Pathophysiology

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- Course website: rci.rutgers.edu/~advis
- Lectures, tests, grades, office hours, textbook,
- Material to be covered:
  Lectures 1-2: Introduction to Pathophysiology (2)
  Lectures 3-4: Mechanisms of Self-Defense and Stress (2)
  Lectures 5-8: Endocrine and Nervous System Dysfunctions (4)
  Lecture 9: Alterations of Skeletal Muscle Function (1)
  REVIEW AND TEST #1
  Lectures 12-18: Cardiovascular, Respiratory and Renal Dysfunctions (7)
  REVIEW AND TEST #2
  Lectures 21-24: Alterations of Digestive Function and Intermediary Metabolism (4)
  Lectures 25-26: Alterations of the Reproductive System (2)
  REVIEW AND TEST #3

- About lecture slides:
  - There are not intended to be the sole source for studying the course material !!!!!!!!!!!!!!!!
  - Slides are good to review the course material after you have study your course textbook
  - Slides are a good indicator of the relative importance of lecture topics (see slide # per topic
  - Group slides by titles when using them to review course material. Match lectures and text.

Basic Heart / Vessels Physiology

- Structure / Function
  cardiovascular system, heart / vessels structures, functions, and their control

- Vein occlusive disease
  varicose, CVI, DVT, SVCS

- Hyper- & hypo- tension
  Tr, 2tr, isolated systolic, complicated, and malignant
  HTN, postural hypotension

- Aneurysm, thrombosis, embolism

- Arterial occlusive disease
  troboangiitis obliterans, Reynaud disease

The heart as a pump and their anatomic and functional issues.
Coronary circulation & supply of O2 and nutrients to cardiocytes.
Variable membrane potential and rhythmicity of heart function.
Neuronal and hormonal control of heart and blood vessels.
The length tension curve (Starling law) and heart function.
The relationship of blood flow, pressure, and resistance.
The relationship of cardiac output, heart rate, and stroke volume.
The relationship of CO, MAP, and TPR.

Hormone / neural control of blood volume and blood pressure.

Some information you must recall from basic physiology, as a prerequisite for this CV pathophysiology section (see next slides)
The pulmonary circulatory system is a low pressure system while the systemic circulatory systems is a high pressure system.

**Structure / Function**
cardiovascular system, heart / vessels structures, functions, and their control

**Vein occlusive disease**
varicose, CVI, DVT, SVCS

**Hyper- & hypo- tension**
1ry, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

**Aneurysm, thrombosis, embolism**

**Arterial occlusive disease**
troboanginitis obliterans, Reynaud disease
Basic Heart / Vessels Physiology

Structure / Function
- cardiovascular system, heart / vessels structures, functions, and their control

Vein occlusive disease
- varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
- primary, secondary, isolated systolic, complicated, and malignant
- HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
- troboanginitis obliterans, Reynaud disease

Main structures directing blood flow, the heart walls and the heart valves
Basic Heart / Vessels Physiology

Structure / Function
cardiovascular system, heart / vessels structures, functions, and their control

Vein occlusive disease
varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
1st, 2ndry, isolated systolic, complicated, and malignant
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Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboanginitis obliterans, Reynaud disease

A composite chart of heart functions based on blood pressure and volumes, as well as heart sounds, venous pulse and EKG.

Structure / Function
cardiovascular system, heart / vessels structures, functions, and their control

Vein occlusive disease
varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
1st, 2ndry, isolated systolic, complicated, and malignant
HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboanginitis obliterans, Reynaud disease

A composite chart of heart functions based on blood pressure and volumes, as well as heart sounds, venous pulse and EKG.
Basic Heart / Vessels Physiology

Structure / Function
Cardiovascular system, heart / vessels structures, functions, and their control

Vein occlusive disease
varicose, CVI, DVT, BVCIS

Hyper- & hypo- tension
1ry, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboanginitis obliterans, Reynaud disease

Cardiovascular autonomic inervation and the heart conduction system
Basic Heart / Vessels Physiology

Vein occlusive disease
varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
1ry, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboanginitis obliterans, Reynaud disease

Drawing of arteries and veins, capillaries, valves in veins, and veins as blood reservoirs
Vein occlusive disease
varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
1st, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboangitis obliterans, Reynaud disease
Basic Heart / Vessels Physiology

Structure / Function
- cardiovascular system, heart / vessels structures, functions, and their control

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Aneurysm, thrombosis, embolism

Arterial occlusive disease
- troboanginitis obliterans, Reynaud disease

Factors regulating blood pressure

Blood pressure
- Hypertension

Cardiac output (CO)
- Increased CO

Peripheral resistance (PR)
- Increased PR

Blood viscosity

Vessel diameter
- (arteriolar)

Constrictor (alpha)

Dilator (beta, only for skeletal muscle arterioles)

Local regulation
- Ionic factors (O₂, K⁺, CO₂, H⁺)
- Autoregulation

Humoral regulation
- Vasodilators (NO, PG, EP)
- Endothelial-derived factors (nitric oxide)
- Vasconstrictors (Ang II, ET, NA)
Basic Heart / Vessels Physiology

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varicose, CVI, DVT, SVCS

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1ry, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
troboangiitis obliterans, Reynaud disease

Three mechanisms that influence total plasma volume
Basic Heart / Vessels Physiology

Vein occlusive disease
varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
1st, 2nd, isolated systolic, complicated, and malignant
HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
tuboaangitis obliterans, Reynaud disease

Angiotensins the organs they affect, and their receptors
### Vein Occlusive Diseases

**Structure / Function**
cardiovascular system, heart / vessels structures, functions, and their control

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varicose, CVI, DVT, SVCS

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A varicose vein is a vein in which the blood has pooled due to valve damage or by venous distention, thus they are distended, tortuous, and palpable. Surrounding tissue becomes edematous.

Varicose veins & valvular incompetence can progress to chronic venous insufficiency (CVI) with chronic pooling of blood, hyper-pigmentation of the skin (feet and ankles) and chronic edema.

Any trauma to the area lowers O2 supply by further decreasing area blood flow producing cell death. Necrotic tissue develops into venous stasis ulcers.

Venous thrombi are more common than arterial ones since blood flow and pressure are lower. Venous stasis may lead to inflammation, endothelial injury, hypercoagulability, and deep venous thrombosis (DVT).

Vein occlusive diseases such as varicose veins may progress to CVI and DVT. They are related to gravity, so they occur in the legs.

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Superior vena cava syndrome (SVCS) is a progressive occlusion of the SVC, leading to venous distention in upper extremities and head. Its etiology is bronchogenic cancer, lymphoma, and other cancer’s metastasis.

Cerebral & central nervous system edema may cause headaches, visual disturbances, and impaired consciousness. Respiratory distress may be present because of edema of the bronquial structures or compression of the bronchus by a carcinoma.

SVCS is generally not a vascular emergency but rather an oncological problem. Treatment consist of radiotherapy for the neoplasm and the administration of diuretics, steroids and anticoagulants.

Oclusion of superior vena cava occurs due to the relative low pressure of this vein, that lies in the close thoracic compartment.
Vein Occlusive Diseases

Structure / Function
- Cardiovascular system, heart, vessels, structures, functions, and their control

Vein occlusive disease
- Varicose, CVI, DVT, SVCS

Hyper- & hypo-tension
- Primary, secondary, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
- Treaubingitis obliterans, Reynaud disease

Examples of venous stasis ulcer and multiple venous trombi

Hypertension

Structure / Function
- Cardiovascular system, heart, vessels, structures, functions, and their control

Vein occlusive disease
- Varicose, CVI, DVT, SVCS

Hyper- & hypo-tension
- Primary, secondary, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
- Troboangitis obliterans, Reynaud disease

Hypertension (HTN) begins at a blood pressure of 120 / 80 mmHg. It is caused by an increase in CO, TPR, or both. CO is increased by conditions increasing HR or SV, while TPR is increased by any factor that raises blood viscosity or reduces vessel diameter.

Primary HTN (also known as essential or idiopathic HTN) affects 95% of HTN individuals. It is caused by a combination of genetic and environmental factors. A central process in this HTN is the shift in the pressure – natriuresis relationship. This cause less renal excretion of salt than normal.

Secondary HTN is caused by any process that raises TPR or CO, such as renal disease, adrenal disorders, vascular disease, and drugs (corticosteroids, oral contraceptives, and antihistamines).

Isolated systolic HTN (ISH) is when the systolic pressure is higher than 140 mm Hg and the diastolic pressure is below 90 mm Hg. It is usually caused by rigidity of the aorta. Increase pulse pressure suggests reduced vascular compliance of the large arteries.

A shift in the pressure – natriuresis relationship is a central process in the pathogenesis of primary hypertension.
Hypertension

Structure / Function
- cardiovascular system, heart / vessels structures, functions, and their control

Vein occlusive disease
- varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
- 1st, 2nd, isolated systolic, complicated, and malignant HTN, postural hypertension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
- troboanginitis obliterans, Reynauld disease

Complicated HTN is sustained primary HTN that causes pathological effects in addition to hemodynamic alterations and fluid and electrolytes imbalance. It affects vessels, heart, kidneys, eyes, & brain. Cardiovascular complications include left ventricular hypertrophy, angina pectoris, congestive heart failure, coronary artery disease, myocardial infarction, and sudden death.

Malignant HTN is a rapidly progressive HTN in which the diastolic pressure is above 140 mm Hg. It cause profound cerebral edema that disrupts cerebral function and cause loss of consciousness.

Generally the early stages of HTN have no specific clinical signs (silent disease), even when it is damaging other organs. Beside elevated blood pressure, the signs and symptoms are specifics for the organs or tissues affected.

HTN treatment starts with reducing or eliminating the risk factors. Among the drugs used are thiazide diuretics, ACE inhibitors, AgII receptor blockers, and adrenergic blockers.

A shift in the pressure – natriuresis relationship is a central process in the pathogenesis of primary hypertension.
Hypertension

Structure / Function
- cardiovascular system,
- heart / vessels structures, functions, and their control

Vein occlusive disease
- varicose, CVI, DVT, SVCS

Hyper- & hypo- tension
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Aneurysm, thrombosis, embolism

Arterial occlusive disease
- tibioangitis obliterans,
- Reynaud disease

Factors that cause a shift in the pressure – natriuresis relationship
Genetics

Increased SNS

Increased RAA (especially aldosterone)

Endothelial dysfunction

Dysfunction of the natriuretic hormones

Renal glomerular and tubular inflammation

DECREASED RENAL SALT EXCRETION
(shift in pressure natriuresis relationship)

Decreased dietary potassium, magnesium and calcium

Increased dietary sodium intake

Insulin resistance

Obesity

DECREASED RENAL SALT EXCRETION
(shift in pressure natriuresis relationship)

Hypertension

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1st, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

Aneurysm, thrombosis, embolism

Arterial occlusive disease
tibiofemoral, infrapopliteal, tibio- and popliteal, arterial insufficiency

Summary of treatment recommendations for hypertension
Hypotension

HYPOTENSION

Orthostatic or postural hypotension is a drop in systolic and diastolic arterial blood pressure on standing from a reclining position. The compensatory vasoconstriction response to standing is replaced by marked vasodilation & blood pooling in muscle vasculature and in the splanchnic and renal beds.

Acute postural hypotension might be caused by anatomic variations, altered body chemistry, antihypertensive and anti-depressant therapy, prolonged immobility due to illness, starvation, physical exhaustion, fluid volume depletion, and venous pooling.

Chronic postural hypotension may be secondary to a specific disease, such as adrenal insufficiency, diabetes mellitus, intracranial tumors, cerebral infarcts, and peripheral neuropathies.

Summary of treatment recommendations for hypertension
Aneurysms

Aneurysms are a localized dilation or outpouching of a vessel wall or cardiac chamber. Wall tension increases as the wall becomes thinner, so the possibility of rupture increases. The stretching produces infarct expansion, a thin layer of necrotic muscle and fibrous tissue that bulges with each systole. With time, the aneurysm can leak, cause pressure on surrounding organs, impair blood flow, or rupture.

A true aneurysm involves all layers of an arterial wall and there is weakening of the vessel wall. A false aneurysm (or saccular aneurysm) is usually the result of trauma. They are caused by a break in the wall or dissection of the layers of the arterial wall, and blood is contained by the adventitial layer.

Treatment of aneurysms is nearly always surgical. Leaking cerebral aneurysms are treated with clot-stabilizing drugs and a number of clinical measures designed to reduce intracranial pressure and promote hemodynamic stability before surgical intervention.
A thrombus is a blood clot that remains attached to a vessel wall. Thrombi tend to develop where intravascular conditions promote activation of the coagulation cascade. In arteries, this is caused by roughening of the tunica intima by arteriosclerosis or infection. In veins, thrombi formation is associated with inflammation. They also form in heart valves if there is an endocarditis or rheumatic heart disease. A thrombus might occlude an artery and cause ischemia or it may dislodge and travel until it occludes a distal systemic or pulmonic vascular bed. They are treated with heparin, warfarin, streptokinase or using a balloon-tipped catheter.

An embolus is a bolus of matter that circulates in the bloodstream that may occlude a blood vessel. It may be a dislodged thrombus, an air bubble, or an aggregate of fat, bacteria, or cancer cells. A pulmonary embolism originates mostly from deep leg veins or from the heart. Systemic emboli most commonly originate from the left heart and are associated with thrombi after myocardial infarction, valvular disease, left heart failure, endocarditis, & dysrhythmias.

**Difference between a thrombus and an embolus**

**Thrombosis and Embolisms**

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1st, 2ndry, isolated systolic, complicated, and malignant HTN, postural hypotension

**Aneurysm, thrombosis, embolism**

**Arterial occlusive disease**
troboaingitis obliterans, Reynaud disease
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Thrombosis and Reynard Disease

**Thromboangiitis obliterans** is an inflammatory disease of peripheral arteries. Inflammation, thrombus formation, and vasospasm can occlude and obliterate portions of small and medium size arteries in feet & hands. Although its pathogenesis is unknown, it is associated with cigarette smoking. Its symptoms are pain and tenderness of affected parts. Its clinical manifestations are caused by sluggish blood flow, rubor caused by dilated capillaries, and cyanosis due to blood that remains in the capillaries after its O2 has diffused into the interstitium. Treatment include vasodilators, sympathectomy, and if gangrene ensues, amputation.

**Reynard phenomenon** and Reynard disease are characterized by vasospasm attacks in small arteries and arterioles of fingers and toes. The former is secondary to systemic diseases such as collagen vascular disease, pulmonary hypertension, thoracic outlet syndrome, myxedema trauma, serum sickness, or long-term exposure to vibrating machinery or cold in the workplace. The latter, Reynard disease, is a primary vasospastic disorder of unknown origin that tend to affect women.

**Difference between a thrombus and an embolus**