HEART STRUCTURE AND FUNCTION

General considerations:

The heart is the first organ to form in the embryo. In mammalians and birds it consists of 4 chambers (2 atria and 2 ventricles). 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. In the adult animal the left ventricle is thicker than the right.

The heart is composed of three layers: pericardium, myocardium (heart muscle) and endocardium.

Pericardium and Epicardium: These two serosal membranes are composed by 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 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 (striations). Myocardial fibres are branched with nucleus in the centre
of the fibre and some connective tissue between muscle fibres. Myocardial muscle has characteristic intercalated disks in which fibres connect to each other. 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:** It is equivalent to the tunica intima of blood vessels and is 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 which allow for unidirectional blood flow. The tricuspid valve (right AV valve); bicuspid or mitral (left AV valve); aortic (semi-lunar) valve; and pulmonic valve (pulmonary artery). The normal valvular leaflets (cusps) are thin, smooth, partially translucent and lined by endothelium. AV valves attach to the papillary muscles of the ventricular myocardium by the chordae tendinae.

**Post-mortem examination:** There is no universal method to open the heart and largely depends on the species, disease suspected and pathologist preference. The most important external features to be first 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>Post-mortem changes</td>
</tr>
<tr>
<td>Wall thickness</td>
<td>Valves</td>
<td>Endocardium</td>
<td>Great vessels and coronary</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.

Although the functional reserve capacity of the heart is reasonably good, any cardiac dysfunction that is not properly compensated eventually leads to heart failure and clinical signs. There is a difference between cardiac disease and cardiac failure. Some cardiac diseases do not progress to heart failure. Overall enlargement of the heart is referred to as cardiomegaly.

**Basic pathophysiological mechanisms involved in heart failure:**

<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>Compressed heart</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
Cardiac Hypertrophy and Dilation are two distinct changes that occur in the heart in response to increased cardiac demand. Cardiac hypertrophy can be left ventricular, right ventricular, or bi-ventricular.

**Hypertrophy**: It could be primary (idiopathic cardiomyopathy) or secondary to another underlying condition that increases workload demand. Primary hypertrophy is rare, irreversible and most commonly seen in dogs and cats. Secondary hypertrophy is a physiologic and partially reversible increase in cardiac mass that results from an attempt to meet increased work demand. Cardiac hypertrophy occurs in two distinct morphological types:

1. **Concentric Hypertrophy**: Increase in myocardial mass with thick walls and reduced ventricular chamber volume.

2. **Eccentric Hypertrophy (Dilation)**: Increase in myocardial mass with enlarged ventricular volume. In this type of hypertrophy the myocardial fibres stretch thereby increasing the contractile force, stroke volume and cardiac output (*Starling’s Law*).

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.

<table>
<thead>
<tr>
<th><strong>Gross Changes in Cardiac Hypertrophy:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected side</strong></td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Right side</td>
</tr>
<tr>
<td>Left side</td>
</tr>
<tr>
<td>Bi-ventricular</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%

**Myocardial Hypertrophy (Histopathology)**: Myocardial hypertrophy is hard to
evaluate microscopically without morphometric methods. Myofibers increase in width, nuclei increase in size, while sarcomeres, myofilaments and mitochondria increase in number. Hyperplasia, increase in the number of cells, does not occur in heart muscle cells.

CONGESTIVE HEART FAILURE

Congestive heart failure could be unilateral 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.

- **Left heart failure** → pulmonary congestion and edema (acute); intraalveolar haemorrhage → alveolar siderophages known as *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**.

- **Right heart failure** → chronic passive congestion of liver (*nutmeg liver*), anasarca and ventral edema (horses and cattle), hydrothorax (cats) and hydroperitoneum (dogs). *Brisket disease* in cattle. *Ascitic (ascites) syndrome* in chickens. *Cor pulmonale* is a common cause of right heart failure.

CONGENITAL HEART AND BLOOD VESSEL DEFECTS

The 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 few others are just incidental and clinically irrelevant. The etiology of congenital heart defects is diverse including genetic, toxic, nutritional and possibly infectious.

There are many types and combinations of congenital heart or vessel diseases. The most frequently found in veterinary practice are:

**Ectopia cordis**: (rare; > bovine). Heart is located in abnormal sites such as extrathoracic, intraabdominal or pre-sternal. It is mostly found in stillbirths or aborted fetuses but the sporadic animal may survive for few days or weeks.

**Patent Ductus Arteriosus (PDA)**: Common defect in all species particularly in dogs: > Poodle, Collie, Pomeranian. Diagnosed in dogs if fails to close in 3 weeks. The ductus arteriosus is a normal communication between pulmonary artery and aorta in fetal circulation. This arterial communication normally closes few hours after birth forming
the ligamentum arteriosum. In PDA the ductus fails to close. Hemodynamics: blood shunts left to right. Aorta ↩ pulmonary artery ↩ pulmonary hypertension. **Note:** closure of the ductus areteriosus normally takes several days in foals.

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

**Atrial Septal Defect:** This form of septal defect could be 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 most commonly in dogs and cattle. Atrial communication results in L to R shunt and RV volume overload. Minor defects show no clinical signs (in 10% of humans and animals a probe can be passed through foramen, yet no functional shunt is present). **Hemodynamics:** Large defect: Excessive blood flow from LA ↩ RA; volume overload RV ↩ RV hypertrophy (from increase blood flow, not resistance). Pulmonary congestion (oxygenated blood return to lungs).

**Ventricular Septal Defect (VSD):** One of the most common cardiac defects in domestic animals (> horses, cattle) which is characterized by inter-ventricular communication in postnatal life. Embryologically, muscular septum grows up, membranous septum grows down, and infundibulum meets both muscular and membranous septum. Failure to do this results in VSD. Relative to the position in the septum, VSD could be low when it is close to the apex (rare) or high when close to the AV valve. **Hemodynamics:** LR shunt ↩ RV overload ↩ increase RV pressure ↩ RV hypertrophy ↩ if uncompensated ↩ right heart failure ↩ LV hypertrophy as well. Blood shunts could later reverse R ↩ L and cause cyanosis.

**Pulmonic Stenosis:** (> dogs). It is characterized by 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. Post-stenotic arterial dilation is generally found in the artery, distal to the stenosis site. **Hemodynamics:** pressure overload of RV ↩ RV hypertrophy ↩ if uncompensated, right heart failure.

**Subaortic Stenosis:** (>pigs, dogs). Bands of fibrous tissue encircle the left ventricular outflow tract below the aortic valve. **Hemodynamics:** Pressure overload LV, ↩ increase LV pressure ↩ LV hypertrophy ↩ post-stenotic dilation of aorta; if uncompensated, left heart failure and pulmonary edema.
Tricuspid Dysplasia: (>cats > dogs; Retrievers). Dysplastic valves are characterized by thickened fibrous cusps, missing or abnormally short chordae tendinae or thick papillary muscles; abnormal fusion of chordae to the ventricular wall. Tricuspid dysplasia caused RV hypertrophy and R atrial distension.

Mitral Dysplasia: Dogs and cats often characterized by a narrow valve outflow (mitral stenosis).

Tetralogy of Fallot: (>dogs, cattle). Three congenital defects plus one acquired alteration: i. ventricular septal defect; ii. pulmonic stenosis; iii. dextraposition of aorta; iv. right ventricular hypertrophy. Hemodynamics: pulmonic stenosis → overload RV → RV hypertrophy → if uncompensated, right heart failure. In addition, increase RV pressure → blood shunts RV to LV (via septal defect) → venous blood into systemic circulation → cyanosis.

Other important congenital heart diseases include transposition of the great vessels, Eisenmenger complex, overriding aorta, coarction of the aorta, etc. [For information only]

PATHOLOGY OF THE PERICARDIUM

The pericardium is formed by serosal surfaces, one thin which is adhered to the myocardium called epicardium, and another much thicker covering the heart and the base of major vessels, called pericardial sac. The pericardial sac contains traces of fluid that act as a lubricant. Overall size of the pericardium can progressively increase when there is increased physical demand such as in cases of severe hydropericardium and pericarditis.

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 a post-mortem examination and, according to the size of the hemorrhage, are classified in petechial, ecchymotic or "paint brush." 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 agonic states and these lesions should be interpreted accordingly.

Hydropericardium: Accumulation of fluid (transudate) with low protein and cellularity in the pericardial sac. The serosal surface remains smooth and glistening. According to the pathogenesis hydropericardium can be classified as follow:

a. Hydrostatic: i.e., right heart failure, pulmonary hypertension.

b. Hypoproteinemia: i.e., severe emaciation, anasarca, or parasitosis, extensive loss of protein such as in protein losing enteropathy and protein losing nephropathy.
c. **Altered vascular permeability:** i.e., sepsis, disseminated intravascular coagulation (DIC), mulberry heart disease.

**Hemopericardium:** Accumulation of blood in pericardial sac. Common causes include: spontaneous atrial ruptures (hemangiosarcoma in dogs), intra-pericardial aortic rupture (horses), traumatic, iatrogenic (cardiac puncture). Accumulation of blood in the pericardium causing heart failure is referred to as cardiac tamponade which can cause acute death. **Caution:** blood tinged fluid is frequently found as a post-mortem change in animals that have been dead for several hours.

**Pericarditis:** Inflammation of the pericardium. According to exudate can be classified as fibrinous, purulent (suppurative), fibrino-hemorrhagic or granulomatous. According to the duration of the inflammatory process can be acute, subacute or chronic. Most forms of pericarditis tend to be diffuse involving both the pericardium and epicardium (epicarditis). When the fibrin accumulates and becomes partially organized, the exudate on the pericardial surface takes a peculiar appearance known as “bread and butter”. Fibrin strands on the pericardium surface are often seen in pigs with mulberry heart disease and Glasser’s Disease (*Haemophilus parasuis*) in pigs and with blackleg and malignant edema in ruminants. Chronic pericardial inflammation generally leads to fibrosis and fibrous adhesions between pericardium and epicardium, and between pericardium and pleura. Presence of purulent exudate in the pericardial sac is also referred to as pericardial empyema. In chronic cases formation of granulation tissue and fibrosis results in constrictive pericarditis with concurrent myocardial hypertrophy and possible heart failure.

**PATHOLOGY OF THE ENDOCARDIUM AND VALVES**

**Endocardial Fibrosis and Fibroelastosis:**

Generalized (primary) fibroelastosis occurs as a hereditary disease in humans and cats (Burmese and Siamese). It is characterized by diffuse thickening of the endocardium accompanied by left ventricular hypertrophy and dilation in animals with no other cardiac abnormalities (primary fibroelastosis).

Acquired (secondary) focal fibroelastosis 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. Grossly, the endocardium appears white, thick, and roughened. Generalized fibroelastosis may impair and reduce stroke volume leading to congestive heart failure.
Endocardial (Subendocardial) Mineralization: Abnormal deposition of calcium or mineral in the endocardium occurs in all species. It is generally the result of hypervitaminosis D (iatrogenic Vit D toxicity) or ingestion of Vitamin D analogs present in some rodenticides or toxic plants such as 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 young calves. Cyst may be filled with clear yellow fluid (lymphocyst) or with blood (hemocyst). There are no clinical signs. Cysts rupture and disappear with age.

Myxomatous Valvular Degeneration (Endocardiosis): Perhaps the most common cardiac lesion in dogs found at necropsy. The incidence increases notably with age, for instance, in 1 year-old dogs it is only 5% while in dogs older than 13 years incidence can reach 75%. Endocardiosis affects typically the mitral valve and is characterized by nodular proliferation of fibroelastic tissue with increase mucinoid substance in the valve. The cause is unknown but presumed genetic. Grossly, affected valves are thickened and nodular but the surface is always smooth and glistening. Mitral endocardiosis can produce valvular insufficiency, "jet lesions" and eventually left heart failure in dogs. In severe cases it causes rupture of chordae tendinae 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). According to the surface can be vegetative, in which a cauliflower-like mass of exudate and fibrin attached to the valve or endocardium, or ulcerative when the endocardium is ulcerated. Vegetative valvular endocarditis is common particularly in farm animals suffering from bacteremia with organisms such as Streptococcus equi in horses; Staphylococcus aureus in dogs; Truperella (Archanobacterium) pyogenes (cattle); Erysipelothrix rhusiopathiae and Streptococcus suis II in pigs; Bartonella and Streptococcus sp. in cats. Endocarditis may rarely result from migrations of Strongylus vulgaris larvae in horses. 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 cause lung infarcts. Ulcerative endocarditis is commonly seen in dogs with uremia.

**PATHOLOGY OF THE MYOCARDIUM**

General response to myocardial injury: The types of cellular degeneration (Zenker's), cellular necrosis and mineralization of the myocardiocytes are remarkably similar to those seen in skeletal muscle. However, myocardial cells are particularly vulnerable to anoxia and injury caused by free radicals (peroxidation of cell membranes). Unlike skeletal muscle, repair in myocardium is practically absent and
therefore myocardial necrosis always results in myocardial fibrosis (scar). If the number of affected fibres is considerable, myocardium appears grossly pale (focal, multifocal, or diffuse). Myocardial calcification is a common sequel due to failure of Ca++ pump to extrude calcium from the sarcoplasmic reticulum. If extensive, myocardial degeneration and necrosis may result in heart failure. Microscopically, myocardial degeneration and necrosis is similar to skeletal muscle and consists primarily in myofiber swelling, hypereosinophilia, loss of striation and dissolution of the sarcoplasm. 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 exceptional in animals (see atherosclerosis).

**Toxic Myocardial Necrosis:** The most common causes of toxic myocardial injury occur by ingestions of toxic plants such as *Lantana camara*, cardiotoxic drugs such as adriamycin, monensin and furazolidone, and by excessive ingestion of NaCl in birds. T-2 mycotoxin and uremia can also cause myocardial degeneration.

**Nutritional Myopathy:** *White Muscle Disease (WMD).* Myocardium is particularly vulnerable to free radical peroxidation due to lack of adequate free radical scavengers such as vitamin E and glutathione peroxidase, a selenium containing enzyme. 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 (lipoperoxidation) 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 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, all of which have 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 (*brain-heart syndrome*). This syndrome may be caused by the sudden release of catecholamines since endogenous (i.e., functional adrenal pheochromocytomas) and exogenous injections of catecholamines cause myocardial degeneration.

**Septic Cardiomyopathy:** Recent studies have shown that patients with severe sepsis and septic shock suffer reversible cardiac contractile and relaxation dysfunctions which account for 10% of fatalities. These cardiac changes are largely functional rather than
structural, nonetheless, some patients develop focal myocardial degeneration and necrosis similar to what years ago was described as Zenker’s degeneration in patients dying of typhoid fever. There are speculations that septic cardiomyopathy also occurs in veterinary patients.

INFLAMMATORY DISEASES OF MYOCARDIUM

Myocarditis: Inflammation of the myocardium rarely occurs alone and it is typically part of a systemic disease. According to the type of exudate, myocarditis can be classified in suppurative (neutrophils), lymphocytic, eosinophilic (eosinophils), haemorrhagic or granulomatous. In some cases suppurative myocardial tissue evolves into myocardial abscesses. Grossly the myocardium shows focal, multifocal or diffuse areas of palor 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 in domestic animals are caused by viruses such as Parvovirus-2 in young puppies, Porcine circovirus-2 or Porcine Reproductive and Respiratory Syndrome (PRRS) in pigs; bacteria such as *Histophilus somni* and *Archanobacterium pyogenes* in cattle; Apicomplexan parasites such as *Toxoplasma gondii*, *Neospora caninum*, *Sarcocystis* sp in many animal species, *Trypanosoma cruzi* in dogs; Cysticerci in ruminants (*Taenia* sp).

CARDIOMYOPATHIES

The term “Cardiomyopathy” is used to describe cardiac diseases in which a primary myocardial abnormality results in changes in cardiac wall thickness (hypertrophy or dilation), electrical disturbances and often sudden unexpected death. It is a diagnosis of exclusion, which is absence of cardiovascular anomalies (including shunts), absence of coronary disease or absence of hypertension. In humans it is characterized by cardiomegaly, left mural thrombosis, and myocardial fibrosis. In animals cardiomyopathies are less well defined. In addition, coronary disease and hypertension are rarely present in animals. As in humans, animal cardiomyopathies are morphologically classified in three types:

i. **Dilated or Congestive Cardiomyopathy (DCM):** It is the most common type of cardiomyopathy in humans and dogs. In cats DCM is associated with taurine deficiency. DCM is mostly seen in middle age cats, large breed dogs with strong familial tendency, and sporadically in Holsteins. There is bi-ventricular and atrial dilatation and the hearts show systolic dysfunctions and reduced contractility. The ventricular walls are thin and flabby. Microscopically there is degeneration and loss of fibers with a variable degree of fibrosis. Cats with DCM often have aortic thromboembolism. 

ii. **Hypertrophic Cardiomyopathy (HCM):** (cats > dogs). It is the most common type of feline cardiomyopathy. In humans HCD is inherited in 50% of cases (mutation genes of contractile protein) and in most cases is clinically
characterized by sudden unexpected death. In cats may first appear as anesthetic death. Grossly, affected hearts show massive hypertrophy and atrial dilation. In spite of the myocardial hypertrophy, HCM is characterized by “stiff fibres”, weak systole and impaired ventricular filling. Microscopically there is fibre disarray, hypertrophic cardiomyocytes and some fibrosis. Main clinical signs are those of congestive heart failure. Cats frequently have atrial and aortic "saddle" thrombi with concurrent posterior paresis.

iii. **Restrictive Cardiomyopathy:** This is a rare type of cardiomyopathy characterized by impaired ventricular filling in animals. Grossly and microscopically there is diffuse endocardial fibroelastosis and excessive moderator bands in the left ventricle.

**NOTE:** In veterinary medicine the term secondary (non-idiopathic) cardiomyopathy is sometimes used for **cardiomegaly** secondary to other primary conditions such as congenital heart defect, hypertension, **cor pulmonale**, etc.

**PATHOLOGY OF THE VASCULAR SYSTEM**

**General considerations:** The vascular system is formed by arteries (elastic, muscular), arterioles, capillaries, venules and veins. Also, lymphatic vessels are also considered parts of the vascular system. Microcirculation or systemic capillary bed is formed by arterioles, capillaries and venules where exchange between blood and tissue takes place. The most important vascular diseases and lesions in domestic animals tend to affect arteries, arterioles and capillaries and to a lesser extent 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 and infarction in affected organs.

"**Chicken fat**" clots: Post-mortem clotting of blood where coagulated plasma separates from blood cells. It is a post-mortem change most commonly seen in horses.

**ARTERIOSCLEROSIS, ATHEROSCLEROSIS AND ANEURISMS**

**Arteriosclerosis:**

**Atherosclerosis and atheromas:** This is perhaps one of the most important health problems in humans predisposed by familial hypercholesterolemia. Cholesterol plaques form in the arterial intima and media particularly in the coronary (heart attack) or cerebral (stroke). Atherosclerosis in animals is rare and most commonly reported in dogs with hypothyroidism-hypercholesterolemia, diabetes mellitus, and in pigs,
psittacine birds and pigeons fed a high lipid diet. Atheromatous plaques, also known as atheromas, are composed of large foamy macrophages filled with lipid in the intima and media layers of the arterial wall.

**Arteriolosclerosis (Arterial hypertrophy):** The walls of medium size muscular arteries can thicken as a result of medial (smooth muscle) hypertrophy caused by sustained high pressure (hypertension) or increased volume flow. Similar medial hypertrophy is often seen in the pulmonary arteries of cats and in the past it was associated to *Aelurostrongylus abstrusus*, but this idea has been abandoned since identical lesions are found in Specific Pathogen free (SPF) cats. Medial hypertrophy is seen in the pulmonary arteries of dogs with *Dirofilaria immitis* and secondary to renal hypertension. Medial thickening results in reduced elasticity and increased resistance. Arterioloesclerosis is a histological diagnosis.

**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- Saccular 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 hemothorax, hemoabdomen, hemopericardium, brain hemorrhage (stroke), etc. The most common causes of aneurysms in animals are *Strongylus vulgaris* in horses (aorta, mesenteric), *Spirocerca lupi* in dogs (aorta), and copper deficiency in mares (uterine) and pigs.

**ARTERITIS, VASCULITIS AND PHLEBITIS**

**Arteritis:** Arterial inflammation can affect large arteries like the aorta and mesenteric or small arteries like those found in many organs such as kidney, brain and lungs, among others. Aortitis is most commonly found in horses with *Strongylus vulgaris* where the larval stages migrate through the aorta and mesenteric arteries causing necrosis and inflammation of the intimal wall. Similar aortic changes are found in dogs with *Spirocerca lupi* and in pulmonary arteries affected with *Dirofilaria immitis*.

**Vasculitis:** This is a general term that describes inflammation of small arteries and veins which are detected mostly by histopathology but their consequences are grossly visible such as in hemorrhages, edema or small 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 most of these cases the blood vessel is just a bystander and the inflammatory response may result in thrombosis.

**Fibrinoid necrosis:** This is a unique but non-specific vascular change in small arteries and arterioles which leads to edema and hemorrhage. The walls of affected arteries are necrotic and have deposits of acidophilic pertinacious material, hence the name fibrinoid necrosis. It is generally associated to viral infection such as classical swine fever; toxic
conditions such as uremia and mercury poisoning; bacterial toxins such as in enterotoxemia and edema diseases of swine (E. coli); nutritional deficiencies such as mulberry heart disease; inflammatory vasculitis such as in purpura hemorrhagica (in horses following infections with Streptococcus equi) and in some forms of immune mediated vasculitis such as lupus.

**COMMON EXAMPLES OF DISEASES CAUSING VASCULITIS**

**Multisystemic:** Disseminated intravascular coagulation (DIC).

**Viral Vasculitis:** Malignant catarrhal fever (periarteritis/panarteritis), classical and African swine fever, equine viral arteritis (myoarteritis/panarteritis).

**Bacterial Vasculitis:** Septicemia (i.e. Salmonella spp, Haemophilus somnus, Erysipelothrix rhusiopathiae), Septic thromboembolism (Streptococcus spp, Actinobacillus spp).

**Mycotic Vasculitis:** Mucor spp, Absidia spp, etc (panarteritis)

**Toxic Vasculitis:** Ergotism (fungus: Claviceps purpurea, grass Festuca spp/ mycotoxin Fusarium spp). Vasoconstriction (> peripheral), vascular degeneration, necrosis).

**Immunologic Vasculitis:** Hypersensitivity reaction such as type III hypersensitivity (deposition of immune complex).

**PHLEBITIS**

Phlebitis is common in humans (varicose veins, thrombophlebitis) but rare in animals. Veins undergoing inflammation typically become thrombosed, hence the term thrombophlebitis. Most common forms of thrombophlebitis in veterinary practice are found in cattle with vena cava thrombosis secondary to hepatic abscess, “Downer cow”, neonatal omphalophlebitis in farm animals, iatrogenic phlebitis caused by improper venipuncture. Some parasites such as Schistosoma sp (blood fluke trematode) cause verminous thrombophlebitis in humans and animals.

**THROMBOSIS/ THROMBOEMBOLISM**

**Thrombosis and Thromboembolism:** Common sequela of vascular or endocardial diseases (endothelial damage). Examples: Horses: Strongylus vulgaris (mesenteric arteries); Dogs: Primary cardiomyopathies, Dirofilaria immitis, Spirocerca lupi; Cats: Primary cardiomyopathy; Cattle: valvular endocarditis, post-caval thrombosis,
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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**

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

**Chylothorax** and **Chyloabdomen** (chylous 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 skim milk. Laboratory analysis typically shows a fluid rich in lymphocytes and triglycerides.

**NEOPLASTIC DISEASES**

**PRIMARY TUMORS:**

**Hemangioma:** Benign tumor of endothelial cells. Common in dogs, also found in cats, horses, sheep and pigs. This benign tumor can arise in any tissue but the skin is the most common site. Tumors 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 particularly the lungs. It is most commonly seen in dogs (> German shepherd) and the two most common primary sites in dogs are spleen or right atrium in the heart. Grossly the tumor(s) 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 involvement i.e, splenic can cause hemoabdomen while atrial can cause heart failure or rapid death due to cardiac tamponade. Anemia is also commonly found.

**Rhabdomyomas and Rhabdomyosarcomas of Heart:** Rare neoplasia in domestic
animals (> cattle) and sometimes are congenital. The tumor is grossly characterized by a well circumscribed white mass embedded in heart muscle. The tumor often projects into heart chambers.

**Aortic and Carotid Body Tumor or Chemodectomas (Non-chromaffin paraganglioma):** Tumors of extra-cardiac tissues arising from chemoreceptors (aortic and carotid body are rare and often benign acting mainly as a space-occupying tumor. Aortic body tumor (adenoma, carcinoma) is generally a single mass in the base of the heart inside the pericardial sac. Carotid body tumors (adenoma, carcinoma) are firm white masses arising near the bifurcation of the common carotid artery. Malignant tumors often produce metastasis. Histologically, the tumors are formed by lobules of closely packed cuboidal or polyhedral neoplastic cells surrounded by thin connective tissue.

**SECONDARY TUMORS:**

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

**Lymphosarcoma:** This malignancy commonly metastasizes to heart, producing disseminated white areas due of infiltration of neoplastic cells. Histopathology is required for confirmatory diagnosis.