

# The effect of blood usage protocol on the age of packed red blood cell transfusions administered at 2 veterinary teaching hospitals

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## Abstract

**Background** – Controversy exists regarding the optimal duration of storage of units of canine packed red blood cells (PRBC) prior to transfusion, resulting in different blood usage strategies between hospitals. Two hospitals were studied: At North Carolina State University (NCSU), usage protocol dictates that the oldest units of PRBC (stored the longest) are prioritized for transfusion; whereas, at Ontario Veterinary College (OVC), units of PRBC are sorted according to age (days after collection) and PRBC are selected for transfusion according to clinician or technician discretion, such that PRBC could be administered after any storage duration, with no preference given to older units.

**Objective** – To evaluate differences in the age of PRBC administered to dogs at 2 veterinary hospitals with different age-related PRBC usage protocols during a 1-year period (2010–2011).

**Key Findings** – The average age of units of PRBC administered at NCSU was older than that at OVC ( $P < 0.001$ ). Additionally, a higher number of PRBC units older than 14 days old were transfused at NCSU ( $P < 0.001$ ), and the age of the oldest administered PRBC unit was also older at NCSU ( $P < 0.001$ ). NCSU discarded approximately 15 expired PRBC units, whereas OVC discarded 96 expired PRBC units during the study period.

**Significance** – A standardized protocol for the priority administration of the oldest stored PRBC resulted in the administration of significantly older PRBC, but fewer expired units of PRBC were discarded.

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## Abbreviations

NCSU North Carolina State University  
OVC Ontario Veterinary College  
PRBC packed red blood cells

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## Introduction

The introduction of blood component therapy to veterinary medicine in the late 1980s resulted in a shift in transfusion practice from the administration of whole blood to packed red blood cells (PRBC) and fresh frozen plasma.<sup>1</sup> Strategies to maximize the storage duration and oxygen-carrying capacity of PRBC were investigated, and the addition of RBC preservative solutions<sup>2</sup> to PRBC extended their safe storage time to a maximum of 42 days.<sup>3</sup> Controversy has arisen in recent years regarding the impact of the age of transfused PRBC on morbidity and mortality. Storage lesions are changes in RBC or storage media that occur during PRBC storage.<sup>4</sup> These storage lesions might explain the association of the age of transfused PRBC with the incidence of acute lung injury,<sup>5</sup> infection,<sup>6</sup> acute kidney injury,<sup>6</sup> multiple organ failure,<sup>7</sup> and death in human patients.<sup>6,8,9</sup> The association between transfusion of older stored PRBC units and morbidity and mortality has led to ethical debates regarding

the allocation of stored blood products and the sustainability of the current human blood banking system.<sup>10</sup>

There are few studies investigating the influence of PRBC storage time on transfusion-related complications or outcome in dogs. A recent study included retrospective data from more than 3,000 dogs receiving PRBC transfusions and showed an association between the age of the transfused PRBC and the incidence of coagulation failure and thromboembolic disease.<sup>11</sup> While longer duration of storage of PRBC units was not associated with mortality in all included dogs, it was a negative risk factor for survival in dogs with hemolysis as the reason for the transfusion. However, appropriately designed prospective studies are needed to confirm associations between the transfusion of older stored PRBC and morbidity and mortality in veterinary and human patients.<sup>12</sup>

A recent study compared 2 human ICUs with opposite age-related transfusion strategies.<sup>13</sup> One ICU always transfused older PRBC first, whereas the transfusion of younger PRBC was favored in the other ICU. Although a significant difference was found in the median age of PRBC administered at each ICU (16 vs 7 days), a large overlap in the age of transfused PRBC was found, and very few units of PRBC that were older than 35 days old were transfused.<sup>13</sup> The objective of the present study was to assess the differences in the age of units of PRBC administered to dogs at 2 tertiary referral veterinary teaching hospitals with different age-related blood transfusion protocols.

### Materials and Methods

Information was collected from the medical records of dogs receiving PRBC transfusions at North Carolina State University (NCSU) and the Ontario Veterinary College (OVC) between June 1, 2010 and May 31, 2011. Efforts were made to collect information prospectively onto paper worksheets, which were later transcribed to a commercial spreadsheet program.<sup>a</sup> An electronic medical record search for invoices containing "canine packed red blood cells" was also performed to collect missing data retrospectively from medical records. Dogs were excluded from analysis if the medical record or administered PRBC information was incomplete or missing, or if PRBC from commercial blood banks were administered, because information regarding the age of the purchased PRBC was often unavailable. Dogs receiving PRBC transfusions during more than one visit within the study period were included in the study for each subsequent visit and considered a separately enrolled dog.

Information collected from each dog's medical record included the mean age (days) of PRBC, number of transfused PRBC units that were older than 14 days old,

number of transfused PRBC units that were older than 30 days old, and age of the oldest PRBC unit transfused during that visit. The mean age of PRBC that each dog was transfused was determined by dividing the sum of the age of all of the PRBC units by the total number of units transfused during that visit.

During the study period, NCSU stored units of PRBC in a designated refrigerator, but not separated according to age or volume. Clinicians and veterinary technicians were instructed to first select the oldest PRBC unit of the appropriate volume that was available. Often, newly collected PRBC were not made available for use until the older units were administered, per the discretion of the blood bank coordinator. At OVC, PRBC units were stored in a designated refrigerator according to age (calculated in days from the date of blood collection) and volume (mL). PRBC units were categorized as  $\leq 12$  days old or  $> 12$  days old and small ( $< 200$  mL) or large ( $\geq 300$  mL), and were chosen at the discretion of the clinician or veterinary technician such that fresher PRBC could be administered if desired. Both hospitals had otherwise identical hospital-run canine blood banking programs that performed routine blood collections from client- and staff-owned dogs to meet the needs of the hospitalized dogs. PRBC units were collected at each institution using a triple-bag collection system with added red cell preservative<sup>b</sup> and stored for a maximum of 42 days.

### Statistical analyses

Descriptive statistics were performed to calculate median, range, mean, and standard deviation for all continuous variables. Continuous variables were analyzed for normality with a Shapiro–Wilk test. No continuous variables were normally distributed; therefore, a Wilcoxon–Mann–Whitney test was used to assess differences between hospitals in the median for the total number of PRBC units, total volume of PRBC transfused at each visit (mL), mean age of transfused PRBC, number of transfused PRBC units that were older than 14 days old, number of transfused PRBC units that were older than 30 days old, and the age of the oldest PRBC unit transfused. Commercially available computer software was used for statistical analyses<sup>c</sup> and figure generation.<sup>d</sup> A *P* value  $< 0.05$  was considered significant for all comparisons.

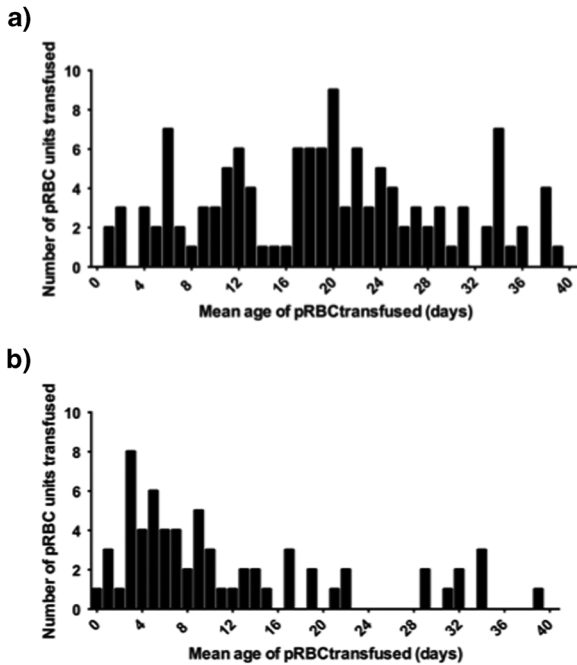
### Results

At NCSU, 166 dogs received PRBC transfusions and 124 dogs were included in the data analysis. Forty-two dogs were excluded because of administration of PRBC units from external commercial blood banks ( $n = 29$ ), incomplete information about the PRBC administered ( $n = 12$ ), and incomplete or missing medical records ( $n = 1$ ). At

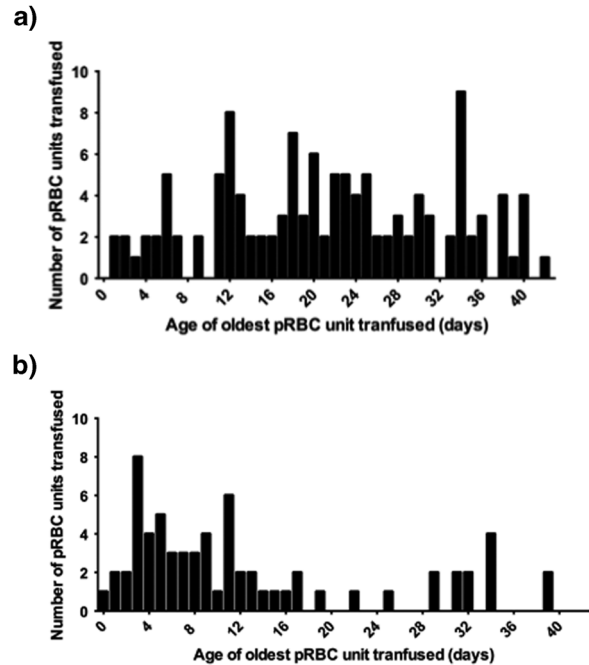
**Table 1:** Comparison of packed red blood cell (PRBC) transfusion variables for each dog transfused at 2 hospitals with different blood banking strategies

Variable	NCSU (n = 124)	OVC (n = 66)	P value
Mean age of PRBC units administered (days)	19.4 (1–39)	8.0 (0–39)	< 0.001
Number of PRBC units > 14 days old administered	1 (0–10)	0 (0–4)	< 0.001
Number of PRBC units > 30 days old administered	0 (0–4)	0 (0–2)	0.051
Age of oldest PRBC unit administered (days)	21 (1–42)	9 (0–39)	< 0.001

Values are presented as median (min-max). NCSU, North Carolina State University; OVC, Ontario Veterinary College.



**Figure 1:** Distribution of the number of PRBC units transfused to dogs at two hospitals (a: NCSU and b: OVC) using different PRBC allocation protocols during a 1-year period, according to the mean age of transfused PRBC. NCSU, North Carolina State University; OVC, Ontario Veterinary College; PRBC, packed red blood cells.



**Figure 2:** Distribution of the number of PRBC units transfused to dogs at 2 hospitals (a: NCSU and b: OVC) using different PRBC allocation protocols during a 1-year period, according to the oldest PRBC unit age. NCSU, North Carolina State University; OVC, Ontario Veterinary College; PRBC, packed red blood cells.

OVC, 73 dogs received PRBC transfusions and 66 dogs were included in the data analysis. Seven dogs were excluded because of incomplete or missing medical records ( $n = 6$ ) and incomplete information about the PRBC administered ( $n = 1$ ).

NCSU administered PRBC with a significantly higher mean age ( $P < 0.001$ ), a higher number of PRBC units older than 14 days ( $P < 0.001$ ), and an older age of the oldest PRBC unit administered ( $P < 0.001$ ) compared with OVC (Table 1). The distributions of the frequency of the mean age of transfused PRBC and age of the oldest PRBC unit transfused to each dog at each institution are depicted in Figures 1 and 2, respectively.

During the study period, specific information regarding the number of discarded expired units of PRBC at NCSU was not recorded; however, it was estimated that approximately 15 expired PRBC units were discarded. In comparison, OVC discarded 96 expired PRBC units during the study period. During the study period, NCSU purchased PRBC from commercial blood banks to keep up with the demand that exceeded the supply of PRBCs, whereas PRBC were not purchased from commercial blood banks by OVC during the study period.

**Discussion**

This study took place over a 1-year period and included information from 190 PRBC transfusions at 2 veterinary

teaching hospitals. NCSU employed a protocol that required the preferential administration of older units of PRBC. Conversely, at OVC, clinician or technician preference determined the age of the PRBC that were transfused. Those selecting PRBC at OVC often selected fresher units ( $\leq 12$  days old), presumably because of the perceived negative consequences associated with transfusing older PRBC.<sup>7,14</sup> Overall, dogs transfused at NCSU received PRBC that were significantly older than those transfused at OVC (mean of  $19 \pm 9.9$  vs  $11.4 \pm 10.1$  days). The median oldest PRBC unit transfused at NCSU was older than at OVC (21 vs 9 days), and more units of PRBC that were older than 14 days old (median of 1 vs 0 units) were transfused at NCSU. A difference in the number of transfused units of PRBC older than 30 days old was not found, but this study was likely underpowered to detect this difference given the small number of PRBC of this age that were transfused at either hospital.

Large numbers of expired units of PRBC were discarded at OVC. The wastage of almost 100 units within 1 year was a troubling finding given the amount of time and resources dedicated to the collection, processing, and storage of each unit, in addition to the canine donor and owner's voluntary time. Unfortunately, the year the present study took place represented a period of reduced caseload and blood product usage at OVC compared with previous years, which likely impacted the overall number of units of PRBC used within 12 days of collection (ie, prior to being allocated to the  $>12$  days old area of the refrigerator, where they were less likely to be used). Since the completion of the present study, the blood transfusion protocol at OVC has been revised and the practice of storing PRBC according to 2 age categories of blood has been discontinued. OVC now stores older blood products in the front and the more recently collected products in the back of the dedicated blood refrigerator. The number of blood products stored has also been decreased in an attempt to reduce the wastage of expired blood products. At both hospitals, an interactive computer spreadsheet system is also used to more closely monitor the supply of blood products in order to match it with demand, to avoid discarding blood products as much as possible.

Atkinson et al. recently investigated the ability of a novel transfusion strategy to enable the transfusion of younger blood, without negatively impacting the blood supply.<sup>15</sup> They proposed always transfusing the oldest blood that is younger than 14 days, and if no blood younger than 14 days was available, to transfuse the youngest blood older than 14 days. Using a simulation model, they determined that for hospitals in which the local blood product supply is greater than the demand, using the aforementioned transfusion strategy would enable a decrease in the mean age of transfused blood

products, while decreasing the fraction of blood brought into the hospital to less than 0.5%.<sup>14</sup> The authors claimed that this system would not work or be necessary in a hospital whose demand for blood exceeded their supply, and instead they recommended that those hospitals continued to administer the oldest blood products first as they were unlikely to administer blood products near the end of their expiration. The present study included 2 hospitals whose supply and demand for blood were different. Although the demand for PRBC at NCSU exceeded the supply and led to the purchase of almost 30 additional units of PRBC from commercial blood banks, the supply of PRBC units at OVC exceeded the demand, resulting in the disposal of expired PRBC units. Therefore, it is possible that the novel transfusion strategy proposed by Atkinson et al. would only be successful at a hospital where supply exceeds demand and blood products are likely to age and expire prior to administration.

In conclusion, a blood banking protocol that dictated preferential administration of the oldest stored units of PRBC resulted in administration of older PRBC units compared to a protocol that allowed clinician or technician discretion to dictate the age of transfused PRBC. The former protocol decreased the number of expired units of PRBC that were discarded. Prospective randomized clinical trials are needed to more accurately assess associations between the age of transfused PRBC units and outcome in dogs before firm recommendations can be made regarding the appropriate duration of storage and allocation of blood products.

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### Footnote

- <sup>a</sup> Microsoft Excel (version 14), Microsoft Office 2010, Microsoft Corporation, Redmond, WA.
- <sup>b</sup> Teruflex blood bag system (CPD with optisol red cell preservative solution for collection of 450 mL of blood), Terumo Corp, Tokyo, Japan.
- <sup>c</sup> SAS OnlineDoc 9.1.3., SAS Institute, Inc, Cary, NC.
- <sup>d</sup> GraphPad Prism 6; GraphPad Software, San Diego, CA.

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