REVIEW ARTICLE

Veterinary Anaesthesia and Analgesia, 2014, 41, 233-242

Canine and feline blood transfusions: controversies and recent advances in administration practices

Caroline Kisielewicz & Ian A Self

Queen Mother Hospital for Animals, Royal Veterinary College, Hatfield, Hertfordshire, UK

Correspondence: Caroline Kisielewicz, Queen Mother Hospital for Animals, Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire AL9 7TA, UK. E-mail: carkis13@yahoo.com

Abstract

Objectives To discuss and review blood transfusion practices in dogs and cats including collection and storage of blood and administration of products. To report new developments, controversial practices, less conventional blood product administration techniques and where applicable, describe the relevance to anaesthetists and anaesthesia.

Databases used PubMed and Google Scholar using dog, cat, blood transfusion, packed red blood cells and whole blood as keywords.

Conclusions Blood transfusions improve oxygen carrying capacity and the clinical signs of anaemia. However there are numerous potential risks and complications possible with transfusions, which may outweigh their benefits. Storage of blood products has improved considerably over time but whilst extended storage times may improve their availability, a phenomenon known as the storage lesion has been identified which affects erythrocyte viability and survival. Leukoreduction involves removing leukocytes and platelets thereby preventing their release of cytokines and bioactive compounds which also contribute to storage lesions and certain transfusion reactions. Newer transfusion techniques are being explored such as cell salvage in surgical patients and subsequent autologous transfusion. Xenotransfusions, using blood and blood products between different species, provide an alternative to conventional blood products.

Keywords autologous transfusion, cell salvage, leukoreduction, storage lesion, transfusion relevance to anaesthesia, xenotransfusion.

Introduction

The first report of a successful blood transfusion in animals was by Richard Lower in 1665 whereby blood was withdrawn from one dog and replaced with blood from another dog (Lower 1665). Despite early experiments, small animal blood transfusions have only become common over the last 30– 60 years (Davidow 2013).

Transfusion aims to replace the missing component of blood and, in the case of anaemia, haemorrhage, haemolysis or ineffective erythropoiesis, to increase oxygen carrying capacity. Blood products are more readily available, due to on-going improvements in processing and storage, and transfusion practices are evolving. However, there are still numerous controversies regarding blood product storage and administration; for instance the ideal duration of storage to minimise storage lesions and the least traumatic method of blood administration to minimise erythrocyte haemolysis (McDevitt et al. 2011; Solomon et al. 2013). There is increasing interest in less conventional blood transfusion techniques which circumvent blood storage considerations, such as cell salvage with autologous transfusion and xenotransfusion, as alternatives to more traditional blood transfusion methods.

This review presents recent research, as identified in PubMed and Google Scholar databases, in veterinary transfusion medicine and where applicable, the particular relevance to anaesthesia, involving packed red blood cells (pRBC) and whole blood (WB), and details some of the controversial aspects of blood transfusion. Where veterinary literature is sparse, human studies are reported. Discussion of either plasma or platelet transfusions in veterinary patients is beyond the scope of this review.

Blood products

Whole blood is withdrawn from a donor animal and transferred to a bag or syringe containing citratephosphate-dextrose (CPD), citrate-phosphate-dextrose-adenine (CPDA-1) or, acid-citrate-dextrose (ACD); citrate-phosphate is the anticoagulant and dextrose and adenine provide nutrients for the cells (Wardrop et al. 1994a). Fresh WB is transfused within 4-6 hours following collection; it contains red blood cells (RBC), platelets, leukocytes and plasma proteins including clotting factors. It is used primarily for managing acute, severe haemorrhage from trauma, surgery or coagulopathies (Prittie 2003). After 6-8 hours, the product becomes stored WB, contains RBC and plasma and has a shelf life of 21-28 days. It no longer provides viable platelets, leukocytes or labile clotting factors (fibrinogen, factor VIII, von-Willebrand's factor).

Blood components can be separated by centrifugation immediately after collection, removing supernatant plasma to produce pRBC containing RBC, leukocytes, platelets, remnant plasma and anticoagulant; this is predominantly used for managing haemolysis and non-regenerative anaemia. Nutrient solutions, sodium chloride-adenine-glucose-mannitol (SAG-M), extend storage times to 35–42 days whilst preserving RBC (Wardrop et al. 1994a,b, 1997; Hess 2006).

The withdrawn plasma contains plasma proteins, labile and non-labile clotting factors, and is frozen for use within a year as fresh frozen plasma, for managing clotting factor or plasma protein deficiencies, disseminated intravascular coagulation and severe necrotising pancreatitis (Davidow 2013). After 1 year of storage, the product becomes known as frozen plasma and can be stored a further 4 years. It has previously been thought that labile clotting factors are not reliably functional after 1 year however a recent study identified that although the activities of factors VIII and X were lower in frozen plasma after 5 years of storage compared to fresh frozen plasma stored for 1 year, the product remained haemostatically active based on thromboelastography findings (Urban et al. 2013).

Cats typically receive fresh or stored WB, as small blood donation volume complicates component separation; blood-banking allows the storage of the different canine blood product components.

Stored blood and storage lesions

The morphologic changes, metabolic derangements and oxidative injuries that occur with storage, which detrimentally affect RBC viability and function, and ultimately contribute to their decreased survival following transfusion are known as storage lesions (Donadee et al. 2011; Pavenski et al. 2012); these are recognised in the human field but veterinary literature is limited.

The pH of stored blood progressively decreases with lactic and pyruvic acid accumulation, promoting 2,3 diphosphoglycerate (2,3-DPG) reduction by 54% within the first 24 hours of storage in canine RBC (Price et al. 1988) to undetectable levels within 2 weeks of human pRBC storage (Raat & Ince 2007). Low 2,3-DPG increases haemoglobin oxygen affinity, thereby reducing oxygen unloading following transfusion, possibly affecting tissue oxygenation and patient morbidity and mortality (Raat & Ince 2007). Levels return to near-normal within 72 hours of transfusion in people (Heaton et al. 1989); this remains unconfirmed in dogs. Cat RBC rely on chloride for oxygen affinity and 2,3-DPG concentrations are naturally low (Bunn 1971; Taketa et al. 1971); the P_{50} of stored haemoglobin in cats decreases relatively little (Wong & Haskins 2007) compared to that of dogs (Ou et al. 1975) in which 2,3-DPG is the major modifier of haemoglobin affinity for oxygen.

Adenosine triphosphate (ATP) levels decrease in stored canine RBC (Price et al. 1988); there is a 60% reduction in intracellular levels after 5 weeks of storage of human blood (Raat & Ince 2007). ATP prevents erythrocyte membrane loss by microvesiculation which leads to the extracellular accumulation of negatively-charged pro-inflammatory and pro-coagulant microparticles (MPs). Negativelycharged phospholipids, specifically phosphatidyl-serine, are transported from the outer to inner surfaces of RBC, by ATP-mediated active transport, thus minimising macrophage clearance following transfusion (Hess 2006). With decreasing ATP concentration, RBC shape degenerates with irreversibly reduced deformability. Free haemoglobin concentration increases proportionately with time due to stored blood haemolysis (Hess et al. 2009) and reacts with circulating nitric oxide, significantly faster than RBC haemoglobin, resulting in vasoconstriction (Raat & Ince 2007; Donadee et al. 2011).

Phosphatidyl-serine-expressing MPs progressively increase in stored canine pRBC (Herring et al. 2013). Microparticles develop physiologically as a result of a protective cellular mechanism against early cell death but are usually removed by the reticulo-endothelial system (Rubin et al. 2008); no removal occurs in storage resulting in their accumulation. They are pro-inflammatory and may have a role in human transfusion reactions (Jy et al. 2011). MPs are also pro-coagulant; they provide negatively-charged membrane surfaces which catalyse the activation of Factors IX and X and they express an inactive form of tissue factor (Rubin et al. 2010).

Dogs with experimentally induced pneumonia receiving 42-day-old stored blood had increased in vivo haemolysis with subsequent pulmonary hypertension and vascular damage, gas exchange abnormalities and risk of death compared to those receiving 7-day-old blood (Solomon et al. 2013). Tissue oxygen saturation decreased in people receiving stored blood >21-days-old compared to people receiving blood of <21-days of age; older blood may affect peripheral vasculature and oxygen delivery (Kiraly et al. 2009). These studies corroborate the findings of several other human papers suggesting that transfusing older blood negatively affects outcome (Napolitano & Corwin 2004; Tinmouth et al. 2006; Weinberg et al. 2010). Some human studies however, have not found a link between stored blood age and increased morbidity and mortality (Vincent et al. 2002; Corwin et al. 2004).

Storage lesions have been documented to start to develop within hours of storage and progressively increase in number and severity with duration of storage. There is limited literature in the veterinary field investigating whether the administration of blood products stored for a longer duration of time is likely to significantly influence patient morbidity and mortality, particularly in different disease states. Nonetheless, due to the accumulating evidence for storage lesions and their potentially negative implications in human and to a lesser extent veterinary medicine, it would appear sensible to administer fresh whole blood or blood that has been stored for as short a time as possible, and ideally for <14-21 days, in all cases but particularly to any critically ill patients. The anaesthetist should consider that transfusion of stored blood likely involves administering an acidic product and that it may not achieve the expected level of tissue oxygenation in dogs due to decreased 2,3-DPG concentrations.

Leukoreduction

Leukoreduction (LR) involves filtering blood prior to storage in order to remove leukocytes and platelets. This is routinely performed in human medicine in numerous countries across the world, but is a relatively uncommon procedure in the veterinary field.

Leukocytes are metabolically active and produce cytokines which accumulate extracellularly during storage (Nielsen et al. 1996) and may contribute to storage lesions in people as increased RBC aggregation and adherence to endothelial cells occurs following transfusion of non-LR stored blood (Lu et al. 2003; Tinmouth et al. 2006). Canine pRBC stored for 42 days had significantly higher erythrocyte counts following reduced haemolysis in the LR group, and a significant decrease in 2,3-DPG which was significantly lower in the non-LR group at each time point measured during storage (Ekiz et al. 2012) again suggesting that LR may decrease storage lesions. Leukocytes degrade in storage releasing bioactive substances such as histamine, vascular endothelial growth factor (VEGF), myeloperoxidase and plasminogen activator inhibitor-1 (Nielsen et al. 1997). Vasoactive compounds and cytokines are likely involved in some RBC storage lesions and may contribute to transfusion reactions in dogs (Graf et al. 2012).

Prestorage LR of canine blood at 4 °C reduces leukocyte counts by 99.9%; it does not adversely affect post-transfusion viability, ATP or haemoglobin concentrations (Brownlee et al. 2000). LR attenuates the inflammatory response to blood transfusion in people (Dzik 2002; Locke et al. 2005) and reduces erythrocyte damage and haemolysis with storage (Ekiz et al. 2012). Segmented neutrophils, fibrinogen and C-reactive protein increased significantly in healthy dogs that received non-LR 21-day-old stored pRBC compared to those that received LR pRBC of the same age in which inflammatory markers did not increase significantly from baseline (McMichael et al. 2010). Leukocytes, platelets and other cells produce VEGF which is essential for wound healing but also facilitates angiogenesis and tumour metastasis. Concentrations

of VEGF increase in stored non-LR canine pRBC but remain undetectable in LR units (Graf et al. 2012). Although the relevance of this finding in dogs is unclear, LR blood is recommended for use in human cancer patients to avoid transfusing excessive VEGF (Werther et al. 2001).

Leukoreduction, however, does not abrogate all inflammatory responses seen with stored-blood transfusions. When comparing LR and non-LR canine pRBC stored for seven and 28 days, older blood, irrespective of the LR status, induced an inflammatory response in healthy recipient dogs characterised by increased monocyte chemo-attractant protein-1 concentrations as well as increased neutrophils, decreased platelets and evidence of extravascular haemolysis producing substantial amounts of circulating non-transferrin-bound iron (Callan et al. 2013).

Leukoreduction has been investigated widely in human medicine and is becoming an area of interest in the veterinary field. The available evidence suggests that it would be beneficial to perform LR on all RBC products intended for storage as it would reduce the occurrence of transfusion reactions, storage lesions, transfusion-induced inflammation and disease transmission etc. Further studies are required to determine whether these benefits would outweigh the cost in veterinary patients.

Blood typing and cross-matching

Canine blood types are classified by the dog erythrocyte antigen (DEA) system based on RBC surface antigens and include DEA 1.1, 1.2, 1.3, 3, 4, 5, 6, 7 and 8 although anti-sera for DEA 6 and 8 are no longer available. The DEA 1.1 frequency of 42-71.2% varies with geographical location and breed (Giger et al. 1995; Gracner et al. 2007; Ekiz et al. 2011; Ferreira et al. 2011). DEA 4 is a high frequency antigen, occurring in 98-100% of dogs whereas other blood types occur with low to moderate frequency (Giger et al. 1995; Iazbik et al. 2010). The Dal antigen was recently documented following the identification of anti-Dal alloantibodies in a pre-sensitised Dalmatian; the alloantibodies are not naturally occurring (Blais et al. 2007). This antigen has a 93% frequency in breeds other than Dalmatians. Administering blood from a Dal-positive dog to a pre-sensitised Dalmatian may result in the development of potentially life-threatening haemolytic reactions therefore emphasising the need for cross-matching in dogs that have previously received blood transfusions.

DEA 1.1 is highly antigenic and should be determined in all donor and recipient dogs before transfusion (Tocci & Ewing 2009). Dogs do not have naturally occurring DEA 1.1 alloantibodies but may have alloantibodies to DEA 3, 5 and 7; acute immunologic haemolytic transfusion reactions have not been reported in previously untransfused dogs (Giger et al. 1995; Hohenhaus 2004). Universal donors are generally accepted as being negative for DEA 1.1, 1.2, 3, 5 and 7 but positive for DEA 4; 52% of greyhounds and 37.5% of non-greyhounds were identified as universal donors in one study (Iazbik et al. 2010). In many cases, only DEA 1.1 is tested and this is often performed with in-house point-ofcare kits. Administering type-compatible blood to dogs is not necessary for the first transfusion due to the lack of DEA 1.1 alloantibodies.

Feline blood groups are described by the AB system and include blood types A, B and AB; cats without A or B antigens have not been identified. Type A is the most common domestic cat blood type with a frequency of 73.3–100% which varies with geographical location (Giger et al. 1991; Griot-Wenk et al. 1996; Juvet et al. 2011; Proverbio et al. 2011). Pedigree cat breeds each have their own blood type frequencies. In the UK, Bengal cats are 100% type A (Gunn-Moore et al. 2009) and type A frequency is highest in Italian Ragdoll cats followed by types AB then B (Proverbio et al. 2013).

Type A and B, but not AB, cats have naturally occurring alloantibodies. Type A cats have weak anti-B alloantibodies, transfused type B erythrocytes to these cats will only survive for several days. In contast type B cats have strong anti-A alloantibodies resulting in acute, severe haemolytic reactions against type A erythrocytes with erythrocyte halflife of several hours (Hohenhaus 2004). Therefore due to the presence of alloantibodies, there are no universal feline donors and type A and B cats should always receive type-compatible blood. Type AB cats, however, are considered universal recipients and could theoretically receive blood of any type for their first transfusion; although type A is recommended over type B.

Mik antigens, independent of the AB blood group, were recently identified following a haemolytic transfusion reaction in a previously untransfused type A cat receiving type-compatible blood; the recipient was presumed to have naturally occurring anti-*Mik* alloantibodies (Weinstein et al. 2007). *Mik* frequency is unknown; however this discovery introduces the concept that cross-matching may need to be considered prior to all transfusions.

Cross-matching should be performed in any dog or cat that has received a blood transfusion >3-5 days previously to assess compatibility; it may need to be considered to identify incompatibilities associated with *Mik*-antigen positive cats. In-house, major and minor cross-match kits have been developed for dogs and cats based on gel technology and can be used despite auto-agglutination (Kessler et al. 2010).

Blood administration

Blood is best administered intravenously although intra-osseous routes could be considered if venous access is not achieved. Intra-peritoneal administration results in slow absorption and therefore has delayed effects. Blood donated from dogs typically is collected into blood bags; these are connected to infusion sets with in-built filters and are volume and rate controlled by a peristaltic fluid pump. Cat blood is typically collected into anti-coagulant containing syringes due to the small volumes obtained and administered via a transfusion line containing a micro-aggregate filter; administration rate is controlled by a syringe driver. Gravity flow is not used commonly due to possible inaccuracies with administration rate and volume. Sterility is maintained by avoiding or minimising any transfusion line disconnections during blood administration.

Transfusion of biotin-labelled autologous RBC to healthy dogs by volumetric, peristaltic infusionpump with a standard transfusion line (in-built 170– 260 μ m filter), syringe infusion-pump with 18 μ m aggregate filter and gravity flow with a standard transfusion line allowed identification of transfused erythrocytes in 4/8, 1/7 and 8/8 dogs, respectively, 24 hours post-transfusion; thereafter cell survival was not significantly different between groups (McDevitt et al. 2011). The initial marked RBC loss over 24 hours was attributed to shearing stress from forcing blood, with microclots following labelling reactions, through microaggregate filters for syringe-pumped cells and mechanical cell damage associated with the infusion pump.

Warming of stored blood prior to transfusion has been considered unnecessary in routine cases unless large volumes or high rates are administered or if patients are hypothermic; it could accelerate erythrocyte deterioration and promote micro-organism growth (Prittie 2003; Davidow 2013). The increased surface area of the transfusion line tubing may allow the blood to achieve near room-temperature levels, particularly at slow administration rates, before reaching the patient.

The blood volume to be transfused (VT) ideally should be guided by goal-directed therapy; historically, it has depended on the severity of anaemia, availability of blood products, body mass and donor PCV. Several formulae have been described for estimating the VT to dogs and cats (Turnwald & Pichler 1985; Griot-Wenk & Giger 1995; Kristensen & Feldman 1995; Castellanos et al. 2004); it is presumed that these formulae apply to cases of stable anaemia rather than those with ongoing severe haemorrhage or haemolysis although this has not been specifically stated in most studies. The accuracy of four formulae in predicting the increase in PCV with pRBC transfusion was investigated in dogs with regenerative anaemia due to ongoing haemorrhage and haemolysis (Short et al. 2012). Two formulae were accurate; these were: VT = [(desired PCV)]- patient PCV)/donor blood PCV] × 90 (canine blood volume) \times kg bodyweight, and VT = required PCV% increase $\times 1.5 \times$ kg bodyweight.

The transfusion administration rate depends on the cardiovascular and hydration status and severity of anaemia. In relatively stable patients that do not have active severe blood loss, the rate should be slow initially (0.25 mL⁻¹ kg⁻¹ for 30 minutes) to allow identification of transfusion incompatibilities or reactions and can be increased thereafter, typically to 2-10 mL⁻¹ kg⁻¹ hour (Turnwald & Pichler 1985; Harrell & Kristensen 1995). The maximum transfusion rate recommended for euvolaemic anaemic animals, to avoid volume overload, is 10-20 mL⁻¹ kg⁻¹ hour. Dogs with major blood loss may require massive transfusion (replacement of blood volume in 24 hours or half the blood volume in three hours) with increased volumes and rates (Jutkowitz et al. 2002). Whole blood transfusion rates in one study were 4 mL^{-1} kg⁻¹ hour for cats with cardiovascular dysfunction, $10 \text{ mL}^{-1} \text{ kg}^{-1}$ hour for euvolaemic cats and 60 mL⁻¹ kg⁻¹ hour for those in hypovolaemic shock; no complications were described for the different rates (Weingart et al. 2004). Packed RBC were administered to dogs at fast (20-30 minutes) or slow (2 hours) rates to determine whether the inflammatory response to transfusion would be dampened with a slower administration rate; pRBC age, rather than transfusion rate, was a significant factor in developing an inflammatory response (Callan et al. 2013).

Transfusion of RBC products should be completed within four hours of removing the product from refrigeration due to the risk of bacterial contamination and growth. This recommendation arises from numerous human studies published in the last 70 years; although some studies are out-dated as storage solutions and techniques have changed, there is no recent research to suggest that prolongation of this time is appropriate (Brunskill et al. 2012).

Cell salvage and autologous blood transfusion

Cell salvage and autologous transfusion is a potential management option for dogs with large volume haemorrhage; it minimises the risks, complications and reactions seen with homologous blood transfusion. Blood shed intra- or post-operatively is collected using a cell separator system, washed and returned to the patient within 6 hours as pRBC suspended in saline; plasma, activated clotting factors, anticoagulants and systemic medications are removed (Hirst & Adamantos 2012; Kellett-Gregory et al. 2013). Leukoreducing blood prior to autologous transfusion reduces bacterial load, leukocytes and neoplastic cells in people (Waters et al. 2003; Nieder et al. 2004), although consensus on the use of LR autologous blood transfusions in people with malignancy is lacking. Cell salvage has been used in human obstetrics and in vascular, orthopaedic, neurological and cardiac surgeries with rare complications apart from coagulopathies resulting from large-volume autologous transfusion of erythrocytes without platelets or clotting factors (Ashworth & Klein 2010). Clinical cell salvage was described in three dogs with haemoperitoneum. All cases received homologous blood transfusions in addition to the autologous transfusion, but it was surmised that the total demand for homologous transfusions was reduced (Hirst & Adamantos 2012). No transfusion reactions or other complications were identified. Depending on the cell salvage device used, the cost of its use may be less than the administration of two pRBC units to dogs (Kellett-Gregory et al. 2013). Prospective trials are warranted to clarify the risks and benefits of cell salvage in veterinary patients; cell salvage may provide a promising alternative to limit homologous transfusion.

Pre-operative blood donation over the weeks prior to a surgical procedure with subsequent autologous transfusion intra- or post-operatively, as required, has been performed in human patients undergoing elective surgical procedures in which haemorrhage and transfusion are likely (Klein et al. 2007; Spahn & Goodnough 2013). This transfusion method reduces the requirement for homologous transfusions and their associated risks (Henry et al. 2002). Pre-operative autologous donation still results in storage lesions and carries the risk of bacterial contamination just as with any blood units (Klein et al. 2007). The procedure is more expensive than homologous transfusion due to the increased costs from donation (Spahn & Goodnough 2013).

Acute euvolaemic haemodilution involves donating blood immediately prior to anaesthesia induction in people with replacement of blood volume loss with crystalloid fluid therapy (Klein et al. 2007). The blood is stored at room temperature in the operating theatre and is transfused during the surgical procedure when required. The fresh blood has minimal storage lesions. The procedure is reserved for elective surgical procedures where severe haemorrhage is expected. It does not necessarily remove the requirement for homologous transfusion, but reduces the number of units of homologous blood used (Segal et al. 2004).

Pre-operative blood donation and acute euvolaemic haemodilution with autologous transfusion have not been reported in clinical veterinary cases. The costs of these procedures would need to be assessed to determine their viability. Acute euvolaemic haemodilution appears to be a viable transfusion option with minimal associated risks; studies in veterinary patients are warranted as this may be another possible alternative transfusion method that could reduce the need for homologous transfusions.

Xenotransfusion

The first reported xenotransfusions, transfusions between different species, were performed by Jean-Baptiste Denis in 1667 where calf blood was administered to dogs; thereafter, lamb and calf blood was transferred to people (Roux et al. 2007). Transfusion practices evolved dramatically following the discovery of human blood groups in 1900 (Landsteiner 1900). However there is continued interest in xenotransfusion, most recently involving pig blood for people (Cooper 2003). Purified polymerised porcine haemoglobin has been successfully transfused to dogs with no agglutination or haemolytic reactions (Jia et al. 2010).

Several studies involving transfusion of dog blood to cats were reported in the 1960's (Bovens & Gruffydd-Jones 2013). A single case report was presented more recently (Gowan 2004). No severe acute adverse reactions occurred, as cats presumably do not have alloantibodies to dog erythrocyte antigens. However, antibodies developed within 4-7 days of the initial transfusion, as demonstrated by positive slide agglutination and in vitro haemolysis tests; the lifespan of transfused RBC was <4 days (Clark & Kiesel 1963). Repeat transfusion with dog blood >6 days after the first transfusion resulted in anaphylaxis which was fatal in >66% of cases (Bovens & Gruffydd-Jones 2013). Xenotransfusion of dog blood to cats could be considered in genuine emergencies where no alternative exists, providing that the cat has not received dog blood before. This may provide time for performing diagnostic procedures or acquiring appropriate blood products.

Oxyglobin (OPK Biopure, Netherlands), an ultrapurified, polymerized bovine haemoglobin-based oxygen carrying solution (average molecular weight of 200 kD), is a form of xenotransfusion which has been studied in dogs and cats for 10-15 years. It has been used predominantly for managing anaemia where it provided similar clinical improvements to pRBC transfusion in dogs (Zambelli & Leisewitz 2009) and efficiently increased haemoglobin concentration in cats (Weingart & Kohn 2008) although the effects are short-lived as 95% is eliminated from the circulation within 5-9 days in dogs (Callan & Rentko 2003). It also effectively increases systolic arterial blood pressure in hypotensive cats (Wehausen et al. 2011) and improves haemodynamic function and tissue oxygenation in dogs, partly due to vasoconstriction (Driessen et al. 2007). Although a suitable alternative to increasing oxygen carrying capacity, there is a risk of circulatory overload in cats with cardiac disease (Weingart & Kohn 2008). It also interferes with any biochemical tests that are based on colorimetric or optical assessment (Wall 1998; Gibson et al. 2002).

Xenotransfusion allows temporary management of anaemia which may provide time for diagnostic or surgical procedures to be performed or for appropriate blood to be collected and transfused. It is not without potentially significant risk and does not supersede homologous or autologous transfusion. Based on the currently available evidence however, xenotransfusion does have a place in veterinary transfusion medicine.

Conclusion

Blood transfusion practices have evolved over time. Storage techniques have improved allowing extension of storage times however increasingly more storage lesions are now being identified; where possible it is preferable to use younger blood products. The benefits of LR are being recognised in both human and veterinary fields and may become standard practice in the future. Promising transfusion options, such as cell salvage with autologous transfusion and xenotransfusion, may provide alternative sources of blood products.

References

- Ashworth A, Klein AA (2010) Cell salvage as part of a blood conservation strategy in anaesthesia. Br J Anaesth 105, 401–416.
- Blais MC, Berman L, Oakley DA et al. (2007) Canine dal blood type: a red cell antigen lacking in some Dalmatians. J Vet Intern Med 21, 281–286.
- Bovens C, Gruffydd-Jones T (2013) Xenotransfusion with canine blood in the feline species: review of the literature. J Feline Med Surg 15, 62–67.
- Brownlee L, Wardrop KJ, Sellon RK et al. (2000) Use of a prestorage leukoreduction filter effectively removes leukocytes from canine whole blood while preserving red blood cell viability. J Vet Intern Med 14, 412– 417.
- Brunskill S, Thomas S, Whitmore E et al. (2012) What is the maximum time that a unit of red blood cells can be safely left out of controlled temperature storage? Transfus Med Rev 26, 209–233.
- Bunn HF (1971) Differences in the interaction of 2,3diphosphoglycerate with certain mammalian hemoglobins. Science 172, 1049–1050.
- Callan MB, Rentko VT (2003) Clinical application of a haemoglobin-based oxygen carrying solution. Vet Clin North Am Small Anim Pract 33, 1277–1293.
- Callan MB, Patel RT, Rux AH et al. (2013) Transfusion of 28-day-old leucoreduced or non-leucoreduced stored red blood cells induces an inflammatory response in healthy dogs. Vox Sang 105, 319–327.
- Castellanos I, Couto CG, Gray TL (2004) Clinical use of blood products in cats: a retrospective study (1997-2000). J Vet Intern Med 18, 529–532.
- Clark CH, Kiesel GK (1963) Longevity of red blood cells in interspecies transfusion. J Am Vet Med Assoc 143, 400– 401.
- Cooper DK (2003) Porcine red blood cells as a source of blood transfusion in humans. Xenotransplantation 10, 384–386.
- Corwin H, Gettinger A, Pearl R et al. (2004) The CRIT study: anemia and blood transfusion in the critically

ill – current practice in the United States. Crit Care Med 32, 39–52.

- Davidow B (2013) Transfusion medicine in small animals. Vet Clin Small Anim 43, 735–756.
- Donadee C, Raat NJ, Kanias T et al. (2011) Nitric oxide scavenging by red blood cell microparticles and cell-free hemoglobin as a mechanism for the red cell storage lesion. Circulation 124, 465–476.
- Driessen B, Zarucco L, Gunther RA et al. (2007) Effects of low-volume haemoglobin glutamer-200 versus normal saline and arginine vasopressin resuscitation on systemic and skeletal muscle blood flow and oxygenation in a canine hemorrhagic shock model. Crit Care Med 35, 2101–2109.
- Dzik WH (2002) Leukoreduction of blood components. Curr Opin Hematol 9, 521–526.
- Ekiz EE, Arslan M, Ozcan M et al. (2011) Frequency of dog erythrocyte antigen 1.1 in 4 breeds native to different areas in Turkey. Vet Clin Pathol 40, 518–523.
- Ekiz EE, Arslan M, Akyazi I et al. (2012) The effects of presotrage leukoreduction and storage duration on the in vitro quality of canine packed red blood cells. Turk J Vet Anim Sci 36, 711–717.
- Ferreira RR, Gopegui RR, Matos AJ (2011) Frequency of dog erythrocyte antigen 1.1 expression in dogs from Portugal. Vet Clin Pathol 40, 198–201.
- Gibson GR, Callan MB, Hoffmann V et al. (2002) Use of haemoglobin based oxygen carrying solutions in cats: 72 cases (1998–2000). J Am Vet Med Assoc 221, 219–225.
- Giger U, Griot-Wenk ME, Bucheler J et al. (1991) Geographical variation of the feline blood type frequencies in the United States. Feline Pract 19, 21–26.
- Giger U, Gelens CJ, Callan MB et al. (1995) An acute haemolytic transfusion reaction caused by dog erythrocyte antigen 1.1 incompatibility in a previously sensitized dog. J Am Vet Med Assoc 206, 1358–1362.
- Gowan R (2004) Canine blood transfusion in a cat with erythrocyte leukaemia. Proceedings of the Australian College of Veterinary Scientists Science Week, Surfer's Paradise, Australia. pp. 29–30.
- Gracner D, Bedrica L, Labura C et al. (2007) Blood groups and hematology in Istrian pointers. Vet Arhiv 77, 95–102.
- Graf C, Raila J, Schweigert FJ et al. (2012) Effect of leukoreduction treatment on vascular endothelial growth factor concentration in stored canine blood transfusion products. Am J Vet Res 73, 2001–2006.
- Griot-Wenk ME, Giger U (1995) Feline transfusion medicine. Blood types and their clinical importance. Vet Clin North Am Small Anim Pract 25, 1305–1322.
- Griot-Wenk ME, Callan MB, Casal ML et al. (1996) Blood type AB in the feline AB blood group system. Am J Vet Res 57, 1438–1442.
- Gunn-Moore DA, Simpson KE, Day MJ (2009) Blood types in Bengal cats in the UK. J Feline Med Surg 11, 826–828.

- Harrell KA, Kristensen AT (1995) Canine transfusion reactions and their management. Vet Clin North Am Small Anim Pract 25, 1333–1364.
- Heaton A, Keegan T, Holme S (1989) In vivo regeneration of red cell 2,3-diphosphoglycerate following transfusion of DPG-depleted AS-1, AS-3 and CPDA-1 red cells. Br J Haematol 71, 131–136.
- Henry DA, Carless PA, Moxey AJ et al. (2002) Preoperative autologous donation for minimising perioperative allogenic blood transfusion. Cochrane Database Syst Rev 2, CD003602.
- Herring JM, Smith SA, McMichael MA et al. (2013) Microparticles in stored canine RBC concentrates. Vet Clin Pathol 42, 163–169.
- Hess JR (2006) An update on solutions for red cell storage. Vox Sang 91, 13–19.
- Hess JR, Sparrow RL, van der Meer PF et al. (2009) Red blood cell hemolysis during blood bank storage: using national quality management data to answer basic scientific questions. Transfusion 49, 2599–2603.
- Hirst C, Adamantos S (2012) Autologous blood transfusion following red blood cell salvage for the management of blood loss in 3 dogs with hemoperitoneum. J Vet Emerg Crit Care 22, 355–360.
- Hohenhaus AE (2004) Importance of blood groups and blood group antibodies in companion animals. Transfus Med Rev 18, 117–126.
- Iazbik MC, O'Donnell M, Marin L et al. (2010) Prevalence of dog erythrocyte antigens in retired racing greyhounds. Vet Clin Pathol 39, 433–435.
- Jia X, Chen L, Ding W et al. (2010) Heterologous transfusion of dog by polymerized hemoglobin of pig. Chin Anim Husb & Vet Med, 9, S858.292.
- Jutkowitz LA, Rozanski EA, Moreau JA et al. (2002) Massive transfusion in dogs: 15 cases. J Am Vet Med Assoc 220, 1664–1669.
- Juvet F, Brennan S, Mooney CT (2011) Assessment of feline blood for transfusion purposes in the Dublin area of Ireland. Vet Rec 168, 352.
- Jy W, Ricci M, Shariatmadar S et al. (2011) Microparticles in stored red blood cells as potential mediators of transfusion complications. Transfusion 51, 886–893.
- Kellett-Gregory LM, Seth M, Adamantos S et al. (2013) Autologous canine red blood cell transfusion using cell salvage devices. J Vet Emerg Crit Care 23, 82–86.
- Kessler RJ, Reese J, Chang D et al. (2010) Dog erythrocyte antigens 1.1, 1.2, 3, 4, 7 and Dal blood typing and crossmatching by gel column technique. Vet Clin Pathol 39, 306–316.
- Kiraly LN, Underwood S, Differding JA et al. (2009) Transfusion of aged packed red blood cells results in decreased tissue oxygenation in critically injured trauma patients. J Trauma 67, 29–32.
- Klein HG, Spahn DR, Carson JL (2007) Transfusion medicine 1. Red blood cell transfusion in clinical practice. Lancet 370, 415–426.

- Kristensen AT, Feldman BF (1995) General principles of small animal blood component administration. Vet Clin North Am Small Anim Pract 25, 1277–1290.
- Landsteiner K (1900) Zur Kentniss der antifermentativen lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe. Zentralbl Bakteriol 28, 357–362.
- Locke R, Paul D, Touch S et al. (2005) Cytokine load in prestorage leukoreduced PRBC transfusions in premature infants. J Perinatol 25, 526–530.
- Lower R (1665) The success of the experiment of transfusing the bloud of one animal into another. Philos Trans R Soc Lond B Biol Sci 1, 352.
- Lu C, Gray-Statchuk L, Cepinkas G et al. (2003) WBC reduction reduces storage-associated RBC adhesion to vascular endothelial cells under conditions of continuous flow in vitro. Transfusion 43, 151–156.
- McDevitt RI, Ruaux CG, Baltzer WI (2011) Influence of transfusion technique on survival of autologous red blood cells in the dog. J Vet Emerg Crit Care 21, 209–216.
- McMichael MA, Smith SA, Galligan A et al. (2010) Effect of leukoreduction on transfusion-induced inflammation in dogs. J Vet Intern Med 24, 1131–1137.
- Napolitano LM, Corwin HL (2004) Efficacy of red blood cell transfusion in the critically ill. Crit Care Clin 20, 255–268.
- Nieder AM, Carmack AJ, Sved PD et al. (2004) Intraoperative cell salvage during radical prostatectomy is not associated with greater biochemical recurrence rate. Urology 65, 730–734.
- Nielsen HJ, Reimert CM, Pedersen AN et al. (1996) Timedependent, spontaneous release of white cell- and platelet-derived bioactive substances from stored human blood. Transfusion 36, 960–965.
- Nielsen HJ, Reimert C, Pedersen AN et al. (1997) Leucocyte-derived bioactive substances in fresh frozen plasma. Br J Anaesth 78, 548–552.
- Ou D, Mahaffey E, Smith JE (1975) Effect of storage on oxygen dissociation of canine blood. J Am Vet Med Assoc 167, 56–58.
- Pavenski K, Saidenberg E, Lavoie M et al. (2012) Red blood cell storage lesions and related transfusion issues: a Canadian Blood Services research and development symposium. Transfus Med Rev 26, 68–84.
- Price GS, Armstrong J, McLeod DA et al. (1988) Evaluation of citrate-phosphate-dextrose-adenine as a storage medium for packed canine erythrocytes. J Vet Intern Med 2, 126–132.
- Prittie J (2003) Triggers for use, optimal dosing, and problems associated with red cell transfusions. Vet Clin Small Anim 33, 1261–1275.
- Proverbio D, Spada E, Baggiani L et al. (2011) Comparison of gel column agglutination with monoclonal antibodies and card agglutination methods for assessing the feline AB group system and a frequency study of feline blood types in northern Italy. Vet Clin Pathol 40, 32–39.

- Proverbio D, Spada E, Perego R et al. (2013) Assessment of blood types of Ragdoll cats for transfusion purposes. Vet Clin Pathol 42, 157–162.
- Raat NJ, Ince C (2007) Oxygenating the microcirculation: the perspective from blood transfusion and blood storage. Vox Sang 93, 12–18.
- Roux FA, Sai P, Deschamps JY (2007) Xenotransfusion, past and present. Xenotransplantation 14, 208–216.
- Rubin O, Crettaz D, Canellini G et al. (2008) Microparticles in stored red blood cells: an approach using flow cytometry and proteomic tools. Vox Sang 95, 288–297.
- Rubin O, Crettaz D, Tissot JD et al. (2010) Microparticles in stored red blood cells: submicron clotting bombs? Blood Transfus 8, s31–s38.
- Segal JB, Blasco-Colmenares E, Norris EJ et al. (2004) Preoperative acute normovolemic hemodilution: a metaanalysis. Transfusion 44, 632–644.
- Short JL, Diehl S, Seshadri R et al. (2012) Accuracy of formulas used to predict post-transfusion packed cell volume rise in anemic dogs. J Vet Emerg Crit Care 22, 428–434.
- Solomon SB, Wang D, Sun J et al. (2013) Mortality increases after massive exchange transfusion with older stored blood in canines with experimental pneumonia. Blood 121, 1663–1672.
- Spahn DR, Goodnough LT (2013) Blood transfusion 2. Alternatives to blood transfusion. Lancet 381, 1855– 1865.
- Taketa F, Mauk AG, Lessard JL (1971) Chain amino termini of the cat hemoglobins and the response to 2,3-diphosphoglycerate and adenosine triphosphate. J Biol Chem 246, 4471–4476.
- Tinmouth A, Fergusson D, Yee IC et al. (2006) Clinical consequences of red cell storage in the critically ill. Transfusion 46, 2014–2027.
- Tocci LJ, Ewing PJ (2009) Increasing patient safety in veterinary transfusion medicine: an overview of pre-transfusion testing. J Vet Emerg Crit Care 19, 66–73.
- Turnwald GH, Pichler ME (1985) Blood transfusion in dogs and cats Part II. Administration, adverse events, and component therapy. Compend Contin Educ Pract Vet 7, 115–122.
- Urban R, Couto CG, Iazbik MC (2013) Evaluation of hemostatic activity of canine frozen plasma for transfusion by thromboelastography. J Vet Intern Med 27, 964–969.
- Vincent J, Baron J, Reinhart K et al. (2002) Anemia and blood transfusion in critically ill patients. J Am Med Assoc 288, 1499–1507.
- Wall RE (1998) Synthetic colloids and blood substitutes. Suppl Compend Contin Educ Vet Pract 20, 4–9.
- Wardrop KJ, Owen TJ, Meyers KM (1994a) Evaluation of an additive solution for preservation of canine red blood cells. J Vet Intern Med 8, 253–257.

- Wardrop KJ, Young J, Wilson E (1994b) An in vitro evaluation of storage media for the preservation of canine packed red blood cells. Vet Clin Pathol 23, 83–88.
- Wardrop KJ, Tucker RL, Mugnai K (1997) Evaluation of canine red blood cells stored in a saline, adenine, and glucose solution for 35 days. J Vet Intern Med 11, 5–8.
- Waters JH, Tuohy M, Hobson D (2003) Bacterial reduction by cell salvage washing and leukocyte depletion filtration. Anaesthesiol 99, 652–655.
- Wehausen CE, Kirby R, Rudloff E (2011) Evaluation of the effects of bovine haemoglobin glutamer-200 on systolic arterial blood pressure in hypotensive cats: 44 cases (1997–s2008). J Am Vet Med Assoc 238, 909–914.
- Weinberg JA, McGwin G, Vandromme MJ et al. (2010) Duration of red cell storage influences mortality after trauma. J Trauma 69, 1427–1432.
- Weingart C, Kohn B (2008) Clinical use of a haemoglobinbased oxygen carrying solution (Oxyglobin[®]) in 48 cats (2002–2006). J Feline Med Surg 10, 431–438.

- Weingart C, Giger U, Kohn B (2004) Whole blood transfusions in 91 cats: a clinical evaluation. J Feline Med Surg 6, 139–148.
- Weinstein NM, Blais MC, Harris K et al. (2007) A newly recognized blood group in domestic shorthair cats: the Mik red cell antigen. J Vet Intern Med 21, 287–292.
- Werther K, Christensen IJ, Nielsen HJ (2001) The association between preoperative concentration of soluble vascular endothelial growth factor, perioperative blood transfusion, and survival in patients with primary colorectal cancer. Eur J Surg 167, 287–292.
- Wong C, Haskins SC (2007) The effect of storage in the P50 of feline blood. J Vet Emerg Crit Care 17, 32–36.
- Zambelli AB, Leisewitz AL (2009) A prospective, randomized comparison of Oxyglobin (HB-200) and packed red blood cell transfusion for canine babesiosis. J Vet Emerg Crit Care 19, 102–112.

Received 23 September 2013; accepted 15 November 2013.

Copyright of Veterinary Anaesthesia & Analgesia is the property of Wiley-Blackwell and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.