

CARDIAC PATHOLOGY

INTRODUCTION

1. Heart disease may be the result of one or more of these pathogenic mechanisms:
 - a. Pump failure – due to weak contractility/chamber emptying or impaired filling.
 - b. Obstruction to forward blood flow – due to valvular stenosis, vascular narrowing, systemic or pulmonary hypertension.
 - c. Regurgitant blood flow - due to valvular incompetence.
 - d. Shunted blood flow – mostly a result of congenital defects (septal, vascular)
 - e. Rupture – can occur at the level of the heart or a major vessel
 - f. Cardiac conduction disorders – these lead to arrhythmia and pump failure.
2. Heart disease may be Primary or Secondary:
 - a. Primary – due to heart functional derangement.
 - b. Secondary –extra-cardiac derangement. This can be due to systemic derangement or specific organ derangement (e.g. systemic hypertension in renal disease, or pulmonary hypertension following pulmonary fibrosis).
3. Pathological changes in the heart frequently result in increased functional demand:
 - a. Increased preload – due to increased volume of blood entering the heart during diastole i.e. 'volume overload' (E.g. 1c, 1d above).
 - b. Increased afterload – due to increased resistance against which the heart must pump blood during systole i.e. 'pressure overload' (E.g. 1b above).

CARDIAC ADAPTIVE MECHANISMS (compensation)

The cardiovascular system has a range of mechanisms to cope with derangement/increased demand: **(1)** cardiac dilation, **(2)** cardiac hypertrophy (*not hyperplasia, as cardiomyocytes do not divide*), **(3)** increased cardiac rate/output, **(4)** blood redistribution to vital organs, and **(5)** increase in blood volume. Those directly involving the heart, cardiac dilation and cardiac hypertrophy are morphological changes that can be assessed grossly/histologically. Changes in rate/output are functional only.

Physiologically, acute increases in preload (e.g. strenuous exercise) result in transient heart dilation to accommodate the extra blood. In addition, the force of contraction, stroke volume and cardiac output increases (Frank-Starling relationship).

Pathologically, in response to chronic increases in preload or afterload the myocardium undergoes hypertrophy and/or dilation. There are two distinctive patterns of cardiac hypertrophy, concentric and eccentric:

1. **Concentric hypertrophy**, is typically the result of **increased afterload**. There is an increase in the mass of the ventricle (i.e. thicker wall), but there is no change (or decrease) in the end diastolic volume (i.e. the ventricular chamber volume).
2. **Eccentric hypertrophy**, conversely, is the result of **increased** preload. Here, the heart has to accommodate a larger blood volume. There is also increase in the ventricular mass but now the wall becomes longer and the chamber dilates (increased end diastolic volume). N.B. *in eccentric hypertrophy the ventricular wall*

may appear thin because it is dilated, but its mass is still greater than normal because the cells have increased in size by elongating.

CARDIAC FAILURE (decompensation)

Depending on the location, extent and duration of the pathological lesion, cardiac compensatory mechanisms may work remarkably well. If compensation is possible, heart disease can be clinically unapparent (i.e. asymptomatic).

Clinical disease occurs when compensation is not possible, which may occur immediately after the insult, or after a long period of compensation. The latter may result from increased demand (E.g. strenuous exercise), or degenerative changes (E.g. during prolonged hypertrophy, the capillary density cannot keep up with the increased myofibre size, resulting in reduced individual cardiomyocyte perfusion. This results in cardiomyocyte hypoxia and consequent degeneration and replacement by fibrosis).

Irrespective of the type of hypertrophy, cardiac dilation may occur when compensation is no longer possible, heralding the onset of failure in a previously compensating heart.

This is why chronic cardiac disease may evolve asymptotically over a period of time and suddenly manifest as acute clinical cardiac failure. Heart disease clinical signs may be predominantly cardiac (e.g. exercise intolerance, syncope) or related to changes in other organs (e.g. respiratory distress). Malfunction of the left or right side of the heart results in very different pathophysiological effects (**understanding of this is very important!**):

- a. Left – leads to pulmonary congestion/oedema and decreased cardiac output.
- b. Right – excessive right atrial pressure and systemic venous congestion.

CONGENITAL CARDIAC ABNORMALITIES

Normal Development:

The heart initially consists of a simple tube lined by endothelium. The anterior portion will form the truncus arteriosus (split later into aorta and pulmonary artery) and ventricles. The caudal portion forms the omphalomesenteric veins which will transform into the sinus venosus and atria. Further development will then involve looping of this tube and then division into left and right heart. The heart is completely formed during the first third of pregnancy and is functional from an early stage in foetal life.

Aetiology of cardiac congenital defects

The aetiology of many congenital heart anomalies is not known, although the following factors may be implicated:

1. Genetic
 - a) Inherited – through genome of sperm or ova.
 - b) Acquired – genomic defect arising in the fertilised zygote.
2. Environmental (note, examples are not comprehensive)
 - a) Infections; particularly viral in early pregnancy (E.g. bluetongue, BVD).
 - b) Physical; hypoxia, hyperthermia, mechanical trauma, ionising radiation.
 - c) Nutritional, i.e. deficiencies or imbalance in diet (e.g. vit A deficiency).
 - d) Chemical, i.e. toxic chemicals (E.g. Thalidomide, griseofulvin).

CLASSIFICATION OF CONGENITAL DEFECTS

Broadly, congenital cardiac defects can be classified as follows:

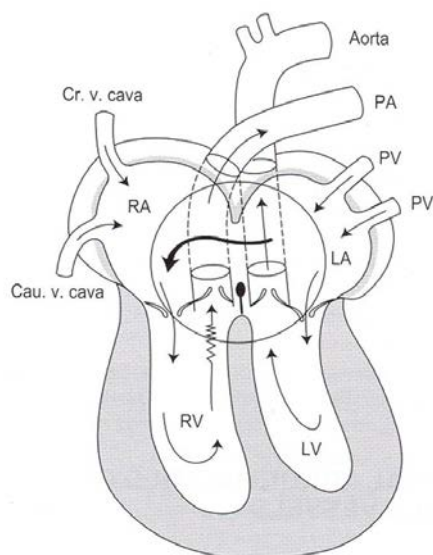
- i) Septal defects: Abnormalities of chamber development or partitioning, resulting in SHUNTS.

- ii) Abnormalities of the great vessels and their origins, resulting in SHUNTS and/or VASCULAR ANOMALIES.
- iii) Abnormalities of valve formation, resulting in DYSPLASIAS.

1. Septal Defects:

a) Atrial defects – These are most commonly a result of a persistent foramen ovale between the atria. NOTE: *Late closure in neonatal foals and lambs is not uncommon up to two weeks post-partum.* Small defects are sometimes found incidentally in slaughtered adult cattle, with no apparent clinical significance.

In some cases there may be failure of fusion of the overlying membranous portion of the atrial septum resulting in a flap-like S-shaped connection between the atria which is physiologically closed by atrial pressure during life and not significant clinically.



Atrial Septal Defect (ASD)

1. LA → RA → RV

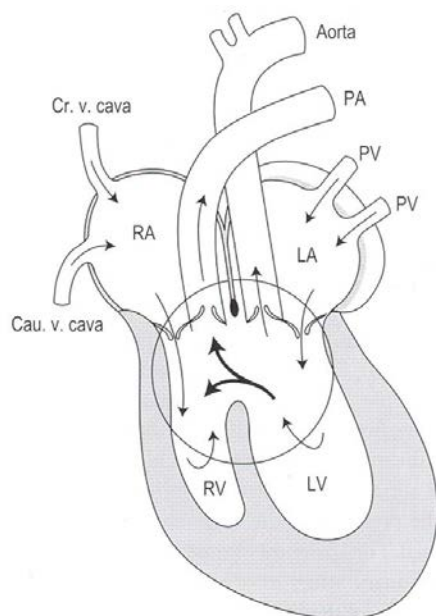
= RA dilation

= ↑ RV preload > eccentric RV hypertrophy

2. ↑ pulmonary return = LA dilation

b) Ventricular defects - may occur singly or associated with other abnormalities (e.g. Tetralogy of Fallot). Seen commonly in cattle, sheep and pigs. This is also the most common congenital cardiac defect in the cat. This defect can be part of a more complex transposition syndrome in cattle, pigs and also dogs.

The majority of defects are situated high up the septum, often below the aortic valve behind the main LAV valve cusp on the left and below the RAV on the right, as a result of failure of the inter-ventricular septum to join with the endocardial cushions. Large defects result in shunting of blood, usually from left to right, with mixing of oxygenated and non-oxygenated blood, and increased right ventricular preload with resulting pulmonary overperfusion.



Ventricular Septal Defect (VSD)

1. LV → RV

= ↑ RV preload > Eccentric RV hypertrophy

2. Pulmonary overperfusion

= ↑ pulmonary return > LA dilation and
↑ LV preload > LV eccentric hypertrophy

2. Defects of the truncus arteriosus:

Normally the ascending aorta and pulmonary artery develop from a spiral partitioning of the truncus arteriosus. This spiral partitioning accounts for the intertwined relationship of the roots of the great vessels in the adult heart.

Normal development of the roots of the great vessels and the semilunar valves (aortic/pulmonic) is dependent upon correct alignment of the spirally partitioned truncus arteriosus with the semilunar endocardial cushions.

A spectrum of anomalies can arise when this development goes wrong:

a) Transposition defects of the roots of the great vessels

Usually the root of aorta is affected, leading to displacement of the normal position. The commonest scenario is where the aorta is misplaced to lie over the right ventricle, known as dextro-rotation.

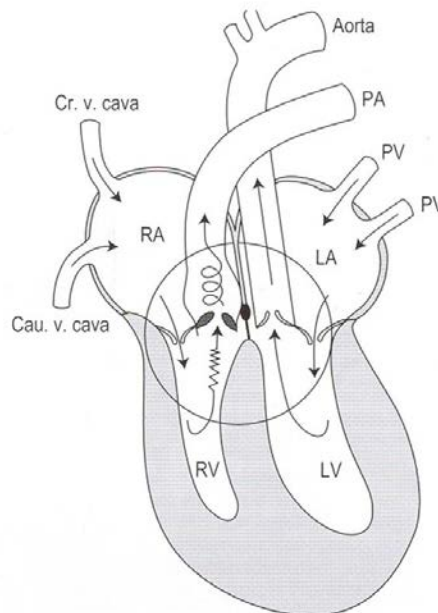
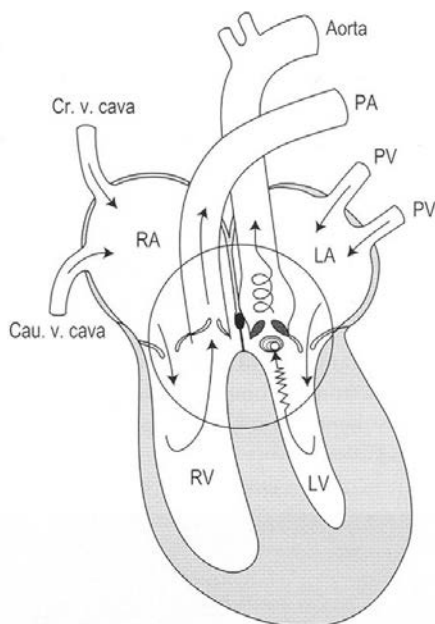
b) Persistent truncus arteriosus

There is failure of normal spiral partitioning of the truncus arteriosus into aorta and pulmonary artery. As a result, a single large artery (i.e. the truncus) leaves the base of the heart into which both left and right ventricles empty.

c) Semilunar valve stenosis

Maldevelopment of semilunar valve endocardial primordia leads to valve cusp distortion and stenosis (valvular stenosis) or formation of a band of muscular or fibrous tissue in the outflow tract beneath the valve (subvalvular stenosis). Occurs in dogs, pigs and less commonly cats.

The aortic or pulmonic valves may be affected; however it is unusual to get both valves affected simultaneously. The associated ventricle is usually markedly hypertrophied (concentric) due to increased afterload.



Aortic Stenosis (left)

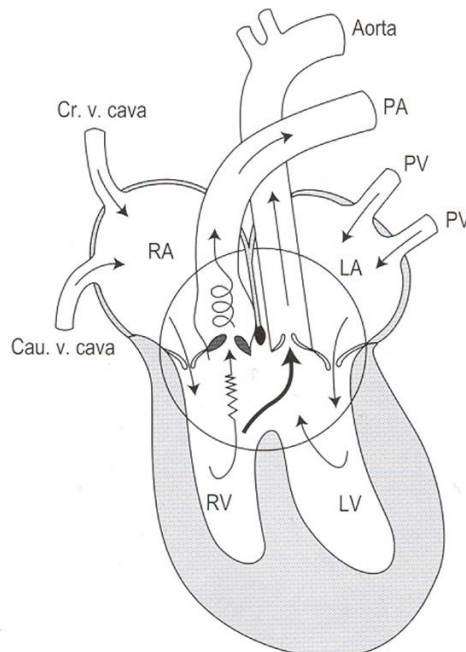
1. ↑ LV afterload
= LV concentric hypertrophy
2. Aortic poststenotic dilation

Pulmonic Stenosis (right)

1. ↑ RV afterload
= RV concentric hypertrophy
2. PA poststenotic dilation

Various congenital defects may occur together with other abnormal features and constitute complex malformations e.g. Tetralogy of Fallot:

- i) Ventricular septal defect
- ii) Pulmonic stenosis
- iii) RV hypertrophy
- iv) Dextro-rotated aorta (i.e. transposed to the right - over RV & VSD)



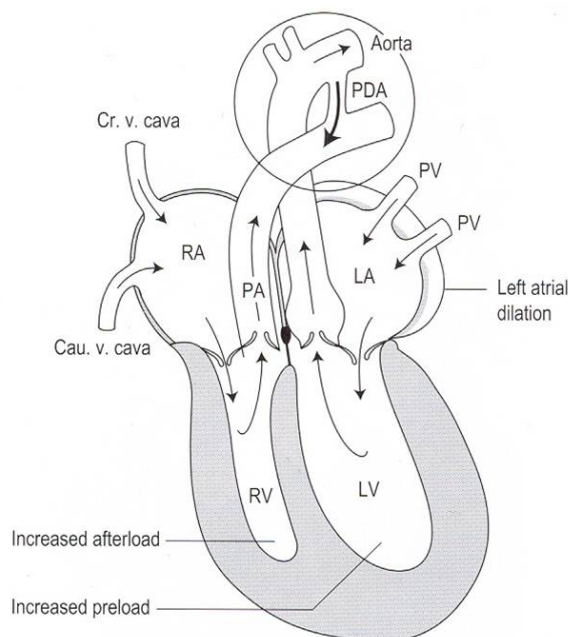
Tetralogy of Fallot

1. Pulmonic stenosis
= \uparrow RV afterload
2. VSD: RV \rightarrow LV
= systemic hypoxia
3. RV hypertrophy (see 1)
4. Dextro-rotated aorta

3. Patent ductus arteriosus (PDA)

Note that in the pig, sheep and horse, ductus patency may be a normal temporary feature of immediate post-natal life (up to two weeks).

If small, PDAs may be subclinical and cause clinical signs only when the animal is forced to exert itself, or where pulmonary hypertension exists. As a result, relatively mature animals may be seen with patent ductus arteriosus.



Patent Ductus Arteriosus (PDA)

1. Aorta \rightarrow Pulmonary Artery
= \uparrow RV afterload
= RV concentric hypertrophy (minor)
2. Pulmonary overperfusion
= \uparrow pulmonary return
= LA dilation and LV preload
= LV eccentric hypertrophy

Shunt reversal (applies to all shunts!)

Chronic injury to the delicate pulmonary vasculature as a result of persistent overperfusion may lead to fibrosis (scarring) and arteriolosclerosis, with gradual increase in pulmonary resistance. Once resistance in the pulmonary circulation exceeds that of the systemic circulation 'shunt reversal' occurs. For example, in PDA, non-oxygenated blood will now flow from the pulmonary artery into the aorta. This is known as 'Eisenmenger's syndrome' and results in systemic hypoxia.

4. **Persistent aortic/branchial arch(es)/vascular ring anomalies**

Of the six pairs of branchial arches present in the early embryo, normally only the left fourth arch (L4) persists as the aortic arch.

Persistent branchial arches are most commonly recognised in dogs and cats. The basic anomaly is constriction of the oesophagus as a result of anomalous vascular rings or associated structures, arising from persistent branchial arches. This results in megaesophagus with regurgitation of undigested food (i.e. food never reaches stomach - as opposed to vomiting, where the food is partially digested).

- a) Persistent right aortic arch - most common manifestation. The vascular ring forms between the ductus arteriosus/ligamentum arteriosum (branchial arch L6) and the anomalous root of aorta (persistent right arch R4).
- b) Double aortic arch
- c) Anomalous subclavian arteries – May be combined with persistent right aortic arch. In this anomaly, the subclavian arteries originate directly from the aortic arch (i.e. no brachiocephalic trunk).

5. **Atrioventricular valvular dysplasia**

In this condition the atrio-ventricular valves fail to form properly leading to A-V valve regurgitation (incompetence) with cardiac dilation and failure. The left A-V valve is most commonly affected. The condition is seen most often in cats, dogs and calves. There are two main morphological presentations:

- a) Web-like valve formations with no clear leaflets.
- b) Short chordae tendinae with small papillary muscle masses.

(Rarely, AV dysplasia can take the form of a stenosis).

MISCELLANEOUS CONDITIONS

- a) *Coarctation of the aorta* - narrowing of the ascending aorta (rare in bovine only).
- b) *Ectopia cordis* - the heart is normal but is situated abnormally in the body. Cattle and pigs show the highest incidence of the condition and the heart is usually situated pre-sternally in the lower cervical region, or more rarely in the abdomen.
- c) *Endocardial fibro-elastosis* - this condition has been described in young dogs, cats (Burmese), pigs and calves. Affected animals usually are found dead at 2-3 months of age often with no previous clinical signs.

The left ventricular endocardium is diffusely thickened with fibro-elastic tissue (valve cusps and chordae may be also affected). The right side may or may not be affected.

- d) *Congenital anomalies of the pericardium* - absence or incompleteness of the pericardial sac may occur in dogs, cats and lambs. In puppies there may also be a concomitant peritoneopericardial diaphragmatic hernia, with liver and/or intestines in the pericardial sac.

ACQUIRED CARDIAC DISEASES

I. PERICARDIAL CONDITIONS

The pericardium encloses the heart and roots of the great vessels. It is a thin, fibrous and inelastic sac with an internal serous membrane lined by flattened mesothelial cells. Any fluid accumulations within this inelastic membrane cause a compressive effect affecting preferentially the thinner walled right side of the heart (tamponade). Normally, it contains a small amount (1-5 mL) of clear serous fluid.

a) Non-inflammatory fluid accumulation:

- i) Hydropericardium - true serous transudate; usually the result of congestive heart failure, commensurate with degree of compensation. May also be seen with neoplasms (chemodectomas, mediastinal lymphoma, ectopic thyroid tumours, mesotheliomas etc.), anaemia, uraemia (due to renal failure), hypoproteinaemia and general debility.
- ii) Haemopericardium - accumulation of whole blood in the pericardium. Usually associated with rupture of large vessels, especially in horses; or dilated atria due to AV valve regurgitation in dogs. Also seen in RTA, puncture wounds, coagulopathies or secondary to ruptured right auricular haemangiosarcoma. Death results from cardiac tamponade.
- iii) Idiopathic pericardial haemorrhagic effusion is relatively common in dogs, predominantly large breeds. Presents as slowly developing right sided heart failure followed by left side.

b) Inflammation - Pericarditis:

Chief complication is restriction of ventricular movement. Symptoms are those of acute circulatory failure.

- i) Haematogenous –due to septicaemia (cattle, pigs).
- ii) Traumatic penetration of pericardium - foreign bodies from oesophagus or reticulum (cattle); fractured rib (dogs, cattle, horses).
- iii) Extension of infection from surrounding tissues - lungs, pleura, mediastinum (pigs, sheep, cattle).
- iv) Extension of myocardial inflammation - primary myocarditis spreads by local invasion; rare.

Acute infections may cause rapid death (especially if young). If the lesion is chronic, it tends to become organised (*i.e.* with fibrosis).

Regarding the nature of the fluid, it is possible that pericarditis is fibrinous (due to increased vascular permeability) or suppurative (with pus formation, due to the presence of pyogenic bacteria).

The possible sequelae of pericarditis are as follows:

- 1. *Resolution* – resolves without further functional/morphological consequences.
- 2. *Adhesion* - organisation of fibrin following serofibrinous pericarditis. Where there is purulence, a 'bread and butter' effect of layers adherent fibrinous matrix and pus accumulate between pericardium and epicardium. It may result in fibrosis.
- 3. *Constriction/atrophy* - if the condition is insidious, gradual tamponade and cardiac atrophy may occur = **constrictive pericarditis**
- 4. *Myocarditis* – associated with traumatic reticulitis/pericarditis, where the sharp foreign body (e.g. wire/nail) penetrates into the myocardium; rare.

II. MYOCARDIAL CONDITIONS

The myocardium constitutes the bulk of tissue in the heart. In it, cardiomyocytes (striated muscle) form myocardial bundles, arranged in complex layers and bands. The atrial myocardium is thin and supported by fibrous and alveolar connective tissue.

Blood supply is from the coronary arteries, arising in the sinuses behind the aortic valve cusps and supplying the myocardium as end-arterioles. The ratio of capillary supply to muscle bundle number and size is important in adult hearts.

In many myocardial diseases, damage must be widespread and severe before clinical signs are observed, and lesions may be detected incidentally at necropsy. If severe, myocardial disease results in heart failure (acute or chronic). Remember, heart muscle cannot undergo hyperplasia or regenerate, therefore compensation attempts are by hypertrophy of surviving muscle.

1. Hypertrophy and dilation

Myocardial hypertrophy (i.e. increase in size of cells) may result from a physiological response (e.g. to increased exercise), or a pathological one (e.g. valvular stenosis, systemic hypertension or renal disease etc.).

Dilation may occur where the disease process is too rapid to allow cardiac compensation. More commonly (especially in dogs), it may herald the onset of failure in a previously compensating heart.

Assessment of hypertrophy and dilation can be difficult and is best done by weighing and measuring thickness of ventricular walls, size of papillary muscles, and dimensions of muscle fibres (see last sheet of chapter).

2. Metabolic disturbances

Hydropic degeneration – The first manifestation of cell injury (hypoxia, toxins, septicaemia), consisting of intracellular accumulation of fluid. Injury causes energy production to decrease and membrane pumps fail due to lack of ATP.

Fatty change/degeneration – Fat accumulates within cardiomyocytes due to inability to metabolise normally. May also result from myocardial hypoxia (e.g. ischaemia, anaemia) or toxicity (e.g. poisons, toxemia in ruminants).

Fatty infiltration - Replacement of muscle bundles by adipocytes (fat cells), with no degeneration. Probably congenital in sheep, calves, and pigs.

Hyaline degeneration - Most commonly a microscopic manifestation of the vitamin E/selenium deficiency 'White Muscle Disease', together with cardiomyocyte necrosis (death), inflammation, and dystrophic calcification. This disease presents as acute left-heart failure or acute ataxia/collapse. Muscles affected in "white muscle disease" include appendicular, intercostal, diaphragmatic and cardiac muscle. These have grey/yellow streaks or patches (in the heart they are on the innermost aspect of the myocardium).

Calcification – Dietary excess of vitamin D, plants with vitamin D analogs, or Calcium therapy in puppies, cattle and reptiles.

Visceral gout –It occurs in reptiles and birds, as in these species uric acid is the nitrogen metabolism's end product (vs. urea in mammals). Uric acid will precipitate in tissues as 'urate tophi' (crystals) under certain circumstances (high protein diet and/or dehydration). Can affect other organs, especially kidneys.

3. **Myocardial infarction**

Relatively uncommon in domestic species, and when it occurs it is usually the result of embolism of coronary vessels (could be sterile, septic, neoplastic).

Myocardial infarction following athero- or arterio-sclerosis of coronary vessels, as seen in man/primates, is rare in domestic animals. Small focal areas of myocardial degeneration may be associated with intimal lesions of the intra-myocardial arterioles in the canine heart but these lesions and similar ones in the horse do not seem to be clinically significant.

4. **Myocarditis**

Inflammation of the myocardium. This is rarely an isolated primary condition and usually follows a generalised infection by bacterial, viral or protozoal agents. Usually results in acute cardiac failure. May be classified as:

Acute (Suppurative) – In most cases, this is the result of septic emboli being released from non-cardiac suppurative foci (e.g. umbilical abscesses, tail bite abscesses, joint-ill, metritis or mastitis), lodging in the heart vasculature. Other possible origins are extension from the endocardium or pericardium, or septic embolism from valvular endocarditis entering the coronary vessels.

Acute (Non-suppurative) - Results from septicaemia or viraemia e.g. pasteurellosis, leptospirosis, Foot and Mouth disease, canine viral hepatitis, parvovirus in puppies, encephalomyocarditis virus in pigs.

Chronic - There is cardiomyocyte loss, with replacement by fibrous tissue. May get granulomas in cattle and sheep. May be a sequel of earlier sub-clinical acute myocarditis in dogs and cats.

5. **Parasitic infestations**

Parasitic larvae may encyst in the myocardium in heavy infestations. They generally produce little or only localised host response:

Cysticercosis - *C. bovis* (cattle), *C. ovis* (sheep), *C. cellulosae* (pigs). Usually have thin connective tissue layer around capsule with a few eosinophils and lymphocytes present. Non-viable cysts tend to calcify.

Sarcocysts – Protozoal organisms in cattle and sheep; also in pigs, horses and dogs. Can only be seen histologically in most cases - elongated cysts containing many zoites (Rainey's corpuscles).

Toxoplasmosis - *T. gondii* (protozoa) may cause cysts or foci of inflammation in myocardium in generalised infections in dogs and cats. In sheep, it is more common to get CNS involvement than heart.

Neosporosis – *Neospora caninum* causes severe myocarditis as well as myositis and encephalitis in dogs. As well as general muscle signs may have arrhythmias. (remember, it also causes abortion in cattle).

Trypanosomiasis - *Trypanosoma cruzi* is the causative agent of 'Chagas' disease'. USA. Causes pyogranulomatous myocarditis and myositis.

6. **Cardiomyopathy**

Myocardial disease leading to cardiac failure:

'White muscle disease': This is the result of lack of vitamin E and/or Selenium, and results in multifocal necrosis of skeletal and cardiac muscle.

'Mulberry Heart' Disease (pigs): Occurs in 3 - 4 month old thriving pigs (usually the best in the litter). This is considered to result from lack of selenium/vitamin E (see also hepatosis dietetica in liver notes). This may be the result of low dietary vit E/Se, high levels of polyunsaturated fats in diet (destroy vit E), or genetic derangements of vit E/Se metabolism. The cardiac presentation is similar to white muscle disease, with necrosis, although in this case, there are also myocardial haemorrhages, resulting from arteriolar fibrinoid necrosis. These result in acute cardiac failure, and affected animals are usually found dead, with pulmonary oedema, sero-fibrinous pericardial fluid and myocardial haemorrhages in the thorax. In the abdomen, there is fibrinous fluid, and hepatic congestion. In the brain, there is bilaterally symmetrical malacia (=softening) of brain cerebral gyri.

Malignant hyperthermia (pigs): (=Hertztod disease/back muscle necrosis). This is a genetic disease, due to a point mutation in the skeletal muscle ryanodine receptor (a Ca^{++} transmembrane channel) – 2-30% pure bred breeding pigs susceptible, with heavily muscled breeds more susceptible. It is triggered by stress (e.g. handling, transportation), and classically by halothane anaesthesia. This results in necrosis of cardiac and skeletal muscles (back, loin, thigh, shoulder). These muscles are then pale, soft and exudative (PSE), interfering with the maturation of these into meat. A similar disease occurs in humans and dogs, known as 'halothane sensitivity'.

Feline hyperthyroidism (cats): This is more common in older cats, and is associated with uni-/bilateral enlargement of thyroid(s) with accompanying hyperfunction of these. This can be the result of benign multinodular hyperplasia (any age, but usually over 5 years old) or neoplasia (older cats). In the latter case, adenomas (microadenomas) are more common than carcinomas. These cats are hyperactive/aggressive, hypertensive, tachycardic, and thin—despite a voracious appetite. Left ventricular hypertrophy is usual and often striking. Rarely the right side is involved, and these cats tend not to develop aorto-iliac 'saddle' thrombi (versus hypertrophic cardiomyopathy, see below). NOTE: Similar cardiac changes are seen as part of acromegaly in cats due to acidophil (somatotroph) adenomas of the pituitary gland which produce excess growth hormone.

Idiopathic cardiomyopathies: These are mostly of unknown aetiology, and may culminate in cardiac dilatation and congestive failure, although some forms are hypertrophic (particularly cats) with a more acute clinical course.

+ Dilated cardiomyopathy (DCM): This condition affects cats, horses, and dogs (giant breeds -Deerhounds, Irish Wolfhounds, St. Bernards; also large-chested individuals of other breeds- Boxers, Dobermans, Labradors). Cases of DCM have been strongly associated with taurine deficiency in cats, and correction of commercially-available diets has reduced the incidence (although cases still occur). In other species the aetiological link is not that strong, and monensin toxicity has been associated with DCM in a horse, and long-term administration of drugs such as doxorubicin and adriamycin has resulted in DCM in dogs. Affected hearts are enlarged (cardiomegaly) with uni-, or more often bi-ventricular dilation ('soup bowl' appearance). They are pale and flabby.

+ Hypertrophic cardiomyopathy (HCM): This disease is common in cats (more frequently male) and rare in dogs. Furthermore, in Maine Coons and Ragdolls causative mutations in sarcomeric genes have been identified. Histologically, the myocardial fibres are hypertrophied, may be arranged haphazardly ('myofibre disarray'), and are accompanied by interstitial fibrosis and frequent arteriosclerosis. There is no evidence of myodegeneration.

There is marked cardiomegaly, resulting from left ventricular concentric hypertrophy, with concurrent thickening of the interventricular septum, and normal or reduced internal left ventricular chamber size. Thrombus formation in the left atrium is common, and when this thrombus breaks (60% of cases), these animals develop leads aortoiliac thromboembolism ('saddle thrombus'), with sudden-onset posterior paresis.

+ Restrictive cardiomyopathy: Occurs less commonly in cats. These animals have marked myocardial fibrosis or endomyocardial fibrosis of the left ventricular endocardium. This leads to loss of compliance and inability to fill adequately in diastole (i.e. diastolic dysfunction). As a result of this, there is marked left atrial dilation with a left ventricle of normal dimensions. These cats often develop cardiac dysrhythmias (atrial fibrillation) with pulmonary oedema and may develop left aortic thromboembolism. Right-sided congestive heart failure, with right atrial dilation can also develop.

+ Arrhythmogenic right ventricular cardiomyopathy (ARVC): This is primarily a familial disease of Boxer dogs, and is rare in cats (and humans). The right ventricular myocardium is replaced by fat and fibrous tissue (may also see similar changes in atria and left ventricle). May present with arrhythmia, syncope, heart failure or sudden death.

+ Eosinophilic myositis: green-grey colour of muscle resulting from myodegeneration and eosinophilic inflammation. Seen in sheep and cattle. Probably related to parasitic infestations (sarcocysts).

NOTE: Idiopathic cardiomyopathies are the result of pathological changes to the cardiomyocytes themselves. In HCM and DCM the hypertrophy and dilation are not associated to functional changes (i.e. increased afterload or preload). They are the result of cardiomyocyte derangement. Despite this, the gross presentation is similar to that of eccentric and concentric hypertrophy due to functional overload. Confusion between these and cardiomyopathies should be avoided, as the pathogenesis is diverse between them.

III. ENDOCARDIAL CONDITIONS

The endocardium lines the cardiac chambers, and is a component of the valve cusps.

a) Endocarditis: Endocarditis is inflammation of the endocardium. Valvular endocarditis is more common in the domestic species than mural (wall) endocarditis. Factors that have been involved in this occurrence are valvular trauma due to blood turbulence, valve tissue aging, the avascularity of valves, valve exposure to blood pathogens, and factors due to the pathogens. In any case, there may be spread from valve lesions to the wall in severe cases.

It is most common in cattle, pigs and sheep, and uncommon in dogs, cats and horses. All the cardiac valves can be affected, but the distribution varies between atrioventricular and semilunar valves, and between species. Briefly, atrioventricular valves are more frequently affected than semilunar valves in all species. The left side of the heart is most commonly affected in all major domestic species, with the exception of cattle, in which the right side of the heart is most commonly affected.

These lesions frequently originate as septic thrombi due to chronic bacteraemia or pyaemia - e.g. infected wounds (e.g. foot puncture), umbilical infection, mastitis, metritis, abscesses (dental), or arthritis. Organisms commonly isolated are:

Cattle -	<i>Arcanobacterium pyogenes</i> .
Pigs -	<i>Erysipelothrix rhusiopathiae</i> ; streptococci (e.g. <i>Strep. suis</i>).
Sheep-	Streptococci; <i>Arcanobacterium pyogenes</i> .
Dogs -	Streptococci; staphylococci; <i>E. coli</i> ; <i>Pseudomonas</i> ; <i>Enterobacter</i>
Horses-	Streptococci.

The lesions are usually 'vegetative' thrombi in gross appearance, invading and distorting normal cusp symmetry. Histologically, the lesions are composed of fibrin (thrombus) matrix, friable necrotic debris, neutrophils and bacteria located mainly on the outflow surfaces of valves. In longer-standing lesions there is often granulation tissue (proliferative fibrovascular tissue) with embedded bacterial colonies.

Possible sequelae:

- i) Rupture of friable vegetations with resulting septic embolism:
 - Right-side lesions (cattle) – pulmonary embolism and abscessation.
 - Left-side lesions (pig, dog, horse) – myocardial and peripheral infarction and infection (especially kidneys).
- (ii) Valvular stenosis/incompetence:

Stenosis means narrowing of the valve orifice, whereas incompetence means inadequacy of the valve to maintain an efficient seal against backflow of blood with consequent leakage or regurgitation. Both of these can be simultaneous. Summarized below are the consequences of the most commonly encountered situations:

Stenosis (semilunar)	Cardiac changes	Non-cardiac changes
Left-sided	Left ventricular concentric hypertrophy	Pulmonary congestion/oedema
Right-sided	Right ventricular concentric hypertrophy	Caval venous congestion
Incompetence (atrioventricular)	Cardiac changes	Non-cardiac changes
Left-sided	Left ventricular eccentric hypertrophy	Peripheral hypoperfusion Pulmonary congestion (if severe)
Right-sided	Right ventricular eccentric hypertrophy	Caval venous congestion

b) Degenerative Valvular Disease:

+ Myxomatous valvular disease or endocardiosis (dogs): Most frequently, changes are seen in AV valves, especially on the left (mitral valve), although others may be affected. The condition is very common in older dogs (>6y). 97% of dogs of 9 years old and over show lesions (of which 40% are considered clinically significant). Toy, small and medium breeds are predisposed (King Charles Cavalier Spaniel).

Grossly, the lesions on main cusps can be graded (Whitney 1→4) from smooth, white, discrete nodules, through coalescent nodules, to plaque-like thickenings with cuspal distortion and chordal involvement and rupture (results in a 'flail leaflet'). Microscopically, the affected valve cusps have marked accumulation of mucopolysaccharide (= 'myxomatous' degeneration).

The valvular changes cause valve cusp distortion with consequent incompetence and leakage of blood into the corresponding atrium during systole.

+ Chronic valvulopathy - HORSES

Valve lesions in equines are not typical of acute inflammation or degeneration. Valves may be distorted by fibrous lesions which may be thickenings, bands or nodules. There are also reports of endocardiosis-like changes in equine AV valves.

Histologically, the changes observed are those of sparse chronic inflammation with fibrous scarring. The most significant lesions affect main mitral and aortic valve cusps.

- 1) Sparse cellular infiltrations (lymphocytes, macrophages and fibroblasts) in the superficial outflow layer of the cusp.
- 2) Variable villous or papillary eruptions of the outflow endothelium.
- 3) The deeper layers often show irregular whorls or meshes of collagen fibres which may be more organised, resulting in cuspal nodulation or distortion seen in the gross.

c) Other Conditions:

+ Necrotising endocarditis - isolated foci of necrosis on the left atrial endocardium just above the LAV valve ring in old dogs with uraemia.

+ Endocardial calcification - deposits of calcium and fibrous tissue which may spread into the myocardium. Affects left atrium and ventricle in calves. Mineral imbalance – high dietary Ca and P, soil rich in K or low in Mg/P, hypervitaminosis D, plant derived vitamin D analogues.

+ Haematocysts and lymph cysts – incidental - in the A-V valve cusps at their attachments to chordae or valve ring (lambs, calves and horses).

+ Melanosis – incidental - melanin deposition on heart valves and mural endocardium of Scottish Blackface sheep and black breeds of cattle.

+ Jet lesions - fibrous thickenings of the endocardium adjacent to an incompetent valve (caused by back flow during systole). Lesions may also occur in the aorta/pulmonary artery as a result of high pressure abnormal jets of blood passing through a narrowed stenotic semilunar valve and striking the vessel endothelium.

CARDIAC NEOPLASIA

True primary neoplasms of cardiac tissue are rare. They often do not cause clinical signs until very large unless they interfere with cardiac function due to their location.

1. Primary cardiac neoplasms:

+ Haemangiosarcoma - arise in the right atrium/auricle and may involve the base of the right ventricle. Other primary sites include liver, spleen and skin. Metastases also occur in these organs and in the lungs and brain. Usually only presents clinically when haemopericardium > tamponade occurs.

+ 'Heart-base' tumours - arise in the chemoreceptor cells in the aortic and pulmonary bodies. Therefore, they are chemodectomas. They may metastasise, and local enlargement usually results in mechanical displacement on adjacent tissues (can result in dyspnoea, cyanosis and/or syncope), and pericardial effusion. Brachycephalic dogs are predisposed.

+ Other – thymomas, ectopic thyroid tumours, sarcomas, rhabdomyomas, neurofibromas can be found in the ventricles rarely. Myxomas are also rare, but can occur in the atrial appendages of dogs.

2. Secondary neoplasia:

+ Metastases from malignant tumours; seen in dogs and cats mainly (mammary and thyroid adenocarcinoma, haemangiosarcomas).

+ Lymphomas are often part of multicentric lymphoid neoplasia (e.g. bovine leukosis).

SECONDARY CARDIAC DISEASE

The heart becomes diseased as a result of abnormality in other organs.

a) Cor pulmonale:

This term is used to describe heart disease which is a consequence of chronic pulmonary disease. It usually features isolated right heart enlargement following raised pulmonary resistance/hypertension. Causes may be:

- i) Primary chronic lung disease - fibrosis, emphysema, bronchiectasis; e.g. diffuse allergic/fibrosing alveolitis in cattle (see respiratory pathology notes)
- ii) Pulmonary thromboembolism - metastatic neoplasia, parasitism e.g. heartworm (*Dirofilaria*) or *Angiostrongylus vasorum* infestation in dogs.
- iii) Mechanical obstruction/obliteration of pulmonary arteries – thromboembolism, fibrosis, neoplasia (primary or metastatic).
- iv) Impairment to respiratory movements - malformations, thoracic trauma.
- v) High altitude/mountain disease - occurs in cattle kept above 6500 feet (~2000m). Related to chronic hypoxia, hypocapnia and respiratory alkalosis leading to pulmonary vasoconstriction, pulmonary hypertension and eventually congestive heart failure. Calves are usually affected. The right heart is markedly dilated, and there is pulmonary and peripheral oedema.

b) Systemic disease:

The heart may be unable to cope with increased peripheral vascular resistance and hypertension. E.g. interstitial nephritis in dogs, or feline hyperthyroidism and chronic renal disease (of unknown aetiology) can both result in left ventricular hypertrophy. Various diseases causing long-term tachycardia can result in chronic injury to the myocardium – 'tachycardia-induced cardiomyopathy'.

VASCULAR PATHOLOGY

DISEASES OF ARTERIES

1. Arterial hypertrophy

Arterial hypertrophy is seen as increase in the tunica media (smooth muscle) and intima of arterioles, and is the response to raised arterial blood pressure or volume (arteriolosclerosis). Local changes are seen typically in renal arteries in cases of chronic interstitial nephritis in dogs and cats. NOTE: Generalised hypertension as seen in man does not occur in the domestic species.

Another pathogenesis is possible, and hypertrophy of the intimal and medial layers of pulmonary arteries is seen in cats affected by the lungworm *Aleurostrongylus abstrusus*, dogs with dirofilariasis, or left-to-right shunting PDA.

2. Arteriosclerosis

This term encompasses a group of vascular diseases of unknown aetiology which are characterised by fibrous thickening with degeneration of the arterial walls. It affects large arteries (typically the abdominal aorta, or branching sites in all large arteries). The pathogenesis of arteriosclerosis is unclear, although it is thought to result from turbulent blood flow. As such, arteriosclerosis is a common feature of feline hypertrophic cardiomyopathy and myxomatous mitral valve disease in small dogs, but most commonly an age related, incidental finding in aged dogs, horses and cattle. Grossly, such lesions may be seen as plaques or grey streak-like thickenings on the arteries. Histologically there is mucopolysaccharide accumulation in the intima, followed by fibrosis, calcification and muscle hypertrophy. The sub-intimal layers are often disrupted as well.

3. Atherosclerosis

Characterized by accumulation of cholesterol in the vascular wall. It is rare in domestic animals, but may occur in canine hypothyroidism or diabetes mellitus.

4. Amyloidosis

Amyloidosis is an insoluble protein derived from serum amyloid A (AA type), immunoglobulin light chain fragments (AL type), pancreatic islet cell amyloidosis (IAPP, produced by β cells) (note: other amyloid types exist). AA type most often occurs in chronic inflammation, but also as an idiopathic familial condition (Abyssinian cats, sharpei dogs). AL type is less frequent, and associated with Ig-secreting plasma cell neoplasia (e.g. multiple myeloma).

Amyloid deposits maybe found in renal vessels and glomeruli, splenic white pulp arterioles, the space of Disse in liver sinusoids, coronary and meningeal arteries. Non-vascular lesions include deposits in adrenal cortex, intestine), renal medulla of cats (leading to necrosis of the papillary region), or pancreatic islet deposits in older cats (of unknown clinical significance). Amyloid is stained with Congo red.

Macroscopically affected organs (kidneys, liver) are pale and firm with a waxy texture when the amyloidosis is marked.

5. Calcification

- a) Dystrophic - following inflammation, thrombosis or necrotic degenerative lesions (e.g. *Strongylus vulgaris* larval lesions in horses).
- b) Metastatic - widespread medial calcification. Large arteries show plaque-like lesions but small arterioles may be completely encircled. Histologically, there is degeneration and calcification of elastic fibres in the tunica media.

6. Fibrinoid necrosis

This is associated with endothelial damage and entry and accumulation of serum proteins, which polymerize along the vessel wall. It is seen in diseases with vascular degeneration (e.g. uremia), or with inflammation (vasculitis).

7. Arteritis

The term arteritis describes inflammation in arterial walls.

a) Infectious

i) Generalised: *Bacterial* - salmonellosis, swine erysipelas, pasteurellosis. *Viral* – feline coronavirus (FIP), swine fever, distemper, equine viral arteritis, bovine malignant catarrhal fever, Border disease in lambs, Aleutian disease in mink. *Mycotic* – aspergillosis, mucormycosis (necrotising thrombotic condition caused by fungi of the Mucorales family). *Parasitic* – strongyloidosis. Vasculitis as a sequela of infection (usually a result of deposit of immunocomplexes) is classically reported with *Streptococcus equi* infection= purpura haemorrhagica.

ii) Localised: Local extension of a focal *bacterial infection*, especially if suppurative or necrotising; e.g. pasteurella pneumonia, meningitis, metritis. Macroscopically, lesions are petechial haemorrhages in serosal surfaces, in adrenal glands and visible mucosae. Often, however, diagnosis is made histologically.

Parasitic lesions - in the UK, a parasite which commonly causes vascular lesions of significance is the equine large strongyle (roundworm), *Strongylus vulgaris*. The larvae and immature adults migrate through and along arterial walls causing intimal damage and arteritis. Lesions are encountered in the ascending aorta, roots of the cranial mesenteric, ileocaecal and renal arteries. In dogs, eosinophilic/granulomatous inflammation of pulmonary arteries caused by *Dirofilaria* or *Angiostrongylus spp* may result in cor pulmonale.

b) Non-infectious:

i) Polyarteritis nodosa - in the domestic species affects principally the media of arteries and arterioles. The lesions have been recorded in dogs, sheep, cattle, horses and pigs. The cause of this condition is unknown but may be related to antigen-antibody immune complex deposition in vessel walls (type III hypersensitivity). Characteristic lesions are often not recognised grossly although petechiation may be present as a result of cutaneous vasculitis. If present, they feature nodules along arteries (e.g. in the mesentery). Histologically, the lesion is a fibrinoid necrosis of the tunica media, which is infiltrated by neutrophils. Nodules characteristic of the chronic lesion form as a result of extensive granulation reaction, with eosinophils, plasma cells and lymphocytes.

8. Aneurysms

Circumscribed, balloon-like dilation of the wall of an artery due to weakening and loss of elasticity. Blood enters the wall of the vessel to form a bulge.

Usually seen as a result of mechanical disturbance (e.g. proximal to a stenotic lesion or following excessive blood flow as in a PDA). Other possibility is *parasitism*, and a classic example is the verminous aneurysm due to *Strongylus vulgaris* infestation in the horse. *Nutritional deficiencies* may result in weaker collagen (e.g. Copper deficiency). *Congenital* derangements of collagen synthesis can also predispose to aneurysms (e.g. Ehler-Danlos syndrome – affects all species).

9. Aortic Rupture

- Rarely - may be traumatic or spontaneous:
In the dog - due to *Spirocerca lupi* lesions in wall (not in UK).
In the horse - Aortic rupture during exercise or intense excitement (e.g. stallions or 3-day eventers). Rupture of the root of the aorta within the pericardium results in haemopericardium and cardiac tamponade. Also, verminous aneurysms may rupture (e.g. at the cranial mesenteric artery).

10. Thrombosis

Aortic thrombosis is most common in male cats with hypertrophic cardiomyopathy or atrial thrombosis. Less common in dogs and rare in horses. Sudden posterior paralysis with hypothermia of hind-limbs and loss of femoral pulse, usually due to embolisation of a left atrial thrombus (the correct terminology is thromboembolism, although these are commonly known as “saddle” thrombus, due to their positioning/location at the iliac bifurcation of the aorta). Grossly, this is a firm, dark red aggregate situated in posterior aorta and extending into iliac arteries (embolus). Renal and mesenteric arteries may also be affected. Occasionally thrombus embolises to a forelimb, usually the right. Rarely. The cause is unknown and the primary focus not identified.

Other sites of thrombosis, associated with damage to the intimal layer are also possible (e.g. intravascular parasitism, septicaemia)

DISEASES OF VEINS

1. Phlebitis/thrombosis

Phlebitis is the inflammation of veins. It frequently accompanies and precedes thrombosis. Jugulars, vena cavae and portal veins are most commonly affected.

Venous thrombosis can be a result of injection (i.e. iatrogenic, e.g. calcium injection into the cattle mammary veins), or extension from an adjacent area of inflammation. For example, in cattle with traumatic reticulitis or liver abscesses the caudal vena cava may become thrombosed (caval thrombosis), or Umbilical lesions or tail biting may result in thrombophlebitis (hepatic and coccygeal thrombophlebitis, respectively).

2. Rupture

Spontaneous rupture of pulmonary veins leading to post-exertional ‘nose bleeds’ (false epistaxis, as the blood originates in the lungs, as opposed to the nose), is common in racehorses or any horse that undergoes intense exercise. This is known as “exercise-induced pulmonary haemorrhage” (EIPH). The effect of this condition on performance is unclear.

NOTE: The Virchow's triad is a list of the factors involved in thrombosis (one or more of these will be involved if there is a thrombus):

1. Damage to the endothelium

2. Altered blood flow

3. Hypercoagulability of the blood

A SUGGESTED METHOD FOR CARDIAC DISSECTION

The objective of this technique is to reveal cardiac abnormalities whilst retaining anatomical relationships.

1. Observe the heart "*in situ*" in the thorax or whilst still attached to the lungs. This allows identification of any abnormality in organ relationships, especially roots of the great vessels, e.g. transposition defects.
2. Observe the pericardium, incise carefully and assess amount and type of pericardial fluid - colour, consistency, volume (measure, if possible). Collect sample for cytology, microbiology or clinical chemistry, if required.
3. Remove the pericardium. Observe the external appearance of the heart from all sides. Assess the cardiac silhouette – including size, consistency, colour and shape of chambers. Note external vasculature, amount of fat and any obvious lesions (e.g. possible scars/infarcts).
4. Orientate from the left side - the ascending aorta curves away to your right. Note the diameter of the roots of the great vessels, and their relationship to each other (possible malformations?).
5. Cut down the pulmonary artery and through the pulmonic valve; cut through valve cusp commissures, so as to preserve cusps.
6. Cut down the right ventricular wall to the apex. Observe and measure moderator band diameter before transecting. Redirect at the apex and cut up towards the common vena cava junction with the right atrium. Be careful to avoid cutting through the A-V valve leaflets. This exposes the right side of the heart.
7. Observe the mitral orifice from the entrance of the pulmonary vein to the left atrium. Cut carefully down the lateral wall of the left ventricle and through the mitral valve orifice taking care to cut to one side of the main valve leaflets. This exposes the mitral valve and left ventricular chamber.
8. Cut down the caudal/ventral wall of the ascending aorta to enable observation of the aortic valve orifice and cusps.
9. After observing the mitral valve and associated chordae, cut to one side of the main mitral valve cusp to reveal the aortic outflow tract and the aortic valve. Continue cutting through the aortic valve commissures to join up with the cut in the aorta.
10. If required, the atrial appendages can be incised laterally from the atria to the appendage apices. The major extra-mural coronary blood vessels can be opened.
11. The myocardial walls may be subjected to serial longitudinal or transverse gross incisions. Care should be taken not to compromise the basal region of the interventricular septum, if histological assessment of the A-V node is required.

WHAT TO LOOK FOR WHEN ASSESSING A HEART

1. Get a relative heart weight by weighing the cadaver and the heart. Weigh the heart after dissection and removal of blood clots (see below).
2. Assess the cardiac silhouette with reference to obvious abnormal enlargements of the chamber. Check the size, shape and relationship of the roots of the great vessels.
3. Assess the colour of the external surface (epicardium/myocardium); note any mottling, focal lesions or scars. Check if the heart stopped in systole or diastole if a fresh heart.
4. Before and during dissection, check A-V valve orifices for dilation or prolapsed valve cusps and/or ruptured chordae.
5. After dissection, assess the presence or absence of chamber dilatation or hypertrophy:
 - a) General shape of chamber - is one larger, i.e. asymmetry present?
 - b) Thickness of chamber wall - thin flaccid walls may mean dilation.
 - c) Diameter of the RV moderator band - a thick band often means hypertrophy but be aware of species variations.

If evidence of hypertrophy is sought, the technique may require modification to include quantification of ventricular myocardium, i.e. relative heart weight may not be enough.

$$\text{In adults} \quad \frac{\text{LV WEIGHT} + \text{SEPTUM WEIGHT}}{\text{RV WEIGHT}} = 2.8-4.0$$

> 4.0 = LV Hypertrophy
< 2.8 = RV Hypertrophy

6. Assess valve cusps for size, shape and consistency and any overt lesions. Include the chordae (length, linearity, number) and papillary muscle masses.
7. Check width of aortic and pulmonic valve outflow tracts. Check for septal defects and transposition of great vessels. Check for any fibrosis of the aortic outflow tract.
8. Assess colour and consistency of myocardium; beware of pale mottling - some fatty deposits between normal muscles can be misleading especially in ruminants and obese animals. Beware of barbiturate (euthanasia solution) crystallisation on the endocardium.
9. Small animal hearts can be fixed whole in 10% formalin; large hearts may require further dissection to ensure proper fixation of ventricular walls. Try to remove clotted blood prior to fixation but only if this is easy. Label specimens with pencilled labels.