Transfusion Medicine - From donor to recipient

Learning Outcomes

- Donor selection criteria and donor screening
- Donation process including donor aftercare
- Blood products, storage requirements and indications for use
- DEA canine blood group system and AB feline blood group system
- Indications for crossmatching and how to perform in practice
- Recognising when a transfusion is indicated
- Understand how to safely administer blood products
- Monitoring transfusions and identifying possible transfusion reactions
- Autotransfusion and appropriate applications in practice
- Xenotransfusion and appropriate applications in practice

Donor selection criteria – Dogs

Blais et al., 2009; Gibson and Abrams-Ogg, 2012; Gibson and Callan, 2018; PBBUK, 2023

Canine blood donors should be healthy, large breed dogs over 25kg (lean weight) and between 1 and 8 years old. They must have a suitable temperament, ideally not requiring the use of sedation. The Pet Blood Bank in the United Kingdom does not permit the use of sedation in canine blood donors. Donors should be up to date with routine preventative healthcare including vaccinations although these must not have been administered within the 10-14 days prior to a donation. The dog must not be receiving any medication excluding ectoparasite and endoparasite prevention and must not have had any medical illness or surgery within the previous 3 months. Any animal that has previously received a transfusion is excluded from becoming a blood donor. Dogs that have travelled outside Ireland or the UK are generally excluded from blood donation although, if necessary, these dogs can donate if additional screening is performed for infectious diseases endemic to the geographical region(s) the animal has entered. Historically, any dog that had previously been pregnant was excluded from becoming a blood donor. However, a 2009 study by Blais *et al.* found no evidence of pregnancy-induced red blood cell alloantibodies in dogs. Therefore, a history of pregnancy is no longer a concern. Animals currently pregnant or nursing should not donate blood due to the potential risk this may cause to the mother and/or neonates.

Donor selection criteria – Cats

VetsNow, 2013; Gibson and Callan, 2018; Taylor et al., 2021; PBBUK, 2023

Feline donor criteria are similar to that of dogs. A healthy cat over 4.5kg (lean weight) between 1 and 8 years is recommended. Many feline donors will require sedation however cats with an agreeable temperament that are not stressed by vet visits are desirable. As with dogs, feline donors should be up to date with preventative healthcare, vaccinations, and parasite prevention. They should have no recent history (previous 3 months) of medical illness or surgery, never received a transfusion, never travelled outside Ireland or UK and not be currently pregnant or nursing. Ideally only indoor cats should donate however outdoor cats can be used if additional infectious disease screening is carried out although there is still a risk to the recipient.

Donor screening

Gibson and Abrams-Ogg, 2012; VetsNow, 2013; Wardrop et al., 2016; Augusto et al., 2018; Gibson and Callan, 2018

Once a potential donor has been identified, screening is required to ensure they are a suitable candidate.

Begin with assessment of the animal's temperament; observe the animal's response to waiting in reception, the physical examination, restraint, and blood sampling. If any signs of fear, anxiety, stress or aggression are noted then the animal is not a suitable candidate for blood donation.

Obtain a full history, perform a physical examination and measure an accurate weight. This is also an opportunity to discuss with the owner about their expectations of the donation process and answer any questions they may have.

Run full haematology and biochemistry to identify potential underlying issues. Use peripheral vessels (eg. cephalic or saphenous veins) for blood sampling to preserve jugular veins for the donation.

Identify the animal's blood type. In cats, it is gold standard to also perform crossmatching prior to blood donation. Feline blood is not stored and therefore every donation is collected for a specific intended recipient. Crossmatching is recommended in cats prior to the first transfusion (this will be discussed further later on). Ensure that the potential donor and intended recipient are compatible prior to performing the donation.

Infectious disease screening is required for all potential blood donors. The American College of Veterinary Internal Medicine have issued a consensus statement which outlines numerous endemic diseases for which potential donors can be tested. Fortunately, in Ireland there are not many to be concerned about.

In cats, screening for Feline Leukaemia Virus (FeLV), Feline Immunodeficiency Virus (FIV) and *Mycoplasma haemofelis* is advised. Annual screening is adequate for indoor only cats however outdoor cats will require infectious disease screening prior to every donation.

In dogs, *Angiostrongylus vasorum* (lungworm) is the main disease of concern. If positive, this poses a risk to donor due to the effects on coagulation. Ensure all canine donors are either receiving routine prophylaxis for lungworm or are screened with a point of care test prior to donation.

Some breeds are at increased risk of developing cardiomyopathies. It can be recommended to perform echocardiogram on these high-risk breeds to rule out occult cardiac disease. Dog breeds of concern include Airedale Terrier, Portuguese Water Dog, Standard Schnauzer, Doberman Pinscher, St. Bernard, Great Dane, Bernese Mountain Dog, Irish Wolfhound and Newfoundland. High risk cat breeds include British Shorthair, Ragdoll, Sphinx, Maine Coon.

The above-mentioned screening protocols are required to initially enrol an animal as a blood donor. Prior to every subsequent donation an up-to-date history should be obtained alongside a physical examination and accurate weight. As a minimum a packed cell volume (PCV) and total solids (TS) should be performed prior to every donation although full haematology and biochemistry is preferred. Outdoor cats require infectious disease screening prior to every donation.

Donation Process

VetsNow, 2013; Augusto *et al.*, 2018; Gibson and Callan, 2018; BSAVA, 2020

It is important to remember that there is no benefit at all to the donor in the donation process, so it is essential to make it as stress free as possible.

Begin by clipping the animal's neck. If it is a regular donor try to alternate the vein used. A topical anaesthetic cream may be used although it is important to be aware of the onset of action time for the specific product used. For example, EMLA™ cream takes 45-60 minutes to take effect so should

be applied during the physical exam or while the bloods are running to allow adequate time for it to take effect.

The use of sedation during blood donations can be controversial. In dogs, ideally no sedation should be used. As previously mentioned, the Pet Blood Bank in the UK does not permit the use of sedation in canine donors. A mild sedative can be administered if the blood is for immediate use however consider whether the dog is a suitable donor candidate if sedation is necessary.

Many feline donors will require sedation so ensure that the animal has been fasted appropriately. A sedation protocol with minimal cardiovascular effects should be used with alpha$_2$ agonists being avoided. Some literature describes the use of propofol and isoflurane combinations in feline donors however if a cat requires this amount of chemical restraint, then they are not a suitable donor candidate!

If sedation is used the animal will require an IV catheter to be placed and should be monitored closely for the duration of the procedure. Apply eye lubricant and provide oxygen.

Donors should be positioned in lateral recumbency on a comfortable table. A rolled towel can be positioned under the neck to aid access and visualisation of the jugular vein. Some cats may prefer a sternal recumbency with the head extended. Ideally four people would be involved in the donation process; 1 to perform venipuncture, 1 to manage the blood bag or syringe and 2 to restrain the animal with 1 monitoring if sedation was administered.

Perform an aseptic skin preparation and raise the jugular vein at the thoracic inlet. Aim for a clean stick venipuncture to minimise platelet loss and clot formation.

A maximum of 20% of the animal's total blood volume can be collected. This is 16-18ml/kg for dogs and 11-13ml/kg for cats. Calculate this before beginning the donation.

During the donation monitor the venipuncture site – the vein may blow, the animal may move or clots may form.

Once the donation is complete, apply direct pressure to the site with a clean swab for 5 minutes. Then apply a neck bandage for a further 30 minutes to minimise haematoma formation. Ensure the neck bandage is not too tight.

Donation Process – closed system

VetsNow, 2013; Higgs *et al.*, 2015; Augusto *et al.*, 2018; Gibson and Callan, 2018

Closed collection systems are commercially available as single, triple or quad bags. They contain the required amount of anticoagulant for the bag size. Prior to the donation, weigh the collection bag and calculate the minimum and maximum collection weights. One unit of whole blood is 450ml. The anticoagulant in the bag will allow +/-10%. 1ml of whole blood weighs 1.06g. Therefore, the minimum collection weight is 429g ([450ml – 10%] x 1.06g) plus the weight of the bag and the maximum collection weight is 524g ([450ml + 10%] x 1.06g) plus the weight of the bag.

Ensure the line is clamped with a guarded haemostat until the needle is within the vein to prevent air contamination. Air contamination can result in red blood cell lysis. If the blood does not flow once the haemostat is removed, check the rest of the line as there may be clips or plastic seals that need to be removed or broken. If repositioning of the needle is required, avoid removing the needle from the skin. The line must be clamped if removing the needle from the skin.

Keep the blood collection bag below the donor for the duration of the donation to aid gravity flow. The bag should be gently mixed and regularly weighed throughout the donation. Once the desired quantity of blood has been collected, clamp the line before removing the needle. The collection line can either be stripped or divided into sections to use for crossmatching later.

Calculate the total volume of blood collected;

$$\frac{\text{(Wt. full bag – wt. empty bag)}}{1.06\text{g}} = \text{volume (ml) WB (+ 65ml AC)}$$

If the facilities are available, the whole blood unit may also be processed into packed RBCs and plasma at this point.

Donation Process – open system

Gibson and Abrams-Ogg, 2012; VetsNow, 2013; Augusto *et al.*, 2018; Gibson and Callan, 2018

Open collection systems are ideal for small volume donations. They are commonly used for feline blood donations. There are small volume closed collection systems available which can be used in cat however they are not currently available in Ireland.

Donations using an open system require the same donor preparation as for closed systems. A key difference is that for cats the required volume should be precalculated based on the recipient's requirements. As feline blood is not stored and is collected for immediate administration to a specific intended recipient, only the volume of blood required by the recipient should be collected. The method for calculating this requirement will be discussed later.

Open collection systems are made up of a butterfly catheter (typically 21G), 3-way tap and 10ml or 20ml syringe. The system requires priming with anticoagulant prior to use. Either CPA or CPDA-1 anticoagulant can be used. An anticoagulant to whole blood ratio of between 1:9 and 1:7 is recommended. This works out as 1ml anticoagulant per 10ml syringe or 1.25ml anticoagulant per 10ml syringe. If too little anticoagulant is added there is increased risk of blood clot formation. If too much anticoagulant is used there is a risk of citrate toxicity in the recipient which can result in hypocalcaemia.

As with the closed method, contact between blood and air should be minimised so ensure the 3-way tap is closed to the room until the needle is within the vein. The syringe should be gently mixed throughout the donation. If multiple syringes are used, they should be capped once full.

Open collection systems carry an increased risk of contamination. Blood collected using this method should therefore be stored for no longer than 24 hours at 4°C.

To administer the blood the syringes can be transferred to a small empty fluid bag or administered individually via a syringe driver. If the syringe driver method is used, then the remaining syringes should be stored in the fridge until required.

Donor Aftercare

Gibson and Abrams-Ogg, 2012; VetsNow, 2013; Augusto *et al.*, 2018; Gibson and Callan, 2018; PBBUK, 2023

Once the donation is completed, dogs can be offered a small amount of food and water. They should be monitored for a short period following donation. It is recommended to record heart rate, pulse quality and mucous membrane colour for approximately 30 minutes following a blood donation. Advise the owner to keep the dog quiet for the remainder of the day with only light exercise for the following 24-72 hours. Ideally a harness should be used to avoid pressure on the venipuncture site.

Cats can also be offered a small amount of food and water after donating. They require closer monitoring for a longer period (3-4 hours). Their heart rate, blood pressure and mucous membrane colour should be closely monitored. If sedation was administered, then it is important to also monitor temperature. Some vets may choose to administer fluid therapy to feline blood donors after the procedure. A total volume of 60ml of crystalloid fluid is typically administered over 3 hours. If the cat is outdoors, advise the owner to keep them inside for 24-48 hours so they can be monitored.

Before discharge, advise the owner to contact the clinic if they have any concerns about their pet. Follow up with the owner the following day to check that the animal has recovered smoothly. Remind the owner that their pet can donate blood a maximum of every 3 months. More frequent donations can result in iron deficiency.

Blood products – whole blood

VetsNow, 2013; Augusto et al., 2018; Gibson and Callan, 2018; Sturgess, 2019

Fresh whole blood

Fresh whole blood is not refrigerated and is administered to the recipient within 4-6 hours of collection. It contains red blood cells, platelets and all plasma proteins including all clotting factors. Fresh whole blood may contain white blood cells depending on the collection system used. Some commercial collection bags contain leucocyte reduction filters within the line.

Fresh whole blood is indicated in cases of whole blood loss (i.e. haemorrhage). It can also be used in anaemia of other causes where there is no access to packed RBCs. The used of fresh whole blood to treat thrombocytopenia is controversial. It is unlikely to have a significant effect however may be used in cases of immune mediated thrombocytopenia while immunosuppressive therapy is taking effect. Daily fresh whole blood transfusions would be required as platelets last less than 24-48 hours. There is risk of volume overload particularly if the patient is normovolaemic. Fresh whole blood may not contain enough clotting factors to treat a consumptive coagulopathy. A fresh frozen plasma transfusion may be a better choice in such cases.

Stored whole blood

Stored whole blood is refrigerated at 1-6°C and is more than 8 hours since collection. It contains red blood cells, plasma proteins and the stable or non-labile clotting factors only. These are the vitamin K dependant factors II, VII, IX and X, as well as factor XI.

The indications for stored whole blood use are whole blood loss (haemorrhage) and other causes of anaemia where there is no access to packed RBCs.

Whole blood can be stored for 21 days if CPD anticoagulant was used and 28 days if CPDA-1 anticoagulant was used. Ideally a specialised blood storage fridge with temperature alarm should be used however a household fridge with low traffic is an acceptable alternative. It is important to note that all red blood cell products should be stored upright to maximise gas exchange and red blood cell viability.

Blood products – component therapy

VetsNow, 2013; Augusto et al., 2018; Gibson and Callan, 2018; Sturgess, 2019

Component therapy maximises the use of a single blood unit. One whole blood unit can be separated into two half units of packed RBCs and one unit of plasma. This can potentially benefit three recipients rather than one. The use of component therapy also reduces the potential transfusion reactions (e.g. volume overload) which can occur as only the required blood component is administered.

Packed red blood cells

Packed RBCs have a PCV of 70 – 80%. Some closed collection systems will have a nutrient solution such as SAGM to extend the shelf life however this will dilute the PCV to approximately 55-65%.

As with whole blood, pRBCs can be stored at 1-6°C for 21 to 28 days in CPD and CPDA-1 anticoagulants respectively. If a nutrient solution is added this can extend the shelf life up to 35 to 42 days depending on the anticoagulant used. There is some concern over formation of storage lesions with prolonged storage of RBC products. These storage lesions can increase recipient mortality and

increase the risk of multiple organ disfunction syndrome and sepsis. In UCDVH blood bank, RBC products from day 36 to 42 are reserved for emergency use only for this reason.

Packed RBCs can be used for anaemia due to haemorrhage, haemolysis or ineffective erythropoiesis.

Fresh Frozen Plasma

Fresh frozen plasma (FFP) is separated from whole blood and frozen within 24 hours of collection. It is stored at -18°C for up to one year. After one year it becomes frozen plasma.

FFP contains plasma proteins including all clotting factors. It also contains lipids and electrolytes. It can be used to treat clotting factor disorders including von Willebrand factor deficiency, disseminated intravascular coagulation, liver failure, vitamin K deficiency and *Angiostrongylus vasorum* (lungworm). FFP is not indicated for use in hypoproteinaemia due to the large volume that would be required to be administered to provide any beneficial effect. In addition there is no evidence of clinical benefit for the use of FFP in cases of pancreatitis.

Frozen Plasma

After one year of storage FFP becomes frozen plasma (FP). FP can be stored for a further four years (five years total). FP contains some plasma proteins including the vitamins K dependent clotting factors (II, VII, IX and X). It also contains lipids and electrolytes.

FP is indicated for use in cases of rodenticide toxicity. Note: Cryosupernatant is also rich in vitamin K dependant factors and would be a more appropriate choice for rodenticide toxicity as a smaller volume if required versus plasma however it is largely unavailable.

Blood typing

Day, 2012; Hale, 2012; VetsNow, 2013; Augusto *et al.*, 2018; Humm and Chan, 2020; PBBUK, 2023

Blood typing determines the presence of antigens on the surface of RBCs.

Dogs

In dogs the Dog Erythrocyte Antigen (DEA) system is used. The most well know antigen group DEA 1.0 has subgroups 1.1, 1.2, 1.3 and 1.0 negative. DEA 1.2 and DEA 1.3 are quite rare. Other antigen groups include DEA 3, 4, 5, 6, 7, 8 and the most recently identified group Dal. Not all DEA groups can be tested for, and some tests are only available in commercial laboratories.

There are no significant naturally occurring alloantibodies in dogs. The term 'universal donor' would describe a dog that is negative for all potential antigen groups. Given that 98% of dogs are DEA 4 positive and 99% are Dal positive, a true universal donor is very unlikely to be found.

DEA 1.0 is the most antigenic group and therefore the group that is most commonly tested for in practice prior to a transfusion. A number of point of care assays for DEA 1.0 are available. These include membrane diffusion tests such as *Canine QuickTest* by Alvedia and card style agglutination tests such as *RapidVet- H Canine* by DMS Laboratories. Visit the manufacturers' websites for 'how to' guides and helpful troubleshooting tips (*www.alvedia.com* and *www.rapidvet.com*).

So what blood type should be given?

In theory

DEA 1 positive blood → DEA 1 positive recipient

DEA 1 negative blood → DEA 1 negative recipient

However…

DEA 1 'weak' positive recipients should ideally receive DEA 1 negative blood to prevent alloimmunisation as they have been found to have fewer antigens on the RBC surface when point of care assay results were compared with laboratory testing methods.

We've run out of blood typing kits, what should we do?

If a dog has <u>never</u> received a transfusion previously then they can receive either DEA 1 positive or DEA 1 negative blood for their first transfusion. An EDTA blood sample should be taken from the recipient and stored for blood typing as a soon as possible. This sample can be stored for up to 5-7 days. The animal's blood type must be known if subsequent transfusions are required. It is not possible to accurately blood type an animal in the 90 day period following a blood transfusion.

Cats
In cats the AB blood group system is used.

Type A cats have mostly A antigens and a small amount of B antigens. Although uncommon, some type A cats also have a low titre of anti-B antibodies.
Type B cats only have B antigens but have a high titre of anti-A antibodies.
Type AB cats have equal quantities of A and B antigens. They do not have antibodies for either. Most domestic short hair and domestic long hair cats are type A. Type B is more prevalent in pedigree breeds. There is a newly identified antigen known as *Mik.* The prevalence of this antigen is unknown although some cats do have antibodies.

Cats (except type AB) develop naturally occurring alloantibodies after a few months as the maternally derived antibodies reduce. For this reason, there is no universal feline donor.

Point of care assays available for feline blood typing are similar to canine test kits.

So what blood type should be given?

Type A blood → Type A recipient

Type B blood → Type B recipient

Type AB blood → Type AB recipient

However, type AB cats are rare so it is unlikely that a type AB donor will be available. In this scenario, type A blood can be given but there is likely to be some reaction due to anti B antibodies that may be present in type A blood.

Type A blood should never be administered to a type B recipient as this will result in a severe acute haemolytic reaction which may be fatal. If type B blood is administered to a type A recipient, the reaction is likely less severe however the RBCs would only last 1-2 days. The half-life of correctly typed and crossmatched RBCs in cats is 30-38 days.

The prevalence of antibodies for *Mik* antigen is unknown. It is therefore gold standard practice to crossmatch prior to every feline transfusion. The presence of *Mik* antigen may explain why haemolytic reactions can occur in type-compatible transfusions when crossmatching has not been performed.

<u>Crossmatching</u>
Barnett, 2012; Gibson and Abrams-Ogg, 2012; Hale, 2012; VetsNow, 2013; Gibson and Callan, 2018; Humm and Chan, 2020

Crossmatching determines the presence of antibodies in blood. It is an in vitro test for potential transfusion reactions. These may be seen as agglutination or haemolysis. In dogs, agglutination is commonly seen while haemolysis is less common. Both agglutination and haemolysis are seen in

cats. Although a positive crossmatch can indicate that a transfusion reaction may occur, a negative crossmatch does not rule out a reaction so close monitoring during the transfusion is still essential.

Crossmatching can be performed either in house or at external laboratories. External laboratories perform a 'complete' crossmatch. This involved both major and minor crossmatching at 4°C, 37°C and room temperature as well as running the Coomb's test, used in the diagnosis of immune mediated haemolytic anaemia. The options for crossmatching in house include various commercial test kits, the rapid slide test and the tube test. If using commercial test kits, visit the manufacturer's website for 'how to' guides and troubleshooting tips.

Commercial test kits are more reliable for predicting haemolytic reactions. The rapid slide test and tube test are preferred for agglutination and haemolysis respectively although their results can be subjective and may detect incompatibilities not clinically relevant i.e. transfusion won't result in haemolytic reaction.

When should we crossmatch?
Crossmatching is required if it is more than 4 days since the animal's previous transfusion. It should also be performed if it is less than 4 days but there was a reaction to a previous transfusion. If an animal's transfusion history is unknown, crossmatching is advised. It is also recommended to crossmatch any animal that has previously had a litter.

In cats, the prevalence of the *Mik* antigen is unknown. Some cats have been found to have anti *Mik* antibodies. It is therefore gold standard to crossmatch cats prior to every transfusion, even if it is their first.

How to perform the rapid slide test

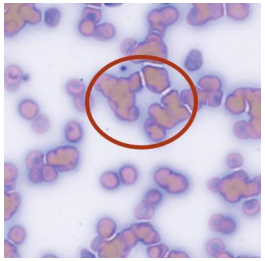
1. Centrifuge an EDTA and serum sample from both donor and recipient. This is where the crossmatching lines made during the collection stage can be used.
2. Mix 1 drop RBCs and 2 drops serum on clean labelled slides as follows:

- **Donor control -** donor RBCs + donor serum
- **Major XM -** donor RBCs + recipient serum
- **Minor XM -** recipient RBCs + donor serum
- **Recipient control -** recipient RBCs + recipient serum

3. Gently rock slides back and forth
4. Observe for macroscopic agglutination within 2 minutes
5. Observe microscopically for microscopic agglutination within 5 minutes

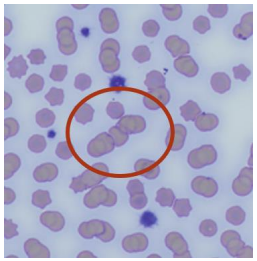
If agglutination is seen this is considered a positive crossmatch. A positive donor control slide likely indicates a handling error with the samples. A positive major crossmatch indicates that a severe acute haemolytic reaction is likely. A positive minor crossmatch indicates that the donor and recipient are incompatible however a reaction is less likely due to dilution in the recipient's blood. A positive recipient control may indicate autoagglutination. This can be seen in cases of immune mediated haemolytic anaemia. If this occurs, crossmatching should be repeated with other donor samples and the 'most compatible' donor blood transfused.

When performing crossmatching using this method it is important to be able to differentiate between agglutination and rouleaux. Agglutination is clumping of RBCs and indicates an incompatible crossmatch. Rouleaux is organised stacking of RBCs which can appear as agglutination macroscopically but is not of clinical concern.



← Agglutination

Rouleaux →



When to transfuse – 'Transfusion Triggers'

Gibson and Abrams-Ogg, 2012; Kohn and Weingart, 2012; Augusto *et al.*, 2018; Gibson and Callan, 2018)

A common question people may ask is 'at what PCV does an animal require a transfusion?'. There is however no specific PCV or single clinical sign that indicates a transfusion is required. The decision is based on an overall clinical assessment of the patient. This includes consideration of a number of factors.

- Chronicity of the anaemia
- Current PCV or haemoglobin concentration
- Ongoing losses e.g. active haemorrhage or haemolysis
- Regenerative ability
- Perfusion status e.g. increasing lactate trends
- Oxygenation status

Clinical signs to look out for, sometimes called transfusion triggers, include:

- Tachycardia
- Tachypnoea
- Lethargy or exercise intolerance
- Collapse
- Bounding pulses
- Weak pulses (cats)

Administration

Gibson and Abrams-Ogg, 2012; Kohn and Weingart, 2012; VetsNow, 2013; Augusto *et al.*, 2018; Gibson and Callan, 2018; Goggs and Hackner, 2018

How much should we give?

Achieving a normal PCV is not the aim of a blood transfusion. The aim is to improve the clinical signs by improving the oxygen-carrying capacity of the blood. The typical target PCV is 25-30%.

As a general rule, 2ml/kg of whole blood or 1ml/kg of packed RBCs will increase the patient's PCV by 1%. A more accurate formula can also be used.

$$\text{Volume (ml)} = \frac{85 \text{ (dog)}}{60 \text{ (cat)}} \times \text{bodyweight (kg)} \times \frac{\text{desired PCV} - \text{actual PCV}}{\text{donor PCV}}$$

The dose for plasma administration is 6-12ml/kg up to a maximum of 20ml/kg/24hrs.

How fast do we give it?

It is very important to start slowing when administering blood products. This allows time for potential reactions to be identified before a large volume of blood has been administered. It is recommended to start at 0.25-1.0ml/kg/hr for the first 15-30 minutes with continuous monitoring during this time. If no issues have been identified after the initial 30 minutes, then the administration rate can be increased to complete the total transfusion within 4 hours. This may be extended up to 6 hours if required but there is increased risk of bacteraemia after 4 hours.

If a patient is at increased risk of volume overload such as those with cardiac or renal disease, then the transfusion should be administered no faster than 3-4ml/kg/hr. With cases of chronic feline anaemia, it can be particularly challenging to balance the rate of administration with the risk of developing volume overload and congestive heart failure.

In an emergency such as haemorrhagic shock, the blood product can be administered as rapidly as necessary.

Gravity flow vs. fluid pump

Fluid pumps and their associated giving sets must only be used for blood product administration if specifically approved for this use by the manufacturer. Use of unapproved equipment can result in haemolysis of RBCs.

All blood products require a filter for administration. This can be either a blood giving set or an in-line filter. Be aware that many in-line filters require changing after a certain volume. Check the specific product being used.

Calculation example

12kg dog Current PCV: 15% Desired PCV: 25% Donor PCV: 42%

$$\text{Volume (ml)} = \frac{85 \text{ (dog)}}{60 \text{ (cat)}} \times \text{bodyweight (kg)} \times \frac{\text{desired PCV} - \text{actual PCV}}{\text{donor PCV}}$$

$$\text{Volume (ml)} = 85 \times 12\text{kg} \times \frac{25\% - 15\%}{42\%}$$

Total volume required = 243ml

1st 15 mins = 0.25ml/kg/hr
0.25ml/kg/hr x 12kg = **3ml/hr** ÷ 4 = **0.75ml**

2nd 15 mins = 0.5ml/kg/hr
0.5ml/kg/hr x 12kg = **6ml/hr** ÷ 4 = **1.5ml**

0.75ml + **1.5ml** = **2.25ml**

243ml - **2.25ml** = 240.75ml ÷ 3.5hrs = **68.8ml/hr**

Check it's safe!

68.8ml/hr ÷ 12kg = 5.7ml/kg/hr ✓ **safe rate if no cardiac/renal disease**

Setting up

Gloves should be worn while handling blood products to minimise contamination. Prior to use blood bags should be inspected for discolouration (purple/brown), clots and haemolysis. Discard if concerned.

Do we need to warm the blood?
Warming of blood products is only indicated for neonates, very small patients, and hypothermic patients. If required, blood can be left at room temperature for 30 minutes or placed in a sealed bag in a warm water bath. Ensure the water bath is less than 37°C as higher temperatures will damage the cells and proteins.

Can crystalloid IVFT continue?
Fluid therapy can continue during a blood transfusion if required. Citrate in the anticoagulant will chelate the calcium in the fluids so a second IV catheter should be placed. Take care with the overall volume (blood and fluids) being administered to the patient and monitor closely for signs of fluid overload.

Other considerations
No medications, unless essential, should be administered during a transfusion. Food should also be withheld. This is to ensure that potential reactions to medications or vomiting/regurgitation following eating are not misidentified as potential transfusion reactions.

Avoid disconnecting a patient from the administration set during a transfusion to minimise potential contamination.

Monitoring
Gibson and Abrams-Ogg, 2012; Proulx and Waddell, 2012; VetsNow, 2013; Gibson and Callan, 2018; Davidow *et al.*, 2021; Morris, Bloch and Brabson, 2021

Record baseline parameters just before starting a transfusion. Patients requiring a transfusion are likely unstable so parameters taken a few hours before may no longer be accurate. Parameters to monitor include:

- Mentation
- Rectal temperature
- Heart rate and rhythm
- Pulse quality
- Respiratory rate and effort
- Mucous membrane colour
- Capillary refill time
- Blood pressure (where possible)
- ECG (where possible)

Ideally continuous monitoring should be provided for the duration of the transfusion and 1 hour following completion. Where this is not possible, the patient should be monitored every 5 minutes for the first 30 minutes and then every 15-30 minutes.

In addition to monitoring patient parameters, ensure that the IV remains patent and if gravity flow is used then ensure the drip rate is correct throughout the transfusion.

When should we recheck the PCV?
This can be quite a controversial topic! Some literature will state that PCV should not be rechecked until 1 hour post transfusion to allow time for a fluid shift to occur. Others have found that checking PCV immediately after finishing the transfusion is just as reliable as checking it up to 4 hours post transfusion.

Checking the PCV immediately can give an indication of destruction if the plasma is pink and PCV is lower than expected. It also gives more time to administer additional blood products should they be required.

The PCV should also be checked again 12 and 24 hours after finishing the transfusion.

Transfusion reactions
Gibson and Abrams-Ogg, 2012; Hale, 2012; Kohn and Weingart, 2012; VetsNow, 2013; Gibson and Callan, 2018; Humm and Chan, 2020; Le Gal, Thomas and Humm, 2020; Martinez-Sogues et al., 2020; Davidow *et al.*, 2021; Yagi, 2021

A transfusion reaction is any undesired side effect of blood product administration. There are currently no veterinary definitions for transfusion reactions, so the human guidelines have been adapted.

Transfusion reactions are divided into immunological and non-immunological reactions. Immunological reactions are hypersensitivity reactions. They are categorised as type I (allergic), type II (cytotoxic) and type III (immune complex). Hypersensitivity reactions are less commonly seen with first exposure although they can occur. Non-immunological reactions can all be minimised with appropriate protocols for donor screening, blood collection, processing, storage and administration.

Type II (cytotoxic)
This is a reaction to foreign RBCs but should be avoidable with correct blood typing and crossmatching.

An acute haemolytic transfusion reaction is the most severe reaction type. This occurs when there are pre-existing antibodies and can be fatal. An example would be when type A blood is administered to a type B cat. The severity of the reaction depends on the amount of RBCs administered. This is why it is important to start a transfusion slowly.

The first clinical sign of a type II reaction is likely a increase in temperature of more than 1°C from baseline. Further investigation would reveal haemoglobinaemia and haemoglobinuria. If the reaction progresses it will result in hypotension, tachycardia (bradycardia in cats), tremors, vomiting and collapse.

If an increased temperature is identified, other potential causes must first be ruled out such as recovery from anaesthesia or external warming (See flowchart below).

A delayed haemolytic reaction can occur up to 21 days following a transfusion. This occurs when there were no pre-existing antibodies. The patient can be asymptomatic or may represent with pyrexia and jaundice with haemoglobinuria and a sudden drop in PCV found on further investigation. To confirm a delayed haemolytic reaction, repeat crossmatching using current plasma from the recipient. A positive crossmatch indicates a delayed reaction has occurred.

Type I (allergic)
This is an acute inflammatory response often mediated by donor immunoglobulins. Mild clinical signs may be seen initially including urticaria, pruritus, facial swelling, vomiting, diarrhoea +/- pyrexia. In severe cases anaphylaxis may occur resulting in haemodynamic collapse (hypotension), hypersalivation (cats), dyspnoea due to bronchoconstriction, and collapse.

Type I reactions should respond to antihistamine and corticosteroid administration.

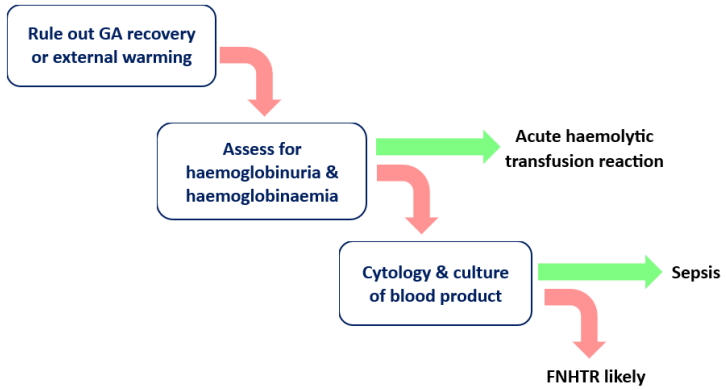
Type III (immune complex)
Type III reactions are reported in dogs following administration of human serum albumin, tetanus antitoxin, snake antivenom and incompatible plasma transfusions. They result in damage to blood vessels, synovial membranes, blood cells and the kidney. Clinical signs typically develop 1-3 weeks

post transfusion and include pyrexia, enlarged lymph nodes, lameness, joint swelling, neutropenia, anaemia, thrombocytopenia, and proteinuria. Treatment is symptomatic.

Sepsis
Sepsis is generally considered a delayed transfusion reaction although clinical signs may develop earlier. Signs include vomiting, diarrhoea, tachycardia, pyrexia, hypotension and haemolysis. If contamination is suspected during administration the transfusion should be stopped. Cytology should be performed on the blood product and a sample sent for culture.

Febrile non-haemolytic transfusion reaction (FNHTR)
This is defined as an increase in temperature of more than 1°C from baseline where all other potential causes have been ruled out. It is a diagnosis of exclusion. FNHTR is thought to be a reaction to WBCs and platelets.

If an increased temperature is identified during a transfusion, follow these steps:



Acute circulatory overload
This can occur when the administration rate is too rapid. Animals that are normovolaemic or have underlying cardiac or renal disease are at increased risk. Clinical signs include coughing, tachypnoea, dyspnoea and tachycardia but if severe, can progress to left atrial enlargement (LA:Ao >1.5), pulmonary oedema and pleural effusion. Thorax radiographs and echocardiogram can be used to identify these changes. Clinical signs should resolve with diuretic treatment such as furosemide.

Transfusion-related acute lung injury (TRALI)
TRALI is defined as an acute onset dyspnoea with hypoxaemia and hypoxia within hours of a transfusion. The pathophysiology is not fully understood, and it can often be misdiagnosed as circulatory overload. However, changes consistent with fluid overload do not occur with TRALI.

Hypothermia
Hypothermia can occur with rapid administration of blood products. There is an increased risk in small patients and neonates.

Hypocalcaemic tetany (citrate toxicity)
Hypocalcaemic tetany, also referred to as citrate toxicity, results from chelation of calcium by the citrate in the anticoagulant. It should be avoidable if the correct blood to anticoagulant ratio is used during the donation. Citrate is metabolised by the liver meaning that patients with marked liver disease are at increased risk. Clinical signs include hyperaesthesia, muscle tremors, vomiting,

arrythmias, collapse and seizures. ECG changes may include tachycardia or bradycardia, prolonged S-T segment, prolonged Q-T segment, and wide T waves.

Other non-immunological transfusion reactions include:

- Dilutional coagulopathy
- Thrombosis
- Hyperammonaemia
- Hyperkalaemia
- Air embolus
- Infectious disease transmission

What should we do if we suspect a transfusion reaction?
Gibson and Abrams-Ogg, 2012; Kohn and Weingart, 2012; VetsNow, 2013; Davidow *et al.*, 2021

1) Stop the transfusion
2) Alert the vet
3) Perform a full patient assessment. This should include TPR, mucous membrane colour, CRT, chest auscultation, blood pressure measurement (where possible), ECG (where possible) and sampling of urine and blood to assess for haemolysis.
4) Depending on the findings of the physical examination and the suspected reaction type, the vet may prescribe medical treatment to be administered.
5) The vet may choose to restart the transfusion. If restarting, reduce the administration rate to 25-50% of the previous rate. The transfusion should only be restarted if there is no evidence of anaphylaxis or haemolysis and the clinical signs have improved.

Should we premedicate?
There is no proven benefit to premedicating animals with antihistamines, antiemetics, corticosteroids or antipyretics prior to administering a blood transfusion. Premedicating may mask the early signs of a transfusion reaction meaning that the reaction has progressed to a more severe state before it is detected. In addition, many transfusion reactions can be minimised or completely avoided with appropriate protocols.

Autotransfusion
Gibson and Abrams-Ogg, 2012; VetsNow, 2013; Higgs *et al*., 2015; Yagi, 2021

Autotransfusion is the collection and reinfusion of a patient's own blood. There are a number of different methods for this but the one most often discussed involves collecting blood from a body cavity for example with haemoabdomen or haemothorax.

There are many advantages to using autotransfusion including avoiding exposure to allogenic blood, preventing the formation of antibodies. There are also fewer potential side effects such as immunological transfusion reactions and transmission of infectious diseases. Autotransfused blood is available immediately and does not require typing or crossmatching. It also reduces demand on blood bank supply.

If performing autotransfusion, aseptic technique is essential and as with any blood collection, contact with air should be minimised to prevent haemolysis. The addition of anticoagulant is not required if the blood has been in the body cavity for more than one hour as by this time clotting factors have already been consumed and fibrinolysis has occurred. If the blood is collected during rapid fresh haemorrhage, then anticoagulant should be added before reinfusion.

There are a number of potential complications associated with autotransfusion. Blood that has been sitting in a cavity for more than 4-6 hours should not be reinfused as there is a higher risk of microbial contamination. If enteric contamination is suspected, it is recommended to avoid reinfusion of this blood. However, a paper by Higgs *et al*. (2015) reports no increase in mortality with

reinfusion of contaminated blood if less than 40% total blood volume is administered or where more than 40% TBV is administered alongside broad-spectrum antimicrobials.

Dissemination of malignancy is often of big concern however studies in people have found no increased risk of metastasis or a poorer prognosis. It is however recommended to use a leucocyte reduction filter to minimise the risk.

Dilutional coagulopathy is another potential complication of autotransfusion, particularly as the reinfused blood will not contain clotting factors. It is recommended to administer a FFP transfusion with autotransfusion of more than 50ml/kg.

Considering these potential complications, autotransfusion should be reserved for life threatening circumstances only.

Xenotransfusion

VetsNow, 2013; Yagi, 2016, Le Gal, Thomas and Humm, 2020; Taylor *et al.*, 2021; Deschamps, Abboud and Roux, 2022

Xenotransfusion is the transfusion of blood from one species to another. Administration of canine blood to cats is the most common use of this technique. Xenotransfusion will result in a delayed haemolytic reaction one to seven days following administration and can only be performed once in the animal's lifetime. Subsequent xenotransfusions are likely to be fatal. Crossmatching prior to xenotransfusion has been found to be unreliable for predicting incompatibilities.

Xenotransfusion should not be common practice and a number of criteria must be met before its use is considered.

- There must be no allogenic blood available
- The patient must be at risk of imminent death or irreversible ischaemia damage and expected to benefit from short term oxygen carrying capacity.
- They must never have received a xenotransfusion previously
- The owner must understand the potential risks of xenotransfusion and provide informed consent

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