Michelle P. Wong, MD, Nadejda Droubatchevskaia, MD, Kate M. Chipperfield, MD, FRCPC, Louis D. Wadsworth, MB, ChB, FRCPC, FRCPath, David J. Ferguson, MD, FRCPC

Guidelines for frozen plasma transfusion

A new document from the Transfusion Medicine Advisory Group of BC describes appropriate use of frozen plasma, fresh-frozen plasma, and cryosupernatant.

ABSTRACT: Guidelines based on a systematic literature review have been developed by the Transfusion Medicine Advisory Group of BC to provide physicians with evidence-based indications for transfusion of frozen plasma. Practices outlined in these guidelines are preferred to practices for blood product use based on anecdotal reports or personal experience, which may lead to unjustified exposure of patients to biological products as well as to overuse of scarce resources. The recommendations in the guidelines prepared by the Transfusion Medicine Advisory Group were graded according to the US Agency for Healthcare Research and Quality (formerly the US Agency for Health Care Policy and Research). At present, transfusion of frozen plasma is indicated for correction of known factor deficiencies for which no factor-specific concentrate is available, multiple-factor deficiencies associated with severe bleeding and/or disseminated intravascular coagulopathy, urgent reversal of warfarin effect, and for massive transfusion to maintain INR and PTT at less than 1.5 times the reference range. Frozen plasma is not indicated for a number of clinical situations, including hypovolemia, wound healing, and treatment of immunodeficiency states.

The Transfusion Medicine Advisory Group (TMAG) of BC has prepared guidelines to assist physicians in their clinical decision-making regarding the appropriate use of frozen plasma products in adults and neonates. These guidelines are available electronically on the British Columbia Provincial Coordinating Office web site (www.bloodlink.bc.ca) and will be updated periodically. Prescribing physicians are responsible for referring to the most recent guidelines, which are intended to guide therapy but are not intended to replace the clinical judgment of the attending physician and appropriate consultation with an expert in transfusion medicine.

How the guidelines were developed

A comprehensive literature search was undertaken on PubMed using combinations of keywords, including the following: plasma, fresh-frozen plasma, guidelines, transfusion, trial, randomized, liver, cardiac surgery, surgical bleeding, thawing, storage, massive transfusion, thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulopathy (DIC), and neonate. Particular attention was paid to the recently published guidelines for the use of fresh-frozen plasma, cryoprecipitate, and cryosupernatant developed by the British Committee for Standards in Haematology (BCSH)[1] and the systematic review by Stanworth and colleagues.[2] The grading of evidence and strength of recommendations were based on those developed by the US Agency for Healthcare Research and Quality (formerly the US Agency for Health Care Policy and Research) (see **Appendix A**) and those referenced in the BCSH guidelines for the use of fresh-frozen plasma, cryoprecipitate, and cryosupernatant.[1]

Dr Wong is a hematopathology resident in the Department of Pathology and Laboratory Medicine at the University of British Columbia. Dr Droubatchevskaia is a hematopathology resident in the Department of Pathology and Laboratory Medicine at UBC. Dr Chipperfield is regional medical leader, Blood Transfusion Medicine, Vancouver Coastal Health, and a clinical assistant professor in the Department of Pathology and Laboratory Medicine at UBC. Dr Wadsworth is a hematopathologist at Children's and Women's Health Centre of BC, a clinical professor in the Department of Pathology and Laboratory Medicine at UBC and is chair of the Transfusion Medicine Advisory Group of BC. Dr Ferguson is the medical director of BC Biomedical Laboratories Ltd., and an assistant clinical professor in the Department of Pathology and Laboratory Medicine at UBC.

Table. Characteristics of four frozen plasma products.

	Frozen plasma (from whole blood collection)	**Fresh-frozen plasma** (from apheresis collection)	**Cryoprecipitate plasma** (cryo)	**Cryosupernatant plasma** (cryo-poor plasma)
Preparation	Whole blood is centrifuged at high speed, allowing separation of plasma, red blood cells (RBCs), and the buffy coat layer (platelets, white blood cells, some RBCs and plasma). Plasma is frozen within 24 hours of collection and is designated as frozen plasma (FP). It is prepared for use by thawing at 37°C, a process that can take up to 30 minutes. Once thawed, the product should be transfused immediately, with completion of transfusion within 4 hours of issuing product.	Whole blood is processed through a cell separator to obtain plasma. Plasma is frozen within 8 hours of collection and is designated as fresh-frozen plasma (FFP). In general, 1 unit of FFP from apheresis collection is equivalent to approximately 2 units of FP from whole blood collection. The two products can be used interchangeably. Once thawed, the product should be transfused immediately, with completion of transfusion within 4 hours of issuing product.	Plasma is frozen for 24 hours, and then thawed at 1°–6°C until insoluble proteins precipitate. The pack is centrifuged to obtain the cryoprecipitate. The cryoprecipitate is then refrozen for storage. Once thawed, the product should be transfused immediately, with completion of transfusion within 4 hours of issuing product.	Plasma is frozen for 24 hours, and then thawed at 1°–6°C until insoluble proteins precipitate. The pack is centrifuged to obtain the supernatant. The supernatant, or cryo-poor plasma, is then refrozen for storage. Once thawed, the product should be transfused immediately, with completion of transfusion within 4 hours of issuing product.
Factors	Contains all of the coagulation factors, including the labile factors (FV and FVIII:C). For product prepared within 24 hours of collection, FVIII:C levels are less than those found in fresh-frozen plasma prepared within 8 hours of collection, but levels are still at or above 0.50 IU/mL. FP can be used for coagulation factor replacement except for isolated or severe FVIII deficiency.	Contains all of the coagulation factors, including the labile factors (FV and FVIII:C).	Contains FVIII:C, von Willebrand factor (vWF), fibrinogen, FXIII, and fibronectin. Cryoprecipitate has the following factor activities: 91 IU of FVIII: C per bag, 113 IU of vWF per bag, and 150 mg of fibrinogen per bag.	Is deficient in high molecular weight vWF multimers and FVIII:C.
Volume	Each bag = 1 unit (200–250 mL)	Each bag = 1 unit (100–600 mL)	Each bag = 1 unit (5–15 mL)	Each bag = 1 unit (>100 mL)
Dose	Typical adult dose of plasma is 10–15 mL/kg body weight. The pediatric dose of plasma is 10–15 mL/kg body weight. Infusion rate is over 2–3 hours, or as required. Will raise factor levels by 25%, assuming there is no ongoing consumption/loss of factors.	Typical adult dose of plasma is 10–15 mL/kg body weight. The pediatric dose of plasma is 10–15 mL/kg body weight. Infusion rate is over 2–3 hours, or as required. Will raise factor levels by 25%, assuming there is no ongoing consumption/loss of factors.	Typical adult dose of cryo is 1 unit/5 kg body weight, up to a total dose of 10 units (bags). The pediatric dose is 1 unit/5–10 kg body weight or 5–10 mL/kg. Will raise fibrinogen by 0.5 g/L, assuming there is no ongoing consumption/loss of fibrinogen.	Typically 1.0–1.5 times plasma volume exchange is performed per plasma exchange (PLEX) run. Indicated as replacement fluid in PLEX for thrombotic thrombocytopenic purpura.

The resulting guidelines were peer-reviewed by hematopathologists and clinicians, including hematologists and critical care physicians, and were subsequently approved by the Transfusion Medicine Advisory Group (see **Appendix B**).

General considerations

Although most plasma products are prepared from whole blood, a small proportion are prepared with plasma collected by apheresis. Physicians contemplating the use of a frozen plasma product (see **Table**), should keep in mind the following general considerations:

- In British Columbia, informed consent is required prior to the transfusion of frozen plasma.
- All routine coagulation parameters should be checked before a product is ordered. This includes complete blood count (CBC), platelet count, international normalized ratio (INR), partial thromboplastin time (PTT), and fibrinogen.
- The Transfusion Medicine Laboratory Service should be made aware of the clinical diagnosis on the request form used to order frozen plasma. The reason for the transfusion should also be clearly and accurately recorded in the patient's chart.
- Frozen plasma should be given only after risks associated with transfusion of allogeneic blood products have been considered and only when the benefits outweigh the risks.
- Most laboratories in British Columbia convert the prothrombin time (PT) to the international normalized ratio to facilitate comparison of results between laboratories. (Throughout the document, we have tried to use the INR where possible, as this is typically what is reported by British Columbia laboratories.)
- If possible, the cause of abnormal coagulation results should be established and the underlying condition should be treated, even if frozen plasma must be given immediately.
- Once the cause of coagulopathy has been established, the transfusion of plasma should not be based solely on the patient's abnormal INR and/or PTT. Only a subset of patients with abnormal coagulation test results will demonstrate clinical bleeding. The decision to transfuse should be based on the patient's clinical condition and, more specifically, the risk and consequences of bleeding.
- Before transfusing a frozen plasma product, a clinician should be aware that:
  - Satisfactory hemostasis may be achieved when coagulation factor levels are at least 20% to 30% of normal, and when the fibrinogen level is above 1 g/L.[3]
  - The concentration of coagulation factors after plasma exchange (PLEX) of 1 blood volume is approximately 30% of normal levels.[4]
  - There is no direct relationship between bleeding and abnormal results of coagulation tests. However, bleeding more often occurs in patients when the INR or the PTT is greater than 1.5 times the upper limit of the reference range.[5]
- Patients who have received plasma should have their clinical status and coagulation tests monitored to assess response to treatment and to guide assessment of ongoing transfusion needs.
- Prophylactic transfusions should not be given in the absence of clinically abnormal bleeding. However, transfusion of blood components may be indicated for patients with severely abnormal INR and/or PTT results or platelet counts prior to a planned invasive bedside procedure, or when urgent reversal of warfarin therapy is warranted.
- The typical adult dose of plasma is 10 mL to 15 mL per kilogram of body weight. Each unit, or bag, contains approximately 100 mL to 600 mL of anticoagulated plasma. It is therefore strongly recommended that plasma be ordered by required volume rather than number of units. The volume of plasma administered should be sufficient to improve hemostasis.
- Prothrombin complex concentrate (Prothromplex/Bebulin) containing FII, FVII, FIX, and FX, is only available through the Canadian Blood Services (CBS) Special Access Program of Health Canada. There may be a role for its use in patients with the effects of excessive warfarin[1,6] and for reversal of anticoagulation in patients who have had an intracerebral hemorrhage.[7] However, availability of this product is limited. To seek approval for the product, please contact your local Transfusion Medicine Laboratory Service.
- Ideally, transfused plasma should be the same ABO group as the patient. If this is not possible, then the local Transfusion Medicine Laboratory Service will issue compatible plasma of a different group according to policies of acceptable transfusion substitutions. With respect to Rh blood group compatibility, plasma that is derived from either Rh-positive or Rh-negative donors may be transfused to any recipient irrespective of their Rh status. There is a small risk of Rh immunization for Rh-negative patients receiving Rh-positive plasma because of potential small amounts of intact red cells or red cell stromal contamination. However, this risk is very low, which means that no Rh immunoglobulin is required if an Rh-negative patient receives Rh-positive plasma.[1]

Clinical indications for use of frozen plasma in adults

The literature and clinical experience support the use of frozen plasma in the following situations.

Single-factor deficiencies. Currently, specific concentrates are available for FXIII, FXI, FIX, FVIII:C, FVIII:C complexed with von Willebrand factor (Humate P), FVII, FVIIa, fibrinogen, antithrombin, protein C, and C1 esterase inhibitor. A Health Canada Special Access Program application may be required for some of the products and consultation with the local Transfusion Medicine Laboratory Service is recommended. Frozen plasma is indicated for replacement of single congenital factor deficiencies for which no specific fractionated product is available in Canada.[8-10] This is mainly applicable to FV replacement. Occasionally, frozen plasma may be used in emergency situations if specific concentrates are unavailable or unattainable, but the patient should be transferred as soon as possible to facilities where the appropriate factor concentrates are available or, alternatively, factor concentrate should be brought in for the patient. (Grade C recommendation, level IV evidence.)

Multiple-factor deficiencies, hypo/dysfibrinogenemia, and/or disseminated intravascular coagulopathy. Frozen plasma is indicated for use in patients with multiple-factor deficiencies associated with severe bleeding and/or disseminated intravascular coagulopathy. DIC can occur as a result of shock, septicemia, massive blood loss, severe vessel injury, tumor lysis syndrome, or obstetrical complications such as amniotic fluid embolism. Treating the underlying cause of DIC is paramount. Transfusion therapy may be useful and necessary, although there is no defined consensus for transfusion policies to manage DIC.[11] Platelets, FP, FPP, and cryoprecipitate should be transfused only when there is active bleeding and coagulation abnormalities.[1,10] Transfusion of blood components is not indicated to normalize laboratory coagulation results in chronic or acute DIC without hemorrhage. Response to transfusion of components and assessment of ongoing needs should be based primarily on the clinical response supplemented by the results of laboratory tests. Addition of antifibrinolytic therapy (e.g., tranexamic acid or aprotinin) may be useful to control hyperfibrinolysis-induced bleeding. (Grade C recommendation, level IV evidence.)

Thrombotic thrombocytopenic purpura. Most patients who develop thrombotic thrombocytopenic purpura are deficient in an active metalloproteinase plasma enzyme due to the presence of a transient antibody directed against the enzyme. The resulting enzyme deficiency allows the accumulation of high molecular weight von Willebrand factor (HMW-vWF) multimers, leading to excess platelet activation, aggregation, and consumption. The syndrome is characterized by microangiopathic hemolysis and thrombocytopenia, usually with neurologic and/or thrombotic complications. Previously, the acute treatment of TTP was daily plasma exchange using frozen plasma for replacement, which results in removal of the antibody and the HMW-vWF, and replacement of the deficient protease.[12] Currently, many hospitals use cryosupernatant or cryo-poor plasma (plasma from which cryoprecipitate has been removed) instead of FP or FPP for replacement as it lacks the HMW-vWF.[13] The choice of cryosupernatant plasma versus frozen plasma is controversial[14,15] and further randomized studies are needed to establish which product should be used as the treatment of choice. Any patient with a presumed diagnosis of TTP must be referred emergently to a centre staffed with a hematology or nephrology consultant and capable of undertaking plasma exchange therapy. As an interim measure, a slow infusion of frozen plasma may be initiated at a rate of 1 unit every 2 hours. However, this should be done only after consultation with the accepting consultant. (Grade B recommendation, level Ib evidence for daily plasma exchange at presentation.)

Need for urgent reversal of warfarin effect. Frozen plasma should only be used to reverse the warfarin effect when there is severe bleeding or hemostasis is required for emergent surgery or an invasive procedure. Frozen plasma should not be used as the first-line therapy for reversal of the warfarin effect except in severe urgent clinical situations, such as limb- or life-threatening hemorrhage (e.g., intracranial hemorrhage) and when prothrombin complex concentrate is not available. Depending on the degree of anticoagulation, the warfarin effect may be reversed more effectively by a number of measures, such as withholding medication and monitoring the INR or the administration of vitamin K. Studies have shown that reversal of anticoagulation with vitamin K is achieved more rapidly with intravenous administration than oral administration.[16]

In addition to vitamin K, a factor concentrate (e.g., prothrombin complex concentrate) or frozen plasma will help to immediately reverse the warfarin effect. However, one study has shown that frozen plasma does not contain sufficient concentrations of vitamin K factors, particularly FIX, to completely reverse the warfarin effect.[17] A factor concentrate rather than

frozen plasma may more readily achieve complete and rapid reversal of over-anticoagulation and decrease the incidence of hematoma enlargement.[17,18] However, as prothrombin complex concentrate is available in British Columbia only through the CBS special access program, frozen plasma is an acceptable alternative for urgent reversal of the warfarin effect. In such instances, frozen plasma (15 mL/kg) is recommended with simultaneous administration of intravenous vitamin K[16] for longer term correction of hemostasis.[19] Response to therapy and the need for additional therapy should be guided by the clinical hemostatic response. Monitoring of the INR is also essential. Of note, clinical trials are being conducted with recombinant FVIIa in the setting of intracranial hemorrhage and, pending the results, this may be an acceptable alternate or preferred product for use in this setting. (Preference of a factor concentrate to frozen plasma—grade B recommendation, level III evidence. Administration of intravenous versus oral vitamin K—grade B recommendation, level IIa evidence.)

Vitamin K deficiency. Many hospitalized or ill patients have inadequate vitamin K intake, especially if they are on a low-lipid diet and/or antibiotics. Body stores of vitamin K last only 2 weeks, so these patients are particularly susceptible to developing a deficiency. These patients may have a prolonged INR[20] (and often a prolonged PTT) and administration of oral or intravenous vitamin K will correct deficits in vitamin K-dependent coagulation factors.[21] Frozen plasma should not be used to correct inadequate vitamin K intake even if clotting times are prolonged, unless urgent invasive procedures are required or the patient is bleeding. Protocols and policies for the administration of vitamin K to patients should be established by each clinical unit. In the presence of normal liver function, the coagulation factors return to hemostatic levels approximately 12 hours after vitamin K administration.[5] (Grade B recommendation, Level IIa evidence.)

Before transfusing a frozen plasma product, a clinician should be aware that there is no direct relationship between bleeding and abnormal results of coagulation tests. However, bleeding more often occurs in patients when the INR or the PTT is greater than 1.5 times the upper limit of the reference range.

Liver disease, especially in the setting of liver biopsy. Patients with liver disease often have coagulation abnormalities that parallel the degree of parenchymal liver damage. Thrombocytopenia secondary to splenomegaly and dysfibrinogenemia may further increase the risk of bleeding. However, spontaneous bleeding seldom occurs without a precipitating event such as surgery, liver biopsy, or vessel rupture. The response to frozen plasma in liver disease is unpredictable and seldom corrects coagulation abnormalities;[22] therefore, routine prophylactic administration of FP is of questionable utility. Of the small percentage of patients who bleed following the procedure, some may require surgical intervention. The risk of bleeding is more likely related to vascular lesions, including malignant tumors, or other patient factors such as poor nutrition. Several authors conclude that pre-procedure coagulation testing fails to predict bleeding outcome.[23-25] There is little evidence to support the routine use of pre-procedure frozen plasma and platelet transfusions prior to liver biopsies for patients with mild to moderate abnormal results of hemostasis (INR and PTT less than 1.5 times the upper limit of the reference range, platelet count greater than 50×10^9/L) as the risk of hemorrhagic complications is not reliably reduced by transfusion of frozen plasma. If the patient has a marked abnormality of coagulation parameters (i.e., outside the parameters listed above) then the prophylactic use of frozen plasma may be undertaken prior to a procedure, based upon the clinician's judgment. However, there are no randomized trials to support this practice. Given the nature and risks involved in the procedure, all patients who undergo the procedure, including those with normal coagulation laboratory values, should be monitored for signs and symptoms of bleeding. (Grade B recommendation, level IIa evidence.)

Preparation for invasive bedside procedures. Invasive bedside procedures are commonly performed in

hospitals and they typically include the following:

- Central venous catheter insertion
- Thoracocentesis/paracentesis
- Gastrointestinal endoscopy and biopsy
- Bronchoscopy, transbronchial lung biopsy, and pulmonary procedures
- Renal biopsy
- Epidural anesthesia, diagnostic lumbar puncture, and neurosurgical procedures
- Angiography

Prior to performing invasive bedside procedures, coagulation tests are commonly ordered with the intention to assess the risk of bleeding complications. However, there is little evidence in the current literature to suggest that mild to moderate abnormalities of the INR and PTT are predictive of hemorrhagic risk, or that these patients will benefit from preprocedure frozen plasma transfusion.[25] Mild to moderate abnormal coagulation results do not imply clinically abnormal bleeding because of the basic design of the INR and PTT assays and the normal physiological reserve of hemostasis. Baseline coagulation factor activity of 40% or higher is required to maintain hemostasis. These are general guidelines and more conservative practices may be justified for higher-risk procedures (e.g., lumbar disc space insertions, neurosurgical procedures, and pulmonary biopsies and procedures). The decision to transfuse blood products can usually be justified when treating hemorrhagic complications. (Grade B recommendation, level IIa evidence.)

During intraoperative cardiopulmonary bypass. The etiology of coagulopathy during intraoperative cardiopulmondary bypass (CPB) is multifactorial and relates to platelet dysfunction, heparinization, and possible dilutional coagulopathy. Transfusion requirements during CPB have decreased in the last 2 decades because of improved surgical techniques and the availability of "near-patient" coagulation tests. Furthermore, the use of antifibrinolytics either prophylactically or in response to excessive hemorrhage has also decreased blood component use. Current evidence does not support the *routine* use of frozen plasma in CPB surgery.[26] (Grade B recommendation, level IIb evidence.)

For massive transfusion. A massive transfusion is defined as the replacement of a patient's whole blood volume with stored blood within a 24-hour period. Other definitions of massive hemorrhage necessitating massive transfusion are more predictive and are defined as 50% blood volume loss within 3 hours or a rate of loss of 150 mL/min.[27] There are many causes of massive hemorrhage, including trauma, surgery (cardiac, transplantation), gastrointestinal bleeding, disseminated intravascular coagulopathy, and obstetrical complications. In all of the above situations, massive transfusion may become necessary and a coagulopathy may ensue that is traditionally ascribed to dilution of platelets and clotting factors as patients lose whole blood while receiving replacement with packed red blood cells (PRBC) and colloid fluids. It is now recognized that the coagulopathy is multifactorial due to the prolonged effects of hypothermia, hypotension, shock, and the development of DIC. Overall, the decision to transfuse frozen plasma or other blood components should be based on clinical judgment and timely coagulation tests. There is no role for the use of replacement "formulae" to guide transfusions[3] except in the rare situation where the rate of blood loss outstrips the clinician's ability to repeat assessments and coagulation testing. In the event of intractable bleeding following transfusion of large volumes of colloid, PRBC, and platelets, frozen plasma and cryoprecipitate may be transfused to maintain the INR and PTT values at less than 1.5 times the upper limit of the reference range[5] and to increase fibrinogen concentration to a minimum of 1.0 g/L.[27] (Grade B recommendation, level IIb evidence.)

Clinical indications for use of frozen plasma in neonates

In addition to the clinical circumstances already described, it may be appropriate to use frozen plasma in the following situations.

Inherited deficiencies of clotting factors. Refer to the section above on single-factor deficiencies. If no factor-specific concentrate is available, then frozen plasma may be indicated.

Hemorrhagic disease of the newborn. Although the incidence of hemorrhagic disease of the newborn (HDN) has decreased since the introduction of routine vitamin K prophylaxis, some infants are still at high risk. This group includes those who are born prematurely, those with liver disease, or those born to mothers on medications such as anticonvulsants, warfarin, or isoniazid. Frozen plasma may also be considered for treatment of severe HDN. Currently, there are no studies to guide the dosage,[1] but a dose of 10 mL to 15 mL per kilogram of body weight is usually well tolerated. (Grade C recommendation, level IV evidence.)

Coagulopathy and bleeding, or coagulopathy with planned procedure. Frozen plasma is indicated for neonates with sepsis, hypotension, hypoxia (respiratory distress syndrome), or liver disease if they have significant coagulopathy and bleeding or if they are at risk of bleeding from an inva-

sive procedure. They should receive approximately 15 mL of frozen plasma per kilogram of body weight and a dose of vitamin K.[1] The response should be monitored clinically and by coagulation studies.[28] (Grade C recommendation, level IV evidence.)

Response to transfusion of components and assessment of ongoing needs should be based primarily on the clinical response supplemented by the results of laboratory tests.

Possible use for frozen plasma

The use of frozen plasma may be considered in the following situation.

Prevention of red blood cell hemolysis related to red cell T antigen activation. Red blood cells carry cryptic antigens that can be exposed when a neonate is infected with neuraminidase-producing bacteria such as clostridia, streptococcus, or pneumococcus in conditions such as necrotizing enterocolitis (NEC). This is known as red cell T antigen activation. Donor plasma contains naturally occurring "anti-T" antibodies. Theoretically, when a plasma product containing anti-T antibodies is administered, the antibodies can damage the patient's T-activated red cells causing hemolysis. Currently, there are no randomized controlled trials to support the use of specially prepared plasma products (i.e., low-titre anti-T plasma) for infants with NEC.[29] For management of patients with NEC and suspected red cell T antigen activation, the physician should consult the transfusion medicine director for product selection as this is a controversial topic and optimal management has not been clearly defined. (Grade B recommendation, level IIa evidence.)

Inappropriate uses for frozen plasma

Because there are many alternatives available for the treatment of the clinical conditions listed below, and because of the risks involved in transfusion, use of frozen plasma products is not indicated in the following situations.

Hypovolemia. Frozen plasma should not be used as a simple intravascular volume expander in adults or children. Crystalloids and/or volume expanders, such as pentastarch, are indicated; they are safer, less expensive, and readily available.

Plasma exchange. Frozen plasma is not routinely indicated for replacement volume in PLEX, except for patients with TTP.

Reversal of prolonged INR in the absence of bleeding. Frozen plasma is not indicated for prolonged INR in the absence of bleeding. If the prolongation is due to an oral anticoagulant, then the medication should be withheld. Depending on the extent of INR elevation and the severity of the patient's clinical condition, vitamin K administration may be helpful.

Prevention of intraventricular hemorrhage in preterm infants. Routine administration of frozen plasma is not indicated for prevention of intraventricular hemorrhage in infants born before 32 weeks gestation.[30]

Treatment of neonates with polycythemia. Frozen plasma is not indicated in the treatment of neonates with polycythemia; crystalloid is considered an effective partial-exchange transfusion fluid.[31] Infants who are clinically well or with only minor symptoms do not necessarily benefit from partial-exchange transfusion.

Wound healing. Frozen plasma is not indicated to enhance or promote wound healing.

Treatment of immunodeficiency states. Frozen plasma is not indicated for treatment of immunodeficiency states. Purified intravenous immunoglobulin preparations are available for these conditions.

Other inappropriate uses. In addition, frozen plasma should not be used for nutritional support, protein-losing states, Guillain-Barré syndrome,[2] acute pancreatitis,[2] or burns.[2]

Competing interests

None declared.

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Appendix A

US Agency for Healthcare Policy and Research guidelines for defining the types of evidence and the grading recommendations.

Levels of evidence

Ia Evidence obtained from the meta-analysis of randomized controlled trials.

Ib Evidence obtained from at least one randomized controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomization.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grades of recommendations

A Required at least one randomized controlled trial as part of a body literature of overall good quality and consistency addressing the specific recommendations (evidence levels Ia, Ib).

B Requires availability of well conducted clinical studies but no randomized clinical trials on the topic of recommendations (evidence levels IIa, IIb, III).

C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV).

Appendix B

The Transfusion Medical Advisory Group advises the BC Ministry of Health. It is composed of transfusion medicine experts who meet regularly to discuss pertinent transfusion-related issues and to endorse transfusion initiatives that will improve the Canadian health care system.

Members

Ms Sheila Armstrong, Administrator, Provincial Laboratory Coordinating Office

Dr Brian Berry, Director Hematopathology and Transfusion Medicine, Vancouver Island Health—South Island, Victoria, BC

Dr Mark Bigham, Medical Officer, Canadian Blood Services—BC and Yukon Centre

Dr Kate M. Chipperfield, Regional Medical Leader, Blood Transfusion Medicine, Vancouver Coastal Health, Vancouver, BC

Dr Jason Doyle, Director, Transfusion Services—Interior Health, Kelowna, BC

Ms Shelley Feenstra, Regional Blood Transfusion Clinician—Vancouver Coastal Health, Vancouver, BC

Dr David Ferguson, Medical Director, BC Biomedical Laboratories Ltd., Surrey, BC

Dr Gershon Growe, Canadian Blood Services—BC and Yukon Centre

Ms Donna Miller, Chair, Nursing Resource Group, Royal Jubilee Hospital, Victoria, BC

Dr Randell Moore, Anesthesiologist, St. Paul's Hospital, Vancouver, BC

Dr Doug Morrison, Director, Transfusion Medicine, Royal Columbian Hospital, New Westminster, BC

Dr David Pi, Director, Provincial Blood Coordinating Office, Vancouver, BC

Ms Pam Quibell, Charge Technologist—Transfusion Services, Northern Health, Prince George, BC

Mr Lyle Unrau, Customer Service Rep, Canadian Blood Services—BC and Yukon Centre

Dr Louis D. Wadsworth, Executive Medical Director, Provincial Health Services Authority (PHSA) Corporate—Lab Services, Vancouver, BC (Chair)

Ms Maureen Wyatt, Assistant Charge Technologist, Interior Health, Kelowna, BC

Mr Ed Yee, Regional Director, Canadian Blood Services—BC and Yukon Centre

Dr Wilson Yeung, Hematopathologist, St. Paul's Hospital, Vancouver, BC

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