Fresh frozen plasma  
*Uses and Abuses*

Jeannie Callum, BA, MD, FRCPC, CTBS
"Under disclosure rules, I'm required to tell you I own stock in the company whose drug I'm prescribing."
Except my country of origin
Why is it important that we use plasma properly?

Adverse reactions

$
Outline

- Basics about plasma
  - Products, content, dose, monitoring, lab testing
- Risks of plasma
- Coagulation testing
  - Do the INR and PTT predict who needs plasma?
- When should you give it?
  - Therapeutic and prophylaxis
- When should you *not* give it?
  - Alternatives
- Can you stop giving it?
The Basics

Everything you must know
Terminology

- Frozen plasma
  - Also known as FP24 - frozen within 24 hours

- Fresh frozen plasma
  - Must be frozen within 8 hours

- Thawed plasma
  - Store liquid and must be used within 5 days

- Therapeutic plasma
  - Plasma used for a bleeding patient

- Prophylactic plasma
  - Plasma used to ‘prevent’ bleeding before a procedure
Basics
Dosage

- 15 mL/kg is the recommended dosage (minimum 3 units for initial dose)
  - No good data to support this dose
- 250 mL per ‘unit’
  - Apheresis ‘jumbo’ bags also available (500 mL)
- Each unit from a different **male** donor
  - With the exception of some units of AB plasma
- Each dose increases the patient’s factor levels by **20%**
Basics
Compatibility

O: Universal Recipient
A: Universal Donor
AB: Universal Donor
B: Emergency Donor
Basics
Thawing

20 minutes

5-10 minutes
How long does the effect of plasma last?

**Procoagulant Recovery and Survival**

- **Fibrinogen** ($t_{1/2}=3\text{ d}$)
- **Factor X** ($t_{1/2}=20\text{ h}$)
- **Factor VIII** ($t_{1/2}=12\text{ h}$)
- **Factor VII** ($t_{1/2}=5\text{ h}$)

For a 70 kg patient with 3000 mL plasma volume receiving FFP (20 mL/kg):

**ASSUMPTIONS:**
- Stable plasma volume after expansion
- 85% procoagulant activity in plasma
- 100% recovery
- Synthetic capacity to maintain pre-transfusion procoagulant activity
Infusion time & Monitoring

**Infusion**
- If time allows, 15 minute test dose
- Maximum infusion time 4 hours (write a rate!)
- Consider furosemide (before)

**Monitoring**
- Vitals pre, 15 minutes, post (minimum)
  - At 15 minutes look for reaction: allergic, TRALI, AHTR
  - Minor urticaria – okay to slow down, give anti-histamine and continue
    - **NOT** a contra-indication to more plasma
  - Watch for TACO (first warning sign is BP going up)
The risks of plasma

Why you don’t want to have plasma
Case

How should this patient have been managed?

- 50 year old male, presents with end-stage cirrhosis
- As part of investigations has a transjugular liver biopsy
- Continued oozing x 3 days from neck puncture site
- Listed for emergency liver transplant
- Administered 4 units of plasma for INR 2.6 (liver failure) and oozy puncture site
- Requires intubation for TRALI from the plasma
- Dies 7 days later of multiorgan failure
Case

How should this patient have been managed?

- 58 year old male presents with triple vessel disease and acute coronary syndrome
- On warfarin for atrial fibrillation
- Requires emergent bypass surgery after cardiac cath shows disease not amendable to stenting
- On day 3 of admission INR 2.4 from warfarin (warfarin held on day 1 but patient eating hospital food)
- Patient on iv heparin
- Anesthesia orders 2 units of FFP to reverse warfarin immediately prior to surgery
- 30 minutes into 1st units patient develop acute anaphylaxis
## Risks

- **Transfusion associated circulatory overload**
  - *Rate 1 in 68 patients administered plasma!*

- **Transfusion-related acute lung injury**
  - Rate 1 in 10,000?
  - United Kingdom the risk decreased from 1:65,000 to 1:317,000 after switch to ‘female-free plasma’

- **Anaphylaxis**
  - Rate 1 in 20,000

- **ABO-immune hemolysis (by mistake)**
  - Rate 1 in 40,000

- **Acute lung injury & multiorgan failure**
TACO – Pretty common
Narick et al, Transfusion 2011; epub ahead of print

- Period of passive reporting – 1 in 1566 plasma transfusion
- Period of active surveillance:
  - 84 patients received a total of 272 units of plasma
  - 4 (4.8%) unreported TACO reactions identified
  - The prevalence rate 1 in 68 (95% CI, 1:250-1:27)
  - Most patients were in the ICU at the time of the plasma infusion
Prospective observational study in a medical ICU over 2 years

51 (6%) of 901 transfused patients develop TACO within 6 hours by ‘rigid criteria’

Compared with matched controls TACO cases had:

- more positive fluid balance (1.4 L vs. 0.8 L)
- larger amount of plasma transfused (0.4 L vs. 0.07)
- faster rate of blood component transfusion (225 mL/hr vs. 168 mL/hr)
Prospective observational study  
Li et al, Transfusion 2011; 51: 338-43

- In a secondary analysis comparing TACO cases and random controls:
  - left ventricular dysfunction before transfusion increased risk of TACO 8.23x
  - & plasma ordered for reversal of anticoagulant increased TACO risk 4.31x
Transfusion-related acute lung injury
Wiersum-Osselton JC, et al. Transfusion 2011; 51:1278-83

Rate per 100K

Male only plasma
Canadian TRALI reduction strategies
Lin et al. Transfusion 2011; epub
TRALI Fatalities
Holness et al. TMR July 2004

- TRALI fatalities reported to FDA (USA)
- Jan 1997 - Jul 2002 - 58 TRALI of 416 (14%) fatalities in USA
- FFP most frequently implicated product (>RBC>PLT>cryoprecipitate)
- 83% positive for anti-HLA or anti-PMN antibodies
- 75% of donors female
## FFP & pulm morbidity after cardiac surgery


<table>
<thead>
<tr>
<th>Outcome</th>
<th>FFP (n = 964)</th>
<th>No FFP (n = 964)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation time (hr)</td>
<td>21.6</td>
<td>15.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>7.4%</td>
<td>4.5%</td>
<td>0.0076</td>
</tr>
<tr>
<td>ARDS</td>
<td>2.6%</td>
<td>1.7%</td>
<td>0.1383</td>
</tr>
<tr>
<td>Intubation morbidity</td>
<td>28.5%</td>
<td>15.9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Reintubation</td>
<td>17.1%</td>
<td>10.8%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Readmission to ICU for pulm reasons</td>
<td>6.6%</td>
<td>3.3%</td>
<td>0.0020</td>
</tr>
<tr>
<td>ICU length of stay (hrs)</td>
<td>93</td>
<td>70</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
ALI and FFP (surgery & non-surgery studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>OR</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>Events / Total Plasma Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leese, 1987</td>
<td>0.78</td>
<td>0.30</td>
<td>2.07</td>
<td>8 / 99 10 / 99</td>
</tr>
<tr>
<td>Leese, 1991</td>
<td>0.97</td>
<td>0.22</td>
<td>4.23</td>
<td>4 / 35 4 / 34</td>
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<tr>
<td>Vanderwerff, 1997</td>
<td>4.30</td>
<td>1.29</td>
<td>14.31</td>
<td>4 / 35 4 / 34</td>
</tr>
<tr>
<td>Martin, 2003</td>
<td>4.10</td>
<td>1.55</td>
<td>10.85</td>
<td>12 / 83 7 / 177</td>
</tr>
<tr>
<td>Gajic, 2004</td>
<td>2.28</td>
<td>1.15</td>
<td>4.54</td>
<td>8 / 44 3 / 71</td>
</tr>
<tr>
<td>Dara, 2005</td>
<td>5.04</td>
<td>1.26</td>
<td>20.16</td>
<td>8 / 44 3 / 71</td>
</tr>
<tr>
<td>Khan, 2007</td>
<td>2.48</td>
<td>1.29</td>
<td>4.75</td>
<td>8 / 44 3 / 71</td>
</tr>
<tr>
<td></td>
<td>2.32</td>
<td>1.46</td>
<td>3.71</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: p=0.14; I²=38%
Quality of evidence: Low ☹☹☺☺

Fig. 4. ALI.
Trauma patients receiving <10 RBC
The coagulation testing

Understanding the INR and the PTT
Are our assumptions correct?

- Basic assumptions that we make about using plasma before bedside or surgical procedures
  - Abnormal test results predict who will bleed during or after a procedure
  - Plasma will correct the hemostatic abnormalities
  - Plasma given before the procedure is more effective than that giving after the procedure for the rare patient that bleeds (because of an oops)
INR and aPTT do NOT predict which patient will bleed

Segal et al. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion. 2005;45:1413-25

<table>
<thead>
<tr>
<th>Reference/Procedure</th>
<th>Abnormal tests</th>
<th>Normal tests</th>
<th>Risk difference</th>
<th>95% CIs</th>
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<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 angiography</td>
<td>1/85</td>
<td>15/915</td>
<td>0.00 [0.00, 0.02]</td>
<td></td>
</tr>
<tr>
<td>12 angiography</td>
<td>0/9</td>
<td>0/200</td>
<td>0.00 [-0.14, 0.14]</td>
<td></td>
</tr>
<tr>
<td>16 bronchoscopy</td>
<td>3/28</td>
<td>28/218</td>
<td>-0.02 [-0.14, 0.10]</td>
<td></td>
</tr>
<tr>
<td>17 bronchoscopy</td>
<td>1/14</td>
<td>43/412</td>
<td>-0.03 [-0.17, 0.11]</td>
<td></td>
</tr>
<tr>
<td>27 liver biopsy</td>
<td>0/27</td>
<td>0/9</td>
<td>0.00 [-0.14, 0.14]</td>
<td></td>
</tr>
<tr>
<td>25 liver biopsy</td>
<td>4/76</td>
<td>4/100</td>
<td>0.01 [-0.05, 0.08]</td>
<td></td>
</tr>
<tr>
<td>22 liver laparoscopy</td>
<td>4/93</td>
<td>4/85</td>
<td>0.00 [-0.07, 0.06]</td>
<td></td>
</tr>
<tr>
<td>13 liver laparoscopy</td>
<td>0/29</td>
<td>1/50</td>
<td>-0.02 [-0.09, 0.05]</td>
<td></td>
</tr>
<tr>
<td>29 transjugular liver</td>
<td>0/112</td>
<td>0/45</td>
<td>0.00 [-0.03, 0.03]</td>
<td></td>
</tr>
<tr>
<td>14 transjugular liver</td>
<td>0/31</td>
<td>0/19</td>
<td>0.00 [-0.08, 0.08]</td>
<td></td>
</tr>
<tr>
<td>31 transjugular liver</td>
<td>3/203</td>
<td>0/168</td>
<td>0.01 [0.00, 0.03]</td>
<td></td>
</tr>
<tr>
<td>32 para/thoracocentesis</td>
<td>1/42</td>
<td>18/556</td>
<td>-0.01 [-0.06, 0.04]</td>
<td></td>
</tr>
<tr>
<td>15 transjugular kidney</td>
<td>2/10</td>
<td>0/15</td>
<td>0.20 [-0.06, 0.46]</td>
<td></td>
</tr>
<tr>
<td>33 kidney biopsy</td>
<td>1/9</td>
<td>33/110</td>
<td>-0.19 [-0.41, 0.03]</td>
<td></td>
</tr>
</tbody>
</table>

Favors treatment  Favors control  Risk Difference
Screening for the Risk for Bleeding or Thrombosis

Mark H. Eckman, MD; John K. Erban, MD; Sushil K. Singh, MD; and Grace S. Kao, MD


- 17 studies
- Role of PT and aPTT in predicting post-operative hemorrhage

- “For nonsurgical and surgical patients without synthetic liver dysfunction or a history of oral anticoagulant use, routine testing has no benefit in assessment of bleeding risk.”
**Screening for the Risk for Bleeding or Thrombosis**

Mark H. Eckman, MD; John K. Erban, MD; Sushil K. Singh, MD; and Grace S. Kao, MD

<table>
<thead>
<tr>
<th></th>
<th>Bleed</th>
<th>No Bleed</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT elevated</td>
<td>2</td>
<td>241</td>
<td>1 in 121</td>
</tr>
<tr>
<td>PT not elevated</td>
<td>23</td>
<td>1561</td>
<td>1 in 68</td>
</tr>
<tr>
<td>All Patients</td>
<td>25</td>
<td>1802</td>
<td>1 in 72</td>
</tr>
</tbody>
</table>
FFP given before a procedure will not correct an INR <2

INR Change per 500 mL FFP

Decrease in INR = 0.37 [pre-Tx INR] – 0.47

Holland and Brooks, Am J Clin Path 2006; 126: 133.
Effect of FFP on patients with INRs between 1.3 and 1.8

The relationship between the INR and coagulation factors

- **INR**
  - 1
  - 1.3
  - 1.7
  - 2.0
  - 2.2
  - 3.0

- Zone of normal hemostasis
- Zone of anticoagulation

- 60 ml/kg FFP = 4 L ‘fresh’ plasma
- 15 ml/kg FFP

---

100 %
90 %
80 %
70 %
60 %
50 %
40 %
30 %
20 %
10 %
0 %
Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials


- 57 trials evaluated
  - Liver disease, cardiac surgery, warfarin-related hemorrhage, massive transfusion, prevention of IVH in infants, burns, etc.
  - …for most clinical situations, the RCT evidence base for the clinical use of FFP is limited…the strongest RCT evidence seems to indicate that the prophylactic use of FFP is not significantly or consistently effective across a range of different clinical settings.
Falsely reassured

- We administer FFP in an attempt to "correct" the INR prior to performing an invasive procedure for ‘borderline’ INR<2.
- Without checking the effect of the FFP on the INR, the procedure is performed and the favorable outcome is attributed to the “protective effect” of FFP.
- Had the INR been checked after the FFP, but before the procedure, the conclusion would have been strikingly different.
- The INR value would be found to be still elevated and the observation made that the procedure was safely done despite an abnormal pre-procedure laboratory test.

- 200 consecutive patients undergoing liver biopsy with laproscopic ‘observation’ for bleeding
- No degree of abnormal lab tests warranted pre-procedure therapy at this institution
- There was no correlation of liver bleeding time and laboratory test results
- Even patients with INR>3 and platelets<50 did not bleed more than patients with ‘better’ test results
Random distribution

Figure 1-5. Lack of relationship between the liver bleeding time and the preprocedure PT. The time that the liver was directly observed to bleed after biopsy is plotted as a function of the percentage of activity of the PT. Use with permission from Ewe et al. 

70
Transbronchial biopsies on 18 pigs who were treated with escalating doses of warfarin

Goal = to determine the INR level at which excess bleeding would occur following the procedure

Excess bleeding - ≥ 100 mL in ≥ 50% of animals

They had planned to apply different post-procedure therapies to staunch the bleeding

But…the warfarin treated animals never developed bleeding despite some having INR levels >10

11 of 18 pigs had INR>7 at the time of the biopsy
Important message about the INR/PTT

You order INR/PTT on two different kinds of patients:

a) BLEEDING patient – once the INR hit 1.5-2.0 your patient might benefit from plasma for ‘global’ coagulation factor deficiencies (from bleeding and dilution)

b) PRE-OPERATIVE patient – you order the test because you took a bleeding history and got concerned – you are looking for a congenital or acquired single factor deficiency – even one second above normal = a positive test and needs further investigation!
Indications for plasma

Irrational exuberance!
Common indications

Liver disease

Trauma/Massive hemorrhage

Procedure

Surgery
Note:

- We will get to when we DON’T use plasma but note that…
  - patients on oral anticoagulant drugs
  - other anticoagulants
  - vitamin K deficiency
  - or those not bleeding with abnormal test results

Are better served with other strategies
What is the evidence for use of plasma before a procedure?

- There is evidence that plasma is rarely needed for any of these common procedures:
  - Central venous catheters
  - Liver biopsy
  - Thoracentesis & paracentesis
  - Bronchoscopy & transbronchial biopsy
  - Renal biopsy
Central venous catheters

- 57 year old woman with AML needs a Hickman line insertion to commence chemotherapy today
- Her INR is 1.9 and PTT 41 this morning
  - she has suspected mild DIC and vitamin K deficiency (not eating and on broad spectrum antibiotics)
  - Given iv vitamin K 10 mg iv this AM
- Platelet count is 38
- No active bleeding and no bleeding history
- **At your hospital would they get plasma?**
- **At your hospital would they get platelets?**
What do we know?

- Bleeding complications relate to inadvertant puncture of the carotid or subclavian artery

- Systematic review of complications of CVC insertion (jugular or subclavian) reported 48 episodes of pneumothorax and/or hemothorax after 3420 procedures (1.4%), although only one-third of the episodes were hemothorax (=0.5% risk of a hemothorax).
What do we know?

- A meta-analysis of 8 RCTs found that the use of doppler ultrasound to guide line placement reduced the incidence of placement complications (OR 0.22, 0.10-0.45)

- Greater experience by the physician performing the CVC insertion reduces the risk of procedural complications
All our Hickman lines are placed with ultrasound guidance by experienced interventional radiologists

0.5% x 0.22 = 0.11% (1 in 909 major bleed rate)
The weight of the evidence
Evidence
Petersen GA. Does systemic anticoagulation increase the risk of internal jugular vein cannulation? (letter) Anesthesiology. 1991;75:1124.

- 516 consecutive patients for internal jugular lines before cardiac surgery
- 252 (49%) were anticoagulated with heparin
- An observer who was unaware of the anticoagulation status of each patient recorded the presence of an insertion site hematoma
- Of the 22 hematomas that occurred
  - 13 were in anticoagulated patients
  - 9 were in non-anticoagulated persons
- This difference was not significant
More evidence

- 202 CVC insertions performed on liver transplant patients with severe hemostatic abnormalities
- No attempts were made to correct laboratory abnormalities before the procedure
- Mean coagulation factor levels were 29% of normal, mean PTT was 92 sec, mean platelet concentration was 47 (range=8-79)
- Despite these values and the lack of any pre-procedure therapy, no serious bleeding complications occurred
More evidence

- 76 patients who received 104 central catheters
- 22 catheters were placed with platelet counts of 50-100, 30 catheters with counts of 20-50, and 11 with counts below 20
- 13 percent of patients had a combination of thrombocytopenia and prolongation of the PT/PTT
- None were given transfusions of platelets or FFP before the procedure
- None had serious complications, intrathoracic bleeding, or an unexpected drop in hematocrit
More evidence

- 658 CVC line insertions
- Median INR was 2.4 (1–16) (580 cases >1.5)
- Median platelet count was 81 (9 – 1,088) (531 <150)
- In 453 cases both abnormalities were present
- Patients were not given any pre-procedure transfusion of FFP or platelets
- 1 patient, with near normal tests, developed a hemothorax after inadvertent puncture of the subclavian artery
- There were no other major hemorrhagic complications
More evidence

- Of 3188 tunneled CVCs placed:
  - 428 had platelet counts <50 (down to 3)
  - 361 had INR>1.5 (up to 3.8)

- Their guidelines:
  - Plt count >25 and INR<2 (some clinicians tolerated even more abnormal numbers)

- Excluded patients transfused components between the last reading and the procedure

- 3 had bleeding complications
  - None had platelet counts <50 or INR>1.5
How much evidence do physicians need?
## TABLE 2: Revised Parameters for Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>INR</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine-needle aspiration, 20-gauge or smaller needle</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Percutaneous aspiration</td>
<td>≤ 0.8</td>
<td>≥ 25,000</td>
</tr>
<tr>
<td>Thoracentesis, liver biopsy, or other invasive procedure</td>
<td>≤ 2.0</td>
<td>≥ 25,000</td>
</tr>
</tbody>
</table>

Note—INR = international normalized ratio.

*AJR 2009; 193:1656–1664*
Practice Guidelines on the management of adult patients with ascites due to cirrhosis, the guideline committee recommended that:

“Because bleeding is sufficiently uncommon, the routine prophylactic use of fresh frozen plasma or platelets before paracentesis is not recommended.”

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minor</strong></td>
<td>NO PLASMA! EVER!!</td>
</tr>
<tr>
<td>• Venous line</td>
<td>No matter how high the INR!</td>
</tr>
<tr>
<td>• Arterial line</td>
<td>[platelets &gt;25 except for first 3 where I don’t even care about the platelet count!]</td>
</tr>
<tr>
<td>• Paracentesis</td>
<td></td>
</tr>
<tr>
<td>• Endoscopy (just looking)</td>
<td></td>
</tr>
<tr>
<td>• Thoracentesis</td>
<td></td>
</tr>
<tr>
<td>• Ultrasound guided central line</td>
<td></td>
</tr>
<tr>
<td><strong>Not minor</strong></td>
<td>INR &lt;2</td>
</tr>
<tr>
<td>• Organ biopsy</td>
<td>PLT &gt;25</td>
</tr>
<tr>
<td>• Endoscopic biopsy/procedure</td>
<td></td>
</tr>
<tr>
<td>• Transbronchial biopsy</td>
<td></td>
</tr>
<tr>
<td><strong>Neuro</strong></td>
<td>INR&lt;1.5 (warfarin – with PCCs)</td>
</tr>
<tr>
<td>• LP</td>
<td>INR&lt;1.7 (liver disease – with FFP)</td>
</tr>
<tr>
<td>• Epidural</td>
<td>PLT &gt;50 (LP) &gt;80 (epidural, brain biopsy)</td>
</tr>
</tbody>
</table>
What about the use of plasma for trauma patients?

- What about 1:1 resuscitation?
Iraq 2003-2005

- >10 units of blood (RBC/whole blood) in 24 hrs
  - This type of trial design may excluded severely injured patients who died before #10
- Divided patients into 3 groups based on similar ratios of FFP:RBC and mortality
- Analyzed to determine the effect of the FFP:RBC ratio on mortality
- Transfusion protocol not disclosed
- Between 2003-05 – 5,293 admitted of whom 246 (4.6%) were included
- 95% penetrating trauma
<table>
<thead>
<tr>
<th>Variable</th>
<th>Not much</th>
<th>Medium</th>
<th>Lots (1:1.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=31</td>
<td>N=53</td>
<td>N=162</td>
<td></td>
</tr>
<tr>
<td>Thorax injury</td>
<td>26%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>94</td>
<td>108</td>
<td>109</td>
</tr>
<tr>
<td>Base deficit</td>
<td>13</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Heart rate</td>
<td>122</td>
<td>118</td>
<td>111</td>
</tr>
<tr>
<td>sBP</td>
<td>90</td>
<td>98</td>
<td>97</td>
</tr>
<tr>
<td>Crystalloid</td>
<td>1.8 L/hr</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>RBC</td>
<td>4 units/hr</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Plasma</td>
<td>2</td>
<td>6</td>
<td>12</td>
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<tr>
<td>Plasma</td>
<td>0.1 unit/hr</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Factor 7a</td>
<td>16%</td>
<td>26%</td>
<td>36%</td>
</tr>
</tbody>
</table>
# Outcomes


<table>
<thead>
<tr>
<th>Variable</th>
<th>Not much</th>
<th>Medium</th>
<th>Lots</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>53</td>
<td>162</td>
</tr>
<tr>
<td>Mortality</td>
<td>65%</td>
<td>34%</td>
<td>19%</td>
</tr>
<tr>
<td>Median time to death</td>
<td>2 hrs (1-4)</td>
<td>4 hrs (2-16)</td>
<td>1.6 days (4 hours – 6.5 days)</td>
</tr>
<tr>
<td>Number of deaths</td>
<td>20</td>
<td>18</td>
<td>31</td>
</tr>
</tbody>
</table>
Their conclusion
Borgman et al. J Trauma 2007; 63: 805-813

- High FFP:RBC ratio results in a 55% absolute risk reduction in mortality!
- High FFP:RBC ratio decreased the hourly transfusion rate

**QUOTABLE**

“If you want to get people to believe something really, really stupid, just stick a number on it.”
Author Charles Seife
Proofiness: The Dark Arts of Mathematical Deception
### Other Retros

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Highest FFP</th>
<th>Lowest FFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duchesne</td>
<td>135</td>
<td>26%</td>
<td>88%</td>
</tr>
<tr>
<td>Maegele</td>
<td>713</td>
<td>24%</td>
<td>46%</td>
</tr>
<tr>
<td>Holcomb</td>
<td>466</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>Scalea</td>
<td>250</td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td>Kashuk</td>
<td>133</td>
<td>8%</td>
<td>40%</td>
</tr>
<tr>
<td>Sperry</td>
<td>415</td>
<td>28%</td>
<td>35%</td>
</tr>
<tr>
<td>Teixeira</td>
<td>383</td>
<td>26%</td>
<td>90%</td>
</tr>
<tr>
<td>Zink</td>
<td>466</td>
<td>26%</td>
<td>55%</td>
</tr>
</tbody>
</table>

**Median**

- **26%**
- **55%**
- **Delta 29%!**
2 way analysis:

1. the effect of the ratio at 24 hours on outcome
2. the effect of the ratio on outcome in a time-dependent analysis

Median time to the first RBC and first FFP was 18 and 93 minutes, respectively
The pre- and post-MTP studies

- Another way to look for effects on outcomes
- Unfortunately:
  - Selection bias results in different patients between the two groups
  - Not the same time period – other changes to care have occurred
Military Before, After
Formula-driven resuscitation was associated with an **increased risk** of MT despite no differences in baseline characteristics.
They successfully managed patients “better”

- Warmer on arrival (96.5 to 98.2°F)
- Less crystalloid exposure in first 12 hours (14 vs. 9 L)
- More FFP (8 to 14 U)
- More platelets (1 to 2 U)
- “Better” ratio (0.54 to 0.76)
- Faster transport
- CAT-tourniquet for every soldier
- New medic resuscitation guidelines
Military Before, After

Mortality for MT Patients

- Pre: CPGs - 24
- Post: CPGs - 19
What should you do until PROPPR study is completed?

A. ONLY RBCS  CBC, INR, fibrinogen q1h
RBCs <10 and surgical control planned

B. LAB DRIVEN  CBC, INR, fibrinogen q1h

C. E=mc²

No bleeding = No components
“Until more data are available, caution should be exercised in using fixed ratios of blood components for all except early resuscitation of the most severe trauma cases as all blood products carry risk that may outweigh therapeutic benefit if used in excess”
“Such strategies should also be regarded as ‘resuscitation’ in the most acute sense and as soon as hemorrhage is controlled and the patient’s clinical status has stabilised, then titration of products based on blood testing should be re-instituted to reduce the risk of overtransfusion.”
When should you not give it?

My NO list
Penalty Avoidance
Don’t do this...

- Bleeding and INR <1.5
- Procedure and INR <1.5
- Bleeding and you’re caught not knowing what the INR/PTT is
- INR >1.5 but the patient is not actively bleeding
- Warfarin reversal
- Heparin/LMWH reversal
- Any other anticoagulant
- High PTT with normal INR
- “2 units” = 33 kg patient
### Why use PCCs for warfarin reversal?

<table>
<thead>
<tr>
<th>PCC</th>
<th>FFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled, virally inactivated Prion reduction process</td>
<td>Not virally inactivated</td>
</tr>
<tr>
<td>Lyophilized</td>
<td>Needs ABO group (10min)</td>
</tr>
<tr>
<td>Needs to be reconstituted</td>
<td>Needs to be thawed (30min)</td>
</tr>
<tr>
<td>Volume 40-80mL</td>
<td>Volume 15mL/kg (~1000mL)</td>
</tr>
<tr>
<td>Infused over 15-30min</td>
<td>Infused over hours</td>
</tr>
<tr>
<td>Less risk of transfusion rxns</td>
<td>Risk of transfusion rxns: TRALI, TACO, anaphylaxis</td>
</tr>
<tr>
<td>$1150 for 1000 units</td>
<td>$1050 for 6 units plasma</td>
</tr>
</tbody>
</table>
Half of plasma is not needed?

Provincial Plasma Orders (n=573)

- Appropriate: 55%
- Inappropriate: 29%
- Indeterminate: 16%
How do we compare with the rest of world?

- Finland - 45% INR >1.5 (not sure about bleeding)

- Australia - 63% appropriate
This group surveyed UK critical care physicians to figure out how diverse were the practices in ICUs across their country.

Of the physicians that responded (22% response rate), half give plasma and half do not when faced with a non-bleeding patient with abnormal coagulation tests and without a planned procedure in the ICU!!!
What do UK physicians actually do?

- 366 FFP transfusion episodes in ICU
- Likely inappropriate:
  - 126 with INR<1.5
  - 93 with INR>1.5 but not bleeding and no planned procedure
  - 29 with INR<2.5 prior to bedside procedure
- 248 episodes of 366
- Could it be that 68% of plasma use in ICU may be unnecessary???
Can you stop your physicians (and nurses) from giving plasma?

Of course you can!
Plasma Use – Prospective auditing
Rhode Island can do even better!
Tavares & Sweeney. Transfusion 2011; 51: 754-61

Mortality 8.4/1000 patient days

80% reduction in plasma use!

Mortality 4.5/1000 patient days
Summary

- The benefits of plasma is probably overstated
  - ½ of the plasma transfused is probably not needed
- The need for prophylactic FP is over-stated
  - The vast majority of time you should use plasma for active bleeding
- Plasma is associated with pulmonary injury
  - Use it judiciously
  - Prevent TACO – Expect TACO
- Abnormal coagulation test results will not tell you who will bleed
- 1:1 resuscitation with plasma is NOT of proven benefit
Case

- 86 year old woman is admitted with a hip fracture after a fall
- She is on warfarin for atrial fibrillation
- It is 1200 and the INR is 3.2
- She is booked for surgery tomorrow on the ‘wait and see’ B list
- The MD orders:
  - 1 mg po vitamin K
  - 2 units of plasma
  - Repeat INR at 1700
INR at 1700 is 2.3
MD orders:
  - Vitamin K 1 mg po
  - 4 units of FFP
  - Repeat INR at 0600
INR at 0600 is 2.1
MD orders:
  - Vitamin K 10 mg po
  - 4 units of FFP
Pre-op needs to be tubed and vented for TACO
What should they have done?

10 mg iv vitamin K
Two choices for vitamin K

Gentle nudge back to 2-3
2 mg po
Works in 24-48 hours

Emergency
5-10 mg iv
Works in 6 hours