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Red blood cell transfusions – when, what and how to do it!

Red cell transfusions are now a relatively common intervention in veterinary practice in the UK and help in the treatment of many patients. This is largely due to the availability of blood products, such as Packed Red Blood Cells (PRBC) , from blood banks supplying directly to practices. After donation, red cells are separated from plasma into a concentrated packed cell form, a nutrient extender is then added to them. This allows the red cells to be stored for up to 42 days before being transfused into patients. DEA 1 blood typing prior to transfusion is essential and cross matching should be performed for second transfusions. Blood products are administered through a filtered giving set and patients monitored closely for transfusion reactions. Transfusion reactions are thankfully rare but potentially life threatening.

Key words: Canine, Packed Red Blood Cells (PRBC), transfusion, blood typing, cross matching, transfusion reactions

Clinical presentation

Without doubt, blood transfusions can be one of the most rewarding interventions in veterinary medicine, as increasing red cell numbers and the associated improved oxygen carriage makes an obvious and immediate difference to the patient. In many instances these transfusions preserve life and many of the advances in veterinary medicine and surgery would not be possible without the ability to transfuse patients.

As with any intervention, there are multiple considerations and with transfusions these must be carefully considered.

Firstly blood is not *'just another fluid'*, but a complex, physiologically balanced, biological mixture. An understanding of its content is important when considering administering transfusions. Red cells are living cells and need to be carefully looked after before administration to the patient which leads to practical storage and transport requirements for these products.

Secondly, blood products are a very precious and limited resource. All blood available for transfusion is donated and so the health and wellbeing of the donor should always be considered. It is also important that these products are used respectfully and rationally, in patients with fair prospects of making a recovery, so that the benefit of this resource can be maximised. Used with forethought and care, the ability to give transfusions is a great addition to the veterinary therapeutic armoury and with the progression of blood banking in the UK, easily within the realms of possibility for all small animal practitioners.

Banked canine PRBC are readily available in the UK and this article primarily covers PRBC transfusion in the dog. However, the general principles of transfusion medicine apply to all of our companion animal species and many exotic species. For specific species, Pet Blood Bank UK (PBB) can guide you on blood collection and banking advice or refer you to an external advisor who has experience with that species.

Red cell products

Red cell products available in the UK are Canine Packed Red Blood Cells (PRBC), Fresh Whole Blood (collected and administered within 4-6 hours) and Stored Whole Blood. Fresh Whole Blood has the advantage of containing platelets but the number and function decline 4-6 hours after collection. Stored Whole Blood is uncommonly used, as platelet numbers and levels of Von Willebrand factor (vWF) and coagulation factors I (Fibrinogen), V and VIII decline quickly. Stored Whole Blood has a shelf life of 21-28 days depending on the anticoagulant used. If blood is to be stored, then separating the plasma and freezing it as Fresh Frozen Plasma (FFP) (Figure 1), and then resuspension of the

Figure 1: PRBC and Fresh Frozen Plasma (FFP)

red cells in a nutrient solution (SAG-M) allows the most efficient use of the whole unit of blood. This extends PRBC shelf life to 42 days and plasma products have a frozen shelf life of up to five years.

Table 1 illustrates the utility of the PRBC versus whole blood, and Table 2, specific differences in their content. If plasma is frozen within 24 hours of collection of the whole blood unit, Fresh Frozen Plasma (FFP) is produced, the use of which is outside the scope of this article but is discussed in more detail in Kit Sturgess's article on fresh frozen plasma (Sturgess 2014).

Indications for red cell transfusions

Patients with a wide variety of conditions causing symptomatic anaemia will benefit from red cell transfusions alongside treatment of their underlying condition. If a diagnosis has not been reached, transfusion can enable further diagnostic tests to be performed safely. Put simply, red cell transfusions are indicated for any patient developing clinical signs of low tissue oxygenation due to anaemia, which usually manifests as weakness and lethargy, pale mucous membranes, tachycardia and tachypnoea on examination. The speed at which the anaemia develops will also impact on the need for transfusion. If red cell numbers fall slowly, for example a chronic anaemia secondary to bone marrow disease, then adaptive mechanisms such as increased 2,3-diphosphoglycerate improve the efficiency of oxygen carriage leading to a delay in the development of clinical signs. Conversely if red cell numbers fall quickly, for example blood loss secondary to a road traffic accident, there is no time for adaptation and the clinical need for transfusion may occur with relatively modest blood loss.

The causes of anaemia are wide ranging but can be broadly defined into three aetiological groups:

- Loss of red cells (e.g. haemorrhage)
- Destruction of red cells (e.g. immune mediated disease)
- Failure of production of red cells (e.g. bone marrow disease)

When to transfuse

A precise trigger point or 'magic number' in terms of red cell number, haemoglobin content or Packed Cell Volume (PCV) for when to transfuse a specific patient cannot be given. Each and every individual patient, their clinical presentation and diagnosis has to be considered before making a decision whether to transfuse or not.

Table 1: The indications for using whole blood and packed red blood cells

Disease Process	Whole Blood	Packed Red Blood Cells
Regenerative anaemia	◆	★
Non regenerative anaemia	◆	★
Pancytopenia	Fresh	
Anaemia with hypoproteinaemia	◆	★
Anaemia with hypovolemia	◆	★
Anaemia with coagulopathy	◆	★
DIC	◆	◆
Liver disease with anaemia	◆	◆
Thrombocytopenia	Fresh	
Thrombocytopathia	Fresh	
Neonatal isoerythrolysis		★

◆ Indicates suitable blood products that can be utilised in treating the disease process.
★ Designates the superior product choice when more than one suitable product can be utilized.
(Courtesy of Dr Anne Hale).

In human medicine, detectable changes in tissues at the cellular level start to occur secondary to reduced oxygenation at a PCV of 30% or less and the same is likely true in our patients. On a clinical level in animals (especially with chronic anaemias), clinical signs are not often seen until PCV drops to a much lower value. Symptomatic anaemias typically present as a weak, tachypnoeic, tachycardic patient with altered mucous membrane colour. Pale mucous membranes are consistent with anaemia, but can also be seen in severe shock. Icteric mucous membranes can be seen in animals with pre-hepatic jaundice secondary to red cell destruction.

In acute instances, transfusion should be considered where whole blood loss is demonstrated to be the cause of clinical symptoms. This should be regardless of the red cell numbers as the PCV recorded may reflect total blood loss without an adjustment in blood volume to allow the PCV to drop. Chronic anaemias in canines are usually relatively well compensated and tend only to cause significant symptoms once PCV drops to less than 20% and occasionally much lower values.

The purpose of a red cell transfusion in companion animals would be to alleviate clinical signs but not to remove stimulus for the patient's own red cell production (if this capacity still exists in the recipient). As a rough guide, in canines capable of regeneration, transfusion to a stable end point of 25-30% PCV would be suggested. In those incapable of regeneration, aiming for mid-range of normal PCV (35%-55%) may be beneficial.

The average lifespan of a canine red cell is usually stated as 120 days. Cellular life expectancy may be reduced due to the collection and storage process, although a consensus as to what degree this impact is has not been reached. The red cells in each unit of transfused blood will be of variable age and as a result the effect of a transfusion will wane over time. Response to transfusion is also dependant on the host response to the red cells and the underlying disease process.

Diagnostic tests

Diagnostic tests useful for the evaluation of anaemic patients include:

Packed Cell Volume (PCV) and Total Solids (TS)

PCV should be measured using a percentage reader and TS should be measured

using a refractometer (this is using the serum protein {SP} gauge which measures in g/L rather than the urine specific gravity scale). At the time of spinning PCV tubes, gross assessment of the serum for hyperbilirubinaemia (yellow) or haemoglobinaemia (pink/red) is also helpful.

Blood Smears

In practice, these can be stained with a Romanowsky stain, such as Diffquick®, and are used to assess red cell morphology, number and regeneration, platelet number, white cell morphology and for the presence of red cell parasites, such as *Babesia canis*.

Slide Agglutination Tests

A drop of blood on a slide and a drop of 0.9% saline mixed together, can be used to visually assess for auto-agglutination in suspected Immune Mediated Haemolytic Anaemia (IMHA). Examination under a microscope will help differentiate:

- Agglutination – red cells attached to each other due to the presence of antibody on the cell surface (Figure 2)
- Rouleaux – which is the normal physiological stacking of red cells (Figure 3)

The presence of rouleaux will disperse if additional saline is added, whereas agglutination will not. Note: This MUST be performed with equipment and samples at room or body temperature.

Coagulation Times

In emergency situations, a rough assessment of global coagulation can be performed by assessing the whole blood clotting time (WBCT). Blood is collected into a plain glass tube and gently rocked within the closed hand of the investigator and regularly assessed for the formation of a clot. Although a relatively crude test, a clot should form within six minutes.

An activated clotting time (ACT) tube uses diatomaceous earth within the tube as an activator, which speeds up the process, with times of 60-110 seconds being normal for canines. Both WBCT and ACT will be prolonged in animals with marked thrombocytopenia (platelet counts $<10x10^9$/l or <1 platelet per high power field on smear analysis).

Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) are now available as patient side tests. These are more accurate and specifically evaluate secondary coagulation. If in house analysis is not available, freezing separated plasma collected into a citrate tube will allow analysis at a later stage.

Table 2: The different make up of whole blood and packed red cell products, indications for use and rates of administration

Component	Whole Blood (Fresh)	Packed Red Blood Cells (PRBC)
Storage instructions and shelf life	• Collected in CPD or CPDA 1 • Must be transfused within 4-6 hours to have any viable platelets and all coagulation factors • 1 unit average volume = 450ml • Average PCV 45% unless measured	• In SAG-M nutrient solution • 2-6°C. 42 days in SAG-M • 1 unit average volume = 250ml • Average PCV 62% unless measured
Indications for use	• Symptomatic anaemia (blood loss) • Platelet deficiency: Fresh Whole Blood is unlikely to have a significant effect on platelet numbers in a severely thrombocytopaenic patient • **GUIDELINE:** 10ml/kg of fresh whole blood raises the PLT count by 10 x 10^9/l	• Symptomatic anaemia in presence of normovolaemia without clotting factor deficits
Action	• Restores O_2 carrying capacity and blood volume, if used promptly post collection • Supplies all coagulation factors and some viable platelets	• Restores O_2 carrying capacity
Not indicated for	• Pharmaceutically treatable anaemias (i.e. those that will respond to specific non-transfusion therapy) because of risks associated with transfusions	• Pharmaceutically treatable anaemias (i.e. those that will respond to specific non-transfusion therapy) because of risks associated with transfusions • Clotting factor and platelet deficits
Hazards	• Infectious disease transmission • Immunologic transfusion reactions (e.g. incompatibility and allergic) • Non-immunologic transfusion reactions (e.g septic, toxic and circulatory overload)	• Infectious disease transmission • Immunologic transfusion reactions (e.g. incompatibility and allergic) • Non-immunologic transfusion reactions e.g septic, toxic and circulatory overload • Ammonia levels can increase in stored red cell products. These should be used with caution in dogs with known liver disease
Rate of infusion *Use an in line blood filter with all products (170-260 microns)*	• To calculated dose, to complete transfusion in < 4 hours • According to patients' fluid status. If hypovolaemic at rates up to shock doses (as fast as blood is being lost), if normovolaemic 5-10ml/kg/hr • If compromised circulation (cardiovascular compromise/renal failure) 1-2ml/kg/hr	• To calculated dose to complete transfusion < 4 hours • According to patients' fluid status. If hypovolaemic at rates up to shock doses (as fast as blood is being lost), if normovolaemic 5-10ml/kg/hr • As PRBC are a lower total volume, they can be given at slightly higher rates if indicated

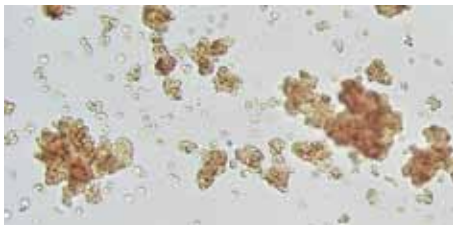

Figure 2: Red cell agglutination, which confirms an incompatible crossmatch (Courtesy of Paola Monti, DWR diagnostics).

Figure 3: Rouleaux formation which is normal physiologically and will disperse with the addition of further saline and gentle agitation of the slide (Courtesy of Paola Monti, DWR diagnostics).

Buccal mucosal bleeding time

This is a simple test used to assess primary haemostasis (platelet function) where platelet numbers are adequate on a smear and clotting times (when measurement is possible) are normal. It should NOT be performed in a confirmed thrombocytopaenia or when coagulation times are prolonged. The time for the bleeding to stop should be 2-4 minutes but may be slightly longer in sedated animals.

A prolonged buccal mucosal bleeding time (BMBT) in this circumstance suggests a thrombocytopathia or Von Willebrand factor deficiency (Von Willebrand factor analysis can be submitted at this stage for confirmation).

Specific tests prior to transfusion

Canine blood typing and Dog Erythrocyte Antigen 1 (DEA 1)

It is no longer appropriate to assume that a patient is likely to only receive one transfusion in their lifetime, or to believe what has previously been quoted that in canines "the first transfusion is free". Incompatibility reactions in canines to first time transfusion are rare, however, if DEA 1 blood type is not known and recorded at the time of the first transfusion, and a subsequent transfusion occurs later on in the animals life - severe and avoidable reactions can occur.

Blood typing is recommended for all donors and recipients as best practice and helps to make the most of the transfusion products available to us. The only blood typing test currently widely available for canines is the test for Dog Erythrocyte Antigen (DEA) 1.

Benchtop methods for DEA 1 typing include agglutination cards and monoclonal antibody impregnated quick tests. These tests are simple to use and allow us to make decisions about which products to use [www.alvedia.com/assets/procedure-quick-test.pdf].

The important concept to note is that a universal canine donation type does not exist. DEA 1 negative donors have been incorrectly termed as "universal donor" in the past and this is a misconception. There have been over 13 canine red cell surface antigens proposed internationally and some identified (Hale 1995). Amongst these red cell antigens, there are some that are also capable of causing reactions and this needs to be considered.

Figure 4: (4a) A buccal mucosal bleeding time is performed using a spring loaded mechanical cutting device such as the Simplate or Surgicutt devices. (4b) the upper lip is folded up and tied to create mild congestion of the oral mucosa. (4c) the device is used to make a standard cut and the wound allowed to bleed. (4d) The wound must not be disturbed but can be blotted from around a 1cm away using the blotting paper and the time for bleeding to stop is recorded. Images courtesy: Amanda Boag Vets Now Emergency Ltd.

Historically DEA 1 was considered to have 3 subgroups and the terminology DEA 1.1, 1.2 and 1.3 was used. With the development of monoclonal antibody and immunofluorescence testing, it has been found that DEA 1.2 and 1.3 are actually red cell populations with a lower density of the DEA 1 antigen on their surface. Testing allows for detection of low level DEA 1 which means an individual canine patient is now only either DEA 1 postive or negative (Acierno *et al.* 2014).

Tests for DEA 1 antigen were developed as DEA 1 was identified as a significant factor involved in causing severe reactions to second transfusions.

DEA 1 is absent in 30-60% of the UK canine population (Barnett *et al.* 2013). Transfusion with untyped blood leads to a reasonable risk of transfusing a DEA 1 negative canine with DEA 1 positive blood and sensitising it to future transfusions.

Sensitisation (alloimmunisation) is when a DEA 1 negative patient is transfused with DEA 1 positive blood. In this scenario the recipient will produce anti-DEA 1 antibodies within a few days of transfusion (4-7 days) and this recipient will remain permanently sensitised to the DEA 1 antigen. If a subsequent transfusion is given at a later date containing DEA 1 positive red cells, an acute reaction will occur. This will involve the production of antigen antibody complexes that shows as an acute type II hypersensitivity reaction, involving agglutination and haemolysis of the donor red cells in the recipient's circulation. This can be a fatal reaction and will, at the very least, negate any benefit of the red cells administered in an already compromised patient. Alloimmunisation is considered to be lifelong in the canine species - so these reactions occur at any time in that patient's life in the case of subsequent incompatible blood administration.

Conversely 40-70% of the canine population are DEA 1 positive. It is completely appropriate to transfuse them with DEA 1 positive PRBC. Knowing the blood type of a canine patient helps reduce the risk of transfusion reactions, but also optimises the use of blood bank resources.

In an acute instance for a first time red cell transfusion when recipient typing is not available for a genuine reason; DEA 1 negative product should be used.

Other canine blood types

Sensitisation can occur to some of the other red cell antigen types also (e.g. DEA 4,7, Kai and Dal) but the reactions associated are either very rare due to low incidence of canines negative for common antigen (DEA 4 and Dal) or can be less acute or severe than those seen with DEA 1 incompatibility (Euler *et al.* 2016). However they may be significant to the overall transfusion picture both around the time of the transfusion and in the weeks following. As canine transfusion medicine develops, more extensive typing may become available, which will, in turn, expand our understanding and help reduce the incidence of incompatibility reactions.

Cross matching

Two common misconceptions that arise are that if both donor and recipient are typed for DEA 1, cross matching is not required, or that typing is the same as cross matching. The lack of comprehensive knowledge of canine blood types and the inability to type beyond DEA 1 means that cross matching is necessary to detect other serious antibody led incompatibilities.

Cross matching is an *in vitro* test mixing donor and recipient components (blood or plasma) to look for potential reactions. Cross matching test result assessment involves looking for agglutination or haemolysis reactions. This test looks for those reactions that could cause severe complications. It is best practice to both type and cross match for any transfusion. However, for second and subsequent transfusion in canines, it is mandatory at any time greater than 4-7 days post the initial transfusion. This is the time it takes for a recipient to produce alloantibody, i.e. antibody against foreign red cell antigens.

Major and minor cross matching is the terminology used depending on whether recipient red cells or plasma are being tested for incompatibility against the donor red cells or plasma. Major cross match tests donor red cells against recipient plasma. Minor cross match tests recipient red cells against donor plasma. Choice of which to run depends on the component being administered and the individual case. In red cell transfusions, the major cross match is the most important to assess.

Blood banks will normally offer a cross match service via an external or internal laboratory to allow assessment for compatibility against multiple donors. On reading the cross match – a suitable

Figure 5*:* Heat sealed aliquots of blood and of red cells allowing crossmatches to be performed without broaching bags of stored packed red cells.

compatible red cell unit is supplied for transfusion by the blood bank. Recipient samples required would normally be 1ml of whole blood in EDTA and 2ml separated serum (4 serum gel tubes) if multiple cross matches are to be run.

Finding a compatible unit requires multiple cross matches as 30% cross match incompatibility has been reported in canines receiving subsequent transfusions even if DEA 1 type matched transfusions have been administered previously (Ferreira *et al.* 2014).

Cross matching should be performed without breaching any stored blood product. With fresh whole blood, donors samples can be collected and submitted before the unit is taken. With stored products blood banks normally supply heat sealed citrated aliquots that are attached to the blood units and can be torn off to submit for cross match (Figure 5). Packed cell or whole blood aliquots can be used by laboratories for the purpose of a major cross match. Plasma aliquots can be used for the minor cross match.

Traditional in-house or benchtop cross matching using slides is a time consuming procedure, although simple enough to perform. Assessing the results can be difficult if it is not a procedure commonly performed by the practitioner. There are now gel tests that act as an in-house test and these are a lot simpler to both perform and read. These tests assess for agglutination and are extremely useful for emergency cross matching in critical cases when external lab cross matching is simply not an option due to the time it would take to receive results. The basis of the test is that the gel matrix will not allow the passage of agglutinated (clumped) red cells during light centrifugation in a normal lab centrifuge. Hence, in a positive cross match where an agglutination reaction occurs, red cells will remain at the top of, or in the top part of the gel column. In a negative cross match, non-agglutinated red cells pass straight through the gel and rest at the bottom of the tube.

Consent for transfusion

When dealing with a patient requiring a transfusion, it must be remembered that these are complex biological products with many components and no absolute guarantee can be made about their safety. As a result, consent for their administration should be obtained, where possible, in writing.

Suggested wording that could be included on a consent form for transfusion product administration would be:

I consent to the administration of whole blood/ blood components to my pet. I accept that there is a risk of reactions to blood/blood components and that rarely these can be life threatening.

WARNING. In spite of serological testing, the risk of transmitting infectious agents to the patient is present. Careful donor selection, care, and available laboratory tests do not eliminate the hazard. Also, septic and toxic reactions can result from transfusion of bacterially contaminated blood and components. Such reactions are rare, but may be life threatening.

In addition, blood components may contain immunizing substances that can cause reactions even in typed and cross matched transfusions.

Dose calculations for red cell transfusion

Initial doses of red cells are usually calculated to an amount in mls, but then adjusted on the basis of whether a full whole or half unit of PRBC should be administered. The aim is to maximise the benefit of the transfusion and make best use of the resource (Short *et al.* 2012). The following equation is used to calculate dose of red cells but the patient's individual response should be monitored closely and therapy adjusted according to response:

$$\text{Blood volume to be transfused (mls)} = k \times \text{Weight (Kg)} \times \frac{\text{(required PCV-Recipient PCV)}}{\text{PCV of red cell product}}$$

k is a constant = 70 for canines and 60 for felines

Average PCV of packed cells in nutrient solution (SAG-M) unless measured is 62%

Alternative dose calculations in a more urgent situation can be used in order to decide a baseline volume in units to transfuse. These are:

To raise the PCV by 1% takes 1 ml/kg of packed red cells or 2ml/kg whole blood. This also equates to a general dose rate of 10ml/kg of PRBC's being expected to raise the PCV by around 10% (5% using whole blood) in an anaemic but normovolaemic patient.

These guidelines can be utilised as a starting dose rate and then adjusted according to required response.

In practice storage

Practices that have a high transfusion caseload (more than one case every six weeks) can order and store PRBC on their premises. A separate blood fridge should be used for PRBC to ensure no regular traffic in and out of the fridge causing fluctuations in temperature. A domestic fridge is a reasonable option; however a specially designed laboratory or blood fridge will allow more accurate temperature regulation. Although tempting, the blood fridge should not be used to store other things such as drugs, food (for staff or patients) and laboratory samples as the storage bags are permeable to allow gaseous exchange for optimum red cell storage. Red cells should be stored only in the labelled blood collection bag they are supplied in and any additional packaging or protection should be removed prior to storage to allow air to circulate around the bag.

The temperature within the storage fridge should be monitored with a maximum/minimum thermometer to ensure that red cell units remain between 2-6°C. The thermometer should be checked daily to ensure product is maintained at an appropriate temperature. Red cell units should be inspected and agitated gently every few days to ensure an even mix of the red cells with the nutrient solution in which they are stored.

Figure 6: A unit of packed red cells alongside the fridge's temperature probe to ensure correct storage.

What about platelets?

Primary haemostasis involves the activation of platelets and their adhesion to an initial site of injury. Clinically - primary coagulopathies arise when this process does not happen, this leads to petechial haemorrhage, ecchymosis and overt bleeding. Problems with primary haemostasis occur due to inadequate platelet numbers (thrombocytopenia), a lack of platelet activation (thrombocytopathia) – this can be genetic or secondary to drug therapy such as aspirin), or due to Von Willebrand Factor (vWF) deficiency (vWF deficiency leads to to an inability of platelets to adhere to the site of injury).

The only available product in the UK (at this time) that provides any level of viable platelets is Fresh Whole Blood (transfused within 4-6 hours of collection). Each unit only provides the normal amount of platelets in 450ml of the donor canine's

circulation and is dependant on skilled collection technique. In a deficient canine patient, this number is not likely to make any significant impact in platelet number in the recipient. However it may provide enough platelets to stop bleeding at a critical site (for example in the central nervous system) limiting the progression of symptoms. As a rough guide it is considered that 10ml/kg whole blood, which is expected to raise the PCV by 5%, will raise the platelet count by $10x10^9/l$.

In the USA canine blood banking industry, they have the market for, and are able to produce, concentrated forms of platelet products similar to those available in human medicine. Platelet Rich Plasma (PRP) is a concentrated version of platelets from one unit of blood. Even more concentrated PRP containing higher levels of platelets can be harvested using the process plasmapheresis. These sensitive products can only be stored at room temperature, under constant agitation and are known to have a high incidence of potential for bacterial contamination due to their special storage requirements. These could be processed in the UK but demand is currently not high enough to support them as a commercial product.

Veterinary surgeons in the USA have access to frozen and Dimeythylsulfoxide (DMSO) preserved platelet concentrates and experimental work to produce a lyophilised (freeze dried) product is ongoing. For specific cases, such as chemotherapy patients with thrombocytopenias or severely affected immune mediated thrombocytopenias, these products could theoretically be obtained from the USA via a Veterinary Medicines Directorate Special Treatment Certificate in the absence of any more suitable UK licenced product. However, canine studies into their efficacy are currently limited (Callan *et al.* 2009).

Preparation of product for administration

Blood products need to be prepared carefully for use and once breached have a very limited lifespan due to the risk of bacterial contamination. The recommendation from human medicine is red cells should be transfused within 4 hours of breach.

Recipients are often critically ill, and therefore administering products at room temperature is recommended. In most instances, refrigerated red cells will warm when passing down a giving set at room temperature. If warming is necessary, this can be achieved by placing the red cell unit in a waterproof zip lock bag to prevent contamination of the ports, and placing this in a commercial water bath of <37°C. A max/min thermometer should be used to monitor the water temperature of warm water in a bowl/sterile litter tray if a water bath is unavailable. Gentle and slow warming of products is sensible if time allows, as red cell viability can be reduced if they are exposed to sudden changes in temperature.

Routes for transfusion

The recipient should be prepared with a central or peripheral intravenous catheter using aseptic technique. The largest gauge catheter suitable for the patient's size and vasculature should be placed. In very moribund patients if intravenous access is not possible, then the intra osseous route can also be utilised as an effective and rapid method of administration.

The catheter should be flushed with normal 0.9% saline and a T-port or sterile cap placed. All blood products should be administered via a filtered giving set to reduce the risk of microthrombi and given to a calculated dose. Pre, during and post transfusion the patient should be monitored closely.

Transfusions should not be administered through the same intravenous catheter as any solutions containing calcium (such as lactated Ringers or Hartmann's solution) due to the risk of calcium chelation and the formation of particulate matter, or administered alongside glucose due to the potential for osmotic damage to the red cells. Normal 0.9% saline can be used to flush giving sets or bags of remaining red cells or to administer concurrent crystalloid requirement.

In the past, PRBC's required resuspension with 0.9%NaCl as their PCV was so high that they could not be infused alone. However, PRBC products today typically have a red cell extender (the SAG-M nutrient solution) added so this is less of a problem and resuspension with saline is rarely necessary.

Rate of transfusion

In stable patients, an initial infusion rate of 0.5-1.0 ml/kg/hr should be used for the first 15-30 minutes. During this time, the patient should be monitored for any evidence of a transfusion reaction. As long as no problems are identified, the rest of the unit should be delivered over 4 hours. The easiest way to calculate this rate is to estimate the remaining volume left in the bag and divide that by 4 for the hourly rate. In an emergency (e.g. severe acute haemorrhage), red cells can be given as fast as necessary.

Due to the nature of the recipient's problems, the calculated dose of product may need to be given more slowly e.g. in an animal with compromised circulation, such as heart failure. However, meticulous sterility and hygiene must be maintained when handling the products. In most instances, it is perfectly possible to administer transfusions within the optimum timescale. In a normovolaemic animal, a maximum transfusion rate of 20ml/kg/hr is suggested.

Monitoring

Monitoring of transfusion patients should be given thought and attention. Constant monitoring is advisable over the initial 30 minutes of a transfusion. After that, if no concerns have arisen and continuous monitoring is not possible, regular checks (i.e. every 15-30 minutes) are appropriate. A monitoring chart is essential as trends are important - an example can be found on PBB's website (https://www.petbloodbankuk.org/media/1184/frmsis0502-transfusion-record.pdf). In anaemic patients heart and respiratory rate will slow during the transfusion as oxygen carriage improves; any sudden or unexpected increase in temperature, heart or respiratory rate should prompt that a transfusion reaction is imminent. A multiparameter monitor recording ECG, blood pressure and temperature can be very useful to aid the member of staff who is monitoring the recipient. However, hands on monitoring of temperature, heart rate and respiratory rate is perfectly adequate in the absence of this equipment.

Infusion pumps and syringe drivers

It is recommended that red cell products are transfused by gravity alone to both canine and feline patients as a recent publication raised a concern that the longevity of red cells transfused by both syringe driver and infusion pump may be reduced compared to transfusion using gravity alone (McDevitt *et al.* 2011). In human medicine however, validated peristaltic type infusion pumps and syringe drivers are used to administer transfusions.

Transfusion reactions

Types of transfusion reaction are summarised in Table 3. Clinically, they present as an increase in temperature, a change in the respiratory and heart rate, change in mucous membrane colour, visible oedema or as gastro-intestinal signs such as vomiting. If any reaction occurs then the transfusion should be stopped to allow assessment of the patient. If the reaction is mild, then slowing the rate of transfusion may be enough to reduce the signs. If reactions are severe, the transfusion should be stopped until the reaction is categorised and a decision made whether drug treatment is necessary or whether restart is appropriate. If not, the transfusion may need to be abandoned. If a severe anaphylactic hypersensitivity (type I) reaction is suspected intravenous antihistamine and/or corticosteroids may be appropriate.

Older red cells have in some studies been associated with an increase in incidence of transfusion reactions and morbidity in canine patients – so the age of the red cells should also be taken into account when administering transfusions.

Summary

Blood transfusions can be lifesaving in a number of clinical situations. Used prudently, with forethought and adequate preparation, the risks associated can be minimized. The availability of Pet Blood Bank products in the UK has opened up many therapeutic options that have enabled many disease processes, trauma cases, anaesthetics and surgical procedures to be carried out with far more positive outcomes.

Table 3: Possible transfusion reactions, causes and clinical presentations. Comparative human information is also included

Transfusion reaction	Pathogenesis	Clinical presentation
Transfusion associated circulatory overload	Rapid or excess volume delivery in a susceptible patient (e.g.small patient, cardiac abnormality, delicate haemo-dynamic status, renal failure)	Within 6 hours of end of transfusion Cough Tachypnoea Tachycardia Signs of volume overload: - jugular venous distension - nasal fluid - Pulmonary oedema
Acute haemolytic transfusion reaction	Known DEA incompatibility Unknown DEA incompatibility Other RBC antigen incompatibilities (for eg Kai, Dal)	Fever Hypotension Haemoglobinaemia/uria
Sepsis	Bacterial contamination in blood product enters recipient Result in bacteraemia and immune reaction	Fever Vomiting Tachycardia, tachypnoea
Delayed haemolytic transfusion reaction	Allo-immunization to other unknown antigens.	Fever Lethargy Unexpected anaemia, usually within first two weeks after transfusion
Febrile non-haemolytic transfusion reaction	Humoral and cellular-mediated inflammatory reaction	Onset 1-2 hours after transfusion Fever Nausea/ vomiting Increase in BP
Allergic transfusion reaction	Inflammatory reaction resulting in release of histamine by mast cells	Urticarial rash Pruritus Nausea, vomiting Diarrhoea, abdominal pain Hypotension (less common) Dyspnoea (less common)
Anaphylactic transfusion reaction	Severe allergic reaction against transfused blood	Immediate respiratory distress (seconds to minutes) Upper airway oedema obstruction Lower airway signs and symptoms – tachypnoea, increased chest noise Depressed mentation Vomiting Hypotension, weak pulses and ultimately circulatory collapse
Transfusion related Acute lung injury (N.B This has yet to be formally recognised in veterinary patients – it is NOT known as yet if it occurs)	IN HUMANS : Leukocyte antibodies in the donor blood react with recipient leucocytes, primarily causing lung injury Associated with higher concentrations of plasma, e.g: fresh frozen plasma	Within 2 to 6 hours of start of transfusion Coughing Tachypnoea, hypoxaemia Tachycardia Fever

Step by Step - Administration of Red Cell Products

Equipment Required:

- Unit of red cells
- Zip lock bag
- Clean bowl/tray to act as a water bath to warm the product
- Thermometer
- Filtered giving set
- IV catheter – largest gauge possible for the patient

Figure 7: Red cells are placed in a protective water-proof zip lock bag and are warmed to room or body temperature in a water bath of no more than 37°C.

Figure 8: PRBC's should be removed from the protective bag and one of the administration ports on the red cell bag should be accessed by tearing the protective cover.

Figure 9a, b and c: A filtered giving set is removed from its outer packaging and prepared for use by closing off the in-line C clamp and the drip wheel. Note the chamber drip rate at this time (a standard filtered giving set will usually be 20 drops/ml).

Figure 10: The insertion spike is unsheathed in an aseptic manner.

Figure 11: Firmly push the insertion spike into the bag of red cells via the port.

Figure 12: The insertion spike has now breached into the bag of red cells, this bag of red cells must be used within 4 hours.

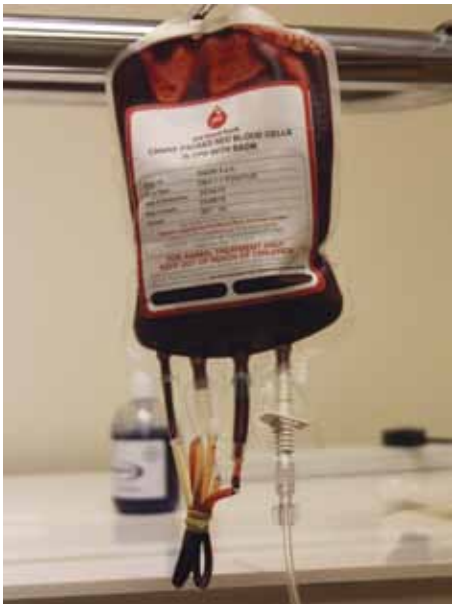

Figure 13: Hang the bag of red cells from a drip stand in order to prime it ready for use.

Figure 14: The in-line clamp should be released and the drip wheel slowly released to allow the blood to flow into the administration set.

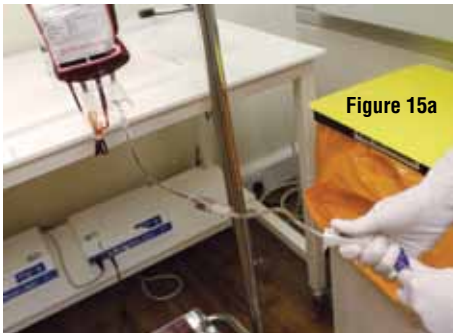

Figure 15 a and b: The filtered drip chamber should be filled to above the filter but not so full that the drip rate cannot be seen.

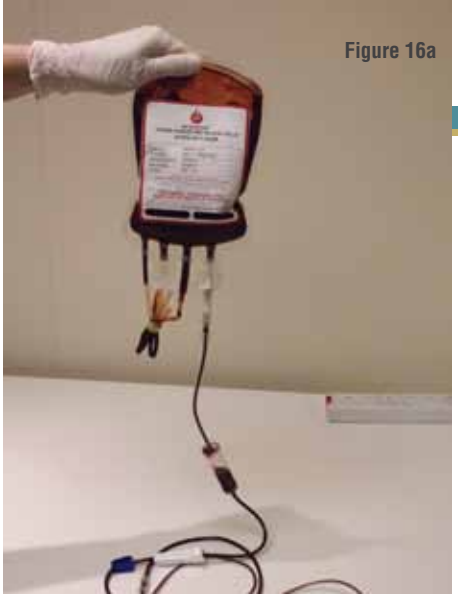
Figure 16a


Figure 16b

Figure 16 a and b: The tubing is fully primed with no air remaining and at this point the end of the giving set can be uncapped and attached to the patient's catheter in a sterile manner. The transfusion can be initiated.


Figure 17a


Figure 17b

Figure 17 a and b: All blood products should be administered through a microaggregate filter (normally 170-260 micron) to facilitate removal of any small clots and other debris that may be present These filters may be present within the lines of blood giving sets as in Figure 18 (a) or may be attached separately as an in line filter (such as Hemo-Nate filters) Fig 17 (b), if using a syringe for the transfusion. This is more common in cats and small canine patients.

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1) A Jack Russell Terrier weighing 10kg has a chronic anaemia associated with renal failure – he has a Packed cell volume (PCV) of 10%. You would like to raise his PCV to 30%. What would you order from Pet Blood Bank UK?

A) Half a unit of packed red cells
B) One unit of packed red cells
C) Two units of packed red cells
D) One unit of fresh whole blood

2) Which of the following statements is false?

A) Red cells should be stored in a refrigerator at 2-6 °C
B) Red cells can be stored in the middle shelf of the practice lab fridge used for insulin and vaccines
C) Red cells should be gently inverted every few days to mix them with the nutrient solution they are stored in
D) Packed red cell units do not contain viable platelets

3) Which of the following statements is true?

A) First transfusions in dogs are "free"
B) DEA 1 –ve donors are universal
C) Blood typing is the same as cross matching so if you know the blood type of the dog you do not need to cross match
D) Cross matching is necessary before a further transfusion in an anaemic 12 year old dog that received a DEA 1 type matched transfusion when he was six weeks old

4) Which of the following statements are true?

A) In saline agglutination tests should be run using refrigerated EDTA blood samples
B) Total protein can be estimated using a refractometer and the serum out of a Heamatocrit tube
C) Blood smears can be stained for in practice red cell examination using diff quick
D) Buccal mucosal bleeding time should be used to diagnose thrombocytopenia

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