



THE UNIVERSITY OF
WESTERN AUSTRALIA

FACULTY OF MEDICINE, DENTISTRY AND HEALTH SCIENCES

Blood Transfusion Therapy in Trauma and Massive Hemorrhage – Putting the Patient First

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- Over last 40 years, transfusion therapy evolved from use of predominately whole blood to now largely component therapy.
- Whole blood: still used in many developing countries and in military situations, however
- Component therapy predominates primarily due to resource utilization and safety.
- Change occurred without strong evidence of clinical outcomes between whole blood and component therapy in multiple trauma patients.
- WWI & WWII: plasma and whole blood
- Vietnam: aggressive crystalloids



- ↘ National blood services funded by government
- ↘ Provide transfusion needs – through components
- ↘ Embedded in the manufacturing/inventory paradigm
 - “Blood factories”
 - GMP, QC etc
 - Detached from clinical environment



- Driven by red cell needs - recovered plasma as a by product
 - Recovered plasma sent for fractionation to derivatives
 - Mostly used for chronic deficiencies
 - Haemophilia
 - Primary Immune Deficiency
 - Etc
- USA - 5 million transfusion recipients each year vs
15000 haemophilia, 30,000 PID etc



↘ RCCs

- “To increase oxygen delivery to the tissues”...but
- Do transfused red cells increase VO_2 ?
 - Yes, around the critical [Hb] ie about 50g/l, but
 - **At 80 g/l, no obvious effect** (Walsh et al 2004)

↘ Platelets

- PLADO study – Low vs Medium vs High dose platelets
- **Same clinical outcome irrespective of dose**

↘ FFP

- Two higher quality trials - Both evaluated prophylaxis
- **No benefit reported in either trial**



Blood components – Questioning dogma

- ↘ ***The move to component therapy was driven by the need for recovered plasma***
- ↘ ***The components produced had little bearing to clinical transfusion***
- ↘ Emerging evidence indicates possible serious morbidity and mortality from the use of stored blood components
- ↘ In the era of Evidence Based Medicine, we need to question our assured dogmas
 - Components are as good as blood ?
 - Fresh blood is impossible to deliver ?



1. Reduced ability of Hb to release bound oxygen at tissue level (*2,3 DPG*)

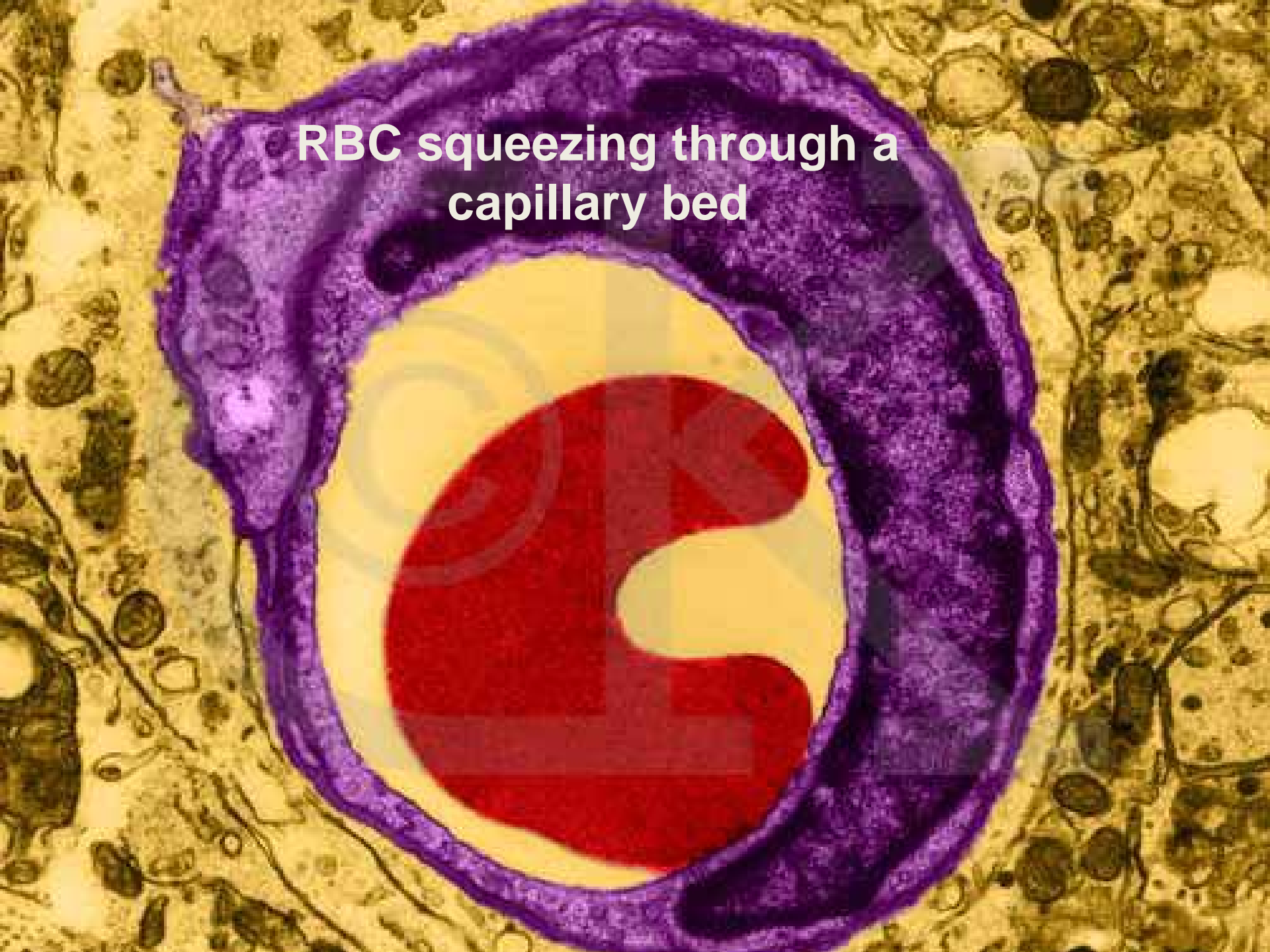
2,3 DPG levels become undetectable after two weeks of storage. Levels are restored within 72 hours after transfusion

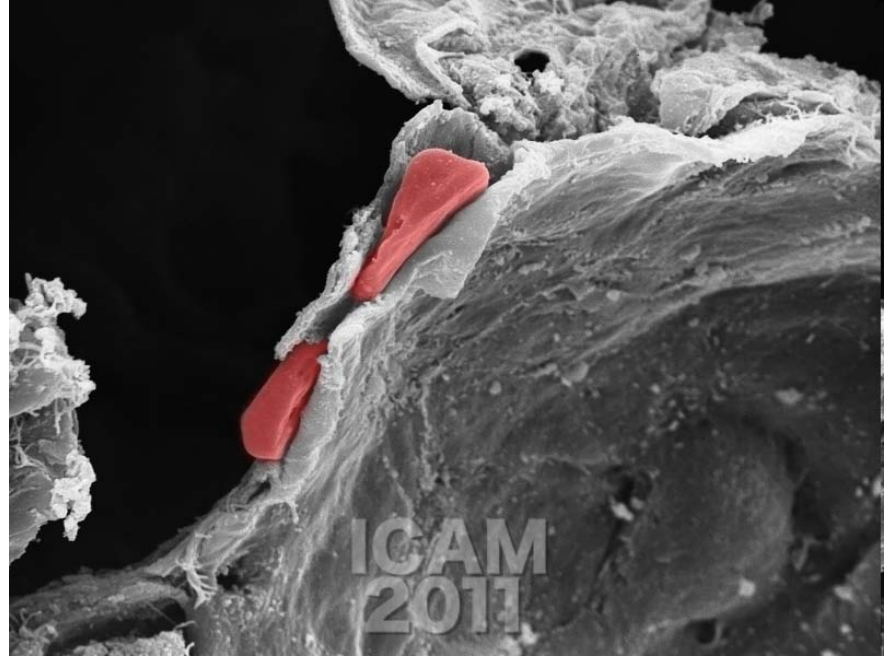


Problems with stored pRBC's

1. Reduced ability of Hb to release bound oxygen at tissue level (*2,3 DPG*).
2. Reduced RBC deformability = potential to block capillary beds

**RBC squeezing through a
capillary bed**





Problems with stored pRBC's

1. Reduced ability of Hb to release bound oxygen at tissue level (*2,3 DPG*)..
2. Reduced RBC deformability = potential to block capillary beds
3. Storage lesion (age dependent defect) = potential to block capillary beds

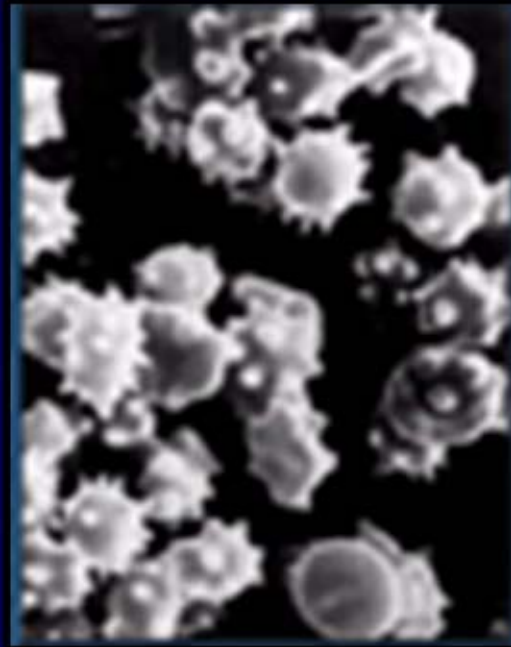


More is known about the risks of transfusion than the benefits

RBC Shape Change During Storage



Day 1



Day 21



Day 35



Problems with stored pRBC's

1. Reduced ability of Hb to release bound oxygen at tissue level (2,3 DPG)
2. Reduced RBC deformability = potential to block capillary beds
3. Storage lesion (age dependent defect) = potential to block capillary beds
4. **Activation of recipients immune system**



Each unit of blood increases the risk of a nosocomial infection by up to 50%!

Transfusion increases the risk of postoperative infections after cardiovascular surgery J Am Coll Surg 2006 Jan;202

An alternative scoring system to predict risk for surgical site infection complicating coronary artery bypass graft surgery Infect Control Hosp Epidemiol 2007 Oct;

Transfusion of red cells is associated with increased incidence of bacterial infection after colorectal surgery; a prospective study Transfusion Feb 2003

Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient Crit Care Med 2002 Vol 30 #10

Transfusion Practice and Blood Stream Infections in Critically Ill Patients Chest 2005:127

Blood transfusions correlate with infections in trauma patients in a dose-dependant manner Am Surg 2002:68



Use of unrefrigerated fresh whole blood (UFWB) in massive transfusion

Australian Study March 1992 to February 1995.

- ↘ Retrospective review of patients who received UFWB.
- ↘ Noting blood usage and outcome in 11 patients receiving UFWB
- ↘ Mean blood usage in the 24 hours before UFWB:
 - 16.5 units RCCs (range, 6-27), 17.1 units PCs (8-32), 14.5 units FFP (6-26) and 13.5 units cryoprecipitate (4-36).
- ↘ *After UFWB ⇒ immediate and substantial reduction in the rate and volume of blood loss in all patients.*
 - This was sustained in seven patients, who had a successful outcome; the other four patients died within 24 hours from recurrent uncontrollable haemorrhage.



Reiteration – The extinction of fresh whole blood transfusion

↘ Bigger inventory – One donor - Many patients

↘ Blood screening

- Donor recruitment
- Donor selection – a million questions
- Testing – a million tests

↘ Need for recovered plasma



Fully tested fresh unrefrigerated whole blood (FUWB) usage for major surgery

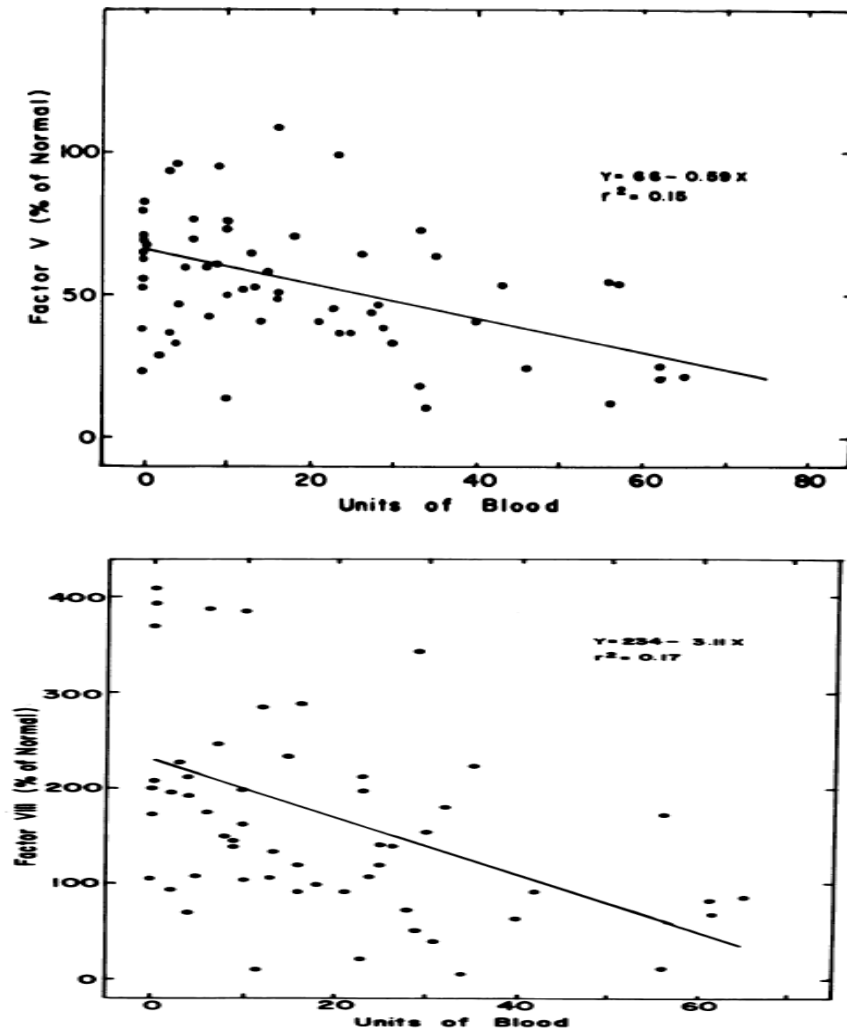
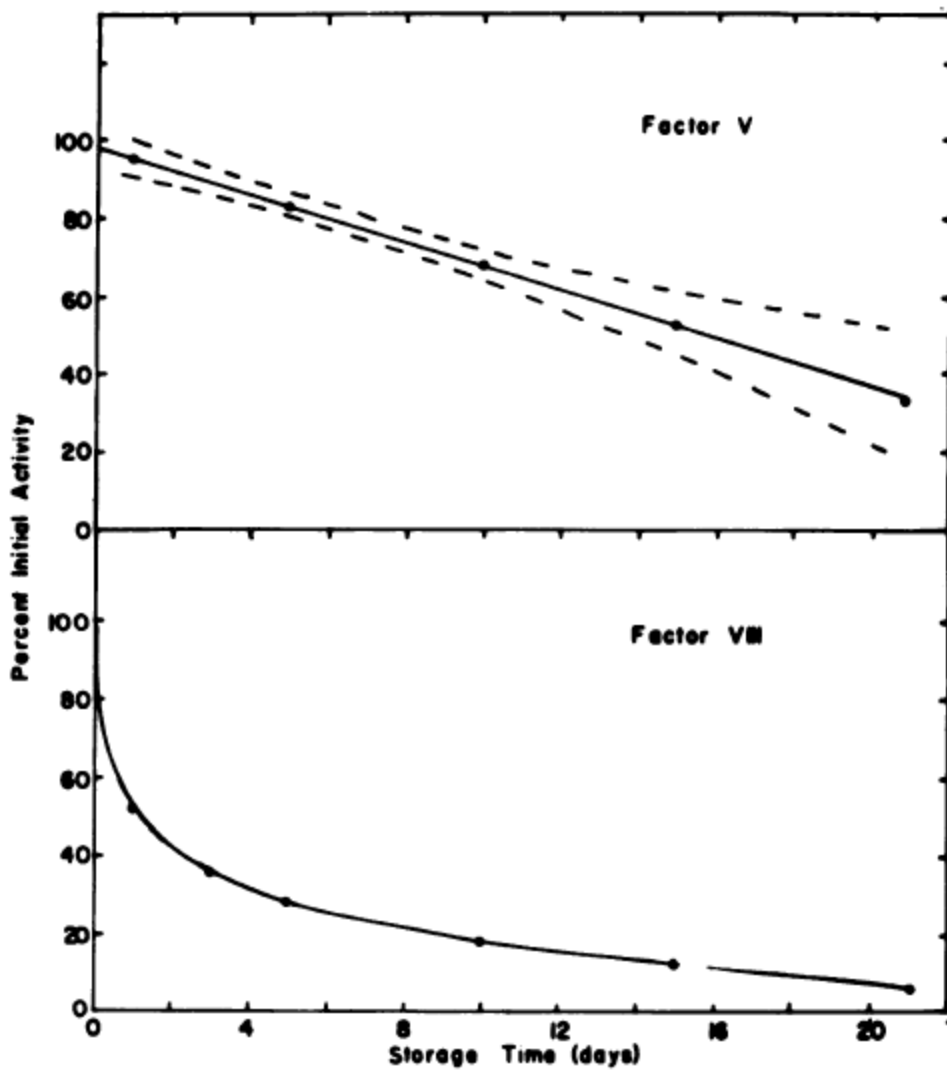
- ↘ Outcomes of FUWB and traditional blood component use
 - 20 cases of cardiac bypass surgery.
 - 23 cases of burns debridement
- ↘ Platelet function also reevaluated.
- ↘ Decreased requirement for blood components following administration of whole blood post cardiac surgery.
- ↘ Whole blood usage for burns debridement surgery eliminated the requirement for additional blood components.
- ↘ Platelet activation was markedly reduced in whole blood compared to component platelets,
 - Possible reason for increased efficacy of FUWB in these clinical settings.
- ↘ .



- ↘ ~1/4 of severely injured trauma pts at ER admission are **coagulopathic**.
- ↘ Not well understood however speculated to be:
- ↘ As a result of tissue hypo perfusion-> release of inflammatory mediators.
- ↘ **Acidosis**: anaerobic metabolism
- ↘ **Hypothermia**-> platelet dysfunction, inhibits coag pathway enzymes
- ↘ “Lethal Triad”: **coagulopathy, hypothermia and acidosis**(Bloody Vicious Cycle)-often cannot be reversed

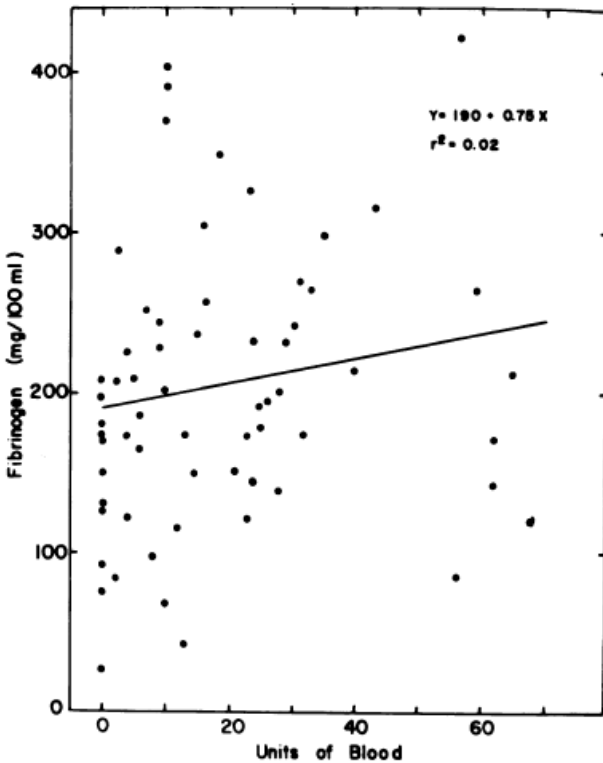


“Labile” coagulation factors in CPD WB

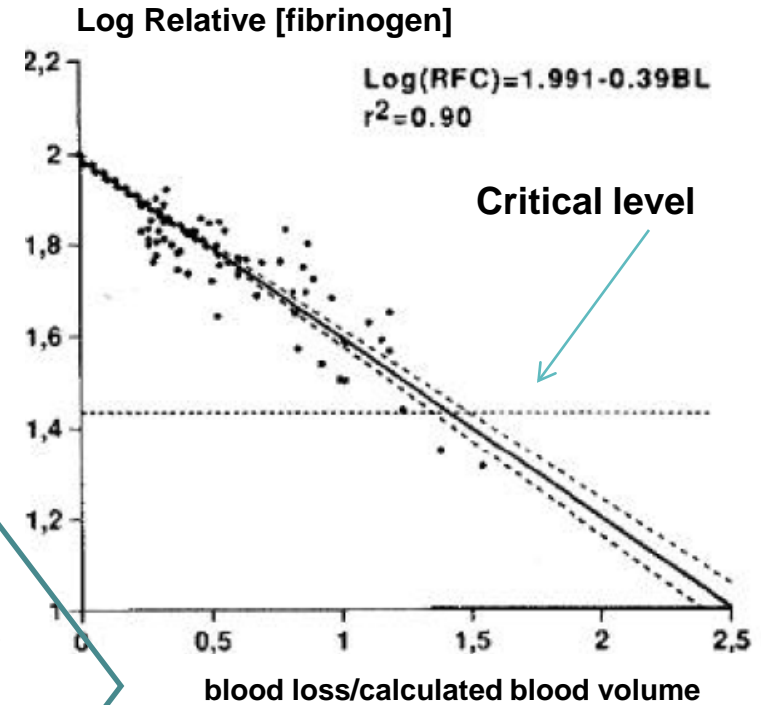




Fibrinogen after massive transfusion of red cells



Between these two studies is the introduction of **total plasma removal** with automated devices

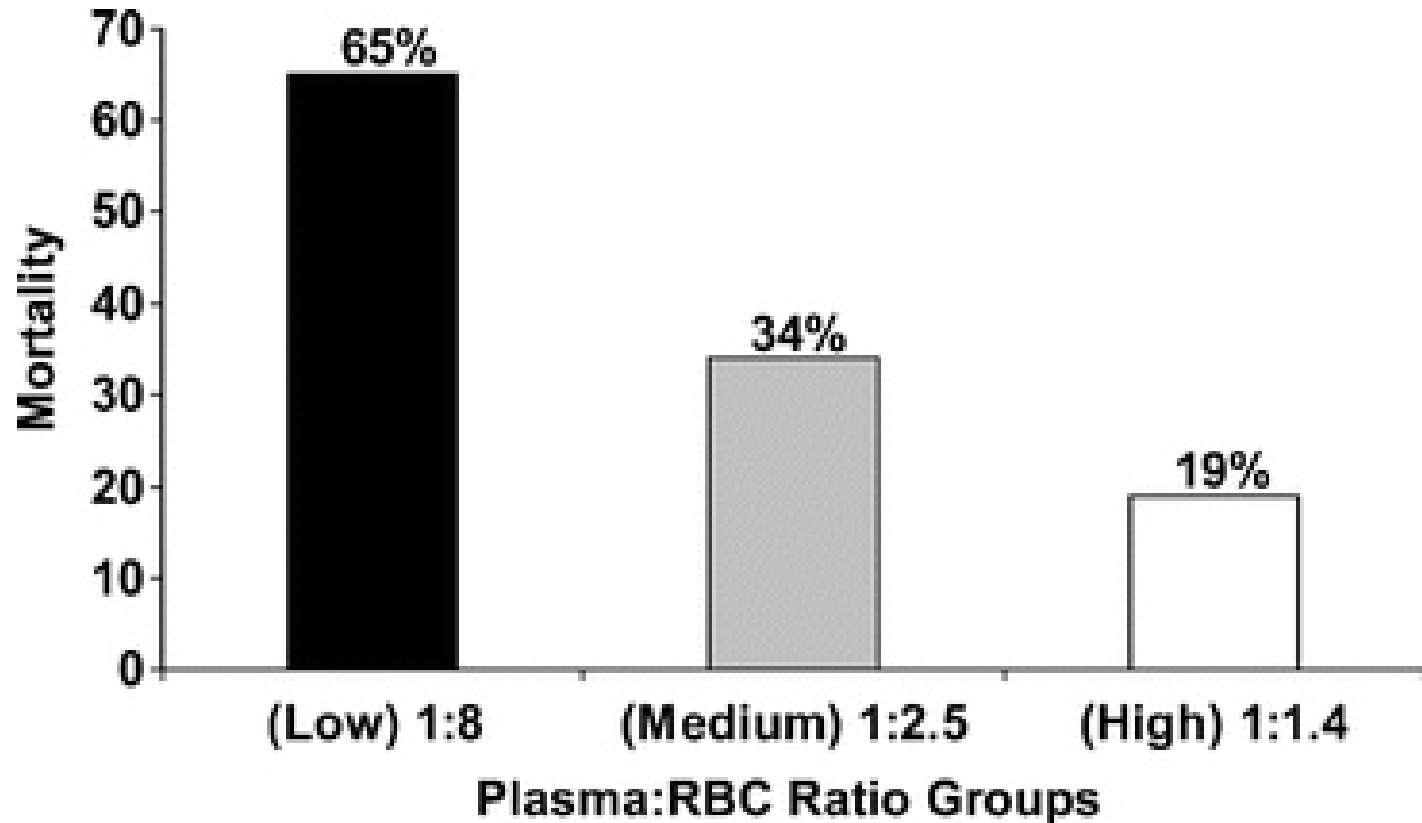


Counts et al 1979
Trauma patients

Hiipala et al 1995
Surgical blood loss

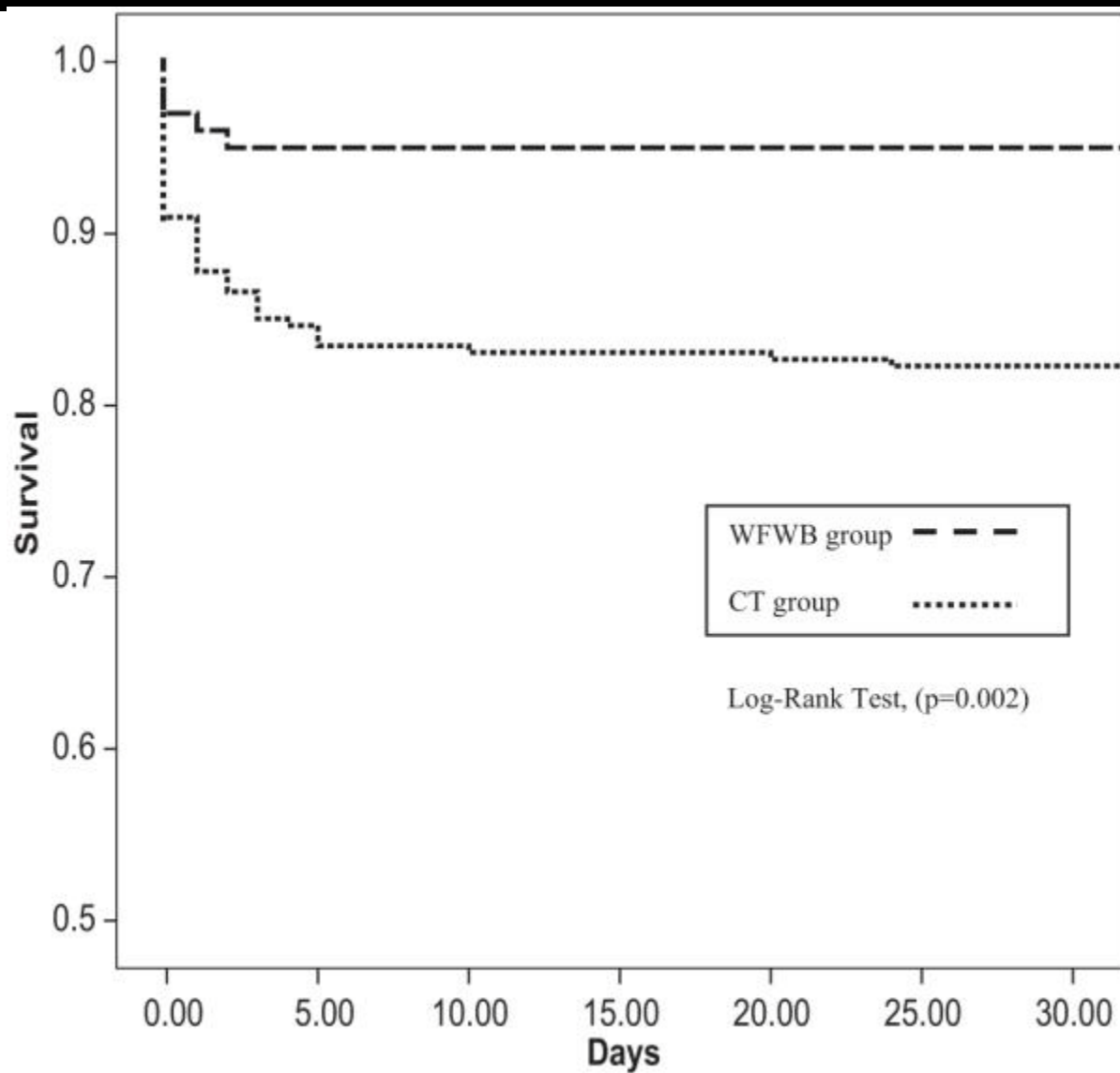


The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support



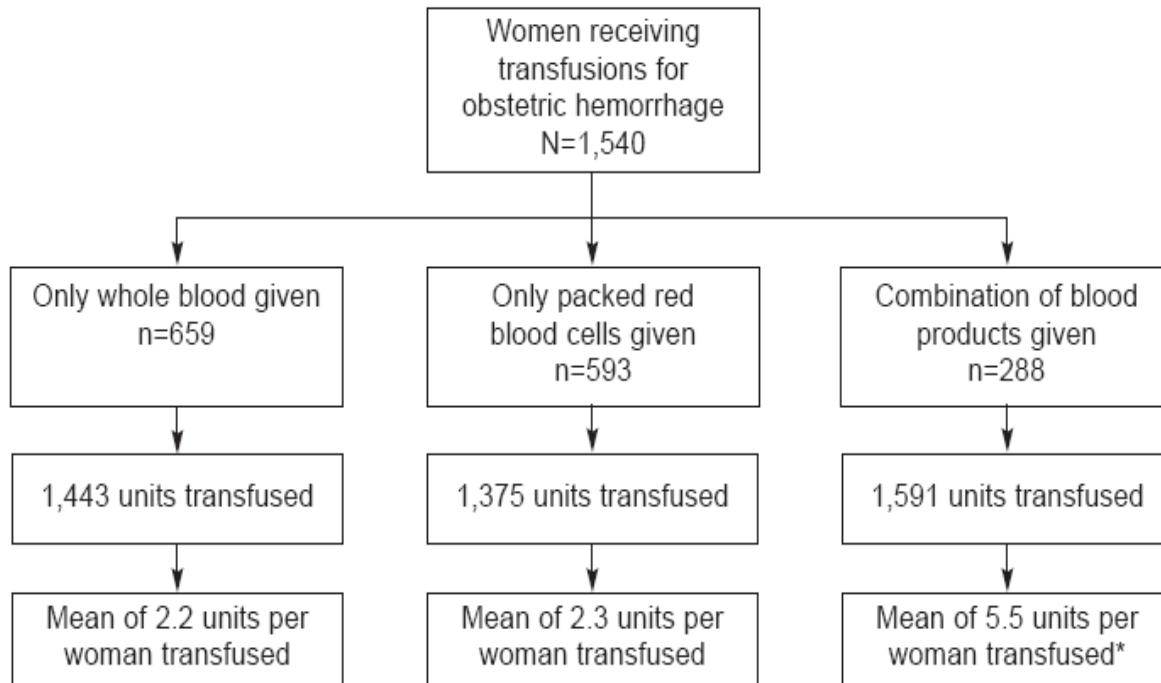


Fresh blood in battlefield trauma





Whole Blood in the Management of Hypovolemia Due to Obstetric Hemorrhage



Complication	Whole Blood Only (n=659)	PRBC Only (n=593)	Combinations of Blood Products (n=208)	P
Acute tubular necrosis	2 (0.3)	12 (2)	11 (4)	<.001*
Adult respiratory distress	3 (0.5)	2 (0.3)	6 (2)	<.01†
Pulmonary edema	47 (7)	24 (4)	39 (14)	<.001‡
Hypofibrinogenemia§	1 (0.2)	2 (0.3)	47 (16)	<.001†
Intensive care unit	4 (1)	7 (1)	23 (8)	<.05†
Maternal death	0	1	2	.03

PRBC, packed red blood cells.



Transfusion of fresh whole blood (FWB) versus platelet concentrates (PC) after cardiac operations

- To evaluate FWB vs PC after cardiac operations
- Platelet aggregation on extracellular matrix model
- 24 patients one unit FWB (12 patients) or 10 platelet units (12 patients) after cardiopulmonary bypass.
- One unit FWB restored platelet aggregation on extracellular matrix to preoperative status (3.0 +/- 1.0), eight PC needed for the same result (3.2 +/- 0.8).
- One unit FWB increased platelet count to level achieved by six PC.
- ***The effect of one unit of FWB on platelet aggregation after cardiopulmonary bypass is equal or superior, to the effect of 8 to 10 PC.***



- Much of transfusion practice lacks an evidence base
- In particular, the assumption that transfusion and resuscitation following massive blood loss requires individual stored components needs to be challenged
- Component therapy in the developed economies was an inevitable outcome of recovered plasma manufacture



More reflections

- Fresh whole blood has been rendered extinct but is therapeutically superior
- We suggest that the emerging Patient Blood Management movement represents the future of transfusion
- This can be achieved by closely integrating the transfusion service within the clinical environment



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NHS
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**PATIENT BLOOD
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BLOOD TRANSFUSION**

Programme

