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Blood Group Systems and Blood Transfusion of Animals

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ABSTRACT
This review provides the reader with an update overview of blood group for animals and blood transfusion basis to be employed for them. The review consist of blood groups in animals blood typing cross matching, donors, blood collection, storage blood component, blood transfusion, blood component therapy, blood substitutes and adverse reaction. The safe use of blood component therapy requires knowledge of blood groups, antibody prevalence and knowledge of the means to minimize the risk of adverse reaction by including the use of proper donors and screening assays that facilitate detection of serological incompatibility. The decision to transfuse and the type of product to administer depend on several factors such as the type of anemia and the size of animal. In conclusion transfusion medicine has become more feasible in small animal practice with improved access to blood products through on-site donors, the purchase blood bank products, external donor program or the availability of blood component substitutes.

Keywords: Animal transfusion, Cross matching, Blood substitutes, Serological incompatibility, Blood groups**.**

INTRODUCTION

Animals and bacteria have cell surface antigens referred to as a blood type. Antigens from the human ABO blood group system are also found in apes such as chimpanzees, bonobos and gorillas. The structure of the blood group antigens in animals is not always identical to those typically found in humans. The classification of most animal blood groups therefore uses different blood typing systems as compared to those used for classification of human blood.

Erythrocytes possess particular antigen (glycoprotein or glycolipids) on the surface of their cell membrane that allow their classification into blood groups. A characteristic of these antigens is their ability to trigger a reaction caused by circulating anti-erythrocytes antibodies in the opponent host or donor. These antibodies may occurs naturally or be induced following a previous transfusion. A severe and potentially life- threatening situation is one in which the interaction leads to the destruction by heamolysis of red blood cells, where the rapid destruction of RBC may be mediated by Igm and complement fixation as well the release of potent vasoactive compounds. This may cause shock and generally occurs when the patient posses antibodies towards the transfused RBCs. In other instances the antibodies red cell antigen interaction is less severe. And the most important outcome is the transfusion losses its efficacy as the mean survival time of transfused RBCs is drastically reduced. [1]

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Do animals also have blood groups like humans?

Human's blood group is applied to single factor. This factor is agglutinogen and is also called antigen. It is found on the surface of red blood corpuscles. Accordingly a person with `A' antigen is designated as a person with A-group, with `B' antigen as B-group, with both A and B antigens as AB-blood group and a person without any antigens is designated as O-blood group. In the case of animals blood group is applied to combinations of blood factors. Hence
it is preferable to call it as blood group systems rather then blood groups. Each system has many factors, which are together called blood group-factors.

Blood types

Blood types (or groups) are determined by specific antigens found on the surface of erythrocytes. In humans, there is the ABO system of blood types, whereas animals have a variety of different blood types (Table 1). Knowledge of blood types in the different species is important as transfusion of incompatible blood (the donor animal has a different blood type from the recipient animal) can result in severe hemolytic transfusion reactions and even death, in some instances. Blood typing (for the most common blood groups) is offered by a few specialized veterinary diagnostic laboratories (e.g. the Comparative Coagulation Laboratory at Cornell University, the Equine Blood Testing Laboratory in Kentucky, the Stormont Laboratory in California) Ideally, any animal that is routinely used as a blood donor should be blood typed for the most common antigens that produce a hemolytic reaction and should be negative for these antigens. Blood type compatibility (or incompatibility) is determined in the laboratory using cross matching procedures. Since administration of typed negative blood will not prevent a

transfusion reaction to less well-characterized red cell antigens, cross matching should always be performed in an individual that has been previously exposed to blood group antigens. [2]

The blood groups of various types of animals are given below:

- Canine Blood Groups
- Equine Blood Groups
- Feline Blood Groups
- Misc. Blood Groups

Canine blood groups

In dogs, at least eleven blood group systems have been identified, A, Tr, B, C, D, F, J, K, L, M and N. (An alternative nomenclature calls them dog erythrocyte antigen, DEA, 1, 2, 3, etc.) the majority of these appear to be inherited as simple mendelian dominants. Only one, the A system, is sufficiently strong to be of clinical significance. [3] About 60 % of dogs are a positive, and the rest are A negative. Naturally occurring antibodies to A occur in about 10 % of A –negative dogs, but these are usually of low titer and not of clinical significance. Therefore, unmatched first transfusions in the dog are usually safe. If, however, an A-negative dog is sensitized by transfusion of A-positive blood, high tittered anti- A may be produced. Subsequent transfusion of A-positive blood into such an animal could lead to a severe reaction. Similarly, if a bitch is sensitized by incompatible transfusion and mated to an A-positive dog, hemolytic disease may occur in her pups. Natural HDN in dogs is extremely rare. The Tr system is a soluble antigen system antigenically related to the human A, cattle J, sheep R, and pig A system. Two antigens belong to the system, Tr and O.There expression is controlled by an epistatic gene.Anti-Tr occurs naturally in some Tr-negative dogs. [4] Agglutination at 4°C, hemolytic tests, and antiglobulin tests has all been used for the detection of canine blood groups. The source of complement can either be fresh dog serum or rabbit serum. Table -2 refers common canine blood types and their approximate incidence of hemolytic reaction. [5]

Feline blood groups

In cat's only one major blood group system, the AB system has been reported. The AB antigens are glycolipids. Cats may be either A, B, or AB. A is completely dominant over B. About 75 % to 95 % of cats are A positive, about 5 % to 25 % are B positive, and less than 1% are AB. [8] This distribution however does differ among countries and among purebred cat breeds. Thus in the united states more than 99 % of domestic shorthair and longhair cats are type A, whereas in the British shorthair breed only about 40 % are type A. Severe transfusion reaction have been described in group B cats that received only very small quantity of group A blood, since 95 % of B cats possess anti- A of the Igm class (Interestingly only about 35% of A cats possess anti-B and it is of the IgG, and IgM classes and is of much lower titer). If completely matched blood is transfused into cats, its half-life is only about two days. [6] If group a blood is transfused into a cat of blood group B, its half-life is just over 1 hour. It is this very rapid destruction that results in severe clinical reactions. Thus a group B cat given as little as 1 ml of group a blood will go into shock-hypotension, apnea and AV block within a few minutes. Cossmatching is therefore, essential in this species. [7]

HDN has been recorded in Persian and related (Himalayan) breeds but is very rare. It occurs in kittens from queen of blood group B bred to sites of blood group A. Although healthy at birth, they develop severe anemia as a result of intravascular hemolysis. Affected kittens show depression and possibly hemoglobinuria. Necropsy may reveal splenomegaly and jaundice. Antibodies to the sites and the kitten's red cells are detectable in the queen's serum. Agglutination and hemolytic tests are used for feline blood typing. Table 3 provides incidence of hemolytic reactions in different breeds. [9]

Equine blood groups

There are over thirty blood groups in horses, of which only eight are major systems. Of these 8 and 7 are internationally recognized (A, C, D, K, P, Q and U), whilst the T system is primarily of research interest. Of these, the Aa and Qa are most important for hemolytic reactions, especially neonatal isoerythrolysis (NI). Other blood groups can occasionally give NI reactions, including Dc, Ua, Ab and Pa. In addition, all horses lack a unique red cell antigen to donkeys, so they will produce antibodies (and NI) when exposed to donkey blood (such as in mule pregnancies). [10] Natural antibodies do exist, particularly to Ca antigens, which cause weak agglutination and hemolytic cross-match reactions, however the antibodies to Ca do not appear to produce a significant hemolytic reaction *in vivo*. The incidence of Aa and Qa is breed-dependent. The table four provides the percentage of animals in the listed breed that are negative for the factor. [11]

Blood groups in other species

Cattles: - There are eleven major blood group systems in cattle, A, B, C, F, J, L, M, R, S, T and Z. The B group has over 60 different antigens, making it difficult to closely match donor and recipient. The J antigen is a lipid that is found in body fluids and is adsorbed onto erythrocytes (therefore, it is not a "true" antigen). Newborn calves lack this antigen, acquiring it in the first 6 months of life. Some animals have only a small amount of J antigen on erythrocytes and none in serum; these so-called "J-negative" animals can develop antibodies against the J-antigen and develop transfusion reactions if transfused with J-positive blood. Neonatal isoerythrolysis is not a naturally occurring phenomenon in cattle. Bouts of NI have occurred secondary to blood-derived vaccines (e.g. against anaplasmosis, babesiosis). The most common antigens that cattle were sensitized to were the A and F-systems.

Sheep: - Seven blood group systems have been identified in sheep (A, B, C, D, M, R and X). Similar to cattle, the B system is highly polymorphic. The R system is similar to the J system in cattle, in that the antigen is soluble. [12] The M-L system is involved in active red cell potassium transport and polymorphisms in this system result in breeds of sheep with varying erythrocyte potassium content. Neonatal isoerythrolysis has been reported in lambs administered bovine colostrum. This is due to the presence of antibodies to sheep erythrocytes in bovine colostrum (called "heterophile" antibodies), which is a common occurrence. They are antibodies produced to common cross-reactive antigens present on the surface of bacteria and protozoa that are identical to epitopes on blood group antigens. [13]

Goats: - Blood group antigens in goats are similar to those in sheep and the same reagents are used to type both species. Five major systems have been identified in goats; A, B, C, M and J.

Pigs: - Fifteen pig blood group systems have been identified. They are identified by the letters from A to O. There

expression is controlled by a gene called S (secretor). In the homozygous recessive state (ss), this gene can prevent the production of the A and O substances. As a result, the amount of these antigens bound to red cells in these animals is reduced to an undetectable level. A and O, like J in cattle and R and O in sheep are soluble antigens found in serum and passively adsorbed onto red cells after birth. Natural anti-A antibodies may occur in A-negative pigs, and transfusion of A- positive blood into such an animal may cause transient collapse and hemoglobinuria. Pig blood groups are detected by agglutination, hemolytic, and antiglobulin tests. [14] Each type of test is characteristic of certain blood groups. Production of either A or O blood group substances by a pig requires the presence of the S gene. Pigs that lack this gene (ss animals) make neither of this blood group substance. [15]

Chickens: - Chickens have at least twelve different blood group systems with multiple alleles. The red cell B system is also the major histocompatibility system in the chicken. A hemolytic disease may be artificially produced in chicken embryos by vaccinating the hen with cock red cells.

Crossmatch

The crossmatch procedure determines whether donor blood is compatible (or incompatible) with recipient blood. A crossmatch should always be performed in the following situations:

- An animal of a species which contains naturally occurring pathogenic antibodies to foreign blood group antigens. This occurs in the cat. In this species, a crossmatch should be performed on the first and every transfusion, unless the blood types of both donor and recipient are known. In cat breeds in which there is a low percentage of type B cats (e.g. Siamese, DSH or DLH in the USA), transfusion of blood from an uncrossmatched or untyped donor can be performed relatively safely. However, there is still a (albeit small) chance of a major transfusion reaction and this procedure is not recommended.

- An animal of a species which does not contain naturally occurring antibodies but has been sensitized to foreign red cell antigens, with the production of acquired antibodies. This is the situation in the dog and horse. In these species, a crossmatch does not need to be performed on the first transfusion the animal receives (as long as you can be sure this is the first transfusion ever), but should be performed at subsequent transfusions (if the interval between the first and subsequent transfusions is more than 5 days). [16]

There are two types of crossmatches:

- **Major cross match:** This is the most important cross match; comparing *donor erythrocytes* to *recipient serum* (i.e. you are checking for preformed (acquired or naturally occurring) antibodies in recipient serum against donor erythrocytes. For the major crossmatch, you need red blood cells from the donor (this can be whole blood from a donor animal or packed red blood cells) in EDTA or citrate and serum from the recipient (non-anticoagulant tube).

- **Minor cross match:** This compares donor serum to recipient erythrocytes and checks for preformed antibodies in donor serum that could hemolyse recipient red cells. This crossmatch is less important as usually the donor serum is markedly diluted after transfusion and is unlikely to produce a significant transfusion reaction. This type of crossmatch could be important if transfusing small patients, in which hemodilution is less likely to occur.

In the crossmatch procedure, washed erythrocytes are incubated with serum. For horses, a source of complement (to hemolyse the erythrocytes) is added, as the antibodies in horses are usually hemolysins that require a source of complement for their hemolytic action. For the major cross matching "*Donor erythrocytes* "are washed and incubated with *recipient serum.*

For the minor cross matching "*Donor serum"* is incubated with washed *recipient erythrocytes.* The mixture of erythrocytes and serum are then observed visually for hemolysis (especially in the horse) and microscopically for agglutination. Any evidence of agglutination or hemolysis indicates an incompatible crossmatch. [17]

When there is an incompatible reaction on the major crossmatch, the donor blood should not be transfused under any circumstances. When there is an incompatible reaction on the minor crossmatch, the transfusion can go ahead. However, if the donated serum is likely to contribute substantially to the plasma volume of the recipient, the serum should be removed from the donor whole blood. The packed cells (washed or unwashed) should be reconstituted in sterile isotonic saline before infusion

Donor selection and blood collection

Several approaches are available in order to obtain blood products. One approach is lo purchase products as the need arises from a blood bank. There are several drawbacks with this option, such as delays in obtaining blood components, limitations as to the availability of certain blood components when requested, and blood components that are not produced by a given blood bank. Another approach is to have access to donors either as in-house donors or from an external donor program a donor log should be kept in addition to the donor's medical file. The log can contain the name, blood type, scheduled dates for yearly or twice yearly screening tests, blood collection dates, and the owner's contact information, if it is an external donor. A transfusion log should also be kept with information on each transfusion, including the date of transfusion, donor, type and volume of blood component used, recipient, diagnosis, and problems encountered, such as adverse reactions. [18]

"The ideal canine donor should have the following characteristics:

It must possess weight more than 30 kg, have taut neck skin that permits easy access to the jugular vein, hate a packed cell volume that is at least 0.40 UL, have demonstrated a good temperament and be in fit physical condition, have no previous history of transfusion or pregnancy, be DEA-1.1 and DEA-l.2negative, and possess adequate levels of Von Willebrand factor (Vwf).

The ideal feline donor should have the following characteristics:

It should be weigh more than 4.5 kg, have a packed cell volume that is at least 0. 35 L/L, have demonstrated a good temperament, and is in fit physical condition. Proper maintenance of donors requires up-to-date vaccinations' fecal floatation every 6 mo if there is contact with new animals; a yearly hemogram, clinical chemistry profile, and

screen for infectious diseases: and in the dog, preventative heartworm therapy in regions where it is appropriate. At each blood collection, the donor's weight, temperature, and packed cell volume should be checked. [19]

Anticoagulants and preservatives

Heparin and citrate are anticoagulants that will not contribute to cell preservation during long-term storage and whole blood collected in these anticoagulants should be used within 24 h. Commonly used preservatives include acid citrate dextrose (ACD), citrate phosphate dextrose (CPD and CP2D), and citrate-phosphate-dextrose-adenine (CPDA-1 K in which the added dextrose, phosphate, and adenine favor the viability of RBCs, permitting their storage for up to 3 to 5 wk, depending on the preservative. [22]

Blood product indications

The choice of blood components to be used cannot be based solely on the packed cell volume; the rate as well as the quantity and type of components lost or missing, influences the clinician's choice. Whole blood is indicated in a patient that requires several blood components or has acutely lost more than 50 % of its total blood volume, in order to replace both oxygen-carrying capacity and oncotic activity. Whole blood is not ideal product where tissue reoxygenation is specifically required and there is need for plasma volume expansion. [20] Examples of this is acute hemorrhage with less than 50 % of total blood volume loss, in which the volume expansion needed may be provided by crystalloid solutions and tissue reoxygenation can be supplied by packed RBCs. Other examples include chronic hemorrhage, hemolytic anemia, or nonregenerative anemia. Packed red cell transfusion is preferable whole blood transfusion in these situations, since whole blood transfusion can lead Co hypervolemia in these patients. [23] Packed RBCs are prepared by removing 200 to 250 ml of plasma tram 450 ml. (I unit) of whole blood after centrifugation. The packed cell volume of the RBC preparation is approximately 0.70 to 0.80 L/L, and the RBCs can be resuspend in a protein-poor additive solution, such as a packed *cell* volume of 0.55 to 0.65 *L/L*, Shelf life depends on the preservative solution used. The transfusion of packed RBCs is indicated for tissue reoxygenation and is ideal for a nonermovolemic$_h$ anemic patient. Fresh frozen plasma (FFP) is plasma that has been separated from RBCs and frozen at -18°C within 8 h of collection (if preserved with CPDA-1. CPD, or CP2D; 6 h if preserved with sodium citrate or ACD (acid citrate dextrose) plasma, frozen after this period is referred to as frozen plasma (FP). One unit of FFP has an approximate volume of 200 to 250 ml and contains labile and stable coagulation factors. The main indications for FFP administration are a lack of coagulation factors associated with hepatic insufficiency, DIC, vitamin K deficiency (rodenticide toxicosis, liver insufficiency, biliary tract obstruction, malas-similalion syndrome, and chronic antibiotic use), a need for plasma volume expansion, or a massive blood loss within a few hours. Other indications include a congenital or a hereditary deficiency in coagulation factors, such as hemophilia A, B, or von Willebrand's disease. On the other hand, FP, which lacks labile coagulation factor activity, maybe used to treat conditions in which stable coagulation factors are needed, such as rodenticide toxicosis or hemophilia B. As much as possible, FFP should be reserved for patients requiring labile coagulation factors (DIC, hemophilia A, and von Willcbrand's disease), and FP used for other disorders. [24]

Special clinical considerations for transfusion of whole blood or packed RBCs

Choosing the proper blood component or components and calculating the amount administer to the patient must be based on a case-by-case evaluation, in acute hemorrhage, packed cell volume may be a poor indicator of the degree of blood loss. Since all blood components are lost in hemorrhage, signs of shock may be seen initially when the packed cell volume is within reference limits. The packed cell volume in such patterns will gradually drop over The 72 h following the initialing incident, as extravascular fluid is redistributed and intravascular space, assuming that there has been no volume replacement with crystalloids in which case the packed cell volume will drop more quickly. [21] The potential for survival depends mainly on 2 factors: reestablishment of the blood volume and Tissue reoxygenation. Initial fluid therapy with crystalloids or colloids is essential to reestablish blood volume. This will be sufficient for losses that do not exceed 20 % of the patient's total blood volume. For losses exceeding 20 % whole blood packed red cell transfusion is indicated. Losses between 20 % and 50 % of blood volume require crystalloids and packed RBCs. [23]

Table 1: List of animals and their respective blood groups

Animal	Blood group
Dog	A1, A2, B, C, D, F, Tr, He.
Cat	A,B,AB.
Horse	A,C.D,K,P,Q,U
Cattle	A,B,C,F,J,L,M,R,S,T,Z.
Pig	A,O.
Sheep	A,B,C,D,M,R,X.
Goat	A,B,C,M,J

Adverse transfusion reactions

The risk of an adverse reaction is minimized under the following conditions the administered product has been properly collected, processed and stored. The donors are healthy animals of known blood group type and proper screening tests have been performed (cross matching). One study determined that up to 13 % of dogs developed an adverse reaction, but all animals survived. There are 2 types of adverse reaction, an immediate reaction that occurs during or within 1h following transfusion or a delayed reaction that may occur days, months or years later. The severity of an adverse reaction varies from mild (fever) to severe (death) the most serious transfusion reaction that practitioner can prevent is an acute hemolytic reaction. This is an immunological reaction that takes place when the patient has circulating natural or acquired antibodies towards donor erythrocyte antigens. Clinical signs in dog include fever, tachycardia or bradycardia, excessive salivation, tearing cardiac arrest. The severity of the signs in dogs depends on the volume administered. A clinician presented with an acute hemolytic reaction should interrupt the transfusion immediately and treat for shock. If present he or she should also verify the blood product being used and retrace the steps that lead to the transfusion, including a repetition of the cross match procedure. In cat, an acute hemolytic reaction is very likely in type B cat receiving type a blood. This risk is minimized if blood is screened for incompatibility, for cat and DEA1.1 and DEA1.2 negative dogs are used. [25]

Conclusion

The present status of research in and the practical use of, blood groups in animals are reviewed. Blood groups in animals are mainly used as genetic markers for the control of doubtful parentages and for genetic studies.

Table 2: Canine blood types and there incidence in United States

"New name" DEA group	"old" name	Population incidence*	Natural antibody	Transfusion significance
1.1	A_1	40-60%	No	Acute hemolytic reaction
1.2	A_2	10-20%	No	Acute hemolytic reaction
3	B	5-20%	Yes	Delayed hemolysis
4	C	85-98%	No	None
5	D	10-25%	Yes	Delayed hemolysis
6	F	98-99%	No	Unknown
7	Tr	10-45%	Yes	Delayed hemolysis
8	He	40%	No	Unknown

Table 3:Feline blood groups

Frequency of blood group	Breeds
None	Siamese and related breeds, Burmese, Tonkinese, Russian blue
1-10%	Maine Coone, Norwegian Forest, DSH, DLH
11-20%	Abyssinian, Birman, Himalayan, Persian, Somali, Sphinx, Scottish fold
20-45%	Exotic and British shorthair cats, Cornish and Devon Rex
Type AB	DSH, Scottish fold, Birman, British shorthair, Somali, Bengal, Abyssinian

Table 4-Eqine blood groups

System	Thoroughbred %	Arabian %	Standardbred %	Quarterhorse %	Morgan %
Aa-	15	18	44	51	43
Qa-	39	79	100	83	99

In animals the role of blood groups in transfusion and in incompatibility, of mating is limited. For cattle, horses, sheep, swine and chickens, studies on blood groups have reached a fairly high level of scientific and practical interest.

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