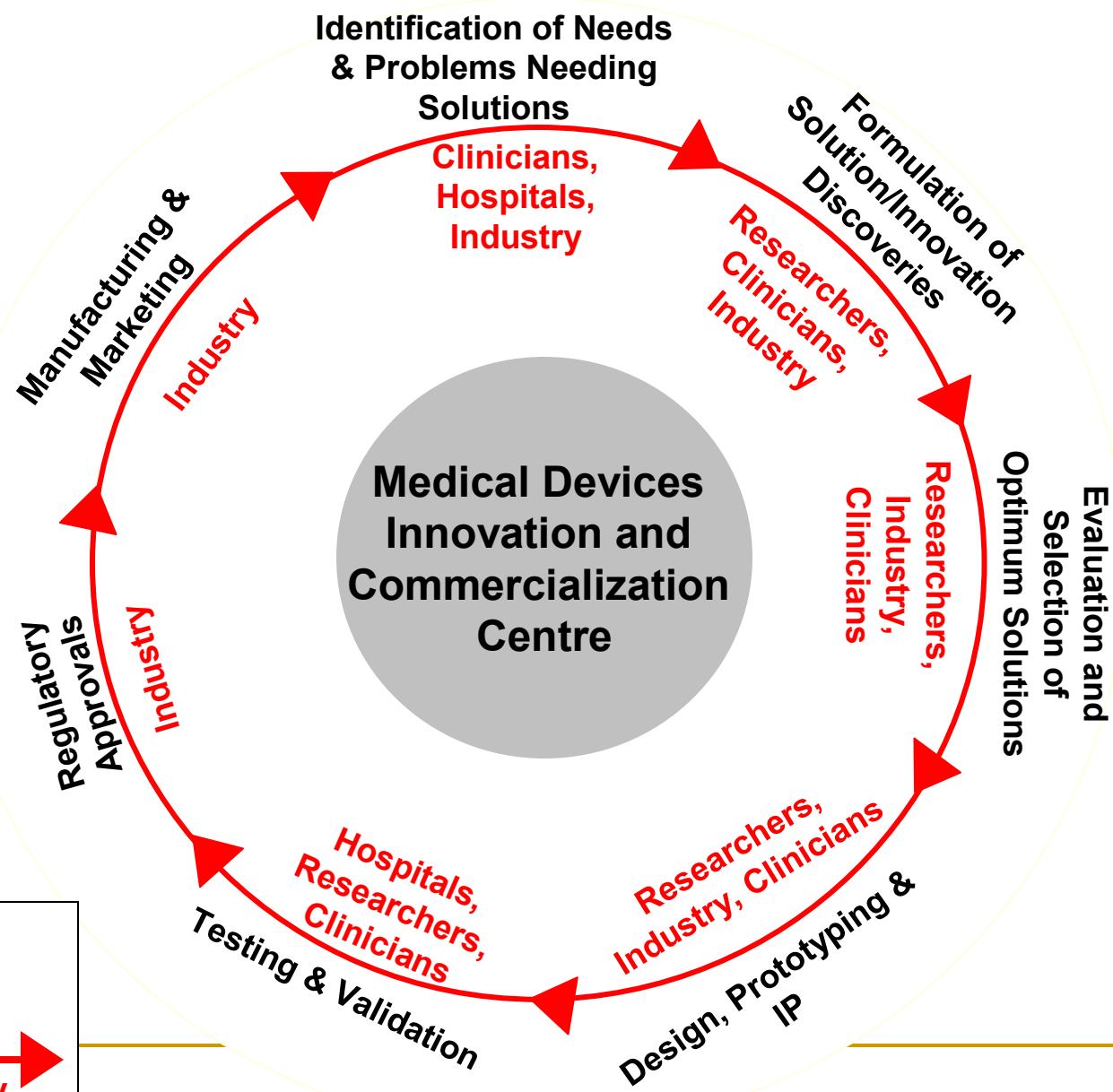




# Medical Devices

## Lecture 6 – Artificial Organs Overview



## Legends:

# Activity

# Responsibility

# Origin

- For the last 60 years or so, human knowledge & skill from various fields have been converging and are now capable of producing devices (prosthesis) for assisting & replacing a variety of cells, tissues, and organs that lack proper function.
- This type of technology are either available or are becoming available for almost all organs of the body.

# History

- For centuries, medications (chemicals) have been used to help patients. More recently, medical devices have also emerged.
- Medical devices are currently in the same stage as medications were 100 years ago. That is, they are expanding exponentially. There are 500,000 medical devices in the market, with 25,000 per year being added to this pool.
- There are many diseases and malfunctioning organs that can be corrected with prosthesis, in many cases with better results than medications.
- The development of artificial organs is regarded as one of the major breakthroughs of the 20<sup>th</sup> century, and continues into the 21<sup>st</sup> century.

# The Need

- About 5 million patients per year are treated with medical devices in the US alone, using devices such as ventricular assist devices (VADs), valves, other prostheses, etc.
- Adding to this statistic, if diagnostic equipment, tools and devices are used, this becomes a huge industry. In fact, it is estimated that the medical devices industry is over \$250 billion in the US alone.

# Characteristics of Artificial Organs

- Human made
- Originate from cells and tissues from the same species or either species
- Hybrid, a mixture of human made and cell/tissue substitution

# Advantages of Medical Devices

- Availability (emergency basis, unlike transplant organs)
- Cost is generally less once amortized for the impact years
- Provide better quality of life
- Effectiveness, especially in late stages of disease
- No side effects, as seen with drugs

# Uses of Medical Devices

- Medical devices are used for:
  - Diagnosis (MRI, X-rays, electrocardiogram, etc.)
  - Treatment (Artificial valves, heart, knees, cochlear implants, hip joints, etc.)
  - Rehabilitation, such as devices used in cardiac & exercise rehabilitation
  - Attempts are being made to produce such devices for prevention. For example, HealthWatch, sensors, etc.

# Transplant vs. Implant

- ***Transplantation*** – Replacing disabled organs with natural tissues
- ***Implantation*** – Replacing disabled organs with a prosthetic device
- Implantation of man-made devices does not require immune suppression drugs, as seen with transplant. The immune response occurs when the natural tissue rejects cells, tissues & organs that have histopathologically different roots. In other words, the DNA and RNA differs. Devices are man-made and do not have DNA and RNA.
- Implants are still primitive with some major limitations, however, they are being advanced to be reliable, durable, functional, and inexpensive.

# Clinically Acceptable Transplantation

- Liver Transplant
- Heart Transplant
- Kidney Transplant (from cadaver or living donor)
- Bone Marrow Transplant
- Bank Bone Transplant
- Corneal Transplant
- Blood Transfusion

# Process for Design & Testing

- First step is to determine the need, the problem, and the function of the organ to be replaced:
  - Study in detail the anatomy, structure and function of the organ in question.
  - Conceptual design & Prototyping
  - Bench-testing (in vitro testing) of the prototype
  - In vivo testing of the prototype (in various animals and/or ex vivo)
  - Formal in vivo testing
  - Feasibility clinical trials in humans
  - IDE or general clinical trials
  - Regulatory approved use of the device

# Progress of artificial organs & transplanted organs

- Conceptual stage
- Experimental stage
- Clinical observations
- Clinically applicable devices have been tested, approved by regulatory agencies, and are in use today

# Conceptual Stage Examples

- Artificial Eye
- Neuro Stimulators
- Blood Pressure Regulators
- Implantable Lung
- Artificial Trachea
- Artificial Gut
- Artificial Fallopian Tube

# Experimental Stage Examples

- Bioartificial Kidney
- Brain Implants
- Myocyte Implants
- Smooth Muscle Cells
- Striated Muscle

# Clinical Examples

- Nerve Guidance Channels
- Artificial Esophagus Oxygenators
- Artificial Blood
- Artificial Limbs
- Artificial Tendons
- Ventricular Assist Devices
- CNF Tissues
- Small Intestine
- Cardiomyoplasty (Almost no longer pursued)
- Artificial Hearts
- Intravenous
- Artificial Pancreas
- Artificial Skin
- Cochlear Implants
- Gene Therapy Product
- Bioartificial Liver
- Pancreatic Islets

# Clinically Acceptable Artificial Organs

- ❑ Chronic ambulatory dialysis                          — Maintenance  
Hemodialysis
- ❑ Skin & Tissue Expanders                          — Dental Implants
- ❑ Hydrocephalus Shunts                                — Intraocular Lenses
- ❑ Ear Oscicle Chain (for middle ear)  
Balloon Pump    — Intra-aortic
- ❑ Prosthetic Cardiac Valves                          — Vascular Grafts (Large)
- ❑ Implantable Defibrillators (ICD)                — Cardiac Pacemaker
- ❑ Bone Fixation System                                — Joint Prosthesis
- ❑ Hip Prosthesis                                         — Heart-Lung Machine

# Lessons Learned from Clinical Use of Artificial Organs

- Improved quality of life
- Restore part, or all, of the human organ function
- Extend life
- Great potential for human life
- Promote a response from tissue when implanted in the body.
  - That is, immediately all implants have response from body tissue such as positioning and attaching of the natural tissue with respect to the implanted device.
- All body fluids and tissue in contact with foreign materials undergo a dynamic sequence of biological reactions, which can continue for days, weeks, and sometimes for years.

# Future of artificial organs

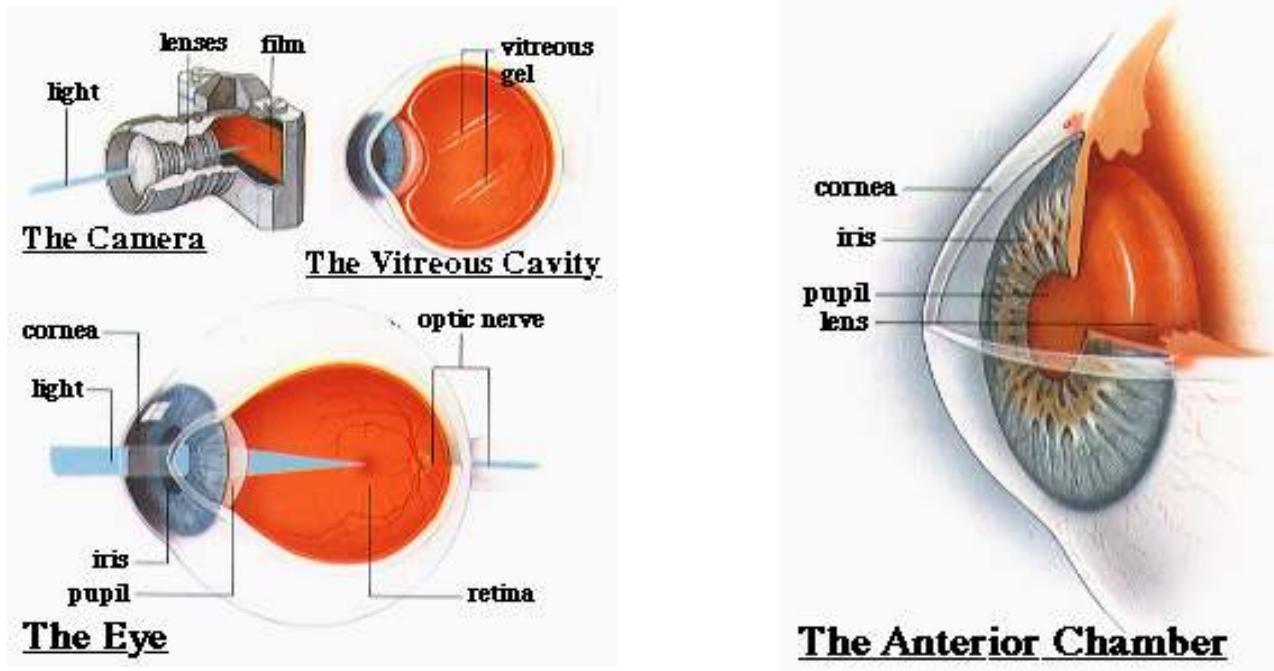
- More advances in artificial organ development
- Improvement of health care
- Cost reduction
- Utilizing new technologies

# Hybrid Examples

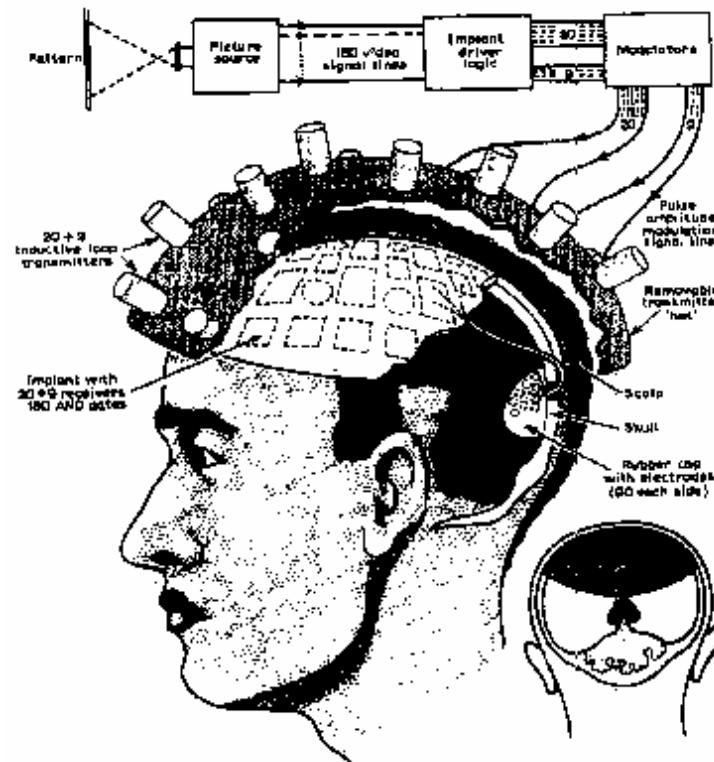
## Combination of Cell Biology & Man-Made Materials

- Matrix provides the building blocks that can be put into an environment for the incorporation of peptides & glucoprotein sequences, which are responsible for cell-cell interactions.
- Create new classes of biohybrid materials, such as bioactive substances for transplants. For example, insulin xenograft tissue protected against immune rejection by a selective envelope that is man-made.
- Composites of synthetic materials with cell biology to accelerate transplant integration within the body. Example is endothelial cell, lined polymer, conduits designed for vascular graft.

# The Structure of the Eye

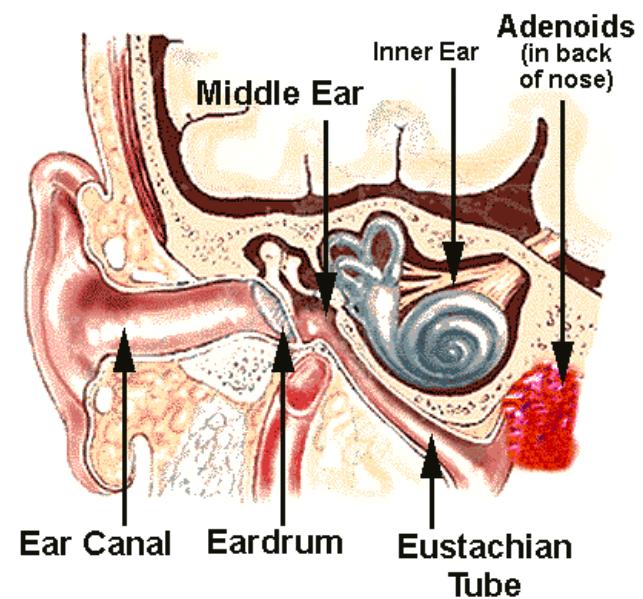
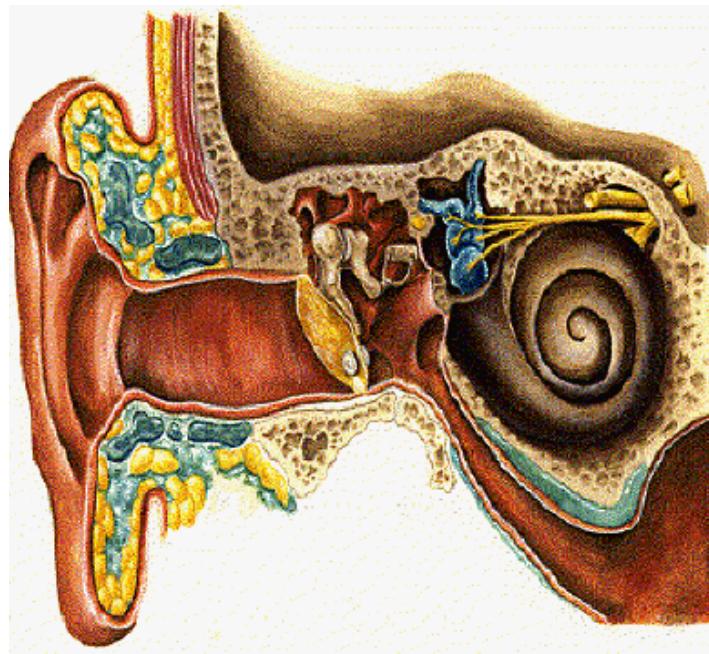


# Stimulated Visual Cortex



# EAR

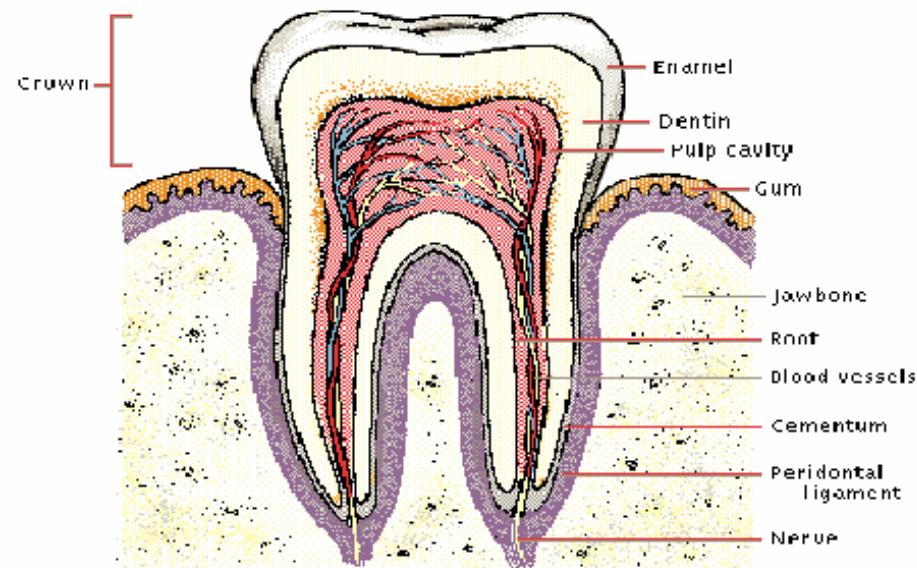
➤ Organ of hearing



# Artificial Hearing Device



# Structure of the Tooth

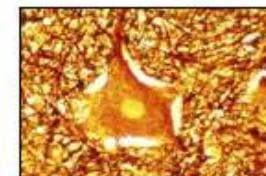


# Dental Implants



# Tissue

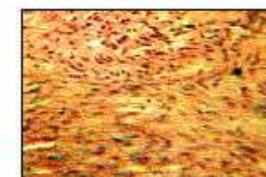
- What is Tissue?
- Types of Tissue
  - ❑ Epithelial Tissue
  - ❑ Connective Tissue (Tendons and Ligaments)
  - ❑ Muscular Tissue
    - Mechanics of Muscle and Bone Motion
    - Sliding Protein Contraction Mechanism
    - Muscle Bioenergetics
    - All or None Mechanism of Contraction
    - The Neuromuscular Junction
    - Production of Tension Force
  - ❑ Nervous Tissue
    - Nerve Cell Structure
    - The Synapse



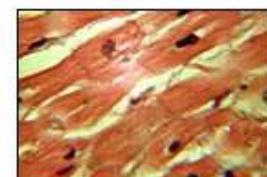
Neuron (Nervous tissue)



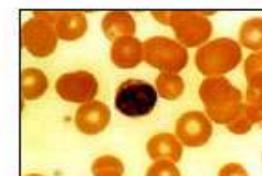
Skeletal muscle



Smooth muscle



Cardiac muscle



Blood



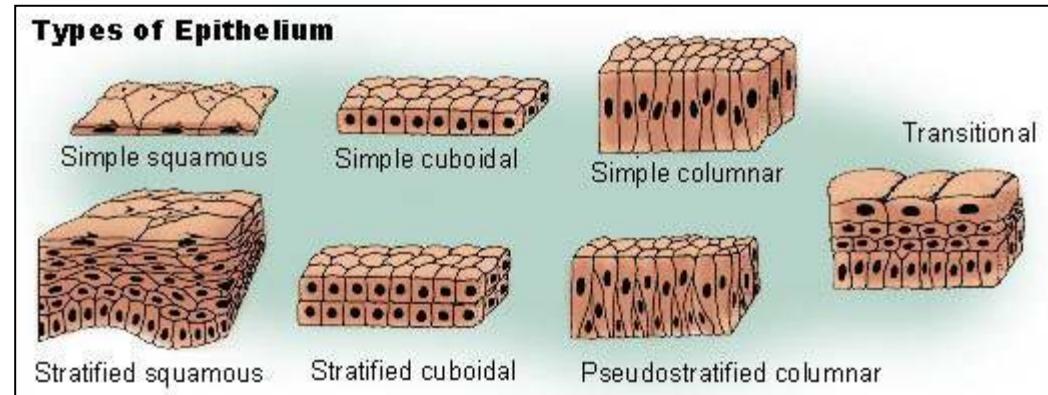
Osseous tissue



Hyaline cartilage

# What is Tissue?

- Tissue: A group of structurally and functionally similar cells specialized in performing a common function.
- Generally, cells cannot function alone. They function within a group of similar cells and are supported by the organism.
- The tissue is the forth level of the basic human structure, defined as Atoms, Molecules, Cells, Tissues, Organs, ...
- Tissue within the body is grouped into four basic types:
  - Epithelial
  - Connective
  - Muscular
  - Nervous



# Epithelial Tissue

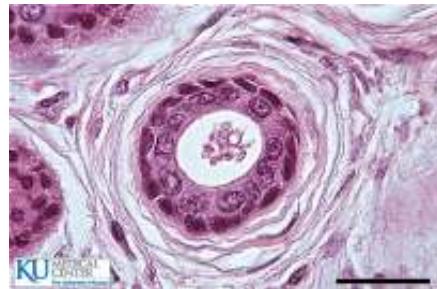


Figure 1. Trachea: The pseudostratified columnar epithelium of the trachea is ciliated and has goblet cells.

<http://www.kumc.edu/instruction/medicine/anatomy/histoweb/epithel/epithel.htm>

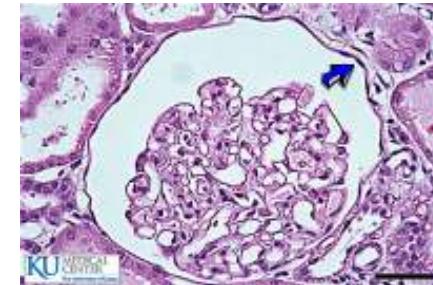
- Cells lining the inside and outside of the body.
- Form glands.
- The cells are closely packed with little or no intercellular material.
- Does not have blood vessels (avascular). The cells obtain their nutrients and dispose of waste material through adjacent connective tissue.
- Attached to connective tissue by a layer (between the epithelium and connective tissue) known as the “basement membrane”.
- Epithelium is exposed to stresses causing:
  - Tear
  - Wear
  - Injury
- The cells can quickly divide and produce new cells to replace those that are damaged (e.g., skin).
- See Figures 1 through 4.

# Epithelial Tissue



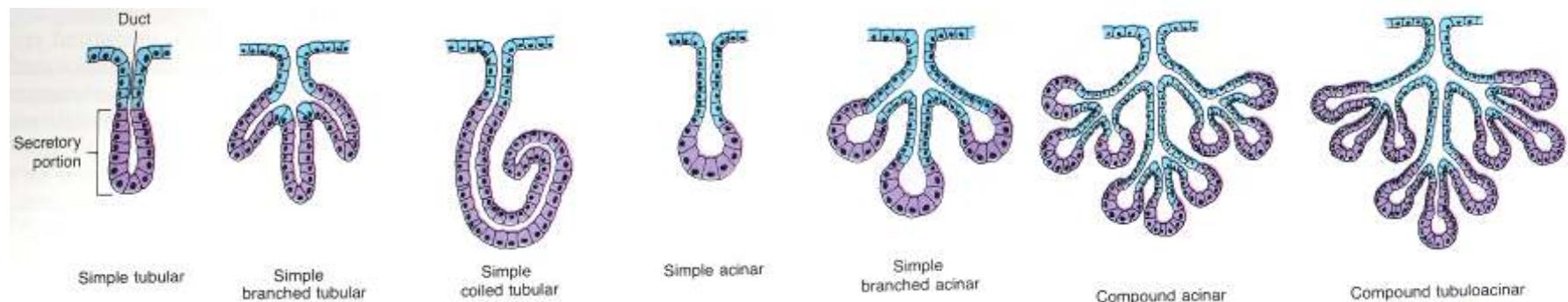
**Figure 2. Sweat Duct:** Cross-sectional view through a duct of a sweat gland illustrating stratified cuboidal epithelium.

<http://www.kumc.edu/instruction/medicine/anatomy/histoweb/epithel/epithel.htm>



**Figure 3. Kidney (Glomerulus):** Simple squamous epithelium (arrow) lines the glomerulus. This is an H & E section and nuclei are blue.

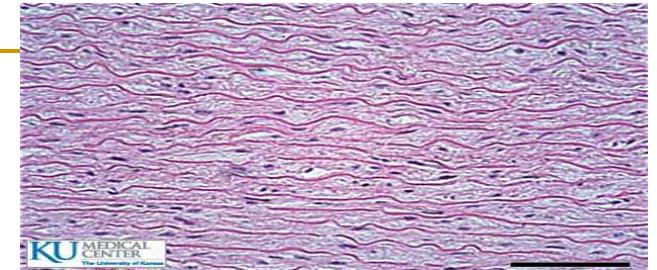
<http://www.kumc.edu/instruction/medicine/anatomy/histoweb/epithel/epithel.htm>



**Figure 4.** Lining of glands by epithelium.

# Connective Tissue

- The most abundant tissue in the body.
- Support tissue for the body.
- Highly vascular (many blood vessels) with a rich blood supply, with the exception of cartilage which is avascular.
- Unlike epithelial tissue, cells are scattered (not closely packed).
- Functions:
  - ❑ Support
  - ❑ Protection
  - ❑ Binding together
- Intercellular matrix (substance between the connective tissue cells) is non-living and can be:
  - ❑ Fluid
  - ❑ Semi-fluid
  - ❑ Mucus-like
- An important subject for biomechanics and medical engineers.



**Figure 5. Elastic Fibers:** Sheets of elastic fibers, called elastic lamellae, are common in the aorta, shown here. These lamellae give a distinctive refractive appearance when you focus through them.

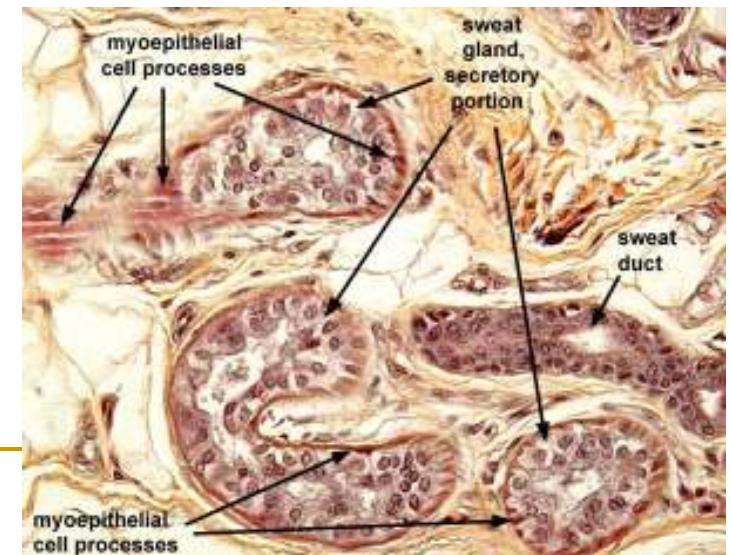
<http://www.kumc.edu/instruction/medicine/anatomy/histoweb/ct/ct.htm>

# Connective Tissue

- Cartilage is a connective tissue composed of firm, but compliant, material.
- Bone is another example of connective tissue with a hard intercellular and non-compliant material.
- Connective tissue produces intercellular substances.
- Connective tissue cells may:
  - Store fat
  - Ingest bacteria
  - Ingest debris
  - Create anticoagulants
  - Form antibodies for protection against disease
- See Figures 5 through 8.

**Figure 6.** a portion of a sweat gland deep in skin, surrounded by mixed fibrous connective tissue and adipose connective tissue at the transition from dermis to hypodermis.

"image copyright 2008 by David G. King, used with permission"

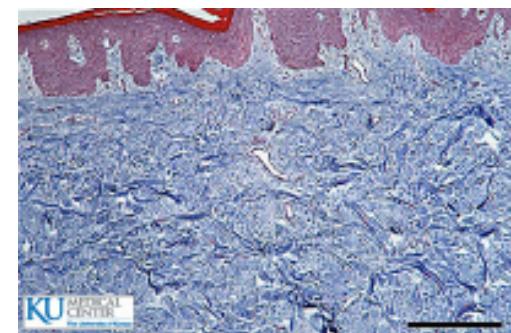


# Examples of Connective Tissue

- **Elastic cartilage** is used to form organs such as auditory tubes, external ears, etc.
- **Fibrous cartilage** connects the pelvic and vertebral bones to provide strength.
- **Hyaline cartilage** is found in the embryonic skeleton, ends of bones, nose, and the respiratory system. It is flexible, permits movement and provides support.
- **Cartilage is a jelly-like matrix made of caliginous and elastic fibres and mature cartilage cells called chondrocytes.**
- Reticular connective tissue has interlacing reticular fibres, providing support and strength.
- Dense (caliginous) connective tissue:
  - Closely packed fibres with less intracellular substance
  - Fibres can be arranged regularly or irregularly
  - This tissue provides resistance to tear against tension.
- Bone is a connective tissue.

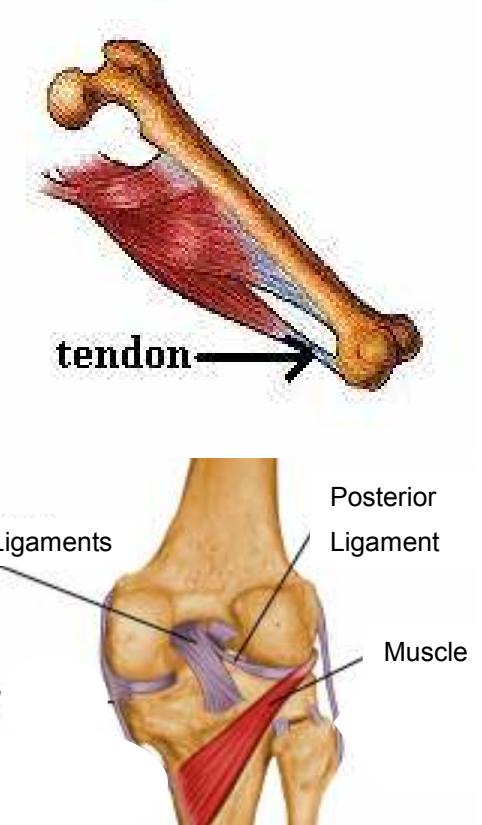
**Figure 7.. Collagen Fibers:** The Masson (trichrome) stain leaves collagen green or blue. In the skin, Type 1 collagen predominates, as shown by the thick, wavy bundles.

<http://www.kumc.edu/instruction/medicine/anatomy/histoweb/ct/ct.htm>



# Tendons and Ligaments

- Tendons attach muscles to bone and are made of regularly arranged fibre.
- Ligaments connect bones together.
- Biomechanical engineers have developed a carbon fibre implant for reconstructing bone ligaments and tendons.
  - Carbon fibres are coated with a plastic called polylactic acid. This material can be sewn in and around torn ligaments and tendons for reinforcement and providing scaffolding around which the body's own caliginous fibre can grow.
  - Within 2-3 weeks, the polylactic acid will be absorbed by the body and the carbon fibres eventually fracture. The fibres are connected by a collagenous material produced by the fibroblasts.

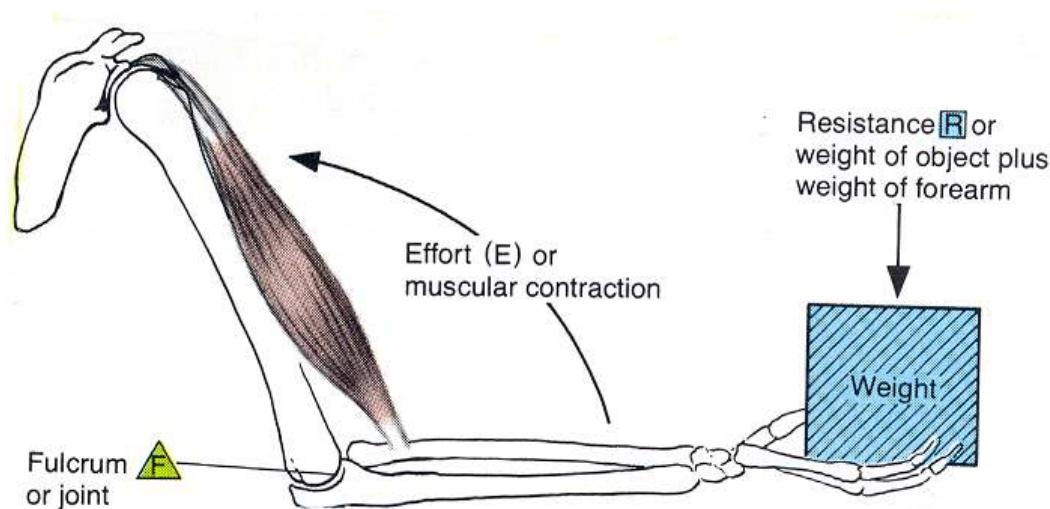


# Muscle Tissue

- Consists of **highly specific cells capable of performing contraction.**
- **Muscle tissue forms about 50% of the total body weight.**
- Muscle tissue characteristics:
  - **Excitability:** Response to stimuli (change in internal or external environment)
  - **Contractility:** Contracts in response to a stimulus
  - **Extensibility:** Capable of stretching
  - **Elasticity:** Ability to deform and return to original shape (zero hysteresis)

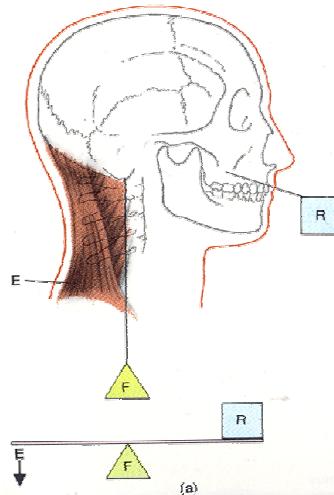
# Functions of Muscle Tissue

- Produce motion by applying force on tendons (a connective tissue), which move the bones.
- Bones act as levers (moving rod on a fixed point).
- Maintenance of posture.
- Creation of force and loss of energy in form of heat.



**Figure 9.** Relationship of skeletal muscles to bones. Bones serve as levers, and joints act as fulcrums for the levers. Here the lever-fulcrum principle is illustrated by the movement of the forearm lifting a weight. Note where the resistance and effort are applied in this example.

# Mechanics of Muscle and Bone Motion



- Motion of body is result of muscle and bone, connected by tendons. See Figure 9 on previous page.
- There are three types of lever systems in the body (Figure 10).

- a. **First class lever.** The fixed point is between the resistance and the muscle contraction (work, effort). Example: Head resting on vertebral column, where the muscle connecting the head to the vertebral column provides force (effort) on the fixed point.
- b. **Second class lever.** This is when the force (effort) and fixed point are located so that one is at each side of the resistance. Example: The toes. In this case, the body is the resistance and the fixed point is the ball of the foot and the muscle of the calf provides the force.
- c. **Third class lever.** In this group, effort (force) is located between the fixed point and the resistance. Example: Forearm and elbow.

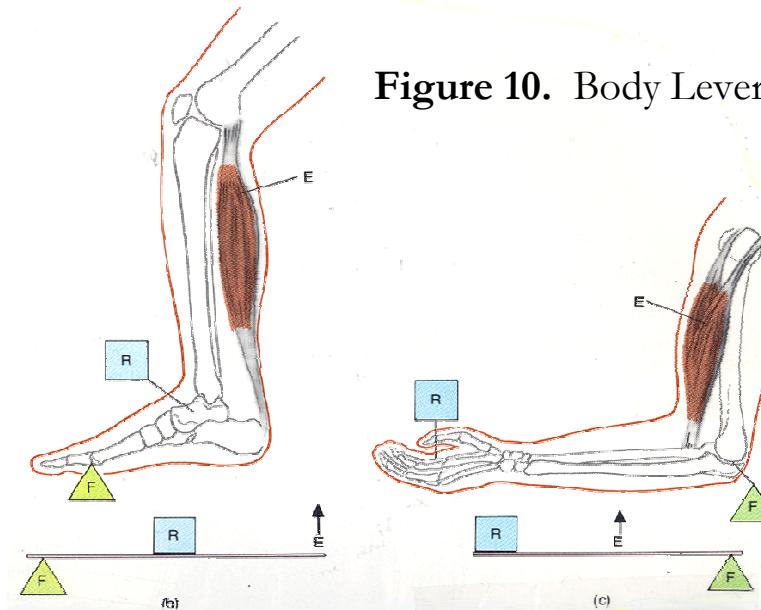
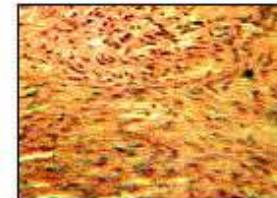


Figure 10. Body Levers.

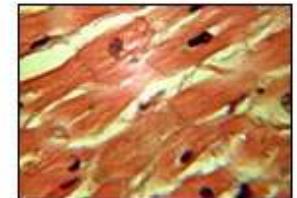
# Muscle Types



Skeletal muscle



Smooth muscle



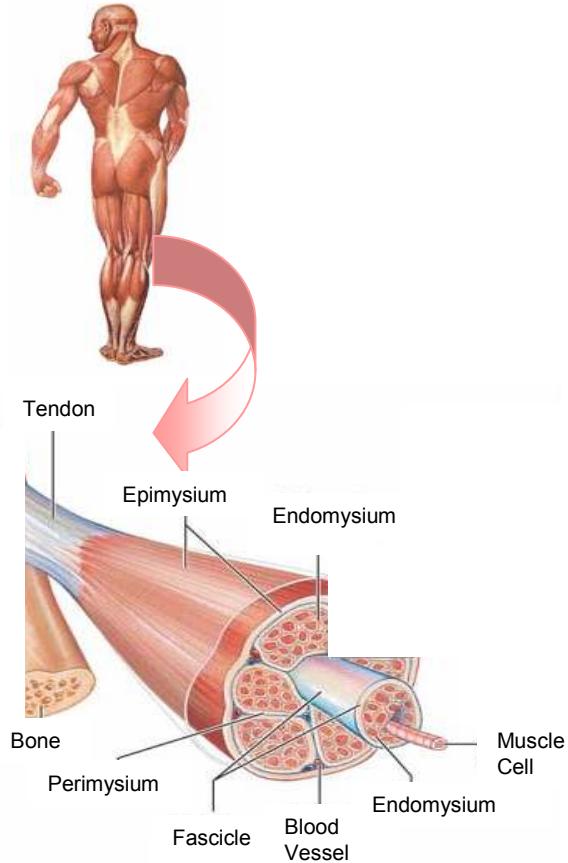
Cardiac muscle

## ➤ There are three types of muscle:

- **Skeletal muscle** or "voluntary muscle" is anchored by tendons (or by aponeuroses at a few places) to bone and is used to effect skeletal movement such as locomotion and in maintaining posture. An adult male: 42% skeletal muscle, an adult female: 36%.
- **Smooth muscle** or "involuntary muscle" is found within the walls of organs and structures such as the esophagus, stomach, intestines, bronchi, uterus, urethra, bladder, blood vessels, and the arrector pili in the skin (in which it controls erection of body hair). Unlike skeletal muscle, smooth muscle is not under conscious control.
- **Cardiac muscle** is also an "involuntary muscle" but is more akin in structure to skeletal muscle, and is found only in the heart.
- Cardiac and skeletal muscles are "striated" in that they contain sarcomeres and are packed into highly regular arrangements of bundles; smooth muscle has neither. While skeletal muscles are arranged in regular, parallel bundles, cardiac muscle connects at branching, irregular angles (called intercalated discs). Striated muscle contracts and relaxes in short, intense bursts, whereas smooth muscle sustains longer or even near-permanent contractions.

# Muscle Mechanics

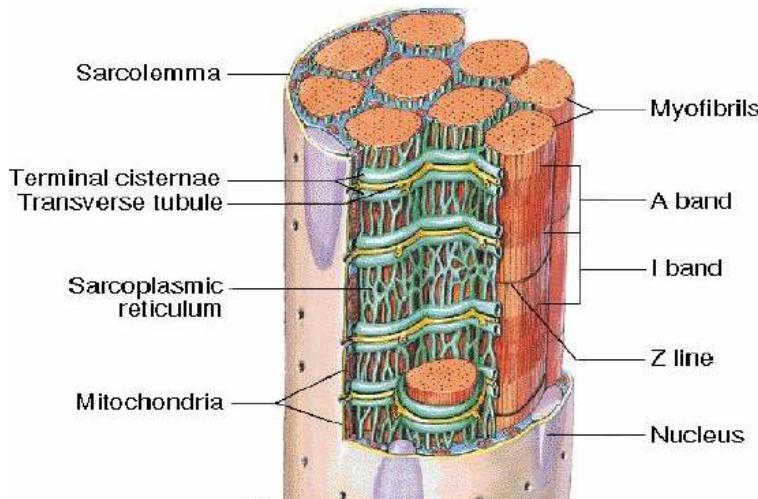
- Skeletal muscle consists of muscle fibres (long, cylindrical cells).
- The muscle fibres (cells) are parallel to one another.
- The diameter of each fibre ranges from 10 -100 microns. The length can reach up to 30 cm (sometimes more).
- Each fibre is enveloped by a plasma membrane called the sarcolemma.
- Inside of the sarcolemma, cytoplasm (sarcoplasm), many nuclei and a number of mitochondria are located.



**Figure 11.** Schematic of the relationship between muscle tissue and connective tissues.

# Muscle Mechanics

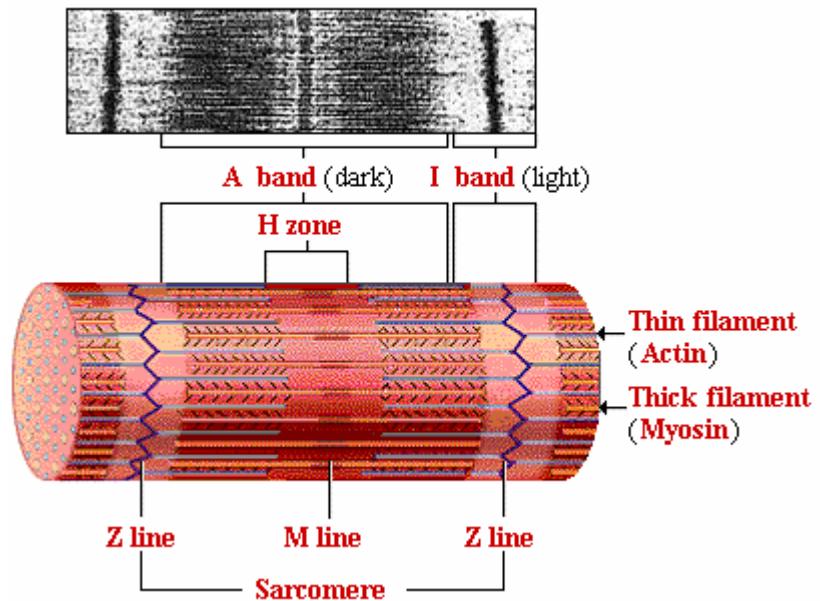
- A network of membrane enclosed tubules form t - tubules.
- Skeletal muscle fibres have thread-like structures about 1-2 microns in diameter (myofibrils).
- Each muscle can contain hundreds to thousands of myofibrils arranged parallel. (Longitudinal)
- Each myofibril consists of two structures called myofilaments. Each is very thin (smaller than a nano millimetre in diameter).
- The myofilaments are separated from one another by a narrow zone of dense material called Z-lines.
- Each sarcomere is about 2.6 microns long.



**Figure 12.** Schematic based on electron micrograph of microfibrils of a muscle fiber.

# Muscle Mechanics

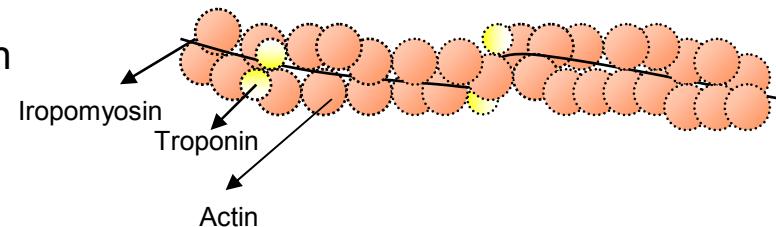
- There are two types of myofilaments - an overlapping thin myofilament and a thick myofilament
- The thick myofilaments are made from myosin protein and thin filaments are composed of actin protein.
- A myosin molecule is rod-shaped forming the thick myofilaments and cross-bridges.
- Cross-bridges are found in pairs and spirals around the main access.
- Thin myofilaments (actin) have two additional protein molecules:
  - Tropomyosin
  - Troponin



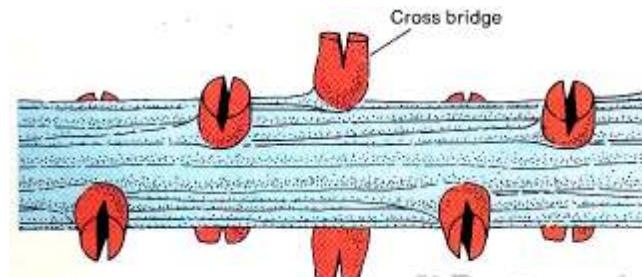
**Figure 14.** Schematic representation of muscle tissue showing the thick and thin myofilaments of a sarcomere.

# Sliding Protein Contraction Mechanism

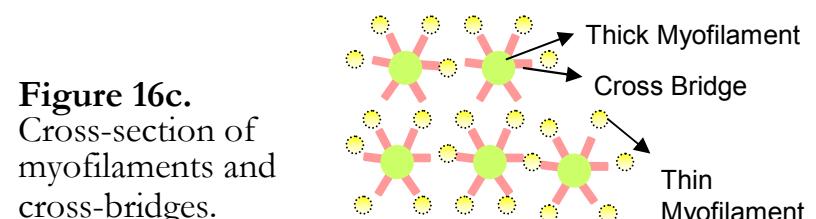
- Myofilaments (actin and myosin) are accordion shaped in cross-section.
- The myofilaments slide inward and the H-Zone is reduced.
- Sarcomere (bag or membrane) shortens, but the length of the myofilaments does not change.
- The cross-bridge of thick myofilaments (myosin) move like the oars of a boat on the surface of thin myofilaments.
- This oar-like motion slides thick and thin myofilaments past each other.
- The H-Zone narrows and disappears.
- The thin myofilaments meet at the centre of the sarcomere and may overlap.
- The sliding filaments and shortening of sarcomeres causes the shortening of the muscle and causes contraction.



**Figure 16a.** Schematic representation of a thin myofilament (actin).



**Figure 16b.** Myofilament showing thick filament (myosin) and cross-bridges.



**Figure 16c.**  
Cross-section of myofilaments and cross-bridges.

# Muscle Mechanics - Applicable Examples

- **Muscle tone** is the partial contraction of portions of skeletal muscle. It is essential for maintaining posture (ex. Muscle in the back of the neck or when standing).
- **Flaccid** is when the muscle has less than normal tone:
  - Damaged.
  - Nerves do not conduct a constant flow of impulses to the muscle.
- **Atrophy:** When flaccid muscle progresses to atrophy (wasting away), muscle cells decrease in size due to a loss of myofibrils.
  - Muscles become flaccid and atrophied if they are not used. For example, muscle atrophies in bedridden individuals and when bones are casted.
  - It takes 6 months to 2 years for the muscle to reduce to 1/4 of the original size. The muscle fibre will be replaced by fibrous tissue.
- **Hypertrophy:** This is the reverse of atrophy. Muscle fibres increase in size due to production of more myofibrils, mitochondria and forceful muscular activity (quick muscular activity does not cause hypertrophy), repetition and forceful activities are required.
- **Rigormortis:** Rigidity after death. Due to chemical changes after death and lack of ATP to cross-bridges of thick myofilaments.

# Muscle Bioenergetics

- Contraction of muscle requires energy.
  - This energy is supplied by adenosine triphosphate (ATP).
  - When a nerve impulse stimulates a muscle fibre, ATP is broken down into ADP + Phosphate + energy.
  - The energy created through the breakdown of ATP is used to create muscle contraction. Muscle contractions are used to perform work by the muscle and create heat. This is why when we exercise we get warmer.
- In order for the muscle to contract, we require the following chemical reaction:  
**ATP - in the presence of activated myosin, breaks down into ADP + P + energy**
- To replenish the ATP for future activity, muscle cells must produce ATP. This is done in the mitochondria as follows:  
**ADP + P + energy → ATP**
- **The energy comes from the breakdown of digested foods and oxygen from the air.**
- Muscle fibres alternate between periods of great activity (contraction) and inactivity (rest).
  - During rest, muscle requires very little energy while producing ATP (more than the body would use).
  - During contraction, muscle energy requirements are high and ATP is synthesized at an accelerated rate.

# Anaerobic Activity

- When exercise (contraction) is strenuous, more ATP is used than created. Thus, the muscle needs to build a reserve supply of energy for such periods. This occurs by:
  - The muscle fibres storing any excess ATP on the thick myofilaments (myosin).
  - Additional ATP combines with a substance called creatine (produced by the liver).
- Creatine can accept high energy phosphate from ATP to become creatine phosphate as follows:



- The formation of creatine phosphate is anaerobic (does not need oxygen).
- Creatine phosphate is produced when the muscle fibres are resting.
- During strenuous exercise (contraction) the creatine phosphate produces ADP, energy and creatine as:



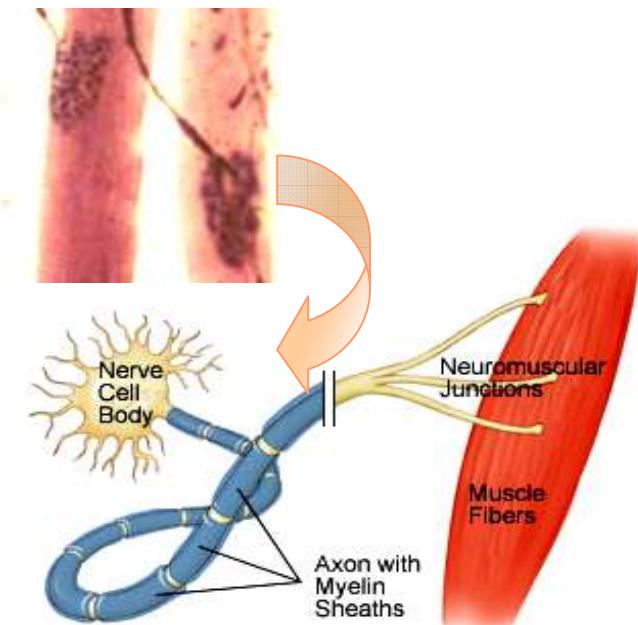
- This reaction is also anaerobic.

# All or None Mechanism of Muscle Contraction

- Individual muscle fibres of a motor unit will contract to their fullest extent under sufficient stimulus or will not contract at all.
- In other words, muscle fibres do not partially contract. Each muscle fibre has an all or none firing mechanism.
- **Threshold:** The weakest stimulus from a neuron capable of initiating a contraction in a muscle fibre.
- **Contraction types:** Different types of contractions can be produced depending on the stimulus frequency:
  - **Twitching contraction:** This is a rapid, jerky response to a single stimulus. This type of twitching can be recorded (a myogram).
  - **Treppe:** When a skeletal muscle contracts more forcefully in response to the same strength of stimulus after it has contracted several times. This can happen by stimulating an isolated muscle with a series of stimuli at the same frequency and voltage.
  - **Isotonos:** iso = equal, tonos = tension (force). During contraction, the muscle shortens and pulls on other structures such as bone producing movement. During such a contraction, the tension remains constant and energy is expended.
  - **Isometric:** when a minimal shortening of the muscle happens and it remains nearly the same length, but the tension on the muscle increases greatly. With isometric contraction, no movement results but energy is still expended.

# How Does Skeletal Muscle Tissue Contract?

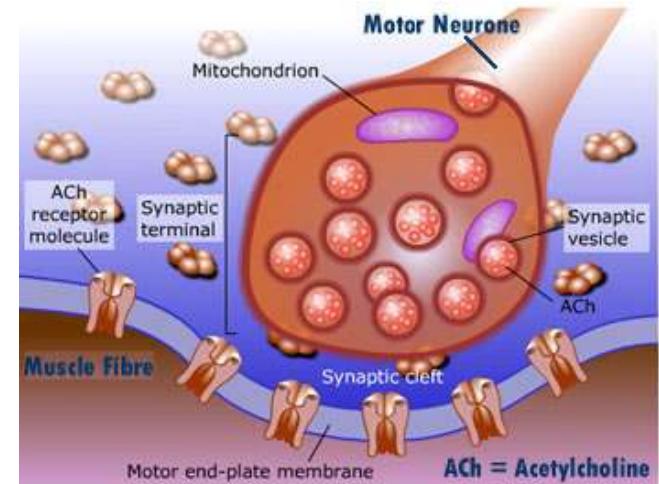
- In order to make myofilaments slide along each other, a stimulus must be applied.
- Such a stimulus is normally transmitted by nerve cells (neurons).
- The neuron has a long axis called an axon that can be up to 90 cm in length.
- A bundle of many axons forms a nerve.
- A neuron that transmits a stimulus to muscle is called a motor neuron.
- The axon of the motor neuron branches into fine endings and these sit in groups at the muscle membrane.
- The portion of the muscle membrane directly under the terminals of axons is called the motor end plate.
- The area contacting the neuron and muscle fibre is called neuromuscular junction (myoneural junction).
- When a nerve impulse (electrical voltage) reaches a terminal at a neuromuscular junction, it causes vesicles to release a chemical (acetylcholine or ACh).



**Figure 17.** Schematic of a photomicrograph of a motor end plate showing end plate and axon termination.

# How Does Skeletal Muscle Tissue Contract?

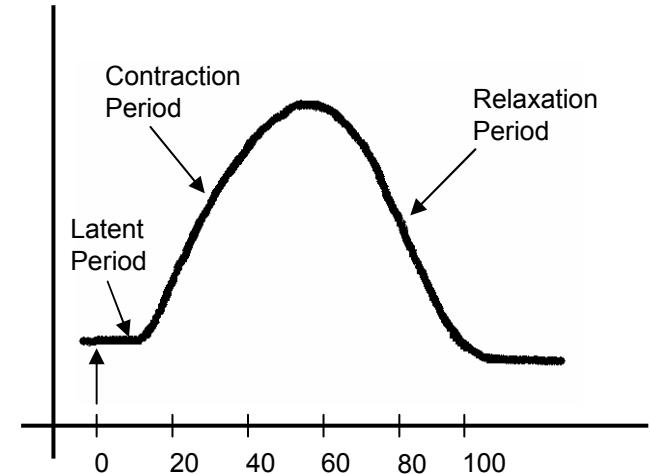
- The ACh transmits the electrical or nerve impulse from the neuron across the myoneural junction to the motor end plate of the muscle of the cell membrane.
- As soon as the impulse (electrical voltage) reaches the motor end plate, contracting activities are initiated.
- The motor neurons and muscle cells, which are stimulated together, is called a motor unit.
- Each motor neuron may deliver up to 150 muscle fibres.
- Those muscle fibres innervated by 1 motor neuron, if stimulated sufficiently, slide and relax simultaneously.
- Those muscles of the body, which require precise control such as the eye, have one motor neuron for approx. 10 muscle fibres.
- Large muscles (biceps) may have as many as 500 muscle fibres for each motor unit.



**Figure 18.** Motor end plate showing the relationship between synaptic vesicles and myofibrils.

# Mechanics of Muscle Movement

- Motor neuron stimulation produces a contraction in all muscle fibres of that particular motor unit.
- The sum of tension in the muscle is the total tension of all of those muscle fibres stimulated to contract. See Figure 19.
- If more force is required, more motor units must fire.
- More motor units firing by excitement is called recruitment.
- The recruitment needs are determined by the amount of force required by the body.
- The various motor neurons fire asynchronously (some are excited and some are not excited). This results in some motor units being active while others are inactive, creating a situation where not all motor units are firing at the same time.
- This mechanism of asynchronous firing of motor neurons prevents fatigue and maintains contraction and rest of some fibres at the same time.
- This alternating resting and contraction of motor units produces smooth contraction force, which can be sustained for long periods of time. This asynchronous firing prevents the jerky movement phenomenon.

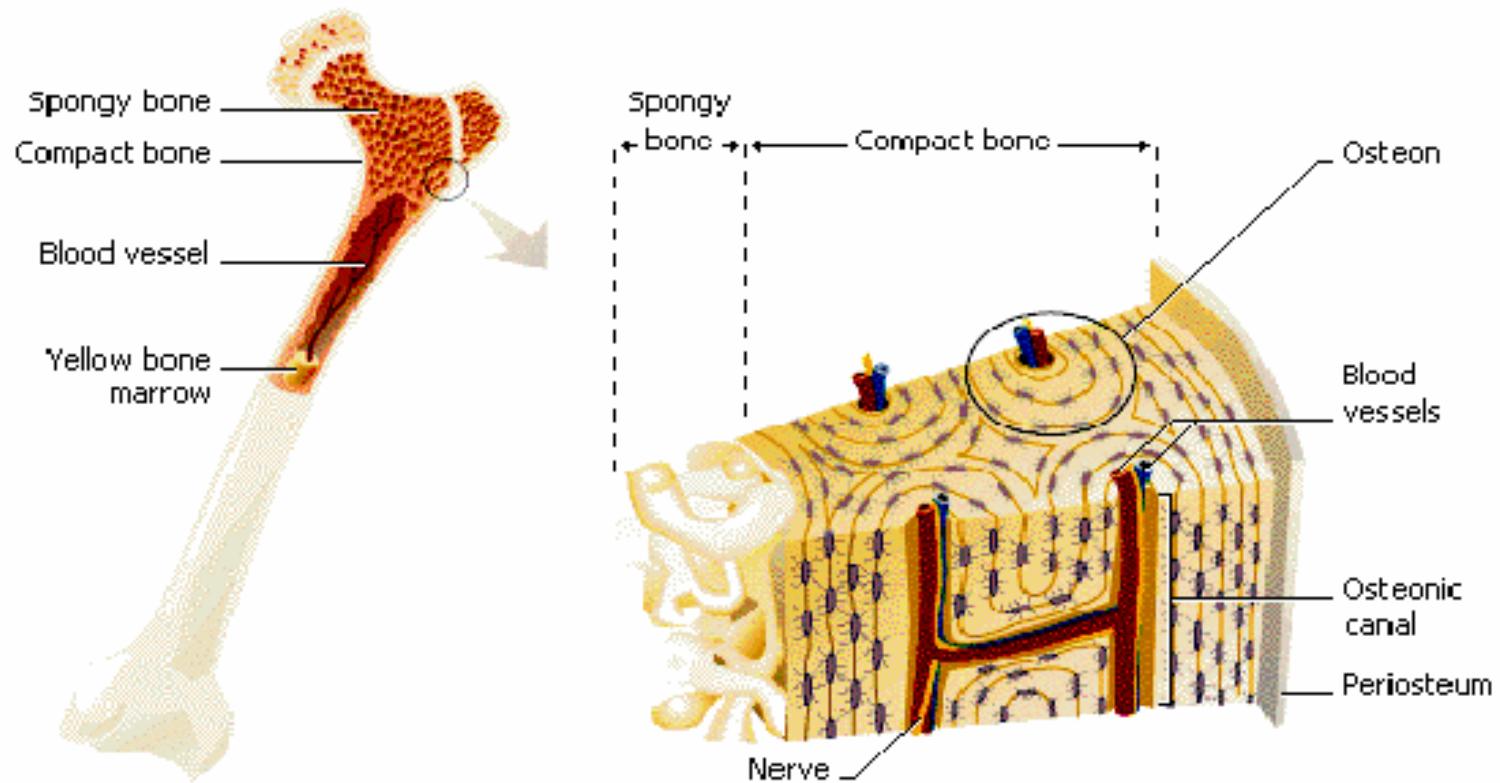


**Figure 19.** Muscle force creation.  
Time is in msec.

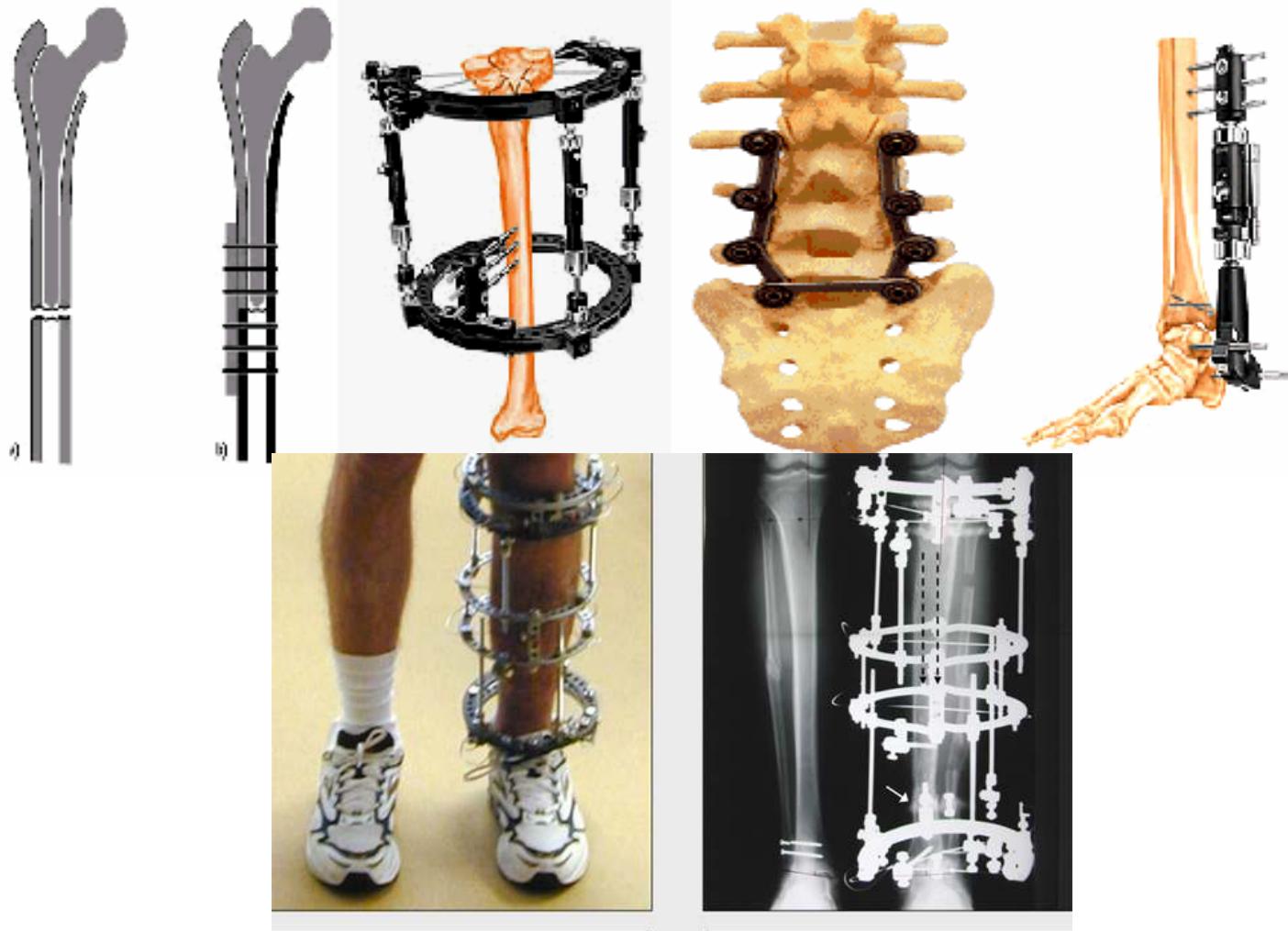
# Biomechanical Events in Producing Tension Force

- Acetylcholine (ACh) released by nerve impulse at synaptic vesicles of motor axon.
- Diffusion of ACh across the myoneural junction.
- Initiation of an impulse (voltage) from the motor end plate over the surface of sarcolemma (membrane of the muscle cell).
- The voltage impulse enters the t-tubule and sarcoplasmic reticulum.
- The voltage inside of the t-tubules and sarcoplasmic reticulum stimulates the release of calcium ions from storage into sarcoplasm.
- Calcium ions activate myosin, thus breaking down ATP.
- The calcium ion also binds with tropomyosin-troponin complex resulting in the split of the complex from thin myofilaments.
- The receptors on the thin myofilaments attach to the myosin of cross-bridges.
- By using the energy from the earlier ATP breakdown, the thin myofilaments slide passing thick myofilaments.
- The sliding draws the Z-lines towards each other, thus the muscle fibres contract.
- Acetylcholine is inactivated by a biochemical material called acetylcholinesterase, thus preventing nerve impulse conduction from axon terminals to motor end plates and finally to muscle fibres.
- In response to the inhibition of nerve impulses, calcium ions are transported back into sarcoplasmic reticulum by a protein called calsequestrin using energy from ATP.
- The low calcium concentration in sarcoplasm stops the enzymatic activity of myosin.

# Bone Anatomy



# Bone Fixation System

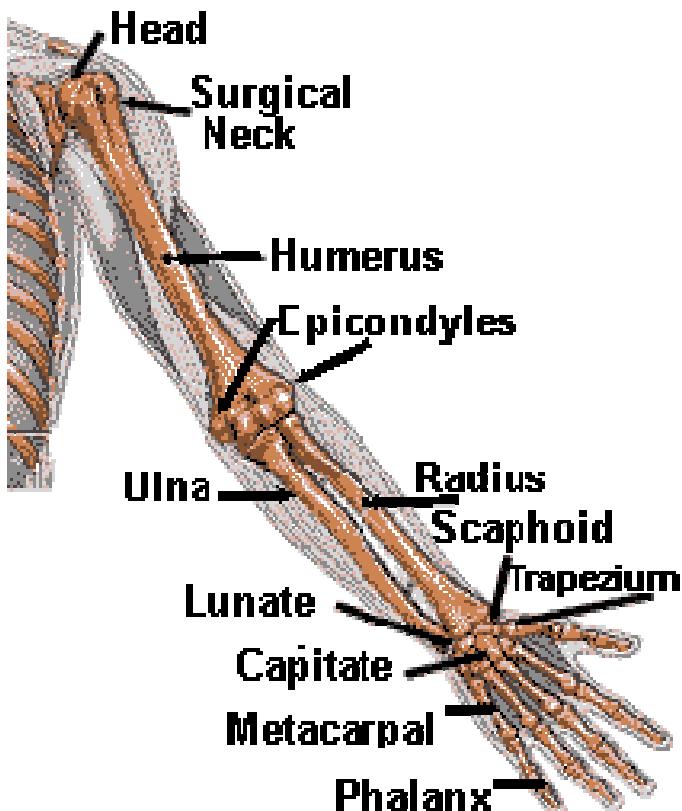


AN ILIZAROV, CIRCULAR FIXATOR USED TO STABILIZE AND LENGTHEN THE TIBIA.

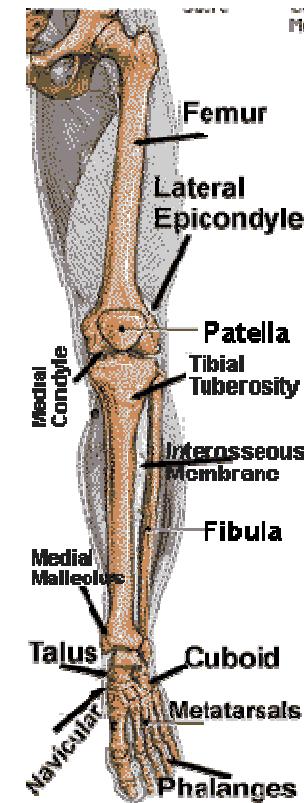
SMALL WIRES AND PINS FIX THE BONE TO THE FRAME UNTIL HEALING OCCURS.

# Anatomy of Limbs

Upper Limb



Lower Limb



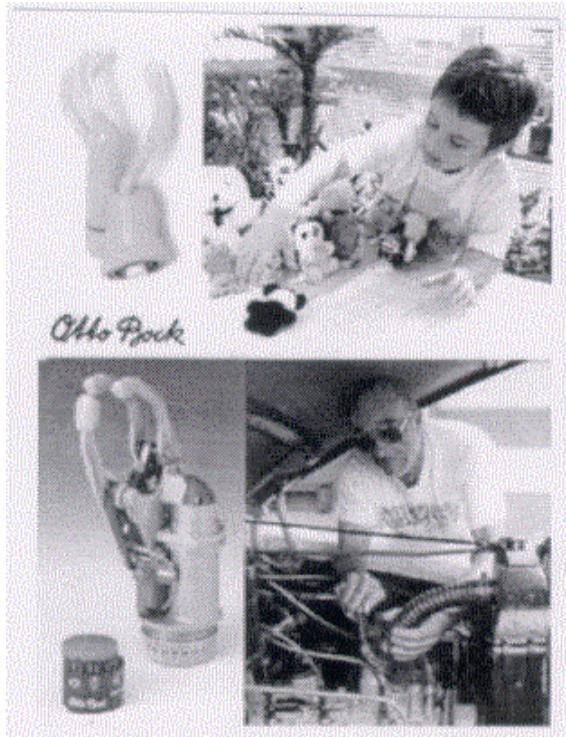
# Artificial Limbs

## Upper Limb - Hand



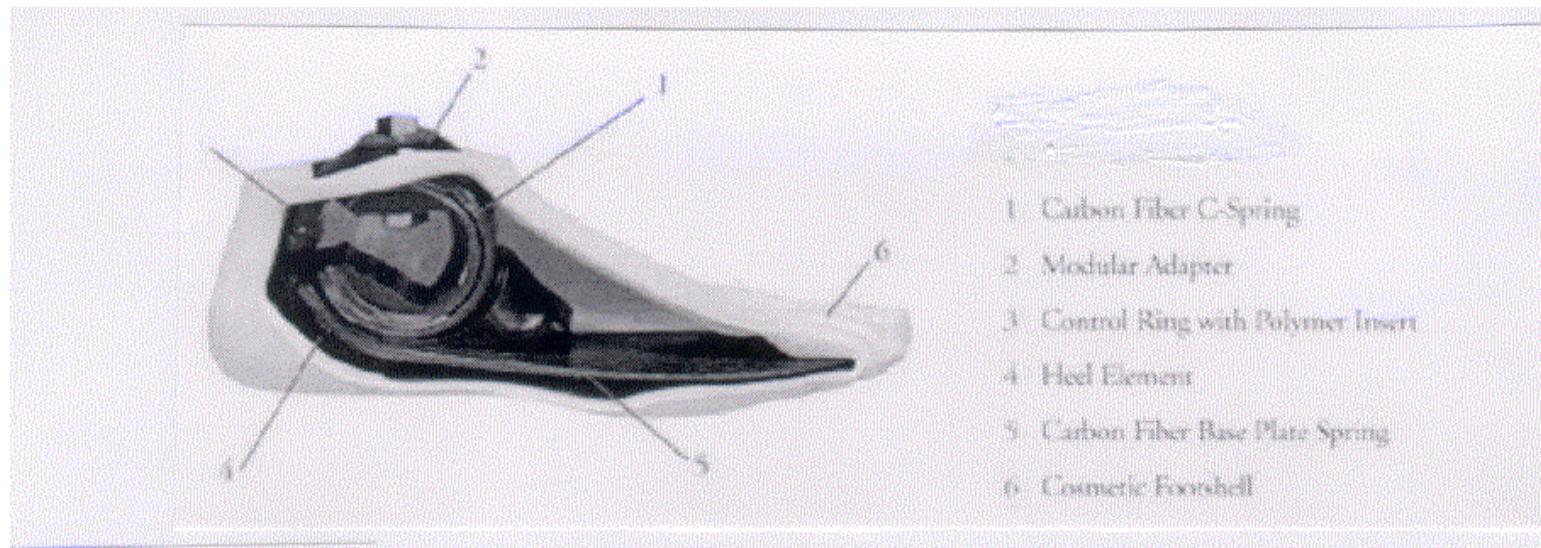
# Artificial Limbs

## Upper Limb - Arm



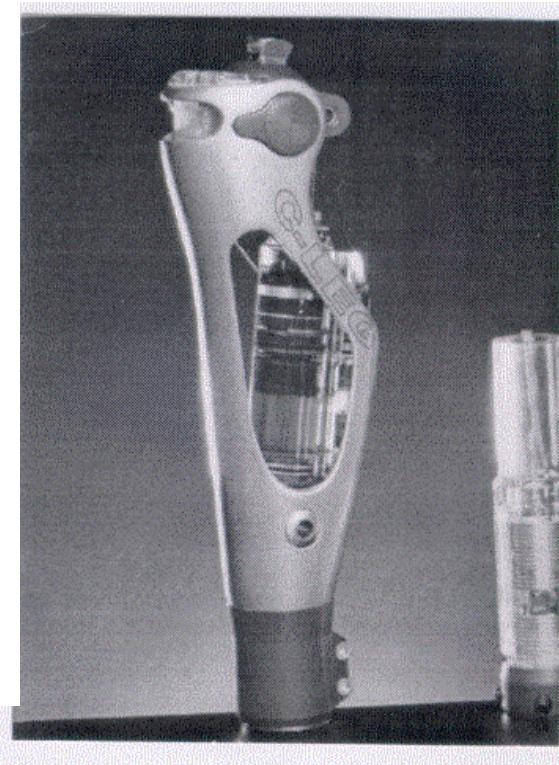
# Artificial Limbs

## Lower Limb - Foot



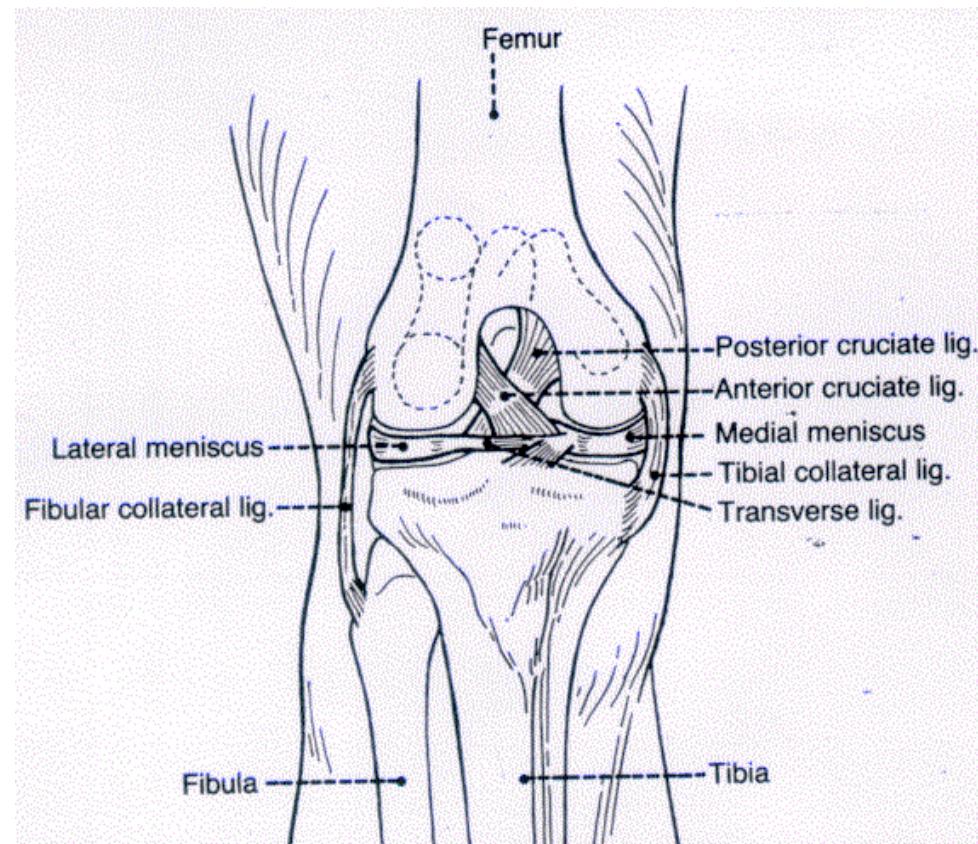
# Artificial Limbs

## Lower Limb - Leg



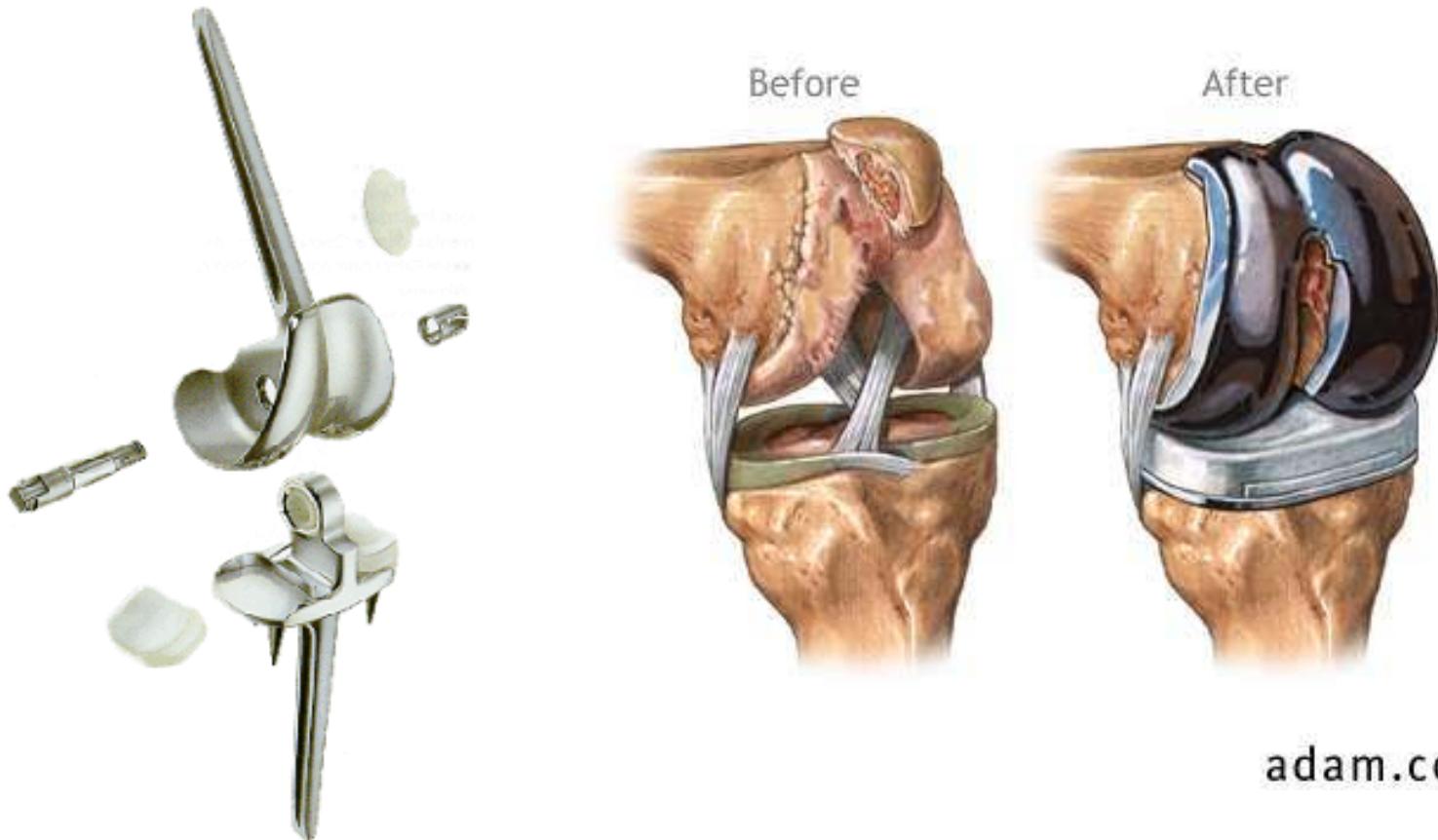
# Structure of Large Joints

## Knee Joint



# Artificial Joints

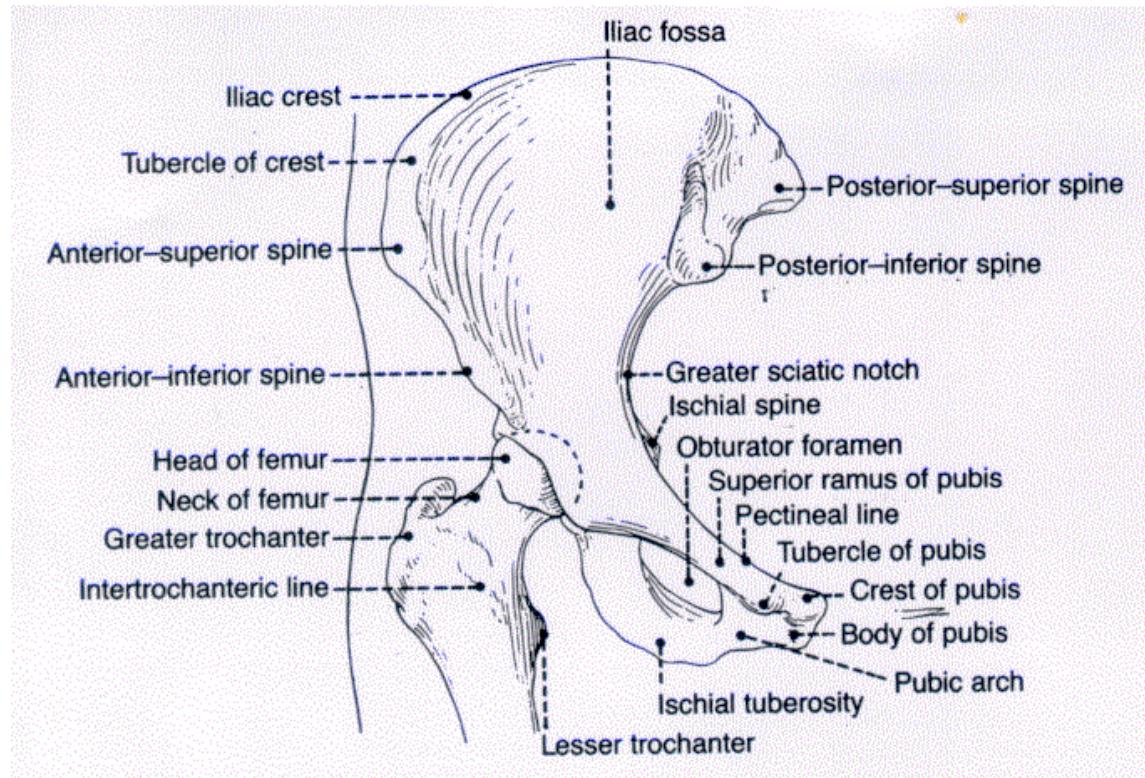
## Knee



[adam.com](http://adam.com)

# Structure of Large Joints

## Hip Joint



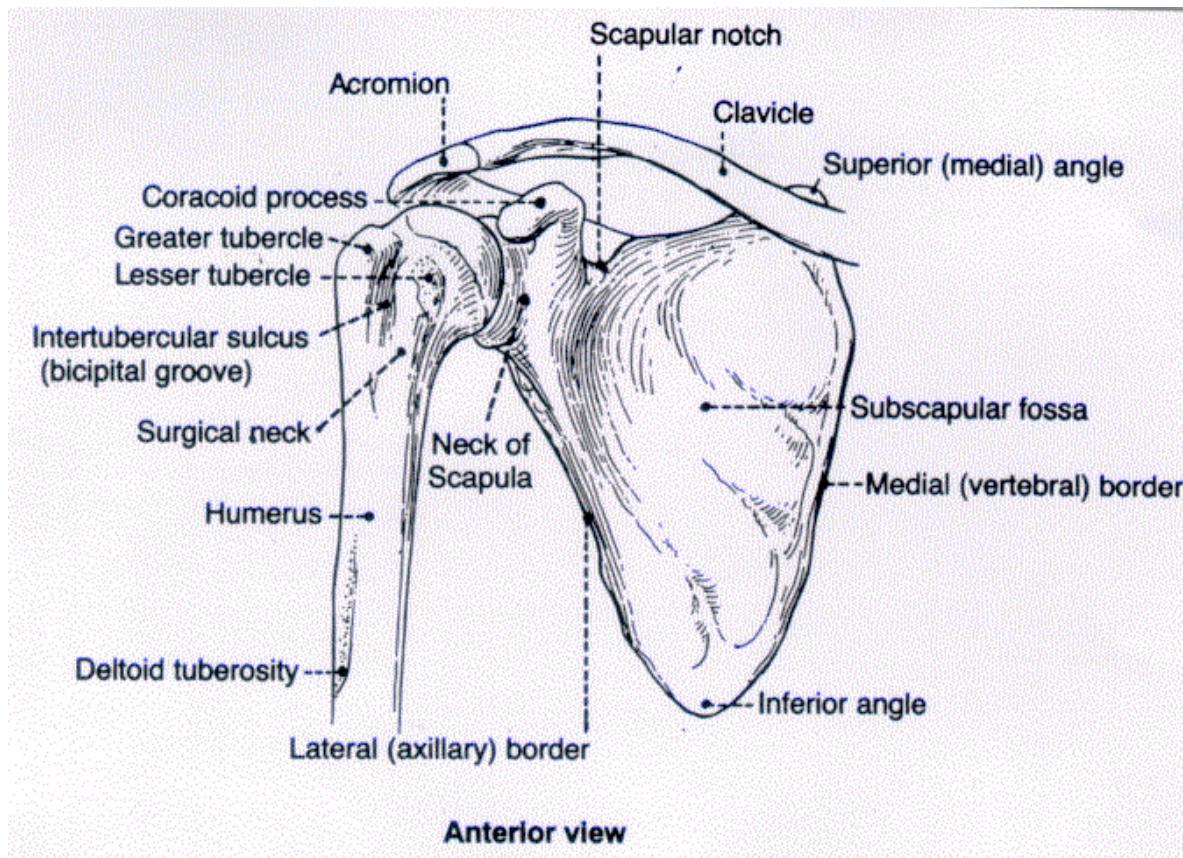
# Artificial Joints

Hip



# Structure of Large Joints

## Shoulder Joint

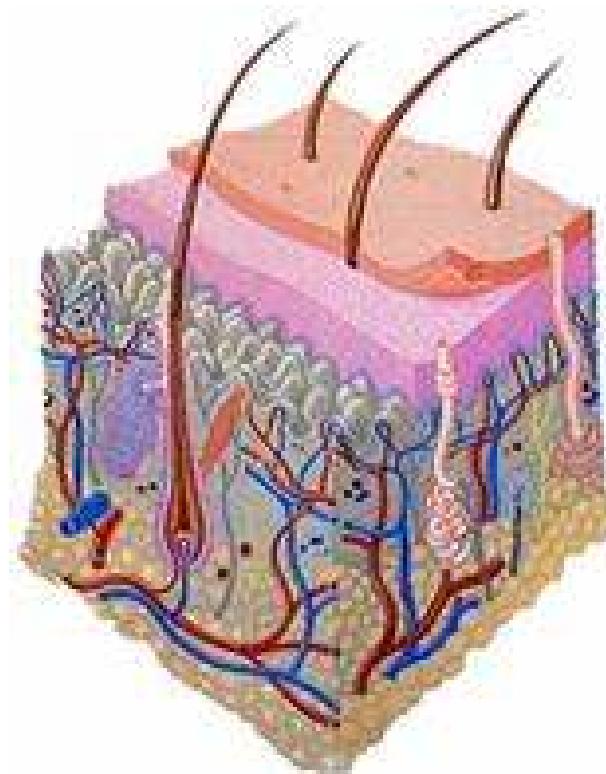


# Artificial Joints

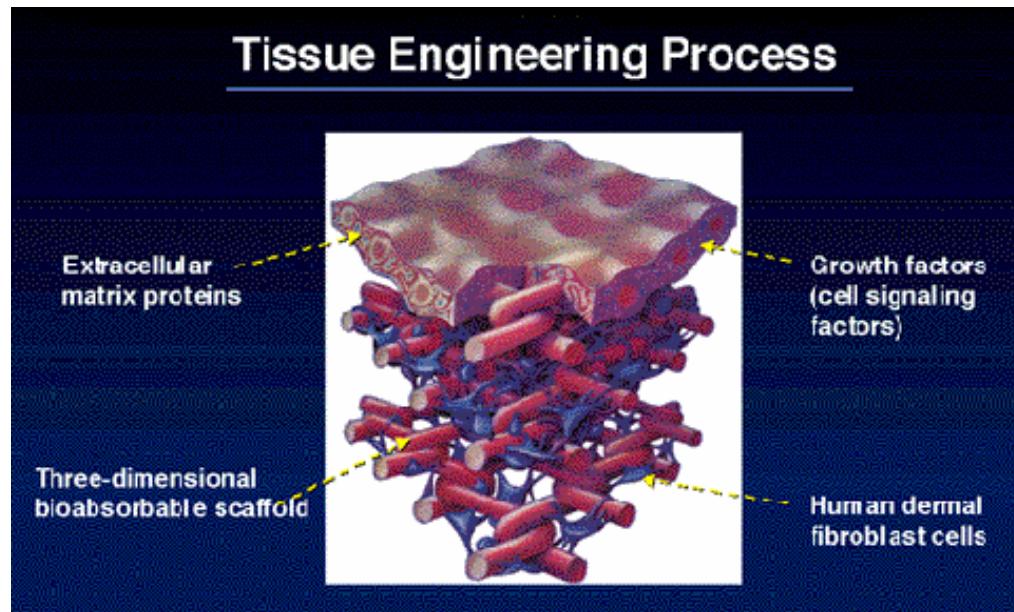
Shoulder



# Structure of the Skin

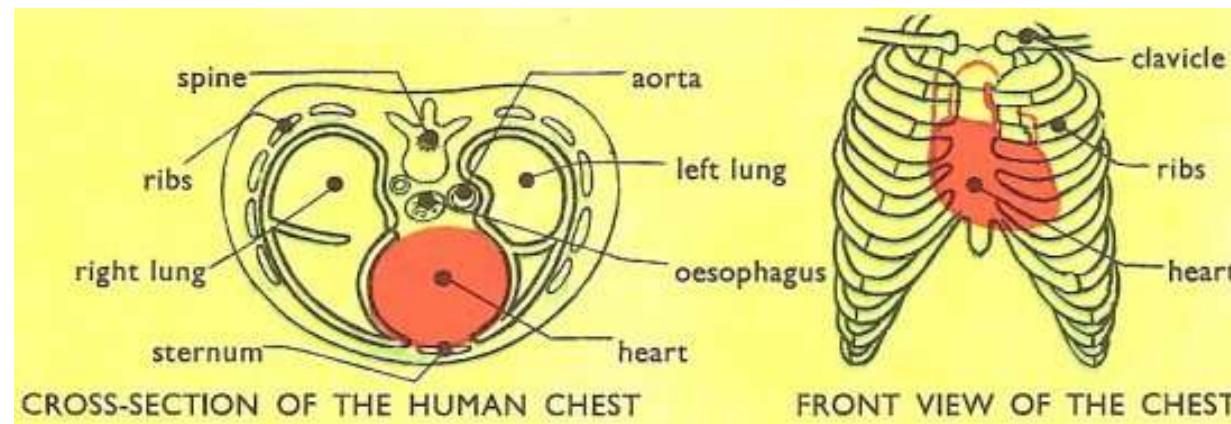
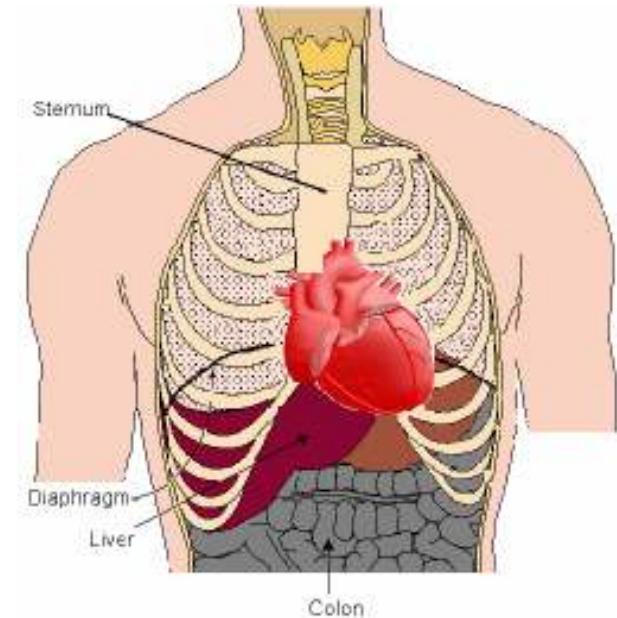


# Tissue Engineering Process



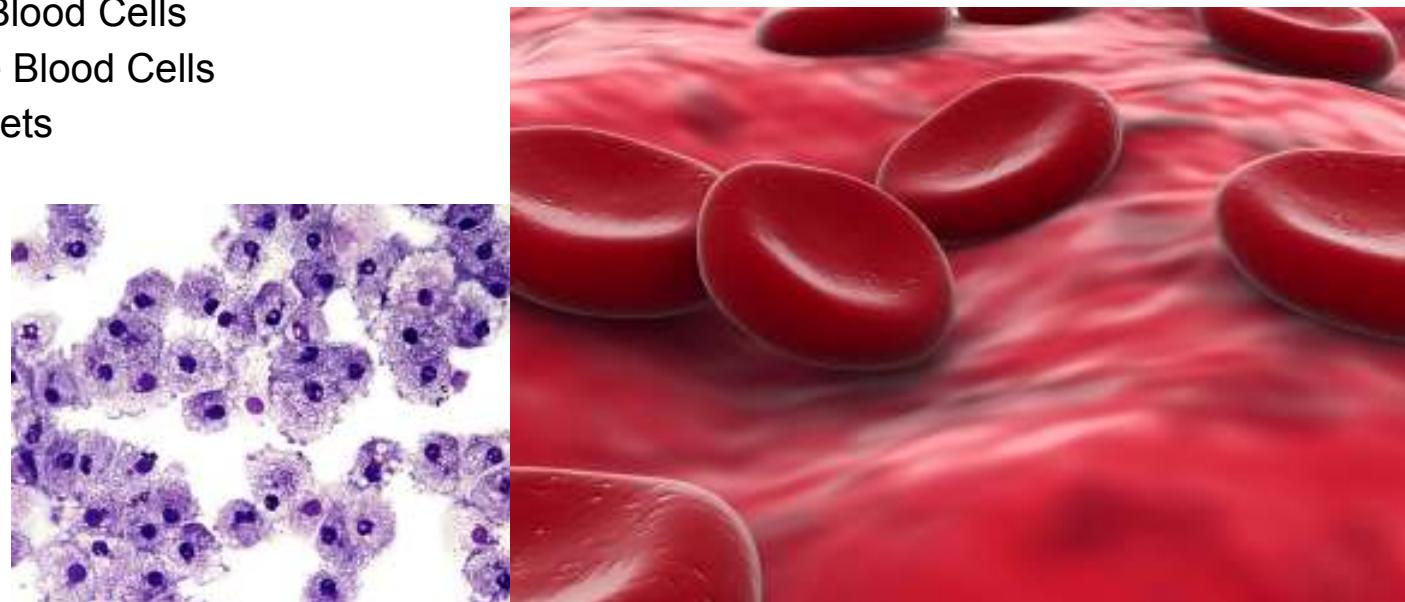
# The Cardiovascular System

- The cardiovascular system is a network of pipelines through the body. Blood is forced through the pipes by the heart pump, eventually returning the blood to the heart.
- The cardiovascular system consists of:
  - Blood
  - Heart
  - Vessels



# Blood

- The volume of blood in an adult human is about 6 to 8% of the body weight.
- The viscosity of blood is about 4.5 to 5.5 times that of water.
- The pH of blood is somewhere between 7.35 - 7.45.
- The salinity is about 0.85 to 0.90% NaCl.
- Blood Density is about 1.057 gm/cm<sup>3</sup>
- Formed Elements:
  - Red Blood Cells
  - White Blood Cells
  - Platelets



# Functions of the Blood



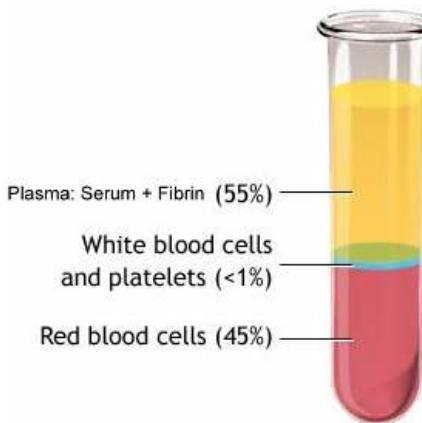
Red Blood Cells  
White Blood Cells

**Mammalian Blood Cells in a Small Blood Vessel**

- **Transportation:** Blood moves oxygen, nutrients, wastes, carbon dioxide, hormones and enzymes.
- **Regulation:** Blood regulates pH, water content of the cells and body temperature.
- **Defense:** Blood defends the body against toxins and microbes.
- **Homeostasis:** Blood maintains an acceptable environment for living cells.

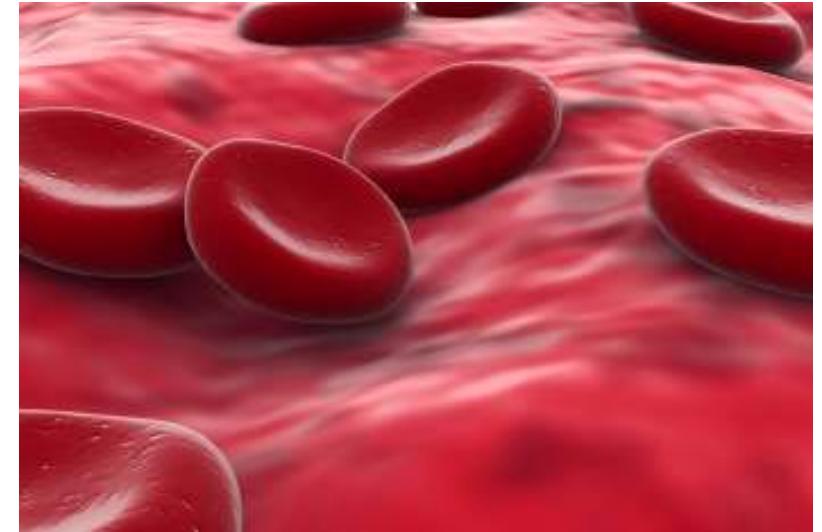
# Components of Blood

- Blood consists of plasma and blood cells. Plasma is what is left after the cellular components of the blood are removed by centrifuging.
- The blood cells are the formed elements in the blood. They include erythrocytes (red blood cells), leukocytes (white blood cells) and thrombocytes (platelets).
- The blood cells are produced by a process called hemopoiesis from bone marrow.



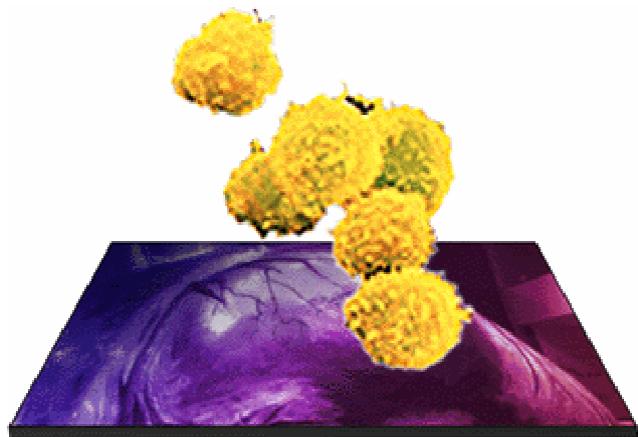
# A. Red Blood Cells

- The Erythrocytes are biconcave disks without nuclei and contain Haemoglobin, which contains four heme groups. The heme groups each contain one atom for each iron and have a strong desire to bond with oxygen. These are used for oxygen transport.
- Red Blood Cells transport oxygen away from and carry carbon dioxide back to the lung. Hemoglobin can combine with a large amount of oxygen (greater than 1 to 1 ratio) under normal conditions. This is oxygenated blood, which has a bright red color. When oxygen is removed, the blood becomes dark.
- The life of Red Blood Cells is about 120 Days.
- The number of Red Blood Cells in a male human is about 5.4 million per mm<sup>3</sup> and in a female, is about 4.8 million per mm<sup>3</sup>.
- Hematocrit is a measurement of the percentage of Red Blood Cells in the whole blood. It is determined by centrifuging heparinized blood. Heparin is used to prevent clotting while waiting for the cells to settle in vertical centrifuge tubes. The packed cell volume contains WBC's and the platelets forming a thin layer on the top, with the remainder Red Blood Cells.



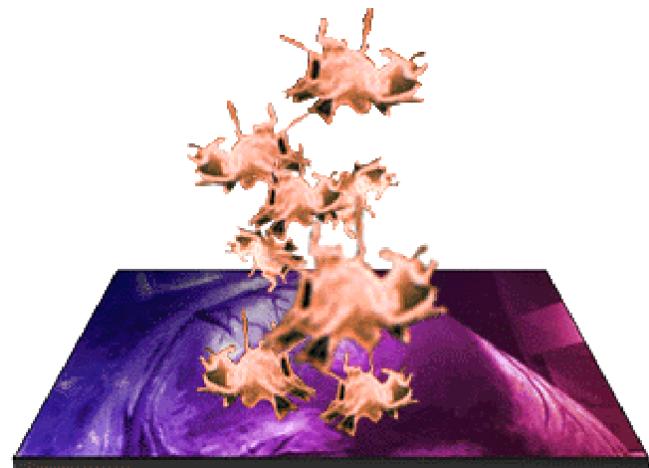
## B. Leukocytes

- Leukocytes are White Blood Cells. They have nuclei. Their main function is defending the body. They are larger than Red Blood Cells; Red Blood Cells are around 8 microns and leukocytes are about 13-14 microns.
- The general function of leukocytes is to fight infection. They are involved in allergic reactions and fighting foreign bodies called antigens. They produce specific defence substance, which are called antibodies, aimed exclusively at the particular invader involved. White Blood Cells number about 5000 to 9000 mm<sup>3</sup> in normal people.



## C. Thrombocytes (Platelets)

- The function of platelets is a process in homeostasis such as blood clotting.
- Platelets are cell fragments without nuclei.
- There are about 250,000  $\text{mm}^3$  to 400,000 per  $\text{mm}^3$  in normal people.

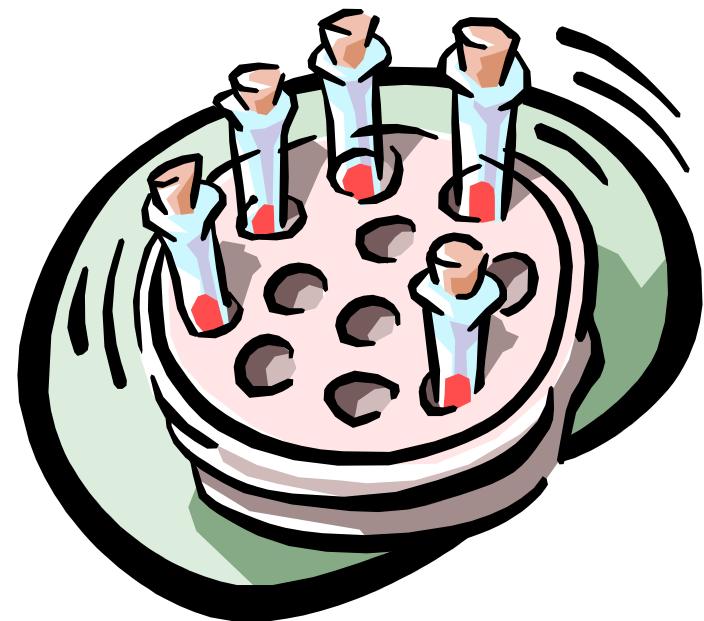


## D. Plasma

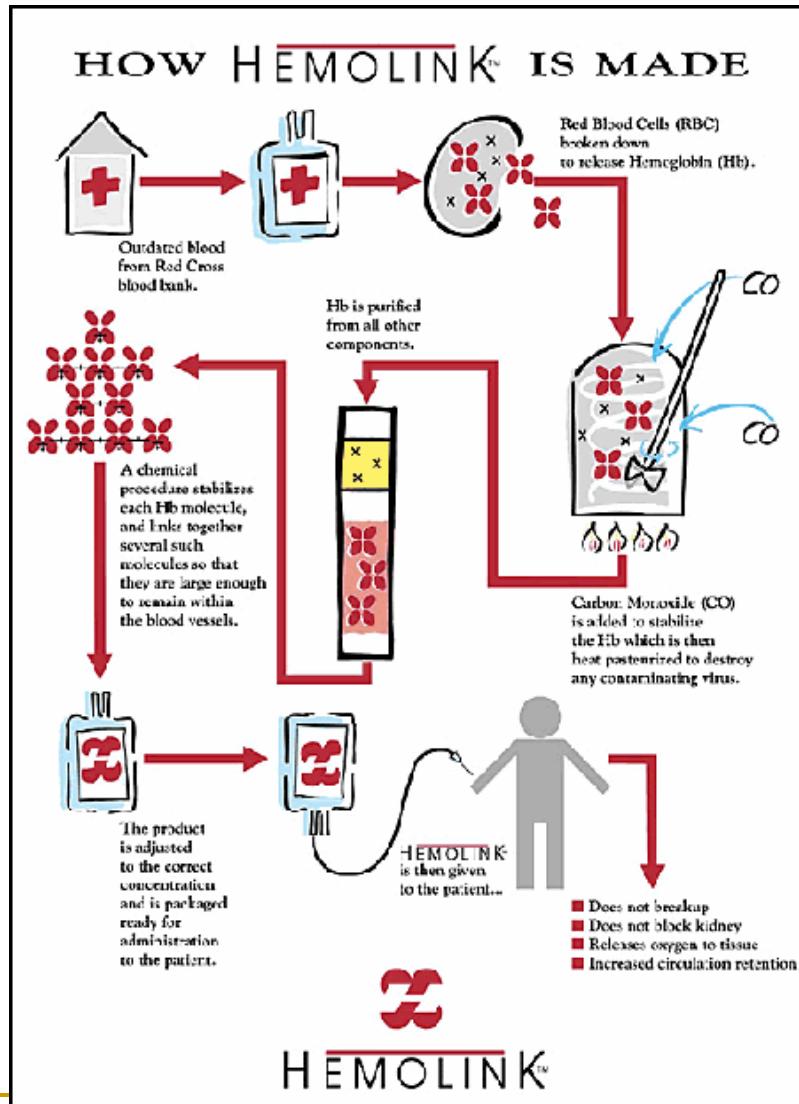
- The liquid non-cellular portion of blood, which consists of about 91.5% water and 8.5% solutes.
- The main solutes are proteins, foods, enzymes, hormones, gases and electrolytes.
- Other substances found in plasma include:
  - Nutrients: amino acids, fatty acids, vitamins, glucose
  - Waste: carbon dioxide, urea, uric acid
  - Proteins: hormones, antibodies

# Blood

- Considered a circulating tissue composed of a fluid portion (plasma) with suspended formed elements (red blood cells, white blood cells, platelets).

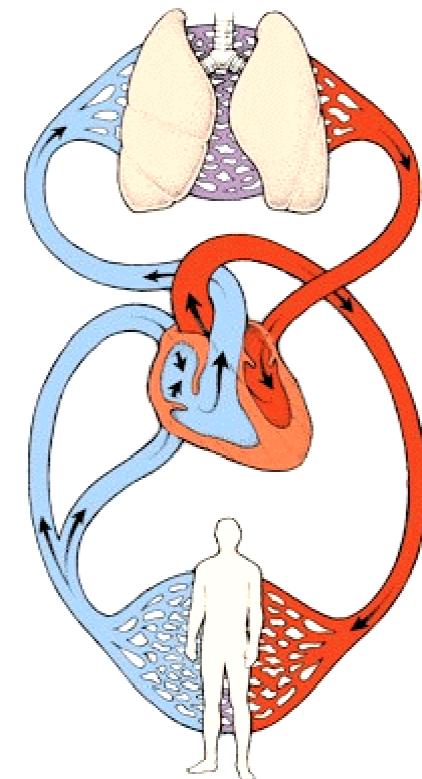


# Hemolink Development Process

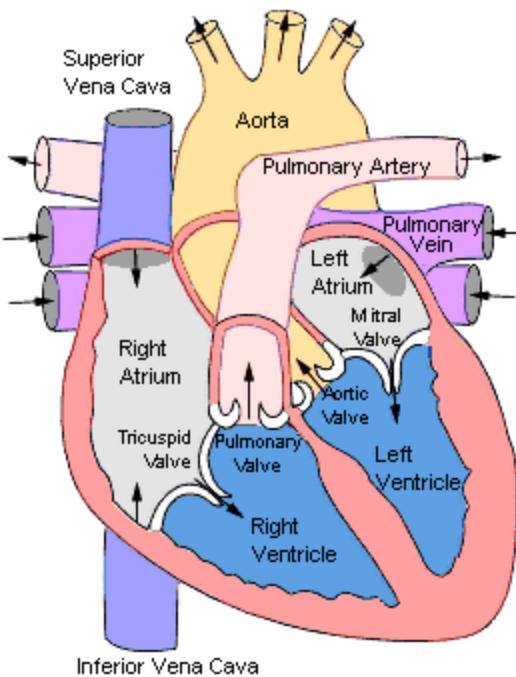


# Cardiovascular System

- ❖ The Cardiovascular System consists of:
  - The heart, arteries and smaller arterioles (carrying blood away from the heart), Capillaries (distributing blood to the cells), as well as small venules and large veins, conducting blood back to the heart.
- ❖ The circulatory system consists of oxygenated blood leaving the left ventricle, traveling through the aorta, arteries and capillaries to the various parts of the body where the oxygen is distributed, and wastes and CO<sub>2</sub> are collected. Deoxygenated blood returns to the right atrium through veins, at a lower pressure. This complete circuit is called **systemic circulation**.
- ❖ **Pulmonary circulation** passes from the right ventricle to the lung where oxygen is obtained and CO<sub>2</sub> is released, returning to the left atrium and then to the left ventricle.
- ❖ Functions of Blood:
  - Transport
  - Disposal
  - Liquid Balance
  - Defence
  - Communication
  - Temperature Control

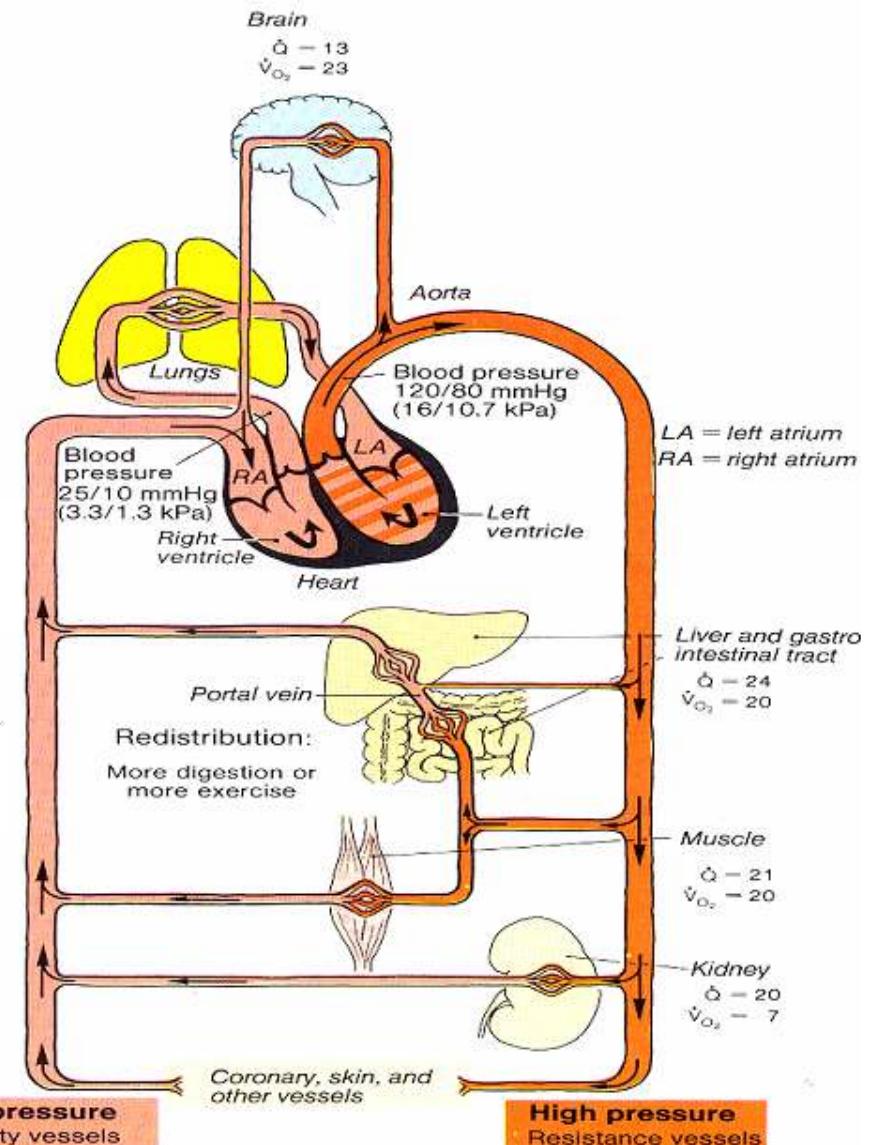


# The Cardiovascular System



Organ blood flow as % of cardiac output  
(output at rest=5.5L/m/70 kg body weight)

$\dot{V}_{O_2}$   
Oxygen utilization as % of total utilization of 0.25 L O<sub>2</sub>/min



# Structures of the Heart

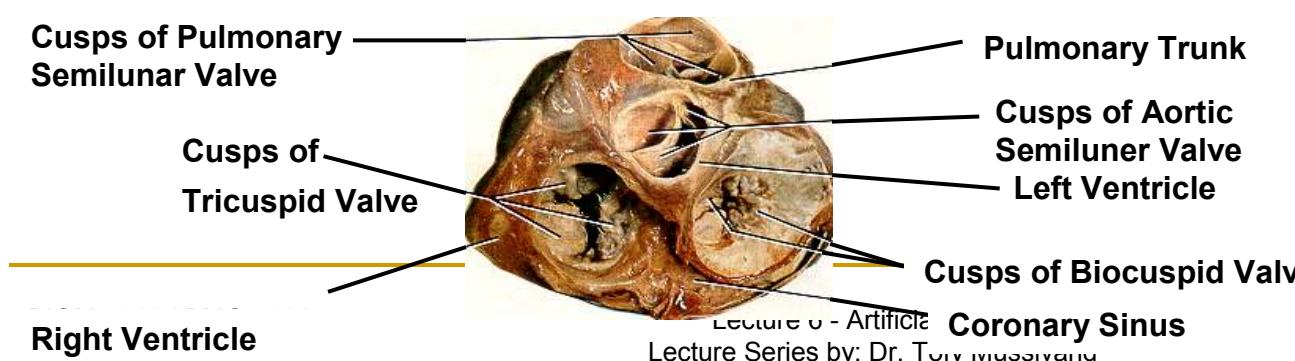
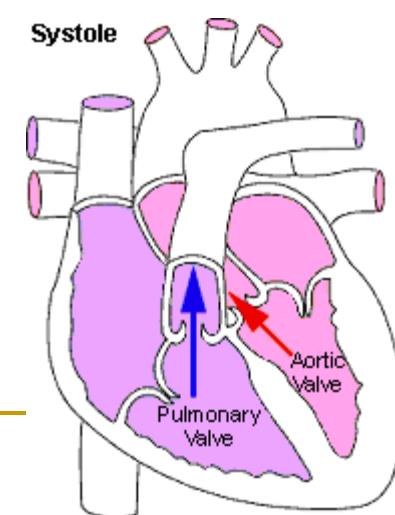
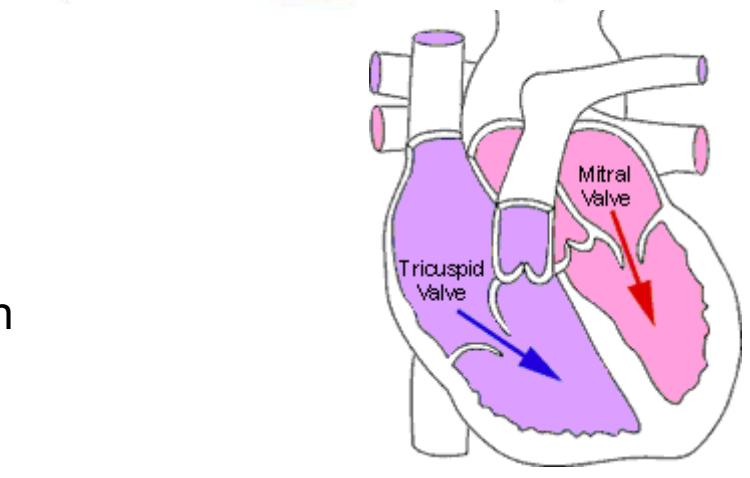
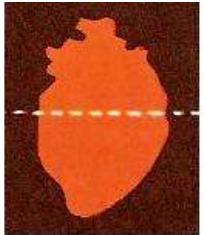
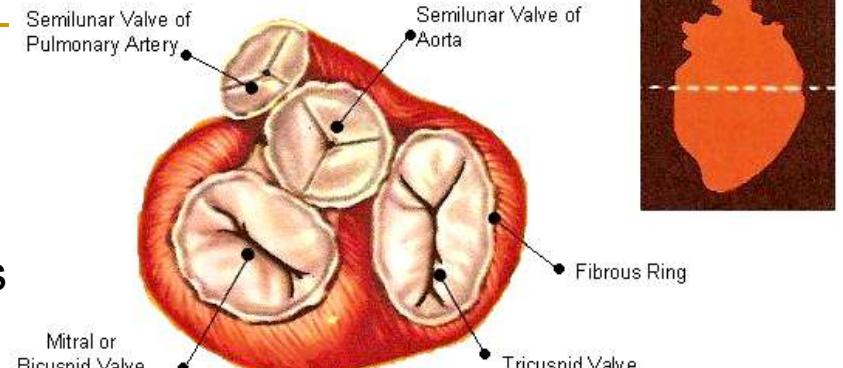
- The human heart consists of four rooms (chambers). The order of receiving blood is numbered by the author in a counter-clockwise fashion:
  - Chamber 1: Right Atrium: This is where low oxygen content blood is received.
  - Chamber 2: Right Ventricle: Where the blood is received from the right atrium in order to be pumped to the lungs for oxygenation.
  - Chamber 3: Left Atrium: Where oxygenated blood is received from the lung.
  - Chamber 4: Left Ventricle: Where oxygenated blood is received in order to be pumped to the aorta and remainder of the body.
- Function of the Heart: The heart's function is to pump the blood to the lungs for oxygenation and to the remainder of the body for perfusion of the tissue. The heart is a muscular organ.
- The heart has four valves: 2 valves between the atrium and ventricles (between chambers, 1,2, and 3,4) and 2 valves for taking blood away from the heart.
  - There are 2 valves between the atriums and ventricles, and 2 valves leaving the ventricles.
  - All valves are one-way and permit flow under normal healthy conditions.

# Heart Muscle

- The heart muscle is striated, meaning it has dark and light lines and has actin and myosin filaments.
- During contraction, these actin and myosin filaments slide over one another and cause contraction force.
- The heart beats and this beating is initiated by a specialized conduction system that starts in the SA Node (pacemaker) and goes to the AV Node and then to the rest of the heart muscle.
- Action potential is the cause of contraction and relaxation of the muscle.
- The whole muscle of the heart, which is composed of many cells, contracts as a whole like one cell.
- Impulses from the atria (Chambers 1 and 3) must pass through the AV Node before triggering ventricular (Chamber 2 and 4) contraction.
- Stimulation of one muscle on cardiac tissue causes all muscles to react. This is due to intercalated disks which conduct the action potential.
- It is about the size of a clenched fist (12 cm long, 9 cm wide) and is tapered at the bottom end (approx. 6cm thick).
- Located at the centre of the chest and tilted to the left side on the front of the thoracic cavity, between the second and the first intercostal space, about 2/3 of the mass of the heart is on the left side.
- The heart is contained in a sac called the pericardium.
- The heart has 4 chambers: right and left atrium, right and left ventricle.
- The right side receives blood from the body and pumps it into the lungs. The left side receives the blood from the lungs and pumps it into the body.
- There are 2 valves between the atrium and ventricular chambers called AV valves:
  - Tricuspid valves between the right atrium and the ventricle.
  - Bicuspid valves between the left atrium and ventricle.
- The Semilunar valves prevent flow from coming back from the aorta to the ventricle and from the pulmonary artery to the ventricle.

# Heart Valves

- There are two atrioventricular (AV) valves between the atria and ventricles:
  - The Tricuspid between the right atrium and right ventricle.
  - The Bicuspid valve between the left atrium and left ventricle.
- Two Semilunar valves:
  - The Pulmonary semilunar valve between the right ventricle and pulmonary artery.
  - The Aortic valve between the left ventricle and aorta.
- All are one-way valves.



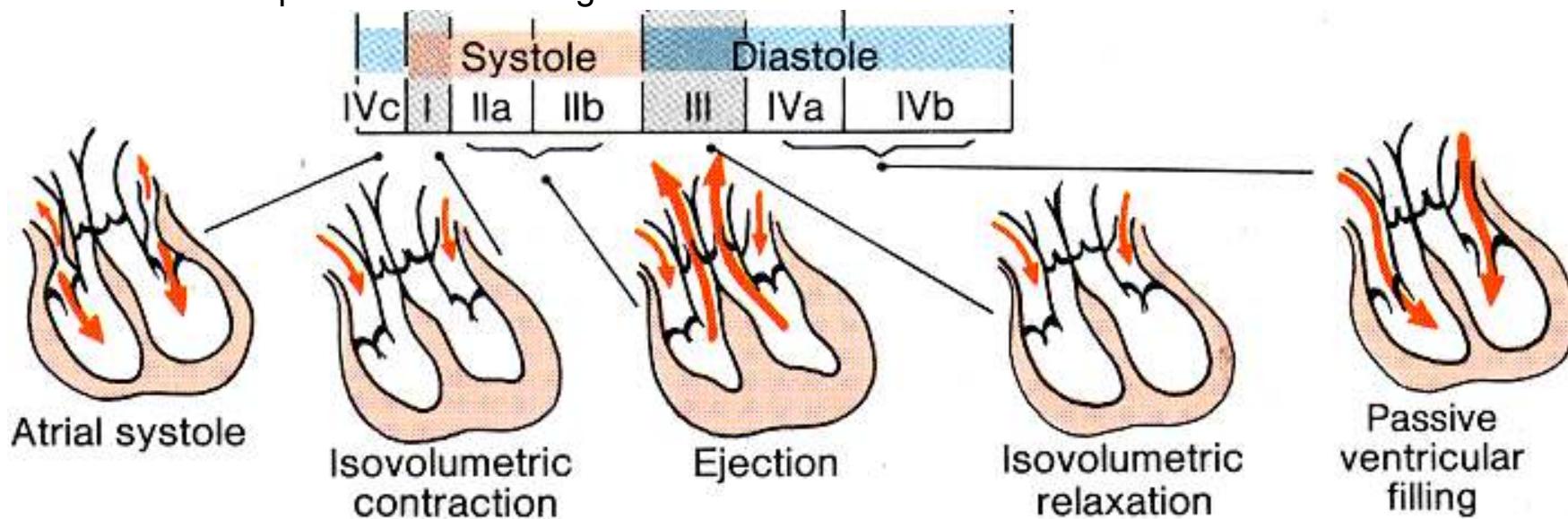
Lecture 6 - Artificial  
Coronary Sinus  
Lecture Series by: Dr. Tony Muzzolini

# Conduction of Action Potential

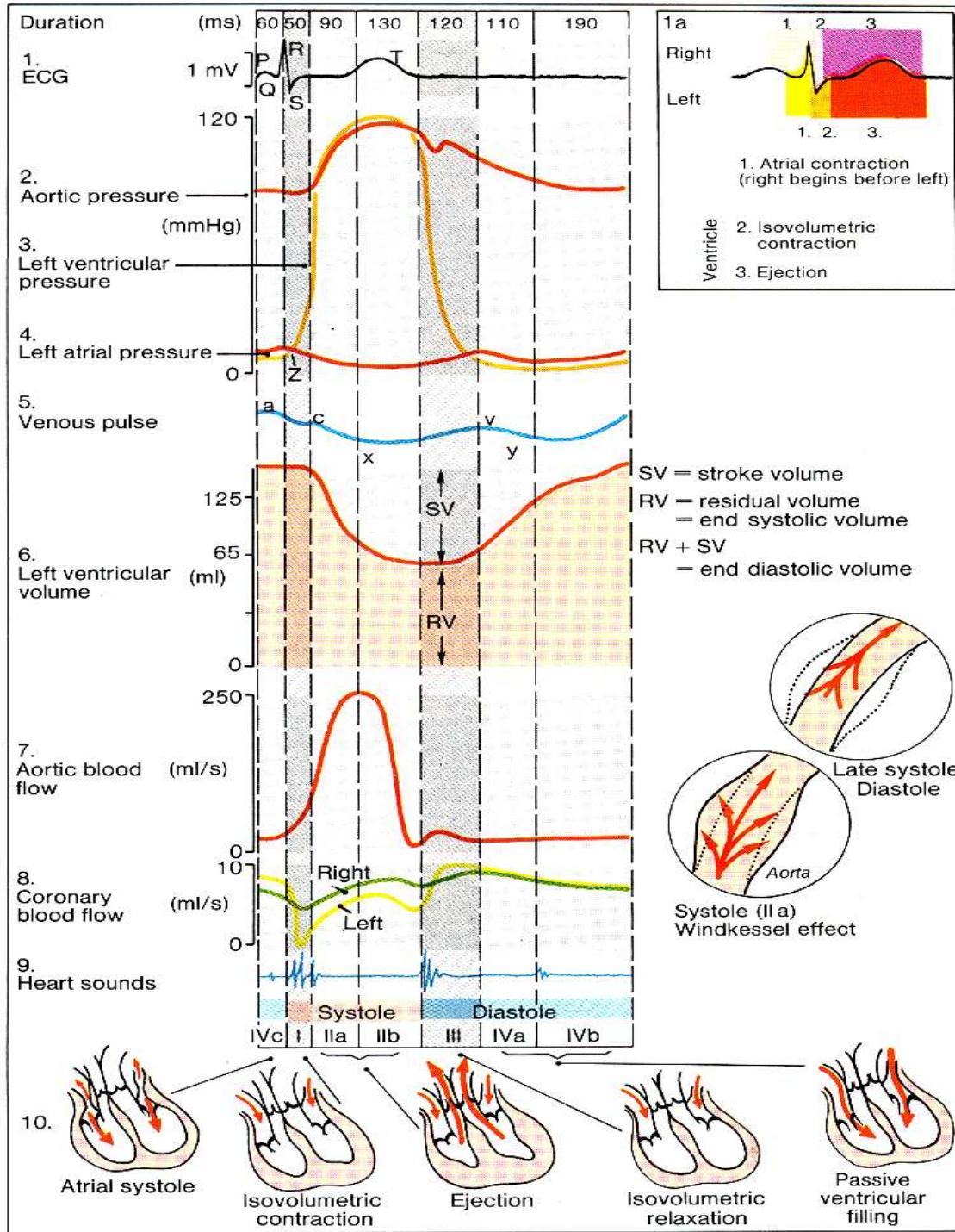
- There is a special system of conduction within the heart.
- The conduction system begins with Sinoatrial (SA) Node, which is a small mass of specialized muscle in the wall of the Right Atrium near the opening of the superior vena cava.
- The SA Node is an automatic, self-excitatory tissue, which initiates each heartbeat.
- This way, it sets the basic rate of the heartbeat and is why it is called the pacemaker.
- With each beat, an electrical action potential is initiated first and travels through all the tissues of the atria and ventricles causing contraction.

# The Heart (Cardiac) Cycle

- One heartbeat is composed of several actions.
- The sequence of these actions during one complete heartbeat is called the cardiac cycle (heart cycle).
- The time of one cycle varies with the heartbeat. However, it is about 0.8 seconds.
- The heart beats about 42 million times per year. Each beat consists of contraction, which produces force to pump blood out of the heart and relaxation in which the heart muscle relaxes, thus permitting the filling of the heart with the blood.
- The duration of contraction is called systole and the time of relaxation is diastole.
- SA Node initiates each cardiac cycle.
- With each heart cycle, several changes happen: Changes in aortic pressure, changes in ventricular pressure and changes in electrical conduction of the heart.

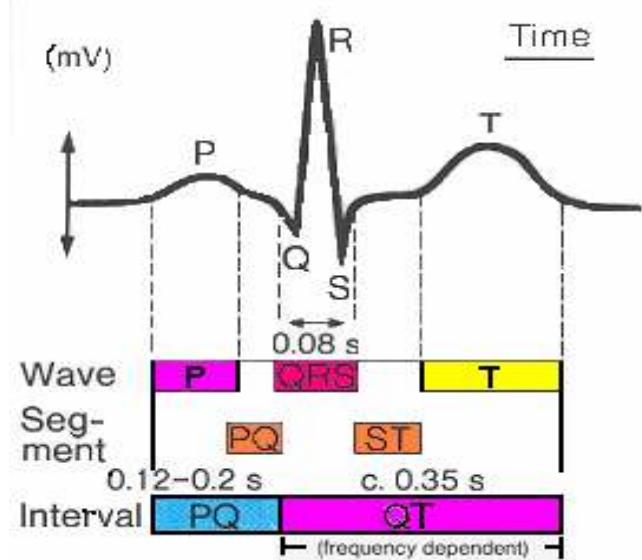


# The Cardiac Cycle



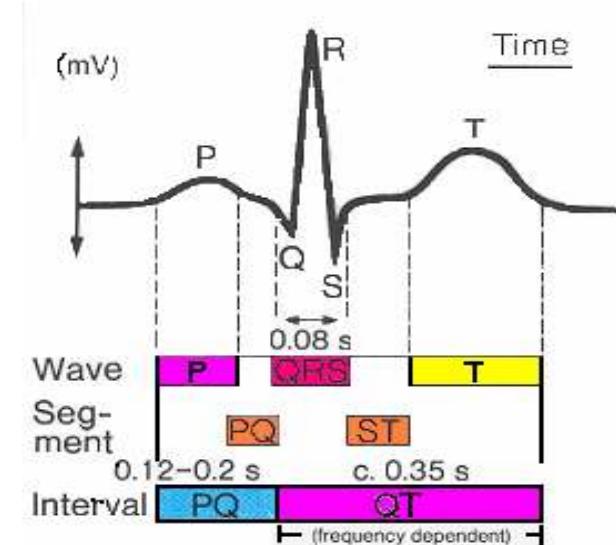
# The Electrocardiogram

- An electrocardiogram is the plot of the wave of depolarization and repolarization of action potential of the heart muscle recorded on the surface of the body.
- The electrocardiogram is used to diagnose disease of the heart.
- An electrocardiogram is recorded by an electrocardiograph, which amplifies and records the electrical activity of the heart. The result is an electrocardiogram or ECG.
- Each electrocardiogram begins with the P wave. This is the graphic record of the spread of the collective depolarization of the multitude of muscle cells in the atria, just prior to atrial contraction.
- Then there is another wave, which is called QRS complex. This is the spread of collective impulses to the ventricles just before ventricular muscles contract.
- There is also the T wave, which is a representation of the repolarization of the ventricular muscles.
- The shapes and the time intervals between the waves are important for evaluation and interpretation of the ECG.



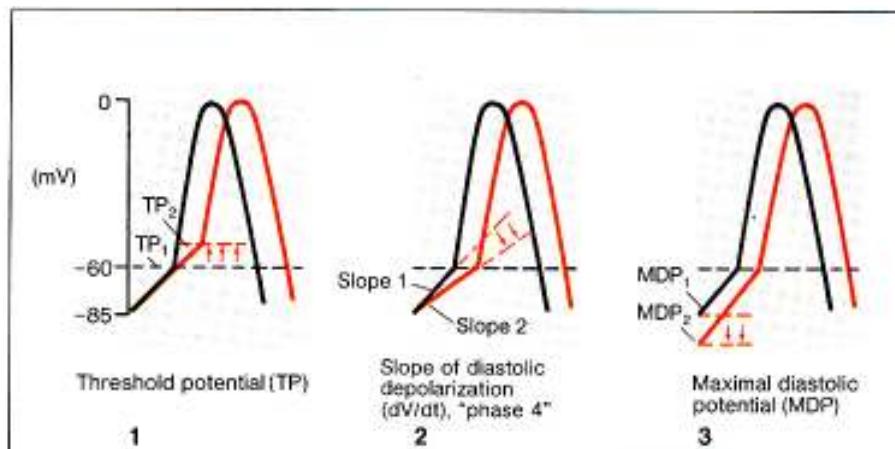
# The Electrocardiogram

- The PR interval is the duration between the beginning of the P wave and the beginning of the QRS wave. It represents the time between the beginning of the contraction of the atrium and the beginning of the contraction of the ventricle.
- In patients with heart disease, having scared or inflamed tissue, PR may be increased.
- This is because more time is required for the PR wave to pass through the atrial muscle and AV Node.
- The QRS duration is the time required for QRS wave represents depolarization of the ventricles.
- The QT interval extends from the beginning of the Q wave to the end of the T wave. It represents the time of ventricle contraction and depolarization.
- The ST interval represents the time during which the ventricle depolarizes. It extends from the S wave to the end of the T wave.



# Disturbances in the Heart Rate and Rhythm

- Any variation from the normal rhythm of the heart is called arrhythmia.
- Tachycardia means fast heart beat and that is defined as when the heart beats more than 100 beats per minute.
- Tachycardia could be caused by several events: fever, drugs, weakening of the heart muscle, sports and nerve stimulation.

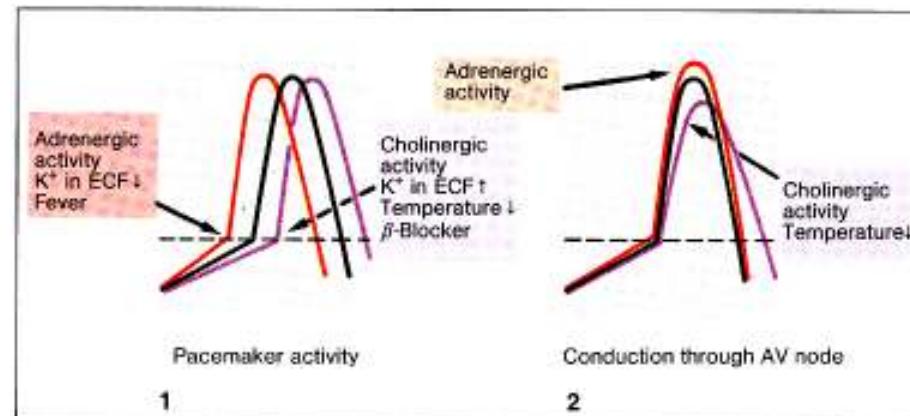


Influences on pacemaker rate.

- When the heart beats less than 60 times per minute; it is called a slow heart beat or bradycardia.
- Bradycardia could also be a result of disease, body temperature, drugs or stimulation.
- A normal ECG has PQRST and appropriate time amplitude.
- Fibrillation is when the heart beats very rapidly and the beat is uncoordinated.
- Ventricular fibrillation can result in death because, with this condition, no blood is pumped into the arteries.

# Disturbances in the Heart Rate and Rhythm

- Ventricular fibrillation may be caused by inadequate oxygen to the heart muscle, heart attacks, injury, electrical shock and drugs.
- Sometimes fibrillation can be corrected by defibrillation. This application of a strong electric current to the chest wall which acts as a stimulator and causes depolarization of all the cardiac muscle fibres simultaneously. Thus, all the contractions stop momentarily.
- If the SA Node then begins to function, normal heart rhythm returns, otherwise death may occur.
- Heart Block: Transmission of action potential is needed for contraction of heart muscles and, if this is delayed or blocked at some point in the conduction system, heart block results.
- **Pacemakers: Artificial pacemakers now are implanted in patients with severe heart block problems.**  
The pacemaker is implanted underneath the skin and electrode nodes are connected to the heart. This device provides pacing for impulses that make the heart beat.



Influences on (1) frequency and (2) conductivity.

# Mechanics of Blood Circulation

## ➤ **Introduction:**

As it was mentioned earlier in the course, physical laws of nature are obeyed by biological systems. The circulation of blood within the blood vessels is no exception. The laws governing the circulation of flow of blood within the heart and vessels are basically grouped into three laws of conservation, as listed below.

## ➤ **Conservation of Mass Laws:**

1. For blood circulation at any given region, the summation of flows into that region must be equal to the summation of all the flows out of that region.

$$Q_i = Q_o$$

Where:  $Q_i$  = All the flows in

$Q_o$  = All of the flows going out

2. This provides us with an explanation for several complex blood circulation problems. For example, if the flow is confined to the blood vessels, then at bifurcations (separation of the vessels), the flow into that junction. Therefore, in abdominal aortic bifurcation, the flow coming from the abdominal aorta will be branched to the left and right. The summation of flows to the left and right iliac.
3. The other problem that can be related to conservation of mass is the velocity in a tube of variable cross section. With a steady flow, the local velocity is inversely proportional to the cross sectioned area.

$$Q = v \cdot A$$

Where:  $Q$  = Flow into that cross section

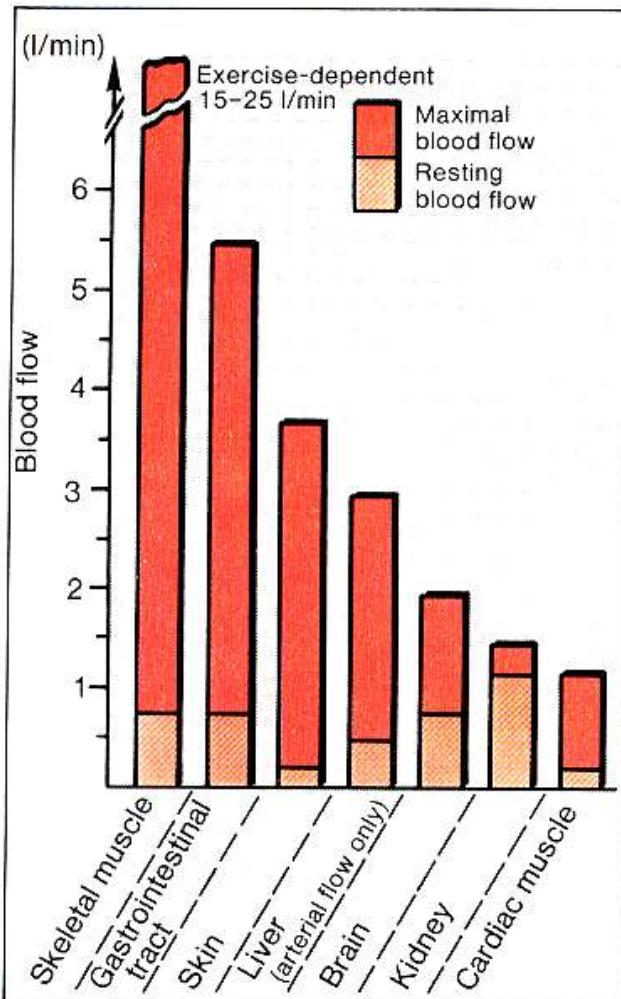
$v$  = Velocity at the cross section

$A$  = The cross-sectional area

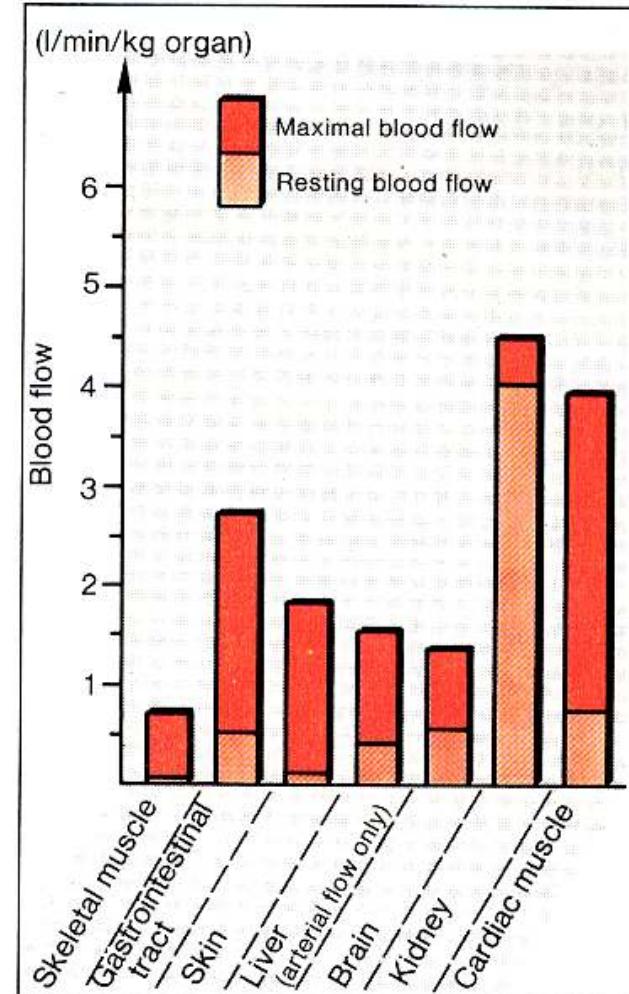
If the vessel cross-section changes along the vessel, the velocity will also change inversely:

$$v_1 \cdot A_1 = v_2 \cdot A_2 = v_3 \cdot A_3$$

# Systemic Blood Flow



**Regional blood flow.**



**Blood flow relative to organ weight.**

# Poiseuille's Law

- ❖ Poiseuille, a French physician, in 1846, described the factors governing non-pulsatile flow of a homogeneous fluid through a rigid tube.
- ❖ He stated that the rate of flow  $Q$  through a cylindrical tube of length  $L$  and radius  $R$  was directly proportional to the driving pressure  $\Delta P$ .
- ❖  $\Delta P$  presents the difference in pressure between the two ends of the tube. This could be written as:

$$Q = \frac{\pi \cdot r^4 \cdot \Delta P}{8 \cdot \eta \cdot L}$$

Where:  $Q$  = Flow rate

$r$  = Internal radius of the tube

$\Delta P$  = Pressure drop

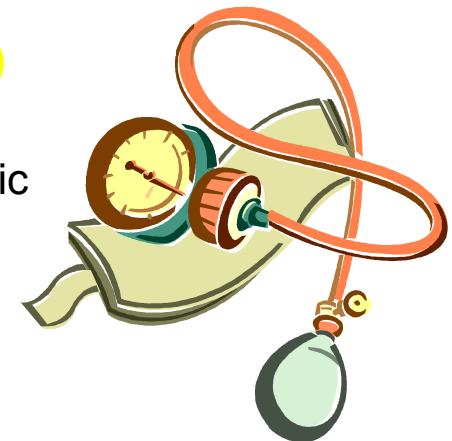
$\eta$  = Fluid viscosity

$L$  = Length of tube

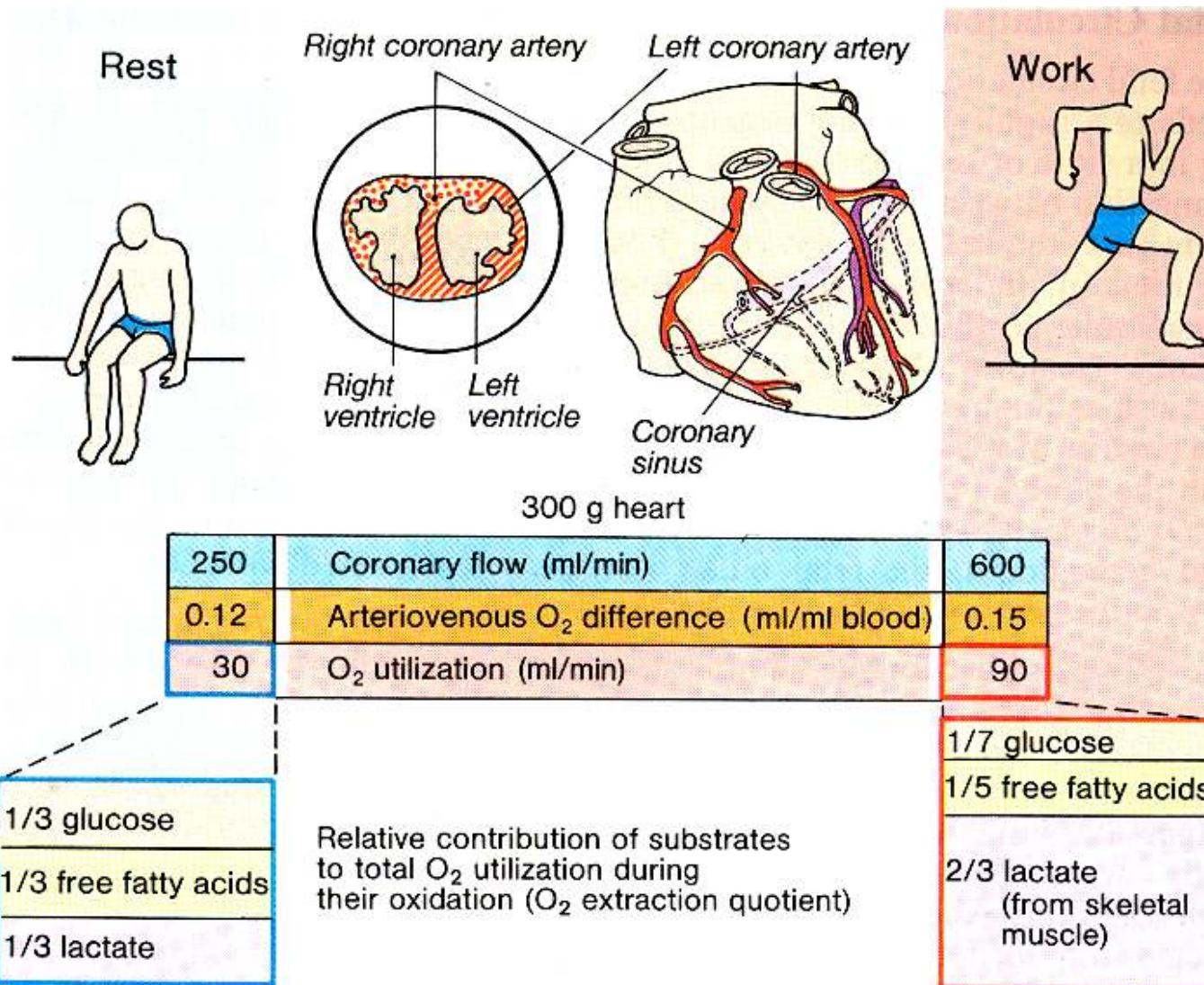
- ❖ Although blood is a non-homogeneous fluid and the tubes are not rigid, Poiseuille's Law, nonetheless, gives a good approximation and is very useful in understanding the blood circulation.

# Blood Pressure

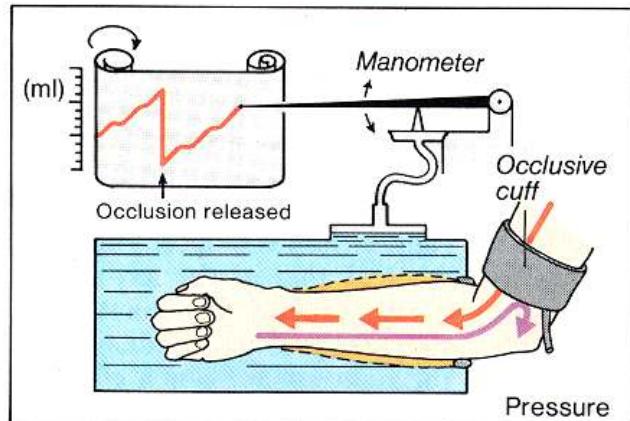
- **What is Blood Pressure?** It is the pressure in the body arteries. This is the pressure exerted by the blood on the vessel wall in order to keep the blood flowing.
- **Systolic Blood Pressure (SP):** The pressure required to push against arterial walls during ventricular contraction. This force is needed to create blood flow.
- **Diastolic Blood Pressure (DP):** The force of blood in the arteries during ventricular relaxation.
- **Pulse Pressure (PP):** The difference between systolic and diastolic pressure is called the pulse pressure:  $PP = SP - DP$
- **Peripheral Resistance (R):** The resistance to blood flow by both friction of flow and the vessel walls.
- **Units of Pressure:**  $100 \text{ mmHg} = 13.3 \text{ KPa}$  or  $8 \text{ mmHg} = 1 \text{ KPa}$ .
- **Cause of Blood Flow:** Blood flows through the body vessels because of differences in pressure. ( $\Delta P$ ) → actual total hydraulic energy gradient



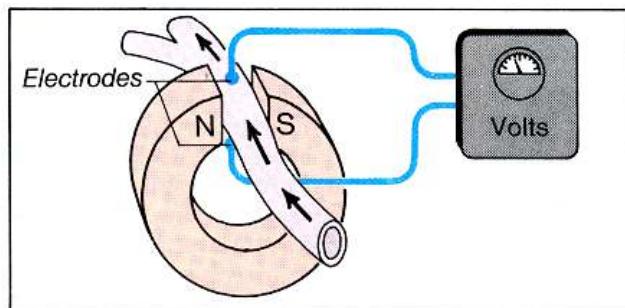
# The Heart – At Rest vs. Exercise



# Measuring Blood Flow

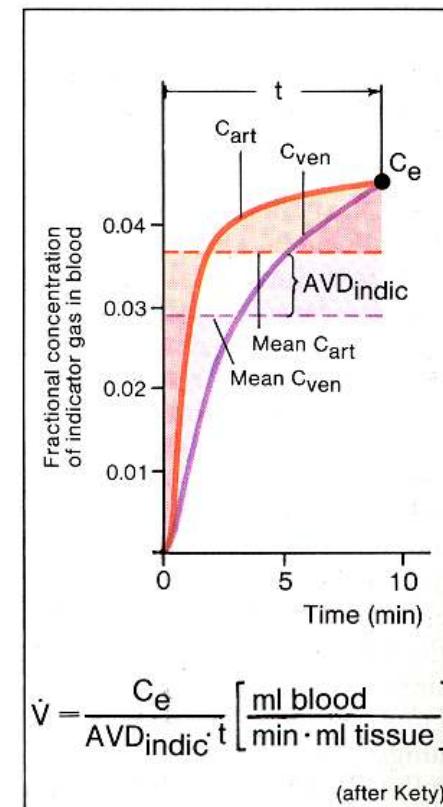


Plethysmography to measure blood flow.



Magnetic flowmeter to measure blood flow.

Indicator gas method to measure blood flow.



# Cardiac Output

- **Cardiac Output:** The blood volume ejected by the left ventricle (Chamber 4) into the aorta each minute (CO) or (Q). The CO is the product of the heart rate (HR) and stroke volume (SV), and also related to pressure drop and vascular resistance:

$$Q = CO = HR \cdot SV = \frac{\Delta P}{R}$$

Where:

Q = CO = cardiac output

HR = heart rate

SV = stroke volume

$\Delta P$  = mean pressure

R = peripheral resistance

Which is analogous to Ohm's Law:

$$I = \frac{E}{R}$$

Where:

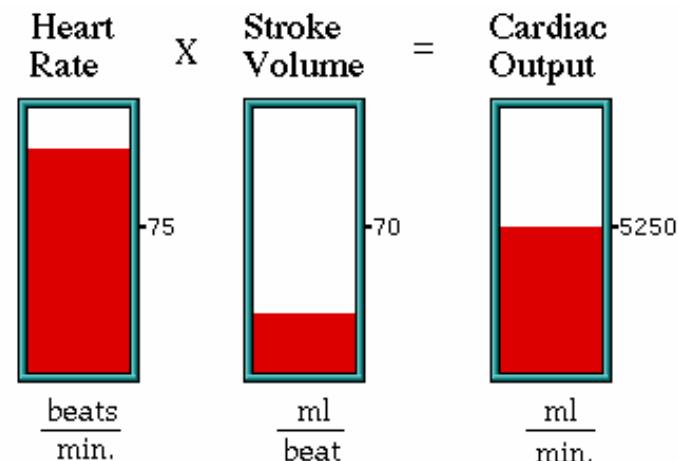
I = current flow

E = voltage drop across the resistance

R = resistance

- **Mean Blood Pressure:** The geometric mean of systolic and diastolic pressure (P).

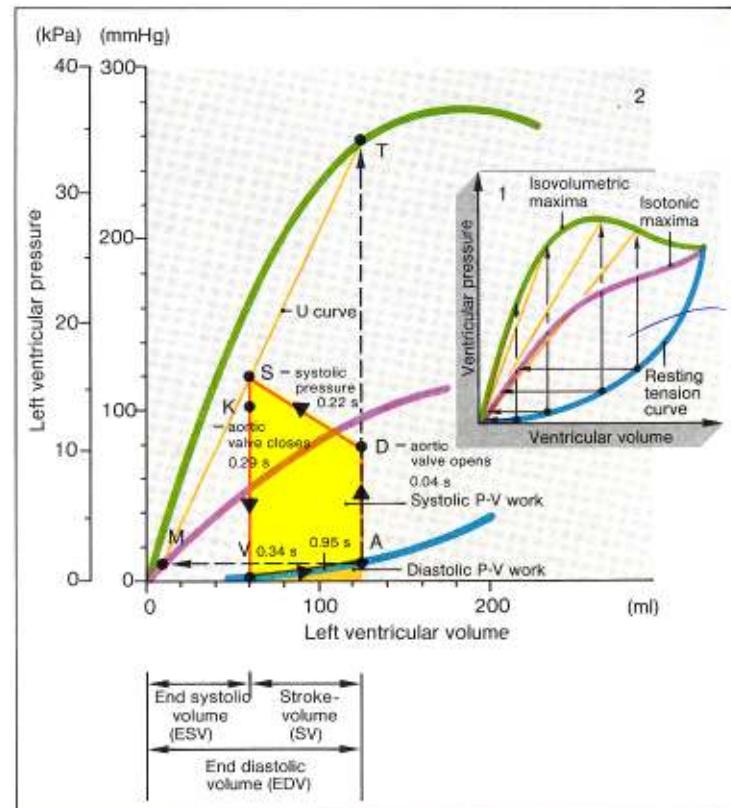
$$P = \frac{SP + DP}{2}$$



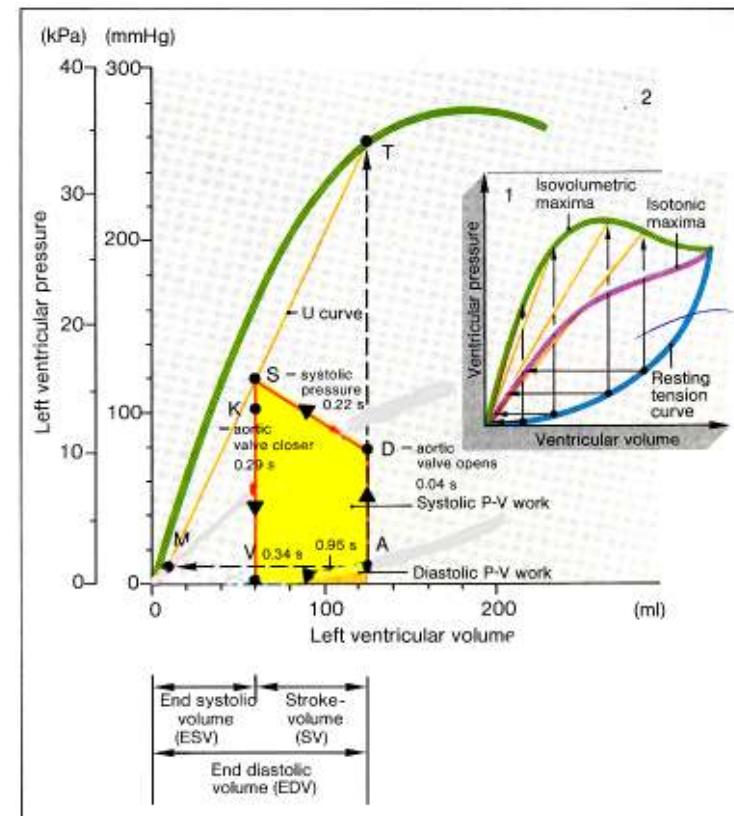
A sudden drop in **blood pressure** (e.g. when getting out of bed) results in low **venous return** and therefore decreased stroke volume. However, heart rate increases due to **sympathetic** activity, and normal cardiac output is maintained.

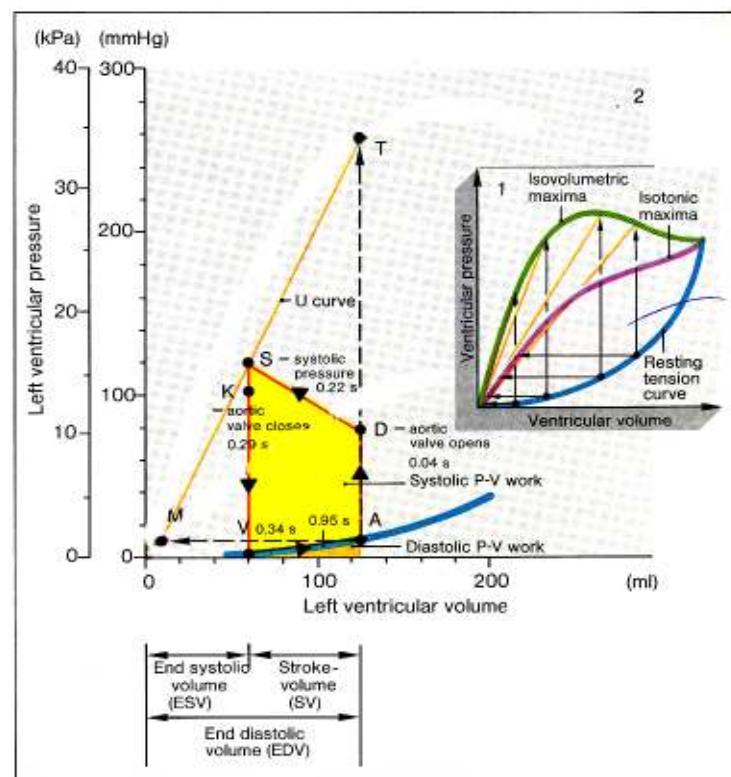
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<http://sorrel.humboldt.edu/~jlg21/Zoo%20310/Lab%2012%20ADAM%20cardiovasc/Cardiac%20Output/cardiac%20output%20home.htm>

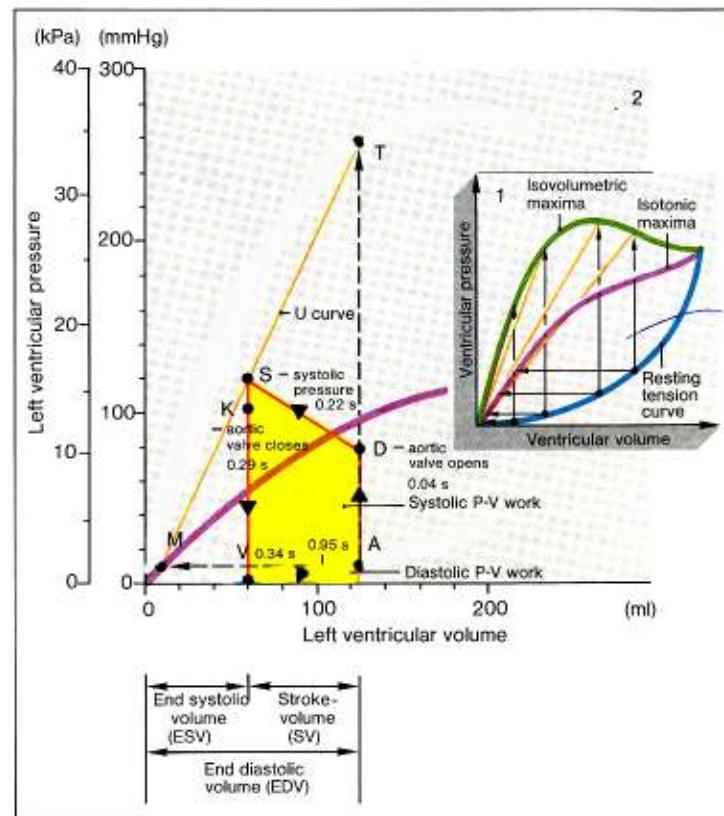


**Cardiac work diagram (left ventricle).**



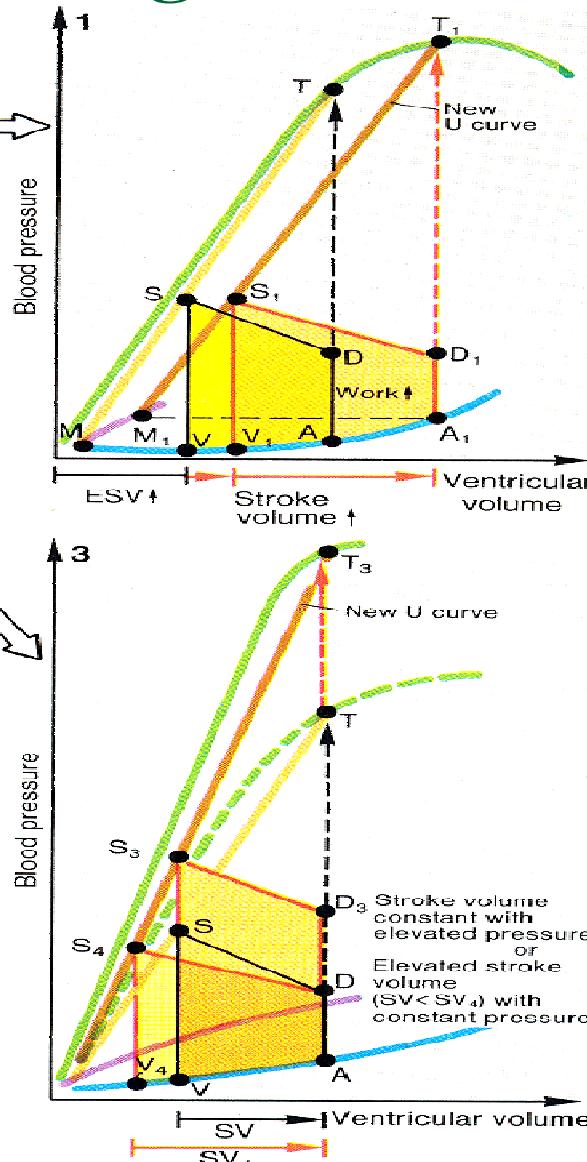
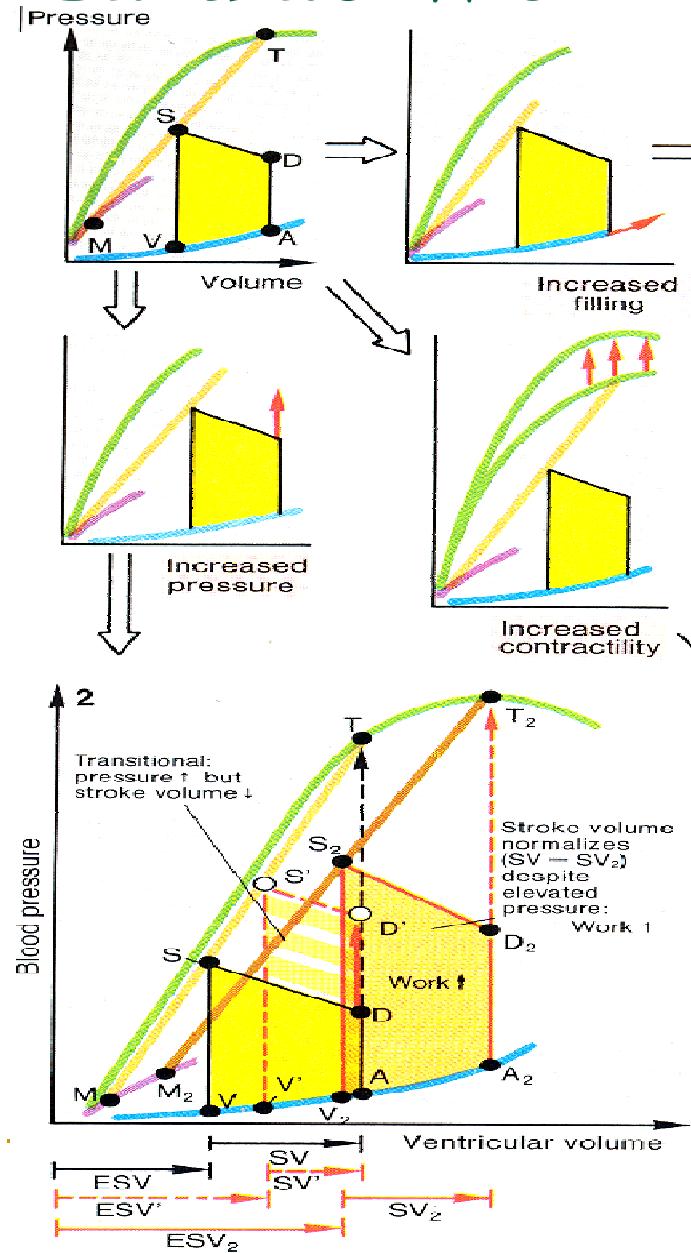


## Resting tension curve (left ventricle).



## Isotonic maxima (left ventricle).

# Cardiac Work Diagram



- (1) increased filling (preload),
- (2) increased pressure (afterload),
- (3) increased contractility.

# Blood Flow Energies

The total hydraulic energy gradient is the force of blood flow. It has three components:

- Pressure
  - Kinetics
  - Gravity
- Pressure Component: Pressure is an expression of energy

$$P = \frac{F}{A}$$

Where:

F = force being applied

A = area the force is being applied onto

- The pressure can be expressed in relation to energy as:

$$E_P = P \cdot Q_V$$

Where:

$E_P$  = pressure energy

P = pressure

$Q_V$  = blood volume

# Blood Flow Energies

- Kinetic Components: Kinetic energy of moving blood can be expressed as:

$$E_K = \frac{1}{2} \rho \cdot Q_V \cdot v^2$$

Where:

$E_K$  = kinetic energy  
 $\rho$  = density  
 $Q_V$  = volume  
 $v$  = velocity

- Gravitational Energy: The potential energy related to position relevant to a reference level can be expressed as:

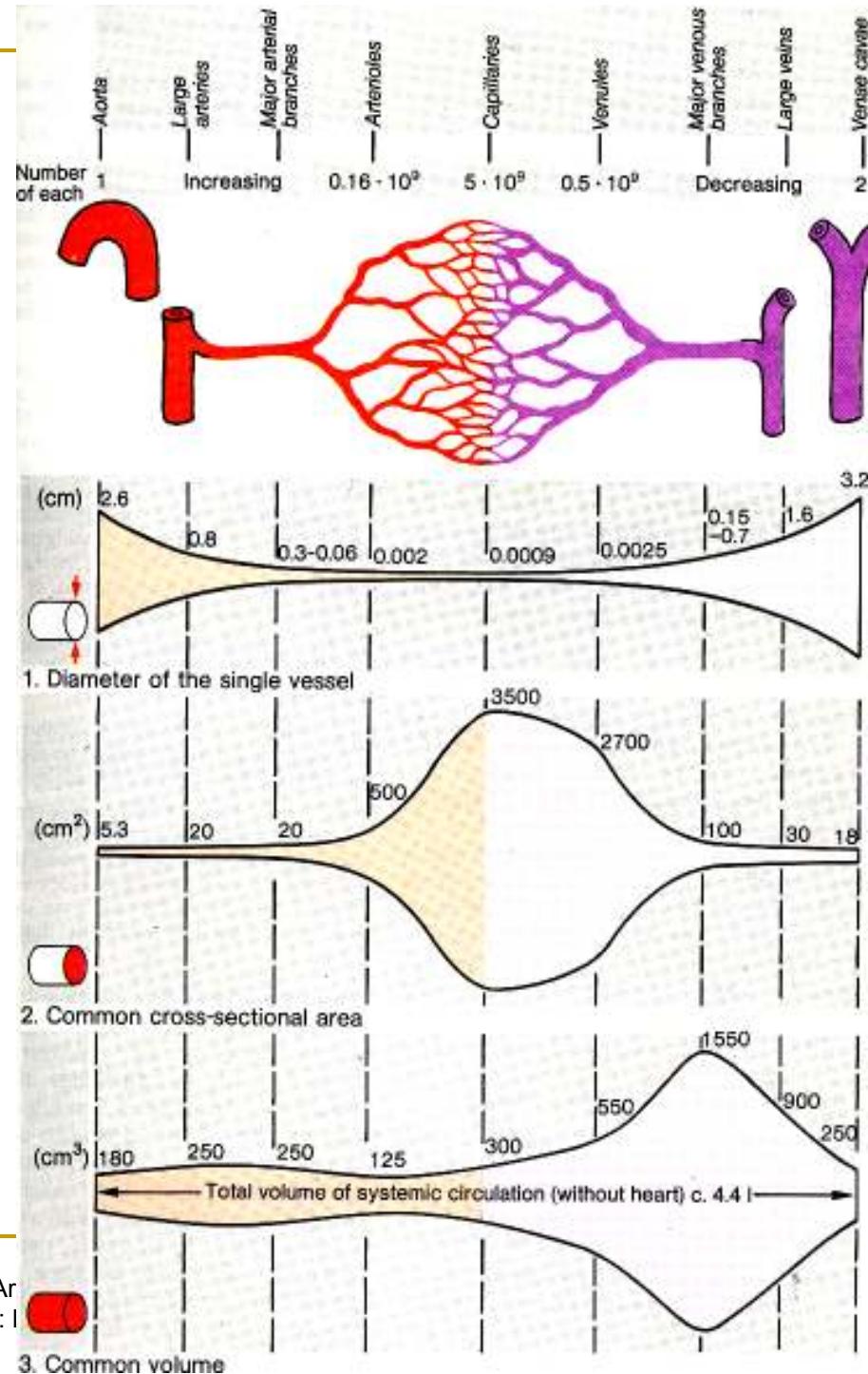
$$E_g = \rho \cdot g \cdot h \cdot Q_V$$

Where:

$E_g$  = potential (gravitational) energy  
 $\rho$  = blood density  
 $g$  = gravitational acceleration constant  
 $h$  = height  
 $Q_V$  = volume

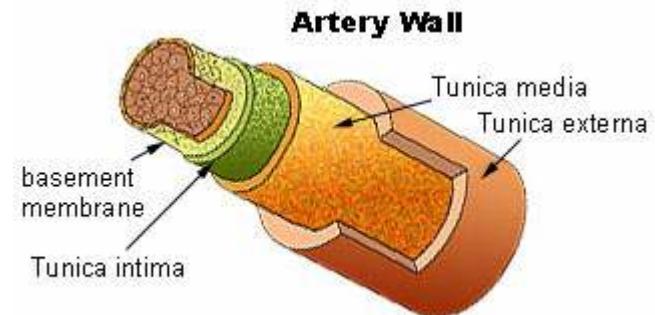
# The Vessels

- Arterial vessels are a network of tubes that carry blood.
- The arteries branch and become progressively smaller in diameter until the precapillary sphincter.
- The blood enters the aorta and then travels to the arteries, arteriole, precapillary sphincters, capillaries, postcapillary sphincters, venules, vein, vena cava, and then to the right atrium (Chamber1)



# Structure of Arteries

- Arteries have three coats (tunics) and a hollow core.
  - The inner core (tunica) is called tunica interna. It is composed of an endothelial lining, which is made up of simple epithelial cells. This layer is in contact with blood.
  - The middle coat, called tunica media, is usually the thickest layer. It consists of elastic fibres and smooth muscle.
  - The outer coat is called tunica externa, which consists mainly of elastic and collagenous fibres.
- All of these have two major properties, elasticity and contractility. When the heart contracts and ejects blood into the large arteries, the arteries expand to contain the extra blood. As the ventricle relaxes, the elastic recoils and forces the blood to move forward.
- The reason for this contractility is the smooth muscle in the middle coat of the wall structure.
- The smooth muscle is arranged longitudinally.

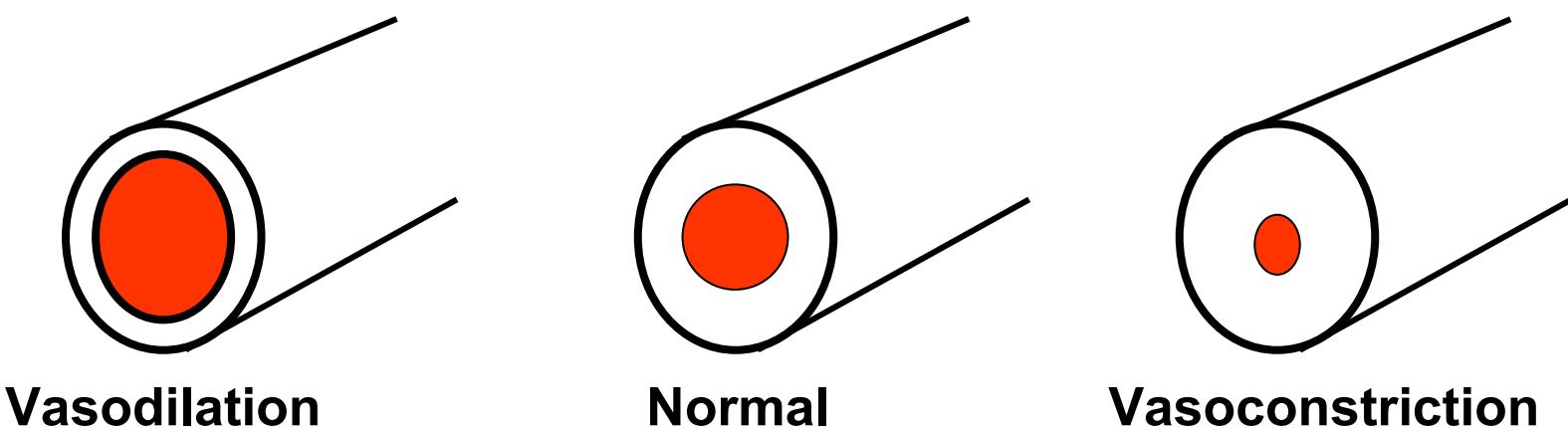


# Structure of Arteries

- o The muscles are innervated by nerve fibres.
- o When nerve fibres are stimulated, the smooth muscle contracts. This is why, when one is under emotional stress and other forms of stress, sympathetic nerves, which innervate the smooth muscle, will cause contraction of the arteries and this may cause higher resistance to blood flow or in other words, higher pressure.
- o This, in turn narrows the vessel.
- o Such a decrease in the size of the lumen is called vasoconstriction. When the sympathetic stimulation of the nerve is removed, the smooth muscle fibres relax and the size of the arterial lumen increases.
- o This, in turn dilates the vessel.
- o Such a decrease in the size of the lumen is called vasoconstriction. When the sympathetic stimulation of the nerve is removed, the smooth muscle fibres relax and the size of the arterial lumen increases dilation.

# Vasoconstriction/Vasodilation

- A decrease in the size of the lumen is called vasoconstriction.
- An increase is called vasodilation.
- The contractility and relaxation of arteries have two major roles:
  - They play a role in homeostasis, or feedback control. When an artery is cut, great quantities of blood can be quickly lost, however, due to the feedback system, its wall constricts so that blood does not escape quite so rapidly.
  - The other important result of artery contractility is a phenomenon called Windkessel (a German word meaning “air vessel”).



# Windkessel Phenomenon

The Windkessel effect is the term used in medicine to describe the recoiling effect of large arteries.

Consider this:

- The heart is the prime force for moving the blood. It is stimulated (contracts) periodically and pumps blood through the body.
  - In each cycle, the left and right ventricles are first filled with blood from the left and right atria.
  - During the diastolic phase of the cycle, due to a deceleration of the blood stream, a pressure force is generated which closes the valves between the atria and the ventricles (AV valves).
  - Then the contraction of the heart muscle begins and the pressure in the ventricles increases.
  - When this pressure exceeds that in the aorta and the pressure in the right ventricle exceeds that in the pulmonary artery, the aortic valve on the left and the pulmonary valve on the right are pushed open and blood is ejected into the aorta and the lungs. This is the systolic phase of the cardiac cycle.
  - The ejection continues until a deceleration of the jets of the blood creates a pressure field to close the valves.
  - Then the muscle relaxes, the pressure decreases and the diastolic phase of the cardiac cycle begins.

Now for an engineering question:

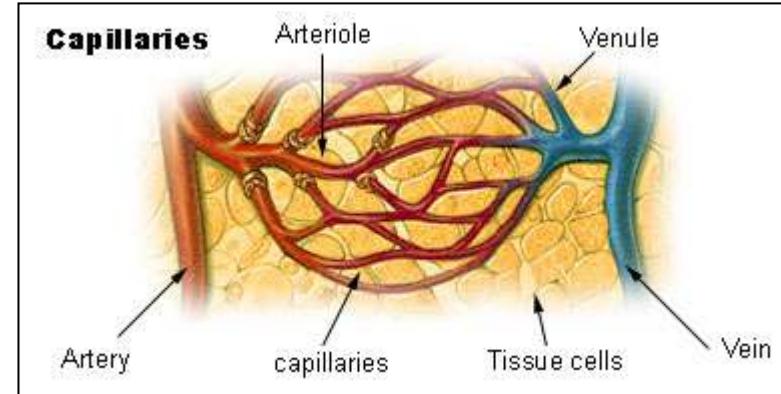
- During this contraction and relaxation, the blood pressure fluctuates in the heart from a low (of 0 to 4 mmHg compared to atmosphere) to a high of 120 mmHg, but in the aorta the pressure fluctuation is much less.
  - How does the aorta do this?
  - How does this large fluctuation of blood pressure in the heart convert to the pressure wave in the aorta with the same mean value but a smaller fluctuation?

# Arterioles

- Arterioles are small arteries that deliver blood to the capillaries.
- The blood enters capillaries after passing through the arterioles.
- Arterioles that are close to the arteries from which they branch have a tunica interna like that of arteries.
- The tunica media is composed of a smooth muscle and very few elastic fibres and the tunica externa is composed of mainly elastic and collagen fibres.
- As arterioles get smaller in size, the tunics change character so that arterioles close to the capillaries consist of little more than a layer of epithelium surrounded by a few scattered smooth muscle cells.
- The smooth muscle of arterioles, like that of arteries, is subject to vasoconstriction and vasodilation.
- During vasoconstriction, blood flow into the capillaries is restricted. During vasodilation, the flow is significantly increased.
- Thus, arterioles play a key role in regulating blood flow.

# Capillaries

- Capillaries are microscopic vessels that usually connect arterioles and venules.
- They are found near almost every cell in the body, especially where there is a lot of activity, such as muscles, liver, kidneys, lungs and nervous system.
- If the area has lower activity, such as tendons and ligaments, the capillary supply is not extensive.
- Some parts of the body do not have capillaries. Examples are the cornea of the eye, epidermis and cartilage.
- The epidermis is the outermost non-vascular layer of the skin.



# Venules

- When several capillaries join, they form a small vein called a venule.
- Venules collect blood from capillaries and then drain into veins.
- The venules closest to the capillaries consist of a tunica interna of endothelium and tunica externa of connective tissue.
- The venules approaching the veins also contain the tunica media.

# Veins

- Veins are composed of the same three coats as arteries, but they have considerably less elastic tissue and smooth muscle and they contain more white fibrous tissue.
- However, they are still distensible enough to adapt to variations in the volume and pressure of blood passing through them.
- By the time blood leaves the capillaries and moves into the veins, it has lost a great deal of pressure.
- The difference in pressure can be observed in blood flow from a cut vessel.
- Blood leaves a cut vein in an even flow rather than in a rapid jet, which is a characteristic of an artery.
- Most of the structural differences between arteries and veins reflect these pressure differences.
- For example, veins do not need walls as strong as those of arteries. The low pressure in veins, however, has its disadvantages.
- When one stands, the pressure pushing blood up the veins in the lower extremities is barely enough to balance the force of gravity pulling it back down. For this reason, many veins, especially those in the limbs, contain valves to prevent back flow.
- Normal valves ensure the flow of blood throughout the body.



# Varicose Veins

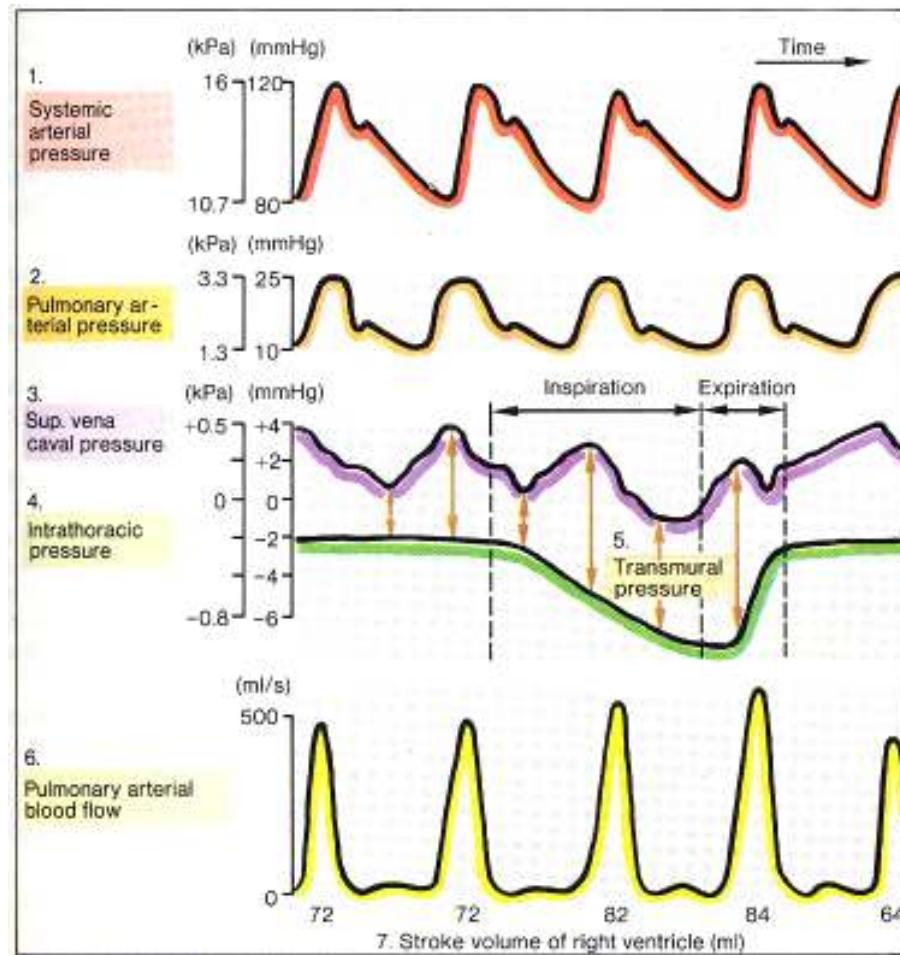
## Clinical Example:

- ❖ In people with bad valves in the veins, large quantities of blood are forced by gravity back down into distal parts of the vein.
- ❖ This pressure overloads the vein and pushes the wall outward. After repeated overloading, the walls lose their elasticity and become stretched and flabby. A vein damaged this way is called a varicose vein.
- ❖ Varicose veins may be caused by prolonged standing or pregnancy. Because this type of vein is not able to exert a firm resistance against the blood, blood tends to accumulate in these veins causing them to swell and forcing fluid into the surrounding tissue.
- ❖ Veins close to the surface of the legs are highly susceptible to varicosities. Veins that lie deeper are not as vulnerable because surrounding skeletal muscles prevent their walls from over stretching.
- ❖ Hemorrhoids are also a form of varicose veins.

# Physiology of Circulation

- Blood flows through the cardiovascular system of closed vessels because of pressure differences in the various parts of the system. It always flows from regions of higher pressure to regions of lower pressure.
- The mean (or average) pressure in the aorta is about 100 mmHg in a normal person.
- This pressure continually decreases rapidly through the arterial system and more slowly through the venous system. Because of the continuous drop in pressure, blood flows from the aorta (about 100 mmHg), to the arteries (about 40 to 100 mmHg), then to venules (8 to 12 mmHg), then to veins (5 to 10 mmHg), then to the vena cava (2 mmHg).
- The pressure in the right atrium is about 0 mmHg.
- When blood leaves the capillaries, it enters the venules and veins, which are large in diameter, thus offering less resistance to flow.
- Contraction of a skeletal muscle around the veins also helps drive blood toward the heart

# Effects of Respiration



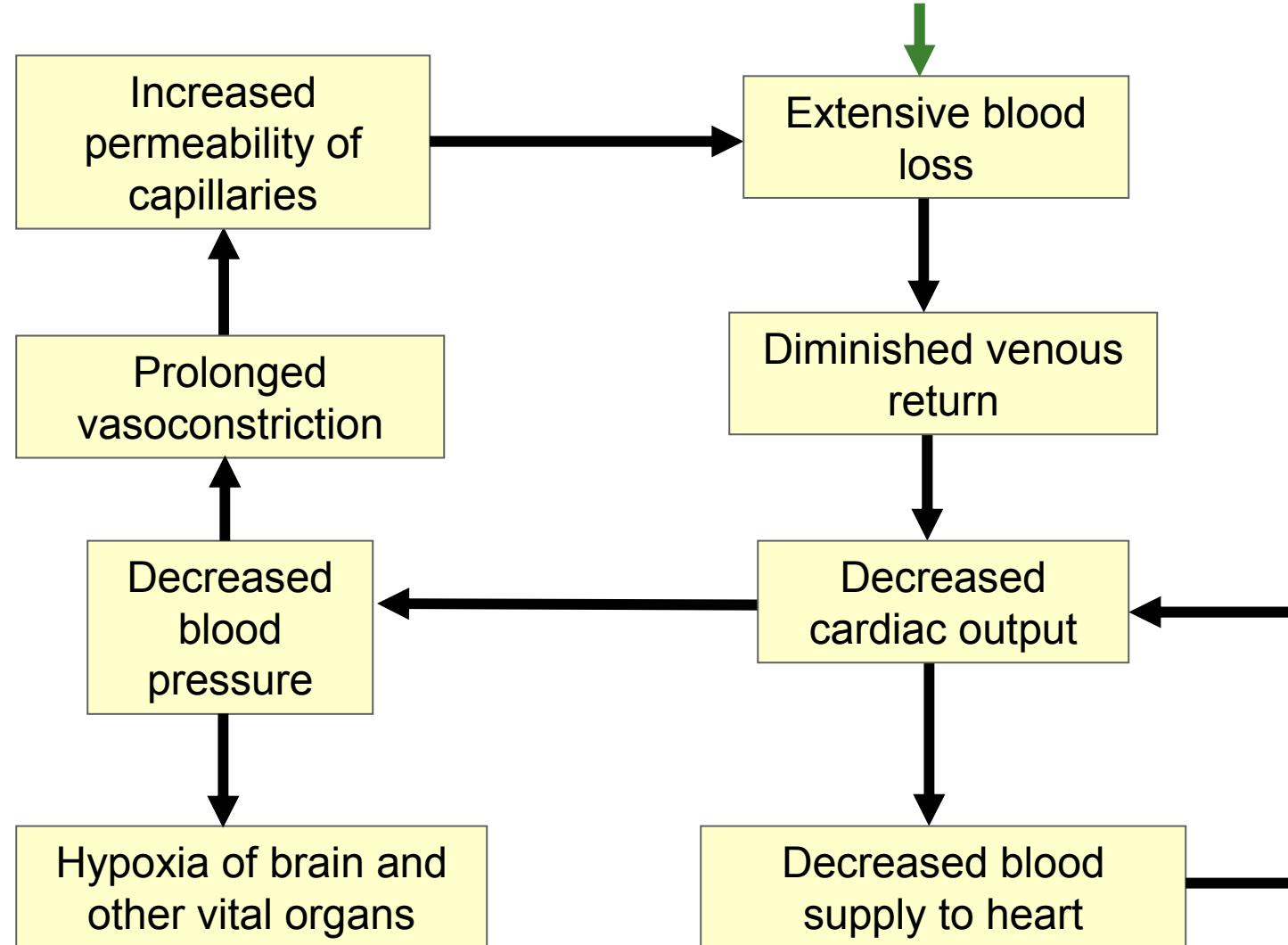
**Effect of respiration  
on pulmonary circulation  
and venous pressure.**

# Factors that Effect Arteriole Blood Pressure

The following factors influence arteriole blood pressure:

- **Cardiac Output (CO):** Cardiac output is the amount of blood ejected by the left ventricle into the aorta each minute. It is the main determinant of blood pressure. Cardiac output is calculated by multiplying stroke volume by the heart rate. In the normal resting adult, it is about 5 l/min (70 ml x 75 beats per minute). Blood pressure varies directly with cardiac output. If the cardiac output is increased by any increase in stroke volume or heart rate, then blood pressure increases. A decrease in cardiac output also causes a decrease in blood pressure.
- **Blood Volume:** Blood pressure is directly proportional to the volume of blood in the cardiovascular system. The normal volume of blood in the human body is about 5l. Any decrease in this volume causes a drop in blood pressure. Any cause that increases blood volume, such as salt intake causing water retention, also increases blood pressure.
- **Peripheral Resistance:** Peripheral resistance refers to impedance to blood flow or resistance to blood flow by the force of friction between blood and the walls of the blood vessel. It is related to the viscosity of blood and blood vessel diameter. The viscosity of blood is the function of the ratio of RBCs and solutes to fluid. Any condition that increases the viscosity of blood, such as dehydration or an unusually high number of RBCs increases blood pressure. A depletion of plasma protein or RBCs, as a result of anemia or hemorrhage, decreases blood viscosity and blood pressure. The smaller the diameter of the vessel, the more resistance it offers to the blood. A major function of arterioles is to control peripheral resistance and, therefore, blood pressure by changing the diameter. The centre for control of circulation is the Vasomotor Centre in the brainstem. Factors that determine heart rate and the force of contraction and, therefore, blood pressure are the autonomic nervous system through the cardiac center, chemicals, temperature, emotion, sex and age.

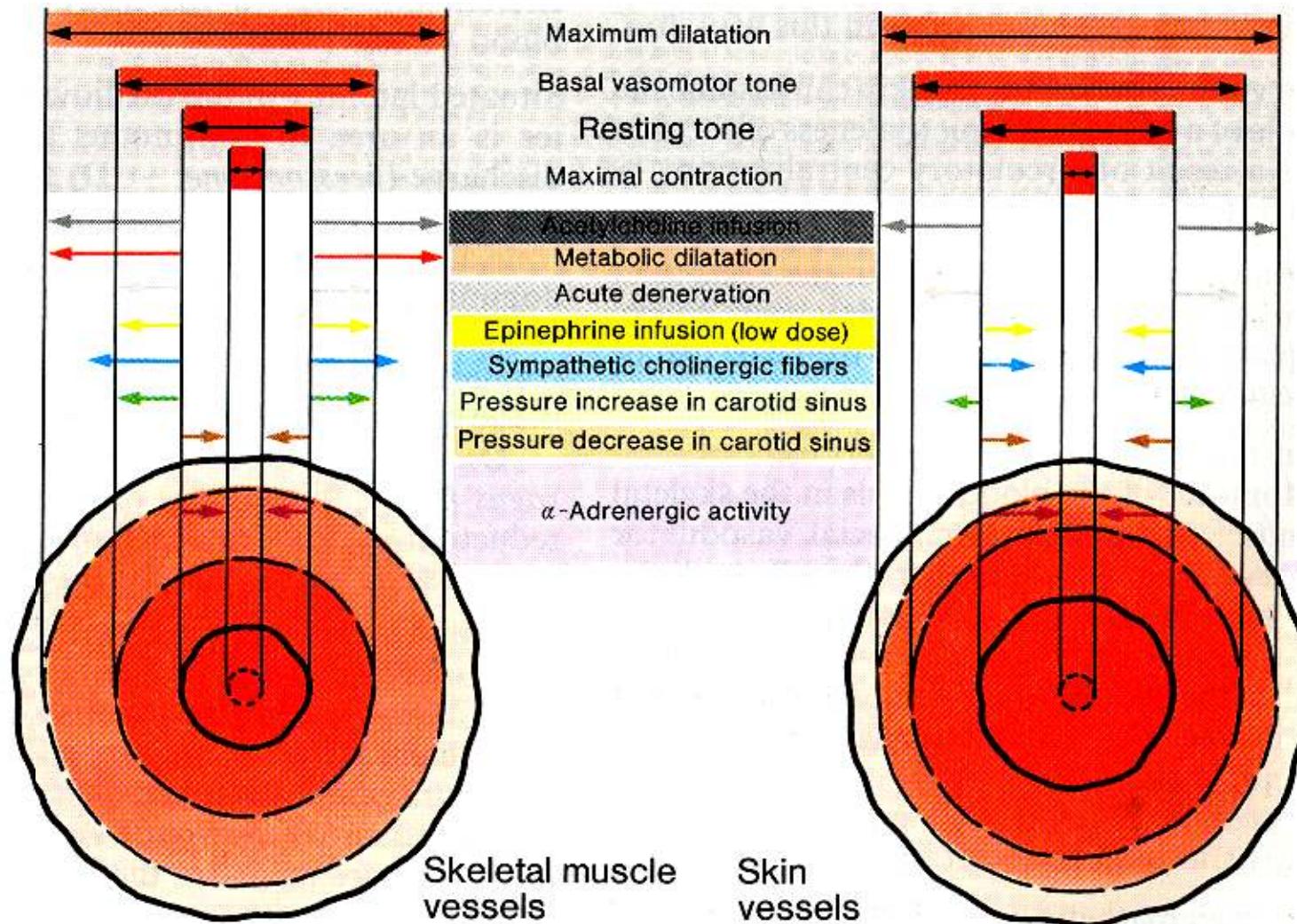
# Pressure Feedback System



# Vasomotor Centre

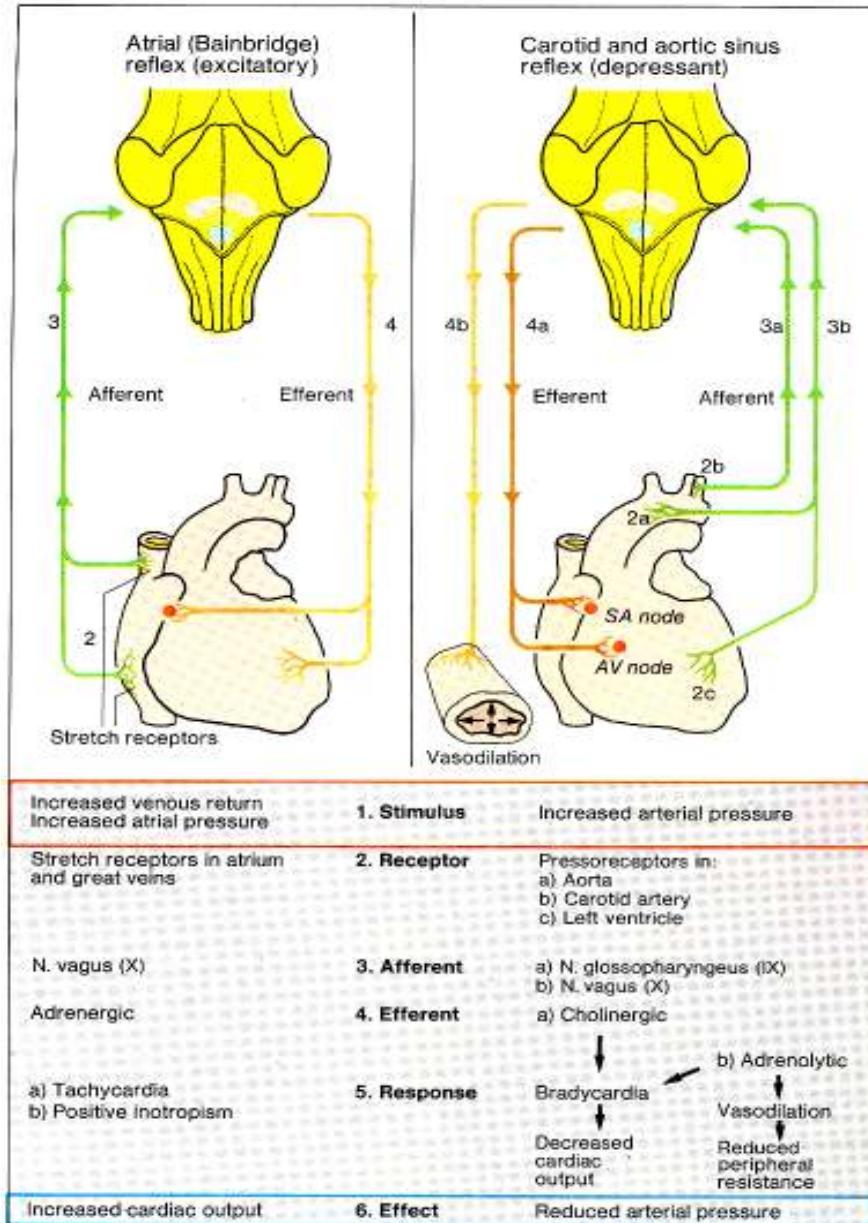
- Within the medulla of the brain there is a cluster of neurons (nerve cells) and this is called the Vasomotor Centre.
- The function of this centre is to control the diameter of blood vessels, especially arterioles.
- It continually sends impulses to the smooth muscle in the arteriole walls that result in a moderate state of vasoconstriction at all times.
- If the number of impulses is increased, the vessels constrict. By decreasing the number of impulses, vasodilation results.

# Vasomotor Influences



# Pressoreceptors

- Pressoreceptors in the carotid sinus and aorta send impulses to the cardiac centre in the brain.
- This signal results in an increase or decrease of cardiac output to help regulate blood pressure.
- The pressoreceptors also send impulses to the vasomotor centre.
- In response, the vasomotor centre decreases or increases impulses sent to the blood vessels.
- Pressoreceptors are sensors of pressure.

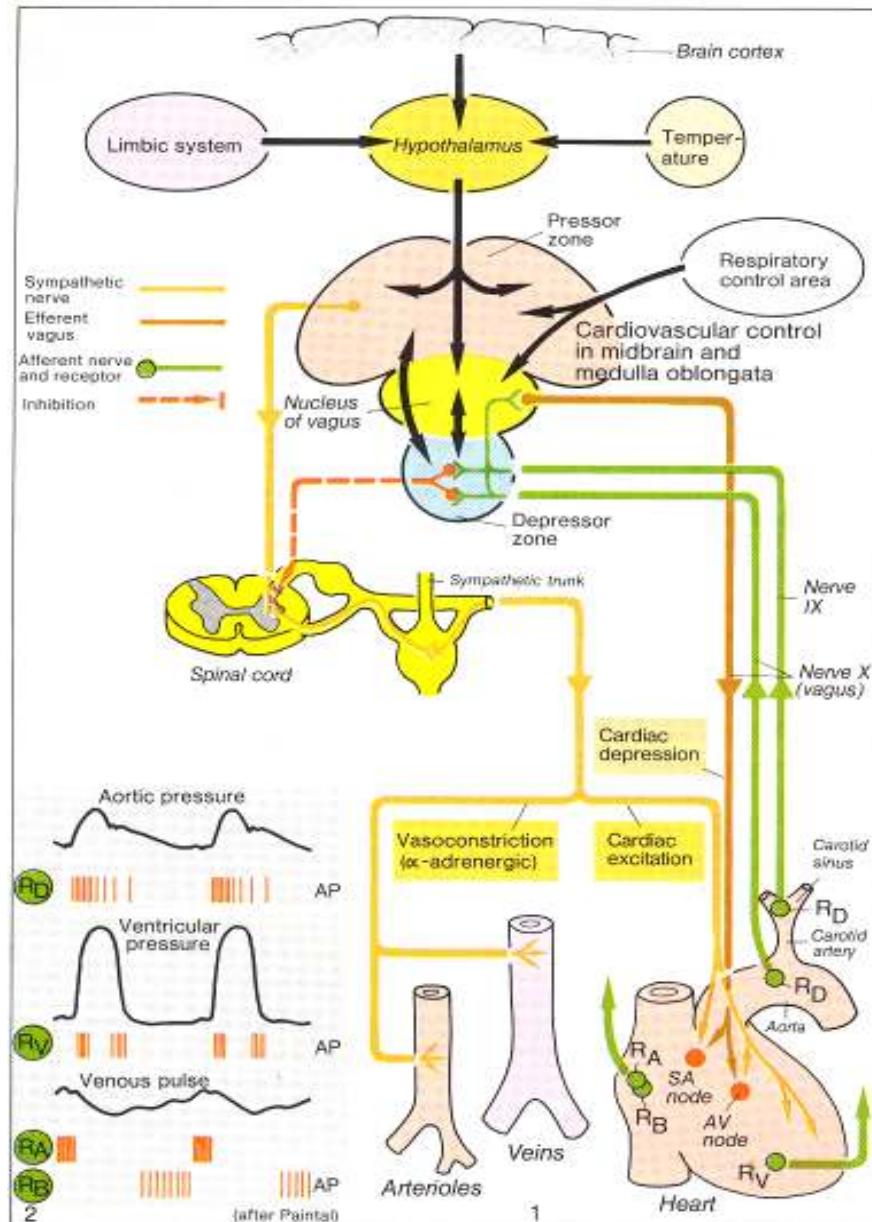


# Chemoreceptors

- These are receptors sensitive to chemicals in the blood.
- Chemoreceptors in the carotid sinus and aorta are called the carotid and aortic bodies.
- They are sensitive to arterial blood, levels of oxygen, carbon dioxide and hydrogen ions.
- Chemoreceptors are stimulated when the oxygen is low (hypoxia), by a decrease in hydrogen ion concentration in the blood or, by an excess of carbon dioxide (hypercapnia).
- The chemoreceptors (when stimulated) send impulses to vasomotor sensors in the brain.
- In response, the vasomotor centre increases sympathetic stimulation to the arterioles.
- This brings about vasoconstriction and an increase in blood pressure.

# Control by Higher Brain Centres

- In response to strong emotions, higher brain centres such as the cerebral cortex can have a significant influence on blood pressure.
- For example, during periods of intense anger, the cerebral cortex stimulates the vasomotor centre to fire sympathetic impulses to arterioles.
- This causes vasoconstriction and an increase in blood pressure.
- When a person is emotionally resting, relax impulses from higher brain centres cause a decrease in sympathetic stimulation via the vasomotor centre.
- This produces vasodilation and a consequent decrease in blood pressure.
- A frequent result is fainting because blood flow to the brain is diminished.



# Chemicals

- Several chemicals affect blood pressure by causing vasoconstriction.
- Epinephrine and norepinephrine, produced by the adrenal glands, increase heart rate and force the heart into contraction and bring about vasoconstriction of the abdominal and subcutaneous arterioles.

**Relationship Between Blood Velocity and Cross Sectional Area**

Vessel	Cross Sectional Area (cm <sup>2</sup> )	Velocity (cm/sec)
Aorta	2.5	40
Arteries	20	10-40
Arterioles	40	0.1
Capillaries	2,500	< 0.1
Venules	250	0.3
Veins	80	0.3-5.0
Vena Cava	8	5-20

- They also bring about dilation of cardiac and skeletal arterioles.
- Antidiuretic hormones produced by the hypothalamus and released from the brain cause vasoconstriction if there is a severe loss of blood due to hemorrhage.
- Angiotensins also help to raise blood pressure by stimulating secretion of aldosterone, which causes increased sodium/on concentration and water reabsorption.
- This causes vasoconstriction due to release of renin.
- These are produced by mast cells and renin found in plasma.
- They are vasodilators and assume key functions during an inflammatory response.

# Autoregulation

- Autoregulation refers to a local automatic adjustment of blood flow in a given region of the body in response to the particular needs of that tissue.
- In most body tissue, oxygen is the principle stimulus for autoregulation.
- In response to low oxygen supplies, the cells in the immediate area produce and release vasodilator substances.
- Such substances are thought to include potassium ions, hydrogen ions, carbon dioxide, lactic acid and adenosine.
- Once released, the vasodilator substance produces a local dilation of arterioles and relaxation of precapillary sphincters.
- The result is an increased flow of blood into the tissue, which restores oxygen levels to normal.
- The autoregulation mechanism is important in meeting the nutritional demand of active tissue, such as muscle tissues, where demand might suddenly increase as much as ten fold.

# Increased Workload on the Heart

- **High blood pressure** and **blood cholesterol** causes narrowing of the vessels and increased resistance to flow, and thus increases the workload:

$$R = \frac{8 \cdot \eta \cdot L}{\pi \cdot r^4}$$

Where: R = flow resistance

L = Length of tube

r = radius of vessel

and  $\eta$  = viscosity of blood, which depends on:

- hematocrit = % of RBC
- velocity of blood flow

- **Cigarette smoking** causes nicotine to stimulate the adrenal gland to over secrete:

- Aldosterone
- Epinephrine
- Norepinephrine

These are all powerful vasoconstrictors, thus increasing the load through restriction of vessels.

- **Obesity causes** extra miles of capillaries to develop to nourish the fat tissue.  
These cause extra resistance, thus overloading the heart.

# Increased Workload on the Heart

- **Lack of Exercise** (couch potatoes): Venous return does not get help from contraction of skeletal muscle.
- **Exercise:**
  - Strengthens the smooth muscle of the blood vessel, thus assisting in circulation.
  - Heart output will increase under exercise.
- **Diabetes mellitus:** Fat metabolism dominates glucose metabolism. This results in increased cholesterol level and plaque formation, causing high blood pressure.
  - **High blood pressure** worsens this by driving fat into the vessel walls.

# Heart Disease

## Heart Muscle Disease

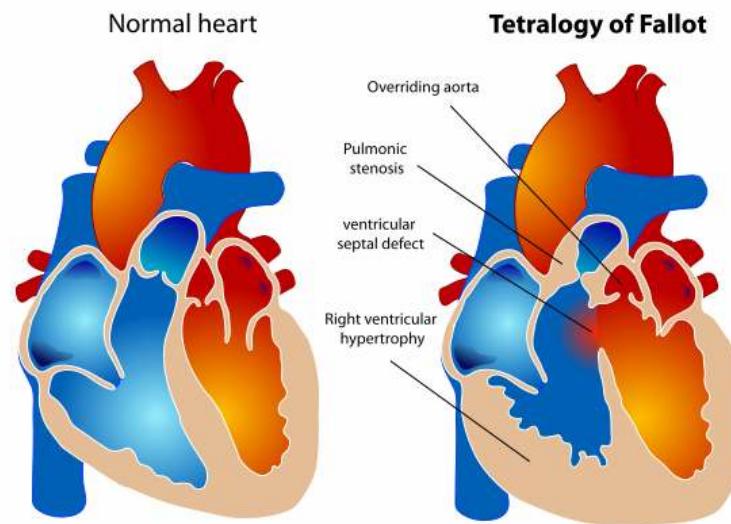
- Is due to inadequate **coronary blood supply**. An insufficient oxygen supply to the myocardium causes:
  - Thrombosis, thus embolus, in a coronary artery
  - Built up fatty deposits in arterial walls

## Congestive Heart Failure

- Is when the heart is not capable of **supplying oxygen to and from the body**.
- The symptoms are:
  - Diminished blood flow to various tissues of the body.
  - Accumulation of blood in various organs because the heart is unable to pump out the blood.
- Potential Treatment:
  - Digitalis: Strengthens the contraction of the heart muscle.
  - Diuretics: Reduces flow (water).
  - Dietary (salt restriction): Reduces flow (water uptake).

# Anatomical Disorders

- **Congenital (inborn) heart defects:**  
Some babies born with these defects may live a healthy life. These include:
  - **Septal Defect:** An opening in the septum that separates the interior of the heart into the left and right side.
  - **Intra-Ventricular Septal Defect**
  - **Valvular Stenosis:** Narrowing and calcification of one of the valves regulating blood flow of the heart.
  - **Tetralogy of Fallot** is a combination of four defects; intra-ventricular septal opening, aorta that emerges from both ventricles, stenosis of the pulmonary valve and an enlarged right ventricle.



# Anatomical Disorders

## ➤ Fault Conductive (**Arrhythmias**):

- At least half of the deaths from myocardial infarction occur before the patient reaches the hospital.
- These early deaths are caused by irregular heart rhythm (arrhythmia).
- Arrhythmia caused by disturbance in the conduction system.
- Arrhythmia can cause cardiac arrest due to lack of oxygen to the heart muscle.
- Serious arrhythmias can be controlled and heart rhythm re-established if detected early on.
- Arrhythmias arise when electrical impulses are blocked at critical points.

# Cardiac Catheterization

- The tip of a long, plastic catheter or tube is introduced into a vein in the arm or leg.
- The catheter is radio-opaque so that it can be seen with a fluoroscope.
- With the help of the fluoroscope, the catheter is threaded through the vena cava and into the right atrium, right ventricle or pulmonary trunk.
- The catheter can be inserted into an artery of the leg or arm and worked up to the aorta, to the left atrium or ventricle.



Coronary Angiogram

# Gloomy Facts

- Some statistics:
  - 44,000-50,000 Canadians die each year due to heart disease.
  - Over 500,000 Americans die every year from heart disease.
  - Over 5 million people worldwide die annually due to heart disease.
  - One in every four people between the ages of 30 and 60 has the potential of dying from heart disease.
- Risk factors in heart disease:
  - High blood cholesterol level
  - High blood pressure
  - Cigarette smoking
  - Obesity
  - Lack of exercise
  - Diabetes mellitus
  - Genetic predisposition
- All, but the last two risk factors place an increased workload on the heart.

# HeartSaver Ventricular Assist Device

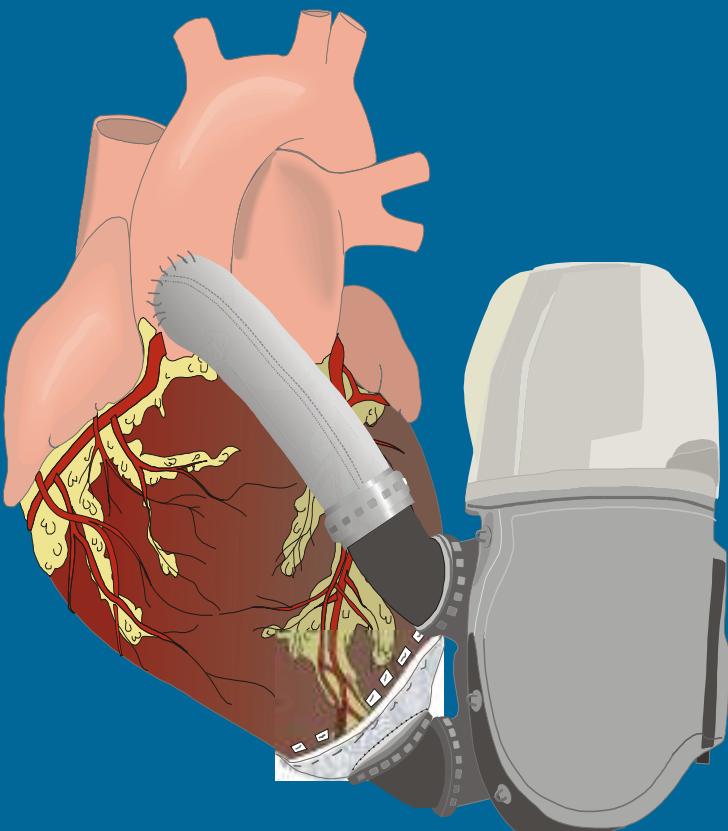


# HeartSaver VAD Development Goals

---

- **Pulsatile Ventricular Assist Device:**
  - ▶ **Implantable in Thoracic Cavity**
  - ▶ **No Percutaneous Connections**
  - ▶ **Remotely Monitored/Controlled**
  - ▶ **Capable of out of Hospital Use**
  - ▶ **Long Term Support Capability**
  - ▶ **Minimal Limitations for Patients**

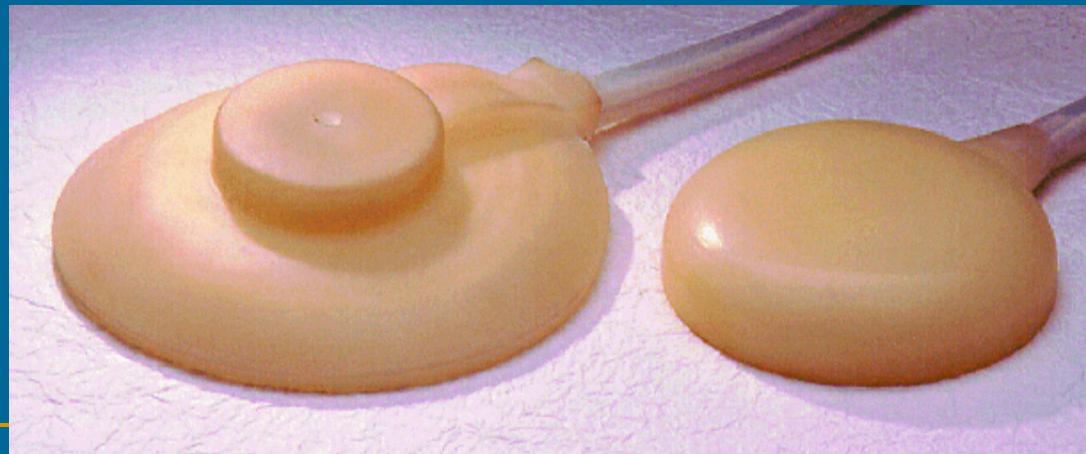
# Blood Pump



- ▶ **Intrathoracic Location**
- ▶ **Electro-hydraulic Actuation**
- ▶ **No Percutaneous Connections**
- ▶ **Titanium Housing**
- ▶ **Biolized Blood Surfaces**
- ▶ **Bioprosthetic Valves (porcine)**
- ▶ **Operating Modes:**
  - ▶ **Full Fill - Full Eject**
  - ▶ **Fixed Rate**
  - ▶ **Single Beat (de-airing)**

# Energy & Information Transmission

- ▶ **Hybrid System:**
  - ▶ Transcutaneous Energy Transfer (RF)
  - ▶ Transcutaneous Information Transfer (IR)
- ▶ **Coil Alignment Monitored by Controller**
- ▶ **Immunity to nearby Metals**
- ▶ **Multiple Redundancy for Information Transfer**



# Power Sources

## Internal Battery



## External Battery



- ▶ **Lithium Ion Technology**
- ▶ **Implantable Internal Battery**
- ▶ **Wearable External Battery**
- ▶ **Fully Monitored Charge/Discharge**

# Remote Patient Monitor



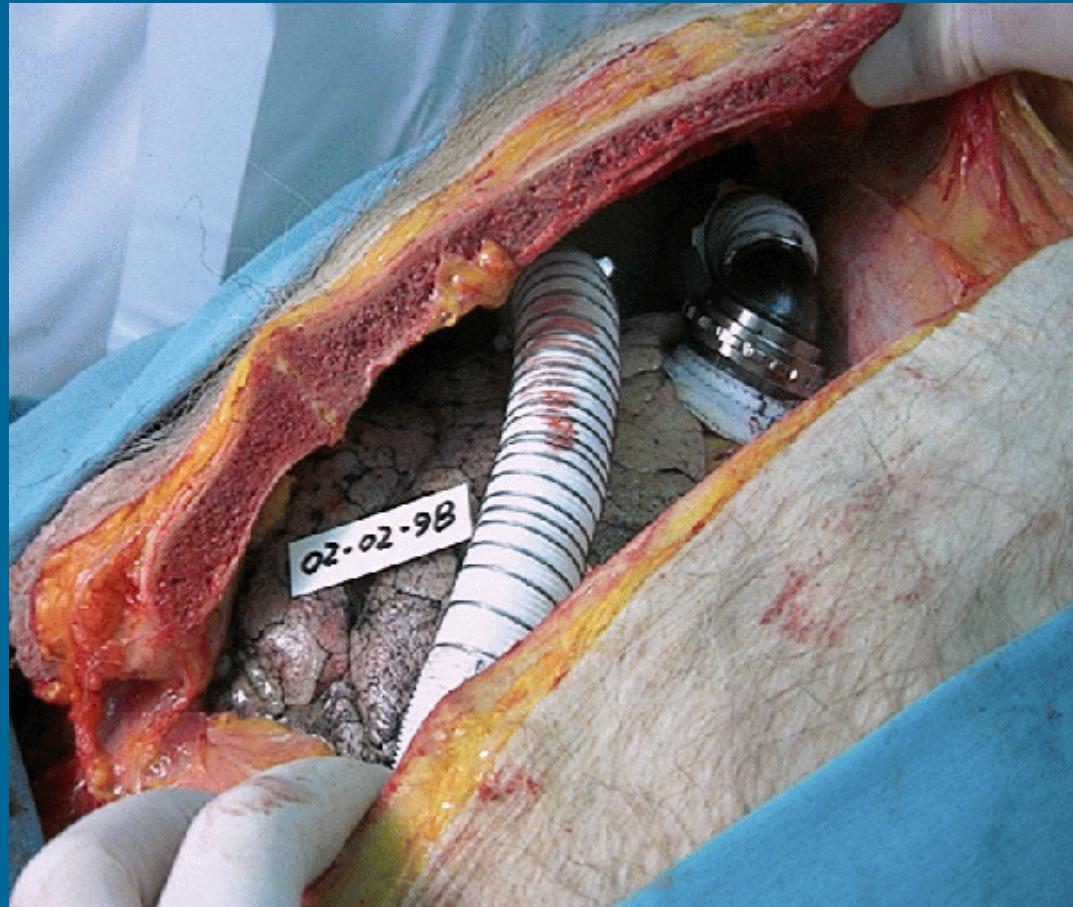
- ▶ **Wearable**
- ▶ **Visual & Audible Alarms**
  - ▶ LEDs
  - ▶ Text Messages
  - ▶ Buzzer
  - ▶ Vibrator
- ▶ **Wireless Communication with Clinical User Interface**

# Clinical User Interface



- ▶ Touchscreen Operated
- ▶ Wireless Communication (RF)
- ▶ Remote Monitoring Capability
- ▶ Online Monitoring of Device Filling & Ejection
- ▶ Separate Control, Monitoring & Clinical Engineering Screens

# Cadaver Fit Trial



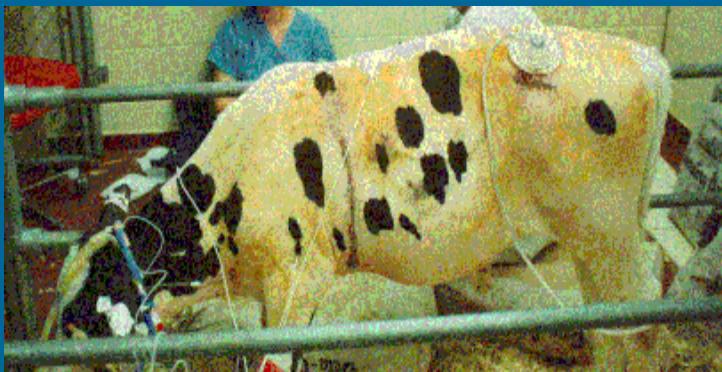
**70 Kg Male - Photo Courtesy of the Cleveland Clinic**

# In Vivo Studies

Series	Cases	Durations
1	12	up to 1 week
2	13	up to 1 month
3	18	acute

**Over 1,360 hours in vivo accumulated**

# In Vivo Study Milestones



**“Willy”**  
**1 month elective explant.**  
**Demonstrated ability of**  
**device to support**  
**dysfunctional heart.**

**“Norman”**  
**1 week elective explant.**  
**Demonstrated feasibility**  
**of totally implantable**  
**system.**

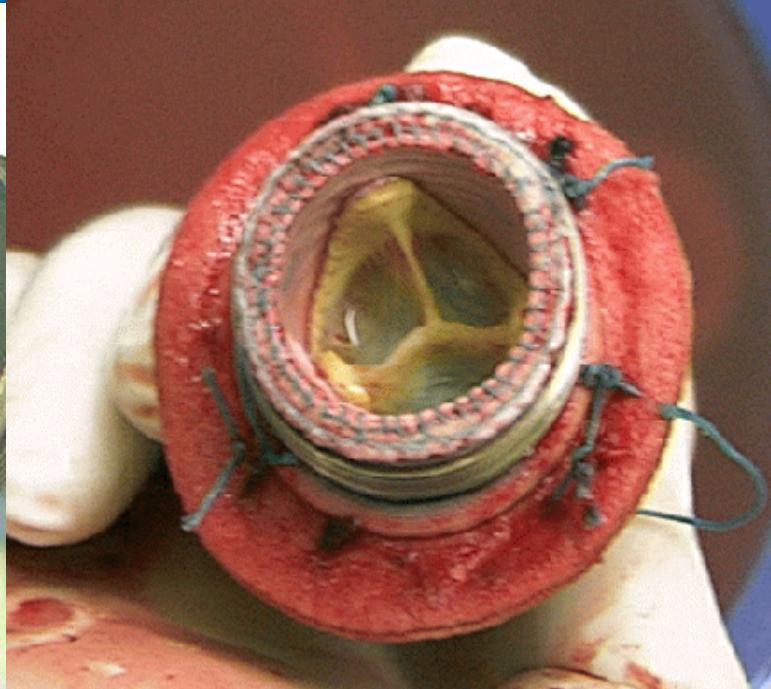


# Valves & Conduits at Explant

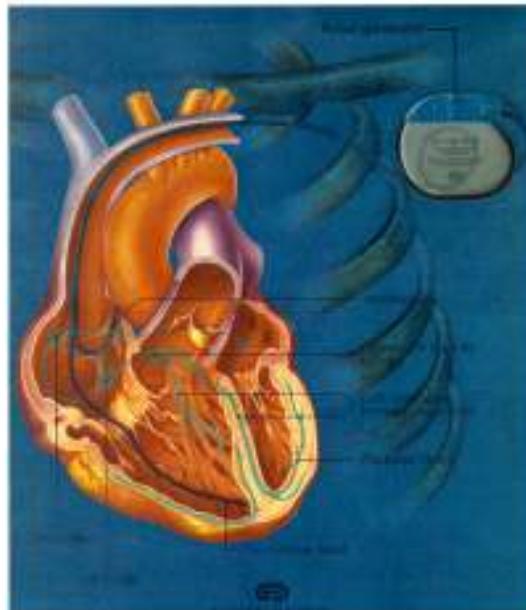
Inflow Conduit



Apical Tip Valve

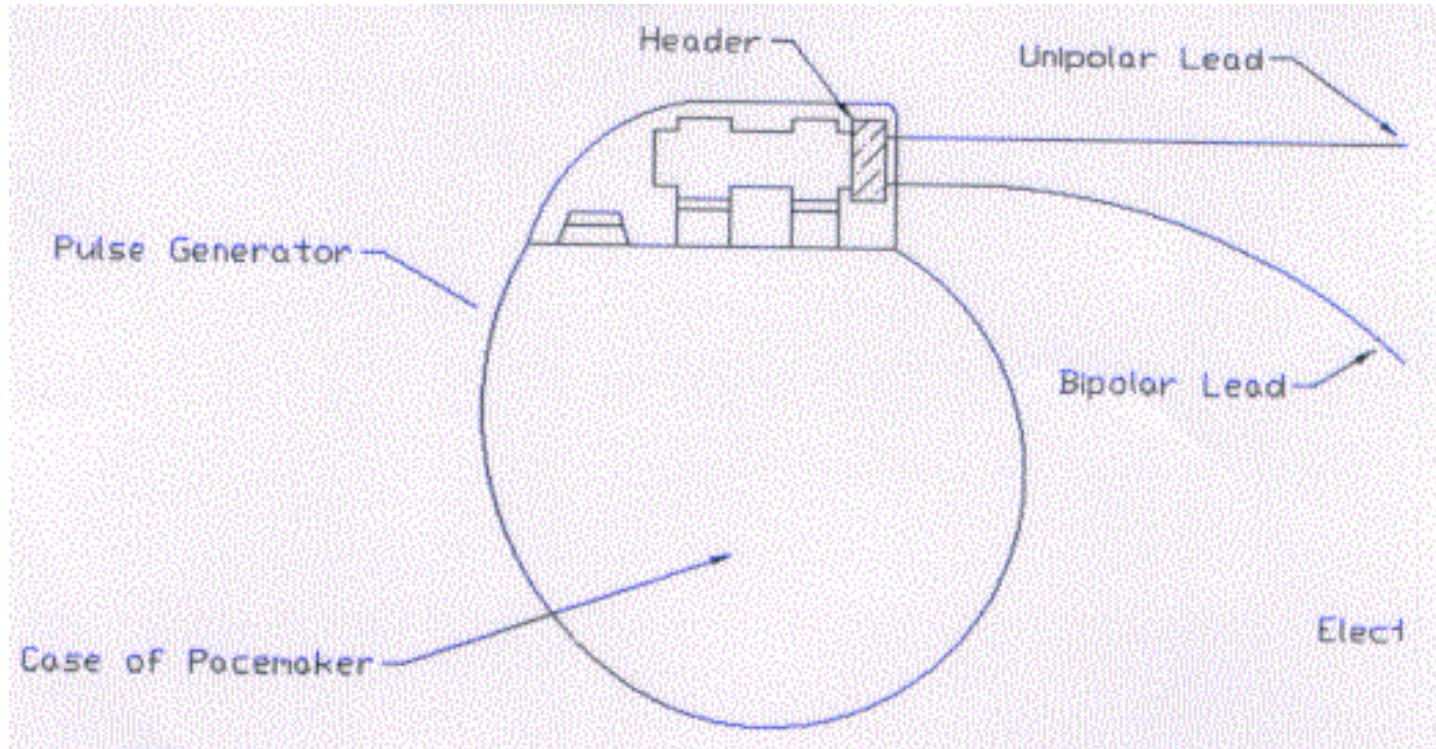


# Pacemaker



# Pacemaker

## Schematic Structure

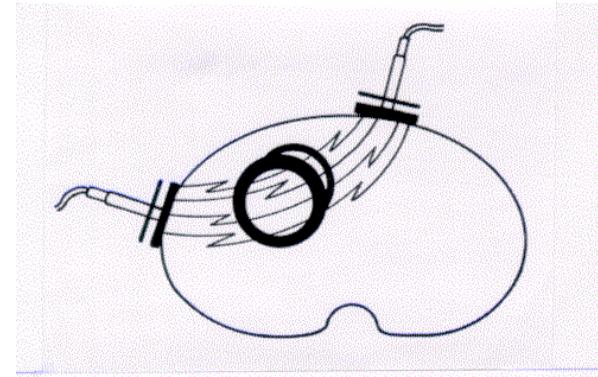
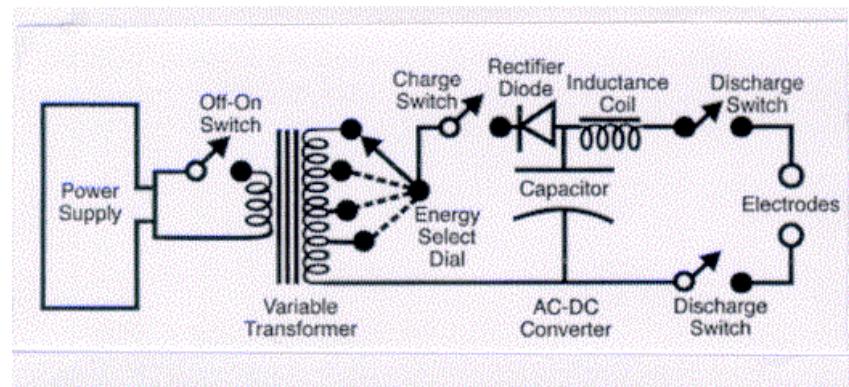


# Defibrillator

External Defibrillator

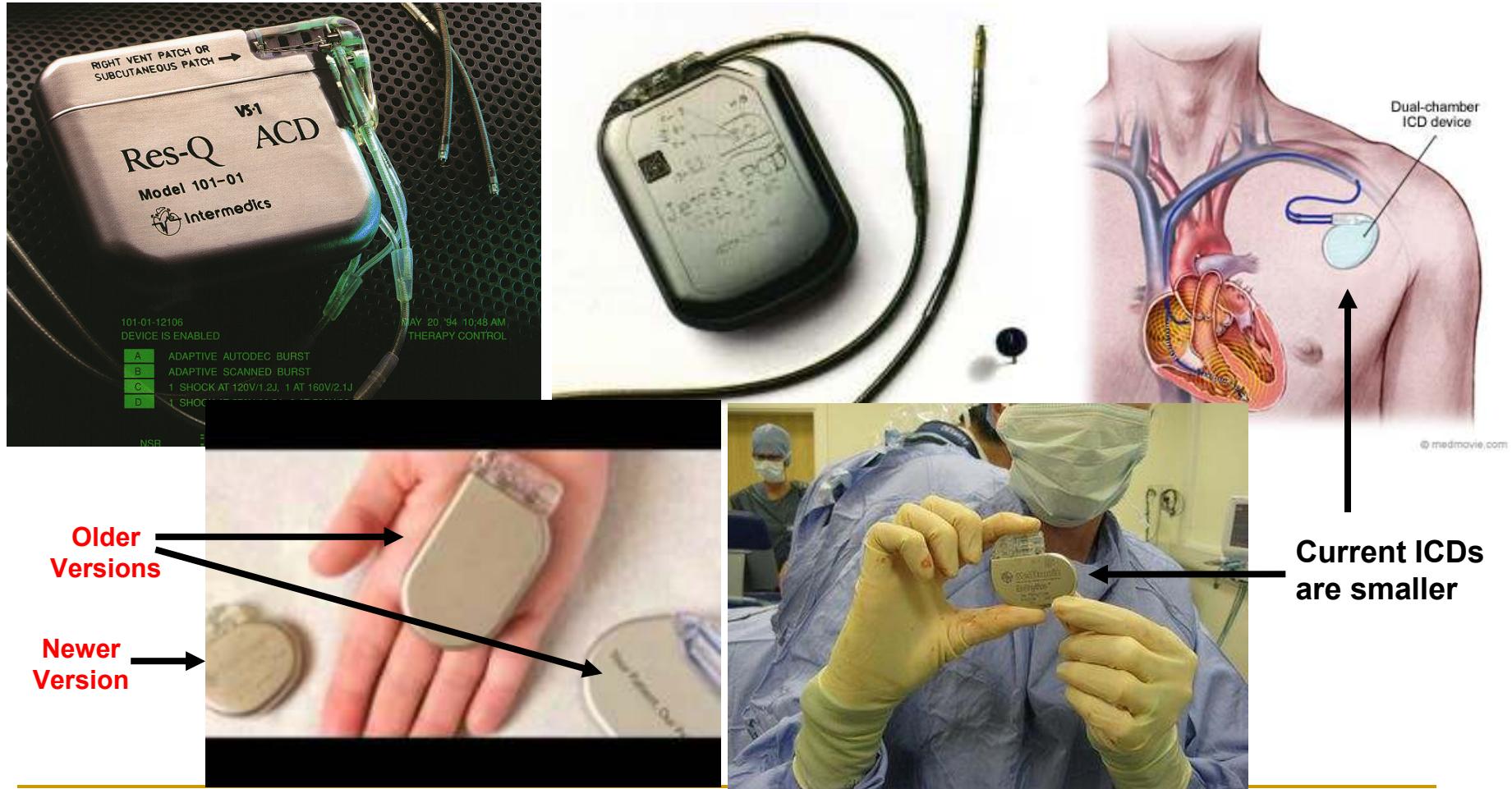


Schematic Structure

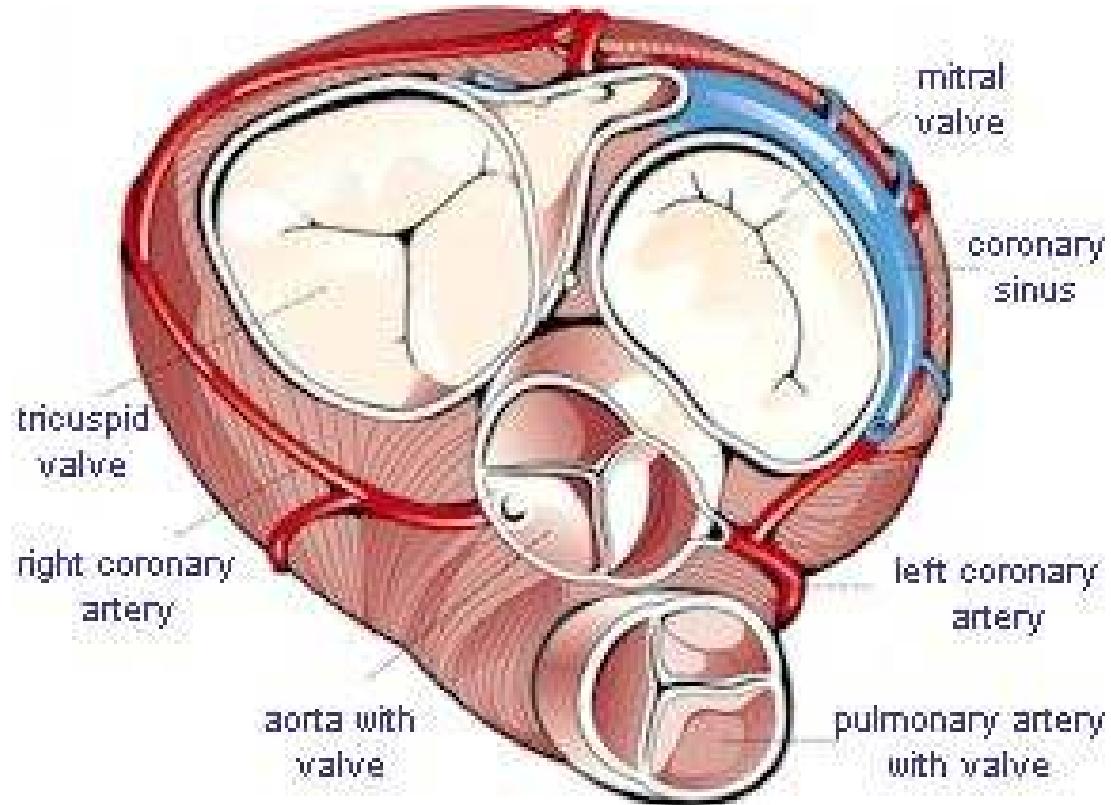


# Defibrillator

## Internal Cardiac



# Anatomy of Heart Valves



# Prosthetic Valves

Starr-Edwards



Magovern-Cromie



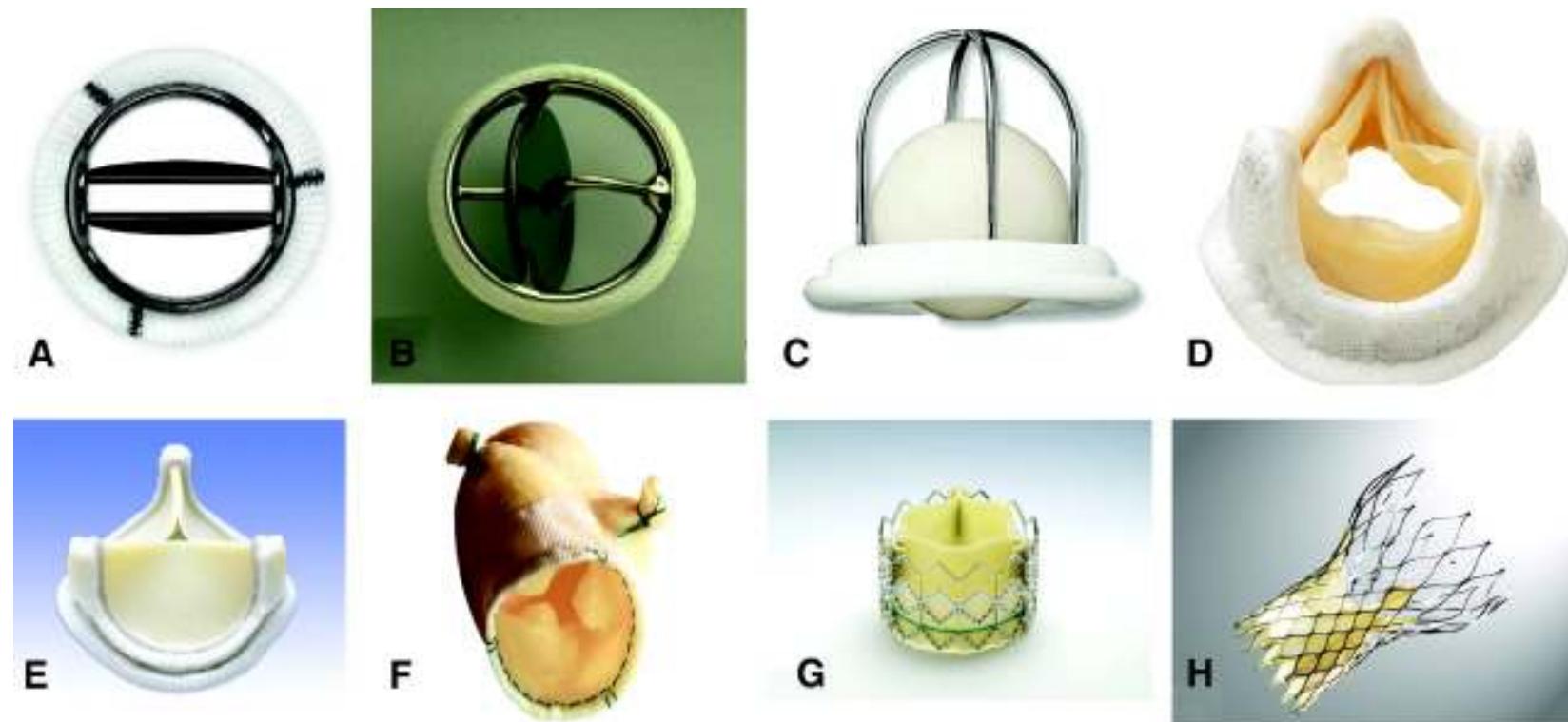
Porcine Valve



Smeloff-Sutter Valves



# Different types of prosthetic valves.



Different types of prosthetic valves. A, Bileaflet mechanical valve (St Jude); B, monoleaflet mechanical valve (Medtronic Hall); C, caged ball valve (Starr-Edwards); D, stented porcine bioprosthesis (Medtronic Mosaic); E, stented pericardial bioprosthesis (Carpentier-Edwards Magna); F, stentless porcine bioprosthesis (Medtronic Freestyle); G, percutaneous bioprostheses expanded over a balloon (Edwards Sapien); H, self-expandable percutaneous bioprostheses (CoreValve).

Pibarot P , Dumesnil J G Circulation 2009;119:1034-1048

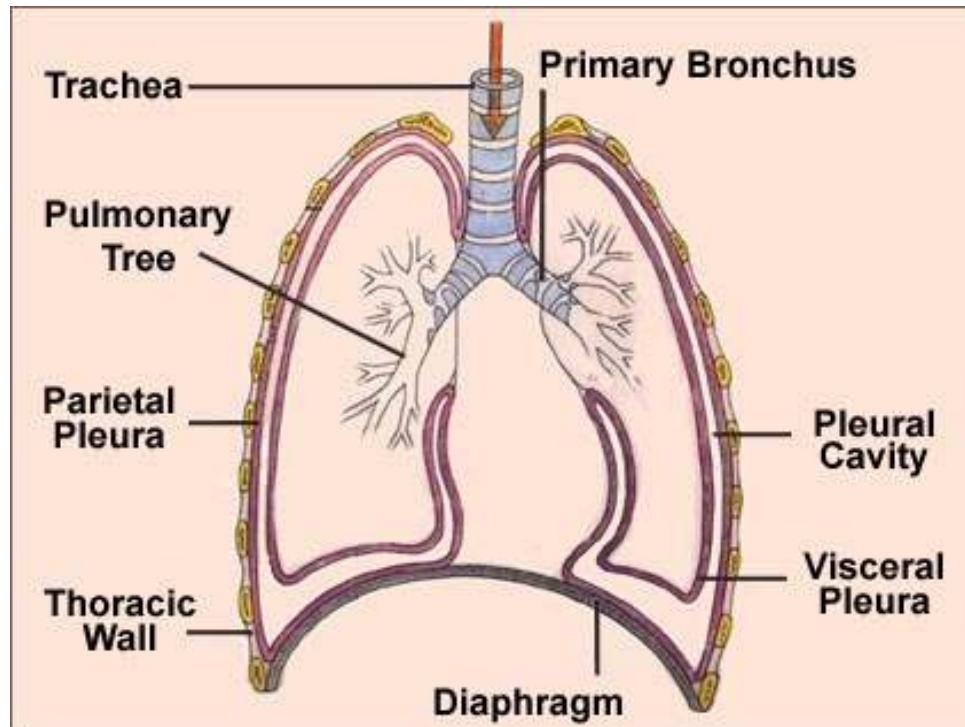


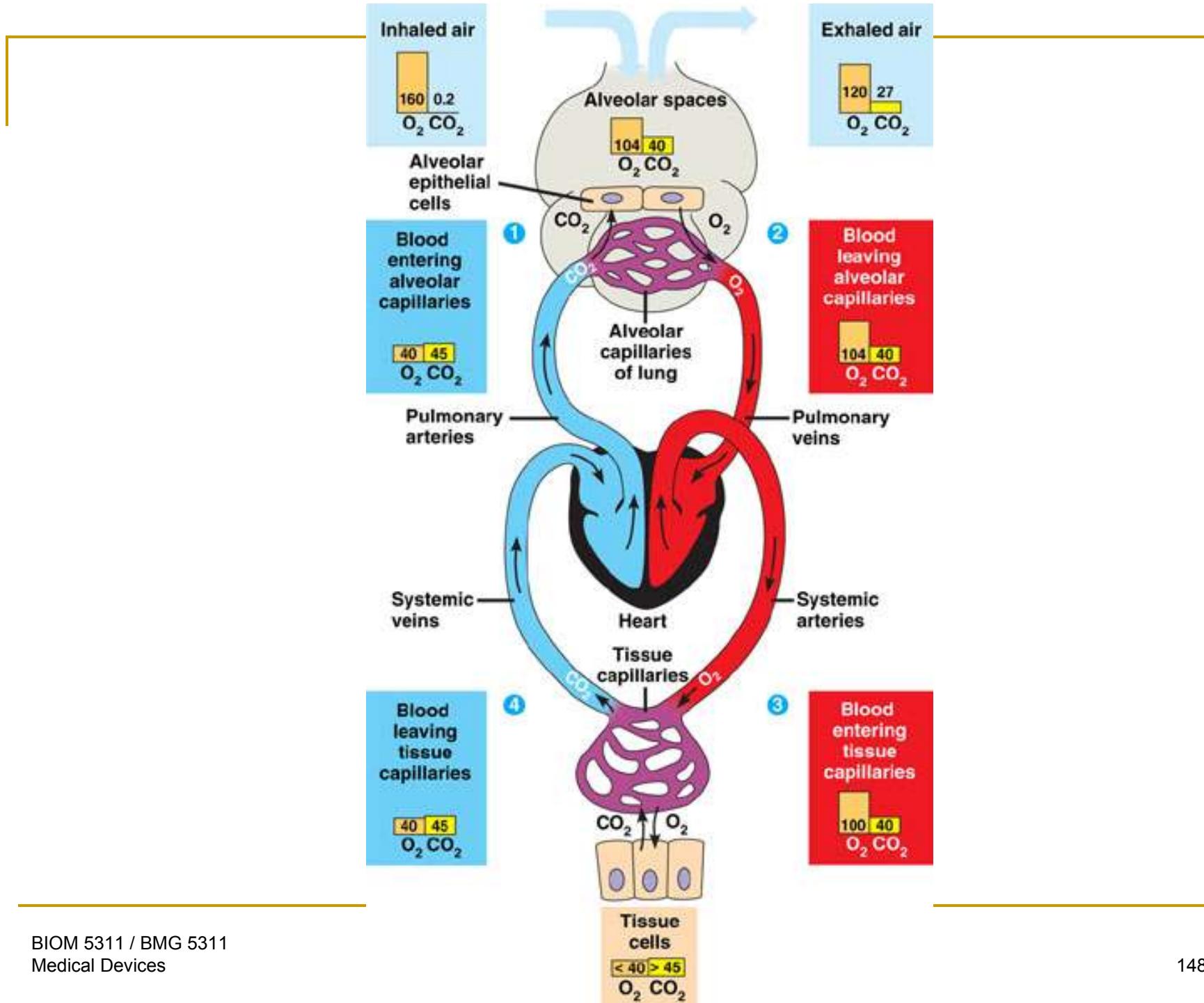
*Learn and Live*

# Transcatheter Aortic Valve Replacement

# CoreValve Aortic Valve Revalving

# Structure of the Lung





# Lungs and Respiration

## 1. The Lungs

- a. The lungs are located inside of the chest cavity.
- b. Normal lungs are light pink in colour. When one smokes or breathes polluted air, the colour of the lungs changes to dark and eventually blocks the function of gas exchange.

## 2. Function

- a. The main function of the lung(s) is respiration.
- b. Assists in metabolism, such as the conversion of Angiotensin I to Angiotensin II.
- c. Play a major role in blood pressure control. Angiotensin II is a potent vasoconstrictor, which acts on arterioles.
- d. Lung (pulmonary) circulation acts as a buffer for blood volume. Pulmonary circulation has a large degree of compliance and, thus, can hold blood volume in the vessels of the lungs and act as reservoir as required.
- e. The lungs trap small blood emboli (clots) helping the prevent clots from going to the brain, heart and other parts of the body.

# Respiration

1. Respiration is the exchange of gases – O<sub>2</sub> and CO<sub>2</sub>.
2. At the cellular level, respiration also means the utilization of O<sub>2</sub> and the production of CO<sub>2</sub>.
3. Diffusion of gases takes place as O<sub>2</sub> in the inspired air moves to the small sacs of the lungs (alveoli) and diffuses into the blood.
4. The movement of air, including O<sub>2</sub>, from the nose to the lung alveoli is called ventilation.
5. The movement of O<sub>2</sub> into the blood is done by diffusion
6. CO<sub>2</sub> from the blood diffuses into the alveoli and then is pushed out of the lungs during expiration.
7. Number of alveoli: There are around 300 million sacs (alveoli) in the lungs. They provide a surface area of about 70 m<sup>2</sup>. Each alveoli is about 0.03 mm and they are surrounded by a dense network of pulmonary capillaries for the exchange of gases.
8. Conduction of oxygen in blood: Once O<sub>2</sub> is exchanged into the blood, part of the O<sub>2</sub> is dissolved in the blood. This portion of dissolved oxygen is small and meets the tissue requirements for oxygen. The major portion of the O<sub>2</sub> is carried in the red blood cells RBCs) attached to hemoglobin (Hb).

# Respiration continued:

9. Hemoglobin:
  - a. Hemoglobin is the chemical in RBCs allowing a huge amount of O<sub>2</sub> to be attached to it.
  - b. Then, by the movement of the RBCs, the O<sub>2</sub> goes to all the tissues of the body.
  - c. Hemoglobin is a protein with molecular weight of 64,800.
  - d. Hemoglobin has four subunits. Each subunit contains a heme.
  - e. Heme is a complex chemical made of:
    - a. One porphyrin
    - b. Fe(II)
  - f. Each of the four Fe(II) combines with one O<sub>2</sub> molecule.
10. Oxygenation: The process of combination of O<sub>2</sub> molecule and Fe(II) is called oxygenation. Please note this is not oxidation. Oxidation is the use of O<sub>2</sub> and the production of H<sub>2</sub>O and CO<sub>2</sub>.
11. Diffusion of O<sub>2</sub> from the RBC to the tissue and CO<sub>2</sub> from the tissue to the blood takes place in the capillary.

# Respiration continued:

12. How much blood goes to the lungs:

- a. At rest, roughly 5 litres of blood per minute, as we discussed under the heart. This blood is returned and goes through the lungs for the exchange of gases. About 0.03 litres/min of  $O_2$  is conveyed at rest from the lungs to the periphery. That is, this is net value or the difference between the amount of  $O_2$  transported in the arteries and in the veins. This is called the  $VO_2$ .
- b. About 0.025 litres /min of  $CO_2$  ( $VCO_2$ ) is exchanged from the periphery (the difference between venous  $CO_2$  and arterial  $CO_2$ ).

13. Respiratory frequency:

- a. At rest, roughly 12-16 breaths/minute.
- b. Intake of air is about 0.5 litres /breath.

14. Tidal volume ( $V_T$ ) is the total ventilation rate. That is, the amount of air taken in each breath multiplied by the number of breaths per minute. It equals 6-8 litres/min (meaning that there are 6 to 8 litres of air taken in by the lungs each minute).

15. During exercise or exertion, this ventilation rate ( $V_T$ ) or tidal volume can go up to 100 litres /min. This is known as the respiratory limit.

16. The respiratory limit is the maximum amount of air taken in litres /minute.

17. Alveolar ventilation ( $V_A$ ) is smaller than the respiratory limit because of dead space ventilation.

18. Dead space ventilation ( $V_D$ ) is a significant fraction of tidal volume ( $V_T$ ).

# Partial Pressure and Dalton's Law

1. The partial pressure of a gas in a mixture of gases is the pressure that each specific gas exerts. It is equal to the total pressure of the gas mixture multiplied by the relative concentration fraction of that specific gas.
2. Dalton's Law: Dalton's Law indicates that the sum of partial pressures of the individual gases equals the total pressure of the gas mixture.
3. Air is a mixture of gases and at sea level the total pressure of this gas mixture is 760 mm Hg, which is equal to 101.3 kPa (kiloPascals).
4. In dry air, at sea level, the inspired air has a partial pressure of 21.2 kPa (159 mm Hg) for O<sub>2</sub>. For CO<sub>2</sub>, the partial pressure is 0.03 kPa (0.23 mm Hg). For N<sub>2</sub> and other inert gases in the air, the partial pressure is 80 kPa (601 mm Hg). While expired air at sea level has partial pressures of 15.33 kPa (115 mm Hg) for O<sub>2</sub>, 4.4 kPa (33 mm Hg) for CO<sub>2</sub>, and now we have H<sub>2</sub>O (because the air went through the mouth and lungs) at 6.27 kPa (47 mm Hg), and 75.33 (565 mm Hg) for N<sub>2</sub>.

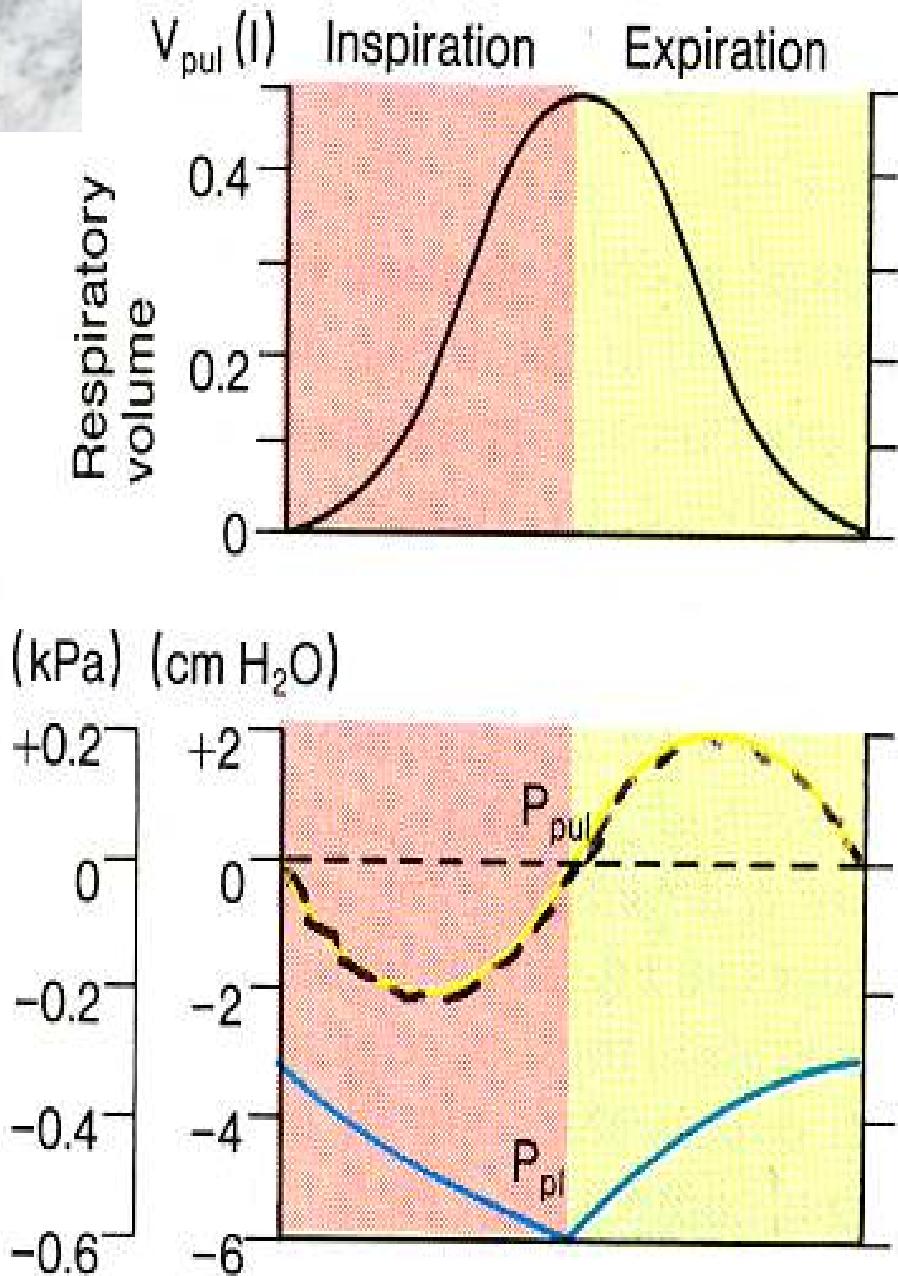
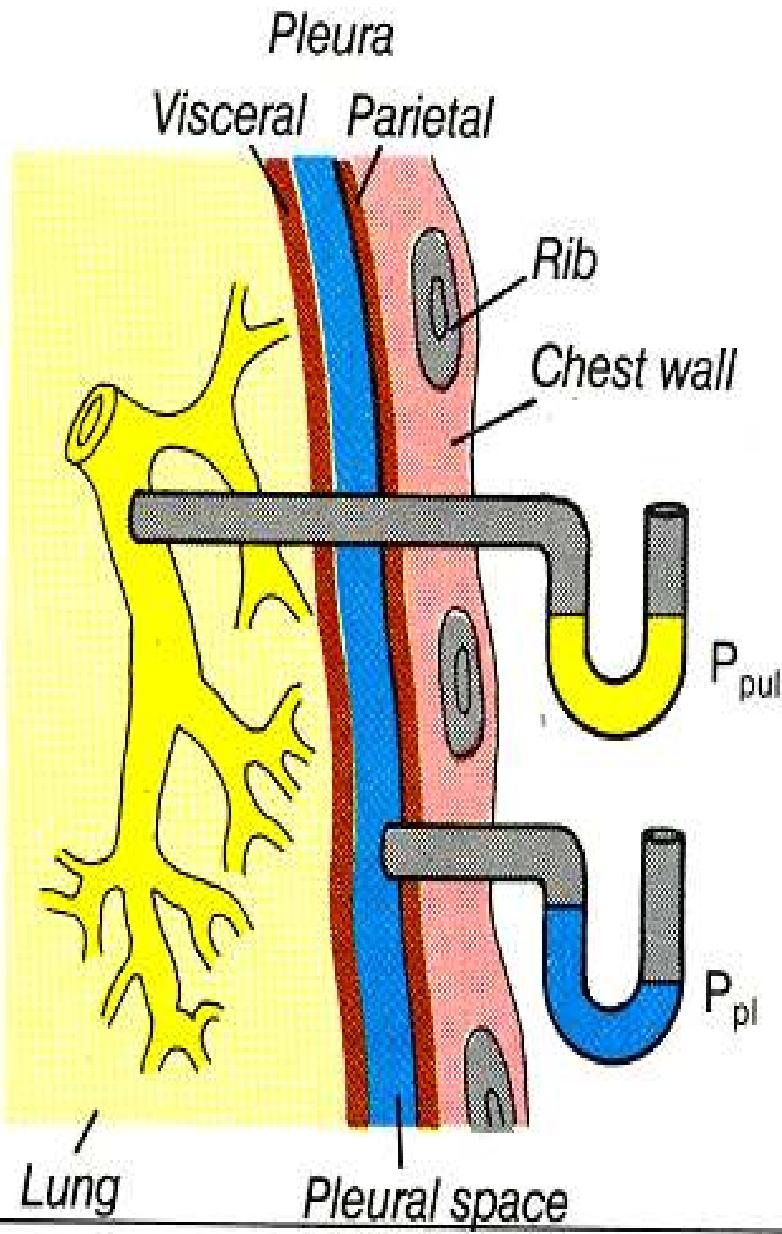
# Mechanics of Respiration

1. The lungs are elastic and, thus, have a tendency to recoil.
2. However, they do not recoil because they are expanded and adapted to the contours of the chest wall.
3. There is a cavity between the lung and chest wall called the pleural space.
4. This cavity has two layers, one attached to the lung (pleura pulmonalis) and the other attached to the chest wall (pleura parietalis). See Figure 1.
5. The space between these two layers is filled with a thin film of fluid, which is not expandable.
6. Because this pleural space has a non-expandable fluid film, the lung remains in contact with the chest wall as long as the pleural space is not punctured.
7. If for some reason this pleural space is punctured, such as opening the chest wall for surgery, air enters the pleural space, and the lungs recoil and collapse. This is called a pneumothorax. See Figure 2.
8. Intrapleural (intrathoracic) pressure is the pressure inside the pleural space, which is equal to the intrathoracic pressure. It is normally negative at – 0.03 kPa. This is about –3 cm of a column of water compared to atmospheric pressure.

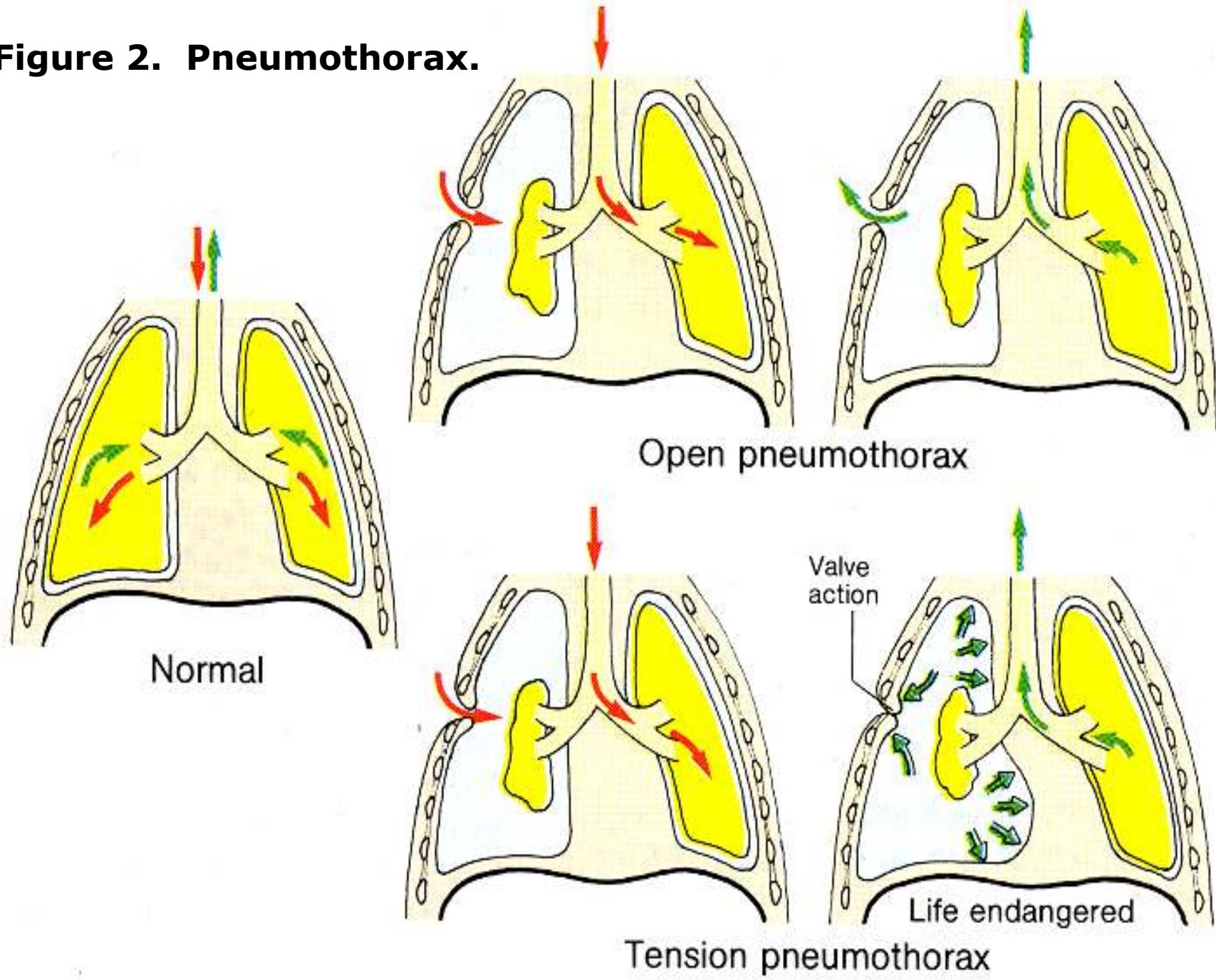
# Mechanics of Respiration continued:

9. At inspiration, this pressure is lowered to – 0.6 kPa causing expansion of the lungs when the inspiration is normal (not much effort is necessary for breathing in).
10. When inspiration is strong, effort is being made to inspire more air, the intrapleural pressure ( $P_{pl}$ ) to be lowered and it goes to around – 4 kPa.
11. On a strong expiration (breathing out), the intrapleural pressure ( $P_{pl}$ ) can become slightly positive.
12. Intrapulmonic pressure: This is the pressure in the alveoli and is important in breathing. Intrapulmonic pressure ( $P_{pul}$ ) must be below the external atmospheric pressure for inspiration (breathing in). On the other hand, for expiration, this pressure ( $P_{pul}$ ) must be positive.
13. The driving force for ventilation is the pressure difference between atmospheric and intrapulmonic pressure ( $P_{pul}$ ) in the alveoli.
14. The reason for this pressure gradient is changing lung volume. That is, lung volume is increased on inspiration and decreased on expiration by action of the diaphragm and thorax.

**Figure 1. Intrapleural and intrapulmonary pressures.**

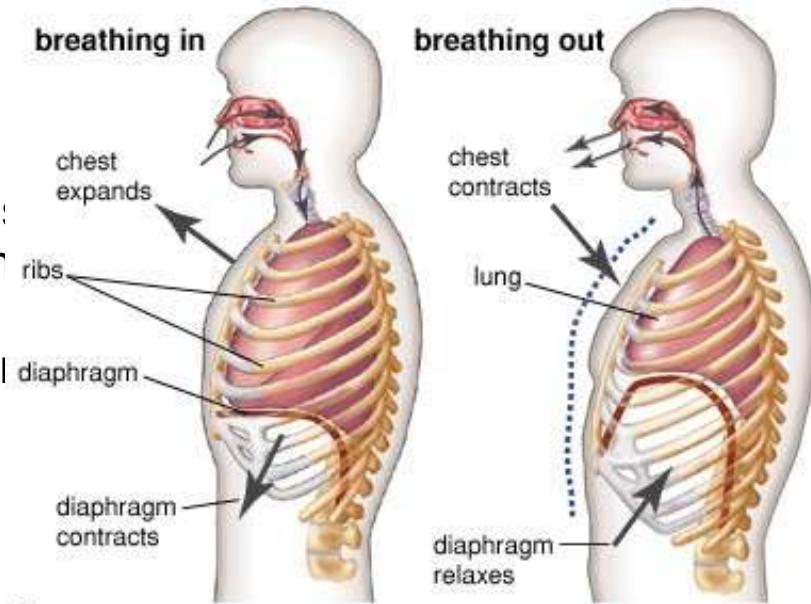


**Figure 2. Pneumothorax.**



# Inspiration

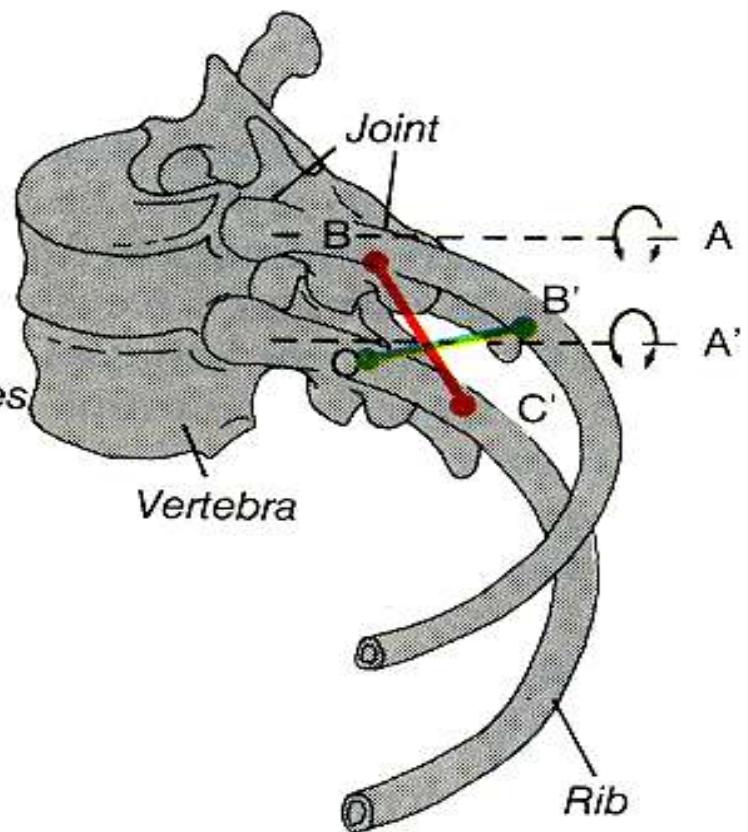
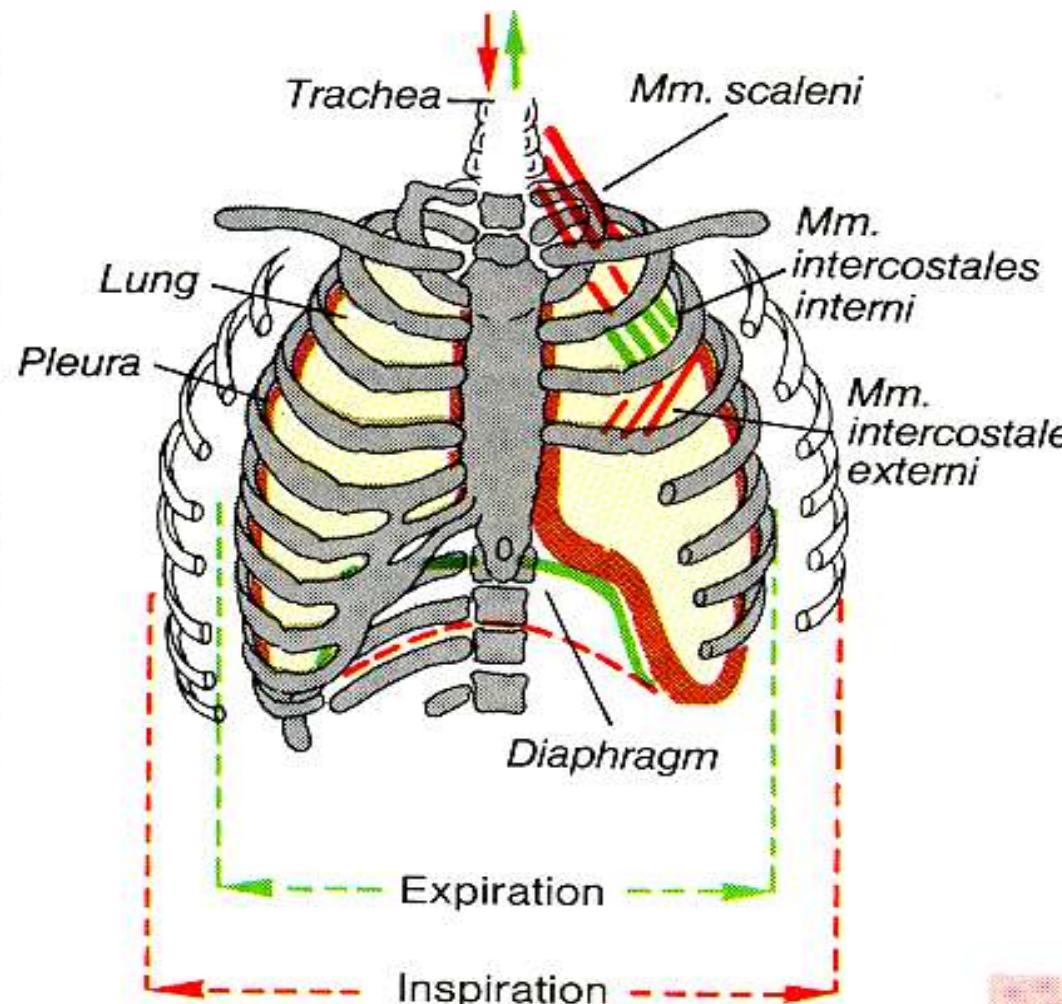
1. Inspiration is an active (requires energy) process.
2. Muscular contraction is required to increase the volume of the chest and inflate the lungs and causes the intrapulmonic pressure (alveoli) to decrease to permit air to flow into the lungs.
3. During inspiration, the diaphragm directly influences the lung volume. It contracts during inspiration and relaxes during expiration. It can go lower (as much as 7 cm) during deep inspiration.
4. Contraction of other muscles of the thorax, such as the external intercostals muscles and other accessory muscles, have an indirect influence on inspiration and expiration.



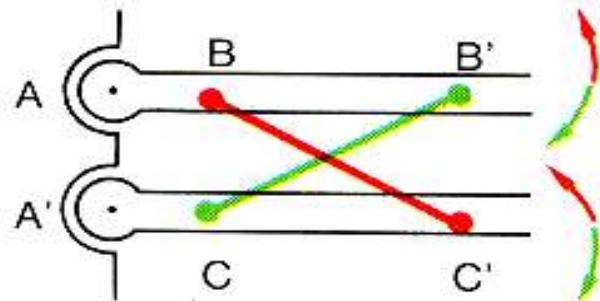
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# Expiration

1. Occurs exclusively by passive recoil of the lungs.
2. Can be assisted by contraction of the abdominal muscles, which increase the intraabdominal pressure, pushing the relaxed diaphragm towards the chest cavity and by contraction of the internal intercostal muscles of the chest. See Figure 3.



Lever  $A-B < A'-C' \rightarrow$  raises rib



Lever  $A-B' > A'-C \rightarrow$  lowers rib

**Figure 3. Respiratory musculature.**

# Cleansing of Inspired Air

1. There are many particles in the inspired air.
2. Thus the air must be filtered before it gets to the lung.
3. These particles are caught by mucus, which covers the nasal and pharyngeal cavities.
4. The bronchial tree is long and has many branches. By the time that air gets near the end of the tree, near the alveoli, many of the remaining particles are attached to the bronchial mucus and then they are:
  - a. Phagocytosed (eaten by white blood cells) or
  - b. Returned toward the glottis (mucociliary excalator) by the cilia of the tracheo -bronchial epithelium. These cilia beat (move) 12-20 times/second and push the mucus film at a speed of 1 cm/min and this is eventually excreted.

# Engineering Measurements of Respiratory Volumes

1. In passive expiration (sometimes called “quiet”) the thorax rests at the resting expiratory level. See Figure 4.
2. At rest or during quiet breathing, the ventilatory exchange is about 0.5 litre per breath.
3. The ventilatory exchange at rest is called tidal volume ( $V_T$ ).
4. In active maximal inspiratory effort, the intake of air is about 2.5 litres in addition to  $V_T$  that is about 3 litres per breath.
5. The difference between maximal inspiration volume and tidal volume is called inspiratory reserve volume.
6. At forced expiration (active maximal expiratory effort) about 1.2 litres of air is yielded. This is called expiratory reserve volume, that is the difference between maximal expiratory volume minus tidal volume.
7. Residual volume is the amount of volume that cannot be expired. It is about 1.5 litres.
8. Vital capacity is the total volume between maximum expiration and maximum inspiration.
9. Spirometer: An instrument that measures the above volumes (Figure 4).

# Engineering Measurements of Respiratory Volumes continued:

10. Pressure-volume (work) of breathing:

1. The pressure-volume curve indicates the work of breathing.
2. By measuring the pressure in the airway (intrapulmonary pressure,  $P_{pul}$ ) at different stages of chest inflation during a respiratory cycle.
3. The intrapulmonary volume ( $V_{pul}$ ) can be measured at different stages.
4. The relationship between these two can be plotted graphically like other engineering PV relationships as shown in Figure 5.

11. Intrapulmonary pressure ( $P_{pul}$ ) is set to be equal to zero relative to the atmosphere.  $V_{pul}$  at the resting expiration level is often set at zero as well.

12. Under static conditions, the pressure-volume curve (PV curve) for lung and thorax can be determined.

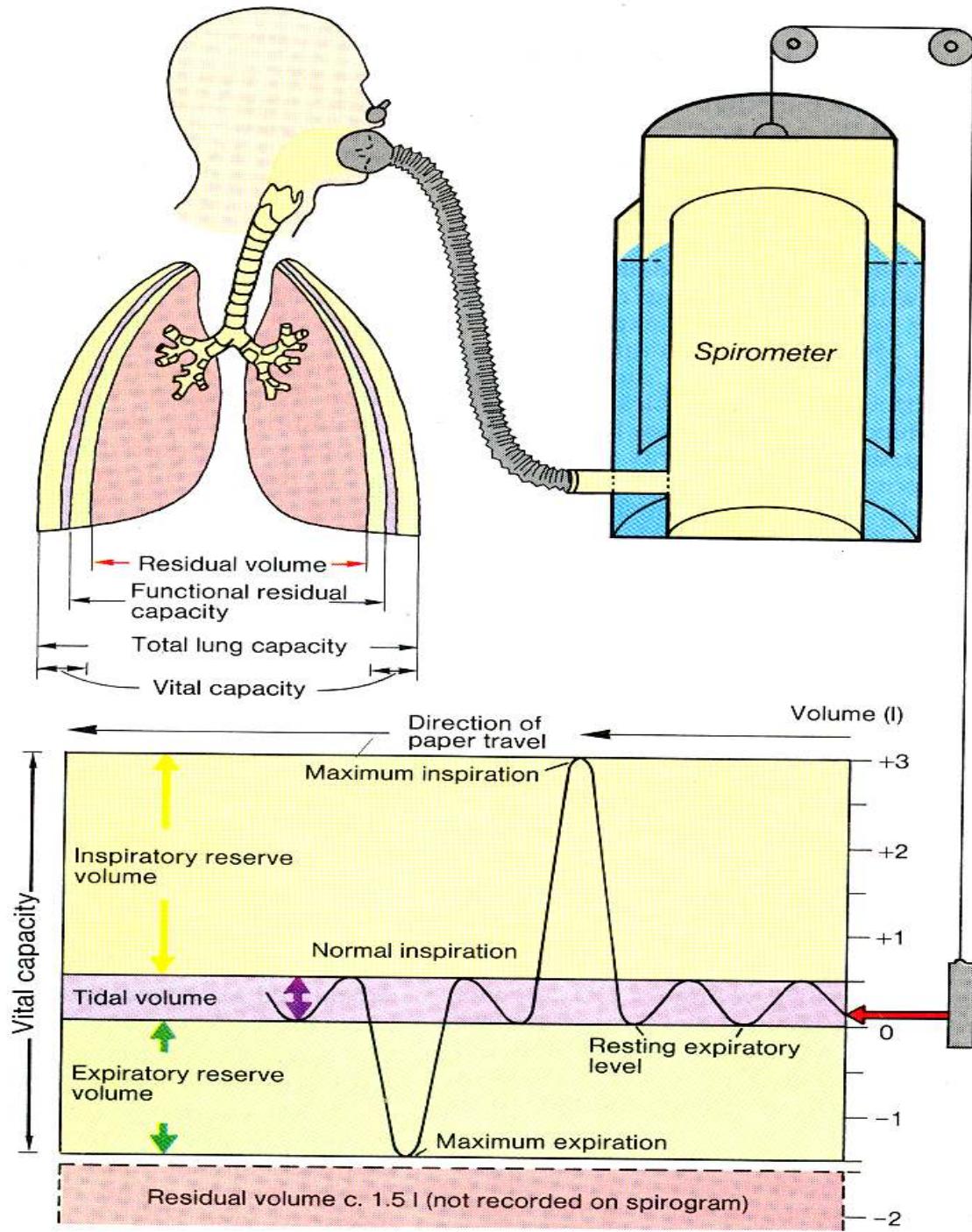
13. The slope of the static PV curve ( $\Delta V_{pul} / \Delta P_{pul}$ ) equals the static compliance as shown in Figure 5.

14. Static compliance is defined as the stretchability of the lungs and thorax.

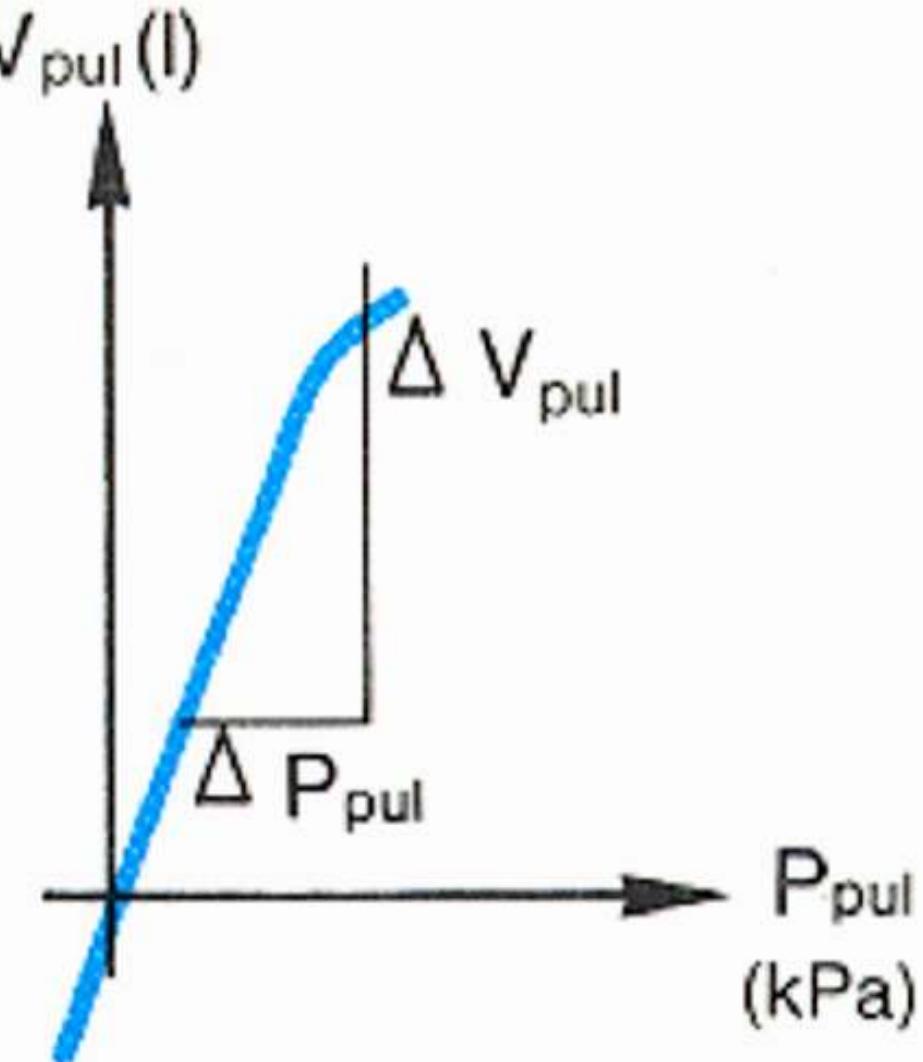
# Engineering Measurements of Respiratory Volumes continued:

15. Breathing work:
  - a. The area enclosed by the curve of inspiration and expiration represent this work.
  - b. This is the work done against the frictional resistance to the airflow and to the lung and chest movements in inspiration or expiration.
16. The total work of expiration and total work of inspiration can be determined from these curves. See Figure 6.

## Figure 4. Measurement of lung volumes

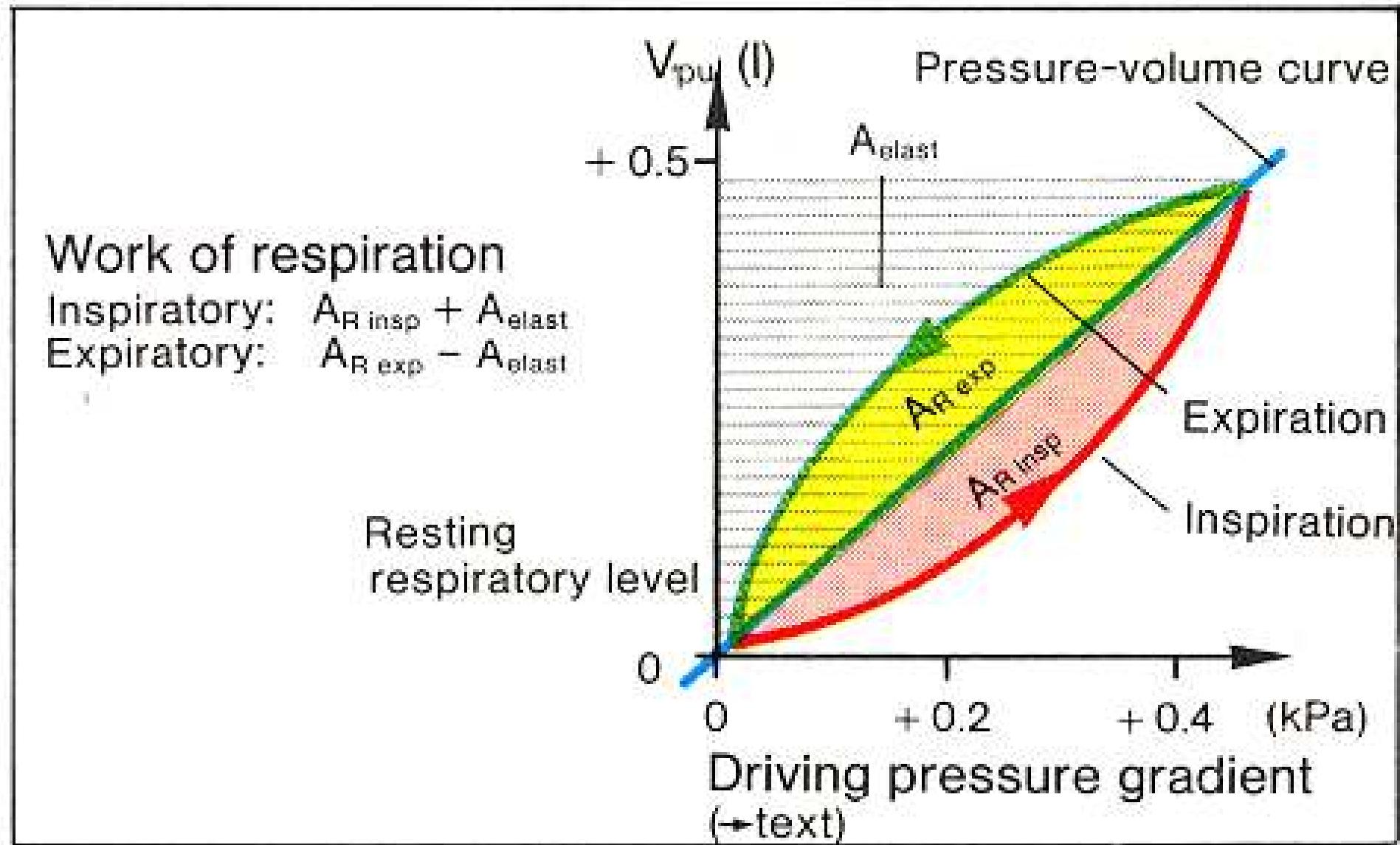


**Figure 5. Static compliance.**



$$\frac{\Delta V_{\text{pul}}}{\Delta P_{\text{pul}}} = \text{Compliance}$$

**Figure 6. Dynamic pressure-volume curves.**



# Gas Exchange Principles

1. In order to have gas exchange, there must be ventilation.
2. Not all the ventilated air is used for gas exchange as it does not all reach the alveoli.
3. The tidal volume ( $V_T$ ) that reaches the alveoli is less than what entered and is called  $V_A$ .
4. The difference is because of dead space ( $V_D$ ).

Thus,  $V_T = V_A + V_D$ ,

Where  $V_T$  = tidal volume

$V_A$  = volume reaching the alveoli

$V_D$  = volume taken by dead space

5. Total Ventilatory Rate: This is equal to tidal volume multiplied by the frequency of breathing.

Thus,  $V_{RT} = V_T \cdot f$ ,

Where  $V_T$  = total ventilatory rate

$V_{RT}$  = tidal volume

$f$  = frequency

6. Alveolar Ventilatory Rate ( $V_{RA}$ ) and Dead Space Ventilatory Rate ( $V_{RD}$ ) can be derived from  $V_A$  and  $V_D$ .

# Gas Exchange Principles continued:

7. At rest, normally  $V_A$  is about 70% of the total ventilatory rate ( $V_T$ ). This is about 5.2 litres/min.
8. Determination of various regulatory rates and shallow rapid breathing.
9. Given  $V_T = 0.5$  litres,  $f = 15$  breaths/min,  $V_D = 0.15$  litres,  $V_A = 0.35$  litres, then determine  $V_{RT}$ ,  $V_{RD}$  and  $V_{RA}$ .
10. If breathing frequency is increased to 25 breaths/min, then determine the same as above. Make assumptions as required.

# Respiratory Gas Diffusion

1. When air enters the lung, oxygen goes (diffuses) into the blood from the air in the alveoli.
2. CO<sub>2</sub> diffuses into the alveoli sac from the cells through the interstitial fluid to the blood and to the alveoli.
3. The laws governing this diffusion of O<sub>2</sub> and CO<sub>2</sub> can be covered by the following laws of physics and/or principles of engineering:
  - a. **Charles' Law:** Charles' Law states that the volume of a gas is directly proportional to its absolute temperature when pressure remains constant.
  - b. **Dalton's Law:** As it was stated, this law says that each gas in a mixture of gases exerts its own pressure as if the other gases were not present. The total pressure of the mixture is calculated by adding up all the pressures of each component gas. The individual pressure of each gas is called its partial pressure. An example for the atmosphere, the pressure is the sum of the pressures of all its components. That is, atmospheric pressure is equal to the sum of the pressures of O<sub>2</sub>, CO<sub>2</sub>, N<sub>2</sub>, and H<sub>2</sub>O added together, and at sea level this is 760 mm Hg.
  - c. **Henry's Law:** The quantity of a gas that will be dissolved in a liquid is proportional to the partial pressure of that gas and its solubility coefficient when the temperature remains constant. When one buys a bottle of club soda, since the bottle is unopened, CO<sub>2</sub> is dissolved. Once the cap is removed, the pressure is released and the gas begins to bubble out.

# Respiratory Gas Diffusion continued:

4. Henry's Law explains what happens to deep-sea divers, scuba divers or caisson workers (those who build tunnels under water) when they breathe air under high pressure. A considerable amount of N<sub>2</sub> goes into solution in the plasma and the interstitial fluid.
5. Air that is inspired contains 79% N<sub>2</sub>. At sea level, the pressure and, therefore, its solubility is very low and, thus, very little N<sub>2</sub> is dissolved in the blood plasma. Therefore, no known impact on physiological body functions. When air under pressure is breathed, the N<sub>2</sub> in the mixture can affect the body because the partial pressure is a function of total pressure. Therefore, the partial pressure of all the components of the mixture increase as the total pressure is increased. Since partial pressure of N<sub>2</sub> is higher in the mixture of compressed air than at sea level, considerable amounts of N<sub>2</sub> are dissolved in the plasma and interstitial fluid. These excess amounts of dissolved N<sub>2</sub> may produce giddiness (laughing) and other symptoms similar to alcohol intoxication. This is called "nitrogen narcosis", and the greater the depth, the more serious the condition.

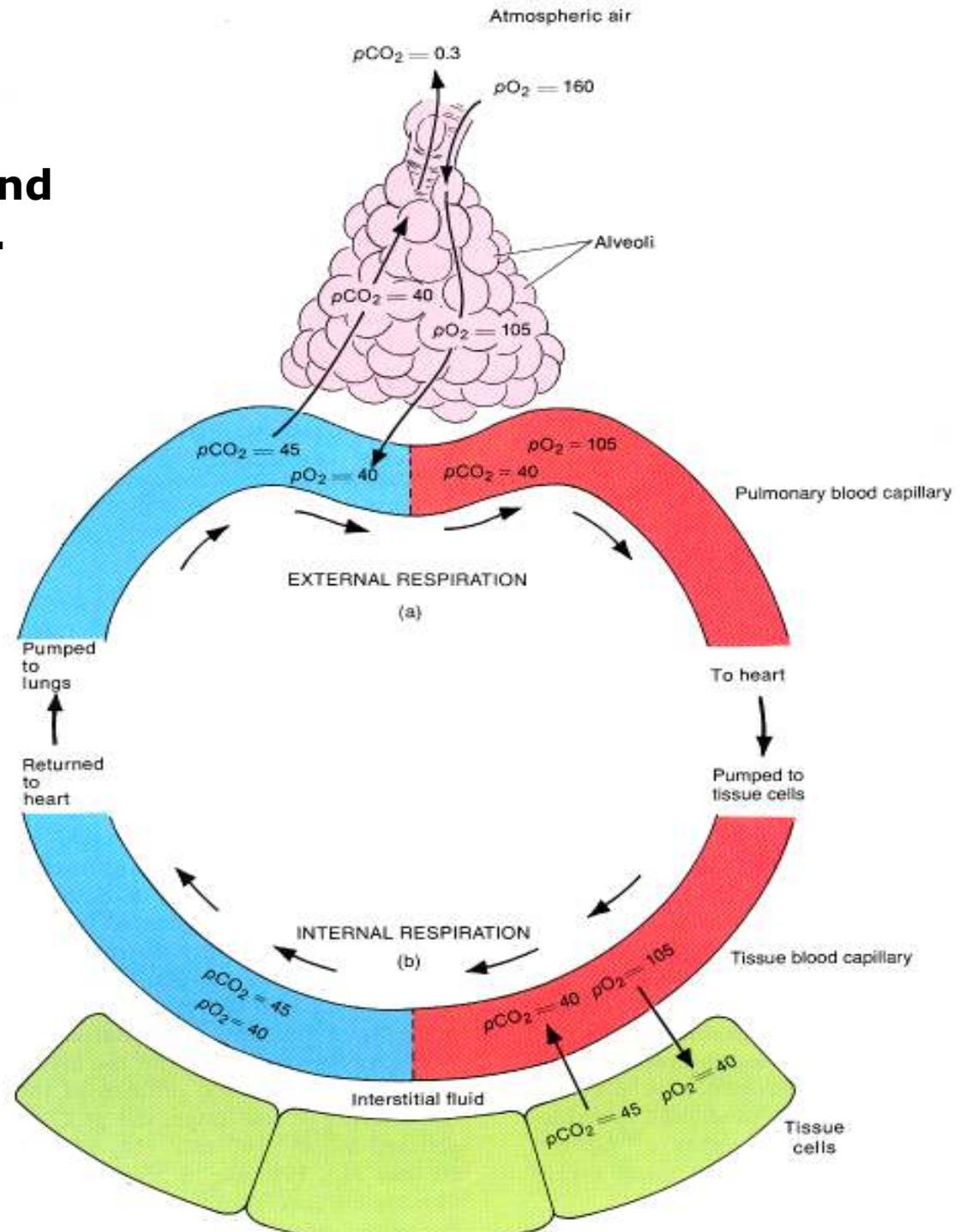
# Respiratory Gas Diffusion continued:

6. If the person comes to the surface slowly, the dissolved nitrogen can be eliminated through the lungs. But if the diver surfaces rapidly, the nitrogen comes out of solution too quickly, and forms a gas bubble in the tissue which results in decompression sickness causing leg pain, dizziness, shortness of breath, extreme fatigue, paralysis and unconsciousness.
7. Slow ascent or the use of a special tank for decompression within 5 minutes of surfacing can prevent decompression sickness.
8. Hyperbaric oxygenation:
  - a. The application of Henry's Law is demonstrated by hyperbaric oxygenation.
  - b. "Hyper" means "higher, over, above" and "baros" means "pressure".
  - c. Hyperbaric oxygenation is using pressure to dissolve more O<sub>2</sub> in the blood.
  - d. This higher oxygenation by pressure is effective method to treat patients who are infected by anaerobic bacteria causing tetanus and gangrene because anaerobic bacteria cannot live in the presence of free oxygen.
  - e. Hyperbaric chamber has oxygen at a pressure of 3 to 4 atm or about 2300 to 3000 mm Hg.
  - f. The tissues pick up the O<sub>2</sub> causing the bacteria to be killed.
  - g. Some have applied hyperbaric oxygenation for the treatment of heart disease and there are other potential applications.

# Types of Respiration

1. **External respiration:** This is the exchange of gases between the alveoli of the lungs and the blood.
2. **Internal respiration:** This is the exchange of gases between the blood and the cells and tissues. See Figure 7.

**Figure 7. Internal and external respiration.**



# External Respiration

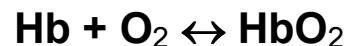
1. The exchange of gases between the alveoli of the lungs and the pulmonary capillaries.
2. The  $pO_2$  of alveolar air is 105 mm Hg and the  $pO_2$  of the deoxygenated blood entering the pulmonary capillaries is 40 mm Hg. Therefore, the difference in this oxygen pressure causes oxygen to diffuse from the alveoli into the deoxygenated blood. This continues until equilibrium. That is, until the pressure reaches 105 mm Hg approximately.
3.  $pCO_2$  of the pulmonary deoxygenated blood is 45 mm Hg and the alveolar  $pCO_2$  is 40 mm Hg. Because of this  $pCO_2$  difference, there is  $CO_2$  going from the blood into the lung. This continues until the  $pCO_2$  of the blood is 40 mm Hg.
4. This exchange of gases is assisted by:
  - a. The thickness of the alveolar capillaries is only 0.05 microns.
  - b. The surface area is large, about  $70.0\text{ m}^2$ .
  - c. A huge number of capillaries are adjacent to the alveoli.
  - d. Capillaries are so narrow that the RBCs must flow through them in single-file, providing time for exchange and maximum exposure of each RBC to the available  $O_2$

# Internal Respiration

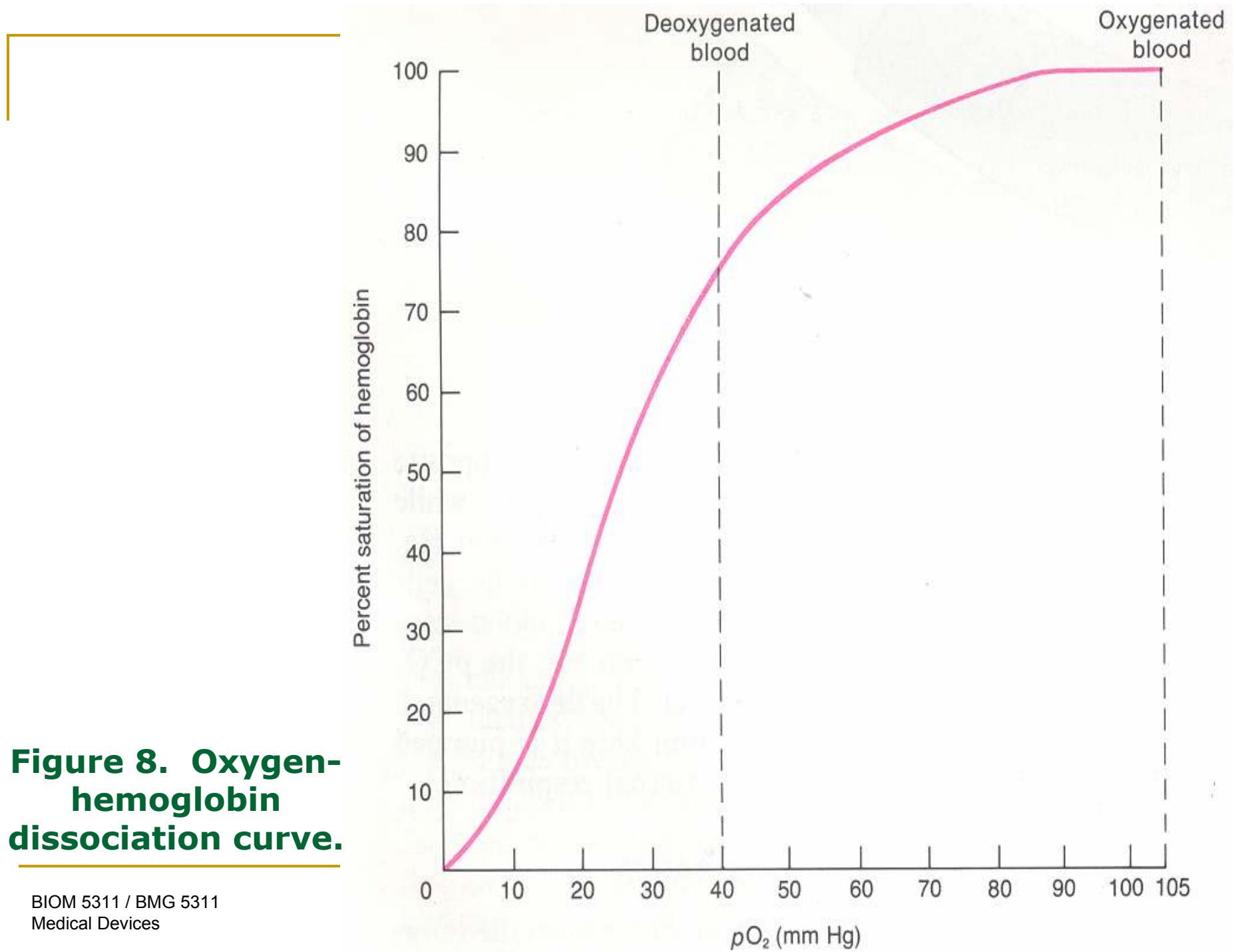
1. This is the exchange of gases between the blood and the tissue cells.
2. Oxygenated blood in the tissue capillaries has a  $pO_2$  of 105 mm Hg, while in the tissue cells  $pO_2$  is 40 mm Hg. Therefore, the  $O_2$  diffuses through the interstitial fluid to the cells until the  $pO_2$  in the blood decreases to 40 mm Hg.
3.  $pCO_2$  of the tissue cells is 45 mm Hg, while that of the tissue capillary oxygenated blood is 40 mm Hg. Then  $CO_2$  diffuses from the tissue cells, through the interstitial fluid, into the oxygenated blood.

# Oxygen Exchange

1. Under normal resting conditions, each 100 ml of oxygenated blood contains 20 ml of O<sub>2</sub>.
2. O<sub>2</sub> does not dissolve easily in water. Thus, very little O<sub>2</sub> is carried in the plasma. Only about 3% of overall O<sub>2</sub> in the blood is carried dissolved in the plasma.
3. 97% of O<sub>2</sub> is carried by the hemoglobin in the RBCs.
4. Hemoglobin is the chemical containing:
  - a. Protein (globin)
  - b. Pigmented component (heme)
  - c. Heme contains four atoms of iron
  - d. Each atom of iron is capable of combining with a molecule of O<sub>2</sub>.
5. O<sub>2</sub> and hemoglobin form a reversible oxyhemoglobin:



6. Fully Saturated Hemoglobin: When hemoglobin is fully converted to HbO<sub>2</sub> (it has taken up all the O<sub>2</sub> that it can), it is referred to as fully saturated.
7. Partially Saturated Hemoglobin: When hemoglobin consists of a mixture of Hb and HbO<sub>2</sub>, then it is called partially saturated.
8. The oxygen-hemoglobin dissociation curve shows the relationship between hemoglobin saturation and the partial pressure of O<sub>2</sub>. As pO<sub>2</sub> increases, more O<sub>2</sub> combines with hemoglobin. See Figure 8.



**Figure 8. Oxygen-hemoglobin dissociation curve.**

# Control of Respiration

1. The respiratory center consists of the rhythmicity area of the medulla, inspiratory and expiratory areas (pneumotaxic and apneustic areas).
2. The inspiratory area has an intrinsic excitability that causes the rhythm of respiration.
3. The pneumotaxic and apneustic areas coordinate the transition between inspiration and expiration.
4. Respiratory rate can be modified by a number of factors such as:
  - a. Brain
  - b. Outside factors
  - c. Inflation reflex
  - d. Chemical stimuli such as the levels of O<sub>2</sub> and CO<sub>2</sub>.
  - e. Blood pressure
  - f. Temperature
  - g. Pain
  - h. Irritation of the respiratory mucosa
  - i. Cortical influences

# Respiratory Crises and Interventions

1. Cardiopulmonary Resuscitation (CPR) is the artificial establishment of respiration and circulation through airways, breathing and circulation.
2. The abdominal thrust (Heimlich) maneuver is a form of first aid procedure used in the case of choking. It consists of an abdominal push or thrust, which elevates the diaphragm causing a compression of the lungs, increasing the air pressure in the bronchial tree and pushing the lodged material out.

# Pittsburgh & IMO Artificial Lung Devices

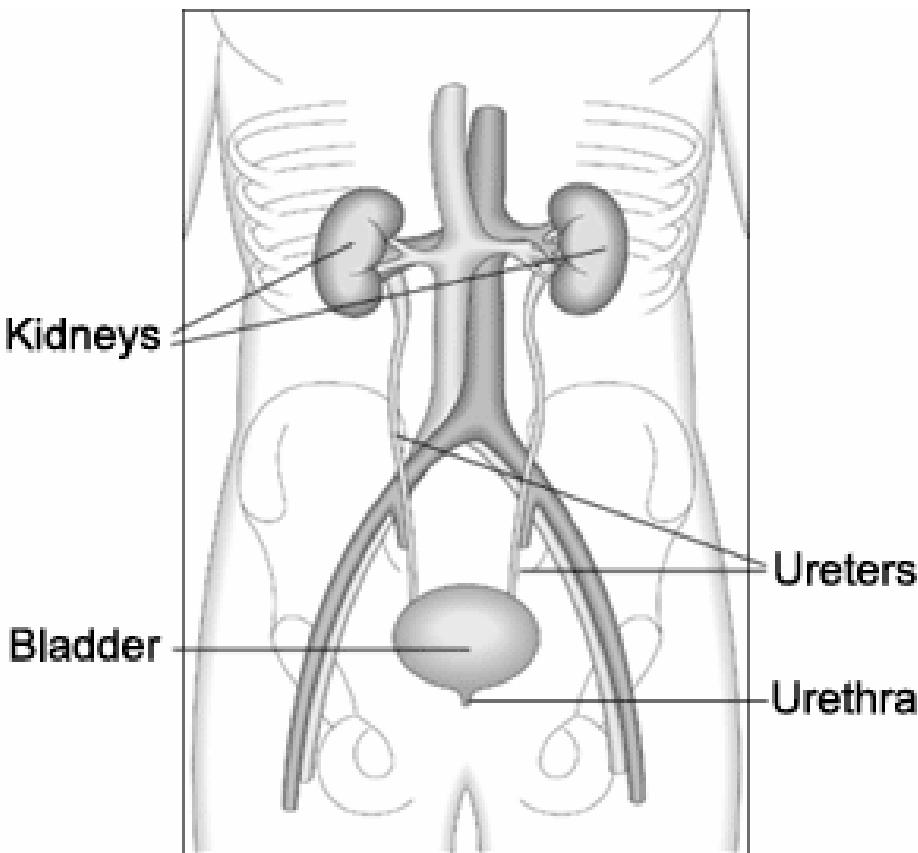


*The core of the Pittsburgh Artificial Lung (PAL) will be an exchange chamber like this prototype, in which many gas-carrying fibers trade the blood's carbon dioxide for fresh oxygen, while a miniature pump circulates blood through the oxygenator.*



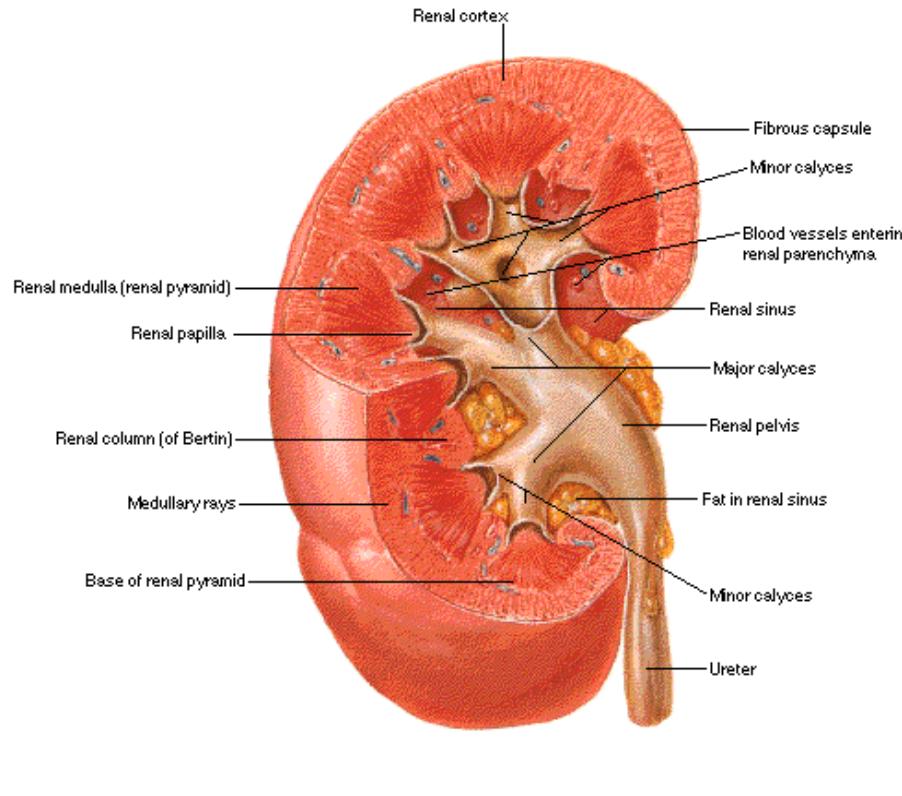
*The IMO artificial lung device*

# Kidney – Anatomy

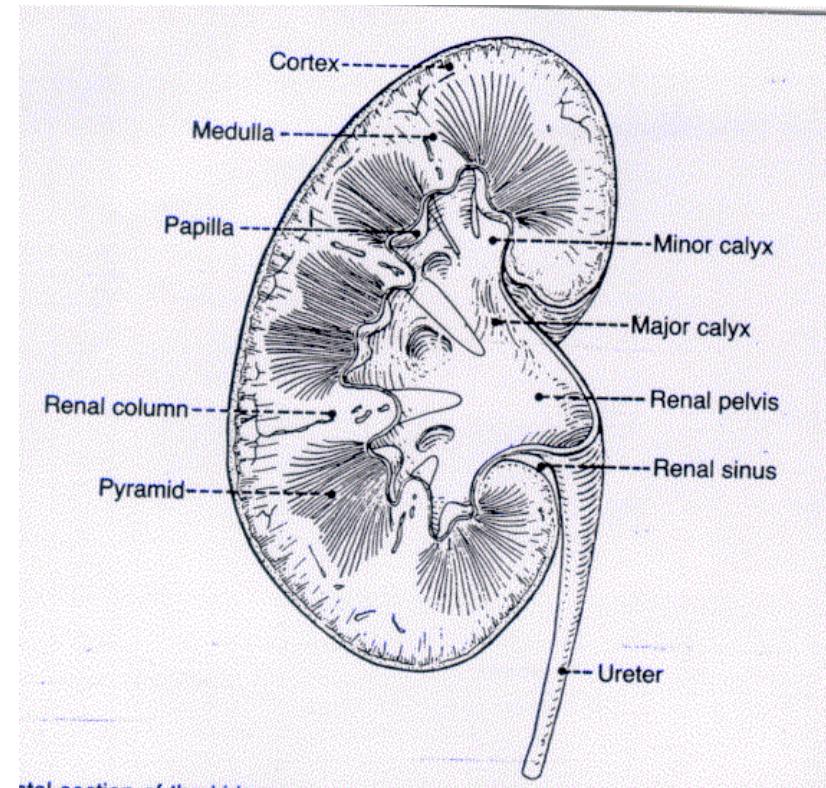
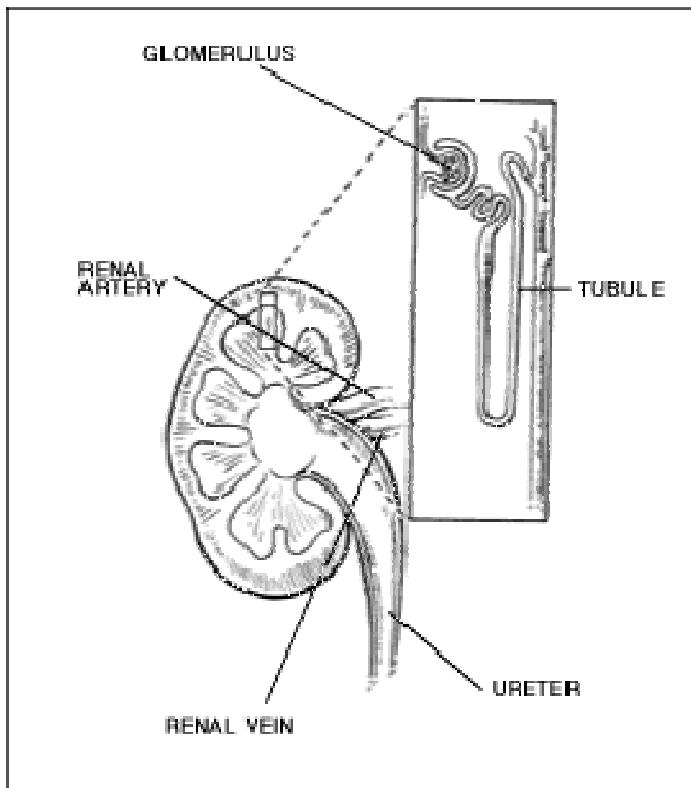


# Structure of the Right Kidney

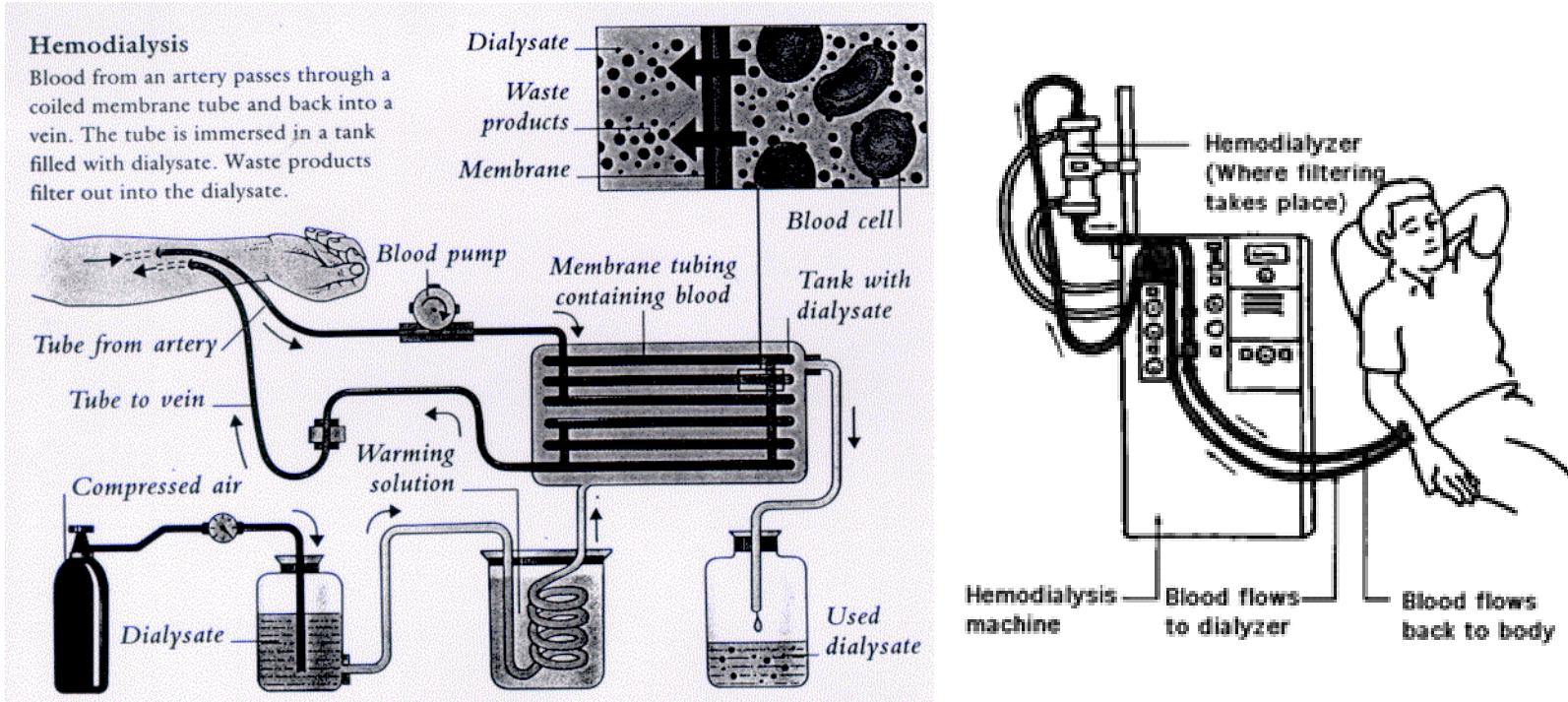
Right Kidney Sectioned in Several Planes



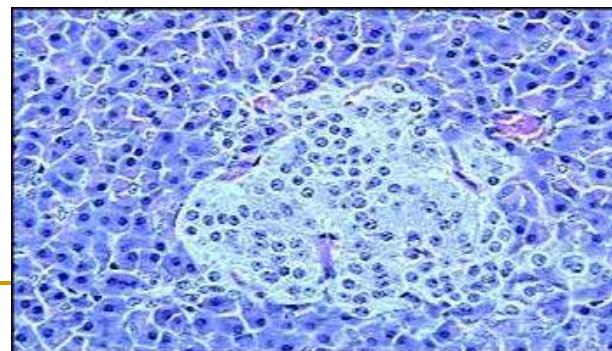
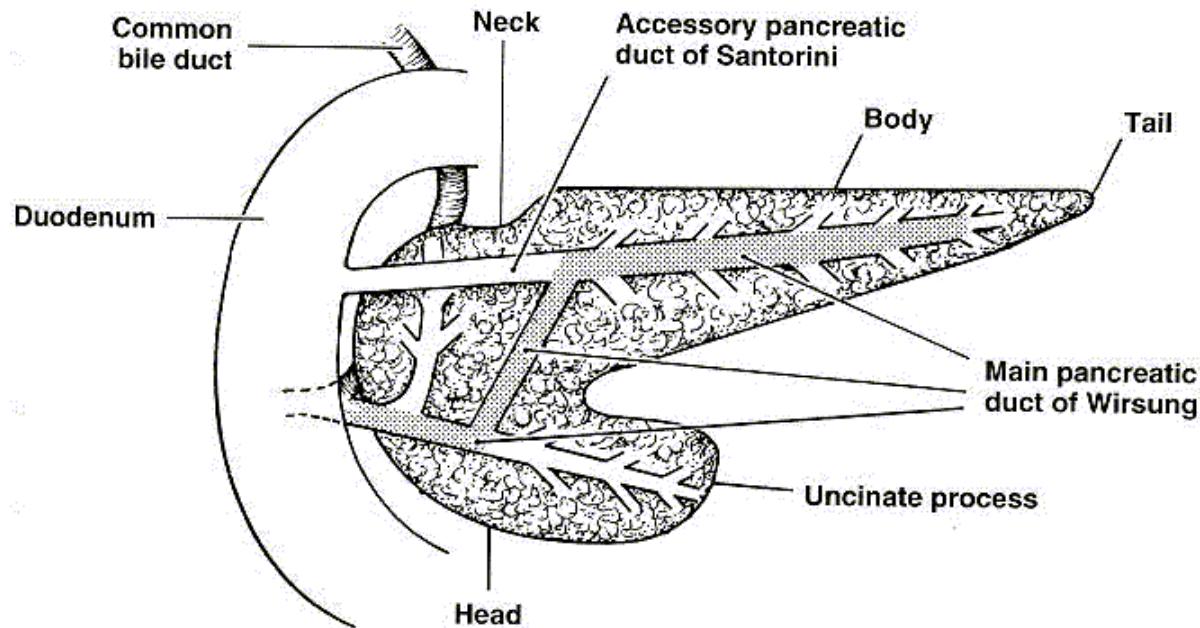
# Kidney – Structure



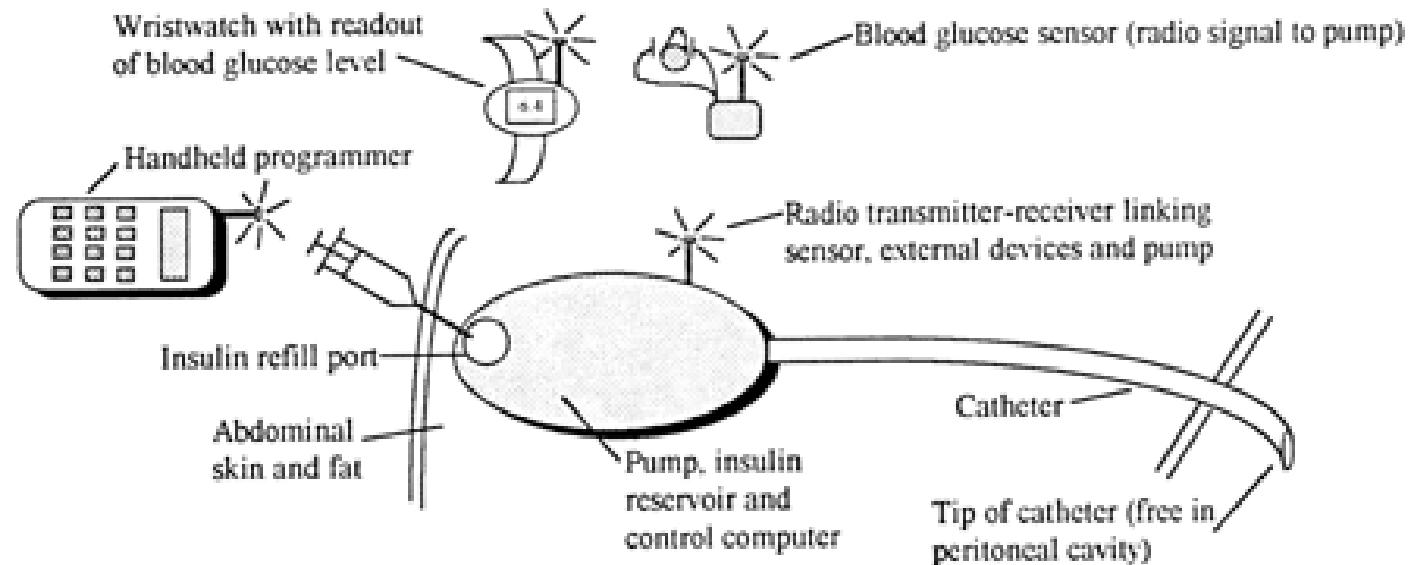
# Hemodialysis



# Pancreas Structure

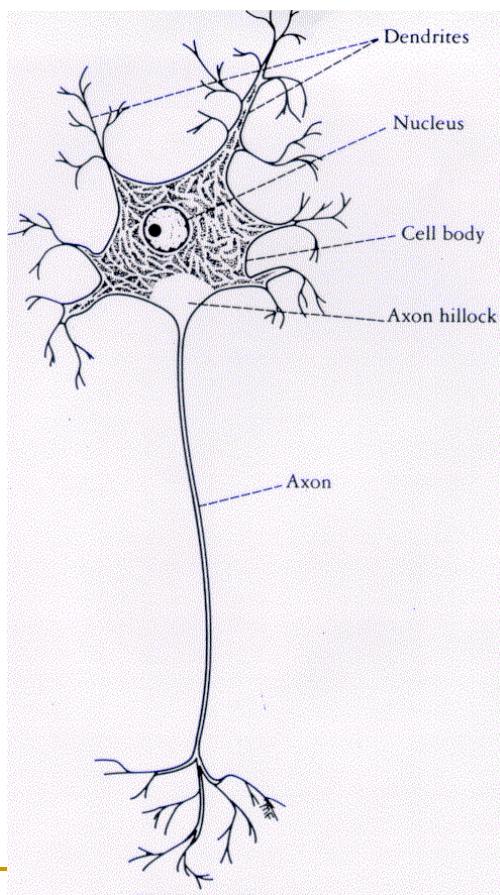


# Artificial Pancreas

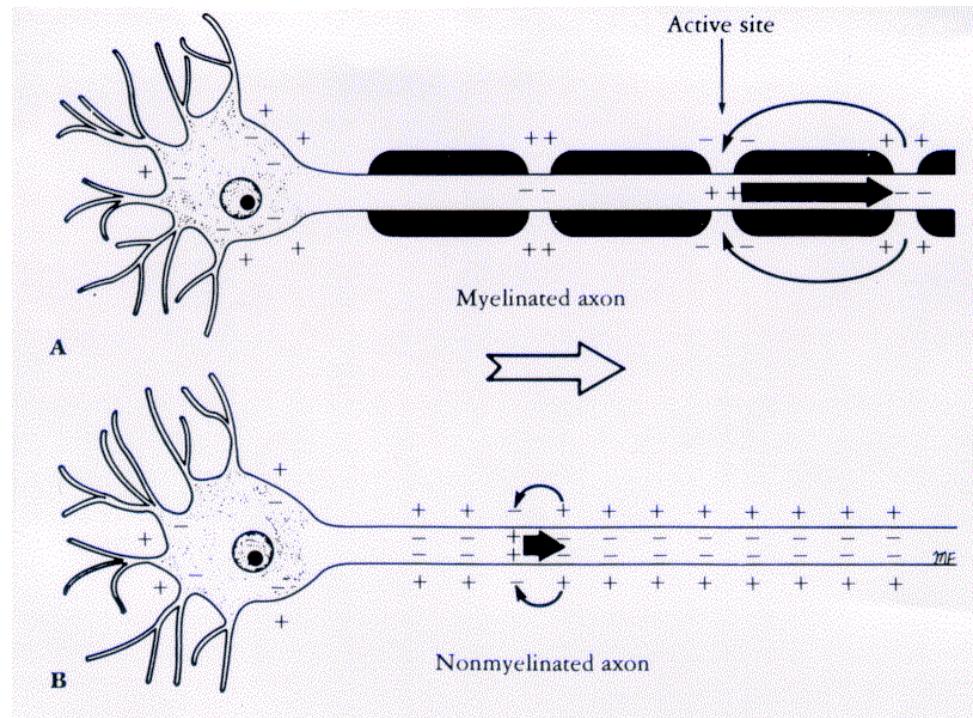


# Neurons

## Neuron Structure



## Myelinated & Unmyelinated



# Nerve Cells (Neurons)

- Nerve cells are excitable (respond to a stimulus).
  - The response is manifested by changing the electrical properties of the cell membrane.
- Transmit an electrical impulse.
- Human nervous system has  $1 \times 10^{10}$  neurons (nerve cells).
- They cannot be recreated, they can only be reduced by such things as smoking, drinking, aging and the environment.
- A cell structure generally has:
  - Body (soma)
  - Axon
  - Dendrites

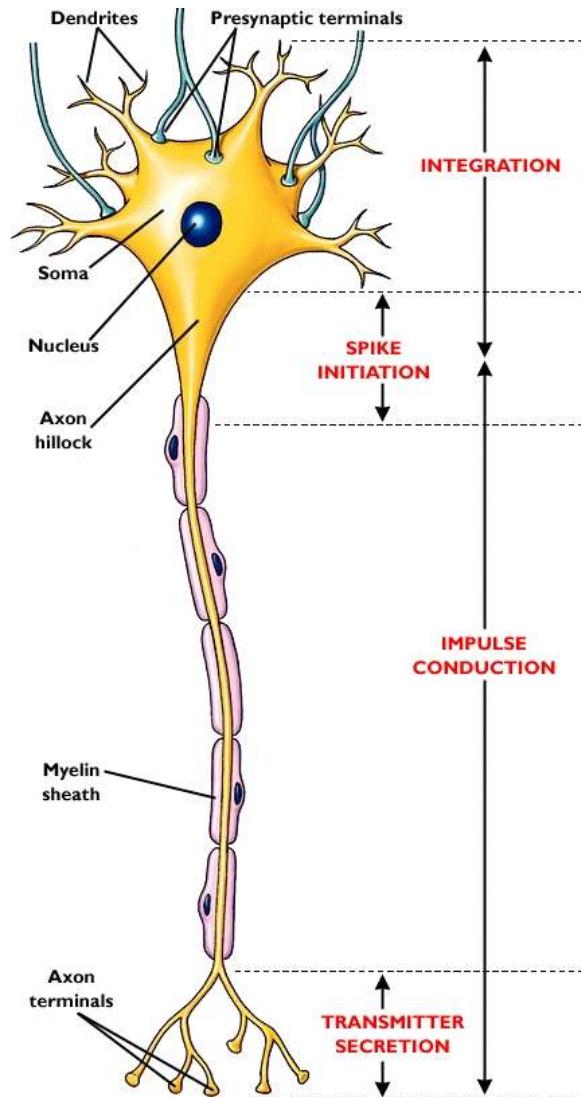


Figure 20. Electrical living cables.

<http://fig.cox.miami.edu/~lfarmer/B1L265/nerves.html>

# Nerve Cells

- The soma contains organelles (mitochondria, neurotubuli and neurofibrils - similar to muscle cells).
- Dendrites provide a large contacting area required for impulse transduction.
- Dendrites receive signals from other neurons and transmit them to the soma.
- Axons transmit signals from the soma to other neurons. The terminals are swellings called synaptic knobs.
- Synaptic knobs contain vesicles containing a neurotransmitter.

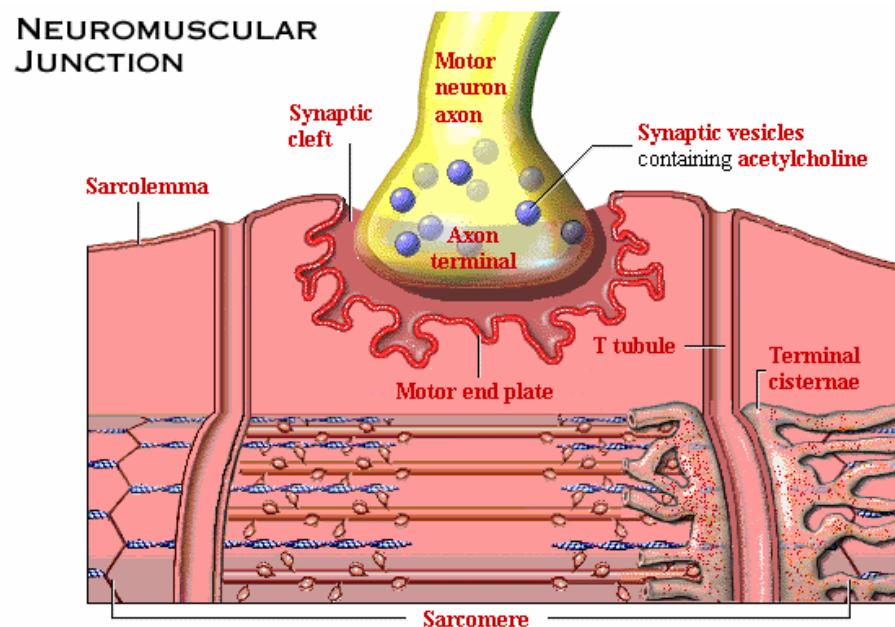
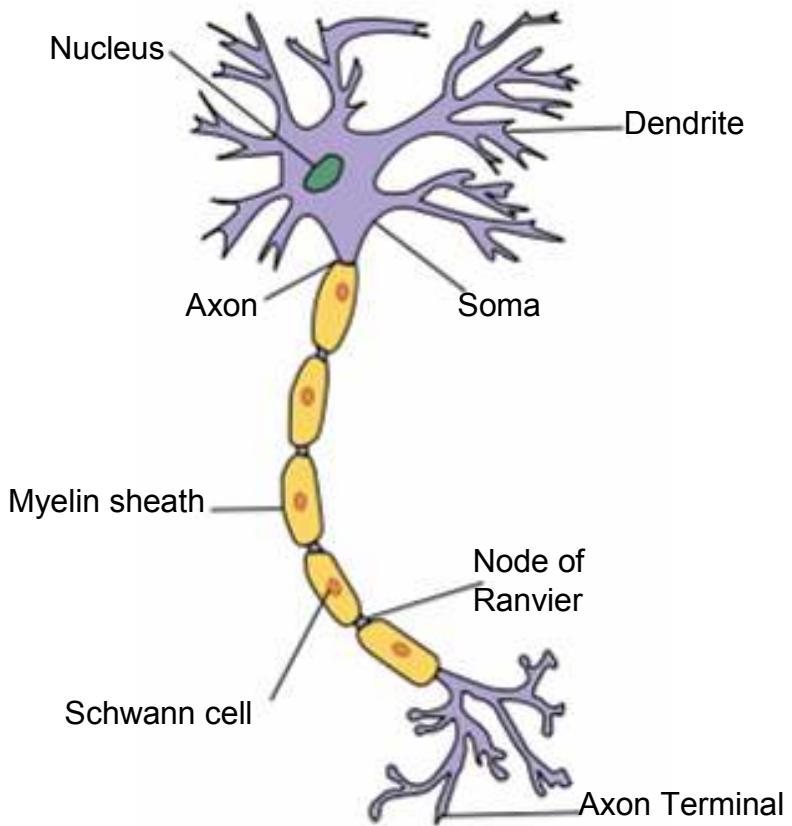


Figure 23. Synaptic structure.

# Myelin Sheath

- The axon is wrapped by Schwann cells, together forming nerve fibre.
- Schwann cells produce myelin, a lipoprotein sheath outside of the axon membrane (axolemma).
- Nodes of Ranvier are intervals along the axon providing areas without myelin.
- Although Schwann cells are present, they do not form the myelin sheath at the Node of Ranvier.
- The velocity of conduction increases at the Node of Ranvier.

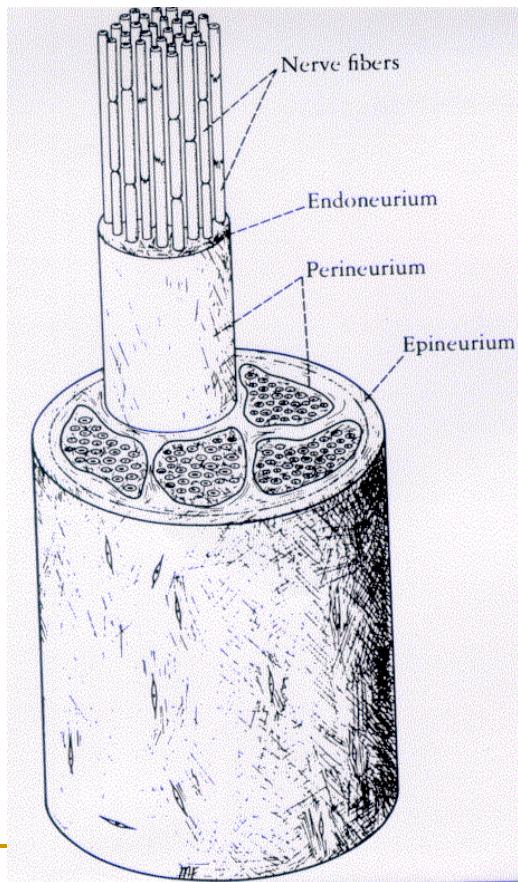


**Figure 21.** Neuron.

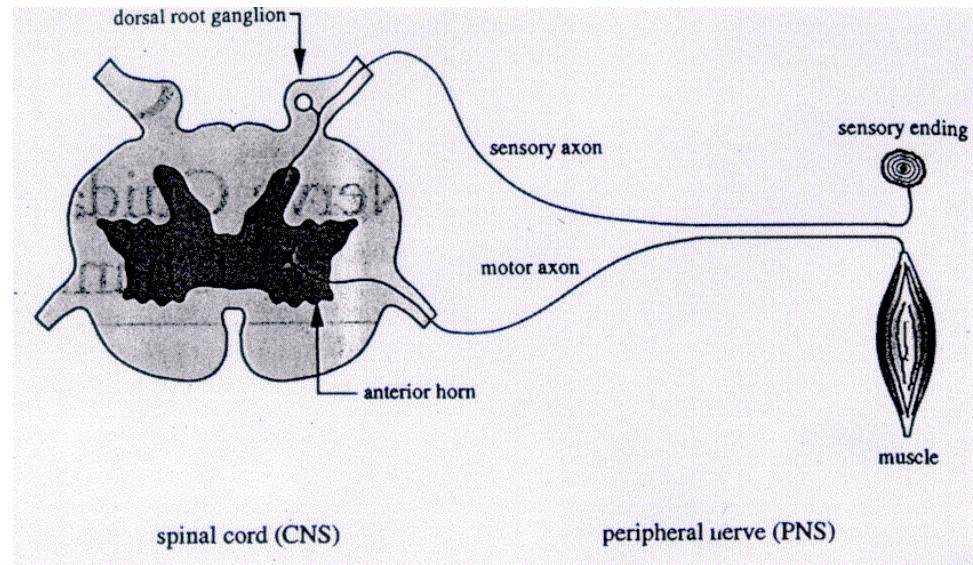
# Nerve Cells (Neurons)

# Nerves

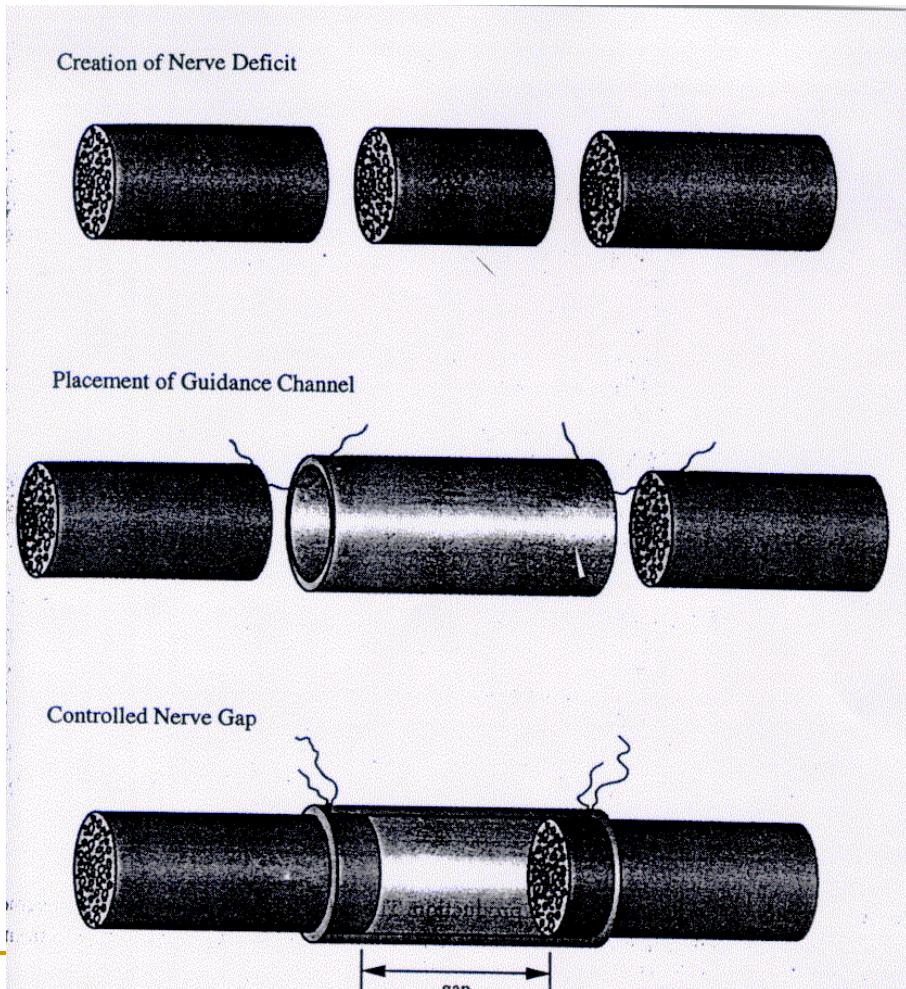
## Peripheral Nerve Structure



## Peripheral Nerve Fiber

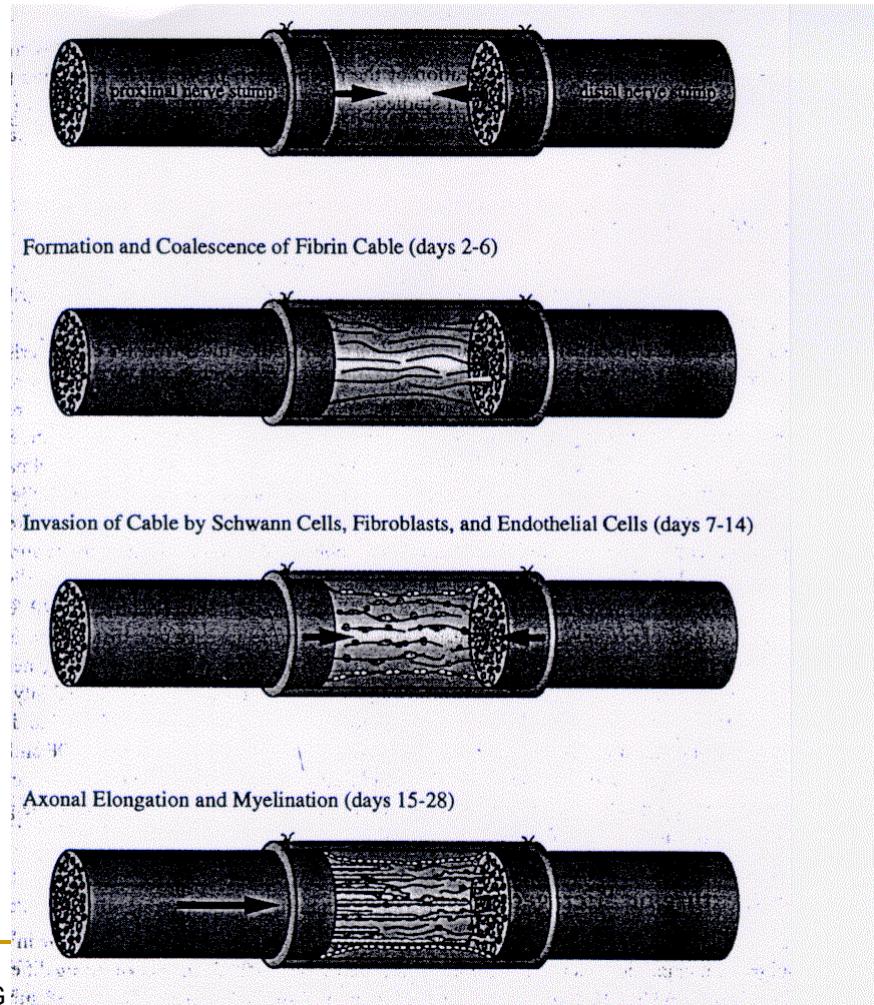


# Nerve Regeneration Techniques



Tube to repair nerve

# Nerve Regeneration Techniques



Nerve Regeneration  
in Guidance Channel