HUMAN MEDICATIONS AS A CAUSE OF TOXICOSIS IN DOGS AND CATS

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Poisoning of dogs and cats by medications intended for human use commonly occurs as a result of owner misuse, off-label administration, or, most frequently, accidental ingestion of drugs that are inadequately stored within the household. In the United States, human pharmaceuticals account for approximately 30 per cent of reported companion animal poisonings, with comparable proportions documented across several European countries[1]. This article focuses on the classes of human medications most frequently implicated in canine and feline poisonings, and aims to provide clinicians with practical guidance for the recognition, diagnosis, and management of these cases.

Non-steroidal anti-inflammatory drugs (NSAIDs):

Exposure

NSAIDs are widely used for their analgesic, antipyretic, anti-inflammatory, and antithrombotic effects[1]. When it comes to NSAID intoxication, dogs are the most affected species and literature identifies ibuprofen as the most frequent agent followed by carprofen, aspirin (acetyl-salicylic acid), and naproxen. Cats are significantly more sensitive to these toxins due to limited glucuronyl-conjugating capacity, which prolongs drug excretion[2].

Mechanism of toxicity

NSAIDs primarily inhibit cyclooxygenase enzymes (COX-1 and COX-2), which decreases the production of prostaglandins. This deficiency impairs the gastric mucosal barrier—reducing protective mucus and bicarbonate secretion—and disrupts the autoregulation of renal blood flow. Additionally, because NSAIDs are weak acids, they can become "ion trapped" within gastric cells, leading to direct local cellular injury[2].

Clinical signs

Gastrointestinal disturbances are the most frequent signs, including anorexia, vomiting (sometimes bloody), melaena, abdominal pain, and gastric perforation[1,3]. Some studies define the threshold for ibuprofen GI toxicosis in dogs as low as >25mg/kg[3], with cats susceptible to ibuprofen toxicosis at approximately half the dose required to cause toxicity in dogs[2]. Renal impairment often manifests as acute kidney injury (AKI) and is recognised at doses of ~175mg/kg. Massive overdoses (e.g., >400mg/kg of ibuprofen in dogs) can trigger CNS signs such as ataxia, seizures, or coma, with fatal doses reported at ~600mg/kg. Dose-dependent or idiosyncratic hepatotoxicity may also occur[2,3].

Treatment and prognosis

Management involves gastric decontamination via emesis (if indicated) and multiple doses of activated charcoal to address enterohepatic recirculation[2,3]. Supportive care includes IV fluid therapy to maintain renal perfusion, use of gastroprotectants (e.g., omeprazole, sucralfate), and misoprostol (a synthetic prostaglandin)[2,4]. Severe cases may require intravenous lipid emulsion (ILE) which sequesters the drug via a 'lipid sink' within the intravascular space, reducing the amount of free drug and aiding elimination, or therapeutic plasma exchange (TPE), a blood purification technique which can remove highly protein bound toxins[1,3]. The prognosis is excellent, with a 99 per cent survival rate in dogs; however, this will vary depending on the clinical severity of the patient and treatment options available[3]. Key predictors of a positive outcome include: a time of presentation of less than 7.5 hours, a baseline creatinine below 1.5mg/dL (132mmol/L), and absence of haemoconcentration (PCV<51 per cent)[3].

Paracetamol

Exposure

Paracetamol (acetaminophen) intoxication in small animals typically occurs through accidental ingestion of improperly stored human formulations or intentional administration by owners attempting to treat fever or pain[1,5]. Cats are significantly more sensitive than other species, with clinical signs of toxicosis reported at dosages as low as 10mg/kg. Dogs are more resistant, generally showing toxicosis at oral doses around 100mg/kg[5].

Mechanism of toxicity

The drug is transformed in the liver via glucuronidation, sulfation, and cytochrome P-450-mediated oxidation. A toxic product of the P-450 pathway, N-acetyl-p-benzoquinone

imine (NAPQI), is usually detoxified by glutathione; however, overdoses deplete glutathione stores, allowing NAPQI to bind irreversibly to hepatocellular proteins and cause oxidative stress. Cats are uniquely vulnerable because they are deficient in glucuronosyltransferase activity and have capacity-limited sulfation. Furthermore, feline haemoglobin contains eight sensitive sulfhydryl groups (compared to four in other species), making their red blood cells exceptionally prone to oxidative injury[5].

Clinical signs

Signs often emerge one to four hours post-ingestion and include depression, vomiting, and oedema of the face and paws. Cats primarily suffer from red blood cell damage, leading to methaemoglobinemia (cyanosis or chocolate-coloured blood), respiratory distress, and haemoglobinuria. Whereas dogs usually develop centrilobular hepatocellular necrosis (liver failure) and icterus, though high doses can also cause methaemoglobinemia[5].

Treatment and prognosis

Management includes gastrointestinal decontamination, intravenous fluid therapy, and the administration of specific antidotes. In cats, treatment should be initiated regardless of the time elapsed since exposure, due to the prolonged half-life of paracetamol in this species[1,5].

N-acetylcysteine is indicated to reduce NAPQI binding by acting as a glutathione precursor. A loading dose of 140mg/kg is recommended, administered either orally or intravenously, followed by a maintenance dose of 70mg/kg every six hours for an additional seven treatments[5,6].

Ascorbic acid (vitamin C) may also be used as an adjunctive antidote in paracetamol intoxication because it promotes the reduction of methaemoglobin. It is typically administered at a dose of 30mg/kg every six hours for a total of seven doses[5,6].

Methylene blue is generally considered a more effective and faster treatment for methaemoglobinemia in dogs, particularly in cases with severe clinical signs. However, it has a narrow therapeutic index and may act as an oxidising agent at higher doses. For this reason, its use is considered contraindicated or requires extreme caution in cats. The recommended dose in both dogs and cats is 1–1.5mg/kg administered slowly intravenously, although repeat dosing is not advised in cats[6,7].

The prognosis for paracetamol (acetaminophen) intoxication in small animals is highly dose-dependent and varies according to the species-specific metabolic vulnerabilities[1,5]. The primary cause of death in cats is typically erythrocyte injury leading to cyanosis and respiratory distress[1].

Baclofen

Exposure

Baclofen is primarily used to prevent and treat spasticity; it is commonly prescribed for humans with conditions like multiple sclerosis, cerebral palsy, or other spinal disorders[8]. While dogs are most affected, cats are highly sensitive. Baclofen has a very narrow margin of safety; clinical signs in dogs have been reported at doses as low as 0.7mg/kg, and fatalities have occurred at 2.3mg/kg[8,9].

Mechanism of toxicity

Baclofen is a synthetic derivative of the inhibitory neurotransmitter GABA. It acts as a centrally-acting skeletal muscle relaxant by stimulating GABA-B receptors on presynaptic nerve terminals. This stimulation inhibits the release of excitatory neurotransmitters, resulting in hyperpolarisation and increased inhibitory tone throughout the central nervous system[8].

Clinical signs

Clinical signs typically emerge within 15 minutes to seven hours post-ingestion, predominantly affecting the CNS. Common signs include ataxia, miosis, vocalisation, and profound CNS depression that can progress to a comatose state. Gastrointestinal disturbances such as vomiting and hypersalivation are also frequent. Severe toxicosis often leads to life-threatening respiratory depression, apnoea, bradycardia, and seizures[8,9].

Treatment and prognosis

Treatment requires rapid gastric decontamination; however, emesis should only be induced in asymptomatic patients after a recent ingestion (<20-30mins). A single dose of activated charcoal is recommended; repeated doses are unnecessary as baclofen does not undergo enterohepatic circulation[8]. Supportive care is critical and may include mechanical ventilation for respiratory arrest, IV fluid therapy, and benzodiazepines for seizures[9].

Specific interventions such as intravenous lipid emulsion (ILE), cyproheptadine, and haemodialysis can effectively mitigate signs and enhance elimination[8]. For ILE, the most widely recommended dosing regimen consists of an initial intravenous bolus of 1.5mL/kg, followed by a continuous infusion of 15mL/kg/h for 30 minutes, additional boluses may be administered at five-minute intervals. Total ILE dose should not exceed 10 per cent of patient's total blood volume[10]. The survival rate for dogs is approximately 83.8 per cent and, with prompt, intensive, supportive care, the prognosis is often excellent even after massive ingestions[8].

Selective serotonin reuptake inhibitor (SSRI) antidepressants

Exposure

SSRI toxicosis in small animals primarily stems from the accidental ingestion of human antidepressants—such as citalopram, fluoxetine, and sertraline—or the misuse of veterinary-specific products that contain them (mainly fluoxetine). Dogs are most frequently exposed due to the growing prevalence of these prescriptions in human and veterinary medicine[11].

Mechanism of toxicity

The mechanism of toxicity involves the specific blockage of presynaptic serotonin reuptake, which leads to excessive concentrations of serotonin within the synaptic cleft[12]. This overstimulates postsynaptic 5-HT receptors, resulting in a range of clinical signs. Unlike tricyclic antidepressants, SSRIs have minimal impact on other neurotransmitters like catecholamines or histamine[11,12].

Clinical signs

Clinical signs are dose-dependent and typically manifest within one to four hours. CNS depression (lethargy, sedation) is the most frequent sign, followed by gastrointestinal upset

(vomiting, hypersalivation) and CNS stimulation (agitation, tremors)[11]. Massive ingestions may trigger serotonin syndrome, characterised by hyperthermia, muscle rigidity, ataxia, and seizures[12].

Treatment and prognosis

Treatment focuses on gastric decontamination—including emesis and activated charcoal—and supportive care. Agitation is managed with phenothiazines, while tremors and seizures require methocarbamol or benzodiazepines. Cyproheptadine (an antihistamine) serves as a specific serotonin antagonist for severe cases[12]. ILE may be used as an adjunct for refractory lipophilic drug overdoses[10]. The prognosis is excellent with prompt veterinary intervention, with studies reporting 100 per cent survival rates in treated dogs[11,12].

Antihistamines

Exposure:

Antihistamines, particularly first-generation H1-receptor antagonists like diphenhydramine, are frequently involved in small animal toxicosis due to their widespread over-the-counter use for allergies, insomnia, and motion sickness. Most exposures (over 93 per cent) occur via accidental ingestion of improperly stored human medications, though intentional administration by owners or injection is also possible[13]. While many animals remain asymptomatic, those receiving doses significantly above the therapeutic 2.2mg/kg level are at risk, with the margin of safety being relatively narrow[14].

Mechanism of toxicity

These drugs function as inverse agonists that stabilise the inactive conformation of G protein-coupled H1 receptors[1,13]. Because they are lipophilic, they readily cross the blood-brain barrier to act on the CNS. Additionally, they antagonise muscarinic, α-adrenergic, serotonergic, and dopaminergic receptors, causing a variety of adverse anticholinergic and neurologic effects[13].

Clinical signs

Signs usually manifest within 30 minutes to three hours post-exposure[1,13]. Diphenhydramine has a narrow margin of safety, with adverse effects reported at doses of as little as 1mg/kg above therapeutic levels. Most dogs exposed to doses up to four times the recommended dose (approximately 8.8–9.1mg/kg) remain asymptomatic. Mild toxicosis has been reported at a mean dose of 13.4mg/kg (approximately six times the therapeutic dose) and is characterised by lethargy and mild central nervous system depression. Moderate toxicosis occurs at a mean dose of 35.3mg/kg (roughly nine to 15 times the therapeutic dose), with clinical signs including tachycardia and hyperactivity. Severe toxicosis has been associated with mean doses of 87.4mg/kg (approximately 13 to 45 times the therapeutic dose) and may result in hyperthermia, tremors, and seizures[13].

Treatment and prognosis

Decontamination via emesis is recommended only for asymptomatic patients; if CNS signs are present, activated charcoal with a cathartic is preferred[13]. Supportive care includes IV fluids and symptom-specific management, such as using diazepam for seizures or agitation. While massive overdoses (e.g., >100mg/kg) can be fatal, the overall prognosis is excellent, as the majority of patients develop only mild signs or no signs at all[14]. Use of ILE is also described for antihistamine intoxication in humans, but there is no reference to its use in veterinary literature[15].

Cannabis

Exposure

Cannabis intoxication in pets, particularly dogs, is an increasingly frequent clinical presentation as societal perceptions and legal landscapes evolve. Exposure primarily occurs through the accidental ingestion of an owner's marijuana supply or medical cannabinoids[16]. While second-hand smoke inhalation is possible, the oral ingestion of concentrated products poses the greatest risk, as these account for roughly 66 per cent of reported animal exposures[17].

Ingestion of concentrated oils is more insidious than inhalation because peak brain levels are achieved hours later and the effects persist for a longer duration[16].

Mechanism of toxicity

The mechanism of toxicity involves the primary psychoactive constituent, Δ-9-tetrahydrocannabinol (THC), which acts upon G protein-coupled receptors known as CB1 and CB2. CB1 receptors are densely located within the CNS and are responsible for psychotropic effects by inhibiting the presynaptic release of neurotransmitters like acetylcholine, dopamine, and serotonin. THC is highly lipophilic, distributing rapidly into the brain, liver, and fat. It undergoes extensive hepatic metabolism and prominent enterohepatic recirculation, contributing to a prolonged biological half-life of approximately 30 hours[17].

Clinical signs

Clinical signs usually appear within 60 minutes of ingestion and include profound CNS depression (lethargy), ataxia, and ptyalism[16]. A hallmark clinical clue, particularly in dogs, is acute urinary incontinence, which is reported in nearly half of all cases. Other common signs include: mydriasis, bradycardia, hypothermia, and hyperesthesia, characterised by a heightened sensitivity to motion or sound[17]. Massive overdoses or exposure to synthetic cannabinoids may result in more severe stimulatory signs, such as agitation, tachycardia, tremors, and seizures[16].

Treatment and prognosis

Management is largely supportive; decontamination via emesis is often unrewarding due to THC's antiemetic properties, but activated charcoal is recommended to interrupt enterohepatic recirculation[17]. Agitated patients may require sedation with benzodiazepines, while severely poisoned animals might benefit from intravenous lipid emulsion (ILE) to bind the highly lipophilic THC. Due to a wide margin of safety, with a minimum lethal dose in dogs exceeding 3g/kg, most animals recover completely within 24 to 72 hours[16].

Summary

Human medications represent a significant and preventable source of toxicosis in companion animals, most often resulting from accidental ingestion or inappropriate owner administration.

Clinical presentations range from mild gastrointestinal upset to severe neurological, renal, hepatic, or respiratory compromise. Early recognition, prompt decontamination, and appropriate supportive or antidote therapy are critical determinants of outcome. Increased owner education and safe medication storage remain essential strategies to reduce the incidence of these potentially life-threatening intoxications in our companion animals.

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READER QUESTIONS AND ANSWERS

1. AT APPROXIMATELY WHAT IBUPROFEN DOSE IN DOGS DOES ACUTE KIDNEY INJURY BECOME A RECOGNISED RISK?

A. >25 mg/kg
B. ~75 mg/kg
C. ~175 mg/kg
D. >600 mg/kg

2. WHICH STATEMENT BEST REFLECTS A KEY TREATMENT CONSIDERATION FOR PARACETAMOL INTOXICATION IN CATS COMPARED WITH DOGS?

A. Methylene blue is the first-line treatment in cats
B. Treatment in cats should be initiated regardless of time since ingestion
C. N-acetylcysteine is contraindicated in cats
D. Activated charcoal is ineffective in cats

3. WHICH CLINICAL SIGN IS CONSIDERED A HALLMARK CLUE OF CANNABIS INTOXICATION IN DOGS?

A. Persistent vomiting
B. Acute urinary incontinence
C. Severe jaundice
D. Hyperglycaemia

4. WHY ARE REPEATED DOSES OF ACTIVATED CHARCOAL GENERALLY UNNECESSARY IN BACLOFEN TOXICOSIS?

A. Baclofen is poorly absorbed
B. Baclofen is rapidly metabolised by the liver
C. Baclofen does not undergo enterohepatic circulation
D. Baclofen binds irreversibly to plasma proteins

5. WHICH MECHANISM BEST EXPLAINS SEROTONIN SYNDROME IN SSRI TOXICOSIS?

A. Blockade of dopamine receptors
B. Excess serotonin in the synaptic cleft overstimulating 5-HT receptors
C. Increased prostaglandin synthesis
D. Direct hepatic necrosis

ANSWERS: 1C; 2B; 3B; 4C; 5B.