Delegate Tasks
- Porters to bring equipment, run blood samples to lab and pick up blood products
- It takes little training or expertise to squeeze on a blood pump set
- Give someone the task of documenting interventions (drugs, IV fluids) and observations
- Checking and signing for blood products
- Arranging postoperative disposition/interhospital transfer

Keep Patient Warm
- Haemostatic cellular enzymes don't work if patient hypothermic
- Warm IV fluids
- Forced air convection warmer
- Turn temperature up in theatre

Correct Acidosis
- Haemostatic enzymes require normal pH to work properly
- Ensure normocarbia
- Correct lactic acidosis by restoring cardiac output and oxygen flux
- Sodium bicarbonate not usually useful unless acute hyperkalaemia

Beware Hyperkalaemia
- May precipitate malignant arrhythmias
- Need frequent ABGs during massive transfusion
- Treatment
  - Calcium
  - Na HC03
  - Insulin/Dextrose

General versus Regional Anaesthesia
- Regional advantages
  - Avoids risks of G/A
  - Reduced blood loss, transfusion requirements
  - Satisfies maternal preferences

G/A May Be Better If…..
- Severe continuing blood loss
- Haemodynamic instability
- Life threatening maternal or fetal compromise
- Coagulopathy
- Anticipated prolonged, difficult surgery
Cardiotocogram
Fetal scalp pH
Fetal Heart presence & rate
Doppler
Pinard’s
Fetal Oxygen Saturation (FspO₂)

What About ME?

Massive transfusion protocol
(email to anaesthetic staff 9/05, 11/06 final)

Protocol
- Activation of MTP by communication with blood bank
- Blood bank supplies initial 4U PRBC
- MTP pack
1. 4U PRBCs, 4U FFP, 4U platelets (1poool;
Alternating with
2. 4U PRBC, 4U FFP, 10U Cryo
3. Suggest additional products in certain circumstances - rFVIIa

Basic review - platelets
- Both NUMBER and FUNCTION important
- Normal count: 150,00-450,000/µL of blood

Administration of platelets
- Compatibility testing not required routinely, but platelets should be ABO and Rh (D) compatible
  - Can give incompatible platelets if type needed not available, can cause low-grade haemolysis due to isoagglutinins present in plasma
  - If Rh(D) +ve platelets are given to a Rh(D) -ve female of child bearing potential, Rh(D) immunoglobulin should be considered for prevention of immunisation
- One unit of platelets expected to raise the platelet count of a 70kg adult by 5-10,000/µL, in an 18kg child by 20,000µL
  - The usual dose in an adult patient is 4 units
Administration of platelets

- Give through clean standard giving set (170 to 260 mm) approved for blood administration
  - Large particle filter which only removes aggregates, other large particles
- NSW has instituted universal leucodepletion for platelets, so no need to use bed-side white cell filters for platelet transfusions
  - For blood requiring bed-side leucodepletion, a white cell filter is also required - removes small particles such as white cells but allows red cells, platelets and proteins through
- Platelets should not be transfused through a line after blood
  - Blood can be transfused through the line after platelets

Basic review – coagulation factors

- All coagulation factors are made in the liver, except for vWF
- VIII & IX - haemophilic factors
- VIII & V – “labile” factors as levels decrease most quickly in stored blood
  - FVIII – 50% by 24hrs, 6% after 21 days
  - FV – 50% at 14d
- Vitamin K dependent coagulation factors
  - Factor II, VII, IX, X
  - Protein C & S
  - Warfarin acts by blocking the reduction of oxidised (inactive) vitamin K

Coagulation cascade

- Classical understanding: intrinsic and extrinsic system
- Converge at a common pathway - the final clotting factor thrombin (F IIa) converts soluble fibrinogen into insoluble fibrin
- Fibrin clot is further strengthened by cross-linking catalysed by F XIIIa

New Cell-based Model of Coagulation

- Coagulant response occurs on platelet surface, regulated by its specific receptors
- Damaged endothelium exposes TF, which binds circulating FVIIa (1% of circulating FVII)
- Platelets and some coagulation factors activated by exposure to TF-FVIIa complex → platelets release mediators (ADP, TXA2, vWF, etc) that promote platelet adherence
- Clotting factors bind to adjacent receptors on membrane, initiating clotting cascade → thrombin generation
F Xa activates prothrombin, enough to activate platelets, FV, FVIII, F IX

Options for coagulation factor replacement

- FFP
- Cryoprecipitate
- Prothrombinex
- Isolated coagulation factors

FFP

- Contains all coagulation factors including ~200u of F VIII, plus the other labile factor, F V
- Stored frozen (colder than -25°C) with a shelf life of up to 12 months
- Plasma separated from whole blood and frozen within 18 hrs after collection
- Volume of each unit 150 – 300ml

Administration of FFP

- Compatibility testing not required, ABO compatible plasma should be used when possible
  - Group AB plasma can be used for all groups in an emergency
  - Restrict Group O recipients to group O plasma
- Volume depends on clinical situation, patient size and laboratory tests
  - General guide is 10 -15mL/kg per dose
    - 4 units (600-1200ml) standard for 70kg person
    - Caution with volume

Cryoprecipitate

- Prepared by thawing FFP between 1°C and 6°C and recovering the precipitate
- Cold-insoluble precipitate is refrozen
- Contains most of the F VIII, Fibrinogen, F XIII, vWF and fibronectin from the FFP
- Volume 10-40 mL if derived from a whole blood collection, ~60 mL if derived from an apheresis
- Fibrinogen >140 mg/unit; FVIIIc >70 IU/unit
- Shelf-life 12 months at -25°C or below

Administration of FFP

- Mix gently by inversion prior to use
- Administer through a standard giving set with an administration filter
- Complete transfusion as soon as possible
  - Over 2-4 hrs unless in an emergency
- Once thawed, use immediately or store at 2-6°C for 24 hrs
  - Can be stored for up to 5 days at this temperature but must not be used for FVIII deficiency
Administration of Cryoprecipitate

- Compatibility testing not required. ABO compatible plasma should be used when possible
  - ABO incompatible can be used with caution, particularly with large volumes
- Once thawed, use immediately and complete transfusion within 6 hrs of thawing
- Mix gently but thoroughly by inversion prior to use
- Administer through a standard giving set with an administration filter

- Volume depends on the clinical situation and patient size, guided by laboratory tests
  - Standard 1-1.5 units per 10kg patient body weight each dose
    - Standard dose 10u for 70kg person
  - Up to 4 units maybe required per 10kg body weight to raise the fibrinogen concentration by ~ 0.5 g/L in the absence of continued bleeding

Recombinant FVIIa

- Introduced to clinical medicine in the 1980s as a prohaemostatic agent for pts with congenital or acquired haemophilia
- Mechanism of action:
  - Thought to act at the site of tissue injury by binding to exposed TF and generating small amounts of thrombin to activate platelets
  - Activated platelet surface can then form a template on which recombinant F VIIa can directly or indirectly mediate further activation of coagulation
  - Need platelet count > 10x10^9/L

- Gene for human F VIIa cloned and expressed in baby hamster kidney cell
- Formulated as a freeze-dried preparation
  - Store at room temperature or refrigerate for up to 3hrs after reconstitution
- Contains non-coagulation factor contaminants – trace amount of hamster, bovine and mouse proteins used in manufacturing
  - Standard dose 90 µg/kg, repeat every 2 hours if bleeding ongoing
- Plasma half-life is ~2-3hrs (shorter in children)
- Guidelines for use dependent on institution
  - >15u PRBCs over 8hrs, or 20u/24hrs

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Recombinant FVIIa

- Effective and relatively potent prohaemostatic agent in approximately 90% of patients with haemophilia and inhibiting antibodies and other types of complex coagulation disorders (acquired von Willebrand disease, F V and F XI deficiency)
- Application in other patients who experience severe bleeding is promising
- Relatively safe
  - 1-2% incidence of thrombotic complications based on published trial

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Massive Bleeding requiring rVIIa: Cases by Presentation

- Trauma: 16%
- Cardiac surgery: 9%
- Other surgery: 5%
- Obstetric: 3%
- Medical/other: 3%
- Haem/oncology: 1%
- Intra-cranial haemorrhage: 1%
- Known coagulopathic state: 1%

Total cases = 696
Position: Feb 2007
Obstetric: 4%

Patients requiring rVIIa: Obstetric makes up 3-5%

Causes of rVIIa failure

- Fibrinogen <0.8 g/L
- Platelets <50 x 10^9/L
- Low pH – acidaemia
- Low body temp

Randwick Campus vs. Total Registry

Effect on Bleeding

- Not Known: 52.6%
- Increased: 63%
- Unchanged: 0.5%
- Decreased: 8.0%
- Stopped: 14.1%

Prince of Wales Hospital
All Registry
**Effects of FVIIa in Platelet Disorders**

- Improved haemostasis in patients with/without bleeding disorders
- Hemostatic plug develops with fewer platelets
- Enhances local platelet adhesion
- Signal for activation of nearby platelets
- Enhanced fibrin deposition on each platelet
- Increased platelet surface thrombin generation

**Blood products used in the 24 hrs to infusion (units):**
- Packed cells: 30
- Platelets: 16
- FFP: 20
- Cryoprecipitate: 16

**Coagulation profile prior to infusion:**
- Platelet count: $83 \times 10^9/l$
- INR: 1.6
- APTT: 75 secs
- Fibrinogen: 2.3 g/l

**Mean dose/kg infused:**
113 µg

**POWH protocol**
- First 4 units RCC
- Then 4 units FFP and 4 units platelets
- Then 4 units RCC, 4 units plasma, 8 units cryoprecipitate
- Continue to alternate until MTP ceased or lab results suggest other therapies

**Recombinant FVIIa**

- **Trauma Surgery**
  - RCT 2005 with 301 pts (143 blunt, 134 penetrating)
  - All centers, no statistical effect
  - When early deaths excluded, reduced need for blood transfusion for blunt trauma by 2.6 and massive transfusions (but not for penetrating trauma)
- **Cardiac Surgery**
  - No solid data
- **Liver Surgery**
  - Some large RCT showed no effect in cirrhotic pts with upper GIB or liver transplantation
- **Neurosurgery**
  - RCT showed early use in ICH to significantly improve functional outcome and reduce mortality

**Drug**

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<th>Side effects</th>
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**Typical “catastrophic bleeding” profile**

- Blood products used in the 24 hrs to infusion (units)
  - Packed cells
  - Platelets
  - FFP
  - Cryoprecipitate
- Coagulation profile prior to infusion
  - Platelet count: $83 \times 10^9/l$
  - INR: 1.6
  - APTT: 75 secs
  - Fibrinogen: 2.3 g/l
- Mean dose/kg infused: 113 µg

**Outcome at 28 Days**

- Decreased 52%
- Unchanged 28%
- Stopped 20%

**Effect on Bleeding**

Haemostasis Registry: rVIIa: First 27 mothers: Jan 2007 Outcome & Effect on Bleeding


**Uterine Bleeding**

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