

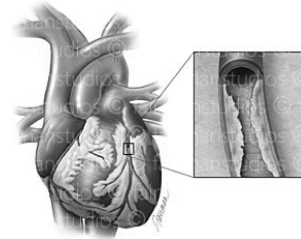
# BME 301

## Lecture Nineteen



## Review of Last Time

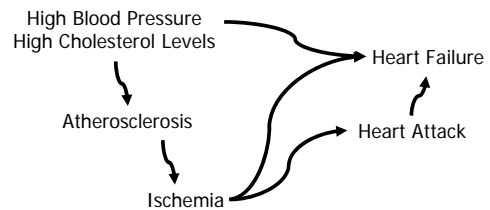
- How do we treat coronary artery disease?
  - CABG
  - PTCA
  - Stent
  - Prevention



## 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



## What is Heart Failure?

## Heart Failure

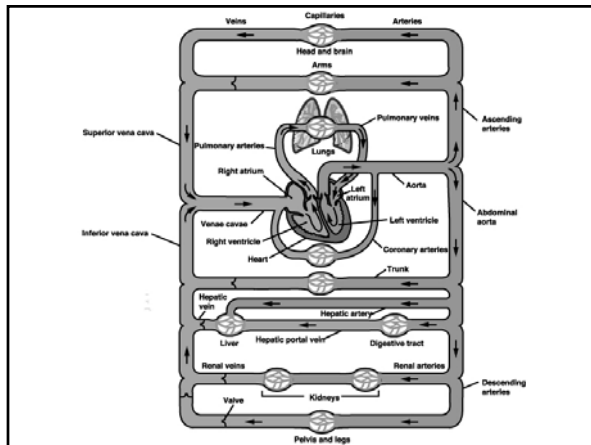
- Heart failure:
  - Occurs when left or right ventricle loses the ability to keep up with amount of blood flow
  - Can involve the heart's left side, right side or both sides
  - Usually affects the left side first
- About 5 million Americans are living with heart failure
- 550,000 new cases diagnosed 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
- Normal echocardiogram
  - <http://www.ardingerphoto.com/pcawebsite/cardiology/movies/sssmovies/normalao2cycle.html>
- Dilated cardiomyopathy
  - <http://www.ardingerphoto.com/pcawebsite/cardiology/movies/sssmovies/dilcardiomyopsss.html>

## 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:
Shortness of breath (also called dyspnea)	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 leak into lungs	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
Persistent coughing or wheezing	Fluid builds up in lungs	Coughing that produces white or pink blood-tinged phlegm.
Buildup of excess fluid in body tissues (edema)	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:
Increased heart rate	To "make up for" loss in pumping capacity, heart beats faster	Heart palpitations, which feel like the heart is racing or throbbing.
Confusion, impaired thinking	Changing levels of blood substances, such as sodium, can cause confusion	Memory loss and feelings of disorientation.
Lack of appetite, nausea	Digestive system receives less blood, causing problems with digestion	Feeling of being full or sick to their stomach.
Tiredness, fatigue	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.

## Heart Failure Video



## How Do We Treat Heart Failure?

## How Do We Treat Heart Failure?

Heart Transplant  
Cardiac Assist Devices  
Artificial Heart

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

## How Do We Treat Heart Failure? Heart Transplant

### Heart Transplant

- 1960s:
  - First heart transplants performed
- 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:
  - 4,000 patients are on the national patient waiting list for a heart transplant
  - Only about 2,300 donor hearts become available for transplantation each year

### Surgical Procedure

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

### Rejection

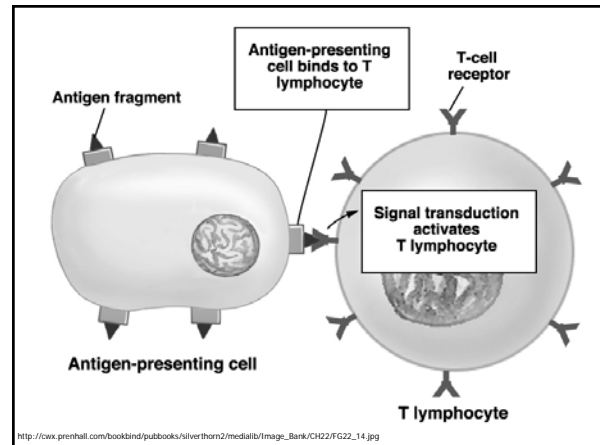
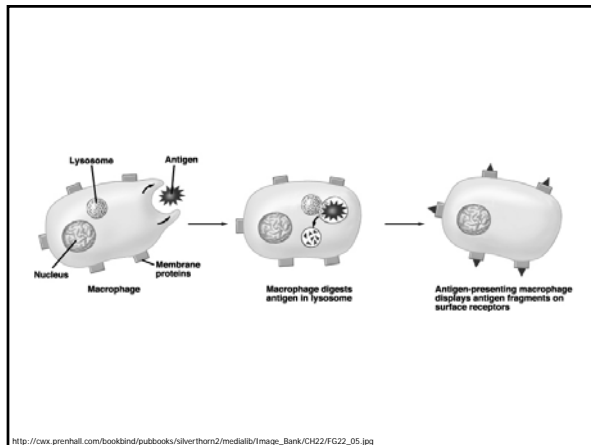
- Risk of rejection is highest right after surgery
  - In one study, first year after transplant:
    - 37% of patients had no rejection episodes
    - 40% had one episode
    - 23% had more than one episode
- Induction therapy:
  - Use of drugs to heavily suppress immune system right after transplant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

## Remember from our vaccine unit:

- How Do T Cells Identify 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 virus-related 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

## 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 the Uniform Organ Donor Card  
<http://www.tdh.state.tx.us/agep/become.htm>

The image shows a sample of a Uniform Donor Card. It is a rectangular form with a black border. At the top, it says "Uniform Donor Card". Below that, there is a line for the donor's name and a line for the date. The text reads: "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:" followed by two checkboxes: "Any needed organs and tissue" and "Only the following organs and tissue: \_\_\_\_\_". Below these are lines for "Donor Signature" and "Date", and two lines for "Witness". At the bottom, there are lines for "Next of Kin" and "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

- <http://www.organdonor.gov>
- <http://www.tdh.state.tx.us/agep/become.htm>
- <http://www.lifegift.org/default.html>
- [http://www.lifegift.org/UD\\_Organ\\_Donation.html](http://www.lifegift.org/UD_Organ_Donation.html)
- <http://www.shareyourlife.org/>

## 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

## Requirements of Mechanical Support

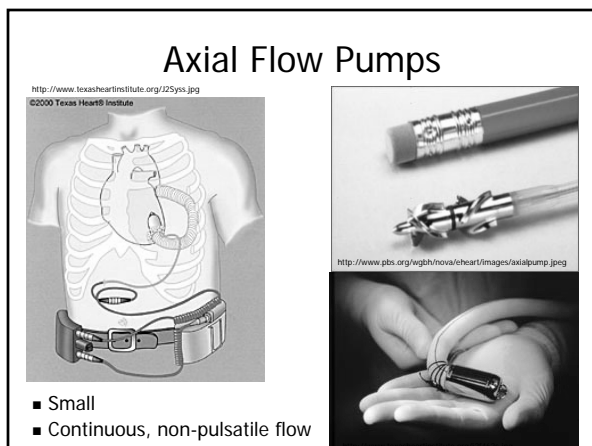
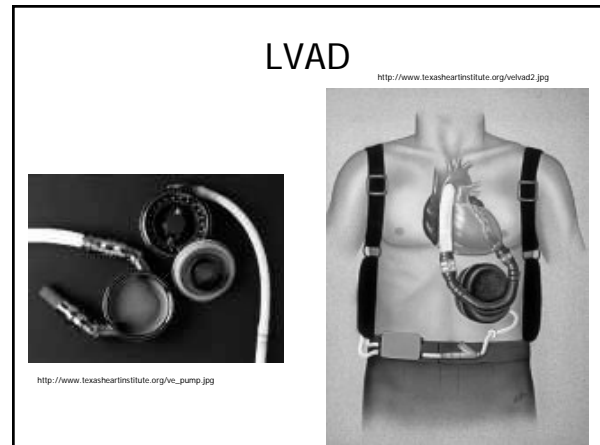
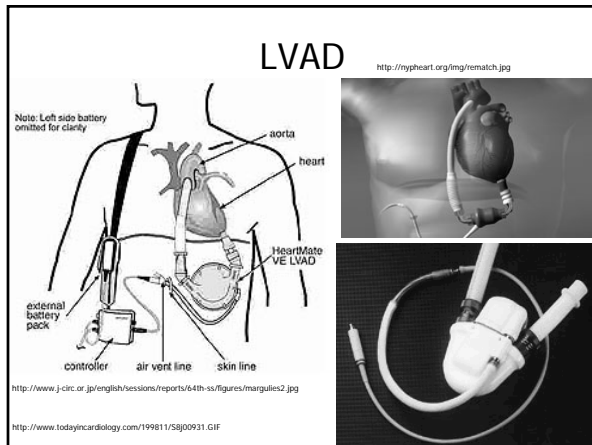
- Non-thrombogenic blood contacting surface
- Pumping action that avoids blood trauma
- Variable output
- Small enough to fit in chest cavity
- Reliable

## Types of Mechanical Support

- Temporary: LVADs
  - Give heart muscle a chance to rest/recover
  - Bridge to transplantation
  - Failure is not catastrophic
- Permanent: Total Artificial Heart
  - Replace damaged heart muscle
  - Failure is catastrophic

## How Do We Treat Heart Failure?

### Left Ventricular Assist Devices



## How Do We Treat Heart Failure?

### Artificial Heart

## Artificial Heart - History

- April 4<sup>th</sup>, 1969
  - Haskell Karp became first human to have artificial heart implanted
  - Surgeon Denton Cooley performed operation

## Artificial Heart - History

- 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 they medial take their pictures
  - Immediately after this was done they put back the tube and opened up everything that had closed up.

## Artificial Heart - History

- Karp survived 5 days with artificial heart
- Human heart transplant was performed
- Karp died 14 hours later

## Artificial Heart - History

- 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 patients consent
  - I think if I had sought permission from the hospital, I think I probably would have been dined and we would have lost a golden opportunity

## Artificial Heart - History

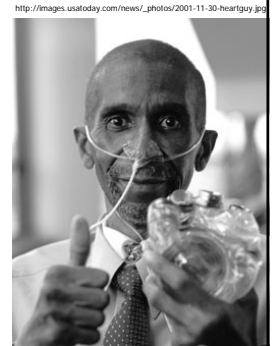
- Dr. Debakey
  - I was in Washington when I read in the morning pagers about the use of this artificial heart
  - I was shocked
  - I didn't know he had taken it from the laboratory

## Artificial Heart - History

- No more human trials until the 1980s...

## History of Artificial Heart

- <http://www.cnn.com/2001/HEALTH/conditions/07/03/artificial.heart/>
- June 2001
  - <http://discover.npr.org/features/feature.jhtml?wfid=1123833>
- August 2001
  - <http://discover.npr.org/features/feature.jhtml?wfid=1127758>
- November 2001
  - <http://discover.npr.org/features/feature.jhtml?wfid=1133260>



## History of Artificial Heart

- 1958:
  - Designed by Drs. Willem Kolff and Tetsuzo Akutsu
  - Polyvinyl chloride device
  - Sustained a dog for 90 minutes
- 1965:
  - Dr. Willem Kolff
  - Silicone rubber heart
  - Tested in a calf



<http://www.accessscience.org/WN/graphics/jarvik.jpg>



<http://www.abimed.com/images/product/h/koff65.jpg>

## History of Artificial Heart

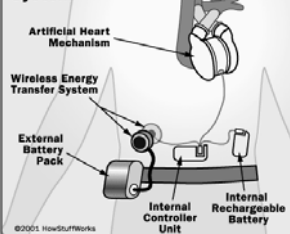
- 1969:
  - Dr. Domingo Liotta
  - First to be implanted in human as bridge to transplant
  - Patient survived for 3 days with artificial heart and 36 hours more with transplanted heart
- 1982:
  - Drs. Willem Kolff, Donald Olsen, and Robert Jarvik, and Jarvik-7
  - First to be implanted in a human as destination therapy



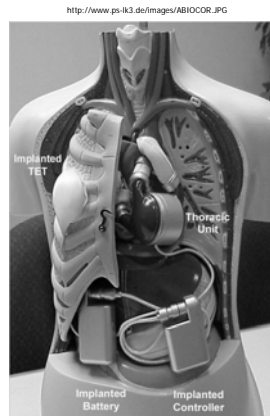
<http://www.abimed.com/images/product/h/liotta.jpg>



### The AbioCor Artificial Heart System



<http://static.howstuffworks.com/gif/artificial-heart-abiocor-diagram.gif>



<http://www.ps-ik3.de/images/ABI0COR.JPG>

## AbioCor Artificial Heart

- <http://www.heartpioneers.com/newsimages.html#>
- Cost: \$70-100k



[http://www.cardiacaribe.com/newsite/images/articulo/feb02/abiocor\\_hand.jpg](http://www.cardiacaribe.com/newsite/images/articulo/feb02/abiocor_hand.jpg)



## Surgical Procedure

- Surgeons implant energy-transfer coil in the abdomen
- The chest is opened and patient is placed on a heart-lung machine
- Surgeons remove the right and left ventricles of native heart. This part of the surgery takes two to three hours
- Atrial cuffs are sewn to native heart's right and left atria
- A plastic model is placed in the chest to determine the proper placement and fit of the heart in the patient
- Grafts are cut to an appropriate length and sewn to the aorta and pulmonary artery
- The AbioCor is placed in the chest. Surgeons use "quick connects" -- sort of like little snaps -- to connect heart to the pulmonary artery, aorta and left and right atria.
- All of the air in the device is removed
- The patient is taken off the heart-lung machine



<http://www.tulsa.edu/hsc/medmag/s01/images/abio-prep.gif>



[http://www.heartpioneers.com/images/news/implant\\_thumb.jpg](http://www.heartpioneers.com/images/news/implant_thumb.jpg)

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