Chapter 4

Cardiovascular and Haemopoietic Systems

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HEART

Introduction

The purpose of gross examination of the cardiovascular system at necropsy is to detect lesions and interpret their significance.

A relatively minor but critically located lesion may cause a marked, possibly fatal, disturbance in cardiovascular function. Some fatal diseases (eg acute phalaris toxicosis and hypomagnesaemia) produce functional cardiac effects only and therefore no detectible lesions. On the other hand, a major structural abnormality (eg an extensive area of cardiac fibrosis) may be an incidental necropsy finding.

Some gross cardiovascular lesions may be sufficiently distinctive to suggest a specific disease (eg focal mural haemorrhage at the base of the pulmonary artery in bluetongue in sheep; a necrotising myocarditis in blackleg in cattle).

History, clinical findings, and evidence at necropsy of **cardiac compensation** (eg cardiac hypertrophy or dilation) or **congestive heart failure** (eg ventral oedema, hepatic congestion and enlargement, or fluid accumulation in body cavities) can assist interpretation of cardiovascular lesions found at necropsy.

A working knowledge of **cardiovascular structure and function** is an important basis for identifying and interpreting gross **pathological patterns of cardiovascular disease**.

Cardiovascular Responses to Maintain Cardiac Output

The role of the cardiovascular system is to maintain an adequate circulation of blood to meet the metabolic (nutritional, oxygen and excretory) needs of body tissues.

The heart (a rate-variable, one-way pump) drives the system.

There are three determinants of heart function, **rate and rhythm**, **haemodynamics**, and **contractility** *(see **Table 1**)*, and they mediate:

- **Disturbances** of heart function in cardiac disease.
- **Compensatory responses** of the heart to demands on cardiac output in both normal and diseased hearts *(see **Tables 1** and **2**)*.

The normal heart has the capacity (cardiac reserve) to increase its output up to five-fold, as seen, for example, during physical exertion.

Compensatory responses can maintain an adequate cardiac output and circulation of blood for some time in animals with severe cardiac disease and compromised cardiac function.

Determinants of Heart Function	Disturbances	Compensatory Responses in Normal and Diseased Hearts
1. Rate and Rhythm (ability to depolarise regularly but variably).	**Arrhythmias** (disturbed impulse formation or conduction) may be: • **Intrinsic.** • **Secondary to myocardial damage** (necrosis, fibrosis, or infiltration by inflammatory or neoplastic cells).	• Increased heart rate
2. Haemodynamics (ability to maintain efficient, one-way blood flow). *Haemodynamics involve:* • *Heart chamber **pressures.*** • *Heart chamber **volumes.***	**Haemodynamic disturbances**, affecting one or both ventricles, include: • **Systolic (pressure) overload** (eg outflow stenoses and hypertension). • **Diastolic (volume) overload** (eg valvular insufficiencies). • **Diastolic (volume) underload** (eg constrictive pericarditis).	• Hypertrophy. • Hyperplasia.

3. Contractility
(ability to contract with vigour).
	Contractility deficits (myocardial failure) may be:
	• **Intrinsic** (eg cardiomyopathies).
	• **Secondary to myocardial damage.**
		• Increased contractile force:
		  • From sympathetic stimulation.
		  • In stretched myofibres in cardiac dilation.

Table 1. Determinants of heart function.

Cardiovascular Responses to Maintain Adequate Cardiac Output	Outcomes
1. Systemic Responses • **Increase in peripheral resistance.** • **Redistribution of blood flow to vital organs.** • **Venular constriction.** • **Increase in blood volume** *(modulated by sodium and water retention, a renal response to hypovolaemia, and by sodium retention due to renin / angiotensin / aldosterone activation).*	**Systemic responses** enhance venous return to the heart. ***Circulatory filling pressure*** *is the "tightness" with which the circulation is filled with blood (it depends on peripheral resistance, venous tone, vascular compliance and blood volume) and is central to the events that follow the onset of heart failure.* ***Venous return*** *is proportional to* ***circulatory filling pressure*** *minus* ***atrial pressure. Cardiac output*** *is directly proportional to* ***atrial pressure****.* *As the heart fails, renal compensation increases circulatory filling pressure to enhance venous return and restore cardiac output, but at the price of an increase in atrial pressure.*
2. Intrinsic Cardiac Responses • **Increase in heart rate**	**Increase in heart rate** (from sympathetic stimulation) increases cardiac output per minute. Stroke volume is maintained by more rapid filling and emptying of ventricles.
• **Cardiac dilation** *Dilation is a compensatory response that can increase cardiac output, as stretching of myofibres increases the contractile force (Frank-Starling phenomenon) and increased stroke volume results. However stretching beyond certain limits results in decreased contractile force.* **Cardiac dilation** results from: • **Diastolic (volume) overload** (eg in heart shunts; atrioventricular and semilunar valvular insufficiencies).	**Cardiac dilation** is indicated by: • Rounded (globose) cardiac profile. • Enlarged ventricular lumen(s) (with or without change in wall thickness). • Changes in size of atrioventricular rings (AVR) (normal ratio of circumference LAVR / RAVR is 0.8 - 0.9). *Dilation occurs terminally in many cardiac diseases.* *In both* ***cardiac dilation*** *and* ***eccentric hypertrophy*** *the heart tends to be globose and the ventricular wall is usually thin, especially relative to the overall chamber dimensions. The papillary muscles may be attenuated.*
• **Cardiac hypertrophy (concentric or eccentric)** *Hypertrophy is an important long-term compensatory response to sustained changes in pressure or volume loads.* **Concentric hypertrophy** results from: • **Systolic (pressure) overload** (eg in aortic stenosis; pulmonic stenosis; pulmonary hypertension). • **Diastolic (volume) underload** (eg in constrictive pericarditis; hydropericardium; restrictive cardiomyopathies). **Eccentric hypertrophy** results from: • **Diastolic (volume) overload** (eg in cardiovascular shunts; atrioventricular and semilunar valvular insufficiencies).	**Cardiac hypertrophy** is indicated by: • Increased heart mass (normally 0.5 - 1.0 % of body weight). • Concentrically or eccentrically thickened ventricular walls *(in normal animals, the left ventricular wall is thicker than the right, except in neonates where they are of similar thickness).* • *Hypertrophy of the right side broadens the base of the heart.* • *Hypertrophy of the left side increases heart length.* • *Bilateral hypertrophy produces a globose heart.* In **concentric hypertrophy**: • Ventricular mass is increased **without** increase in end-diastolic volume (ventricular lumen volume may be **decreased**). • Affected ventricular wall is thicker than normal as are papillary muscles, muscle ridges (*trabeculae carneae*) and moderator bands, especially the large band in right ventricle. In **eccentric hypertrophy**: • Ventricular mass is increased **with** increase in end-diastolic volume. • Affected ventricular wall is **not** thicker and may be thinner.

Table 2. Cardiovascular responses to maintain adequate cardiac output.

Circulatory Failure

There are **three syndromes of cardiovascular circulatory failure** that should be considered at necropsy *(see **Table 3**).* History and clinical findings assist in this assessment.

Circulatory Failure Syndromes	Pathological Outcomes
1. Acute Heart Failure (cardiac syncope). *Causes include:* • *Reflex vagal inhibition.* • *Tachycardia or fibrillation.* • *Conduction failure.* • *Terminal congestive heart failure.*	Outcome of acute heart failure is: • No detectible lesion (except in terminal congestive heart failure).
2. Congestive Heart Failure. *Congestive heart failure develops when the compensatory cardiovascular responses to sustained **arrhythmias, pressure or volume overloads**, or **myocardial damage** can no longer maintain an adequate cardiac output from a diseased heart to meet the metabolic needs of body tissues.*	Pathophysiological features of congestive heart failure are: • **Accumulation of fluid** (due to retention of sodium and water). • **Tissue and organ ischaemia.** *The compensatory response of increased blood volume is initially beneficial as it enhances venous return and cardiac output, but it also results in an **increase in capillary hydrostatic pressure,** which tends to promote **interstitial oedema** ("waterlogging").*
• **Left-sided failure** results in increased hydrostatic pressure in the pulmonary venous system (and decreased forward blood flow to peripheral tissues). *Causes include:* • *Disease of mitral or aortic valves.* • *Several congenital heart diseases.* • *Contractility loss from myocardial necrosis, myocarditis, or cardiomyopathy.*	Outcomes of left-sided failure are: • **Pulmonary congestion and oedema** (with white frothy fluid in airways). • **Hydrothorax** (possible).
• **Right-sided failure** results in increased hydrostatic pressure in the systemic and portal venous systems (and decreased forward blood flow to lungs and left ventricle). *Causes include:* • *Pulmonary hypertension.* • *Disease of tricuspid and pulmonary valves.* • *Contractility loss from myocarditis, myocardial necrosis or cardiomyopathy.*	Outcomes of right-sided failure in ruminants are: • **Ventral oedema.** • **Hepatic congestion and enlargement** ("nutmeg liver", congestive hepatic nodularity). • **Fluid accumulation in body cavities** (ascites, hydrothorax and hydropericardium). *Sodium and water retention and resulting increase in blood volume are more severe in right-sided than in left-sided failure.*
3. Peripheral Circulatory Failure *Causes include:* • *Reduced circulatory blood volume due to acute blood loss, shock, or splanchnic venous pooling.*	Outcomes of peripheral circulatory failure include: • Evidence of blood loss. • Congestion of viscera.

Table 3. Cardiovascular circulatory failure. Their pathological outcomes are summarised.

Dissection of the Heart

An essential part of any necropsy is a systematic examination of the heart, including:

- **Pericardium.**
- **Endocardium (mural and valvular).**
- **Myocardium.**
- **Large vessels.**

Always follow the same procedure for dissection and examination of the heart, to optimise detection of **gross lesions** as well as **changes in size**, **shape** and **position** of the heart, its components and associated thoracic structures. There are several ways to open a heart:

- **Inflow-Outflow Method**: The heart is opened by incisions A and B on the right side and incisions C and D on the left *(see **Appendix 1. Dissection and Gross Examination of the Heart**)*.

  This common method allows good access to all chambers, preserves atrioventricular valves and moderator bands, and allows easy measurement of atrioventricular valve rings.

  *Measurements of body weight, circumference of atrioventricular valves and weights of whole heart, right ventricular free wall, combined left ventricular free wall plus interventricular septum, and combined atria allow assessment of **heart to body weight ratios** and degree of chamber dilation (see **Appendix 1**).*

- **Ventricular Slice Method**: The heart is preferably fixed first, and then sliced transversely, perpendicularly to the septum from apex to base at 1-cm intervals.

  This 'breadloaf" method is used to determine ventricular mass, extent of ventricular lesions (eg necrosis, fibrosis), chamber dimensions and wall-to-lumen relationships.

- **Four Chamber Method**: The heart is preferably fixed first, and then bisected longitudinally perpendicularly to the septum from base to apex to reveal all walls and chambers.

  This method is used to compare thickness of the ventricular septum and free walls.

For **histological examination:**

- Collect and formalin-fix 5mm-wide sections from myocardial lesions or a minimum of five standard sites (sites 1. 2, 4, 6 and 9) *(see **Appendix 2. Standard Sites for Histological Examination of the Heart**)*.
- With special cases or small animals, **fix the whole opened heart** before collecting samples from lesions and standard sites.

Postmortem Changes in the Heart

Rigor mortis of the myocardium occurs earlier than in skeletal muscle, and produces contracted rigid ventricular walls in a freshly dead animal (within an hour of death). The left ventricle is affected first. As blood clots relatively slowly in the unopened carcass, rigor usually expresses blood completely from the left ventricle and incompletely from the right. Clotted blood in the left ventricle suggests incomplete rigor due to myocardial degeneration. Postmortem blood clots in the atria, right ventricle and large vessels at the base of the heart are dark red ("current jelly"). As sedimentation of red cells is slow in ruminants, so-called "chicken-fat" clots do not occur except in severely anaemic animals.

As rigor passes (after 12 to 24 hours) and **autolysis** proceeds, the appearance of the heart changes. Unclotted or haemolysed blood may flow back into the ventricles. Postmortem leakage and haemolysis of erythrocytes can cause dark-red, haemoglobin staining of pericardial fluid and endocardium, and should not be mistaken for antemortem haemorrhage. The autolysed myocardium is inelastic and pale grey, with a partially-cooked appearance.

Congenital Developmental Abnormalities of Heart and Large Vessels

The embryological development of the heart and large vessels is complex and consequently anomalies can occur. The most severe defects result in death *in utero* and the mildest remain subclinical throughout life. It is only animals with anomalies of intermediate severity that, after surviving the circulatory changes from foetal to neonatal life, develop signs of cardiac disease.

Most congenital cardiac anomalies in ruminants appear to be spontaneous diseases of low incidence. In other species, and particularly in dogs, some anomalies are genetically determined. They can be produced experimentally by various chemicals and drugs, physical agents (x-radiation and hypoxia), and nutrient deficiencies and excesses.

Necropsy of any foetus or neonate, with or without signs of cardiac failure, should include systematic examination of the heart for the most common cardiac anomalies *(see **Appendix 1**)*. Always examine the heart and large vessels *in situ*, and do **not** separate them from the lungs until after the locations and connections of the large vessels at the base of the heart have been evaluated.

Congenital cardiac anomalies can be broadly classified as:

- **Anomalies from failure of closure of foetal cardiovascular shunts.**
- **Anomalies from failure of normal valvular development.**
- **Anomalies from malpositioning of large vessels.**
- **Other cardiac anomalies.**

Anomalies from failure of closure of foetal cardiovascular shunts

A **patent ductus arteriosus** may be an anatomical finding in neonatal ruminants, but is rarely functional. *In utero*, blood is shunted from pulmonary artery to aorta, bypassing the lungs. *If it persists after birth, there is a shunt from the left to right ventricle and pulmonary hypertension results.*

A congenital **atrial septal defect** may result from a **true septal defect** or from **failure of closure of the foramen ovale** (in the unborn foetus this is a right-to-left interatrial septal shunt; it may still be anatomically-patent but functionally-closed in neonates and occasionally in adults due to the higher pressure in the left ventricle). *Left-to-right interatrial shunt produces right ventricular dilation and hypertrophy, relative pulmonary stenosis and bilateral atrial dilation.*

A **ventricular septal defect** is one of the commonest seen in ruminants, and usually is located in the dorsal membranous septum (rather than the ventral muscular septum), or in the subpulmonary septum. It may be hereditary in Hereford and Limousin breeds. *In utero* there is no flow across the defect as pressures in both ventricles are the same. *After birth there is a left-to-right shunt, which produces bilateral ventricular hypertrophy (more eccentric in left ventricle).* Always check for concurrent defects, such as **dextropositioning of the aorta**, which will straddle the ventricular septal defect.

The **tetralogy of Fallot** is a relatively common complex cardiac anomaly comprising three primary defects of high ventricular septal defect, pulmonic stenosis and dextropositioning of the aorta and a fourth, secondary defect, compensatory hypertrophy of the left ventricle. **Eisenmenger's complex** is similar to tetralogy of Fallot, with pulmonary hypertension but without a pulmonary stenosis.

Anomalies from failure of normal valvular development

Pulmonic stenosis (subvalvular, valvular or supravalvular)) causes post-stenotic dilation and thinning of the wall of the pulmonary trunk and concentric right ventricular hypertrophy. It is usually reported in dogs, but occurs in other domestic animals.

Subaortic and aortic stenosis (most commonly the former) causes post-stenotic dilation of the aorta, and concentric right ventricular hypertrophy and frequently multifocal myocardial necrosis. It occurs frequently in Danish pigs and dogs.

Congenital haematomas (haematocysts) are common, blood-filled cysts lined by endothelium frequently seen on the margins of the atrioventricular valves of young ruminants. They measure up to 10 mm in diameter and usually regress after several months. They occasionally enlarge and persist up to a year with serous fluid content replacing blood.

Anomalies from malpositioning of large vessels.

Transposition of the aortic and pulmonary trunks is a severe cardiac anomaly that occurs in calves and involves **dextropositioning of the aorta** so that it receives blood from the right ventricle. It occurs in four types: **overriding aorta** (aorta straddles a defective septum); **partial transposition** (both aorta and pulmonary artery leave the right ventricle); with **overriding pulmonary artery** (pulmonary artery straddles a defective septum, and the aorta leaves the right ventricle) and **complete transposition** (aorta leaves the right ventricle, and the pulmonary artery leaves the left).

Persistence of right aortic arch in calves results in the aortic trunk ascending on the right rather than on the left side of the trachea and oesophagus (because the right fourth aortic arch persists instead of the left, as is normal, to form the ascending trunk of the aorta). The ductus arteriosus (ligamentum arteriosum) passes from the aorta to the pulmonary artery from right to left over the oesophagus, compressing it against the trachea. This eventually leads to obstruction and proximal dilation of the oesophagus (mega-oesophagus).

Other cardiac anomalies.

Ectopia cordis is congenital displacement of the heart (cervical, sternal, or abdominal) and is usually reported in calves. It is not strictly a malformation of the heart but of adjacent structures.

Ventricular hypoplasia, aortic hypoplasia, aortic coarctation (aorta constricted at the site of entry of the ductus arteriosus), **persistent truncus arteriosus** (common aortic trunk: one vessel arises from the heart base and the aorta and pulmonary artery arise from it), **abnormal origin of carotid arteries** (arise from pulmonary artery instead of the aorta), **cor triloculare biatriatum** (complete absence of interventricular septum, resulting in three heart chambers: two atria and one ventricle) and **endocardial fibroelastosis** are also reported.

In a 14-year Kansas study of calves with cardiac defects, 36 calves had 78 congenital cardiac defects: ectopia cordia cervicalis (10 defects), common aortic trunk (3), dextraposed aorta (8), duplicated major trunks (1), hypoplastic aorta (2), interventricular septal defect (11), interatrial septal defect (2), left ventricular hypoplasia (10), patent ductus arteriosis (5), patent foramen ovale (5), right ventricular hypoplasia (10), cor triloculare biatriatum (1), endocardial fibroelastosis with calcification (3) and valvular haematomas (7). All septal defects were high in location and ranged from 5 to 35 mm in diameter.

Reference:

Gopak T, Leopold H W and Dennis S M (1986) Congenital cardiac defects in calves. *Am J Vet Res* 47: 1120-1121.

Cardiac Haemorrhages

Haemorrhages may be localised in the epicardium, endocardium or myocardium.

Epicardial and **endocardial haemorrhages** are common, non-specific, terminal lesions in ruminants. They are seen particularly in animals that have died acutely (eg from bloat, infectious diseases, blue-green algal toxicosis) and reflect terminal anoxia. They range from petechial to ecchymotic to suffusive, and may be extensive. They occur in **bluetongue** in sheep, in addition to the distinctive **focal, mural haemorrhage at the base of the pulmonary artery** (and aorta).

Ecchymotic endocardial haemorrhages particularly in the **left ventricle** are seen in **clostridial enterotoxaemia** in lambs and calves.

Epicardial and **endocardial haemorrhages** are consistent gross lesions in ruminants poisoned by cardiac glycosides in plants such as *Bryophyllum* tubiflorum (mother of millions) and its *B daigremontianum* hybrid, *Nerium oleander* (oleander) and *Homeria* spp (cape tulips).

Pericardial Diseases

Noninflammatory lesions of the pericardium

After death, there may be some transudation of red (haemolysed) fluid into the pericardial sac.

Hydropericardium is the accumulation of clear, colourless to light yellow, watery fluid in the pericardial sac. In chronic cases there is fibrous or fibrovascular villous thickening and opacity of the pericardial and epicardial surfaces; vessel rupture within villous areas can cause blood-staining of the fluid. *In those diseases causing generalised oedema, there may be concurrent ascites, hydrothorax and pulmonary oedema.*

High-protein pericardial oedema fluid (**exudate**, which forms fibrin clots, particularly on exposure to air), results from:

- **Increased vascular permeability** in acute systemic diseases (eg clostridial toxaemias, and heartwater (*Cowdria ruminantium*).

Low-protein pericardial oedema fluid (**transudate** which does not clot) results from:

- **Decreased capillary osmotic pressure** due to **hypoproteinaemia** (eg. illthrift and undernutrition, severe anaemia as in haemonchosis and fascioliasis, and protein-losing enteropathy or nephropathy).
- **Increased hydrostatic pressure** in **congestive heart failure**.

- **Obstruction to lymphatic drainage**, (eg by pericardial, and other thoracic granulomatous lesions or neoplasms, including mesothelioma and lymphoma).

When hydropericardium develops rapidly, cardiac tamponade (compression) compromises cardiac filling, especially of the atria, as the pericardium cannot stretch quickly. When it develops slowly, the pericardium can stretch to accommodate a large volume of fluid without tamponade.

Haemopericardium is the accumulation of pure blood (clotted blood indicates a true haemocardium) in the pericardial sac. Death is usually sudden due to cardiac tamponade. The source of haemorrhage is usually rupture or puncture of the heart or a major vessel.

Serous atrophy of pericardial fat occurs in cachectic animals. The fat is grey and gelatinous and may contain small white foci of fat necrosis.

Pericarditis

Fibrinous pericarditis results usually from systemic (haematogenous) infection, and less frequently from local spread of infection from adjacent thoracic organs (lungs and pleura). Extending from the base of the heart, fibrinous exudate is grey to yellow (neutrophils), to red (blood) and covers epicardial and pericardial surfaces, which when peeled apart have a characteristic "bread and butter" appearance. Fluid is not prominent. Organisation of the exudate can produce patchy or diffuse adhesion between these surfaces. Causes include sporadic bovine encephalomyelitis, pasteurellosis, blackleg, clostridial haemoglobinuria, contagious bovine pleuropneumonia, and neonatal coliform (umbilical) infections. *Heart function may be minimally affected.*

Suppurative pericarditis, invariably of pyogenic bacterial cause, occurs mainly in cattle with a foreign body perforating from the reticulum. The pericardial surfaces are thickened by a shaggy mass of fibrous tissue enclosing a yellow to grey, foul-smelling, fibrinopurulent exudate. *Animals may survive for weeks to months before dying of congestive heart failure (usually right-sided) and septicaemia.*

Constrictive pericarditis occurs as an end stage of a chronic pericarditis where organization results in formation of extensive fibrous adhesions, which may obliterate the pericardial sac and constrict the heart. *Compensatory ventricular hypertrophy with reduced heart chamber volumes (concentric hypertrophy) and congestive heart failure may follow.*

Strong, localised, fibrous adhesions within the pericardial sac at necropsy are usually longstanding, incidental findings.

Endocardial Diseases

Noninflammatory lesions of the endocardium

Endocardial mineralisation and **fibrosis** may occur alone or concurrently in the atria and left ventricle in chronically dilated hearts, and in a variety of chronic debilitating diseases (eg Johnes disease in cattle). A severe form involving also the aorta has been seen in India in climatically-stressed Australian Corriedale sheep (Jackson, 1987).

Focal endocardial fibrosis (**"jet lesions"**) result from abnormal jets of blood or turbulence associated with congenital or acquired valvular disorders.

Endocarditis

Vegetative valvular endocarditis is usually caused by bacterial infections. Lesions first develop on the free margin of the valves at the line of closure, and then extend onto the valves and into myocardium. One or more heart valves have friable grey masses of fibrinonecrotic material colonised by bacteria (or occasionally fungi) and covered by a thin blood clot. Embolic fragments (either bland or septic) may be found in the vessels of other organs (eg causing pulmonary thrombosis or abscessation). In cattle, *A. pyogenes* is the usual cause (a primary infection source such as an hepatic abscess, metritis or mastitis may be found) and enteric *Streptococcus* spp. have also been isolated. Neonatal umbilical and post-marking bacterial infections can be the cause in lambs and calves.

Mural endocarditis is usually an extension from a valvular lesion.

Acute ulcerative mural endocarditis can accompany the haemorrhagic, necrotising myocarditis of *Clostridium chauvoei* infection (blackleg) in ruminants.

Myocardial Diseases

Myocardial degeneration

Myocardial degeneration occurs in a variety of systemic diseases, including infections, toxaemias and severe anaemia. Gross changes may be minimal and difficult to distinguish from autolysis. **Hyaline degeneration** may produce gross, dull-grey discolouration, friability, and, on cut section, a homogeneous appearance of the myocardium. **Fatty degeneration** (fatty change) produces uneven patchy yellow discolouration of the myocardium or more diffuse change, with the heart flabby and paler than normal. **Atrophy** of the heart in chronic wasting diseases and malnutrition may be associated with gross brown discolouration (brown atrophy) due to lipofuscin accumulation in myocytes.

Myocardial necrosis and mineralisation

Myocardial necrosis in ruminants occurs in acute infections, nutritional deficiencies, chemical and plant toxicoses, ischaemia (infarction) and physical injuries. It produces focal, multifocal and diffuse gross changes of discolouration, pallor or reddening, often accompanied by prominent chalky-white areas of **mineralisation**. The left ventricular subepicardial myocardium and papillary muscles are the most common sites for ischaemic degeneration, necrosis and mineralisation, as these areas develop the greatest intramural tension during systole. A necrotic area is difficult to detect during the first day after injury, but by 2 to 4 days it is more sharply defined as inflammatory cells infiltrate it. The necrotic myocytes are replaced over the next 6 weeks by fibrous tissue, which is initially dark-red to tan (fibrovascular) and later white and opaque. Myocardial necrosis is followed by **replacement fibrosis,** as myocardium does not regenerate (except possibly in neonates), in contrast to skeletal muscle, which does regenerate.

Nutritional myopathy (selenium/vitamin E-responsive disease) in young ruminants can cause cardiac lesions of necrosis with mineralisation or so-called **cardiac "white muscle disease"**. In lambs this syndrome is usually congenital, with involvement mainly of the **right** ventricle. In calves the syndrome is usually delayed in clinical onset until several weeks after birth (so-called delayed white muscle disease) with cardiac lesions mainly in the **left** ventricle. Skeletal muscle lesions are also present, but may be detectible only microscopically. *The predilection for the right ventricle in congenital disease in lambs may reflect right ventricular workload in utero, and for the left ventricle in calves may reflect left ventricular relative workload after birth.*

Cardiomyopathy and woolly haircoat syndrome (**CWH**) in **Poll Hereford** calves in Australia, is an autosomal recessive congenital disease caused by a presumed defect of desmosomal intercellular junctions. Affected calves have a distinctive woolly haircoat and gross **congenital** cardiac lesions of fibrosis and / or necrosis and mineralisation in the ventricular myocardium. Gross lesions are often prominent in the **right** ventricular free wall; the epicardial surface may be irregularly depressed by extensive dark-red areas of fibrovascular (granulation) tissue extending 3 mm into the myocardium. Death usually occurs within two months of birth and may be sudden (from ventricular fibrillation) or follow a period of congestive heart failure. Necrosis and mineralisation of the **left** ventricle, identical to that described for nutritional myopathy, have been seen in CWH calves dying several weeks after birth. Affected calves are not selenium-deficient and do not have skeletal muscle lesions. If the woolly haircoat is overlooked, CWH may be misdiagnosed as nutritional myopathy.

Falling disease in Western Australia occurs in **copper-deficient** dairy cattle that collapse and die suddenly, with pale, flabby hearts, generalised venous congestion, and microscopic lesions of myocardial fibrosis.

Toxic agents and **plants** that cause **myocardial necrosis** (frequently detectible only microscopically) in ruminants include:

- Sodium fluoroacetate (1080) in baits used to control rabbits can accidentally poison ruminants. Plants that accumulate fluoroacetate in Australia include *Gastrolobium* spp, *Oxylobium* spp, and *Acacia georginae. In sodium fluoroacetate toxicosis in ruminants there are usually minimal gross lesions of myocardial pallor and mottling. There are microscopic lesions of myocardial necrosis.*
- Ionophores (monensin, lasalocid, salinomycin, narasin).
- Gossypol (in cottonseed products), which is cardiotoxic to preruminant calves, and also in goats but not orally to sheep.
- *Persea americana* (avocado) leaves, which are cardiotoxic to sheep and goats *They also cause a sterile mastitis and agalactia in goats and horses.*
- *Cassia occidentalis* (coffee senna), which also affects skeletal muscle.
- *Ixiolaena brevicompta* (flat billy button), which primarily affects skeletal muscle.
- *Lantana camara,* which causes myocardial necrosis in sheep.
- Cardiac glycosides in plants. ***Epicardial*** *and* ***endocardial haemorrhages*** *are consistent gross lesions.*

Myocarditis

Gross lesions of myocarditis may appear as areas of reddening (congestion), focal to diffuse pallor or discolouration, with or without evidence of suppuration or abscessation. In **chronic myocarditis** there may be **reactive** or **replacement fibrosis**.

Suppurative myocarditis can result from septicaemia (eg *Listeria monocytogenes*) or secondary spread from other suppurative foci (eg *A. pyogenes, Corynebacterium pseudotuberculosis*).

Haemorrhagic necrotising myocarditis is a feature of *Clostridium chauvoei* infection.

Necrotic myocarditis due to *Fusobacterium necrophorum* can be from secondary spread from necrobacillosis in other tissues.

Acute myocardial necrosis with a **lymphocytic myocarditis** is a feature of **foot and mouth disease** in neonatal ruminants and pigs. Lesions are seen as irregular opaque grey streaks in the ventricular myocardium ("tiger heart").

Eosinophilic myocarditis in cattle, with or without accompanying skeletal muscle lesions, produces poorly-circumscribed, yellow-green foci within the myocardium. The cause is unknown, but the lesions may be associated with degenerating *Sarcocystis* spp.

Granulomatous eosinophilic myocarditis, severe enough to be detectible grossly as extensive, confluent, off-white areas in the ventricular myocardium, is present in some cases of **woolly-pod** and **popany vetch** (*Vicia villosa* ssp *dasycarpa* and *V benghalensis*) **toxicosis.** This disease syndrome of pruritic dermatitis, diarrhoea, illthrift and death usually affects Friesian and Angus cattle. It causes a generalised granulomatous, eosinophilic inflammation, particularly involving the renal cortex, skin, myocardium, adrenal glands, lymph nodes and liver.

Cysticercus bovis and ***Cysticercus ovis*** in cattle and sheep respectively are the intermediate metacestode stages of the human tapeworm *Taenia saginata* and dog tapeworm *Taenia ovis*. They may be seen as an intact small vesicle (viable form) or as a degenerate fibrotic focus up to 1cm in diameter within the myocardium. **Hydatid cysts** of *Echinococcus granulosus* occur infrequently in the myocardium.

Reference:
Harper PAW, Cook RW, Gill PA, Fraser GC, Badcoe LM, Power JM Vetch toxicosis in cattle grazing *Vicia villosa* spp. *dasycarpa* and *V. benghalensis*. *Aust Vet J* 1993;70:140-144.

Cardiomyopathies

Cardiomyopathies are primary diseases of the heart that are of idiopathic cause. Morphological and clinical classifications such as hypertrophic cardiomyopathy, dilated (congestive) cardiomyopathy, and restrictive cardiomyopathy, are currently applied. However, many are inherited diseases that will eventually be classified on a molecular genetic basis.

A number of cardiomyopathies have been reported in cattle.

Cardiomyopathy of adult Friesian-Holsteins in Australia, Canada, Japan and Britain, and in Simmental-Red Holstein crossbreds in Switzerland results in right-sided heart failure including ventral oedema, hepatomegaly, pericardial effusion, and ascites associated with bilateral ventricular dilation. There are microscopic lesions of myofibre atrophy and vacuolar hypertrophy with interstitial and replacement fibrosis and myofibre necrosis. Autosomal recessive transmission is probable.

Cardiomyopathy and woolly haircoat syndrome (CWH) in Poll Hereford calves in Australia *(see above). Cases of a* ***cardiomyopathy with bilateral ventricular dilation*** *have been observed in calves from a horned Hereford herd in Australia (Cook RW, unpublished).*

Cardiomyopathy in Japanese Black calves causes death suddenly or after a short period of dyspnoea, usually at less than 30 days of age. The necropsy findings are of left and right-sided congestive heart failure, with left ventricular dilation and extensive myocardial degeneration, necrosis and fibrosis of the left ventricle and less frequently the right. An autosomal recessive mode of transmission is suspected.

Bovine generalised glycogenosis type II (**Pompe's disease**) is not a primary cardiomyopathy. Most affected animals have a generalised muscle weakness. Some have eccentric cardiac hypertrophy and signs of left-sided heart failure.

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Conduction System Diseases

The conduction system of the heart comprises the sinoatrial node, internodal atrial pathways, atrioventricular node, atrioventricular trunk (bundle of His), right and left crura (right and left bundle branches), and cardiac conducting fibres (Purkinje fibres). An awareness of the general location of the major components of this system during dissection of the heart at necropsy allows them to be included in samples collected for histological examination *(see **Appendix 2**)*.

In ruminants, most dysrhythmias (that can cause intermittent collapse and sometimes sudden death) are not due to primary lesions within the conduction system, but secondary to myocardial degeneration and necrosis, inflammation or neoplasia.

Neoplasms

Primary neoplasms of the heart are rare.

In **sheep**, in a United Kingdom series of 891 tumours, 22 were from the cardiovascular system. Cardiac tumours were **rhabdomyoma** (1), **neurofibroma** (1), **fibromas** (3). The remaining 17 tumours were **haemangiomas** of liver (4), spleen (9), subcutis (3), and intestine (1).

In **cattle**, **bovine leucosis** can cause nodular or diffuse lesions in the heart. **Bovine neurofibromas** may involve cardiac nerves, and form single or nodular masses on the epicardial surface or in the myocardium. **Mesotheliomas** arising from the pericardial, pleural, and peritoneal serosa produce multiple, small, firm nodules or villous projections from these surfaces; lymphatic obstruction and fluid effusion can follow.

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VASCULAR SYSTEM

Introduction

The vascular system comprises **arteries**, **microcirculation** (arterioles, capillaries and venules), **veins** and **lymphatics**.

Pathogenesis of Vascular Lesions

Gross vessel-associated lesions result from:

- **Vessel wall damage and increased permeability** (causing oedema, haemorrhage).
- **Vessel obstruction** (causing congestion, oedema, ischaemia / infarction).
- **Coagulopathy and thrombocytopathy** (causing haemorrhage).

Vessel Wall Damage and Increased Vessel Permeability

Petechial haemorrhage and **oedema**, with **ischaemia** in some tissues, follow generalised damage to small vessels. Haemorrhage (often massive) is the hallmark of damage to large vessels. Generalised petechiation reflects anoxic capillary damage in acute septicaemic or toxaemic disease.

Altered capillary permeability appears to be the basis of the mild lesions of **bovine ephemeral fever** (oedema of lymph nodes, polyserositis) and the more severe lesions of **heartwater** (pulmonary oedema, hydrothorax and hydropericardium*). Heartwater, a tick-borne rickettsial disease (Cowdria ruminantium), does not occur in Australia.*

Viral-induced endothelial damage within the microcirculation produces microthrombosis and increased permeability with associated ischaemic necrosis, oedema and haemorrhage in many tissues in **orbiviral infections**. These include **bluetongue** of sheep, **epizootic haemorrhagic disease** (EHD) of deer and **Ibaraki disease** of cattle (the last is caused by an EHD 2 virus). In **bluetongue** in sheep, **focal haemorrhage within the tunica media at the base of the pulmonary artery** (also of the base the aorta, and in the endocardium and epicardium of the heart) is a distinctive finding. *In bluetongue in cattle overseas, only 5% of infected animals show signs of disease (fever, lameness, and erosive muzzle and oral lesions). In Australia, infection by bluetongue and EHD viruses occur in cattle but clinical disease has not been reported.*

Generalised necrotising arteritis and arteriolitis are associated with a range of gross lesions in **bovine malignant catarrh**, including lymphadenopathy, exudative dermatitis, erosive stomatitis and gastroenteritis, keratoconjunctivitis, erosive, possibly pseudomembranous, rhinitis and tracheitis, renal infarcts (or foci up to 4

mm of nonsuppurative interstitial nephritis), white foci of nonsuppurative periportal hepatitis. and oedema and scattered petechiae within leptomeninges.

Generalised vasculitis in *Chlamydophila psittaci* infections causes gross lesions of fibrinous polyserositis in **sporadic bovine encephalomyelitis** of cattle, and polyarthritis and conjunctivitis in sheep (both species have more generalised microscopic lesions including meningoencephalomyelitis).

Although there is microscopic submucosal arteritis in the lower alimentary tract in **mucosal disease** (caused by **bovine pestivirus**), the gross alimentary tract lesions are attributable to the direct necrotising effect of pestivirus on epithelium in the upper alimentary and on aggregated lymphoid tissue (eg Peyer's patches) in the intestines.

Massive haemorrhage (often fatal) following rupture of large vessels is rare but can follow trauma. Fatal pulmonary haemorrhage can result from pulmonary arterial wall erosion and rupture following pulmonary thromboembolism from **thrombosis of the caudal vena cava**.

Vessel Obstruction

Congestion, **oedema**, **ischaemia** and **infarction** (**necrosis**) can follow vessel obstruction. When infective agents cause a generalised vasculitis, microvascular obstruction can occur (in addition to vessel damage and increase in permeability). **Arteriole thrombosis** in salmonellosis can cause digit necrosis.

Gangrene of the extremities follows sustained vasoconstriction of arterioles and endothelial damage caused by alkaloids in *Claviceps purpurea*, the ergot of rye and other grain crops and grasses. Tall fescue grass, which causes an identical condition, harbours endophytic fungi that can produce ergot alkaloids *in vitro*.

Constriction of the muscular pulmonary venules produces **post-capillary pulmonary hypertension** and right-sided heart failure with right ventricular dilation (but never hypertrophy), ventral oedema and hydrothorax in cattle with **St George disease**, caused by the ingestion of *Pimelea* spp. There is also a severe haemodilution anaemia and diarrhoea. A daphnane ester, simplexin, isolated from *P. simplex* produces most of the signs of the disease. Pathogenesis of the associated **hepatic peliosis**, which causes the liver to be enlarged and blue-black, is uncertain.

Hypoxia-induced vasoconstriction in **high altitude disease of cattle** produces **pre-capillary pulmonary hypertension**, with medial hypertrophy of pulmonary arteries and arterioles, and right-sided heart failure with right ventricular hypertrophy, ventral oedema and ascites.

Venous stasis in the hind limbs of "downer cows" can lead to thrombosis and venous infarction with necrosis of medial thigh muscles.

Thrombosis of the caudal vena cava caused by localised phlebitis associated with hepatic abscessation, can produce pulmonary thromboembolism and arteritis, pulmonary abscessation (organisms isolated include *Fusobacterium necrophorum* and *A pyogenes*) and fatal pulmonary haemorrhage. Massive septic embolism can follow erosion of the posterior vena cava by an hepatic abscess.

Omphalophlebitis in newborn calves can produce disseminated bacterial infection and hepatic thrombophlebitis.

Arterial medial calcification is a sporadic finding in aged and often debilitated cattle and sheep. Overseas, it occurs, with mineralisation of other tissues, in cattle grazing plants containing 1,25 dihydroxycholecalciferol or a related compound.

Granulomatous serosal lymphangitis in **Johnes disease** of ruminants may be severe enough to produce a characteristic gross **"cording" of lymphatics** in the serosa of the intestines and mesentery.

Coagulopathy and Thrombocytopathy

Haemorrhagic diathesis is the hallmark of:

- Coagulation system defects.
- Reduced platelet numbers or function.

Most cases of haemorrhagic diathesis in sheep are associated with hepatic injury. In **blue-green algal toxicosis** caused by *Microcystis aeruginosa*, blood clots slowly and poorly in the opened carcass. As well as hepatic liver damage, there is generalised petechial and ecchymotic haemorrhage (involving subcutaneous tissue, skeletal muscle fascia, serosal surfaces and particularly the intestinal mucosa) within 24 hours of algal consumption.

Accidental **warfarin** consumption or ingestion of **dicoumarol** (dicoumarin or dihydroxycoumarin) in mouldy sweet clover hay causes haemorrhages, including large subcutaneous haematomas most commonly in cattle, and less so in sheep. *Wikstroemia indica* (tiebush) contains diydroxycoumarin compounds and causes diarrhoea and possible dysentery in cattle and deer; widespread haemorrhages are present in deer at necropsy.

Factor VIII deficiency has been reported in horned Hereford cattle; 5% of male calves died within a day of marking in affected herds.

Pancytopaenic disease in cattle following ingestion of bracken (*Pteridium* spp) and rock fern (*Cheilanthes seiberi*) causes generalised haemorrhages ranging from petechiae to large extravasations of blood (due to thrombocytopaenia). Red or yellow bacterial infarcts can occur in liver, heart and kidney, and, in calves, in the oral mucosa. The bone marrow is pink and soft.

In **disseminated intravascular coagulation**, the activation of the coagulation system to produce generalised microthrombosis within arterioles and capillaries can sufficiently deplete coagulation factors to cause a haemorrhagic diathesis (consumptive coagulopathy). The microthrombotic obstruction of arterioles and capillaries is thought to contribute to the lesion of bilateral haemorrhagic renal cortical necrosis in septicaemic or endotoxaemic post partum cows, and to lesions of haemorrhagic adrenal necrosis, microangiopathic haemolytic anaemia and gangrene of the extremities in septicaemic calves. *Unfortunately, microthrombi are not readily seen at microscopic examination as fibrinolysis continues after death and most thrombi can be lysed within three hours of death.*

Pulmonary Oedema

Oedematous lungs are wet, heavy and do not collapse. However, sections placed in formalin solutions will float. The lungs are frequently congested. The interlobular septa are distended with fluid, which may be clear, or pink from haemorrhage. Fluid oozes from the cut lung surface and the airways may contain foam. Fluid accumulates in the interstitium and lymphatics of the compliant hilar areas of the lung before alveoli are flooded. ***Hydrothorax*** *can accompany pulmonary oedema.*

High-protein pulmonary oedema (permeability oedema with **exudate**) results from:

- **Increased vascular permeability** caused by damage to alveolar capillary endothelium or alveolar type 1 epithelial cells. Causes include bacteria (in peracute pneumonias), pneumotropic viruses, clostridial exotoxins, ingested or inhaled toxins such as 3-methyl indol (produced in the rumen from L-tryptophan in pasture to cause so-called atypical interstitial pneumonia), endotoxic shock, disseminated intravascular coagulation, and anaphylaxis.

Low-protein pulmonary oedema (haemodynamic oedema with **transudate**) results from:

- **Decreased capillary osmotic pressure** due to **hypoproteinaemia** (eg illthrift and undernutrition, severe anaemia, and protein-losing enteropathy or nephropathy).
- **Increased pulmonary capillary hydrostatic pressure** in **left-sided heart failure** (cardiogenic oedema) and systemic vasoconstriction following acute brain damage (neurogenic oedema).
- **Obstruction of lymphatic drainage** (usually by neoplastic invasion of pulmonary lymphatic vessels).

Hydrothorax

Hydrothorax is the accumulation of clear, colourless to light yellow, watery fluid in the thoracic cavity. Causes are the same as those involved in oedema of the pericardium and lungs and include:

- **Increased vascular permeability** (eg clostridial toxaemias),
- **Decreased capillary osmotic pressure** due to **hypoproteinaemia** (eg illthrift and undernutrition, severe anaemia, and protein-losing enteropathy or nephropathy).
- **Increased hydrostatic pressure** in **right-sided heart failure** (including **cor pulmonale** associated with pulmonary hypertension, as in pre-capillary pulmonary hypertension in bovine brisket disease and post-capillary pulmonary hypertension in St George disease, and left-sided congestive heart failure).
- **Obstruction of lymphatic drainage** (eg by thoracic granulomatous lesions or neoplasms including mesothelioma and lymphoma).

In chronic hydrothorax there is fibrosis and reactive hyperplasia of the pleura.

HAEMOPOIETIC SYSTEM

The haemopoietic system comprises **blood** and **blood-forming tissues**, and **lymphoreticular tissues and organs**.

It includes **bone marrow**, **spleen**, **haemolymph nodes**, **thymus**, **lymph nodes**, and **mucosa-associated lymphoid tissue (MALT)**, the last including large discrete lymphoid aggregations forming the **tonsils** and intestinal **Peyer's patches**.

This presentation focuses on the gross lesions of **diseases of blood**, and particularly those affecting red blood cells.

*See **Chapter 3. Lymphoreticular System**, for information on the immunological arm of the haemopoietic system.*

BLOOD

Introduction

Changes in the cellular and plasma components of blood are best assessed by examining a peripheral blood sample from the live animal. It is useful to routinely collect an EDTA, lithium heparin and clotted blood sample when a live animal is presented for necropsy.

Signs of blood disorder include:

- anaemia
- generalised oedema (hypoproteinaemia).
- haemorrhagic diathesis
- splenomegaly
- haemoglobinuria / icterus

At necropsy, if a haemopoietic disorder is suspected, make impression smears from haemopoietic marrow (femur) for Wright / Giemsa staining. Air-dry and pack these smears **before** you open containers of formalin solution. Then collect and formalin-fix marrow samples for histological examination.

For suspected bovine babesiosis, make impression smears of kidney, brain, liver and heart. Brain smears from the cerebral cortex of animals dying of *B. bovis* infection commonly have capillaries choked with sludged erythrocytes, many of which are parasitised. This phenomenon does not occur in *B. bigemina* infection.

Anaemia

The carcass is pale and the blood watery. The heart is pale and flabby, and there may be pulmonary oedema, hydrothorax and hydropericardium. In severe anaemias there may be a fine, reticulated mottling of the liver due to periacinar degeneration.

The spleen is small in haemorrhagic anaemias, and enlarged in haemolytic anaemias.

Haemorrhagic anaemia

In **acute haemorrhagic anaemias**, the site of extensive haemorrhage sufficient to cause anaemia with acute circulatory failure is usually obvious, whether blood loss is internal or external.

Parasitic causes in cattle and sheep include internal parasites (including *Fasciola hepatica*, *Haemonchus* spp, hookworms and coccidia) and massive infestations by external parasites (ticks, sucking lice).

Other causes in cattle include pulmonary haemorrhage following pulmonary thromboembolism from the posterior vena cava, abomasal haemorrhage (sometimes associated with a bovine leucosis lesion), bladder haemorrhage in enzootic haematuria, renal haemorrhage in pyelonephritis, ruptured middle uterine artery from uterine prolapse, castration of calves with Factor VIII deficiency, cardiac tamponade from coronary artery or cardiac ventricle rupture (traumatic pericarditis), haemorrhagic diathesis in mouldy sweet clover toxicosis, and gastrointestinal and generalised haemorrhage due to bracken (*Pteridium* spp) toxicosis.

In **chronic haemorrhagic anaemias**, with blood loss from the body, **there is also oedema due to hypoproteinaemia**. Causes are those of chronic haemorrhage into the gastrointestinal tract (abomasal ulceration, internal parasites (including, *F. hepatica, Haemonchus* spp, hookworms, *Oesophagostomum radiatum* in calves, and coccidia), into the urinary tract (enzootic haematuria, pyelonephritis), or through the skin (bloodsucking external parasites: ticks and sucking lice).

Haemolytic anaemia

Haemolytic anaemias are characterised by:

- **Icterus**, which may obscure (and also be accentuated by) the pallor of the anaemic carcass.
- **Splenomegaly**.
- **Haemoglobinuria**, when haemolysis is **acute** and **intravascular** (eg in bovine babesiosis and *L. pomona* infections). The kidneys are brown to black.

  *Haemoblobinuria does **not** occur in diseases where haemolysis is **extravascular** (eg bovine anaplasmosis and ovine eperythrozoonosis).*

Causes of haemolytic anaemia include babesiosis, anaplasmosis and theileriosis (particularly in splenectomised cattle), eperythrozoonosis, bacillary haemoglobinuria, leptospirosis (*L. pomona*, not *L. hardjo*), postparturient haemoglobinuria, poisoning by *Brassica* spp. (eg canola, kale, chou moellier), onions and copper, ingestion of cold water, and isoerythrolysis in calves (where dams vaccinated against babesiosis / anaplasmosis). ***Heinz body formation*** *in erythrocytes, due to denaturation of haemoglobin, is a feature of haemolyic anaemias caused by Brassica spp and onions, and is involved to some degree in postparturient haemoglobinuria in cattle and chronic copper toxicosis in sheep.*

Chronic copper toxicosis is the most common cause of haemolytic anaemia in sheep in certain parts of Australia. It is associated with accumulation of copper in livers damaged by pyrrolizidine alkaloids in plants, and release of stored copper to produce the acute haemolytic episode in which up to 60% of circulating erythrocytes may be lysed. There is sufficient haemoglobin in the urinary system to produce brown to black kidneys and gross haemoglobinuria. The liver is swollen and yellow, and the spleen is enlarged and soft.

Calves accumulate excessive levels of liver copper if their diets (eg milk replacer) contains in excess of 30 mg copper per kg DM. Haemolytic episodes occur in these calves, but these may be overshadowed by a clinical syndrome of hepatic failure with marked icterus resulting from **progressive hepatic fibrosis** associated with the copper accumulation.

Eperythrozoon ovis is the usual cause of infectious haemolytic anaemia in sheep in Australia. It is widespread and can cause severe anaemia in lambs and weaners but not in adult sheep. There is barely discernible, mild icterus but **no** haemoglobinuria. Fatal cases have flabby hearts, excessive pericardial fluid, brown liver and kidneys, and an enlarged soft spleen with white pulp hyperplasia.

Congenital erythropoietic porphyria in Holstein and Shorthorn cattle causes a mild to moderate haemolytic anaemia associated with the more dramatic signs of photosensitization and **porphyrin pigmentation of teeth**, **bones** and **urine**, all of which fluoresce red under UV light. ***Erythropoietic protoporphyria*** *in Limousin and Limousin-cross cattle causes only photosensitization (without anaemia or discolouration of teeth and bones).*

Haemolytic anaemia of Murray Grey calves is a chronic progressive, fatal, genetic, presumed autosomal recessive disorder. Signs are first detected between two weeks and two months of age and include retarded growth, poor exercise tolerance, progressive weakness, marked icterus and death. There is a **regenerative anaemia**. At necropsy there is anaemia, icterus and splenomegaly, the heart may be flaccid and globose (due to anaemia), the liver has a very enlarged dark-green right (dorsal) lobe and often an atrophic tan fibrotic left (ventral) lobe, the kidneys are enlarged and dark green-brown, urine is brown, and bone marrow is red and gelatinous.

Anaemia of defective haemoglobin formation

The depression anaemias of chronic disease (eg. neoplastic, inflammatory and uraemic) are listed in this category, as iron may be rate limiting for erythropoiesis in these disorders. Iron deficiency probably causes the usually subclinical anaemia of calves on solely milk diets.

In the absence of parasitism, anaemia without icterus in adult sheep is most likely of nutritional origin; frank malnutrition will produce anaemia probably due to deficiency of protein or iron.

Copper and cobalt deficiencies are inconsistently associated with anaemia in ruminants

Anaemia of deficient cell production

In bracken toxicosis in cattle, **pancytopaenia** results in a peripheral neutropaenia, haemorrhagic anaemia (from gastrointestinal and generalised haemorrhage due to thrombocytopaenia) that is **non-regenerative** (due to bone marrow depression of erythropoiesis). Rock fern and trichlorethylene extracted soya bean meal cause similar disease syndromes. In St George disease (*Pimelea* spp. toxicosis) in cattle there is a severe **non-regenerative, haemodilutional anaemia** caused by progressive expansion of plasma volume.

Toxic Anoxias (Nitrate and Cyanide Toxicoses)

Nitrate toxicosis results when the normal conversion of nitrate via nitrite to ammonia by ruminal microorganisms is inadequate and **nitrite** is absorbed and causes methaemoglobinaemia (nitrite oxidises the ferrous iron of haemoglobin to ferric iron to form methaemoglobin, which is incapable of transporting oxygen). Plants containing >1.5% DM nitrate are potentially toxic. Cattle are more susceptible than sheep. The blood is dark with a brownish colour ("chocolate") and clots poorly. There is cyanosis of mucous membranes and light brown discolouration of tissues. There are petechial or ecchymotic serosal haemorrhages, and the pericardial sac contains an excess of blood-stained fluid.

Cyanide (hydrocyanic or prussic acid) toxicosis results when cyanogenic glycosides in ingested plants are metabolised by ruminal microorganisms to release hydrocyanic acid. The cyanide ion produces a cellular hypoxia (cytotoxic anoxia) by forming a stable complex with cytochrome oxidase which can then not function in electron transport (oxyhaemoglobin is unable to release oxygen for electron transport). Death is rapid, with signs of anoxia. The blood is bright red and often clots slowly or not at all. The mucous membranes are pink and appear well oxygenated. There may be an odour of bitter almonds in fresh rumen contents.

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Appendix 1. Dissection and Gross Examination of the Heart

General
A systematic examination of the heart (including **pericardium, endocardium (mural and valvular), myocardium** and **large vessels**) is an essential part of any necropsy. Always follow the same procedure to optimise detection of **gross lesions** as well as **changes in size, shape** and **position** of the heart, its components and associated thoracic structures.
• **Weigh the animal at the start of the necropsy.** *The following relates to the examination of the heart.*
• Examine heart and lungs *in situ* for changes in size, shape or position. eg ectopia cordis (cervical, sternal, or abdominal).
• Examine pericardium (normally smooth, shining and transparent). Open pericardial sac. Note amount and type of fluid.
• Remove heart and lungs from thoracic cavity with trachea, oesophagus and tongue attached.
• Examine trachea and lungs.
• Do **not** separate heart from lungs unless there are special reasons for doing so. If separation is required, **examine large vessels at base of heart before cutting them 1 to 3 cm from their cardiac origin.**
• Examine epicardial surface of heart and large vessels at base of heart.
• **Dissect and examine the heart (Inflow-Outflow Method)**: The attached diagrams illustrate opening of heart chambers by four incisions, **Incisions A** and **B** on the right side and **Incisions C** and **D** on the left. Blood flow is followed from right atrium (RA) to right ventricle (RV) to pulmonary artery and lungs. Then from left atrium (LA) to left ventricle (LV) and aorta.

Heart Measurements at Necropsy
Circumference of atrioventricular valve rings • After opening and completing the examination of the heart by the Inflow-Outflow Method, use a flexible ruler or string to measure the circumference of the opened atrioventricular valve rings. *The circumference of the left atrioventricular ring (LAVR) is compared with that of the right (RAVR) and expressed as a ratio (LAVR / RAVR). Deviation from the normal ratio of 0.8 to 0.9 indicates AV ring dilation.*
Weights of heart components • Dissect the heart free of extraneous tissue attached to its base, and weigh it (HW). • Separate the right ventricular free wall (RV) from the right atrium at the right coronary groove (it has already been separated from the interventricular septum during Inflow-Outflow Method dissection), and weigh it. • Dissect the rest of the combined atria (A) from the remaining ventricular mass at the left coronary groove. Weigh the combined left ventricle plus interventricular septum (LV + S). Weigh the combined atria (A). *The total heart weight, right ventricular free wall weight, and combined left ventricle plus septum weight are then compared with total body weight of the animal and expressed as a ratio.* *The right ventricular free wall weight and combined left ventricle plus septum weight are compared with total heart weight and expressed as a ratio.* *The combined left ventricle plus septum weight is compared with right ventricular free wall weight and expressed as a ratio.*
Thickness of interventricular septum and ventricular free walls Avoiding *trabeculae carneae*, papillary muscles and supraventricular crest, measure thickness of: • Interventricular septum at its thickest point, one third to half way from aortic valve to apex of left ventricle. • Left ventricular free wall between the papillary muscles. • Right ventricular free wall near the ring of the right AV (tricuspid) valve.

Body Weight, Heart Weight and AV Ring Ratios Assessed at Necropsy
(Indicative values for young cattle)

BW (kg) HW (g) A (g)	HW / BW (g / kg)	RV / BW (g / kg)	LV+S / BW (g / kg)	RV / HW (g / g)	LV+S /HW (g / g)	LV +S / RV (g / g)	LAVR / RAVR
	5 - 12	1.0 – 3.0	4.0 - 7.0	0.18 - 0.25	0.55 - 0.75	2.20 – 4.20	0.8 - 0.9

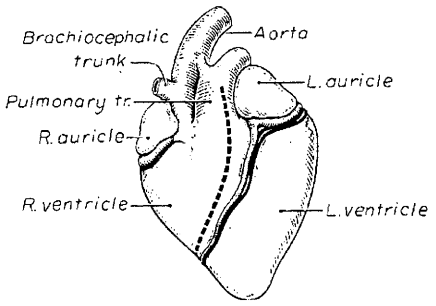
A = atria (combined); BW = body weight; HW = total heart weight; LV + S = left ventricle plus septum; RV = right ventricular free wall; LAVR = left atrioventricular ring circumference; RAVR = left atrioventricular ring circumference.

Appendix 1. Dissection and Gross Examination of the Heart (continued)

Dissection of Heart *(See attached diagrams)*	**Heart Structures Examined** *Congenital abnormalities detected.*
"Starting position": Hold the heart in the left hand with the right side of the heart on the left and the left side on the right, with the apex pointing towards you. The left longitudinal sulcus is uppermost. For orientation, return the heart in this "starting position" before making each of the following four incisions.	• *Transposition of large vessels (often associated with other cardiac anomalies, eg ventricular septal defect).*
Incision A: Cranial border of right ventricle (RV) dorsoventrally from pulmonary trunk to apex of RV, along interventricular septum parallel to left longitudinal sulcus (with knife or scissors).	• Semilunar valves of pulmonary trunk. • *Patent ductus arteriosus* • *Ventricular septal defect*
Incision B: Caudal border of right ventricle (RV) ventrodorsally from apex of RV along interventricular septum to right atrium (RA) and last part of the caudal vena cava (with knife or scissors). ***Atrial Incision B (optional): Right atrium (RA), 1 cm above and parallel to coronary groove*** *from caudal vena cava forward into right auricle (with scissors). Avoid the cranial vena cava to preserve for histological examination the sinoatrial node, which lies along the junction (sulcus terminalis) between the cranial vena cava and right atrium.*	• Remove blood clots from lumen; distinguish between postmortem clots and antemortem thrombi. • Right atrioventricular (tricuspid) valve. • Openings of cranial vena cava and caudal vena cava. • Fossa ovalis (foramen ovale in neonates may be probe-patent but functionally closed). • Coronary sinus. • *Patent foramen ovale.*
Atrial Incision C (optional): Left atrium (LA), 1 cm above and parallel to coronary groove *from pulmonary vein opening forward to left auricle (with scissors).* **Incision C: Centre of left atrium (LA) and left ventricle (LV)**, dorsoventrally through parietal cusp of left atrioventricular valve, between cranial and caudal papillary muscles in the left ventricular free wall (with knife).	• Left atrioventricular (mitral) valve. • Openings of pulmonary veins. • Foramen ovale remnant. • *Congenital haematomas of A/V valve margin; common in neonates, but do not persist.*
Continue with heart held as for Incision C. **Incision D: Under centre of septal cusp of left atrioventricular valve**, ventrodorsally through septal cusp, left atrium and along aortic trunk (with knife or scissors).	• Semilunar valves of aortic trunk. • Openings of right and left coronary arteries. • Opening of brachiocephalic trunk. • Measure circumference of right atrioventricular ring (RAVR) and left atrioventricular (LAVR). *Normal LAVR / RAVR = 0.8.-.0.9).* • *Subaortic stenosis, aortic hypoplasia.*

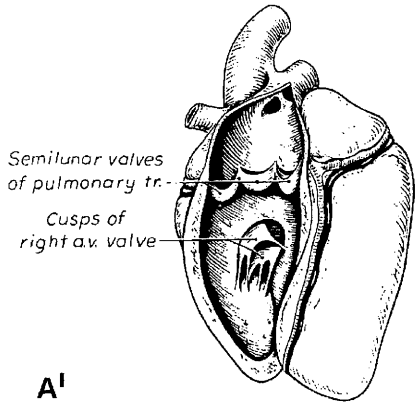
Incision variations *(See Appendix 2)*	
Incision C (v): Caudal border of left ventricle (LV) dorsoventally from last part of the pulmonary vein and left atrium (LA) to apex of LV along interventricular septum (with knife or scissors).	• As for **Incision C** above.
Incision D (v): Cranial border of right ventricle (RV) ventrodorsally from apex of LV, along interventricular septum, parallel to left longitudinal sulcus, **under** septal cusp of left atrioventricular valve **and along aortic trunk** (with knife or scissors).	• As for **Incision D** above.

Appendix 1. Dissection and Gross Examination of the Heart (continued)



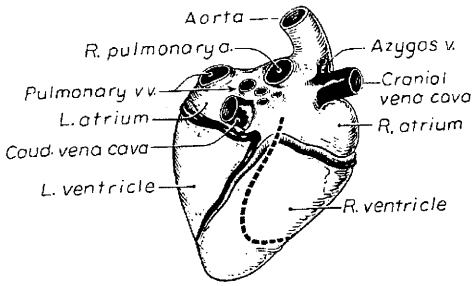
A

To open right ventricle, hold heart in left hand with left side of heart towards you. Make incision, starting at pulmonary trunk, into right ventricle, close to interventricular septum.



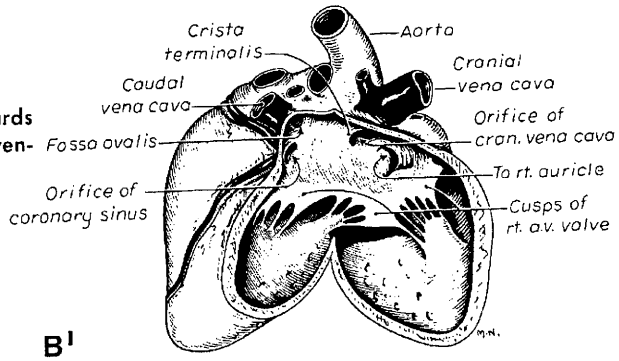
A'

Open pulmonary trunk past bifurcation. Check semilunar valves.



B

Turn heart over with its right side towards you. Continue incision, following interventricular septum, into right atrium.

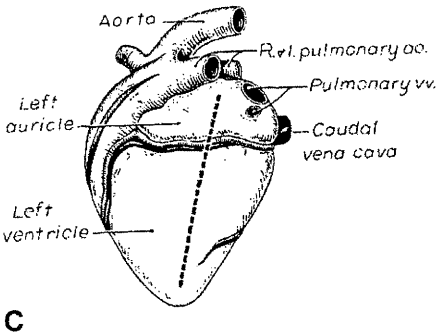


B'

Open right ventricle and atrium.
Check right atrioventricular valve, orifices of cranial vena cava, caudal vena cava, fossa ovalis and coronary sinus.

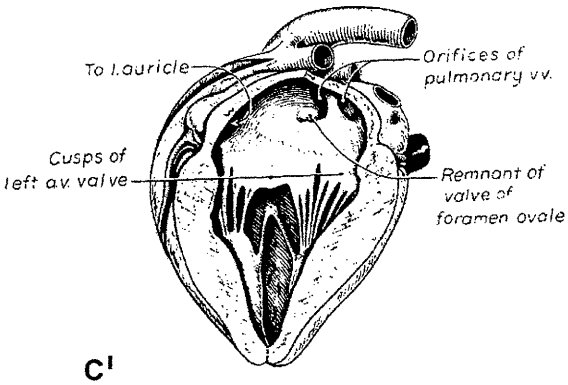
Diagrams are reprinted from King JM, Dodd DC, Newson ME. *Gross Necropsy Technique for Animals* 1979: pages 9-10, with permission from JM King.

Appendix 1. Dissection and Gross Examination of the Heart (continued)



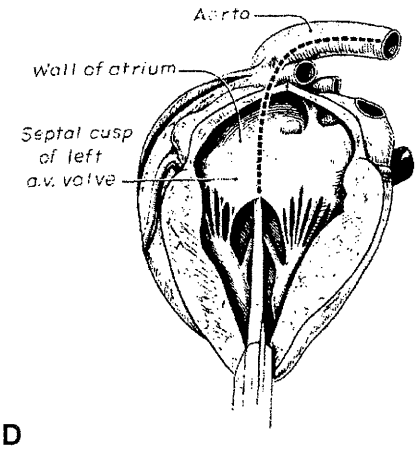
C

Open left atrium and ventricle with straight incision.
Incise through parietal cusp of left atrioventricular valve.



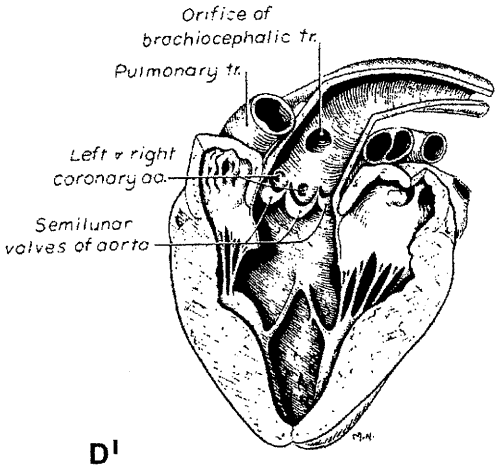
C'

Check left atrioventricular valve and openings to pulmonary veins.



D

To open aorta, insert knife under septal cusp of left atrioventricular valve.
Incise through wall of atrium, out and down aorta.



D'

Check semilunar valves of aorta, orifices of right and left coronary arteries, orifice of brachiocephalic trunk.
Make multiple inspection slices through organ.

Open abdominal aorta and its major branches (mesenterics, iliacs, etc.).

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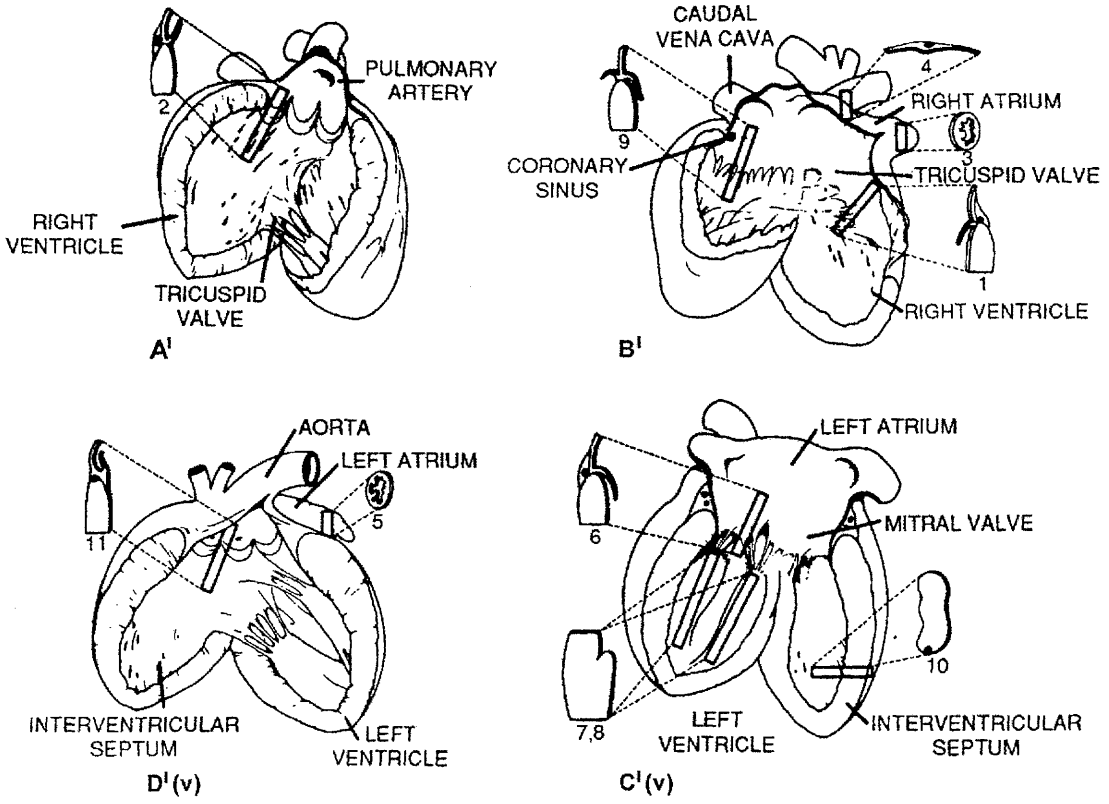
Appendix 2. Standard Sites for Histological Examination of the Heart



A¹	Right ventricle and pulmonary outflow tract.	**B¹**	Right ventricle and right atrium.
D¹(v)	Left ventricle and aortic outflow tract.	**C¹(v)**	Left ventricle and left atrium.

Standard sites for histological examination of heart	
1*	Right ventricular free wall, parietal cusp of right atrioventricular (tricuspid) valve and right atrium.
2*	Right ventricular outflow tract, including pulmonic semilunar valve and pulmonary artery.
3	Right auricular appendage.
4*	Right atrium and cranial vena cava at sulcus terminalis to include sinoatrial node.
5	Left auricular appendage.
6*	Left ventricular free wall, parietal cusp of left atrioventricular (mitral) valve and left atrium.
7	Cranial papillary muscle of left ventricular free wall.
8	Caudal papillary muscle of left ventricular free wall.
9*	Interventricular septum base (including atrioventricular node), septal cusps of left and right atrioventricular valves, and interatrial septum.
10	Interventricular septum near apex of left ventricle, including terminal branches of left coronary artery.
11	Left ventricular outflow tract, including aortic semilunar valve and aorta.
***Sites sampled for modified histological study of myocardium.**	

Diagrams are reprinted from *Textbook of Canine and Feline Cardiology. Principles and Clinical Practice.* 2nd edn. (Fox PR, Sisson D, Moisse NS, editors), Bishop SP. *Necropsy techniques for the heart and great vessels.* page 846, Copyright 1999, with permission from Elsevier Science.