The circulatory system has three main components:

- The heart establishes a pressure gradient to pump the blood.
- The blood vessels are passageways for the distribution of pumped blood throughout the body.
- The blood is a transport medium, serving the needs of body cells.
  - The pulmonary circulation is a loop of blood vessels between the heart and the lungs.
  - The systemic circulation is the circuit of blood vessels between the heart and other body systems.

From: http://www.cameron.edu/~gabrielr/ch09_lecture.ppt

The Cardiovascular System: Major Functions

- Delivers O₂, nutrients
- Removes CO₂, other waste
- Transports hormones, other molecules
- Temperature balance and fluid regulation
- Acid-base balance
- Immune function

The Heart

- Location
  - Thorax between the lungs
  - Pointed apex directed toward left hip
- About the size of your fist
  - Less than 1 lb.
The Heart: Coverings

- Pericardium – a double serous membrane
  - Visceral pericardium
  - Next to heart
  - Parietal pericardium
  - Outside layer
- Serous fluid fills the space between the layers of pericardium

The Heart: Heart Wall

- Three layers
  - Epicardium
    - Outside layer
    - This layer is the parietal pericardium
    - Connective tissue layer
  - Myocardium
    - Middle layer
    - Mostly cardiac muscle
  - Endocardium
    - Inner layer
    - Endothelium

The Myocardium

- Epicardium
  - Outside layer
  - This layer is the parietal pericardium
- Myocardium
  - Middle layer
  - Mostly cardiac muscle
- Endocardium
  - Inner layer
  - Endothelium

External Heart Anatomy

- Brachiocephalic artery
- Superior vena cava
- Right pulmonary artery
- Ascending aorta
- Pulmonary trunk
- Right pulmonary veins
- Right atrium
- Right coronary artery
  - Aorta
  - Left coronary artery
  - Coronary artery
  - Circumflex artery
- Anterior cardiac vein
- Right ventricle
- Left ventricle
- Great cardiac vein
- Anterior interventricular artery
  - Left coronary artery
  - Apex

Heart Anatomy

- Aorta
- Right and left pulmonary arteries
- Pulmonary trunk
- Right aorta
- Aortic valve
- Left pulmonary vein
- Left aorta
- Mitral valve
- Left atrioventricular groove
- Coronary sinus
- Left atrium
- Left ventricle
- Left ventricular cavity
- Left ventricular septum
- Descending aorta
- Right atrium
- Right pulmonary vein
- Pulmonary trunk
- Right aortic root
- Right atrioventricular groove
- Right atrium
- Right ventricle
- Right atrioventricular groove
- Right atrial appendage
- Right atrioventricular orifice
- Inferior vena cava
- Superior vena cava
- Right atrioventricular groove
- Right atrial appendage
- Right atrioventricular orifice
- Inferior vena cava
Myocardial Blood Supply

- **Right coronary artery**
  - Supplies right side of heart
  - Divides into marginal, posterior interventricular

- **Left (main) coronary artery**
  - Supplies left side of heart
  - Divides into circumflex, anterior descending (LAD)

- **Atherosclerosis → coronary artery disease**
  - Reduces blood flow through these vessels!!!!

Blood Flow Through the Heart

- **Right heart:** pulmonary circulation
  - Pumps deoxygenated blood from body to lungs
  - Superior, inferior vena cavae → RA → tricuspid valve → RV → pulmonary valve → pulmonary arteries → lungs

- **Left heart:** systemic circulation
  - Pumps oxygenated blood from lungs to body
  - Lungs → pulmonary veins → LA → mitral valve → LV → aortic valve → aorta

The action of heart valves ensure that blood flows in the proper direction.

- The AV valves are the tricuspid on the right and bicuspid on the left. They allow blood to flow from the atria into the ventricles. This occurs when atria pressure is greater than ventricular pressure, during ventricular filling.
- During ventricular ejection, when ventricular pressure exceeds atrial pressure, the AV valves close. This prevents the blood from flowing backwards. The AV valves are anchored by chordae tendineae to papillary muscles.
- The other pair of valves are the semilunar, pulmonary on the right and aortic on the left. They are forced open when the ventricular pressures exceed the pressures in the pulmonary arteries and aorta.
- The semilunar valves close when the pressures in the ventricles fall below the pressures in these vessels. This prevents the blood from flowing backwards.
- A fibrous skeleton separates the atria from the ventricles.
Valve Pathology

- Incompetent valve = backflow and repump
- Stenosis = stiff= heart workload increased
- May be replaced
- Lup Dub Heart Sound
Myocardium

- Myocardium: cardiac muscle
  - LV has most myocardium
    - Must pump blood to entire body
    - Thickest walls (hypertrophy)
    - LV hypertrophies with exercise and with disease
    - But exercise adaptations versus disease adaptations very different

Cardiac Muscle Cells:

- Autorhythmic
- Myocardial
- Intercalated discs
- Desmosomes
- Gap Junctions
  - Fast signals
  - Cell to cell
- Many mitochondria
- Large T tubes

Structural and Functional Characteristics of Skeletal and Cardiac Muscle

- Only one fiber type (similar to type I)
  - High capillary density
  - High number of mitochondria
  - Striated
- Cardiac muscle fibers connected by intercalated discs
  - Desmosomes: hold cells together
  - Gap junctions: rapidly conduct action potentials

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Mechanism of Cardiac Muscle Contraction

**Figure 14-11:** Excitation-contraction coupling and relaxation in cardiac muscle

- **Mechanism of Cardiac Muscle Excitation, Contraction & Relaxation**

- **Compare and Contrast Cardiac vs Skeletal Striated Muscle**

- **Regulation of Cardiac Contractility**

- **Modulation of Contraction**

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Comparison of isolated **skeletal** (RED) and **cardiac** muscle fibers in-vitro. Note that in reality they may not develop the same force; that is not the point of this comparison. The point is skeletal muscle has plenty of Ca++ in the SR; whereas the SR in the cardiac fibers is dependent upon the influx/efflux of Ca++ with each heart beat.

**Calcium Movement**

- Ca++ comes into cell
- Larger amounts of Ca++ from SR flood the cell (via Ca++ induced Ca++ release)
- Ca++ and TroponinC bind
  \[ \rightarrow \text{cardiac contraction} \]
- cAMP activates phosphokinase (PK)
  \[ \rightarrow \text{phosphorylates:} \]
  - Ca channel to allow more Ca in
  - Phospholamban: ↑ SR Ca++-ATPase pump (more Ca available for release in subsequent beats)
  - Troponin: increase myofilament activity

**Relaxation**

1. SR Ca++ ATPase pump
2. Na+K pump Na++ out
3. Allows the Na-Ca exchanger to pump Ca++ out

**Cardiac Glycosides (i.e. Digitalis)**

1. Inhibit Na-K pump = more Na intracell
2. Inhibit Na-Ca exchanger
3. More Ca inside the cell
4. End result: greater contraction of heart muscle (used to treat patients in Brugada failure)

**β-Adrenergic activation increases cardiac inotropy, chronotropy and lustropy**
ISOTONIC CONTRACTIONS

WHAT IS PRELOAD?

STARLING’S LAW OF THE HEART

PRELOAD & THE ISOTONIC CONTRACTION

BIOCHEMICAL BASIS FOR STARLING’S LAW

Contractility and Starling Curves
Common Factors that Alter Contractility

- Changes in sympathetic nervous system activity
- Catecholamines and other hormones
- Oxygen supply
- Changes in extracellular calcium
- Cellular pH changes

Electrical conduction in the heart

- The Sinoatrial node (SA node), a group of autorhythmic cells (main pacemaker of the heart) in the right atrium near the entry of the superior vena cava.
- An internodal pathway connects the SA node to the atrioventricular node (AV node), a group of autorhythmic cells found near the floor of the right atrium.
- From the AV node action potentials move into fiber known as the bundle of his or atrioventricular bundle. The bundle passes from the AV node into the wall of the septum between the ventricles.
- A short way down the septum the bundle divides into left and right bundle branches.
- These fibers continue downward to the apex where they divide into many small Purkinje fibers that spread outward among the contractile cells.

Preload and Afterload in the Heart

- INCREASE IN FILLING PRESSURE = INCREASED PRELOAD
- PRELOAD REFERS TO END DIASTOLIC VOLUME.
- AFTERLOAD IS THE AORTIC PRESSURE DURING THE EJECTION PERIOD/AORTIC VALVE OPENING.

http://www.mdl.rcm.upr.edu/physiology/cardio.ppt
Cardiac Conduction

SA node
AV node
Common bundle
Bundle branches
Purkinje fibers

From: http://www.servier.com/

Electrical activity of the heart

• 99% of the cardiac muscle cells are contractile
• 1% of the cardiac muscle cells are autorhythmic cells, noncontractile
• The heart contracts rhythmically – autorhythmicity
• The rhythmic cells have pacemaker activity

The spread of cardiac excitation

• Each heart chambers contracts as a unit to accomplish efficient pumping
• Atria and ventricles are functionally coordinated
• Attrial excitation and contraction is complete before the ventricular contraction
• Fibrillation is random, uncoordinated excitation and contraction of cardiac cells
• Ventricular fibrillation causes death rapidly

Coordinating the Pump: Electrical Signal Flow

Intrinsic Conduction System

Function: initiate & distribute impulses so heart depolarizes & contracts in orderly manner from atria to ventricles.
Intrinsic Control of Heart Activity:
Cardiac Conduction System

- Spontaneous rhythmicity: special heart cells generate and spread electrical signal
  - Sinoatrial (SA) node
  - Atrioventricular (AV) node
  - AV bundle (bundle of His)
  - Purkinje fibers
- Electrical signal spreads via gap junctions
  - Intrinsic heart rate (HR): 100 beats/min
  - Observed in heart transplant patients (no neural innervation)

SA node: initiates contraction signal
- Pacemaker cells in upper posterior RA wall
- Signal spreads from SA node via RA/LA to AV node
- Stimulates RA, LA contraction

AV node: delays, relays signal to ventricles
- In RA wall near center of heart
- Delay allows RA, LA to contract before RV, LV
- Relays signal to AV bundle after delay

AV bundle: relays signal to RV, LV
- Travels along interventricular septum
- Divides into right and left bundle branches
- Sends signal toward apex of heart

Purkinje fibers: send signal into RV, LV
- Terminal branches of right and left bundle branches
- Spread throughout entire ventricle wall
- Stimulate RV, LV contraction

Electrocardiogram (ECG or EKG)
- The ECG is a recording of the electrical activity induced in the body fluids by the cardiac impulse that reaches the surface of the body
- The electrocardiograph represents a comparison in voltage detected by electrodes at two different points on the body surface, not the actual potential

ECG components
- P wave represents atrial depolarization (recorded when impulse spreads across the atria)
- QRS complex represents ventricular depolarization
- T wave represents ventricular repolarization
THE CONDUCTION SYSTEM OF THE HEART
Conduction of the action potential (AP)

- The AP originates at the s-a node.
- AP propagates across the atrial walls.
- The AP is delayed at the a-v node.
- The AP propagates rapidly down the bundles.
- The ventricular myocardium is depolarised homogeneously.

SPREAD OF THE CARDIAC IMPULSE
The impulse originates at the sino-atrial node and invades the atria.

- Atrial depolarisation generates a 'P wave' on the ECG.
- The impulse is delayed at the atrio-ventricular node.

SPREAD OF THE CARDIAC IMPULSE contd
Ventricles invaded by impulse generating a QRS complex.
Ventricles uniformly depolarised - ST segment.

INTERPRETING THE ELECTROCARDIOGRAM

- PR interval - 0.12 - 0.20 s determined by delay of the AP at the a-v node.
- QRS complex time - 0.08 s the time for AP propagation along the conduction system.
- ST segment. Isoelectric region corresponding to the ventricular AP plateau.
- QT interval. The mean duration of the ventricular AP. Interval is heart rate dependent.

ECG Deflection Waves
**ECG Deflection Waves**

60 seconds ÷ 0.8 seconds = resting heart rate of 75 beats/minute

1st Degree Heart Block = P-Q interval longer than 0.2 seconds.

---

**Abnormal electrical patterns (Arrhythmias)**

- **Abnormalities in rate:**
  - Tachycardia (>100 beats/minute)
  - Bradycardia (<60 beats/minute)

- **Abnormalities in rhythm (arrhythmias):**
  - Extrasystoles or premature ventricular contractions (PVCs) (ectopic focus)
  - Atrial fibrillation (300 to 300 beats/minute)
  - Atrial flutter (200 to 300 beats/minute)
  - Ventricular fibrillation (rapid, irregular, uncoordinated depolarizations)
  - Heart block (defects in cardiac conducting system)
    - Complete heart block (complete dissociation between atrial and ventricular activity)

- **Cardiac myopathies:**
  - Myocardial ischemia; myocardial infarction

---

**Extrinsic Control of Heart Activity: Parasympathetic Nervous System**

- **Reaches heart via vagus nerve (cranial nerve X)**
- **Carries impulses to SA, AV nodes**
  - Releases acetylcholine, hyperpolarizes cells
  - Decreases HR, force of contraction
- **Decreases HR below intrinsic HR**
  - Intrinsic HR: 100 beats/min
  - Normal resting HR (RHR): 60 to 100 beats/min
  - Elite endurance athlete: 35 beats/min

---

**Extrinsic Control of Heart Activity: Sympathetic Nervous System**

- **Opposite effects of parasympathetic**
- **Carries impulses to SA, AV nodes**
  - Releases norepinephrine, facilitates depolarization
  - Increases HR, force of contraction
  - Endocrine system can have similar effect (epinephrine, norepinephrine)
- **Increases HR above intrinsic HR**
  - Determines HR during physical, emotional stress
  - Maximum possible HR: 250 beats/min

---

**Parasympathetic stimulation**

- **Decreases the heart rate (influence on SA node)**
- **Decreases the AV node excitability**
- **Shortens the action potentials in contractile atrial cells (atrial contraction is weakened)**
- **Has little effect on ventricular contraction** (sparse parasympathetic innervation)
**Sympathetic stimulation**

- Increases the rate (increase the rate of SA node depolarization)
- Reduces AV nodal delay
- Speeds up the propagation of action potential throughout conduction pathways
- Increase of contractile strength in both atria and ventricles

---

**Heart Rate and Endurance Training**

Resting heart rates in adults tend to be between 60 and 85 beats per min. However, extended endurance training can lower resting heart rate to 35 beats or lower. This lower heart rate is thought to be due to increased parasympathetic stimulation.

---

**Cardiac Cycle**

- Systole – contraction and emptying
- Diastole – relaxation and filling
- Mechanical events of the cardiac cycle:
  - Early ventricular diastole
  - Late ventricular diastole
  - End of ventricular diastole
  - Ventricular excitation and onset of ventricular systole
  - Isovolumetric ventricular contraction
  - Ventricular ejection
  - End of ventricular systole
  - Ventricular repolarization and onset of ventricular diastole
  - Isovolumetric ventricular relaxation
  - Ventricular filling

---

**Cardiac Cycle: Heart Chambers and the Beat Sequence**

1. Late diastole: all chambers relax, filling with blood
2. Atrial systole: atria contract, add 20% more blood to ventricles
3. Isovolumic ventricular contraction: closes AV valves ("lub"), builds pressure
Cardiac Cycle: Finish and Around To the Start

4. Ventricular ejection: pushes open semi lunar valves, blood forced out
5. Ventricular relaxation: aortic back flow slams semi lunar valves shut (“dup”)
   AV valves open refilling starts – back to start of cycle

Summary of Heart Beat: Electrical, Pressure and Chamber Volumes

Cardiac Cycle

- All mechanical and electrical events that occur during one heartbeat
- Diastole: relaxation phase
  - Chambers fill with blood
  - Twice as long as systole
- Systole: contraction phase

Cardiac Cycle: Ventricular Systole

- QRS complex to T wave
- 1/3 of cardiac cycle
- Contraction begins
  - Ventricular pressure rises
  - Atrioventricular valves close (heart sound 1, “lub”)
  - Semilunar valves open
  - Blood ejected
  - At end, blood in ventricle = end-systolic volume (ESV)
Cardiac Cycle: Ventricular Diastole

- T wave to next QRS complex
- 2/3 of cardiac cycle
- Relaxation begins
  - Ventricular pressure drops
  - Semilunar valves close (heart sound 2, “dub”)
  - Atrioventricular valves open
  - Fill 70% passively, 30% by atrial contraction
  - At end, blood in ventricle = end-diastolic volume (EDV)
Of four heart sounds only two (S₁ & S₂) generally are heard with a stethoscope.

S₁ is generally the longest and loudest. It occurs at the beginning of systole.

S₂ occurs at the end of systole.

S₃ is low pitched and occurs early ventricular filling.

S₄ is coincident with atrial contraction.

Major Events of Cardiac Cycle

- Quiescent period
- Atrial systole
- Isovolumetric contraction
- Ventricular ejection
- Isovolumetric relaxation
- Ventricular filling
Stroke Volume, Ejection Fraction

- **Stroke volume (SV): volume of blood pumped in one heartbeat**
  - During systole, most (not all) blood ejected
  - EDV − ESV = SV
  - 100 mL − 40 mL = 60 mL

- **Ejection fraction (EF): percent of EDV pumped**
  - SV / EDV = EF
  - 60 mL/100 mL = 0.6 = 60% (average at rest)
  - Clinical index of heart contractile function
    - Clinically, 40% or less is considered ‘impaired’ function

Cardiac Output (Q)

- **Total volume of blood pumped per minute**
  - Q = HR x SV
    - RHR ~70 beats/min, standing SV ~70 mL/beat
    - 70 beats/min x 70 mL/beat = 4,900 mL/min
    - Use L/min (4.9 L/min)

- **Resting cardiac output ~4.2 to 5.6 L/min**
  - Average total blood volume ~5 L
  - Total blood volume circulates once every minute

**CAlculations of SV, EF, AND Q**

**Stroke Volume:** major determinant of CR endurance: determined by:

- 1. Volume of venous blood returned to the heart (preload)
- 2. Ventricular distensibility or capacity to enlarge the ventricle
  - 1 & 2 influence filling capacity; and thus, how much blood available to be pumped (think Frank-Starling ‘Law’)
- 3. Ventricular contractility
- 4. Aortic pressure (afterload) (pressure against which the ventricle must contract)
  - 3 & 4 influence the ventricle’s ability to empty
    - note that there a drop in total peripheral resistance during exercise, due to vasodilation in skeletal muscle. This helps keep aortic pressure, and thus afterload, from increasing facilitating ↑SV.

**Regulation of Stroke Volume**

- End-diastolic volume (EDV)
  - Volume of blood in the ventricles at the end of diastole (‘preload’)
  - Ventricular distensibility
- Average aortic blood pressure
  - Pressure the heart must pump against to eject blood (‘afterload’)
- Strength of the ventricular contraction
  - ‘Contractility’
The LV Pressure-Volume Relation

Regulation of cardiac output

- Depends on the control of the heart rate and stroke volume
- The heart is innervated by the ANS, both parasympathetic and sympathetic nerves
- Under resting conditions, parasympathetic control is dominant (vagus nerve)

The vascular system is a series of parallel pathways. Parts of it are distributed to different body regions. Each region receives a fresh blood supply. Depleted blood (low oxygen, high carbon dioxide) returns to the right side of the heart.

- The right and left pumps can be compared.
  - Oxygen-poor blood on the right side soon becomes the same volume of oxygen-rich blood pumped from the left side.
  - The pulmonary circulation is low pressure and low resistance. The systemic circulation is the opposite.
  - Pressure is the force exerted by pumped blood on a vessel wall. Resistance is the opposition to blood flow.

From: Coyle, Gatorade Science Exchange, #34
**Vascular System**

- Arteries: “Volume and Pressure Storers”
- Arterioles: Control the DISTRIBUTION (flow) of blood! (and thus, indirectly, the blood pressure)
- Capillaries: “Exchange” vessels
- Venules: collect blood from capillaries
- Veins: Provide a low pressure storage system for blood.
  At rest, ~66% of blood volume in this system.

**BLOOD DISTRIBUTION AT REST**

**Arterioles** - Control the DISTRIBUTION (flow) of blood! (and thus, indirectly, the blood pressure)

**Arteries** (low compliance)

- **HEART**
- **VEINS**
- **CAPACITY VESSELS**
- **CAPILLARIES**

**DIASTOLE** 80 mmHg

**SYSTOLE** 120 mmHg

**VEINS**

- **Lumen**
- **Valve**
- **Endothelium of tunica interna**
- **Connective tissue (elastic and collagenous fibers)**
- **Tunica media**
- **Tunica externa**

**Artery**

**Vein**

**Tissue fluid**

**Endothelial cell**

**Silt**

**Tissue fluid**

**Capillary**
Coronary circulation

- Coronary arteries (from aorta)
- Q is only during diastole
- Coronary veins (empty in the right atrium)
- Coronary blood flow is adjusted in response to changes in the heart’s O₂ requirements
- Atherosclerotic coronary artery disease

Blood Pressure

- Systolic pressure (SBP)
  - Highest pressure in artery (during systole)
  - Top number, ~110 to 120 mmHg
- Diastolic pressure (DBP)
  - Lowest pressure in artery (during diastole)
  - Bottom number, ~70 to 80 mmHg
- Mean arterial pressure (MAP)
  - Average pressure over entire cardiac cycle
  - MAP = 2/3 DBP + 1/3 SBP

Blood Pressure - Diagrams

Figure 3: Systole: ‘inflow’ > ‘outflow’

Blood Pressure = Cardiac Output x Total Peripheral Resistance

Figure 3: Systole blood ‘inflow’ > ‘outflow’

Resting conditions

Δ volume & thus pressure increases in large arteries
This build up of volume & pressure is SYSTOLIC BP

Figure 3: Diastole blood ‘inflow’ < ‘outflow’

Resting conditions

Heart is at rest: NO inflow of volume into the large arteries, only ‘outflow’ to the arterial system: and so, Volume & thus pressure decreases in large arteries
This loss of volume & pressure is DIASTOLIC BP

Blood Pressure = Cardiac Output x Total Peripheral Resistance
From: Coyle, Gatorade Science Exchange, # 34

**Systole:**

- much more blood ‘inflow’ > ‘outflow’
- Δ volume & thus pressure increases in large arteries
- This build up of extra volume increases Systolic BP pressure even more than during resting conditions
- Dynamic Exercise conditions

**Diastole:**

- NO blood ‘inflow’ > ‘outflow’ is much greater!
- Because TPR decreases during rhythmic exercise, much more blood volume can leave the large arteries to perfuse the working muscles. This results in a DBP that is the same as rest.
- Dynamic Exercise conditions

**Blood Pressure Response to Dynamic Graded Exercise**

Based on the model, can you know *see WHY* SBP increases, whereas DBP remains the same or even decreases? Think ‘inflow – outflow’ & of course, how changes in SV & TPR come into play!!!

Also, based on this model, you might now have a better appreciation as to the treatment of hypertension. A physician might try to decrease the overall volume in the system by having the patient decrease his/her sodium intake or even give the patient a diuretic. Or, the ‘inflow’ side might be treated by trying to decrease either HR or SV by a calcium channel blocker or a Beta blocker. Alternatively, the ‘outflow’ side might be altered by prescribing an ACE inhibitor to decrease TPR. Recall that Angiotension Converting Enzymse (ACE) converts the vasoinactive Angiotension I to the potent peripheral vasoconstrictor, Angiotension II. This should provide some insight into Friday’s laboratory experience!

**Pressure Rate Product: ~ MVO²**

---

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treadmill Running</th>
<th>Snow Shoveling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>175 ± 15</td>
<td>175 ± 15</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>150 ± 25</td>
<td>190 ± 30</td>
</tr>
<tr>
<td>Oxygen consumption (METS)</td>
<td>9.5 ± 1.8</td>
<td>5.7 ± 0.8</td>
</tr>
<tr>
<td>Rating of perceived exertion (6-20 scale)</td>
<td>17.9 ± 1.5</td>
<td>16.7 ± 1.7</td>
</tr>
</tbody>
</table>

Note: The energy expenditure required for sexual activity is 3-4 METs (metabolic equivalents) before and after orgasm and 4-6 METs during orgasm.
Blood pressure and workload of the heart

- The arterial blood pressure – afterload
- High blood pressure – ventricular pressure increases
- Chronically elevated afterload leads to heart failure (decrease heart contractility)
- Sympathetic stimulation – compensatory
- Decompensated heart failure

Measuring Arterial Blood Pressure

General Hemodynamics

- Blood flows from a region within the vessel of high pressure to a region within the vessel with lower pressure (pressure gradient)
- Pressure gradient across the entire cardiovascular system = 100 mmHg
- Blood vessels and the blood itself provide resistance to blood flow
- Resistance to blood flow = \( \eta L / r^4 \)
  - \( \eta \) = viscosity of the blood
  - \( L \) = length of the vessel
  - \( r^4 \) = radius of the vessel to the 4th power

Changing Blood Flow

Blood Flow = \( \Delta \text{pressure} / \text{resistance} \)

- Blood flow can change by either changing pressure or resistance or a combination of the two
- Changing resistance has a larger effect on blood flow because of the fourth power mathematical relationship between vascular resistance and vessel radius
- Vasoconstriction: radius of the vessel decreases, decreasing blood flow
- Vasodilation: radius of the vessel increases, increasing blood flow
Pressure Changes Across the Systemic Circulation

General Hemodynamics:

\[ \text{Blood flow} = \frac{\Delta P}{R} \]

- Easiest way to change flow \(\Rightarrow\) change R
  - Vasoconstriction (VC)
  - Vasodilation (VD)
  - Diverts blood to regions most in need
- Arterioles: resistance vessels
  - Control systemic R
  - Site of most potent VC and VD
  - Responsible for 70 to 80% of P drop from LV to RA

General Hemodynamics: Blood flow = \(\Delta P/R\) (continued)

- Blood flow: \(Q\)
- \(\Delta P\)
  - Pressure gradient that drives flow
  - Change in P between LV/aorta and vena cava/RA
- \(R\)
  - Small changes in arteriole radius affect R
  - VC, VD

Distribution of Cardiac Output at Rest and During Heavy Exercise

What mechanisms are responsible for the change in DISTRIBUTION?

Distribution of Blood

- Blood flows to where needed most
  - Often, regions of \(\uparrow\) metabolism \(\Rightarrow\) \(\uparrow\) blood flow
  - Other examples: blood flow changes after eating or exposure to heat.
- At rest (\(Q = 5\) L/min)
  - Liver, kidneys receive 50% of Q
  - Skeletal muscle receives \(~20%\) of Q
- During heavy exercise (\(Q = 25\) L/min)
  - Exercising muscles receive 80% of Q via VD
  - Flow to liver, kidneys decreases via arteriole VC

CARDIAC OUTPUT DURING EXERCISE

Note the changes in blood DISTRIBUTION!!!
Organ Blood Flow Balance

Locally Produced Vasodilators/Constrictors

Extrinsic Control (Mainly SNS)

Intrinsic (local) Control of Blood Flow

Stimuli to increase local blood flow
1. Metabolic factors
   - increased oxygen demand
   - increases in metabolic by-products
   - inflammatory chemicals
2. Endothelium released factors
   - Nitric oxide
   - Prostaglandins
   - Endothelium-derived hyperpolarization factors (EDHF)
3. Myogenic responses

Intrinsic Control of Blood Flow

- Ability of local tissues to constrict or dilate arterioles that serve them
- Alters regional flow depending on need
- Three types of intrinsic control
  - Metabolic
  - Endothelial
  - Myogenic

Metabolic Mechanism

- Adenosine, CO₂, H⁺
- Increased Metabolic Rate
  - Increased Metabolic Concentration
  - Arteriolar Dilation
  - Increased Blood Flow
- Decreased Metabolic Rate
  - Decreased Metabolic Concentration
  - Arteriolar Constriction
  - Decreased Blood Flow

Intrinsic Control of Blood Flow

- Metabolic mechanisms (Vaso Dilation)
  - Buildup of local metabolic by-products
  - O₂, CO₂, K⁺, H⁺, lactic acid
- Endothelial mechanisms (mostly VD)
  - Substances secreted by vascular endothelium
  - Nitric oxide (NO), prostaglandins, EDHF
- Myogenic mechanisms (VC, VD)
  - Local pressure changes can cause VC, VD
  - P → P → VC, P → VD

Figure courtesy of Dr. Donna H. Korzick, Pennsylvania State University.
Intrinsic Control of Blood Flow

Extrinsic Neural Control of Blood Flow

- Upstream of local, intrinsic control
- Redistribution of flow at organ, system level
- Sympathetic nervous system innervates smooth muscle in arteries and arterioles
  - Baseline sympathetic activity → vasomotor tone
  - ↑ Sympathetic activity → ↑ VC
  - ↓ Sympathetic activity → ↓ VC (passive VD)

Distribution of Venous Blood

- At rest, veins contain 2/3 blood volume
  - High capacity to hold blood volume
  - Elastic, balloon-like vessel walls
  - Serve as blood reservoir
- Venous reservoir can be liberated, sent back to heart and into arteries
  - Sympathetic stimulation
  - Venoconstriction

Figure 6.13

How Is Vascular Tone Regulated?

Extrinsic Control Factors
1. SNS (Most Important)
2. Circulating Neurohumoral Agents e.g. Norepinephrine, Epinephrine, Angiotensin II

Local Control Factors
Vasodilator and Vasoconstrictor Substances Released From the Vascular Endothelium and Vascular Smooth Muscle Cells Including By-Products of Metabolism

Blood Distribution (summary)

- Matched to overall metabolic demands
- Autoregulation—arterioles within organs or tissues dilate or constrict in response to the local chemical environment
- Extrinsic neural control—sympathetic nerves within walls of vessels are stimulated causing vessels to constrict
- Determined by the balance between mean arterial pressure and total peripheral resistance
Integrative Control of Blood Pressure

Blood pressure is maintained and controlled by the autonomic nervous system. Receptors that modify blood pressure control through the cardiovascular control centers:

- **Baroreceptors**: stretch receptors in the aortic arch and carotid arteries that are sensitive to changes in blood pressure.
- Sensitive to changes in arterial pressure.
- Afferent signals from baroreceptor to brain.
- Efferent signals from brain to heart, vessels.
- Adjust arterial pressure back to normal.

Return of Blood to the Heart

- The heart can only pump what it 'sees'!!!
  - (That's why we elevate one's feet after they pass out)
- Venous return is the main determinant of CO! Not the contractile state of the heart!

Return of Blood to the Heart

- Upright posture makes venous return to heart more difficult.
- Three mechanisms assist venous return:
  - One-way venous valves
  - Muscle pump
  - Respiratory pump.
Control of Blood Flow

Key Points
• Blood is distributed throughout the body based on the needs of individual tissues
• Redistribution of blood is controlled locally by the release of chemical substances, which cause vasodilation
• Extrinsic neural control of blood flow distribution is accomplished through vasoconstriction through the sympathetic nervous system
• Blood returns to the heart through veins, assisted by valves, the muscle pump, and respiratory pump

Blood: 3rd component of cardiovascular system
functions + facts

• Three major functions
  – Transportation (O₂, nutrients, waste)
  – Temperature regulation
  – Acid-base (pH) balance
• Blood volume: 5 to 6 L in men, 4 to 5 L in women
• Whole blood = plasma + formed elements
• Regulating blood volume supports efficient circulation to cells, tissues, organs & systems

COMPOSITION OF TOTAL BLOOD VOLUME

Red Blood Cells

• No nucleus, cannot reproduce
  – Replaced regularly via hematopoiesis
  – Life span ~4 months
  – Produced and destroyed at equal rates
• Hemoglobin
  – Oxygen-transporting protein in red blood cells
    (4 O₂/hemoglobin)
  – Heme (pigment, iron, O₂) + globin (protein)
  – 250 million hemoglobin/red blood cells
  – Oxygen-carrying capacity: ~20 mL O₂/100 mL blood

Transport of oxygen (primarily bound to hemoglobin)

Key Points
• ~ 15 g of hemoglobin per 100 ml of blood
  – ‘Heme’ contains iron, which binds oxygen
  – Each gram of hemoglobin can combine with ~ 1.34 ml of oxygen, so that:
    • 20 ml of oxygen can be bound to each 100 ml of blood
      – (15 g X 1.34 ml oxygen per gram) = ~20 ml of oxygen per 100 ml of blood
    – Thus, 1Liter has (10 X 20ml = 200ml of oxygen)
  – And so, 5 Liters of blood (a normal CO) has (5 X 200ml) = 1,000 ml of oxygen
Anemia - reduced O₂ carrying capacity of the blood

- Insufficient number of RBCs:
  - Hemorrhagic - due to blood loss associated with an injury, undiagnosed bleeding ulcer, etc.
  - Hemolytic - due to blood loss due to transfusion reactions & certain bacterial and parasite infections.
  - Aplastic - due to destruction or inhibition of red marrow by drugs, ionizing radiation or certain bacterial toxins.

- Insufficient hemoglobin content in RBCs:
  - Iron Deficiency - inadequate intake or absorption of iron.
  - Pernicious - dietary deficiency of Vitamin B₁₂ or inadequate production of intrinsic factor for absorption of Vitamin B₁₂.

Anemia - reduced O₂ carrying capacity of the blood

- Abnormal hemoglobin in RBCs:
  - Sickle Cell - one amino acid in the 287 forming the beta chains is wrong.

In low O₂ conditions the beta chains form stiff rods which cause RBCs to sickle blocking small vessels.

Blood Viscosity

- Thickness of blood (due to red blood cells)
- Twice as viscous as water
- Viscosity ↑ as hematocrit ↑
- Plasma volume must ↑ as red blood cells ↑
  - Occurs in athletes after training, acclimation
  - Hematocrit and viscosity remain stable
  - Otherwise, blood flow or O₂ transport may suffer

Sickle Cell Anemia

ACSM and CHAMP Summit on Sickle Cell Trait:
CHANGES IN a-VO₂ diff

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<th>a-VO₂ diff</th>
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