BLOOD TRANSFUSION IN THE CAT

by

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Literature Review

Introduction

Whole blood transfusion is a widely used treatment in a variety of pathologic conditions in many animal species. Despite its replacement in recent years by plasma expanders, reconstituted platelets, fresh frozen plasma and cryoprecipitates in the treatment of selected disorders, whole blood still enjoys some distinct advantages. Whole blood provides the recipient with a balanced electrolyte solution, utilizable energy substrates, clotting factors, as well as cellular elements.

Although erythrocytes can be the cause of many adverse reactions associated with transfusion, they may be the most essential component of the transfusion because of their role in carrying oxygen to the tissues. Anemia can occur due to hemorrhage, intravascular destruction, bone marrow depression or pooling in the microvasculature. If an animal is deprived of adequate red cells for too long, death or tissue damage will result from anoxia. Problems associated with blood transfusions have stimulated research into the hemodynamics of red cell exchange and the erythrocyte antigens and serum antibodies that precipitate many of these problems. For all species studied, the problems of blood group incompatibilities, transfusion reactions, and neonatal isoerythrolysis apply to varying degrees. Currently, for most domestic animals, information on erythrocyte antigens and their effect on transfusion

safety and efficacy is understood and applied in clinical situations.

Cats are among the species in which whole blood transfusions are most widely practiced for routine treatment. This is due in part to the many anemias that affect cats, the ease of transfusion, the clinical record of safety and the relative inexpense of maintaining donors. Unfortunately, research has not provided a sound basis for the widespread use of this therapy. There have been studies of the blood grouping systems of cats[1,2,3] and the methodology of and clinical indications for blood transfusions in cats are described,[4,5] but little is known about how the cat reacts to the transfused red cells.

History

The once popular belief that blood types were only important in man has, since the early 1900's, given way to research which produced considerable information on blood typing, blood transfusion, and the problems associated with blood transfusion. Ingebrigsten[6] reported the existence of isoagglutinins in cat serum, in 1912, in a study on tissue transplantation. Of 40 cats examined in groups of 10, isoagglutinins were found in the serum of 6, which reacted to the cells of between 1 and 7 of the other cats in their test group. No attempt was made to form groups based on the occurrence of antibodies. Ottenberg and Thalhimer[7] confirmed the results of that study and reported the first experimental

transfusions in cats. They concluded that isoagglutinins in cats are weak antibodies that fluctuate significantly and do not form distinct groups, while isohemolysins are not found in the blood of normal cats, but can be elicited by transfusion. It appeared that there were possible groups associated with the induced isohemolysins.

There was no further research on cat transfusions for some years. In that period, the clinical use of blood transfusion therapy in cats became an accepted practice. Kirk[8] advocated whole blood transfusion to treat the anemia and agranulocytosis associated with feline panleukopenia, in 1948, and explained the mechanics of the exchange process. In 1950, Holmes[9] undertook the first of two projects to blood type cats in Manchester, England. In his first survey, he used the isoagglutinin found in the blood of normal cats, designated group O, to type 477 cats. He reported the population to consist of two groups. The larger group (EF) exhibited the antigens, designated E and F, on the surface of their red cells and made up 97% of the population sample. A second group O, whose serum contained the antibodies to those red cell antigens, made up the remaining 3%. In 1952, Holmes[1] surveyed an additional 103 cats and reported a third group, F, whose red cells were agglutinated by type O serum and whose serum weakly agglutinated the cells of group EF. The population percentages given in the second survey were 95% EF, 4% O and 1% F. The EF and O groups of Holmes correspond

to groups A and B respectively, of later studies.[2] The one cat designated group F corresponds to none found in later studies and is unexplainable because the antigens E and F seem to be one antigen. In addition to the blood groups, Holmes reported that isoagglutinins remained relatively constant throughout the year and that natural isohemolysins are found in normal cat blood. Holmes attempted to make an analogy between the blood groups of cats and those of man but no firm conclusions were made.

In 1952, Eyquem and Podliachouk[2] surveyed 350 cats and reported the existence of two groups, with the population consisting of 85% group A and 15% group B. They found normal isoagglutinins in 20% of the cats studied and found that normal titers of between 1:16 and 1:512 could be increased to 1:8000 by isoimmunization.

A more extensive study of blood group systems of domestic cats and their mode of inheritance was undertaken by Auer and Bell[3] in 1981. When they surveyed 1,895 cats in Brisbane, Australia, they found 73.3% group A, 26.3% group B and .4% of a previously unreported blood group in which the erythrocytes contained both antigens and was, therefore, designated group AB. By absorbing sera against incompatible red cells, they showed that no important subgroups to the AB system existed. Anti-A was found to be a strong agglutinin and a strong hemolysin, occurring in 95% of group B cats. Anti-B was a weak agglutinin and a strong hemolysin, occurring

in only 35% of group A cats. The levels of antibodies fluctuated throughout the study. Although they speculated on two hypothetical inheritance patterns, Auer and Bell were unable to form any firm conclusions. The simplicity of the AB system makes it relatively simple to determine the blood groups in a sample of the cat population. Only one small sample of cats in the U.S. is reported, which found 18 group A cats and 2 group B cats in New York City.[10] These results could easily fit the previously reported population proportions.

Indications for Transfusion

Whole blood or reconstituted red blood cell transfusion is most often used in cats in the treatment of acute or chronic anemias or for maintaining cats with nonresponsive anemias.[11] It is a well accepted adjunct for treating acute blood loss,[12] hemobartonellosis,[13] aplastic anemia,[14] feline respiratory disease complex[15] and myeloproliferative disorders[16] associated with feline leukemia virus. Unlike the dog, fatal bleeding rarely occurs in the cat due to trauma and the need for transfused blood seldom arises during surgical procedures.[11] Why cats suffer more often and more severely from anemia is not known but it is appropriate that cats also seem to have the greatest ability to withstand anemia without showing any clinical signs.[11] When anemia affects the cat to the point of debility, blood transfusions may provide the recipient with the needed time to respond on its own or simply provide the red cells necessary to ameliorate most clinical signs.

Although whole blood can be given to supply platelets or clotting factors,[13] it is preferable to separate plasma or platelets for these procedures.[17]

The decision of whether to transfuse an anemic cat must take many factors into consideration. There is no magic degree of anemia at which a transfusion becomes necessary, because each cat will differ in its ability to tolerate anemia. A cat's ability to tolerate anemia is determined partly by the rapidity of onset and the general health of the cat. Hemobartonella, for example, can cause a 10-15% drop in packed cell volume (PCV) in one day,[4] while causing fever and otherwise depressing the cat. Chronic anemias are, in contrast, characterized by minor decreases of 1-2% per day in PCV[4] and can be free of other manifestations. The more rapid the drop in PCV and hemoglobin (Hb), the more debilitating the anemia. Clinical evaluation remains the most important deciding factor of whether a transfusion is indicated. Schall and Perman[18] recommend transfusion if the PCV is 12% or less, while Norsworthy[4] begins transfusion therapy in some cases at a PCV of 15%. Enough blood should be given to produce clinical improvement but not so much as to suppress erythropoetic stimulus. That dosage is not agreed upon by all researchers. Norsworthy[4] recommends returning the PCV to 18%. Others prefer to give a standard dose to the average size cat which they feel has produced the best results. Clark states 2-5 ml/lb is usually sufficient.

Schall and Perman[18] state the arbitrary does of 10-20 ml/kg. Flint et al[12] gives a standard dose of 40 ml in feline infectious anemia and Cotter[22] calls for a standard dose of 100 ml in chronically anemic cats for maintenance. In chronic cases where bone marrow response is poor, inhibition of erythropoetic stimulus is not as great a concern. Final judgement depends on the amount, the clinician feels produces desired results, but which still leaves the cat anemic, so that the bone marrow will respond if possible. Whole blood transfusion may be contraindicated in autoimmune hemolytic anemia and when distinct incompatibility is evident in crossmatching tests.

Methodology

The methods of removing and administering blood are limited only by feline anatomy and the skill of the clinician. With few exceptions the administration of the transfusion will not pose a major problem. Donors should be feline leukemia virus negative and be free of hemobartonellosis. Blood can be taken from the jugular vein, cephalic vein or ventricle of the heart. The jugular vein is probably the easiest to isolate and the safest. The heart should be reserved for those donors which are terminal. The expense of maintaining a donor cat is minimal compared to the usefulness of the procedure. The amount of blood taken from a donor varies but a healthy cat can lose up to 30% of its blood volume without going into shock. Clark states 10 ml/lb can be withdrawn and replaces it with plasma expander.[5] Thornton[19] recommends taking 50-60

ml per bleeding and resting the donor for 3 weeks before another bleeding. Byars and Divers state that 20% of a cat's blood volume of 35 ml/lb may be donated safely. A sacrificial donor of average size will yield approximately 175 ml from the heart.[19] If the blood is to be used immediately, it should be collected in heparin, because the safety of citrate anticoagulants is questioned in the cat.[5] The amount of heparin is not critical but it is possible to give too much in a large transfusion, approximately .25 ml (1000 units/ml) should be used for 10 ml of blood.[5] Heparin can be diluted in 3 ml of saline to aid in mixing. Heparin will eventually be broken down by plasma heparinases and therefore cannot be used for storing blood. Acid-citrate-dextrose (ACD) or citrate-phosphate-dextrose (CPD) are used for storage, because these solutions maintain erythrocyte viability better. It has been recommended that dog blood may be stored for 3 weeks in ACD at 4°C.[21]

Blood can be administered with a needle, but a catheter well seated in the cephalic vein is preferable. The rate of transfusion is disputed because rapid infusion can result in pronounced cardiovascular disturbances and methods of slow infusion are difficult to adapt for use in cats. Schall and Perman[18] recommend a 5 ml/lb/hr rate and Cotter[22] states a full 100 ml dose can be given in 30 min. in an average size cat. If vomiting or excitement occurs, the transfusion should be stopped until the cat has recovered. If the blood is cool

it should be warmed for rapid transfusion. Tranquilizers or anesthetics can be used before transfusion but are generally not needed. Blood should be given in the peritoneal cavity only as a last resort. Intraperitoneally infused erythrocytes are absorbed into the blood,[19] but the process is usually not fast enough to provide relief in a severely anemic cat. Thornton[20] reports poor results with the procedure in puppies and kittens.

Transfusion Reactions

Adverse reactions due to the transfusion of whole blood in cats have been alluded to since the first experimental transfusions were done. Most are credited to red cell incompatibility, but unfavorable effects could be due to immunologic reactions to leukocytes, infusion of cold blood, infusion of extraneous matter or infusion of toxic amounts of anticoagulant. Ottenberg and Thalhimer[7] concluded that direct transfusion of red cells agglutinable by the recipient's serum has no immediate harmful effects. Cells which are susceptible to hemolysis by the recipient's serum did cause some negative reactions. When transfused with these cells the recipients exhibited a marked hemoglobinemia, hemoglobinuria, with intravascular hemolysis, phagocytosis, a reactive leukopenia and usually glycosuria. Because they did not report the existence of natural isohemolysins, all of these reactions were in previously transfused cats. Thornton[19] mentions complications which occurred after single

and multiple transfusions and states that information on blood groups in cats might help avoid these problems. The vast majority of feline transfusions are done with complete safety[10,22] even on a repeat basis. The caution by most investigators, that blood should be crossmatched or repeat transfusions avoided, seems to be designed to catch the infrequent problem case rather than the rule.

Despite the widespread use of transfusions in cats, only one death caused by transfusion of incompatible blood has been reported.[23] A feline surgery patient was given citrated whole blood two hours after surgery because of pallor and a history of anemia. Apparently, it was the cat's first transfusion. After infusion of only 4 ml of blood, the cat reacted with periods of dyspnea, stretching increased heart rate and force, and retching. Death occurred 15-30 minutes later. The case report does not provide sufficient information to conclude whether death was due to red cell incompatibility or to a reaction to something in the plasma or the anticoagulant solution. The donor cat had group A erythrocytes but the recipient's blood group was unknown, and its anti-A titer was not measured. No necropsy results were given. In an experimental follow-up severe shock reaction occurred in 17 of 32 unsensitized cats of blood type B given 1 ml of 50% saline suspension of group A cells. No deaths resulted. If the population of cats is 75% group A and 25% group B,[3] then with a randomly chosen

donor and recipient, a transfusion of incompatible blood should occur 37.5% of the time. Adverse reactions occurred in approximately one-half of the group B cats given group A erythrocytes and in none of the group A cats given group B erythrocytes. An adverse reaction would then be expected 4.68% of the time with randomly chosen donors. In a clinic doing a large number of feline transfusions such a high rate of adverse reactions would hardly go unnoticed, unless the reaction lacks sufficient manifestations to be noticed clinically. Even though the death report and high rate of experimental transfusion reactions are questionable, it is substantive enough to raise concern about how adverse reactions can be prevented. Crossmatching will prevent some but not all of the incompatible transfusions, by revealing recipients with high titers of antibody against the donors blood group antigens. Agglutination crossmatch tests are simple and quick to perform but hemolytic crossmatches require a source of complement not readily available to most clinicians. An even more complete, but less feasible solution to the problem would be the typing of all donor and recipient cats.

The citrate in ACD or CPD has also caused problems in the transfusion of whole blood to cats.[5] Citrate intoxications occur in dogs and man.[24,25] It is due largely to chelation of calcium. Because citrate is metabolized rapidly by the liver, rapid infusions of large amounts of citrate are needed to produce toxicity in dogs (2-5 ml/kg/min).[25]

Whether the feline liver is less efficient at metabolizing citrate or whether cats are more susceptible to the effects of decreased serum calcium is not known, but the use of citrated blood in cats has been questioned.[5] This problem can be avoided by restricting use of stored blood and preserving fresh blood in heparin. If stored blood must be used, reconstitution of red cells in saline will decrease the amount of citrate infused. The adverse effects of citrate can be counteracted by infusion of 1 mg $CaCl_2$ per 10 ml of whole blood infused.[24]

The occurrence of neonatal isoerythrolysis in cats following blood transfusion is unknown. All of the prerequisites of the problem have been reported in cats. Colostrum can contain levels of antibodies directed against blood group antigens[2] and red cell antigens are found on the cells of the liver and spleen of the fetus.[2] Fetal erythrocytes also show evidence of antigen development as early as 38 days of gestation.[3] It is possible, therefore, that transfusions which cause antibody development in an intact female, might cause colostral antibodies to be present in later pregnancies, which could be high enough in titer to cause problems in the kittens of a different blood group. Nothing substantive is known about the inheritance patterns of feline erythrocyte antigens, but "fading kitten syndrome" has been associated with an incompatibility reaction between queen and kitten due to sensitization with panleukopenia tissue vaccine.[26]

Rationale for Thesis

The purpose of this study was to determine the life-span of erythrocytes after autologous and allogeneic transfusions in the cat, to determine the role that red cell antigens and antibodies against those antigens play in the fate of the red cells and to determine the maximum time feline blood can be stored.

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Paper 1. Survival of Erythrocytes After Autologous and Allogeneic Transfusion in Cats

Summary

Apparent mean survival time of ^{14}C-cyanate labeled feline erythrocytes was determined after autologous and allogeneic transfusion. Mean survival time was defined as that time when one half of the transfused cells have been removed from circulation. Autologously transfused cells had a mean survival time of 38.0 days $\pm$ 2.02. Allogeneic transfusion between cats of the same blood type showed a near normal mean survival time of 30 days. Primary allogeneic transfusion between cats of differing blood groups showed a mean survival time between 10 and 14 days, while repeat transfusions of this type showed a mean survival time of less than 5 days. The life-span of cross-transfused red cells can be significantly effected by blood type. For maximum effectiveness, survival of cells, blood transfusions should be between cats of the same blood type. First-time transfusions between cats with different blood groups can be given safely but erythrocyte life-span will be shortened.

Introduction

Blood transfusion is one of the most used and discussed treatments for a wide variety of ailments in all animal species. It contains many elements essential to life. Whole blood or reconstituted red cells must be used when treating losses of blood or cellular elements of the blood, of a magnitude that could seriously compromise an animal's ability to deliver oxygen to the tissues. Effective numbers of erythrocytes can

be reduced with hemorrhage, intravascular hemolysis, pooling in the microvasculature, and bone marrow depression. Transfusions in cats are especially appropriate, because bone marrow depression and neoplastic anemias occur frequently. Clinically, many transfusions are performed under a variety of conditions[1,2] on a regular basis, and although results are not always optimal, neither the safety nor the efficacy of the practice is seriously questioned. The indications for and the mechanics of blood transfusions in cats are well outlined,[3,4] but very little attention has been directed toward the hemodynamics and complications of transfusions.

Several techniques are available to estimate red cell life-span and the normal erythrocyte life-spans of many species are known.[5,6,7,8] Cells removed from an individual and reinfused into the same individual provide a reliable estimate for normal red cell life-span.[8] Cells transfused between compatible humans last approximately as long as normal cells,[9] while erythrocytes of random cross-transfusions in animals tend to have shorter than normal life-spans.[5,6,10,11,12] The simplest and most widely used of these techniques is ^{51}Cr labeling of erythrocytes. Among its other shortcomings, is the fact that it reports a T 1/2 that is only useful from a comparative point of view. Other methods, DF^{32}P, ^{14}C-glycine and ^{59}Fe labeled erythrocytes yield data which can give a concrete estimate of normal life-span. The reported erythrocyte life-span in cats is 76.2 days[13] and 72.6 days,[14] for DF^{32}P and ^{14}C-glycine studies respectively.

Blood groups occur in cats and isoantibodies to those groups are also found in normal cat blood.[15,16,17] The cat population is approximately 75% group A and 25% group B, with group AB occurring rarely.[17] Erythrocyte incompatibilities have been incriminated as the cause of complications following single and multiple transfusions in cats,[18] and possibly as a cause of neonatal isoerythrolysis in kittens.[19] Only one death due to blood group incompatibility in a transfused feline surgery patient has been reported.[20]

The purpose of the present study was to determine the life-span of erythrocytes after autologous and allogeneic transfusions in the cat, and determine the role that blood groups and isoantibodies play in the fate of the transfused cells and the safety of the transfusion.

Materials and Methods

Five domestic shorthair cats were used in the study. The group consisted of one intact male and four intact females of various color patterns. To our knowledge none of the cats were related and none had received any previous transfusions.

Initially, the cats were crossmatched against each other. A 3 ml blood sample was taken from the jugular vein. Red cells were separated by centrifugation, washed twice and diluted to 2% with isotonic saline. Washed cell suspension (50 µl) was mixed with undiluted serum (100 µl) and incubated for 30 min. at 37° C, then the mixture was centrifuged at 1000 rpm for 1 minute. Agglutination was determined grossly and

microscopically. Appropriate controls were used in all cases.

Erythrocyte life-span was determined after autologous and allogeneic transfusion. Erythrocytes were labeled in vitro with $K\ ^{14}CNO_4$.[a] Blood (5 ml/transfusion) was taken from the jugular vein into heparin. Red cells were separated by centrifugation and reconstituted in sterile isotonic buffered saline. The labeling preparation (50 µl/ml) was added to the red cell suspension and incubated at 37° C for one hour with slight agitation. The cells, separated by centrifugation, were washed 3 times in sterile saline and reconstituted to 5 ml. The resulting solution was transfused with a cephalic catheter into cats anesthetized with ketamine.[b] The cats were observed closely for post-transfusion reactions. Post-transfusion blood samples (1 ml) were taken from the jugular vein into heparinized syringes. Samples were taken at 30 min, 24 hours, 48 hours and 2-3 times/week. The packed cell volume (PCV) of each sample was determined by microhematocrit and hemoglobin (Hb), as the cyanmethemoglobin derivative. The radioactivity was counted by placing whole blood (20 µl) onto small pieces of filter paper and decolorizing with 30% H_2O_2 (.5 ml). After thorough drying, the filter paper was

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[a]Potassium (^{14}C) Cyanate, Amersham/Searle, Arlington Heights, Ill.

[b]Ketaset, Veterinary Products Bristol Laboratories, Syracuse, N.Y.

immersed in liquid scintillation counting fluid[c] (10 ml). The samples were refrigerated and counted in a Betatrac 6895 liquid scintillation counter.[d] The radioactivity is reported as counts per minute as a percent of the 24 hour count. The data of the autologous transfusions were evaluated using linear regression. Mean survival time was defined as the time when one half of the transfused cells had been removed from circulation, as determined by the regression line. It represents approximately one half of the full life-span.

The cats were blood typed after being sensitized by tri-weekly injections of allogeneic whole blood (1 ml) from randomly selected partners. The cells and serums of the cats were tested against each other using the agglutination test along with a test for hemolysis. The hemolytic test modified the agglutination procedure by adding 50 µl of pooled guinea pig complement,[e] which had been absorbed against pooled cat red cells for 5 min. After observing for agglutination, complement was added and incubated for 1 hour at 37° C. Hemolysis was determined visually at 1 hour and 90 minutes. Types were assigned based on the assumption that anti-A was

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[c]Scintisol, Isolab Inc., Akron, Ohio.

[d]Betatrac 6895, Tracor Analytic, Inc., Elk Grove Village, Ill.

[e]Guinea Pig Complement, Lyo & Diluent, Miles, Elkhart, Ind.

a strong agglutinin and a strong hemolysin while anti-B, a strong hemolysin and weak agglutinin.[17]

Results

Erythrocytes transfused autologously declined at an approximately linear rate as would be expected with a random labeling procedure. The results are plotted in Figure 1. There was an initial 10-20% drop in activity between the 30 min and 48 hr samples probably due to damage to cells during the labeling procedure. Most of the nonviable cells are removed from circulation within 24 hrs after transfusion.[21] The remaining erythrocytes had a mean survival time of 38.9 days $\pm$ 2.02 which corresponds to a life span of 77.8 days. Counts in the 0-10% range proved to be unreliable but transfused cells were essentially gone by day 82 in all four transfusions.

Because crossmatching of cats by agglutination tests showed no pronounced incompatibilities, the initial transfusions were random. In figure 2, three distinct groups of results can be seen. Transfusion between cats of the same blood type (G) shows an approximately linear decrease in number of erythrocytes surviving and a nearly normal mean survival time of 30 days corresponding to a life span of 60 days. First time transfusions between cats of differing blood types (D, E, F), show shorter more variable life-spans, with a mean survival time of between 10 and 14 days. The number of surviving cells dropped below 10% by 15 to 22 days. Second

or third transfusions between cats of differing blood types, cats which have been previously sensitized to the red cell antigens of the transfusion, showed rapid destruction of cells. In all cases (A, B, C), there was a mean survival time of less than 5 days, with less than 10% of the cells surviving at 10, 5.5 and 5 days respectively. Neither signs of transfusion reactions, nor hemoglobinemia was observed.

Blood grouping tests revealed one group B cat which developed a high titer agglutinating antibody directed against the red cells of the other four cats, which were then designated group A. The group A cats sensitized with injections of group B blood developed a high titer hemolytic antibody against group B red cells, confirming the blood group distinctions.

Discussion

The present data indicate that the life-span of normal feline erythrocytes is 77.8 days $\pm$ 4.04. That is slightly longer than reports by other investigators using other isotopes. Because ^{14}C-cyanate binds firmly to the hemoglobin of the red cell, it may be a more accurate reflection of potential life span.

The life-span of cross-transfused cells can be affected significantly by the blood types. When blood is transfused between cats of the same blood type (A or B) erythrocyte life-span is almost normal. That indicates that no subgroups of consequence occur within the three main blood types in

cats, which would cause immunologic destruction of the cells. Transfusions of this kind should provide long term benefit to the patient. Cross-blood group transfusions into cats not previously sensitized to red cell antigens can provide adequate numbers of red cells with a life-span long enough to allow their use in many situations. Recipient cats can develop an immunological response to incompatible cells that is accompanied by rapid destruction of transfused erythrocytes at approximately 2 weeks. Although adverse reactions were not observed in the present experiment with this immune response, they can occur. Repeated transfusions between the same two individuals or between cats of differing blood types may be unwise because cells may not live long enough to benefit the recipient. An apparent anamnestic response to red cell antigens rapidly destroys the incompatible cells. The possibility that transfusion reactions or hypersensitivities to the antigens could occur is also greater. The present experiment does not indicate any grave hazards in transfusion of incompatible blood even on a repeat basis. On three occasions cats were given incompatible blood to which they had already been sensitized and no adverse effects were noted. The safety may be real, but in this experiment all cats were healthy at the time of transfusion and the volumes used were much smaller than those of clinical transfusions. These transfusions were also done in anesthetized cats and consisted of cells reconstituted in sterile saline, thus removing

foreign serum antigens. Because there are reports of problems, the matter of safety should not be viewed as unimportant.

This experiment indicates, as does clinical experience, that transfusions in the cat can provide the oxygen carrying erythrocytes with a high degree of viability and relative safety. Further, unlike other species[5,6,11,12] the erythrocytes can be quite long lived due to the single red cell antigen system of cats. If feline blood groups are distributed in the United States similar to their distribution in other countries,[17] there should be a high rate (37.5%) of incompatible transfusions done when donors are chosen randomly but a much smaller rate of repeated incompatible transfusions. Primary incompatible transfusions will apparently provide benefit to the patient for a significant period of time but are potentially more hazardous. The potential hazards can be minimized by blood typing of cats or in some cases through simple crossmatches. For maximum benefit, especially in treating chronic anemias where bone marrow response is poor, cats should be transfused with cells of the same blood group or at least not transfused with cells to which they have been previously sensitized.

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Figure 1. Percentage of transfused erythrocytes surviving, determined by counts/min as a percent of the 24 hr counts. Results of four autologous transfusions.

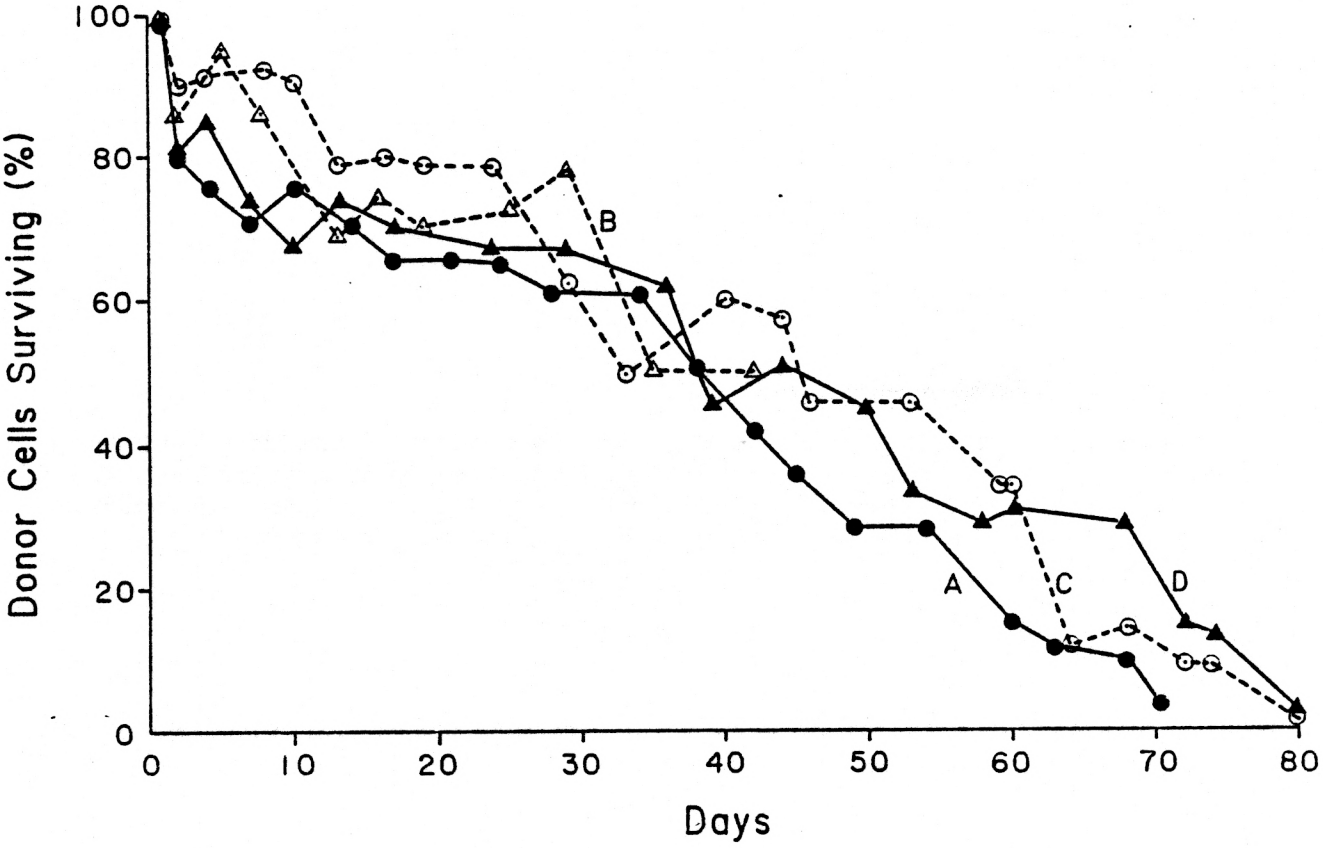
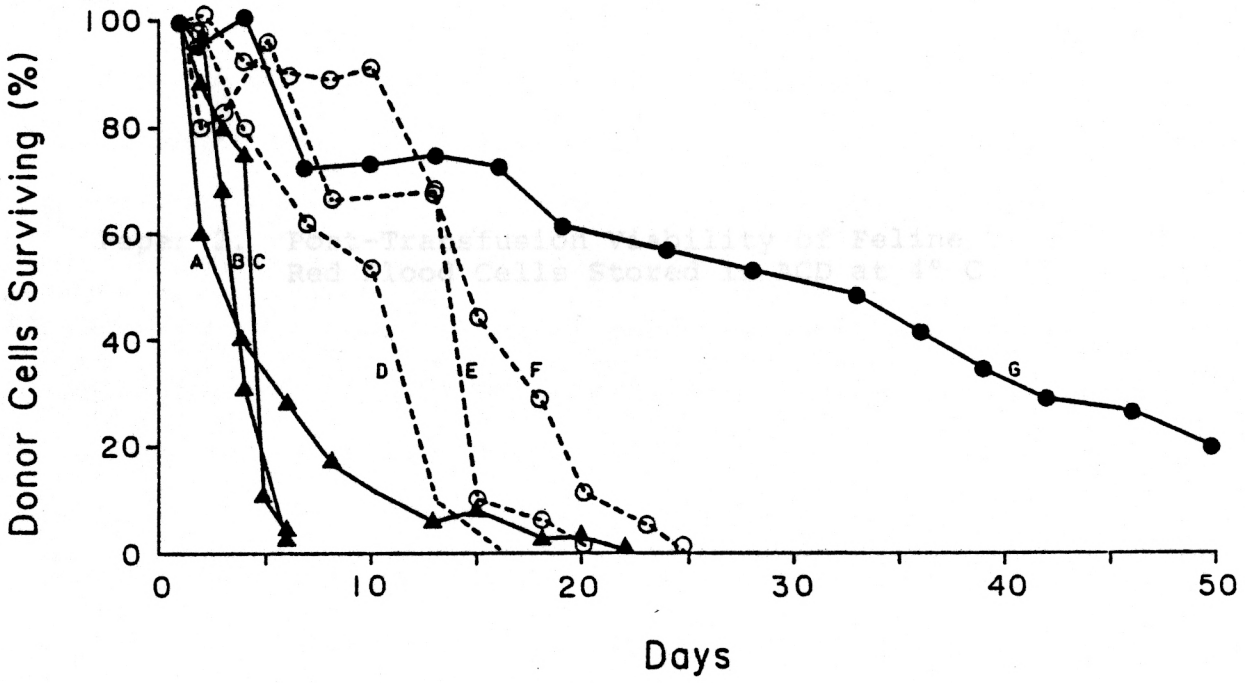

Donor Cells Surviving (%)
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
Days
A
B
C
D

Figure 2. Percentage of transfused erythrocytes surviving, determined by counts/min as a % of the 24 hr radioactivity counts. ●—● Transfusion between cats of the same blood group, o—o between cats of different groups not previously transfused and ▲—▲ repeated between cats of different groups.


Donor Cells Surviving (%)
100
80
60
40
20
0
0
10
20
30
40
50
Days
A
B
C
D
E
F
G

Paper 2. Post-Transfusion Viability of Feline Red Blood Cells Stored in ACD at 4° C

Summary

The 24-hour post-infusion erythrocyte viability was determined in feline blood stored in acid-citrate-dextrose (ACD) solution "B" with ^{51}Cr-labeling. Viability decreased significantly ($p < .01$) during 40 days of storage. Feline blood can be stored in ACD at 4° C for 30 days and retain high erythrocyte viability.

Introduction

The use of stored blood for transfusions in cats, although not a common technique, may, under certain circumstances, be the most convenient alternative. It allows more efficient use of blood from sacrifical cats and may eliminate the cost of maintaining a donor cat. If stored blood is to be used, it is important to know the length of time that the red cells can be kept while retaining their viability.

Erythrocyte viability limits storage of human blood. Post-storage viability is defined as the percent of transfused red blood cells present in the circulation 24 hours after the transfusion, as determined by radioactive chromate labeling. The National Institute of Health (NIH) recommends that at least 70% of the transfused cells be viable at 24 hours; therefore, human blood stored in acid-citrate-dextrose (ACD) is limited to three weeks. In some countries, ACD has been replaced by solutions containing adenine or phosphate for human blood storage, but it remains a widely used, widely available and efficient media for blood storage.

Post-storage viability of stored feline blood is unknown. It has been assumed that cats will follow closely the results obtained with dogs. Canine blood remains viable for up to four weeks in ACD at 4° C,[1] but recommendations for maximum storage rarely go beyond the human standard of 21 days.[2]

Materials and Methods

Four domestic shorthair cats were used in this study. One was an intact male, the other three intact females. The cats weighed between 8 and 12 lbs.

ACD solution "B" was prepared and sterilized by passage through a .22um membrane filter.[a]

Blood (30 ml) was removed from each donor by jugular venipuncture and added to the anticoagulant at a ratio of 4 ml of blood to 1 ml of ACD in 150 ml plastic bags.[b] The bags were mixed by gentle rotation biweekly while being stored at 4°C.

Approximately 1 hour after collection and every 10 days thereafter 5 ml of the blood-anticoagulant mixture was drawn into syringes. Radioactive sodium chromate[c] (25 μCi) was added to the mixture. After a 30 minute incubation at 37°C, ascorbic acid (50 mg) was added to terminate the labeling process. Cells were washed 3 times with equal volumes of sterile isotonic saline, and suspended in 5 mls of isotonic saline.

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[a]Millex, G. S. Millipore Corporation, Bedford, Mass.

[b]Viaflex, Travenol Laboratories, Inc., Deerfield, Ill.

[c]Radioactive sodium chromate, Amersham/Searle, Arlington Heights, Ill.

Labeled blood samples were infused into each cat via a cephalic catheter.[d] Blood samples (1 ml) were taken from the jugular veins just prior to transfusion, at 30 minutes post-transfusion and at 24 hours post-transfusion. The radioactivity of whole blood samples were counted in a well type gamma counter and reported as counts/min/ml. The 24-hour post-transfusion viability percentages were calculated using the radioactivity of the 30 minute sample as 100% and comparing it to the 24-hour post-infusion radioactivity. The counts were corrected for the radioactivity present from the previous weeks experiment. Experimental data were analyzed by analysis of variance, with the significant effects of time localized by least significant difference (LSD).

Results and Discussion

The 24-hour post-transfusion viability of feline red blood cells, stored in ACD, decreased significantly by the 40th day of storage ($p < .01$). Visible hemolysis became apparent by the end of the fifth week.

The data presented here indicate that cat whole blood can be stored up to 40 days in ACD solution "B" at 4°C and mtaintain a high degree of viability (> 70%). It is noteworthy that using the same criteria recommendation for storage of dog blood is 21 days.[2] It appears from this data that cat blood storage can be extended to 1 month.

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[d]Sovereign indwelling catheter, Sherwood Medical, St. Louis, Mo.

Most transfusions in cats are not given in emergency situations, but rather used in the treatment of acute or chronic anemias.[3] The ability to use stored blood is, therefore, probably more of a convenience than a necessity, but with the availability of blood from cats to be euthanized and the length of storage possible, it can be an attractive alternative.

Questions have been raised about the safety of citrate anticoagulant use in the cat.[4] Citrate toxicity occurs in dogs and humans[5,6] when large amounts of citrated blood are infused. Many transfusions have been performed in cats using citrate anticoagulant with apparent safety but the problem needs further study.

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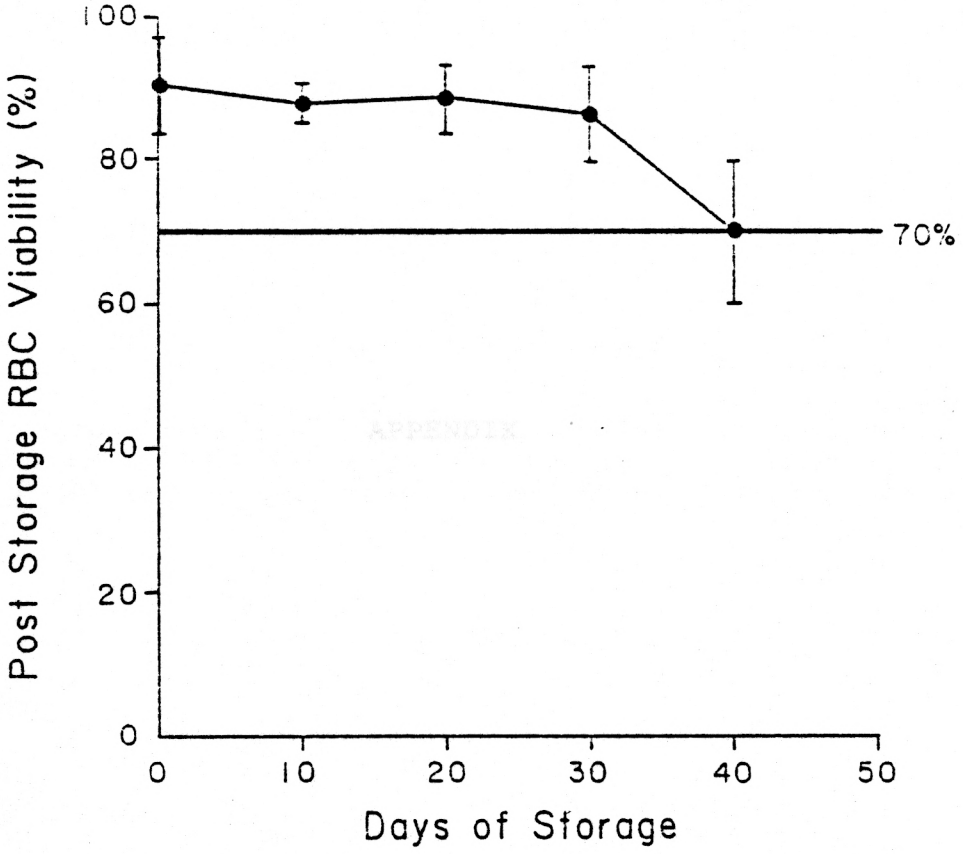
Figure 1. Post-storage viability of feline erythrocytes stored in ACD at 4°C (S.D. = 3.87). The NIH minimum standard is indicated at the 70% level.


Post Storage RBC Viability (%)
100
80
60
40
20
0
70%
0
10
20
30
40
50
Days of Storage

APPENDIX

Autologous 1 Sample (days)	Counts avg.	%24 hr. count	Hb.	Hct.
1	972	100	11.2	40
2	765	79	11.4	38
4	731	75	11.4	38
7	690	71	11.3	38.5
10	740	76	11.2	39
14	679	70	11.3	39.5
17	643	66	11.4	38.5
21	641	66	11.5	38
24	634	65	11.4	40
28	589	61	11.4	40.5
34	583	60	11.5	40
38	486	50	11.5	40.5
42	410	42	11.5	41.5
45	342	35	11.6	39.5
49	271	28	11.4	39.5
54	276	28	11.4	40
60	148	15	11.3	40
63	116	12	11.2	38.5
68	92	10	11.3	39
70	38	4	11.0	39.5
Autologous 2				
1	1154	100	9.8	36
2	983	85	9.4	36.5
5	1097	95	9.6	35.5
8	980	85	9.6	37
13	785	68	10.1	37.5
16	851	74	10.0	36.5
19	807	70	10.2	37.5
25	831	72	10.1	36
29	903	78	9.6	38
35	577	50	9.8	37.5
42	576	50	9.4	38.5

Table 1 - Daily radioactivity data, hemoglobin and hematocrit values for 4 autologous and 7 allogeneic transfusions.

Autologous 3

Sample (days)	Counts avg.	%24 hr. count	Hb.	Hct.
1	231	100	10.2	38.5
2	208	90	10.0	38.5
4	214	92	10.3	36
8	217	93	9.9	36.5
10	211	91	9.9	35.5
13	181	78	10.0	35
16	184	80	10.1	35
19	179	78	10.4	35
24	182	78	10.4	36.5
29	141	62	10.5	36
33	111	49	10.3	37
40	138	60	10.2	36
44	130	57	10.4	36
46	103	45	10.0	35.5
53	105	45	10.7	36.5
59	78	34	10.5	37.5
60	79	34	10.5	37
64	28	12	10.5	38.5
68	34	15	10.7	38
72	20	9	10.7	39
74	19	9	10.9	37
80	3	1	10.7	39
Autologous 4				
1	179	100	11.2	41.5
2	146	81	11.2	41
4	150	85	11.0	39
7	132	73	10.9	39.5
10	120	67	10.9	38.5
13	130	73	10.6	36
17	125	70	10.8	36
24	122	67	10.9	37
29	119	67	10.3	37.5
36	111	62	10.4	36
39	81	45	10.3	34
42	90	51	10.3	35
50	80	45	10.0	35.5

53	59	33	10.3	34.5
58	53	29	10.3	34.5
60	55	31	10.1	35
68	52	29	10.4	34
72	29	16	10.3	36.5
74	25	14	10.3	36
80	4	2	10.7	36
Sample (days)	Counts avg.	%24 hr. count	Hb.	Hct.
Allogeneic 1				
1	63	100	12.4	40
2	51	80	12.2	39
3	52	83	10.9	39.5
5	61	97	12.0	38
8	42	66	11.6	38
13	43	68	11.8	39
15	28	44	10.6	38
18	19	29	11.8	39.5
20	8	12	12.1	39.5
23	4	6	12.4	40.5
25	1	2	12.3	39
Allogeneic 2				
1	200	100	11.6	41
2	192	96	11.8	41
4	204	102	11.5	40
7	144	72	11.5	41.5
10	146	73	11.6	41.5
13	150	75	11.9	40.5
16	144	73	11.8	39.5
19	124	62	11.7	39
28	108	54	11.6	39.5
33	94	47	11.5	38.5
39	70	35	11.4	38
42	58	29	11.2	38
46	54	27	11.4	38.5
53	30	15	11.3	39.5
58	38	19	11.1	38
60	8	4	11.1	38
64	4	2	11.3	37.5

Allogeneic 3 Sample (days)	Counts avg.	%24 hr. count	Hb.	Hct.
1	229	100	11.9	37.5
2	224	98	11.4	38
4	183	80	10.6	36,5
7	142	62	10.8	37.5
10	121	53	11.6	36.5
13	23	10	11.4	37
16	2	1	11.0	37
Allogeneic 4				
1	343	100	11.2	39
2	202	59	10.6	38
4	134	39	11.8	38
6	93	27	10.8	39.5
8	58	17	11.6	37
10	41	12	11.4	37
13	21	6	12.2	39
15	27	8	12.4	40.5
18	10	3	12.2	40.5
20	10	3	11.6	41
Allogeneic 5				
1	1238	100	11.1	33.5
2	1263	102	10.6	35
4	1139	92	10.5	35
6	1111	90	9.6	36
8	1102	89	11.1	36.5
10	1139	92	10.9	35.5
13	830	67	11.2	37
15	124	10	10.6	35
18	74	6	10.2	36
20	25	2	10.8	36

Sample (days)	Counts avg.	%24 hr. count	Hb.	Hct.
Allogeneic 6				
1	323	100	12.2	39
2	325	100	11.9	38
3	216	67	11.6	39.5
4	101	31	12.2	38.5
6	7	2	10.9	37
Allogeneic 7				
1	883	100	10.8	34
2	769	87	11.1	33
3	710	80	10.8	35.5
4	662	75	11.4	34
5	88	10	11.2	34
6	35	4	10.8	32.5

Cat 18 Storage (days)	30 min count	24 hr count	24 hr %	Hb.
1	1452	1249	86	9.0
10	1559	1340	86	9.4
20	1866	1720	92	8.8
30	1367	1179	86	8.6
40	6402	5028	79	8.8
Cat 19				
1	825	805	98	10.5
10	940	788	84	10.3
20	1320	1078	82	10.7
30	772	715	93	10.4
40	3471	2594	75	10.8
Cat 20				
1	1173	1119	95	10.8
10	1323	1166	88	11.2
20	1523	1387	91	11.3
30	967	832	86	10.9
40	4042	2712	67	11.5
Cat 21				
1	1189	983	83	10.4
10	1288	1184	92	11.2
20	1267	1112	88	11.4
30	1035	776	75	11.5
40	4861	2829	58	11.1

Table 2 - 24 hr post-storage viability data and hemoglobin values for 4 cats.

BLOOD TRANSFUSION IN THE CAT

by

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D.V.M., Kansas State University, 1982

AN ABSTRACT OF A MASTER'S THESIS

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requirements for the degree

MASTER OF SCIENCE

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College of Veterinary Medicine

Kansas State University
Manhattan, Kansas

1983

Whole blood transfusion is a widely used therapeutic procedure in cats, but little is known about the hemodynamics and complications of the transfusion and the effect of feline blood groups on the safety and efficacy of the process. Autologous transfusion in other species and transfusion between compatible humans provides red cells with near normal life-spans, while allogeneic transfusion in animals can result in shortened life-span of transfused erythrocytes. Problems of red cell incompatibilities, transfusion reactions, and neonatal isoerythrolysis, have been associated with blood group antigens and antibodies in most species studied, but reports in the cat are few. There are only three blood groups known in cats. The population consists of 75% group A, 25% group B, and .4% group AB.

Apparent mean survival time of ^{14}C-cyanate labeled feline erythrocytes was determined after autologous and allogeneic transfusion. Mean survival time was defined as that time when one half of the transfused cells have been removed from circulation. Autologously transfused cells had a mean survival time of 38.0 days $\pm$ 2.02. Allogeneic transfusion between cats of the same blood type showed a near normal mean survival time of 30 days. Primary allogeneic transfusion between cats of differing blood groups showed a mean survival time between 10 and 14 days, while repeat transfusions of this type showed a mean survival time of less than 5 days. The life-span of cross-transfused red cells can be significantly

affected by blood type. For maximum effectiveness, survival of cells, blood transfusions should be between cats of the same blood type. First-time transfusions between cats of differing blood types can be given safely but erythrocyte life-span will be shortened.

The 24-hour post-infusion erythrocyte viability was determined in feline blood stored in acid-citrate-dextrose (ACD) solution "B" with ^{51}Cr-labeling. Viability decreased significantly ($p < .01$) during 40 days of storage. Feline blood can be stored in ACD at 4°C for 30 days and retain high erythrocyte viability.