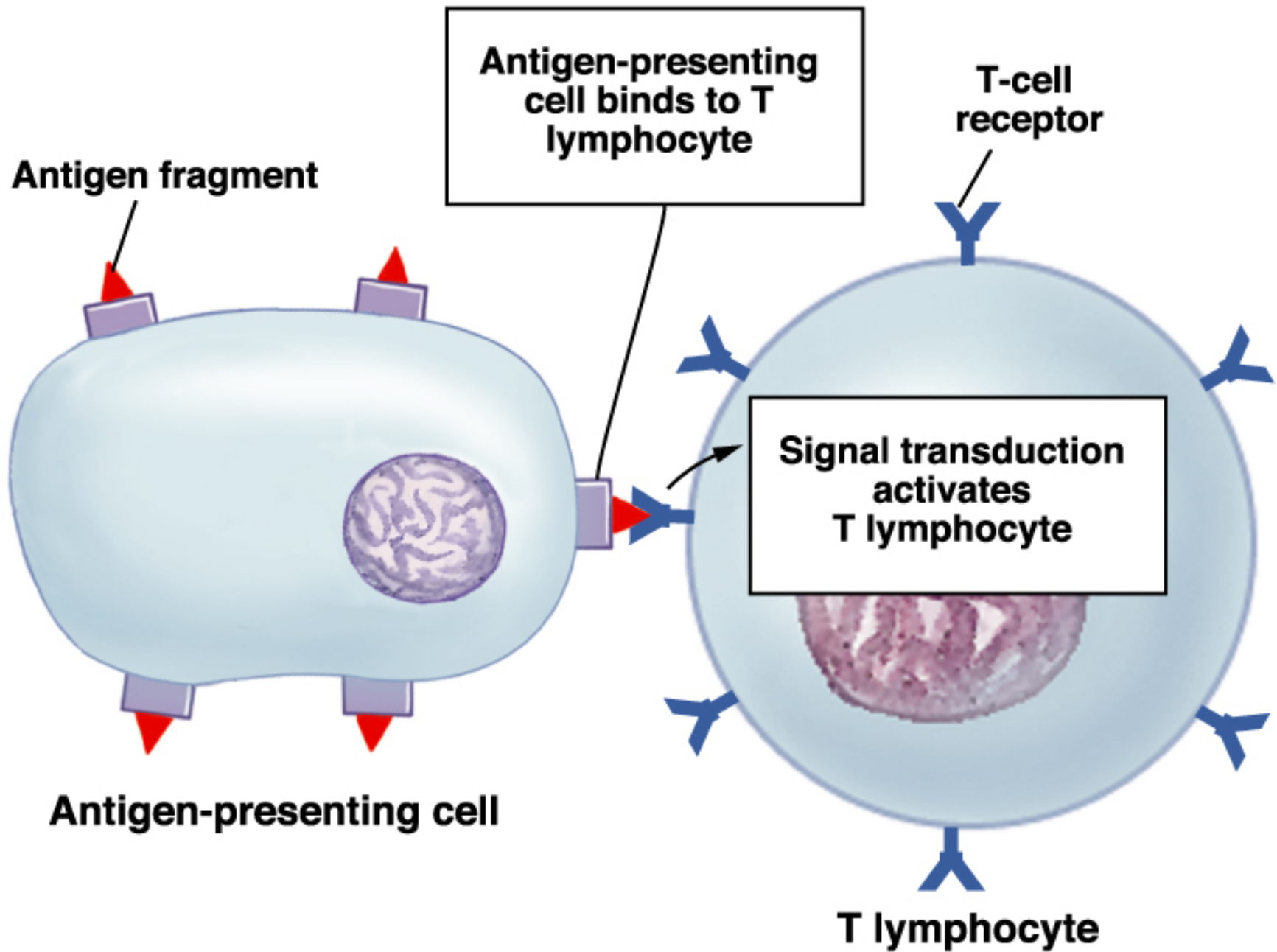


Bioprosthetic Valve

Remember from Our Vaccine Unit:

- Two branches of immune system
 - Innate
 - Adaptive
 - B-lymphocytes -- make antibodies (humoral)
 - T-lymphocytes -- cell-mediated
- Adaptive immune system gives immunologic memory!
- How do T Cells recognize virus infected cells?
 - Antigen presentation
 - All cells have MHC molecules on surface
 - When virus invades cell, fragments of viral protein are loaded onto MHC proteins
 - T Cells inspect MHC proteins and use this as a signal to identify infected cells





MHC Receptors

- Two types of MHC molecules
 - Class I MHC molecules are found on all nucleated cells
 - Class II MHC molecules are found on antigen presenting immune cells
- Self-Tolerance
 - T cells which recognize class I MHC self-antigens are destroyed early in development
- When this fails: auto-immune disease
 - Type 1 diabetes

Donor MHC Matching

- The greater the difference in peptide sequences of MHC receptors between donor and recipient:
 - The stronger the immune response
 - The greater the chance of organ rejection
- Matching:
 - 200 different histocompatibility antigens
 - Each person has a certain “set”
 - Odds that 2 unrelated people will have the same set are about 1 in 30,000
 - Transplant coordinators try to match histocompatibility antigens of the donor and the recipient as well as possible to minimize rejection

Immunosuppressive Rx

- Cyclosporine, azathioprine and low-dose steroids
 - Reduce T-cell activation:
 - T-helper cell
 - CTL activity
- Immuno-compromised state
 - Recipient susceptible to opportunistic viruses/diseases:
 - B-cell lymphomas (Epstein-Barr virus)
 - Squamous cell carcinomas (human papilloma virus)
 - Kaposi's sarcoma (a herpes virus)
 - Viral infections (cytomegalovirus)
- Graft-versus-host disease
 - Caused by alloreactive T-cells within the donor tissue that can cause tissue damage in the recipient
- Routine heart biopsies to monitor for rejection

Winds of Change??

<http://www.reuters.com/article/scienceNews/idUSSYD90620080125>

<http://www.npr.org/templates/player/mediaPlayer.html?action=1&t=1&islist=false&id=18349971&m=18352567>

How To Become An Organ Donor

Three steps:

1. Speak with your family about your decision to donate. Make sure they know about your wish to be an organ donor.
2. Sign a Uniform Donor Card, and have two family members sign the card as witnesses.
3. Carry the card in your wallet at all times.

Uniform Donor Card

- Department of Public Safety (where you obtain drivers licenses)
- Download a Uniform Organ Donor Card
- In Texas, Glenda Dawson Donate Life (formerly DEAR)
 - Donor Education, Awareness, and Registry
 - <http://www.dshs.state.tx.us/organdonation/default.shtm>
 - https://www.donatelifetexas.org/TXDear_Secure/default.aspx

rd!

Uniform Donor Card	
I, _____, have spoken to my family about organ and tissue donation. The following people have witnessed my commitment to be a donor. I wish to donate the following:	
☐ Any needed organs and tissue.	
☐ Only the following organs and tissue: _____	
Donor Signature	Date
Witness	
Witness	
Next of Kin	Telephone

Why Inform Your Family?

If you haven't told your family you're an organ and tissue donor -- you're not!

Sharing your decision with your family is more important than signing a donor card. In the event of your death, health professionals will ask your family members for their consent to donate your organs and tissues. This is a very difficult time for any family, and knowing your wishes will help make this decision easier for them. They will be much more likely to follow your wishes if you have discussed the issue with them.

Remember - signing an organ donor card is NOT enough. Discuss your decision with your family!

More About Organ Donation

- <https://www.texasdear.org>
 - Texas state organ donor registry
- <http://www.shareyourlife.org/>
- <http://www.organdonor.gov/>
 - Government site about organ donation
- <http://www.unos.org/>
 - Organization that coordinates transplants

How Do We Treat Heart Failure?

Cardiac Devices

History of Cardiac Devices

- 1950s and 1960s:
 - Heart-lung machine
 - Prosthetic materials to close holes between heart chambers
 - Replacement valves
 - Implantable pacemakers
 - Coronary angiography to diagnose/treat coronary artery disease
 - Intra-aortic balloon pump (IABP)
- 1970s and 1980s:
 - IABP gains wide acceptance as temporary cardiac assist system
 - Cyclosporine, an anti-rejection drug, makes human heart transplants feasible
 - PTCA to treat coronary artery disease with a balloon catheter
 - External & implantable ventricular assist devices enter clinical trials
- 1990s:
 - External and implantable left ventricular assist devices approved for temporary support as a bridge-to-transplantation

Design Requirements of Devices

- Non-thrombogenic blood contacting surface
- Pumping action that avoids blood and tissue trauma
- Variable output
- Small enough to fit in chest cavity
- Reliable

Types of Mechanical Support

- Temporary: LVADs
 - Give heart muscle a chance to rest/recover
 - Surprisingly, this can be enough to downgrade heart failure to a somewhat manageable level
 - Bridge to transplantation
 - Failure is not catastrophic
- Permanent: Total Artificial Heart
 - Replace damaged heart muscle
 - Failure is catastrophic

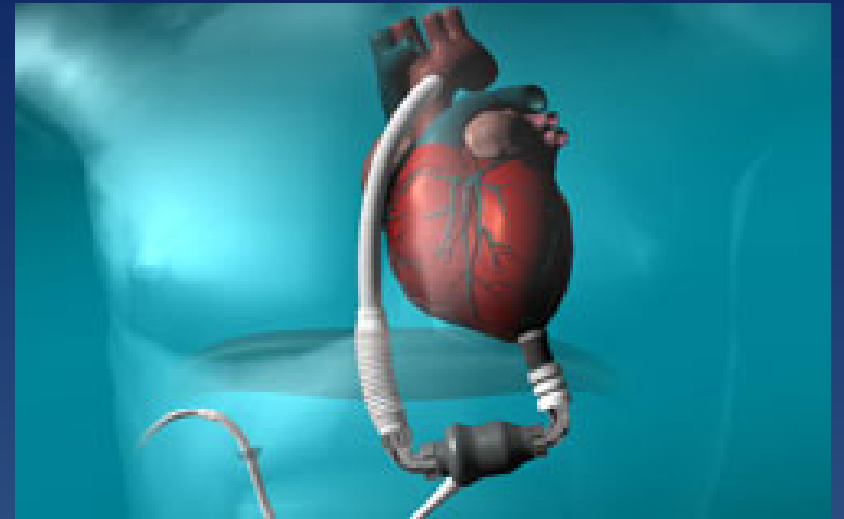
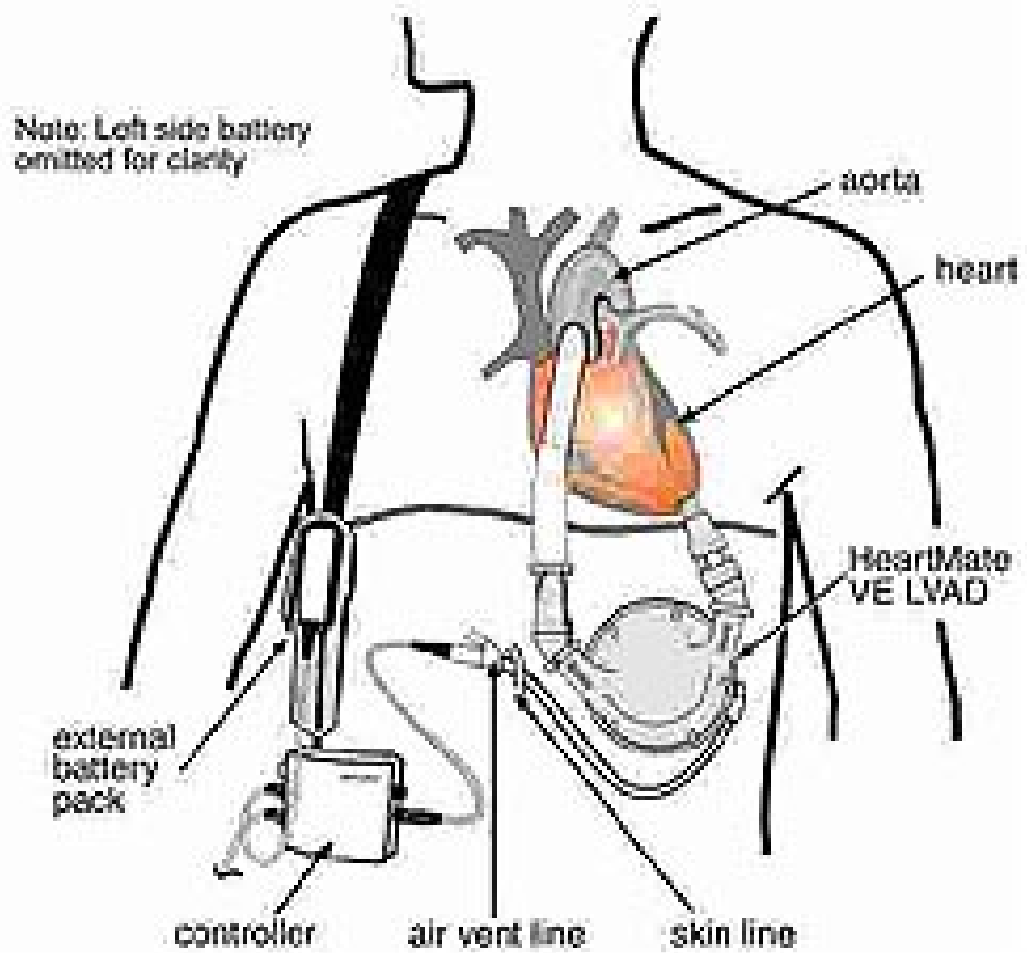
How Do We Treat Heart Failure?

LVADs



LVAD

<http://nypheart.org/img/rematch.jpg>



<http://www.j-circ.or.jp/english/sessions/reports/64th-ss/figures/margulies2.jpg>

<http://www.todayincardiology.com/199811/S8j00931.GIF>

LVAD

<http://www.texasheartinstitute.org/velvad2.jpg>

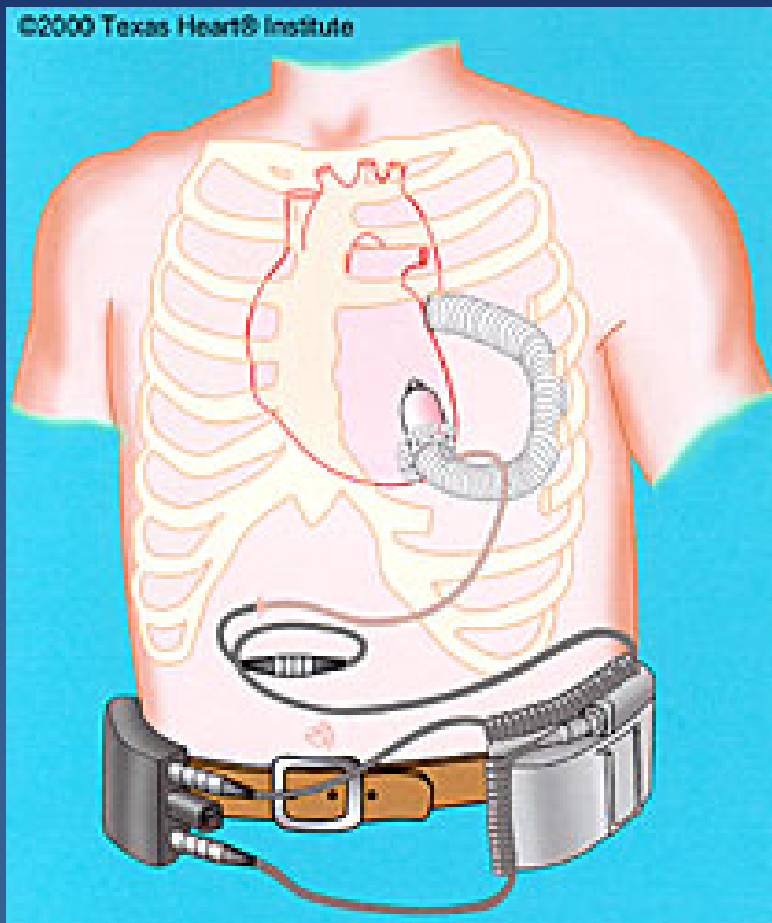


http://www.texasheartinstitute.org/ve_pump.jpg



Axial Flow Pumps

- Small
- Continuous, non-pulsatile flow



<http://www.texasheartinstitute.org/J2Syss.jpg>



<http://www.pbs.org/wgbh/nova/eheart/images/axialpump.jpeg>

<http://www.texasheartinstitute.org/j2f462s.jpg>

How Do We Treat Heart Failure?

Artificial Heart

Artificial Heart - History

- April 4th, 1969
 - Haskell Karp became first human to have artificial heart implanted
 - Surgeon Denton Cooley performed operation
 - Founded the Texas Heart Institute in 1962
 - Artificial heart had two chambers and blood was pumped by external airbags
 - Karp lived for ~2.5 days until a donor heart was available
 - Although, he died shortly after transplant
- No more human trials until the 1980s

Artificial Heart – Success?

- Denton Cooley
 - Mr. Karp has regained organ function indicated the mechanical heart is feasible
- Mrs. Shirley Karp
 - He could not say anything
 - I don't think he was really conscious
 - One day they removed the tube from his throat, they put a sheet over all the apparatuses in back of him and had the media take their pictures
 - Immediately after this was done they put back the tube and opened up everything that had closed up.

Artificial Heart - Outcome

- Dr. Debakey
 - Led team testing artificial heart in animals
- Dr. Liotta
 - Principal scientist developing artificial heart
- Liotta's proposal:
 - Even though 4 of 7 calves died after implant
 - Implant heart in human
 - Debakey rejected proposal
 - Liotta secretly went to Dr. Cooley who agreed
 - IRB was not informed

Artificial Heart - History

- Dr. Cooley
 - Dr. DeBakey seemed to show little interest in ever using it
 - Dr. Liotta thought he was just wasting his years in a laboratory
 - The time had come to really give it a test and the only real test would be to apply it to a dying patient
 - In those days I didn't feel like we needed permission
 - I needed the patient's consent
 - I think if I had sought permission from the hospital, I think I probably would have been denied and we would have lost a golden opportunity

Artificial Heart - History

- Dr. DeBakey
 - I was in Washington when I read in the morning papers about the use of this artificial heart
 - I was shocked
 - I didn't know he had taken it from the laboratory
- This left all three physicians at odds

Artificial Heart - Current

- AbioCor – first self-contained artificial heart
 - Must have large frame
 - Lasts ~ 18 months
- Robert Tools received first in 2001
 - Heart failure, diabetes and high blood pressure
 - Lived for ~ 150 days
 - Died of other complications
- AbioCor II
 - Soon to begin clinical trials
 - Longer device life



History of Artificial Heart

1997:

http://www.chron.com/CDA/archives/archive.mpl?id=2007_4456849

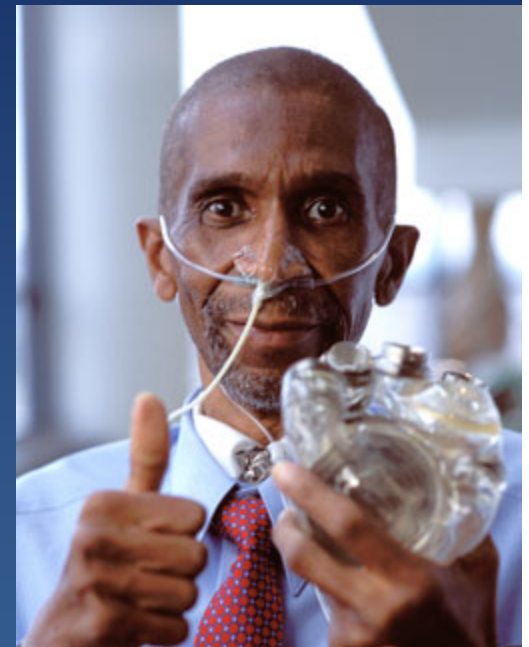
http://www.nytimes.com/2007/11/27/health/27docs.html?pagewanted=1&_r=1

July 2001: Robert Tools (right) receives AbioCor's artificial heart

<http://www.cnn.com/2001/HEALTH/conditions/07/03/artificial.heart/>

Nov 2001:

http://www.pbs.org/newshour/updates/november01/heart_11-30.html



http://images.usatoday.com/news/_photos/2001-11-30-heartguy.jpg

Recent Advances

<http://www.npr.org/templates/player/mediaPlayer.html?action=1&t=1&islist=false&id=18023493&m=18060872>

<https://mediamill.cla.umn.edu/mediamill/embed/7238>

Next Time (Thurs. 3/27)

- Homework 8 is due
- This was my last lecture
 - Evaluations
- Clinical trials & sample size calculation