Cardiovascular System

Major Functions

- Main functions of the cardiovascular system:
  - Respiration
    - Transport of O_2 and CO_2
  - Nutrition
    - Supply of carbs, amino acids, fats, vitamins, etc.
  - Excretion
    - Removal of metabolic products, urea and creatinine
  - Maintenance of hydration
    - Intracellular and interstitial fluids

Major Functions

- Main functions (continued)
  - Maintenance of body temperature
    - Supply and removal of heat from tissue
  - Regulation of tissue and organ function
    - Delivery of hormones
  - Protection
    - Delivery of sentinels: antibodies, leukocytes
  - Responsiveness
    - All above functions must meet varying demands of the tissues

Cardiovascular System

- Major structures
  - Perfusion fluid: medium for mass transfer
    - Blood
      - Red blood cells
        - Hemoglobin
      - White blood cells
      - Plasma
        - Electrolyte fluid
        - Non-cellular constituents of blood

Cardiovascular System

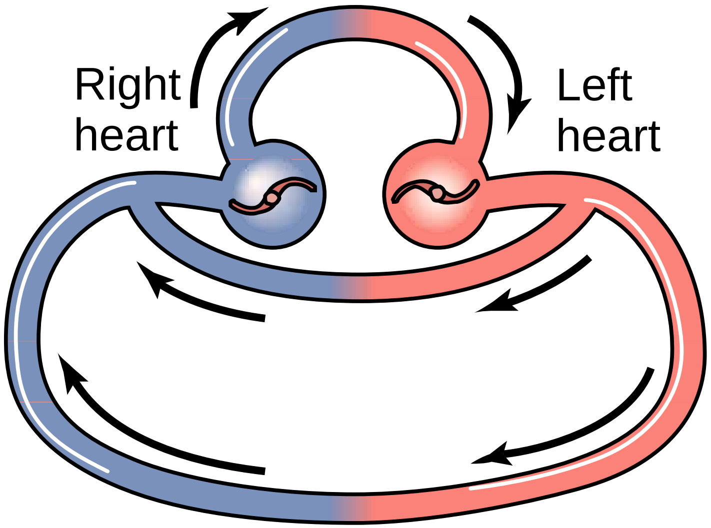
- Distribution conduits
  - Blood vessels
    - Arteries (supply)
    - Veins (return)
    - Capillaries (mass transport)
- Energy source – Pump
  - Heart

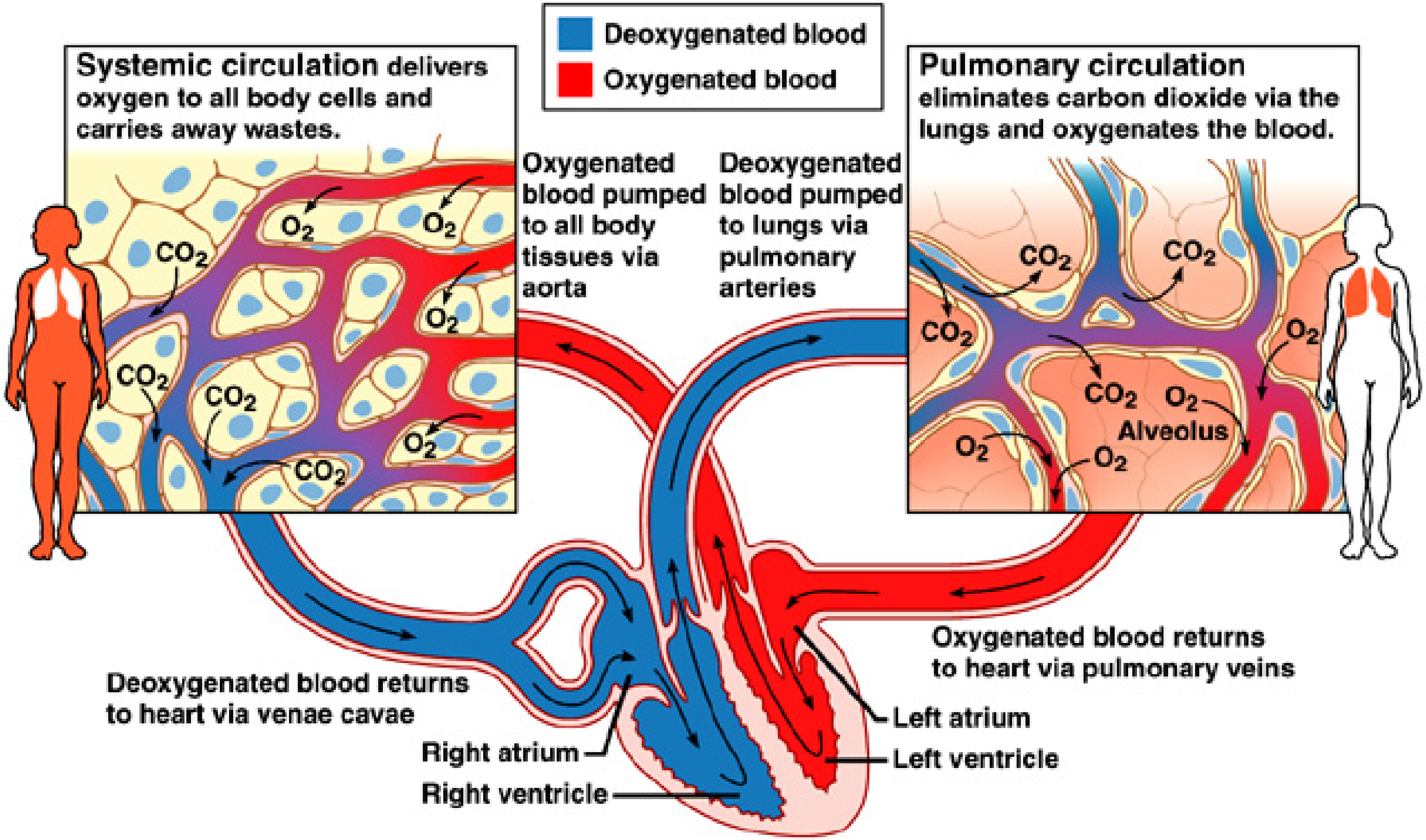
Cardiovascular System

- Regulators
  - Feedback system
    - Autonomic nervous system
    - Autoregulation
    - Hormonal control
- Focus of this module will be on:
  - Conduits, pump, and their combined function

General Anatomy

- Heart
  - 2 pumps in series
    - One pumps de-oxygenated blood to the lungs
      - Pulmonary circulation – right side
    - One pumps oxygenated blood to the body
      - Systemic circulation – left side



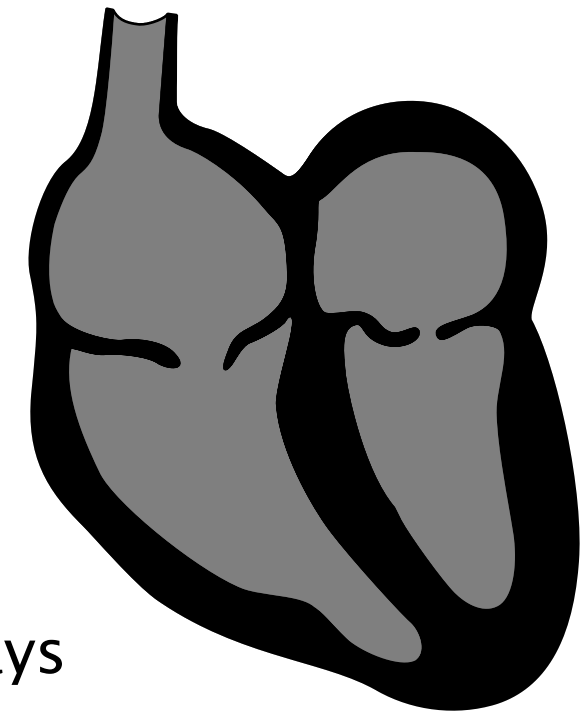


The double pump

General Anatomy

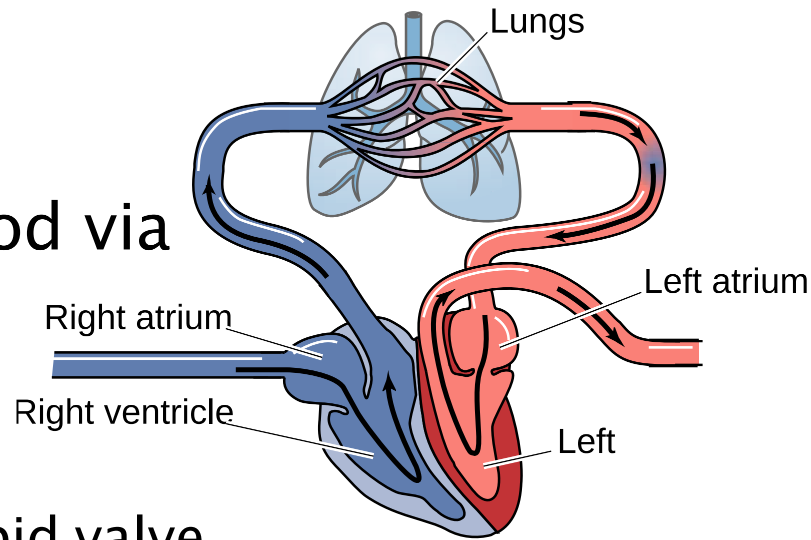
- Each side has two chambers
  - Atrium
    - Priming pump
  - Ventricle
    - Higher pressure pump

  - Heart weighs ~ 300g
  - Pumps 100,000 times per day
  - Moves 7000 L of blood per day
  - Runs continuously for ~ 30,000 days



Circulation Route

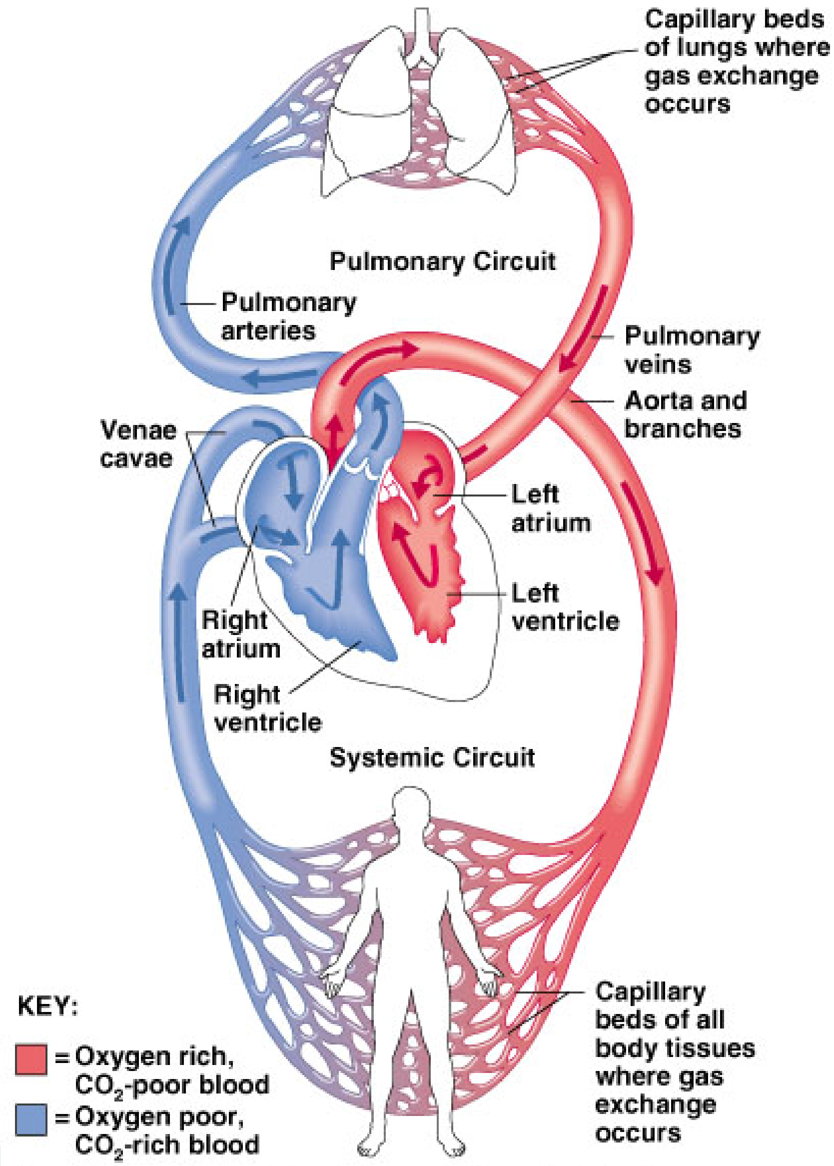
- Right Heart
  - Receives deoxygenated blood via
    - Inferior and superior vena cava
      - Empty into the right atrium
  - Right Atrium contracts
    - Blood flows through the tricuspid valve
      - Into the right ventricle
  - Right Ventricle contracts
    - Blood flows through the pulmonary valve (3 leaflets)
    - Out the pulmonary arteries (left and right)
  - To the lungs
    - Returns through the pulmonary veins



Circulation Route

- Pulmonary veins fill the Left Atrium
- Left Atrium contracts
  - Blood flows through the bicuspid (mitral) valve
    - Fills the left ventricle
- Left Ventricle contracts
  - Blood flows through the aortic valve (3 leaflets)
  - Into the Aorta
    - To the systemic circulation

Blood Circulation

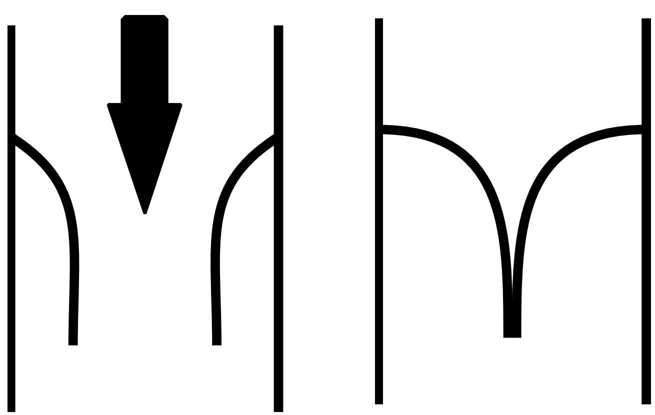


Valves

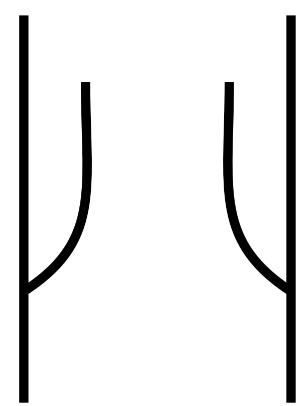
- 4 main valves to prevent backflow
  - Tricuspid, pulmonary, mitral, and aortic
  - Keep blood moving in the correct direction
  - Failure leads to various pathologies including heart failure
    - Many successful engineered heart valves

Valves

- A / V valve (atrioventricular) structure
  - Mitral and tricuspid valves
  - Made of leaflets
    - Which are pushed closed by back pressure



Prolapse

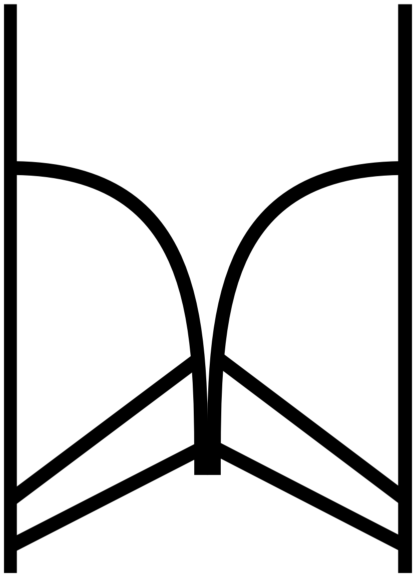


Why doesn't this happen?

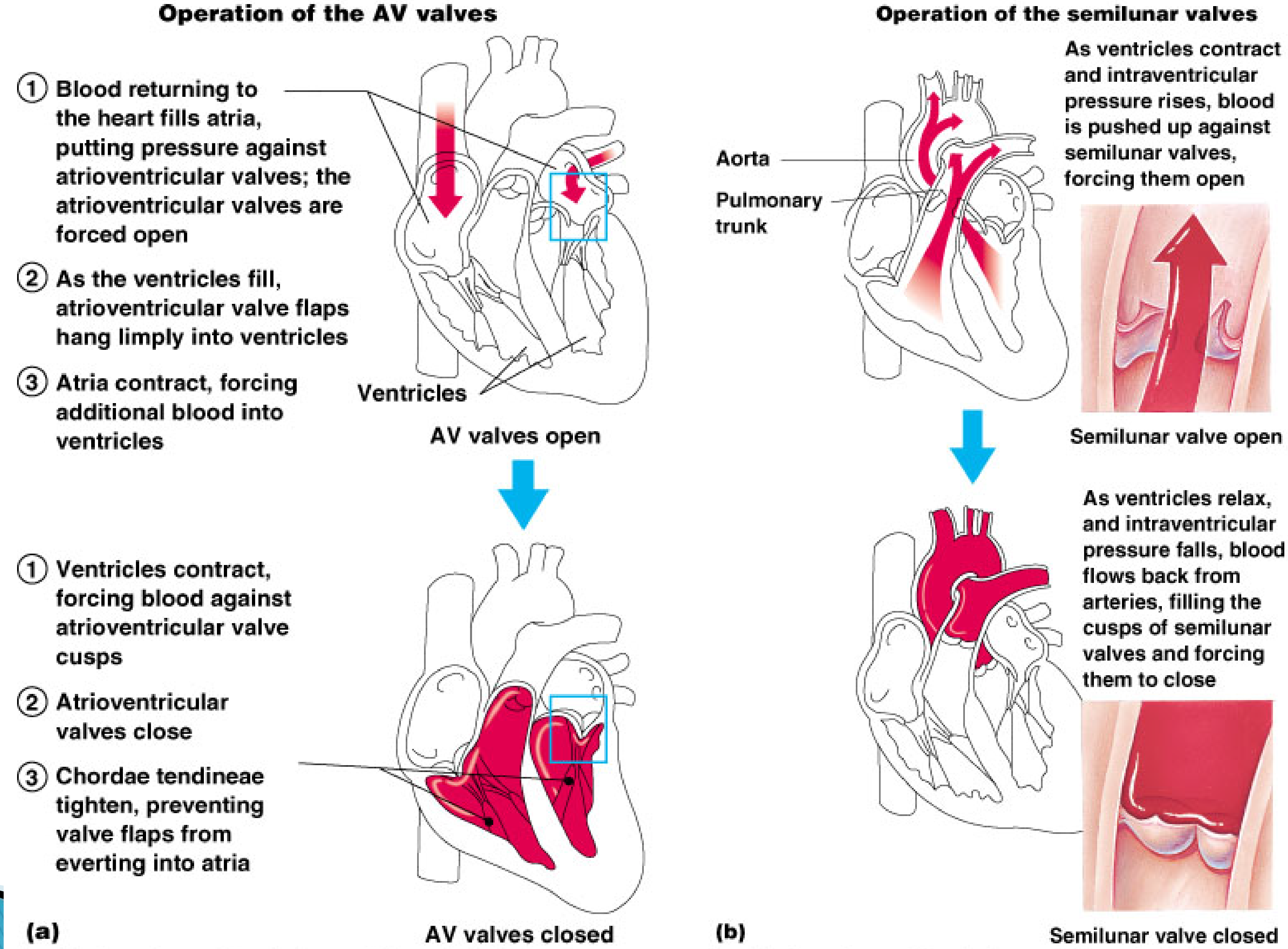
Valves

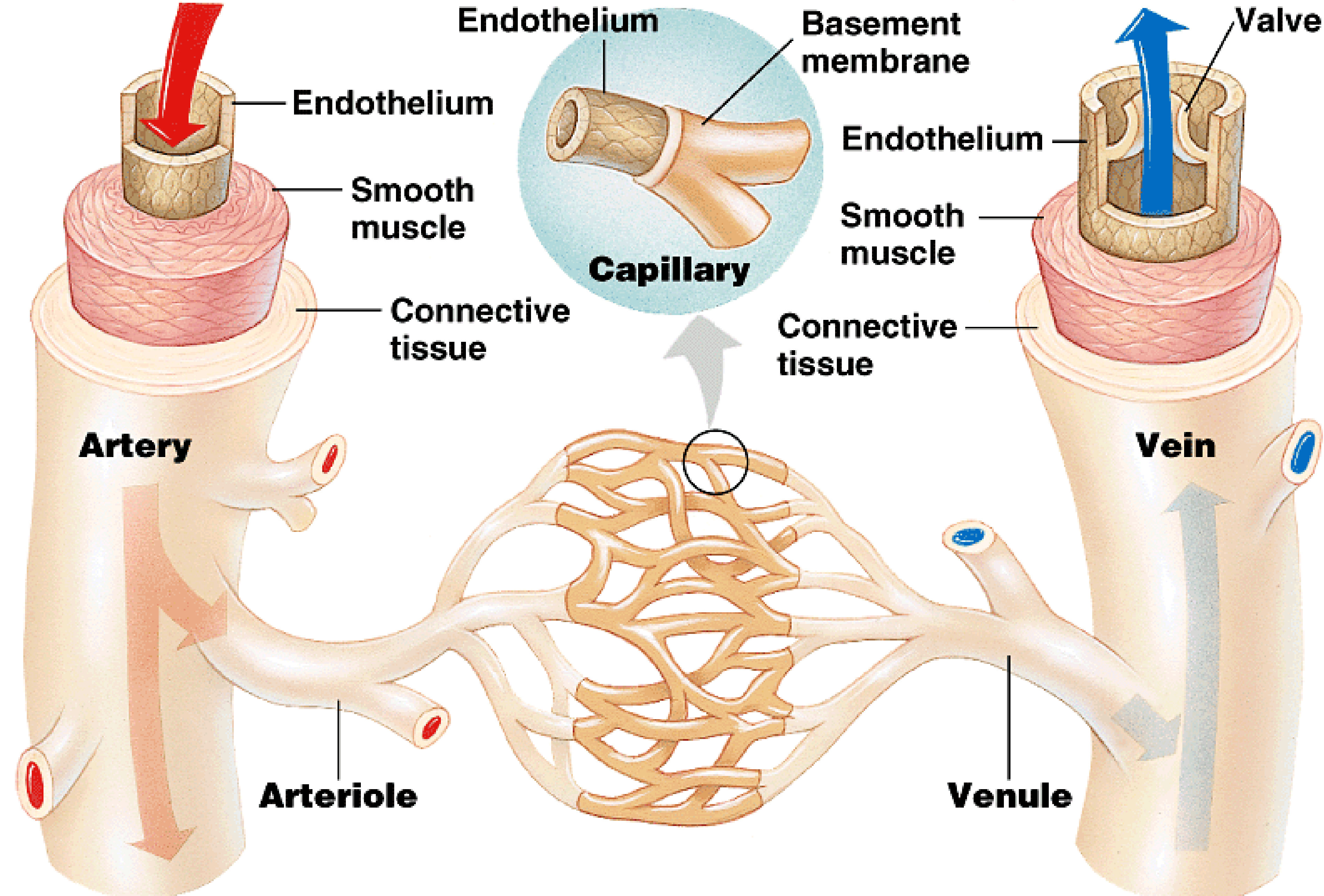
- End of leaflets are tethered to the wall by
  - Chordae Tendinae
  - Tension is regulated by small muscles
    - Papillary muscles
  - Prevents prolapse under pressure
  - Held in place by chordae tendineae

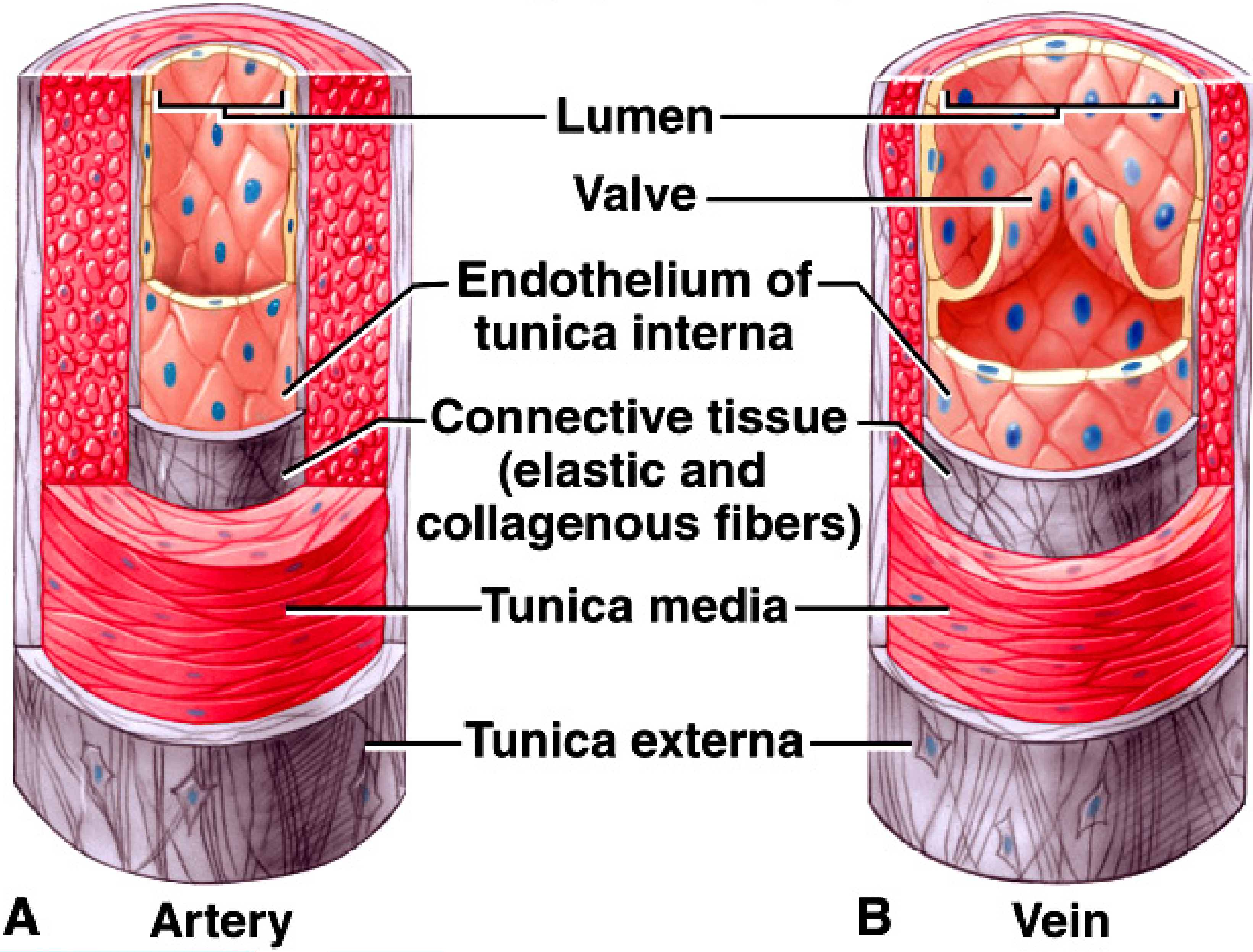
(“heart strings”)

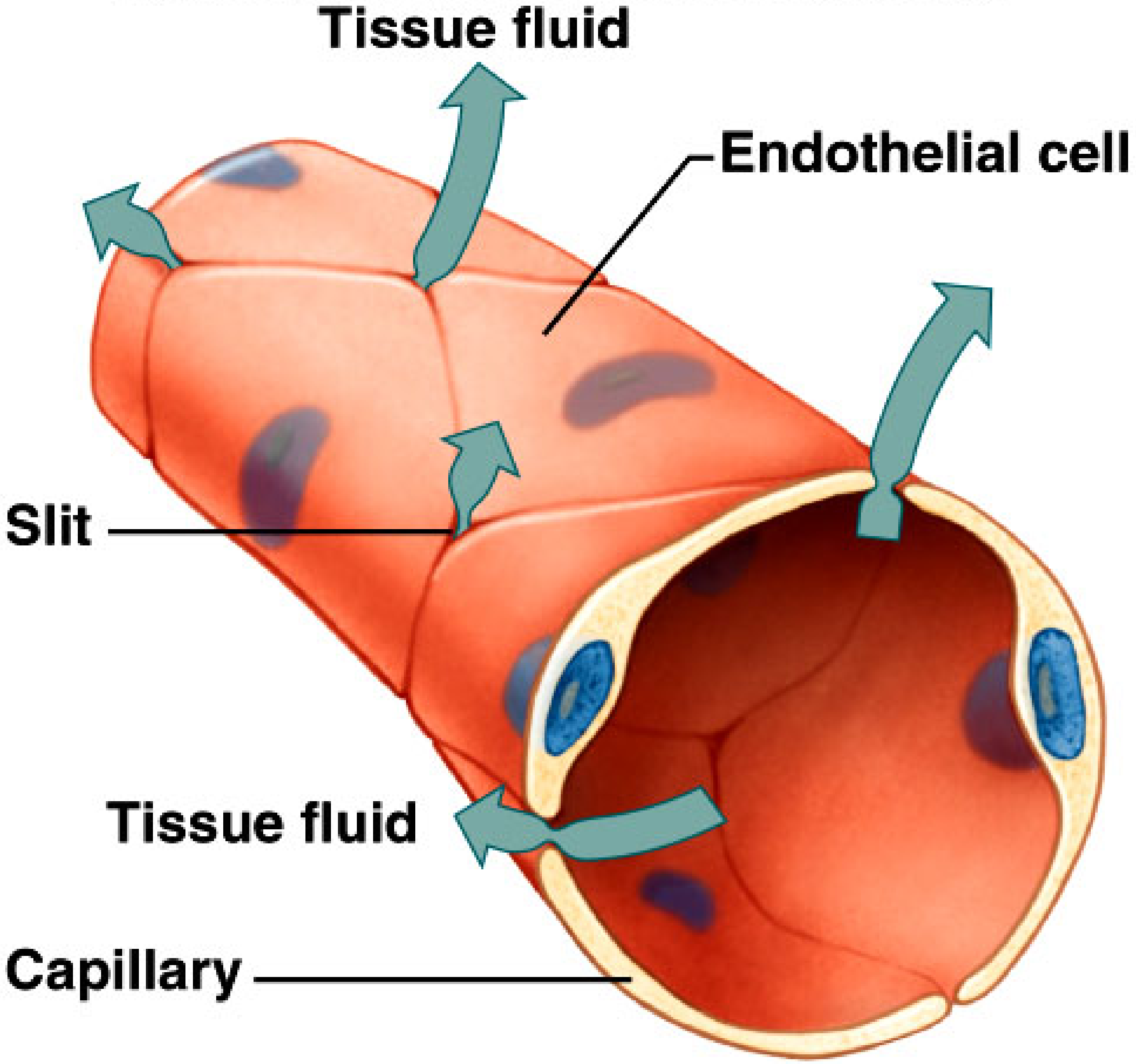


Operation of Heart Valves



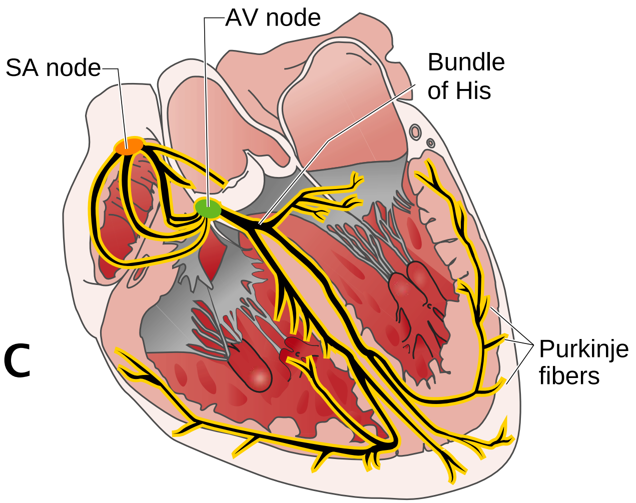

Endothelium
Basement membrane
Valve
Endothelium
Endothelium
Smooth muscle
Smooth muscle
Connective tissue
Connective tissue
Capillary
Artery
Vein
Arteriole
Venule

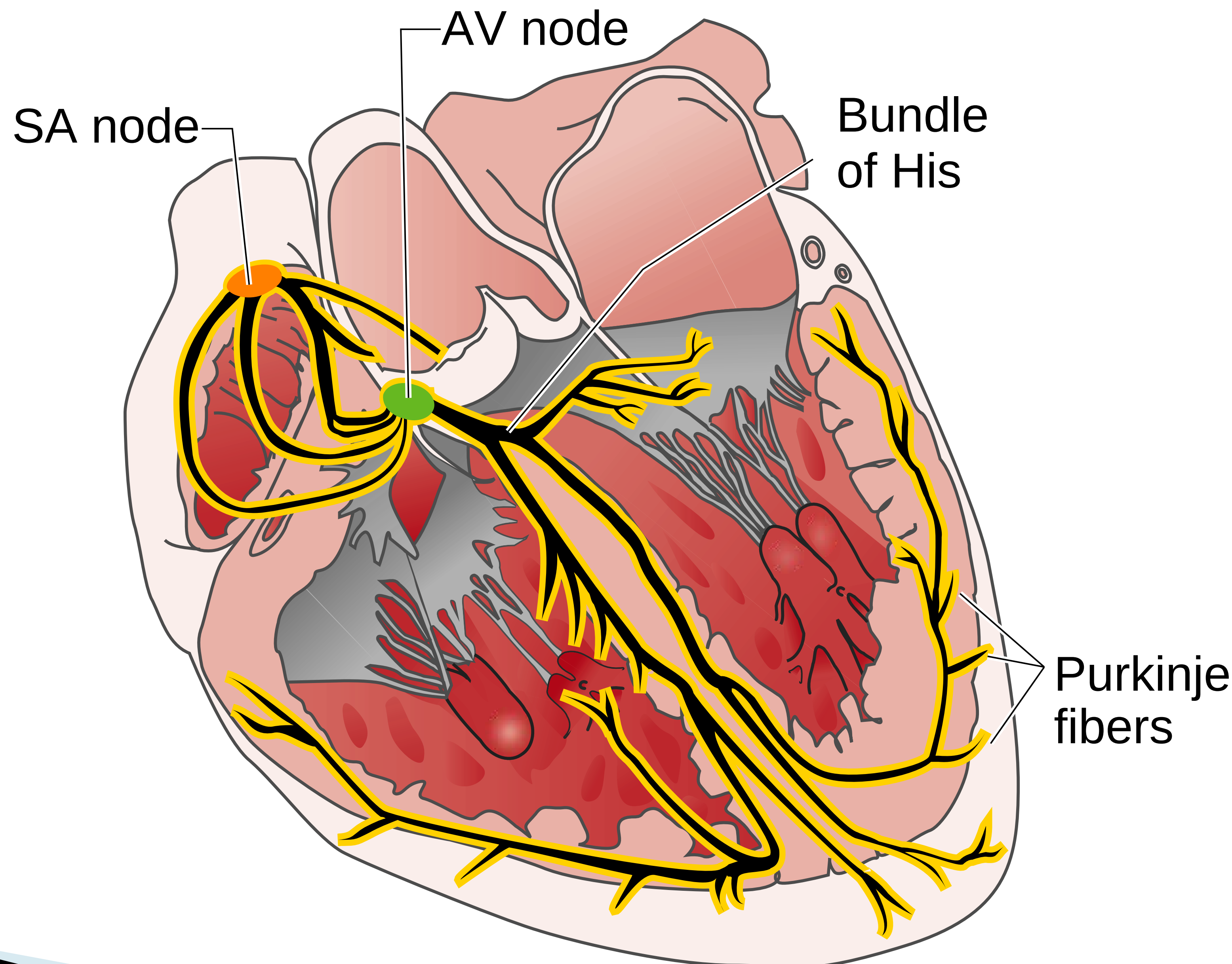

Lumen
Valve
Endothelium of tunica interna
Connective tissue (elastic and collagenous fibers)
Tunica media
Tunica externa
A
Artery
B
Vein


Tissue fluid
Endothelial cell
Slit
Tissue fluid
Capillary

Pacemaker Cells

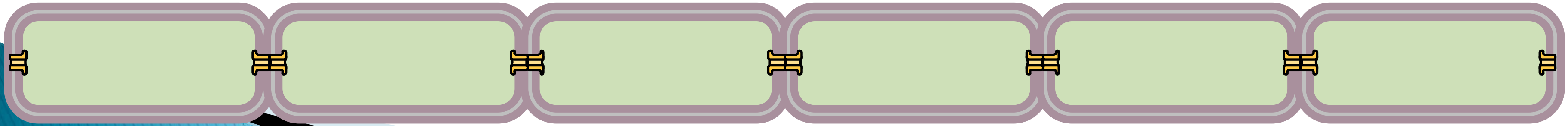
- Distinct structures control the electrical impulses
  - Sino Atrial Node (SA)
  - Atrioventricular Node (AV)
  - Purkinje fibers
- Pacemakers of the heart
  - Spontaneously generate rhythmic depolarizations




AV node
SA node
Bundle of His
Purkinje fibers

Myocytes

- The electrical impulses in the fibers
  - Depolarize the surrounding tissue
  - Myocytes undergo contraction
  - Electrical signal is propagated between myocytes through gap junctions
    - The muscle cells are electrically coupled
      - Propagation is similar to cable equation
        - Dead tissue can break conduction
        - Result of heart attacks



20.2

Propagation

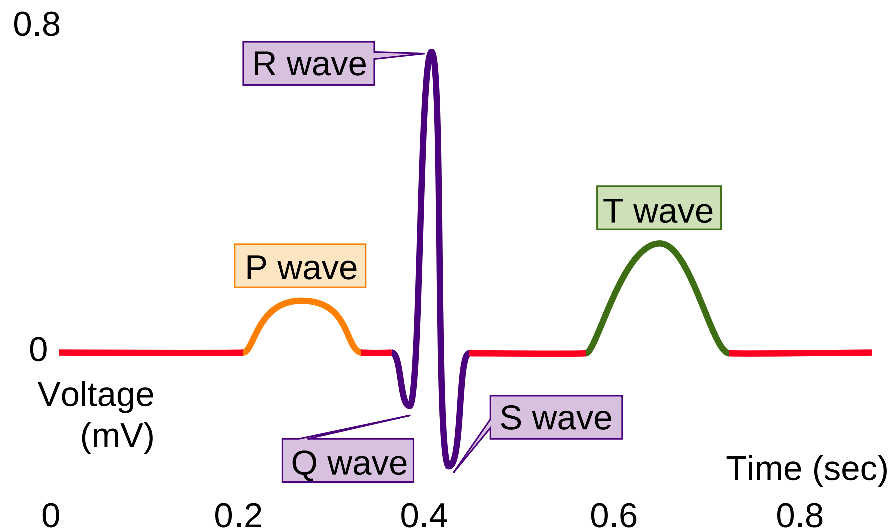
- Depolarization begins at the fibers
  - Depolarizes neighboring cells
  - Potential is propagated to surrounding cells
    - Through gap junctions
- Cable equation in 3-D
  - Passive propagation
  - Active propagation (channel kinetics)
    - Myocytes have a threshold
    - Fire a cardiac action potential
      - $V_{rest} \sim -80mV$
      - $V_{th} \sim -60mV$

Cardiac Action Potential

- The myocytes fire an action potential
  - Similar to neuronal action potential
    - Different phases
    - Different currents are active
- 3 main currents
  - I_{Na+} rapid depolarization
  - I_{Ca++} rapid depolarization and plateau
  - I_{K+} repolarization

Clinical ECG

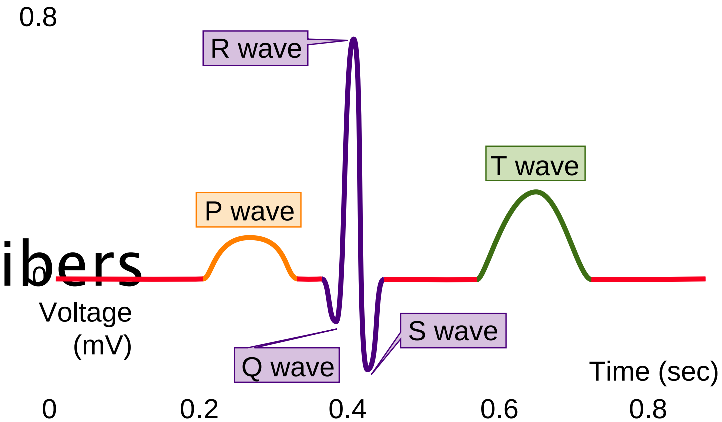
- A simplified ECG recording (~V_{III})
- Major waves are given names
  - Correspond to structures



Clinical ECG

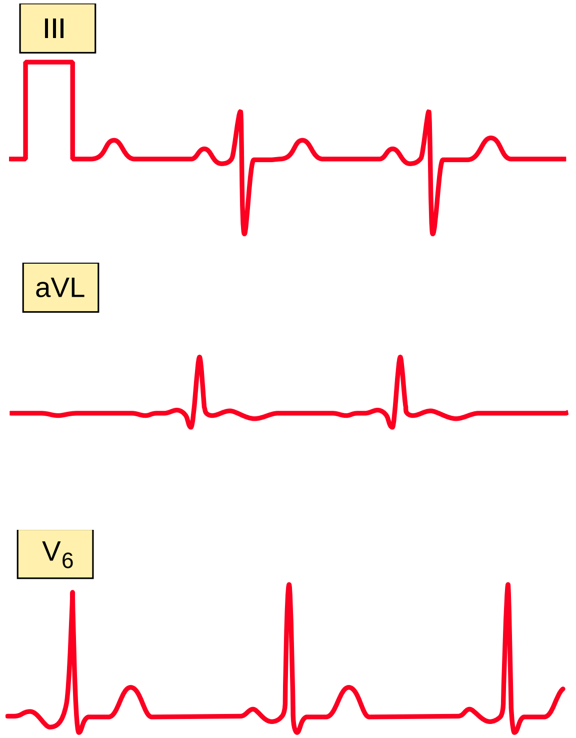
- P: depolarization of the atria
- QRS: depolarization of the ventricles
- T: repolarization of the ventricles

- Can’t see certain events
  - Repolarization of the atria
  - Depolarization of the Purkinje fibers



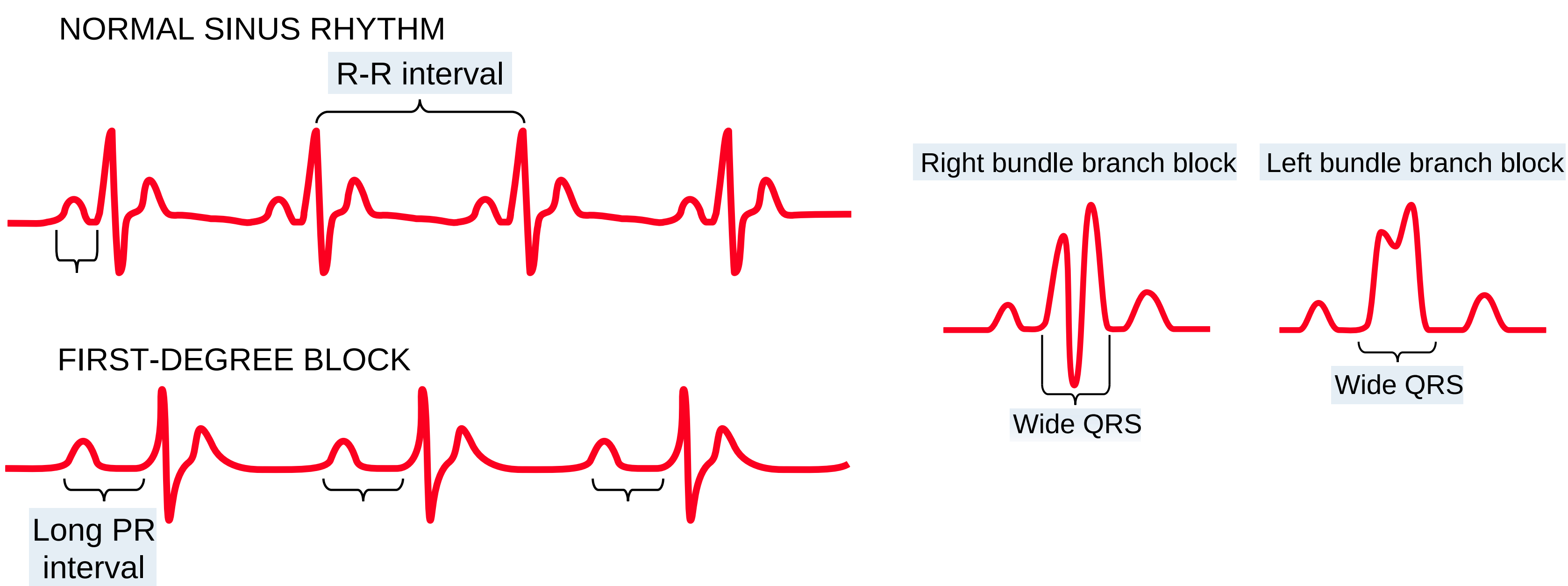
Clinical ECG

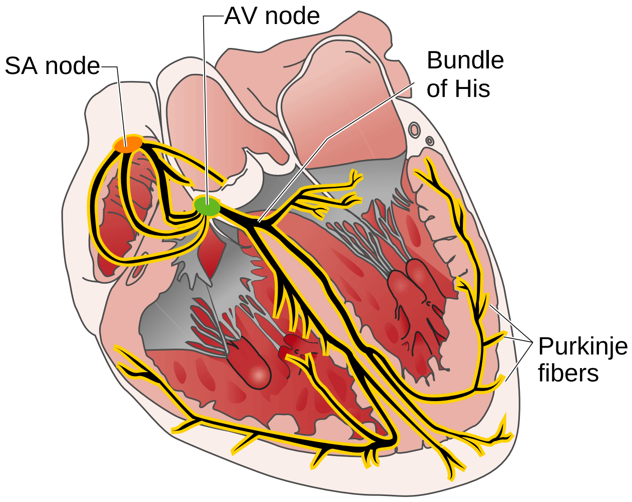
- The heart vector is displayed differently on each lead
  - Signal was recorded synchronously on all channels



ECG as a Diagnostic Tool

- Study the output of all 12 leads
  - Pathology displays a characteristic change





Pacemaker

Historical Perspective

- 1958 – Senning and Elmqvist
  - Asynchronous (VVI) pacemaker implanted by thoracostomy and functioned for 3 hours
  - Arne Larsson
    - First pacemaker patient
    - Used 23 pulse generators and 5 electrode systems
    - Died 2001 at age 86 of cancer

Historical Perspective

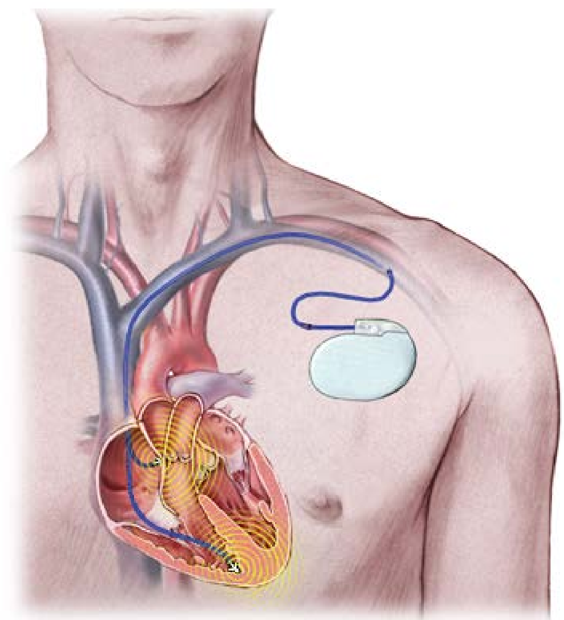
- 1960 – First atrial triggered pacemaker
- 1964 – First on demand pacemaker (DVI)
- 1977 – First atrial and ventricular demand pacing (DDD)
- 1980 – Griffin published first successful pacemaker intervention for supraventricular tachycardias

Historical Perspective

- 1981 – Rate responsive pacing by QT interval, respiration, and movement
- 1994 – Cardiac resynchronization pacing
- 1998 – Automatic capture detection
- Now
    - Approximately 3 million with pacemakers

Pacemaker Basics

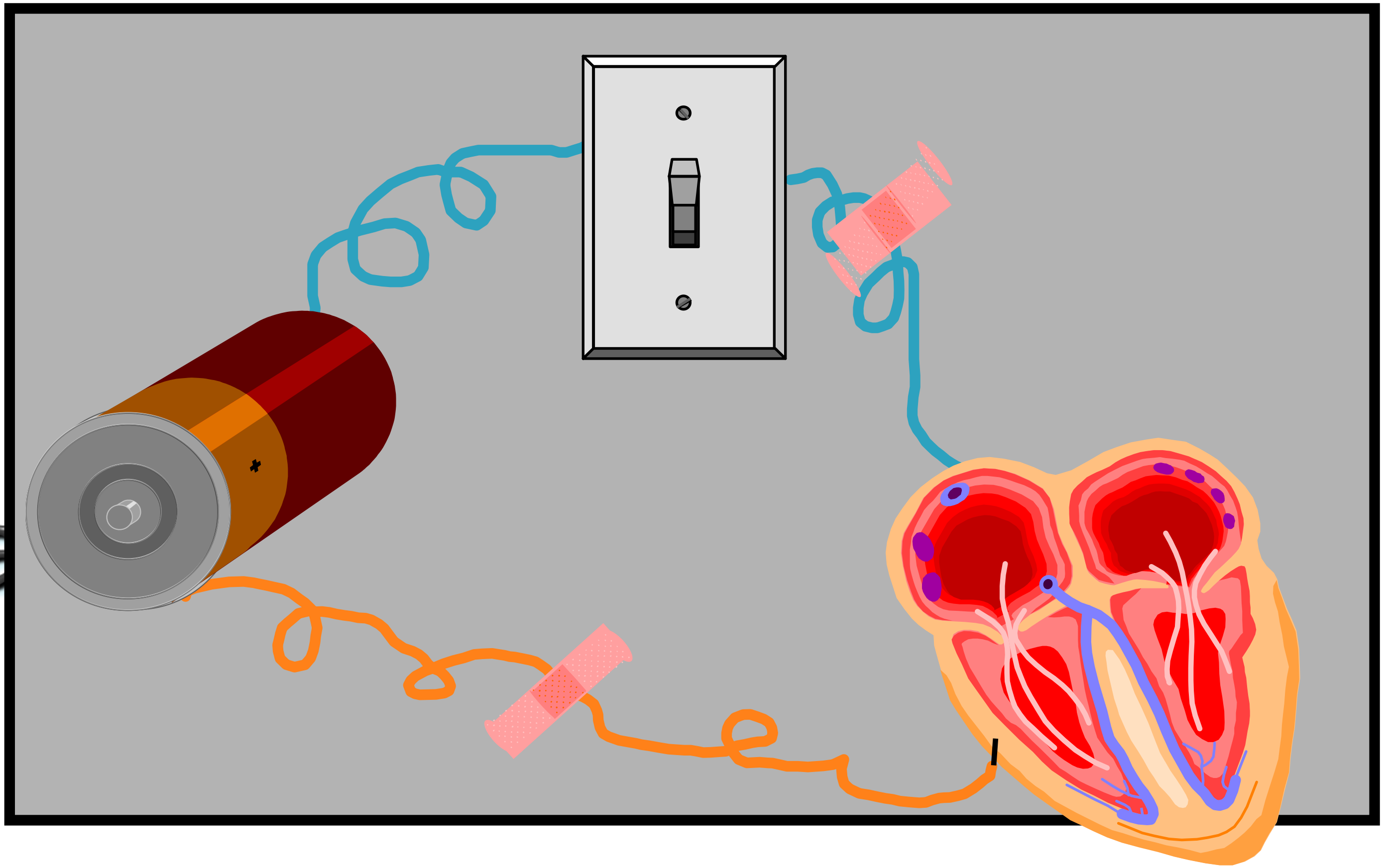
- Provides electrical stimuli to cause cardiac contraction when intrinsic cardiac activity is inappropriately slow or absent
- Sense intrinsic cardiac electric potentials



Pacemaker Basics

- Designed to treat a cardiac tachydysrythmia
- Performs cardioversion/defibrillation
  - Ventricular rate exceeds programmed cut-off rate
- ATP (antitachycardia pacing)
  - Overdrive pacing in an attempt to terminate ventricular tachycardias
- Some have pacemaker function (combo devices)

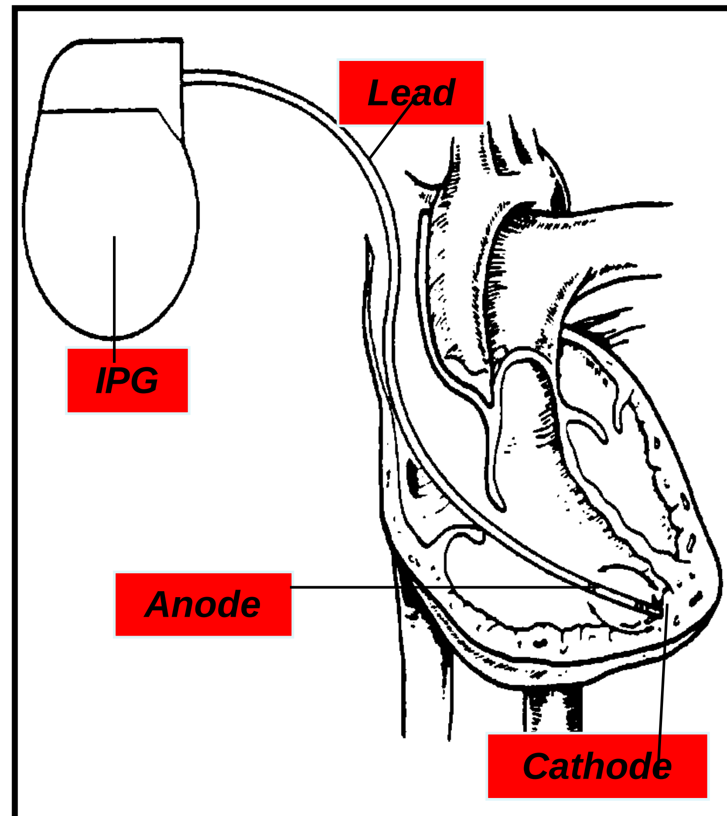
Wha



- A Pacemaker System consists of a **Pulse Generator** plus **Lead (s)**

Implantable Pacemaker Systems Contain the Following Components:

- Pulse generator– power source or battery
- Leads
- Cathode (negative electrode)
- Anode (positive electrode)
- Body tissue



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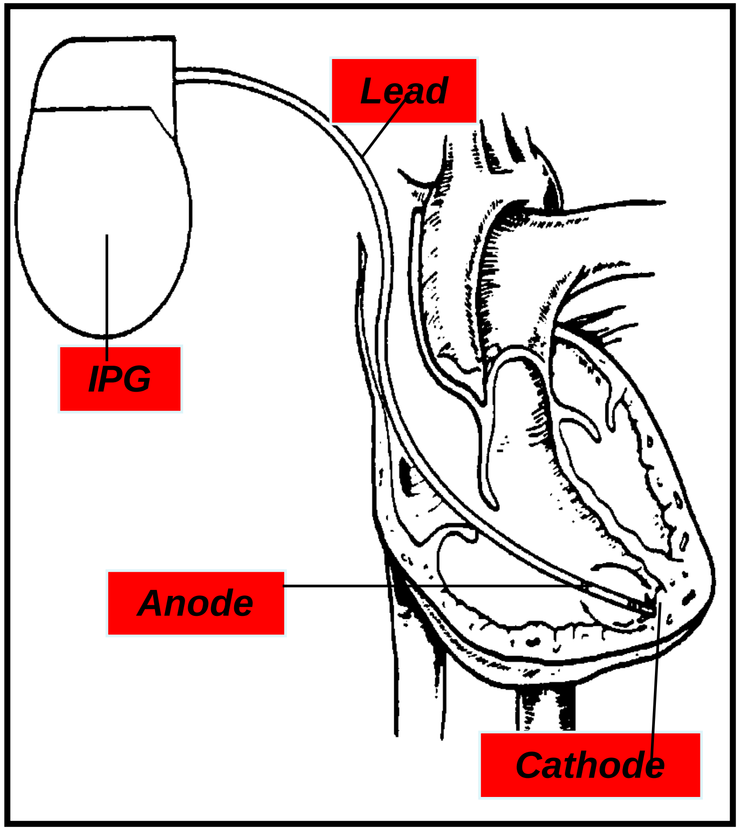
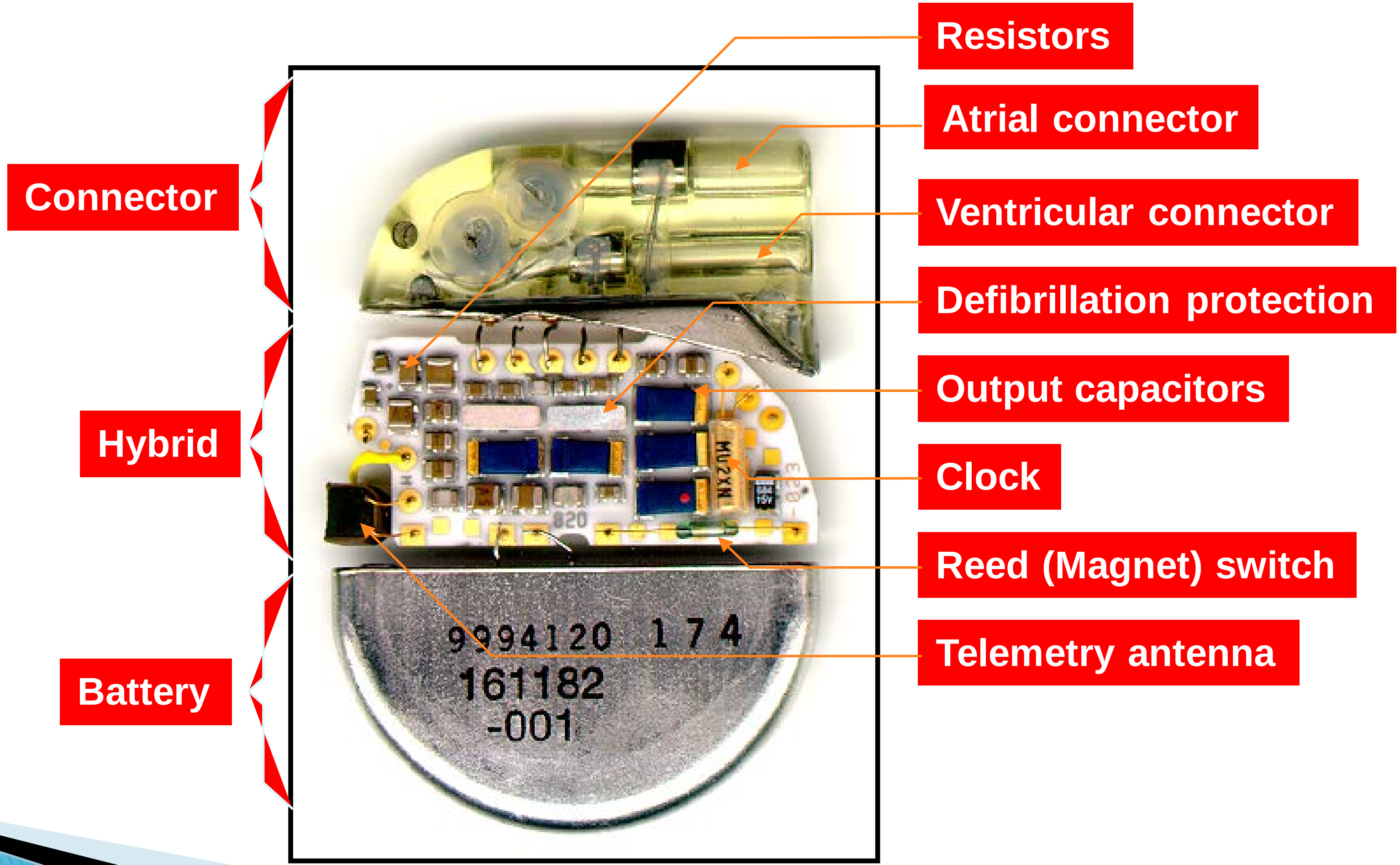
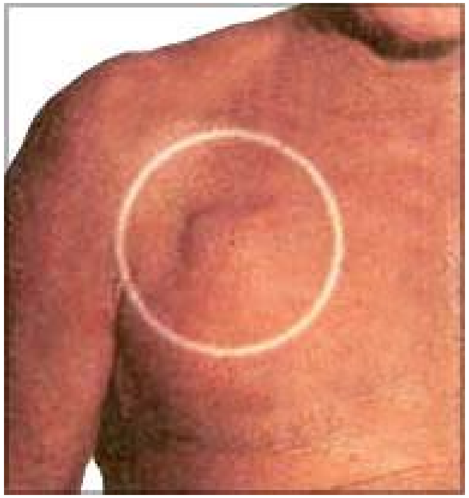


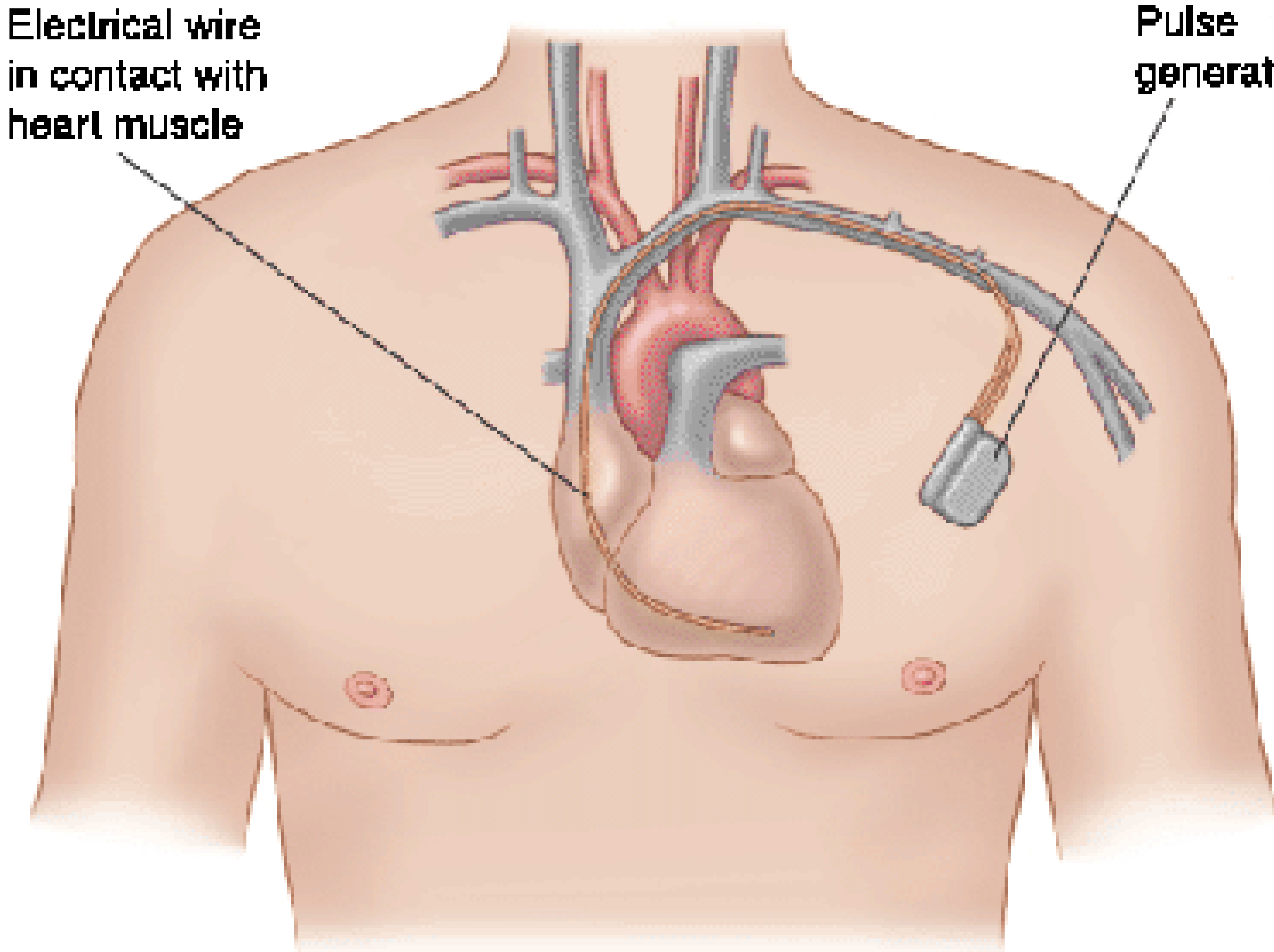
Anatomy of a Pacemaker



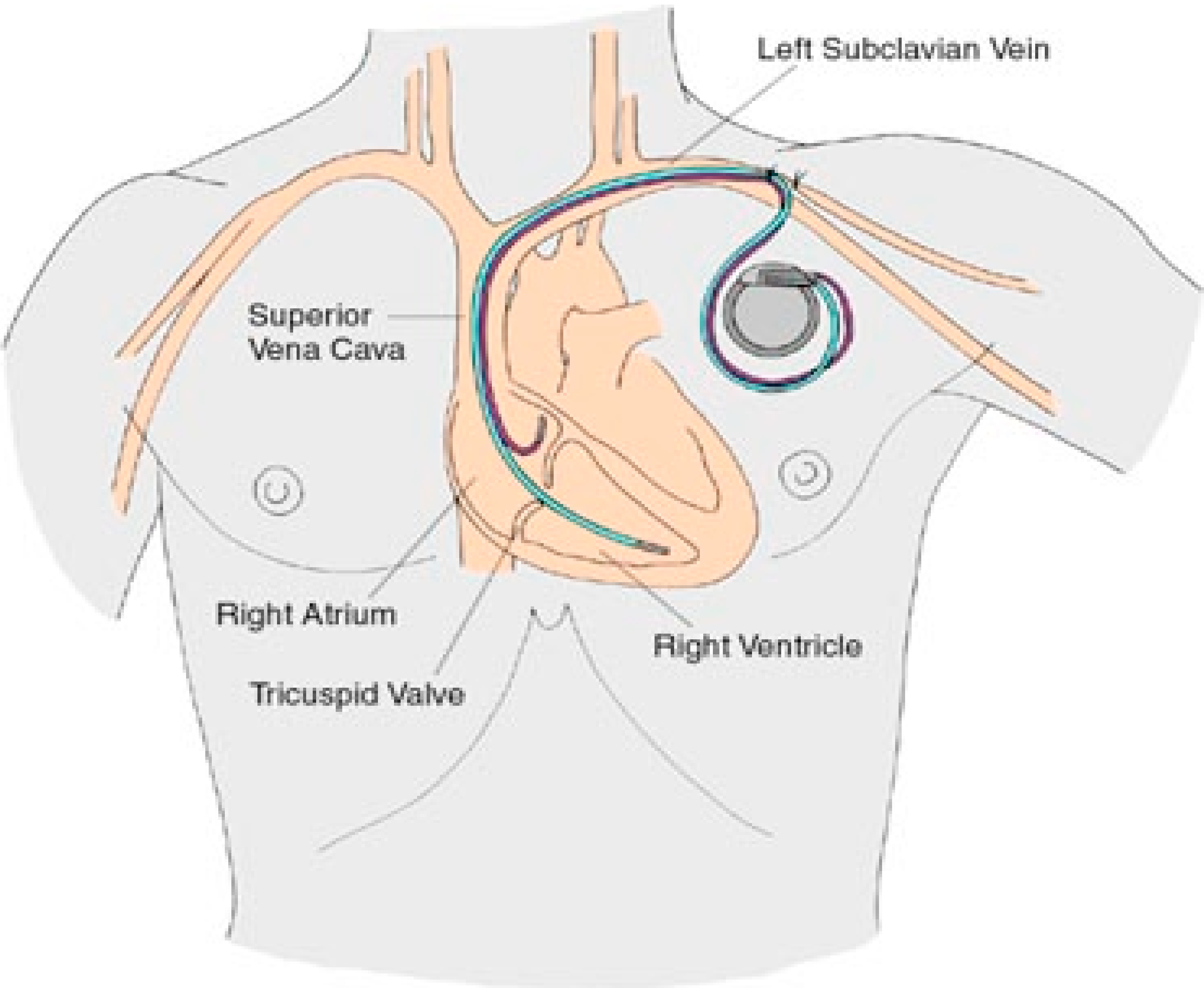
Pacemaker Basics

- Pulse Generators
  - Placed subcutaneously or submuscularly
  - Connected to leads
  - Battery
    - Most commonly lithium-iodide type
    - Life span 5 to 8 years
    - Output voltage decreases gradually
      - Makes sudden battery failure unlikely



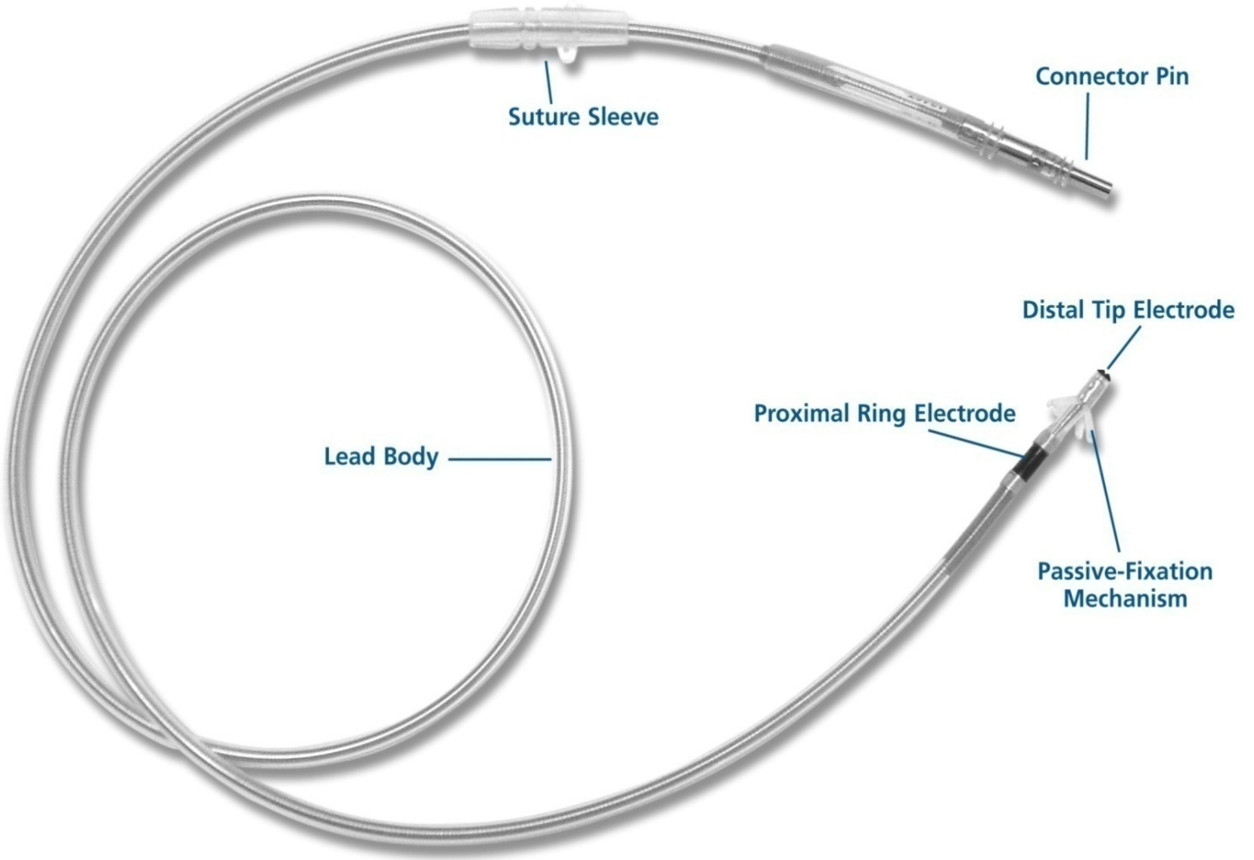

Electrical wire
in contact with
heart muscle
Pulse
generator

Dual-Chamber Pacemaker



Lead components

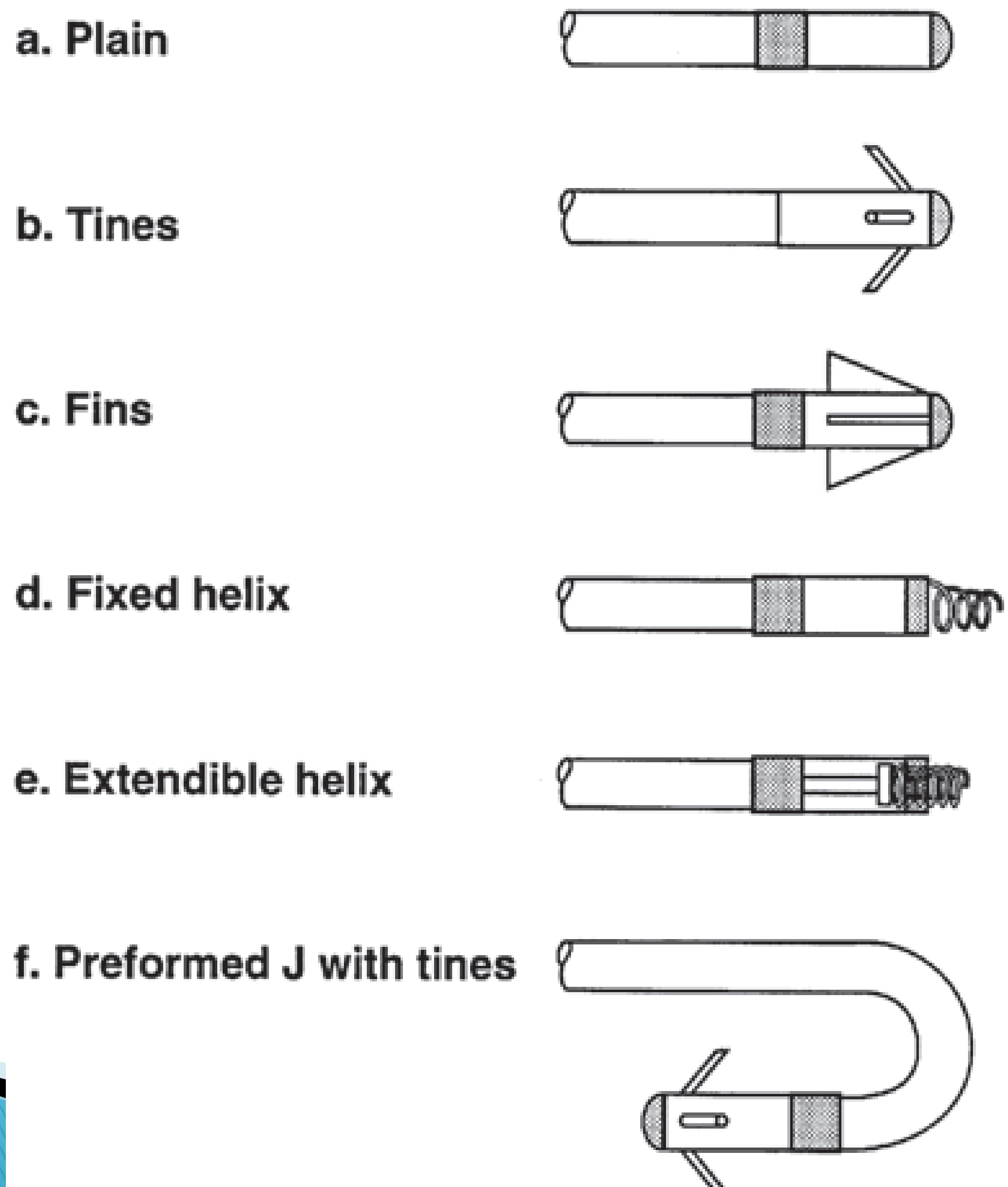
- Conductor
- Connector Pin
- Insulation
- Electrode



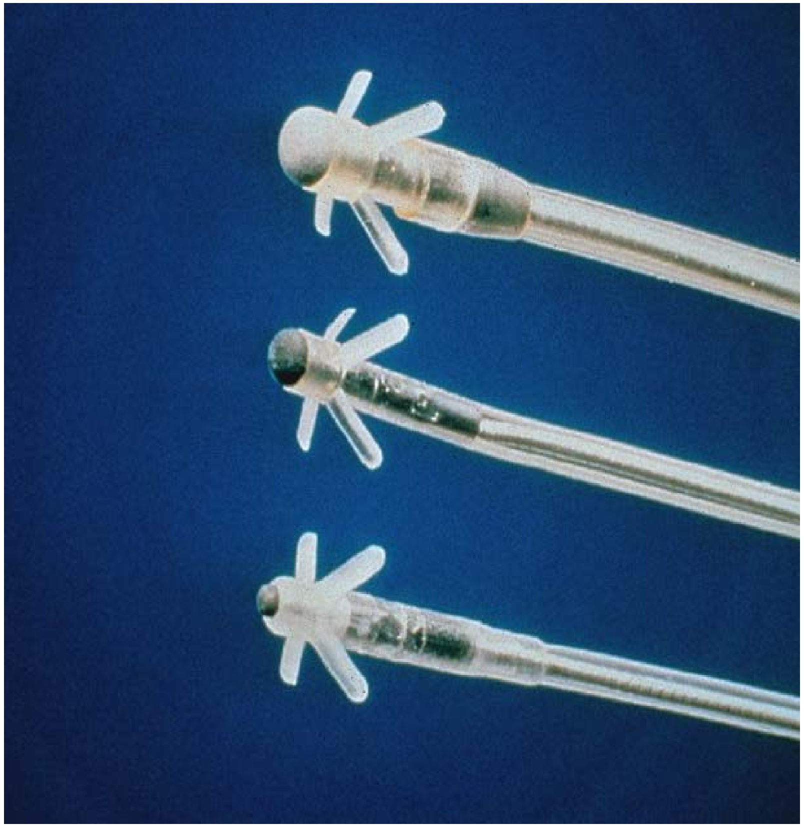
Lead Characterization

- Position within the heart
  - Endocardial or transvenous leads
  - Epicardial leads
- Fixation mechanism
  - Active/Screw-in
  - Passive/Tined
- Shape
  - Straight
  - J-shaped used in the atrium
- Polarity
  - Unipolar
  - Bipolar
- Insulator
  - Silicone
  - Polyurethane

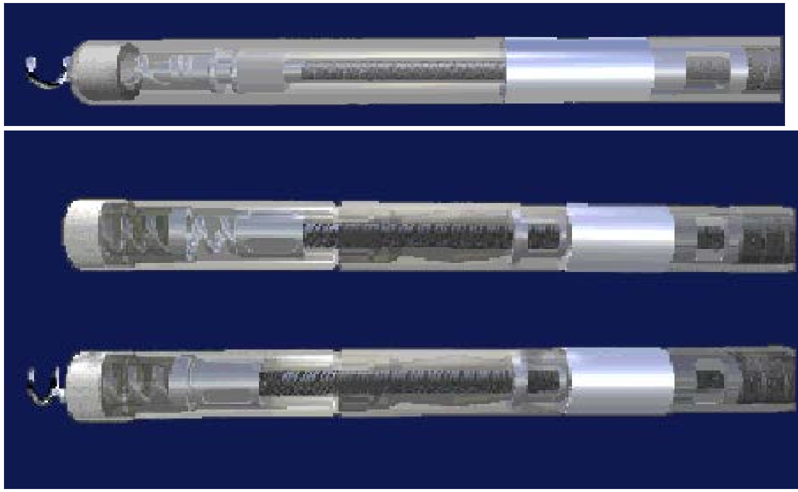
Transvenous Leads – Fixation Mechanisms



- Passive fixation
  - The tines become lodged in the trabeculae

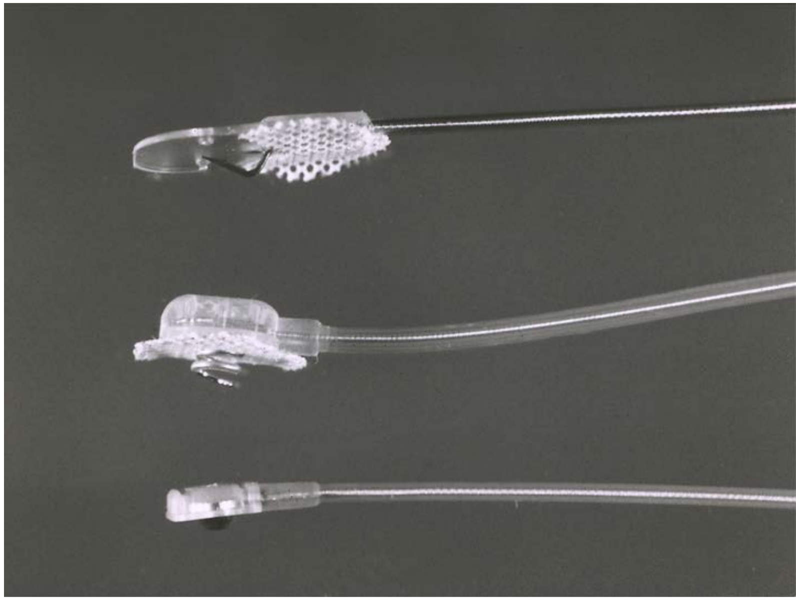


- Active Fixation
  - The helix (or screw) extends into the endocardial tissue
  - Allows for lead positioning anywhere in the heart's chamber



Myocardial and Epicardial Leads

- Leads applied directly to the heart
  - Fixation mechanisms include:
    - Epicardial stab-in
    - Myocardial screw-in
    - Suture-on



	Active Fixation	Passive Fixation
Advantages	Easy fixation Easy to reposition Lower rate of dislodgement Removability	Less expensive & simple Minimal trauma to patient Lower thresholds
Disadvantages	More expensive >Complicated implantation	Higher rate of dislodgement (>a/c) Difficult to remove chronic lead

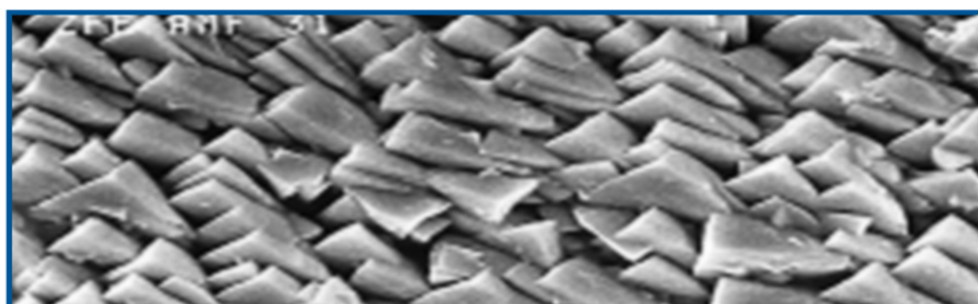
Electrodes

- Deliver an electrical stimulus, detect intrinsic cardiac electrical activity, or both

- Electrode performance can be affected by
  - Materials
  - Polarization
  - Impedance
  - Pacing thresholds
  - Steroids

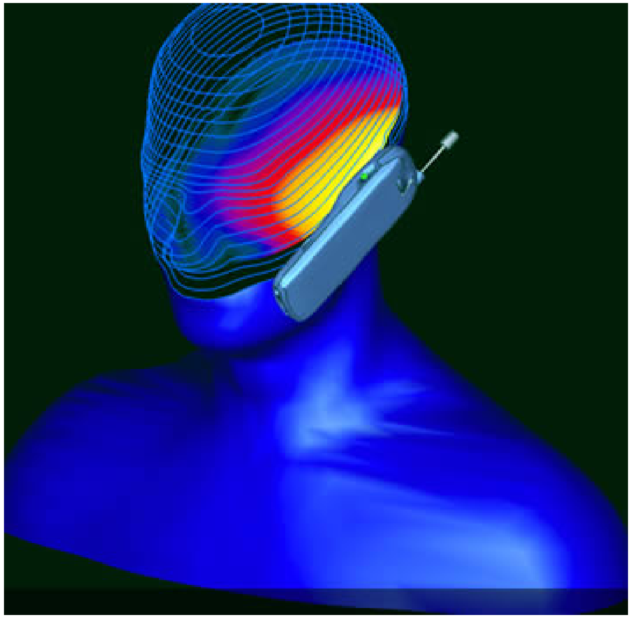
Electrode Materials

- The ideal material for an electrode
  - Porous (allows tissue ingrowth)
  - Should not corrode or degrade
  - Small in size but have large surface area
  - Common materials
    - Platinum and alloys (titanium-coated platinum iridium)
    - Vitreous carbon (pyrolytic carbon)
    - Stainless steel alloys such as Elgiloy



Electromagnetic Interference

- Can interfere with function of pacemaker or ICD
- Device misinterprets the EMI causing
  - Rate alteration
  - Sensing abnormalities
  - Asynchronous pacing
  - Noise reversion
  - Reprogramming



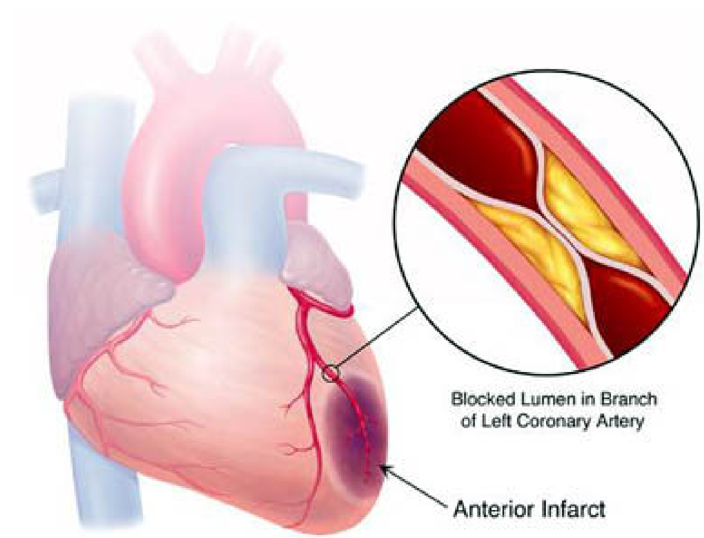
Electromagnetic Interference

- Examples
  - Metal detectors
  - Cell phones
  - High voltage power lines
  - Some home appliances (microwave)

Stent

Coronary Artery Disease

- Leading cause of death in United States for men and women
- Caused by buildup of plaque in arteries
- Heart tissue is deprived of nutrients
- Risk factors:
  - Age
  - Gender
  - Genes

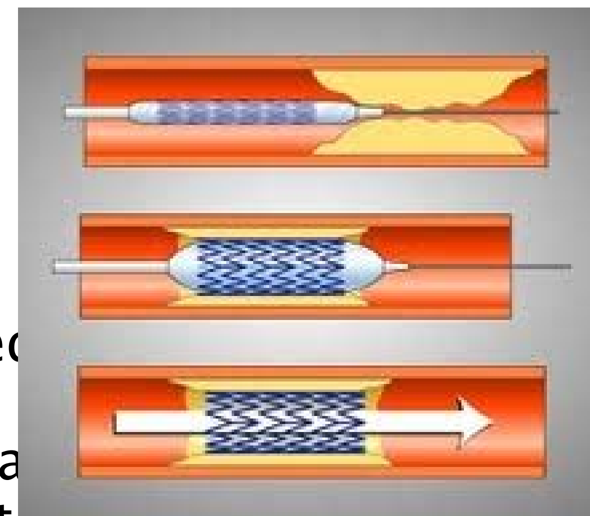


Symptoms and Tests for Coronary Artery Disease

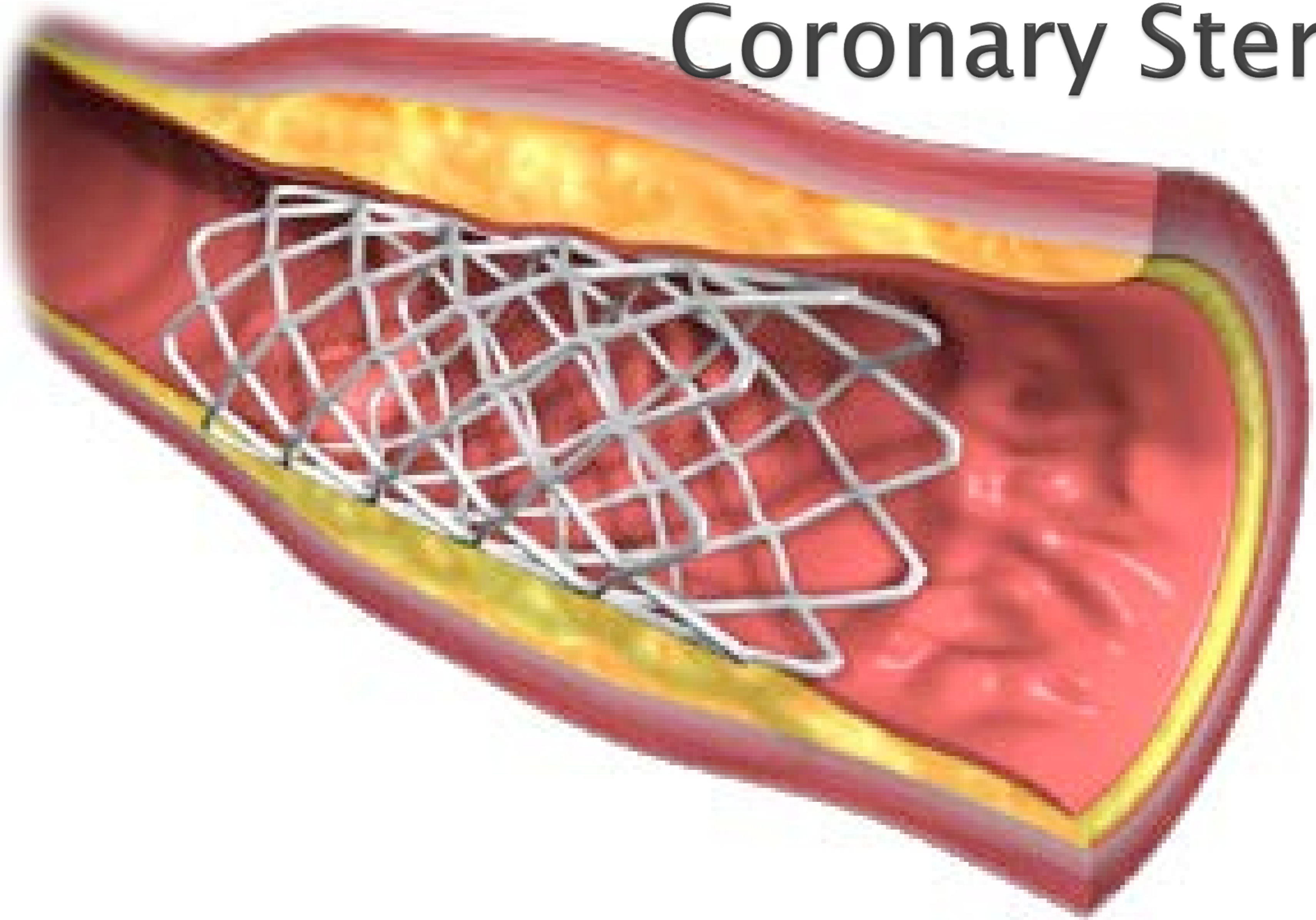
- Symptoms:
  - Vary in strength
  - Chest pain
  - Fatigue
  - Shortness of breath
  - Weakness
- Tests:
  - ECG
  - Exercise Stress Test
  - Nuclear Stress Test
  - CT Scan
  - Coronary Angiograph

Coronary Angioplasty with Stents

- Common treatment for Coronary Artery Disease
- Process:
  - Blockage is defined through coronary angiography
  - Incision is made
  - Cardiac catheter is guided to the heart through an artery of the groin or arm
  - Guide wire is manipulated to lie across the blockage
  - Heparin is a given to thin the blood and prevent clotting
  - Stent balloon catheter is transported along the guide wire and is positioned over the blockage
  - Saline is pumped into the balloon to infla
  - Balloon is inflated for 30 to 60 seconds to expand the stent



Coronary Stent



What is a Stent

- A small, mesh-like device made of metal
- Acts as a support or scaffold, in keeping the vessel open
- Stent helps to improve blood flow to the heart muscle and reduce the pain of angina
- 80% of patients who have balloon angioplasty will have a stent placed as well.

Types

Bare metal stents:

- Traditional method
- May have an increased rate of re-narrowing due to growth of scar tissue in the stent, a condition called Restenosis.

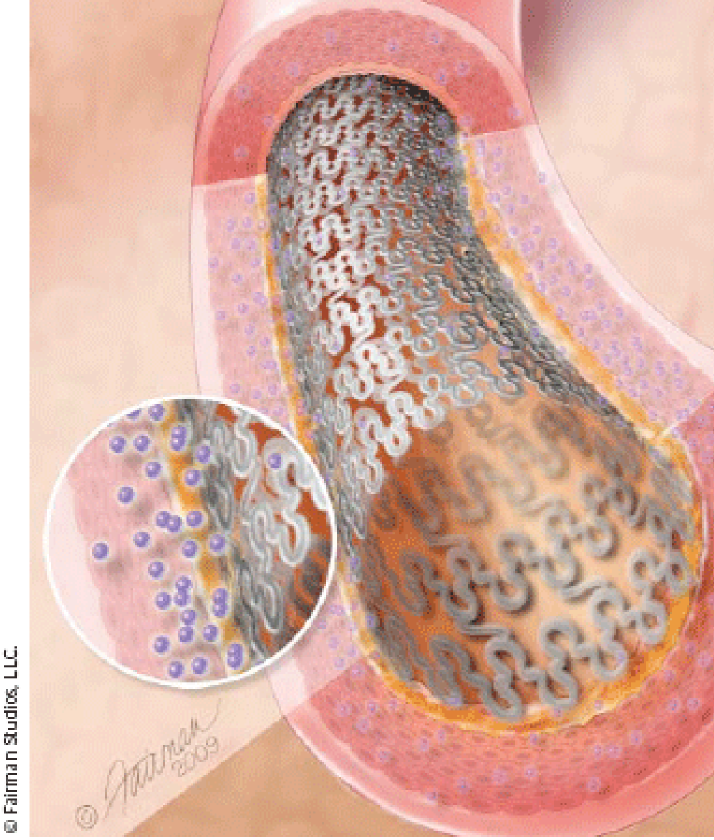


FIGURE 1. A drug-eluting stent consists of a backbone, a drug, and a polymer coating that controls the drug's release.

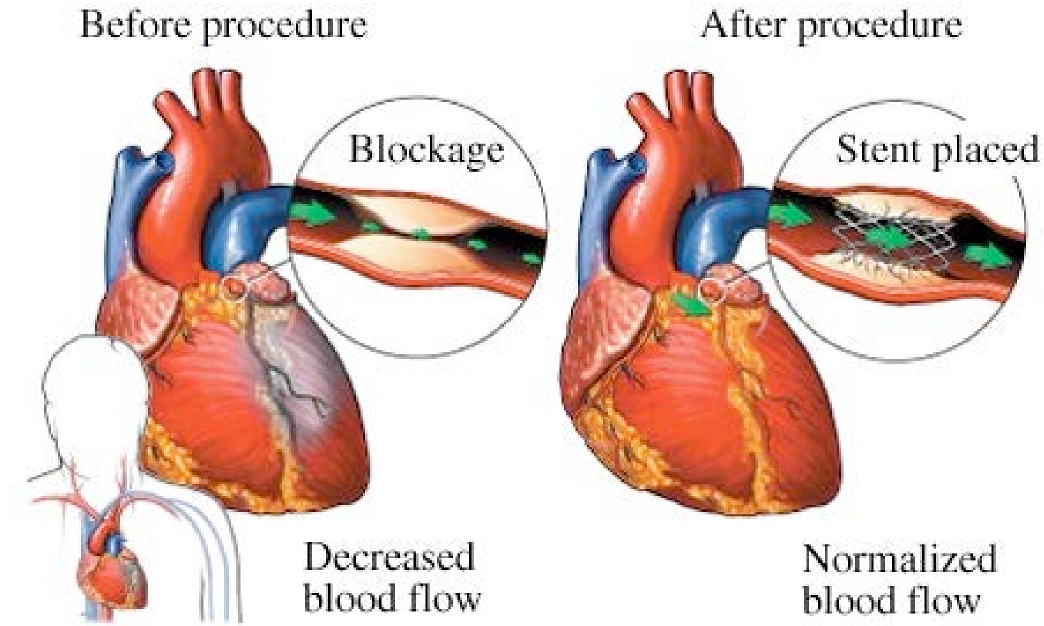
Drug-eluting stents:

-Combat Restenosis

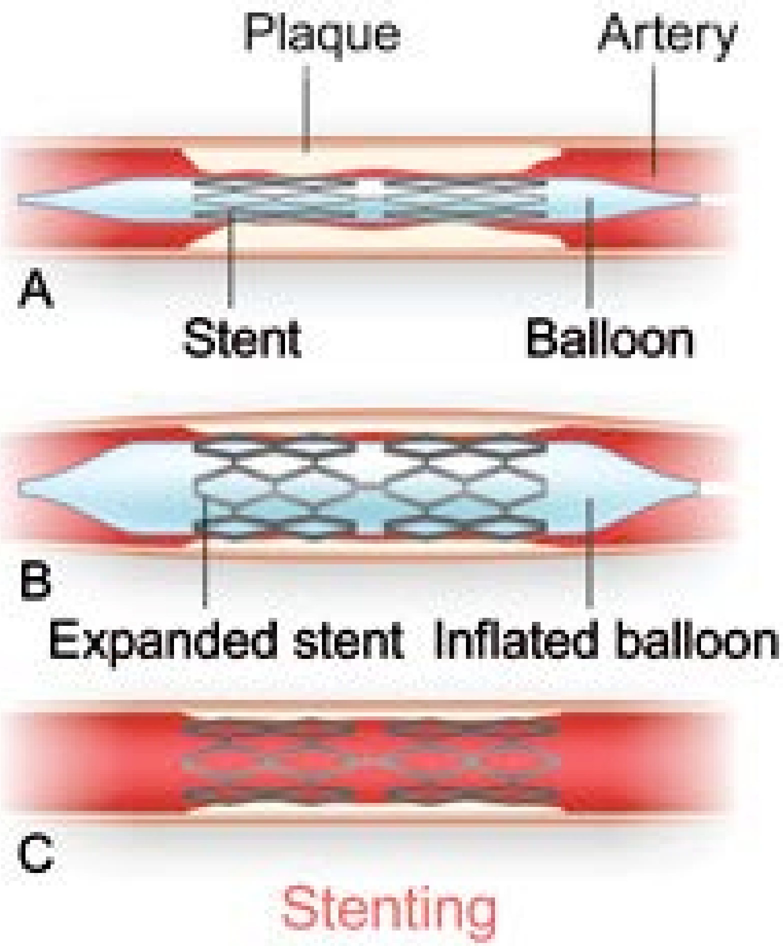
-Coated with medications that are slowly released to block the body's ability to form scar tissue around the stent.

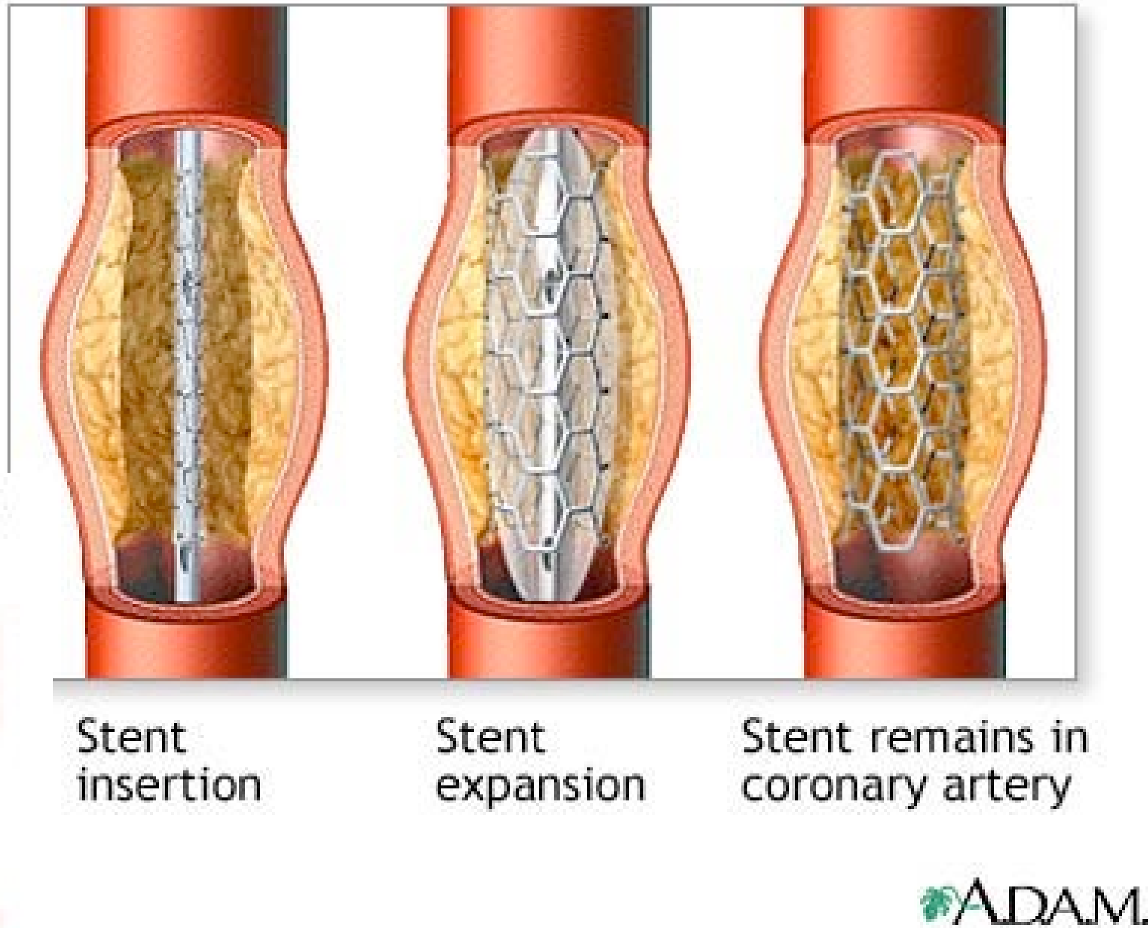
--The medication is delivered directly to the site of the artery blockage.

History



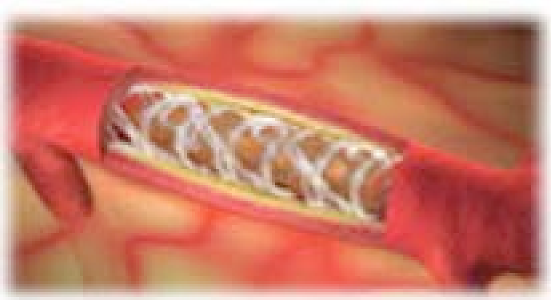
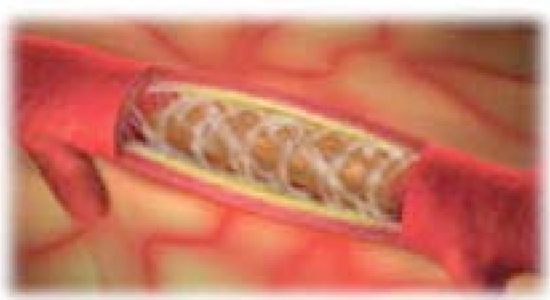
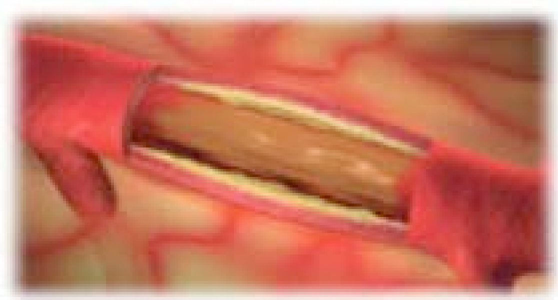
- Percutaneous transluminal coronary angioplasty (PTCA) by Gruntzig in 1977
- Puel and Sigwart, in 1986, deployed the first coronary stent to act as a scaffold
- In 2001, drug-eluting stents (DES) were introduced as a strategy to minimize restenosis


Plaque
Artery
A
Stent
Balloon
B
Expanded stent
Inflated balloon
C
Stenting

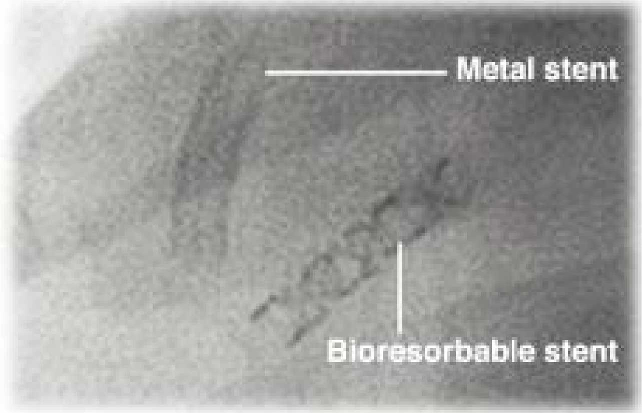

Stent insertion
Stent expansion
Stent remains in coronary artery
A.D.A.M.

Future Advancements

- The ReZolve™ stent integrates a proprietary drug-eluting polymer and a novel design to create a stent with metal-like performance out of a polymer material.
- The stent restores blood flow and supports the artery through healing, then completely dissolves from the body, leaving the patient free of a permanent implant.

Future Advancements



- Unlike permanent metal alloys, the REVA polymer dissolves from the body after healing of the artery has occurred, leaving additional treatment options available in the future.
- Another unique feature of the polymer is that it is visible under x-ray, allowing the stent to be visualized during the implant procedure and at follow up. Other bioresorbable polymer stents are invisible and require permanently attached radiopaque markers to aid in their placement.

Microscale shear activated-nanoparticles disperse into nanoparticles

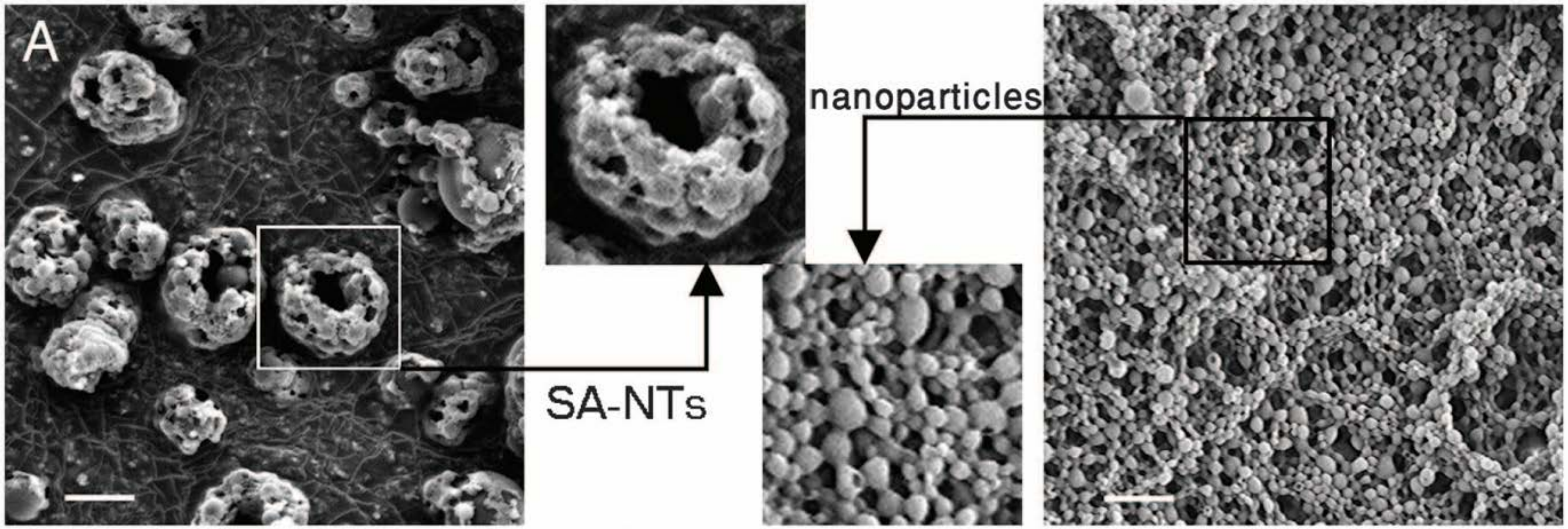


Fig.A. SEM of the microscale SA-NTs and the PLGA NPs

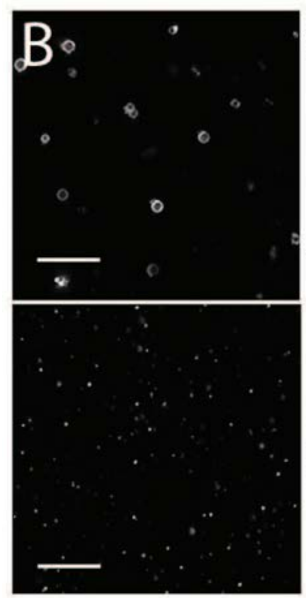


Fig.B. Intact SA-NTs dispersed into the PLGA NPs after exposure to shear stress

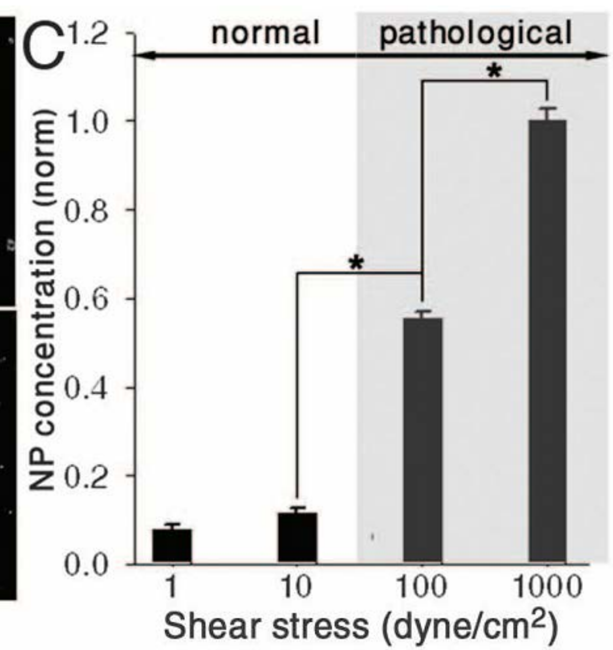


Fig.C. Quantification of released NPs from SA-NTs.

Schematic of the experimental strategy