

# Sudden and unexpected death in small animal patients: Part 1

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## INTRODUCTION

Veterinary surgeons are sometimes asked to examine animals that have been found dead without premonitory signs. When death occurs in this manner and without explanation, the term 'sudden unexpected (unexplained) death' (SUD) is used. This does not necessarily imply that death was instantaneous, but is usually defined as the death of an animal that appears healthy but dies suddenly within a few minutes or several hours due to pre-existing disease or functional disorder.

Although SUD is a common occurrence in farm animals, especially due to the range of bacterial infections that may arise in neonatal animals, by contrast, true cases of SUD in small animals are uncommon. This article, the first in a two-part series on sudden death in small animals, describes some of the more common causes of this problem in cats and dogs.

## CAUSES OF SUDDEN UNEXPECTED DEATH

Documentation in the veterinary literature of cases of SUD in small animals is scarce, although two review articles originating from Canada (2000 and 2001) described the causes and incidence of SUD in 79 cats and 151 dogs over a 10-year period (Table 1). Some of the more important conditions leading to SUD in some of these systems will now be discussed.

**TABLE 1: Causes of SUD in small animals**

CAUSE	DOGS	CATS
Heart disease	21.9%	20.3%
Toxicity	16.6%	-
Gastrointestinal disease	13.2%	7.6%
Trauma	12.6%	39.2%
Non-traumatic haemorrhage (E.g. associated with HSA)	6.6%	1.3%
Malnutrition or dehydration	5.3%	-
Respiratory disease	4.0%	6.3%
Urogenital disease	3.3%	5.1%
Central nervous system disease	1.3%	1.3%
Peritonitis	1.3%	-
Pancreatic disease	1.3%	-
Undetermined	12.6%	12.7%
FeLV-related disease	-	3.8%
Hepatic disease	-	1.2%
Sepsis	-	1.2%

SUD can occur due to disease in any physical system, but in reality some causes predominate. In general, causes are categorized as either traumatic or non-traumatic in origin:

### • Traumatic

Trauma is a very common cause of SUD in cats in particular, and is probably most frequently associated with road traffic accidents, although other incidents such as 'high-rise syndrome' (animals falling from a high building), gunshot, physical abuse or fatal bite wounds can produce similar consequences. Such traumatic events produce various types of lesions including bone fracture, internal haemorrhage, diaphragmatic rupture, splenic or hepatic rupture (Fig. 1), abdominal organ displacements, and skin abrasions. Inevitably affected animals tend to be those with outdoor access.



**Fig. 1:** Traumatic hepatic rupture in a cat: One lobe (asterisk) is dark and haemorrhagic and the remainder of the liver is pale due to subsequent blood loss.

### • Non-traumatic causes

The leading non-traumatic cause of SUD in cats and dogs is considered to be cardiovascular disease, although underlying respiratory tract problems are also an extremely important cause.

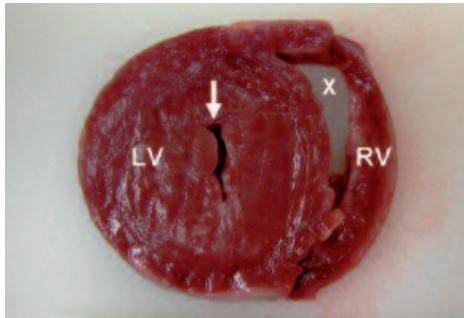
#### Cardiovascular disease

In cardiovascular disease, the cause of SUD usually relates to either organic or functional cardiac disease or peripheral cardiovascular collapse (shock).

**Some conditions may be associated with grossly evident lesions:** The most common types of heart disease involved, the idiopathic **cardiomyopathies** (hypertrophic (HCM) and dilated (DCM) forms in

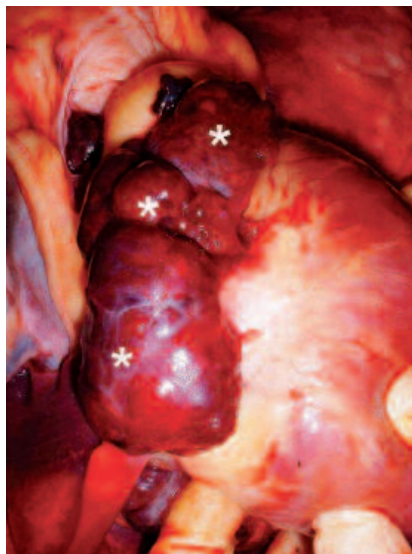


dogs and HCM in cats), are good examples of this. In HCM (Fig. 2), for example, the cause of death is due to pronounced hypertrophy of the myocardium, which impinges on and reduces left ventricle (LV) lumen diameter, interfering with its outflow. Such patients die of acute low output cardiac failure associated with massive reduction of LV output. Affected cats are typically middle aged to older and often male, although inevitably females and younger animals (as young as five months of age) can be affected.



**Fig. 2:** Transverse section of heart from a cat with HCM. There is severe thickening of the left ventricular free wall (LV) with marked stenosis of the left ventricular lumen (arrow). The adjacent right ventricle (RV) and its lumen (X) are unaffected.

Acute cardiac failure can occur as a consequence of cardiac tamponade associated with bleeding from **atrial haemangiosarcoma** (HSA) (Fig. 3). This neoplasm typically arises in the right atrium, presenting as a dark-red haemorrhagic mass that may bleed over short or long periods of time into the pericardial sac. It may also invade through the atrial myocardium. Massive cardiac tamponade develops when the pericardium fills with blood, impairing venous return and acutely reducing cardiac output. Consequently the patient dies apparently suddenly, although inevitably the lesion will have been present for some time. Affected animals are typically middle aged to older (>6 years old) dogs (rare in the cat).



**Fig. 3:** Right atrial haemangiosarcoma in a dog: the entire right atrium (asterisks) is expanded by this vascular neoplasm.

**Stenosis of the great vessels** (including the pulmonary valve, aortic arch and subaortic area) (often in young dogs, 2 months to 2 years) represents another cardiac cause of SUD and is often considered to be congenital. Obstruction of the left ventricular outflow tract (LVOT) due to subaortic stenosis is the most common congenital heart defect in large breed dogs. LVOT obstruction results in a ventricular pressure overload which requires higher systolic pressure to maintain stroke volume. Ventricular hypertrophy results and increases the demand for myocardial blood flow. Aortic pressures are normal but left ventricular luminal pressures increase, such that the coronary driving pressure may be inadequate and sometimes coronary flow reverses direction in systole. Papillary muscles and subendocardial regions are most commonly affected by the myocardial ischaemia predisposing the myocardium to ventricular arrhythmias and syncope.

In regions where it is prevalent, **heartworm disease** is a cardiac cause of SUD. Although it occurs in both cats and dogs, the disease in cats is more severe. Death usually relates to obstruction of pulmonary arterial vessels due to endothelial villous proliferations that arise due to the presence of the parasites, emboli caused by live or dead parasites or even microfilariae, secondary thrombosis due to endothelial damage and parasite tissue. Embolisation even associated with a single worm can be fatal. It is curious that heartworm disease (and cardiomyopathy for that matter) can be serious enough to cause death often with almost no warning at all, but this is definitely the case at times.

#### **Other conditions may not produce gross lesions:**

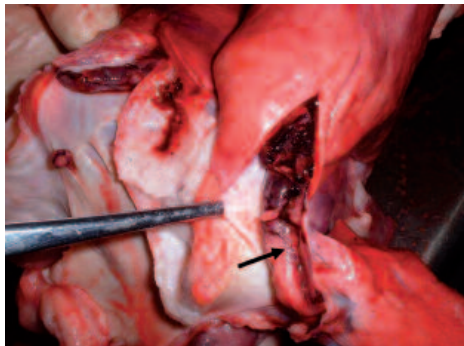
Examples of such cases include cardiac syncope or breed related dysrhythmias. Animals with **cardiac syncope** may die suddenly during sleep without previous clinical signs or evidence of cardiac dysfunction. They show no evidence of struggle in their sleep and typically no other significant findings are seen at post-mortem examination to account for SUD. In these cases, examination of the myocardium, valves and conducting tissue often reveals no evidence of organic disease to explain death, so it is usually speculated that cardiac arrest has occurred due to physiological abnormality of conduction through the myocardium/conduction system. Similar consequences also arise in dogs with clinical signs of cardiac impairment due to **breed-related dysrhythmias** (Doberman Pinschers and Boxers, for instance).

#### **Respiratory disease**

##### **Pulmonary arterial thrombosis (Fig. 4)**

Thromboembolism represents not only an extremely important cause of SUD but is the major cause involving the respiratory system. Inevitably this does not represent a primary respiratory disease *per se* but involves the vasculature. The underlying problem in pulmonary arterial thrombosis arises in the

peripheral pulmonary arterial bed and is related to spontaneous intravascular coagulation in these larger vessels. The latter may occur as a result of imbalance between plasma pro- and anticoagulant factors. Thrombus propagation leads to occlusion of progressively larger vessels and outflow to the lungs is eventually occluded. Such acute low output cardiac failure due to right ventricular outflow occlusion can arise as a consequence of a hypercoagulable state and two common causes of its onset include underlying **chronic glomerular diseases** (such as amyloidosis) leading to a protein-losing nephropathy and severe **protein losing enteropathy** (PLE) (associated usually with lymphangiectasia, small intestinal lymphoma or 'inflammatory bowel disease'). In both conditions there is increased plasma protein loss, including anticoagulation proteins, the most important of which is the loss of antithrombin III, one of the major components accounting for anticoagulant activity in the blood. Other conditions also associated with pulmonary arterial thrombosis include endocrinopathies (such as hyperadrenocorticism), sepsis or severe inflammatory diseases (such as acute pancreatitis), cardiac disease, immune-mediated haemolytic anaemia, neoplasia and heartworm disease.



**Fig. 4:** Lung from a dog: one of the pulmonary arteries has been dissected open to demonstrate a thrombus within its lumen (arrow).

Other respiratory conditions that can feasibly cause SUD include large **inflammatory or neoplastic lesions**. These can result in SUD due to massive haemoptysis associated with haemorrhage of the lesions. Additionally, asphyxiation due to upper respiratory tract (pharyngeal or tracheal) foreign bodies for example may cause SUD.

**Problems arising in other body systems are less common causes of SUD, but examples include:**

#### **Gastrointestinal system**

Although less commonly causative than cardiac or respiratory disease, some gastrointestinal tract disorders are well-known causes of SUD.

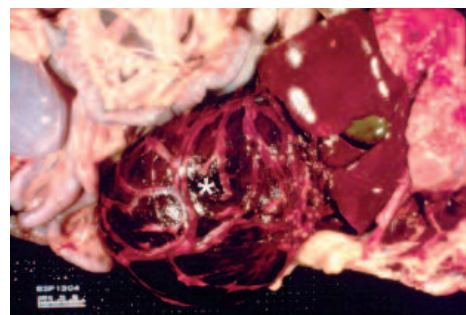
Such problems may have an underlying **vascular or mechanical** origin. Vascular problems may arise due to severe bleeding from a gastric or intestinal ulcer or

other haemorrhagic lesion for example, although conditions that initially begin as mechanical problems (such as displacements/obstructions (torsion, foreign body, strangulation, intussusception (Fig. 5)) may ultimately progress to become vascular problems, with SUD possible due to a variety of mechanisms. Conditions that may lead to SUD due to a final common pathway of peripheral circulatory collapse include gastric dilatation and volvulus syndrome (GDV) and the entity known as haemorrhagic gastroenteritis (HGE).



**Fig. 5:** Intestinal tract from a dog: an intussuscepted portion of bowel is seen (asterisks). The white asterisk marks the compromised intussusceptum, which is telescoping into the adjacent region, the intussusciens (black asterisk).

**GDV** (Fig. 6): This potentially catastrophic condition is not uncommonly responsible for SUD in predominantly deep chested or large/giant breed dogs. Although the underlying pathogenesis of this condition is not completely understood, it is considered to be multifactorial. The final common pathway of gastric dilatation involves increased intragastric pressure, which eventually results in decreased blood flow to the stomach wall, leading to necrosis. Gastric distension eventually increases such that occlusion of the caudal vena cava and portal vein occurs, resulting in decreased venous return from the abdomen to the heart. This leads to decreased cardiac output, myocardial hypoxia, hypovolaemic shock, and hypotension. The cardiac problems may lead to arrhythmias and hypotension, and decreased portal blood flow can result in an increased rate of endotoxin release by gram-negative



**Fig. 6:** Gastric dilatation and volvulus in a dog: the stomach (asterisk) is markedly distended and covered by omentum. Its red-black discoloration denotes devitalisation due to vascular compromise subsequent to associated volvulus.



bacteria, both of which enter the circulation. Simultaneously, portal vein occlusion reduces the ability of the reticuloendothelial system to handle such toxins and bacteria. SUD is therefore mostly a consequence of peripheral circulatory collapse and endotoxaemia.

**HGE** can develop very quickly, causing death within a few hours. The name of this condition is somewhat of a misnomer as it is not a true enteritis, but rather is associated with massive acute haemorrhage into the gastrointestinal tract lumen, most likely as a consequence of gram-negative endotoxic shock. Various bacteria can also cause haemorrhagic cases of gastroenteritis, including agents such as *Clostridium perfringens* where associated enterotoxaemia can cause SUD as a result of systemic effects of several bacterial toxins.

Another example is the **impacted foreign body**, which may erode through the gastrointestinal wall resulting in peritonitis, sepsis and /or lethal haemorrhage if an adjacent major arterial branch is perforated.

Although less likely, **canine parvovirus** or **feline panleucopaenia virus** infection in young animals in some instances can cause severe enough intestinal disease to cause death without premonitory signs. SUD associated with parvovirus infection, however, if it occurs, is probably more likely to result from myocarditis that can sometimes develop in infected pups.

#### **Nervous system**

Occasionally disease in the central nervous systems is responsible for causing SUD in pets. **Cerebrovascular accidents (strokes)** are being increasingly recognised in dogs and involve sudden onset of non-progressive, focal signs of brain dysfunction due to ischaemia and infarction or haemorrhage. This interruption of arterial blood flow to the affected area of the brain is associated with a thrombus or thromboembolus. Such cerebrovascular diseases can alter cardiovascular and autonomic function, and stroke can produce changes in autonomic function, leading to cardiac arrhythmia and myocardial damage, which in turn can result in SUD.

#### **Urogenital system**

The urogenital tract is an infrequent location of diseases likely to cause sudden death. Gestational complications in pregnant females, such as uterine rupture or torsion, may cause SUD, however, as may pyometra (Fig. 7) in unspayed bitches. Although obstructions in the urinary tract could lead to SUD, usually such cases are associated with premonitory clinical signs.



**Fig. 7:** Cystic endometrial hyperplasia and pyometra in a bitch. The uterus has been dissected open to show the cystically thickened wall and lumen filled with purulent fluid.

#### **Miscellaneous causes**

A relatively under recognised cause of SUD particularly in dogs is **Addison's disease**. Acute hypoadrenocorticism involves diffuse adrenal cortical atrophy with reduced output of adrenocorticosteroids. This condition usually presents as a well-defined clinical condition that can be easily diagnosed due to the combination of history, clinical signs and biochemical abnormalities. Sometimes, however, the process of atrophy may be chronic and well tolerated and thus go unrecognised initially until some form of stress (psychological stress such as boarding, or physiological stress such as general anaesthesia) is encountered. At this time their output of mineralocorticoid and glucocorticoids is inadequate and they die acutely from hypotensive shock. Adrenocortical failure results partly from low mineralocorticoid output due to atrophy, leading to increased urinary sodium and water loss and total body sodium, which is reflected in low plasma sodium. There is also marked elevation of plasma potassium, altering the sodium: potassium ratio such that the animal becomes hyperkalaemic. If the hyperkalaemia is severe enough, myocardial conduction disturbances (severe bradycardia) can result in SUD. A contributing factor to death in these patients is hypotension due to reduced blood volume as a result of low sodium and water levels. At post-mortem examination, adrenocortical atrophy should be recognised both grossly and microscopically.

Occasionally pets die suddenly during kennel or cattery visits. Although underlying organic disease is frequently discovered, the possibility of non-medical causes should not be overlooked.

**Electrocution**, for instance, should be considered in such instances. Although this may arise from unsafe heating systems, direct contact with a wire is not necessarily required as electric current can travel some distance along a solid, wet kennel floor from a compromised circuit.

**Intoxications:** More usually there are some clinical signs associated with intoxications, but these cases can certainly lead to unexpected illness and death in pets, often causing owners to suspect foul play. Some of the more common causes of intoxication in

small animals that may lead to unexpected death include:

- **Anticoagulant rodenticides:** Pets may be poisoned either directly from baits or indirectly by consumption of poisoned rodents. Although the 'first-generation' anticoagulants (such as warfarin) require multiple feedings to result in toxicity, 'second-generation' anticoagulants (brodifacoum and bromadiolone) are highly toxic to dogs and cats after only a single feeding.

These anticoagulants antagonise vitamin K, thereby interfering with hepatic synthesis of coagulation proteins that depend on this cofactor (factors I, II, VII, IX, and X). Inactivity of these factors leads to a coagulation defect. More usually animals become depressed and anorectic initially and subsequent clinical signs reflect some manifestation of haemorrhage (such as anaemia, haematoma formation, melaena, haemothorax, epistaxis, haemoptysis, haematuria) but owners will occasionally find their pet suddenly or unexpectedly dead as a consequence of haemorrhage.

- **Ethylene glycol (EG):** Dogs and cats are highly susceptible to this agent and most episodes of poisoning are associated with radiator antifreeze (95% ethylene glycol) ingestion which is widely available, sweet tasting and has a small minimum lethal dose.

EG is rapidly absorbed from the gastrointestinal tract and although half of what is ingested is excreted unchanged by the kidneys, the remainder is metabolised by the liver and kidneys, forming oxalate and other toxic metabolites that produce severe metabolic acidosis. Oxalate is also cytotoxic to the renal tubular epithelium causing acute tubular necrosis which combined with the metabolic acidosis can lead to relatively sudden death.

- **Non-steroidal anti-inflammatory drugs (NSAIDs):** Aspirin, ibuprofen and acetaminophen (paracetamol) are the most commonly involved. Cats in particular are more sensitive to NSAID toxicosis because they are deficient in glucuronyl transferase, an enzyme integral to metabolism of these drugs. Accidental ingestion of any of these drugs by cats may therefore lead to death within a short period of time due to renal and/or hepatic necrosis.
- **Lily plants:** Although cats are finicky eaters, for some reason they eat the leaves and flowers of lily plants, both of which are toxic to this species. Ingestion of small amounts of this plant can cause death due to acute renal failure, although the mechanism of toxicity still remains somewhat unclear.

Although infrequent causes of SUD in pets, some other intoxications that deserve mention in this article include:

- **Carbon monoxide poisoning:** Acute carbon monoxide (CO) poisoning is rare in pets but can occur. CO is a colourless, odourless and tasteless gas that forms when fuels such as charcoal, wood, gasoline, kerosene and propane fail to burn off completely. Much intoxications occur during the winter due to malfunction of furnaces or gas heaters, as well as car exhausts and the use of gas heaters as a heat source. Aeroplane cargo areas may also accumulate CO, so toxicity should not be overlooked in cases of SUD of pets transported by air. Although death by CO poisoning is usually not sudden, it can certainly be perceived this way by owners who may find their pet unexpectedly dead. People and animals are poisoned when they inhale CO because it replaces oxygen in erythrocyte haemoglobin, producing carboxyhaemoglobin, resulting in impaired oxygen delivery to tissues. Haemoglobin acquires a bright red colour when converted to carboxyhaemoglobin, so CO-poisoned patients are described as having a 'classic' cherry-red appearance to their blood, skin, mucous membranes and viscera even after death. This is not always seen, however, so the diagnosis should not be precluded even if this appearance is not noted.

- **Chocolate poisoning:** Dogs are sensitive to methylxanthines, naturally occurring alkaloids found in numerous plants. Theobromine and caffeine are examples found in cocoa bean derived products such as chocolate. Deaths have been reported in dogs that have ingested less than 100 mg/kg theobromine (1g of theobromine is reported to correspond to about 1 kg of chocolate). The main pharmacological manifestations of methylxanthines, and hence chocolate toxicity in the dog, include central nervous system stimulation, diuresis and cardiovascular dysfunction. Clinical signs therefore usually include restlessness, excitement, ataxia, muscle tremors, seizure, vomiting, diarrhoea and cardiac arrhythmia. Death may occur 6-24 hours post-ingestion and chronic exposure can result in sudden death after several days, likely due to cardiac failure. Analysis of gastric contents and samples of non formalin-fixed liver is recommended to rule out such a diagnosis.

## CONCLUSION

True sudden death is actually a fairly rare event in dogs and cats and although problems in any physical system can be causative, the leading cause is probably cardiovascular disease. Most cases that are perceived by owners as SUD actually turn out to be due to underlying problems that have gone unnoticed for

some time. Regardless, a thorough post-mortem examination is advised when clients present you with such cases, and where possible, involvement of a trained pathologist is strongly advised, especially in cases that are likely to become medico-legal issues.

Inevitably there are times when this may not be feasible, however, and you may be requested to perform a post-mortem examination at your practice. The second article in this series will discuss some of the more important aspects of how best to approach investigation of such cases in practice.

#### FURTHER READING

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*These multiple choice questions are based on the above text. Answers appear on page 99.*

**1. Disease in which body system is most commonly implicated as a cause of sudden death in small animal patients:**

- a. nervous
- b. urogenital
- c. cardiovascular
- d. gastrointestinal

**2. Which condition is most likely to produce lesions that are grossly evident at post-mortem examination:**

- a. third degree atrioventricular block
- b. hypertrophic cardiomyopathy
- c. ventricular dysrhythmia
- d. cardiac syncope

**3. Which gastrointestinal condition would be most likely to cause sudden death in a dog:**

- a. gastric foreign body
- b. parvoviral enteropathy
- c. inflammatory bowel disease
- d. haemorrhagic gastroenteritis