CPD article

Winter poisoning hazards for pets

In this final article on seasonal poisoning risks to pets, winter poisoning hazards are discussed. Some hazards in this season are associated with cold weather such as carbon monoxide poisoning, antifreeze and medicines for the symptomatic relief of colds and flu. Carbon monoxide poisoning in winter is often associated with use of a faulty heating appliance and may be missed as the effects are vague and non-specific but other members of the household may also be unwell. Ethylene glycol antifreeze poisoning results in renal failure and requires prompt antidotal treatment to prevent the formation of metabolites which are responsible for the toxic effects. If a pet has eaten a cold and flu product it is important to obtain information on the name and ingredients as these products contain various analgesics and decongestants that require different management. Christmas foods (chocolate, foods containing dried vine fruits, macadamia nuts) and decorative plants such as holly, poinsettia and mistletoe are also a potential risk to pets at this time of year. These plants usually only cause mild signs despite their poisonous reputation. Macadamia nuts can cause self-limiting signs in dogs and chocolate commonly causes neurological and cardiovascular signs, but severe cases are uncommon. Ingestion of dried vine fruits requires prophylactic treatment to prevent acute kidney injury. https://doi.org/10.12968/coan.2022.0040

Nicola Bates BSc (Brunel) BSc (Open) MSc MA, Senior Information Scientist, Veterinary Poisons Information Service (VPIS), 2nd Floor, Godfree Court, 29-35 Long Lane, London, SE1 4PL. nicola.bates@vpisglobal.com

Key words: decongestant poisoning | Christmas poisoning | antifreeze poisoning | carbon monoxide poisoning

Winter poisoning risks are discussed in the final article on seasonal poisoning in pets. This includes substances associated with cold weather such as antifreeze, carbon monoxide from faulty heating appliances and treatments for winter infections such as colds and flu. In addition, in the northern hemisphere Christmas is a winter festival and associated with some festive foods and decorative plants. Contact a poisons information service for more specific and individual case advice, if required.

Antifreeze

A common antifreeze ingredient is ethylene glycol (also known as ethanediol). It is not toxic itself, but is metabolised to toxic compounds by the action of alcohol dehydrogenase. This enzyme oxidises ethylene glycol to glycoaldehyde that is ultimately metabolised to oxalate which cause renal damage and hypocalcaemia by binding to calcium to form calcium oxalate (crystals of which may be present in urine). Calcium oxalate crystal formation within the renal tubules has been shown to be the cause of the renal effects in ethylene glycol poisoning (de Water et al, 1999). A post-mortem finding of a large amount of calcium oxalate crystals in the kidney is diagnostic for ethylene glycol poisoning (Amoroso et al, 2017). The lethal dose of ethylene glycol in cats is commonly reported as 1.5 ml/kg (Milles, 1946). In another study 1 g/kg was fatal to cats within 48 hours (Gessner et al, 1961). This is equivalent to approximately a teaspoon of undiluted antifreeze in a cat. Dogs can tolerate a higher dose. In experimental studies dogs given ethylene glycol or antifreeze (95% ethylene glycol) at a dose 6 ml/kg and above died (Sanyer et al, 1973; Hewlett et al, 1989).

A poster on the risks of antifreeze poisoning for display in practices is available to download from the International Cat Care website (*Figure 1*).

Clinical signs

Although the progression of clinical signs in ethylene glycol toxicosis can be divided into stages these may overlap and not be clearly defined in many cases, particularly in cats.

In the early stages of ethylene glycol poisoning (from 30 minutes to 12 hours) there are central nervous system (CNS) signs caused by unmetabolised ethylene glycol including ataxia and weakness. Vomiting and tachycardia may occur. These early signs may be easily missed, particularly in an outdoor cat. Polyuria, dehydration, tachypnoea, acidosis and hypothermia may occur. Polydipsia, although

Figure 1. International Cat Care have a free downloadable poster outlining the dangers of antifreeze available on their website https://icatcare.org/app/uploads/2019/09/antifreeze-warning-poster.pdf

common in dogs, is generally not seen in cats. Seizures can occur at this stage in severe cases.

From 12–24 hours in cats and 36–72 hours in dogs, cardiopulmonary signs develop with tachypnoea, tachycardia, acidosis, hyper- or hypotension, pulmonary oedema, arrhythmias, congestive heart failure and circulatory shock. Cats remain depressed. Cerebral oedema may be present, and death can occur in this stage in some cases.

In the third stage of poisoning (which occurs from around 24 hours onwards) renal system signs including oliguria, azotaemia and/or uraemia develop and the kidney injury exacerbates acid/base and electrolyte disturbances. Kidneys may be swollen and painful and there may be vomiting, anorexia, oral ulcers and severe depression, lethargy, coma and convulsions as a result of uraemia (Thrall et al, 1984).

Increased urea and creatinine are generally seen from about 12 hours in cats and 24–48 hours in dogs (Grauer et al, 1984). There is also low urine specific gravity (because of osmotic diuresis induced by ethylene glycol); proteinuria, glucosuria, haematuria and albuminuria. Calcium oxalate crystals can appear in the urine within 3–6 hours after ingestion (Sanyer et al, 1973; Grauer et al, 1984; Thrall et al, 1985; Connally et al, 2010), but the absence of oxalate crystals does not rule out ethylene glycol poisoning. The crystals are light yellow, arranged in rosettes, sheaves or prisms and are birefringent in polarised light.

There may also be hyperglycaemia, hypocalcaemia (because of binding of calcium to oxalate), hyperphosphataemia and hyperkalaemia (because of reduced excretion and acidosis). Clinical signs of hypocalcaemia generally do not occur in ethylene glycol poisoning because of the shift to the active, ionised form of calcium when metabolic acidosis occurs (Winek et al, 1978a; Thrall et al, 1984).

Treatment

Diagnosis of ethylene glycol poisoning is generally based on history, clinical signs and laboratory findings. Ethylene glycol poisoning should be suspected in any animal with acute onset of signs, raised urea, creatinine, hypocalcaemia, hyperglycaemia, and other nitrogenous compounds in the blood (azotaemia or uraemia) and low or fixed urine specific gravity (Grauer and Thrall, 1982), CNS depression, metabolic acidosis with or without a high anion gap or calcium oxalate crystalluria (Stuckey et al, 2012).

The aim of therapy in ethylene glycol poisoning is to prevent metabolism and the production of toxic metabolites, reverse electrolyte and acid/base disturbances and maintain the glomerular filtration rate.

Decontamination is recommended for any quantity, but gut decontamination is probably only worthwhile within 1 hour of ingestion. Adsorbents such as activated charcoal are not useful and in many cases animals, particularly cats, do not present until the onset of signs, hours after ingestion.

In symptomatic animals the blood pH, electrolytes and renal function should be monitored. Intravenous (IV) fluids 2–3 times maintenance is essential to ensure adequate hydration and to promote diuresis. If possible, the central venous pressure and renal output should be monitored in animals with renal dysfunction because of the risk of fluid overload and subsequent pulmonary oedema. Regular weighing may help assess risk of fluid overload. If there is oliguria or anuria the fluid rate can be increased and diuretics such as mannitol or furosemide can be given if there is no response. Haemodialysis is very effective in ethylene glycol toxicosis if started before onset of azotaemia and can be used in animals with uraemia while waiting for possible return of renal function (Rollings et al, 2004), but is rarely available.

Ionised calcium concentration should be monitored in animals with renal failure or severe acid/base disturbances (Connally et al, 2010). Calcium gluconate can be given if there are clinical signs of severe hypocalcaemia and sodium bicarbonate to correct severe acidosis (Jandrey, 2016). Animals should be offered food and water if their condition allows.

The aim of antidotal therapy in the management of ethylene glycol toxicosis is to prevent formation of the toxic metabolites. This is achieved through administration of ethanol or fomepizole. Ethanol has a higher affinity for alcohol dehydrogenase than ethylene glycol, whereas fome-

pizole is a potent selective competitive inhibitor of alcohol dehydrogenase. With the enzyme either busy with ethanol or inhibited by fomepizole there is time for renal excretion of the unchanged parent compound. Ethanol is cheap and readily available whereas fomepizole is generally unavailable and is very expensive. In addition, cats require six times the dose used in dogs and humans. Ethanol therapy will cause sedation and recumbency and these patients need appropriate nursing care.

The sooner antidotal therapy is started, preferably within the first few hours after ingestion, the better the outcome. A potentially lethal dose of ethylene glycol can be survived if treatment is prompt, but it should be noted that administration of an antidote is usually necessary for a prolonged period and animals with ethylene glycol poisoning require intensive management for several days with regular monitoring, evaluation and blood tests. Prognosis is poor in cats with ethylene glycol toxicosis.

Carbon monoxide

Carbon monoxide is a colourless, odourless, tasteless, non-irritating, flammable gas. It is most commonly formed when there is incomplete combustion of organic fuels. Many incidents of carbon monoxide poisoning are associated with the use of badly installed, poorly maintained or malfunctioning domestic combustion appliances using gas, oil or solid fuel, or the use of such appliances in inadequately ventilated areas. There is limited information on carbon monoxide poisoning in domestic animals, but poisoning is similar to that seen in humans.

Carbon monoxide combines reversibly with the oxygen carrying sites of the haemoglobin molecule with an affinity 200 times greater than oxygen itself. Consequently, carbon monoxide reduces the availability of oxygen to tissues by combining with haemoglobin (to form carboxyhaemoglobin) and reducing the amount of oxygen it can carry, and preventing the release of bound oxygen to tissues (Ashbaugh et al, 2012).

The clinical effects of carbon monoxide toxicosis are non-specific and variable depending on concentration, duration, animal size and underlying condition. Some groups are more at risk: those with pre-existing cardiovascular and cerebral vascular disease (e.g. elderly), anaemia or increased affinity of haemoglobin for carbon monoxide (e.g. fetuses). When taking a history, questions to ask include whether the heating was recently switched on, if the boiler is regularly serviced, if the pet sleeps near the boiler, whether any other gas-fuelled heating devices are used or if anyone in the household has been feeling unwell. Owners of any animal with suspected carbon monoxide poisoning should be advised to seek medical attention. Any suspect appliance should be switched off and serviced. Cats and dogs (and children) have higher alveolar ventilation because of an increased metabolic rate and may show signs of carbon monoxide toxicosis before adult humans.

Clinical signs

Signs of carbon monoxide toxicosis include vomiting, depression, tremor, drowsiness, lethargy and listlessness, anorexia, tachycardia, tachypnoea, weakness and ataxia (Fitzgerald, 2013). Deafness and blindness may occur and there may also be behavioural changes with aggressive behaviour (Hipwell, 1995). In severe cases there may be lactic acidosis, hypotension, convulsions, coma, arrhythmias and cerebral oedema (Berent et al, 2005). Permanent neurological damage may result, and in most cases, if signs persist for >3 weeks then complete recovery is unlikely (Fitzgerald, 2013).

Carbon monoxide poisoning is often misdiagnosed because the effects are vague and non-specific. The cherry-red colouration often quoted as a classic sign of carbon monoxide poisoning is rarely observed (Fitzgerald, 2013).

Treatment

The most important initial treatment for carbon monoxide toxicosis is removal from exposure and 100% oxygen by endotrachael tube or tight-fitting mask. For cats or small dogs, it may be more practical to place the animal in an incubator and supply high flow oxygen (Fitzgerald, 2013), but most pets can be managed in an oxygen cage or with nasal oxygen (Hall, 2016). The half-life of carboxyhaemoglobin in a person breathing air is about 4–5 hours, and 60–80 minutes if breathing 100% oxygen.

Management of clinical signs is supportive with intravenous fluids for hypotension, diazepam for convulsions and mannitol for cerebral oedema (Berent et al, 2005). If possible, the patient's electrocardiogram (ECG) should be monitored, and arrhythmias managed supportively (Fitzgerald, 2013). Blood gases should be monitored in animals with severe toxicosis.

The formation of carboxyhaemoglobin is a useful biomarker of exposure to carbon monoxide but is rarely measured in veterinary medicine. The amount of carboxyhaemoglobin formed depends on a range of factors including duration and concentration of carbon monoxide exposure and the health status of the animal. In a case series involving cats and dogs the carboxyhaemoglobin concentration did not correlate well with clinical outcome (Berent et al, 2005).

Christmas foods

Chocolate

Chocolate ingestion in pets is common around Christmas (Noble et al, 2017); about 20% of all chocolate enquiries to the UK's Veterinary Poisons Information Service occur in December (VPIS data). Chocolate toxicosis in cats is uncommon, presumably because they usually only eat a small amount compared wih dogs.

Chocolate contains the methylxanthine theobromine, which produces CNS stimulation with cardiac and respiratory hyperactivity. The type of chocolate is defined by the quantity (percentage) of cocoa solids the chocolate con-

tains. Dark or plain chocolate is made without milk and contains a higher concentration of cocoa solids and theobromine than milk chocolate. White chocolate is not real chocolate as it does not contain any cocoa solids, but it is made primarily of cocoa butter, sugar and milk solids.

Signs of chocolate toxicosis generally occur within 2–4 hours of ingestion (Dolder, 2013) but can sometimes occur after 6–12 hours (Gwaltney-Brant 2001). Initially there may be vomiting, abdominal discomfort, diarrhoea, polydipsia, polyuria, excitability and hyperactivity; then ataxia, tremors, tachycardia, hypertension and hyperthermia. Hypokalaemia can occur as a result of vomiting and polyuria.

Convulsions can occur after ingestion of chocolate but are rare. Other less common effects include bradycardia, haematemesis, haematuria, bloat, tachypnoea, cyanosis and arrhythmias (classically premature ventricular contractions (PVC)). Renal dysfunction is also uncommon. Pancreatitis may result 24–72 hours after ingestion because of the high fat content of some chocolate products (Gwaltney-Brant, 2001). Recovery from theobromine toxicosis can occur within 24 hours but may take 48–72 hours.

White chocolate, although low in theobromine, is high in fat and sugar and ingestion may cause gastrointestinal signs. Pancreatitis is also a potential risk with white chocolate.

If a potentially toxic dose has been ingested gut decontamination should be attempted. An emetic can be given but emesis is best avoided in animals with hyperactivity or excitability because of theobromine toxicity, however activated charcoal can be given, if practical. In late-presenting animals activated charcoal should be given. Repeated doses of adsorbents may be useful in enhancing elimination as theobromine appears to undergo enterohepatic re-circulation and has a long half-life.

Treatment is supportive with anti-emetics if there is severe or persistent vomiting. If possible, in symptomatic animals the heart rate, body temperature and ECG should be monitored. Fluids are recommended to support the cardiovascular system and enhance excretion (as theobromine is excreted renally). Diazepam or methocarbamol can be used for the management of tremors with diazepam or barbiturates for hyperactivity or convulsions.

Where tachycardia (>180 beats per minue (bpm) in dogs) is persistent a beta-blocker such as propranolol, metoprolol or esmolol (Verschoor-Kirss et al, 2022) can be given, although care should be taken when using these drugs as severe hypotension may result from unopposed alpha-adrenergic effects. Lidocaine is the drug of choice for ventricular arrhythmias unresponsive to a beta-blocker. In dogs with bradycardia atropine can be given. Prognosis in pets with chocolate toxicosis is excellent. Severe cases are uncommon and deaths are rare.

Grapes and their dried fruits

Grapes are available all year round, but many Christmas foods contain dried vines fruits (sultanas, raisins, currants),

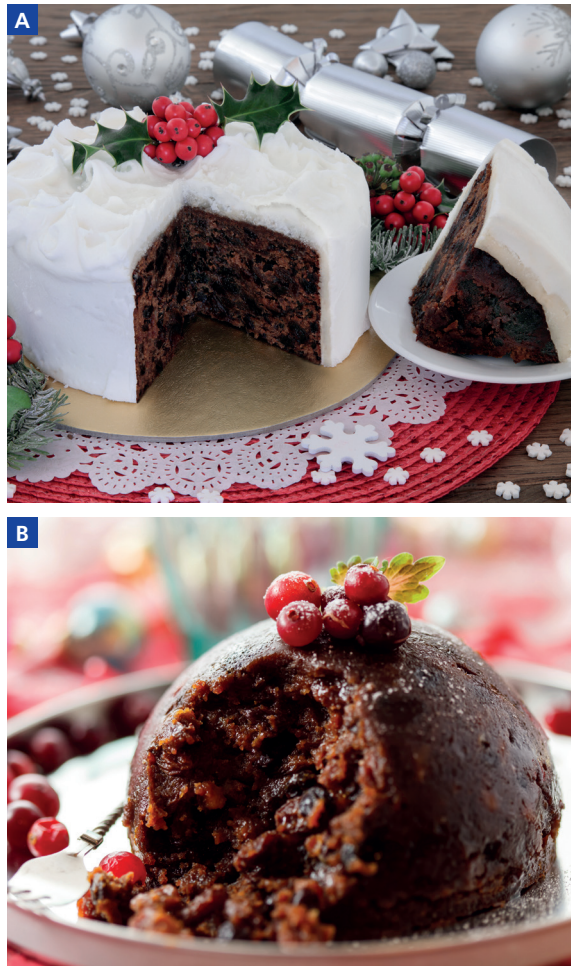

Figure 2. Christmas cake (a) and Christmas pudding (b) contain dried vine fruits and ingestion can cause acute kidney injury in dogs.

such as Christmas cake (*Figure 2a*) and pudding (*Figure 2b*), stollen and mince pies. The toxic dose of raisins, currants, sultanas or grapes has not been established and there does not appear to be a dose-response relationship (Eubig et al, 2005). Individual variation in response may also occur, and some dogs have been reported to eat grapes and dried fruits without apparent adverse effects. It is now thought that tartaric acid in grapes is the cause of the acute kidney injury that occurs (Wegenast et al, 2021, 2022), but there is still much to learn about grape toxicosis in dogs.

Clinical signs of poisoning usually occur within 6 hours and are always present within 24 hours. Initially, there is vomiting, diarrhoea, hypersalivation, haematemesis, bloody stools, anorexia, tender abdomen, ataxia, weakness and lethargy. Grapes or dried fruit may be present in the vomitus or faeces (Eubig et al, 2005). From 24–72 hours renal failure may develop with oliguria or anuria. Some animals appear dehydrated and may be polydipsic and there may be evidence of pancreatitis (Eubig et al, 2005). Bradycardia, tachycardia, hypo- or hyperthermia, anaemia, leucocytosis, cyanosis, respiratory depression, tremor, rigidity and seizures had been reported in some cases. Fortunately, symptomatic

acute kidney injury is rare in pets with grape or dried fruit ingestion (Reich et al, 2020; Dijkman et al, 2022).

Chocolate-coated raisins are also available, and ingestion would present the additional risk of chocolate poisoning.

Gut decontamination should be considered following ingestion of any quantity of grapes, raisins, sultanas or currants (Mazzaferro et al, 2004). Digestion of grapes and dried fruit appears to be slow and gastric decontamination several hours after ingestion is possibly worthwhile, particularly if a large volume has been ingested. In addition, raisins are hygroscopic and can double or triple in volume on contact with water (Eshel et al, 1988). Whole grapes and swollen raisins have been recovered in dogs even after they have remained in the stomach overnight (Eubig et al, 2005). Activated charcoal can be given.

Aggressive intravenous fluid therapy (e.g. twice the normal maintenance rate) for at least 48 hours for rehydration and to support renal function is recommended to prevent acute kidney injury. An anti-emetic should be given if vomiting is protracted.

Electrolytes and renal function should be monitored every 24 hours for 72 hours. Animals should be monitored for signs of fluid overload (tachypnoea, chemosis, serous nasal discharge, pulmonary crackles, increased body weight). Where necessary use of furosemide or mannitol may be considered to re-establish urine output, but efficacy is unproven and there is evidence that tubular necrosis and obstruction of the renal tubules occurs preventing urine flow (Mazzaferro et al, 2004). Dopamine may be used to enhance renal perfusion.

Haemodialysis and peritoneal dialysis have been employed in several cases reported in the literature (e.g. Mazzaferro et al, 2004; Eubig et al, 2005; Stanley and Langston, 2008) in dogs, although in practice they will rarely be available because of cost and accessibility.

Prognosis is good if treatment is started before the onset of renal signs, but prognosis is poor in dogs with oliguria or anuria after ingestion of grapes and grape products (Gwaltney-Brant et al, 2001).

Macadamia nuts

Macadamia nut toxicosis has been reported in dogs, although the mechanism of toxicity is unknown. Toxic effects can also occur following ingestion of macadamia butter (which is like peanut butter) (McKenzie et al, 2000). A toxic dose has been estimated to be approximately 2–3 g/kg which equates to about one nut/kg (Gwaltney-Brant, 2007). Note that chocolate-coated macadamia nuts are available, and in these cases, there is an additional risk of chocolate toxicosis.

Signs of macadamia nut toxicosis usually start within about 12 hours (Hansen et al, 2000; McKenzie et al, 2000) and last 24–48 hours (Hansen et al, 2000; McKenzie et al, 2000). Signs reported in dogs include weakness and ataxia (more pronounced in hind limbs), abdominal tenderness, lethargy, vomiting, diarrhoea, pyrexia, bloat, lameness, stiffness, joint pain and recumbency. Mild elevations in serum triglycerides (macadamia nuts are rich in oils) and alkaline phosphatase (APL) may occur (Hansen et al, 2000).

Treatment of macadamia nut toxicosis is supportive. If the quantity ingested is large, then administration of a laxative will hasten passage of the nuts through the gastrointestinal tract. Analgesia may be given if required, but most cases can be managed at home (Hansen et al, 2000, 2002) since effects are self-limiting, although management should be assessed on a case by case basis.

Cold and flu products

Medicines for the symptomatic relief of colds and flu (*Figure 3*) are commonly used over the winter season. They typically contain an analgesic (usually ibuprofen or paracetamol) and a decongestant.

Decongestants

Cold and flu products usually contain pseudoephedrine or phenylephrine as a decongestant. These drugs cause vasoconstriction, which in turn relieves nasal congestion, but they also have direct and indirect effects on adrenergic receptors resulting in peripheral vasoconstriction, cardiac stimulation and increased blood pressure.

Individual response to these decongestants is very variable and unpredictable. Common signs are hyperactivity, agitation, dilated pupils, tachycardia and pyrexia. There may also be vomiting, hypertension and reflex bradycardia (Kang and Park, 2012; Wegenast, 2012). Severe effects are generally not expected with phenylephrine because of low oral bioavailability but pseudoephedrine may cause cyanosis, arrhythmias, tremors and seizures. Animals with cardiac disease may be more at risk.

Figure 3. Medicines for the symptomatic relief of colds and flu commonly include paracetamol or ibuprofen and a decongestant such as phenylephrine or pseudoephedrine.

Animals that have ingested pseudoephedrine or phenylephrine will require monitoring of heart rate and blood pressure. An emetic is usually only recommended if ingestion occurred within 30 minutes (Gwaltney-Brant, 2016) but could be considered later for modified-release pseudoephedrine products. Activated charcoal can be given.

IV fluids are recommended to promote excretion (and reduce the risk of rhabdomyolysis-induced renal impairment in animals with severe poisoning). Acepromazine is recommended for stimulatory signs or hypertension (Pascoe et al, 1994; Wegenast, 2012; Gwaltney-Brant, 2016), as it has antihypertensive and anxiolytic effects. A barbiturate is recommended for tremors or convulsions, as diazepam is best-avoided because it can exacerbate sympathomimetic-induced agitation (Means, 1999). Bradycardia usually does not require intervention and will resolve if hypertension is corrected. Esmolol is recommended for marked supraventricular tachycardia as propranolol is best avoided as it is a non-specific beta-blocker and beta-2 blockade may exacerbate hypertension (Holding, 2012). Carvedilol has been used to manage tachycardia and hypertension in a dog after ingestion of pseudoephedrine (Kang and Park, 2012). Nitroprusside is recommended for severe hypertension (Wegenast, 2012) but this is not likely to be readily available.

Paracetamol

Paracetamol (also known as acetaminophen or APAP in some countries) is a very widely and readily available analgesic. It is metabolised in the liver by glucuronidation, sulphation and oxidation. The glucuronide and sulphate conjugates are non-toxic and are excreted in bile and urine. In most species the oxidation pathway is minor while glucuronidation is the major pathway of paracetamol metabolism. Cats and ferrets (Court, 2001), however, have a restricted ability to conjugate with glucuronic acid as they have low levels of glucuronyl transferase, the enzyme that catalyses the final step of the glucuronidation pathway. These species therefore have a limited ability to metabolise paracetamol to non-toxic metabolites.

The oxidation pathway produces a highly reactive compound called N-acetyl-p-benzoquinoneimine (NAPQI), which conjugates with glutathione, and is metabolised to non-toxic compounds. Glutathione becomes depleted and NAPQI then binds with cellular molecules and proteins causing cell death in the liver. In addition, alternative metabolic pathways also allow accumulation of oxidising metabolites that may induce methaemoglobin formation, Heinz body formation and denaturation of erythrocyte membranes. Cats are at increased risk of Heinz body formation because their haemoglobin is different to that of dogs and has eight reactive sulfhydryl groups (Taketa et al, 1967), twice the number in canine haemoglobin. This results in increased susceptibility to oxidative damage and increased Heinz body formation.

In cats and dogs, clinical manifestations of paracetamol ingestion may occur within 4 hours (Marcella, 1983), but definitely within 6–24 hours (Kolf-Clauw and Keck, 1994). Early signs can be non-specific and the animal may present many hours later. There may be progressive cyanosis, which is associated with tachycardia, tachypnoea and dyspnoea. Mucous membranes appear brown in colour, and weakness and lethargy may be observed. Other signs include depression, vomiting, diarrhoea, anorexia and facial and paw oedema. Haematuria, anaemia, and evidence of haemolysis may be present. In animals with severe facial oedema there may be reduced tear production and there is risk of ocular damage. Keratoconjunctivitis sicca (KCS) has been reported in a small number of dogs with facial oedema after paracetamol overdose (Mariani, 2001; Burwell, 2008).

Liver damage is evident within 24–36 hours. Death, usually from progressive methaemoglobinaemia or from severe hepatic necrosis (less commonly in cats), occurs between 2–6 days post-ingestion in cases that present late or remain untreated. Recovery may take several days (Aronson and Drobatz, 1996), depending on the severity of signs, but biochemical abnormalities may take several weeks to return to normal concentrations.

Haemoglobinuria, intravascular haemolysis, jaundice and other evidence of liver damage may be seen in animals that survive the initial stages of paracetamol poisoning. Coma, convulsions and pulmonary oedema are occasionally reported. Oliguria and renal damage can also occur, but less commonly (Richardson, 2000).

The aim of treatment for an animal with paracetamol poisoning is to ensure adequate oxygenation and prevent further metabolism of paracetamol to toxic metabolites with the use of antidotes and to prevent damage to the liver and erythrocytes. Any animal with signs consistent with paracetamol toxicosis should be treated irrespective of the time since ingestion or the dose ingested.

If ingestion was recent (within 1–2 hours) an emetic and activated charcoal can be considered, depending on the animal's clinical condition. Antidotal therapy should be started in any animal with signs of poisoning or that has ingested a potentially toxic dose. Acetylcysteine is the antidote of choice. It can be given by intravenous infusion or orally; however it has a sulphurous smell and taste which can cause hypersalivation, so it needs to be diluted to improve palatability if administered orally. S-adenosyl-L-methionine (SAMe) can be given in combination with acetylcysteine.

Other treatment is essentially supportive with monitoring for signs of hypoxia, methaemoglobinaemia, liver damage, anaemia, haemolysis and renal impairment. Oxygen will be required in animals with cyanosis. Whole blood transfusions may be required in animals with evidence of severe haemolysis, significant decrease in packed cell volume (PCV) or severe anaemia.

Ibuprofen

Ibuprofen ingestion is very common in dogs and can cause gastrointestinal, neurological, renal and hepatic

KEY POINTS

- Carbon monoxide poisoning caused by a faulty heating appliance can be easily missed as the effects are vague and non-specific. Other members of the household may also be unwell.
- Ethylene glycol antifreeze poisoning requires prompt antidotal treatment to prevent the formation of metabolites which are responsible for the toxic effects.
- If a pet has eaten a cold and flu product it is important to obtain information on the product name and ingredients involved as these products can contain different analgesics and decongestants.
- Ingestion of the common Christmas plants poinsettia, holly and mistletoe generally causes only mild effects, despite their reputations of being poisonous.
- Christmas is also a time of excess food consumption, and some foods are hazardous to pets such as chocolate (cardiac effects and central nervous system stimulation), macadamia nuts (neurological signs, lameness, gastrointestinal signs) and grapes and dried vine fruits (acute kidney injury).
- Various foods such as raisins and macadamia nuts are also available coated in chocolate and may present an additional toxicological risk.

signs in overdose. Initial signs are vomiting, haematemesis, diarrhoea, abdominal tenderness and anorexia. Ingestion of a large dose may result in rapid (within 1–2 hours) onset of neurological signs with agitation, hyperactivity, hyperaesthesia, tremors, twitching or seizures and coma. Death can occur following ingestion of a very large dose.

Renal failure can occur from 12 hours but can be delayed. There may be protracted vomiting, pyrexia, anaemia, anorexia, polyuria, polydipsia, dehydration and collapse. Signs of liver damage (raised liver enzymes, bleeding, jaundice) are uncommon but can occur in severe cases.

Treatment of ibuprofen toxicosis is aimed at preventing or treating gastrointestinal and renal signs. After a large dose treatment may also be required for neurological signs. An emetic and activated charcoal can be given if ingestion was recent. In animals that have ingested a large quantity, emesis is best avoided because of rapid onset neurological signs. Animals with dehydration, hypotension or pre-existing renal insufficiency are more at risk of toxic effects.

In all cases where treatment has been necessary ulcer-healing or ulcer-preventing drugs should be started. Gastroprotectants (e.g. omeprazole) should be given for 7–14 days or longer depending on clinical condition and the dose ingested (Schell and Gwaltney-Brant, 2011). Misoprostol (a synthetic prostaglandin) can be used for prevention (rather than treatment) of ulcers. Misoprostol should not be used in pregnant animals as it can cause uterine contractions and abortion. If activated charcoal has been given, parenteral administration is recommended for other drugs or a lapse of 2 hours between the administration of charcoal and oral drugs. Sucralfate is only recommended if ulceration is suspected or confirmed. It is therefore not used in animals that present early and do not develop ulceration.

If there is severe or persistent vomiting, then anti-emetics should be administered as vomiting may result in dehydration and subsequent renal failure.

Renal function should be monitored in an animal with ibuprofen toxicosis. The renal function should be checked at 24 and 48 hours post-ingestion (Tegzes, 2016), although renal failure may occasionally be delayed for up to 5 days post-ingestion. If possible, blood gases and electrolytes should be checked and corrected, especially if there is evidence of renal dysfunction and/or oliguria. Liver toxicity occurs occasionally, and routine monitoring is not required except after ingestion of a significant quantity.

Comatose animals should be managed supportively with regular turning. Diazepam or barbiturates may be given if there is any convulsant activity. In animals with non-steroidal anti-inflammatory drug (NSAID) toxicosis it is important to ensure adequate hydration and good urine output with monitoring for signs of fluid overload (tachypnoea, chemosis, serous nasal discharge, pulmonary crackles), and with monitoring of central venous pressure if possible (otherwise assess by using clinical signs and bodyweight). If the dose ingested may cause renal impairment or the animal is vomiting, fluid therapy appropriate to its hydration and perfusion status but at least maintenance IV fluids should be given for at least 24 hours. The duration of therapy should be adjusted depending on the renal parameters.

Christmas plants

Poinsettia

Poinsettia (*Euphorbia pulcherrima*, *Figure 4a*) is an ornamental perennial houseplant that is commonly available at Christmas. The flowers are very small and surrounded by large red (sometimes white, cream pink or multicoloured) bracts, which are often mistaken for petals.

E. pulcherrima has the reputation of being a toxic plant, but this has been greatly exaggerated (Winek et al, 1978b; Jackson, 1986; Krenzelok et al, 1996; Krenzelok and Mrvos, 2015). *Euphorbia* species contain diterpene esters, but they are present in a very low concentration in *E. pulcherrima* and as a consequence this plant is not as irritant as other *Euphorbia* species.

Many cats and dogs remain well after ingestion of poinsettia (VPIS case data). Vomiting, hypersalivation, anorexia, lethargy and depression may occur, but effects are usually rapid in onset and self-limiting (Volmer, 2002). Although two deaths have been reported in dogs (Jasperson-Schib, 1976; Klug et al, 1990), signs reported were not consistent with poinsettia ingestion. Of 10 cats reported to the Hennepin Regional Poisons Center in America that ingested poinsettia, one developed hypersalivation and the others remained well (Hornfeldt, 1989).

Gut decontamination is not required after ingestion of poinsettia and treatment is supportive, with rehydration and an antiemetic as required.

*Figure 4. Common decorative Christmas plants include (a) poinsettia (*Euphorbia pulcherrima*), (b) mistletoe (*Viscum album*) and (c) holly (*Ilex *species*).*

Mistletoe

Mistletoe (V*iscum album*, Figure 4b) contains alkaloids (Anderson and Phillipson, 1982), polypeptides (viscotoxins) and lectin proteins (viscumin) (Franz et al, 1981; Olsnes et al, 1982). The toxic components are mainly found in the foliage (i.e. leaves and stems) (Anderson and Phillipson, 1982; Frohne and Pfänder, 2005). The toxicity of the fruits is considered to be low; viscotoxins are not present in the berries (Frohne and Pfänder, 2005), however, the ingestion of lots of berries could cause gastrointestinal signs (Anderson and Phillipson 1982; Frohne and Pfander, 2005). Following ingestion, it has been suggested that the action of protease enzymes during the digestion process removes the toxins (Samuelsson, 1973). The American mistletoe (*Phoradendron leucarpum*) is also regarded as of low toxicity although gastrointestinal signs can occur (Krenzelok and Mrvos, 2015).

Many animals remain asymptomatic but can develop gastrointestinal irritation (hypersalivation, vomiting, diarrhoea, abdominal discomfort) after ingestion of mistletoe. Gut decontamination is generally not necessary, and treatment is symptomatic and supportive with rehydration and an antiemetic, if required.

Holly

Holly such as English holly (*Ilex aquifolium*, *Figure 4c*) is used for decoration at Christmas. The female plants bear fruits, which remain on the plant through the winter. The plant is considered to be of low toxicity, but the leaves and berries contain saponins which have local irritant effects on mucous membranes. The clinical signs are thought to be mainly caused by the saponins (Volmer, 2002).

In cats and dogs, ingestion of holly may cause hypersalivation, vomiting, inappetence, diarrhoea, lethargy and depression. Animals may also shake their head and smack their lips (Volmer, 2002). Choking on the leaves is also a potential hazard and has been reported in other animals (Simpson, 1992).

Gut decontamination is not required after ingestion of holly and treatment is supportive, with rehydration and an antiemetic as required.

Conclusions

Some winter seasonal poisoning hazards are associated with cold weather such as carbon monoxide poisoning, antifreeze and medicines for the symptomatic relief of colds and flu. Plants brought into the home for decoration over the Christmas season are also a potential risk, however, although the common plants available at Christmas, such as poinsettia, holly and mistletoe, all have the reputation of being poisonous, in most cases effects are mild or absent. Christmas is also a time of excess food consumption, and some foods are hazardous to pets such as chocolate, macadamia nuts and grapes and dried vine fruits. CA

References

Amoroso L, Cocumelli C, Bruni G et al. Ethylene glycol toxicity: a retrospective pathological study in cats. Vet Ital. 2017;53(3):251–254. https://doi.org/10.12834/VetIt.1159.6409.2

Anderson LA, Phillipson JD. Mistletoe – the magic herb. Pharm J. 1982;229(6197):437–439

Aronson LR, Drobatz K. Acetaminophen toxicosis in 17 Cats. J Vet Emerg Crit Care. 1996;6(2):65–69. https://doi.org/10.1111/j.1476-4431.1996.tb00034.x

Ashbaugh EA, Mazzaferro EM, McKiernan BC, Drobatz KJ. The association of physical examination abnormalities and carboxyhemoglobin concentrations in 21 dogs trapped in a kennel fire. J Vet Emerg Crit Care. 2012;22(3):361–367. https://doi.org/10.1111/j.1476-4431.2012.00759.x

Berent AC, Todd J, Sergeeff J, Powell LL. Carbon monoxide toxicity: a case series. J Vet Emerg Crit Care. 2005;15(2):128–135. https://doi.org/10.1111/j.1476-4431.2005.00140.x

Burwell B. Case report — unusual case of acetaminophen toxicity. Vet Forum. 2008;25(9):38-47

Connally HE, Thrall MA, Hamar DW. Safety and efficacy of high-dose fomepizole compared with ethanol as therapy for ethylene glycol intoxication in cats. J Vet Emerg Crit Care. 2010;20(2):191–206. https://doi.org/10.1111/j.1476-4431.2009.00492.x

Court MH. Acetaminophen UDP-glucuronosyltransferase in ferrets: species and gender differences, and sequence analysis of ferret UGT1A6. J Vet Pharmacol Ther. 2001;24(6):415–422. https://doi.org/10.1046/j.1365-2885.2001.00366.x

de Water R, Noordermeer C, van der Kwast TH et al. Calcium oxalate nephrolithiasis: effect of renal crystal deposition on the cellular composition of the renal interstitium. Am J Kidney Dis. 1999;33(4):761–771.

https://doi.org/10.1016/S0272-6386(99)70231-3
Dijkman MA, van Roemburg RG, De Lange DW, Hugen S, Robben JH. Incidence of VITIS fruit-induced clinical signs and acute kidney injury in dogs and cats. J Small Anim Pract. 2022;63(6):447–453. https://doi.org/10.1111/jsap.13483
Dolder LK. Methylxanthines: caffeine, theobromine and theophylline. In: Peterson ME, Talcott PA, eds. Small animal toxicology, 3rd edition. Elsevier, St Louis, Missouri; 2013: 647-652
Eshel G, Broide E, Azizi E. Phytobezoar following raisin ingestion in children. Pediatr Emerg Care. 1988;4(3):192–193. https://doi.org/10.1097/00006565-198809000-00008
Eubig PA, Brady MS, Gwaltney-Brant SM, Khan SA, Mazzaferro EM, Morrow CM. Acute renal failure in dogs after the ingestion of grapes or raisins: a retrospective evaluation of 43 dogs (1992-2002). J Vet Intern Med. 2005;19(5):663–674. https://doi.org/10.1111/j.1939-1676.2005.tb02744.x
Fitzgerald KT. Carbon monoxide poisoning. In: Peterson ME, Talcott PA, eds. Small animal toxicology, 3rd edition. Elsevier, St Louis, Missouri; 2013: 479-487
Franz H, Ziska P, Kindt A. Isolation and properties of three lectins from mistletoe (*Viscum album* L.). Biochem J. 1981;195(2):481–484. https://doi.org/10.1042/bj1950481
Frohne D, Pfänder HJ. Poisonous plants: a handbook for doctors, pharmacists, toxicologists, biologists and veterinarians, 2nd edition. Timber Press, Portland, Oregon; 2005: 270-271
Gessner PK, Parke DV, Williams RT. Studies in detoxication. 86. The metabolism of 14C-labelled ethylene glycol. Biochem J. 1961;79(3):482–489. https://doi.org/10.1042/bj0790482
Grauer GF, Thrall MA. Ethylene glycol (antifreeze) poisoning in the dog and cat. J Am Anim Hosp Assoc. 1982;18:492–497
Grauer GF, Thrall MA, Henre BA, Grauer RM, Hamar DW. Early clinicopathologic findings in dogs ingesting ethylene glycol. Am J Vet Res. 1984;45(11):2299–2303
Gwaltney-Brant S. Chocolate intoxication. Vet Med. 2001;96(2):108–111
Gwaltney-Brant SM. Garbage ingestion. Clinician's Brief. 2007;June: 45-46. https://www.cliniciansbrief.com/columns/56/garbage-ingestion
Gwaltney-Brant S. Decongestants (pseudoephedrine, phenylephrine). In: Hovda LR, Brutlag AG, Poppenga RH, Peterson KL, eds. Blackwell's Five minute veterinary consult clinical companion. Small Animal Toxicology, 2nd edition. Wiley Blackwell, Ames, Iowa; 2016: 327-332
Gwaltney-Brant S, Holding JK, Donaldson CW, Eubig PA, Khan SA. Renal failure associated with ingestion of grapes or raisins in dogs. J Am Vet Med Assoc. 2001;218(10):1555–1556
Hall JM. Carbon monoxide. In: Hovda LR, Brutlag AG, Poppenga RH, Peterson KL, eds. Blackwell's Five minute veterinary consult clinical companion. Small animal toxicology, 2nd edition. Wiley Blackwell, Ames, Iowa; 2016: 881-884
Hansen SR, Buck WB, Meerdink G, Khan SA. Weakness, tremors, and depression associated with macadamia nuts in dogs. Vet Hum Toxicol. 2000;42(1):18–21
Hansen SR. Macadamia nut toxicosis in dogs. Vet Med. 2002;97(2):274–276
Hewlett TP, Jacobsen D, Collins TD, McMartin KE. Ethylene glycol and glycolate kinetics in rats and dogs. Vet Hum Toxicol. 1989;31(2):116–120
Hipwell F. Suspected carbon, monoxide poisoning in a dog. Vet Rec. 1995;136(11):275–276. https://doi.org/10.1136/vr.136.11.275
Holding JK. Phenylpropanolamine toxicosis in dogs and cats. Vet Med. 2012;107(1):32–34
Hornfeldt CS. Confusion over toxicity of poinsettia. J Am Vet Med Assoc. 1989;194(8):1004
Jackson EM. The Poinsettia. J Toxicol Cutaneous Ocul Toxicol. 1986;5(4):231–232. https://doi.org/10.3109/15569528609036299
Jandrey KE. Ethylene glycol and diethylene glycol. In: Hovda LR, Brutlag AG, Poppenga RH, Petersen KL, eds. Blackwell's five-minute veterinary consult clinical companion small animal toxicology, 2nd edition. Ames, Iowa, Wiley-Blackwell; 2016: 78-84
Jaspersen-Schib R. Exotische Halsketten aus Toxischen Samen und Früchten. Schweiz Apoth Ztg 1976;114:391-393
Kang M-H, Park H-M. Application of carvedilol in a dog with pseudoephedrine toxicosis-induced tachycardia. Can Vet J. 2012;53(7):783–786
Klug S, Saleem G, Honcharuk L, Marcus S. Toxicity potential of poinsettia, is the plant really toxic?. Vet Hum Toxicol. 1990;32(4):368
Kolf-Clauw M, Keck G. Paracetamol poisoning in dogs and cats. Eur J Companion Anim Pract. 1994;4:85–92.
Krenzelok EP, Jacobsen TD, Aronis JM. Poinsettia exposures have good outcomes… just as we thought. Am J Emerg Med. 1996;14(7):671–674. https://doi.org/10.1016/S0735-6757(96)90086-8
Krenzelok EP, Mrvos R. Toxic Christmas and New Year holiday plants… or are they? Asia Pac J Med Toxicol. 2015;4:64–67
Marcella KL. Acetaminophen poisoning in cats and man. J Am Vet Med Assoc. 1983;183(8):836
Mariani CL, Fulton RB Jr. Atypical reaction to acetaminophen intoxication in a dog. J Vet Emerg Crit Care. 2001;11(2):123–126. https://doi.org/10.1111/j.1476-4431.2001.tb00078.x
Mazzaferro EM, Eubig PA, Hackett TB et al. Acute renal failure associated with raisin or grape ingestion in 4 dogs. J Vet Emerg Crit Care. 2004;14(3):203–212. https://doi.org/10.1111/j.1534-6935.2004.00114.x
McKenzie RA, Purvis-Smith GR, Allan SJ et al. Macadamia nut poisoning of dogs. Aust Vet Pract. 2000;30(1):6–8
Means C. Ma huang: all natural but not always innocuous. Vet Med. 1999;94(6):511–512
Milles G. Ethylene glycol poisoning; with suggestions for its treatment as oxalate poisoning. Arch Pathol. 1946;41:631–638
Noble PJM, Newman J, Wyatt AM, Radford AD, Jones PH. Heightened risk of canine chocolate exposure at Christmas and Easter. Vet Rec. 2017;181(25):684. https://doi.org/10.1136/vr.104762
Olsnes S, Stirpe F, Sandvig K, Pihl A. Isolation and characterization of viscumin, a toxic lectin from *Viscum album* L. (mistletoe). J Biol Chem. 1982;257(22):13263–13270. https://doi.org/10.1016/S0021-9258(18)33440-9
Pascoe PJ, Ilkiw JE, Stiles J, Smith EM. Arterial hypertension associated with topical ocular use of phenylephrine in dogs. J Am Vet Med Assoc. 1994;205(11):1562–1564
Reich CF, Salcedo MC, Koenigshof AM et al. Retrospective evaluation of the clinical course and outcome following grape or raisin ingestion in dogs (2005–2014): 139 cases. J Vet Emerg Crit Care. 2020;30(1):60–65. https://doi.org/10.1111/vec.12905
Richardson JA. Management of acetaminophen and ibuprofen toxicoses in dogs and cats. J Vet Emerg Crit Care. 2000;10(4):285–291. https://doi.org/10.1111/j.1476-4431.2000.tb00013.x
Rollings CE, Francey T, Cowgill LD. Use of hemodialysis in uremic and non-uremic dogs with ethylene glycol toxicity [abstract 117]. Proceedings of the 22nd ACVIM Forum, Minneapolis 9-12 June 2004, p44
Samuelsson G. Mistletoe toxins. Syst Biol. 1973;22(4):566–569
Sanyer JL, Oehme FW, McGavin MD. Systematic treatment of ethylene glycol toxicosis in dogs. Am J Vet Res. 1973;34(4):527–534
Schell MM, Gwaltney-Brant S. OTC drugs. In: Poppenga RH, Gwaltney-Brant SM. Small animal toxicology essentials. Wiley-Blackwell; 2011: 236-238
Simpson VR. 'Ilex choke' in lambs. In Pract. 1992;14(1):39. https://doi.org/10.1136/inpract.14.1.39
Stanley SW, Langston CE. Hemodialysis in a dog with acute renal failure from currant toxicity. Can Vet J. 2008;49(1):63–66
Stuckey JA, Ramirez CJ, Berent LM, Kuroki K. Pathology in Practice. J Am Vet Med Assoc. 2012;241(10):1301–1303. https://doi.org/10.2460/javma.241.10.1301
Taketa F, Smits MR, DiBona FJ, Lessard JL. Studies on cat hemoglobin and hybrids with human hemoglobin A. Biochemistry. 1967;6(12):3809–3816. https://doi.org/10.1021/bi00864a026
Tegzes JH. Human NSAIDs (ibuprofen, naproxen). In: Hovda LR, Brutlag AG, Poppenga RH, Peterson KL, eds. Blackwell's Five minute veterinary consult clinical companion. Small animal toxicology, 2nd edition. Wiley Blackwell, Ames, Iowa; 2016: 339-346
Thrall MA, Grauer GF, Mero KN. Clinicopathologic findings in dogs and cats with ethylene glycol intoxication. J Am Vet Med Assoc. 1984;184(1):37–41
Thrall MA, Dial SM, Winder DR. Identification of calcium oxalate monohydrate crystals by X-ray diffraction in urine of ethylene glycol-intoxicated dogs. Vet Pathol. 1985;22(6):625–628. https://doi.org/10.1177/030098588502200618
Verschoor-Kirss M, Rozanski E, Rush JE. Use of esmolol for control of tachycardia in 28 dogs and cats (2003–2020). J Vet Emerg Crit Care. 2022;32(2):243–248. https://doi.org/10.1111/vec.13162
Volmer PA. How dangerous are winter and spring holiday plants to pets? Vet Med. 2002;97(12):879–884
Wegenast C. Phenylephrine ingestion in dogs. What's the harm? Vet Med. 2012;107(11):476–478
Wegenast CA, Meadows ID, Anderson RE, Southard T. Unique sensitivity of dogs to tartaric acid and implications for toxicity of grapes. JAVMA. 2021;258(7):704–707. https://doi.org/10.2460/javma.258.7.704
Wegenast CA, Meadows ID, Anderson RE, Southard T, González Barrientos CR, Wismer TA. Acute kidney injury in dogs following ingestion of cream of tartar and tamarinds and the connection to tartaric acid as the proposed toxic principle in grapes and raisins. J Vet Emerg Crit Care. 2022;32(6):812-816. https://doi.org/10.1111/vec.13234
Winek CL, Shingleton DP, Shanor SP. Ethylene and diethylene glycol toxicity. Clin Toxicol. 1978a;13(2):297–324. https://doi.org/10.3109/15563657808988239
Winek CL, Butala J, Shanor SP, Fochtman FW. Toxicology of Poinsettia. Clin Toxicol. 1978b;13(1):27–45. https://doi.org/10.3109/15563657808988227