Disorders of Circulation
MHD 2018-19

Concepts

- Hyperemia vs Congestion vs Hemorrhage
- Edema
- Thrombosis/Embolism/Infarction
- Shock

Hyperemia vs Congestion

- Both refer to
  - increased intravascular blood volume
    - in tissue, an organ, or body part
Hyperemia

- **Active process**
  - Arteriolar dilatation and increased blood flow
    - Caused by sympathetic neurogenic discharge or chemical mediators
  - Tissues appear “redder”
  - Examples
    - Sites of inflammation
    - Exercising skeletal muscle

Congestion

- **Passive process**
  - IMPAIRED OUTFLOW of VENOUS blood from a tissue
- Systemic process vs isolated process
- Acute vs chronic
- Tissues have abnormal “red-blue” color

Congestion

- **Clinical example**
  - Congestive heart failure
    - Hepatic congestion
Hemostasis - Definition

- A series of regulated processes that
  - maintain blood in a fluid clot-free state in normal vessels
  - rapidly form a localized hemostatic plug at the site of vascular injury

Self-check:
- Describe the necrotic area.
- What are the cellular features?
- Compare to normal.
Hemorrhage - Definition

- Flow of blood from a ruptured blood vessel
  - Blood may flow into tissue, into a body cavity or outside the body

Hemorrhage - Mechanisms

- Bleeding occurs when large or small blood vessel is disrupted by
  - a mechanical force (trauma)
  - pathologic process (congestion, inflammation, neoplastic erosion of vessel)

- Abnormal hemostasis causes a predisposition to bleeding

Hemorrhage – Clinical Correlation

- Except for ______________, hemorrhage of any kind should be considered abnormal.
Hemorrhage – Clinical Correlations

- Seriousness depends on site as well as rate/amount of blood loss

Edema - Definition

- Result of movement of fluid from vasculature into interstitial spaces or body cavities

Normal Physiology
Normal physiology

- Near equilibrium created by hydrostatic pressure and oncotic pressure allows for most fluid to remain within vascular compartment
  - note: even under normal conditions, some fluid may accumulate in the interstitium
    - this slight excess fluid is removed and returned to circulation by lymphatics

Why does my patient have edema?

- Increased hydrostatic pressure
  - Systemic: Heart failure
  - Local: Impaired venous return post deep venous thrombosis
- Decrease colloid osmotic pressure, due to reduced plasma albumin
  - Decreased synthesis (liver disease, malnutrition)
  - Increased loss (nephrotic syndrome)
- Lymphatic obstruction
  - Neoplasm
- Increased vascular permeability
  - Inflammation
- Sodium Retention
  - Renal failure
Pathways leading to systemic edema

- Heart Failure
  - Capillary hydrostatic pressure
  - Renal blood flow
  - Activation of the renin-angiotensin-aldosterone system
  - Retention of Na⁺ and H₂O
  - Blood volume
  - Plasma osmotic pressure
  - EDEMA

- Malnutrition, Hepatic Synthesis, Nephrotic Syndrome
  - Plasma albumin

Renal Failure

- Retention of Na⁺ and H₂O

Thrombosis - Definition

- Formation of blood clot (thrombus) within intact vessel
- Pathologic process
Mechanisms of Thrombosis

- **Endothelial injury**
  - Clinical examples: Inflammation; advanced atherosclerosis

- **Altered blood flow**
  - Clinical examples: Turbulence (atherosclerotic vessel narrowing) vs. stasis (atrial fibrillation, bed rest)

- **Hypercoagulable state**
  - Predisposition to easy clot formation
    - Clinical examples:
      - Inherited: Protein C deficiency
      - Acquired: woman who smokes and uses oral contraceptives; disseminated cancer
Virchow’s triad in thrombosis. Endothelial integrity is the most important factor. Abnormalities of procoagulants or anticoagulants can tip the balance in favor of thrombosis. Abnormal blood flow (stasis or turbulence) can lead to hypercoagulability directly and also indirectly through endothelial dysfunction.
Hypercoagulable States

Primary (Genetic)

- Factor V mutation (Arg to Glu substitution in amino acid residue 506 leading to resistance to activated protein C; factor V Leiden)
- Prothrombin mutation (G20210A noncoding sequence variant leading to increased prothrombin levels)
- Increased levels of factors VIII, IX, XI, or fibrinogen (genetics unknown)

Rare

- Antithrombin III deficiency
- Protein C deficiency
- Protein S deficiency

Very Rare

- Fibrinolysis defects
- Homozygous homocystinuria (deficiency of cystathione β-synthetase)

Secondary (Acquired)

High Risk for Thrombosis

- Prolonged bed rest or immobilization
- Myocardial infarction
- Atrial fibrillation
- Tissue injury (surgery, fracture, burn)
- Cancer
- Prosthetic cardiac valves
- Disseminated intravascular coagulation
- Heparin-induced thrombocytopenia
- Antiphospholipid antibody syndrome

Lower Risk for Thrombosis

- Cardiomyopathy
- Nephrotic syndrome
- Hyperestrogenic states (pregnancy and postpartum)
- Oral contraceptive use
- Sickle cell anemia
- Smoking

Fate of a Venous Thrombus

- Organization - Ingrowth of endothelial cells, smooth muscle cells, fibroblasts into thrombus
- Recanalization - Capillary channels may form within length of thrombus
  - Somewhat re-establish vessel lumen
- Overtime thrombus may be incorporated into well of remodeled vessel

“Organization/Recanalization”
Emboli - Definition

- Intravascular substance (solid, liquid, gas) which is carried by blood from point of origin to distant site.

  - Greek term “plug” or “stopper”

Types of Emboli

- Fragments of thrombi (thromboembolism)
- Atherosclerotic
- Amniotic fluid
- Air (gas)
- Fat

Emboli derived from a lower-extremity deep venous thrombus lodged in a pulmonary artery branch.
Fat and Marrow Emboli develop in patients with severe skeletal injuries

"Fat Embolism" syndrome is systemic (pulmonary insufficiency, neurologic
-Symptoms, anemia, thrombocytopenia, petechial rash)
Fatal in up to 10% of patients

Amniotic Fluid Emboli
-uncommon complication during active labor
-maternal mortality rate "80% world-wide
-neurologic deficits, dyspnea, cyanosis, shock
56-year old woman develops a popliteal venous thrombosis after hip replacement surgery. She recovers and returns to her job as a teacher. Three months later, which of the following terms would describe the process mostly likely seen in the popliteal vein?
A. Acute inflammation
B. Granulomatous inflammation
C. Embolization
D. Organization
E. Propagation

Infarction - Definition

- Infarct - area of ischemic necrosis caused by occlusion of vascular supply to affected tissue
  
  Self check – what is the pattern of necrosis?

- Majority of infarcts are associated with thromboembolism and involve arterial occlusions.

Types of Infarcts

- White (pale) infarct
  - Arterial occlusions
    - Solid organ with end-arterial circulation
      - Heart, spleen, kidney

- Red infarct
  - Tissues with dual circulations
    - Lung, small intestine
  - Venous occlusions
    - Ovarian torsion
  - Loose tissues
    - Lung
  - When flow re-established after infarction
    - S/p angioplasty of arterial obstruction
Infarcts

Lung

Spleen

Remote kidney infarct, now replaced by a large scar
Self-check – what is the “scar” composed of? Did any regeneration of kidney tissue occur? Why?

Factors That Influence Infarct Development

- Nature of vascular supply
- Rate of development of occlusion
- Vulnerability of tissue to hypoxia
- Oxygen content of blood
Clinical Outcome of Thrombosis

- Depends on many factors
  - Degree of occlusion of vessel lumen, collaterals, size of infarct
    - Partial occlusion may allow enough blood to flow to vital tissue
    - Complete occlusion usually results in infarction
      - Unless there is enough collateral circulation to support oxygen requirements of the tissue
    - Survival of patient determined by size and location of infarct as well as collateral circulation.

Shock

- Final common pathway for a number of serious events
- Characterized by systemic hypoperfusion of tissues with resultant
  - Impaired tissue perfusion
  - Cellular hypoxia
Three Major Types of Shock

• **Cardiogenic**
  - low cardiac output due to myocardial pump failure
    • MI
    • Ventricular Rupture
    • Arrhythmia
    • Cardiac Tamponade

• **Hypovolemic**
  - low cardiac output due to loss of blood or plasma volume
    • Hemorrhage
    • Fluid loss (vomiting, diarrhea, burns, trauma)

• **Septic**
  - arteriolar vasodilatation and venous blood pooling that stems from systemic immune response to microbial infection
    - Upcoming 1 hour lecture in Pulmonary Block

A 65-year old previously healthy man is hospitalized for bilateral pneumonia. On hospital day #8 he is found to have swelling and tenderness of his left leg. An ultrasound examination reveals findings consistent with acute left common femoral vein thrombus. Which of the following conditions is most likely to have contributed the most to this finding?

A. Protein C deficiency  
B. Prolonged immobilization  
C. Hypertension  
D. Left ventricle mural thrombus  
E. Chronic alcohol use

Summary

• Hyperemia vs Congestion vs Hemorrhage  
• Edema  
• Thrombosis/Embolism/Infarction  
• Shock
• On sectioning of an organ from a 69-year old woman at the time of autopsy, a focal wedge-shaped area that is firm is accompanied by extensive hemorrhage, giving it a red appearance. The lesion has a base on the surface of the organ. In which of the following situations did this lesion most likely develop?

A. Spleen with embolized mural thrombus
B. Kidney with septic embolus
C. Heart with coronary thrombosis
D. Lung with pulmonary thromboembolism