General Pathology

Thrombosis & Embolism
Infarction
Shock
(Web)

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**Terminology**

**Thrombosis**
- inappropriate activation of hemostatic process in uninjured or slightly injured vessels
- formation or presence of a solid mass (thrombus) within CV system

**Thrombus (pl. Thrombi)**
- aggregate of platelets and fibrin with entrapment of rbc’s/wbc’s
- can lead to vascular obstruction and embolism
- adherent to vascular wall (vs post-mortem blood clot)
Thrombosis

Human - Coronary artery with thrombus
(top left) External surface of the heart, where a coronary artery has been cross-sectioned, revealing a thrombus filling and completely occluding the lumen. Thrombi in coronary arteries are almost always due to endothelial damage resulting from atherosclerosis.
(bottom left) radiograph showing occlusion of a coronary artery and histiologic section showing almost complete filling of the lumen of a coronary vessel with a thrombus.
(top right) myocardial infarct resulting from coronary artery thrombosis.
Pathogenesis of Thrombosis → Virchow’s Triad

**Endothelial injury**
- dominant influence
  - thrombosis by itself

**Alterations in blood flow**
- turbulence
  - endothelial injury / activation
- stasis
  - no dilution of clotting factors
  - build-up of thrombi

**Hypercoagulability**
- ↑ prothrombotic factors
- ↓ inhibitory factors

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Fig. 2-24 (Zachary) Virchow triad in thrombosis. Endothelial integrity is the single most important factor. Note that injury to endothelial cells can affect local blood flow and/or coagulability; abnormal blood flow (stasis or turbulence) can, in turn, cause endothelial injury. The elements of the triad may act independently or may combine to cause thrombus formation.
Thrombi

Location in Cardiovascular System

Cardiac chambers

Mural thrombus left ventricular chamber – Feline Heart

Atrial thrombus (ball thrombus) in an enlarged left atrium of a cat with hypertrophic cardiomyopathy (note thickened wall of left ventricle)
Thrombi on the heart valves is often associated with infection / inflammation of the valves (ie septic thrombi of bacterial endocarditis)
Arterial thrombi • grow away from heart

Venous thrombi • grow toward the heart

Fig. 2-25 (Zachary) Thrombus (mural), artery. Thrombus formation is usually initiated by endothelial damage, forming a site of attachment for the thrombus. Growth of the thrombus is downstream, resulting in a tail that is not attached to the vessel wall. Portions of the tail can break off to form thromboemboli.
Arterial Thrombi

- usually form at sites of turbulence &/or endothelial injury
- often paler & “meater” than venous thrombi

Figure 02-26 (Zachary) Arterial thrombus, pulmonary artery, dog. Arterial thrombi are composed primarily of platelets and fibrin because of the rapid flow of blood, which tends to exclude erythrocytes from the thrombus; thus they are usually pale beige to gray (arrow).

Fig. 2-30 (Zachary) Large thrombus, pulmonary artery, cow. Large thrombi are less readily dissolved by thrombolysis and therefore heal by other methods. This thrombus consists of a large coagulum of fibrin that has undergone little to no resolution H&E stain.
Cardiac and larger arterial thrombi often have a laminated appearance characterized by alternating layers of platelets (white-gray) and fibrin (white) intermixed with erythrocytes and leukocytes (lines of Zahn). These lines are the result of rapid blood flow in the heart and arteries/arterioles that favors the deposition of fibrin and platelets and the exclusion of erythrocytes from the thrombus. This horse had verminous arteritis (Strongylus vulgaris fourth stage larvae) in the affected artery.
Venous Thrombi

- usually form in slow flow environments
- fibrin strands with entrapped rbc’s → more red colored
- sometimes difficult to differentiate from post-mortem blood clot

Figure 02-29 (Zachary) Venous thrombi, pulmonary vein, lung, horse
Venous thrombi become molded to the shape of the lumen of the vein.
Blood Clot

- can refer to thrombus or post-mortem blood clot (so be specific)
- PM blood clots are not associated with pathological change & not attached to wall
Chicken-Fat Clot

- gelatinous, yellow, post-mortem blood clot
- due to rapid erythrocyte sedimentation rate
- mostly horses, pigs

Erythrocytes settle due to gravity in a post-mortem blood clot similar to blood in a test tube; giving “chicken fat” appearance to the upper part of the clot.
Outcome of Thrombi

- Lysis (resolution)
- Propagation
- Embolization
- Organization / Recanalization
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**Fig. 2-32 (Zachary) Occlusive mural thrombus, recanalization, cat.** In occlusive and large thrombi, the healing process may occur by fibrosis and the invasion and growth of endothelial-lined vascular channels through the fibrosed area (recanalization). Note the vascular channel, horizontally in the middle of the thrombus. This provides alternate routes for blood flow to reestablish through or around the original thrombus. The permanent vascular narrowing and altered, more turbulent blood flow at the site of a healed thrombus result in an increased risk for subsequent thrombosis at the site. H&E stain.
Embolism

- passage through the venous or arterial circulation of any material capable of lodging in a blood vessel and thereby obstructing the lumen

Emboli (pl. Emboli)

- detached intravascular material carried via the blood to a site distant from its origin
- most emboli arise from thrombi (however other types can occur)
Thromboembolism

- occlusion of a blood vessel by an embolus that has broken away from a thrombus
- localizes at point where it can not longer "fit" through

Thromboembolus / Thromboemboli (pl.)

- the piece(s) of thrombotic material transported in the bloodstream to another site
Cardiac thromboemboli usually lodge at the bifurcation of the aorta into the external iliac arteries with a portion of the thromboembolus entering each iliac vessel to form a saddle thromboembolus. A saddle thromboembolus is not attached to the wall of the aorta or iliac arteries and is easily removed at necropsy. The thromboembolus is composed of layers of platelets and fibrin in which there are enmeshed erythrocytes.
Parasites - nematodes
- Dirofilaria immitis
Arteritis with thrombosis, cranial mesenteric artery, horse. Damage to the cranial mesenteric artery, by strongyle larval migration is relatively common in horses. Strongyle larvae are often found within the lesion (image to the right) and occasionally may be found within the resulting thromboemboli (most emboli don’t contain the larvae).
Fibrocartilagenous embolism, spinal cord, dog. Note vessel occluded with a cartilaginous embolism (large black arrow). As a result of the blocked vessel there is ischemic necrosis of the spinal cord (myelomalacia) with a focal area of hemorrhage (white arrow). At higher magnification (inset) the cartilaginous material in vessels stains bright blue with an Alcian blue stain.
**Composition of Emboli**

Fat
- bone fractures
- prolonged surgery
- osteomyelitis

*Fat embolus in a pulmonary artery, human.* Note, bone marrow embolus (mixture of fat and hematopoietic cells) in a medium-sized artery in the lung of a human patient that died of a heart attack with attempted CPR (ie the trauma of the CPR fractured a rib with resultant fragments of bone marrow gaining entry into a vein and embolism to the lung).
Composition of Emboli

Other

- foreign material (eg hair, air bubbles)
- tumor cells
- amnionic fluid
- etc

Pulmonary embolus containing fragments of hair. The hair has embolized to the lung, ie an injection with a large bore needle or some other form of trauma has resulted in fragments of skin / hair gaining entry into a vein with embolism to the lung.
Infectious causes of Thrombosis or Thromboembolism

- bacteria or viruses can cause localized or widespread endothelial damage (thrombosis, +/- thromboembolism)

Bacterial endocarditis in cattle often involves the right AV valves. They often give rise to septic thromboemboli which shower and implant in small branches of the pulmonary artery, resulting in scattered inflammatory foci (ie embolic pneumonia)
Infectious causes of Thrombosis or Thromboembolism

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Fig. 14-89 (Zachary) Thrombotic meningoencephalitis (previously referred to as thromboembolic meningoencephalitis), cerebrum, steer.

A, On the surface of the cerebral cortex (arrows) are several red-brown lesions. These lesions are areas of necrosis, hemorrhage, and inflammation secondary to vasculitis and thrombosis caused by Histophilus somni (formerly Haemophilus somnis). Such septic infarcts are distributed randomly (hematogenous portal of entry) throughout the CNS, including the spinal cord. The lesions depicted here are unusually severe. B, A thrombus (arrow) is present in the vascular lumen. Note the acute inflammatory response, edema, fibrinogenesis, and hemorrhage in the vessel wall.
Disseminated Intravascular Coagulation (DIC)

- sudden onset of widespread fibrin thrombi in microcirculation
- often *consumptive coagulopathy* (via consumption of platelets / coagulation factors)
- causes:
  - Severe burns
  - Heatstroke
  - Systemic viral disease
  - Shock (toxemia / septicemia)
  - Widespread metastatic tumors
  - Heartworm disease
  - Many other causes

Note fibrin thrombi with glomerular capillaries (PTAH) stain
Infarction

- **definition**: an area of ischemic necrosis resulting from occlusion of either arterial supply or venous drainage

- most due to **thrombosis**, **embolism** or **vascular occlusion** due to twisted vessels

- ~40% of human deaths result of CV disease, esp infarction (heart & brain)

- pulmonary, intestinal and renal infarction most common in domestic animals
Factors that Influence Development of an Infarct

1. Nature of the vascular supply
2. Rate of development of occlusion
3. Vulnerability to hypoxia
4. \( O_2 \) content of blood at time of infarct
The size of the renal infarct (represented by the 2 red triangles) is proportional to the caliber of vessel obstructed.
Red Infarct

- sometimes in acute renal infarcts with damaged vessels & hemorrhage

**Fig. 2-39 (Zachary) Acute hemorrhagic infarct, kidney, dog.** There is a focal wedge-shaped hemorrhagic area of cortical necrosis. The capsular surface of the infarct bulges above that of the adjacent normal kidney, indicating acute cell swelling and hemorrhage.
Infarction – Gross

Red Infarct

- venous infarction (no drainage)

Fig. 2-42 (Zachary) Venous infarction, small intestinal volvulus, pig. Note the intensely congested loops of small intestine undergoing early venous infarction. The veins have been compressed by a volvulus that has compressed the veins but not the arteries, thus preventing the venous return. If the volvulus had rotated further, it would also have compressed the arteries. (note, because arterial pressure is higher than venous pressure, the arterial wall is thicker and more resistant to compression, some blood can get into the gut but the compressed veins results in blood backing up & stagnating in the gut).
Pulmonary infarcts are typical dark areas at the margins of the lobes.

[Note: The lung receives blood flow from two circulatory systems: most is poorly-oxygenated blood from the pulmonary circulation and a smaller amount of well-oxygenated blood from the bronchial circulation]
Infarction – Gross

Pale Infarct

- lack of blood → mostly arterial occlusions in solid organs (heart, kidney)
- often zone of red at periphery

Fig. 2-40 (Zachary) Acute pale infarcts, kidney, rabbit. Multiple, pale white to tan pyramidal-shaped infarcts extend from the renal cortex to the medulla. The infarcts bulge above the capsular surface (center top), indicative of acute cell swelling. The glistening areas on the right are highlights from the photographic lamps.
• ischemic necrosis of affected tissue
Infarction – Repair

- scar tissue replaces parenchyma
- parenchymal loss + fibrous tissue contraction = depression / indent on surface
Myocarditis, necrosuppurative focal. dog. This focal area of myocardial necrosis and inflammation is due to a septic infarct resulting from valvular endocarditis due to *Staphylococcus* spp.
Venous Obstruction

- severe obstructions cause venous infarction
- mostly due to twisting of vessels (eg intestinal volvulus) \(\rightarrow\) shock / death
- occasionally obstruction (eg thrombosis or tumor) of portal vein or vena cava

note, vessels of the stomach, spleen & intestine are prone to constriction / compression when volvulus occurs of these organs (ie “torsion” of the supporting mesentery which includes vascular supply)
Gastric volvulus (torsion) in a dog → twisting of vessels → obstructs gastric portion of portal venous system → severe venous congestion (acute, local, congestion) → ischemia (necrosis) → loss of endothelial integrity → hemorrhage → shock → death

Acute Blockage of Portal Venous System

Venous infarction of a segment of small intestine due to strangulation by a pedunculated lipoma
Blockage of Posterior Vena Cava

Etiology

- in dogs, heartworm (high burdens) or tumor invasion

With heavy burden of heartworm, adults can sometime be in right heart (ventricle & atria) and caudal vena cava.

Pheochromocytoma (adrenal medullary tumor), dog. Note local invasion of vena cava which would impair venous return.
Blockage of Posterior Vena Cava

Etiology

• in ruminants with rupture of hepatic abscesses into caudal vena cava
Pulmonary Artery Thrombosis

- can be due to a variety of causes, eg:
  - pneumonia
  - parasites (eg heartworm)
  - hypercoagulability (eg nephrotic syndrome, hyperadrenocorticism)
  - liver abscess rupture into vena cava (ruminants)
  - deep vein thromboembolism (eg humans, downer cows)

note large thrombus in the pulmonary artery of a dog with hypercoagulability due to Cushing’s disease (hyperadrenocorticism)
Pulmonary Artery Thrombosis

Result
- depends upon size of artery blocked: Large artery → death

Small artery → infarction (usually red)

Note several pulmonary infarcts
• systemic hypotension due to reduced cardiac output or reduced blood volume

• final common pathway for:  
  • microbial sepsis
  • severe hemorrhage
  • extensive trauma or burns
  • myocardial damage
  • severe pulmonary embolism

• results in impaired tissue perfusion and cellular hypoxia

• brain and heart are organs most susceptible to ischemic damage from shock

3 General Categories

1. **Cardiogenic Shock**

2. **Hypovolemic Shock**

3. **Blood Maldistribution (Vasogenic Shock)**
Cardiogenic Shock

Failure of heart to adequately pump blood

- myocardial infarction
- arrhythmias (eg ventricular tachycardia)
- cardiomyopathy
- obstruction of blood flow
- etc
Hypovolemic Shock

Decreased circulating blood volume

- blood loss from hemorrhage
- fluid loss (eg vomiting, diarrhea, burns)
Blood Maldistribution (Vasogenic Shock)

- decrease in peripheral vascular resistance ➔ pooling of blood in peripheral tissues
- especially vasodilation due to:
  a) Anaphylactic Shock - release of vasoactive amines
  b) Neurogenic Shock - loss of ANS signals to arterioles
  c) Septic Shock - release of chemical mediators associated with infections
Pathogenesis

microbial substances (esp LPS) are released from bacteria

activation / injury of endothelial cells + stimulates WBC’s to release cytokines

vasodilation, prothrombotic (DIC), complement activation, etc
Three Stages of Shock

Figure 02-45. Shock. In hypovolemic shock, there is initially compensation characterized by increased cardiac rate and output, vasoconstriction of nonessential vascular beds, and predominantly oxidative metabolism by morphologically normal cells. With progression, cardiac output falls as peripheral vasodilation occurs and cell metabolism shifts to glycolysis with progressive morphological changes in cells.
Lesions of Shock

- pulmonary congestion & edema (cattle and horses)
- hepatic congestion (dog)
- heart - hemorrhage and necrosis
- brain - neuronal cell death
- kidneys - acute tubular necrosis
- blood vessels - endothelial damage (thrombosis / DIC)
- adrenal glands - hemorrhage
- GI tract - congestion and necrosis
- Skeletal muscle - pallor