

Clinical and clinicopathologic variables in adult horses receiving blood transfusions: 31 cases (1999–2005)

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Objective—To determine clinical and clinicopathologic abnormalities in horses administered a blood transfusion and evaluate effects of blood transfusion on these variables.

Design—Retrospective case series.

Animals—31 adult horses that received ≥ 1 blood transfusion.

Procedures—Medical records of horses receiving a blood transfusion were reviewed to obtain clinical findings, laboratory test results before and after transfusion, adjunctive treatments, transfusion type and volume, response to transfusion, results of donor-recipient compatibility testing, adverse reactions, and outcome.

Results—31 horses received 44 transfusions for hemorrhagic anemia (HG; $n = 18$ horses), hemolytic anemia (HL; 8), or anemia attributable to erythropoietic failure (EF; 5). Tachycardia and tachypnea were detected in 31 of 31 (100%) and 22 of 31 (71%) horses, respectively, before transfusion. The PCV and hemoglobin concentration were less than the reference range in 11 of 18 horses with HG, 8 of 8 horses with HL, and 5 of 5 horses with EF. Hyperlactatemia was detected in 16 of 17 recorded values before transfusion. Heart rate, respiratory rate, and PCV improved after transfusion, with differences among the types of anemia. Seventeen (54%) horses were discharged, 9 (29%) were euthanized, and 5 (16%) died of natural causes. Adverse reactions were evident during 7 of 44 (16%) transfusions, varying from urticarial reactions to anaphylactic shock.

Conclusions and Clinical Relevance—Abnormalities in clinical and clinicopathologic variables differed depending on the type of anemia. Colic, cold extremities, signs of depression, lethargy, tachycardia, tachypnea, low PCV, low hemoglobin concentration, and hyperlactatemia were commonly detected before transfusion and resolved after transfusion. (*J Am Vet Med Assoc* 2007;231:267–274)

Blood transfusions are often administered to horses as a treatment for acute life-threatening hemorrhage, hemolytic anemia, or anemia caused by erythropoietic failure.¹ The purpose of a transfusion is to restore oxygen delivery to tissues by increasing the oxygen-carrying capacity of blood through restoring blood volume, increasing hemoglobin concentration in blood, or a combination of both. The choice between transfusion of whole blood or PRBCs is influenced by the type of anemia (normovolemic vs hypovolemic) and products available for transfusion. For instance, whole blood is preferred for animals with hemorrhagic disease,² whereas for horses with anemia attributable to hemolytic disease or erythropoietic dysfunction, transfusion of PRBCs is often sufficient to improve tissue oxygenation while minimizing the likelihood of volume overload.^{3,4} There is limited information on the usefulness of transfusion of whole blood or PRBCs for improving oxygen delivery or clinical signs in horses with naturally developing anemia. Furthermore, there is limited empirical information on the clinical and clinicopatho-

ABBREVIATIONS	
PRBCs	Packed RBCs
rhEPO	Recombinant human erythropoietin
EIA	Equine infectious anemia

logic abnormalities that prompt transfusion of blood to adult horses.

Evidence-based guidelines for the decision to perform a transfusion have not been reported for equine medicine and critical care of horses. Consequently, recommendations of transfusion triggers for large animals are based on recommendations developed for humans, dogs, and cats. Identifying the indications for transfusion is not simple, and because of the risk to recipients and cost of the procedure, blood transfusion should be performed only when indicated. Conversely, the severe adverse effects of anemia mean that animals should not be denied a transfusion when it is needed. The PCV may be used as a guide⁵; however, there is no variable for which a single value is a transfusion trigger, and the decision to provide a transfusion should not be made on the basis of Hct, hemoglobin concentration, or RBC count alone. Rather, the decision to provide a transfusion should be made on the basis of a holistic evaluation of an animal, which would include the medical history, physical abnormalities, and clinicopathologic

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data. However, we are not aware of any reports on objective clinical or clinicopathologic abnormalities in anemic horses that subsequently received a transfusion of whole blood or PRBCs, except in animals with experimentally induced anemia.⁶ Additionally, the efficacy of transfusion for improving these variables in horses has not been reported.

An important concern when performing a blood transfusion is the risk to a recipient. Acute reactions vary in severity from mild urticarial skin reactions to acute anaphylaxis and may even result in death.⁵ Development of alloantibodies in a recipient and subsequent problems with repeat transfusions or development of neonatal alloimmune hemolytic anemia in progeny of female recipients is a concern.⁵ To our knowledge, the incidence of these adverse events has not been recorded for large animals.

The purposes of the study reported here were to identify the clinical and clinicopathologic abnormalities in horses with severe hemorrhagic anemia, hemolytic anemia, or anemia attributable to erythropoietic failure; to determine the effect of transfusion of whole blood or PRBCs on those variables; and to describe the incidence and type of adverse reactions in horses receiving a transfusion of whole blood or PRBCs.

Criteria for Selection of Cases

Medical records of horses admitted to The Ohio State University Veterinary Teaching Hospital from 1999 to 2005 were reviewed. Search criteria were the performance of crossmatching by the clinical pathology service or a financial charge to the account for a blood transfusion. Only records for horses ≥ 6 months old were evaluated. Clinical and laboratory variables from before and after transfusion were abstracted from the medical records.

Each horse's clinical condition that necessitated transfusion was categorized into 1 of 3 classifications: hemorrhagic anemia or hypovolemic shock secondary to blood loss, hemolytic anemia, or erythropoietic failure (nonregenerative anemia). Classification was based on the consensus opinion of the authors, especially when the anemia had a multifactorial cause. The hemorrhagic group included horses that had external, intraoperative, or internal hemorrhage with evidence of hypovolemia. The hemolytic group included horses with euvoolemia and clinicopathologic or clinical evidence of hemolysis (hemoglobinemia or hemoglobinuria) with supportive evidence of identification of immunoglobulin on RBCs by use of fluorescent antibody cell sorting, with or without positive results for the Coombs test. Erythropoietic failure was defined as euvolemic anemia, negative results for the Coombs test, a history of administration of rhEPO,⁵ lack of evidence of chronic blood loss or hemolysis, and histologic changes in bone marrow characteristic of erythroid hypoplasia or myelophthitic disease.

Procedures

The clinical and laboratory response to each blood transfusion and overall outcome of each horse (survival, euthanasia, or death resulting from natural causes)

were recorded from the time of admission or within 6 hours preceding transfusion (data before transfusion) and within 6 hours after transfusion (data after transfusion). Concurrent treatment at the time of blood transfusion was also abstracted from the records. Volume of blood transfused was recorded in addition to any data regarding agglutination crossmatching status, recipient compatibility, and any acute reactions to transfusion. Clinical and clinicopathologic data were included for variables collected and recorded within 6 hours after transfusion. Clinicopathologic variables were measured on jugular venous blood samples.

Sixty-two records were retrieved. Two horses were excluded on the basis of age (< 6 months old), 24 horses were prepared for transfusion by crossmatch testing of blood but were euthanized or not administered a blood transfusion, and 5 horses were excluded from the study because of incomplete records. Therefore, 31 horses met the criteria for inclusion, and these horses received a total of 44 transfusions.

Statistical analysis to evaluate differences for selected physical examination and clinicopathologic variables among groups of horses and before and after transfusion within groups of horses was conducted by use of the Kruskal-Wallis test and Wilcoxon signed rank test, respectively, after assessment by use of the Shapiro-Wilk test to determine a normal distribution. Nonparametric statistical analysis was used because of the non-Gaussian distribution of the data, evident skewness of data distribution for a large number of the variables, and small sample size. The proportion of horses with specific abnormalities detected during physical examination was examined by use of the Pearson χ^2 test. Values were considered significant at $P < 0.05$. Results were reported as median and range, unless otherwise stipulated.

Results

Horses—The 31 horses ranged from 6 months to 26 years of age (median, 6.3 years). Body weight ranged from 88 to 826 kg (194 to 1,817 lb; median, 450 kg [990 lb]). Horses comprised 7 Quarter Horses; 6 Thoroughbreds; 4 Tennessee Walking Horses; 4 Arabians; 3 Standardbreds; 2 American Paint Horses; and 1 horse each for Morgan, Miniature, Percheron, Criollo, and American Saddlebred. There were 15 females (all sexually intact) and 16 males (12 geldings and 4 sexually intact).

Clinical signs—One horse was anesthetized at the time of transfusion and could not be assessed for physical examination characteristics. For the remaining 43 transfusions, physical examination revealed that horses had lethargy (34 [79%]), inappetence (31 [72%]), signs of depression (29 [67%]), colic (20 [47%]), sweating (15 [35%]), and cold extremities (16 [37%]) prior to administration of a blood transfusion (Table 1). There was no significant difference in the proportion of horses with colic, cold extremities, or inappetence among classifications of anemia, but the proportion of horses sweating was significantly ($P = 0.024$) higher for horses with hemorrhagic anemia. The proportion of horses with signs of depression varied significantly ($P = 0.005$) among groups of horses.

Transfusions—Of 31 horses that received a blood transfusion, 18 (58%) received a transfusion because of hypovolemic anemia secondary to blood loss, 8 (26%) because of hemolytic anemia, and 5 (16%) because of euvoletic anemia secondary to erythropoietic failure. The most frequent reason for transfusion of horses with anemia secondary to blood loss (ie, hemorrhage) was colic surgery (5/18). The most prevalent disease necessitating transfusion because of hemolytic anemia was immune-mediated erythrocyte lysis or agglutination (4/8). Administration of rhEPO accounted for 3 of 5 horses with erythropoietic failure.

Twenty of 31 (64%) horses received a single transfusion, 9 (29%) received 2 transfusions, and 2 (6%) were administered 3 transfusions. The majority (40/44 [91%]) of transfusions were whole blood, and the remaining 4 (9%) were PRBCs. Median volume of whole blood administered was 15 mL/kg (6.8 mL/lb; range, 5 to 26 mL/kg [2.3 to 11.8 mL/lb]), whereas median volume of PRBCs administered was 8 mL/kg (3.6 mL/lb; range, 4 to 10 mL/kg [1.8 to 4.5 mL/lb]). The PCV of donor blood was recorded for only 5 of 44 transfusions, and median PCV was 38% (range, 35% to 40%). The PCV of transfused horses increased significantly ($P < 0.001$) after transfusion (median increase of 4%; range, -11% to 13%). Horses that received whole blood had a PCV of 12% (range, 4% to 37%) before transfusion, which increased to 17% (range, 6% to 39%) after trans-

fusion. Horses that received PRBCs had a PCV of 9% (range, 8% to 12%) before transfusion, which increased to 15% (range, 12% to 22%) after transfusion.

Transfusion resulted in significant changes in several variables. Significant decreases in heart rate ($P < 0.001$), respiratory rate ($P = 0.001$), and serum creatinine concentration ($P = 0.014$) and a significant ($P = 0.040$) increase in venous oxygen saturation were detected after transfusion (Table 2).

During the 44 transfusions, 7 (16%) adverse reactions were recorded for 7 horses. Adverse events during or soon after completion of a transfusion were mild urticarial reactions ($n = 3$), acute anaphylactic shock (1), and worsening hemolysis in horses with hemolytic disease (3). Crossmatching status was recorded for 6 of 7 transfusions in which there were adverse reactions (2 were compatible on major and minor crossmatching, 3 were compatible only on major crossmatching, and 1 was compatible only on minor crossmatching).

The majority (24/31 [77%]) of horses in the study received concomitant crystalloid fluids. None of the horses that had anemia attributable to erythropoietic failure received concomitant crystalloid or other fluids.

Seventeen of 31 (54%) horses were discharged from the hospital. Nine (29%) horses were euthanized because of a poor prognosis for health and function or as a result of financial limitations. Five (16%) horses died as a consequence of disease progression.

Table 1—Physical examination findings for horses in each of 3 classifications of anemia before receiving a blood transfusion.

Classification of anemia	Colic	Cold extremities	Lethargy	Signs of depression*	Inappetence	Sweating*
Erythropoietic failure	1/5	1/5	5/5	5/5	4/5	0/5
Hemolytic anemia	3/8	2/8	3/8	8/8	6/8	3/8
Hemorrhagic anemia	12/18	11/18	12/18	8/18	12/18	12/18

Values are expressed as the number of horses with the finding/total number of horses within each classification.
*Within a column, proportions differ significantly ($P < 0.05$) among groups.

Table 2—Median (range) values for clinical, biochemical, and hematologic variables of 31 anemic horses before and after receiving 44 blood transfusions.

Variable	Before	After	No. of transfusions*	P value†
Heart rate (beats/min)	80 (48 to 130)	60 (46 to 116)	44 and 43	< 0.001
Respiratory rate (breaths/min)	28 (8 to 70)	20 (12 to 72)	44 and 43	0.001
Rectal temperature (°C)‡	38.2 (36.8 to 40.3)	NR	44 and 0	NA
PCV (%)	12 (4 to 37)	16 (6 to 39)	44 and 43	< 0.001
Hemoglobin (g/dL)	5.8 (2.2 to 25.0)	6.6 (2.0 to 9.0)	44 and 43	0.470
Total protein (g/dL)	5.5 (2.8 to 9.6)	6.2 (3.5 to 9.2)	41 and 39	0.050
Lactate (mmol/L)	4.6 (1.6 to 11.0)	3.2 (0.8 to 14.2)	17 and 11	0.054
PvO ₂ (mm Hg)	27.6 (9.9 to 41.0)	29.3 (25.0 to 46.3)	28 and 14	0.058
Base excess (mmol/L)	0.05 (-17.00 to 17.30)	-0.40 (-14.00 to 7.00)	30 and 14	0.951
Bicarbonate (mmol/L)	24 (7 to 34)	22 (14 to 31)	32 and 19	0.720
Venous oxygen saturation (%)	51 (29 to 75)	55 (31 to 79)	17 and 11	0.040
SUN (mg/dL)	21.5 (5.0 to 97.0)	21.0 (16.0 to 64.0)	28 and 13	0.074
Creatinine (mg/dL)	2.1 (0.7 to 10.6)	1.9 (1.0 to 6.1)	28 and 13	0.014
pH	7.37 (7.09 to 7.46)	7.38 (7.14 to 7.49)	30 and 15	0.680

*Represents the number of horses for which measurements were obtained before and after transfusion, respectively. †Values were considered significantly different at $P < 0.05$. ‡To convert to degrees Fahrenheit, multiply the value by 1.8 and then add 32 to the product.
NR = Not recorded. NA = Not applicable; statistical analysis was not performed because of paucity of data after transfusion.

Anemia attributable to erythropoietic failure—Five horses had anemia attributable to erythropoietic failure and received 9 transfusions. Median age of the 5 horses was 3 years (range, 2 to 14 years), and median body weight was 458 kg (1,008 lb; range, 371 to 518 kg [816 to 1,140 lb]). Causes of erythropoietic failure included myelophthistic disease ($n = 1$ horse), rhEPO administration (3), and pure RBC aplasia (1). Eight of 9 blood transfusions administered were whole blood, with the remaining transfusion consisting of PRBCs. Median volume of whole blood and PRBCs administered was 17 mL/kg (7.7 mL/lb; range, 13 to 26 mL/kg [5.9 to 11.8 mL/lb]) and 7 mL/kg (3.2 mL/lb), respectively. Median PCV was 6% (range, 4% to 8%) before transfusion and 9% (range, 7% to 17%) after transfusion (Table 3). There was an overall increase in PCV of 4% (range, 1% to 13%).

Heart rate ($P = 0.004$) and respiratory rate ($P = 0.004$) decreased significantly after transfusion in horses with anemia attributable to erythropoietic failure. However, there was a significant increase in PCV ($P = 0.039$) and total plasma protein concentration ($P = 0.008$) after blood transfusion in this group of horses.

Two horses with anemia attributable to erythropoietic failure had adverse reactions during transfusion. One had a mild urticarial reaction despite full crossmatching compatibility. The second horse had a presumed anaphylactic reaction; this horse had compatibility only for the major crossmatch and received a transfusion of whole blood.

In this group, 2 of 5 horses were discharged from the hospital. The remaining 3 horses in this group were euthanized.

Hemolytic anemia—Eight horses had hemolytic anemia and received 15 transfusions. Causes of hemolysis included immune-mediated hemolytic anemia ($n = 4$) and toxins (4), which included methemoglobinemia subsequent to red maple leaf ingestion in 3 horses.

The majority (13/15) of transfusions administered were whole blood, and the remaining 2 were PRBCs. Median volume of whole blood administered was 15 mL/kg (range, 10 to 20 mL/kg [4.5 to 9.1 mL/lb]), whereas the median volume of PRBCs administered was 9 mL/kg (4.1 mL/lb; range, 4 to 10 mL/kg). For horses

that received whole blood, the PCV before transfusion was 14% (range, 6% to 19%) and it increased to 16% (6% to 22%) after transfusion. The PCV before transfusion in horses that received PRBCs was 11% (range, 8% to 12%), and it increased to 18% (12% to 22%) after transfusion. The change in PCV was an increase of 4% (range, -4% to 10%). This included an increase of 4% for horses that received whole blood (range, -4% to 6%) and 6% for horses that received PRBCs (range, -4% to 10%).

Heart rate ($P < 0.001$) and serum concentrations of creatinine ($P = 0.03$) and urea nitrogen ($P = 0.003$) were significantly lower after blood transfusion. Blood methemoglobin concentration did not decrease significantly ($P = 0.25$) after transfusion; however, for each horse in which it was measured, there was a reduction in blood methemoglobin concentration after transfusion (Table 4).

Three of the 7 recorded blood transfusion reactions were in 3 horses with hemolytic anemia; 1 of these horses developed signs of acute anaphylactic shock and was euthanized. The remaining 2 reactions were classified as worsening of ongoing hemolysis. All 3 horses had incomplete compatibility testing, with 2 of 3 being compatible only on major crossmatching and the remaining horse being compatible only on minor crossmatching. Incompatibilities resulted despite testing of multiple potential donors and were ascribed to the disease process in the affected recipient horses.

Three of 8 horses in this group survived to be discharged from the hospital. Two horses in this group were euthanized, and 3 died of natural causes.

Hemorrhagic anemia—Eighteen horses had hemorrhagic anemia or hypovolemia secondary to blood loss and received 20 transfusions. Causes of blood loss included hemorrhage during or after surgery ($n = 8$), reproductive tract bleeding (5), hemorrhage secondary to coagulopathies (4), and nonreproductive tract trauma (1). All 20 transfusions administered were whole blood. Median volume of whole blood administered was 13 mL/kg (range, 4 to 25 mL/kg [1.8 to 11.4 mL/lb]). Seven of 18 horses had a PCV $> 25\%$ (within the reference range) before transfusion. Overall, for

Table 3—Median (range) values for clinical, biochemical, and hematologic variables of 5 horses with anemia secondary to failure of erythropoiesis before and after receiving 9 blood transfusions.

Variable	Before	After	No. of transfusions*	P value†
Heart rate (beats/min)	76 (56 to 84)	48 (48 to 60)	9 and 9	0.004
Respiratory rate (breaths/min)	20 (12 to 42)	18 (12 to 30)	9 and 9	0.039
Rectal temperature (°C)‡	38.6 (37.7 to 40.0)	NR	9 and 0	NA
PCV (%)	6 (4 to 8)	9 (7 to 17)	9 and 9	0.004
Hemoglobin (g/dL)	2.7 (2.2 to 2.5)	4.8 (3.3 to 6.7)	5 and 4	0.630
Total protein (g/dL)	5.6 (2.8 to 8.0)	6.2 (3.5 to 8.4)	9 and 9	0.008
Lactate (mmol/L)	3.8 (2.5 to 9.8)	3.3 (0.9 to 14.2)	6 and 5	0.630
PvO ₂ (mm Hg)	25.1 (22.9 to 40)	28.9 (25.9 to 40.0)	7 and 5	0.440
Base excess (mmol/L)	0.70 (-3.40 to 4.40)	2.00 (-12.00 to 5.80)	9 and 5	1.000
Bicarbonate (mmol/L)	24 (22 to 25)	26 (14 to 30)	7 and 4	NA
Venous oxygen saturation (%)	47.0 (29.0 to 75.0)	55.3 (31.2 to 74.9)	6 and 5	NA
SUN (mg/dL)	14 (11 to 25)	21§	7 and 1	NA
Creatinine (mg/dL)	1.4 (1.1 to 1.7)	5.1§	7 and 1	NA
pH	7.38 (7.24 to 7.42)	7.4 (7.21 to 7.44)	9 and 5	NA

§The range was not determined because there was a value for only 1 horse after transfusion.
See Table 2 for remainder of key.

Table 4—Median (range) values for clinical, biochemical, and hematologic variables of 8 horses with hemolytic anemia before and after receiving 15 blood transfusions.

Variable	Before	After	No. of transfusions*	P value†
Heart rate (beats/min)	84 (60 to 130)	64 (42 to 116)	15 and 15	< 0.001
Respiratory rate (breaths/min)	24 (16 to 68)	20 (12 to 72)	15 and 15	0.270
Rectal temperature (°C)‡	38.7 (37.0 to 40.3)	NR	15 and 0	NA
PCV (%)	12 (6 to 19)	17 (6 to 22)	15 and 15	0.003
Hemoglobin (g/dL)	5.6 (2.6 to 9.2)	6.5 (2.0 to 8.6)	13 and 9	0.720
Methemoglobin (g/dL)	0.79 (0.12 to 2.51)	0.31 (0.18 to 1.10)	4 and 4	0.250
Methemoglobin proportion of hemoglobin (%)	13.5 (2.73 to 45.6)	4.3 (2.1 to 20.1)	4 and 4	0.250
Total protein (g/dL)	7.6 (4.6 to 9.6)	7.7 (5.2 to 9.2)	13 and 12	0.460
Lactate (mmol/L)	5.4 (4.1 to 8.0)	3.9 (3.2 to 5.3)	6 and 3	0.250
PvO ₂ (mm Hg)	23.1 (9.9 to 41)	28.75 (25.8 to 46.3)	12 and 6	0.310
Base excess (mmol/L)	−1.7 (−17 to 8.8)	−0.9 (−14 to 6.2)	12 and 6	0.560
Bicarbonate (mmol/L)	22 (10 to 34)	22 (14 to 30)	13 and 9	0.840
Venous oxygen saturation (%)	53.4 (42.0 to 67.7)	51.6 (48.9 to 77.6)	8 and 5	0.060
SUN (mg/dL)	27.5 (5.0 to 97.0)	23.5 (16.0 to 64.0)	12 and 8	0.031
Creatinine (mg/dL)	3.4 (1.0 to 10.6)	1.85 (1.0 to 6.1)	12 and 8	0.031
pH	7.37 (7.19 to 7.46)	7.37 (7.14 to 7.49)	12 and 7	0.810

See Table 2 for key.

Table 5—Median (range) values for clinical, biochemical, and hematologic variables of 18 horses with hemorrhagic anemia before and after receiving 20 blood transfusions.

Variable	Before	After	No. of transfusions*	P value†
Heart rate (beats/min)	86 (48 to 124)	66 (40 to 84)	20 and 19	< 0.001
Respiratory rate (breaths/min)	39 (8 to 70)	20 (12 to 60)	20 and 19	0.010
Rectal temperature (°C)‡	37.8 (36.8 to 39.2)	NR	20 and 0	NA
PCV (%)	16 (8 to 37)	18 (10 to 39)	20 and 19	0.110
Hemoglobin (g/dL)	10.8 (3.3 to 13.2)	7.1 (6.2 to 9.0)	9 and 5	NA
Total protein (g/dL)	4.1 (3.3 to 9.0)	5.2 (3.6 to 7.0)	19 and 18	0.150
Lactate (mmol/L)	4.1 (1.6 to 11.0)	1.1 (0.8 to 1.5)	5 and 3	0.250
PvO ₂ (mm Hg)	33.5 (21.7 to 41.0)	34.7 (25.0 to 41.2)	9 and 3	0.250
Base excess (mmol/L)	−2.5 (−11.5 to 17.3)	−5.0 (−14.0 to 7.0)	9 and 3	0.500
Bicarbonate (mmol/L)	23.8 (7.0 to 29.0)	23.0 (14.0 to 31.0)	12 and 6	0.810
Venous oxygen saturation (%)	56.2 (29.3 to 57.9)	78.8§	3 and 1	NA
SUN (mg/dL)	22 (9 to 30)	19 (17 to 26)	9 and 4	NA
Creatinine (mg/dL)	2.1 (0.7 to 4.4)	1.8 (1.4 to 2.5)	9 and 4	NA

See Tables 2 and 3 for key.

horses with hemorrhagic anemia, PCV increased by 5% (range, −11% to 10%) after transfusion, but this change was not significant ($P = 0.11$).

Heart rate decreased significantly ($P < 0.001$) after the administration of whole blood (Table 5). Similarly, respiratory rate decreased significantly ($P = 0.01$) after the administration of whole blood.

Two of the 7 adverse transfusion reactions were in horses with hemorrhagic anemia. The reactions were mild urticarial reactions that required no specific treatment. The reaction developed in 1 horse despite a fully compatible crossmatching status; the other horse did not have the crossmatching status recorded.

Twelve of 18 horses in this group survived to be discharged from the hospital. Four horses were euthanized, and 2 horses in this group died of natural causes.

Discussion

In the study reported here, we determined that blood transfusion to horses has beneficial effects on clinical and clinicopathologic variables and that the de-

gree of improvement and variables used to characterize the improvement varied with the cause of anemia. We also determined that there was a low incidence of fatal adverse reactions to administration of whole blood or PRBCs.

Whole blood was administered more frequently than PRBCs, which is consistent with the greater proportion of horses treated for hemorrhagic anemia. Other reports^{2,7-9} indicate that the most common reason for transfusion in horses is surgery of the paranasal sinus or ethmoid, and the transfusions are administered during surgery. This was an uncommon reason for transfusion of horses in the study reported here (only 2 horses), although the reasons for this discrepancy are unclear. There is also some variability regarding the reasons for transfusion administration among domestic species. Hemorrhage secondary to trauma¹⁰ and immune-mediated hemolytic anemia^{10,11} are common reasons reported in dogs, and hemorrhage^{3,12,13} and erythropoietic failure secondary to chronic renal failure^{3,13,14} represent the most common reasons for transfusion in cats. Transfusions in these instances often consist of PRBCs.

Again, the reason for these differences among species is unclear but could be attributable to differences in clinician preferences in use of colloids, crystalloids, and blood products for the various species.

Variation in abnormalities detected during physical examination was evident within and among groups of horses. Lethargy and inappetance were reported in 79% and 72% of horses, respectively, and 67% of horses had signs of depression. These are nonspecific clinical findings that may be indicative of inadequate oxygen delivery and malaise associated with an underlying disease. However, the high frequency of these findings in horses that were subsequently administered blood transfusions suggests that these clinical signs may be indicators of the need for transfusion of whole blood or PRBCs. However, these signs are not pathognomonic of the need for transfusion and can be caused by diseases that do not require blood transfusions.

The proportion of horses within a group with sweating, cold extremities, and signs of depression varied with the cause of anemia. Sweating was not detected in horses with anemia caused by erythropoietic failure but was detected in 12 of 18 horses with hemorrhagic anemia. Conversely, signs of depression were evident in all horses with aplastic or hemolytic anemia but in only 8 of 18 horses with hemorrhagic anemia. It appeared that horses with hemorrhagic anemia were more likely to have cold extremities and colic and less likely to have signs of depression than the horses in the other groups, but this difference was not significant. If real, this difference would likely be related to the hypovolemic and acute nature of the anemia, with blood pressure and blood flow to vital organs preserved at the expense of flow to tissues such as the skin. However, any or all of these findings are abnormal and may be indicators of the need for transfusion, volume resuscitation, or a combination of both when used in conjunction with objective data that support the need for transfusion of horses.

The rate of development of anemia also influences the clinical findings in horses with anemia.^{1,9,15} Horses with prolonged chronic destruction of RBCs or failure of erythrocyte production are more stable clinically than horses with acute hypovolemic hemorrhagic anemia or severe hemolysis. This was evident as a relatively lower heart rate; lower respiratory rate; and lack of signs of colic, sweating, and cold extremities in horses of the erythropoietic failure group, compared with findings for horses with hemorrhagic anemia. The physiologic adaptation to a chronically developed hypoxic environment causes an increase of 2,3-diphosphoglycerate concentration within the remaining erythrocytes, which favors oxygen affinity to hemoglobin and results in a shift of the oxygen delivery dissociation curve.¹⁶ These compensatory mechanisms augment oxygen delivery to tissues, which allows animals to tolerate anemia when the rate of development of anemia is slow.⁹

We determined that transfusion of whole blood or PRBCs significantly lowered heart rate and respiratory rate for all classes of anemia. Decreases in heart rate can be attributed to restoration of blood volume, hemoglobin concentration, or both, with a subsequent increase in oxygen delivery to tissue.¹ Volume replacement improves cardiac preload, stroke volume, and cardiac out-

put, whereas hemoglobin replacement improves the oxygen-carrying capacity of each unit of blood. Clinical condition of horses with hemorrhagic disease improved as a result of blood volume restoration as well as increases in erythrocyte count, whereas clinical condition of horses with hemolytic anemia and anemia attributable to erythropoietic failure likely improved because of improvements in RBC numbers and hemoglobin concentration.

Increases in respiratory rate could have been attributable to reduced oxygen delivery and a compensatory increase in ventilation rate. Increased respiratory efforts were evident when there was physical exertion, an increase in body temperature, or both. However, no direct causation was established for this finding among horses in the study reported here. We attributed the increase in respiratory effort to an increased oxygen requirement because an increase in body temperature of 1.0°C (1.8°F) increases oxygen requirement by 12%.⁵ The decrease in respiratory rate after transfusion may have been attributable to improved tissue oxygenation through combinations of corrected hypovolemia, improved RBC numbers, and an increase in hemoglobin concentration.¹

It is recommended^{7,9} that anemic horses be administered 10 to 20 mL of blood/kg, and this volume was achieved in the horses of the study reported here. Our findings are consistent with a report³ in cats in which administration of 15 mL/kg resulted in an increase in PCV of 4.0%. The PCV improved significantly in horses with hemolytic anemia and anemia attributable to erythropoietic failure but not horses with hemorrhagic anemia. However, 7 of 18 horses with hemorrhagic anemia had a PCV of > 25% (within the reference range) before transfusion, and administration of whole blood to these horses may not have resulted in a measurable increase in Hct. Hemorrhage causes equal losses of circulating red cell mass and plasma proteins, and acute hemorrhagic shock is not associated with a reduction in PCV.⁵ The rate for restoration of circulating blood volume through transcellular and transcompartmental shifts in fluid is slow and requires a longer duration of time than that required to lose whole blood. Therefore, there is a disparity between the measurable PCV and the actual RBC content of the vascular space. Resuscitative fluids shift from the extracellular fluid compartment to maintain blood volume, and similar shifts are evident with blood transfusions and IV administration of other fluids; thus, there is a decrease in Hct after transfusion despite maintenance of or improvement in circulating red cell mass. Therefore, PCV is not a good indicator of the efficacy of transfusion in all horses with hemorrhagic anemia.

It has been postulated¹⁷ that blood lactate concentrations may be a useful indicator for the need to perform a transfusion in human and veterinary medicine because lactate concentration increases when tissue perfusion and oxygenation decreases. The study reported here revealed that blood lactate concentrations were increased in all horses in which that variable was recorded prior to receiving a transfusion. However, the results did not reveal a significant reduction in blood lactate concentrations after transfusion. This may have been attributable to the limited number of recorded blood

lactate values before and after transfusion ($n = 17$ and 11 , respectively). The cause or causes of the increase in blood lactate concentration was not determined but may have been attributable to increased production or decreased hepatic clearance. In all classes of anemia, blood lactate concentration shifted toward the reference range after transfusion (overall, $P = 0.054$). The greatest degree of improvement was evident for horses with hemorrhagic anemia in which the median blood lactate concentration decreased (improved) from 4.1 mmol/L before transfusion to 1.1 mmol/L after transfusion ($P = 0.25$). These results parallel results for studies of progressive anemia of lambs¹⁷ and horses⁶ in which blood lactate concentrations increased as blood hemoglobin concentrations decreased and vice versa. The beneficial effect of transfusion on blood lactate concentration in horses with hemorrhagic anemia could have been attributable to decreased lactate production or increased lactate consumption by the liver and muscles or it may have been secondary to improved tissue oxygenation through volume restoration and increases in hemoglobin concentration and subsequent oxygen delivery.

Azotemia was a consistent finding overall and within each anemia classification with the exception of horses with anemia attributable to erythropoietic failure. We believed the increases in SUN and creatinine concentrations were the result of hypovolemia (prerenal causes), hypoxia, nephrotoxic effects of hemoglobinuria, or a combination of these factors with subsequent renal dysfunction, although the exact mechanisms are unknown. There was a significant decrease in SUN and creatinine concentrations after transfusion; however, given that most of the horses in the study also received crystalloids, resolution of azotemia could have been a result of transfusion or the adjunctive fluid treatment.

Potential complications of blood transfusion in horses and other species include transfusion reactions^{7,18-20} and transmission of infectious diseases.^{4,5,21} Transfusion reactions can vary in severity from mild urticarial reactions that require no intervention to anaphylactic shock that requires emergency resuscitative procedures.^{9,19} Despite the identification of erythrocyte surface antigens and crossmatching methods, there are still transfusion reactions in horses. However, with these testing methods and the use of autologous blood transfusions^{18,20} for elective surgical procedures, it is likely that the incidence of reactions is at a lower rate in crossmatched horses than in unmatched recipients.^{1,18,19} The recognized risk of transmitting infectious diseases in horses through transfusions is low, compared with that reported for humans, with EIA virus being the most substantial potential risk.⁹ None of the horses in the study reported here was believed to have contracted EIA because all donor horses had a negative Coggin's test prior to blood collection.

Analysis of our results revealed that the adverse effects of transfusion administration can be evident for all disease states and clinically important even when a compatible donor-recipient agglutination crossmatching status is determined. Seven horses in this study had some type of adverse reaction during or shortly after transfusion. Two reactions were in horses with anemia attributable to erythropoietic failure. One of these horses

had mild urticaria despite compatibilities on both major and minor crossmatching, and the second horse had acute colic, dyspnea, and excitation consistent with anaphylaxis. That horse was incompatible on minor crossmatching (donor plasma vs recipient RBCs), and despite resuscitative efforts, it was necessary to euthanize the horse shortly after blood administration. Incompatibility for minor crossmatching could have led to a severe hemolytic crisis in which the donor plasma contained anti-RBC antibodies against the remaining recipient cells.⁹

Three adverse reactions were in horses with hemolytic anemia. One horse had signs of anaphylaxis, and the remaining 2 horses were suspected of having varying degrees of ongoing hemolysis. All 3 had at least 1 incompatibility on crossmatching. Two of the 3 horses had compatibility on major crossmatching and incompatibility on minor crossmatching, whereas the third horse had incompatibility on major crossmatching but compatibility on minor crossmatching. It was assumed that the adverse effects in these 3 horses were a continuation of the underlying disease, rather than directly attributable to the administration of a transfusion. Therefore, blood transfusions were administered to these horses with the recognition that the donor blood may have been incompatible with that of the recipient, where incompatibilities were a consequence of the disease process (eg, immune mediated).

Two of 7 reactions were in horses with hemorrhagic anemia. These reactions were mild and consisted of a mild urticarial skin reaction that did not require treatment. One of the horses did not have a crossmatching status recorded. The second horse had compatibility on both major and minor crossmatching, yet it still developed a mild urticarial reaction, which indicated that crossmatching compatibilities are not 100% sensitive in identifying compatibility between donors and recipients. When choosing a potential donor horse, thorough assessment of disease status (eg, testing to detect EIA), size of the donor horse, and potential volume of blood to be harvested should be considered. It would be ideal to know the blood type of both the donor and recipient; at the least, the crossmatching compatibility status should be assessed to determine compatibility and minimize potential adverse reactions.

On the basis of results of the study reported here, administration of 15 mL of whole blood/kg and 8 to 10 mL of PRBCs/kg can yield an expected increase in PCV of 4% when the donor PCV is 35% to 40% . Such a transfusion would be expected to result in improvements in clinical and clinicopathologic variables in anemic horses.

References

1. Hunt E, Wood B. Use of blood and blood products. *Vet Clin North Am Food Anim Pract* 1999;15:643-661.
2. Wong PL, Nickel LS, Bowling AT, et al. Clinical survey of antibodies against red blood cells in horses after homologous blood transfusion. *Am J Vet Res* 1986;47:2566-2571.
3. Klaser DA, Reine NJ, Hohenhaus AE. Red blood cell transfusions in cats: 126 cases (1999). *J Am Vet Med Assoc* 2005;226:920-923.
4. Jutkowitz LA, Rozanski EA, Moreau JA, et al. Massive transfusion in dogs: 15 cases (1997-2001). *J Am Vet Med Assoc* 2002; 220:1664-1669.
5. Radostits OM, Gay CC, Hinchcliff KW, et al. Diseases of the hemolymphatic and immune systems. In: *Veterinary medicine*.

A textbook of the diseases of cattle, horses, sheep, goats, and pigs. 10th ed. Philadelphia: Elsevier Health Sciences, 2007;458–459.

6. Magdesian KG, Fielding CL, Rhodes DM, et al. Changes in central venous pressure and blood lactate concentration in response to acute blood loss in horses. *J Am Vet Med Assoc* 2006; 229:1458–1462.
7. Durham AE. Blood and plasma transfusion in the horse. *Equine Vet Educ* 1996;8:8–12.
8. Specht TE, Colahan PT, Nixon AJ, et al. Ethmoid hematoma in nine horses. *J Am Vet Med Assoc* 1990;197:613–616.
9. Slovis NM, Murray G. How to approach whole blood transfusions in horses, in *Proceedings*. Am Assoc Equine Pract 2001; 47:266–269.
10. Callan MB, Oakley DA, Schofer FS, et al. Canine red blood cell transfusion practice. *J Am Anim Hosp Assoc* 1996;32:303–311.
11. Kerl ME, Hohenhaus AE. Packed red blood cell transfusions in dogs: 131 cases (1989). *J Am Vet Med Assoc* 1993;202: 1495–1499.
12. Castellanos I, Couto CG, Gray TL. Clinical use of blood products in cats: a retrospective study (1997–2000). *J Vet Intern Med* 2004;18:529–532.
13. Weingart C, Giger U, Kohn B. Whole blood transfusions in 91 cats: a clinical evaluation. *J Feline Med Surg* 2004;6:139–148.
14. Morris DD. Blood products in large animal medicine: a comparative account of current and future technology. *Equine Vet J* 1987; 19:272–275.
15. Trim CM, Eaton SA, Parks AH. Severe nasal hemorrhage in an anesthetized horse. *J Am Vet Med Assoc* 1997;210:1324–1327.
16. Murphy MF, Wallington TB, Kelsey P, et al. Guidelines for the clinical use of red cell transfusion. *Br J Haematol* 2001;113:24–31.
17. Widness JA, Lowe LS, Bell EF, et al. Adaptive responses during anemia and its correction in lambs. *J Appl Physiol* 2000;88:1397–1406.
18. Byars TD, Divers TJ. Clinical use of blood transfusions. *Calif Vet* 1981;1:14–16.
19. Kallfelz FA, Whitlock RH, Schultz RD. Survival of ⁵⁹Fe-labeled red cells in cross-transfused equine blood. *Am J Vet Res* 1978; 39:617–620.
20. Smith JE, Dever M, Smith J. Post-transfusion survival of ⁵⁰Cr-labeled erythrocytes in neonatal foals. *J Vet Intern Med* 1992; 6:183–185.
21. Hardy J. Current status of transfusion triggers for red blood cell concentrates. *Transfus Apher Sci* 2004;31:55–66.