Blood Management Issues and Opportunities

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Reengineering transfusion and cellular therapy processes hospitalwide: ensuring the safe utilization of blood products

Brooks, Transfusion 2005;45S

- "Blood donor centers have done a remarkable job of making the blood in the bag safer than it has ever been."
- "The actual process of transfusion, however, is an area that has languished while public attention and healthcare resources have been focused on blood centers."
- "The most significant risks associated with blood transfusion reside with the transfusion process rather than the unit of blood."
- "If blood safety is to improve, reengineering must occur at the hospital level."

The mantra of blood safety: time for a new tune?

Farrugia, Vox Sanguinis 2004;86

- " Optimal blood usage should be viewed as an essential component of the complex nexus of blood safety measures."
  - ***European Commission 'Kreuth Initiative'***
- " It is important that the blood safety focus shifts from the product considerations which underlie the traditional 'Safety Tripod' concept and focus more strongly on blood product usage as part of the transfusion medicine process."

What is Blood Management?

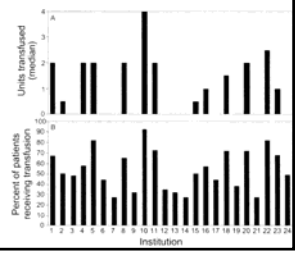
- Blood management is a comprehensive, multidisciplinary process that is designed to promote the optimal use blood products throughout the hospital.
- The goal of blood management is ensure the safe and efficient use of the many resources involved in the complex process of blood component therapy.

Is Blood Utilization Efficient?

Variation in Transfusion Practice- Cardiac Surgery

- Primary CABG patients at 24 institution
- Transfusion rates:
  - RBC 27- 92%
  - Platelets 0- 36%
  - FFP 0- 36%
  - Cryo 0- 17%

Why does this occur?



Stover et al, JCTVA 2000;14

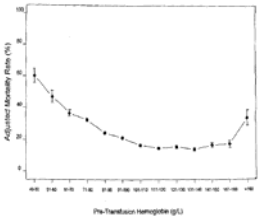
Anemia Management vs. Transfusion Management

- Although mild anemia is well tolerated in most patients, moderate to severe anemia appears to be harmful in high risk patients, particularly in those with significant cardiovascular disease
- Logically, the traditional treatment of anemia has been blood transfusions, which carry their own set of risks
- What physicians are making is an individualized trade-off decision between the risks of anemia vs. the risks and benefits of transfusion

Does transfusion practice affect mortality in critically ill patients?

Hebert- Am J Respir Crit Care Med 1997;155

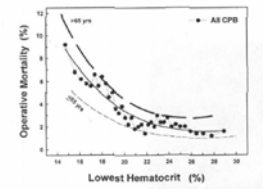
- **Prospective observational cohort of 4470 critically ill patients (~20% CV disease)**
- **In patients with cardiac disease, there was a trend toward an increased mortality when hemoglobin values were < 9.5 g/dL**
  - **increasing hemoglobin values in anemic cardiac patients was associated with improved survival**
- **"We conclude that anemia increases the risk of death in critically ill patients with cardiac disease. Blood transfusions appear to decrease this risk."**



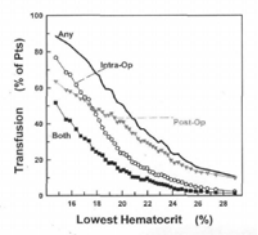
Adverse effects of low hematocrit during CPB in the adult: Should current practice be changed?

Habib-JTCVS 2003;125

- **Retrospective review of 5000 CPB cases at a single center 1994- 2000**
- **Nadir HCT <22% on CPB was independently associated with:**
  - **increased operative mortality**
  - **increased ICU and hospital LOS**
  - **increased total costs**
  - **decreased long term survival**
- **"Changes to several areas of practice in CPB patients can alter the level of hemodilution… (including) freer use of transfusions to maintain HCT at predetermined levels"**



"Confounding By Indication"



Habib, JTCVS 2003;125

Do Transfusions Improve Outcomes in Anemic Patients?

A multicenter, randomized controlled clinical trial of transfusion strategies in critical care

Hebert et al, NEJM 1999;340(6)

- Prospective, randomized multicenter Canadian study with 838 critically ill ICU patients
- Liberal transfusion strategy (Hb 10.0 g/dL) vs restrictive strategy (Hb 7.0 g/dL)
  - Restrictive transfusion group had a mean HgB of 8.5 and received 2.6 +/- 4.1 units
  - Liberal transfusion group mean HgB 10.7 and received 5.6 +/- 5.3 units

A multicenter, randomized controlled clinical trial of transfusion strategies in critical care

Hebert et al, NEJM 1999;340(6)

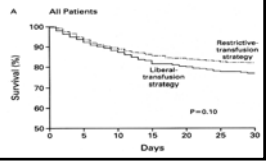
- Overall, the adjusted multi-organ dysfunction score and in-hospital mortality were significantly higher in the *liberal* transfusion group than in the restrictive transfusion group
- No sub-group of these critically ill patients demonstrated an added benefit of higher Hgb levels, and most patients in the liberal transfusion group had worse outcomes.

Hebert et al. Outcomes and Morbidity

	Restrictive (%)	Liberal (%)	P
• MI	0.7	2.9	0.02
• Pulm edema	5.3	10.7	<0.01
• Angina	1.2	2.1	0.28
• ARDS	7.7	11.4	0.06
• Infections	10.0	11.4	0.38

Hebert et al. Outcomes and Mortality at 30 days

	Restrictive (%)	Liberal (%)	p
• All patients	18.7	23.3	0.10
• APACHE ≤20	8.7	16.1	0.03
• <55yo	5.7	13.0	0.02
• Cardiac Dx	20.5	22.9	0.69
• Death (Hosp)	22.2	28.1	0.05



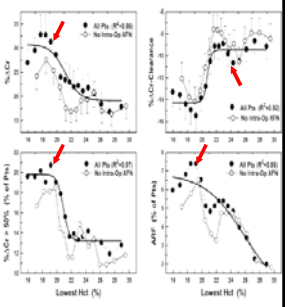
"A restrictive strategy of red cell transfusions is at least as effective as and possibly superior to a liberal strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction or unstable angina."

Hebert et al, NEJM 1999;340(6)

Role of hemodilutional anemia and transfusion during CPB in renal injury after CABG

-Habib, CritCareMed 2005:33(8)

- Retrospective review of 1760 CABG patients
- Impact of nadir HCT, CPB time and transfusion on renal dysfcn using mulitvariate analysis and propensity scores
- Nadir HCT <24% assoc with renal dysfcn and ARF
- Transfusion *increased* renal injury at HCT < 24%
  - Renal inj 14.4%-> 26.0%
  - ARF 3.4% -> 12.0%
  - LOS 6.3d -> 8.1d
  - Mortality 1.4% -> 3.8%



"This need (to test the efficacy of methods aimed at minimizing CPB hemodilution) is amplified by growing evidence, including from this study, of the adverse effects and ineffectiveness of packed RBC transfusions as a means to avoid excessive hemodilutional anemia."

-Habib, CritCareMed 2005:33(8)

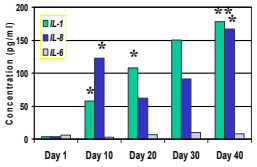
Why Don't Transfusions Necessarily Improve Outcomes in Anemic Patients?

Stored allogeneic blood is different than endogenous hemoglobin!

- Storage Defects
  - Impaired tissue oxygen delivery due to storage defects
- Transfusion Complications
  - Adverse effects and immune system changes as a consequence of allogeneic transplantation

Storage Defects and Microvascular Perfusion

- Decreased 2,3- DPG, ADP
- Poor deformability
- Build-up of cytokines, free hemoglobin, K+



Kristiansson, Acta Anesth Scand 1996; 40

Hovav, Transfusion 1999;39

Microvascular perfusion with stored RBCs
-Tsai, Transfusion 2004; 44

- **Hamster model of hemorrhagic shock and resuscitation with fresh or 28 day stored RBCs**
- **Hamster window chamber model to measure functional capillary density, microvascular blood flow and O2 distribution**
- **Stored RBC resulted in malperfused and under-oxygenated microvasculature (75% reduction) that was not detected at the systemic level**

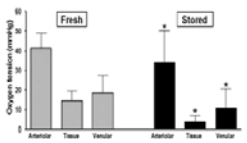
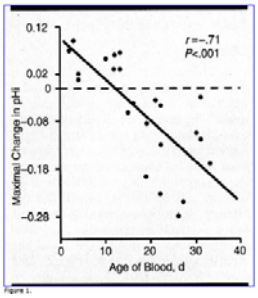


Fig. 4. Comparison of microvascular oxygen distribution in arterioles, venules, and tissue after Level 2 hemodilution and the two experimental groups: fresh (gray) and stored RBCs (black). Data are presented as means ± SD. In both experimental groups, the changes were significantly different from Level 2 and from each other (*) ($p < 0.05$).

Effect of stored blood transfusion on oxygen delivery in patients with sepsis

-Bone,Marik,Sibbald- JAMA 1993;269(23)

- 33 ICU patients with sepsis
- Transfusion of 3U PRBC for Hb <10g/dL
- ↑SVR, ↑ PVR
- DO2 increased
- VO2 unchanged
- Lactate increased
- Gastric pHi decreased for RBC> 15 days



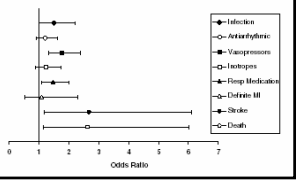
Adverse Effects of Allogeneic Blood ("Excess Baggage")

- Infectious Complications
  - Viral, bacterial contamination of platelets (1:3000), other (nvCJD, West Nile, Chagas)
- Febrile and allergic reactions
- Hemolytic transfusion reactions (clerical)
  - Leading cause of morbidity and mortality
- Other
  - TRALI, ARDS, GVH, SIRS, TACO
  - Microchimerism

Perioperative Adverse Events and Platelet Transfusions

Spiess, Transfusion 2004;44

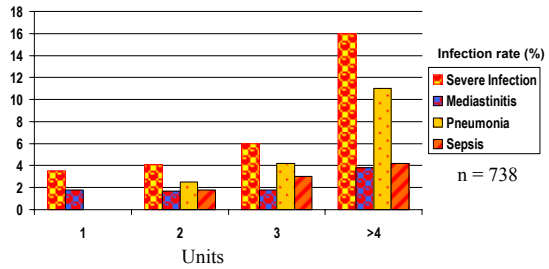
- Retrospective review of aprotinin data base- 1720 CABG patients
- Stepwise multiple regression to account for confounding factors
- Platelet transfusions independently associated with increased risk of :
  - pulmonary injury
  - infection
  - stroke
  - death



Transfusion Related Immunomodulation (TRIM)

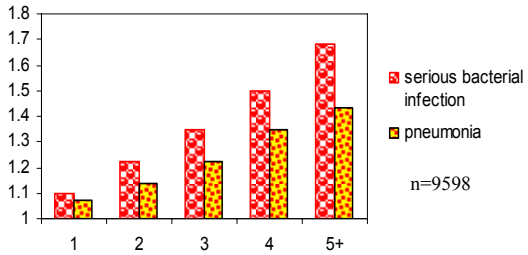
- Dose-dependent alterations in immune function
  - Upregulation of humoral immunity
  - Decreases in NK cell and macrophage activity, activation of T-suppressor cells (anergy)
  - Effect has been known and well-documented for years
- 7- 10 fold increase in postoperative infection rates leading to increased LOS, resource consumption, total hospital costs
- Increased cancer recurrence rates in transfused patients, increased 5 year mortality in CABG
- A linear dose- response curve of adverse clinical effects is well documented with large studies using multivariate analysis

Dose-Response for Transfusion and Infection in Cardiac Surgery



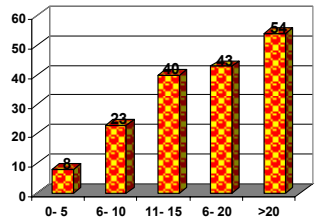
Leal-Noval et al. Chest 2001;119:1461

Dose-Response for Transfusion and Infection in Hip Replacement



Carson et al, Transfusion 1999;39:694-700

Dose Response for Post-injury Multiple Organ Failure

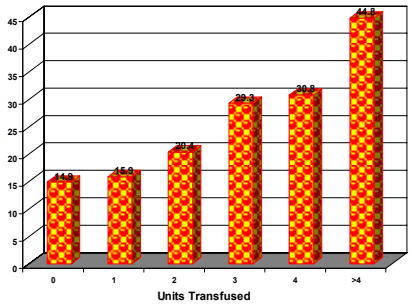


MOF(%)

OR 7.4- 13.2
n = 513

Moore et al, Arch Surg 1997;(132)

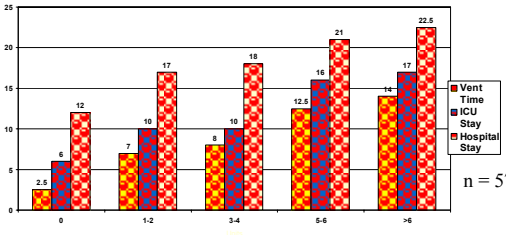
Dose Response for Mortality and Transfusion in Critical Care



OR 1.4
n= 1136

Vincent et al, JAMA 2002; 288(12)

Dose Response for Length of Stay in Critical Care



n = 576

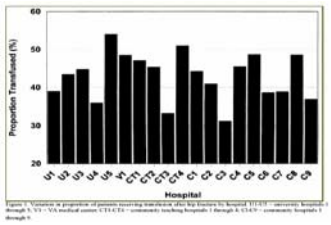
Shapiro et al, J Trauma 2003;55

Are we using this hazardous therapy wisely?

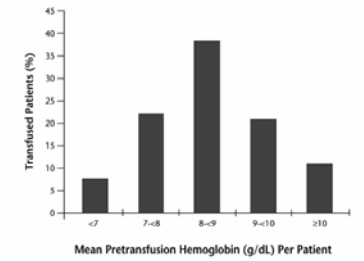
Can four hours a year of committee time adequately develop, promote and monitor appropriate blood utilization practices throughout the hospital?

Variation in Transfusion Practice- Orthopaedics

- Review of transfusion practice for hip fractures at 19 institutions
- RBC transfusion rate varied from 31.2% to 54.0%



Poses et al, Am J Medicine 1998;105(3)



Corwin- Crit Care Med 2004;32(1)

Emily Cooley Lecture 2002: transfusion safety in the hospital

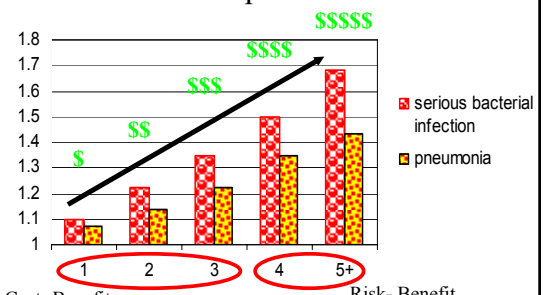
Dzik, Transfusion 2003; 43

"Blood use decisions are probably more akin to those applied to common antibiotics than to those applied to specialized medicines like chemotherapy agents or seizure-control medications."

"… it is perhaps not surprising that many transfusion decisions are ill informed, outdated, or, simply incorrect."

Integrated Blood Management Strategies

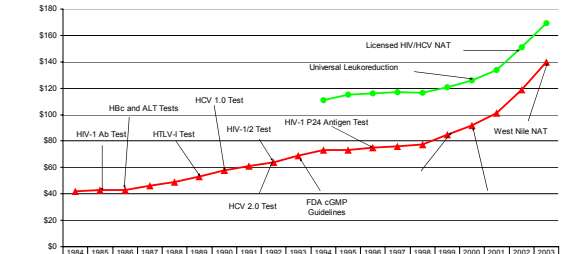
Blood Management and the Dose- Response Curve



Cost- Benefit
Transfusion Alternatives

Risk- Benefit
Transfusion Guidelines

America's Blood Centers
Safety Measures and Average Red Blood Cell Service Fees
1984 - 2003



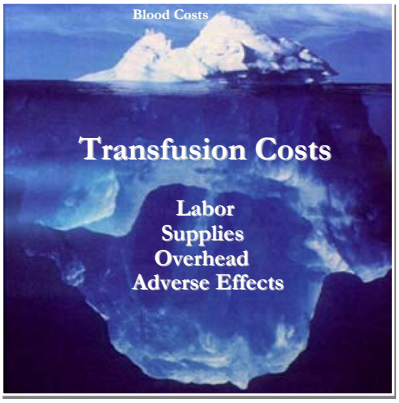
	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
RBCs	$42	43	43	46	49	53	58	61	64	69	73	73	75	76	77	85	92	101	119	140
RBCs, LR											111	115	116	117	116.7	121	126	134	151	169.5

Author, Year	Facilities	Study Technique	Acquisition Cost %	Patient Sample	Cost/ Unit (2004 $)*
Forbes, 1991 (11)	19 Teaching Hospitals with Level I or II Trauma	Survey of blood related charges	37%	Mixed Population	$405
Mohandas, 1995 (12)	Outpatient Cancer Center	Review of blood related charges for 219 patients	26%	Solid Tumors	$660
				Hematologic Tumors	$711
Cantor, 1998 (13)	Outpatient Cancer Center	Survey of blood related cost activities	15%	Solid Tumors	$512
				Hematologic Tumors	$525
Crémieux, 2000 (14)	Outpatient Cancer Center	Cost activities recorded for 517 patients	19%	Solid Tumors	$678
				Hematologic Tumors	$718
				Complex Patients	$753

*2004 Medical Services CPI, base acquisition cost $178

Hospital Resource Variable Costs

Hospital Resource	Variable Cost (2004$)
Operating room variable time	$1730- $2880/ hour
Postoperative hospital day	$1200/ day
ICU day	$3400/ day
ICU day- ventilated patient	$4400/ day
Ventilator-associated pneumonia	$15,500
Serious postoperative infection- orthopedic surgery patient	17,500- $18,800
Postoperative deep sternal infection- cardiac surgery patient	$25,600
Post procedure bleeding- Percutaneous Coronary Intervention	$13,700
Reoperation for bleeding- cardiac surgery patient	$26,900- $28,600
*Red blood cell transfusion- variable cost per unit	$1700- $2500/ unit



Applied Blood Management

- Management goals- *Woody Allen's Law*
  - Avoid/ minimize anemia
  - Avoid/ minimize transfusions
  - Efficient utilization of resources
    - ***Stewardship***
- Organizational principles
  - *Attention to detail*
  - Utilization of evidence-based guidelines and clinical best practices
  - Multidisciplinary teams
  - Proactive approach

Maintain RCM!

ST. VINCENT HOSPITALS AND HEALTH SERVICES

- **USE THIS FORM FOR ALL BLOOD COMPONENT TRANSFUSION ORDERS.**
- **Check off at least one indication for each type of blood component order.**
- **The minimal effective dose of all blood components should be used. SINGLE UNIT transfusions of red cells are often effective.**
- **Compliance with transfusion guidelines will be monitored by the transfusion committee.**
- **The blood bank phone # is 803-0421 (86th Street).**

❑ **Blood Transfusion Consent signed**

TRANSFUSION ORDER (indicate type and amount): _____

Request for special red cell products: _____ Irradiated _____ Washed _____ CMV negative

Patient location (SE, ICU, OR, PACU, etc) _____ Utilization review ❑

INDICATION (check all that apply):

Packed Red Cells **Most recent hemoglobin _____ g/dL or hematocrit _____%**

One unit of packed red cells in an adult, 8 mL/kg pediatric dose, will increase hematocrit by approximately 3% and hemoglobin by 1 g/dL.

❑ Hematocrit ≤ 21% or hemoglobin ≤ 7 g/dL

❑ Hematocrit ≤ 24% or hemoglobin ≤ 8g/dL in a patient with coronary artery disease and unstable angina/ myocardial infarction/ cardiogenic shock

❑ Rapid blood loss with > 30- 40% of estimated blood volume (>1500- 2000 mL) not responding to appropriate volume resuscitation, or with ongoing blood loss.

❑ The patient has been determined to be normovolemic and there is evidence to support the need for increased oxygen carrying capacity as witnessed by (indicate):

NOTE- *these indications will be tracked and may be peer reviewed.*

❑ Tachycardia, hypotension not corrected by adequate volume replacement alone

❑ PVO_2 < 25 torr, extraction ratio > 50%, VO_2 < 50% of baseline- *specify* _____

❑ Other- *specify*. _____

❑ Autologous predonate red cells: hematocrit ≤ 30% or hemoglobin ≤ 10 g/dL

Platelets **Most recent platelet count _____/ ec^3**

A single dose of platelets (adult: one apheresis or 6 concentrates; pediatric dose 1 unit/10 kg) will increase the platelet count by 25,000- 33,000/ ec^3

❑ Platelet count ≤ 10,000/ ec^3 prophylactically in a patient with failure of platelet production

❑ Platelet count ≤ 20,000/ ec^3 and signs of hemorrhagic diasthesis (petechiae, mucosal bleeding)

❑ Platelet count ≤ 50,000/ ec^3 in a patient with (indicate):

❑ Active hemorrhage

❑ Invasive procedure (recent, in-progress, planned)

❑ Platelet dysfunction as documented by- *specify* _____

Fresh Frozen Plasma **Most recent coag. studies: PT ___ INR ___ PTT ___ Fibrinogen _____**

A dose of 10- 15 mL/ kg is usually adequate to correct a coagulopathy. **Patient weight _____ kg**

❑ Abnormal coagulation studies and significant hemorrhage

❑ Prophylactic use for PT/ APTT > 1.5 times the mean of the reference range

❑ Emergent reversal of coumadin

Cryoprecipitate **Most recent coag. studies: PT ___ INR ___ PTT ___ Fibrinogen _____**

One unit per 10 kg is usually adequate when cryoprecipitate is required. **Patient weight _____ kg**

❑ Fibrinogen ≤ 100 mg/ dL

❑ Fibrinogen ≤ 150 mg/dL with active hemorrhage

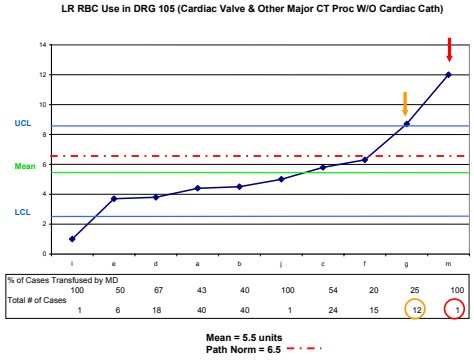
_____/_____ _____ _____ _____

Physician's signature / printed name Pager # Date Time

Trust…
but verify.
-Ronald Reagan

Speak softly…
and carry a big stick.
-Theodore Roosevelt

Peer Blood Utilization Profiling



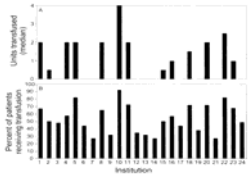
Multidisciplinary Team- Cardiac Surgery

- Cardiac surgeons
- Anesthesiologists
- Perfusion
- Nurses- Preop/OR/CR/ CVPV Ward
- Physician's Assistants
- Pharmacists
- Laboratory/ Blood Bank
- Administrators
  - Supervisory
  - Purchasing
  - Quality
  - Financial

Blood Management Opportunities- CABG

- **Preoperative**
  - Risk stratification and intervention
  - Anemia management
  - Iatrogenic blood loss (cath lab)
  - Cessation of drugs that increase bleeding
- **Intraoperative**
  - Avoidance of hemodilution
  - Heparin management protocols
  - Pump prime volumes
  - Pump circuit coatings
  - Perfusion/ autotransfusion techniques
- **Intraoperative (cont)**
  - Surgical techniques
  - Anesthetic techniques
  - Pharmacologic therapies
  - Topical hemostatic agents
  - Point of care
    - Hemoglobin
    - Coagulation status
  - Coagulation management protocols
  - Rewarming protocols
- **Postoperative**
  - Point of care
  - Postoperative autotransfusion
  - Evidence-based guidelines

Variation in transfusion rates among institutions is the end result of the actions or inactions of organizations to manage the series of events that ultimately lead to blood transfusions.



Further, this series of events is largely predictable and to a great extent is controllable.

Final Thoughts:

Transfusion Committee

vs.

Blood Utilization Committee

Which do you have?

Blood Management Issues and Opportunities- Summary

- Blood products are increasingly scarce and increasingly expensive
- Blood component therapy is inherently hazardous
- Blood utilization is less than optimal
- Better management of blood resources presents a tremendous opportunity for patients, physicians, hospitals and communities

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www.BloodManagement.com

Blood Management References

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