The University of Jordan

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Blood Transfusion in Surgical Practice

The University of Jordan

Blood and Blood Products

Indications for transfusion

Complications of transfusion

Massive blood Hemorrhage and transfusion

Approximately 15 million red blood cell (RBC) units are transfused annually in the United States (1)

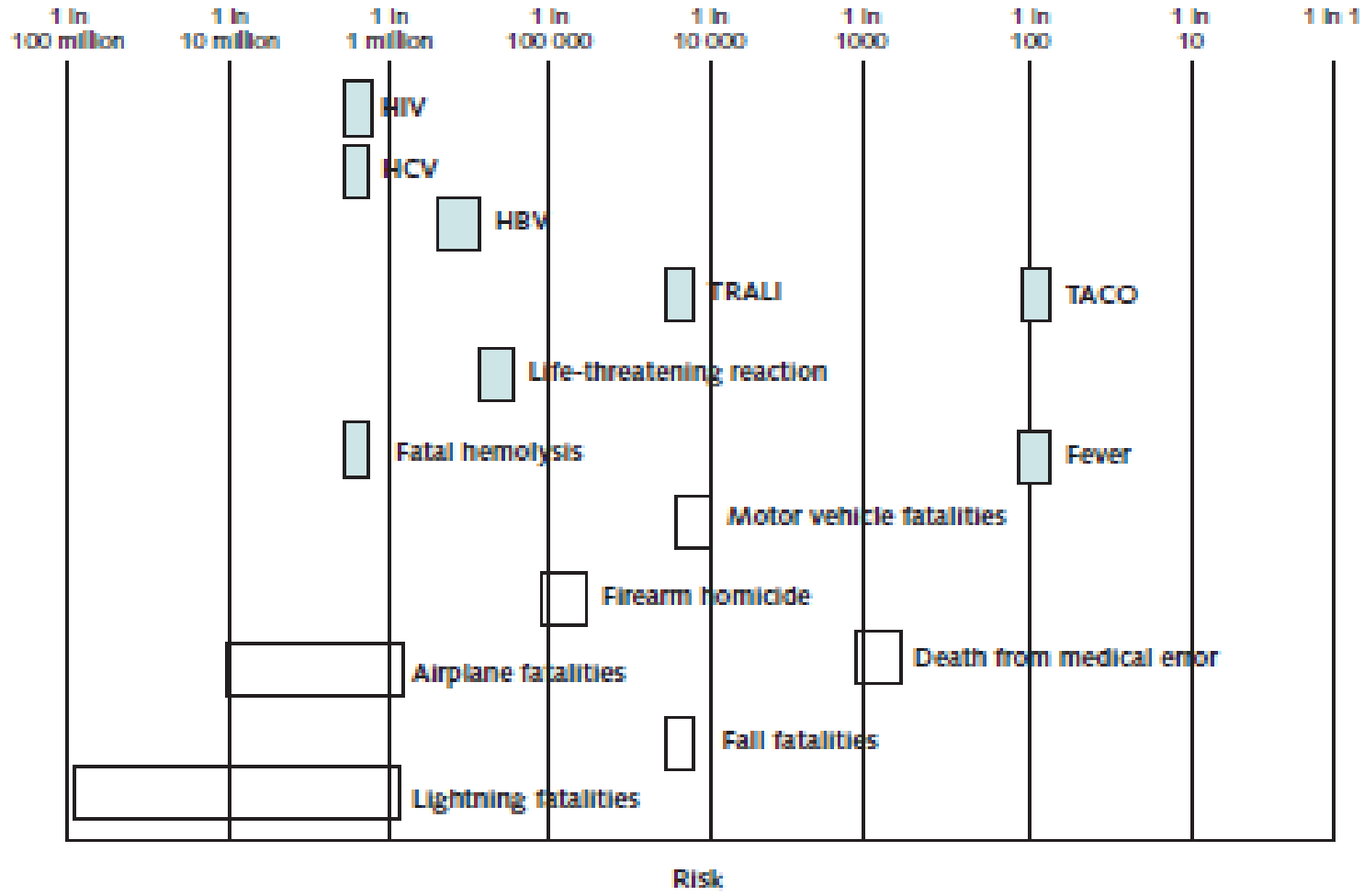
1. U.S. Department of Health and Human Services. The 2009 national blood collection and utilization survey report. Washington, DC: U.S. Department of Health and Human Services, Office of the Assistant Secretary for Health; 2011.

About 85 million are transfused annually worldwide.

Takei T, Amin NA, Schmid G, Dhingra-Kumar N, Rugg D. Progress in global blood safety for HIV. J Acquir Immune Defic Syndr. 2009;52 Suppl 2:S127-31. [PMID: 19901625]

Clinicians should offer RBC transfusion to patients only when benefits outweigh harms

Figure. Adverse effects of RBC transfusion contrasted with other risks.



RATIONALE FOR TRANSFUSION

Role of blood in oxygen delivery

Impact of anemia on morbidity and mortality

Why?

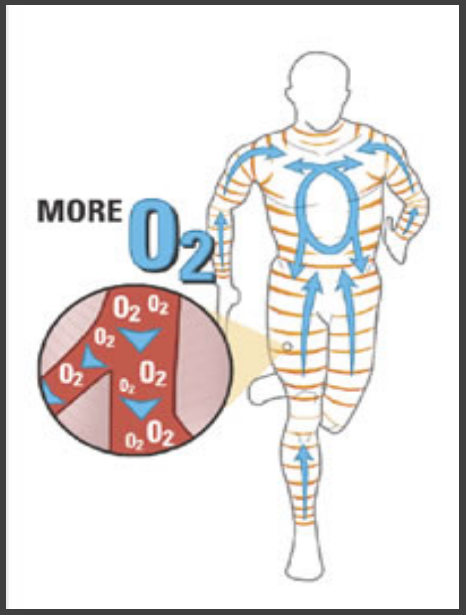
- The body at rest uses approx **250ml O2/L blood**
- O2 delivery can fall with a reduction in any of:
  - Cardiac Output
  - Hb concentration
  - O2 saturation
- Organs most sensitive to hypoxia are Heart and Brain

Why?

- **The purpose of a red cell transfusion is to improve the oxygen carrying capacity of the blood.**
- Oxygen delivery to tissues (O2 Flux)

= Cardiac Output x Oxygen content of blood

Hb x SaO_2

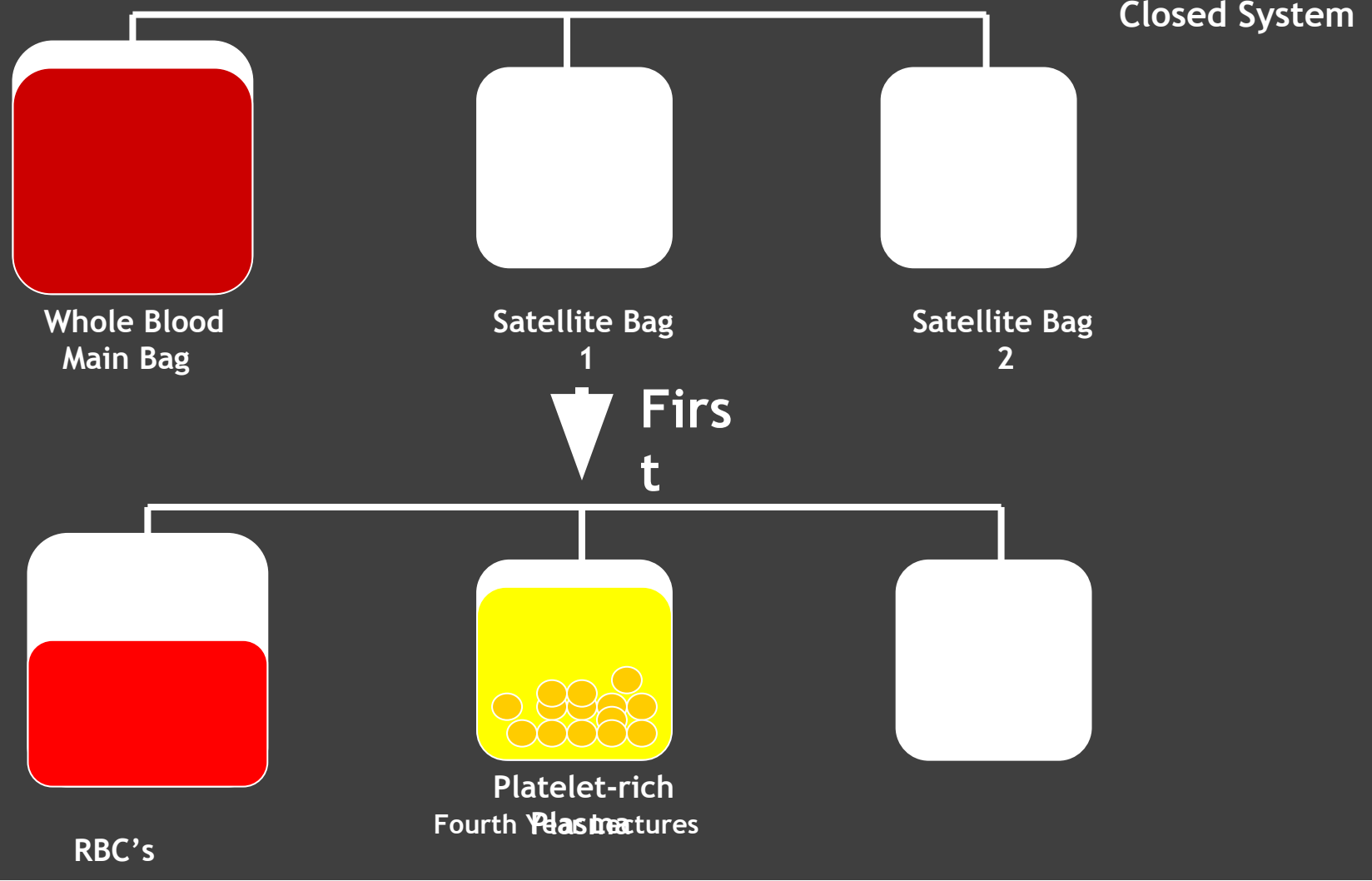


Blood Components

- Prepared from Whole blood collection or apheresis
- Whole blood is separated by differential centrifugation
  - Red Blood Cells (RBC's)
  - Platelets
  - Plasma
    - Cryoprecipitate
    - Others
- Others include Plasma proteins—IVIg, Coagulation Factors, albumin, Anti-D, Growth Factors, Colloid volume expanders

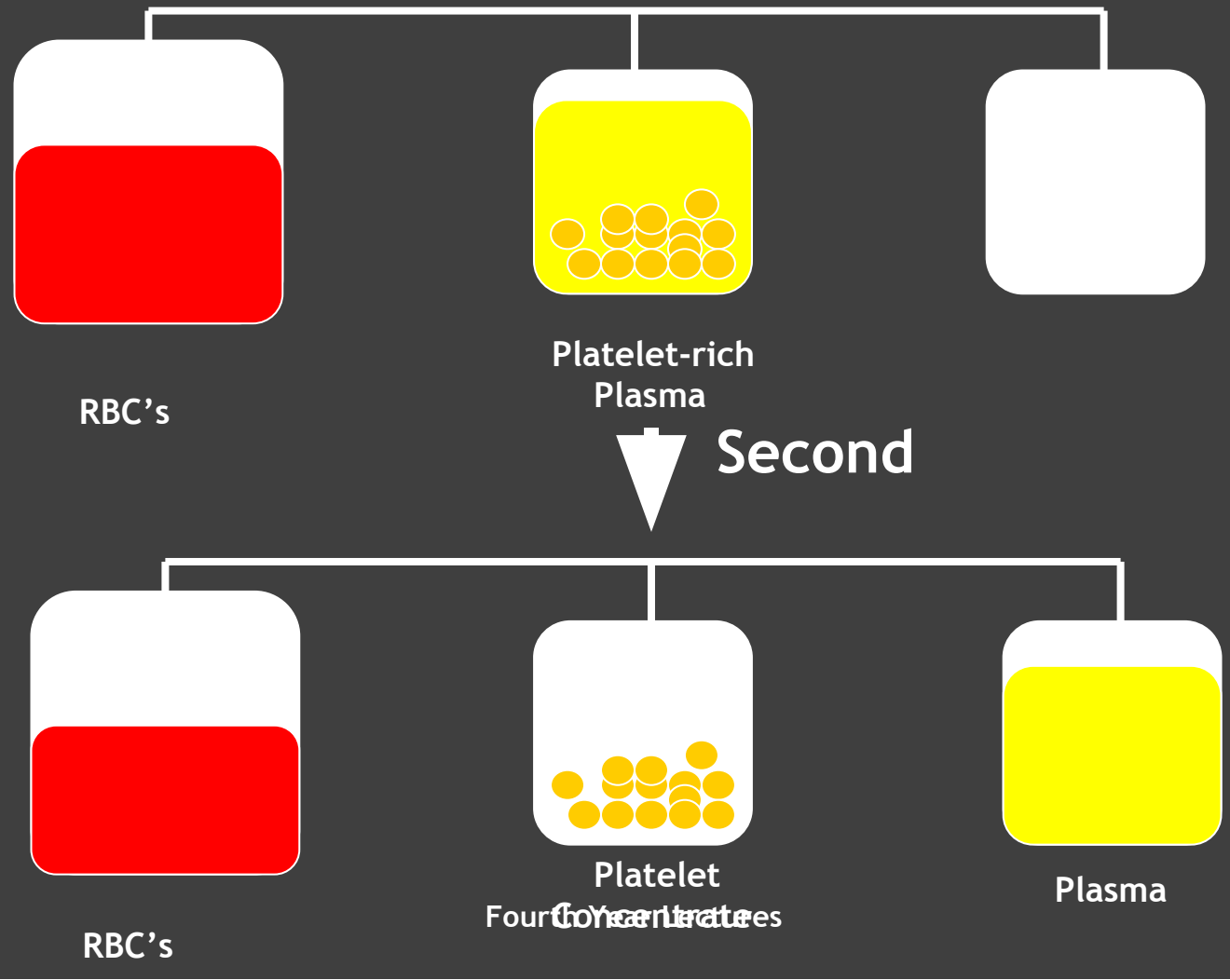
Differential Centrifugation

First Centrifugation



Differential Centrifugation

Second Centrifugation



Whole Blood

- Storage
  - 4° for up to 35 days
- Indications
  - Massive Blood Loss/Trauma
- Considerations
  - Use filter as platelets and coagulation factors will not be active after 3-5 days
  - Donor and recipient must be ABO identical

RBC Concentrate

- Storage
  - 4° for up to 42 days, can be frozen
- Indications
  - Many indications—ie anemia, hypoxia, etc.
- Considerations
  - Recipient must not have antibodies to donor RBC's
  - Usual dose 10 cc/kg (will increase Hgb by 2.5 gm/dl)
  - Usually transfuse over 2-4 hours (slower for chronic anemia(

Platelets

- Storage
  - Up to 5 days at 20-24°
- Considerations
  - Contain Leukocytes and cytokines
  - 1 unit/10 kg of body weight increases Plt count by 50,000
  - Donor and Recipient must be ABO identical

Indications

10,000/mm3 in stable, non-bleeding patients,

20,000/mm3 in unstable non-bleeding patients

50,000/mm3 in invasive procedures or actively bleeding.

- Neurologic or ophthalmologic or Cardiac procedures require a platelet count near 100,000/mm3.

FFP

- Contents—Coagulation Factors (1 unit/ml)
- Storage
  - FFP--12 months at –18 degrees or colder
- Indications
  - Coagulation Factor deficiency, fibrinogen replacement, DIC, liver disease, exchange transfusion, massive transfusion

FFP transfusion must be ABO-compatible with the recipient

Does not need to be Rh-compatible since it lacks red blood cells.

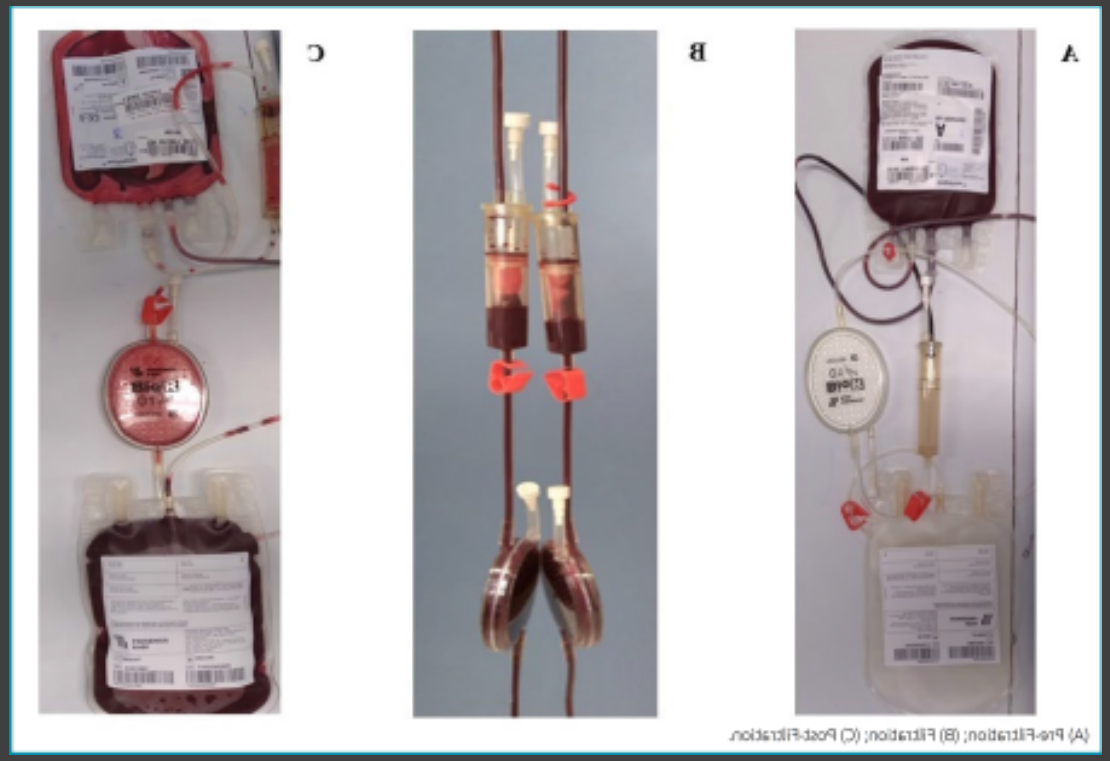
Cryoprecipitate

- Description
  - Precipitate formed/collected when FFP is thawed at 4°
- Storage
  - After collection, refrozen and stored up to 1 year at -18°
- Indication
  - Fibrinogen deficiency or dysfibrinogenemia
  - vonWillebrands Disease
  - Factor VIII or XIII deficiency
  - DIC

- Considerations
  - ABO compatible preferred (but not limiting)
  - Usual dose is 1 unit/5-10 kg of recipient body weight

Leukocyte Reduction Filters

- Used for prevention of transfusion reactions
- Filter used with RBC's, Platelets, FFP, Cryoprecipitate
- May reduce RBC's by 5-10%



When to transfuse

ICU Transfusions

George S. Patton: "A pint of sweat saves a gallon of blood."

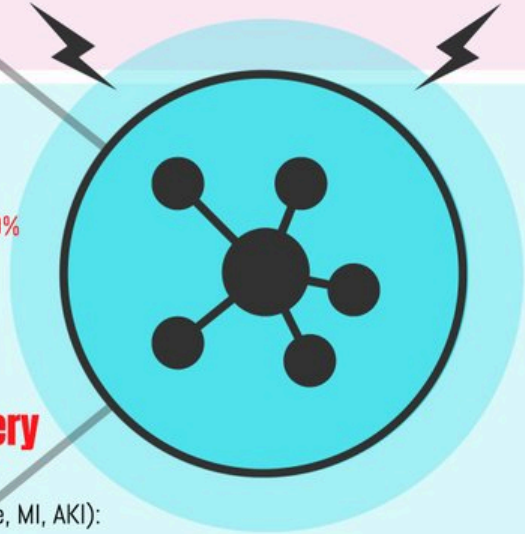
Columbia CCM Fellowship EBM MM

TRICC: NEJM 1999: ICU Patients

- RCT: N = 833; ICU patients with Hb < 9
- 7-9 g v 10-12 g (Non-leukocyte reduced blood)
- No difference in 30 day mortality: Underpowered
- Trend towards reduced mortality in restrictive group: (18.7% v 23.3%).

FOCUS: NEJM 2011: Hip Surgery

- RCT: N = 2016 with Hb < 10; High risk elderly patients
- Target > 8 v > 10; Outcome: 60 day mortality or inability to walk
- No difference: 35.2% v 34.7%



Villaneueva: NEJM 2013: UGIB

- RCT: N = 921
- 7-9 v 9-11; Outcome: 45 day mortality
- Improved mortality in restrictive group: 5% vs 9%

TRISS: NEJM 2014: Sepsis

- RCT: N = 921
- ≤ 7 v < 9: 90 day mortality
- 43% v 45%: No difference

TRICS3: NEJM 2018: Cardiac Surgery

- RCT: N = 5243 High risk patients
- < 7.5 v < 9.5: 6 mos composite (death, stroke, MI, AKI):
- No difference: 17.4% v 17.1%

Background

- Carson et al. “Mortality and morbidity in patients with very low **postoperative** Hb levels who decline blood transfusion.” Transfusion 2002
  - Mortality
    - Hgb 7.1 to 8.0 (n = 99) — zero percent
    - Hgb 5.1 to 7.0 (n = 110) — 9 percent
    - Hgb 3.1 to 5.0 (n = 60) — 30 percent
    - Hgb ≤3.0 (n = 31) — 64 percent

The TRICC Study

- Enrolled 838 euvolemic, anemic, critically ill pts who were admitted to 1 of 25 Canadian ICUs
- Patients were stratified according to center and disease severity (APACHE II) and placed into one of two groups

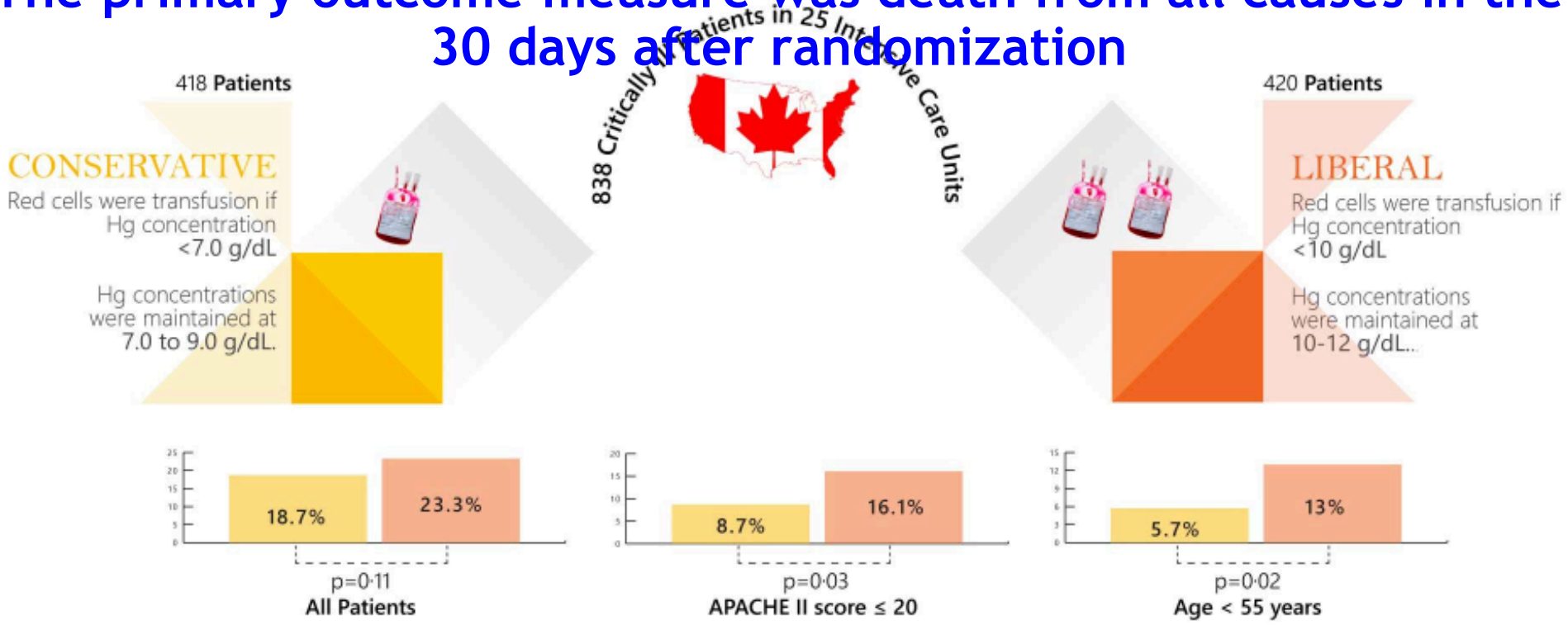
- ❑ **Restrictive group**: Transfuse if Hb < 7 and maintain between 7 and 9
- ❑ **Liberal group**: Transfuse if Hb < 10 and maintain between 10 and 12

- The primary outcome measure was death from all causes in the 30 days after randomization

Herbert PC, et al. NEJM 1999

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

The primary outcome measure was death from all causes in the 30 days after randomization



A RESTRICTIVE STRATEGY OF RED-CELL TRANSFUSION IS AT LEAST AS EFFECTIVE AS AND POSSIBLY SUPERIOR TO A LIBERAL TRANSFUSION STRATEGY IN CRITICALLY ILL PATIENTS, WITH THE POSSIBLE EXCEPTION OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND UNSTABLE ANGINA.

February 11, 1999

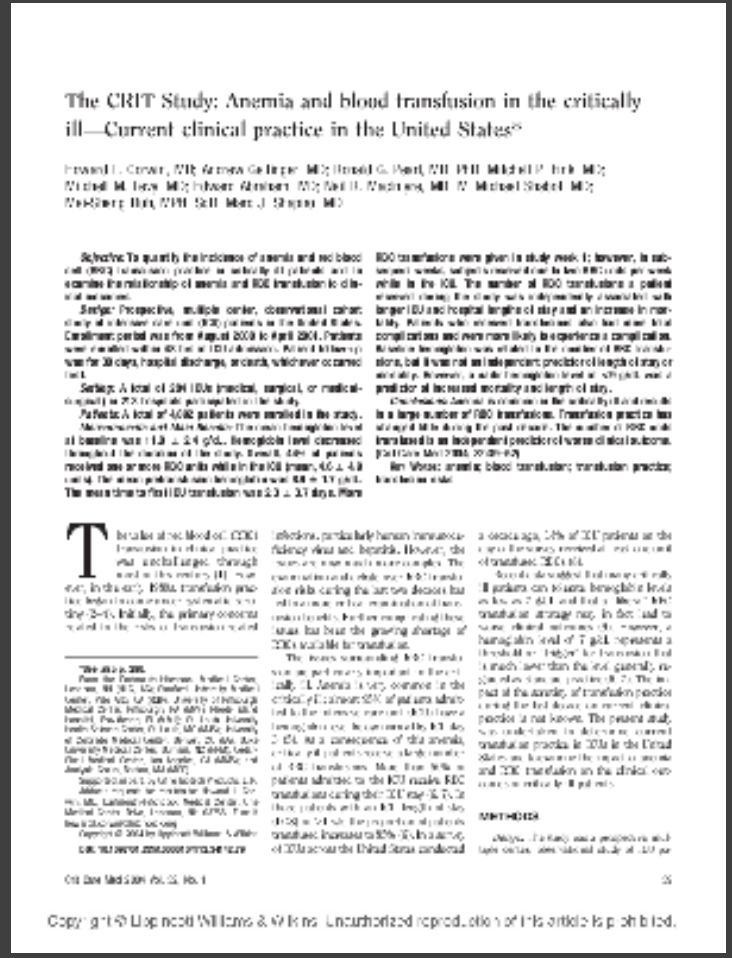
N Engl J Med. 1999;340(6):409-417

“A restrictive red blood cell transfusion strategy generally appears to be safe in most critically ill patients with cardiovascular disease…

with the possible exception of patients with acute myocardial infarction and unstable angina.”

CRIT Study

- Prospective, multiple center, observational cohort
- 4,892 ICU pts in the US
- Propensity score matched
- relationship of anemia and RBC transfusion with clinical outcomes

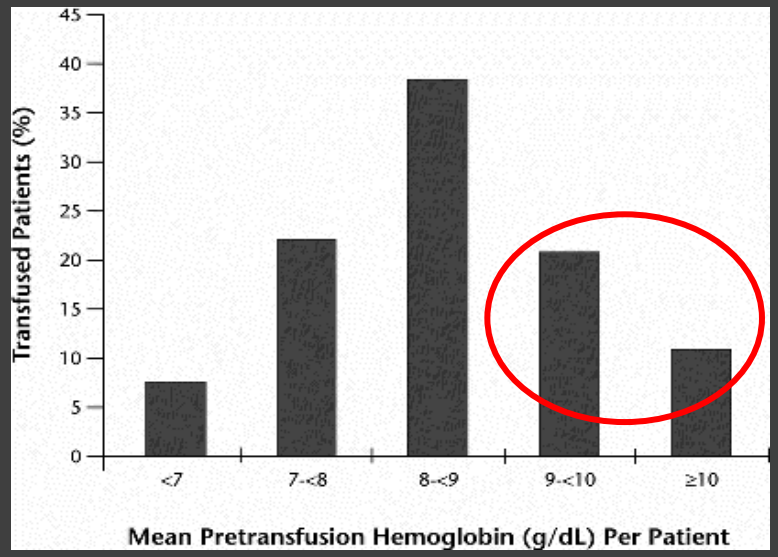


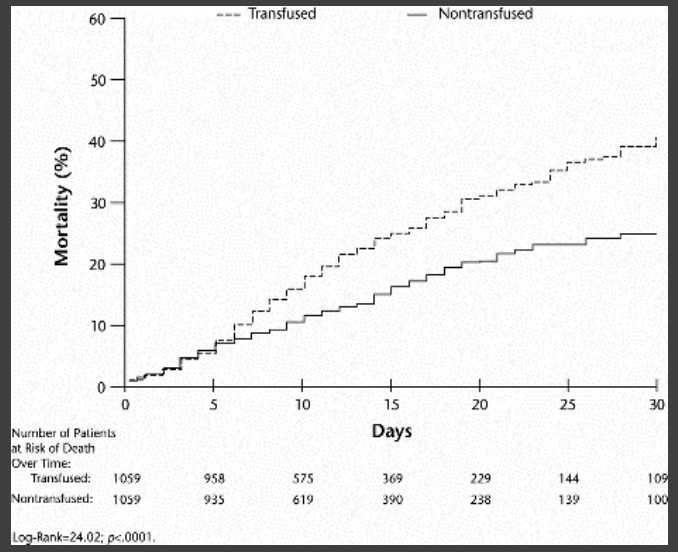
The CRIT Study: Anemia and blood transfusion in the critically ill—Current clinical practice in the United States*

Crit Care Med. 2004 Jan;32(1):39-52

CRIT Results

Overall, 44% of pts admitted to the ICU received one or more RBC units while in the ICU





35% of Blood transfused in patients with Hgb ≥ 9

The mean pre-transfusion Hb was 8.6 ± 1.7 g/dL

RBC transfusion was independently associated with higher mortality (OR 1.65 CI 1.35-2.03).

OR 2.62 if 3-4 units transfused p < 0.0001

When to Pull the “transfusion Trigger?”

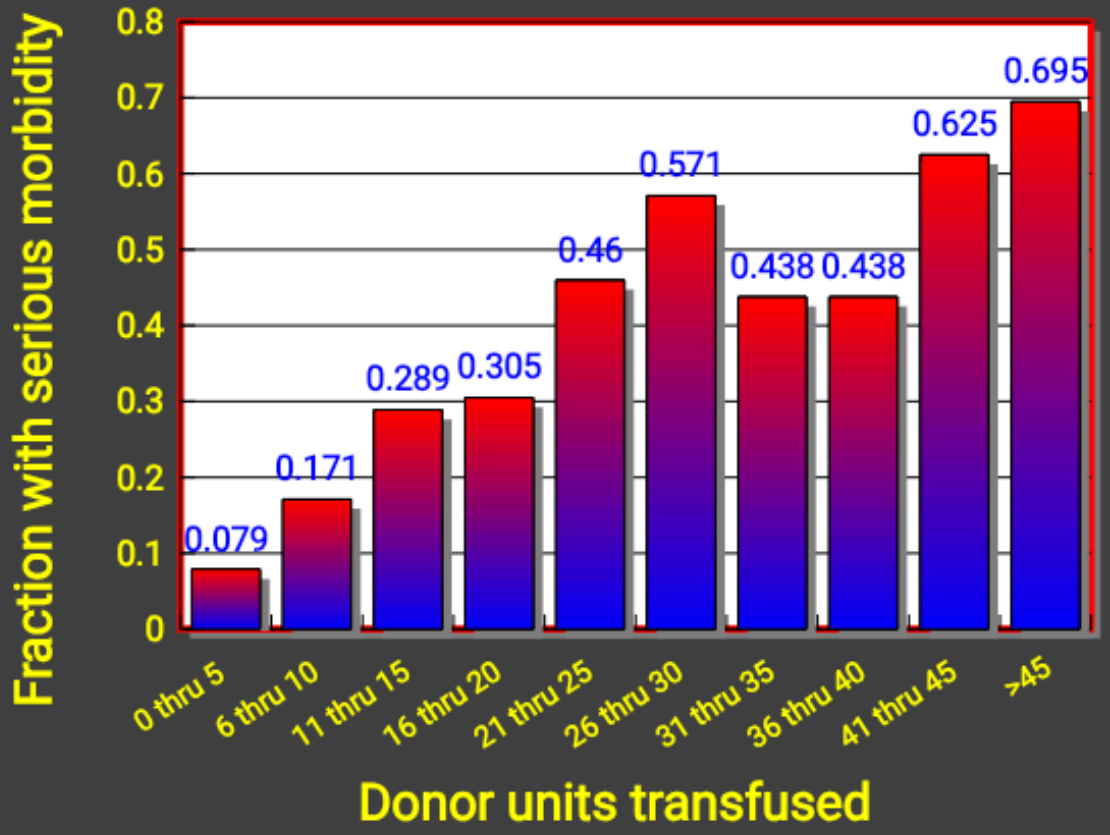
Should not be based solely on hemoglobin number.

Decision should consider clinical scenario, patient characteristics, and symptoms.

Blood Transfusion in the Operating Room Is Bad!

- Cardiac Surgery
- Thoracic operations
- Vascular operations
- Cancer procedures
- General Surgery
- Cardiology doesn’t get a pass! PCI outcomes worse w/ blood transfusion

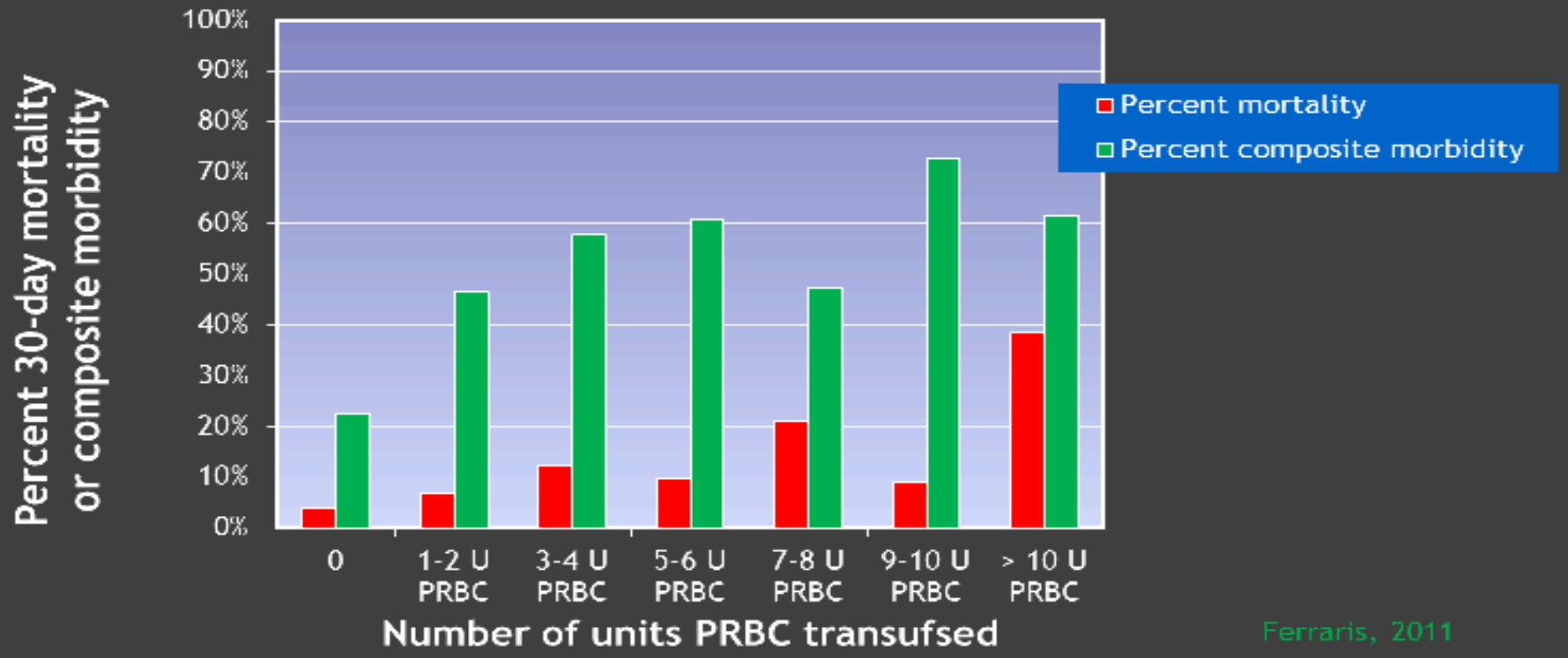
Transfusion & Serious Morbidity in 4,445 Cardiac Surgical Patients



Serious morbidity and mortality increase with the amount transfused.

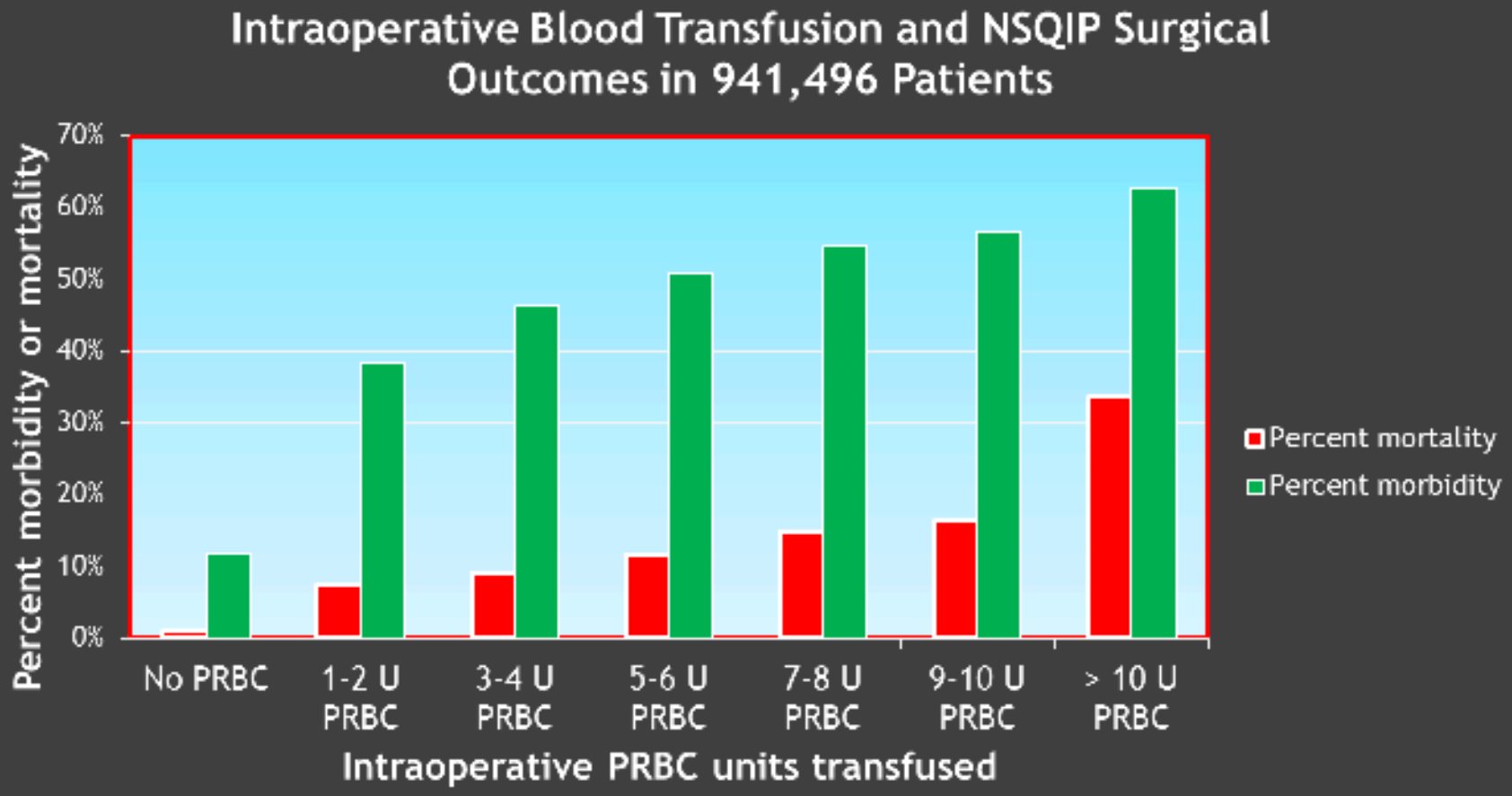
Ferraris, Intl J Angiol, 2006

Intraoperative Blood Transfusion & Lung Surgery



Ferraris, 2011

Blood Transfusion in General Surgical Population



Scenario 1: Trauma – Massive Hemorrhage

- **Setting:** Emergency Department.
  Patient: 28-year-old male, stabbed in the right upper quadrant. Arrives hypotensive (BP 80/50), tachycardic (130 bpm). FAST exam positive for intra-abdominal fluid. Hb on arrival 10.2 g/dL. After 2 L crystalloid, BP 85/55, HR 120.
- **Question:** Transfuse?

Scenario 2: Upper GI Bleed – Cirrhosis

- **Setting:** Gastroenterology ward.
  Patient: 55-year-old with alcoholic cirrhosis (Child-Pugh B), presents with hematemesis. Endoscopy shows esophageal varices, banded. Now post-banding day 1. Hb 6.8 g/dL. Hemodynamically stable. No active bleeding. INR 1.6, platelets 70,000/µL.
- **Question:** Transfuse RBCs? Any other considerations?

Scenario 3: Hematology – Myelodysplastic Syndrome

- **Setting:** Outpatient oncology clinic.
  Patient: 74-year-old with MDS, transfusion-dependent. Hb 7.1 g/dL. Asymptomatic, no cardiac history, tolerating daily activities. Last transfusion 3 weeks ago.
- **Question:** Transfuse?

Scenario 4: Obstetrics – Postpartum Hemorrhage

- **Setting:** Labor and delivery.
  Patient: 32-year-old, vaginal delivery, now 2 hours postpartum. Estimated blood loss 1500 mL. Uterine atony controlled with uterotonics and balloon tamponade. Hb 6.5 g/dL (baseline 11.0). BP 100/60, HR 110. Ongoing oozing.
- **Question:** Transfuse?

Scenario 5: Orthopedic Surgery – Postoperative Asymptomatic Anemia

- **Setting:** Postoperative day 2 after total hip arthroplasty.
  Patient: 70-year-old female, no cardiac history. Hb 7.8 g/dL (pre-op 12.5). Vital signs normal. Ambulating with physical therapy. No active bleeding. Drain output minimal.
- **Question:** Transfuse?

When to Pull the “transfusion Trigger?” American Association of Blood Banks Guidelines

- Hgb <7
- Hgb 7-8

- Transfusion recommended
- **Restrictive Transfusion Strategy** for stable patients

  Consider transfusion only if symptomatic (chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure).

- Hgb 8 – 10
- TRANSFUSION GENERALLY NOT INDICATED

  Can consider Tx in special circumstances (ie ACS w/ active ischemia, symptomatic anemia, active bleeding).
- Hgb >10
- TRANSFUSION NOT INDICATED

Transfusion Complications

- Acute Transfusion Reactions (ATR's)
- Chronic Transfusion Reactions
- Transfusion related infections

Acute Transfusion Reactions

- Hemolytic Reactions (AHTR)
- Febrile Reactions (FNHTR)
- Allergic Reactions
- TRALI
- Coagulopathy with Massive transfusions
- Bacteremia

Acute Hemolytic Transfusion Reactions (AHTR)

- Occurs when incompatible RBC's are transfused into a recipient who has pre-formed antibodies (usually ABO or Rh)
- Antibodies activate the complement system, causing intravascular hemolysis
- Symptoms occur within minutes of starting the transfusion
- This hemolytic reaction can occur with as little as 1-2 cc of RBC's
- Labeling error is most common problem
- **Can be fatal**

Symptoms of AHTR

- High fever/chills
- Hypotension
- Back/abdominal pain
- Oliguria
- Dyspnea
- Dark urine
- Pallor

What to do?

If an AHTR occurs

- **STOP TRANSFUSION**
- **ABC's**
- Maintain IV access and run IVF (NS or LR)
- Monitor and maintain BP/pulse
- Give diuretic
- Obtain blood and urine for transfusion reaction workup
- Send remaining blood back to Blood Bank

Blood Bank Work-up of AHTR

- Check paperwork to assure no errors
- Check plasma for hemoglobin
- DAT (Direct AntiglobulinTest)
- Repeat crossmatch
- Repeat Blood group typing
- Blood culture

Labs found with AHTR

- Hemoglobinemia
- Hemoglobinuria
- Positive DAT
- Hyperbilirubinemia
- Abnormal DIC workup

Monitoring in AHTR

- Monitor patient clinical status and vital signs
- Monitor renal status (BUN, creatinine)
- Monitor coagulation status (DIC panel– PT/PTT, fibrinogen, D-dimer/FDP, Plt, Antithrombin-III)
- Monitor for signs of hemolysis (LDH, bili, haptoglobin)

Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Definition--Rise in patient temperature >1°C (associated with transfusion without other fever precipitating factors)
- Occurs with approx 1% of PRBC transfusions and approx 20% of Plt transfusions
- FNHTR caused by alloantibodies directed against HLA antigens

What to do?
If an FNHTR occurs

- STOP TRANSFUSION
- Use of Antipyretics
- Use of Corticosteroids for severe reactions
- Use of Narcotics for shaking chills
- Future considerations
  - May prevent reaction with leukocyte filter
  - Use single donor platelets
  - Washed RBC's or platelets

Allergic Nonhemolytic Transfusion Reactions

- Etiology
  - May be due to plasma proteins or blood preservative/anticoagulant
  - Best characterized with IgA given to an IgA deficient patients with anti-IgA antibodies
- Presents with urticaria and wheezing
- Treatment
  - Mild reactions—Can be continued
  - Severe reactions—Must STOP transfusion and may require steroids or epinephrine
- Prevention—Premedication (Antihistamines)

TRALI

Transfusion Related Acute Lung Injury

- Clinical syndrome similar to ARDS
- Occurs 1-6 hours after receiving plasma-containing blood products
- Caused by WBC antibodies present in donor blood that result in pulmonary leukostasis
- Treatment is supportive
- High mortality

Bacterial Contamination

- More common and more severe with platelet transfusion (platelets are stored at room temperature)
- Organisms
  - Platelets—Gram (+) organisms, ie Staph/Strep
  - RBC's—Yersinia, enterobacter
- Risk increases as blood products age (use fresh products for immunocompromised)

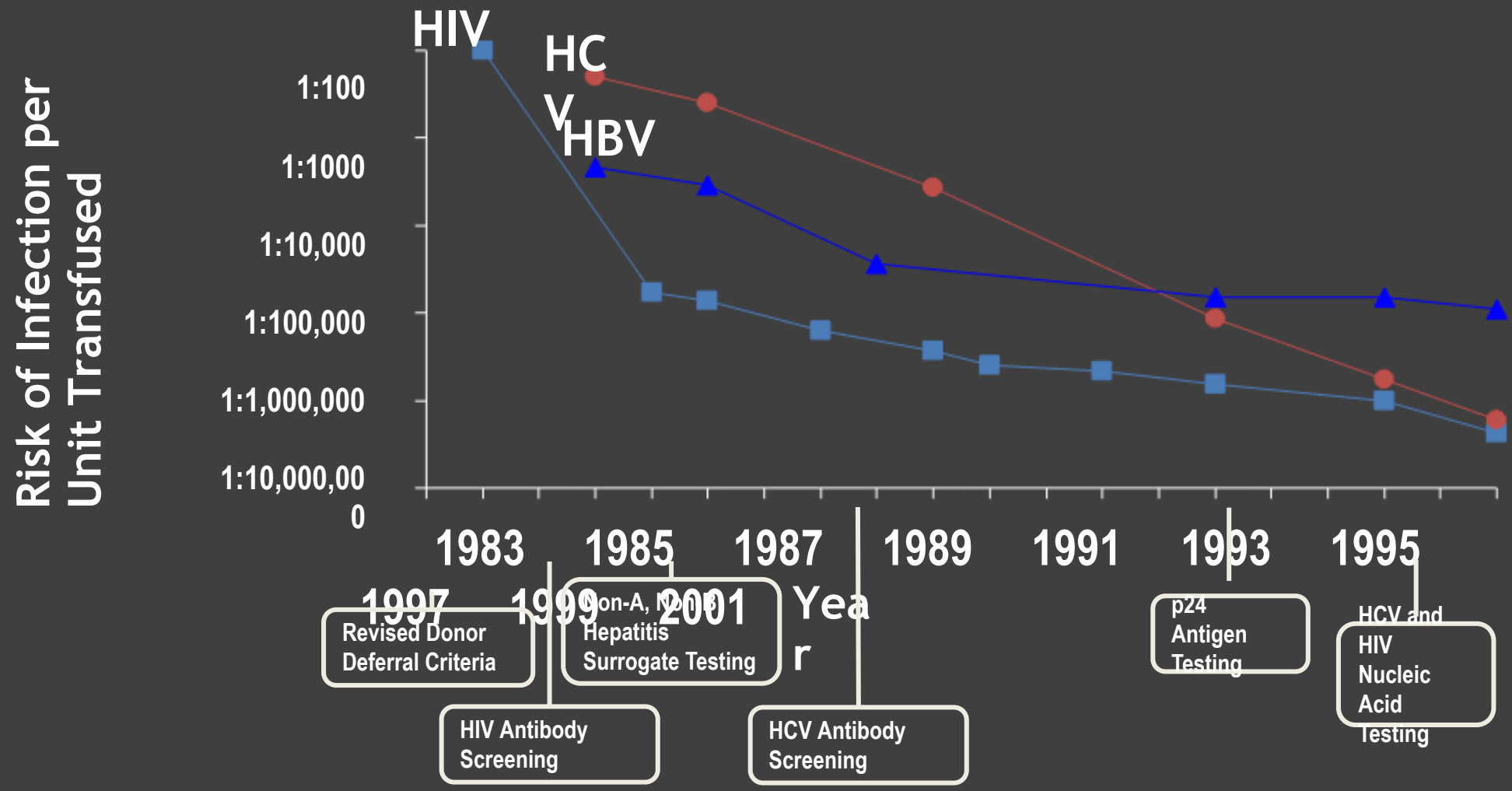
Chronic Transfusion Reactions

- Alloimmunization
- Transfusion Associated Graft Verses Host Disease (GVHD)
- Iron Overload
- Transfusion Transmitted Infection

Transfusion Associated Infections

- Hepatitis C
- Hepatitis B
- HIV
- CMV
  - CMV can be diminished by leukoreduction, which is indicated for immunocompromised patients

Decline in HIV, HBV, HCV Risks of Transmission via Blood Tx



Busch MP, et al. *JAMA*. 2003;289:959-62.

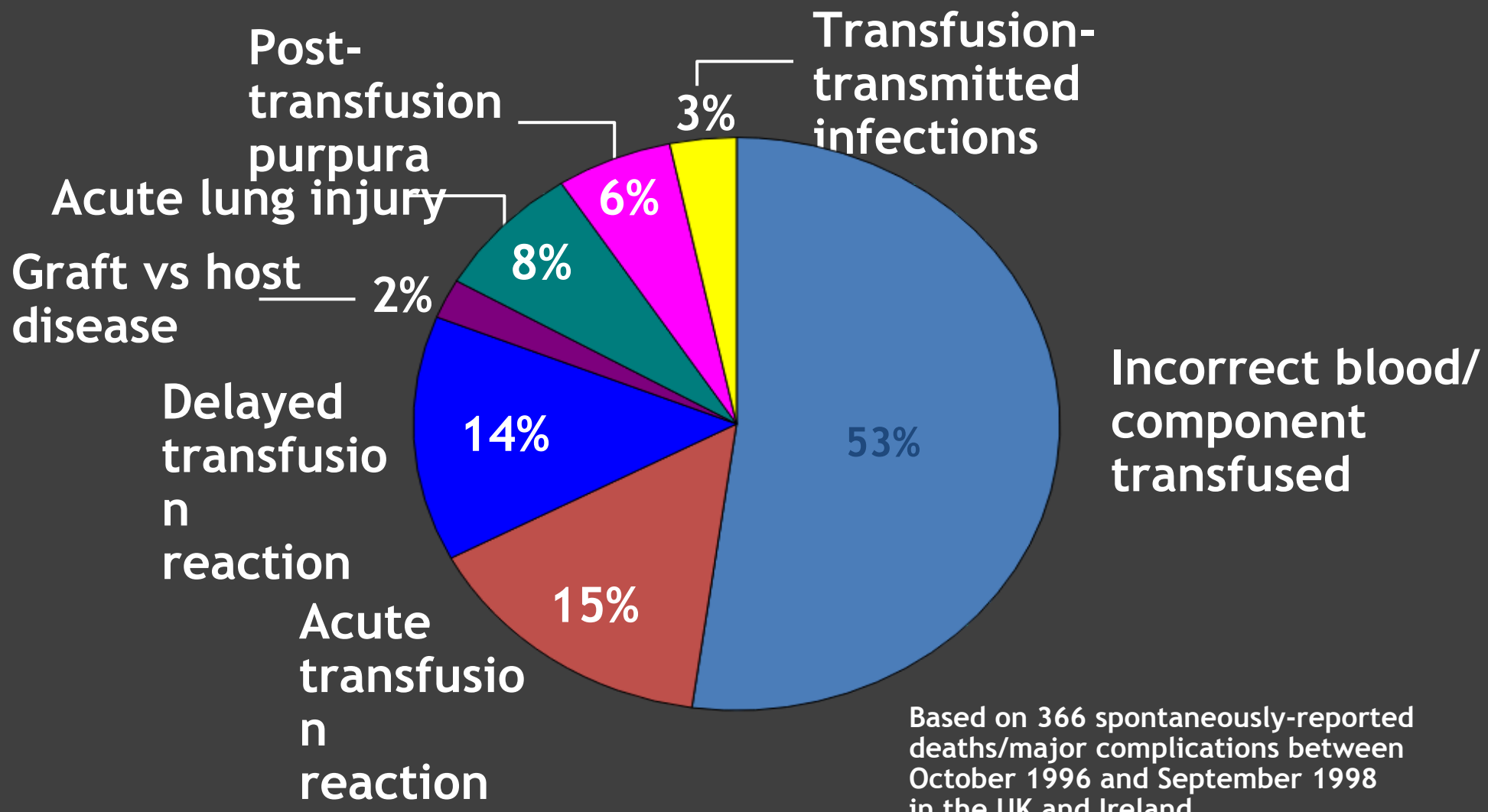
Risks of Transfusion: Infectious Disease

- ✔ HIV = 1 in 1.8 million
- ✔ HCV = 1 in 1.6 million
- ✔ HBV = 1 in 220,000

HIV = human immunodeficiency virus.
HCV = hepatitis C virus.
HBV = hepatitis B virus.

Busch MP, et al. *JAMA*. 2003;289:959-62.

Serious Hazards of Transfusion



Based on 366 spontaneously-reported deaths/major complications between October 1996 and September 1998 in the UK and Ireland.

Williamson LM, et al. *BMJ*. 1999;319:16-9.

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- **Setting:** Emergency Department.
  Patient: 28-year-old male, stabbed in the right upper quadrant. Arrives hypotensive (BP 80/50), tachycardic (130 bpm). FAST exam positive for intra-abdominal fluid. Hb on arrival 10.2 g/dL. After 2 L crystalloid, BP 85/55, HR 120.
- **Question:** Transfuse?
- **Answer: Yes – initiate massive transfusion protocol.** In hemorrhagic shock, Hb is not the primary trigger. The patient remains unstable despite initial resuscitation. Early balanced transfusion (RBC:plasma:platelets 1:1:1) is indicated to prevent coagulopathy and improve outcomes, regardless of initial Hb.

Scenario 2: Upper GI Bleed – Cirrhosis

- **Setting:** Gastroenterology ward.
  Patient: 55-year-old with alcoholic cirrhosis (Child-Pugh B), presents with hematemesis. Endoscopy shows esophageal varices, banded. Now post-banding day 1. Hb 6.8 g/dL. Hemodynamically stable. No active bleeding. INR 1.6, platelets 70,000/µL.
- **Question:** Transfuse RBCs? Any other considerations?
- **Answer: Yes, but cautiously.** Restrictive threshold (Hb <7 g/dL) is appropriate in stable cirrhotic patients with variceal bleed. However, **over-transfusion** (target >9 g/dL) increases portal pressure and rebleeding risk. Transfuse to a target of 7–8 g/dL. Concurrently, consider platelet transfusion if platelet <50,000/µL with ongoing bleeding; here, no active bleeding, so platelets not indicated.

Scenario 3: Hematology – Myelodysplastic Syndrome

- **Setting:** Outpatient oncology clinic.
  Patient: 74-year-old with MDS, transfusion-dependent. Hb 7.1 g/dL. Asymptomatic, no cardiac history, tolerating daily activities. Last transfusion 3 weeks ago.
- **Question:** Transfuse?
- **Answer: No.** In chronic anemia without symptoms, a higher threshold is not required. Guidelines recommend a restrictive strategy (Hb 7–8 g/dL) for stable, asymptomatic patients with myelodysplasia to minimize iron overload and transfusion reactions. Reassess with symptoms (fatigue, dyspnea, angina) or if Hb drops further.

Scenario 4: Obstetrics – Postpartum Hemorrhage

- **Setting:** Labor and delivery.
  Patient: 32-year-old, vaginal delivery, now 2 hours postpartum. Estimated blood loss 1500 mL. Uterine atony controlled with uterotonics and balloon tamponade. Hb 6.5 g/dL (baseline 11.0). BP 100/60, HR 110. Ongoing oozing.
- **Question:** Transfuse?
- **Answer: Yes.** Postpartum hemorrhage with ongoing bleeding and hemodynamic changes warrants transfusion. In obstetrics, a lower trigger (Hb <6–7 g/dL) is often used in stable patients, but here with tachycardia and continued oozing, immediate RBC transfusion is indicated. Also assess coagulation: consider fibrinogen <200 mg/dL as an early trigger for cryoprecipitate.

Scenario 5: Orthopedic Surgery – Postoperative Asymptomatic Anemia

- **Setting:** Postoperative day 2 after total hip arthroplasty.
  Patient: 70-year-old female, no cardiac history. Hb 7.8 g/dL (pre-op 12.5). Vital signs normal. Ambulating with physical therapy. No active bleeding. Drain output minimal.
- **Question:** Transfuse?
- **Answer: No.** In asymptomatic, hemodynamically stable postoperative orthopedic patients, a restrictive threshold (Hb <8 g/dL) is safe and reduces transfusion-associated risks. No evidence of impaired functional recovery or wound healing with restrictive strategy. Recheck Hb if symptoms develop.

Massive Transfusion

Massive Hemorrhage

Massive Blood Transfusion

Massive Blood Transfusion Protocol

- Massive hemorrhage, also known as major hemorrhage or massive bleeding, is defined as a severe blood loss that is life-threatening and often requires immediate transfusion support.

Loss of blood volume:

- One common definition is the loss of one or more circulating blood volumes (approximately 70ml/kg in adults) within a 24-hour period.
- Another definition is the loss of 50% of a patient's total blood volume within

Rapid rate of blood loss:

- Massive hemorrhage can also be defined by a rate of bleeding exceeding

Transfusion requirements:

- Requiring the transfusion of 10 or more units of red blood cells within a 24-hour period.
- ≥ 4 units of any blood component transfused within 2 h of injury

Massive Blood Transfusion

Definitions

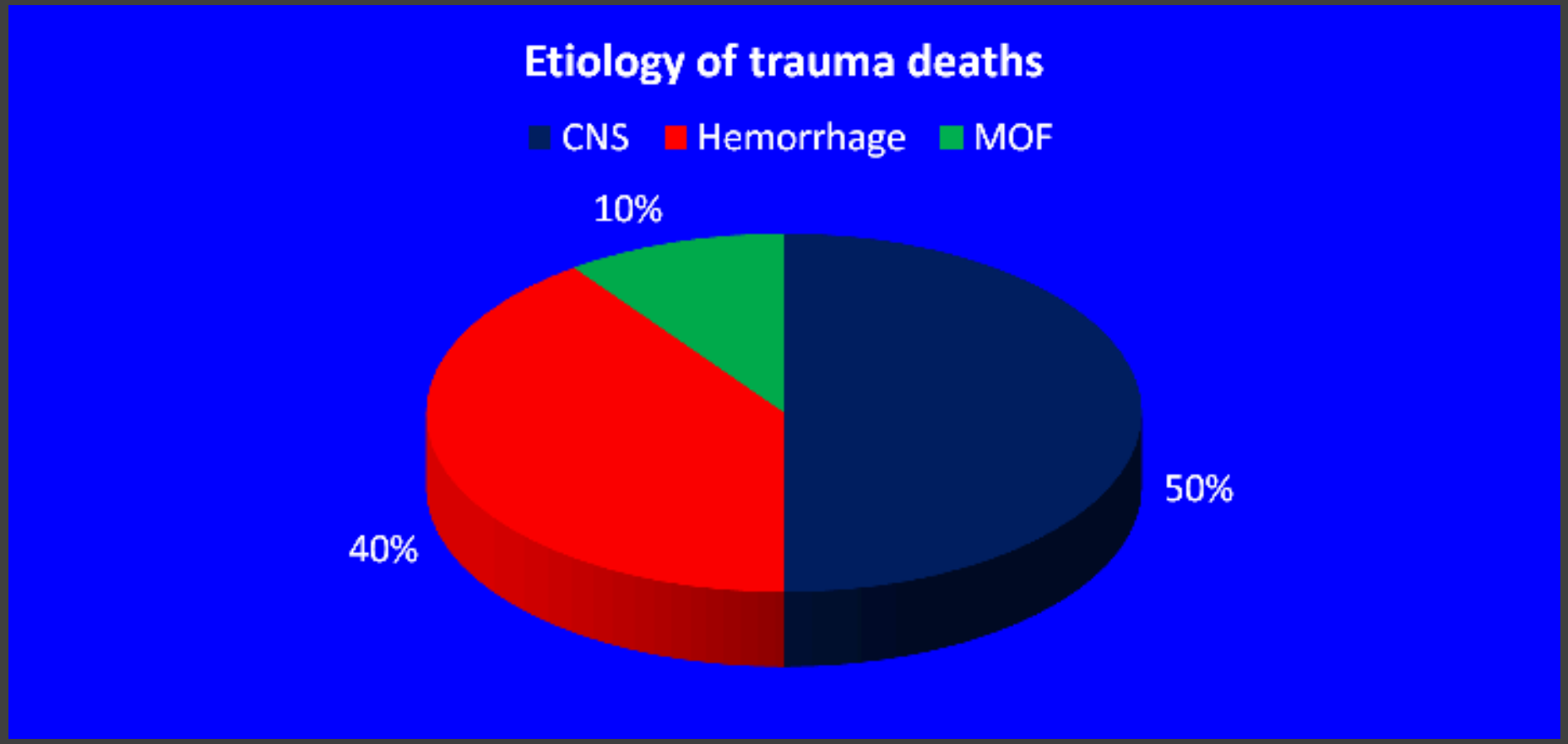
- Replacement of one blood volume in a 24 hour period
- Replacement of >50% of the total blood volume within 3-4 hours
- Transfusion of 3 or more RCC within 1 hour or 4 blood component units in 30 min. when ongoing need is foreseeable

Classification of Hemorrhage

American College of Surgeons Committee on Trauma
Advanced Trauma Life Support Program

	CLASS I	CLASS II	CLASS III	CLASS IV
Blood loss (ml)	Up to 750	750-1,500	**1,500-2,000**	**≥ 2,000**
Blood loss (% blood volume)	Up to 15%	15%-30%	**30%-40%**	**≥40%**
Pulse rate	<100	>100	**>120**	**≥140**
Blood pressure	Normal	Normal	**Decreased**	**Decreased**
Pulse pressure (mmHg)	Normal or increased	Decreased	Decreased	Decreased
Capillary refill test	Normal	Positive	Positive	Positive
Respiratory rate	14-20	20-30	30-40	>35
Urine output (ml/hr)	≥30	20-30	5-15	Negligible
CNS — mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic

Causes of death following multiple trauma



Current Orthopaedics (2004) 18, 304-310

Massive Blood Transfusion Management

- Haemostatic Resuscitation
- Fluid management
- Metabolic acid base correction
- Normal temperature
- Calcium management
- Management of Coagulopathy

Maintain Hb> 8 g.dl

- Assess degree of urgency
- Employ blood salvage to minimize allogeneic blood use
- Give red cells
- Group O Rh D negative In extreme emergency Until ABO and Rh D groups known
- Use blood warmer and/or rapid infusion device if flow rate >50 ml/kg/h in adult

Maintain adequate coagualtion

- Anticipate platelet count <50 after 2 blood volume replacement.
- Maintain PT & APTT < 1.5 · mean control
- Give FFP 12–15 ml/kg guided by tests
- Anticipate need for FFP after 1–1.5 blood volume replacement
- Allow for 30 min thawing time

Maintain adequate coagulation

- Maintain Fibrinogen > 1.0 g/l
- If not corrected by FFP give cryoprecipitate (Two packs of pooled cryoprecipitate for an adult)
- Allow for 30 min thawing time
- Keep ionised Ca2+

Suggested criteria for activation of MTP

- Actual or anticipated 4 units RBC in < 4 hrs, + haemodynamically unstable, +/– anticipated ongoing bleeding
- Severe thoracic, abdominal, pelvic or multiple long bone trauma
- Major obstetric, gastrointestinal or surgical bleeding

Initial management of bleeding

- Identify cause
- Initial measures:
  - compression
  - tourniquet
  - packing
- Surgical assessment:
  - early surgery or angiography to stop bleeding

Specific surgical considerations

- If significant physiological derangement, consider damage control surgery or angiography

Cell salvage

- Consider use of cell salvage where appropriate

Dosage

Platelet count < 50 x 10^9/L	1 adult therapeutic dose
INR > 1.5	FFP 15 mL/kg[a]
Fibrinogen < 1.0 g/L	cryoprecipitate 3–4 g[a]
Tranexamic acid	loading dose 1 g over 10 min, then infusion of 1 g over 8 hrs

[a] Local transfusion laboratory to advise on number of units needed to provide this dose

Resuscitation

- Avoid hypothermia, institute active warming
- Avoid excessive crystalloid
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled
- Do not use haemoglobin alone as a transfusion trigger

Special clinical situations

- Warfarin:
  - add vitamin K, prothrombinex/FFP
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate
- Head injury:
  - aim for platelet count > 100 × 10^9/L
  - permissive hypotension contraindicated

Considerations for use of rFVIIa[b]

The *routine* use of rFVIIa in trauma patients is not recommended due to its lack of effect on mortality (Grade B) and variable effect on morbidity (Grade C). Institutions may choose to develop a process for the use of rFVIIa where there is:

- uncontrolled haemorrhage in salvageable patient, and
- failed surgical or radiological measures to control bleeding, and
- adequate blood component replacement, and
- pH > 7.2, temperature > 34°C.

Discuss dose with haematologist/transfusion specialist

[b] rFVIIa is not licensed for use in this situation; all use must be part of practice review.

ABG	arterial blood gas	FFP	fresh frozen plasma	APTT	activated partial thromboplastin time
INR	international normalised ratio	BP	blood pressure	MTP	massive transfusion protocol
DIC	disseminated intravascular coagulation	PT	prothrombin time	FBC	full blood count
RBC	red blood cell	rFVIIa	activated recombinant factor VII		

Haemostatic Resuscitation: FFP

- Meta-analysis from 2010-2012: Patients undergoing massive transfusion, high FFP to RBC ratios was associated with a significant reduction in the risk of death (odds ratio (OR) 0.38 (95%CI 0.24-0.60) and multiorgan failure (OR 0.40 (95%CI 0.26-0.60).

- Murad MH, Stubbs JR, Gandhi MJ, Wang AT, Paul A, Erwin PJ, Montori VM, Roback JD: The effect of plasma transfusion on morbidity and mortality: a systematic review and meta-analysis. *Transfusion* 2010, 50:1370-1383

Haemostatic Resuscitation: FFP

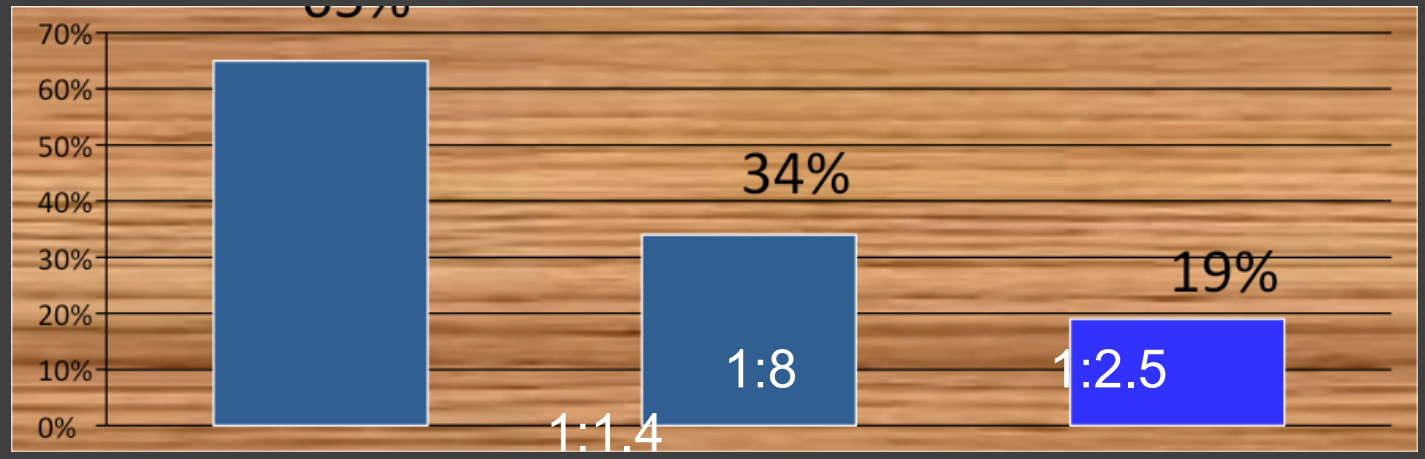
- Meta-analysis from 2012 reports of reduced mortality in trauma patients treated with the highest FFP or PLT to RBC ratios.

- Johansson PI, Oliveri R, Ostrowski SR: Hemostatic resuscitation with plasma and platelets in trauma. *A meta-analysis. J Emerg Trauma Shock* 2012, 5:120-125.

Coagulopathy of Massive Transfusion

Mortality Vs FFP/RBC ratio

- Retrospective review of 246 patients receiving a massive transfusion (> 10 units of blood)



Borgman MA. et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital J trauma, 2007. 66:805-813

Haemostatic Resuscitation: Plts

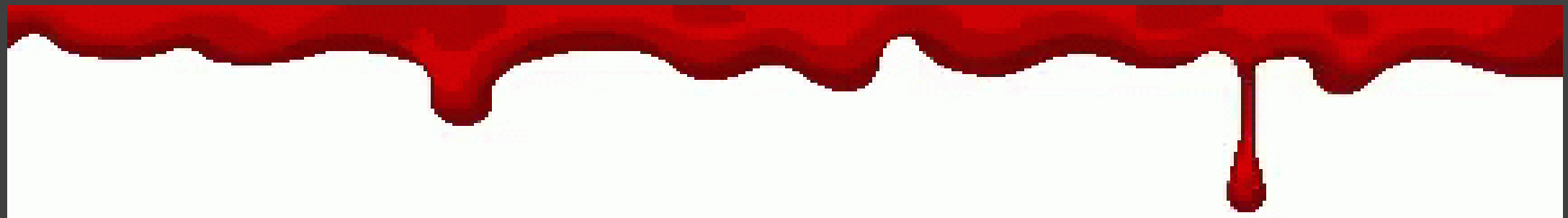
- Platelets are also pivotal for hemostasis: low Plts increases mortality.
- The highest survival was established in patients who received both a high PLT:RBC and a high FFP:RBC ratio.

- Holcomb JB, Wade CE, Michalek JE, Chisholm GB, Zarzabal LA, Schreiber MA, Gonzalez EA, Pomper GJ, Perkins JG, Spinella PC, Williams KL, Park MS: Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. *Ann Surg* 2008, 248:447-458.

What is the optimal ratio of blood products ?

Massive blood Transfusion

Massive transfusion protocol (MTPs)



- Established to provide rapid blood replacement in a setting of severe haemorrhage
- Early optimal blood transfusion is essential to sustain organ perfusion and oxygenation

What is Massive transfusion?

- 10 units of red cells in 24 hours
- Total blood volume is replaced within 24 hours
- Three units over one hour with ongoing bleeding
- 50% of total blood volume is replaced within 3 hours

Massive Transfusion-Clinical Settings

- Trauma
- Surgery (e.g. Liver, Cardiovascular)
- Less frequent
  - abdominal aortic aneurysm
  - liver transplant
  - obstetric catastrophes
  - GI bleeding

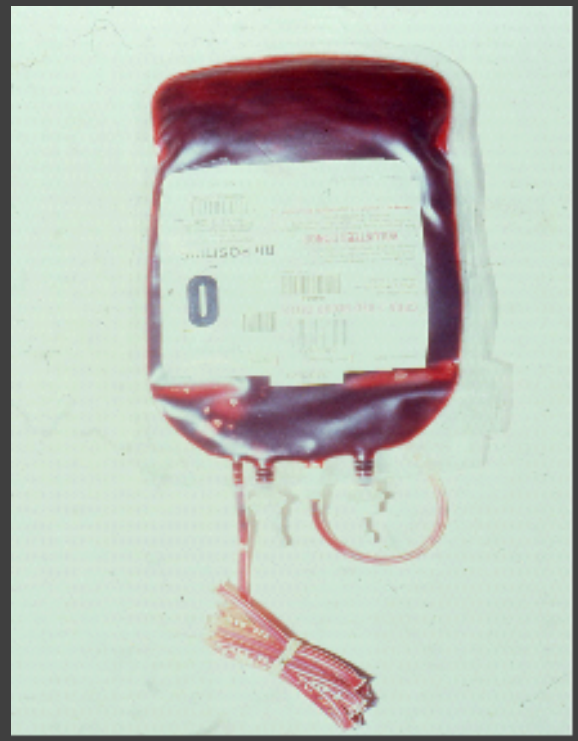
- **Cardiac surgery** — Most common cause of massive transfusion
- **Obstetric hemorrhage** — Gravid and parturient women are hypercoagulable with compensatory hyperfibrinolysis.
- **Liver disease** —
  - leads to the reduced production of normal coagulation factors
  - production of abnormal factors

Challenges

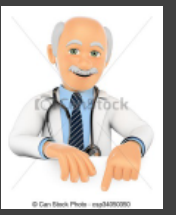
- Types of components to be administered
- Selection of the appropriate amounts
- TIME

Emergency Release Blood - Universal Donor

- O, RhD neg/pos RBCs – 5 min
- AB or A Plasma/Platelets



Important



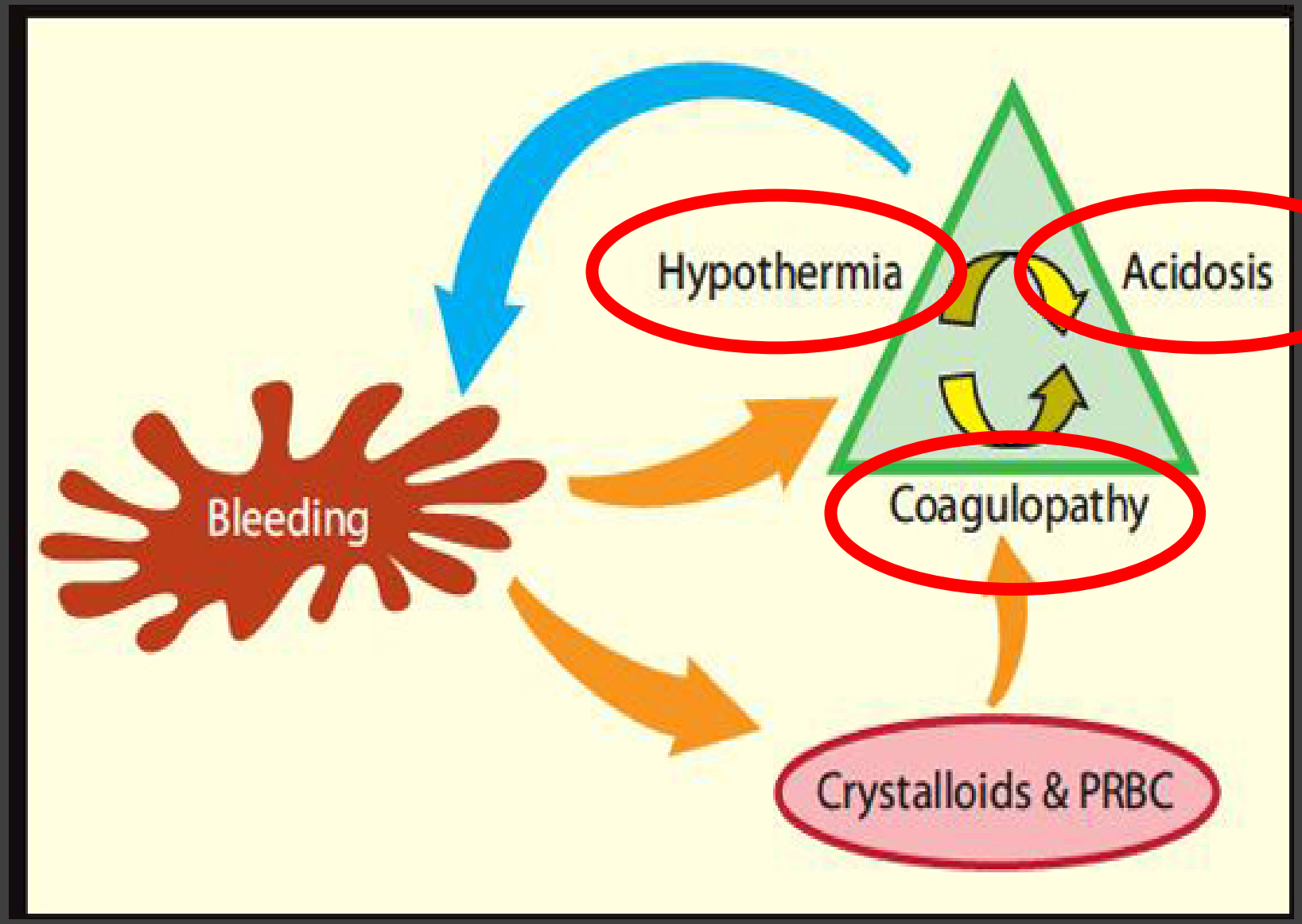
At the onset - aggressive fluid replacement and bleeding control can reduce the tissue injury, inflammation, and hypoperfusion

Untimely or incomplete control of massive bleeding- systemic consumptive coagulopathy with hemodilution and endothelial damage

If uncorrected, concurrent hypothermia and acidosis can further exacerbate coagulopathy and lead to irreversible multiorgan failure (MOF).

Complications of Massive Transfusion

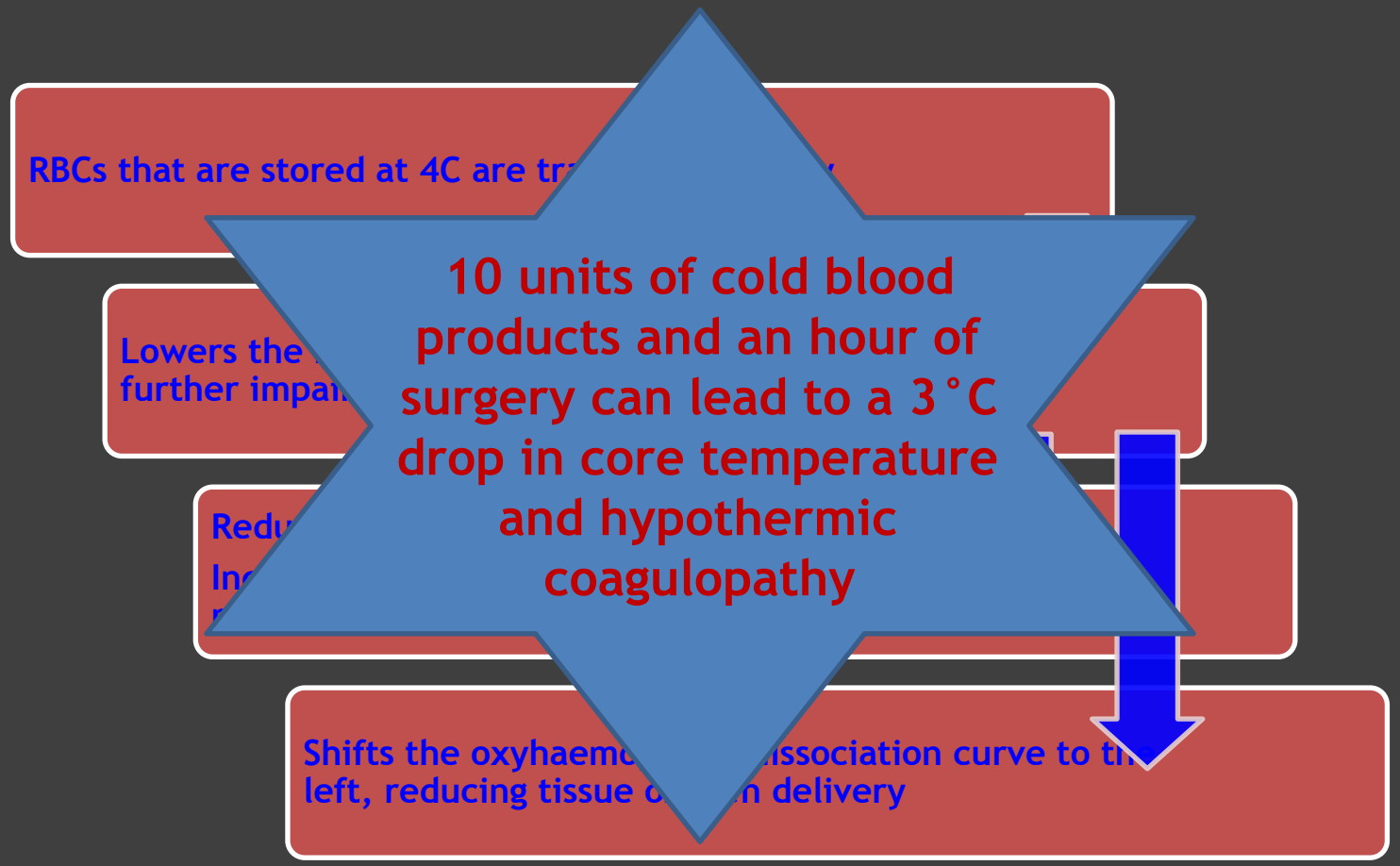
- Hypothermia
- Acid/base derangements
- Coagulopathy
- Citrate toxicity
- Electrolyte abnormalities
  - hypocalcemia
  - hypomagnesemia
  - hypokalemia
  - hyperkalemia
- Transfusion-associated acute lung injury


Hypothermia
Acidosis
Bleeding
Coagulopathy
Crystalloids & PRBC

Acidosis and hypothermia

- Acidosis
  - Interferes with formation of coagulation factor complexes
- Hypothermia
  - Reduces enzymatic activity of coagulation factors
  - Prevents activation of platelets

Hypothermia



Passive methods: remove wet clothing, apply vapor barriers (like heat-reflective blankets), use insulation, and keep the patient from cold surfaces.

Active external methods: use heat packs and forced warm air to warm the patient's body.

Active internal methods: administer warmed IV fluids and perform lavage with warm fluids in severe cases.

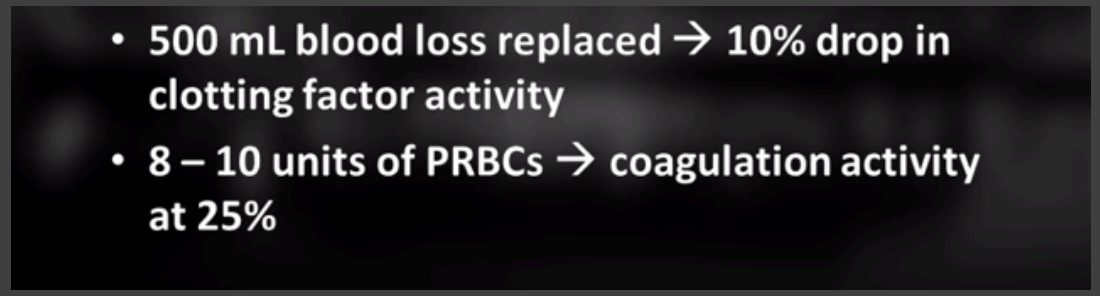
Prevention of hypothermia

- A high capacity commercial blood warmer should be used to warm blood components


3M Bair Hugger
43

Coagulopathy

- Dilutional coagulopathy
- Disseminated intravascular coagulation.
- Consumption of platelets and coagulation factors



ALTERATIONS IN HEMOSTASIS

- Acute DIC
  - microvascular oozing
  - prolongation of the PT and aPTT in excess of that expected by dilution
  - significant thrombocytopenia
  - low fibrinogen levels
  - increased levels of D-dimer

Hypocalcaemia

- Citrate binds calcium
- Results in hypotension, small pulse pressure, flat ST-segments and prolonged QT intervals on the ECG.
- Slow i.v. injection of calcium gluconate 10%

Hyperkalaemia

- The potassium concentration of blood increases during storage, by as much as 5–10 mmol u1 .

- Hyperkalaemia rarely occurs during massive transfusions unless the patient is also hypothermic and acidotic

Monitoring recommendations

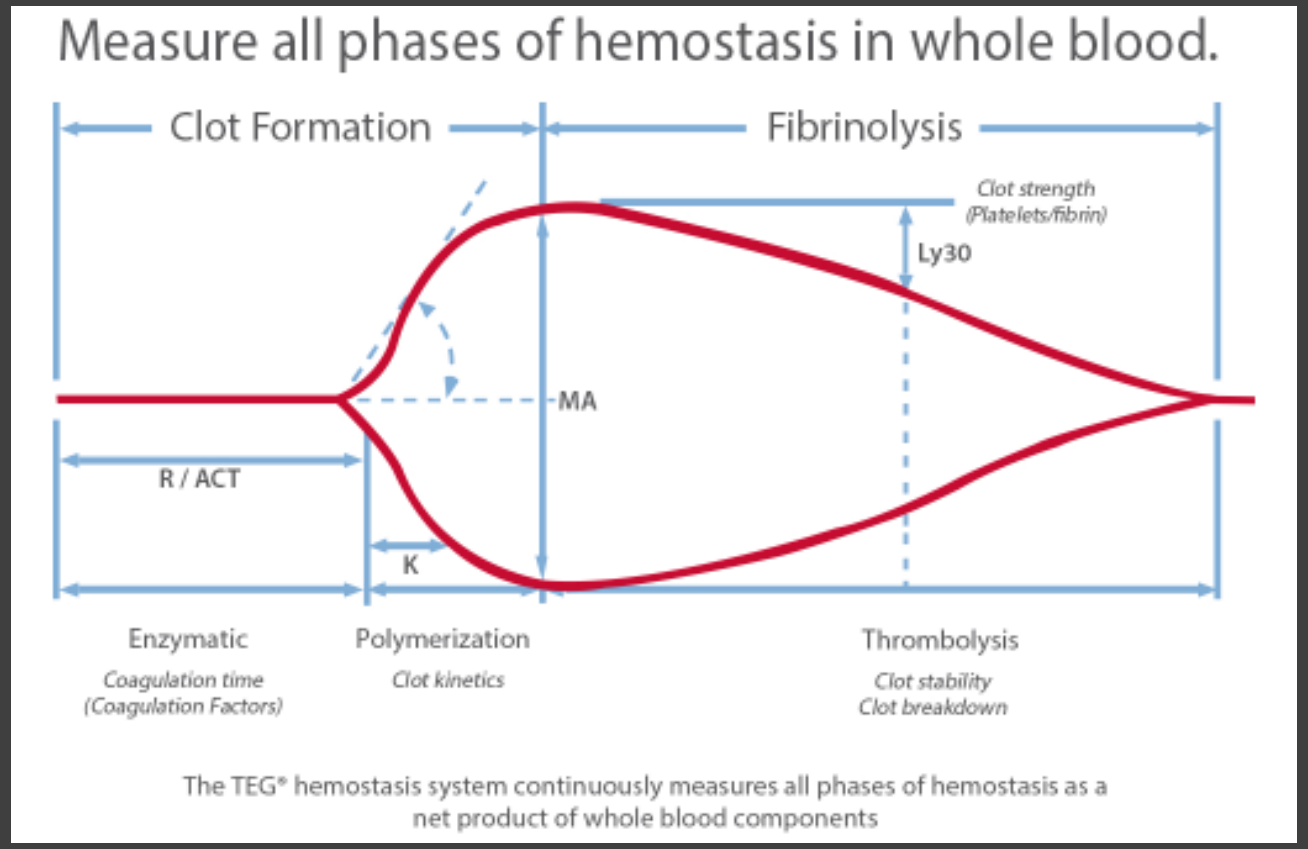
- PT, aPTT
- Platelet count
- Fibrinogen
- Electrolytes
- Viscoelastic test
  - after the administration of every five to seven units of red cells.

Goals

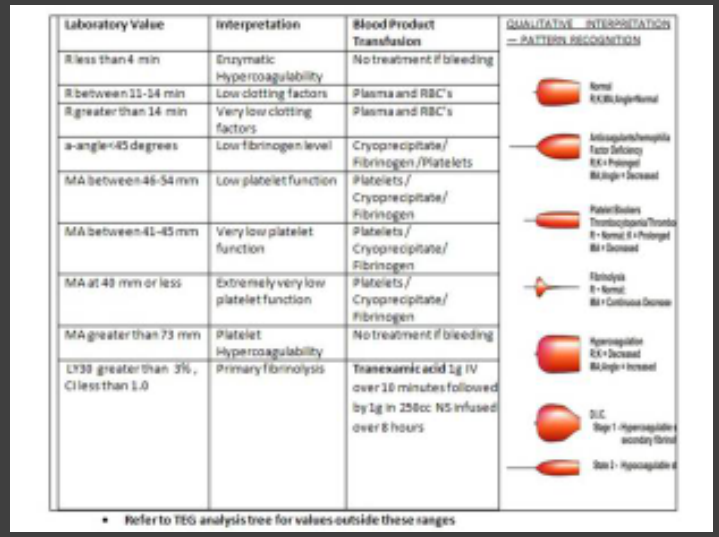
Investigation	Target value
Haemoglobin	10 gm/dl
Hematocrit	32%
Platelet count	> 50 x 10 9 /l
PT	< 1.5 x control
PTT	< 1.5 x control
Fibrinogen	> 0.8 g/l

Viscoelastic whole-blood assays

- TEG® and ROTEM®
- provide information on the coagulation process through the graphic display of clot initiation, propagation and lysis.
- used to guide transfusion of blood components


Measure all phases of hemostasis in whole blood.
Clot Formation
Fibrinolysis
Clot strength
(Platelets/fibrin)
Ly30
MA
R / ACT
K
Enzymatic
Coagulation time
(Coagulation Factors)
Polymerization
Clot kinetics
Thrombolysis
Clot stability
Clot breakdown
The TEG® hemostasis system continuously measures all phases of hemostasis as a net product of whole blood components

- Costeffective -since it reduces inappropriate transfusions, thus improving transfusion management and patients' clinical outcome



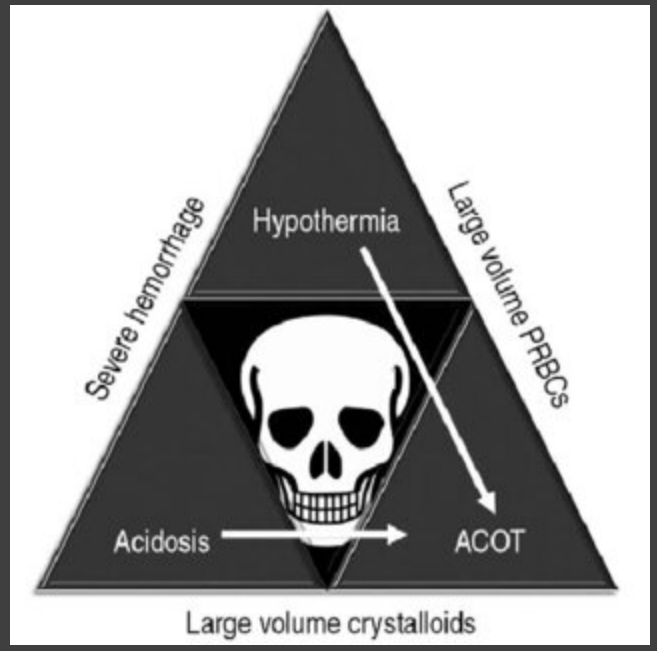
Laboratory Value	Interpretation	Blood Product Transfusion
R less than 4 min	Enzymatic Hypercoagulability	No treatment if bleeding
R between 11-14 min	Low clotting factors	Plasma and RBC's
R greater than 14 min	Very low clotting factors	Plasma and RBC's
a-angle<45 degrees	Low fibrinogen level	Cryoprecipitate/ Fibrinogen /Platelets
MA between 46-54 mm	Low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA between 41-45 mm	Very low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA at 40 mm or less	Extremely very low platelet function	Platelets / Cryoprecipitate/ Fibrinogen
MA greater than 73 mm	Platelet Hypercoagulability	No treatment if bleeding
LY30 greater than 3% , CI less than 1.0	Primary fibrinolysis	**Tranexamic acid** 1g IV over 10 minutes followed by 1g in 250cc NS infused over 8 hours

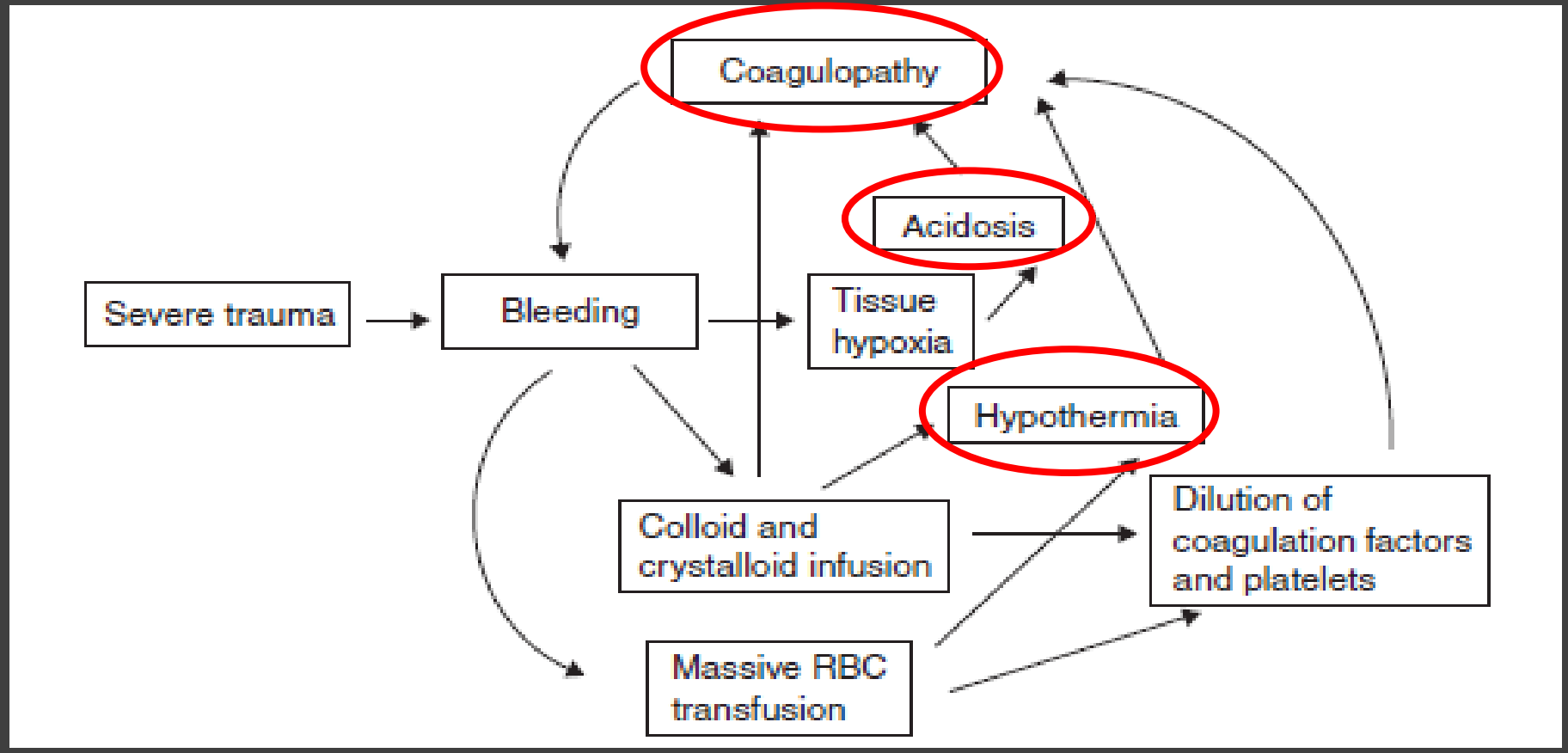
QUALITATIVE INTERPRETATION – PATTERN RECOGNITION

- Refer to TEG analysis tree for values outside these ranges

Thank You

The Lethal Triad in Trauma




Coagulopathy
Acidosis
Severe trauma
Bleeding
Tissue hypoxia
Hypothermia
Colloid and crystalloid infusion
Dilution of coagulation factors and platelets
Massive RBC transfusion

Coagulopathy

- Activation and consumption of coagulation factors secondary to tissue trauma
- Reduced activity of coagulation factors from prolonged shock, hypoxia, hypothermia, or failure to clear activation peptides that act as competitive inhibitors
- Acute disseminated intravascular coagulation (acute DIC)

- Coagulation abnormalities may be induced by the dilutional effects of blood replacement on coagulation proteins and the platelet count
- Consumption of coagulant proteins, and fibrinolysis
- Extensive blood loss
- Dilutional effects of physiologic vascular refill

Hypothermia

A temperature < 35°C is associated with an increase in mortality.

- Trauma patients that are hypothermic are not perfusing their tissue

- The coagulation cascade is an enzymatic pathway that degrades with temperature and ceases at 33.3C
  - Reduces activity of clotting factors by 50% at 34 C
  - Platelet activation almost eliminated at 30 C

- The replacement of blood loss with red cells and a crystalloid volume expander will result in gradual dilution of plasma clotting proteins, leading to prolongation of the prothrombin time (PT) and the activated partial thromboplastin time (aPTT)

- A similar dilutional effect on the platelet concentration can be seen with massive transfusion

- Hypothermia reduces the enzymatic activity of plasma coagulation proteins, but has a greater effect by preventing the activation of platelets via traction on the glycoprotein Ib/ IX/V complex by von Willebrand

Acidosis

Base deficit (BD) ≥ 6 identifies patients that

- require early transfusion,
- increased ICU days and
- risk for ARDS and MOF

- BD of ≥ 6 is strongly associated with the need for MT and mortality.
- Patients have an elevated BD before their blood pressure drops to classic “hypotension” levels.
- Acidosis contributes more to coagulopathy more than hypothermia (not reversible)

- Acidosis specifically interferes with the assembly of coagulation factor complexes involving calcium and negatively-charged phospholipids.

- Activity of the factor Xa/Va prothrombinase complex is reduced

%	50	70	80
Ph	7.2	7.0	6.8

- The resulting delayed production and reduced concentrations of generated thrombin lead to
- Delayed fibrin production, altered fibrin structure, and increased susceptibility to fibrinolysis .