

COMPANION OR PET ANIMALS

Suspected anaphylaxis following intravenous amoxicillin clavulanate administration under general anaesthesia in nine dogs

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SUMMARY

Nine dogs undergoing general anaesthesia for various procedures between April and May 2015 at the University of Liverpool Small Animal Teaching Hospital experienced suspected anaphylaxis following intravenous administration of 20 mg/kg amoxicillin clavulanate. Common clinical signs, which developed during or immediately after antibiotic administration, included periorbital and muzzle oedema, erythematous wheals and moderate to severe hypotension. Each of these cases was anaesthetised by different people so a standardised intervention protocol was not employed. However, treatment generally consisted of discontinuation of antibiotic administration, anti-histamine administration, intravenous crystalloid fluid therapy and sympathomimetic drugs depending on severity of hypotension. All nine dogs recovered uneventfully from general anaesthesia although some mild dermatological signs persisted for several hours after recovery. No long-term complications have been reported. The two most severely affected cases are described in detail in this report and the rest are summarised in Table 1.

BACKGROUND

Anaphylactic and anaphylactoid reactions are a result of mast cell degranulation which may result in multisystemic effects due to release of inflammatory mediators including histamine, prostaglandin and leucotrienes. Type I anaphylactic reactions are IgE-mediated hypersensitivity reactions that occur with prior exposure to antigens, whereas anaphylactoid reactions are IgE independent, causing direct activation of mast cells and basophils with no prior immune trigger necessary. Anaphylactic and anaphylactoid reactions are clinically indistinguishable (Hepner and Castells 2003).

Most drugs given during the perioperative period have the potential to cause an anaphylactic or anaphylactoid reaction (Armitage-Chan 2010). Surveys of hypersensitivity reactions identified neuromuscular blockers, antibiotics and natural rubber latex as the most common causes of perioperative anaphylaxis in adult human beings (Mertes and others 2011, Dong and others 2012). Less commonly reported causes of anaphylactic reactions include colloids, iodinated contrast agents, opioids and local anaesthetics (Hepner and Castells 2003).

Intravenous amoxicillin clavulanate is commonly administered to cats and dogs perioperatively as

therapeutic plasma concentrations are reached more rapidly than with other routes of administration (Boothe 2001). However, there are currently no licensed intravenous preparations for animals in the UK so human preparations are utilised under the Cascade (Veterinary Medicines Directorate 2013).

This case series presents nine cases of apparent anaphylaxis after intravenous administration of amoxicillin clavulanate (1.2 g Augmentin, GlaxoSmithKline) at a dose of 20 mg/kg under general anaesthesia in dogs presented for surgery at the University of Liverpool Small Animal Teaching Hospital (SATH) between April and May 2015. Salient clinical features and treatments of the nine dogs are presented in Table 1 and the two most severely affected cases are described in detail below.

Published reports of anaphylactic reactions in veterinary patients are rare (Armitage-Chan 2010). To the authors' knowledge, there has been one previously reported case series describing anaphylactic reactions to amoxicillin clavulanate in two dogs (Bosmans and others 2014), but this is the first report of such a large case series over a relatively short time period. The authors consider the reporting of this case series important for general veterinary practitioners to increase awareness of recognising anaphylaxis under general anaesthesia to allow rapid and effective intervention.

CASE PRESENTATION**Case 1**

A one-year nine-month-old, 31.5 kg, body condition score 5 out of 9 (Laflamme 1997), neutered male American bulldog was presented with a 10 week history of left pelvic limb lameness and stifle effusion. No other concurrent conditions were noted. The dog had not improved with conservative management or with oral meloxicam (Metacam; Boehringer Ingelheim). There was a positive cranial drawer and tibial thrust under sedation for radiographs, confirming instability of the left stifle joint. Accordingly a tibial plateau levelling osteotomy was planned.

On the day of surgery, physical examination was unremarkable except for the general concerns associated with brachycephalic breeds such as increased risks associated with the airway control under anaesthesia. Serum biochemistry and haematology were not performed as it was not deemed necessary. An American Society of Anesthesiology grade of 2 was assigned to the dog (American Society of Anesthesiologists 2014).



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TABLE 1: Case details and treatment for anaphylactic reactions following intravenous amoxicillin clavulanate (Augmentin, GlaxoSmithKline) administration in nine dogs

Breed	Sex	Age	Medication(s) prior to GA	Procedure	Premedication	Induction	Maintenance	Perioperative/intraoperative drugs	Adverse reaction(s)	Treatment/interventions	Concentration of amoxicillin clavulanate given and speed of administration
Bulldog	NM	1y9m	0.1 mg/kg meloxicam PO q.24 hours	Tibial plateau levelling osteotomy	3 µg/kg medetomidine, 0.2 mg/kg methadone, 6 µg/kg acepromazine IV	1.6 mg/kg propofol and 1 mg/kg ketamine IV	Isoflurane+O ₂	10 mg/kg paracetamol IV, femoral+sciatic nerve block with 1 mg/kg levobupivacaine	Facial oedema, paw oedema and urticaria, hypotension (MAP 20 mm Hg at nadir)	0.3 mg/kg chlorphenamine IV repeated again after 1 hour. 10 mg/kg bolus Hartmann's solution, 0.1 mg/kg ephedrine IV then 0.06 mg/kg/hour phenylephrine CRI	100 mg/ml with a target administration of 2–5 minutes
Crossbreed	NF	1y5m	0.1 mg/kg meloxicam PO q.24 hours and 10 mg/kg paracetamol PO q.8 hours	Tibial tuberosity transposition	5 µg/kg medetomidine, 0.2 mg/kg methadone IM	1 mg/kg propofol and 1 mg/kg ketamine IV	Isoflurane+O ₂	1 mg/kg maropitant SC, 10 mg/kg paracetamol IV, femoral+sciatic nerve block with 1 mg/kg levobupivacaine, 1 µg/kg fentanyl IV	Periorbital+muzzle oedema with urticarial wheals (lasting four hours), tachypnoea and hypotension	0.4 mg/kg chlorphenamine IV. 10 mg/kg bolus Hartmann's solution, 0.1 mg/kg ephedrine IV then 5 µg/kg/min dopamine CRI	12 mg/ml over 20 minutes via a syringe driver
French bulldog	F	1y10m	None	Tibial tuberosity transposition	0.02 mg/kg ACP, 0.2 mg/kg methadone IM	3 mg/kg propofol and 1 mg/kg ketamine IV	Isoflurane+O ₂	10 mg/kg paracetamol IV, 0.1 mg/kg meloxicam IV, femoral+sciatic nerve block with 1 mg/kg bupivacaine	Mild periorbital oedema and erythema, tachypnoea and hypotension	0.4 mg/kg chlorphenamine IV, 0.1 mg/kg ephedrine and 7 µg/kg/min dopamine CRI	12 mg/ml over 20 minutes via a syringe driver
Crossbreed	NF	3y8m	0.1 mg/kg meloxicam PO q.24 hours	Tibial plateau levelling osteotomy	6 µg/kg medetomidine, 0.2 mg/kg methadone IM	1.7 mg/kg propofol IV	Isoflurane+O ₂	10 mg/kg paracetamol IV, 1 mg/kg omeprazole IV, femoral+sciatic nerve block with 1 mg/kg levobupivacaine	Generalised urticaria	None required	100 mg/ml with a target administration of 2–5 minutes
Border collie	F	8y8m	10 mg/kg paracetamol PO q.8 hours	MRI +hemilaminectomy	5 µg/kg medetomidine, 0.25 mg/kg methadone IM	1.2 mg/kg propofol and 0.5 mg/kg ketamine IV	Sevoflurane in MRI, Isoflurane in theatre	10 mg/kg paracetamol IV, 10–15 µg/kg/min fentanyl CRI and 50–80 µg/kg/min lidocaine CRI	Hyperthermia (38.2 -> 39.7°C) immediately post second Augmentin dose	Active cooling with use of cold air, HME removal and increased fresh gas flow	12 mg/ml over 20 minutes via a syringe driver
Rottweiler	M	1y	0.1 mg/kg meloxicam PO q.24 hours	Elbow arthroscopy	15 µg/kg medetomidine, 0.2 mg/kg methadone IM	1.1 mg/kg propofol IV	Isoflurane+O ₂	0.1 mg/kg meloxicam IV, 0.2 mg/kg morphine IA	Facial oedema for one hour post infusion	0.2 mg/kg chlorphenamine IM	12 mg/ml over 20 minutes via a syringe driver
Pug	M	5m	1 ml lactulose PO q.8 h and 12.5 mg/kg amoxicillin clavulanate PO q.12h	Portosystemic shunt attenuation	4 µg/kg medetomidine, 0.2 mg/kg methadone IM	1.3 mg/kg propofol IV	Isoflurane+O ₂	5 mg/kg/hour remifentanyl CRI	Facial oedema	0.7 mg/kg chlorphenamine IV	12 mg/ml over 20 minutes via a syringe driver
Rottweiler	NM	5y1m	10 mg/kg paracetamol PO q.8 hours (vomited after meloxicam)	Tibial plateau levelling osteotomy	5 µg/kg medetomidine, 0.2 mg/kg methadone IM	1 mg/kg propofol and 0.15 mg/kg midazolam IV	Isoflurane+O ₂	Lumbar plexus+sciatic nerve block with 1 mg/kg bupivacaine, 2 µg/kg fentanyl IV, 2 mg/kg robenacoxib SC	Periorbital oedema and generalised urticaria	0.2 mg/kg chlorphenamine IV	12 mg/ml over 20 minutes via a syringe driver
Labrador	NF	6y6m	0.1 mg/kg meloxicam PO q.24 hours	Modified Maquet procedure	4 µg/kg medetomidine, 0.2 mg/kg methadone IM	0.75 mg/kg alfaxalone and 1 mg/kg ketamine IV	Isoflurane+O ₂	Femoral+sciatic nerve block with 1 mg/kg levobupivacaine, 10 mg/kg paracetamol IV, 0.1 mg/kg meloxicam IV, 1.5 µg/kg fentanyl followed by 0.5 µg/kg/min fentanyl CRI	Periorbital oedema and mild hypotension (lowest MAP 56 mmHg)	0.3 mg/kg chlorphenamine IV	12 mg/ml over 20 minutes via a syringe driver

CRI, constant rate infusion; GA, general anaesthesia; HME, heat and moisture exchanger; IA, intra-articular; IM, intramuscular; IV, intravenous; MAP, mean arterial pressure; O₂, oxygen; PO, per os (orally); q., every; SC, subcutaneous.

A catheter was placed in the right cephalic vein and intravenous premedication with 0.2 mg/kg methadone (Comfortan, Dechra), 0.003 mg/kg medetomidine (Dormilan, Lintbells) and 0.006 mg/kg acepromazine (ACP injection, Novartis) was administered. General anaesthesia was induced with 1.6 mg/kg propofol (Propofol Plus, Abbott) and 1 mg/kg ketamine (Ketamidol, Chanelle). The trachea was intubated using a cuffed 9.0 mm endotracheal tube, which was connected to a circle breathing system. General anaesthesia was maintained with isoflurane (IsoFlo, Abbott) in 100 per cent oxygen with vapouriser settings between 1 per cent and 2 per cent. Fluid therapy with Hartmann's solution (Aquapharm-11, Animalcare) was administered at 2 ml/kg/hour. Anaesthetic monitoring included electrocardiography, pulse oximetry, capnography, oesophageal temperature probe and non-invasive oscillometric blood pressure measurement using a multiparameter machine (Datex-Ohmeda, GE Healthcare). A femoral (preiliac approach) and sciatic nerve block was performed shortly after induction using 1 mg/kg of levobupivacaine (Chirocaine 0.5 per cent, Abbott).

After the local block, 20 mg/kg amoxicillin clavulanate (Augmentin, GlaxoSmithKline) was administered intravenously over one to two minutes at a concentration of 100 mg/ml. After five minutes, the dog became hypotensive with mean arterial blood pressure (MAP) of 30 mm Hg and heart rate increased from 60 bpm to 120 bpm. Angio-oedema and facial swelling also developed. The lowest MAP recorded was 20 mm Hg, which was seen 20 minutes after administration of amoxicillin clavulanate.

Hypotension persisted despite two crystalloid boluses of 10 mg/kg over 15 minutes and two doses of 0.1 mg/kg ephedrine (Ephedrine hydrochloride, Martindale) intravenously. To prevent any further histamine release, chlorphenamine (Chlorphenamine maleate, Archimedes Pharma) at 0.3 mg/kg (Chlorphenamine maleate, Archimedes Pharma) was administered intravenously. Phenylephrine (Phenylephrine, AMDIPHARM) at 0.06 mg/kg/hour was started as a constant rate infusion (CRI) intravenously. After 10 minutes of infusion, MAP increased over 60 mm Hg and heart rate increased to 200 bpm. Concurrent Hartmann's solution bolus 5 ml/kg was given over 15 minutes as the blood pressure was still not satisfactory. Subsequently heart rate decreased to 110 bpm and MAP stabilised at 100 mm Hg. The phenylephrine CRI was discontinued after 45 minutes. A second dose of 0.3 mg/kg chlorphenamine was given intramuscularly 100 minutes after the first dose. At this point the dog was considered cardiovascularly stable with a heart rate of 110 bpm and a MAP over 85 mm Hg. The rest of the surgery and recovery were uneventful. No further doses of antibiotics were given intravenously to the patient.

Case 2

An 18-month-old, 26.4 kg, body condition score 6 out of 9, neutered female crossbreed dog was presented with a two-week history of acute onset, intermittent non-weightbearing lameness of the left hindlimb. Orthopaedic examination and radiography revealed left stifle effusion and grade 3 out of 4 medial patella luxation. Treatment was commenced with 0.1 mg/kg meloxicam orally once a day and 10 mg/kg paracetamol (Pardale-V, Dechra) orally once a day and tibial tuberosity transposition surgery was performed one week later.

Preoperative serum biochemistry and haematology were unremarkable except for mild hypokalaemia (3.2 mmol/L, reference range: 3.4–4.9 mmol/L). Physical examination on the day of surgery was unremarkable except for hypersalivation for which

the patient received 1 mg/kg maropitant (Cerenia, Zoetis) subcutaneously on admission following reported travel sickness by the owner. An American Society of Anesthesiology grade of 1 was assigned to the dog.

The dog was premedicated with 0.005 mg/kg medetomidine and 0.2 mg/kg methadone intramuscularly. A catheter was placed in the right cephalic vein and general anaesthesia was induced with 0.75 mg/kg propofol and 1 mg/kg ketamine 35 minutes after premedication. The trachea was intubated using a cuffed 9.0 mm endotracheal tube which was connected to a circle breathing system. Oxygen was administered at 4 l/minute for 10 minutes (reduced to 1 l/minute thereafter). General anaesthesia was maintained with isoflurane in 100 per cent oxygen with vapouriser settings between 1 per cent and 2 per cent. Anaesthetic monitoring included electrocardiography, pulse oximetry, capnography, oesophageal temperature probe and non-invasive oscillometric blood pressure measurement using a multiparameter machine (Datex-Ohmeda, GE Healthcare). Fluid therapy was commenced with Hartmann's solution (Aquapharm-11, Animalcare) with 27 mmol/L potassium chloride added at a rate of 4 ml/kg/hour. A femoral and sciatic nerve block was performed on the left limb with 1 mg/kg levobupivacaine using a nerve stimulator prior to surgery. Intravenous 10 mg/kg paracetamol (Perfalgan, Bristol-Myers Squibb) was administered. Then 20 mg/kg amoxicillin clavulanate (Augmentin, GlaxoSmithKline) was administered intravenously over 20 minutes at a concentration of 12 mg/ml. Immediately following the antibiotic infusion, the dog developed marked periorbital and labial oedema with erythematous wheals. The dog also developed tachypnoea (respiratory rate 40–45 bpm) and mild hypotension (MAP of 50 mm Hg). Pulse oximetry reading remained above 98 per cent. Intravenous 0.4 mg/kg chlorphenamine was administered and a bolus of 10 ml/kg Hartmann's solution was administered over 15 minutes. Intravenous 0.1 mg/kg ephedrine was administered at the same time as the fluid bolus. MAP increased to 100 mm Hg following ephedrine and fluid bolus administration. After 15 minutes, MAP decreased to 80 mmHg and steadily decreased to 70 mm Hg over 10 minutes. At this point, in order to avoid further hypotension, a CRI of 5 µg/kg/minute dopamine (Dopamine, Hospira, UK) was commenced for the remaining duration of surgery. MAP increased to 90 mm Hg and was maintained between 90 mm Hg and 100 mm Hg. Body temperature remained between 35–36°C throughout anaesthesia despite use of a heated mat (HotDog, Augustine Biomedical) and gloves filled with warm water.

OUTCOME AND FOLLOW-UP

Case 1

Once the surgery was completed, remaining signs of muzzle swelling and angio-oedema were assessed. The muzzle and skin appeared to be back to normal which was 180 minutes after the antibiotic dose was given. Visual airway examination via a laryngoscope appeared to be unremarkable at this point. As the airway did not appear compromised, the isoflurane was switched off and the dog was allowed to recover. The dog was extubated once the swallowing reflex had returned and was adequately saturating (>95 per cent) on room air. Recovery was uneventful.

Postoperative analgesia was provided with 0.2 mg/kg methadone (Comfortan, Dechra) intravenously every four hours and 0.1 mg/kg meloxicam (Metacam, Boehringer Ingelheim) orally once a day. Vital parameters (heart rate, pulse quality, respiratory rate and effort, mucous membrane colour, capillary refill

Veterinary Record Case Reports

time and oscillometric blood pressure) were closely monitored postoperatively. No further adverse reactions were noted.

Twelve hours after anaesthesia the dog was bright, alert, responsive and appeared comfortable. The facial swelling and angio-oedema had completely resolved and the dog was continued on 0.02 mg/kg buprenorphine (Vetergesic, Ceva) every eight hours instead of methadone. Within 48 hours the dog was discharged and sent home with the following oral medications: 0.1 mg/kg of meloxicam (Metacam; Boeringer Ingelheim) once a day, 3 mg/kg of tramadol (Tramadol hydrochloride, Accord Healthcare) every eight hours and 2 mg/kg marbofloxacin (Marbocyl, Vetoquinol) once a day.

Case 2

Dopamine administration was discontinued on recovery and MAP was maintained above 90 mm Hg without pharmacological intervention. No signs of respiratory distress were present after extubation and recovery was uneventful except for mild salivation. Periorbital and labial oedema resolved approximately four hours after recovery. Postoperative analgesia was provided with 0.2 mg/kg methadone intravenously every four hours and 10 mg/kg paracetamol intravenously every eight hours. The dog was discharged from hospital after 24 hours with 0.1 mg/kg meloxicam orally every 24 hours, 10 mg/kg paracetamol every 8 hours and 17 mg/kg cephalexin (Cephacare, Animalcare). Oral 0.04 mg/kg chlorphenamine (Piriton, GlaxoSmithKline) was also continued every eight hours for three days post surgery. No further complications were reported.

DISCUSSION

The authors report suspected anaphylactic reactions following administration of intravenous amoxicillin clavulanate under general anaesthesia in nine dogs between April and May 2015, with two cases described in detail above.

Anaphylaxis is a severe, life-threatening, systemic hypersensitivity reaction ([Johansson and others 2004](#)). Anaphylaxis generally occurs on re-exposure to a specific antigen, requiring release of inflammatory mediators, but can also occur upon first exposure due to cross-reactivity among many drugs whereas anaphylactoid reactions occur upon first exposure due to activation of complement, basophils and mast cells ([Hepner and Castells 2003](#)). Both reactions can occur within seconds to minutes of antigen exposure with rapid progression. Common clinical features include urticaria, angio-oedema, tachycardia, hypotension, vomiting, diarrhoea, laryngeal oedema and bronchospasm ([Shmuel and Cortes 2013](#)). Cardiovascular collapse and severe bronchoconstriction can be rapidly fatal ([Hepner and Castells 2003](#)). Full clinical histories were not available for all of the cases so it was not possible to deduce whether there had been prior exposure to penicillin-based antibiotics and if the adverse reactions were as a result of an anaphylactic or anaphylactoid reaction. As both reactions are clinically indistinguishable and treated in the same way, the distinction is not important in terms of case management ([Armitage-Chan 2010](#)). Therefore, for the remainder of this discussion, both reactions will be described using the term 'anaphylaxis'.

Anaphylactic reactions frequently occur during the perioperative period due to multiple drug administrations in close succession ([Armitage-Chan 2010](#)). As anaphylaxis is uncommon and visualisation of the anaesthetised patient is limited by surgical draping, the cardiorespiratory symptoms of anaphylaxis (hypotension, tachycardia and bronchospasm) are often the first to be detected. However, these complications may occur for different reasons, which could delay recognition of anaphylaxis as the

cause. Prompt recognition and intervention are essential in order to stabilise the patient and prevent fatalities ([Association of Anaesthetists of Great Britain and Ireland 2009](#)).

It can be difficult to determine which drug is responsible for causing an anaphylactic reaction in patients receiving multiple drugs under general anaesthesia ([Armitage-Chan 2010](#)). [Naranjo and others \(1981\)](#) developed a scale to estimate the probability of drugs causing an adverse reaction. This scale is not easy to apply to anaesthetised veterinary patients due to the required criteria. In all dogs presented in this report, clinical signs of anaphylaxis were noted either during or immediately after intravenous antibiotic administration. We conclude that antibiotic administration was most likely responsible for the adverse reactions reported.

The estimated incidence of anaphylactic reactions in human anaesthesia is between 1 in 5000 to 1 in 20000 cases ([Mills and others 2014](#)). Muscle relaxants and antibiotics are the largest triggers for perioperative anaphylaxis in human beings ([Dong and others 2012](#)). Penicillins and other β -lactam antibiotics cause approximately 70 per cent of antibiotic-induced anaphylaxis ([Association of Anaesthetists of Great Britain and Ireland 2009](#)).

Published reports of anaphylactic reactions in veterinary patients are rare ([Armitage-Chan 2010](#)). Suspected perioperative hypersensitivity reactions in dogs to gadolinium-based contrast material ([Girard and Leece 2010](#)) and buprenorphine ([Rossanese and Rigotti 2015](#)) have been reported. [Bosmans and others \(2014\)](#) reported suspected anaphylaxis in two dogs following administration of intravenous amoxicillin clavulanate under anaesthesia. This report presents nine cases of suspected perioperative anaphylaxis following administration of intravenous amoxicillin clavulanate.

The dogs in this report were treated by different anaesthetists and were affected with varying severity. Therefore, a standardised treatment protocol was not employed but the priority in all cases was to maintain cardiovascular stability, particularly in counteracting hypotension, as anaesthesia may exacerbate the hypotension induced by anaphylaxis ([Ansari and others 2012](#)).

The speed of administration of a drug may play a role in the extent of histamine release. If drugs are administered slowly in diluted solutions they are less likely to cause a noticeable response despite histamine being still measurably increased ([Guedes and others 2006](#)). In the nine cases reported here, two received 100 mg/ml intravenous amoxicillin clavulanate administered over two to five minutes. Following these two reactions, the remaining seven cases received a 12 mg/ml solution of the same antibiotic administered over 20 minutes with a syringe driver. However, of the two most severely affected cases described, one received 100 mg/ml solution and one received 12 mg/ml solution.

Seven out of the nine dogs reported were treated with chlorphenamine as part of the first line treatment following development of clinical signs of anaphylaxis. Although histamine 1 receptor antagonists are recommended in the presence of urticaria and angio-oedema ([Hepner and Castells 2003](#)), there is little evidence to support the use of antihistamines in the immediate management period in human beings ([Association of Anaesthetists of Great Britain and Ireland 2009](#)). Pretreatment with corticosteroids and antihistamines is widely practised with little evidence of benefit and they do not prevent a severe anaphylactic response ([Liccardi and others 2008](#)).

Although management of anaphylaxis should be tailored to individual patients, the general consensus in human anaesthesia is that adrenaline should be administered as early as possible

(Association of Anaesthetists of Great Britain and Ireland 2009). Adrenaline has α -agonist and β -agonist activity, resulting in vasoconstriction, bronchodilation, positive inotropic effects as well as reducing further inflammatory mediator release. Current recommendations for immediate management of anaphylaxis include removal of all potential causative agents, airway maintenance, oxygen provision, intravenous adrenaline administration and high rate intravenous fluid therapy with isotonic crystalloids (Association of Anaesthetists of Great Britain and Ireland 2009). Secondary management could consist of antihistamine and corticosteroid administration, alternative vasopressors with refractory hypotension and β -2 agonists for persistent bronchospasm (Association of Anaesthetists of Great Britain and Ireland 2009). These guidelines could easily be applicable to animals. For example, a constant rate infusion of adrenaline between 0.005 μ g/kg/minute and 0.5 μ g/kg/minute significantly improved the haemodynamic status of dogs in anaphylactic shock when compared with bolus administration (Mink and others 2004).

Adrenaline was not used in any of the cases presented here but may be beneficial as a treatment for anaphylaxis in dogs. Most dogs in this report received chlorphenamine and some received intravenous fluid boluses and/or alternative vasopressors including ephedrine, dopamine and phenylephrine depending on the severity of hypotension. All dogs recovered uneventfully with no lasting harmful effects.

Corticosteroids can be used to decrease airway swelling during anaphylactic reactions (Hepner and Castells 2003). However, they were not used in any of the dogs in this report as none developed any clinical signs suggestive of laryngeal oedema or bronchospasm and most of the affected patients were undergoing orthopaedic surgery and had already received NSAIDs which precluded their use due to increased risk of gastrointestinal ulceration (Lanza and others 2009).

In order to reduce the incidence of anaphylaxis in human beings, it has been recommended that intravenous antibiotics should be administered 20–30 minutes prior to anaesthetic induction so that the patient can be monitored closely for signs of anaphylaxis (Lockey and others 2011). Therefore, this should also be considered for veterinary patients, as current practice at the University of Liverpool SATH is to administer intravenous antibiotics shortly after induction. As a result of this case report and literature review, the authors recommend that a standard, step-by-step hospital protocol for the management of perioperative anaphylaxis should be developed and utilised.

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Contributors Both the authors were involved in all the cases presented in the case report. Each author took responsibility for one of the two main cases discussed and subsequently drafted the article together and revised it critically.

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REFERENCES

- American Society of Anesthesiologists (2014) ASA Physical Status Classification System. <https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>. Accessed March 3, 2016
- Ansari M. M., Gupta K., Bhandari S., Haleem S. (2012) Amoxicillin/clavulanic acid-induced anaphylaxis during anesthesia. *Journal of Anaesthesia and Clinical Pharmacology* 28, 531–532
- Armitage-Chan E. (2010) Anaphylaxis and anaesthesia. *Veterinary Anaesthesia and Analgesia* 37, 306–310
- Association of Anaesthetists of Great Britain and Ireland (2009) Suspected anaphylactic reactions associated with anaesthesia. *Anaesthesia* 64, 199–211
- Boothe, D. M. (2001) Principles of antimicrobial therapy. In *Small Animal Clinical Pharmacology and Therapeutics*. Ed. D. M. Boothe, 1st edn. Philadelphia: W.B. Saunders Company. pp 125–149
- Bosmans T., Melis S., De Rooster H., Van Goethem B., Defauw P., Van Soens I., Polis I. (2014) Anaphylaxis after intravenous administration of amoxicillin/clavulanic acid in two dogs under general anaesthesia. *Vlaams Diergeneeskundig Tijdschrift* 83, 14–19.
- Dong S. W., Mertes P. M., Petitpain N., Hasdenteufel F., Malinovsky J. M. (2012) Hypersensitivity reactions during anesthesia. Results from the ninth French survey (2005–2007). *Minerva Anestesiologica* 78, 868–878
- Girard N. M., Leece E. A. (2010) Suspected anaphylactoid reaction following intravenous administration of a gadolinium-based contrast agent in three dogs undergoing magnetic resonance imaging. *Veterinary Anaesthesia and Analgesia* 37, 352–356
- Guedes A. G., Rude E. P., Rider M. A. (2006) Evaluation of histamine release during constant rate infusion of morphine in dogs. *Veterinary Anaesthesia and Analgesia* 33, 28–35
- Hepner D. L., Castells M. C. (2003) Anaphylaxis During the Perioperative Period. *Anaesthesia and Analgesia* 97, 1381–1395
- Johansson S. G. O., Bieber T., Dahl R., Friedmann P. S., Lanier B. Q., Lockey R. F., Motala C., Ortega-Martell J. A., Platts-Mills T. A., Ring J., Thien F. Van Cauwenberge P., Williams H. C. (2004) Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *Journal of Allergy and Clinical Immunology* 113, 832–836
- Lafamme D. (1997) Development and validation of a body condition score system for dogs. *Canine Practice* 22, 10–15
- Lanza F. L., Chan F. K. L., Quigley E. M. M. (2009) Guidelines for prevention of NSAID-related ulcer complications - ACG practice guidelines. *The American Journal of Gastroenterology* 104, 728–738
- Liccardi G., Lobelato G., Di Florio E., Di Iorio C., Occhiochiuso L., Romano L., Savoia G., Massa R. M., D'amato G. (2008) Strategies for the prevention of asthmatic, anaphylactic and anaphylactoid reactions during the administration of anesthetics and/or contrast media. *Journal of Investigational Allergology and Clinical Immunology*, 18, 1–11
- Lockey R. F., Kaliner M. A., Simons F. E. R., Motala C., Lanier B. Q. (2011) Global Resources in Allergy (GLORIA) Module 8: Anaphylaxis. http://www.worldallergy.org/educational_programs/gloria/international/materials.php
- Mertes P. M., Alla F., Trechot P., Auroy Y., Jougle E. (2011) Anaphylaxis during anaesthesia in France: an 8-year national survey. *Journal of Allergy and Clinical Immunology* 128, 366–373
- Mills A. T. D., Sice P. J. A., Ford S. M. (2014) Anaesthesia-related anaphylaxis: investigation and follow-up. *Continuing Education in Anaesthesia, Critical Care & Pain* 14, 57–62
- Mink S. N., Simons F. E., Simons K. J., Becker A. B., Duke K. (2004) Constant infusion of epinephrine, but not bolus treatment, improves haemodynamic recovery in anaphylactic shock in dogs. *Clinical and Experimental Allergy* 11, 1776–1783
- Naranjo C. A., Busto U., Sellers E. M., Sandor P., Ruiz I., Roberts E. A., Janacek E., Domecq C., Greenblatt D. J. (1981) A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology and Therapeutics* 30, 239–245
- Rossanese M., Rigotti C. (2015) Suspect anaphylaxis following intravenous buprenorphine administration in a dog. *Veterinary Record Case Reports* 3, 1–3
- Shmuel D. L., Cortes Y. (2013) Anaphylaxis in dogs and cats. *Veterinary Emergency and Critical Care* 23, 377–394
- Veterinary Medicines Directorate (2013) *Veterinary Medicines Guidance Note No. 13* [Online] Available from <http://www.vmd.defra.gov.uk>. Accessed November 7, 2015

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