

# Influence of cross-match on posttransfusion packed cell volume in feline packed red blood cell transfusion

Joel G. Weltman, DVM; Daniel J. Fletcher, PhD, DVM, DACVECC and Catherine Rogers, DVM, DACVECC

## Abstract

**Objective** – To evaluate the influence of major cross-match on transfusion efficacy based on the change in PCV following packed red blood cell (pRBC) administration in cats.

**Design** – Retrospective study from January 2000 to December 2010.

**Setting** – University Teaching Hospital.

**Animals** – Two hundred nine cats received 233 type-specific pRBC transfusions as treatment for anemia. Forty-three transfusions were cross-match compatible and 190 were not screened with cross-match.

**Interventions** – Pretransfusion major cross-match.

**Measurements and Main Results** – Signalment, body weight, dosage of pRBC transfusion, pretransfusion PCV, posttransfusion PCV, IV fluid volumes administered between the measurement of the pretransfusion PCV and posttransfusion PCV, time delay between pretransfusion PCV measurement and transfusion administration, time between administration of transfusion and posttransfusion PCV measurement, and major cross-match testing data were extracted from the medical records of cats receiving pRBC transfusions and were evaluated for their influence on posttransfusion PCV scaled to dose of pRBC administered. The mean pretransfusion PCV was significantly lower for cross-match compatible transfusions ( $13.7 \pm 4.2\%$ ) compared to noncross-matched transfusions ( $16.1 \pm 4.5\%$ ; independent samples *t*-test,  $P < 0.0001$ ). The PCV increase posttransfusion scaled by dose was significantly greater for cross-match compatible transfusions ( $1.02 \pm 0.51\%/mL/kg$ ) than for noncross-matched transfusions ( $0.74 \pm 0.65\%/mL/kg$ ; independent samples *t*-test,  $P = 0.0093$ ). Of age, dose of pRBCs, cross-match status, reason for transfusion, pretransfusion PCV, and dose of IV fluids administered between the pretransfusion and posttransfusion PCV, only pRBC dose, cross-match status, and pretransfusion PCV were independent predictors of change in PCV with transfusion on multiple regression analysis (coefficient = 0.507,  $P < 0.0001$ ; coefficient = 1.64,  $P = 0.041$ ; coefficient =  $-0.235$ ,  $P = 0.0009$ , respectively).

**Conclusions** – In this retrospective study, administration of type-specific, cross-match compatible pRBC transfusions resulted in significantly greater increases in the posttransfusion PCV when compared to administration of typed, noncross-matched pRBCs. Future prospective studies evaluating the effect of cross-match on transfusion efficacy in cats are warranted.

(*J Vet Emerg Crit Care* 2014; 24(4): 429–436) doi: 10.1111/vec.12204

**Keywords:** anemia, efficacy, resuscitation

## Introduction

Feline blood transfusion has become more commonplace over the past 10 years, likely due to increasing availability of species-specific blood components.<sup>1,2</sup> The presence

From the Department of Clinical Sciences, Cornell University, College of Veterinary Medicine, Ithaca, NY 14853.

Presented in part as an abstract at the International Veterinary Emergency and Critical Care Symposium, San Antonio, TX, September 8–12, 2012.

Address correspondence and reprint requests to Dr. Daniel J. Fletcher, Cornell University College of Veterinary Medicine, DCS Box 31, Ithaca, NY 14853. Email: dan.fletcher@cornell.edu  
 Submitted October 31, 2012; Accepted May 26, 2014.

## Abbreviations

CM+	cross-matched, type-specific transfusion
CM–	noncross-matched, type-specific transfusion
pRBC	packed red blood cell

of alloantibodies against RBC antigens has been well established in feline blood, and alloantibodies have been identified in kittens as young as 2 months old.<sup>3–5</sup> Alloantibodies are thought to arise from exposure to structural epitopes to endogenous RBC antigens.<sup>3</sup> Common

antigens present on feline RBCs have been identified and labeled using the AB blood group system. The prevalence of these antigens has been evaluated in Australia, Austria, Brazil, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Portugal, Spain, Switzerland, Turkey, the United Kingdom, and the United States of America.<sup>2-4,6-14</sup>

Previous reports have advocated the use of type-specific blood in cats naïve to blood transfusion and recommend the use of cross-match only in previously transfused cats.<sup>1,2,15,16</sup> In 2007, Weinstein *et al*<sup>5</sup> documented a novel RBC antigen in a group of domestic shorthair cats and labeled it *Mik* antigen. Four type A recipient cats (all *Mik* negative) were reported to have incompatible cross-match results against 30 *Mik*-positive type A donor cats.<sup>5</sup> The authors also described an acute, hemolytic transfusion reaction following administration of type-specific RBCs to one *Mik*-negative recipient.<sup>5</sup> The results of this report suggest a high prevalence of naturally occurring alloantibodies in the *Mik*-negative recipient cats against the *Mik* antigen expressed by the donor cats. These alloantibodies were not identified through traditional AB blood typing.

Although the prevalence of alloantibodies other than those against AB antigen have yet to be established, it is possible that such alloantibodies, such as those against the *Mik* antigen, could lead to transfusion reactions or decreased efficacy of packed red blood cell (pRBC) transfusions. Pretransfusion major cross-matching could potentially identify incompatibilities due to these alloantibodies. The purpose of this retrospective study was to investigate the influence of cross-matching on the efficacy of feline pRBC transfusion measured by the change in recipient PCV after transfusion. Our hypothesis was that type-specific, cross-match compatible transfusions of pRBCs would yield significantly higher PCV increases posttransfusion per volume of pRBCs transfused than type-specific, noncross-matched transfusions.

## Materials and Methods

### Data collection

Cats receiving pRBC transfusions from January 1, 2000 to December 31, 2010 were identified. Information obtained from all records included age, sex, breed, weight, reason for transfusion, dose of intravenous fluid administered between the measurement of pretransfusion and posttransfusion PCV (mL/kg), transfusion dose (mL/kg), pretransfusion PCV, length of time between pretransfusion PCV measurement and pRBC administration, posttransfusion PCV, and length of time between pRBC administration and posttransfusion PCV measurement. Patients receiving type-specific transfusions identified as compatible by major cross-match and

cats for which incompatible pRBCs units were identified by cross-matching were recorded. Patients receiving a minor cross-match as a part of pretransfusion screening were also recorded. The reason for transfusion was assigned to one of the following groups based on data extracted from the medical record: (1) blood loss, (2) decreased production, and (3) destruction. This classification scheme was chosen based on previous literature.<sup>1,2</sup> Several transfusions were administered as a result of multiple causes, and were therefore coded with all applicable causes. Patients were excluded from analysis if we were unable to retrieve pretransfusion PCV, posttransfusion PCV, or dose of pRBC transfusion from their medical record.

### pRBC sources

Packed red blood cells were obtained from either client owned cats participating in our institution's blood banking program or from one of two commercial blood banks.<sup>a,b</sup>

Screening for blood donor cats at our institution prior to 2009 included physical examination, complete blood count, serum biochemistry analysis, urinalysis, feline blood typing, and infectious disease testing including feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis, and toxoplasmosis. After 2009, feline blood donor screening by our hospital for client owned blood donors included a physical examination, complete blood count, serum biochemistry analysis, urinalysis, feline blood typing, echocardiogram, and infectious disease testing including feline leukemia virus, feline immunodeficiency virus, heartworm, *Mycoplasma haemofelis*, *Mycoplasma haemominutum*, and *Bartonella*. Although the age of each individual pRBC unit was not available in the medical records, all pRBCs were administered within 35 days of collection if obtained from a commercial blood bank or within 30 days if obtained from client owned cats within our institution's blood bank. All blood was administered prior to these expiratory dates. All blood was collected into citrate, dextrose, and phosphate anticoagulant and preservative solutions. All units of pRBCs from commercial blood banks contained adenine, and the majority of the units collected in our institution's blood bank program contained adenine. Information on degree of hemolysis and PCV of transfused pRBCs was not available in this study population.

### Blood type identification

When possible, patient blood type identification was performed by trained laboratory personnel according to the slide or tube agglutination procedures described previously.<sup>17</sup> If immediate transfusion was necessary or the clinical pathology laboratory was not

available, the patient's blood type was identified by either the immunochromatographic cartridge<sup>c</sup> or the card agglutination<sup>d</sup> technique as described previously.<sup>17</sup>

### Cross-match procedure

During the period of investigation, major cross-match procedures were performed in all patients that received a red blood cell transfusion greater than 3 days previously or if requested by the clinician in naïve or recently transfused cats. For a number of the type-specific cross-match compatible transfusions it was not possible to determine if the recipient was naïve or previously transfused. Additionally, the rationale for cross-match in documented naïve cats was not available in the medical record. Trained laboratory personnel performed all cross-match procedures. To perform major cross-match, 500 microliters of anti-coagulated donor blood was placed into a 12 × 75 mm tube. To wash RBCs, donor pRBCs were centrifuged (1000 × *g*, room temperature, 2 minutes) and the RBC pellet was reconstituted in 5 mL saline solution.<sup>e</sup> This procedure was repeated 2–3 times. The donor RBCs were then reconstituted to a two percent solution in saline. Coagulated recipient blood was centrifuged and the serum harvested as previously described.<sup>18</sup> The recipient serum was diluted 1:2 in saline. Five hundred microliters of recipient serum solution was added to 500 microliters of the donor RBC solution. A recipient auto-control was performed by adding recipient serum solution to a recipient RBC solution prepared in the same manner as described for donor RBC solution. In addition, a minor cross-match was performed in a subset of patients in the same manner utilizing donor serum or plasma and recipient RBC suspension as substrates. The samples were covered and allowed to incubate for 30 minutes. Samples were subsequently centrifuged and observed for evidence of hemolysis. RBC pellets were then resuspended and observed for evidence of agglutination both macroscopically and microscopically. Any procedure resulting in any detectable hemolysis or agglutination was deemed incompatible.

### Statistical analysis

Data were evaluated for normality with the Kolmogorov-Smirnov test. All normally distributed data are presented as the mean plus or minus standard deviation whereas all nonnormally distributed data are presented as a median and range. Comparisons between characteristics of type-specific, cross-match compatible transfusions (CM+) and type-specific, noncross-matched transfusions (CM-) were done using independent samples *t*-tests if data were normally distributed and Mann-Whitney *U* tests if data were not

normally distributed, and comparisons of proportions between groups were done using Fisher's exact test due to the small sample size. A stepwise multiple linear regression model (backward elimination method) was used to determine which of the following parameters were independently associated with the change in PCV following transfusion: age, reason for transfusion, dose of pRBCs (mL/kg), cross-match status, pretransfusion PCV, and dose of intravenous fluid administered concurrently (mL/kg). Reason for transfusion (a categorical variable) was evaluated as three individual dichotomous variables (blood loss, decreased production, and destruction) in the multiple linear regression analysis. Statistical significance was set at a *P* value < 0.05. All statistical analyses were performed with commercial statistical software.<sup>f</sup>

### Results

Medical records of 391 cats receiving 458 transfusions were considered for inclusion in the study. A total of 209 cats receiving 233 transfusions met the inclusion criteria and were included in the study. One hundred and seventy-three cats received a total of 190 type-specific, noncross-matched transfusions and 36 cats received 43 type-specific, cross-match compatible transfusions. In addition, 3/43 (7.0%) type-specific, cross-match compatible transfusions were also evaluated by minor cross-match and considered compatible. A total of 91 cross-match procedures were performed in these 43 pretransfusion screenings. An incompatible unit of pRBCs was identified in a total of 15/91 cross-matches (16.5%), and at least one incompatible unit of pRBCs was identified in 11/43 pretransfusion screenings (25.6%). Red blood cell transfusions were administered greater than 3 days previously in 34/43 cross-match compatible transfusions (79%). The transfusion history for 7/43 cross-match compatible transfusions (16.3%) was not available in the medical record, and the blood typing card test was considered inaccurate due to patient auto-agglutination in 1/43 cross-match compatible transfusion in a naïve recipient (2.3%). The remaining transfusion was cross-matched one day following a previous type-specific noncross-matched transfusion, and the rationale for cross-match testing in this cat is not documented in the medical record. The median age of the cats at the time of transfusion was 8 years (range 0.08–20), and the median weight was 4.12 kilograms (range 0.38–10.2 kilograms). There were 120 males (intact 5/120, castrated 115/120) and 89 females (intact 4/89, spayed 85/89). Breeds represented include mix breeds (181/209), Maine Coon (7/209), Siamese (5/209), Himalayan (3/209), Persian (3/209), Ocicat (2/209), Angora (1/209), Burmese (1/209), Jungle Bob (1/209), Korat

(1/209), Manx (1/209), Ragdoll (1/209), Rex (1/209), and Russian Blue (1/209).

The mean dose of pRBCs administered was not significantly different between CM+ and CM- transfusions (CM+:  $8.85 \pm 3.22$  mL/kg; CM-:  $8.47 \pm 3.22$  mL/kg;  $P = 0.11$ ). The volume of IV fluids administered between the measurement of pretransfusion PCV and posttransfusion PCV was available in 217/233 transfusions. Intravenous fluids were administered during this period in 130 transfusions, and there was no difference in median concurrent fluid administration dose between the groups (N = 28, CM+: 3.70 mL/kg, range 0–50.4 mL/kg; N = 189, CM-: 3.33 mL/kg, range 0–109 mL/kg;  $P = 0.80$ ). There was no difference in the median ages of cats receiving a type-specific, cross-match compatible transfusion compared to those that did not (CM+: 9 years, range 1–20 years; CM-: 8 years, range 0.1–20 years;  $P = 0.70$ ). There was no statistically significant difference in the proportion of purebred cats between the CM+ and CM- groups (11.9% versus 13.7%,  $P = 1.0$ ). The proportions of transfusions from each pRBC source were similar between the groups (in house blood bank: CM+ 16.7%, CM- 10%,  $P = 0.87$ ; commercial blood bank 1: CM+ 57%, CM- 51%,  $P = 0.59$ ; commercial blood bank 2: CM+ 26.3%, CM- 39%,  $P = 0.20$ ).

For transfusions for which these data were available, there was a significantly greater delay between pretransfusion PCV measurement and start of transfusion for CM+ transfusions (N = 38, median 3 hours, range 0.3–23 hours) when compared to CM- transfusions (N = 165, median 1.75 hours, range 0–30 hours,  $P = 0.0012$ ). No difference was found in the duration of time between the end of the transfusion and measurement of posttransfusion PCV between CM+ transfusions (N = 42, median 2 hours, range 0–14 hours) and CM- transfusions (N = 187, median 2 hours, range 0–19 hours,  $P = 0.89$ ).

CM+ transfusions yielded a significantly larger mean change in PCV scaled to dose of pRBCs administered than CM- transfusions (Figure 1 – CM+:  $1.02 \pm 0.51\%/mL/kg$ ; CM-:  $0.74 \pm 0.65\%/mL/kg$ ;  $P = 0.0093$ ). Mean pretransfusion PCV was significantly lower for CM+ transfusions than for CM- transfusions (Figure 2 – CM+:  $13.7 \pm 4.2\%$ ; CM-:  $16.1 \pm 4.5\%$ ;  $P < 0.0001$ ). There were no significant differences in the proportions of CM+ compared to CM- transfusions due to presumed blood loss (23.3% versus 40.2%,  $P = 0.053$ ), hemolysis (11.4% versus 8.2%,  $P = 0.55$ ), or decreased production (75% versus 64.3%,  $P = 0.21$ ).

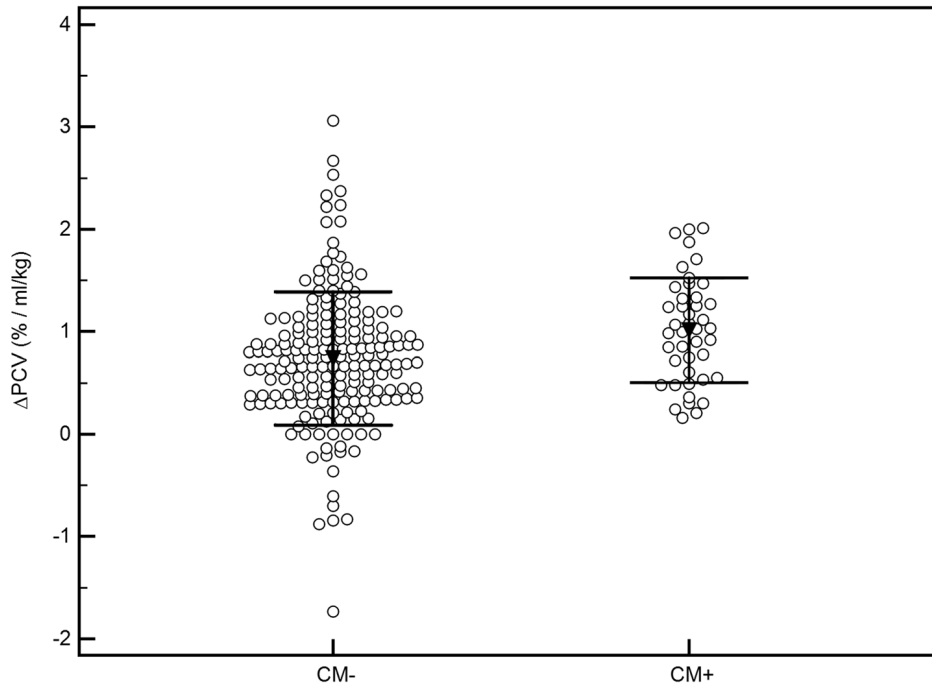
A significant multiple linear regression model emerged ( $F_{3,229} = 20.7$ ,  $P < 0.001$ , adjusted  $r^2 = 0.206$ ). Of age, dose of pRBCs administered (mL/kg), cross-match status, reason for transfusion (blood loss, decreased production, and/or destruction), pretransfusion PCV, and dose of IV fluid administered between the measure-

ment of the pretransfusion PCV and posttransfusion PCV (mL/kg) only dose of pRBCs (coefficient = 0.507,  $P < 0.0001$ ), cross-match status (coefficient = 1.64,  $P = 0.041$ ), and pretransfusion PCV (coefficient =  $-0.235$ ,  $P = 0.0009$ ) were independent predictors of the change in PCV with transfusion.

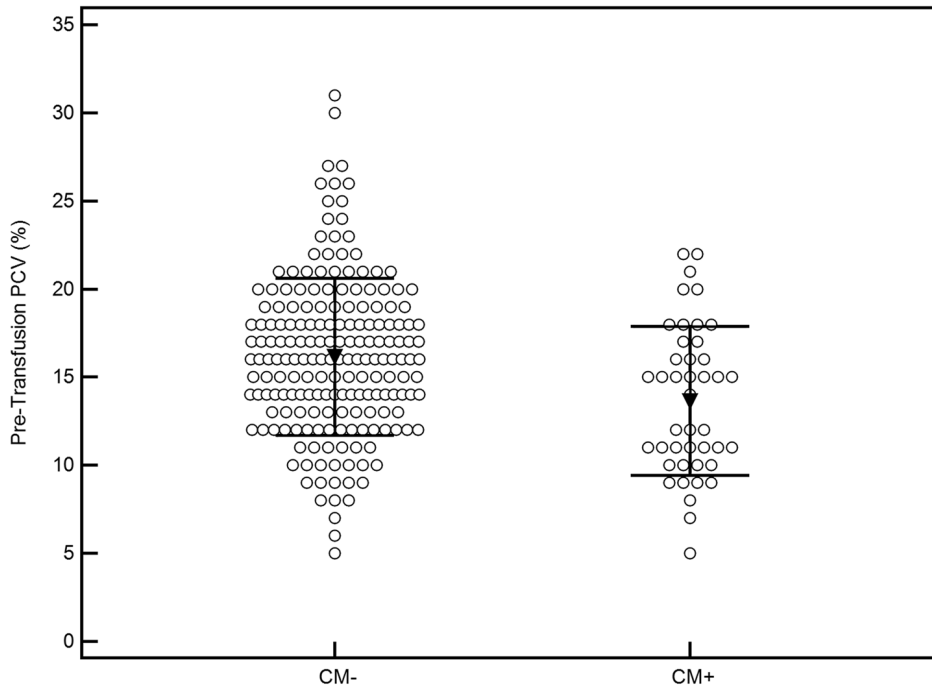
## Discussion

Alongside the rapid growth in availability of feline blood components, there has been a growing interest in pretransfusion compatibility testing.<sup>1,2,5,17</sup> Previous studies investigating compatibility of RBC units in cats have predominantly focused on the use of feline AB blood typing.<sup>1–4,6</sup> As all cats in our study received type-specific pRBC transfusions, AB antibodies cannot account for the difference in efficacy between CM+ and CM- transfusions. Cross-matching may aid in identifying cats with antibodies to RBC antigens other than AB, and with the recent identification of *Mik* antigen,<sup>5</sup> more thorough pretransfusion compatibility screening may be warranted. In this study, cats receiving pRBC units deemed compatible by major cross-match showed a significantly greater increase in the posttransfusion PCV scaled by dose of pRBCs administered ( $1.02 \pm 0.51\%/mL/kg$ ) than cats receiving type-specific, noncross-matched units ( $0.738 \pm 0.65\%/mL/kg$ ). While the differences in efficacy between the groups may have been due to many factors, it is possible that the cross-matches performed in these cats identified incompatibilities due to antigens other than AB and contributed to the improved efficacy in the CM+ group.

Two recent studies have investigated the efficacy of RBC transfusion in cats. In 2004, Weingart *et al* retrospectively compared the expected rise in HCT to the actual rise in HCT in 91 cats receiving 163 whole blood transfusions.<sup>2</sup> They found that in 22.6% of transfusions, the actual rise in HCT was less than expected based on the dose of blood administered. This study asserted an expected HCT rise of 1% for each 2 mL/kg of whole blood administered, and previous veterinary publications have stated an expected PCV rise of 1% for each 1 mL/kg of pRBCs administered.<sup>2,16,19,20</sup> In 2005, Klaser *et al* reported a mean PCV increase of 7.3% in cats receiving a mean dose of 9.3 mL/kg of pRBCs.<sup>1</sup> Although the authors did not specifically evaluate the relationship between the change in PCV and the dose of pRBCs administered in each individual cat, the data show an approximate increase of 0.78%/mL/kg (7.3%/9.3 mL/kg), very similar to our finding of 0.738%/mL/kg in CM- transfusions. While the effect of cross-matching was not evaluated in these studies, they demonstrated less than expected increases in PCV or hematocrit following RBC transfusion in their study populations, and these data are



**Figure 1:** The change in PCV per dose (in mL/kg) of pRBCs administered ( $\Delta$ PCV) was significantly higher for cross-match compatible transfusions (CM+:  $1.02 \pm 0.51\%/mL/kg$ ) than for noncross-matched, type-specific transfusions (CM-:  $0.74 \pm 0.65\%/mL/kg$ ; independent samples *t*-test,  $P = 0.0093$ ). The open circles represent all individual data points, the black triangle is the mean and the error bars denote the standard deviation.



**Figure 2:** The pretransfusion PCV was significantly higher for noncross-matched, type-specific transfusions (CM-:  $16.1 \pm 4.5\%$ ) than for cross-match compatible transfusions (CM+:  $13.7 \pm 4.2\%$ ; independent samples *t*-test,  $P < 0.0001$ ). The open circles represent all individual data points, the black triangle is the mean and the error bars denote the standard deviation.



consistent with the findings in noncross-matched cats in our study.

In human medicine, pretransfusion compatibility testing is more extensive than in veterinary medicine, and is designed to minimize the likelihood of reaction. For routine testing, human medical guidelines for pretransfusion screening recommend initial group (AB and D) identification followed by screening for clinically significant antibodies.<sup>21</sup> The indirect antiglobulin test, performed by exposing the recipient plasma or serum to a solution of known antigenicity, is considered the most reliable screening test for the presence of clinically relevant antibodies.<sup>21</sup> Manual cross-match procedures are recommended in human transfusion medicine if the recipient currently has or has previously had clinically relevant antibodies identified on antibody screening tests or if antibody screening tests are not available.<sup>21</sup> Based on standards in human medicine, it could be argued that cross-match procedures are indicated for all feline transfusions until an accurate antibody screening method equivalent to the indirect antiglobulin test is available for cats. The results of our study provide evidence that such pretransfusion cross-matching may be warranted.

Pretransfusion PCV was found to be an independent predictor of the change in PCV in this study. To the authors' knowledge, there are no studies investigating this phenomenon in the veterinary or human literature. The association between lower pretransfusion PCV and greater changes in PCV with transfusion in our study is unclear, but possible causes may include a reduction in endogenous clearance of transfused RBCs or a reduction in continued RBC loss in patients with more severe anemia. The immunosuppressive consequences of RBC transfusion have been recognized in human clinical medicine for many decades, and descriptions of this phenomenon have been published in both human and veterinary literature.<sup>22,23</sup> While transfusion-associated immune modulation has not been related to a prolonged survival of transfused RBCs, this could explain the reduced clearance of transfused RBC in some cats in this study, particularly those receiving multiple transfusions in the CM+ group. Further investigation into this phenomenon is warranted. Although, the CM+ cats had significantly lower pretransfusion PCVs than CM- cats, pretransfusion PCV and cross-match status were independent predictors of the change in PCV with transfusion, suggesting the cross-match procedure resulted in improved efficacy independent of the effect of the lower pretransfusion PCVs in the CM+ group. The reason for lower pretransfusion PCV in CM+ cats compared to CM- cats is unclear. Because the majority of CM+ cats had been previously transfused, these cats may have had chronic anemias resulting in physiologic tolerance to low

PCV, fewer clinical signs of anemia, and a lower clinical transfusion threshold.

Pretransfusion compatibility screening by cross-match can take several hours, and at our institution this procedure is only performed by trained laboratory personnel. Not surprisingly, there was a significant delay between the measurement of PCV and the start of pRBC transfusion in type-specific, cross-match compatible transfusions (median 3 hours) compared to noncross-matched, type-specific transfusions (median 1.75 hours), while there was no difference between the CM+ and CM- groups in the duration of time between the end of transfusion and measurement of the posttransfusion PCV in cats in which these data were available. Unfortunately, due to the retrospective nature of this study, these times could only be roughly estimated from the medical record, and could not be determined at all for 33 of 233 transfusions. However, it seems likely that pretransfusion delays would result in lower posttransfusion increases in PCV due to the underlying diseases that lead to anemia, and the fact that our records show greater increases in PCV despite these delays in CM+ transfusions arguably strengthens the main conclusion of this study that cross-matching may lead to better transfusion efficacy. Future prospective studies will be required to more fully investigate the effects of these delays.

Although pRBC are administered to alleviate the harmful consequences of anemia, recent studies in human medicine have documented serious dose-dependent risks of transfusion as well. In addition to acute hemolytic and nonhemolytic reactions, administration of pRBCs to critically ill humans has been associated with immunosuppression and microcirculatory dysfunction.<sup>24,25</sup> Both prospective and retrospective evaluations in people have shown that the incidence of infection, multi-organ failure, systemic inflammatory response syndrome, and mortality is increased in patients receiving transfusions.<sup>26-32</sup> Due to these risks, more conservative transfusion guidelines in hemodynamically stable patients have become the standard of care in human medicine.<sup>25,33</sup> Pretransfusion compatibility testing in our study resulted in significantly higher posttransfusion PCV for a given dose of pRBCs, potentially reducing the number of transfusions necessary and mitigating some of these risks of transfusion. Future prospective studies to investigate these phenomena in cats are warranted.

This study has several important limitations, and findings should be interpreted cautiously until further, prospective studies are performed. Because the study population included all cats receiving transfusions at one hospital, there was heterogeneity in the etiology of the anemia. Previous retrospective analyses investigating feline blood transfusions showed no

effect of anemia etiology on the efficacy of whole blood or pRBC transfusions.<sup>1,20</sup> Similarly, we found no effect of the reason for transfusion on transfusion efficacy, but our ability to definitively determine the reason for transfusion was limited based on the retrospective nature of this study. In addition, the simplified etiology scheme used in this study may have failed to identify clinically relevant differences between the individuals. In future studies, a uniform population consisting of a simple, well-documented disease process could offer a more homogenous population.

Based on previously published recommendations,<sup>1,2,15,16</sup> most cats naïve to transfusion in this population were administered type-specific, noncross-matched pRBCs whereas the majority of cats receiving type-specific, cross-match compatible transfusions had been previously administered red blood cell transfusions. Although this contributes to the inhomogeneity of the study populations, the consequences of previous exposure to foreign red blood cell antigens in the CM+ cats would likely predispose them to transfusion reaction and decreased transfusion efficacy, opposing our hypothesis, and reducing our chances of documenting a difference between groups. While this represents a significant limitation in the retrospective analysis of this population, it also highlights the importance of the divergence in posttransfusion PCV between CM+ and CM- cats in our study. A randomized, prospective, controlled trial including only naïve transfusion recipients would eliminate this variable between patient groups, and it is possible that the effect size may be even greater than we documented in this study.

Comparison of the method of blood typing was not possible in this population as this information was not routinely documented in the medical record during the study period. A recent study investigating feline blood typing procedures reported a 95% agreement of immunochromatographic cartridges and 91% agreement of card agglutination kits to laboratory methods described above, suggesting this variable likely had little influence on the results.<sup>17</sup> In future prospective studies, standardized blood typing should be employed. As our clinical pathology laboratory does not routinely perform a minor cross-match during pretransfusion compatibility screening in cats for pRBC transfusion, the majority of our patients did not receive minor cross-matches. Although pRBCs contain minimal donor plasma, without a documented compatible minor cross-match, the influence of donor antibody against recipient red blood cell antigen in this study cannot be evaluated. While this is a limitation, the presence of donor antibody would likely influence both study groups. The utility of minor cross-match should be evaluated in future, prospective analyses. The method of blood product administration

has recently been investigated in dogs, and the use of mechanical delivery systems was associated with early loss of transfused RBCs.<sup>34</sup> Syringe and fluid pumps are commonly used to regulate the speed of pRBC transfusions in our practice, and the use of these devices may have resulted in less effective transfusions. Because the method of delivery is not routinely documented in our pRBC transfusion records, evaluation of delivery technique was not possible, although it is unlikely that there were differences in method of delivery between the two groups of cats.

Previous retrospective studies have reported frequencies of acute, nonhemolytic transfusion reactions (elevation in body temperature, gastrointestinal signs, face rubbing, and angioedema) to be 1.2–7.9%.<sup>1,2</sup> In Klaser et al, one patient presumed to have an acute hemolytic transfusion reaction showed evidence of pigmenturia, fever and a subsequent decline in PCV.<sup>1</sup> In Weingart et al, 4 of 29 patients with total bilirubin measurements were suspected to have hemolytic transfusion reactions leading to posttransfusion hyperbilirubinemia with a lower than expected posttransfusion HCT.<sup>2</sup> We could not report the rate of transfusion reaction in our study population as this information was not well documented throughout the study period in the pRBC transfusion records, although this information would have helped determine the contribution of premature destruction of transfused RBCs to decreased transfusion efficacy. Although we could not definitively determine if any of the cats in this study had acute reactions, by reporting the pRBC volume received by each cat, not the pRBC unit size, we ensured that our data was not affected by premature discontinuation of the transfusion. Thorough documentation of both nonhemolytic and hemolytic transfusion reactions should be included in future, prospective studies.

In addition to the previously described limitations, there are several drawbacks of this study shared by many retrospective analyses. It was often challenging to accurately extract information about the timing of diagnostic tests and transfusion administration, the rationale for individual transfusions, and the presumed causes of the anemias from the medical records. Packed red blood cells were obtained from multiple sources, leading to some variability in the anticoagulant and preservative solutions used and potentially in the handling of individual units. However, all pRBCs were obtained from one of 2 high quality commercial blood banks or from our institution's blood bank, which follows standard veterinary blood banking protocols. It was not possible to determine the age of each unit administered because these data are not routinely recorded in our medical records, but all units administered were within recommended storage intervals (a maximum of 35 days old at the time of

administration if obtained from a commercial blood bank and a maximum of 30 days old at the time of administration if obtained from our institution's blood bank).

Historically the identification of AB blood type in the cat has been accepted as adequate for compatibility testing in naïve feline RBC recipients, with cross-match procedures generally reserved for previously transfused cats. In this study, we found that administering type-specific, cross-match compatible pRBCs to cats led to a greater increase in the posttransfusion PCV as compared to administering AB type-specific, noncross-matched pRBCs. While this analysis provides evidence suggesting more thorough compatibility testing in cats may be warranted before administration of pRBC transfusion, given the previously described limitations inherent in this retrospective study, prospective studies evaluating the effect of cross-match on the efficacy of RBC transfusion in cats, particularly those naïve to transfusion, are necessary before specific alterations to recommendations for clinical transfusion practice can be made.

### Footnotes

- <sup>a</sup> Northwest Veterinary Blood Bank, Bellingham, WA.
- <sup>b</sup> Animal Blood Resources Blood Bank, Dixon, CA.
- <sup>c</sup> Quick Test A + B, Alvedia, Limonest, France.
- <sup>d</sup> RapidVet-H Feline Blood typing card, DMS Laboratories, Flemington, NJ.
- <sup>e</sup> 0.9% Saline, CardinalHealth, Dublin, OH.
- <sup>f</sup> MedCalc Software version 12.3.0.0, Mariakerke, Belgium.

### References

1. Klaser DA, Reine NJ, Hohenhaus AE. Red blood cell transfusions in cats: 126 cases (1999). *J Am Vet Med Assoc* 2005; 226(6):920–923.
2. Weingart C, Giger U, Kohn B. Whole blood transfusions in 91 cats: a clinical evaluation. *J Feline Med Surg* 2004; 6(3):139–148.
3. Knottenbelt CM, Day MJ, Cripps P, et al. Measurement of titres of naturally occurring alloantibodies against feline blood group antigens in the UK. *J Small Anim Pract* 1999; 40(8):365–370.
4. Bücheler J, Giger U. Alloantibodies against A and B blood types in cats. *Vet Immunol Immunopathol* 1993; 38(3):283–295.
5. Weinstein NM, Blais M-C, Harris K, et al. A newly recognized blood group in domestic shorthair cats: the Mik red cell antigen. *J Vet Intern Med* 2007; 21(2):287–292.
6. Giger U, Bücheler J, Patterson DF. Frequency and inheritance of A and B blood types in feline breeds of the United States. *J Hered* 1991; 82(1):15–20.
7. Juvet F, Brennan S, Mooney CT. Assessment of feline blood for transfusion purposes in the Dublin area of Ireland. *Vet Rec* 2011; 168(13):352.
8. Medeiros M, Soares AM, Alviano DS, et al. Frequencies of feline blood types in the Rio de Janeiro area of Brazil. *Vet Clin Pathol* 2008; 37(3):272–276.
9. Arıkan S, Gurkan M, Ozaytekin E, et al. Frequencies of blood type A, B and AB in non-pedigree domestic cats in Turkey. *J Small Anim Pract* 2006; 47(1):10–13.
10. Malik R, Griffin DL, White JD, et al. The prevalence of feline A/B blood types in the Sydney region. *Aust Vet J* 2006; 83(1–2):38–44.
11. Ruiz de Gopegui R, Velasquez M, Espada Y. Survey of feline blood types in the Barcelona of Spain. *Vet Rec* 2004; 154(25):794–795.
12. Jensen A, Olesen A, Fukui M. Distribution of feline blood types detected in the Copenhagen area of Denmark. *Acta Vet Scand* 1994; 35(2):121–24.
13. Silvestre-Ferreira AC, Pastor J, Almeida O, et al. Frequencies of feline blood types in northern Portugal. *Vet Clin Pathol* 2004; 33(4):240–243.
14. Giger U, Gorman N, Hubler M, et al. Frequencies of feline A and B blood types in Europe. *Proceedings of the 23rd Conference of the International Society of Animal Genetics (Suppl)*. 1992;23:17–18.
15. Hohenhaus AE. Blood transfusions, component therapy, and oxygen-carrying solutions. In: Ettinger SJ, Feldman EC. eds. *Textbook of Veterinary Internal Medicine*, 7th ed. St. Louis: Saunders Elsevier; 2010, pp. 537–544.
16. Giger U. Transfusion medicine. In: Silverstein DC, Hopper K. eds. *Small Animal Critical Care Medicine*. St. Louis, MO: Saunders Elsevier; 2009, pp. 281–286.
17. Seth M, Jackson K V, Giger U. Comparison of five blood-typing methods for the feline AB blood group system. *Am J Vet Res* 2011; 72(2):203–209.
18. Vap LM, Harr KE, Arnold JE, et al. ASVCP quality assurance guidelines: control of preanalytical and analytical factors for hematology for mammalian and nonmammalian species, hemostasis, and cross-matching in veterinary laboratories. *Vet Clin Pathol* 2012; 41(1):8–17.
19. Callan MB. Red blood cell transfusion in the dog and cat. In: Boudreaux MK, Brooks MB, Callan MB, et al. eds. *Schalm's Veterinary Hematology*, 6th ed. Ames, IA: Blackwell Publishing; 2010. pp. 738–743.
20. Castellanos J, Couto CG, Gray TL. Clinical use of blood products in cats: a retrospective study (1997–2000). *J Vet Intern Med* 2004; 18(4):529–532.
21. Chapman JF, Elliott C, Knowles SM, et al. Guidelines for compatibility procedures in blood transfusion laboratories. *Transfus Med* 2004; 14(1):59–73.
22. Prittie JE. Controversies related to red blood cell transfusion in critically ill patients. *J Vet Emerg Crit Care* 2010; 20(2):167–176.
23. Dellinger EP, Anaya DA. Infectious and immunologic consequences of blood transfusion. *Crit Care*. 2004; 8(Suppl):2S18–2S23.
24. Hebert PC, Wells G, Blajchman M, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med* 1999; 340(6):409–417.
25. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Crit Care Med* 2008; 36(9):2667–2674.
26. Claridge JA, Sawyer RG, Schulman AM, et al. Blood transfusions correlate with infections in trauma patients in a dose-dependent manner. *Am Surg* 2002; 68(7):566–572.
27. Taylor RW, O'Brien J, Trotter SJ, et al. Red blood cell transfusions and nosocomial infections in critically ill patients. *Crit Care Med* 2006; 34(9):2302–2308.
28. Ciesla DJ, Moore EE, Johnson JL, et al. A 12-year prospective study of postinjury multiple organ failure: has anything changed? *Arch Surg* 2005; 140(5):432–440.
29. Vincent JL, Baron JF, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. *JAMA* 2002; 288(12):1499–1507.
30. Croce MA, Tolley EA, Claridge JA, et al. Transfusions result in pulmonary morbidity and death after a moderate degree of injury. *J Trauma* 2005; 59(1):19–24.
31. Corwin HL, Gettinger A, Pearl RG, et al. The CRIT study: anemia and blood transfusion in the critically ill-current clinical practice in the United States. *Crit Care Med* 2004; 32(1):39–52.
32. Dunne JR, Malone DL, Tracy JK, et al. Allogenic blood transfusion in the first 24 hours after trauma is associated with increased systemic inflammatory response syndrome (SIRS) and death. *Surg Infect* 2004; 5(4):395–404.
33. Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. *Ann Intern Med* 2012; 157(1):49–60.
34. McDevitt RI, Ruau CG, Baltzer WI. Influence of transfusion technique on survival of autologous red blood cells in the dog. *J Vet Emerg Crit Care* 2011; 21(3):209–216.



Copyright of Journal of Veterinary Emergency & Critical Care is the property of Wiley-Blackwell and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.