BLOOD IS A LIQUID TRANSPLANT

TRANSFUSE PATIENTS NOT NUMBERS

INFORMED CONSENT

INFORMED CHOICE

RISKS

versus

BENEFITS

versus

ALTERNATIVES

TRANSFUSION INFECTIONS

- HIV 1 / 2: 1 in 1,467,000 per unit
- HCV: 1 in 1,149,000 per unit
- HBV: 1 in 765,000 to 1,006,000 unit
- Bacterial sepsis: 1 in 5,000 per apheresis unit
- HTLV I /II: 1 in 4,364,000 units
- West Nile Virus: 11 cases to date
- Syphilis: None since 1960's
- ZIKA: 4 cases to date
- Babesiosis CT MA MN: 1 in 18,000 per unit
- Dengue virus PR: 0 from screened blood
- CMV (reduced risk): 1% to 4%

TRANSFUSION INFECTIONS
Emerging Pathogens

- Malaria
- Lyme disease
- Chikungunya virus
- Parvoviruses
- vCJD
- Hepatitis E
- Brucella
- Leishmaniasis
- Rickettsia
- EBV
- Babesiosis
- Herpes viruses

TRANSFUSION REACTIONS IMMEDIATE TYPE

- Allergic – wide range from urticaria to anaphylactoid
- Febrile non-hemolytic
- Acute hemolytic
- Anaphylactic --- check for severe food allergies!!
- Acute hypotension
- Acute pain syndrome
- Hypothermia – can use a blood warmer
- Bacterial contamination --- especially with platelets!!
- Transfusion associated dyspnea (TAD)
- Transfusion associated circulatory overload (TACO)
- Transfusion related acute lung injury (TRALI)

Arch Pathol Lab Med. 2007;131:708-718

DELAYED TRANSFUSION REACTIONS (DAYS TO MONTHS)

- Formation of red cell antibodies
- Formation of neutrophil / HLA antibodies
- Formation of platelet specific antibodies
- Immune modulation (TRIM)
- Graft versus host disease (GVHD)
- Iron overload (TRIO)

Arch Pathol Lab Med. 2007;131:708-718.

TRALI

Transfusion Related Acute Lung Injury

- TRALI has been the #1 cause of transfusion related deaths to the FDA since 2004 till 2017. Now #2.
- Estimated incidence (1:1000 to 1:5000)
  - Any blood product can cause TRALI

TRALI

- Any blood product can cause it
- **Non-cardiogenic pulmonary edema** within **6 hours** of transfusion with **hypoxemia**
- **HYPOXEMIA**, hypotension, fever, crackles
- HLA/PMN antibodies/ monocytes/ chemokines
- Mortality 5% to 25%
- Supportive care -- may need ventilator
- Do **NOT** use diuretics

TACO

Transfusion associated circulatory overload

Since 2017 #1 cause of transfusion deaths

- 1 to 11% in critically ill patients (1:350)
- **CARDIOGENIC PULMONARY EDEMA**
- Tachypnea, dyspnea, tachycardia, **hypertension**, increased pulmonary artery pressure, jugular venous distention
- Mortality up to 20%
- Treatment with diuresis and vent support

TRANSFUSION RELATED IMMUNE MODULATION (TRIM)

- *Immune Activation*
  - TA-GVHD
  - TRALI
  - Alloimmunization
    - Red Cells
    - Platelets
    - Leukocytes
- *Immune Suppression*
  - Nosocomial Infections
  - Postoperative Infections
  - Cancer Recurrence
  - Enhanced Allograft Survival
  - Microchimerism
  - SLL/CLL

Chest 2005;127:295-307

TRIO

- **T**ransfusion **R**elated **I**ron **O**verload
- Can occur with greater than 20 units
- Serum ferritin greater than 1,000
- Most common with sickle cell, thalassemia, myelodysplastic syndromes, aplastic anemia, and leukemia
- Chelation therapy – oral now available

THROMBOEMBOLISM

- ACS-NSQIP data base of 750,937 patients
- Surgeries 1/2014 to 12/2014
- 525 teaching hospitals
- Dose dependent increase in VTE
- All subspecialities
- Perioperative RBC transfusions may be associated with development of new or progressive postoperative VTE
- JAMA SURGERY 6/13/2018 online

RBCs ARE DAMAGED GOODS

- Decreased 2,3 DPG
- Decreased ATP
- Decreased nitric oxide
- Decreased deformability
- Increased adhesiveness and aggregation
- Increased free hemoglobin
- CAPILLARY CONSTI

RISKS

versus

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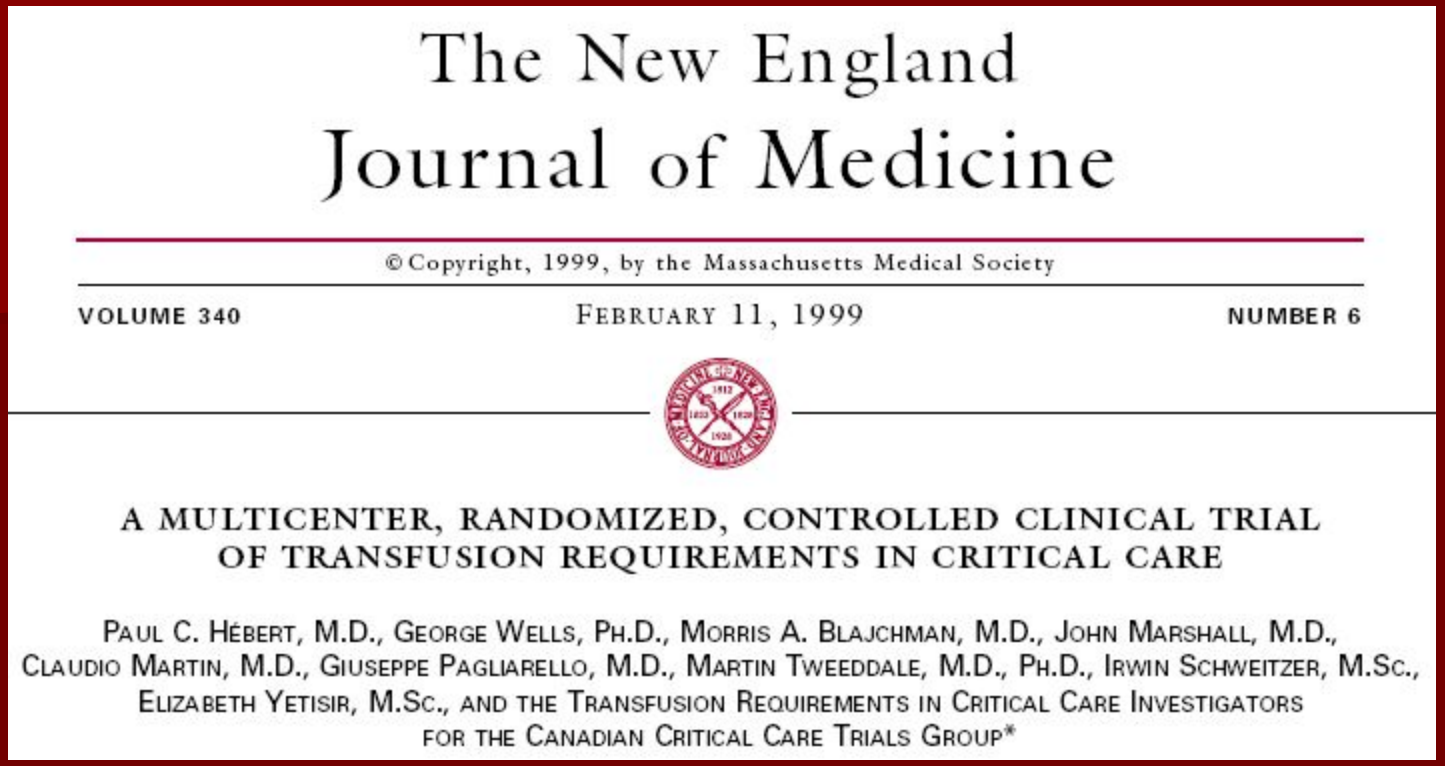
ALTERNATIVES

RBC TRANSFUSIONS

- Hemorrhagic shock and acute hemorrhage with hemodynamic instability
- **Adequate saline replacement**
- **SYMPTOMATIC ANEMIA**
  - Chest pain
  - Orthostatic hypotension or tachycardia NOT responsive to saline fluids
  - Congestive heart failure



The New England Journal of Medicine

VOLUME 340 FEBRUARY 11, 1999 NUMBER 6

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

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D., CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.SC., ELIZABETH YETISIR, M.SC., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

- Known as the TRICC study
- First randomized controlled trial regarding blood transfusion thresholds done
- Labeled one of the single most important studies in transfusion medicine

TRICC STUDY

Transfusion requirements in critical care

- Prospective , randomized, controlled trial
- Multiple ICUs (25 centers)
- 838 critically ill patients
  - 418 pts restrictive strategy (<7g/dl)
  - 420 pts liberal strategy (<10g/dl)
- 30 day mortality: 18.7% vs 23.3%
- Hospitalization mortality: 22.2% vs 28.1%

Herbert PC et al. *NEJM 1999;* 340:409-417

JAMA CLINICAL EVIDENCE SYNOPSIS

- *"Outcomes Using Lower vs Higher Hemoglobin Thresholds for Red Blood Cell Transfusions"*
- JAMA January 2, 2013
- 19 randomized trials with 6264 patients
- Threshold of 7 to 8 g/dl **NOT** associated with mortality, cardiac morbidity, functional recovery or length of stay compared to higher hemoglobin levels

FOCUS RCT

- 2016 patients with average age 82 with cardiovascular disease or risk factors
- Hip surgery
- Results showed that the restrictive strategy (Hgb<8) was NOT inferior to liberal strategy (Hgb<10) with respect to mortality, morbidity or function.
- NEJM 2011;365:2453-62

2016 Cochrane Review

- Review of 31 randomized clinical trials
- 12,587 medical and surgical patients
- Compared 7-8 g versus 9-10 g hemoglobin
- Results
  - No difference in 30 day mortality
  - No difference in hospital/intensive care stay
  - No difference in functional recovery
  - No increase risk of myocardial infarction

JAMA Clinical Practice Guidelines From the AABB Transfusion Thresholds. October 2016

IMPROVED PATIENT OUTCOMES!!

- "**Restricted** blood transfusion practices are associated with **improved** patient outcomes" Goodnough et al, Trans 2014
- Study done at Stanford 2008 – 2013
- Hemoglobin 7g/dl used
- Decreased mortality
- Decreased length of stay

Promoting High Value Practice by Reducing Unnecessary Transfusions With a Patient Blood Management Program

RBC transfusion is not indicated in hemodynamically stable adult patients with hemoglobin of 7 or more. Critically ill included.

RBC transfusion is not indicated in orthopedic or cardiac surgery patients or patients with underlying cardiovascular disease with hemoglobin of 8 or more

Single unit transfusion followed by reassessment should be standard of care in hemodynamically stable patients not actively bleeding

RBC TRANSFUSIONS HBG LESS THAN 7

- Resuscitated critically ill patients
- Critically ill with hemodynamically stable
- Critically ill with mechanical ventilation
- Critically ill with stable cardiac disease
- Chemotherapy patients
- **Acute Upper GI bleeds** (NEJM 2013)

GI BLEEDS

- Acute Upper GI bleeds (NEJM 2013;368)
  - 921 pts with 461 in restrictive (<7) vs 460 in liberal (<9) had better survival (95% vs 91%)
  - Need endoscopy within 6 hours!!!!
  - Bleeding most commonly from varices that results from increased portal hypertension
  - PARADOXICALLY --- when you increase the blood volume with transfusion you can make the bleeding worse!!!

LIVER DISEASE

- "Rebalanced Hemostasis"
- INR does **NOT** predict bleeding!!!
- Liver anticoagulants (C,S,AT) decreased
- Compensatory increase in VWF!!!
- Treat existing infections
- Optimize renal function
- **NO** prophylactic transfusions!!!!!!!!!!!!!!!
- Based on liver transplant data (Trans Med Reviews 2014).

LIVER DISEASE

- Pre-procedural phase (paracentesis, thoracentesis, central lines, LPs, even liver biopsies)
  - No prophylactic correction of hemostasis
  - Treat existing infections
  - Optimize renal status
  - **BE PROACTIVE AND GIVE IV VITAMIN K DAILY !!!!!**

PARACENTESIS

2009 American Association for the Study of Liver Diseases Practice Guidelines states --

"Because bleeding is sufficiently uncommon, the routine prophylactic use of FFP or platelets before paracentesis is **NOT** recommended"

RBC TRANSFUSIONS HBG 8 TO 10

- Acute coronary syndromes
  - Various studies with data to support transfusions as low as 8 and as high as 10
  - As with all transfusions, clinical judgment with regard to risk-benefit analysis

RISKS

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BENEFITS

versus

ALTERNATIVES

IRON THERAPY

- ALWAYS consider oral or IV iron therapy as an ALTERNATIVE to RBC transfusions
- Usually have maximal reticulocytosis in 7 to 10 days
- Usually see 2 gram rise in hemoglobin
  2 weeks with normal values in 1 month
- Iron dextran vs iron gluconate

- Do **NOT** use in critically sick patients!!!

YELLOW BLOOD

- PLATELETS
- FRESH FROZEN PLASMA (FFP)
- CRYOPRECIPITATE (CRYO)

HEMOSTATIC RANGE

- MUST DIFFERENTIATE ***HEMOSTATIC RANGE*** FROM *REFERENCE* RANGE
  - Platelets: 50,000 (hemostatic)
  - INR: less than 2 (hemostatic)
  - Fibrinogen: 100 (hemostatic)

  - Reference platelets: 150,000-450,000
  - Reference INR: 0.9-1.1
  - Reference fibrinogen: 200-400

PLATELETS

- Prophylaxis < 10,000
- Bleeding < 50,000
- Bleeding brain, spinal cord, eye < 100,000
- Central venous tunneled lines – 20,000
- Spinal catheters – 80,000
- Lumbar puncture – 40,000
- Liver biopsy - 50,000 vs transjugular
- **Uremic** platelet dysfunction -- use **DDAVP**
- Platelet dysfunction (drugs) --- consider TXA and DDAVP before platelet transfusion

PLATELET NO-NOs

- Do **NOT** transfuse platelets for
  - Thrombotic thrombocytopenic purpura (TTP)
  - Immune thrombocytopenia (ITP)
  - Post-transfusion purpura (PTP)
  - Heparin induced thrombocytopenia (HIT)
  - Drug-induced thrombocytopenia (DIT)
- **UNLESS life threatening bleeding**
- **Intracranial bleed on anti-platelet drugs (PATCH study)**

COAGULATION FACTOR HEMOSTATIC LEVELS

Fibrinogen	50mg/dl
Prothrombin	20-30%
Factor V	15-20%
Factor VII	15-20%
Factor VIII	15-20%
Factor X	15-20%
Factor XIII	2-5%

Mannuci, Blood, 2004;104:1243

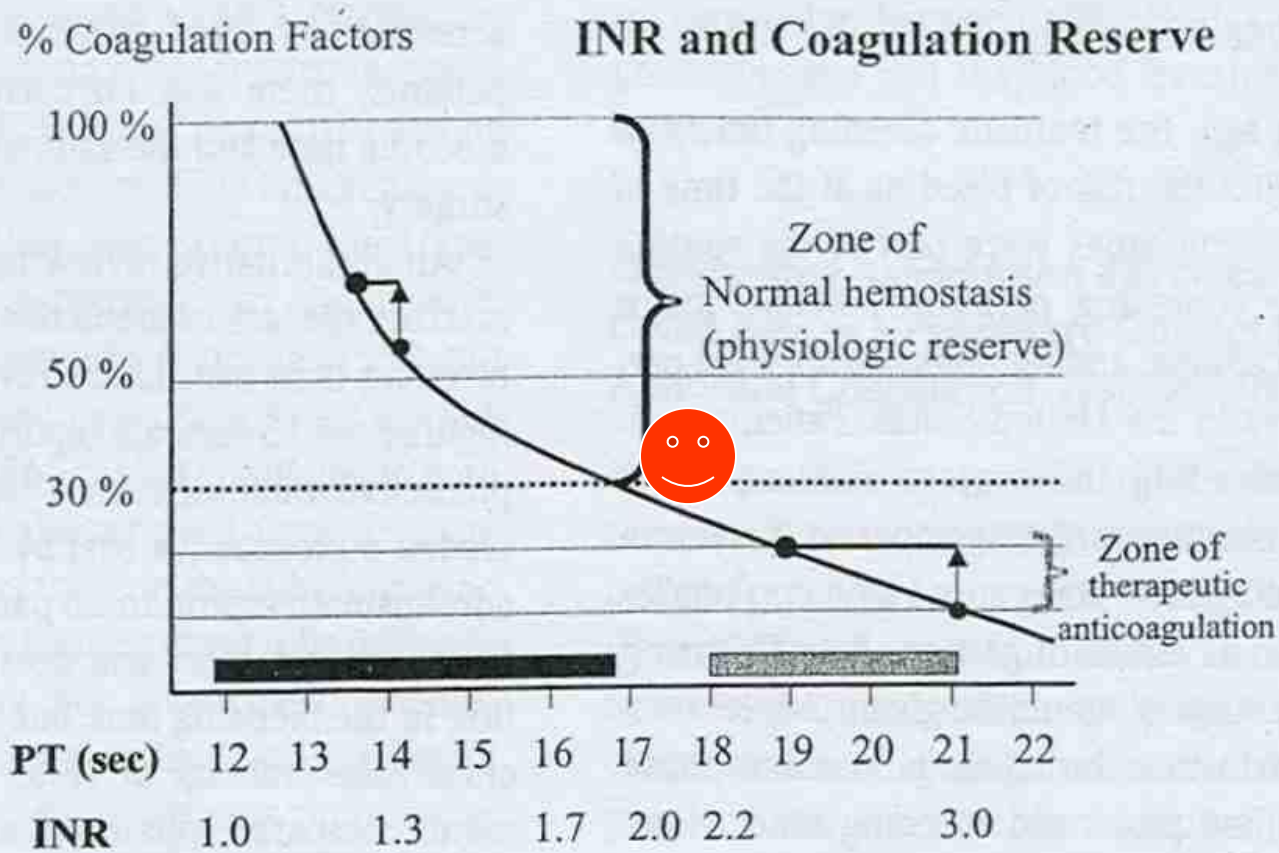

Figure 1-3. General relationship between the concentration of coagulation factors and the result of the prothrombin time (PT) test. In any laboratory, the local position of the curve will vary as a result of technical factors. Results will also vary depending on whether there are single or multiple factor defects. See text for explanation. Note that the zone of physiologic reserve is much larger than the zone of therapeutic anticoagulation.

INR OF FFP

- INR of FFP was actually measured
  - Only 20% had INR 0f 1.0
  - 60% had INR of 1.1
  - 10% had INR of 1.2
  - 5% had INR of 1.3
- THEREFORE 75% of FFP has an INR >1.0

FRESH FROZEN PLASMA

- **Bleeding with INR of 2 or greater NOT due to warfarin**
- Massive blood transfusion
- Factor deficiencies without concentrates

FFP

MUST BE ADEQUATE DOSE

- USUAL DOSE -- 10 to 20 ml/kg
- Average volume of one FFP is 300 ml
- So minimum dose is usually at least 3 FFP in 70 kg patient (up to 5 FFP)
- **SO INCREASED TACO RISK!!!**

FFP

MUST BE GIVEN AT **RIGHT** TIME

- Only give within 4 hours of a surgery or when actually bleeding
- Coagulation effect only lasts 6 hours
- NEVER give the night before a procedure
- NEVER give to “normalize” INR

FFP NO NOs

- Do **NOT** transfuse FFP
  - To reverse elevated INR secondary to warfarin if 4 Factor PCC and IV vitamin K available
  - –Normalize abnormal PT/ INR results
  - –Patients on heparin (unless heparin resistant)
  - –Increase blood volume except MBT
  - –Increase albumin level
  - –To reverse elevated INR secondary to poor nutrition that can be corrected with vitamin K

RISKS

versus

BENEFITS

versus

ALTERNATIVES

FOUR FACTOR PCC

- **Kcentra** – 4 Factor PCC - FDA approved

- **URGENT warfarin reversal**
  - IV Vitamin K 10mg IV
  - **4** Prothrombin Complex Concentrate (PCC)
  - ONE dose is all you need!
  - **Do NOT give FFP!!!!!!!!!!!!!!!!**

IV VITAMIN K

- GREAT stuff ---use oral or IV, but **NOT** SQ
- May work as quick as 2 hours
- INR <5 without bleeding: hold warfarin
- INR 5-9 without bleeding: hold +/- Vit K
- INR >9 without bleeding: hold plus Vit K
- Serious or life-threatening bleeding
  - 10 mg IV Vit K
  - 4-PCC (Kcentra)

Chest 2008;133:160S
Transfusion March 2013

IV VITAMIN K

IF you use ONLY 1.0 to 2.5 mg vitamin K ,

THEN you will NOT make patient resistant to restarting coumadin.

Risk of anaphylaxis same as penicillin or IV contrast !

CONSIDER PROPHYLACTIC USE !!

CRYOPRECIPITATE

- Bleeding with fibrinogen less than **100**
- Congenital fibrinogen deficiencies
- Factor XIII deficiency

- REMEMBER that if fibrinogen is under a 100 it may increase PTT and PT/INR
- SO correct fibrinogen FIRST before considering FFP to correct PTT or PT/INR

SPECIFIC SITUATIONS

CENTRAL VENOUS LINE INSERTION

- **No** study has shown that pre-procedure transfusion of FFP or platelets decreases risk of hemorrhage
- 20,000

THORACENTESIS

- **No** study has shown that pre-procedure transfusion of FFP or platelets decreases risk of hemorrhage

DIAGNOSTIC LUMBAR PUNCTURE

- Studies have shown > 10,000 is safe in children with leukemia and > 20,000 in adults with leukemia
- 40,000 to 50,000

Key Messages From the Literature

Overutilization of blood is a Patient Safety issue

- Blood Transfusions are inherently hazardous
- PRBC transfusions have been associated with:
  - Increased mortality
  - Complications (cardiac, neurologic, renal, respiratory, thromboembolic, wound)
  - Infections

Restrictive blood practices are evidence-based

- A restrictive approach to blood transfusions (Hgb <7 to 8) conserves the blood supply, reduces costs and improves or does not harm patient outcomes
- Administration of blood to a stable hospitalized patient (Hgb >7 to 8) has not been shown to improve patient outcomes or quality of life