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Xenotransfusion of canine blood to cats: a review of 49 cases and their outcome.

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Abstract

Objectives: To describe the use of a xenotransfusion protocol, the outcome of xenotransfusion in recipient cats and to assess owner memory of the xenotransfusion.

Methods: Cats administered xenotransfusions in two hospitals between January 2016 and July 2018 were included. Adherence to xenotransfusion protocol, cause of anaemia, blood type, packed cell volume (PCV), transfusion volume, transfusion reactions, PCV 12 hours after transfusion and survival to discharge were recorded. Owners of surviving cats were questioned to assess if they remembered that a xenotransfusion had been performed.

Results: Forty-nine cats underwent the xenotransfusion protocol. The most common causes of anaemia were surgical blood loss (n = 17), immune-mediated haemolytic anaemia (n = 14) and neoplasia (n = 14). Median PCV before transfusion was 10%. Six cats (12%) had febrile non-haemolytic transfusion reactions. Median PCV 12 hours after transfusion was 25%. Ten cats (20%) died or were euthanased within 24 hours of xenotransfusion. A delayed haemolytic transfusion reaction occurred in 25 of 39 (64%) cats manifesting as icterus in 15 cats after a median of 1.9 days and haemolytic serum in 19 cats after a median of 2 days. Of the 18 cats alive at 1 week after discharge, 15 (83%) were still alive at a median of 173 days after xenotransfusion. All owners contacted remembered that their cats had received a xenotransfusion.

Clinical significance: Xenotransfusion of canine blood to cats is possible but haemolysis should be expected between 1 and 6 days post transfusion. Repeat transfusion with feline blood is often required.

Introduction

Xenotransfusion of canine blood to cats is a recognised veterinary technique, having been used to treat anaemic cats in emergencies when compatible feline blood was not available (Oron et al. 2017, Bovens & Gruffydd-Jones 2013). Although in vitro data suggest that transfusion of cats with dog blood could cause an acute haemolytic transfusion reaction (Euler et al. 2016, Priolo et al. 2018), no severe acute adverse reactions have been reported in cats receiving a single canine blood transfusion (Bovens & Gruffydd-Jones 2013, Klainbart et al. 2018). However, delayed haemolytic transfusion reactions are frequent and fatal anaphylaxis has been described following repeated xenotransfusion (Hessler et al. 1962, René 1968, Lautié et al. 1969, Bovens & Gruffydd-Jones 2013). Despite this, canine to feline xenotransfusion has regained popularity because of the withdrawal of Oxyglobin from the market and the relative difficulty of sourcing feline blood donors. Although there have been some recent clinical reports of successful xenotransfusion (Oron et al. 2017, Weingram et al. 2014, Klainbart et al. 2018), large studies and literature regarding the peri-transfusion time period, long-term follow-up and owner awareness of the significance of xenotransfusion are lacking.

Indications for feline transfusion with feline blood products have been well described (Barfield & Adamantos 2011), but no protocol has been described to help clinicians decide when xenotransfusion is appropriate. Reported clinical indications for xenotransfusion include previous transfusion reaction to feline blood (Euler et al. 2016), insufficient time to blood type the recipient (Oron et al. 2017), non-readily available compatible feline blood products (Oron et al. 2017, Weingram et al. 2014, Euler et al. 2016, Klainbart et al. 2018), financial constraints (Weingram et al. 2014, Klainbart et al. 2018) and life-threatening emergencies (Oron et al. 2017, Euler et al. 2016, Klainbart et al. 2018).

The aims of this study were to describe a xenotransfusion protocol and assess adherence to this protocol, to describe the clinical situations in which xenotransfusion was used, to determine crossmatch compatibility between canine donors and feline recipients and its relevance, to describe the short- and long-term

outcomes of cats administered a xenotransfusion, and to determine whether owners remembered that their cat had received a xenotransfusion and that repeat xenotransfusion was contraindicated.

Material and methods:

This was a prospective observational study. All cats receiving a xenotransfusion at two university teaching hospitals between January 2016 and July 2018 were enrolled in the study. In case of unavailability of appropriate feline blood products or donors, a xenotransfusion protocol was applied, that required fulfilment of set criteria (document 1, Supporting Information). If the clinicians involved in the case considered the cat likely to die within 6 hours without blood product administration due to the severity of their clinical signs they were considered potential candidates for transfusion. In the absence of suitable feline blood products, the clinicians then had to ensure the cat had never been administered dog blood previously and obtain informed consent for xenotransfusion from the owners. A member of the hospital Transfusion Medicine Service had to review the case and agree to the patient's suitability for xenotransfusion. The owners were then informed of the risks of sudden death, rapid haemolysis and likely requirement for a subsequent transfusion with feline blood products. They were also informed that xenotransfusion could not be repeated. For the cats that were discharged, written instructions that reiterated this information were given to the owners.

Adherence to the xenotransfusion protocol, recipient signalment, pre-transfusion PCV, cause of anaemia, xenotransfusion volume and survival to discharge were recorded. Blood type, PCV after transfusion and creatinine before and after transfusion were recorded when clinically possible. The recipients and donors were typed using a commercial immunochromatographic test (respectively Lab test QuickTest A + B and dog erythrocyte antigen (DEA) 1, Alvedia, Limonest, France). One millilitre of packed red blood cells per kilogram was transfused for every percentage point of PCV increase desired, generally aiming for a PCV after transfusion of 25%, although the decision was left to the attending clinician. When sufficient recipient blood was available, both major and minor crossmatches were performed. Crossmatches were performed by trained personnel using washed erythrocytes and a standard slide crossmatch technique as previously described (Tocci & Ewing

2009) although, due to the emergent situations in which the xenotransfusions were performed, crossmatch results were not available before administration.

A standard transfusion monitoring sheet was used during the transfusion, to record temperature, pulse, respiration rate, mucous membrane colour, capillary refill time, urine colour (if applicable), appearance and demeanour at least hourly starting with a baseline before starting the transfusion. The transfusion was administered via syringe and in-line filter (Hemo-Nate) on a syringe driver at 1 mL/kg/hour for the first 30 minutes and then increased to allow each syringe of blood to be given over no longer than 6 hours, with further syringes being administered as required to provide the volume desired by the attending clinician. After the end of the transfusion the patient was monitored as required by the attending clinician with a minimum of once daily full physical examination including body temperature, pulse and respiration assessment until discharge from hospital. Recipient PCV was measured 12 hours after the end of the xenotransfusion when possible. Acute development of urticaria, angioedema or pruritus during the transfusion was recorded as a suspected allergic reaction. If a recipient had an increase in rectal temperature of greater than 1°C from baseline at the beginning of the transfusion, non-pathological reasons including external warming and recovery from general anaesthesia were considered. If no such reason was found, then recipient serum and packed red blood cell supernatant (obtained via centrifugation of haematocrit tubes) were checked for haemolysis (as was recipient urine, if available) and, if present, a haemolytic transfusion reaction was suspected. If absent, the blood product was cytologically examined for bacteria and cultured. If abnormalities were noted the transfusion was stopped and a suspected septic transfusion was recorded. If neither a septic nor an acute haemolytic transfusion reaction were suspected, then a febrile non-haemolytic transfusion reaction was recorded. In these cases, the transfusion was stopped temporarily, the patient was monitored and the transfusion was restarted if the temperature normalised. Transfusion-associated circulatory overload was recorded if a cat developed respiratory distress (defined as increased effort and respiratory rate >40 breaths per minute) during or within 24 hours after the transfusion, echocardiography performed by the attending clinician demonstrated an enlarged left atrium (with a left atrium-to-aorta ratio >1.5) and the

respiratory distress resolved with treatment with furosemide. Other causes of respiratory distress, including transfusion-related acute lung injury were investigated if transfusion-related circulatory overload was not diagnosed. A delayed haemolytic transfusion reaction was recorded if a patient developed haemolysed serum and/or haemoglobinuria, an increase in total bilirubin or bilirubinuria and concurrent decrease in PCV more than 24 hours after transfusion that could not be explained by any concurrent disease process. Serum creatinine concentration was measured at approximately 24 hours and 5 days after transfusion (deemed the time when a delayed haemolytic transfusion reaction was likely) at the attending clinician's discretion, to assess for acute kidney injury secondary to the haemoglobinaemia caused by a haemolytic reaction.

For cats that survived to discharge, referring veterinary practices were contacted and asked for an update on the cats in the study. For those that were still alive, owners were contacted with a standardised telephone questionnaire (document 2, Supporting Information) incorporating five set questions with progression to the next question only if xenotransfusion was not mentioned in the previous answer. The number of questions (from 1 to 5) asked to prompt mention of xenotransfusion was recorded. The owners were then asked if any warning had been given to them regarding future treatments and also if their cat had fully recovered from its disease.

Ethical approval was granted for this study by the university teaching hospital Ethics and Welfare committee (ref: SR2017-1162).

Statistical analysis

Statistical analyses were performed using the statistical software Tanagra version 1.4.50 (Lyon, France, 2003). Data were analysed and presented as median ± range. Data were assessed for normality using the Shapiro-Wilk test. Paired t tests were used to examine whether creatinine values were significantly different before and after xenotransfusion and chi squared test or Fisher's exact test was used to assess the

association of the results of crossmatch with transfusion reactions. Differences were considered significant at a P value <0.05.

Results

Population

Forty-nine cats received a xenotransfusion between January 2016 and July 2018 and were included in this study. The protocol was followed in all cases. Twenty-three were neutered females, three were entire females and 23 were neutered males. Twenty-eight were domestic shorthair cats, four were domestic long hairs, four were British shorthairs, three were Bengals, two were Persians, two were Siamese, two were ragdolls and one each was Burmese, Chantilly-Tiffany, Tonkinese and Abyssinian. Median age was 8.0 years old [range 0.6 to 16.5 years].

The most common reasons for anaemia were surgical blood loss (17 of 49, 34.7%) with the xenotransfusion either given intra- (five of 17 cases) or post-operatively (12 of 17 cases), immune-mediated haemolytic anaemia (IMHA, eight regenerative IMHA and six non-regenerative; 14 of 49, 28.6%) and neoplasia (14 of 49, 28.6%). There was one case each of inflammatory bowel disease, coagulopathy of undetermined cause, acute kidney injury and oral ulcerations (feline eosinophilic granuloma). Nine cats (nine of 49, 18.4%) had received a feline blood transfusion of feline packed red blood cells before the xenotransfusion.

Blood tests

Thirty cats were blood type A (61.2%), 14 were type B (28.6%) and three (6.1%) were type AB. Two cats were not blood typed (one was administered a xenotransfusion during cardiopulmonary resuscitation and one was deemed at risk of imminent cardiopulmonary arrest and died within 2 hours of starting the xenotransfusion). Median PCV before transfusion was 10% [Range 4 to 16%].

Crossmatches between the feline recipients and the donated dog blood were performed in 29 cases. Major crossmatches were incompatible in 20 of 29 cases (69.0%) and minor crossmatches were incompatible in eight of 26 cases (30.8%) (with three minor crossmatches being non-interpretable due to the recipient being saline agglutination positive). Both major and minor crossmatches were incompatible in six of 29 cases (20.7%) and both crossmatches were compatible in seven of 29 cases (24.1%). Major and minor crossmatches only were incompatible in 14 of 29 cases (48.3%) and two of 29 cases (6.9%), respectively.

Transfusion

Thirty-five cats (35 of 49, 71.4%) received DEA-1-positive packed red blood cells and 14 received DEA-1-negative packed red blood cells (14 of 49, 28.6%). The median volume transfused was 14.6 mL/kg [range 2.6 to 28.0 mL/kg]. Six cats (six of 49, 12.2%) had a febrile non-haemolytic transfusion reaction during the xenotransfusion. For two of these cats, the xenotransfusion was stopped (for 20 minutes in one case and 2 hours in the other) and was then continued when their temperature normalised. For one cat, the reaction occurred towards the end of the transfusion and it was not restarted because the temperature remained elevated. The occurrence of febrile non-haemolytic transfusion reaction was not significantly different between cats with a compatible or incompatible crossmatch ($P = 0.75$). No other acute transfusion reactions were noted.

Short-term outcome

PCV after transfusion was obtained in 39 cases. Five cats died or were euthanased during the xenotransfusion (one was undergoing cardiopulmonary resuscitation when the xenotransfusion started, two were euthanased due to the results of diagnostics that were performed during this time (biliary carcinoma and pulmonary thromboembolism) and two did not stabilise, leading to the recommendation for euthanasia). Three cats were euthanased before the 12-hour PCV check because of poor prognosis associated with the primary disease (gastro-intestinal large granular lymphocytic lymphoma, ulcerative gastropathy and subcutaneous haemangiosarcoma) and two cats survived but did not have a PCV reported 12 hours after the

xenotransfusion. Median PCV was 25% [range 10 to 50%], when evaluated at a median of 12 hours [range 4 to 14 hours] after xenotransfusion. Two cats (one with gastric lymphoma and one with diffuse splenic and hepatic neoplasia) went home between 12 and 24 hours after xenotransfusion to be euthanased by their referring veterinary surgeons.

Of the remaining 39 patients (39 of 49), a delayed haemolytic transfusion reaction occurred in 25. Haemolytic serum was noted in 19 of 25 cats after a median of 2 days [range 1 to 6 days], and icterus or icteric serum in 15 of 25 cats after a median of 1.9 days [range 1 to 6 days]. Nine cats had both haemolysed and icteric serum. Of the 14 cats without delayed haemolytic transfusion reaction, nine died or were discharged from the hospital for euthanasia at home due to their underlying disease within 48 hours of the end of the xenotransfusion. The remaining five were hospitalised for at least 6 days after xenotransfusion without developing overt haemolysis, but one of them did receive a feline packed red blood cell transfusion 3 days later. Of the 25 cats that developed a delayed haemolytic transfusion reaction, 14 (of 25) were discharged from the hospital, among which one was discharged within 48 hours after xenotransfusion for euthanasia at home and two of them died or were euthanased within a week. Overall, 14 cats (of 39) were administered a cat blood transfusion after a median of 4 days [range 1 to 6 days].

Of the 20 cats with incompatible major crossmatch, 12 (12, 60%) developed a delayed haemolytic transfusion reaction compared to three out of nine cats (33.3%) that were major crossmatch compatible. Two of the eight cats with incompatible minor crossmatch and 10 of 18 (55.6%) cats with compatible crossmatch developed a delayed haemolytic transfusion reaction (Table 1). Major or minor crossmatch did not apparently differ in the occurrence of delayed haemolytic transfusion reaction (respectively $P = 0.24$ and $P = 0.28$). Delayed haemolytic transfusion reactions occurred at a median of 2 days [range 1 to 6 days] after xenotransfusion in patients with incompatible major crossmatch and 1 day [range 1 to 1.5 days] in cats that received compatible blood on major crossmatch. Incompatibly on major crossmatch did not significantly affect the time between xenotransfusion and development of a delayed haemolytic transfusion reaction ($P = 0.26$). However, time between

xenotransfusion and discharge for the crossmatched patients was a median of 2 days [range 0 to 16 days] and 21 of 29 (72.4%) patients were discharged or died before 6 days after xenotransfusion.

Twenty-three cats of the original population of 49 (46.9%) were discharged from the hospital. Five of these 23 cats (21.7%) died or were euthanased within a week after xenotransfusion: two were diagnosed with leukaemia, two with hepatic and splenic neoplasia and one with gastric lymphoma. Of the remaining 18 cats which survived more than 1 week after xenotransfusion, 11 (61.1%) had had a delayed haemolytic transfusion reaction. However, five of seven cats that did not develop a delayed haemolytic transfusion reaction were discharged before 7 days after xenotransfusion. Ten of the 18 surviving cats (55.6%) were administered a cat blood transfusion after a median of 4 days [range 2 to 6] after xenotransfusion.

Creatinine

Creatinine measurements before and 1 day after xenotransfusion were available for 20 cats and at approximately 5 days after xenotransfusion (median 4 days [range 2 to 10]) for 13 cats (Table 2). Median value was 142 µmol/L [range 54 to 800 µmol/L] before and 108 µmol/L [range 52 to 824 µmol/L] at 1 day and 100 µmol/L [range 50 to 1099 µmol/L] at approximately 5 days after xenotransfusion.

Urine specific gravity was available for 12 cases before xenotransfusion. Among the 22 cats for which a creatinine measurement was recorded before xenotransfusion, seven were azotaemic (creatinine >140 µmol/L). Six of these azotaemic cats had a urine specific gravity of less than 1.035 (Table 2).

Long-term outcome

Eighteen cats (18 of 49, 36.7%) were still alive 7 days after xenotransfusion. Of these 18, nine (50.0%) received a xenotransfusion for surgical blood loss, six (33.3%) for IMHA, two for neoplasia (11.1%) and one for inflammatory bowel disease (5.6%). One cat, diagnosed with mesenteric and splenic large cell lymphoma,

was euthanased 10 days after xenotransfusion due to lack of response to chemotherapy, and one was euthanased 184 days after xenotransfusion due to a relapse of IMHA.

All surviving cats' owners were contacted, at a median of 173 days [range 157 to 570 days] after xenotransfusion. One cat was lost to follow-up, so 15 owners were questioned. A median of two questions [range 1 to 5] was necessary for the owners to mention the xenotransfusion, with all owners stating that their cat had received a xenotransfusion by question 5. Nine owners (of 15, 60.0%) remembered their cat could not receive a repeat xenotransfusion. Eight cats were reported to be recovered from their primary disease, all of which had received a xenotransfusion for surgical blood loss.

Discussion

This study is the first to examine the long-term outcome of a large number of clinical feline recipients of canine blood. The most common reason for xenotransfusion administration was surgical blood loss. The urgency and unpredictability of these situations explains the use of xenotransfusions, because it was not possible to find a cat donor sufficiently rapidly. The hospitals involved in this study do not have access to in-house donors or a national cat blood bank (as is common for many veterinary surgeons around the world), and so organising a feline donation relies on contacting an owner with a cat on the donation list and arranging a donation for a mutually convenient time which can be many hours or even days after the urgent need for blood has arisen (Doolin et al. 2017).

The high level of adherence to the protocol minimised potential unnecessary use of xenotransfusion and suggests that xenotransfusions were only used in urgent situations where the cat was thought likely to die within the next 6 hours. Canine to feline xenotransfusion described previously also mainly involved life-threatening situations (Oron et al. 2017, Euler et al. 2016, Klainbart et al. 2018); although lack of affordability of cat blood is also a suggested indication (Weingram et al. 2014, Klainbart et al. 2018). The protocol described in this study could be used by any clinician to help decide whether a xenotransfusion is

appropriate, with objective parameters and specific indications. In the protocol described here, the attending clinician needed to review the case with a member of the Transfusion Medicine Service and both had to agree to the patient's suitability for xenotransfusion, but in primary care practice this step could be substituted with a colleague, meaning that each case is carefully considered for suitability.

The proportion of cats developing a febrile non-haemolytic transfusion reaction in this study was comparable to that reported in a previous smaller study of xenotransfusions in which 10% (two of 20) of cats developed hyperthermia, although it was unclear whether other possible transfusion reactions that could cause an elevated temperature had been excluded (René 1968). Interestingly, similar febrile non-haemolytic transfusion reaction rates of 13 and 29%, for crossmatch compatible and non-crossmatched blood respectively, were reported in a recent prospective study of cat blood administration to cats (Sylvane et al. 2018) but other studies have a much lower rates of 2.2 to 2.5% (Castellanos et al. 2004, Weingart et al. 2004, Klaser et al. 2005, Roux et al. 2008, McClosky et al. 2018). Given the latter studies were retrospective or surveys, it is possible that febrile non-haemolytic transfusion reactions were overlooked and that there is little difference in febrile non-haemolytic transfusion reaction rate between cat and dog blood administration to cats. In a recent study (Sylvane et al. 2018), febrile non-haemolytic transfusion reactions did not appear to be associated with crossmatch incompatibilities between donor and recipient blood; our findings were similar, although further studies with more crossmatched cases would be required for confirmation.

Two cases were euthanased during xenotransfusion because they failed to stabilise and, although the signs they displayed were not suggestive of an acute transfusion reaction, they could have been secondary to the xenotransfusion and were difficult to interpret in a critical patient.

Our results may under-report the incidence of delayed haemolytic transfusion reaction because nine of 14 cats in which it was not detected died or were discharged from hospital within 48 hours of the

xenotransfusion. Furthermore, of the remaining five cats without signs of a febrile non-haemolytic transfusion reaction (which were hospitalised for at least 6 days post-xenotransfusion), one cat diagnosed with IMHA was administered a cat blood transfusion 3 days after xenotransfusion, which suggests haemolysis might have been overlooked or that haemolysed serum or haemoglobinuria was not displayed by this patient.

Delayed haemolytic transfusion reactions occurred after a mean of 2.3 days but there was evidence of haemolysis as early as 1 day after the end of xenotransfusion administration in nine cases. The latest day that evidence of haemolysis was first apparent was 6 days after xenotransfusion. Incompatibilities between donors and recipients did not predict the development of a delayed haemolytic transfusion reaction or influence the time between the xenotransfusion and the occurrence of a delayed haemolytic transfusion reaction although in vitro results of major crossmatch between a canine donor and a feline recipient suggest a potential high risk of acute transfusion reactions (Priolo et al. 2018). Haemolysis following xenotransfusion can therefore occur much earlier than suggested by previous studies in which haemolysis was reported to occur at day 4 to 7 (Bovens & Gruffydd-Jones 2013).

Creatinine monitoring was only available in a limited number of cases but showed azotaemia was frequent after xenotransfusion. Most of the azotaemic cats had a urine specific gravity of less than 1.035 suggesting renal azotaemia. Unfortunately, specific gravity was not measured concurrent with creatinine measurement after xenotransfusion and so whether any azotaemia detected was genuinely renal in origin cannot be determined, although by this point the cats had been hospitalised for several days and were monitored for hydration or volume deficits and should have been normally hydrated. No significant difference in creatinine levels was apparent after xenotransfusion which would suggest that marked acute kidney injury did not occur secondary to haemoglobinaemia due to a delayed haemolytic transfusion reaction. However, assessment of kidney injury with creatinine alone is suboptimal. Ideally, concurrent measurement of urine

specific gravity and sediment analysis would have been performed as recommended by the IRIS acute kidney injury guidelines (Cowgill 2012).

All the non-surviving cats in this study died or were euthanased because of their underlying disease process with long-term follow-up showing no evidence of complications of xenotransfusion after the delayed haemolytic transfusion reactions at 1 to 6 days. It is impossible to state definitively that the xenotransfusions did not contribute to mortality in this study, but the reasons for death or euthanasia given by the attending clinicians described underlying disease process progression.

Owners received verbal instructions when they gave consent for the xenotransfusion and a written warning was handed to them with their discharge because it has been shown to increase retention of information in human medicine (Johnson et al. 2003). Follow-up showed that owners generally remembered that their cat had had a xenotransfusion, but that they were less reliably aware that a repeat xenotransfusion was not advisable. Strict protocols and excellent communication between veterinary practices therefore need to be in place to make sure that repeat xenotransfusion is avoided.

Although there are clearly concerns about the use of xenotransfusion, most prominently the high frequency of delayed haemolytic transfusion reactions meaning that many cats in this study required a further feline blood transfusion and the previously described risk of death with repeat transfusion (Bovens & Gruffydd-Jones 2013), there can be benefits to xenotransfusion administration in certain circumstances. First, in emergencies, the period between a xenotransfusion and likely delayed haemolytic transfusion reaction provides the clinician with the opportunity to source compatible feline blood if necessary. In cats with adequate regeneration, a second transfusion of feline blood may not be required, as was the case in seven of 18 cats that survived over a week after discharge. Secondly, administration of a xenotransfusion may allow further investigations to be pursued, if the prognosis of the cat is expected to be poor or for owners to have more time to consider their options, including euthanasia in terminal cases. Clinicians may also have

ethical concerns about using feline blood products in patients with a guarded prognosis due to the generally accepted greater impact donation has on cats compared to dogs (Taylor & Humm 2016). This could well have been relevant in this study given 31 of 49 cats had died by day 7 after xenotransfusion.

There were several limitations to this study. Although well defined, identification of acute and delayed transfusion reactions required appropriate monitoring. A standardised protocol was used during the xenotransfusion, to maximise recognition of acute transfusion reactions. However, delayed transfusion reactions could have been overlooked because some patients died or were discharged from the hospital before the 7 days previously reported as the latest time a delayed haemolytic transfusion reaction could occur after xenotransfusion (Bovens & Gruffydd-Jones 2013). Also, as this was a clinical study, blood sampling allowing identification of icteric or haemolysed serum did not occur in a standardised fashion, although it was generally performed daily. The minimum monitoring was a once daily full physical examination; however, these cases were critically ill initially and received very close monitoring during this critical period in all cases.

Additionally, some tests were only performed on a subset of our cohort (crossmatches and creatinine measurements). These tests were not imposed in the protocol due to the limited availability of blood in these critical patients and were left at the clinician's discretion. Therefore, further studies with more cases are required to investigate the trends outlined here.

It is also worth noting that there are no standardised guidelines regarding transfusion reactions in veterinary medicine. Therefore, a delayed haemolytic transfusion reaction was diagnosed in this study using compatible clinical signs. In human medicine, delayed haemolytic transfusion reaction is classed as definitive by the Centres of Disease Control and Prevention when development of novel antibodies can be demonstrated after transfusion in conjunction with a rapid decrease in PCV back to pre-transfusion levels (U.S. Centers for Disease Control and Prevention 2018). Antibodies were not measured in our cases, but the clinical signs seen

in the patients were compatible with a delayed haemolytic transfusion or haemolysis (rapid decrease in PCV and development of jaundice which self-resolves) as described by the CDC (U.S. Centers for Disease Control and Prevention 2018).

In conclusion, this study demonstrates that xenotransfusion of canine blood to cats is a potentially life-saving procedure in emergencies when feline blood products are not available. No acute adverse reactions other than febrile non-haemolytic transfusion reactions (which are short-lived and self-limiting) were seen in this study. Delayed haemolytic transfusion reactions are to be expected between 1 and 6 days after xenotransfusion. Close monitoring of cats that receive a xenotransfusion is therefore advised because feline blood products may be rapidly required.

The protocol used here was followed by clinicians and could be easily adapted for use in other clinics. For some veterinarians the need for the administration of a xenotransfusion will never arise, but for those working without access to feline blood banks or stored feline blood products, this information should increase confidence that xenotransfusion can be performed. It also allows understanding of the adverse effects that can arise, meaning owners can be fully informed and appropriate patient monitoring performed. Finally, our study shows that the long-term outcome for these cats appears to be associated with their primary disease and those who recover from this have no notable adverse effects that could be directly attributed to xenotransfusion.

Table 1. Occurrence of reaction depending on crossmatch results

	Total	FNHTR	Haemolysis	Icterus	Icterus + haemolysis	No haemolysis	No icterus	No icterus or haemolysis	Discharge/Death after (median in days post transfusion)
Major and minor cross matches incompatible	6	2	0	2	0	3	1	1	2 [0 to 3]
Major cross match incompatible	14	2	8	6	4	5	4	2	2.5 [0 to 16]
Minor cross match incompatible	2	0	0	0	0	2	2	2	5 [0 to 10]
Compatible minor and major cross matches	7	1	3	1	1	2	3	2	2.5 [0 to 7]
FNHTR Febrile non haemolytic transfusion reaction									

384 Table 2. Creatinine measurements pre and post-xenotransfusion

	Creatinine pre-xenotransfusion (µmol/L)	USG	Creatinine 1-day post-xenotransfusion (µmol/L)	Creatinine post-xenotransfusion (µmol/L)	Number of days post-xenotransfusion measurement taken
Cat 1	**270**		**238**	**1099**	4
Cat 2	**726**	1.011	**824**		
Cat 3	**219**	1.026	**228**	**603**	5
Cat 4	**800**	1.014	**741**	**671**	5
Cat 5	69		125		
Cat 6	**155**		**172**		
Cat 7	57		68	50	2
Cat 8	**252**		**321**		
Cat 9	73	1.032	64	69	3
Cat 10	**339**	1.02	114	68	6
Cat 11	74	1.023	61		
Cat 12	**144**	1.038	108	100	2
Cat 13	94	1.018	98	79	6
Cat 14	66		97		
Cat 15	**155**	1.012	**214**		
Cat 16	**142**		96		
Cat 17	**181**		69	75	2
Cat 18	**455**	1.018	**242**	**212**	2
Cat 19	81		64	**181**	2
Cat 20	76	1.032	52		
Cat 21	88			57	10
Cat 22	54	1.025		120	4

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