Guide to blood plasma products and their applications – part one

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Amanda Boag and Jenny Walton discuss indications for the use of plasma products, their production, and storage within the practice in the first of a three-part series

FOLLOWING changes in legislation in 2005, veterinary blood banking and component therapy has developed rapidly within the UK.

Practitioners now have easy access to canine blood and its products – notably, packed red cells and various plasma products. This series of articles will focus on indications for plasma product use, their production and storage, the administration and monitoring of plasma transfusions and will include a series of five case studies that have used plasma products.

Indications for plasma component therapy

Although well-defined indications exist for the use of plasma products in single or multiple coagulation deficiencies, indications for many of its other uses are empiric.

Haemostatic disorders

Plasma components are most commonly used to treat haemostatic disorders and are generally effective in treating both inherited and acquired conditions. Specific diagnosis enables selection of the optimum replacement product. It is important to remember that any samples drawn for diagnostic purposes (for example, measurement of clotting factor levels) must be taken either
before or at least 36 hours after transfusion to allow the measurement of endogenous levels.

**Inherited bleeding disorders**

Plasma components are administered to control active haemorrhage or as preoperative prophylaxis. Inherited bleeding disorders are associated with deficiency of a specific factor and the optimal product for treatment depends on which factor is lacking.

The most common disorders are:

- von Willebrand factor (vWF) deficiency; and
- haemophilia
  - factor VIII deficiency (haemophilia A).
  - factor IX deficiency (haemophilia B).

Cryoprecipitate is the treatment of choice for known deficiencies of vWF, factor VIII and fibrinogen. Fresh frozen plasma (FFP) should be used if cryoprecipitate is unavailable. All other factor deficiencies can be treated with cryosupernatant or frozen plasma (FP). In an emergency situation, if an inherited bleeding disorder is suspected, but not yet diagnosed, FFP would be the treatment of choice as it is the most reliable source of all factors.

**Acquired disorders of haemostasis**

Acquired disorders of haemostasis are associated with simultaneous deficiencies of many factors. They may be categorised as:

- deficiency in production of factors – for example, liver insufficiency/failure;
- failure to activate specific factors dependent on vitamin K – for example, anticoagulant rodenticide toxicity;
- excessive consumption of factors – for example, disseminated intravascular coagulation (DIC); and
- depletion or dilution of factors – for example, severe acute blood loss or excessive colloid/crystalloid therapy.

Generally the above disease processes are thought to require replacement of all factors and FFP would be the product of choice. Cryosupernatant or FP are also suitable for use in conditions
associated with the lack of activation of vitamin K-dependent factors as these factors are all present in these products.

**Hypoalbuminaemia**

Acute vasculitis, hepatic disease, protein-losing enteropathies and nephropathies, and peritonitis have all historically been treated in the short term with plasma products – largely in the hope that their use will lead to an increase in albumin levels. Very large amounts of a plasma product are needed to achieve this and the benefits are likely to be very short-lived. The cost and risks involved with these large transfusions are likely to outweigh the benefits.

In the acutely unwell animal, multimodal therapies involving synthetic colloids, with or without plasma components, should always be considered to manage the animal’s intravascular volume status. Longer-term treatment for the underlying disease is the most effective way of raising albumin levels. However, if haemostatic issues are present alongside hypoalbuminaemia, using standard doses of FFP to treat the concurrent coagulopathy is indicated.

**Hypoglobulinaemia**

The use of plasma products as a source of immunoglobulins is sometimes considered. Although it is likely that plasma components will come from healthy vaccinated dogs with normal levels of immunoglobulins, in the UK there is no source of hyperimmunised plasma, as no programme using hyperimmunised canine donors exists.

A common scenario may involve puppies with a disease that adult dogs are vaccinated against, such as parvovirus. Although parvovirus antibody is likely to be present in the plasma, its efficacy in this scenario has not been evaluated and it is not known whether therapeutic levels of antibody exist. For neonates with inadequate antibody transmission and for dogs with suspected hypoglobulinaemia, FP and cryosupernatant have been used as a short-term treatment. Again, no substantial veterinary studies are available to support this regime.

**Plasma products: what are they and how are they prepared?**

Canine plasma products are prepared in the UK from units of whole blood. Although in human medicine, and canine medicine in the US, a technique known as plasmapharesis may be used to harvest plasma from patients without the need for red cell collection, this technique is not yet available for veterinary blood banking in the UK.

Following the collection of whole blood into a proprietary blood collection bag, the whole blood units are centrifuged to separate them into the component parts (Figure 1) of red cells and plasma. Following centrifugation, the plasma and cells are separated (Figure 2). Proprietary blood bags
consist of the primary collection bag, which is connected to one or more satellite bags. This allows separation of the red cells and plasma within a completely closed system and ensures there is no potential for bacterial contamination during the processing.

If it is separated and frozen solid within eight hours of collection, the plasma product is termed fresh frozen plasma and contains all the labile (for example, vWF and factor VIII) and non-labile clotting factors. If freezing is not completed within eight hours, the product is termed frozen plasma. This may not contain therapeutic levels of active labile clotting factors. FFP can be further prepared by slow thawing into cryoprecipitate and cryo-poor plasma (also known as cryosupernatant). Plasma products are stored at less than -20°C (Figure 3). At these temperatures FFP has a shelf life of up to one year and FP a shelf life of up to five years; the lower and more stable the temperature the longer and more reliable the shelf life is thought to be.

Blood banks package and transport plasma product in frozen coolant to ensure it remains frozen en route to the practice. The practice can then choose to thaw it for immediate use or to place it within a freezer for continued storage.

Storage in the practice

Although plasma products can be provided by same day or next-day delivery, there are many clinical situations where plasma is needed urgently. It is therefore recommended that all practices consider stocking and storing a unit of FFP on site for use in emergencies.

Plasma has a long shelf life and having it directly to hand can be life saving in some patients with severe bleeding secondary to disorders of coagulation.

Plasma products can be kept in a normal household freezer set at less than -20°C. Freezers with an automatic defrost should not be used, to minimise the risk of inadvertent thawing.

Plasma products are fragile and prone to breakage when frozen. Large hospitals will often invest in a -30°C or -80°C freezer for keeping larger stocks. Small practices could consider using a small upright freezer. These usually maintain a reliable temperature of -20°C. To check the freezer’s reliability it is recommended that practices monitor the temperature maintained by any freezer for a week before purchasing stock.

Considering space and equipment availability it is, however, common and acceptable practice to store products in a multi-use chest freezer. It must be recognised that the risk of breakage is higher and uniform storage temperatures are harder to maintain in this environment. These risks can be minimised by storing the products towards the bottom of the freezer within their protective packaging and then placing in a sturdy polystyrene box or small cool box. Efforts should also be made to prevent the inadvertent placement of heavy objects on top of the stored product.
A maximum/minimum temperature thermometer with its probe next to the product should be used and checked daily to ensure the product is maintained at an appropriate temperature. The freezer compartment in a fridge is not adequate.

Historically, practical methods of checking whether inadvertent defrost had occurred were used. Elastic bands were placed around the bag prior to freezing then removed before storage. This meant that if the product had defrosted the “waist” created by the elastic band during freezing was no longer present.

Alternatively, as the product is frozen while lying flat at the blood bank, it would subsequently be stored standing vertically at the practice. Inadvertent defrost can then be suspected by a change in the shape of the plasma, from completely flat to bulbous, within the dependent portion of the bag.

When retrieved for use, products thought to have defrosted during storage will have to be discarded. These methods are not routinely recommended as reliable measures of correct storage. Regular and routine recorded maximum/minimum temperature checks of stock are the best way to ensure correct storage conditions.

• In part two, the administration and monitoring of plasma transfusions is examined.

Reference