SECTION II – AN APPROACH TO BLOOD UTILIZATION

BLOOD COMPONENT THERAPY

A recent subcommittee survey of the American Society of Anesthesiologist found that anesthesiologists administer greater than half of all blood products given to patients. It is therefore important to develop expertise in the management of blood component therapy.

Blood Components

A major advance in the field of blood banking is the fractionation of whole blood into individual components that are subsequently used to treat specific deficiencies. Figure I demonstrates the method for blood fractionation and the commonly available therapeutic components.

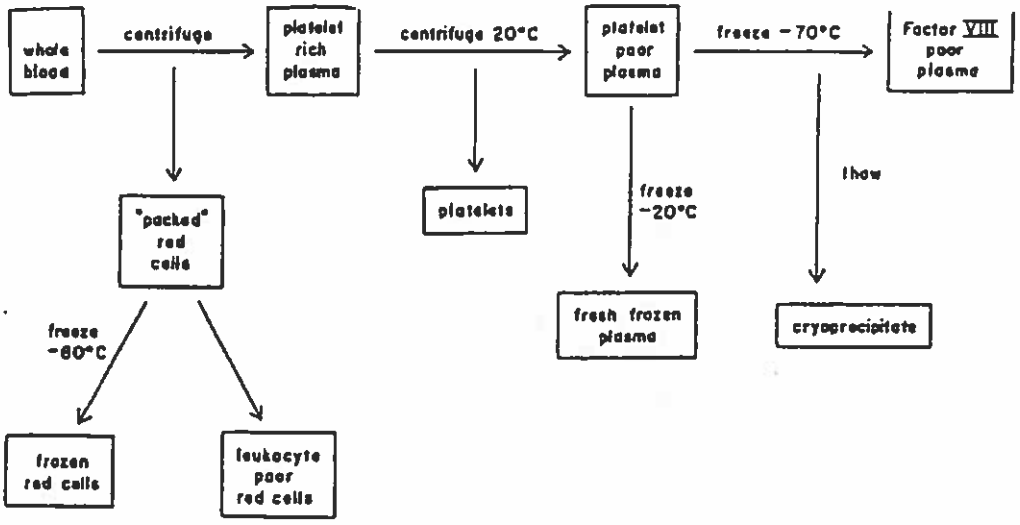


Fig I

Fig I

Typing, Crossmatch and Screen

Red blood cells ("packed cells") are the most common component administered. There are several standard blood bank orders depending on the urgency of a situation or most cost effective route in an elective case. Rational decision making regarding packed red cells requests requires an understanding of how red cells are prepared for transfusion. The following is a synopsis of these procedures.

Type

Typing refers to the determination of a patient's ABO and Rh status. This is done by testing the red cells for A and B antigens while the serum is tested for A and B antibodies. Additional Rh antigen testing completes red blood cell typing. A blood type compatibility and recipient chart is shown in Fig. 2

ABO COMPATIBILITY TESTING				
	Red Cells Tested With		Serum Tested With	
Blood Group	Anti-A	Anti-B	A Cells	B Cells
A	+	-	-	+
B	-	+	+	-
AB	+		-	-
O	-	-	+	+

Fig. 2

Crossmatch

The crossmatch is performed when DONOR red blood cells are mixed with RECIPIENT serum. This is an in vitro trial transfusion that is carried out in three distinct stages. A complete crossmatch requires 45-60 min regardless of circumstances. The following diagram shows the phases of crossmatching and the antigens detected in each.

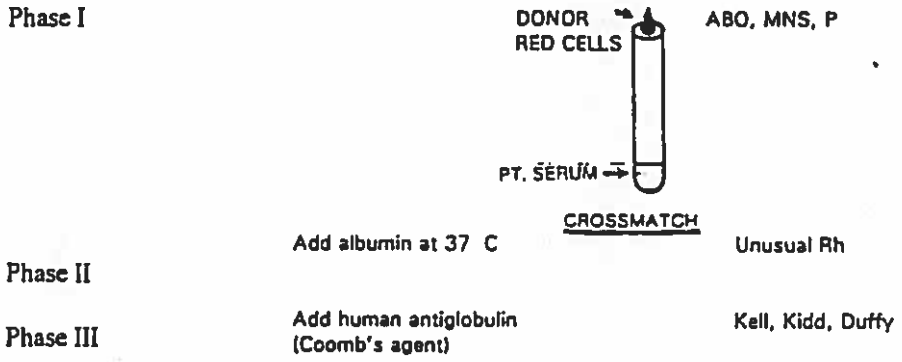


Fig 3

Screen

This refers to the detection of ANTIBODIES in the serum of donor or patient blood. The test is conducted in three phases similar to crossmatch studies. All donated blood is screened shortly after collection for unusual antibodies by combining serum with commercially obtained red blood cells that contain antigens known to cause hemolytic reactions.

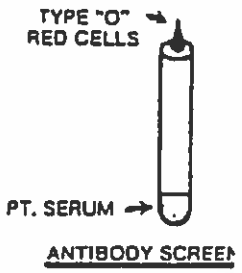


Fig. 4

Emergency Protocols

In an emergent situation blood may have to be administered without a full crossmatch. There are set orders that the blood bank can respond to under these circumstances. The following are the most common emergency orders.

Type Specific Partial Crossmatch

Typed RECIPIENT serum is combined with DONOR red blood cells (from previously screened blood) in saline at room temperature and centrifuged for 5 minutes. This is called an immediate spin crossmatch. Macroscopic agglutination is checked. This requires 5-10 minutes.

Type Specific Uncrossmatched Blood

All blood that is collected from donors undergoes serum screening to identify potentially dangerous antibodies. In an emergency situation where blood is required immediately, screened type specific packed red cells are available. This is considered relatively safe since in a patient without prior transfusion or pregnancy, an unexpected antibody is found in only 1/1000 crossmatches.

Type O Rh-Negative/Rh-Positive Uncrossmatched Blood

Generally type 0 red blood cells lack the A and B antigens and cannot be hemolyzed by antibodies in the recipient's blood (Fig 5). However, some 0 donors contain high titers of hemolytic anti A and B ANTIBODIES. Emergency units of type 0 blood are available when there is insufficient time for patient typing. There are several safety features to protect patients. First, only type 0 blood with low serum antibody titers are chosen as emergency units. Second, this is only available as packed red cells so that exposure to donor serum can be minimized. This is most important when transfusing females of childbearing age. Finally, Rh negative blood can be chosen to prevent alloimmunization. In the operating room at University Hospital 10 units of low titre type 0 Rh negative/positive blood is kept in Central Laboratory for emergency use.

DONOR BLOOD GROUPS WHOSE BLOOD PATIENT CAN RECEIVE	
DONOR	RECIPIENT
0	0, A, B, AB
A	A, AB
B	B, AB
AB	AB

Fig. 5

Indications for Blood Administration

Blood is mainly given to increase the oxygen carrying capacity. The hematocrit at which blood should be administered is not simply answered. A young healthy patient with normal cardiorespiratory function may easily compensate for anemia while an elderly patient with vital organ impairment may be unable to tolerate an identical hematocrit.

General guidelines are, chronic anemia is tolerated much better than acute blood loss. Decreased physiological reserve as found in disease of the cardiorespiratory, renal or hepatic systems may influence the decision when to transfuse. The anticipation of ongoing losses may also influence transfusion decisions. A standard "safe" hematocrit has not been established under these conditions.

The FDA proposed that adequate oxygen carrying capacity can be met by a hemoglobin of 7g/dl or less if perfusion is maintained by adequate intravascular volume. Certain medical conditions may justify, giving blood at a higher hematoglobin. At University Hospital there is a Blood Utilization Committee that reviews blood component ordering and administration for quality assurance.

The figure below gives a means of estimating red cell replacement based on physiological findings in emergent conditions. In elective cases, an equation is given that will help determine the timing of transfusion based on known patient variables. Always indicate the reason for transfusion in some manner on the anesthesia chart for example by a recent hematocrit, exceeding the calculated allowable blood loss or hemodynamic variable.

Emergency

ESTIMATED FLUID AND BLOOD REQUIREMENTS 1N A 70KG MALE				
	INITIAL PRESENTATIONS			
	CLASS I	CLASS II	CLASS III	CLASS IV
Blood loss (ml)	< 750	750-1500	1500-2000	z 2000
Blood loss (% BV)	<15%	15-30%	30-40%	z 40%
Pulse rate	< 100	> 100	> 120	z 140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or Increased	Decreased	Decreased	Decreased
Capillary blanch test	Normal	Positive	Positive	Positive
Respiratory rate	14-20	20-30	30-40	> 35
Urine output (mL/h)	30 or more	20-30	5-15	Negligible
CNS-mental status	Slightly anxious	Mildly anxious	Anxious and confused	Confused and lethargic
Fluid Replacement (3:1 rule)	Crystalloid	Crystalloid	Crystalloid + blood	Crystalloid + blood

Elective Allowable Loss = EBV x $(Hb_{initial} - Hb_{target})/Hb_{initial}$

Fig. 6

Storage

Belle Bonfils Blood Center supplies blood units for transfusion to University Hospital. Citrate, phosphate and dextrose (CPD) are added to donated blood for storage at 4C. Citrate acts as an anticoagulant while phosphate buffers changes in pH. Dextrose provides a source of energy for red blood cell metabolism. To further prolong shelf life, adenine saline solution, another energy substrate is added to the CPD solution. This extends the shelf life to 42 days.

Short Dated Blood

A unit of blood marked as short dated means that its shelf life will expire within 14 days. This is important information as changes take place in the biochemical composition of blood solutions with time. These changes are illustrated below.

PROPERTIES OF WHOLE BLOOD AND PACKED CELL CONCENTRATES STORED IN CPDA-1			
Parameter	DAYS OF STORAGE		
	0	35 (Whole Blood)	35 (Packed Cells)
pH	7.55	6.98	6.71
Plasma hemoglobin (mg/dl)	8.2	46.1	246.0
Plasma potassium (mEq/L)	4.2	27.3	76.0
Plasma sodium (mEq/L)	169	155	122
Blood dextrose (mg/dl)	440	229	84
2,3-Diphosphoglycerate (μ M/ml)	13.2	< 1	< 1
Percent survival	-	79	71

[a]Percent recovery of O_R-tagged red blood cells at 24 hours.
Abbreviation: CPDA-1, citrate phosphate dextrose adenine-1.

Fig. 7

Autologous Blood

There are three methods of collecting autologous blood units: preoperative donation and storage, acute preoperative phlebotomy and hemodilution and Perioperative blood salvage from the surgical site. Despite the relative safety of autologous transfusion, it is currently not recommended to transfuse these units unless there is a specific indication since the most common cause of lethal hemolytic transfusion reaction is clerical error, which may occur in this setting.

Frozen Blood

Packed red blood cells can be frozen which allows storage for up to 10 years. This is commonly done for rare blood types and occasionally with multiple collections of autologous units. It is an expensive process and therefore not often used.

Dilutants

A compatibility list is given in figure 8. Some dilutants can cause hemolysis due to a reduced tonicity of the solution. Other solutions such as Lactated Ringers may promote clotting due to the presence of calcium. The latter occurs as micro debris.

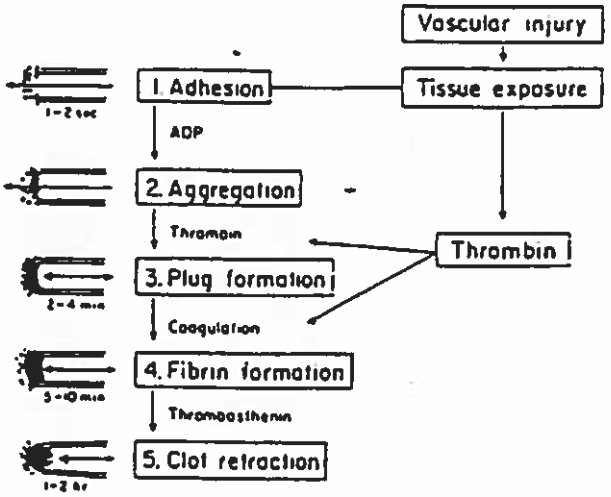
COMPATIBILITY OF BLOOD WITH INTRAVENOUS SOLUTIONS		
Blood to Intravenous Solution 1 : 1 Ratio	Hemolysis at 30 Min	
	Room Temperature	37°C
5% dextrose in water	1+	4+
Plasmanate	1+	3 +
5% dextrose in 0.2% saline	0	3+
5% dextrose in 0.4% saline	0	0
5% dextrose in 0.9% saline	0	0
0.9% saline	0	0
Normosol-R, pH, 4	0	0
Lactated Ringer's Solution	0 (clotted)	0 (clotted)

Fig.8

COAGULATION FACTORS

Coagulation components may be required peri or intraoperatively for treatment of patients with bleeding disorders. It is important to have guidelines for effective treatment. Figure 9 shows the major stages involved in hemostasis. It is important to remember that coagulation is a multistage process that is influenced through injury and treatment at many points.

Fig 9



Coagulation Tests

Bleeding disorders can vary from subtle defects that increase the risk of blood loss to major deficits that are immediately life threatening. Diagnosis is often based on the clinical and/or laboratory observations and are complimentary for diagnosis. Figure 10 shows the routine tests of coagulation and their indications. An isolated laboratory number should never be treated without consideration of the clinical scenario.

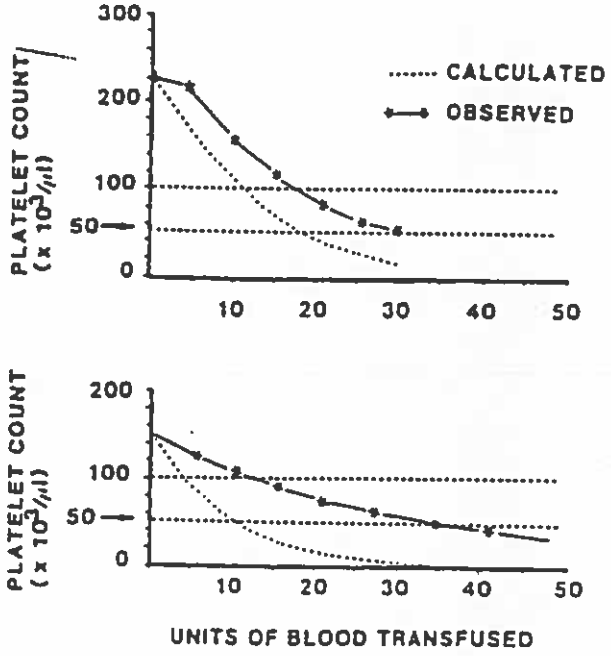
PRIMARY (SCREENING) TESTS OF HEMOSTASIS USED TO CONFIRM THE PRESENCE OF A DISORDER HEMOSTASIS	
Activated coagulation time (ACT)	Can be done in OR: observe for clot retraction and lysis
Fibrinogen level	Depressed in DIC
Prothrombin time (PT)	Prolonged in liver disease, vitamin K deficiency, coumarin anticoagulation, DIC
Partial thromboplastin time (aPTT)	Prolonged in Factors V, VIII deficiency (massive transfusion), the hemophilias, or The presence of heparin
Platelet count	Decreased in thrombocytopenia and DIC

Fig 10

Platelets

Platelets are involved in all phases of the coagulation cascade. They form the initial hemostatic plug and activate the coagulation cascade. Clinical coagulopathy during massive blood transfusion is often initially due to dilutional thrombocytopenia. However, the spleen and bone marrow provide a reserve supply. Therefore, the platelet count is never as low as predicted on a dilutional basis alone. Figure 11 illustrates this point.

Fig. 11



In the past platelets transfusions were only available from pooled or multiple donors. This increases the risk of infectivity and autoimmunization. Currently pheresis units are available which are derived from one donor. At University Hospital, PLP are platelets derived from a single donor are equivalent to 3-4 pooled units. PLA is single donor platelets equivalent to approximately 6-8 pooled units.

Pooled units are only used in times of shortage. Once fractionated, platelets are stored at room temperature and should not be refrigerated. They have a shelf life of 5 days and must be agitated. Assuming normal platelet function, the correlation between platelet count and bleeding is shown in figure 12.

CORRELATION BETWEEN PLATELET COUNT AND INCIDENCE OF BLEEDING		
PLATELET COUNT (cells/mm^3)	TOTAL NUMBER OF PATIENTS	NUMBER OF PATIENTS WITH BLEEDING
More than 100,000	21	0
75,000-100,000	14	3
50,000-75,000	11	7
Less than 50,000	5	5

Fig. 12

Fresh Frozen Plasma

These units are obtained from centrifuged whole blood from which the platelets have been removed. Each unit is derived from one donor and can be held frozen up to a one year period. Currently **40 minutes** are required for thawing and the units cannot be refrozen. Plasma units are only usable for 24 hours following thawing. Fresh frozen plasma contains soluble coagulation factors required for hemostasis. It should never be used for volume expansion in a patient with normal coagulation.

Cryoprecipitate

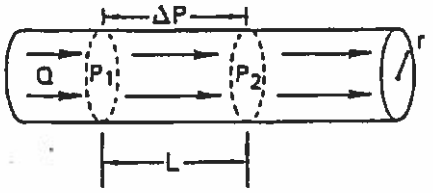
This is a concentrated source of fibrinogen, Von Willebrand's factor, fibronectin and factor VIII and is derived from platelet poor plasma. Once thawed, the shelf life is only 4 hours. Each unit is derived from a single donor and is subsequently pooled. Although cryoprecipitate is usually administered as ABO compatible, this is not critical since the concentration of antibodies is extremely low. Prevention of alloimmunization due to Rh is more important as cryoprecipitate can contain red blood cell fragments. In addition to the above mentioned products, there are factor concentrates available for treatment of congenital hemophilia. There is now a recombinant DNA factor VIII concentrate available for Hemophilia A. Figure 13 shows the minimal factor levels needed for hemostasis and the appropriate therapeutic agent.

BLOOD PRODUCTS FOR HEMOSTATIC DISORDERS			
HEMOSTATIC FACTOR	MINIMUM LEVEL NEEDED FOR SURGICAL HEMOSTATIS (% Normal)	IN VIVO HALF LIFE	THERAPEUTIC AGENT
I	50-100	3-6 days	Cryoprecipitate
II	20-40	3-4 days	Plasma
V	5-20	12 hours	Fresh Plasma Fresh Frozen Plasma
VII	10-20	4-6 hours	Plasma
VIII	30	10-18 hours	Cryoprecipitate Antihemophilic factor
von Willebrand's	30		Desmopressin Plasma
IX	20-25	18-24 hours	Plasma Prothrombin complex concentrate
X	10-20	2-4 days	Plasma
XI	20-30	2-3 days	Plasma
XII	0		Plasma
XIII	1-3	5+ days	Plasma .
Platelets	50,000-100,000	variable	Platelet concentrates

Fig. 13

DELIVERY SYSTEMS

Rapid blood component delivery may be critical in emergency situations. There are a number of physical factors, which govern flow velocity. Poiseuille's law is shown below (Fig 14) and illustrates the variables that determine the rate of flow.



POISEUILLE'S LAW

$$Q = \frac{\Delta P \; r^4 \; \pi}{\eta L \; 8}$$

. Poiseuille's law. In an artificial system, flow through a cylindrical tube or any segment of a tube is directly proportional to ΔP, the driving pressure along the tube, and the fourth power of the radius, r. Flow is inversely proportional to L, the length of the segment and to η, the viscosity of the liquid. The proportionality constant is $\pi/8$.

Fig 14

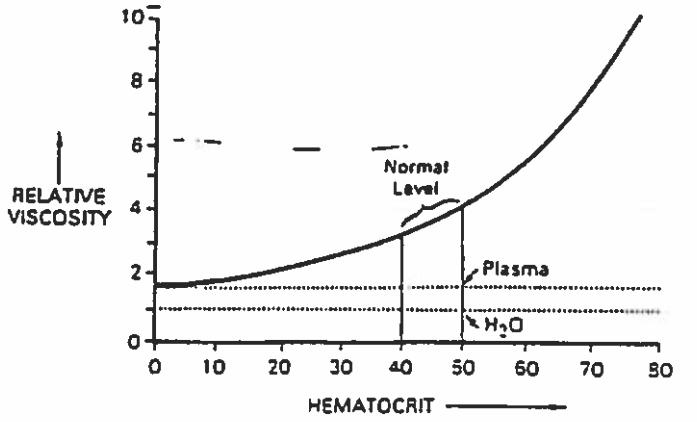
Radius or Size

As can be seen from this formula, intravenous catheter and tubing size are the most important determinants of flow velocity in a delivery system. Due to this it is important to select sizes that do not limit the rate of delivery. The effect of sizing on flow rate is illustrated in Figure 15. It is also important to remember that length is negatively related to flow. It becomes apparent that short and wide radius delivery systems promote rapid flow.

FLOW RESISTANCE OF SELECTED CATHETERS			
DESCRIPTION	ED* (mm)	R_L,+ (mmHg.s/ml)	R_r.+ (mmHg.s/ml)
10 G,7.6cm	3.4	0.2	0.2
12G,7.6cm	2.8	0.3	0.3
14 G, 5.1 cm	2.1	2.0	0.9
14G,5.7cm	2.1	4.9	1.9
16 G, 5.1 cm	1.7	1 1.2	8.7
18 G, 5.1 cm	1.2	28.0	25.0
20 G, 3.2 cm	0.9	57.5	57.4
22 G, 2.5 cm	0.7	76.8	162.1
*Stubb's needle gauge, CRC Handbook of Chemistry and Physics. +Data from Philip and Philip.ED=approximate external diameter, R_L = resistance to laminar flow.R_r = resistance to turbulent flow.			

Viscosity

Blood viscosity is related to hematocrit (Fig. 16). As observed from Poiseuille's law, viscosity affects rate of delivery. Since the hematocrit of packed red blood cells is approximately 70%, dilution may be required in certain systems to ensure rapid delivery.

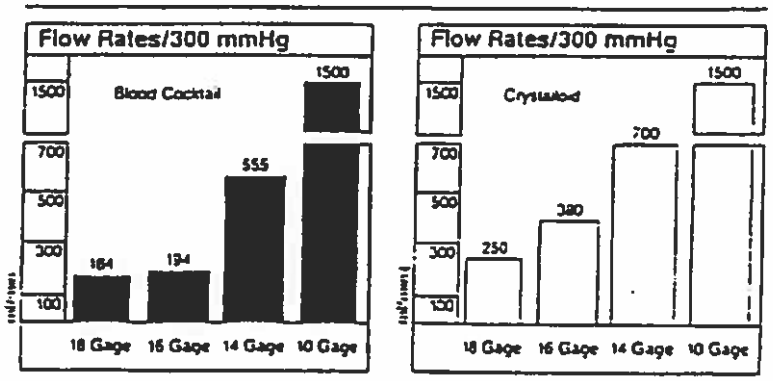


Effect of hematocrit on relative viscosity of blood. Note that as hematocrit increases, the relative viscosity increases disproportionately.

Fig 16

Pressure Gradient

Finally it is noted that the pressure gradient also determines flow velocity. A gradient is established in a delivery system by pressurizing the delivery system at the source. Pneumatic bags are provided in the operating room for this purpose. In addition the Level 1 warmers incorporate pneumatic devices into their system. In contrast, the Rapid Infusion System (RIS) found in OR 2 uses a roller device to push fluid at a constant pressure along its tubing. The combined effects of catheter size, viscosity and pressure gradient are shown in Figure 17.



This blood cocktail produces a 28% hematocrit product. It may be desirable to conserve a higher hematocrit product during the period of uncontrolled blood loss.

Fig 17

Warming Devices

There are a wide variety of products on the market available for warming intravenous solutions. Each system functions within an optimal range for flow rates and this should be checked. If flow rates are too fast, there is insufficient time for equilibration between the heating device and fluid. If the flow rate is too slow or there is copious tubing beyond the heating box then the fluid will cool before it reaches the patient.

At University Hospital, we commonly use the Hotline and Level 1 warmers. The Hotline is unique in that it heats tubing outside the warmer box by a water heated jacket. It is not advantageous to add multiple extensions to the system since this will increase resistance to flow and promote cooling. The Level I and RIS are single channel counter current exchangers and capable of heating solutions during high flow. The heating capacity is shown in Figure 18 while cost is illustrated in Figure 19.

APPARENT THERMAL CLEARANCE OF WARMING DEVICES			
TYPE	V_{rc}(ml/min)		Q CALCULATED (ml/min)
	Saline*	PRBC*	
Single-coil immersion (Hemokinetitherm)	184	15	8
Single-channel dry wall (Fenwal)	256	275	148
Multiple-channel countercurrent (Infuser 37™)	831	341	231
Single-channel countercurrent (System 500™)	1356	658	446
*Data from Flancbaum et al. V_{TC}= apparent thermal clearance. PRBC=packed red blood cells. Q calculated=the calculated flow rate of PRBC infused at 5°C producing an outlet temperature of 32°C.			

Fig. 18

COST OF WARMING BLOOD		
TYPE OF WARMER	UNIT	DISPOSABLE SET
American Pharmaseal DWI000A (Single-channel dry wall)	$500	$10
System 2501™	$2,500	$25
System 500™	$5,000	$50
Infuser 37™	$4,000	$330
Rapid Infusion System™	$51,700	$590
Approximate prices of commercially available warmers and their disposable sets (December 1990)		

Fig 19