Avian Transfusion Medicine

Abstract: Anemia is defined as a decreased capacity of the blood to carry oxygen and is recognized by packed cell volume, erythrocyte, and hemoglobin values below reference ranges. Causes of anemia in birds include blood loss, heavy metal toxicosis, parasitic infection, and chronic disease. Several differences exist between avian and mammalian physiology, including the avian ability to tolerate greater losses of blood. However, the use of blood products has become an effective tool for treating anemic avian patients. Whole blood transfusions (autologous, homologous, and heterologous) and administration of hemoglobin-based, oxygen-carrying solutions are the treatments used most commonly in birds.

History of Transfusion Medicine
The use of transfusion medicine for avian patients is a relatively new application of intravenous blood administration. In 1666, Richard Lower reported blood administration from the carotid artery of one dog to the jugular vein of another, which is often credited as the first allogeneic blood transfusion.1,2 The following year, Lower and Jean-Baptiste Denis performed an intravenous transfusion from an animal to a human patient in an attempt to cure mental illness.3,4 In 1795, Philip Syng Physick performed the first transfusion between humans,1 but it was more than 150 years later that E.A. Hewitt described blood transfusion as the preferred treatment for hemorrhage and anemia in veterinary medicine.3 By the mid 20th century, blood groups had been established in most domestic animal species.1

Avian Hematology
Transfusing incompatible blood into a patient may be fatal. Therefore, before blood transfusion in humans and domestic animal species, patients’ blood is commonly typed, a process based on erythrocyte surface antigens, or is cross-matched with the donor blood for serologic compatibility. Avian blood typing is still very rudimentary, with extensive investigation and description currently limited to chickens, in which 28 blood groups have been described.3,4 In contrast to mammalian erythrocytes, avian erythrocytes are nucleated and oval. The long axis of an avian erythrocyte has an average length of 13.5 µm, whereas the average diameter of a mammalian erythrocyte is 6.3 µm.5 The average avian erythrocyte has a shorter maximum life span (35 and 42 days for chicken and duck erythrocytes, respectively) than its mammalian counterpart (115 and 120 days for canine and human erythrocytes, respectively).6 The comparatively shorter life span of avian erythrocytes may be associated with birds’ higher body temperature and metabolic rate.7 The consumption rate of oxygen by erythrocytes is greater in avian species than in mammals.7

The average packed cell volume (PCV) and total erythrocyte count vary considerably among avian species. For example, Chilean flamingos have a PCV of 41% to 51% and an erythrocyte count of 2.44 × 10^6/µL to 2.93 × 10^6/µL, whereas ostriches have a PCV of 31.4% to 38.6% and an erythrocyte count of 1.48 × 10^6/µL to 1.52 × 10^6/µL.8 Juvenile birds tend to have fewer erythrocytes and lower hematocrits than adults because erythrocyte numbers increase with age.9,10 In some species, PCVs are lower in females than in males, which has been attributed to the effects of estrogen.11 Other factors that affect erythrocyte variability include season and altitude.12,13

At a Glance
- History of Transfusion Medicine Page E1
- Avian Hematology Page E1
- Anemia Page E1
- Therapy Page E2

Abstract:
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Anemia
Anemia is diagnosed by a decrease in total erythrocytes, hemoglobin, or PCV and may be classified as regenerative or nonregenerative.

Regenerative
Regenerative anemia can be caused by hemorrhage or hemolysis. Blood loss may be associated with trauma (e.g., broken blood feather), surgical procedures, gastrointestinal bleeding (e.g., ulcers, parasites), and cloacal bleeding (e.g., from papillomas, egg laying, severe cloacitis, cloacal or uterine prolapse). Coagulopathies are described in other companion animal species as causes of blood loss. There is currently no standardized testing for coagulopathy in birds; therefore, primary coagulopathies have not been reported in avian species. Secondary coagulopathies due to toxins (e.g., aflatoxicosis, rodenticides) have been described in birds, and brodifacoum toxicosis was reported to be the cause of anemia in a white-winged wood duck.15,16

Avian physiology is unique with regard to circulatory homeostasis and aids in recovery after significant blood loss. The large capillary density and surface area within the avian skeletal muscles promote interstitial fluid absorption and an increase in circulating blood volume.17 By allowing blood to enter the caudal vena cava directly, bypassing the liver and kidneys, the renal portal system may also contribute to an increase in the circulating blood volume in anemic patients.18 Contraction of the spleen as a mechanism for increasing circulating erythrocytes does not occur in birds. Hypoxia-induced erythropoietin stimulates increased production and maturation of erythrocytes in the bone marrow.

Birds do not appear to be as sensitive to hypoxia as mammals. One study determined that the lethal dose for 50% (LD50) of mallard ducks subjected to acute blood loss (over 10 to 20 minutes) was 60% of total blood volume.19 For mammals, the LD50 is reported to be 40% to 50% of total blood volume.19 The study also found marked erythrocyte regeneration after 36 hours in the ducks, which is much sooner than regeneration would occur in mammals. In some avian species, tissue damage following blood loss may be spared by the lack of precapillary constriction, as demonstrated in chickens.20

Hemolytic anemia in birds may be caused by infection (e.g., with Plasmodium, Aegyptianella, Haemoproteus, or Leucocytozoon spp) or toxicoisis from ingestation of crude oil or lead.21–26 Autoimmune hemolytic anemia, although rarely diagnosed, has been described in an eclectus parrot (Eclectus roratus).27

Nonregenerative
Nonregenerative anemias can be caused by chronic inflammatory processes (e.g., neoplasia, toxicosis, infection).28,29 Due to the comparatively short life span of avian erythrocytes, birds are thought to be more susceptible than mammals to developing nonregenerative anemias resulting from chronic inflammation.27 Infectious conditions that result in nonregenerative anemia include bacterial (e.g., chlamydiosis, mycobacteriosis), viral, and fungal infections.29 Chronic renal disease and folic acid deficiency are uncommon causes of nonregenerative anemia in birds; iron-deficiency anemia has been induced experimentally in poultry but has not been reported in any pet bird species.30–32

Clinical Signs
The clinical signs of anemia in avian patients can include weakness progressing to collapse and tachypnea or tachycardia.17 Additional signs associated with the underlying cause may be seen. The diagnosis of anemia is made with hematocrit evaluation. A blood smear evaluation can classify anemia as regenerative or nonregenerative. Polychromasia, anisocytosis, reticulocytosis, and mitotic figures may be observed on blood samples from birds with regenerative anemia. Birds with lead toxicosis may have erythrocytes that appear hypochromic and misshapen.26 Basophilic stippling is not seen in all species but has been observed in trumpeter swans and Canadian geese with lead concentrations >3 mg/L.26 Nonregenerative anemias are typically normocytic and normochromic, lacking any of the associated signs of regeneration listed above.

Therapy
Treatment for anemia includes supportive therapy as well as finding and correcting the underlying cause. Crystalloid or colloid fluid products may be used to restore circulating blood volume, thus increasing tissue perfu-
sion and oxygen delivery. In stable patients with mild dehydration, balanced isotonic solutions may be administered subcutaneously; for patients with severe blood loss or dehydration, intravenous and intraosseous routes are preferred. Vitamin K, which is essential to the coagulation cascade, can be supplemented in patients with acute blood loss or excessive clotting times. Vitamin K supplementation has been shown to reduce prothrombin time. A bird’s main sources of vitamin K are diet and bacterial production in the gastrointestinal tract. Iron, which is necessary for hemoglobin production, may be supplemented after hemorrhage to help restore a bird’s circulating erythrocytes. Anemic raptors have shown dramatic responses to a single iron injection.

Administration of Oxyglobin (Biopure, Cambridge, MA) and whole blood transfusions have also been used in avian species. The criteria for blood product use in avian species are not well established. Blood product use should be considered in patients with severe anemia (PCV <20%). Blood product administration may be useful after acute blood loss, as loss of 60% of blood volume may result in death. The severity of clinical signs of anemia may also indicate a need for blood products.

Oxyglobin

Oxyglobin is a modified lactated Ringer’s solution containing 13 g/dL of polymerized bovine hemoglobin. It is a colloidal solution with an average molecular weight of 200 kD that expands plasma volume. The labeled indications for Oxyglobin in dogs are to improve the clinical signs of anemia and increase tissue oxygen content. Because it has a lower affinity for oxygen, Oxyglobin delivers oxygen to the tissues more efficiently than erythrocytes. Furthermore, Oxyglobin molecules are smaller than erythrocytes and can reach areas of the microcirculation that erythrocytes cannot. Other advantages to using Oxyglobin instead of whole blood include reduced potential for disease transmission, elimination of the need for crossmatching, and the ability to safely store the product (unopened) for up to 3 years.

Oxyglobin carries oxygen to the tissues via plasma; therefore, its use does not increase circulating erythrocytes. If a higher dosage of Oxyglobin is used, the PCV may decrease due to a dilutional effect. Hemoglobin values are used to evaluate the physiologic effects of this synthetic blood product. Research conducted on chickens showed that a single dose of Oxyglobin, administered at 15 mL/kg IV, increased blood hemoglobin from 0.04 mg/dL to 4.29 mg/dL. Mallard ducks that were resuscitated with Oxyglobin and crystalloid solutions had decreased mortality compared with ducks that were resuscitated with crystalloid solutions alone or hetastarch and crystalloid solutions.

Oxyglobin has been associated with discoloration of mucous membranes, sclera, and urine in small mammals, though these adverse effects have not been observed in birds. As with any colloidal blood volume expander, Oxyglobin may contribute to circulatory overload. Caution should be used when administering Oxyglobin to euvolemic or hypovolemic patients, particularly those predisposed to congestive heart failure or severe renal disease.

Whole Blood

Fresh whole blood may be used to treat anemic conditions in avian species. Whole blood provides erythrocytes, plasma proteins, and coagulation factors. Crossmatching is often recommended before transfusion. However, it does not appear to be an accurate means of predicting transfusion reactions in avian species. In psittacines, safety of a single blood transfusion from a pigeon donor has been demonstrated. Most birds have not received a previous blood transfusion; therefore, a single blood transfusion from a donor bird can be given in an emergency situation. Efforts have been made to determine the safety and efficacy of transfusions from different donors: autologous (donor and recipient are the same bird), homologous (donor and recipient are of the same species), or heterologous (donor and recipient are of different species). The efficacy of homologous blood transfusions has been demonstrated in domestic pigeons (Columba livia) after blood loss. A faster rate of removal...
of erythrocytes has been demonstrated when homologous rather than autologous transfusions are used in ring-necked pheasants (Phasianus colchicus).\(^4\)

Although heterologous blood transfusions are also effective, the half-life of the transfused erythrocytes is even shorter than that of erythrocytes that are homologously transfused.\(^4\) In a study of blood transfusion in sun conures (Aratinga solstitialis),\(^4\) the longest erythrocyte half-life occurred with autologous transfusion (9.9 days), followed by homologous transfusion (8.5 days). The shortest half-life (4.5 days) was associated with heterologous transfusion from white-eyed conures (Aratinga leucophthalmus). Transfused erythrocytes in cockatiels were found to have longer half-lives when autologous (12.2 to 16.8 days) and homologous (10.5 to 13.1 days) transfusions were given than when the cockatiels received heterologous transfusions from either blue-fronted Amazon parrots (Amazona aestiva; 0.1 to 2.6 days) or pigeons (Columba livia; 0.1 to 1.9 days).\(^4\) Thus, when blood transfusion from the same species of bird is not possible, blood from a donor of a closely related species may have the longest therapeutic effect.

Blood collection from donors must be performed aseptically.\(^4\) The jugular vein is the collection site of choice in most donor birds, and a butterfly catheter is the preferred means of blood collection (FIGURE 1). Blood can also be collected from the basilic and medial metatarsal veins. No more than 1% of body weight should be collected at one time from a single bird (7% to 10% of blood volume).

To maintain erythrocyte viability and prevent coagulation, an anticoagulant is added to the collected blood at a ratio of one part anticoagulant to six to nine parts blood. Commonly used anticoagulants include citrate phosphate dextrose adenine 1 (CPDA-1), acid citrate dextrose (ACD), heparin, and citrate phosphate dextrose. A study evaluating the use of 0.9% citrate, ACD, and CPDA-1 showed decreased viability of avian erythrocytes when any of these media were used for storage, resulting in increased serum potassium and concurrent decreased adenosine triphosphate levels.\(^6\) Citrate has been shown to reduce levels of ionized calcium in the blood in people when blood transfusions are given too rapidly or in the presence of liver dysfunction, as the liver provides a major role in citrate metabolism.\(^4\)–\(^5\)

Therefore, the use of citrate should be avoided in avian patients with hypocalcemia. Signs of citrate intoxication in mammals include cardiac arrhythmia and tremors.\(^5\)–\(^5\)

Blood should be warmed before administration to prevent hypothermia\(^4\) and can be administered through a catheter in the jugular, basilic, or medial metatarsal vein (FIGURE 2). Avian blood transfusions have also been given intraosseously, most often with the catheter placed in the distal ulna, although the tibiotarsus may be used as an alternative site. The bone marrow is rich in capillaries, allowing rapid blood uptake.\(^5\) The humerus should not be used for blood transfusions because it is pneumatic and, depending on species, communicates with air sacs in the cranial aspect of the body.\(^5\)

The total blood volume needed to raise avian PCV to a desired level has not been established. Clinicians are often limited by the amount of blood that can be safely collected from the donor bird. A dose of 1% of body weight or 10% of blood volume has been suggested.\(^5\) The recommended rate at which to transfuse anticoagulated blood into an avian patient is 0.5 mL/kg for the first 20 minutes, with the total time from collection of donor blood to transfusion not to exceed 4 hours, to prevent bacterial growth.\(^4\) A slow bolus can be given manually or with the aid of a syringe pump (FIGURE 2).

A blood filter should be included with the blood administration set to remove microaggregates and prevent microembolism\(^6\)–\(^5\) (FIGURE 3). Screen filters with defined pore
sizes are used most commonly. Hemolysis associated with blood filtration has been described in people. Because most filters are designed for mammalian use and do not account for the greater size of avian erythrocytes, birds may be at greater risk for postfiltration hemolysis.

Parameters used for monitoring an anemic patient include heart rate, respiratory rate, mucous membrane color, and mentation (alert versus lethargic). Refill time of the basilic vein can be used as an estimate of vascular volume in birds. The effects of a blood transfusion should be monitored through an evaluation of the PCV 1 to 2 hours after the transfusion. The patient should be closely monitored for signs of a transfusion reaction. Transfusion reactions in dogs can include hemolysis, febrile reactions, angioedema, and vomiting.52 Adverse transfusion reactions that have been reported in birds include regurgitation, hemoglobinuria, and death.56 Regurgitation after blood transfusion is thought to be due to circulatory overload.57 Signs of circulatory overload can also include coughing or dyspnea. Multiple heterologous transfusions may cause fatal transfusion reactions.41 Improperly stored blood may contribute to transfusion complications such as hyperkalemia.47

Disease transmission is another possible sequela of blood transfusion. Specific diseases for which blood could be screened before transfusion include avian chlamydiosis, polyomavirus, and psittacine beak and feather disease; blood parasites, including Leucocytozoon (FIGURE 4), Plasmodium, and Haemoproteus spp, may also be detected.46 At a minimum, screening of the donor should include evaluation of a blood smear, PCV, and total leukocyte count. In an emergency situation, complete screening of donors may not be practical because rapid on-site tests are not available and would delay the transfusion. Most commercial blood banks do not store avian products, and veterinary hospitals may benefit from prescreening avian donors.
Conclusion
The use of blood products in avian species can be very beneficial when treating anemia. We have observed positive effects of whole blood transfusions in a bald eagle diagnosed with lead toxicosis and an Amazon parrot with blood loss from traumatic injury. For avian patients to fully benefit from blood product therapy, much research is needed in the areas of avian blood typing, administration techniques, and efficacy of heterologous transfusions.

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1. Compared with the life span of the mammalian erythrocyte, the life span of the avian erythrocyte is:
   a. shorter.
   b. longer.
   c. equivalent.
   d. shorter only in chickens.

2. Oxyglobin increases tissue oxygenation by:
   a. expanding plasma volume.
   b. increasing oxygen offloading into tissues.
   c. increasing blood hemoglobin content.
   d. all of the above.

3. Which statement is true regarding the survival of avian erythrocytes after transfusion?
   a. It is longer after autologous transfusion than after either homologous or heterologous transfusion.
   b. It is longer after heterologous transfusion than after homologous transfusion.
   c. It is longer after homologous transfusion than after autologous transfusion.
   d. It is similar after autologous and homologous transfusions.

4. Which of the following should not be a part of avian blood transfusion?
   a. blood filtration
   b. administration of a rapid bolus
   c. warming before administration
   d. intraosseous catheter placement

5. Which of the following may cause a bird to develop nonregenerative anemia?
   a. traumatic blood loss
   b. infection with Plasmodium, Aegyptianella, Haemoproteus, or Leucocytozoon spp
   c. crude oil ingestion
   d. neoplasia

6. Which therapy would be expected to increase a bird’s PCV in 1 to 2 hours?
   a. vitamin K supplementation
   b. crystalloid/colloid fluid administration
   c. Oxyglobin administration
   d. whole blood transfusion

7. Clinical signs of ________ are seen with citrate toxicity.
   a. hyperkalemia
   b. hypokalemia
   c. hypocalcemia
   d. hypercalcemia

8. Which of the following does not help a bird recover circulating blood volume after blood loss?
   a. the renal portal system
   b. splenic contractions
   c. rapid erythrocyte regeneration
   d. capillary density and surface area in skeletal muscles

9. Which route of administration and site would be inappropriate for whole blood transfusion?
   a. intravenous; jugular vein
   b. intraosseous; humerus
   c. intraosseous; ulna
   d. intravenous; medial metatarsal vein

10. A blood filter should be used to prevent:
    a. hyperkalemia
    b. hemolysis
    c. microembolism
    d. circulatory overload.