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International Society of Feline Medicine Consensus Guidelines on the collection and administration of blood and blood products in cats

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Abstract

Practical relevance: Blood and blood products are increasingly available for practitioners to use in the management of haematological conditions and can be lifesaving and therapeutically useful for patients with anaemia and/or coagulopathies. It is important for feline health care that donors are selected appropriately, and transfusions of blood or blood products are given to recipients that will benefit from them. Complications can occur, but can be avoided with careful donor management, understanding of blood type compatibility, recipient selection and transfusion monitoring.

Clinical challenges: Feline blood transfusion can be a lifesaving procedure but also detrimental to donor and recipient without precautions. Cats have naturally occurring alloantibodies to red cell antigens and severe transfusion reactions can occur with type-mismatched transfusions. Blood transfusions can also transmit infectious agents to the recipient, so donor testing is essential. Finally, donors must be in good health, sedated as appropriate and blood collected in a safe and sterile fashion to optimize the benefit to recipients. Transfusion reactions are possible and can be mild to severe in nature. Autologous and xenotransfusions may be considered in certain situations.

Evidence base: These Guidelines have been created by the authors and The International Society of Feline Medicine (ISFM) based on available literature. They are aimed at general practitioners to provide a practical guide to blood typing, cross-matching, blood collection and administration.

Introduction

Although feline blood transfusions are infrequently performed in primary care veterinary practice, they can be lifesaving [1, 2]. Availability of donors has limited the utility of this technique, but with growth of blood banks providing access to feline blood, the procedure may become more routine. It is important that veterinary practitioners select appropriate recipients and donors (in-clinic or stored blood) and administer blood correctly and with monitoring to mitigate the risks. These guidelines are written to provide practical information for practitioners on blood types and cross-matching, indications for transfusion, donor management, recipient preparation and monitoring and potential complications.

Feline blood types

Alloantigens

Blood types arise due to the presence of genetically determined antigenic markers on the surface of red blood cells (RBCs). Blood type antigens are alloantigens as they exist in alternative (allelic) forms in different cats and can induce an immune response when one blood type is transferred to a cat that lacks it. One blood group system, the AB system, has been extensively defined in cats. Within the AB blood group system there are three blood type phenotypes, namely type A, type B and type AB:

- Blood type A is common – N-glycolylneuraminic acid is the alloantigen on the RBC surface
- Blood type B is less common, but common in some pedigree breeds e.g. British Shorthair, Birman, Devon Rex – N-acetylneuraminic acid is the alloantigen on the RBC surface
- Blood type AB is rare – N-glycolylneuraminic acid and N-acetylneuraminic acid are the alloantigens on the RBC surface.

Blood type prevalence varies geographically (see Table 1). Type A is the most common worldwide and in some breeds 100% of cats are believed to be type A (e.g. Siamese [3]). The

prevalence of type B is much lower than type A but it has been reported to be as high as 36% in non-pedigrees in Australia [4] and some breeds can contain high numbers of type B cats (especially the British Shorthair). Type AB is less common. Blood typing is essential to avoid what can be fatal transfusion reactions.

Table 1: Blood types reported in different geographic locations in different breeds of cat in published studies.

Country source of data (reference)	Breed	No. of cats	Type A %	Type B %	Type AB %
UK [5]	Non-pedigree	139	87.1	7.9	5.0
	British shorthair	121	39.7	58.7	1.6
	Birman	24	62.5	29.2	8.3
	Persian	17	88.2	11.8	0
	Other pedigrees	45	77.8	6.7	15.5
UK [3]	Non-pedigree	105	67.6	30.5	1.9
	Siamese	13	100.0	0	0
	Other pedigrees	38	76.3	21.1	2.6
UK [6]	Bengal	100	100.0	0	0
Denmark [7]	Non-pedigree	105	98.1	1.9	0
	Persian	56	96.4	3.6	0
	British shorthair	30	66.7	33.3	0
	Abyssinian	20	100	0	0
	Other pedigrees	33	90.9	9.1	0
Australia [4]	Non-pedigree	355	62	36	1.6
	Siamese	12	100	0	0

Country source of data (reference)	Breed	No. of cats	Type A %	Type B %	Type AB %
	Devon Rex	70	45	54	1.4
	British shorthair	8	38	62	0
New Zealand [8]	Non-pedigree	245	70.6	13.9	0.8
France [9]	Non-pedigree	320	83.8	14.4	1.9
	Pedigree	37	89.2	10.8	0
Central Italy [10]	Non-pedigree	483	89.8	7	3.1
North Italy [11]	Non-pedigree	233	91.0	5.2	3.8 ~~1~~
South Italy [11]	Non-pedigree	215	77.2	12.1	10.7
Italy[12]	Ragdoll	61	77.1	4.9	18.0

Alloantibodies

In contrast to dogs, cats can possess naturally occurring alloantibodies against the 'foreign' (non-self) alloantigen that they are lacking. These alloantibodies will recognise the alloantigens of another cat. Kittens develop these antibodies at 6-8 weeks of age. In the UK, for example, over 70% of type A cats have anti-B alloantibodies [13], which are mostly present at low concentrations, whilst all type B cats have anti-A alloantibodies, often present in high concentrations. In a report from the USA all type A cats had anti-B alloantibodies [14]. Type AB cats never have alloantibodies to either type A or type B antigens. The reaction between the blood type alloantigens and any existing alloantibodies is observed during cross-matching donor and recipient blood.

Alloantibodies are responsible for potentially fatal feline blood transfusion reactions that can arise when cats undergo their first blood transfusion, as they are already present in the cat's circulation, ready to destroy RBCs of a different blood type phenotype. These alloantibodies are also responsible

for neonatal isoerythrolysis [15, 16], a cause of neonatal death. The severity of a blood transfusion reaction also depends on the quantity (i.e. higher titres or concentrations worse) and nature (e.g. strongly agglutinating) of any alloantibodies present in the recipient (or donor).

Donor and recipient cats must always be blood typed before transfusions. Type-compatible blood should be administered, i.e type A blood is given to type A cats, type B blood to type B cats, and type AB blood to type AB cats if possible. For type AB cats, if type AB blood is not available, type A blood (or ideally just the type A RBCs following separation) may be given

BOX OUT START

Blood Typing (Phenotyping)

- Blood typing can be performed by submitting anticoagulated blood to a commercial laboratory or by using an in-clinic test kit.
- Different kits are available for in-clinic feline blood typing; examples useful for general practitioners include RapidVet-H cards (DMS Laboratories Inc, Flemington, NJ, USA) based on agglutination (Figure 1a and Figure 1b) [17], RapidVet-H immunochromatographic (IC) tests (DMS Laboratories) (Figure 1c) and the QuickTest A**+**B (Alvedia, Limonest, France) (Figure 1d to Figure 1h) [17], also based on IC methodology. The Lab.Test A+B (Alvedia) is similar to the QuickTest A+B but can be run on multiple (up to 20) samples and requires a microplate, pipette and test tube to be provided by the user. A gel tube in-clinic blood typing kit is also available (Rapid Vet-H Gel, DMS Laboratories Inc.) that relies on agglutination; this method includes a step that requires use of a centrifuge.
- One study [18] found that the in-clinic QuickTest A+B performed slightly better than the RapidVet-H card test, and may be more reliable in cats with autoagglutination, but the new RapidVet-H IC test also appears to be reliable [19]. A more recent publication, focusing on the Lab.Test A+B found it to outperform the RapidVet-H cards [20]. The study also confirmed that the QuickTest A+B performed

well on blood that had been stored in the fridge and at room temperature. A recent study [21] confirmed that the Lab.Test A+B was very reliable, performing as well as flow cytometry in the blood type phenotyping of a sample of 49 cats (34 A, 13 B and two AB).

- The QuickTest A+B is a migration IC methodology test strip cartridge (Figure 1d to Figure 1h) that uses monoclonal antibodies (further details not given) to differentiate the blood antigens, whereas the RapidVet-H cards use a murine monoclonal antibody as the anti-A reagent and a lectin from *Triticum vulgaris* as the anti-B reagent. These different reagents may explain why the RapidVet-H cards wrongly describe some blood types, as one study [20] showed that the cards were found to sometimes mistype blood type AB cats as type B and occasionally blood type A cats as type AB.
- An automated method for blood typing is available (QuickVet® Feline Blood Typing Test™), for use with the QuickVet® Analyzer (Zoetic ApS, Denmark). The QuickVet® Diagnostic System consists of an analyzer and single use disposable test cartridges based on capillary driven microfluidic technology.
- If a sample to be blood typed is from a cat with severe anaemia (packed cell volume [PCV] <14%), the RBCs can be concentrated by centrifugation of the blood (2-3 mins, remove some of the plasma supernatant and resuspend the remaining RBCs in the remaining plasma supernatant) to get a higher concentration of RBCs, and repeat the test; this can be useful if insufficient RBCs reach the top of the test strip due to the low number present in a very anaemic sample. In a similar way, if agglutination of the sample precludes movement of the RBCs along the strip, the RBCs can be washed in phosphate buffered saline and the test repeated.
- One study [18] found that some feline leukaemia virus (FeLV) infected anaemic cats were mistyped using multiple blood typing methods.
- Cats with less common blood types (type AB and type B) may be mistyped by commercially available blood typing in-clinic methods and results should ideally be confirmed at an external laboratory by a method that uses antibody testing or genetic screening. However, a ‘back typing’

technique for antibody screening can be used in-clinic where type B is suspected: EDTA blood from the suspected type B cat is centrifuged at 1000 *g* for two minutes; 30 µl plasma is removed and mixed with 15 µl EDTA blood collected from a known type A cat on a glass microscope slide and observed for agglutination; if positive this confirms the B blood type, as the plasma of the type B cat contains alloantibodies that agglutinate the type A RBCs.

BOX OUT END

Non-AB feline blood groups

Evidence published in 2007 suggested that other, non-AB, blood group systems existed in cats because blood transfusion reactions have occurred in cats given AB-matched blood transfusions. A study from the USA [22] reported the absence of a novel feline RBC antigen named Mik in three of 65 type A cats tested, in association with the presence of naturally occurring anti-Mik alloantibodies, which mediated a clinically significant transfusion reaction despite the blood donor and recipient cat being AB-matched. However, one study in UK cats [23], and another in German cats [24], found no evidence of anti-Mik alloantibodies in the cats sampled in those studies, as no positive cross-matches between AB-matched blood samples were found in transfusion naïve cats. Other studies [21, 25, 26] have, however, documented the presence of positive cross-matches between AB-matched blood samples, suggesting the presence of non-AB blood group systems, although the clinical significance of these is not always clear and tests for the Mik and other RBC antigens are not available commercially. In the most recent study [27], type A cats were evaluated for naturally occurring non-AB alloantibodies by cross-matching and at least 7% of the type A cats had incompatible cross-matching, documenting the presence of naturally occurring alloantibodies. Five distinct RBC antigens were hypothesized to be present outside of the AB blood group system and one of these was thought to correspond to the previously described Mik antigen.

Cross-matching

Cross-matching can be performed in-clinic or at an external laboratory; the latter is ideal as the test is complex and takes time but obviously this results in a delay in obtaining results. In-clinic cross-matching kits are available. Based on all existing studies, the clinical effectiveness and need of cross-matching before a first transfusion remains controversial, however, given that transfusion-naive cats may have incompatible major cross-matches, cross-matching, as well as blood typing, is recommended by some before each transfusion where possible in cats [27-29], although others have acknowledged that the strength of evidence for this is weak [30]. A recent Australian study [31], questioning primarily general practitioner vets, reported that compatibility testing, including cross-matching, before feline blood transfusions was commonly performed; cross-matching alone in 26%, blood typing alone in 27.6% and both in 34.1% of respondents.

In emergency situations cross-matching may not be possible. However, it is strongly recommended that cross-matching is performed before a transfusion when the recipient has an unknown transfusion history or has had a previous transfusion reaction or has received a transfusion two or more days previously. The two day timeline stipulated is because incompatibilities have been identified by major cross-match testing as early as two days after a first whole blood cross-match compatible transfusion [24].

BOX OUT START

How to perform in-clinic cross-matching

Cross-match methodology

- 1 ml EDTA blood tube and a 1 ml serum (plain) tube obtained from each of the donor & recipient. Label tubes.
- Centrifuge (3,000 rpm for 5 minutes) & separate plasma & serum from RBCs in both tubes. Discard the plasma if not required for other diagnostic investigations. Store serum in a separate tube & label.

- Wash EDTA RBCs - add 2-3 mls of normal saline solution to the RBCs, mix gently & centrifuge (3,400 rpm for 1 minute) & remove the supernatant saline. Repeat twice.
- After the 3rd wash, decant the supernatant & resuspend the RBCs with saline to give a 4% RBC suspension (0.2 mls RBCs with 4.8 mls saline).
- Label four tubes & place the following into each:-

Major cross-match	1 drop recipient serum & one drop donor RBC suspension
Minor cross-match	1 drop donor serum & one drop recipient RBC suspension
Recipient control	1 drop recipient serum & one drop recipient RBC suspension
Donor control (optional)	1 drop donor serum & one drop donor RBC suspension

- Incubate the tubes for 15 minutes at 37°C
- Centrifuge the tubes for 15 seconds (3,400 rpm)
- Read the tubes macroscopically and microscopically:

Macroscopic cross-match reading

In a compatible reaction there should be no clumping nor haemolysis nor agglutination present; when the tubes are gently rolled and rotated, RBCs should be able to float off freely from the centrifuged "pellet" of RBCs. The supernatant should be free of haemolysis (Figure 2).

Microscopic cross-match reading

A drop of the RBC/serum mixture from the tubes is placed on a microscope slide, cover slipped & viewed microscopically (within 60s of placing the blood on a microscope slide). The RBCs should be visible as individual cells & not in clumps. Rouleaux formation, where RBCs stick together as stacks of coins, can look macroscopically like agglutination but rouleaux formation (Figure 3a) can be differentiated from agglutination (Figure 3b) on microscopic examination. Rouleaux formation is not a clinical concern but agglutination indicates an incompatible cross-match reaction.

NB. Others have modified the above protocol to use plasma, rather than serum (as both can be used for cross-matching [32]), along with a 3-5% suspension of RBCs in phosphate buffered saline (rather than

saline), and to not perform the donor control but just the recipient control test [24]. The study describing this modified method also reported that cross-matching could be done with as little as 250 µl (0.25 mls) of blood, which is encouraging as minimising the amount of blood taken from anaemic cats is important.

How to perform routine in-clinic cross-matching using kits

In-clinic cross-match kits are available such as the RapidVet-H Major and Minor Cross-match kits (DMS Laboratories), which use serum, and the QuickTest XM EmMatest test or Lab.Test XM (both Alvedia), which use plasma. All kits can be used to perform both the major and minor cross-matches. A feline Gel.Test (Alvedia), which uses plasma, is also available for cross-matching, but this requires the mandatory use of a specific centrifuge. With all such kits, instructions should be carefully followed, but studies have yielded variable results with different methods and it is difficult to compare results [27].

BOX OUT END

BOX OUT START

How to perform emergency cross-matching

If cross-matching is required in an emergency, the following method can be used which omits the washing of RBCs described above:

- EDTA is collected from donor and recipient then centrifuged to separate plasma and RBCs
- Major cross-match: 2 drops of recipient plasma and 1 drop of donor RBCs (so ~ major cross-match) are then placed on a glass microscope slide and the slide examined microscopically for agglutination between 1 and 5 minutes, as described above. Agglutination must be differentiated from rouleaux formation microscopically as described above for routine cross-matching
- Controls should also be performed using recipient plasma and RBCs and, if possible, donor plasma and RBCs, and examined microscopically

- Note that drying out of blood on the slide can result in rouleaux formation but this takes > 5 minutes to occur

BOX OUT END

Selecting a donor

Infectious disease screening

Risks from transfusion include the transmission of infectious agents from donor to recipient, which can be avoided largely through donor selection and screening. Such a process must vary between countries/regions and practices and will depend on locally endemic diseases, the practicalities in selecting donors that do not carry them and the cost/availability of screening compared to the risk of not having any available blood.

In addition to the considerations above, individual donor factors such as indoor/outdoor status, ectoparasite control and time of last testing will influence the likelihood of infectious agent presence. These will in turn determine which agents should be screened for, the most appropriate methodology and also the required frequency, which may be deemed to be annually, or at the time of every blood donation if there is a high risk of novel exposure or intermittent circulation of a pathogen [33,34].

Core infectious agents to test blood donors for

Haemotropic Mycoplasmas

The pathogenic *Mycoplasma haemofelis* can be transmitted by blood products, although it appears to be inactivated during storage of whole blood for one week [35]. Blood smear evaluation is insensitive for diagnosis and also lacks specificity and thus the diagnostic test of choice for screening blood donors is PCR. PCR testing for '*Candidatus* Mycoplasma haemominutum' (which may survive for a week in stored blood [35]) and '*Candidatus* Mycoplasma turicensis' can also be considered, but as these agents

are of lower pathogenicity [36], donors may not be excluded if positive for these organisms if the donor pool is very limited. Ideally, however, cats should be negative for these agents too.

Bartonella spp.

Numerous *Bartonella* species can be present in the blood of cats and have been associated with several clinical conditions [37]. *Bartonella henselae* has been shown to survive in stored blood [38]. Donors should ideally be serology and PCR negative for *Bartonella* spp. but seropositivity may be common in endemic areas and sensitive testing methods are not always readily available. Seropositive cats may have intermittent bacteraemia [39] but can be considered for donation if PCR negative.

Feline leukaemia virus/feline immunodeficiency virus (FIV)

Both FeLV and FIV can be transmitted by blood transfusion and thus donor cats need to be negative for both of these agents [40]. Antigen tests for FeLV are commonly available, such as ELISA or IC in-clinic tests, but proviral DNA testing (by PCR) should be performed, if at all possible, as transmission of FeLV infection via blood transfusion has been documented by FeLV provirus positive, antigen negative blood (e.g. PCR positive, ELISA negative) [41]. Antibody tests for FIV are commonly available as ELISA or IC in-clinic tests too and cats should be negative for FIV antibody before being used as donors. Although certain FIV antibody tests may be able to differentiate true FIV infected cats from those cats that have been vaccinated for FIV (in those countries where FIV vaccination is, or has been, available for use in cats), it is recommended that only FIV antibody negative cats are used as blood donors due to the potential for confusion in interpretation of test results [42].

Additional agents to consider testing blood donor cats for

Anaplasma spp.

Anaplasma phagocytophilum can cause illness in cats, can be transmitted by blood inoculation, and exist as a persistent infection [43, 44]. Donor cats with potential tick exposure (particularly *Ixodes ricinus*)

from endemic areas should ideally be screened by serology and PCR, if available. Seropositive, PCR-negative cats may be used in endemic regions if no other suitable donor can be identified. Infection with *Anaplasma platys* has been documented in cats [43] and so cats living in areas endemic to *Rhipicephalus* spp. ticks should be screened for this agent by PCR.

Cytauxzoon felis, Babesia felis, Ehrlichia canis, Leishmania infantum and *Neorickettsia risticii*

These are all vector-borne agents[43-49], which may be transmittable by blood products. Although pre-donation physical examination and blood smear examination should minimize transmission risk, the optimal standard would be to have cats negative by PCR, if available, for these agents in blood donor cats living in endemic areas.

Other infectious agents

Screening for coronavirus, *Rickettsia felis* and *Toxoplasma gondii* is not recommended for donor cats. Transmission of these agents by blood products has not been documented.

Donor characteristics

Donors should be healthy, between one and eight years old and with a lean body weight above 4.5kg. They should be of calm temperament and easy to handle to reduce sedation requirements. They should be current with all applicable vaccinations and parasite control and ideally live indoors without recent introduction of other cats to the household, to reduce their exposure to infections. No other recent medications should have been given and they should never have received a transfusion nor be currently pregnant. Cats that have previously had a litter may still be donors. Annual health screening of potential blood donors, including haematology and serum biochemistry profiles, is recommended. In addition, a complete history and physical examination, as well as determination of PCV or haemoglobin concentration, should be completed before each blood collection.

Occult cardiomyopathy is excluded with echocardiography by some clinicians prior to allowing cats to join a donor program, given that up to 30% of cats with cardiac disease will not have a murmur [50]. However, others would omit echocardiography and exclude cats with murmurs, gallops or arrythmias from donation, or perform quantitative NT-proBNP serum testing, which has been shown to reliably discriminate normal cats from those with occult cardiomyopathy [51].

BOX OUT START

Donor selection criteria

- Between one and eight years of age
- Lean body weight above 4.5kg
- Calm temperament
- Up to date with relevant vaccination, worming and ectoparasite treatments
- No current medications
- Ideally living indoors
- No history of having received a transfusion
- Annual haematology and serum biochemistry screening within reference intervals
- FeLV antigen and FIV antibody testing negative (can be done in-clinic) and FeLV provirus PCR negative
- Haemotropic mycoplasma & *Bartonella* spp. PCR testing negative
- Negative for vector borne pathogens in endemic areas

BOX OUT END

Indications for blood transfusion

Due to restrictions on storage of animal blood, most cats in the UK and in Europe in need of a blood transfusion will receive fresh whole blood (FWB), which contains all of the blood components: RBCs, platelets, coagulation factors, and plasma proteins. However, in countries where blood storage is available, feline FWB donations are processed into packed red blood cells (pRBCs) and fresh-frozen plasma (FFP) components. The use of these blood components has many advantages including extending resources, allowing specific replacement therapy, and potentially reducing the number of transfusion reactions.

RBC products

Red blood cell products, namely FWB and pRBCs, increase the oxygen-carrying capacity of the blood and thereby improve oxygen delivery to tissues. While FWB and pRBC transfusions can be used interchangeably in most anaemic cats, administration of pRBCs would be preferable to FWB to those, for example, with underlying cardiac disease to help avoid circulatory overload, and depending on the cause of the anaemia (e.g. if due to haemolysis rather than blood loss). The decision to administer a RBC product transfusion is frequently based on measurement of the cat's PCV, haematocrit, or haemoglobin concentration. However, a "transfusion trigger" or threshold PCV below which a RBC transfusion is administered has not been clearly defined in human or veterinary medicine, and accompanying clinical signs are very important to consider in deciding if a transfusion should be considered. In two recent studies involving RBC transfusions in more than 265 cats, the pre-transfusion PCV was 15% (median value [25]) and 17% (mean value [26]), with a range of 5-40%. In some cats with peracute blood loss and hypovolaemia, RBC transfusions may be indicated even though their PCV is normal. These patients will predictably develop a low PCV following fluid resuscitation with asanguineous fluids.

BOX OUT START

The decision to transfuse RBC products is based on several factors in addition to PCV, including the onset of anaemia (if acute in nature, there may be more of a need compared to chronic onset anaemia), presence of ongoing RBC losses and, most importantly, the clinical signs of the patient. Tachycardia, bradycardia, bounding peripheral pulses, collapse, lethargy, and weakness are all signs that should prompt consideration of RBC transfusion.

BOX OUT END

In approximately 5-25% of cats, ineffective erythropoiesis and blood loss are the most common general causes of anaemia reported in cats receiving RBC transfusions, with haemolysis noted less frequently [25, 26, 29]. Underlying conditions frequently associated with development of non-regenerative anaemia in cats, and the potential need for a RBC transfusion, include chronic kidney disease, lymphoma, systemic inflammatory disease, infectious diseases, and bone marrow disorders [52] and chronic unspecified diseases [29]. An often-overlooked factor contributing to development of anaemia in hospitalized critically ill cats is repeated phlebotomy for blood sampling, with 74% of non-anaemic cats developing anaemia during an ICU stay in one study [53]. In this study cats that required a pRBC transfusion had significantly more daily blood samples taken (median 3, range 1–6) than cats that did not require a transfusion (median 2, range 1–4).

Plasma products

Plasma separated from RBCs within eight hours of blood collection is referred to as *fresh plasma*, but in countries where stored veterinary blood products are available, fresh plasma is more often frozen after preparation and stored (-20 to -30°C) for up to one year; this type of plasma is referred to as *fresh-frozen plasma* (FFP). Fresh plasma and FFP contain haemostatic proteins (coagulation factors, von Willebrand factor, anticoagulant proteins, and fibrinolysins), albumin and immunoglobulins. The main indication for use of fresh plasma or FFP is bleeding due to inherited or acquired coagulopathies, but its use has also been reported in cats with hypotension, liver disease, neoplasia

and sepsis [54]. Although the benefit of prophylactic administration of plasma to cats with a coagulopathy (but not showing clinical signs of bleeding) undergoing an invasive procedure is unclear, it was reported to be the main reason for FFP transfusions in cats in another study [55]. Anticoagulant rodenticide toxicity is uncommon in cats compared to dogs, but may occur after consumption of poisoned prey, and FFP as well as FWB may be included in the treatment protocol [55-57].

Hereditary haemostatic disorders are diagnosed infrequently in cats. There are two case reports of type 3 von Willebrand disease (VWD) [58, 59] and sporadic reports of haemophilia A and B ([55, 60, 61]) causing bleeding in cats. Plasma would be appropriate to provide replacement of von Willebrand factor in cats with VWD or factor VIII or IX in cats with haemophilia A or B, respectively, experiencing bleeding, though FWB would be an alternative if fresh plasma or FPP was not available or the cat was also anaemic.

The effect of plasma on colloid osmotic pressure is less than that of synthetic colloids, and the use of plasma for volume expansion is not recommended [62].

Platelet products

Due to technical challenges associated with preparing platelet-rich plasma from a small volume feline FWB unit, cats in need of a platelet transfusion generally are administered FWB, although this will not provide adequate platelets to correct thrombocytopenia. There are few indications for platelet transfusions in cats, but include uncontrolled or life-threatening haemorrhage (e.g. pulmonary haemorrhage) with thrombocytopenia or thrombopathia, and possibly massive transfusion (rare but is when a high number of pRBCs have been given, which can cause by a dilutional effect on the recipient's clotting factors and platelets). While platelet disorders are uncommon in cats, primary immune-mediated thrombocytopenia can lead to severe blood loss anaemia, which can be managed with FWB transfusions [63]. Cats with bleeding secondary to a

thrombopathia typically require administration of functional platelets (for practical reasons in the form of FWB) to control bleeding [64].

Xenotransfusion

Xenotransfusion is defined as the transfer of blood from one species to another. Successful administration of whole blood or pRBCs from dogs to cats has been documented and can be performed if absolutely necessary and only as a single, one-off transfusion [65, 66]. In some circumstances, dog blood may be more readily available than cat blood, and available in larger volumes, leading to its occasional use [31]. Potential indications for xenotransfusion include previous transfusion reaction to feline blood products, insufficient time to blood type the recipient, non-availability of suitable feline blood products in sufficient quantities or financial constraints. Xenotransfusion is mainly used for short-term stabilisation of an anaemic cat, allowing time for investigations or to obtain compatible feline blood or time for endogenous erythropoiesis to correct the anaemia [65-68] with or without appropriate treatment. Typically, 30-50 mls of canine blood is administered using the same administration rates (see later) as feline blood.

Antibodies to donor canine RBCs are detected 4-7 days following transfusion of canine blood into cats [67], resulting in destruction of donor RBCs and a late haemolytic reaction and hence a shorter life span of the donor canine RBCs compared to the life span of appropriately typed feline RBCs (30 days [69]). Subsequent repeat transfusion of canine blood to the cat will result in a severe transfusion reaction, anaphylaxis and likely death [65]. Reported short-term complications following xenotransfusion are similar to cat to cat transfusions (allotransfusions), with minor febrile non-haemolytic transfusion reactions seen in 12% of cases [68]. A severe acute anaphylactic transfusion reaction immediately upon administration of canine whole blood to a transfusion naïve cat has been reported (Korman, personal communication). Delayed haemolysis, often manifesting as icterus, occurs in 64% of cats at a median of 2 days (range of 1 to 6 days) after transfusion [68], meaning the benefits of xenotransfusion are short

lived compared to allotransfusion. Pre-xenotransfusion cross-matching results do not appear to predict the development of transfusion reactions[67, 68]. In one study [68] the long-term outcome of cats given xenotransfusions appeared to be associated with their primary disease and those that recovered appeared to have no notable adverse effects that could be directly attributed to xenotransfusion.

Chemical restraint of the donor for blood transfusion

It is possible to perform blood collection in conscious cats with a skilled veterinary care team; however, these patients must be cooperative and blood donation may be a negative experience for donors. Movement during donation and signs of anxiety have been reported in conscious cats much more often than in sedated cats [70]. Additionally, stress produced by handling may affect the cellular and chemical composition of the blood (e.g. hyperglycaemia) [71]. Therefore, chemical restraint or general anaesthesia is now commonly used for both in-clinic and client-owned feline donors. The choice of a short-term (30 minutes) protocol for chemical restraint will avoid an uncomfortable experience for the cat and failed, repeated interventions that could produce injuries to the veterinary care team. It will also influence owner satisfaction with the donor experience [72].
Chemical restraint for feline blood donors is no different to any other anaesthetic procedure in the sense that preoperative examination and appropriate fasting (6 hours) are mandatory. An anaesthetic plan, including monitoring and careful choice of dosage regimens, is required. The use of local anaesthetic creams (see Figure 4) and pheromones may be part of the overall management of the patient to help reduce stress.

The intravenous route of administration is often preferred due to the rapid onset of action and the use of lower doses of anaesthetic agents when compared with the intramuscular and subcutaneous routes. Several studies have reported the feasibility, and effects, of different drug combinations on major blood analytes in cat donors (see Table 2). Overall, each protocol has its unique advantages and disadvantages. Ideally, the drug combination should have a short onset with adequate depth

and duration of action and include a smooth and rapid anaesthetic recovery with minimal cardiorespiratory depression on the donor. The choice will be also dependent on drug availability and the familiarity of the veterinary care team with the protocol. Eye lubricant should be applied to all cats regularly (every 10-15 minutes) to avoid eye ulcers and lesions. Ideally, the cat should return to its normal behaviour, and eat and drink, shortly after the end of anaesthesia.

α2-adrenergic receptors agonists (xylazine, medetomidine and dexmedetomidine) are to be avoided for several reasons (see Table 2). Propofol produces significant cardiorespiratory depression and may lead to the formation of Heinz bodies, so is also best avoided. Ketamine is often used as part of drug protocols; however, it should not be administered alone since muscle jerks, hallucinogenic behaviour, hyperaesthesia and emergency delirium (growling, biting, scratching, lunging at the cage) have been observed. Sevoflurane has been used for feline blood donation since induction of, and recovery from, anaesthesia is rapid and predictable (Table 2).

Table 2: Summary of different drug combinations that can be used in blood donors and their effect on major blood analytes. RBC: red blood cell; HCT: haematocrit; Hb: haemoglobin; WBC: white blood cells; PCV: packed cell volume, IV intravenous, IM intramuscular.

Drugs	Dose or dosage or inhalant concentration commonly reported	Comments	Changes in blood analytes reported in studies	References
Ketamine and diazepam	10 mg ketamine + 0.5 mg diazepam, both IV	Protocol for short-term venipuncture (5 minutes). Short onset and duration of action with excellent chemical restraint but may not be enough to complete phlebotomy. Note: diazepam should not be administered IM	Minimal decreases in plasma triglycerides and albumin, and minimal increases in activated partial thromboplastin and prothrombin times, likely without clinical relevance	[73]
Ketamine and midazolam	4-6 mg/kg ketamine + 0.4 mg/kg midazolam, both IM	Mixed in the same syringe for IM injection. Prolonged anaesthetic effects, with ataxia and recumbency for up to 4-6 hours after phlebotomy. Alternative protocols include the addition	Decreases around 24-25% in RBC count, Hb concentrations and PCV after higher doses of ketamine (10 mg/kg) and midazolam (0.5 mg/kg) IV. Based on	[74-76]

Drugs	Dose or dosage or inhalant concentration commonly reported	Comments	Changes in blood analytes reported in studies	References
		of butorphanol (0.3 mg/kg) or buprenorphine (0.01 mg/kg) IM. Hyperthermia may occur with ketamine-based protocols	these PCV changes, some donors may be falsely diagnosed with anaemia	
Dexmedetomidine and butorphanol	0.01 mg/kg dexmedetomidine + 0.2 mg/kg butorphanol, both IM	Ease of administration with short onset of action and possibility of dexmedetomidine reversal with atipamezole (0.1 mg/kg IM). Good muscle relaxation. Adverse effects include emesis, bradycardia, increased systemic vascular resistance and decreases in cardiac output. Peripheral vasoconstriction poses an additional challenge to venous catheterization and blood collection; several donations were aborted due to this. Higher doses of dexmedetomidine might be required in some cats	Decreases in RBC count, Hb concentration and HCT values (i.e. sequestration of erythrocytes by the spleen induced by reduced sympathetic activity)	72 74 77
Alfaxalone and butorphanol	2 mg/kg alfaxalone + 0.2-0.4 mg/kg butorphanol, both IM	Minimal cardiorespiratory changes. Large volume of IM injection. Rapid recovery from anaesthesia (just over 30 minutes). Additional sedation or gentle physical restraint might be required in some cats; further administration of alfaxalone (0.1 mg/kg IV) can be used but will prolong duration and recovery of anaesthesia. In the author's experience (PS), twitching can be observed	No changes in complete blood count or serum biochemical values in experimental cats after doses of 5 mg/kg and 15 mg/kg IV	72, 78, 79
Tiletamine and zolazepam	2.5 mg/kg of each of tiletamine and zolazepam, both IM	Short onset of action. Hypothermia can be observed. Increases in heart rate and blood pressure due to hypovolemia and drug-induced sympathetic stimulation.	RBC, HCT, Hb, WBC, platelet, neutrophil and monocyte counts decreased, and lymphocyte, eosinophil and basophil counts increased after blood collection (not statistically significant)	80
Sevoflurane	Mask or "box" induction with sevoflurane (4-5% for induction followed by 2-3% for maintenance using 2 L/min of oxygen)	Potentially stressful to the cat. Anaesthesia is best induced by wrapping the cat in a towel with gentle restraint using a snug-fitting mask to the face. Possibility of	Not reported	75

Drugs	Dose or dosage or inhalant concentration commonly reported	Comments	Changes in blood analytes reported in studies	References
		profound agitation during recovery. Environmental exposure of the veterinary care team to the inhalant anaesthetic. Higher prevalence of hypotension when compared with ketamine combinations. An endotracheal tube should be available if intubation is required		

Monitoring of mucous membrane colour, temperature, pulse and respiration rate of the donor cat should be performed throughout the anaesthetic procedure and blood collection. Pulse oximetry (SpO_2) can be used as a non-invasive method to determine the percentage of arterial haemoglobin saturated with oxygen. The device can be placed over the plantar digit of a pelvic limb during collection. Hypothermia is prevented by positioning the cat over a circulating warm water blanket or other warming device (with appropriate safety measures). Blood donation implies controlled losses of up to 20% (40-60 ml) of a cat's blood volume over a short period of time. As hypotension (systolic < 80–90 mmHg, mean < 60–70 mmHg, and diastolic <40 mmHg) is commonly observed with both injectable and inhalant anaesthetic protocols [75, 81], blood pressure monitoring is recommended due to potential hypovolaemia and the effects of anaesthetics. Depending on the donor protocol, balanced crystalloid solutions may be provided via intravenously or via the subcutaneous route immediately after donation. Arterial partial pressure of oxygen can decrease during chemical restraint and oxygenation via a tight facemask is recommended. Desaturation (SpO_2 < 90%) indicates hypoxaemia and oxygenation must be administered in this case especially with protocols using a combination of opioid-dexmedetomidine-ketamine or alfaxalone [82]. Other measures may be required including drug reversal and termination of the procedure.

Practical blood collection

The anticoagulant-preservative solutions most often used for collection of blood for transfusion purposes are ACD-A (anticoagulant citrate-dextrose solution), CPD (citrate-phosphate-dextrose) or CPDA-1 (citrate-phosphate-dextrose-adenine). The volume of anticoagulant used and the duration of time for which the blood product can be stored vary depending on the anticoagulant-preservative solution and the collection method. ACD-A, CPD and CPDA-1 typically are used in a ratio of 1 ml anticoagulant to 7ml of blood. Sodium citrate (3.2 or 3.8%) alone (without RBC preservatives) may be used at a ratio of 1 ml anticoagulant to 9 ml of blood if the blood is to be administered within 24 hours of collection. Use of heparin as an anticoagulant for blood collected for transfusion is not recommended.

Blood collection systems are described as “open” or “closed”. A closed system is one in which the only exposure of the collection bag or its contents to air prior to administration is when the needle is uncapped to perform venipuncture during collection. An open system is one in which there is one or more additional sites of potential bacterial contamination during blood collection or processing, with examples being the use of syringes or empty bags with added anticoagulant to collect blood, as frequently used in cats (Figure 5). Blood products collected in an open system should be ideally administered within four hours, or if stored in a refrigerator (1-6°C) they should be administered within 24 hours.

A commercially available feline closed collection system (Figure 6a and Figure 6b) has been evaluated for storage of feline blood for 35 days, with one of eight blood units showing bacterial growth (*Serratia marcescens*) on day 35 but not day zero [83], highlighting the fact that bacterial contamination of a blood unit during collection is an issue regardless of whether using an open or closed collection system. Another closed feline blood collection system was recently evaluated which permits blood collection by suction using a vacuum chamber, which accelerated the process without being detrimental to the blood donor, therefore optimizing collection [84]. In addition, this

study directly compared this closed system to an open system, for evidence of bacterial contamination, and did not observe any difference in bacterial contamination of the units between the two collection systems [84]. Also, blood units and blood products collected using open systems have previously been stored successfully without microbial growth, although all blood banking was done by experienced staff and blood was collected with appropriate aseptic collection methods, processing and careful storage to prevent contamination [85], which may have contributed to this result.

The volume of blood that may be collected safely from feline donors is approximately 20% of their blood volume (blood volume approximately 50-60 ml/kg) every four weeks; thus a recommended volume limit is approximately 10-12 ml/kg for cats based on lean body weight [81]. For practical purposes, a routine feline blood collection is a total volume of approximately 40-60 ml, including anticoagulant. Most volunteer donor schemes using client-owned pets as donors extend the donation interval to every 8-12 weeks, and at this frequency supplementation with iron is not required unless a deficiency is detected.

The jugular vein is the recommended venipuncture site in cats because of its size and accessibility. Strict aseptic technique minimizes the possibility of bacterial contamination (see text box for collection procedure). In a retrospective observational study of 115 feline blood donations (70 non-sedated and 45 sedated), evidence of cardiovascular or respiratory distress was noted in three non-sedated cats after donation; panting, tachypnoea, and collapse were each observed in one cat, all of which were determined to be normotensive within minutes of the untoward event [70] and recovered fully. Further study is required to assess the complication rate between sedated and non-sedated donors but, in most cats, sedation is preferred to reduce patient anxiety and potential movement and trauma to the jugular vein during donation. Assessment of patient demeanour should form part of the pre-donation assessment and examination.

After blood collection and during recovery from chemical restraint donors should continue to be monitored as indicated above (mucous membrane colour, pulse and respiratory rate, and systolic blood pressure if indicated) and optionally provided subcutaneous or intravenous fluids. The patient may be discharged once vital parameters are in the normal range, and ideally after food is eaten, before discharge.

BOX OUT START

Fluid therapy for feline blood donors

Provision of fluid therapy prior, during or after collection of blood from a donor varies between centres and clinicians. No detrimental effects are reported in large donor programs when crystalloid fluids are not supplemented (Penn Animal Blood Bank, personal communication) and other authors provide 90 ml lactated Ringer's solution subcutaneously prior to collection of the donation, and the same solution is administered intravenously at 10 ml/kg starting halfway through the donation [86]. Others supplement with a balanced crystalloid solution such as Hartmann's or lactated Ringer's solution at 2-3 times the volume of blood collected, given immediately intravenously after the donation is completed [87].

BOX OUT END

BOX OUT START

Feline blood collection procedure using open system (equipment shown in Figure 5)

1. A pre-donation blood sample can be collected from an intravenous catheter or peripheral vein for measurement of PCV or haemoglobin via a haemoglobin monitor. Perform the blood collection only if PCV or haemoglobin is in the reference interval.
2. Syringes (several 10, 20, or one 60 ml) are pre-filled with an appropriate volume of anticoagulant (1 ml of ACD-A, CPD or CPDA-1 per 7 ml of blood to be collected).

3. The donor is restrained in the position preferred by the phlebotomist e.g. a sitting position with head raised (especially if not sedated); if sedated, the cat can be placed in sternal recumbency with forelimbs over the edge of a table and the head raised (Figure 6a) or in lateral (Figure 6b and Figure 6c) or dorsal recumbency with the neck extended (Figure 6d).
4. The hair over the jugular vein is clipped and the venipuncture site is prepared using an aseptic technique (Figure 6c).
5. Pressure is applied at the thoracic inlet to raise the jugular vein, and a butterfly catheter (19 or 21 gauge) is inserted into the jugular vein.
6. The phlebotomist keeps the butterfly needle within the jugular vein as still as possible, whilst each syringe is filled in turn and gently rocked to ensure mixing of blood and anticoagulant during collection by an assistant. Sometimes occlusion of both jugular veins can accelerate blood collection if syringe filling flow has slowed down.
7. After collection, the butterfly needle is removed from the jugular vein, and pressure is applied to the venipuncture site to prevent haematoma formation.

If a blood clot is found in one syringe only, that syringe should be discarded if possible.

A more detailed step-by-step photo guide of blood collection is available elsewhere [87]

BOX OUT END

BOX OUT START

Feline blood collection procedure using closed system (equipment shown in Figure 7)

A TEC 724 blood collection kit for cats (Futurlab Srl, Limena, Padova, Italy) can be used for closed blood collection, as previously described [83, 88]. Figure 7a and Figure 7b show the system set up with a description of its use below.

1. Close clamp 3, leave clamps 1 and 2 open.
2. Push the plunger of the 10 ml syringe ‘C’ up to the first thick black permanent marker line to put around 3 ml of anticoagulant into the system (on 1st occasion before the first withdrawal of blood

from the donor make sure the anticoagulant solution reaches the break-valve ‘B’ to prevent subsequent coagulation in the collection line. This means around 3 ml of anticoagulant will be in the closed collection system to go into the blood collection syringe ‘D’ alongside around 20 ml of blood aspirated from donor; this maintains the approximate correct 1:7 ratio of anticoagulant to blood).

3. Close clamp 1.
4. Remove the cap of the luer lock connection ‘A’ and connect it to the butterfly needle of the desired gauge to collect blood from the donor cat.
5. Obtain donor jugular vein access with the butterfly needle, ensuring it is correctly inserted and then held still.
6. Break the break-valve ‘B’ (this valve means that the donor blood is never in contact with the air, ensuring the system remains closed).
7. Draw the 20ml of blood into the ‘D’ syringe via aspiration – the blood comes into contact with, and will mix with, the anticoagulant previously placed in the system.
8. Once the ‘D’ syringe has been filled with blood mixed and anticoagulant, open clamp 3 and push the plunger of syringe ‘D’ so that the blood goes through the unidirectional valve ‘E’ into the primary bag ‘F’ (see Figure 7b).
9. Close clamp 3, open clamp 1 and then repeat steps 2, 7 and 8.
10. Repeat step 9 until collection of blood complete; the anticoagulant solution allows collection of up to 60 ml ± 10% of blood (primary bag capacity is 80 ml).
11. When the blood collection is complete, close clamp 2 and remove the butterfly needle from the donor, applying pressure to the jugular vein.
12. Separate the equipment at the point indicated by the black cross in Figure 6a by means of an electric or manual sealer (a sealer is a tool used to close off the blood bag by sealing the tube using heat or metal; used mainly in blood banks, but available for purchase, but metallic clamps can be used if not available) – this separates the blood-filled primary bag ‘F’ of blood (and the

plasma satellite bag 'I') from the syringes and rest of the kit.

13. To infuse the collected blood in 'F', connect the luer lock infusion adapter 'K' (provided with the kit) to the valve 'G' and remove the butterfly cap from the other end to connect with an infusion set with spike. If not given to the recipient immediately, the collected blood can be stored at 4-6°C. It is possible to take samples from the bag by connecting a luer lock syringe to the needle free valve 'G'.

14. Although very unlikely in general practice, as blood bank centrifuges are usually only available in blood banking organisations, the closed collection kit shown can also be used to divide the FWB collected into one packed red blood cell (pRBC) unit and one plasma unit. This is done by centrifugation of the primary and satellite bags in specialized blood bank centrifuges, then breakage of the break-valve 'H' and transfer of plasma to the bag 'I' which is then sealed at the position of the blue cross in Figure 7a. Plasma can then be stored frozen at -20°C for up to one year (as fresh frozen plasma - FFP) or from one to five years (as frozen plasma - FP). Samples from the plasma bag can be taken by connecting a luer lock syringe to the needle free valve 'J'. The luer lock infusion adapter 'K' can be attached to the valve 'J' and connected to an infusion set with spike for administration.

BOX OUT END

While most cats in need of a transfusion in clinical practice receive FWB, the high erythrocyte sedimentation rate of feline blood allows for the separation of plasma and RBCs by simply placing blood-filled syringes upright for approximately one hour at room temperature [89] (Figure 8a). Plasma can then be expressed into a transfer pack and frozen within 8 hours of collection, if not immediately needed (Figure 8b). Packed RBCs can then be administered directly from the syringe or expressed into a transfer pack containing 10 ml of an additive solution, such as SAGM - saline, adenine, glucose, and mannitol, and stored in a refrigerator [90]. This is could useful when feline blood components are not readily available from a commercial blood blank.

Practical blood administration

Blood products are usually given intravenously via a peripheral vein, but occasionally via a central vein or via an intraosseous route in small patients. A dedicated intravenous line should be used.

Blood products should not be administered with intravenous fluids containing calcium or glucose supplementation (e.g. Hartmann's, lactated Ringer's). Calcium overwhelms the chelating ability of the citrate anticoagulant in stored blood and increases risk of clot formation. Appropriate fluid choices would be 0.9% saline or Plasmalyte.

Blood products must be administered using an appropriate filter to reduce red cell aggregates and microthrombi entering the recipient's circulation. Filters in standard fluid therapy administration sets are too small and blood will clot if administered through them. Use of a syringe and microaggregate filter system does not appear to damage transfused RBCs [91]. Gravity administration using a standard blood giving set can be used but control of administration rate is more difficult. Ideally, a syringe and syringe driver with an inline microaggregate filter system (e.g. Hemo-Nate 18 µm filter, IMS, UK) is best. In most centres the filter is placed in the administration line as close to the patient as possible (Figure 9). Some authors will filter the blood as it is removed from the bag into a syringe, prior to administration to the patient. Either is an appropriate method for removing microthrombi from the FWB or pRBCs.

Transfusion volume and rate

The volume of blood product administered to a patient can be calculated with various formulae, with the following formula performing best in one study, although formulas frequently fail to accurately predict post-transfusion recipient PCV [92].

PCV% increase = volume of blood transfused in ml/ (2 x bodyweight in kg)

Practically, administration volume is rounded to the nearest unit (40-60 ml whole blood) unless the recipient is very small in which case a half unit or 10 ml/kg may be administered.

The rate of administration of the transfusion is determined by the condition of the patient. Patients with severe clinical signs associated with anaemia (e.g. weakness, tachycardia, tachypnoea, hyperdynamic or weak pulses, hypotension, dull mentation) may require blood products faster i.e. as a bolus or over 1-2 hours. Alternatively, as cats with severe or chronic anaemia may have signs of left heart overload [93], transfusions may need to be given over a longer period (e.g. 4-6 hours) to reduce the risk of transfusion associated circulatory overload. However, recent work described a lack of transfusion-associated circulatory overload in anaemic cats and dogs receiving transfusions [94], suggesting that such an adjustment may not be required routinely, although it is still a risk in patients with underlying cardiac disease, for example, and so close monitoring is indicated. If blood products are kept at room temperature for more than 4 hours there is a greater risk of bacterial contamination, which should also be considered when calculating administration rates.

BOX OUT START

Rate of transfusion administration

In patients not requiring rapid volume replacement, transfused blood should be administered at 0.5 ml/kg/hour for the first 30 minutes and the patient monitored constantly for signs of a transfusion reaction (see below) such as vocalization, tachycardia, hypersalivation, vomiting, diarrhoea, facial swelling/urticaria, piloerection, or tachypnoea/respiratory distress. After this time, the rate may be increased to 1 ml/kg/hr for 30 minutes. If there is still no evidence of a transfusion reaction, the administration rate is increased so the total transfusion volume remaining is administered within a 4-hour period, although some follow the 1 ml/kg/hr rate with a period of 20 minutes at 2 ml/kg/hr before increasing the rate further.

BOX OUT END

712

713 **Monitoring the recipient**

714 Patients must be monitored very closely whenever receiving a blood transfusion, particularly within
715 the first 30 minutes of administration as this is the most common time for a severe transfusion
716 reaction to develop. A baseline check of vital signs is performed before commencing the
717 transfusion, including temperature, heart rate, pulse quality, blood pressure, mucous membrane
718 colour, respiratory rate/effort, oxygen saturation and patient mentation.

719

720 These parameters are checked very frequently (initially every five minutes) for the first 30-60
721 minutes (Figure 10a and Figure 10b). Depending on the clinical status of the patient, a
722 multiparameter machine may be used to allow continuous monitoring of heart rate,
723 electrocardiogram, SpO2, blood pressure and temperature throughout the transfusion. Assessment
724 of vital parameter data trends (e.g. gradual increase in heart rate, respiratory rate, temperature) is
725 key to early identification of a transfusion reaction and ensuring detailed records are kept
726 throughout the transfusion is extremely important (Table 3).

727

728 Table 3: An example of a blood product administration sheet used for monitoring cats to help allow
729 for early detection of any problems. T = temperature. P = pulse rate. R = respiration rate. BP = blood
730 pressure. MMemb = mucous membrane. PCV = packed cell volume.

Example Blood Product Administration Sheet for Cats

Date ……

Weight …… kg Vet …….

Blood type ……

Donor reference ……..

Cross-matched? Y □ N □

Patient Sticker

Blood product *(likely whole blood)*

…… Unit size …… mls

Dose estimation: ≈1% increase in PCV is seen for every 2ml/kg of whole blood

Time	**Rate**	**Volume given (mls)**	**Actual Rate Given**	**Monitoring – see below**
Start ……	**0.5 ml/kg/hr** for 1st 30 mins	Volume =	……ml/hr	T, P, R, BP Q 15 mins for 1st hour & then at end; can do this more frequently if any concerns
	1.0 ml/kg/hr for next 30 mins	Volume =	……ml/hr	
Finish ……	As prescribed – *but should not really exceed 10 ml/kg/hr*	**Remainder of unit volume given over 4 hours** Volume =	……ml/hr	

Complete the transfusion within 4 hours

	Time	**T (°C)**	**Pulse rate & quality**	**MMemb colour & CRT**	**RR & pattern**	**BP (mmHg)**	**PCV %**	**Comments**
Start								
15mins								
30mins								
45mins								
1 hour								
Optional time points								
End								

Total volume given (mls) _____

Any transfusion reactions?

_____

_____

____

Please record any notes and further checks on the patient's sheet

Signs of a transfusion reaction include pyrexia, restlessness, vomiting, salivation, change in RR and/or pattern (dyspnoea), change in HR and/or rhythm, change in BP, weak pulses, vocalization, diarrhoea, urticaria.

If any reaction is seen, **the transfusion should be stopped immediately,** and the **vet contacted**. The volume infused, and rate of infusion is recorded (do not discard the blood, line or fluids). Other considerations may be required under vet guidance:

- Start cardiopulmonary resuscitation (CPR) if necessary
- Examine the unit for haemolysis by spinning a microhaematocrit tube containing a sample of the donor blood and look for haemoglobinaemia
- Examine the recipient for haemolysis by spinning a microhaematocrit tube of blood from the recipient and look for haemoglobinaemia
- Consider starting IVF therapy (e.g. crystalloid bolus at 10 ml/kg) – this may be required to avoid renal damage if severe intravascular haemolysis or if signs of shock are present (hypotension, pallor, tachycardia/bradycardia)
- Consider treatment with adrenaline (10-20 μg/kg of a 1: 10,000 solution (100 μg (0.1 mg) per ml) IV or IM) and antihistamines (e.g. diphenhydramine 1 mg/kg IV or IM)
- If volume overload has resulted in pulmonary oedema, diuretic treatment and oxygen support may be required – chest imaging and/or echocardiography may be indicated
- Culture (or e.g. PCR) of a sample of the donor unit may be required if infection or contamination is suspected, but bacterial contamination is unlikely in fresh well-handled blood
- Antipyretics (e.g. meloxicam) may be required in some cases (renal function must be ok)

Transfusion Reactions

Despite appropriate screening, transfusion reactions in cats remain unpredictable and can vary in severity. Transfusion reactions can be defined as acute or delayed (see Table 4). The most common transfusion reactions seen in cats include febrile non-haemolytic transfusion reactions, allergic reactions and transfusion-associated circulatory overload. Transfusion reactions may cause immune-mediated haemolysis, which can result in jaundice, pigmenturia and/or pyrexia, mainly due to anti-blood type reactions. Transfusion reactions can also cause non-haemolytic reactions e.g. transient increases in body temperature, facial pruritis, facial swelling (Figure 11), vomiting and salivation. Increased vocalisation or agitation can often be a preceding sign to a non-haemolytic reaction.

Table 4: Association of Veterinary Haematology and Transfusion Medicine (AVHTM) Consensus Working Group definitions of transfusion reactions (reproduced with permission from AVHTM [95]).

ACUTE TRANSFUSION REACTION DEFINITIONS	
Acute Haemolytic Transfusion Reaction (AHTR)	Acute, non-infectious, immunologic, or non-immunologic reaction that occurs secondary to accelerated destruction of transfused or recipient RBCs and is characterized by acute haemolysis. Acute haemolytic transfusion reactions occur during or within 24 hours of blood product administration. Causes of AHTRs can be divided into blood type incompatibilities and other causes of damage to transfused blood cells. Blood type incompatibilities are immunologic acute haemolytic reactions that are type II hypersensitivity reactions due to major or minor incompatibilities between donor and recipient RBCs. A classic example would be in the case of a type A unit of blood given to a type B cat. Non-

	immunologic causes of AHTRs may include thermal, osmotic, mechanical, or chemical factors that damage transfused blood cells.
Allergic Reaction	Acute immunologic reaction that is secondary to a type I hypersensitivity response to an antigen within a blood product. This reaction occurs during or within 4 hours of transfusion. It is characterized by clinical signs varying from transient and self-limiting to life-threatening anaphylaxis. Feline type I hypersensitivity reactions are typically respiratory (due to upper respiratory tract oedema, bronchoconstriction, and excessive mucus production) although gastrointestinal signs and severe pruritus can also occur.
Febrile Non-Haemolytic Transfusion Reaction (FNHTR)	Acute non-immunologic or immunologic reaction characterized by a temperature > 39°C (102.5°F) AND an increase in temperature of > 1°C (1.8°F) from the pre-transfusion body temperature during or within 4 hours of the end of a transfusion where external warming, underlying patient infection, AHTR, TRALI, and TTI have been ruled out.
Transfusion Associated Circulatory Overload (TACO)	Acute, non-immunologic reaction that is secondary to an increase in blood volume mediated by blood transfusion, characterized by acute respiratory distress and hydrostatic pulmonary oedema. This reaction occurs during or within 6 hours of transfusion. It is associated with clinical, echocardiographic, radiographic, or laboratory evidence of left atrial hypertension or volume overload. These patients typically have a positive response to diuretic therapy.

Transfusion Associated Lung Injury (TRALI)	Acute, immunologic reaction that is secondary to antigen-antibody interactions in the lungs. TRALI is characterized by acute hypoxemia with evidence of non-cardiogenic pulmonary oedema on thoracic radiographs, during or within six hours of allogenic blood transfusion. Patients diagnosed with TRALI have no prior lung injury, no evidence of left atrial hypertension and no temporal relationship to an alternative risk factor for ARDS.
Transfusion Associated Dyspnoea (TAD)	Acute transfusion reaction characterized by the development of acute respiratory distress during or within 24 hours of the end of a transfusion where TACO, TRALI, allergic reaction, and underlying pulmonary disease have been ruled out.
Hypotensive Transfusion Reaction	Acute, non-immunologic reaction that is secondary to the infusion of stimulators of vasodilation and hypotension. It is characterized by the rapid onset of significant hypotension during or shortly after the completion of a transfusion, with the absence of other causes of hypotension, and improvement with cessation of the infusion. There is usually a decrease in systolic blood pressure of at least 30 mmHg from baseline.
Citrate Toxicity	Acute, non-immunologic reaction that is secondary to the transfusion of a large volume of blood, with citrate as the anticoagulant, and is characterized by a significant systemic hypocalcaemia within hours of initiating transfusion.

Hyperammonaemia	Acute, non-immunologic reaction that is secondary to hyperammonaemia and characterized by signs of development of encephalopathy (neurologic signs as ataxia, head pressing, circling, seizures and vomiting), during or immediately after (minutes to few hours) blood transfusion of stored blood or stored blood components. It is a potentially life-threatening reaction in patients with liver disease (liver failure, portosystemic shunt, premature neonates with immature functioning liver) who are unable to metabolize and excrete ammonia properly.
ACUTE-TO-DELAYED TRANSFUSION REACTION DEFINITIONS	
Transfusion Transmitted Infection (TTI)	Acute or delayed, non-immunologic reaction secondary to the transfusion of pathogen contaminated blood or blood components. A TTI can occur hours to years after the transfusion due to the presence of the infectious agent in the blood/blood component unit collected from an infected donor, or from pathogen contamination of blood/blood component units during processing, storage or transfusion. Clinical signs are highly dependent on pathogen transmitted and its pathogenicity for dogs and cats and the clinical status of the recipient.
Transfusion-associated graft vs. host disease (TAGVHD)	Acute to delayed immunologic reaction that is secondary to donor lymphocytes engrafting on and eventually attacking host tissue. TAGVHD occurs 48 hours to 6 weeks following transfusion and has a high mortality rate in human patients (>90%). The reaction is characterized by a skin rash, diarrhea, fever, hepatic dysfunction, and bone marrow hypoplasia. Liver and skin histopathology have a characteristic appearance. In humans, it is

	most common in immunocompromised individuals or when special circumstances cause transient immunosuppression.
DELAYED TRANSFUSION REACTION DEFINITIONS	
Delayed Haemolytic Transfusion Reaction (DHTR)	Delayed, non-infectious, immunologic or non-immunologic, reaction that occurs secondary to lysis or accelerated clearance of transfused RBCs. Delayed haemolytic transfusion reactions occur 24 hours to 28 days after blood product administration. Immunologic DHTRs are typically caused by a secondary immune response to the donor's RBCs. Non-immunologic HTRs occur due to thermal, osmotic, mechanical, or chemical factors that damage transfused blood cells, causing delayed haemolysis.
Delayed Serologic Transfusion Reaction (DSTR)	Delayed, immunologic reaction that is secondary to the development of new clinically significant antibodies against the transfused product without evidence of haemolysis. DSTRs occur 24 hours to 28 days after a transfusion [24].
Post-Transfusion Purpura (PTP)	Delayed, immunologic reaction that is secondary to alloimmunization against platelet antigens. It is characterized by thrombocytopenia arising 5-12 days following transfusion of any platelet-containing blood product.

In a group of 126 cats receiving blood transfusions, non-haemolytic reactions (7.9%) were more common than haemolytic reactions (0.8%) [96]. In another study of 91 cats, a transfusion reaction was only noted in 1.2% [57].

The risk of a transfusion reaction increases with subsequent transfusions (typically from 2 days after an initial transfusion) [24]. Appropriate record keeping is essential so that subsequent veterinarians are

789 aware that the patient has received a blood transfusion. However, in 27 cats that received multiple
790 blood transfusions, transfusion reactions remained uncommon [97].
791
792 Should the patient develop mild signs of a transfusion reaction (e.g. mild 1-2◦C increase in
793 temperature or one episode of vomiting) then the transfusion rate should be reduced. If marked
794 clinical signs develop the transfusion should be stopped and blood replaced with a crystalloid
795 solution. Monitoring of the patient should be continued for evidence of shock (temperature, pulse
796 rate, mucous membrane colour and systolic blood pressure). Serum and urine should be assessed
797 for haemolysis and haemoglobinuria with sample centrifugation (Table 3) to look for evidence of
798 haemolysis of the transfused red cells (e.g. red discolouration of serum or urine).
799
800 In the event of a severe transfusion reaction, the transfusion should be discontinued, and the
801 patient assessed. If signs of shock (hypotension, pallor, tachycardia/bradycardia) a crystalloid fluid
802 bolus (10 ml/kg) and adrenaline (10-20 μg/kg of a 1: 10,000 solution (100 μg (0.1 mg) per ml) IV or
803 IM) should be administered and can be followed by a continuous rate infusion (CRI) of adrenaline.
804 Antihistamines (e.g. diphenhydramine 1 mg/kg IV or IM) and corticosteroids (e.g. hydrocortisone 2-
805 4mg/kg IV or IM or dexamethasone 0.05-0.1mg/kg IM or IV) may also be considered, although
806 evidence for use of corticosteroids in acute transfusion reactions is limited and patient
807 contraindications and potential adverse effects should be taken into account. The donor blood
808 sample/unit should be assessed by checking a PCV for evidence of haemolysis and potentially
809 submitting a sample for bacterial culture.
810
811 Cats may develop signs of volume overload following transfusion. This is of particular concern in
812 patients with cardiac disease, normovolaemic to hypervolaemic anaemic patients (e.g. immune-
813 mediated haemolytic anaemia), and chronically or severely anaemic patients although, as
814 mentioned above, this alone may be less of a clinical concern [94]. If patients become tachypnoeic

following a transfusion, or develop a serous nasal discharge or conjunctival oedema, thoracic radiographs or thoracic ultrasound should be performed to evaluate for pleural effusion or pulmonary oedema. If pleural effusion is present, thoracocentesis should be performed. If pulmonary oedema is present, furosemide 1-2mg/kg IV every two hours as required (based on respiratory auscultation, respiratory rate and response) and oxygen therapy should also be instigated.

Autologous blood transfusion

Autologous blood transfusion (autotransfusion) is the administration of a patient's own blood as a transfusion. This can be considered in patients with haemothorax or haemoperitoneum. Cross-matching or blood typing is not required. Blood is collected in a sterile fashion using a 23G butterfly needle and 10 or 20 ml syringes. Administration of the collected blood is otherwise similar to standard donor-recipient transfusions. There is no clear evidence regarding whether anticoagulant should be added to the transfusion. Blood in contact with the peritoneal surface is reported to become defibrinated within one hour and anticoagulant administration may be unnecessary or lead to hypocalcaemia. The use of a blood filter (18 µm) is strongly recommended to prevent platelet and leukocyte passage. A recent report of eight cats with haemoperitoneum receiving autologous transfusion did not identify any adverse reactions [98].

Conclusion

Feline blood donation and transfusion can be performed safely and effectively in veterinary practice, but the decision to do so must be made carefully. Donor and recipient cats should be blood typed, and ideally cross-matched if possible, prior to transfusion to avoid severe transfusion reactions. The decision to administer a transfusion is based on the potential recipient's clinical condition and cause of anaemia rather than PCV alone. Donors should be assessed for health, temperament and infectious agents and, in most cases, sedated appropriately for blood collection. Blood can be

collected using an open or closed system and recipients should be monitored for signs of a transfusion reaction. Xenotransfusion may be given only once, allowing for short-term stabilisation of the recipient but destruction of donated RBCs occurs after a short time.

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