BLOOD TRANSFUSION IN BIRDS

TRANSFUSÃO SANGUÍNEA EM AVES

Filipe Martinho

Centro de Investigação em Ciências Veterinária - Faculdade de Medicina Veterinária, Universidade Lusófona de Humanidades e Tecnologias.

Abstract: *Birds, both companion and wild, have become frequent patients in veterinary clinics and hospitals as well in wildlife rehabilitation centers in the last two decades. In emergency situations, it is imperative to give the best critical care to these patients, which frequently implies reversing shock and re-establishing homeostasis. In order to do so, a blood transfusion can be life-saving.*
It is important to the clinician to properly evaluate these critical patients and decide when to administer blood or blood products.

KEY-WORDS: Birds, anemia, shock, blood transfusion.

Resumo: *As Aves, exóticas ou silvestres, têm-se tornado pacientes frequentes em clínicas veterinárias, assim como em centros de recuperação de fauna silvestres, nas últimas duas décadas. Em situações de urgência é fundamental fornecer a estes animais os melhores cuidados médicos possíveis, o que frequentemente implica reverter situações de choque e restabelecer a homeostase. Para isso, uma transfusão sanguínea pode ser vital.*
É importante para o clínico avaliar correctamente estes pacientes e decidir em que situações administrar sangue ou os seus subprodutos.

PALAVRAS-CHAVE: Aves, anemia, choque, transfusão sanguínea.

ERYTHROPOIESIS AND HEMOSTASIS IN BIRDS

The blood of every bird contains erythrocytes or Red Blood Cells (RBCs), leukocytes or White Blood Cells (WBCs) and Thrombocytes, the avian equivalent to mammal platelets.

Avian RBCs (Figure 1) are usually oval, although their shape can vary slightly between different bird species and overall larger than mammal's RBCs, with the long axis measuring in average 13,5 µm and the short axis 7,5 µm. However, the most important feature of avian RBCs is that they are nucleated, usually with an oval and centrally placed nucleus, with uniformly clumped chromatin. With Giemsa and Romanowsky-based colorations, the nucleus stains deep purple and the cytoplasm light pink. A small degree of anysocitosis is usually seen in clinically healthy birds (Campbell, 1994; Campbell, 1995; Mitchell & Johns, 2008; Clark *et al*., 2009).

Besides typical mature RBCs, lesser numbers of other cells representing different stages of RBC development can be found on the blood of healthy birds. Immature or polychromatophilic RBCs, the penultimate stage of RBC development, have a more rounded shape and round nucleus, with more lightly clumped chromatin, and the cytoplasm stains lighter blue. The presence of small numbers (between 1 to 5% of total circulating RBCs) of these immature cells in peripheral blood is normal and common in healthy birds but elevated counts are described as polychromasia or polychromatophylia and indicative of increased erythropoiesis as seen in regenerative anemias. Less frequently, other stages of RBC development, such as rubrycites, can be observed on peripheral

blood as well as erythroid cells undergoing division and exhibiting mitotic figures.

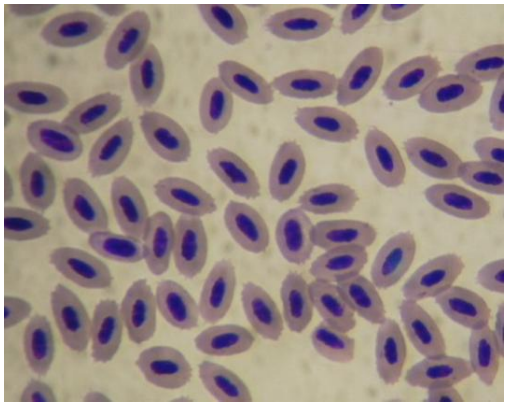

Figure 1 - Blood smear of an African Grey Parrot (*Psittacus erithacus*) stained with Diff Quick®.

A very small number (less than 1%) of avian circulating RBCs are anucleated and refered as erythroplastids.

Normal erythropoiesis takes place in the bone marrow although ectopic erythropoiesis can be occasionally found on the spleen and liver (Campbell, 1995). This process comprises seven sequential stages of cell development:

Rubryblasts (or erythroblasts) are the first stage of RBC development. These are large cells with central and round nuclei with coarse chromatin and large nucleoli. The Nucleus:Cytoplasm (N:C) ratio is high and the cytoplasm is deeply basophilic with clear spaces (mitochondrial spaces).

Prorubrycites are the second stage of RBC development and resemble rubryblasts: They differ from the later by the lack of nucleoli and mitochondrial spaces in the cytoplasm.

Basophilic rubrycites are the third stage of RBC development and have homogenous basophilic cytoplasm and round nuclei with clumped chromatin.

Initial polychromatic rubrycites are the fourth stage of RBC development and are smaller than basophilic rubrycites. The cytoplasm of these cells is basophilic to slightly eosinophilic, an indication of the beginning of hemoglobin synthesis.

Late polychromatic rubrycites are the fifth stage of RBC development, with round to oval shape and with a more eosinophilic cytoplasm.

Polychromatic RBCs are the sixth stage of RBC development. These cells resemble mature RBCs, the seventh and last stage of RBC development, but are more oval in shape, their cytoplasm is slightly basophilic and chromatin appears less condensed (Campbell, 1995).

Erythropoiesis is controlled by a number of factors such as hormones and oxygen concentration in tissues. Hypoxia stimulates the production and release of erythropoietin, a glycoprotein produced in kidneys, which has a direct positive effect on erythropoiesis. Other hormones, such as androgens and adrenocorticoids also have a positive effect on this process. On the other hand, polycitemia tends to suppress erythropoiesis.

Avian RBCs have a shorter half-life (25 to 45 days) than mammal cells. This rapid cell turnover may be associated with a higher body temperature in birds and rapid metabolic rate of avian RBCs, which consume higher rates of oxygen and nutrients than their mammal counterparts (Campbell, 1994; Campbell, 1995).

Blood volume in birds is estimated between 4,4 and 8,3 % of body weight (converting grams to mililiters) with younger birds having a higher blood volume than adults. Compared to mammals, avian blood is more viscous because RBCs are larger and less deformable. Blood density is mostly influenced by the concentration of plasma proteins, although birds have lower blood albumin concentration and lower oncotic pressure than mammals (Sturkie & Griminger, 1986; Campbell, 1994).

RBCs can be clinically evaluated in birds with some tests such as a hematocrit or Packed Cell Volume (PCV), total RBC count, Haemoglobin concentration, estimation of Mean Corpuscular Volume (MCV) and Mean Corpuscular Hemoglobin (MCH), reticulocyte count and RBC morphology.

PCV is calculated by centrifugation of microhematocrit capillary tubes and varies

between 35 and 55% in birds. A PCV less than 35% suggests anemia and higher than 55% is indicative of dehydration or polycitemia. Within the same species, PCV varies with age, gender, hormones and other physiologic factors. For instance, males and older birds tend to have a higher PCV (Campbell, 1995; Mitchell & Johns, 2008).

Total RBC count in birds is usually estimated by manual methods but more recent flow cytometric analysers properly adjusted can also be employed. Total RBC count is lower in birds (1,5 to 4,5 x 10^6 cells/µL) than in mammals. Again, these values can vary with age, sex, hormones, hypoxia and other environmental factors (Campbell, 1995; Mitchell & Johns, 2008).

MCV is estimated based on the formula PCV/RBC x 10 and MCH by Hemoglobin concentration/RBC x 10. These indexes are useful to classify the type of anemia (Campbell, 1995).

RBC morphology also gives important information to evaluate normal erythroid function. A slight polychromasia (between 0,4 and 6,78 % in psittacine birds is normal) and anysocitosis are expected to be seen in avian blood smears. Other changes in morphology include poiquilocytosis, nuclear abnormalities (fragmentation, binucleation, pycnosis, abnormal shapes, Howell-jolly bodies), basophilic stippling of the cytoplasm, spherocytosis, Heinz bodies and erythroplastids (Campbell, 1995; Mitchell & Johns, 2008).

Reticulocytes are immature RBCs that can be counted in blood smears stained with new methylene blue, which stains residual cytoplasmatic RNA dark blue. Most avian Mature RBCs also show some residual cytoplasmic RNA so, in birds, the term "Reticulocyte" should only be used in cells with a distinct ring of RNA surrounding the nuclei. Reticulocyte counts vary between 1 and 5% in healthy birds and increased counts are indicative of RBC regeneration. This parameter also gives a more precise idea of the regenerative response than polychromasia (Campbell, 1995; Mitchell & Johns, 2008).

ANEMIA AND SHOCK IN BIRDS

Anemia is defined by a decrease of PCV, RBC count and/or Hemoglobin concentration and can be classified in three groups: blood loss anemia, regenerative anemia and non-regenerative anemia (table 1) (Pendl, 2001; Mitchell & Johns, 2008).

Clinical signs vary, depending on the severity of the anemia and the underlying diseases. Usually, birds are presented with depression to coma, weakness, pale mucous membranes, tachycardia and/or tachypnea.

In **regenerative** or haemolytic anemia there is increased erythropoiesis on the bone marrow, stimulated by hypoxia and increased erythropoietin levels. Usually, increased numbers of polychromatophilic RBCs and other immature cells can be seen on peripheral blood. Causes for regenerative anemia include hemoparasites, sepsis, toxicosis or secondary to skin burns. Immune-mediated hemolytic anemia is rarely documented in birds, with only described cases in an eclectus parrot (*Eclectus roratus*) (Johnston *et al*., 2007) and in a blue-crowned conure (*Aratinga acuticaudata*) (Jones *et al*., 2002).

In **non-regenerative anemia** there is usually no response from the bone marrow and no immature RBCs are seen in peripheral blood. This type of anemia develops quickly in birds because of shorter RBC half-life and can be caused by chronic infections, neoplasia, hypothiroidism, hyperestrogenism, toxicosis, nutritional imbalances, leukaemia, myeloblastosis and hepato or nephropathies.

Blood loss anemia appears non-regenerative on the acute phase of blood loss but becomes progressively regenerative. Possible causes include trauma, parasites, primary coagulopathies (rare in birds), coagulopathies secondary to toxicosis (Murray & Tseng, 2008) or nutrition and other causes. Currently, there are no standard tests for coagulation in birds and diagnosis of primary coagulopathies can be

challenging although Prothrombine time has been estimated for the chicken and some psittacine species (Morrisey *et al*., 2003).

Figure 2. - Causes of anemia in avian patients. Upper left: yellow-legged gull (*Larus michaelis*) with crude oil intoxication. Upper right: bald eagle (*Haliaetus leucocephalus*) with lead poisoning causing head-tilt. Lower left: blood smear of tawny owl (*Strix aluco*) with heavy Leucocytozoon and Haemoproteus infection. Lower right: booted eagle (*Hieraetus fasciatus*) with extensive injury of left wing which led to serious blood loss.

Blood loss	Regenerative anemia	Non-regenerative anemia
Trauma Lacerations Broken pin feathers Fractures Surgery Parasites Ticks *Dermanyssus* mites Coccidia Primary coagulopathies Secondary coagulopathies Rodenticide toxicosis Aflatoxins Vitamin K deficiency Gastro-intestinal bleeding Parasites Ulcers Cloacal bleeding Ulcerated papillomas Lacerations Prolapse Infections Ulcerated neoplasms	Blood parasites *Plasmodium* *Aegyptianella* *Haemoproteus* *Leucocytozoon* Infection, sepsis Toxicosis Mustard Crude oil Secondary to skin burns Immune-mediated	Chronic infection Tuberculosis Chlamydiosis Aspergilosis Neoplasia Leukemia Hypothiroidism Hyperestrogenism Toxicosis Lead Zinc Aflatoxins Nutricional deficits Hypoproteinemia Iron Vitamin B Myeloblastosis Renal failure Liver failure

Table 1 - Causes of anemia in birds.

Birds can deal with acute blood loss and adapt better to chronic blood loss than mammals. It has been shown that chickens return to normal PCV 72 hours after removal of 30% of blood volume (Ploucha *et al*., 1981). Pigeons return to normal PCV 7 days after removal of 60% of blood volume without clear clinical signs (Finnegan *et al*., 1997) and ducks can also tolerate loss of 60% of blood volume before presenting significant mortality (Lichtenberger *et al*., 2005). Birds have a unique physiologic mechanisms that helps them deal with these situations and quickly recover: there is a large capillary density with a large surface area within the skeletal muscles that absorbs interstitial fluids and rapidly replaces them to the vascular space, increasing blood volume; the bone marrow has the ability to mobilize large numbers of immature RBCs to peripheral blood starting as early as 12 hours after significant blood loss (Lichtenberger *et al*., 2005); the portal renal system, which allows the blood to bypass the liver and kidneys and directly enters the caudal vena cava, also increases blood volume. The absence of some autonomic responses, which have deleterious effects, to hypovolemic shock in birds also increases survival. Birds lack some other mechanisms, such as splenic contraction, that are present in mammals (Ploucha *et al*., 1981; Campbell, 1997; Lichtenberger *et al*., 2005; Matos & Morrisey, 2005; Speer, 2005; Bowles *et al*., 2007; Lichtenberger, 2007; Mitchell & Johns, 2008).

Hypovolemic shock can develop either when there is a decreased blood volume or inadequate distribution of blood flow. This decreased blood flow can be absolute, as seen in hemorrhages or coagulopathies, or relative, as seen in dehydration or polycitemia.

When there is a considerable hypovolemia, with loss of more than 30% of blood volume, there is also a decrease of blood pressure and activation of baroreceptors and the vasomotor center in the medulla

oblongata. This leads to activation of the sympathic nervous system which has two effects: first, vasoconstriction of peripheric veins and arterioles and increased heart rate and myocardial contraction and, second, increased production and release of cathecolamines, such as adrenaline and noradrenaline, and activation of the justaglomerular cells in the kidneys, release of renine and activation of the renine-angiotensine-aldosterone system. The ultimate goal of all these mechanisms is restoration of a normal blood pressure.

Shock can also be classified in three distinct stages: in the initial/compensatory stage, when there is a loss of less than 20% of blood volume, birds can present with tachycardia, normal or increased blood pressure, strong and fast pulses and mucosal Capillary Refill Time (CRT) of less than one second. Outcome is usually benign only with crystalloid fluids administration. In the next stage, or early decompensatory, when there is either a continuous loss of blood or a decrease of 25 to 30% of blood volume, birds present with hypothermia, cold extremities and skin, tachycardia, normal or decreased blood pressure, pale mucous membranes, increased CRT and mental depression. To treat these patients, aggressive fluid therapy both with crystalloids and colloids is warranted. The final stage, or late decompensatory, when there is important blood loss (more than 60% of blood volume), autonomic neuroendocrine responses to shock become ineffective and there is generalized organ failure. Birds present with bradycardia, severe hypotension, pale or cyanotic mucous membranes, absent CRT, weak or absent pulses, hypothermia, olyguria or anuria, pulmonary edema, stupour or coma and, finally, cardio-respiratory arrest. Usually these situations have a very poor prognosis, despite every therapeutic effort (Lichtenberger *et al*., 2005; Lichtenberger, 2007; Mitchell & Johns, 2008).

Birds also tolerate hypoxia better than mammals and because they appear to lack extensive constriction of capillaries in hypoxia/hypovolemia situations, tissue and organ failure caused by ischaemia is rare.

BLOOD TRANSFUSION

Blood transfusion is rarely used in the early stages of hypovolemic shock except in severe and acute hemorrhage or in some coagulopathies (e.g. rodenticide toxicosis). It is indicated when there is a lack of RBCs, thrombocytes, coagulation factors, albumine or anti-thrombine.

A blood transfusion is needed in birds suffering from loss of more than 20% of blood volume, when PCV is less than 20% or in patients with chronic anemia subjected for surgery. In every situation, the patient's ability to deal with the stress of administration and the risk of further blood loss or adverse reactions to the blood transfusion should be considered.

Blood transfusion should not be performed in normovolemic or dehydrated patients, in birds with mild/moderate chronic anemia but otherwise healthy, in anemic and dehydrated patients (more than 7% dehydration) and in anemic patients with hypoproteinemia (Ploucha *et al*., 1981; Campbell, 1997; Morrisey, 1999; Lichtenberger, 2004; Speer, 2005; Bowles *et al*., 2007).

Collection and administration of blood products

Whenever possible, homologous (between same species) transfusions are preferred, as the donor's RBCs survive longer in the recipient organism. Frequently, it is difficult or impossible to perform a homologous transfusion, so a heterologous (between different species) transfusion should be attempted. Since birds don't have pre-formed antibodies for blood groups, the first heterologous transfusion is usually safe, although hemolysis of donor RBCs always leads to some degree of physiologic stress

(Morrisey, 1999; Lichtenberger, 2004; Matos & Morrisey, 2005).

The efficiency of homologous/heterologous transfusions have been studied in some species of birds and the mean donor RBC half-life was about 7,1 days in homologous transfusions in pigeons but only 12 hours in heterologous pigeon-to-red tailed hawk (*Buteo jamaicensis*) transfusions (Sandmeier *et al*., 1994); 10 to 16,8 days in homologous transfusions in cockatiels but only 0,1 to 2,6 days in heterologous transfusions (Degernes *et al*., 1999a); 8,5 days in homologous transfusions in *Aratinga* conures and 4,5 days in heterologous transfusions in two different species of *Aratinga* conures (Degernes *et al*., 1999b). Based on this evidence, heterologous transfusions should be performed between related species (same genus) to increase donor RBCs survival. If a related donor species is not available, at least a donor of the same taxonomic Order (Psittaciformes, Falconiformes, Columbiformes, etc.) should be used.

In the domestic chicken, there are about 28 blood groups described and three different blood group systems (B, L and N) (Finnegan *et al*., 1997). Blood groups have also been studied in a few other galliformes and anseriformes species but are unknown on the vast majority of species currently seen in exotic practice. There is no readily available method to the clinician to typify donor and receptor blood before a transfusion.

As a safe measure before every blood transfusion, but specially in heterologous or in birds that have previously received blood, a cross-matching should always be performed (table 2). Nevertheless, this procedure doesn't seem to accurately predict if reactions to the transfusion will occur.

1	Centrifuge (3500 rpm, 1 minute) 1 drop of whole blood without anti-coagulant in order to obtain serum and 1 drop of blood with EDTA in order to obtain RBCs from both the donor and recipient.
2	RBC washing: resuspend the RBCs in 0,5 ml of NaCl 0,9%, centrifuge 1 minute and discard supernatant. Repeat this procedure twice.
3	Resuspend the washed RBCs in 0,5 ml of NaCl 0,9% in order to obtain a RBC solution.
4	Major cross-matching: in a tube place 2 drops of patient serum and 1 drop of donor RBC solution.
5	Minor cross-matching: in a tube place 2 drops of donor serum and 1 drop of patient RBC solution.
6	Controls: one tube with 1 drop of patient serum and 2 drops of patient RBC solution and another tube with 1 drop of donor serum and 2 drops of donor RBC solution.
7	Incubate all tubes 15 minutes at 37º C.
8	Centrifuge all tubes 15 seconds.
9	Look for macroscopic agglutination and hemolysis. Resuspend the RBCs and place 1 drop on a slide, apply a coverslip and look for signs of microscopic agglutination under a microscope. Agglutination should be differentiated with rouleaux formation, which is plasma-related phenomenon, where RBCs are clumped in piles by effect of electrostatic forces. If a cross-match is compatible, the RBCs are individually distributed and there are no signs of hemolysis.

Table 2 - Cross-matching procedure in birds.

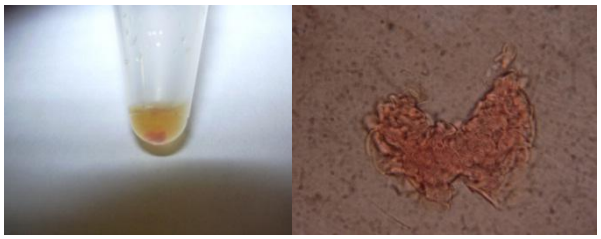

Figure 3 - Cross matching procedure. Left: Macroscopic agglutination. Right: Microscopic agglutination.

Blood should be aseptically collected from healthy birds, usually under isoflurane or sevoflurane anesthesia given by face mask, and mixed with appropriate anticoagulants. Blood should be ideally collected from the jugular vein, because of its larger diameter (although ulnar or medial metarsal veins can also be used), and the volume should be 1% of bodyweight (converting grams to milliliters). This volume should be replaced in the donor bird with crystalloid fluids given endo-venous (IV) or subcutaneous (SC). Citrate-Phosphate-Dextrose-Adenosine (CPDA) or sodium citrate are the anticoagulants of choice because they are metabolized faster by the recipient and this is less likely to develop coagulation problems. They should be used in the proportion of one part anticoagulant to 9 parts of blood. If these are not available, heparin can be used in the proportion of 0,25 ml of heparin to 10 ml of blood. Fresh blood is preferred as prolonged storage of blood leads to increased release of potassium and mammal storage medium are not adequate

for storage of avian blood (because of increase avian RBC metabolism) (Morrisey *et al*., 1997; Morrisey, 1999). Citrate has been shown to decrease calcium blood levels if given to rapidly or in patients with liver failure, because most of the citrate is metabolized in the liver. Therefore, this anticoagulant should not be used in patients with pre-existing hypocalcaemia or liver disease.

Although the volume of blood needed to raise the PCV to a desired level has not been established in birds, the receptor should receive 10 to 20 ml of whole blood/kg previously heated to body temperature (37-38º Celsius) in order to keep its PCV above 25% and blood pressure above 90 mmHg. Blood can be administered IV (jugular, ulnar or medial metatarsal veins) or intra-osseous (IO) with a blood filter, to remove micro cloths and prevent microembolism, by slow bolus injection (5 to 10 minutes) or by an injection pump over a four-hour period (Lichtenberger, 2007). In birds, IO administration is preferred because it is difficult to keep an IV catheter for prolonged time. The preferred IO administration sites are the distal ulna and the proximal tibiotarsus. Blood transfusions can be performed as a first-line treatment in patients with severe hemorrhage but are usually made after stabilization of the avian patient with oxygen, crystalloid and/or colloid fluid therapy and other supportive care (Campbell, 1997; Morrisey, 1999; Lichtenberger, 2004; Matos & Morrisey, 2005; Speer, 2005; Bowles *et al*., 2007; Lichtenberger, 2007).

Figure 4 - Clinical procedures during blood transfusion: Left: blood collection from the right jugular vein from a common guillemot (*Uria aalge*) under isoflurane anesthesia. Right: intra-osseous access of the left distal ulna of a domestic pigeon (*Columba livia domestica*).

During the whole procedure and up until 2 hours post-transfusion, the receptor bird should be monitored for mental status (alert versus depressed) and a few vital parameters assessed (heart rate, respiratory rate, CRT, mucous membranes colour, blood pressure).

Despite all efforts and care, blood transfusion reactions can occur and include hemolysis of donor RBCs, fever, urticaria and anaphylaxis, which can, ultimately, lead to death. These situations are sometimes difficult to assess in birds but have been reported in patients receiving multiple blood transfusions and can be prevented by previously performing a cross-matching. Regurgitation and dyspnea has been reported in birds secondarily to hypervolemia if blood is given too quickly or in an excessive volume. The use Improper or prolonged storaged blood may lead to other complications such as hypercalemia (Morrisey, 1999; Lichtenberger, 2004).

Another potential problem with blood transfusion is the transmission of infectious disease. Although this has not been described in birds, it would be wise to screen the donor animal for hemoparasites such as *Plasmodium* and *Leucocytozoon* and some selected avian pathogens, such as *Chlamydophila psittaci*.

ALTERNATIVES TO BLOOD TRANSFUSION

As an alternative to blood or blood products, oxyglobin can be used. This is a hemoglobin-based oxygen carrier, consisting in purified bovine hemoglobin in a modified Ringer's Lactate solution. It acts as a colloid, delivers oxygen to tissues and has a slight vasoconstrictor effect, which all help to counteract shock effects. It is not imunogenic, so no cross-matching is needed and a blood filter is not necessary for administration. It can be stored at room temperature for 3 years but after the vial is opened it should be used in the following 24 hours, because of the formation of meta-hemoglobin. Birds should receive 5 ml/kg

IV or IO by bolus injection over some minutes (Morrisey, 1999; Meyer, 2002; Lichtenberger, 2004; Matos & Morrisey, 2005; Bowles *et al*., 2007; Lichtenberger, 2007).

Despite all these advantages, oxyglobin has some side effects, as it gives the plasma a red colour, which can be mistaken with hemolysis, and sometimes mucous membranes are stained red. Recently, some concerns about the use of oxyglobin in dogs and humans have aroused because oxygen delivery to tissues might not be that effective as expected because of its vasoconstrictive effect and the reduced cardiac output that accompanies shock. There has also been reported some deaths in dogs with autoimmune haemolytic anemia and gastro-intestinal irritation and hypertension in humans after oxyglobin treatment. Although no adverse reactions in birds have been reported, caution should be used when oxyglobin is administered and the patient should be carefully monitored (Meyer, 2002).

Crystalloid fluids (Sodium Chloride 0,9% or Ringer's Lactate solution) given IV, SC or IO with or without iron-dextran administration can also be an effective treatment in a hypovolemic or anemic patient if whole blood or oxyglobin are not available. It has been demonstrated that at least, in pigeons and quails, ringer's lactate or NaCl 0,9% administration is as effective as a blood transfusion to restore a normal PCV (Schindler *et al*., 1987; Bos *et al*., 1990).

However, crystalloid fluids are not very useful when dealing with birds in severe shock since only 25% of its volume remain on the vascular space. In order to maintain proper blood pressure and tissue perfusion in these patients, colloid fluids, such as Hetastarch, should be added to the treatment plan (Lichtenberger *et al*., 2002; Lichtenberger *et al*., 2005).

In anemic or critically ill birds it is also imperative to provide the best supportive care, address and correct other complications and diagnose and treat the underlying cause to the anemia.

CONCLUSIONS

Although blood transfusions are seldom performed in birds, they can be life saving in some situations. Proper evaluation of the avian patient by means of physical examination and some simple diagnostic tests such as a hemogram can detect and classify a possible anemia.

Since birds respond very well to crystalloid fluids administration and supportive care, a blood transfusion should probably be reserved only to severely anemic patients.

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