Ontario Regional Blood Coordinating Network

Inspiring and facilitating best transfusion practices in Ontario.

FIBRINOGEN CONCENTRATE & PROTHROMBIN COMPLEX CONCENTRATE: TRANSFUSIONISTS CONCENTRATE ON …

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September 27, 2023

Speaker Disclosure

- No commercial product conflicts of interest to declare
- Transfusion Transmitted Injuries Surveillance System, member Education Committee
- Using Blood Wisely initiative, member nursing education development
- Canadian Society of Transfusion Medicine, member Standards Committee

Pre Transfusion Knowledge Question 1

Select the correct statement(s) regarding fibrinogen concentrate [FC]:

a) The principal indication is major or massive hemorrhage.
b) FC can be reconstituted at the bedside with 50 mL of 0.9% sodium chloride.
c) If a patient's fibrinogen is less than 2 g/L, FC is indicated.
d) For bleeding patients, FC can be given at a rate of 20 mL per minute.

Pre Transfusion Knowledge Question 2

Select the correct statement(s) regarding prothrombin complex concentrate [PCC]:

a) PCC is indicated for patients with major bleeding, an elevated INR, and taking warfarin.
b) Vitamin K must be given concurrently with PCC.
c) Symptoms of minor allergic reaction (urticaria) are common with PCC administration.
d) For bleeding patients, PCC can be given at a rate of 20 mL/minute.

Fibrinogen Concentrate (FC) & Prothrombin Complex Concentrate (PCC): Transfusionists, Concentrate On …

Objectives:

- To understand the role of FC & PCC and the clinical indications.
- To define nursing actions to safely administer FC & PCC (reconstitution, tubing, infusion rate, monitoring, possible adverse reactions).

Outline:

- Hemostasis: the blood clotting system.
- What is FC / PCC?
- Indications/Transfusion Guidelines FC / PCC
- Administration FC / PCC.
- FC / PCC Use If Plasma is Not Available
- Possible Adverse Reactions FC / PCC

Hemostasis: the blood clotting system (1)

Hemostasis

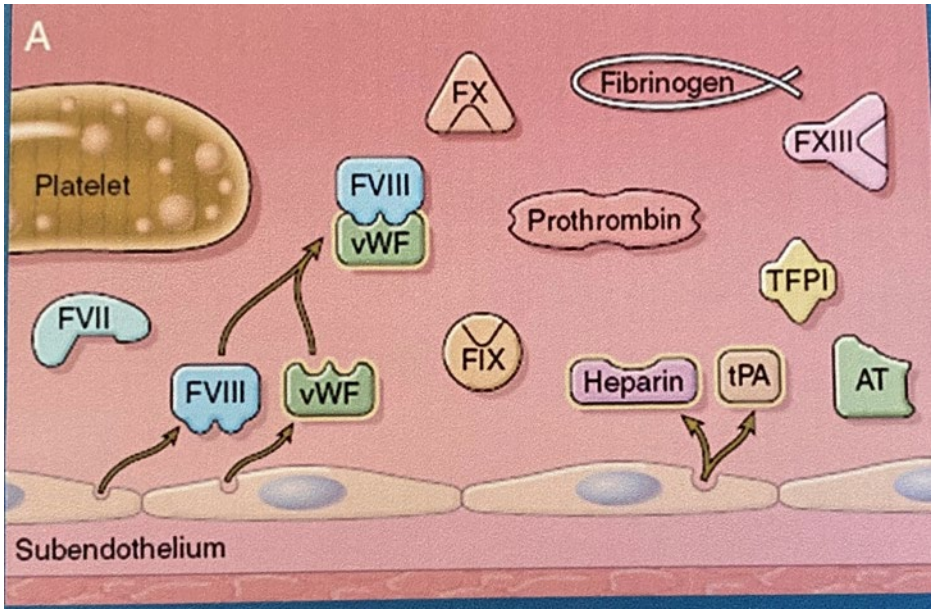
- injury to a blood vessel leads to activation of several parts of the blood clotting system to control bleeding.
- 4 main elements
    1. Primary hemostasis
    2. Secondary hemostasis
    3. Fibrin clot: formation & stabilization
    4. Inhibition of coagulation

Hemostasis: the blood clotting system (2)

Hemostasis
(cross-section of blood vessel)

System in its natural balance

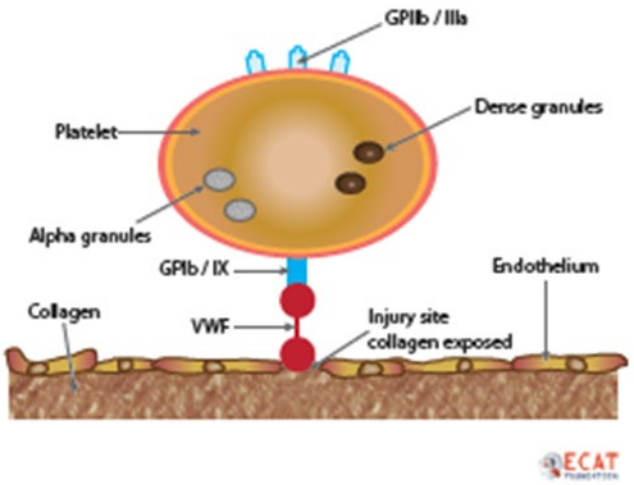
- Plasma coagulation proteins (factors), not activated
- Physiologic antithrombotic mechanism
- Platelets
- Endothelium is intact

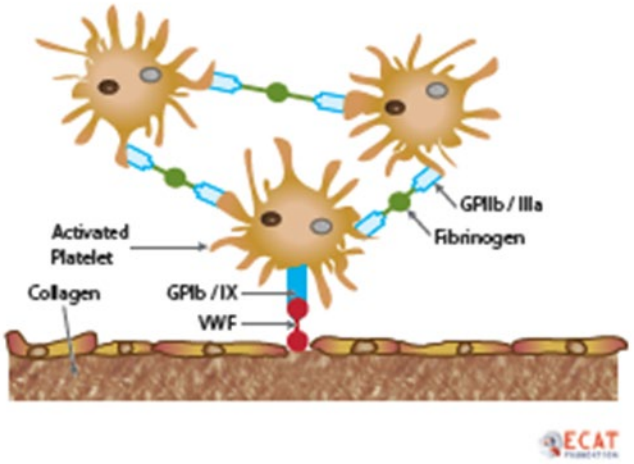


Hemostasis: the blood clotting system (3)

1. **Primary Hemostasis**

- **Trigger:** Blood vessel wall injury, exposes subendothelial collagen.
- **Vasoconstriction:** Defense mechanism.
- **Adhesion:** Platelets adhere to the collagen that has been exposed via von Willebrand Factor [VWF] and platelet receptors.
- **Aggregation:** With the help of fibrinogen, platelets aggregate with each other. This provides the phospholipid surface needed to activate clotting factors.





Hemostasis: the blood clotting system (4)

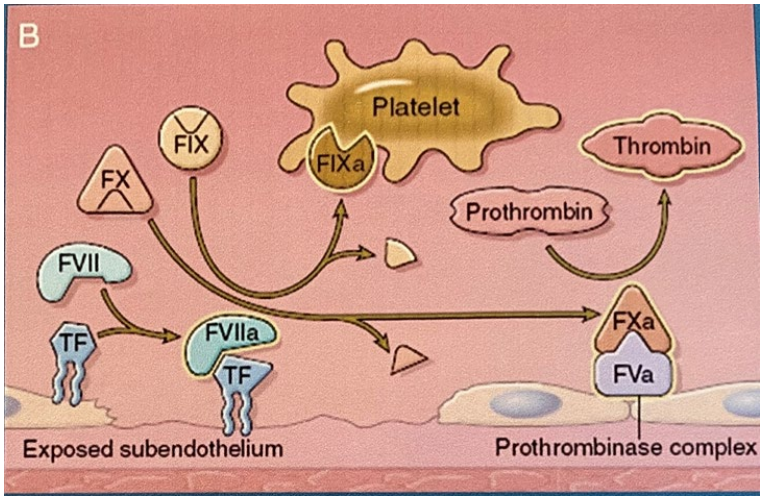
2. Secondary Hemostasis

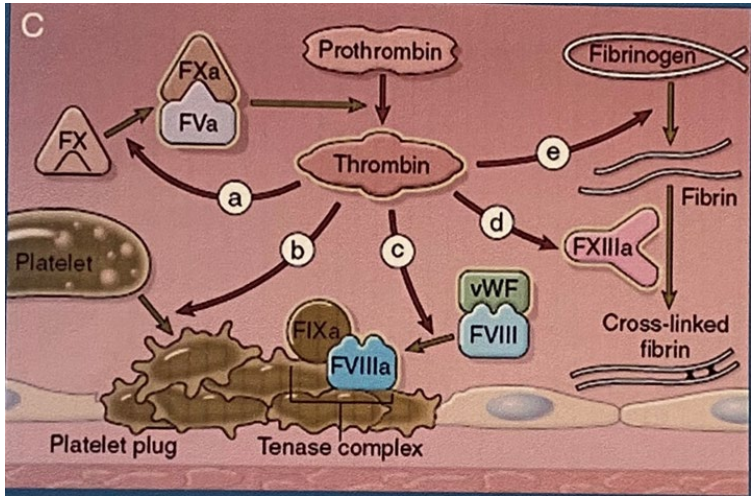
(Factor [F] + letter "a" means activated)

- **Initiation of coagulation:**
  - Injured tissue cells release Tissue Factor [TF].
  - TF & FVIIa form the TF/FVIIa complex.
  - TF/FVIIa complex activates FIX & FX, producing a small amount of thrombin.

- **Amplification phase:**
  - Thrombin activates FV, FVIII, FXI, & more platelets.

- **Propagation phase:**
  - When the TF/FVIIa complex activates FIX, more FXa is created.
  - FIXa & FVIIIa form the tenase complex & more FXa is produced.
  - FXa & FVa with calcium & the phospholipid surface (activated platelets) form the prothrombinase complex which converts prothrombin to large amounts of thrombin.

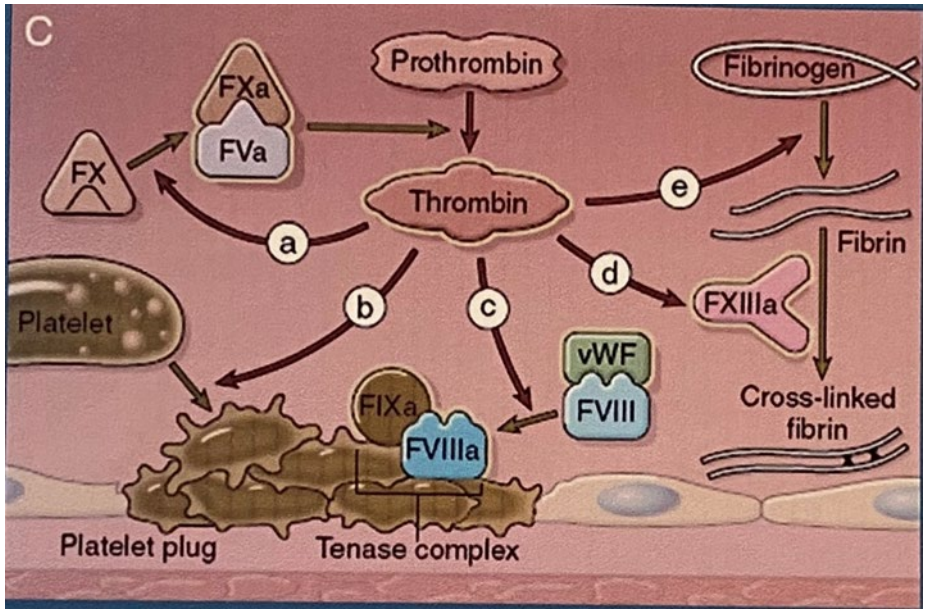




Hemostasis: the blood clotting system (5)

3. Fibrin clot: formation & stabilization

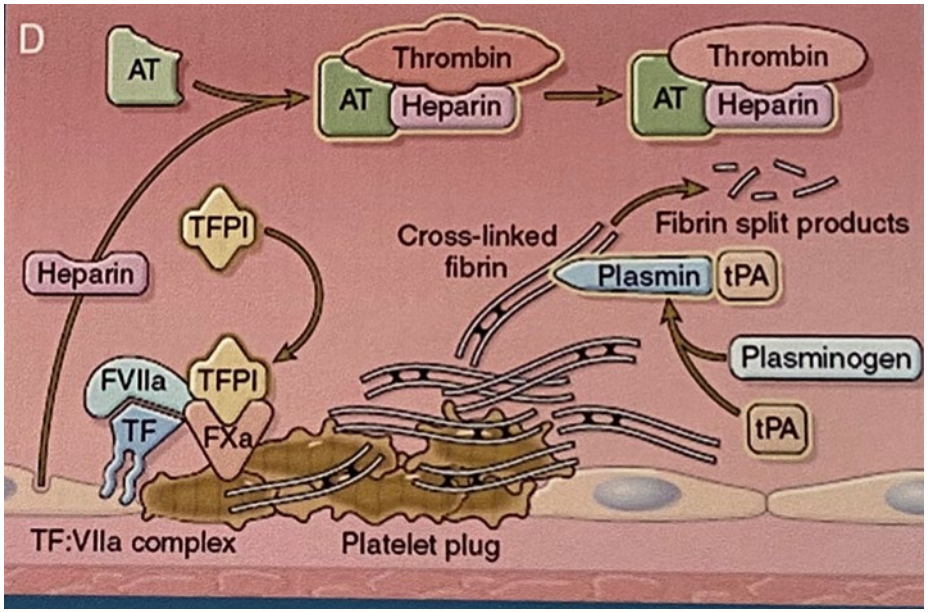
- **Thrombin:**
  Converts fibrinogen to fibrin monomers (soluble).
- **Thrombin:** Activates FXIII.
- **FXIIIa:**
  Cross-links the fibrin monomers (insoluble) which leads to a stable clot.



Hemostasis: the blood clotting system (6)

4. Inhibition of coagulation

- **Inhibition of thrombin generation:**
  - Thrombin binds to thrombomodulin (a membrane receptor) & activates Protein C to Activated Protein C [APC].
  - APC joins with Protein S which inhibits FVa & FVIIIa (slows down coagulation).
  - Thrombin bound to thrombomodulin becomes inactive (can't activate procoagulant factors or platelets).
  - Antithrombin [AT], a naturally occurring anticoagulant, inhibits thrombin & other activated factors, mainly FXa.
- **Fibrinolysis:**
  - Tissue plasminogen activator [tPA] converts plasminogen to plasmin.
  - Plasmin breaks down cross-linked fibrin (to Fibrin Degradation Products [FDP]).
  - Fibrinolysis is suppressed by several inhibitors (thrombin activatable fibrinolysis, anti-plasmin, & plasminogen activator inhibitors).



Fibrinogen Concentrate (FC)

Fibryga®

RiaSTAP®

Vial size:
1 g/50 mL

What is FC?

Brand	Fibryga®	RiaSTAP®
Composition per 1 g vial	Human Fibrinogen 1000 mg	Human Fibrinogen 900-1300 mg
	Nonmedicinal ingredients: Glycine, sodium chloride, L-Arginine hydrochloride, sodium citrate dihydrate.	Nonmedicinal ingredients: Human albumin, sodium chloride, L-arginine hydrochloride, sodium citrate, sodium hydroxide (for pH adjustment).

NOTE (per National Advisory Committee on Blood & Blood Products [NAC])
Cryoprecipitate is manufactured (by Canadian Blood Services [CBS]) from slowly thawed frozen plasma and is indicated for replacement of fibrinogen.
In terms of clinical effectiveness, there is no evidence of superiority of one fibrinogen replacement source.
FC is pathogen inactivated and thus its safety profile (transmissible disease risk) is favoured.
Also, FC provides a precise fibrinogen dose and simpler preparation (thawing is not required; bedside reconstitution is an option).

FC Patient Case 1

Charlotte, a 19-year-old female was brought to your **Trauma Centre**; her car collided with a transport truck.

Massive Hemorrhage Protocol (MHP) was ordered.

She was intubated, given tranexamic acid, and transfused; given 2 transfusion packs totalling
8 units red blood cells [RBC], 4 units frozen plasma[FP]).

Lab tests have been sent; results are pending.

FC Patient Case 1: Question

The next transfusion pack (Pack # 3) should include (in addition to RBC and FP units):

a) Albumin 25% 100 mL, 2 bottles.
b) Prothrombin Complex Concentrate 2000 IU.
c) Fibrinogen Concentrate 4 g.
d) Intravenous Immune Globulin 2 g per kilogram.

FC Patient Case 2

Joe, a 69-year-old male has undergone complex cardiac surgery (coronary artery bypass grafting and aortic valve replacement) is admitted to your intensive care unit.

During the surgery, he was transfused 9 units RBC, 6 units FP and 2 doses platelets.

Lab tests results (sent at the end of the surgery) include:
Hb 78 g/L, platelets 88 X 10^9/L, INR 1.5, fibrinogen 1.2 g/L.

Chest tube blood loss, initally moderate, is increasing.

FC Patient Case 2: Question 1

Joe's physician is likely to order:

a) Albumin 25% 100 mL, 2 bottles.
b) Prothrombin Complex Concentrate 2000 IU.
c) Fibrinogen Concentrate 4 g.
d) Intravenous Immune Globulin 2 g per kilogram.

Review: Fibrinogen's Impact on Hemostasis

Hemostasis: main elements

1. Primary hemostasis: In the Aggregation phase, **fibrinogen** helps platelets aggregate with each other which then provides the phospholipid surface needed to activate clotting factors.

2. Secondary hemostasis

3. Fibrin clot: formation & stabilization: Thrombin converts **fibrinogen** to fibrin monomers which are then cross-linked to form a stable clot.

4. Inhibition of coagulation

FC Indications/Transfusion Guidelines

(Lab test: Clauss fibrinogen assay; Normal fibrinogen 1.5 to 4 g/L)

Brand	Fibryga®	RiaSTAP®
Per product monograph	➢ "treatment of acute bleeding episodes & perioperative prophylaxis in adult & pediatric patients with congenital afibrinogenemia & hypofibrinogenemia" ➢ a therapy for management of uncontrolled severe bleeding in patients with acquired fibrinogen deficiency during surgical interventions	➢ "treatment of congenital fibrinogen deficiency which comprises congenital afibrinogenemia and hypofibrinogenemia"
National Advisory Committee on Blood & Blood Products [NAC]	➢ As per product monographs ➢ "The use … in acquired hypofibrinogenemia is supported by studies, including a high-quality randomized trial in bleeding patients undergoing cardiovascular surgery" ➢ including bleeding obstetrical patients "among others" ➢ "both fibrinogen concentrates appear to have similar efficacy in improving clot firmness in a dilutional hypofibrinogenemia model in vitro"	
Bloody Easy 5.1 [BE 5.1] (p.127)	➢ As per product monographs ➢ "Major or massive hemorrhage from surgery or trauma when fibrinogen <1.5 g/L." ➢ "Acute phase of acute promyelocytic leukemia with fibrinogen <1.5 g/L." ➢ "Hemorrhage after cardiac surgery or peripartum with fibrinogen <2.0 g/L." ➢ "Intracranial hemorrhage secondary to treatment with Tissue Plasminogen Activator with fibrinogen <2.0 g/L."	

FC Patient Case 2: Question 2

Joe's physician has ordered FC 4 g IV now.
(Joe is the patient admitted to ICU post complex cardiac surgery)
Select the correct statement(s):

a) Transfusion Medicine Lab [TML] will/may issue 2 vials of FC to be reconstituted at the bedside.
b) TML will/may reconstitute the FC and issue it in a mini-bag.
c) When reconstituting FC, it should be shaken vigorously for 1 - 2 minutes to ensure it is completely dissolved.
d) FC is compatible with 0.9% sodium chloride. Flush the infusion site prior to and following administration.
e) FC must be given IV direct/IV push, as quickly as possible.

FC Administration 1

(Informed consent; product checks – patient identification, lot number, expiry & visual inspection)

Brand	Fibryga®	RiaSTAP®
Dose	- Acquired fibrinogen deficiency: adults 4 g (4 of 1 g vials), final volume 200 mL per 4 g dose. - Congenital afibrinogenemia & hypofibrinogenemia: dose calculation per product monograph	
TML Storage	Room temperature, up to 36 months	Refrigerator, up to 60 months
Reconstitution	- Packaged with solvent Sterile Water for Injection vial (50 mL), Octajet transfer device, & particle filter. - Use Aseptic technique. - Gently swirl the vial to ensure fully dissolved (from 5 up to 30 minutes). Do not shake. - Do not use solutions that are cloudy or have deposits. - Reconstituted, fibrinogen concentration is 20 mg/mL. - Label product appropriately.	- Packaged with diluent Sterile Water for Injection vial (50 mL), mini-spike® dispensing pin, & syringe filter. - Bring diluent & product vials to room temp. - Use Aseptic technique - Gently swirl the vial to ensure fully dissolved (about 5 to 10 minutes). Do not shake. - Should be clear & colourless, otherwise do not use. - Reconstituted, fibrinogen concentration is 20 mg/mL. - Label product appropriately.
Expiry post reconstitution	Should be used immediately, otherwise responsibility of the user. (Stability has been demonstrated for up to 24 hours at +25°C).	Stable for 8 hours after reconstitution when stored at room temperature & should be administered within this time.

FC Administration 2

Brand	Fibryga®	RiaSTAP®
Tubing	Standard IV tubing (filtered as part of reconstitution procedure)	
IV Fluid	Flush infusion site with 0.9% sodium chloride prior to & following administration.	
Infusion Rate	For patients with acquired fibrinogen deficiency (i.e., bleeding patient), maximum rate of 20 mL per minute (1,200 mL/hour).	Slow intravenous infusion, not exceeding 5 mL per minute (300 mL/hour).
Patient Monitoring	- Assess for signs & symptoms of allergic transfusion reaction (hives, rash, facial or airway edema, difficulty breathing, tachycardia, hypotension). - Use of FC is associated with risk of thrombosis. Monitor for signs & symptoms: leg or arm swelling, feeling warm to touch, red discolouration, tenderness or cramping; shortness of breath, chest/back pain with breathing).	
Lab test monitoring	Following infusion, repeat fibrinogen immediately/within 60 minutes Expected fibrinogen increment is approximately 0.5-1.0 g/L.	

FC:
Neonate Notes & Pediatric Pearls

NAC

In neonates and pediatric patients, it is recommended to consult with the product monograph and a specialist with expertise in managing pediatric/neonatal coagulopathy prior to administration of fibrinogen concentrates. In published studies (13-14) of acquired hypofibrinogenemia in neonatal or pediatric populations, fibrinogen concentrate dosing has ranged between 30-60 mg/kg.

Bloody Easy 5.1 p. 126-7

Pediatrics

Dose: [18]

- **Neonates and Children:** 50 mg/kg infused over 10 minutes for bleeding patients.[18]

Prothrombin Complex Concentrate (PCC)

Beriplex®

Octaplex®

Vial sizes:
500 IU/20 mL
1000 IU/40 mL

What is PPC?

Brand	Beriplex®	Octaplex®
Composition per mL reconstituted solution	Factor II 20 – 48 IU/mL Factor VII 10 – 25 IU/mL Factor IX 25 IU/mL Factor X 22 – 60 IU/mL Protein C 15 – 45 IU/mL Protein S 12 – 38 IU/mL	Factor II 14 – 38 IU/mL Factor VII 9 – 24 IU/mL Factor IX 25 IU/mL Factor X 18 – 30 IU/mL Protein C 13 – 31 IU/mL Protein S 12 – 32 IU/mL
	Nonmedicinal ingredients: heparin, human antithrombin III, human albumin, sodium chloride, sodium citrate, hydrochloric acid or sodium hydroxide in small amount for pH adjustment, solvent (water for injection)	Nonmedicinal ingredients: heparin, sodium citrate, small amounts of solvent detergent reagents TNBP and Polysorbate, solvent (water for injection)

Prothrombin is FII.
Thrombin is the activated form, FIIa.

PCC Patient Case 1

Flo, a 60-year-old female was admitted with a complex left hip fracture related to a fall and requires urgent surgical intervention.

She has a history of 3 previous left hip surgeries (congenital hip dysplasia). Flo also takes warfarin for remote post-operative deep vein thrombosis and pulmonary embolism.

She is scheduled for the operating room in 4 hours.
Her international normalized ratio [INR] is 2.3.
Additional lab investigations are within normal ranges.

Her weight is 70 kg.

PCC Patient Case 1: Question 1

Flo's physician is likely to order (select all that are indicated):

a) Vitamin K 10 mg IV.
b) FC 4 g IV.
c) PCC 1000 IU IV.
d) Post infusion, re-check INR immediately.

PCC Patient Case 2

Jim, a 68-year-old male presented to Emergency Department with hematemesis and abdominal pain.
He is being transfused a 4th RBC for symptomatic anemia (Hb 69 g/L, BP 88/50 mmHg).

Three months ago he was diagnosed with atrial fibrillation, which has been medically managed, including apixaban for stroke prophylaxis.

His INR is 1.4. Other than Hb, lab investigations are within normal ranges. His weight is 75 kg.
Gastroenterology has scheduled an urgent endoscopy for evaluation and likely endoscopic hemostasis.

PCC Patient Case 2: Question 1

Jim's physician is likely to order (select all that are indicated):

a) Vitamin K 10 mg IV.
b) FC 4 g IV.
c) PCC 2000 IU IV.
d) Post infusion, re-check INR immediately.

Review: PCC Impact on Hemostasis

Hemostasis: main elements

1. Primary hemostasis
2. Secondary hemostasis: FVII, FIX, & FX are activated, large amounts of thrombin (FIIa) are generated
3. Fibrin clot: formation & stabilization
4. Inhibition of coagulation: In the inhibition of thrombin generation, Protein C is activated to Activated Protein C [APC]. APC joins with Protein S which inhibits FVa & FVIIIa (slows down coagulation).

PCC Indications/Transfusion Guidelines

In clinical practice, currently available 4-factor PCCs are considered interchangeable.

Brand	Beriplex®	Octaplex®
Per product monograph	➢ Urgent treatment or perioperative prophylaxis of **major bleeding** in acquired deficiency of the prothrombin complex coagulation factors (i.e., deficiency due to vitamin K antagonist treatment, warfarin) ➢ Administer vitamin K simultaneously; monitoring of INR is mandatory. ➢ Use only when rapid correction of levels is necessary. In other situations, reducing the dose of the vitamin K antagonist and/or administration of vitamin K is usually adequate.	
National Advisory Committee on Blood & Blood Products [NAC]	➢ As per product monographs ➢ "Treatment of bleeding in patients receiving direct FXa inhibitor anticoagulants - PCCs should only be considered in patients with severe or life-threatening bleeding … no randomized trials published." - "The optimal dosing strategy is uncertain with 2000 IU (fixed dose) or 25-50 IU/kg (to a maximum of 3000 IU) being the most common" ➢ NAC also lists some unique patient scenarios (if plasma is refused) as well as some with limited evidence that are not promoted (coagulation defects/bleeding in cardiac surgery).	
Bloody Easy 5.1 [BE5.1] (p.127)	➢ As per product monographs ➢ "Reversal of anti-Xa inhibitors: PCCs at a dose of 2,000 IU (repeated in 1 hour if hemostasis is not achieved) is being used across Canada. Data to support its use is limited …"	

PCC is **CONTRAINDICATED** in patients with heparin-induced thrombocytopenia [HIT] or with known allergies to heparin (both Beriplex® & Octaplex® contain heparin).

PCC Patient Case 2: Question 2

Jim's physician has ordered PCC 2000 IU IV now.
(Jim has hematemesis, symptomatic anemia required RBC transfusion, on apixaban re: atrial fibrillation, INR 1.4, for urgent endoscopic treatment).
Select the correct statement(s):

a) If a second dose of PCC is reconstituted but not required for the endoscopy, it could be refrigerated and given later.

b) Jim does not require PCC as his INR is ≤ 1.5.

c) Reconstituted PCC should be colourless, otherwise it must not be given.

d) When reconstituting PCC, it should be shaken vigorously to ensure it is completely dissolved.

e) PCC is compatible with Ringer's lactate. Flush the infusion site prior to and following administration.

PCC Administration 1

(Informed consent, product checks – patient identification, lot number, expiry & visual inspection)

Brand	Beriplex®	Octaplex®
Dose	- No clear consensus approach to dosing, observational studies demonstrated various dosing strategies lead to similar outcomes. A single dose should not exceed 3000 IU. - Dosing options include INR based, weight based, and combination INR/weight based. - Per NAC & BE 5.1: For urgent vitamin K antagonist (warfarin) reversal & INR known, **INR < 3**, PCC 1000 IU; **INR 3-5**, PCC 2000 IU; **INR > 5**, PCC 3000 IU. - If major bleeding and INR unknown/taking direct FXa inhibitor anticoagulants: PCC 2000 IU	
TML Storage	Refrigerator or room temperature. Shelf life 36 months.	Room temperature. Shelf life 36 months.
Reconstitution	- Packaged with solvent Water for Injection vial (20/40 mL), Mix2Vial® transfer device (filter). - Bring solvent & product vials to room temp. - Use Aseptic technique. - Gently swirl vial to ensure fully dissolved. Do not shake. - Should be clear or slightly opalescent, do not use if cloudy or has deposits. - Label product appropriately.	- Packaged with solvent Water for Injection vial (20/40 mL), Mix2vial® transfer device (filter). - Use Aseptic technique - Gently swirl vial to ensure fully dissolved Do not shake. - Should be slightly blue to colourless, do not use if cloudy or has deposits. - Label product appropriately.
Expiry post reconstitution	Should be used immediately, may store at room temperature up to 3 hours.	Should be used immediately, may store at room temperature up to 8 hours.

PCC Administration 2

Brand	Beriplex®	Octaplex®
Tubing	Standard IV tubing (filtered as part of reconstitution procedure)	
IV Fluid	Flush IV tubing/infusion site with 0.9% sodium chloride prior to & following administration.	Flush IV tubing/infusion site with 0.9% sodium chloride or 5% dextrose in water prior to & following administration.
Infusion Rate	- Not more than 3 IU/kg/minute. - Maximum 8 mL per minute (480 mL/hour). i.e., 1000 IU/40 mL over 5 minutes	- Initial rate 1 mL per minute (60 mL/hour). - Maximum 3 mL per minute (180 mL/hour). - In practice,1000 IU/40 mL over 5 minutes.
Patient Monitoring	- Monitor vital signs before, during and after infusion (observe for tachycardia). - Assess for signs & symptoms of allergic transfusion reaction (hives, rash, facial or airway edema, difficulty breathing, tachycardia, hypotension). - Use of PCC is associated with risk of thrombosis/thromboembolic complications (including myocardial infarction) & especially with repeated dosing. Monitor for signs and symptoms of thromboembolic events (leg or arm swelling, feeling warm to touch, red discolouration, tenderness or cramping; shortness of breath, chest/back pain with breathing). - Use of PCC is associated with risk of disseminated intravascular coagulation [DIC].	
Lab test monitoring	- Post infusion, repeat INR immediately. Target for vitamin K antagonist reversal: INR ≤ 1.5. - An INR of 1.5 is considered likely equivalent to vitamin-K dependent factor levels of 30-50% (adequate for hemostasis; 100% factor levels are not required for hemostasis).	

PCC:
Neonate Notes & Pediatric Pearls

NAC

Pediatric patients – retrospective studies of PCC use in pediatric patients did not demonstrate any signals of harm. However, there is only observational published evidence available informing a recommendation for dosing and/or use of these products in this patient population.

FC & PCC Use in Bleeding/Massive Hemorrhage Protocol, if Plasma is Unavailable

- FC & PCC can be substituted for plasma when plasma is not readily available (supported by NAC & by Ontario's Massive Hemorrhage Protocol Toolkit).
- Based on viscoelastic point-of-care testing guided trauma resuscitation. Data is limited but similar outcomes to plasma found.
- Dosing: FC 4 g IV over 10 minutes
  PCC 2000 IU IV over 10 minutes

- Operational issues – reconstitution of the products by …
- Prepare/plan to establish processes as simple as possible
  e.g., instructions with diagrams, practice kits from the manufacturer, pre-prepared supplies and labels, minibag & infusion pump.
- Priority: ASAP transfer to a hospital that can provide definitive treatment/control of hemorrhage.

FC Patient Case 1 – Review - Small Hospital

Charlotte, a 19-year-old female was brought to your **Trauma Centre**; her car collided with a transport truck.

Massive Hemorrhage Protocol (MHP) was ordered.

She was intubated, given tranexamic acid, and transfused
2 transfusion packs totalling
8 units red blood cells [RBC],
4 units frozen plasma [FP].

Lab tests have been sent; results are pending.

Charlotte, a 19-year-old female was brought to your **Small Hospital**; her car collided with a transport truck.

Massive Hemorrhage Protocol (MHP) was ordered.

She was intubated, given tranexamic acid, and transfused blood available
2 - 4 units RBC,
4 g FC
2000 IU PCC

Transfer to large hospital for definitive treatment/hemorrhage control plan established

Possible Adverse Reactions: Question

Whenever blood is being given, which one of these medications must always be readily available:

a) Piperacillin/tazobactam.
b) Cetirizine.
c) Epinephrine.
d) Acetaminophen.

FC & PCC: Adverse Reactions

- If a possible acute transfusion reaction is suspected:
  - 

Stop the transfusion
  - Maintain IV access
  - Check vital signs
  - Verify patient armband identification matches with transfusion label
  - Notify prescriber
  - Patient care as per order
  - Report reaction to TML
  - Document all details

- All unexpected, unusual or serious symptom(s) must be identified, managed and reported to TML for investigation.
- TML must report certain reactions to the Manufacturer/CBS/Health Canada.

FC & PCC: Acute Reaction Chart

IMMEDIATE ACTIONS!

1. **STOP** the transfusion
2. Maintain **IV access**
3. Check **vital signs**
4. Verify **patient ID matches** transfusion label/tag
5. **Notify physician**
6. **Patient care** per order, **report every reaction to Transfusion Medicine Lab (TML), document** per policy

TTISS-ON
Acute Transfusion Reaction Chart

SIGNS AND SYMPTOMS

FEVER, URTICARIA, DYSPNEA, HYPOTENSION

Airway or Facial Edema, Anxiety, Coughing, Diffuse bleeding/oozing, Hemoglobinuria, Hypertension, Itching, Nausea/Vomiting, Pain (Back, Headache, IV site), Rash, Shaking Chills/Rigors, Subjective chills, Tachycardia, Urine colour– dark/red, Wheezing

Consider Recommended Investigations and Suggested Treatment and Actions in the context of each patient's specific clinical scenario and blood component/product transfused.
The initial presenting sign/symptom may evolve, if so re-contact TML. Close patient monitoring is essential.
For additional assistance, call TML at extension: _____

SIGNS & SYMPTOMS		TIMING	POSSIBLE ETIOLOGY	RECOMMENDED INVESTIGATIONS	SUGGESTED TREATMENT AND ACTIONS
FEVER: Temperature of at least 38° C and an increase of at least 1° C from pre-transfusion **and/or** Shaking Chills/Rigors NOTE: Isolated symptom subjective chills, may consider as Low Risk	**Low Risk:** 38° C to 38.9° C but **NO** other symptoms	During or up to 4 hours post transfusion.	Febrile non-hemolytic transfusion reaction	No testing required	• Antipyretic • With physician order and if blood still viable, may resume transfusion with close patient assessment • If recurrent reactions, possible trial of antipyretic premedication
	High Risk: a) at least 38° C but **with** other symptoms **or** b) 39° C or greater **or** c) Shaking Chills/ Rigors	Often within first 15 minutes. During or up to 4 hours post transfusion.	Febrile non-hemolytic transfusion reaction Bacterial contamination Acute hemolytic transfusion reaction	• TML: Group & Screen, DAT • TML: Blood component culture • Patient blood culture (from a different peripheral site) • Urinalysis (first void post-reaction) • Hemolysis work-up: CBC, bilirubin, LDH, AST, haptoglobin, reticulocyte count, blood film • If indicated, assess for - AKI {Acute Kidney Injury} (electrolytes, creatinine) - DIC {Disseminated Intravascular Coagulation} (INR, PTT, fibrinogen, D-dimer)	**DO NOT restart transfusion** • Return blood to TML for clerical check & culture • Broad spectrum IV antibiotics; DO NOT wait for culture results • Aggressive hydration; maintain good urine output • Supportive care per physician's discretion: IV fluid, vasopressors, oxygen, respiratory support • Monitor for hypotension, renal dysfunction, DIC {Disseminated Intravascular Coagulation} • If severe rigors, consider meperidine (if no patient contraindications) • **Serious reaction, call TML immediately**
URTICARIA (Hives) Rash **or** Itching	Less than 2/3 body surface but **NO** other symptoms	During or up to 4 hours post transfusion.	Minor allergic	No testing required	• Antihistamine • With physician order and if blood still viable, may resume transfusion with close patient assessment • If recurrent/severe reactions, possible trial of antihistamine premedication
	2/3 body surface or more but **NO** other symptoms	Often early in transfusion. During or up to 4 hours post transfusion.	Minor allergic (Extensive)	No testing required	**DO NOT restart transfusion** • Antihistamine; may require steroid if symptoms slow to resolve • If recurrent/severe reactions, possible trial of antihistamine /steroid premedication • If continued reactions with premedication, possible trial of washed/plasma depleted components
	With other symptoms, i.e., Airway or Facial Edema, DYSPNEA, HYPOTENSION	Often early in transfusion. During or up to 4 hours post transfusion.	Anaphylactoid reaction /Anaphylaxis	• If also DYSPNEA: chest X-ray, • If also hypoxia: blood gases • Suggest consult Transfusion Medicine physician: explore if indication for - TML: Group & Screen, DAT - Haptoglobin - IgA level (if pre-transfusion sample available) - Anti-IgA testing (performed via Canadian Blood Services, TML will assist in sending samples)	**DO NOT restart transfusion** • **Epinephrine;** consider steroid, antihistamine • Return blood to TML for clerical check • Supportive care per physician's discretion: oxygen, respiratory support, vasopressors • Pending outcome of investigations, washed/plasma depleted components • **Serious reaction, call TML immediately**

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FC & PCC: Acute Reaction Chart

cont'd

SIGNS & SYMPTOMS		TIMING	POSSIBLE ETIOLOGY	RECOMMENDED INVESTIGATIONS	SUGGESTED TREATMENT AND ACTIONS
DYSPNEA **or** SpO_2 (oxygen saturation) of 90 % or less and a decrease of at least 5 % from pre-transfusion **or** intervention required to maintain SpO_2 (oxygen saturation)	With **Hypertension,** tachycardia, +/- FEVER	During or up to **12 hours** post transfusion	TACO* (Transfusion Associated Circulatory Overload)	• TML: Group & Screen, DAT • Consider chest x-ray: Findings - pulmonary edema, Kerley B lines, peri bronchial cuffing; may be pleural fluid • Cardiac biomarkers (as available)	**DO NOT restart transfusion** • Oxygen, high fowler's position, diuretics (document fluid balance) • **Future transfusion:** Slow transfusion rate Pre-transfusion diuretics ** Consider TML to divide unit (as available)
	ACUTE DYSPNEA With **HYPOTENSION,** tachycardia, +/- FEVER	During or up to **6 hours** post transfusion	TRALI (Transfusion Related Acute Lung Injury)	• TML: Group & Screen, DAT • Chest x-ray: Findings – bilateral interstitial /alveolar infiltrates without elevated pulmonary pressures • If also hypoxia: blood gases • Canadian Blood Services requires follow up information & patient blood tests, contact TML, will assist in sending samples	**DO NOT restart transfusion** • Supportive care per physician's discretion: oxygen, respiratory support, vasopressors (benefit uncertain for diuretics (document fluid balance), steroids, and bronchodilators) • **Serious reaction, call TML immediately**
	With FEVER +/- HYPOTENSION	Possible Etiology: Bacterial contamination, Acute hemolytic transfusion reaction **Consider/Follow FEVER, High Risk:** Timing, Recommended Investigations, Suggested Treatment and Actions			
	With URTICARIA, Airway or Facial Edema, HYPOTENSION	Possible Etiology: Anaphylactoid Reaction / Anaphylaxis **Consider/Follow URTICARIA, With other symptoms:** Timing, Recommended Investigations, Suggested Treatment and Actions			
	Mild respiratory symptoms that do not align with TACO or TRALI	During or up to **24 hours** post transfusion	TAD (Transfusion Associated Dyspnea)	• Consider chest x-ray: Findings - normal/unchanged, no pulmonary edema, No bilateral interstitial/alveolar infiltrates	**DO NOT restart transfusion** • Supportive care per physician's discretion: oxygen, respiratory support
HYPOTENSION SBP (Systolic blood pressure) 80 mmHg or lower **AND** from pre-transfusion SBP: - 30 mmHg or greater absolute decrease **or** - 15 to 25 % or greater relative decrease **or** - intervention required to maintain SBP	Alone or with facial flushing	During or up to 4 hours post transfusion	***Bradykinin mediated hypotension	No testing required	**DO NOT restart transfusion** • Supportive care per physician's discretion: IV fluids • If taking ACE (angiotensin converting enzyme) inhibitor medication, consider an alternative anti-hypertensive agent prior to additional transfusion
	With FEVER, +/- DYSPNEA	Possible Etiology: Bacterial contamination, Acute hemolytic transfusion reaction **Consider/Follow FEVER, High Risk:** Timing, Recommended Investigations, Suggested Treatment and Actions			
	With URTICARIA, Airway or Facial Edema, DYSPNEA	Possible Etiology: Anaphylactoid Reaction / Anaphylaxis **Consider/Follow URTICARIA, With other symptoms:** Timing, Recommended Investigations, Suggested Treatment and Actions			
	With ACUTE DYSPNEA, tachycardia +/- FEVER	Possible Etiology: TRALI **Consider/Follow ACUTE DYSPNEA:** Timing, Recommended Investigations, Suggested Treatment and Actions			

*** TACO: Pre-transfusion assess patients for TACO risk factors:** advanced age, history heart failure, history myocardial infarction, left ventricular dysfunction, renal dysfunction, positive fluid balance

**** Pre-transfusion diuretics:** Furosemide PO: onset 30 to 60 minutes, maximal effect 1-2 hours, effect persists about 6-8 hours
Furosemide IV: onset 5 minutes, maximal effect 20-60 minutes, effect persists about 2 hours

***** Bradykinin mediated hypotension**
Bradykinin is believed to have a major role in producing hypotension. Patients taking ACE (angiotensin converting enzyme) inhibitor medication - decreased bradykinin degradation related to increased angiotensin converting enzyme. Also, some individuals have genetic polymorphism leading to decreased bradykinin degradation.

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FC & PCC: Transfusion Checklist

TRANSFUSION CHECKLIST

For references, refer to Bloody Easy Blood Administration Version 3, Summary: Transfusionist's Accountability: Transfusion Checklist (page 80-89).

Unequivocal (unmistakeable) identification of the patient is mandatory.

Patient must be wearing a patient identification armband. Patient identification information must remain attached to the blood for the duration of the transfusion.

PRE-TRANSFUSION

✓ **Informed Consent**
- Per policy/procedure, questions addressed
- Exception: emergent, life-threatening bleed

✓ **Transfusion Order**
- Indication supported: labs, signs, symptoms
- Complete, required information included

✓ **Group & Screen Testing**
- Requi… …patible blood components
- ABO, R… …d groups, antibody screen (clinic… …nt antibodies)
- Label t… …of …ood at patient's bedside

✓ **Prepare the Patient**
- Educate: symptoms indicative of reaction
- Assess for transfusion history and TACO risk factors; follow up if indicated

✓ **Prepare the Equipment**
- Dedicated, patent IV (peripheral or central)
- Compatible IV fluid (only 0.9 % NaCl [sodium chloride] for blood components)
- Bloo… …nents – tubing/filter (170-260 micro… …hange after 4 units or 4 hours
- Platelets – always NEW/FRESH tubing/filter
- Prime tubing/filter: blood or compatible IV fluid
- IV setup to stop abruptly & maintain TKVO: 0.9% NaCl flush syringes + any fluid IV line or 0.9% NaCl IV line
- Infusion Devices: if Health Canada approved

✓ **Pick Up Blood from TML** (Transfusion Medicine Lab)
- Patient identification (surname, first name, unique identification number) and order

TRANSFUSION

✓ **Checking Blood Components/Blood Products**
- Blood received matches transfusion order
- At bedside, in physical presence of patient
- **1. Patient Identification:** surname, first name, unique identification number **identical** on armband, order, transfusion & chart label/tag
- **2. ABO, Rh(D) Blood Groups (only for Co… …): identical/compatible** on Group & sc… …t, CBS (Canadian Blood Services) label, tra… …usion & chart label/tag
- **3. Unit (Components) / Lot (Products) Number: identical on** CBS label (Components) / manufacturer label (Products), transfusion & chart label/tag
- **4. Visual Inspection & Expiry Comp… …s:** no clots, usual colour, ports intact… …es 4 hours after issue from TML **Products:** packaging/seal intact, colour as per manufacturer, vials/glass bottles – once entered/spiked, expires after 4 hours

✓ **Patient Assessment and Vital Signs** (for each unit)
- Close monitoring/observation required
- Minimum: within 30 minutes of starting, 15 minutes after starting, upon completion
- Temp, BP, pulse, respiratory rate, oxygen saturation; if TACO risk - chest auscultation

✓ **Infusion Rate** (for each unit)
- 50 mL/hour for first 15 min… …n be deferred if acute bleeding
- Re-check after 15 minutes, if no indication of reaction then increase to rate as ordered

✓ **Possible Transfusion Reaction**
- If any adverse/unexpected/serious symptoms, **STOP** transfusion; refer to TTISS Reaction Chart

POST-TRANSFUSION

✓ **Completing the Transfusion**
- Comply with expiry time specific for blood component/blood product
  Outside the expiry time, discard remainder
- Component tubing: flush with 0.9 % NaCl
- Products given IV: flush (tubing/IV site) with compatible IV fluid
- Some hospitals require returning the empty blood bag to TML
  Otherwise dispose of blood tubing/bags in biohazardous waste
- Re-assess patient and re-check vital signs:
  - at end of transfusion
  - periodically post-transfusion (reactions may occur 4 hours post-transfusion; for dyspnea reactions up to 24 hours post transfusion)

✓ **Documentation**
- File completed chart label/tag for each component or product transfused on patient's health record (include start and stop times)
- Some hospitals require a completed "transfusion record" form returned to TML
- Record volume transfused, vital signs and patient assessments
- If a transfusion reaction is suspected: report to TML, document signs and symptoms, patient care

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Post Transfusion Knowledge Question 1

Select the correct statement(s) regarding fibrinogen concentrate [FC]:

a) The principal indication is major or massive hemorrhage.
b) FC can be reconstituted at the bedside with 50 mL of 0.9% sodium chloride.
c) If a patient's fibrinogen is less than 2 g/L, FC is indicated.
d) For bleeding patients, FC can be given at a rate of 20 mL per minute.

Post Transfusion Knowledge Question 2

Select the correct statement(s) regarding prothrombin complex concentrate [PCC]:

a) PCC is indicated for patients with major bleeding, an elevated INR, and taking warfarin.
b) Vitamin K must be given concurrently with PCC.
c) Symptoms of minor allergic reaction (urticaria) are common with PCC administration.
d) For bleeding patients, PCC can be given at a rate of 20 mL/minute.

Acknowledgements MOH

The Ontario Regional Blood Coordinating Network (ORBCoN) gratefully acknowledges funding support provided by the Ontario Ministry of Health. The views expressed in this presentation are those of the authors and of ORBCoN and do not necessarily reflect those of the Ontario Ministry of Health or the Government of Ontario.

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Fibrinogen Concentrate (FC) & Prothrombin Complex Concentrate (PCC): Transfusionists, Concentrate On …

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