

Circulation: Blood Vessels, Flow, and Regulation

Adapted From:

Textbook Of Medical Physiology, 11th Ed.
Arthur C. Guyton, John E. Hall
Chapters 14, 15, 16, 17, 18, & 19

John P. Fisher

© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Introduction

- Circulation allows transport of nutrients to the tissues, transport of waste away from the tissues, the movement of hormones, and the maintenance of fluid environment for overall survival and function of the cells
- Overall circulation is divided into two portions
 - Systemic circulation
 - Pulmonary circulation

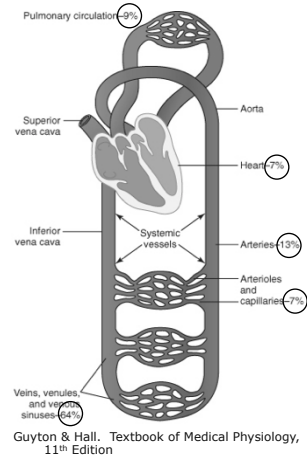
© Copyright 2012, John P. Fisher, All Rights Reserved



Overview of Circulation

Functional Parts of the Circulation

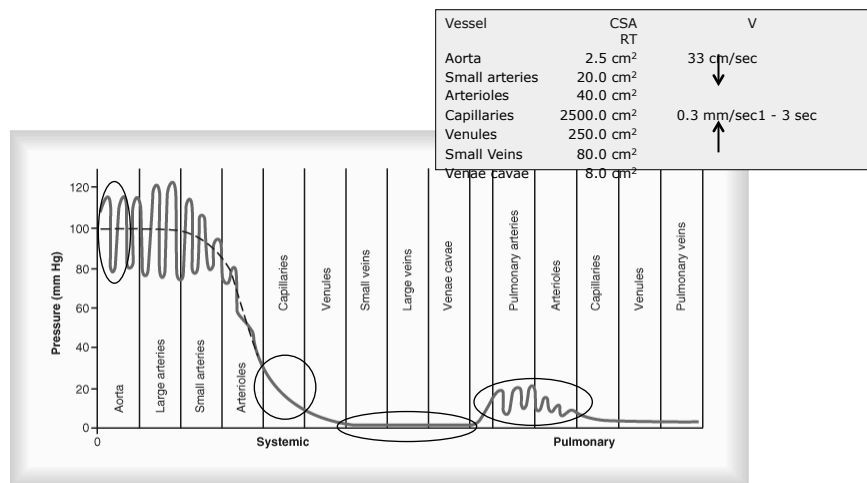
- Arteries
 - Transport blood under high pressure
- Arterioles
 - Acts as control valves through which blood is transported into the capillaries
- Capillaries
 - Allows exchange of fluid, nutrients, electrolytes, hormones, and other substances
- Venules
 - Collect blood from the capillaries
- Veins
 - Conduits for transport of blood from tissues back to the heart and reservoir of blood



© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Functional Parts of the Circulation



© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Principles of Circulation

know and understand this slide

- Blood flow to tissues matches needs of tissues
 - Changes in cardiac output cannot meet the high and low demands of blood from a variety of tissues
 - Microvessels regulate the flow of blood, allowing tissues in need to receive more blood flow
 - *Don't swim after eating*
- Cardiac output is controlled by the sum of all local tissue flows
 - Increased demand causes an increase in output (to a point)
- Arterial pressure is controlled independently of local blood flow control and cardiac output control
 - Arteriole contraction (short term)
 - Venous contraction (short term)
 - Renal hormone control (long term)

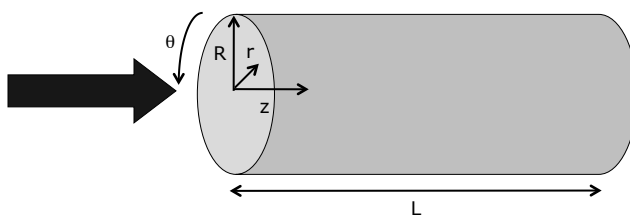


© Copyright 2012, John P. Fisher, All Rights Reserved

Elementary Fluid Mechanics

Flow Through a Cylindrical Tube

- Consider flow through a cylindrical tube



$$P = P_0 \text{ at } z = 0$$

$$P = P_L \text{ at } z = L$$

$$v_z = 0 \text{ at } r = R$$

$$\frac{\partial v_z}{\partial r} = 0 \text{ at } r = 0$$

- Conservation of Momentum (z component of equation of motion in cylindrical coord.)

$$\rho \left(\frac{\partial v_z}{\partial t} + v_r \frac{\partial v_z}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_z}{\partial \theta} + v_z \frac{\partial v_z}{\partial z} \right) = - \frac{\partial \rho}{\partial z} - \left(\frac{1}{r} \frac{\partial}{\partial r} (r \tau_{rz}) + \frac{1}{r} \frac{\partial \tau_{\theta z}}{\partial \theta} + \frac{\partial \tau_{zz}}{\partial z} \right) + \rho g_z$$

- Assuming a Newtonian fluid with constant density

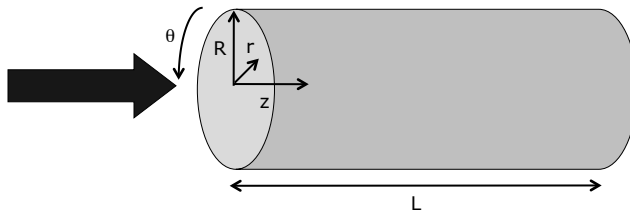
$$\rho \left(\frac{\partial v_z}{\partial t} + v_r \frac{\partial v_z}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_z}{\partial \theta} + v_z \frac{\partial v_z}{\partial z} \right) = - \frac{\partial \rho}{\partial z} + \mu \left(\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v_z}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2 v_z}{\partial \theta^2} + \frac{\partial^2 v_z}{\partial z^2} \right) + \rho g_z$$

© Copyright 2012, John P. Fisher, All Rights Reserved

Elementary Fluid Mechanics

Flow Through a Cylindrical Tube

- Consider flow through a cylindrical tube



$$P = P_0 \text{ at } z = 0$$

$$P = P_L \text{ at } z = L$$

$$v_z = 0 \text{ at } r = R$$

$$\frac{\partial v_z}{\partial r} = 0 \text{ at } r = 0$$

- Velocity Profile, Volumetric Flow Rate, and Resistance to Flow

$$v_z = \frac{(P_0 - P_L)R^2}{4\eta L} \left(1 - \frac{r^2}{R^2}\right)$$

$$Q = \frac{(P_0 - P_L)}{8\eta L} \pi R^4$$

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

Hagen-Poiseuille
Flow



© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Biological Implications of Hagen-Poiseuille Flow

- About 2/3 of the resistance to flow in the peripheral circulation is in the small arterioles
- The resting diameters of small arterioles vary from 4 to 25 μm
- However, these diameters may be dilated or constricted enormously, as much as four times
 - Diameter can be altered by nervous or hormonal control
 - Due to Hagen-Poiseuille Flow and the variability of small arteriole diameter, flow can change up to $4^4 = 256$ times!!!



© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Biological Implications of Hagen-Poiseuille Flow

$$Re = \frac{\rho v D}{\mu}$$

	Diameter (cm)	Blood Velocity (cm/s)	Reynolds Number	
Ascending Aorta	2.0 - 3.2	63	3600 - 5800	turbulent
Descending Aorta	1.6 - 2.0	27	1200 - 1500	
Large Arteries	0.2 - 0.6	20 - 50	110 - 850	laminar
Capillaries	0.0005 - 0.001	0.05 - 0.1	0.0007 - 0.003	
Large Veins	0.5 - 1.0	15 - 20	210 - 570	
Venae Cavae	2.0	11 - 16	630 - 900	



© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Blood

- A viscous (~ 3 cP) fluid mixture of plasma and cells
- Major proteins include
 - Albumin (69 kDa, 4.5 g/100ml) regulates pH and osmotic pressure
 - Globulins (35 - 100 kDa, 2.5 g/100ml) are mainly immune mIcs
 - Fibrinogen (400 kDa, 0.3 g/100ml) is involved in clotting
- Major cell types include
 - Erythrocytes (95%), or red blood cells, direct oxygen transport
 - More dense than serum
 - Biconcave discoid shape
 - Platelets (4.9%) are involved in blood coagulation and hemostasis
 - Leukocytes (0.1%), or white blood cells, are the cellular participants in the immune response
- Hematocrit: cell volume fraction (40% - 50%)



erythrocyte (RBC)

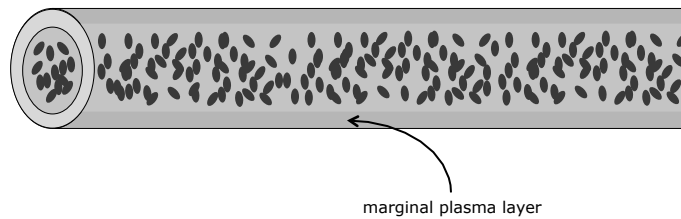


© Copyright 2012, John P. Fisher, All Rights Reserved

Overview of Circulation

Blood Flow

- RBCs are not evenly distributed within vessels
- RBCs tend to accumulate along the axis of the vessel
- Thus a thin cell free layer, called a marginal plasma layer, is created within vessels



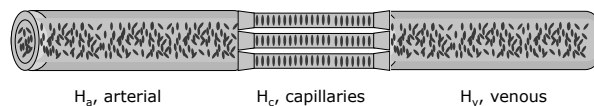
© Copyright 2012, John P. Fisher, All Rights Reserved



Overview of Circulation

Blood Flow

- Blood is non-Newtonian (H-P cannot wholly apply)
 - Above 100 /s shear rates, blood is Newtonian
 - Above 100/s: large vessels including arteries and veins
 - Below 100/s: microcirculation (rouleaux formation)
 - Without fibrinogen, blood is Newtonian down to 0.1 /s shear rates
- Fahraeus effect
 - Large vessel hematocrit > Small vessel hematocrit ($H_a = H_v > H_c$)



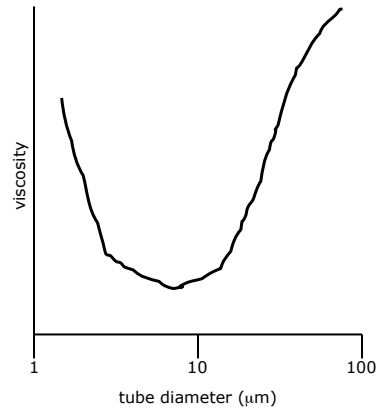
© Copyright 2012, John P. Fisher, All Rights Reserved



Overview of Circulation

Blood Flow

- Fahraeus-Lindquist Effect
 - As vessel diameter decreases, the apparent viscosity of blood decreases
 - Marginal wall viscosity is less than the central core viscosity
 - As vessel diameter decreases, marginal wall proportion increases
- Less than 4 – 6 microns, apparent viscosity increases
- A vessel of 2.7 microns is the smallest a RBC can enter



$$\eta_{\text{apparent}} = \frac{(P_0 - P_L)}{8LQ} \pi R^4$$



© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Introduction

- All blood vessels are distensible
 - Increased in diameter, decreases resistance, and increases blood flow
- Arterial distensibility allows the pulsatile cardiac output to be dampened
- Veins are about 8 times more distensible than arteries
- Definition of Distensibility

$$\text{Vascular Distensibility} = \frac{\text{Increase in Volume}}{(\text{Increase in Pressure} \times \text{Original Volume})}$$

- Definition of Compliance

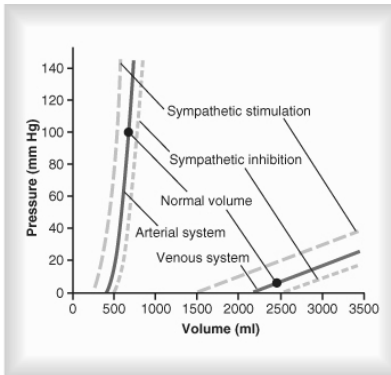
$$\text{Vascular Compliance} = \frac{\text{Increase in Volume}}{\text{Increase in Pressure}}$$



© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Volume-Pressure Relationships



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

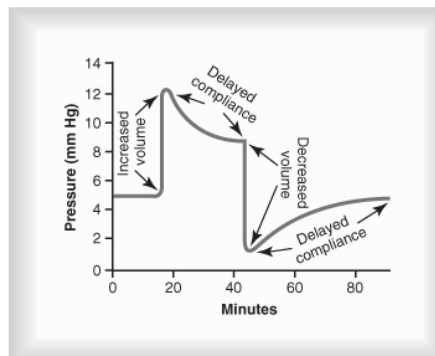


© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Delayed Compliance (Stress Relaxation)

- An increase in vessel volume will increase pressure, but slowly pressure is returned to near normal levels



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

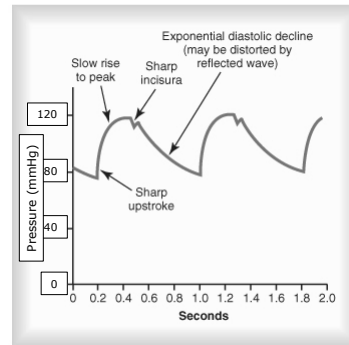


© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Arterial Pressure Pulsations

- Arterial compliance allows for blood flow during diastole
- Difference between systolic and diastolic pressure is the pulse pressure
- Pulse pressure is determined by
 - Stroke volume output
 - Arterial compliance
- Factors changing pulse pressure include
 - Arteriosclerosis (Inc PP)
 - Aortic stenosis (Dec PP)
 - Aortic regurgitation (Dec PP)



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

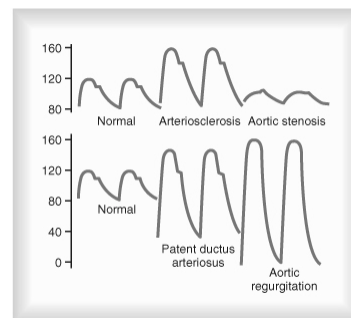


© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Arterial Pressure Pulsations

- When the heart ejects blood into the aorta, a pressure front is transmitted along the aorta
 - Transmission of the pressure pulse
- Typical values include
 - Aorta: 3 - 5 m/sec
 - Large arteries: 7 - 10 m/sec
 - Small arteries: 15 - 35 m/sec
 - *Increasing compliance implies an decrease in the transmission rate of the pressure pulse*



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

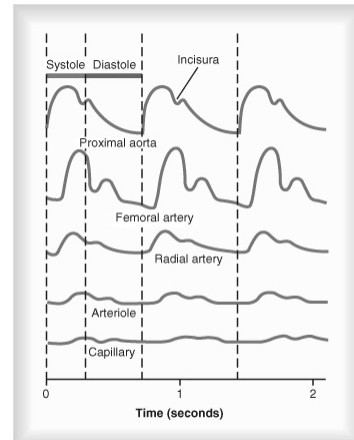


© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Damping of the Pressure Pulse

- As the pressure pulse is transmitted throughout the peripheral circulatory system, the pressure pulse falls in magnitude
- Damping occurs for two reasons
 - Increasing resistance in the smaller blood vessels
 - Decreasing compliance in the smaller blood vessels
- Degree of damping is almost directly proportional to the product of resistance and compliance



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

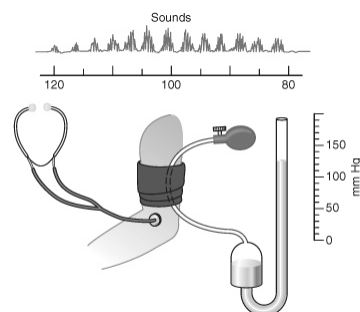


© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Measuring Blood Pressure

- A stethoscope is placed over the antecubital artery and a blood cuff is inflated around the upper arm to > 200 mmHg
 - Brachial artery is collapsed
- Pressure is released slowly in the cuff
- When pressure falls below systolic pressure, blood flow is partially restored and heard
 - Korotkoff sounds - sound quality changes with pressure
- When pressure equals diastolic pressure, sound diminishes - and the sound disappears 5 to 10 mmHg lower



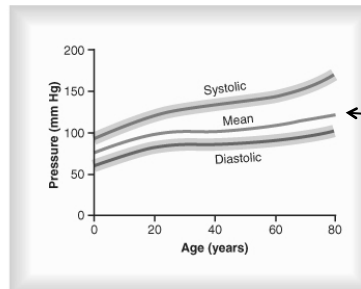
Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Blood Pressure



Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Veins and Their Functions

- As all the systemic veins flow back into the right atrium, the pressure here is called the central venous pressure
- Central venous pressure is regulated by both cardiac output and venous blood flow
 - Increase in cardiac output decreases central venous pressure
 - Increase in venous flow increases central venous pressure
 - Increased blood volume
 - Increased in vessel tone and thus venous pressure
 - Dilation of arterioles and thus decrease in peripheral resistance
- Normal right atrial pressure is 0 mmHg (*gauge pressure*)
- Lowest right atrial pressure is -3 to -5 mmHg, which is the pressure in the chest cavity



© Copyright 2012, John P. Fisher, All Rights Reserved

Vascular Distensibility

Veins and Their Functions

- Large veins provide little inherent resistance when they are distended
- However, external resistance exists in the large veins through other means
 - Surrounding tissues
 - Atmospheric pressure (neck and head)
 - Abdominal pressure
- An increase in right atrial pressure (+4 to 6 mmHg) causes large veins to open
- An increase in abdominal pressure (+15 to 30 mmHg) forces leg venous pressure to increase in order to return blood to the heart

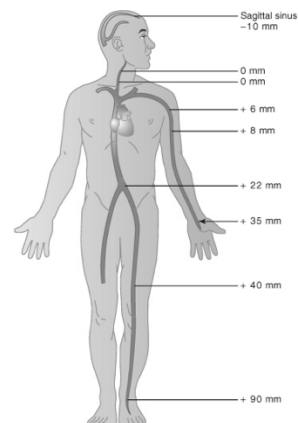
© Copyright 2012, John P. Fisher, All Rights Reserved



Vascular Distensibility

Hydrostatic Pressure

- A column of liquid exerts pressure due to the weight of the liquid
 - Pressure rises 1 mmHg for each 13.6 mm below the liquid surface
- Thus, a person standing still has
 - Right atrial pressure = 0 mmHg
 - Venous pressure in the feet = 90 mmHg
 - Venous pressure in the hands = 35 mmHg
- Also, a standing person also has collapsed neck veins (0 mmHg) due to atmospheric pressure
 - Veins in the skull do not collapse
 - Sagittal sinus = -10 mmHg



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

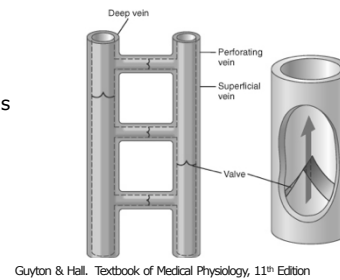
© Copyright 2012, John P. Fisher, All Rights Reserved



Vascular Distensibility

Venous Valves and Venous Pumps

- Veins contain small “valves” that allow blood to flow towards the right atrium and prevents it flow back into the arterial system
- A standing person would have a +90 mmHg pressure in the feet
 - However, skeletal muscle and other movements compresses the veins, moves blood unidirectionally through the valve system - *venous pump*
 - Pressure in walking feet is + 25 mmHg
- Standing without movement allows venous pressure to rise, movement of fluid into the interstitial space, loss of circulating blood volume - and eventually unconsciousness
- Varicose veins result from valve dysfunction and result in edema



© Copyright 2012, John P. Fisher, All Rights Reserved



Vascular Distensibility

Veins as Blood Reservoir

- More than 60% of the circulating blood is in the veins
- In response to up to 20% blood loss, venous constriction can maintain arterial blood pressure
- Other reservoirs
 - Spleen
 - Liver
 - Abdominal veins
 - Venous plexus beneath the skin
 - Heart and lungs

© Copyright 2012, John P. Fisher, All Rights Reserved



Microcirculation and the Lymphatic System

Introduction

- Microcirculation is the site of nutrient transport
- About 10 billion capillaries with a total surface area of 500 - 700 m² provide an interface between the circulation and surrounding tissues
- Most cells are within 20 to 30 μm of a capillary

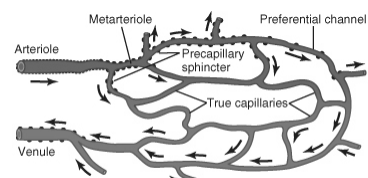


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Structure

- An artery branches 6 to 8 times, forming arterioles ($< 20 \mu\text{m}$)
- Arterioles then branch 2 to 5 times to form capillaries ($< 9 \mu\text{m}$)
 - Metarterioles are intermediate vessels
 - Precapillary sphincters, formed from smooth muscle fibers, regulate the opening and closing of capillaries
- Venules are formed on the venous side of the capillary bed
 - Weak, but pressure here is low



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

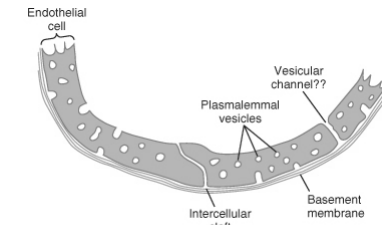


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Capillary Wall

- Formed from a unicellular layer of endothelial cells surrounded by a basement membrane
 - Wall thickness is $0.5\ \mu\text{m}$
 - Capillary diameter is $4 - 9\ \mu\text{m}$
- Contains intercellular clefts
 - Thin slit ($6 - 7\ \text{nm}$) between adjacent endothelial cells that allows fluid transport
 - Allows rapid water and small molecule transport
- Contains plasmalemmal vesicles



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

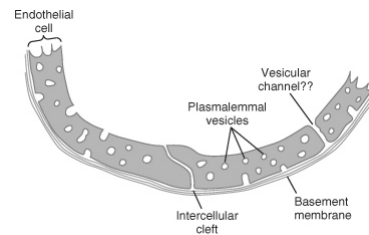


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Specialized Capillary Pores

- Brain capillaries have tight junctions that tightly regulate transport
 - Blood-brain barrier
- Liver capillaries are quite open, allowing free transport
- Kidney capillaries (glomerular tufts) contain fenestrae that allow regulated transport



Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Vasomotion

- Blood flow through capillaries is intermittent, regulated by the contraction of metarterioles and precapillary sphincters
- Oxygen is the key indicator, where increased oxygen demand opens metarterioles and precapillary sphincters
- Despite intermittent flow, the vastness of the capillary bed allows for key averages to be considered
 - Average rate of blood flow through the capillary bed
 - Average capillary pressure
 - Average rate of transfer of substances between the blood and surrounding tissues

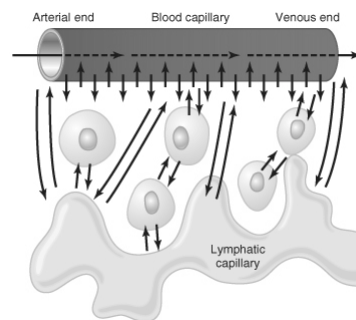
© Copyright 2012, John P. Fisher, All Rights Reserved



Microcirculation and the Lymphatic System

Nutrient Exchange

- Nutrient exchange from the capillary to the interstitial fluid is dominated by passive diffusion induced by thermal fluctuations (Brownian Motion)
- Lipid soluble molecules (oxygen and carbon dioxide) can diffuse directly through endothelial cell membranes
- Water soluble molecules (water, Na^+ , Ca^{++} , and glucose) must pass through capillary pores
 - Diffusion is incredibly fast
 - *Water diffuses through the capillary membrane 80x faster than the rate of plasma flow along the capillary!!!*
- The transport of molecules through the capillary pore depends upon molecule size and molecular concentration gradient



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved



Microcirculation and the Lymphatic System

Relative Permeability of Muscle Capillary Pores

Substance	Molecular Weight	Permeability
Water	18	1.00
NaCl	58	0.96
Urea	60	0.80
Glucose	180	0.60
Sucrose	342	0.40
Inulin	5,000	0.20
Myoglobin	17,600	0.03
Hemoglobin	68,000	0.01
Albumin	69,000	0.001

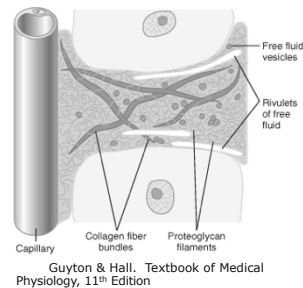


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Interstitium and Interstitial Fluid

- About 1/6 of the body consists of space between cells, interstitium, containing interstitial fluid
- Structural components include
 - Collagen fiber bundles, providing tensile strength
 - Proteoglycan filaments
- Interstitial "gel" fluid
 - Interstitial fluid contains the same components as plasma, but a significantly lower protein concentration, and forms a gel like material with the proteoglycan filaments
 - Little convective transport, mostly diffusion which is 90-95% the rate seen in free fluids
- Interstitial "free" fluid
 - Much less than 1% of tissue volume, however can expand rapidly during edema

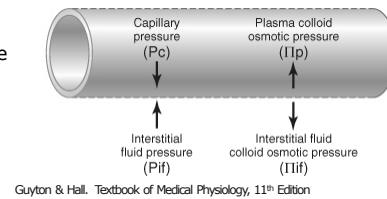


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Fluid Exchange Through the Capillary Membrane

- Four forces affect the movement of fluid between the capillaries and the interstitial spaces
- Capillary pressure (P_c)
 - Tends to drive fluid to the interstitial space
- Interstitial fluid pressure (P_{if})
 - Tends to drive fluid to the capillary
 - Can also pull fluid to the interstitial space
- Plasma osmotic pressure (Π_p)
 - Tends to cause osmosis of fluid to the capillary
- Interstitial fluid osmotic pressure (Π_{if})
 - Tends to cause osmosis of fluid to the interstitial space



Understand these forces !!!



© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Fluid Exchange Through the Capillary Membrane

- The sum of these forces gives us the following at the arterial end of the capillary
 - Outward Forces
 - Capillary pressure 30 mmHg
 - Interstitial fluid pressure 3 mmHg
 - Interstitial osmotic pressure 8 mmHg
 - Inward Force
 - Plasma osmotic pressure 28 mmHg
 - Net Force 13 mmHg Outward



© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Fluid Exchange Through the Capillary Membrane

- The sum of these forces gives us the following at the venous end of the capillary
 - Outward Forces
 - Capillary pressure 10 mmHg
 - Interstitial fluid pressure 3 mmHg
 - Interstitial osmotic pressure 8 mmHg
 - Inward Force
 - Plasma osmotic pressure 28 mmHg
 - Net Force 7 mmHg Inward

© Copyright 2012, John P. Fisher, All Rights Reserved



Microcirculation and the Lymphatic System

Starling Equilibrium

- Mean forces
 - Outward Forces
 - Capillary pressure 17.3 mmHg
 - Interstitial fluid pressure 3.0 mmHg
 - Interstitial osmotic pressure 8.0 mmHg
 - Inward Force
 - Plasma osmotic pressure 28.0 mmHg
 - Net Force 0.3 mmHg Outward

© Copyright 2012, John P. Fisher, All Rights Reserved



Microcirculation and the Lymphatic System

Starling Equilibrium

- A near state of equilibrium exists, where the amount of fluid filtering outward from some capillaries equals almost exactly the quantity of fluid that is returned to the circulation by absorption through other capillaries
 - The difference accounts for the volume of fluid returned by the lymphatic system
- Net filtration, movement of fluid to the interstitial space is about 2 ml/min, or 6.67 ml per minute per mmHg - *filtration coefficient*
- *Average filtration coefficient is about 0.01 ml/min/mm Hg/100 g tissue*

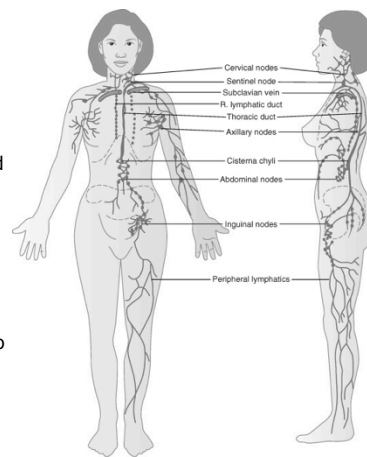


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

The Lymphatic System

- The lymphatic system is an accessory route by which fluid can flow from the interstitial spaces into the blood
- Lymphatics carry proteins and large particulate matter away from the tissue spaces, neither which can be removed by absorption into the capillary bed
- Almost all tissues have lymphatics or prelymphatics
- All the lymph from the lower part of the body flows into the thoracic duct and empties into the venous system
 - Lymph from the left side of the upper body also enters the thoracic duct
 - Lymph from the right side enters the right lymph duct and then into the venous system



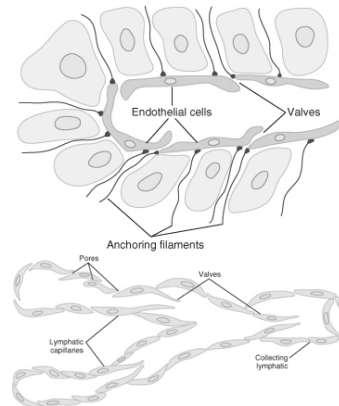
Guyton & Hall, Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

The Lymphatic System

- The lymphatic system provides a vital pathway for the recirculation of large proteins
- Lymphatic capillaries contain endothelial cells that use attaching filaments to connect to surrounding connective tissue
- A minute valve is formed that opens to the interior of the capillary
- Interstitial fluid, with suspended particles, push the valves open and move fluid into the lymphatics



Guyton & Hall, Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Lymph Components

- Protein concentration in the interstitial fluid is about 2 gm/dl and the protein concentration in the lymph flowing from these tissues is the same
- Liver lymph contains proteins at 6 gm/dl
- Intestinal lymph contains proteins at 3 - 4 gm/dl
- Lymph from the body contains proteins at 3 - 5 gm/dl, reflecting large proportion of lymph derived from the liver and intestines (about 2/3)

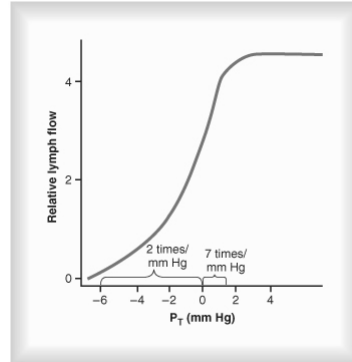


© Copyright 2012, John P. Fisher, All Rights Reserved

Microcirculation and the Lymphatic System

Lymph Flow Rate

- Total lymph flow rate is about 120 ml/hr
- Flow rate increases with increasing interstitial fluid pressure, due to
 - Elevated capillary pressure
 - Decreased plasma osmotic pressure
 - Increased interstitial fluid protein content
 - Increased capillary permeability



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

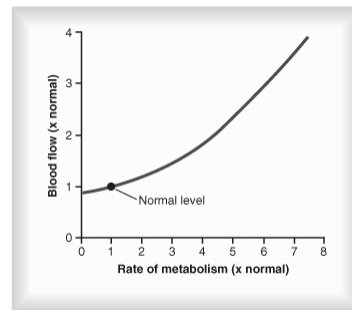


© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Introduction

- Each tissue controls its own blood flow, maintaining the necessary flow but not exceeding it, so as to
 - Provide oxygen
 - Provide nutrients, including glucose, amino acids, and fatty acids
 - Remove carbon dioxide
 - Remove hydrogen ions
 - Maintain ion balance
 - Transport hormone
- In general, the greater the metabolic needs of a tissue, the greater the blood flow
- Maintenance of needs allows for efficient use of supply



Effect of increasing metabolism on tissue blood flow.

Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Mechanisms of Blood Flow Control

- Control is either acute or long term
 - Acute
 - Seconds to minutes
 - Long term
 - Days, weeks, or months
 - Provides far better control to meet the needs of tissues

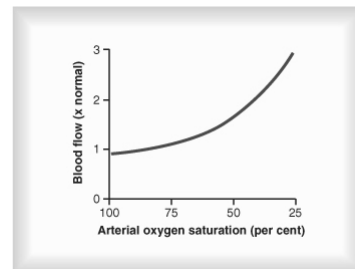


© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Acute Blood Flow Control

- Metabolic needs can dramatically alter blood flow
- Oxygen deficiency is a major determinant
 - High altitude
 - Pneumonia
 - Carbon monoxide poisoning
 - Cyanide poisoning
- Oxygen deficiency is thought to function through one of two mechanisms
 - Vasodilator theory
 - Oxygen demand theory



Effect of arterial oxygen saturation on blood flow through an isolated dog leg.

Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Acute Blood Flow Control

- Vasodilator Theory
 - Decreased oxygen (or other nutrients), increases the formation of vasodilator compounds, which increases vessel dilation in local tissues (paracrine signaling)
 - Possible vasodilators include adenosine, carbon dioxide, lactic acid, adenosine phosphates, histamine, potassium ions, and hydrogen ions
 - Adenosine may be the most potent of these signaling molecules
 - However, it has been difficult to demonstrate that any individual molecule is produced in significant quantities to effect significant dilation
 - Perhaps synergistic effect?



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Acute Blood Flow Control

- Oxygen Demand Theory
 - In the absence of oxygen, as well as other critical nutrients, vessel muscle tone may be diminished due to the simple lack of nutrients
 - In the increased usage of oxygen, as well as other nutrients, vessels would see decreased availability of oxygen and thus initiate vasodilation
 - For example
 - A tissue unit may regulate the number of precapillary sphincters that are open in response to changes in oxygen availability, thereby regulating oxygen delivery and blood flow
 - Similarly, a tissue unit may regulate the strength of precapillary contraction based upon the nutritional supply, thereby regulating oxygen delivery and blood flow
 - The oxygen demand theory is opposed by data demonstrating that vascular smooth muscle can remain contracted for long times while in oxygen debt
 - Other nutrients could regulate blood flow in a similar manner to the oxygen demand theory



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Acute Blood Flow Control

- Reactive Hyperemia
 - When a tissue unit has been lacking in blood flow and blood flow is returned, flow usually increases beyond normal levels
 - Hyperemia lasts in accordance with diminished blood flow - for seconds if blood flow has been interrupted for seconds, hours if blood flow has been interrupted for hours
 - Likely due to local vasodilation
- Active Hyperemia
 - When tissue is highly active (skeletal muscle during exercise), the rate of blood flow increases
 - Activity increases nutritional needs, increases the production of vasodilators, and thus increases blood flow
 - Skeletal muscle blood flow can increase 20x during times of exercise

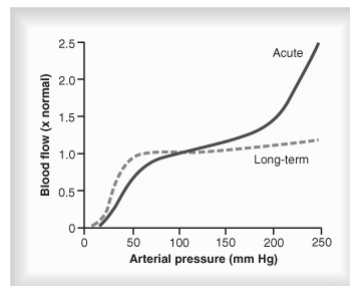
© Copyright 2012, John P. Fisher, All Rights Reserved



Local Control of Blood Flow

Acute Blood Flow Control

- Autoregulation of Blood Flow
 - An increase in blood pressure, increases blood flow, but within a minute blood flow returns to normal - autoregulation
- Metabolic Theory
 - Arterial pressure increases, blood flow increases, nutrition is too high, blood vessels contract, flow decreases
- Myogenic Theory
 - Sudden pressure increase causes a stretch of small blood vessels and smooth muscles to contract, causing vasoconstriction, and reduced blood flow
 - Such a theory implies a possible positive feedback loop and a potential vicious cycle leading to death
 - Thus theory likely only applicable to a few tissues and in limited circumstances



Effect of increasing arterial pressure on blood flow through a muscle. The solid curve shows the effect when change occurs quickly (minutes), the dashed curve shows the effect when change occurs slowly (weeks).

Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved



Local Control of Blood Flow

Acute Blood Flow Control

- Endothelial Derived Relaxing Factor
 - Local mechanisms for controlling tissue blood flow can dilate only small microvessels in local areas available to these controlling factors
 - Upstream and large vessels are largely unaffected
 - However, an endothelial-derived relaxing factor - nitric oxide - is highly upregulated in response to rapid blood flow
 - Increased flow increases endothelial shear stress, which induces endothelial stretch in the direction of flow, and causes the release of nitric oxide
 - Nitric oxide then causes arterial dilation
 - Remember, arterioles provide much of the resistance to flow, thus they play a critical role in overall regulation



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Long Term Blood Flow Control

- Acute control acts quickly, but does not provide perfect control
 - An increase in arterial pressure from 100 mmHg to 150 mmHg causes blood flow to increase 100%, and within 30 to 180 sec blood flow returns to 15% above normal flow
 - Long term control moves this 15% elevation back to nearly normal levels within a few weeks



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Long Term Blood Flow Control

- Tissue Vascularity
 - In the presence of decreased blood flow that is not meeting the needs of a tissue unit, the number of vessels perfusing the tissue unit can increase to provide sufficient blood flow
 - Vessel construction can occur in a matter of days in young organisms, new tissue growth, and cancerous growth
 - Degree of vascularity also significant
 - Vessel construction occurs more slowly in the elderly and the degree of vascularity can be reduced
 - Oxygen is a key regulator in long term control
 - High vascularity in organisms in reduced oxygen environments, such as high elevation or reduced fetal oxygen environments

© Copyright 2012, John P. Fisher, All Rights Reserved



Local Control of Blood Flow

Long Term Blood Flow Control

- Angiogenesis - the growth of new blood vessels
 - Occurs in response to angiogenic factors released from ischemic tissues, growing tissues, highly metabolic tissues
 - Potent angiogenic factors include
 - Endothelial cell growth factor
 - Fibroblast growth factor
 - Angiogenin
 - Angiogenesis mechanism - vessels sprout from either small venules or capillaries
 - Basement membrane supporting endothelial cells is dissolved
 - Endothelial cells proliferate
 - Endothelial migration in the direction of the angiogenic factor
 - Cells divide and fold over into a tube
 - Tubes connect with one another and form a capillary loop through which blood can flow
 - Significant blood flow can induce smooth muscle invasion

© Copyright 2012, John P. Fisher, All Rights Reserved



Local Control of Blood Flow

Long Term Blood Flow Control

- Collateral Circulation
 - If an artery or vein is blocked, a mechanism allows for the circumnavigation of the blockage
 - First, vascular loops dilate around the blockage within minutes
 - Collateral vessels grow size, forming many small channels rather than one large vessel
 - Normal blood flow is restored, though maximal blood flow capability may not be attainable
 - Illustrates both levels of blood flow control
 - Acute: Vascular dilation
 - Long term: Angiogenesis

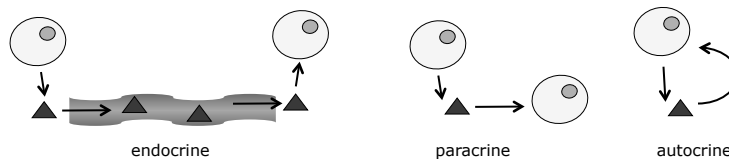


© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Humoral Regulation of Blood Flow

- Humoral regulation occurs by substances secreted or absorbed into the bodily fluids
- Regulation can occur in an endocrine or paracrine manner
 - Endocrine signaling
 - Excreted signals travel through the bloodstream to target cells widely distributed in the body
 - Paracrine signaling
 - Signals that act as local mediators, affecting only cells in the immediate environment of the signaling cell
 - Autocrine signaling
 - Signals that bind to the receptors on the signaling cell itself



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Humoral Regulation of Blood Flow

Vasoconstrictors

- Norepinephrine is a powerful vasoconstrictor, while epinephrine is less potent
 - When sympathetic nervous system is stimulated
 - Nerve ending release norepinephrine that excites the heart, veins, and arterioles
 - Adrenal medullae releases both norepinephrine and epinephrine into the blood
 - Hormones circulate throughout the body, causing systemic vasoconstriction
- Angiotensin
 - Potent vasoconstrictor (1 μg causes 50 mmHg rise in arterial blood pressure)
 - Causes powerful constriction of small arterioles
 - Typically acts systemically to increase total arterial pressure



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Humoral Regulation of Blood Flow

Vasoconstrictors

- Vasopressin
 - More powerful vasoconstrictor than angiotenin
 - Formed in the hypothalamus, transported to the pituitary gland from which it is secreted
 - Also affects water reabsorption in the renal tubules of the kidney
- Endothelin
 - Also powerful, requiring only nanograms to elicit vasoconstriction
 - Present in the endothelial cells of most blood vessels
 - Released after traumatic damage and acts to reduced blood loss



© Copyright 2012, John P. Fisher, All Rights Reserved

Local Control of Blood Flow

Humoral Regulation of Blood Flow

Vasodilators

- Bradykinin
 - Causes powerful arteriolar dilation as well as capillary porosity
 - Acts especially in damaged tissues, the skin, and gastrointestinal glands
- Serotonin
 - Present in the chromaffin tissues of abdominal structures
 - Acts as both a vasoconstrictor and vasodilator, depending upon environment
 - Doubtful role in systemic regulation
- Histamine
 - Released in response to traumatic damage
 - Causes powerful arteriolar dilation as well as capillary porosity
- Prostaglandins
 - Some vasoconstrictors, but mostly vasodilators
 - Probably acts locally



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Introduction

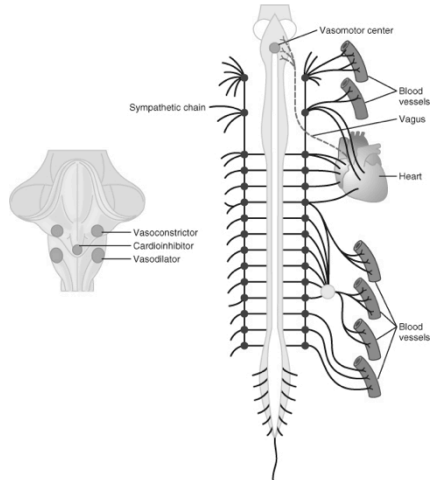
- Nervous regulation occurs almost entirely through the autonomic nervous system
 - The autonomic nervous system acts through the sympathetic and parasympathetic systems
- Sympathetic System
 - Nerve fibers leave the spinal cord through all the thoracic and the first two lumbar spinal nerves
 - Sympathetic nerves innervate the vasculature of the internal viscera and heart
 - Spinal nerves innervate the vasculature of the peripheral areas
 - Innervation of small arteries acts to increase resistance and decrease blood flow
 - Innervation of large arteries acts to decrease vessel volume
- Parasympathetic System
 - Little effect beyond innervation of the vagus nerves in the heart, where stimulation causes a decrease in cardiac output



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Anatomy of Sympathetic Nervous Control of the Circulation



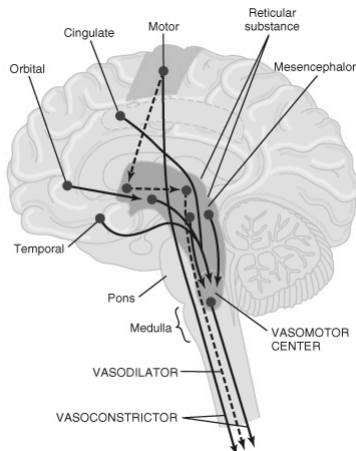
Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved



Nervous Regulation of Blood Flow

Participants in the Brain that Play Critical Roles in Nervous Regulation of the Circulation



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved

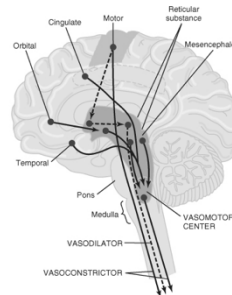


Nervous Regulation of Blood Flow

Sympathetic Vasoconstrictor System

Basic Anatomy

- Areas of the reticular substance of the pons, mesencephalon, and diencephalon can excite and inhibit the vasomotor center
- The hypothalamus can excite and inhibit the vasomotor system
- Similarly, the cerebral cortex can excite and inhibit the vasomotor system
- Widespread areas of the brain can have profound effects on cardiovascular function



Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Sympathetic Vasoconstrictor System

- The vasomotor system is located bilaterally in the reticular substance of the medulla and lower third of the pons
 - System transmits parasympathetic impulses through the vagus nerves to the heart and sympathetic impulses through the spinal cord and peripheral sympathetic nerves to most blood vessels
- Vasoconstrictor area
 - Located in the anterolateral portions of the upper medulla
 - Neurons secrete norepinephrine; fibers excite vasoconstrictor neurons of the sympathetic nervous system
- Vasodilator area
 - Located bilaterally in the anterolateral portions of the lower half of the medulla
 - Inhibit function of the vasoconstrictor area
- Sensory area
 - Located bilaterally in the tractus solitarius in the posterolateral portions of the medulla
 - Receive signals from the vagus and glossopharyngeal nerves
 - Controls functions of the vasoconstrictor and vasodilator areas

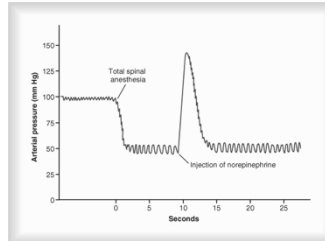


© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Sympathetic Vasoconstrictor System

- Under normal conditions, the vasomotor center sends signals that act to maintain sympathetic vasoconstrictor tone
- Blockage by spinal anesthesia causes a loss of vessel tone, and thus arterial pressure
- Stimulation by norepinephrine restores tone, until hormone is consumed



Guyton & Hall. Textbook of Medical Physiology, 11th Edition



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Sympathetic Vasoconstrictor System

- Sympathetic vasoconstrictor system also functions to control cardiac output
- Lateral portions of the vasomotor system send excitatory impulses that increase heart rate and contractility
- Medial portions send impulses through the vagus nerves to decrease heart rate
- Typically, cardiac functions occur in concert with vessel stimulation
 - Increase in cardiac output with vasoconstriction
 - Decrease in cardiac output with vasodilation



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Rapid Control of Arterial Pressure

- For a rapid increase of arterial pressure, the entire vasoconstrictor and cardioaccelerator systems function, while parasympathetic vagal inhibitory signals are also sent to the heart
- Results include
 - All arterioles of the body are constricted
 - Veins, and especially the large vessels of the circulation are constricted
 - Heart is directly stimulated by the autonomic nervous system to enhance cardiac pumping
 - *Both heart rate and contractility are upregulated*
 - *Response begins within seconds, and pressure can be doubled in 5 to 10 seconds*



© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Rapid Control of Arterial Pressure

- During exercise, skeletal muscle requires significant increases in blood flow
 - Increases result from local vasodilation of the muscle vasculature
 - Increases also result from an increase in arterial pressure
- Results include a 30 to 40% increase in arterial pressure, and an approximate doubling of blood flow to skeletal muscle
- As the nervous system stimulates the increase in activity, the reticular activating system of the brain stem is also activated, causing systemic vasoconstriction and increased cardiac output – raising arterial pressure
- Similar reactions occur in response to other events, including extreme fright



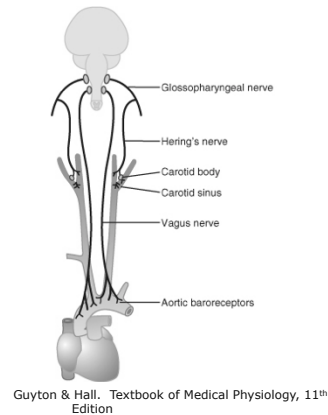
© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Baroreceptors

- Large systemic arteries contain cellular stretch receptors in their wall
- A rise in pressure stretches the baroreceptors, causing them to transmit signals to the central nervous system, and feedback signals are then sent through the autonomic nervous system to the circulation to reduce arterial pressure by vasodilation
- Baroreceptors are extremely abundant in the wall of each internal carotid artery slightly above the carotid bifurcation as well as the aortic arch
 - Signals are transmitted from each carotid sinus through Hering's nerve to the glossopharyngeal nerve and then to the tractus solitarius in the medullary of the brain
 - Signals from the aortic arch are transmitted through the vagus nerve into the same area of the medulla



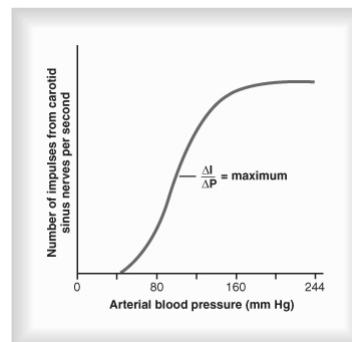
© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Baroreceptors

- Arterial pressure has a significant effect upon the rate of impulse transmission in Hering's nerve
- At normal arterial pressure, a slight change in pressure causes a significant change in the autonomic reflex
 - *Steep slope*
- Also, the rate of autonomic reflex is directly related to the rate of change in arterial pressure
 - *Linear relationship*



Response of the baroreceptors at different levels of arterial pressure

Guyton & Hall. Textbook of Medical Physiology, 11th Edition



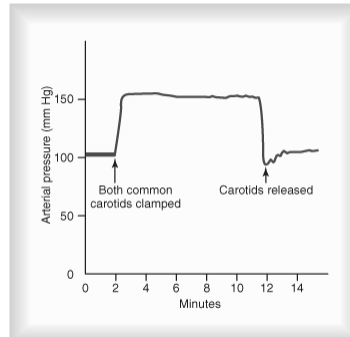
© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Baroreceptors

- Once signals enter the tractus solitarius, secondary signals inhibit the vasoconstrictor center of the medulla, causing
 - Vasodilation of the veins and arteries
 - Decreased heart rate and decrease in the strength of cardiac contraction
- Thus, baroreceptor excitation initiates a decrease in arterial pressure
- Similarly, baroreceptor inhibition initiates an increase in arterial pressure
 - This is the effect you sense upon standing quickly after lying down



Typical carotid sinus reflex on arterial pressure caused by clamping both common carotids after cutting the two vagus nerves

Guyton & Hall. Textbook of Medical Physiology, 11th Edition



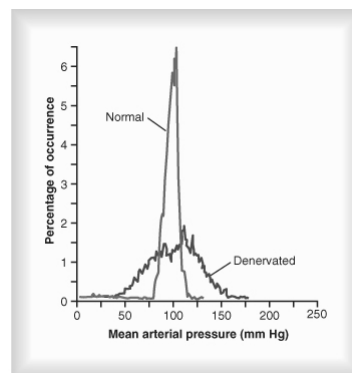
© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Baroreceptors

- The ability of the baroreceptor system to oppose both increases and decreases in arterial pressure changes defines the baroreceptor system as a buffering system
- Baroreceptor system plays no role in the long term maintenance of arterial pressure
- System resets after 1 to 2 days



Frequency distribution curves of arterial pressure for 24 hr in a normal dog and after denervation of the baroreceptor system

Guyton & Hall. Textbook of Medical Physiology, 11th Edition



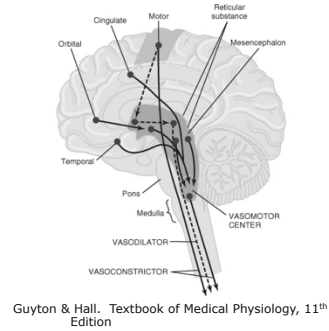
© Copyright 2012, John P. Fisher, All Rights Reserved

Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Carotid and Arterial Chemoreceptors

- Carotid bodies and aortic bodies contain chemoreceptors sensitive to the lack of oxygen
- When arterial pressure falls, chemoreceptors become stimulated because of lack of blood flow and thus oxygen
- Chemoreceptors send signals into the vasomotor center by way of Hering's nerve and the vagus nerves
- Excitation does not occur until arterial pressure falls below 80 mmHg, thus the chemoreceptors have a limited role in regulation



© Copyright 2012, John P. Fisher, All Rights Reserved



Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Central Nervous System Ischemic Response

- When blood flow to the vasomotor center is decreased (cerebral ischemia), the neurons of the center become extremely excited
 - Stimulus likely is an increase in carbon dioxide concentration
- Excitation initiates an increase of systemic arterial pressure to the limit of cardiac output
- Ischemic effect is extreme
 - Arterial pressure can increase 250 mmHg for up to 10 min
 - Some of the peripheral vessels become partially or totally occluded
- Initiated only when arterial pressure falls below 60 mmHg and thus is not a typical regulator mechanism

© Copyright 2012, John P. Fisher, All Rights Reserved



Nervous Regulation of Blood Flow

Reflex Mechanisms of Arterial Pressure Maintenance

Roles of Skeletal Nerves and Muscles

- Any stimulation of the sympathetic vasoconstrictor system also initiates the increase in basal tone in abdominal muscles, pushing blood out of the abdomen and thus increasing blood available to cardiac output
 - Abdominal compression reflex
 - Those with paralyzed skeletal muscle are susceptible to hypotensive episodes
- Both the anticipation of exercise and exercise itself causes skeletal muscle contraction, pushing blood from the peripheral vessels to the heart and lungs - thus increasing cardiac output

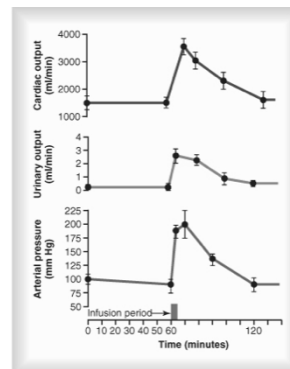


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Introduction

- While the nervous system provides an excellent means for acute blood flow regulation, it does not provide significant control in the long term
- The kidneys play a dominant role in long term blood flow regulation
 - When the body contains too much extracellular fluid, arterial pressure rises, causing the kidneys to excrete the excess extracellular fluid, thus returning arterial pressure to a normal level
- An increase in arterial pressure can augment kidney function
 - Renal output of water - pressure diuresis
 - Renal output of salt - pressure natriuresis



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

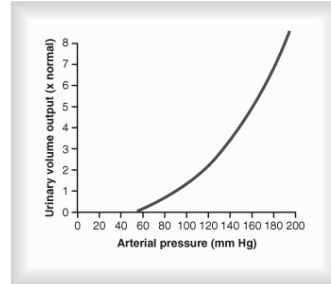


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Pressure Diuresis

- As arterial pressure rises, there is an increase of renal output volume
- This relationship can be plotted as a renal output curve or a renal function curve
- An infusion of blood volume increases both urinary output and cardiac output almost instantaneously - and both return to normal levels within an hour



Renal output curve measured in a perfused kidney showing pressure diuresis when arterial pressure rises above normal

Guyton & Hall. Textbook of Medical Physiology, 11th Edition

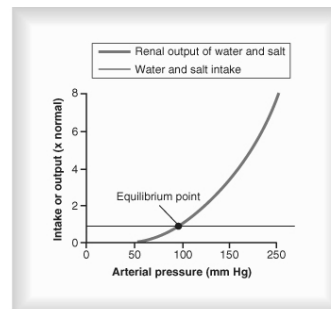


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Infinite Gain of Renal System

- Two curves define the renal system
 - The renal output curve for water and salt
 - The line of water and salt intake minus the amount of water and salt lost to the body in other ways than through the kidneys
- An equilibrium is established such that arterial pressure is always returned exactly back to the equilibrium point between these two relationships



Analysis of arterial pressure regulation by equating the renal output curve with the salt and water intake curve. The equilibrium point describes the level to which the arterial pressure will be regulated.

Guyton & Hall. Textbook of Medical Physiology, 11th Edition

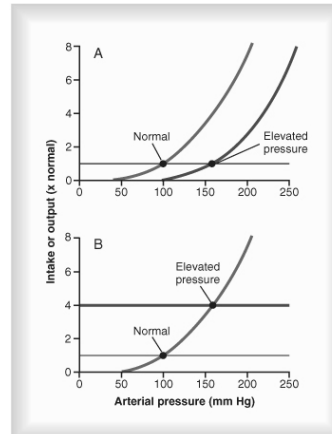


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Long Term Arterial Pressure Maintenance

- As long as the renal output curve for water and salt as well as the line of net water and salt intake remain constant, long term arterial pressure will remain at 100 mmHg
- Equilibrium can only be changes by shifting one of the two relationships
- Thus, long term arterial pressure is determined by
 - The degree of shift of the renal output curve
 - The level of the water and salt intake line



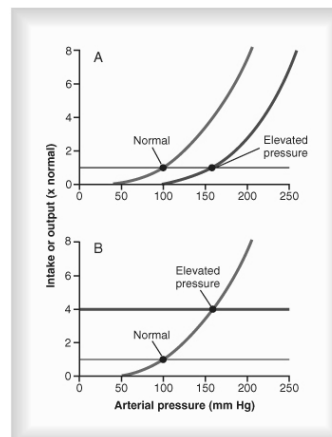
Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Long Term Arterial Pressure Maintenance

- Remember that an acute increase in total peripheral resistance elevates arterial pressure
- Yet, normally functioning kidneys should return arterial pressure
- The solution is that a change peripheral resistance does not necessarily change renal resistance and renal pressure
- Thus kidneys will act to excrete water and salt until arterial pressure is reestablished
- If renal pressure is altered, a different response is observed



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Long Term Arterial Pressure Maintenance

- The relationship between extracellular volume and arterial pressure is the following
 - Increased extracellular fluid volume, increases blood volume, increases mean circulatory filling pressure, increases venous return, increases cardiac output, which increases arterial pressure
 - An increase in cardiac output causes an increase in arterial pressure by
 - Direct effect of increased output increasing pressure
 - Indirect effect of tissue autoregulation of blood flow
 - *Increased blood volume increases blood flow, causing tissue induced vasoconstriction and thus increased peripheral resistance and arterial pressure*

© Copyright 2012, John P. Fisher, All Rights Reserved



Integrated System for Pressure Control

Long Term Arterial Pressure Maintenance

- The role of salt is far more likely to elevate arterial pressure than water intake
 - Water is excreted as quickly as it is ingested
 - Salt is slower in transport
- Salt indirectly increases extracellular fluid volume in two ways
 - Increased salt increases body fluid osmolality, causing a thirst response and an increase in bodily water volume
 - Increase body fluid osmolality stimulates the hypothalamic-posterior pituitary gland secretory mechanism to secrete antidiuretic hormone, inducing kidney reabsorption of water, and an increase in bodily water volume

© Copyright 2012, John P. Fisher, All Rights Reserved



Integrated System for Pressure Control

Hypertension

- Hypertension, or high blood pressure, is diagnosed when mean arterial pressure is above 110 mmHg, where normal is 90 mmHg
 - This occurs when diastolic blood pressure is above 90 mmHg and systolic pressure is above 135 mmHg
- Moderate elevation of arterial pressure leads to a shortened life expectancy due to
 - Excess heart work load leading to congestive heart disease, coronary heart disease, or both - leading to a heart attack
 - Cerebral infarct or stroke - rupture of a major cerebral blood vessel
 - Hemorrhage in the kidneys and kidney failure

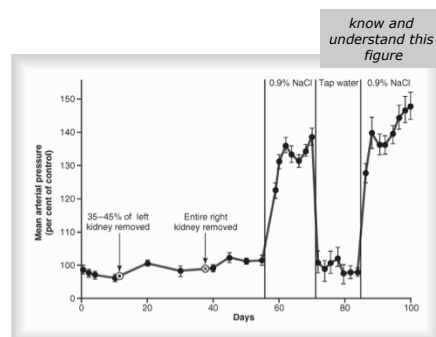


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Hypertension

- Hypertension due to reduced renal mass and increase in salt intake
- Reduction of kidney mass reduces the ability of the kidney to remove salt, thus increasing arterial pressure - shifting the renal function curve to the right
- The intake of both salt and water also causes increased arterial pressure - shifting the water and salt intake line up



Guyton & Hall, Textbook of Medical Physiology, 11th Edition

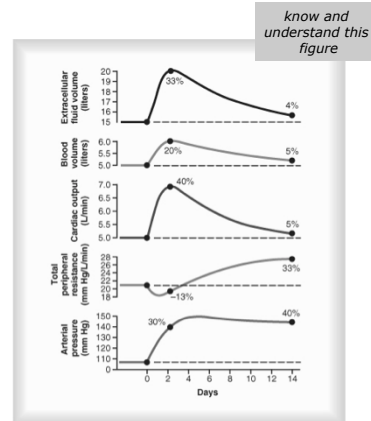


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Hypertension

- Again, the effects of reduced renal mass and increased salt & water intake is examined
- Initially, peripheral resistance falls in an attempt to keep arterial pressure low (baroreceptor mechanism)
 - After this fails, pressure rises
- Then, long term blood flow autoregulation takes over, where resistance increases, while fluid volume, blood volume, and cardiac output decrease
- *Hypertension induces an increase in peripheral resistance*



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

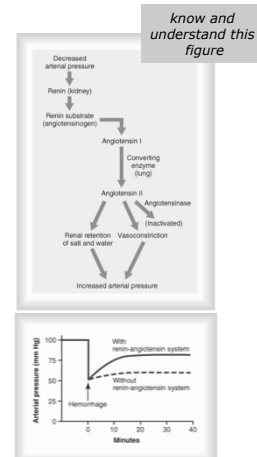


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Renin-Angiotensin System

- Renin is a small protein produced by the kidneys and released in response to a fall in arterial pressure
- Once released, renin acts on angiotensinogen to form angiotensin I
- Angiotensin II, a fragment of angiotensin I, is then formed by cleavage
- Angiotensin II is a powerful vasoconstrictor (increasing resistance and therefore pressure) and inhibitor of renal excretion of salt and water (increasing volume and therefore pressure)
- System actively maintains arterial pressure in response to significant changes in salt intake
- Angiotensin II is inactivated by angiotensinase



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

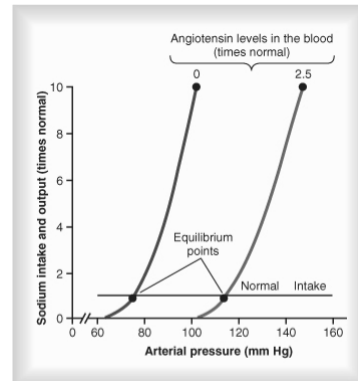


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Hypertension and Angiotensin

- Genetic conditions may lead to decreased or increased renin production
- Assuming sodium intake remains constant, the elimination of angiotensin will cause a dramatic reduction in arterial pressure
- Equally, an increase in angiotensin will cause a significant increase in arterial pressure
- Angiotensin can determine renal retention of water and salt, therefore altering arterial pressure



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

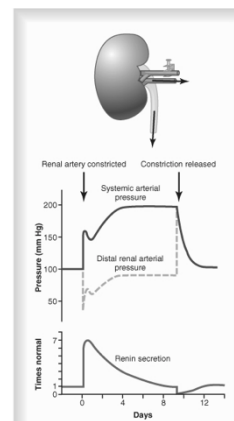


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Goldblatt Hypertension

- Here, one kidney is removed and the renal artery in the remaining kidney is constricted
- Renal pressure falls quickly, but arterial pressure rises over the course of days to reestablish renal pressure
 - Initial response due to renin-angiotensin system
 - Long term response due to increased volume resulting from fluid retention
 - Here, however, volume loading hypertension does not result directly from an increase in blood volume or cardiac output, but rather an increase in peripheral resistance



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

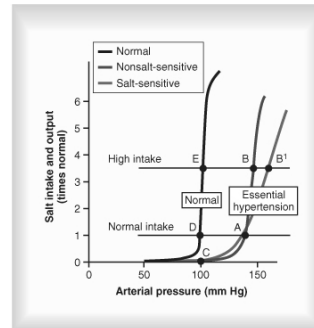


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Essential Hypertension

- Essential hypertension is a form of hypertension with unknown origin, but with typical characteristics
 - Mean arterial pressure is increased 40 - 60%
 - Renal blood flow is reduced by 50%
 - Renal resistance is increased 2 to 4 times
 - Cardiac output is about normal
 - Peripheral resistance is increased 40 - 60%
 - Renal excretion of salt and water requires high arterial pressure (150 mmHg)
- Treatments include drugs to increase renal blood flow (vasodilators) or decrease renal reabsorption of salt and water (diuretics or natriuretics)



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

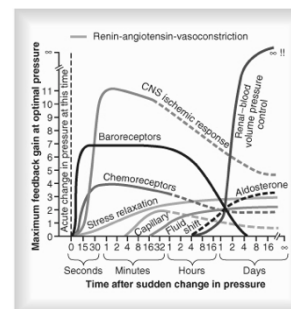


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Summary

- Arterial pressure is regulated by a variety of mechanisms
- Trauma leading to severe blood loss causes
 - Efforts to return arterial pressure, then
 - Efforts to return blood volume
- Acute changes are dominated by the nervous control system
- Kidneys dominate long term control system
- However, other systems do participate



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

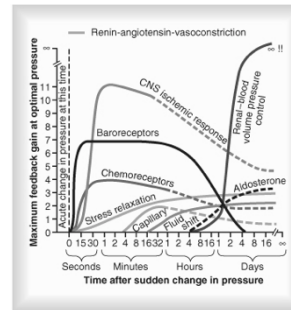


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Summary

- Initially, acute nervous reflexes or nervous responses provide fast acting control
 - Baroreceptor feedback mechanism
 - Central nervous system ischemic mechanism
 - Chemoreceptor mechanism
- These mechanisms result in increased arterial blood pressure due to
 - Constriction of veins and transfer of blood to the heart
 - Increased heart rate and heart contractility
 - Constriction of the arterioles to impede blood flow to peripheral arteries



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

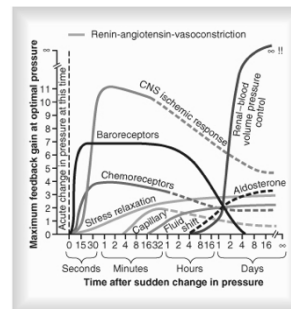


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Summary

- Next, intermediate control mechanisms take over
 - Renin-angiotensin vasoconstrictor mechanism
 - Stress-relaxation of the vasculature
 - Increased pressure causes increased stretch, which decreases pressure
 - Fluid movement between the capillary and interstitial volume to control blood volume
- These mechanisms result in increased arterial blood pressure over the course of minutes to hours



Guyton & Hall. Textbook of Medical Physiology, 11th Edition

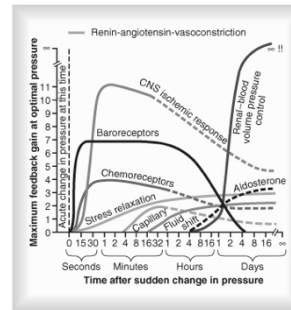


© Copyright 2012, John P. Fisher, All Rights Reserved

Integrated System for Pressure Control

Summary

- Finally, renal-blood volume control mechanisms dominate
 - Aldosterone effects are also significant
- These mechanisms have an almost infinite gain, bringing arterial blood pressure nearly always back to normal levels



Guyton & Hall, Textbook of Medical Physiology, 11th Edition

