HEART STRUCTURE AND FUNCTION (for your information only)

General considerations:
The heart is the first organ to form in the embryo. In mammals and birds it consists of 4 chambers (2 atria and 2 ventricles). The heart functions to maintain adequate blood flow (cardiac output) with the purpose of delivering oxygen and nutrients to the tissues and the removal of waste metabolic products.
The systemic circulation returns non-oxygenated blood to the right atrium via the vena cava, passes to the right ventricle and from here is pumped to the lungs via the pulmonary (pulmonic) arteries. The oxygenated blood returns to the left atrium via the pulmonary veins and finally the blood is pumped to the systemic circulation by the left ventricle. The heart is composed of three layers: pericardium (epicardium), myocardium (heart muscle) and endocardium.

Pericardium and Epicardium: The pericardium is a double layered serosal membrane that covers the heart and the proximal part of the great vessels. These two serosal membranes are composed of thin mesothelium and connective tissue supporting blood and lymphatic vessels, nerves and adipose tissue. The epicardial fat generally follows the coronary grooves. The lymphatic vessels on the epicardial surface are occasionally prominent and can be mistaken for lesions. The pericardial space present between the epicardium and pericardium contains small amounts of clear lubricant fluid.

Myocardium: The myocardial muscle is histologically similar but not identical to skeletal muscle. Myocardial fibres (myocardiocytes) are striated, branched, and contain a nucleus in the centre of the fibre; connective tissue is present between myocardiocytes. Myocardial muscle has characteristic intercalated disks through which fibres connect to each other allowing them to work as a single functional unit. The sarcoplasm contains myofilaments arranged in discrete bands (A, I, Z, bands), large numbers of mitochondria and abundant myoglobin. Purkinje fibers are specialized modified cardiac cells responsible for impulse conduction.

Endocardium: The inner lining of the heart and the valves are formed by endothelium (superficial), basal lamina and sub-endothelial connective tissue (elastic and collagen).
Endocardium also holds part of the conductive system (*Purkinje fibres*).

**Valves:** The heart has four valves that allow for unidirectional blood flow. These are the tricuspid valve (right AV valve); mitral valve (left AV valve or bicuspid valve); aortic valve; and pulmonic valve. The normal valvular leaflets (cusps) are thin, smooth, and partially translucent. The valves are lined by endothelium. AV valves attach to the papillary muscles of the ventricular myocardium by the chordae tendineae.

**Post-mortem examination:** There is no universal method to open the heart. The method chosen largely depends on the species, disease suspected and pathologist preference. The most important external features to be checked are:

<table>
<thead>
<tr>
<th>Silhouette in situ</th>
<th>Shape</th>
<th>Size</th>
<th>Weight (total and ratios)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Pericardial fluid</td>
<td>Fat deposits</td>
<td>Coronary vessels</td>
</tr>
<tr>
<td>Wall thickness</td>
<td>Valves</td>
<td>Endocardium</td>
<td>Great vessels</td>
</tr>
</tbody>
</table>

Once the heart has been opened, it is recommended to gently wash away excess blood from atria, ventricles and major blood vessels. Any abnormal change should be recorded and photographed for second opinion, if it is deemed necessary.

**RESPONSE TO INJURY**

**Important Consideration Regarding Cardiac Damage:**

Keep in mind that myocardiocytes lose their ability to regenerate soon after birth – therefore healing following damage is limited. Fortunately, the functional reserve of the heart is reasonably good and compensatory mechanisms exist to mitigate damage. Cardiac disease, therefore does not necessarily progress to heart failure. When cardiac function is impaired, several physiologic mechanisms act to maintain cardiac output and tissue perfusion of vital organs. The most important mechanisms are: activation of neurohumeral systems, cardiac dilation, and cardiac hypertrophy.

**NEUROHUMORAL ACTIVATION**

Decreased cardiac output and the resulting decreased circulating blood volume lead to the release of norepinephrine by cardiac nerves causing increased heart rate, augmentation of cardiac contractility and increased vascular resistance (via vasoconstriction). Similarly, there is activation of the renin-angiotensin-aldosterone system, which results in increased reabsorption of sodium and water by the kidneys and vasoconstriction. The resulting expansion of the blood volume induces secretion of atrial natriuretic peptide; this enhances sodium and water excretion and induces vasodilation as a counter mechanism.

**CARDIAC DILATION AND CARDIAC HYPERTROPHY**

Overall enlargement of the heart is referred to as cardiomegaly.

**Cardiac dilation** is a response to an increased workload in both physiologic and pathologic states. In cardiac dilation, the myocardial fibres stretch thereby increasing the contractile force, stroke volume and cardiac output (*Frank Starling relationship*). Continued stretch increases contractile force, up to a limit, after which increased stretch
will result in a decrease in tension developed. Chronic dilation of a ventricle can occur through addition of sarcomeres and hence lengthening of myocytes. Various disease conditions can cause an increased diastolic workload (also called preload) and hence dilation of the heart, such as vascular shunts and valvular insufficiencies. Acute overload of a chamber is expected to lead to dilation, whereas chronic volume overload may lead to the development of cardiac hypertrophy.

**Cardiac hypertrophy** can be primary or secondary to an increase in mechanical work or to trophic signals (as in hyperthyroidism in cats). Cardiac hypertrophy can be left ventricular, right ventricular, or bi-ventricular. Primary hypertrophy (ie cardiomyopathy) is less common, irreversible and most commonly seen in dogs and cats. Secondary hypertrophy is a physiologic and reversible increase in cardiac mass that results from an attempt to meet increased work demand. In pathologic states, hypertrophy is an adaptive response of limited benefit, where myocytes have impaired intrinsic contractility, impaired ventricular relaxation, and decreased compliance. This can cause increased end-diastolic pressure and ultimately lead to heart failure. Cardiac hypertrophy occurs in two distinct morphological types:

1. **Concentric hypertrophy**: Increase in myocardial mass with thick ventricular walls and reduced ventricular chamber volume. This is usually associated with pressure overload.

2. **Eccentric hypertrophy**: Increase in myocardial mass with enlarged ventricular chamber volume and relative thinning of the walls. This type of cardiac hypertrophy is accompanied by dilation and is usually associated with volume overload.

### Gross Changes in Cardiac Hypertrophy:

<table>
<thead>
<tr>
<th>Affected side</th>
<th>Gross changes*</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right side</td>
<td>Heart broader at the base</td>
<td>Pulmonary (arterial) stenosis, pulmonary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hypertension (Cor Pulmonale)</td>
</tr>
<tr>
<td>Left side</td>
<td>Increase heart length (axial)</td>
<td>Sub-aortic stenosis, systemic hypertension, feline hyperthyroidism</td>
</tr>
<tr>
<td>Bi-ventricular</td>
<td>Globose (rounded) shape</td>
<td>Hypertrophic cardiomyopathy, various congenital heart defects e.g., tetralogy of Fallot</td>
</tr>
</tbody>
</table>

Objective evaluation of myocardial hypertrophy can only be achieved using weight ratios; Overall normal heart weight to BW ratio < 1.0%

Cardiac hypertrophy has three sequential cellular stages:

1. **Initiation**: increase in cell size by increasing the number of sarcomeres and mitochondria.

2. **Compensation**: stable hyperfunction of the heart; absence or minimal clinical signs of heart failure.

3. **Deterioration**: degeneration of hypertrophied cardiomyocytes, loss of myocardial contractility and frank evidence of heart failure.
Myocardial Hypertrophy (Histopathology): Myocardial hypertrophy can be hard to evaluate microscopically without morphometric methods (measurement of cell size). Myocardiocytes increase in width, nuclei increase in size, while sarcomeres, myofilaments and mitochondria increase in number. Hyperplasia (an increase in the number of cells) does not occur in heart muscle cells.

CARDIAC FAILURE

If cardiac dysfunction is not properly compensated, it eventually leads to heart failure and clinical signs. When the heart fails, it occurs as a result of decreased blood outflow via the aorta and/or pulmonic arteries (low output heart failure) or because of inability to adequately empty the venous reservoirs (congestive heart failure): often these mechanisms will occur together. Signs of low cardiac output include depression, lethargy, syncope, and hypotension. Signs of congestive heart failure include swollen abdomen (ascites), tachypnea and dyspnea (resulting from pleural effusion and pulmonary edema).

Basic pathophysiological mechanisms involved in cardiac dysfunction*:

<table>
<thead>
<tr>
<th>Change</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump failure</td>
<td>Weak contractility and emptying of the chambers caused by myocardial degeneration, fibrosis, inflammation, and/or neoplasia.</td>
</tr>
<tr>
<td>Outflow obstruction</td>
<td>Vascular or valvular stenosis, systemic or pulmonic hypertension</td>
</tr>
<tr>
<td>Blood flow regurgitation</td>
<td>Valvular insufficiency, endocardiosis, endocarditis, volume overload</td>
</tr>
<tr>
<td>Shunted blood</td>
<td>Congenital heart defects or persistence of fetal circulation</td>
</tr>
<tr>
<td>Restricted atrial / ventricular filling</td>
<td>Cardiac tamponade, pericarditis, tumor</td>
</tr>
<tr>
<td>Conduction disorders</td>
<td>Arrhythmias caused by functional or structural abnormalities in the conduction system.</td>
</tr>
</tbody>
</table>

Adapted from PBVD

CONGESTIVE HEART FAILURE*

Congestive heart failure occurs when the heart is unable to pump blood at a rate sufficient to meet the metabolic demands of the tissues. It can be unilateral (left or right) or bilateral, and acute or chronic. It is most commonly found in dogs and cattle. Fluid retention, edema, venous congestion and, in some cases, cyanosis are the most common signs of heart failure.

- **Right heart failure*** → systemic venous and portal hypertension → generalized edema and chronic passive congestion of liver (**natumg liver**). Right heart failure may occur secondary to pulmonary hypertension (cor pulmonale)
  - Horses and cattle: Hydrothorax, ascites, and ventral (dependent) edema
Cats: Hydrothorax
Dogs: Ascites

- **Left heart failure**\(^*\) → pulmonary venous congestion → pulmonary congestion and edema (acute) → intraalveolar haemorrhage → alveolar siderophages (=**heart failure cells**) and pulmonary fibrosis in chronic cases. Fluid accumulation in lungs caused by left heart failure is clinically referred to as **cardiogenic pulmonary edema**.

**CONGENITAL HEART AND BLOOD VESSEL DEFECTS**

Embryonic development of the heart and vasculature is complex and subject to many forms of malformations. In fetal circulation there are venous-arterial shunts in atria, ventricles and great vessels (pulmonary artery and aorta). Atrial and ventricular communications close early in fetal life while the foramen ovale (atrial communication) and ductus arteriosus (pulmonic and aortic communication) close after birth. Some cardiac malformations are incompatible with intrauterine life resulting in embryonic resorption or fetal abortion; others can cause heart failure and clinical signs in postnatal life, while others are incidental (causing no clinical signs). The etiology of congenital heart defects is diverse including genetics (ie, gene/chromosomal abnormalities), maternal infections (eg, Parvovirus, Bluetongue virus, BVD virus), nutritional deficiencies (vitamin A, riboflavin), drugs (eg, thalidomide, ethanol, salicylates), and other teratogens (eg, radiation, fetal hypoxia, maternal diabetes). The cause may be multifactorial (ie, genetic and environmental factors). Often the cause is undetermined.

There are many types and combinations of congenital heart or vessel diseases. They can be divided somewhat into categories based on the pathophysiology.

1. **DEFECTS THAT CAUSE VOLUME OVERLOAD**
   a. **Left to Right shunts**: When a defect is present between the right and left cardiac chambers, blood flows down the pressure gradient from the left to right side.

   - **Patent Ductus Arteriosus (PDA)**\(^*\): A common defect in all species, particularly dogs (Poodles, Collies, and Pomeranians). The ductus arteriosus is a normal communication between the pulmonary artery and aorta in fetal circulation. This arterial communication normally closes functionally (via smooth muscle contraction) a few hours after birth and ultimately forms the **ligamentum arteriosum**. In PDA, the ductus fails to close. **Hemodynamics**: blood shunts from the Aorta → Pulmonary artery → leading to pulmonary hypertension. Pressure overload of the right ventricle (RV) and volume overload of the left ventricle (LV) occur, leading to hypertrophy of both sides. If pulmonary hypertension is severe enough, right to left shunting (reversal) of the blood may occur leading to cyanosis (= Eisenmenger syndrome). **Note**: functional closure of the ductus arteriosus normally takes several days in foals.
• **Atrial Septal Defect***: Can occur due to 1) persistence of the fetal *foramen ovale* or 2) a true defect in the closure of the atrial septum. It occurs in all species but is most common in dogs and cattle. Atrial communication results in a L to R shunt and RV volume overload. Minor defects show no clinical signs. **Hemodynamics**: Large defect: Excessive blood flow from Left atrium (LA) \(\rightarrow\) Right atrium (RA) causing volume overload of the RV \(\rightarrow\) RV hypertrophy.

• **Ventricular Septal Defect (VSD)***: One of the most common cardiac defects in domestic animals (esp. horses, cattle) which is characterized by inter-ventricular communication in postnatal life. Embryologically, the interventricular septum is formed by upward growth of the muscular septum, downward growth of the conotruncal ridge, and the membranous septum, which is derived from the endocardial cushion. Defects in any of these 3 structures may result in a VSD. Relative to the position in the septum, VSD can be low (close to the apex - rare) or high (close to the AV valves - common). **Hemodynamics**: Blood flow from LV to RV \(\rightarrow\) RV overload \(\rightarrow\) RV hypertrophy \(\rightarrow\) right heart failure (if uncompensated). LV hypertrophy often occurs as well. Blood shunts could later reverse from R\(\rightarrow\)L and cause cyanosis. This is called Eisenmenger complex when it occurs with VSD.

b. **Valvular Regurgitation**: Regurgitated blood from the ventricles to the atria leads to progressive atrial dilation and eccentric ventricular dilation of the affected side.

• **Tricuspid Dysplasia***: (most common in cats and dogs; Labrador retrievers). Dysplastic valves are characterized by thickened fibrous leaflets, short or rolled leaflets, missing or abnormally short chordae tendineae, thick papillary muscles, and/or abnormal fusion of chordae or valve leaflets to the ventricular wall. Tricuspid dysplasia causes RV hypertrophy and R atrial enlargement.

• **Mitral Dysplasia*** *(left atrioventricular valvular insufficiency or stenosis)*: It is probably the most common congenital cardiac anomaly in cats; in dogs, it has been most commonly seen in Cavalier King Charles Spaniels, Great Danes, and English Bull Terriers. Anatomically, there is an enlarged annulus, short thick leaflets, short thickened chordae tendineae, upward malposition of atrophic or hypertrophic papillary muscles, and enlargement of the left atrium and ventricle. Mitral valve dysplasia is often accompanied by tricuspid dysplasia, VSD or ASD.

2. **DEFECTS THAT CAUSE PRESSURE OVERLOAD**

Ventricular outflow obstruction causes a progressive /chronic increase in intraventricular pressure resulting in concentric hypertrophy of the affected side.

• **Pulmonic Stenosis***: (common in dogs; beagles, English bulldogs). It is characterized by an abnormally reduced lumen in the pulmonary artery. Depending on the location, pulmonic stenosis is classified as valvular, subvalvular or supravalvular. The stenotic site is formed by a constricting band of fibrous or muscular tissue. In some dogs, an anomalous coronary artery
obstructs the right outflow tract. Post-stenotic arterial dilation is generally found in the pulmonic artery, distal to the stenotic site. **Hemodynamics**: Obstruction of right ventricular outflow → pressure overload of RV → RV hypertrophy → post-stenotic dilation of the pulmonary artery → if uncompensated, right heart failure.

- **Subaortic Stenosis***: (most common in pigs and dogs; bull terriers, boxers, Newfies). Bands of fibrous tissue encircle the left ventricular outflow tract below the aortic valve. **Hemodynamics**: Obstruction of the LV outflow → LV pressure overload → LV hypertrophy → post-stenotic dilation of the aorta; if uncompensated, left heart failure and pulmonary congestion with edema. Dogs with subaortic stenosis often have concurrent mitral valve disease. Myocardial necrosis and fibrosis are not uncommon in affected dogs.

3. **DEFECTS THAT CAUSE CYANOSIS**

In these diseases, nonoxygenated blood from the right heart compartments flows to the left heart compartments or directly into the systemic circulation. This also occurs in cases of PDA and VSD when there is reversal of shunting from R to L.

- **Tetralogy of Fallot***: (>dogs, cattle). Three congenital defects plus one acquired alteration: 1) *Ventricular septal defect*; 2) *Pulmonic stenosis*; 3) *Dextraposition of the aorta (overriding aorta)*; 4) acquired *Right ventricular hypertrophy*. **Hemodynamics**: pulmonic stenosis → RV overload → RV hypertrophy → if uncompensated, right heart failure. In addition, increased RV pressure → right to left blood shunts (through the VSD) → venous blood enters systemic circulation → cyanosis.

4. **MISCELLANEOUS**

- **Persistent Right Aortic Arch***: (most common in dogs). In PRAA, the aorta is incorrectly formed from right rather than from left aortic arch. The trachea and esophagus are enclosed by the aortic arch, pulmonary artery and the *ligamentum arteriosum* which results in localized esophageal constriction causing esophageal dysphagia, regurgitation and megaesophagus. There are no cardiovascular anomalies or cardiac clinical signs.

- **Ectopia cordis**: (rare; mostly in cattle). Heart is located in an abnormal site. It may be extrathoracic, intraabdominal or pre-sternal. It is mostly found in stillbirths or aborted fetuses, but rare animals may survive for a few days or weeks.

**PATHOLOGY OF THE EPICARDIUM/PERICARDIUM**

**Serous atrophy of fat**: Typically seen in severe emaciation and cachexia. The pericardial, visceral and bone marrow fat appear gelatinous.

**Pericardial Hemorrhages**: These vascular changes are commonly seen during post-mortem examination and, according to the size of the hemorrhage, are classified as
petechial, ecchymotic or "paint brush" hemorrhages. Common causes of pericardial hemorrhages are septicemia, sepsis, toxemia, acute myocarditis, disseminated intravascular coagulation (DIC), and coagulopathies. Please note that pericardial hemorrhages are commonly seen in anoxic or in agonal states and these lesions should be interpreted accordingly.

**Pericardial Effusions**: Given time, the overall size of the pericardium can progressively increase to accommodate the presence of fluid or exudate in the pericardial sac. Rapid filling of the pericardium, however, can compress the heart preventing filling of the chambers during diastole resulting in decreased cardiac output and potentially heart failure (*cardiac tamponade*).

- **Hydropericardium**: Accumulation of fluid (transudate) with low protein and low cellularity in the pericardial sac. The serosal surface remains smooth and glistening. Chronically the epicardium may become opaque, rough and thick. According to the pathogenesis, hydropericardium can occur as a result of:
  - *Increased hydrostatic pressure*: Right heart failure or pulmonary hypertension.
  - *Decreased colloidal osmotic pressure (hypoproteinemia)*: Via loss of protein (protein losing enteropathy / nephropathy), decreased intake of protein (malnutrition / emaciation), decreased production of protein (liver disease)
  - *Altered vascular permeability*: Sepsis, disseminated intravascular coagulation (DIC), mulberry heart disease.
  - *Decrease lymphatic drainage*: Heart base or pericardial tumours

- **Hemopericardium**: Accumulation of blood in pericardial sac. Common causes include: atrial rupture (hemangiosarcoma in dogs), intra-pericardial aortic rupture (stallions), trauma, and iatrogenic (cardiac puncture). Accumulation of blood in the pericardium may cause cardiac tamponade and acute death. Caution: blood tinged fluid is frequently found as a post-mortem change in animals that have been dead for several hours.
  - Idiopathic hemorrhagic pericardial effusion has been reported in large/giant breed dogs. The effusion may be hemorrhagic or serosanguinous.

- **Pericarditis**: Inflammation of the pericardium. Pericarditis tends to be diffuse involving both the pericardium and epicardium (epicarditis). The most common types of exudate are fibrinous and suppurative.

- **Suppurative pericarditis** is most commonly seen in cattle as a complication
of traumatic reticuloperitonitis (hardware disease)*. Metal foreign bodies (wire, nails) may penetrate the reticulum and extend through the diaphragm into the pericardium and introduce bacteria from the reticulum.

- **Fibrinous pericarditis** typically results from hematogenous spread of bacteria to the pericardium.
  - Common causes in ruminants: *Mannheimia haemolytica*, *Clostridium chauvoei* (Blackleg disease), *E coli* (septic calves), *Streptococcus*, *Pasteurella multocida*
  - Common causes in pigs: *Haemophilus parasuis* (Glasser's Disease), *Streptococcus suis*, Mulberry heart disease (usually scant fibrin and abundant fluid)

- **Chronic pericarditis** generally leads to fibrosis and fibrous adhesions between the pericardium and epicardium, and between the pericardium and pleura. The formation of granulation tissue and fibrosis can result in **constrictive pericarditis** with concurrent myocardial hypertrophy and possible right heart failure. In constrictive pericarditis, the heart is encased in a dense fibrous scar that limits diastolic expansion and cardiac output. The fibrous scar may obliterate the pericardial space or become calcified.

**PATHOLOGY OF THE ENDOCARDIUM AND VALVES**

**Endocardial Hemorrhage**: This is a very common finding on post-mortem examination. Endocardial hemorrhages occur in sepsis, toxemia, asphyxia, coagulopathies and as an agonal change.

**Endocardial Fibrosis and Fibroelastosis**: 

- **Acquired localized endocardial fibrosis** occurs in the so-called "jet lesions" caused by mechanical injury to the endocardium due to abnormal blood turbulence. Jet lesions are often seen in valvular insufficiencies and typically occur in the atria.
- **Acquired generalized endocardial fibrosis** occurs whenever a ventricle or an atrium is dilated for a prolonged period. This is particularly prominent in dogs with dilated cardiomyopathy.
- **Primary endocardial fibroelastosis** occurs as a hereditary disease in cats (Burmese cats). It is characterized by diffuse thickening of the endocardium accompanied by left ventricular hypertrophy and dilation in animals with no other cardiac abnormalities (not acquired). Lesions begin at ~ 1 day of age.
- When generalized, these lesions can impair and reduce stroke volume leading to congestive heart failure.
- Grossly, the endocardium appears white, thick, and roughened.
- Histologically, the endocardium is thickened by the abnormal deposition of collagen and elastic fibres.
**Endocardial Mineralization***: Abnormal deposition of calcium or mineral in the endocardium and arteries (arterial medial calcification) occurs in all species. It can occur as a result of dystrophic or metastatic mineralization.

- Possible causes include hypervitaminosis D (iatrogenic Vit D toxicity) or ingestion of Vitamin D analogs present in some rodenticides (calciferol) or toxic plants (*Solanum malacoxylon* and *Cestrum diurnum*).
- Mineralization is also found in the endocardium of cachectic animals (i.e. tuberculosis, paratuberculosis) and in uremic dogs (uremic endocarditis).
- Grossly, the endocardium is hardened and its surface is roughened due to the presence of pale yellowish plaques.

**Valvular Cysts***: These are common incidental findings, particularly in cattle. Cysts may be filled with clear yellow fluid (*lymphocyst*) or with blood (*hematocyst*). There are no associated clinical signs.

**Myxomatous Valvular Degeneration (Endocardiosis)***: Perhaps the most common cardiac lesion in dogs. The incidence increases notably with age, for instance, in 1 year-old dogs it is only 5% while in dogs older than 13 years, the incidence can reach 75%. Lesions are most common in toy, small and medium breed dogs and the disease is particularly prevalent in Cavalier King Charles spaniels. The cause is unknown but presumed to be genetic. Lesions most commonly involve the mitral valve and less commonly involve the tricuspid, aortic and pulmonary valves.

- Grossly, affected valves are thickened and nodular but the surface remains smooth and glistening.
- Histologically the lesion is characterized by nodular proliferation of fibroelastic tissue with increase mucinoid substance in the valve.
- Mild myxomatous mitral valve degeneration is a common incidental finding at necropsy. More severe lesions can produce mitral valvular insufficiency, *jet lesions*, left atrial dilation, left ventricular hypertrophy and eventually left heart failure. In severe cases, rupture of chordae tendinae can cause valve prolapse and sudden death.

**Endocarditis***: Inflammation of the endocardium is most frequently caused by bacteria and to a much lesser extent by fungi or parasites. According to location, endocarditis can be classified as valvular or mural (myocardial wall). It can be further classified as vegetative, in which a cauliflower-like mass of exudate and fibrin is attached to the valve or endocardium, or ulcerative when the endocardium is ulcerated. Typical clinical signs include pyrexia, lameness (from thromboemboli) and murmurs.

- Vegetative valvular endocarditis is particularly common in farm animals suffering from bacteremia. Common causes include:
  - *Streptococcus equi* and *Actinobacillus equuli* in horses
  - *Trueperella pyogenes* in cattle (most commonly involves right AV valve)
  - *Erysipelothrix rhusiopathiae* and *Streptococcus suis* in pigs
  - *Staphylococcus aureus* and *Streptococcus* sp in dogs
  - *Bartonella* and *Streptococcus* sp. in cats.
Congenital heart defects and "jet lesions" can predispose animal to bacterial endocarditis. Thromboembolism is a common sequel to vegetative endocarditis; mitral or aortic valve endocarditis causes renal infarcts while tricuspid and pulmonic lesions lead to pulmonary thromboemboli. Ulcerative mural endocarditis is commonly seen in dogs with uremia.

PATHOLOGY OF THE MYOCARDIUM

General response to myocardial injury
Myocardial degeneration and necrosis*:
The types of cellular degeneration and cellular necrosis of the cardiomyocytes are remarkably similar to those seen in skeletal muscle. Myocardial cells are particularly vulnerable to anoxia and injury caused by free radicals. Myocardial degeneration and necrosis may result in heart failure. This occurs when lesions are extensive, but also with mild lesions, if they are distributed along conduction pathways.

- Gross appearance: if the number of affected fibres is considerable, the myocardium may appear pale (focal, multifocal, or diffuse).
- Microscopically: myocardial degeneration and necrosis consists primarily of myofiber swelling, hypereosinophilia, loss of striation and dissolution of the sarcoplasm.
- Myocardial calcification is a common sequel due to failure of Ca++ pump to extrude calcium from the sarcoplasmic reticulum.
- Necrosis of myocardiocytes is followed by leukocytic invasion and phagocytosis of sarcoplasmic debris by macrophages.
- Unlike skeletal muscle, repair in myocardium is practically absent and therefore myocardial necrosis always results in myocardial fibrosis (scarring).

Myocardial degeneration and necrosis can be ischemic, toxic, nutritional or neurogenic:

Ischemic Myocardial Necrosis: The classical heart attack which is so prevalent in humans is rarely seen in domestic animals, perhaps because coronary atherosclerosis is rare in animals (see atherosclerosis).

Toxic Myocardial Necrosis: The most common causes of toxic myocardial injury occur by ingestion of toxic plants such as white snakeroot (horses) or gossypol (pigs), cardiotoxic drugs such as doxorubicin, and ionophores such as monensin.

Nutritional Myopathy*: White Muscle Disease (WMD). The myocardium is particularly vulnerable to free radical peroxidation, which occurs when there is a lack of adequate free radical scavengers. The occurrence of WMD is unpredictable and the theory of a geographic predisposition has been recently challenged. WMD is occasionally found in the neonate and fetus. The pathogenesis of WMD is related to the oxidation of cell membrane lipids (lipid peroxidation) by free radicals due to lack of oxygen radical-scavengers such as tocopherol (Vitamin E) and selenium containing enzymes
(glutathione peroxidase / reductase). Membrane peroxidation induces a positive influx of Ca++ into the sarcoplasm and mitochondria. Since muscle activity relates to the production of free radicals, muscles with higher activity such as heart, diaphragm, intercostal muscles and tongue (predominately type I fibers), are more severely affected. For unknown reasons, myocardial degeneration in WMD is typically on the left side of the bovine heart, while in ovine is on the right side.

**Neurogenic Myocardial Necrosis**: Various types of CNS injury are known to cause myocardial degeneration (*heart-brain syndrome*). This syndrome is thought to be caused by the sudden release of catecholamines since endogenous (i.e., functional adrenal pheochromocytomas) and exogenous (injections) catecholamines can cause myocardial degeneration.

**INFLAMMATORY DISEASES OF MYOCARDIUM**

**Myocarditis**: Inflammation of the myocardium rarely occurs alone and is more commonly part of systemic disease. According to the type of exudate, myocarditis can be classified in suppurative, lymphocytic, eosinophilic, haemorrhagic or granulomatous. In some cases suppurative myocardial tissue evolves into myocardial abscesses. Grossly the myocardium shows focal, multifocal or diffuse areas of pallor or discoloration. Some types such as lymphocytic myocarditis can only be diagnosed microscopically.

Most forms of myocarditis are infectious or parasitic in origin. The most common forms:
- **Dogs** – *Canine parvovirus in young puppies*, *Trypanosoma cruzi* (Chaga’s disease)
- **Pigs** - Encephalomyocarditis virus, Porcine circovirus-2 and Porcine Reproductive and Respiratory Syndrome (PRRS) as part of a systemic infection
- **Cattle** - *Histophilus somni* (vasculitis and papillary muscle infarction or multifocal abscesses) and *Trueperella pyogenes*, Cysticerci in ruminants (*Taenia sp*).
- **Sheep** – *Staphylococcus aureus* (“tick pyema”)
- Apicomplexan parasites such as *Toxoplasma gondii*, *Neospora caninum*, *Sarcocystis* sp in many animal species.

**CARDIOMYOPATHIES**

The term “Cardiomyopathy” is used to describe cardiac diseases in which a primary myocardial abnormality results in changes in cardiac wall thickness (hypertrophy and/or dilation), electrical disturbances and often sudden unexpected death. The underlying cause is genetic or idiopathic (typically suspected to be genetic). It is often a diagnosis of exclusion, requiring us to rule out other causes of cardiac enlargement, such as cardiovascular shunts, valvular disease, and hypertension. **NOTE**: The term secondary cardiomyopathy is sometimes used for cardiomegaly secondary to other primary conditions such as hyperthyroidism, taurine deficiency, etc.
In humans, cardiomyopathies are characterized by cardiomegaly, left mural thrombosis, and myocardial fibrosis. In animals, cardiomyopathies are less well defined. Cardiomyopathies are morphologically classified in three types:

i. **Hypertrophic Cardiomyopathy (HCM)***: (cats > dogs). It is the most common type of feline cardiomyopathy. Clinical signs may include lethargy, anorexia, dyspnea, tachypnea, cardiac murmur and abdominal distension. In cats, HCM may first appear as anesthetic death. Grossly, affected hearts show massive hypertrophy (LV*, IVS +/- RV) and atrial dilation. In spite of the myocardial hypertrophy, HCM is characterized by “stiff fibres”, weak systole and impaired ventricular filling which leads to diastolic dysfunction. Microscopically there is myofibre disarray, hypertrophic cardiomyocytes and some fibrosis. Cats frequently (1/3) have aortic “saddle” thrombi with concurrent posterior paresis and less often have atrial thrombi. Maine Coon and Ragdoll cats are predisposed with HCM in this breed resulting from a defect in the cardiac myosin binding protein C3 gene. Hyperthyroidism can result in similar gross and histologic changes in cats.

ii. **Dilated or Congestive Cardiomyopathy (DCM)***: It is the most common type of cardiomyopathy in humans and dogs. In cats, secondary DCM is associated with dietary taurine deficiency. DCM is mostly seen in large breed dogs (Irish Wolfhound, St Bernard, Doberman, etc) with strong familial tendencies, in middle aged cats, and sporadically in Holsteins. Typical clinical signs include cough, depression, dyspnea, weight loss, syncope, murmurs, arrhythmias, or sudden death. There is bi-ventricular and atrial dilatation and the hearts show systolic dysfunction and reduced contractility. The ventricular walls are thin and flabby. Microscopically there is wavy attenuation, degeneration and loss of fibers with a variable degree of fibrosis; these changes are often subtle. Cats with DCM often have aortic thromboembolism. A variant of DCM occurs primarily in Boxer dogs and is called arrhythmogenic right ventricular cardiomyopathy. In this cardiomyopathy, there is right heart failure and disturbances in cardiac rhythm resulting in sudden death.

iii. **Restrictive Cardiomyopathy**: This is a rare type of cardiomyopathy characterized by impaired ventricular filling and diastolic dysfunction; it occurs primarily in cats. Murmurs and dysrhythmia are common. In this species, the disease has also been termed “left ventricular endocardial fibrosis” where endomyocarditis may be an antecedent condition. Grossly and microscopically there is diffuse endocardial thickening primarily involving the left ventricle and sometimes accompanied by mural thrombosis. **Excessive moderator bands** (false tendons) in the left ventricle can bridge the ventricular septum and free wall entangling the papillary muscles. This may be considered another form of restrictive cardiomyopathy, and has been associated with left-sided heart failure in mature cats. It appears to be a congenital defect that is only manifest later in life. **Congenital endocardial fibroelastosis** in Burmese cats may be considered as an example of restrictive cardiomyopathy.
PATHOLOGY OF THE VASCULAR SYSTEM

**General considerations:** The vascular system is formed by arteries (elastic, muscular), arterioles, capillaries, venules and veins. Additionally, lymphatic vessels are considered part of the vascular system. The microcirculation is formed by arterioles, capillaries and venules and is where all exchanges between blood and tissue take place. The most important vascular diseases and lesions in domestic animals tend to affect arteries, arterioles and capillaries and to a lesser extent the veins and venules. Primary vascular lesions should be differentiated from secondary vascular changes. Vascular lesions may progress and cause partial or complete flow obstruction, ischemia, infarction and hemorrhage in affected organs.

**DEGENERATIVE ARTERIAL DISEASES**

**Arteriosclerosis:** It literally means “hardening of the arteries”, and is more fully defined as chronic arterial change consisting of hardening, loss of elasticity and luminal narrowing resulting usually from proliferative and degenerative changes of the media and intima. The term *atherosclerosis* is applied to lesions of arteriosclerosis in which degenerative fatty changes also occur. In domestic animals, arteriosclerosis is common, but of little importance. The elastic arteries (abdominal aorta) are most frequently affected. Lesions are often localized around the orifices of arterial branches. The etiology/pathogenesis is not well defined, but the significant role of hemodynamic influences (turbulent blood flow) at arterial branching sites has been suggested. The lesions consist of slightly raised, firm, white plaques due to the accumulation of mucopolysaccharides, and later by the proliferation of smooth muscle cells in the tunica media and fibrous tissue infiltration of the intima.

**Atherosclerosis and atheromas:** While perhaps one of the most important health problems in humans, atherosclerosis in animals is rare. Cholesterol plaques form in the arterial intima and media, particularly in the arteries of the heart, brain, mesentery and kidneys. Affected vessels are thickened, firm and yellow-white. Atheromatous plaques (atheromas) are composed of large foamy macrophages filled with lipid in the tunicas intima and media of the arterial wall. In animals, atherosclerosis is seen in:

- **Dogs** with hypercholesterolemia associated with *hypothyroidism, diabetes mellitus*, and hyperlipoproteinemia (miniature schnauzers)
- Pigs, rabbits and birds fed a high lipid diet
- Aged psittacines (parrots)

**Arterial hypertrophy:** The walls of medium size muscular arteries can thicken as the result of medial (smooth muscle) hypertrophy caused by sustained high blood pressure (hypertension) or increased volume flow. Medial hypertrophy of the arteries results in reduced elasticity and increased resistance.

- **Cats** - Medial hypertrophy of the pulmonary arteries occurs commonly. It was speculated to be associated to *Aelurostrongylus abstrusus* or *Dirofilaria immitis*, however, identical lesions are found in Specific Pathogen free (SPF) cats.
Dogs - Medial hypertrophy is seen in the pulmonary arteries of dogs with *Dirofilaria immitis* and secondary to renal hypertension.

Cattle – Medial hypertrophy is seen in the pulmonary arteries in cattle raised at high altitudes (high altitude disease of cattle) due to hypoxia induced pulmonary constriction. The resulting pulmonary hypertension ends in congestive right heart failure.

**Aneurysms**: The word aneurysm refers to a localized weakening and dilation of blood vessels, particularly elastic arteries and to a lesser extent veins. There are two main anatomic types: i- Sacular aneurysm where there is a spherical dilation of the blood vessel resembling a balloon filled with blood; ii- Dissecting aneurysm in which a tear of the intima allows blood to enter into the potential space between the intima and media, progressively dissecting the wall of the vessel. Aneurysms are prone to rupture and cause hemotorax, hemoabdomen, hemopericardium, brain hemorrhage (stroke), etc. Spontaneous aortic rupture may occur in horses (stallions) and turkeys. The most common causes of aneurysms in animals:

- *Strongyulus vulgaris* in horses (aorta, mesenteric)
- *Spirocerca lupi* in dogs (aorta)
- Copper deficiency in mares (uterine) and pigs.
- Idiopathic in stallions and turkeys (dissecting aortic aneurysms with rupture)

**Arterial medial calcification**: Occurs in conjunction with endocardial mineralization.

**Fibrinoid necrosis**: This is a unique but non-specific vascular change. The walls of affected arteries are necrotic and have deposits of acidophilic proteinaceous material (a mixture of fibrin, immunoglobulins, complement, and platelets, hence the name fibrinoid). Fibrinoid change results from endothelial damage and occurs in many acute degenerative and inflammatory diseases of the small arteries and arterioles. Causes include:

- Nutritional deficiencies - *Mulberry heart disease* (vitamin E / Selenium deficiency) in pigs. Characterized by fibrinoid necrosis and thrombosis of small vessels resulting in microhemorrhages and necrosis in the heart
- Viral infections such as classical swine fever and malignant catarrhal fever
- Bacterial toxins - *Edema disease* of swine. In pigs, certain strains of hemolytic *E. coli* produce a cytotoxin that targets the vascular endothelium, resulting in fibrinoid necrosis of arterioles and resultant edema (eyelids, stomach, brain).
- Inflammatory vasculitis - Purpura hemorrhagica (in horses following infections with *Streptococcus equi*)

**VASCULITIS (ARTERITIS AND PHLEBITIS)**

**Vasculitis**: This is a general term that describes inflammation of a vessel (often small arteries and veins) which are detected mostly by histopathology. The consequences of vasculitis are grossly visible, and include hemorrhage, edema, thrombosis, and infarcts. Common causes of vasculitis include systemic infections (virus, bacteria, fungi), hypersensitivities where antigen-antibody complexes attached to the walls of blood
vessels, and adverse drug reactions, among others. In many cases the blood vessel is just a bystander and the inflammatory response may result in thrombosis.

**Arteritis** refers to inflammation of the arteries. Important causes of arteritis include:

- **Strongylus vulgaris** – In horses. The 4th larval stages migrate through the aorta and cranial mesenteric artery causing necrosis and inflammation of the intima (cranial mesenteric arteritis). In severe cases the vessel may be dilated and thick walled (fibrosis) with thrombosis. Larval worms can be observed in the thrombus. May cause colic. Collateral circulation largely prevents infarction of the intestine. Adult worms reside in the intestine.

- **Dirofilaria immitis** – in dogs (less so cats). Adult worms reside in the pulmonary arteries and right ventricle. Inflammation in the arteries (proliferative endoarteritis) causes pulmonary hypertension and may result in thromboembolism. Clinical signs reflect cardiovascular dysfunction and include cough and exercise intolerance, which may progress to congestive heart failure.

**Phlebitis**: Inflammation of veins is rare in animals. Veins undergoing inflammation typically become thrombosed, hence the term thrombophlebitis. Pulmonary thromboembolism is a common sequella. The most common forms of thrombophlebitis in veterinary practice are:

- **Venal caval thrombosis** in cattle – occurs secondary to ruminitis and subsequent hepatic abscesses which can erode through the wall of the venal cava

- Femoral thrombophlebitis in “Downer” cows – results from prolonged stasis

- **Omphalophlebitis** in neonatal farm animals from umbilical infections

- Iatrogenic jugular phlebitis - caused by unsuccessful or repeated venipuncture or the use of indwelling catheters.

### Other examples of diseases causing vasculitis (for your information only)

<table>
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<tr>
<th>Viral</th>
<th>Bacteria</th>
<th>Fungi</th>
<th>Parasites</th>
<th>Toxins</th>
<th>Immune mediated</th>
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<td>Malignant catarrhal fever</td>
<td><em>Salmonella</em></td>
<td><em>Mucor spp</em></td>
<td><em>Angiostrongylus vasorum</em></td>
<td>Ergotism (fungus: <em>Claviceps purpurea</em>)</td>
<td>Systemic lupus erythematosus</td>
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<td>Bovine viral diarrhea</td>
<td><em>Histophilus somni</em></td>
<td><em>Aspergillus sp</em></td>
<td>* Spirocerca lupi*</td>
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<td>rheumatoid arthritis,</td>
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<td>Classical and African Swine Fever</td>
<td><em>Erysipelothrix rhusiopathiae</em></td>
<td><em>Absidia</em></td>
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<td><em>Festuca spp</em> mycotoxin</td>
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<td><em>Fusarium</em></td>
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<td><em>polyarteritis nodosa</em></td>
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<td>Equine infectious anemia</td>
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<td>Equine viral arteritis</td>
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<td>Bluetongue Disease</td>
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<td>Feline infectious peritonitis</td>
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THROMBOSIS/ THROMBOEMBOLISM

Thrombosis and Thromboembolism*: Common sequel of vascular or endocardial diseases (endothelial damage) or coagulopathies. Causes include:
- Horses: *Strongylus vulgaris* (mesenteric arteries)
- Dogs: Primary cardiomyopathies, *Dirofilaria immitis*, *Spirocerca lupi*, nephrotic syndrome, Cushing’s syndrome, pancreatitis
- Cats: Primary cardiomyopathy
- Cattle: Valvular endocarditis, venal caval thrombosis, septicemia, thrombotic meningoencephalitis (TME)
- Pigs: Valvular endocarditis, septicemia, etc.

LYMPHATIC VESSELS

Congenital lymphatic diseases are rare except perhaps for hereditary lymphedema (inherited trait) seen sporadically in dogs, cats and pigs. Lymphedema results in aplasia or hypoplasia of lymphatic vessels causing severe subcutaneous edema particularly in the head, neck and limbs. Acquired lymphedema is caused by obstruction of lymphatic vessels most frequently associated to neoplasia, trauma or inflammation (lymphangitis).

DILATION AND RUPTURE OF LYMPHATIC VESSELS

Lymphangiectasia*: This term implies abnormal dilation of lymphatic vessels. Intestinal lymphangiectasia is a common cause of the “protein losing enteropathy” in dogs and cats.

Chylothorax and Chyloabdomen (chyulous ascites)*. These two conditions result from the rupture of lymphatic vessels and leakage of chyle into the thoracic or abdominal cavities. Most cases are idiopathic and few others are caused by trauma, surgery (iatrogenic), inflammation (lymphangitis) or neoplasia. Chylous effusions obtained by thoracocentesis or abdominocentesis yield a white fluid resembling milk. Laboratory analysis typically shows a fluid rich in lymphocytes and triglycerides.

LYMPHANGITIS (for your information only)

Inflammation of the lymphatic vessels is called lymphangitis and may be seen with specific diseases such as:
- Cattle: Johne’s disease (*Mycobacterium paratuberculosis*), tuberculosis (*Mycobacterium* spp)
- Horses: Glanders (*Burkholderia mallei*), ulcerative lymphangitis (*Corynebacterium paratuberculosis*), epizootic lymphangitis (*Histoplasma farciminosum*), sporotrichosis (*Sporothrix schenckii*), among others.
NEOPLASTIC DISEASES OF THE CARDIOVASCULAR SYSTEM

PRIMARY TUMOURS:

**Hemangioma**: Benign tumour of endothelial cells. Common in dogs, also found in cats, horses, sheep and pigs. This benign tumour can arise in any tissue but the skin is the most common site. Tumours are well circumscribed, red, blood filled masses. Histologically blood-filled vascular spaces are lined by a single layer of well differentiated endothelial cells.

**Hemangiosarcoma**: This is an important malignancy in veterinary patients but is less common than hemangioma. Hemangiosarcoma arises from endothelial cells and frequently metastasizes to other organs (or occurs multicentrically). It is most commonly seen in dogs (German shepherd, Golden retriever) and the two most common primary sites in this species are spleen and right atrium; liver and lung are commonly involved. Grossly these tumours appear as single or multiple red hemorrhagic nodules. Microscopically, the neoplastic cells typically form blood channels lined by pleomorphic endothelial cells with high mitotic rate. Clinical signs are variable depending on the organs involved; splenic masses can rupture and cause hemoabdomen while atrial masses may rupture and cause rapid death due to cardiac tamponade. Anemia is also commonly found.

**Rhabdomyoma and Rhabdomyosarcoma of the heart**: Rare neoplasia in domestic animals (> cattle); sometimes congenital. The tumour is grossly characterized by a well circumscribed white mass embedded in the heart muscle. The tumour often projects into the heart chambers.

**Aortic and Carotid Body Tumor or Chemodectomas (Non-chromaffin paraganglioma)**: Tumours of extra-cardiac tissues arising from chemoreceptors (aortic and carotid body) are rare and often are benign acting mainly as a space-occupying mass. Aortic body tumours form single to multiple masses near the base of the heart inside the pericardial sac. Carotid body tumours are firm white masses arising near the bifurcation of the common carotid artery. Malignant tumours are often invasive and can produce metastasis. Histologically, the tumors are formed by lobules of closely packed cuboidal or polyhedral neoplastic cells surrounded by thin connective tissue. (Ectopic thyroid tumours may produce heart base masses and are an important differential diagnosis)

SECONDARY TUMORS:

Many types of tumors can metastasize to the heart but the most frequent in domestic animals is by far lymphoma.

**Lymphoma**: This malignancy commonly involves the heart, producing multifocal to disseminated white nodules. Microscopically, affected myocardium is infiltrated by neoplastic lymphocytes. This is common in cattle with enzootic lymphoma. Histopathology is required for confirmatory diagnosis.