Plasma Dilution

AATB Quality/Donor Suitability Workshop
November 16, 2011

Gregory Ray, MD, FCAP
Medical Director
CryoLife, Inc.

CryoLife®
Life Restoring Technologies®

Presentation Overview

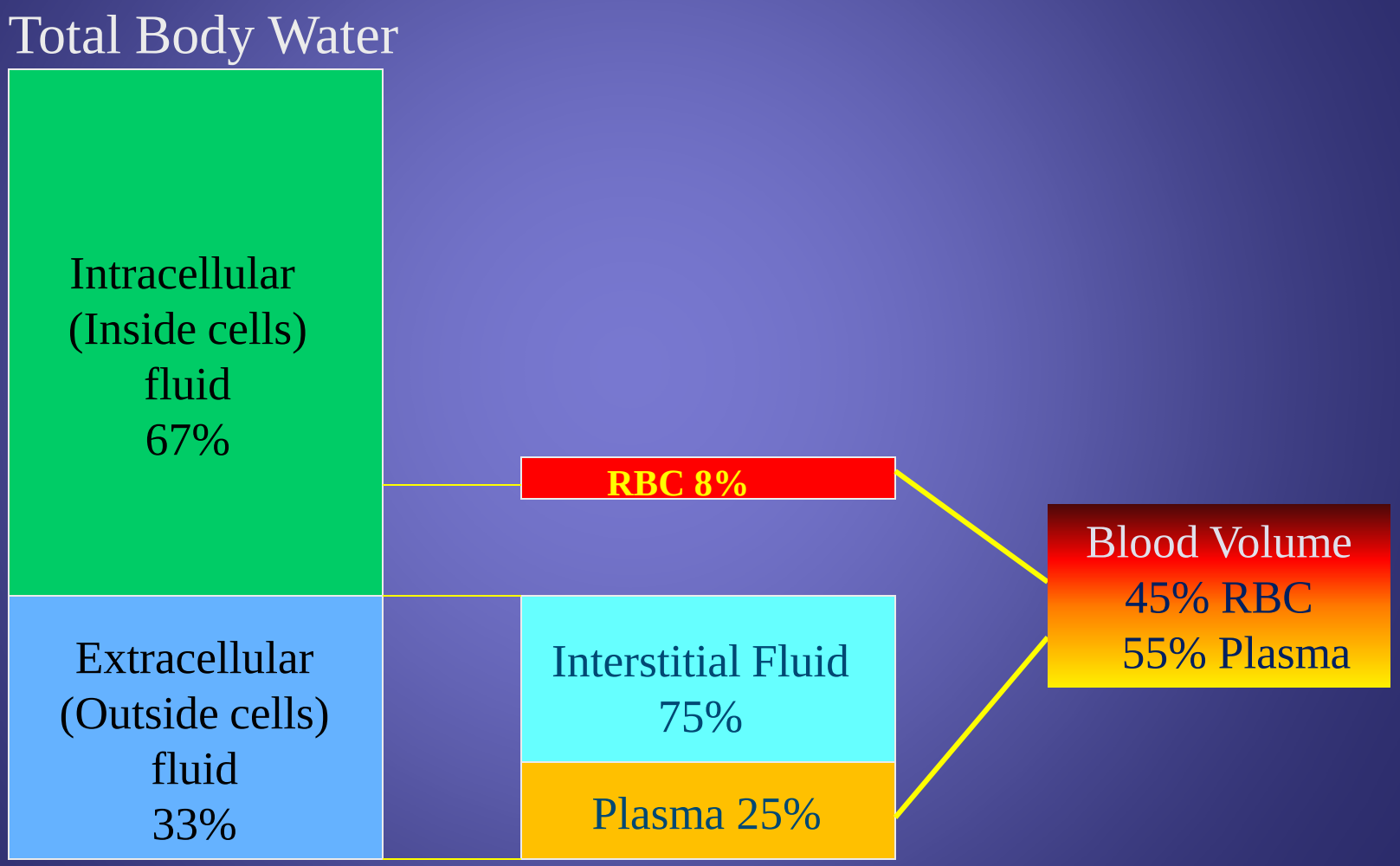
http://www.imdb.com/character/ch0001831/mediaindex

- Basic Body Fluid Physiology
- What is Plasma Dilution and Why Do We Care?
- How Do We Evaluate Plasma Dilution?
- Case Presentations and Discussion
- Gray Matter Exercises

Chapter 1

Basic Fluid Physiology

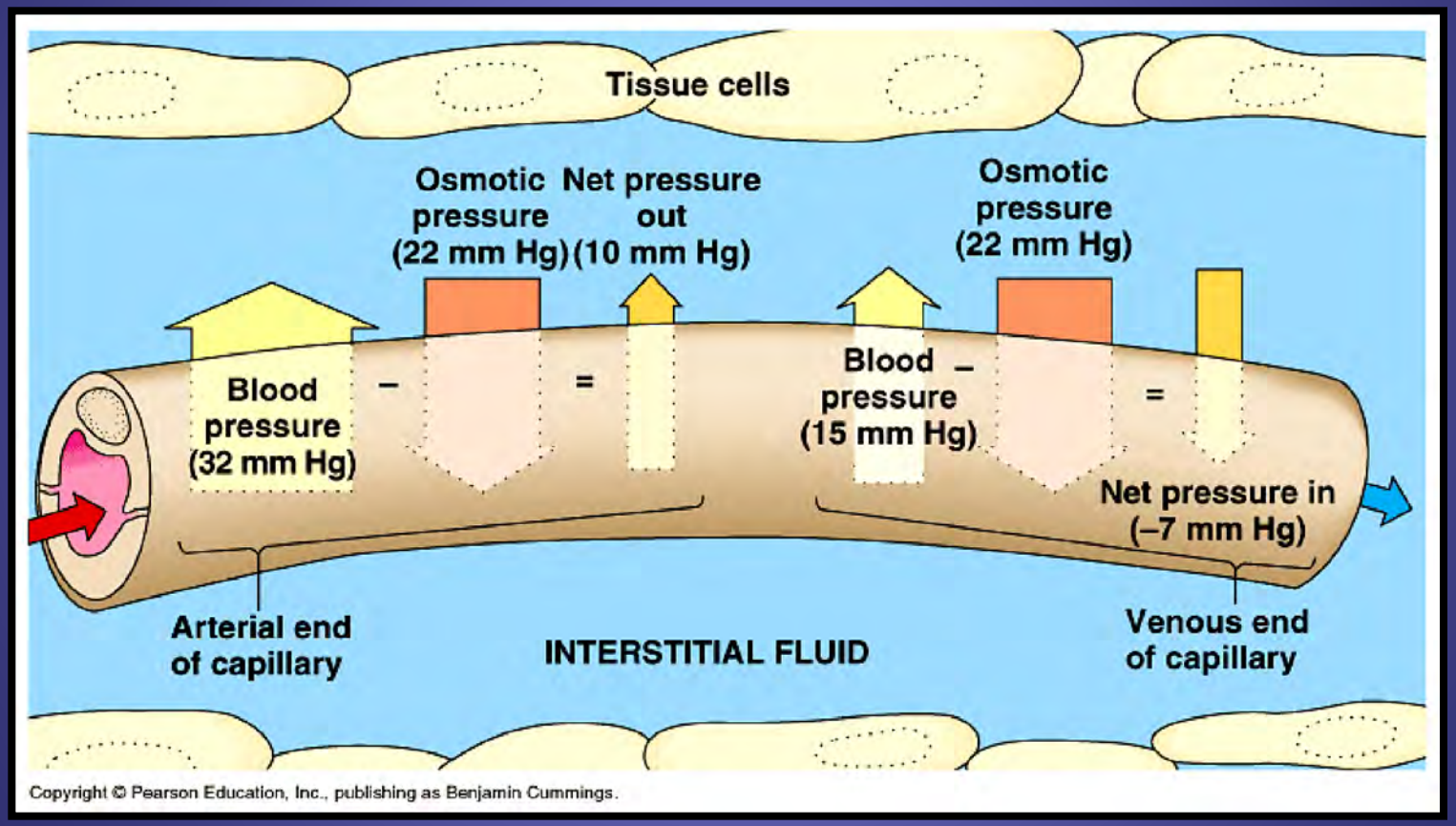
Fluid Compartments



What is Plasma?

- Liquid Portion of Blood ~55% of Blood Volume
- Contents
  - Water
  - Proteins
    - Albumin
    - Globulins/Immunoglobulins (Antibodies)
    - Fibrinogen (removed with clotting-serum)
    - Coagulation Factors
  - Electrolytes
    - Na, K, Cl, HCO_3
  - Hormones, metabolic products, etc.
  - Viral particles/antigens

Blood/Tissue Fluid Equilibrium



Physiologic Response to Hemorrhage

- Loss of blood volume produces a drop in blood pressure
- Increased heart rate and vasoconstriction
- Loss of blood components (RBCs and plasma proteins)
- Initial influx of fluid into vasculature from Interstitial compartment (physiologic dilution)
- Slow redistribution (24-48 hrs) of plasma proteins

Why Do Patients Get IV Fluids?

- Maintenance Therapy
  - Route for administration of medications
    - Crystalloids
  - Fluid/electrolyte balance and nutrition
    - Crystalloids
- Replacement Therapy
  - Correction of deficits
    - Electrolyte and acid/base abnormalities- Crystalloid
    - Anemia- Packed RBCs
    - Coagulation Factors- FFP, cryoprecipitate
  - Volume resuscitation for hemorrhage
    - Crystalloids
    - Colloids
    - Blood Products

IV Fluids Definitions

- Blood
  - Whole Blood
  - Packed Red Blood Cells (PRBCs)
- Colloids (Large Molecules)
  - Fresh Frozen Plasma (FFP), Cryoprecipitate
  - Albumin
  - Platelets
  - Polysaccharide solutions (Hetastarch, Dextran)
- Crystalloids (Small Molecules)
  - Salt solutions (Normal saline, Lactated Ringer's)
  - Glucose solutions (D5W)
  - Total Parenteral Nutrition (TPN)

IV Fluid Distribution

5% Glucose (D5W)

Glucose is rapidly taken up by cells; water distributes proportionally to ALL compartments

1,000 mL D5W → **ICF 670 mL**, **ECF 330 mL** → **ISF 250 mL**, **Plasma 80 mL**

Normal Saline (NS)

Sodium concentration is similar to extracellular fluid; water distributes to ECF compartment

1,000 mL NS → **ISF 750 mL**, **Plasma 250 mL**

Plasma Proteins (FFP)

Large molecules stay in vessels; water distributes only to intravascular compartment

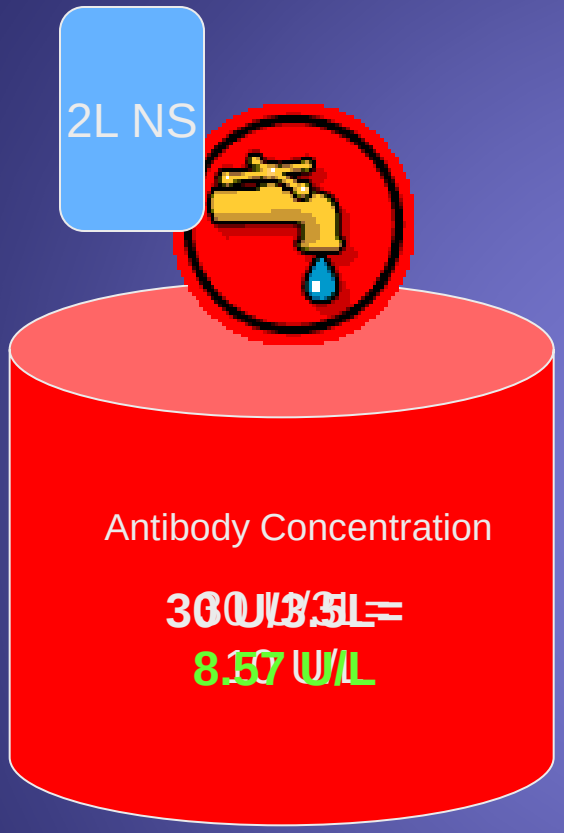
1,000 mL FFP → **Plasma 1,000 mL**

Packed Red Blood Cells (PRBC)

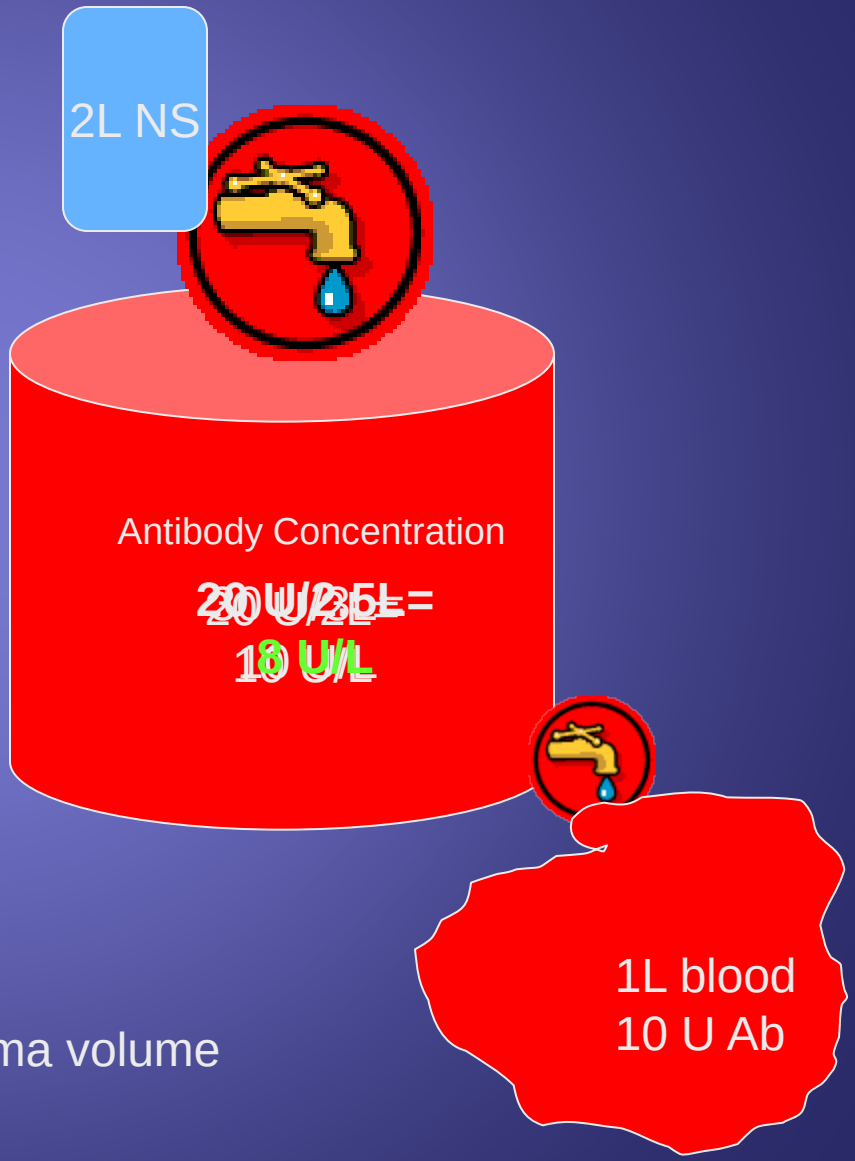
Unit volume is 75-80% RBCs and 20-25% Plasma

300 mL PRBC → **RBC 225-240 mL**, **Plasma 60-75 mL**

No Blood Loss



Blood Loss



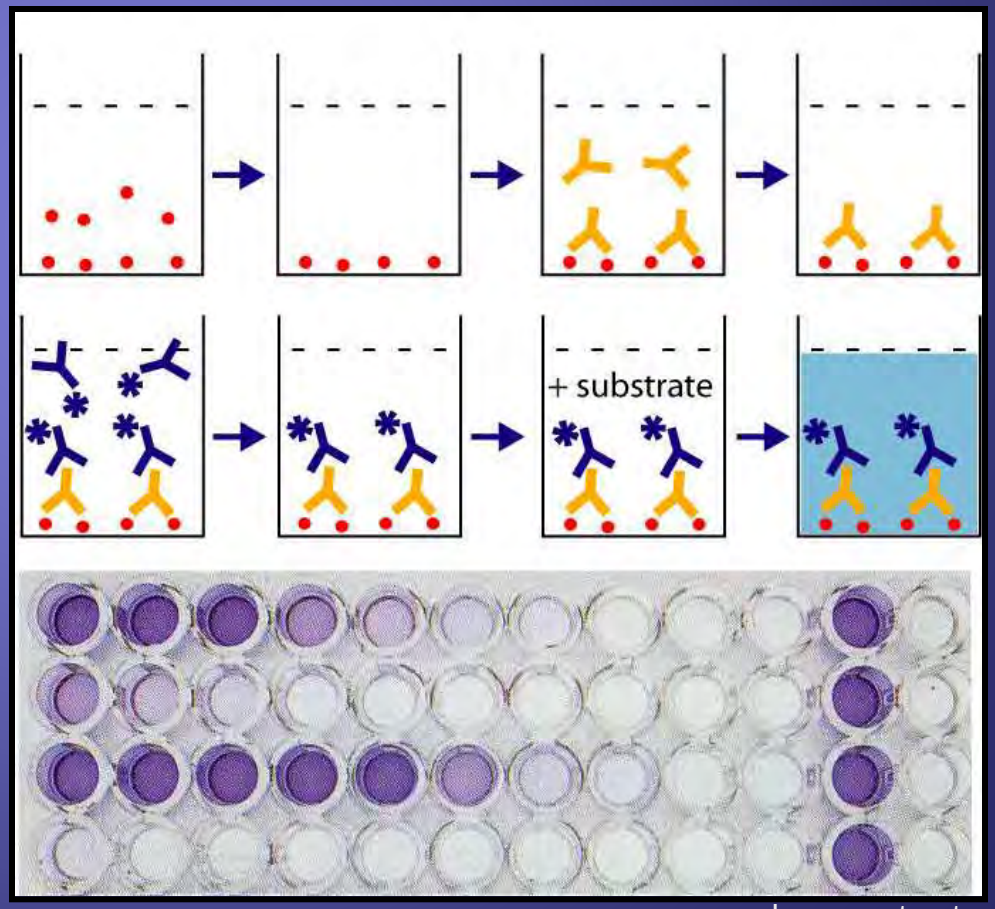
Remember, 1L of NS increases the plasma volume by 250mL!

Chapter 2

What is Plasma Dilution and Why Do We Care?

What Do We Do With Plasma/Serum?

Enzyme Immunoassay (EIA)



cybercarnet.net

So, What is Plasma Dilution and Why Should We Care?

- Loss of plasma proteins (IgG, and other stuff, like virus particles) with hemorrhage
- Addition of IV fluids will further dilute what remains
- The concentration of antibodies and/or viral particles may drop below the detection limit of the test
- 24-48 hours for redistribution of antibodies
- FDA says so- § 1271.80(d)
- This did happen with an organ donor in 1986

Chapter 3

How Do We Evaluate Donors for Plasma Dilution?

Regulations

§ 1271.80 What are the General Requirements for Donor Testing?

- (d) *Ineligible Donors*. You must determine the following donors to be ineligible:
  - (2)(i) A donor in whom plasma dilution sufficient to affect the results of communicable disease testing is suspected, unless:
    - (A) You test a specimen taken from the donor before transfusion or infusion and up to 7 days before recovery of cells or tissue; or
    - (B) You use an appropriate algorithm designed to evaluate volumes administered in the 48 hours before specimen collection, and the algorithm shows that plasma dilution sufficient to affect the results of communicable disease testing has not occurred.

§ 1271.80 What are the General Requirements for Donor Testing?

- (ii) Clinical situations in which you must suspect plasma dilution sufficient to affect the results of communicable disease testing include but are not limited to the following:
  - (A) Blood loss is known or suspected in a donor over 12 years of age [or regardless of blood loss if 12 or under], and the donor has received a transfusion or infusion of any of the following, alone or in combination:
    - (1) More than 2,000 mL of blood (e.g., whole blood, red blood cells) or colloids within 48 hours before death or specimen collection, whichever occurred earlier, or
    - (2) More than 2,000 mL of crystalloids within 1 hour before death or specimen collection, whichever occurred earlier.

1271 Final Guidance Document
Section V (F)

5. Algorithms

*Calculating blood and plasma volumes for donors in the **45-100 kg range**, where there is blood loss with replacement:*

- We recommend that you calculate and assess both blood volume and plasma volume as follows:
  - You may determine the blood volume in mL by dividing the body weight in kilograms by 0.015, or alternatively by multiplying the body weight in kilograms by 70 mL/kg.
  - You may determine the plasma volume in mL by dividing the body weight in kilograms by 0.025, or alternatively by multiplying the body weight in kilograms by 40 mL/kg.

Sample Plasma Dilution Algorithm

Calculations for a 45-100 kg Donor

A = Total volume of blood transfused in the 48 hours before death or sample collection
B = Total volume of colloid infused in the 48 hours before death or sample collection
C = Total volume of crystalloid infused in the 1 hour before death or sample collection

BV = Donor's Blood Volume

- **Calculated Blood Volume =** Donor's weight (kg) / 0.015 OR donor's weight (kg) x 70 mL/kg

PV = Donor's Plasma Volume

- **Calculated Plasma Volume =** Donor's weight (kg) / 0.025 OR donor's weight (kg) x 40 mL/kg

Calculate Both:

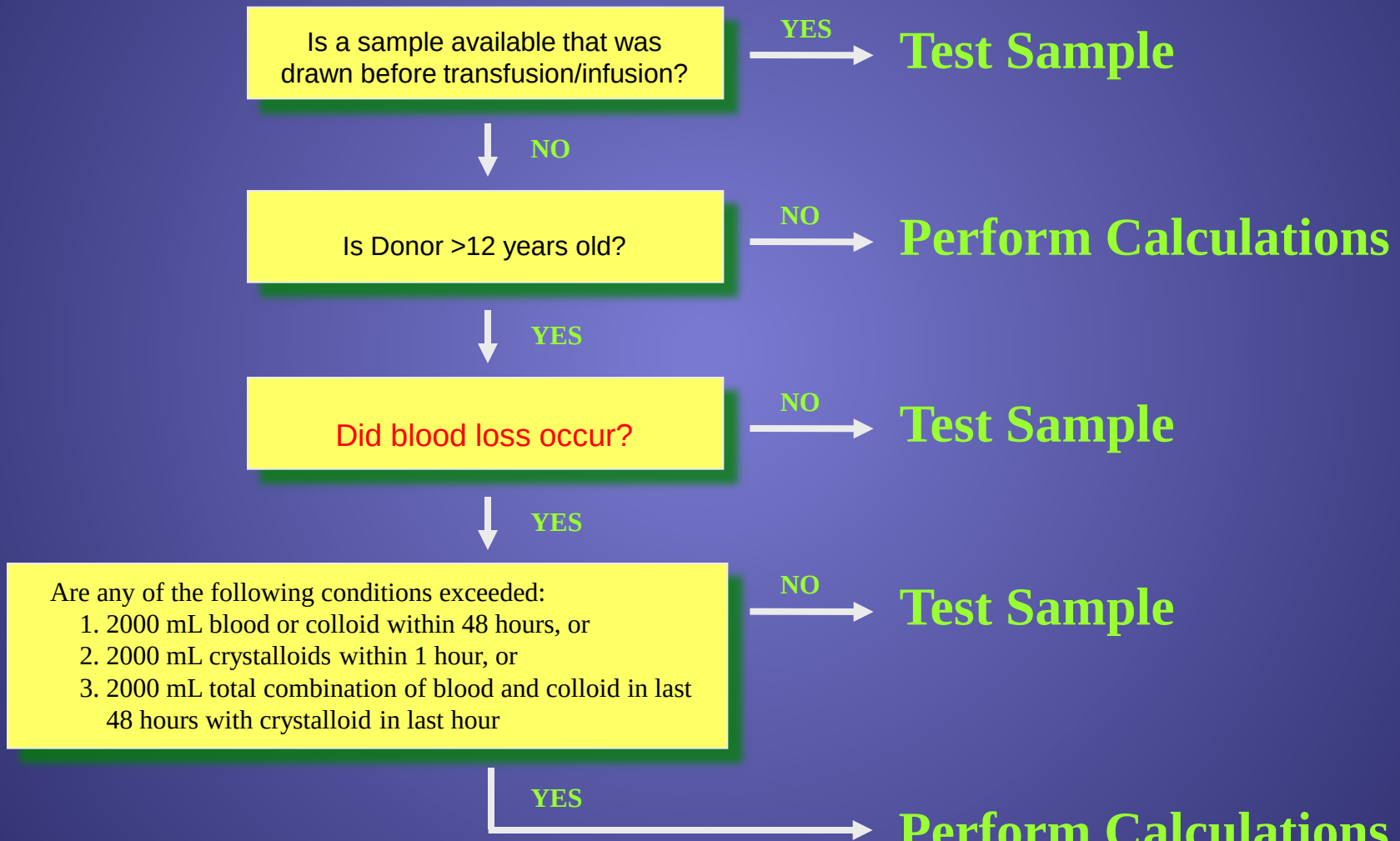
1. Is B + C > PV?	No - Test sample	Yes - Sample Unsuitable
2. Is A + B + C > BV?	No - Test sample	Yes - Sample Unsuitable

1271 Final Donor Eligibility Guidance Document Appendix 2

How Do You Assess Plasma Dilution?

- Use a pre-transfusion/infusion sample for testing if available.
- If such a sample is not available, then you must determine if the donor received fluids sufficient to affect test results.
- The algorithm compares the fluids received within the specified time frames to the donor's blood/plasma volume.
- If the algorithm shows >50% (1:2) dilution, then the sample is UNSUITABLE for ID testing.

Sample Plasma Dilution Algorithm



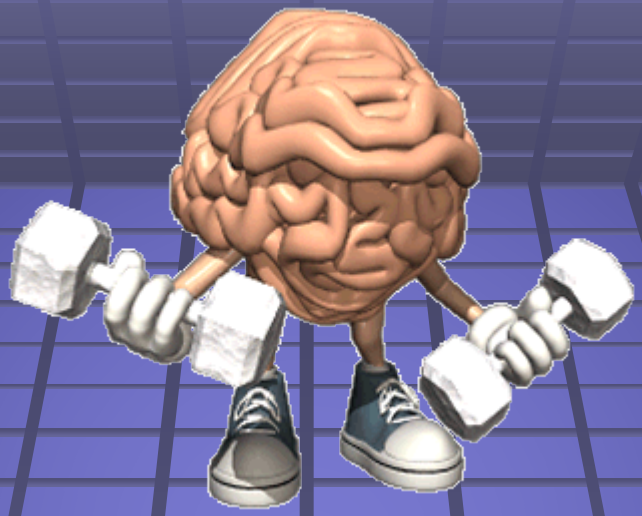
1271 Final Donor Eligibility Guidance Document Appendix 1

Where Do I get the Fluid Information?

- ICU Flowsheets
- Input/Output (I/O) records
- Transfusion Summary from blood bank
- Transfusion slips/records

Problems With Information

- Precise volumes not recorded
  - Look for administration rates
  - TKO (~45-50 mL/hr)
  - Extrapolate from concurrent data
  - Reasonable Maximums
  - Worst case scenarios
- “Units” of blood products
  - Transfusion slips, product label
  - Predefined unit volumes in SOP



Chapter 4

Gray Matter Exercises

Plasma Dilution
Case 1

- 45 year old male presented to ER with severe chest pain and shock
- Became asystolic in ER within 45 minutes of arrival
- Received 1L NS by EMS
- Received additional 1L NS in ER
- 3rd bag of NS started in ER 10 min before code called, exact amount not recorded
- ME declared COD Myocardial Infarction
- Algorithm performed with 3,000 mL NS as “worst case”

Plasma Dilution Case 1

- Donor Weight: 160 lbs (73 kg)
- Donor Height: 5’ 7”
- Estimated Blood/Plasma Volume
  - BV = 73 kg/0.015 = 4,867 mL
  - PV = 73 kg/0.025 = 2,920 mL
- Blood + Colloid + Crystalloid = 3,000 mL <BV
- Colloid + Crystalloid = 3,000 mL >PV
- Is sample acceptable?

Where is the blood loss?

Plasma Dilution Case 2

- 27 year old male; 5’ 8”, 81.8 kg
- Accidental GSW to head
- EMS: 22:38- 18g LAC NS 500mL
  22:42- 16g RAC NS 500mL
- ER: 23:00- TL Cath R Femoral
  Rapid Infuser
- Patient dies at 01:06. Postmortem draw
- Only fluid totals given on code sheet
  - 4 units PRBC (1000mL)
  - 6000 ml NS
- Per Recovery Agency, Nurse said “He got 1000mL NS in the last hour”

Plasma Dilution
Case 2

- Estimated Blood/Plasma Volume
  - BV = 82 kg/0.015 = 5,467 mL
  - PV = 82 kg/0.025 = 3,280 mL
- Blood + Colloid + Crystalloid = 2,000 mL <BV
- Colloid + Crystalloid = 1,000 mL <PV
- Is sample acceptable?

Is 1,000 mL crystalloid appropriate?
If not, what volume should be used?
Can you use 6000 mL/2.5 hrs= 2400 mL?
What other data may be helpful?

Case 2
Lab Tests, etc.

- CBC:
  - 23:33 Hgb 8.5 (13-18 g/dL)
    Hct 24.5% (40-54%)
  - 23:45 Hgb 5.3
    Hct 15.2%
- Chemistry:
  - 23:33 Total Protein 3.6 (6-8.3 g/dL)
    Globulin 1.3 (2.2-4.2 g/dL)
- ER MD estimates blood loss of 2000 mL

Case 2

- Sometimes it is just not clear cut.
- May require a judgment call by the Medical Director.

Vs.

Case 3

- Obese 55 year old male presented to ER with severe abdominal pain and shock
- Severe Hypotensive Shock (60 systolic)
- Taken to OR for repair of aortic aneurysm
- >2.5-3L of free blood in abdomen
- Suffered cardiac arrest in OR
- Only a post-transfusion blood sample is available for infectious disease testing

Case 3

- Fluids Received
  - 48 hours prior to blood draw
    - 11 units PRBC (4070 mL)
    - 4340 mL Colloid
  - 1 hour prior to blood draw
    - 100 mL NS
  - 2.5 hours from EMS arrival to death:
    - 4000mL NS & LR

Case 3

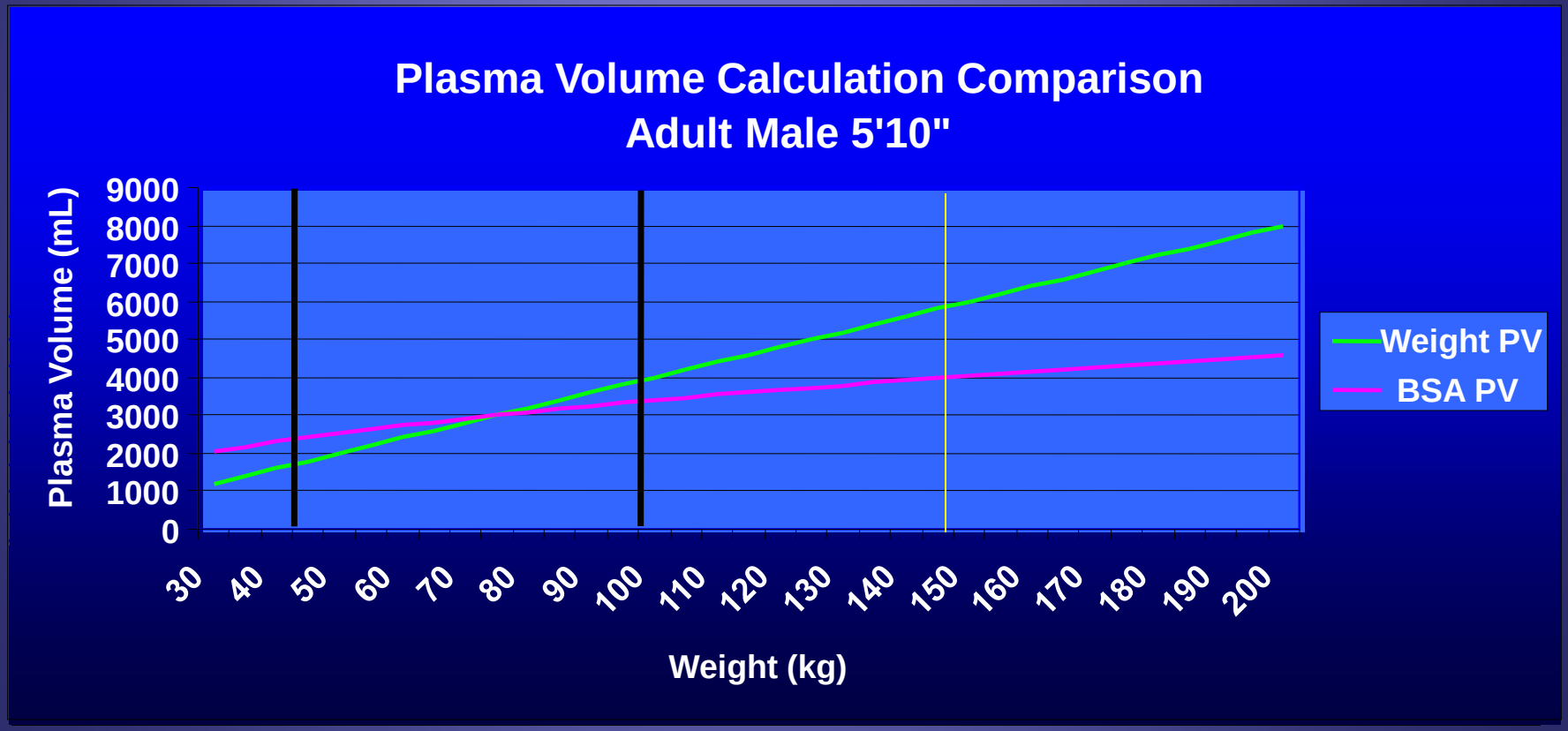
- Donor Weight: 326 lbs (148 kg)
- Donor Height: 5’ 10” (178 cm)
- Estimated Blood/Plasma Volume
  - BV = 148 kg/0.015 = 9,867 mL
  - PV = 148 kg/0.025 = 5,920 mL
- Blood + Colloid + Crystalloid = 8,510 mL <BV
- Colloid + Crystalloid = 4,440 mL <PV
- Is sample acceptable?

Does a 10L blood volume sound reasonable?

Plasma Dilution Calculation Problems

- A donor who is obese
- A donor who weighs <45 kg or >100 kg
- Fat tissue is less vascular than muscle; therefore, less blood volume/gm of tissue mass
- Does the weight based formula recommended in the DE Guidance Document accurately estimate the donor's blood/ plasma volume?

Plasma Volume
Weight vs. Body Surface Area



Case 3
Plasma Dilution Calculation (BSA)

- Donor Weight: 326 lbs (148 kg)
- Donor Height: 5’ 10” (178cm)
- Estimated Blood/Plasma Volume (BSA method)
  - BV[1]=BSA[4](m^2) x 2740= **7,047 mL**
  - PV[2,3]= BSA(m^2) x 1630= **4,192 mL**
- Blood+Colloid+Crystalloid = **8,510 mL > BV**
- Colloid + Crystalloid = **4,440 mL >PV**
- Fails- Sample NOT Acceptable

1. Technical Manual of the American Association of Blood Banks, 15th edition. American Association of Blood Banks. 2005;p. 839.
2. International Committee on Standardization in Haematology. Recommended Methods for Measurement of Red-Cell and Plasma Volume. *J Nucl Med*. 1980; 21:793-800
3. Retzlaff JA, Tause WN, Kieley JM, et al. Erythrocyte volume, plasma volume, and lean body mass in adult men and women. *Blood* 33:649-661, 1969.
4. Dubois D, Dubois EF. A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med*. 1916; 17:863-871.

Case 3
Discussion

- FDA specifically states that calculations provided in the DE Guidance Document are for donors weighing 45-100 kg
- The weight-based calculations provide a good estimate of blood/plasma volume for an average sized adult, but are inaccurate for children and obese adults
- Other more physiologically appropriate calculations should be used in these populations
- What about males vs. females in the 45-100 kg weight range?

PV/BV Calculations for Children

Linderkamp studied 160 children ages 1hr to 14 years.
Used idoinated albumin to establish nomograms for calculating blood volumes from height and weight.

Table 1. Blood volume, plasma volume and red cell mass at different ages (mean ± SD)

Age	No. of cases	Blood volume (ml/kg)	Plasma volume (ml/kg)	Red cell mass (ml/kg)	Hemato-crit
0— 1 day	15	81.9 ± 8.6	43.2 ± 4.6	38.7 ± 9.0	51.8 ± 7.4
2—30 days	15	84.4 ± 7.5	48.5 ± 6.2	35.9 ± 5.8	46.8 ± 5.9
1— 2 months	10	79.4 ± 6.9	53.9 ± 4.9	25.5 ± 3.4	35.4 ± 4.7
3— 6 months	13	76.6 ± 9.0	53.8 ± 7.6	22.8 ± 2.8	32.8 ± 3.3
7—12 months	12	82.4 ± 10.4	57.3 ± 6.9	25.1 ± 4.6	33.5 ± 2.9
13—24 months	10	86.1 ± 9.7	58.7 ± 5.4	27.5 ± 4.6	35.1 ± 2.2
2— 3 years ♂	9	80.5 ± 8.7	52.1 ± 4.3	28.4 ± 5.3	38.6 ± 3.6
♀	8	79.0 ± 7.3	51.6 ± 4.0	27.4 ± 4.6	38.1 ± 3.6
4— 6 years ♂	6	76.7 ± 6.3	48.4 ± 4.7	28.3 ± 2.2	40.8 ± 1.9
♀	10	77.4 ± 4.3	50.9 ± 4.2	26.5 ± 3.8	37.6 ± 4.8
7—10 years ♂	10	79.6 ± 7.1	51.6 ± 1.9	28.0 ± 1.9	38.8 ± 2.9
♀	14	72.7 ± 6.2[a]	46.2 ± 5.1[a]	26.5 ± 2.1	40.3 ± 3.3
11—14 years ♂	14	74.4 ± 5.2	46.7 ± 3.6	27.6 ± 2.4	40.9 ± 2.4
♀	14	68.3 ± 3.5[b]	43.7 ± 2.2[a]	24.6 ± 3.2[a]	39.6 ± 3.8

[a] $P < 0.05$; [b] $P < 0.005$ (t-test) when compared with the values of boys of the same age group

Linderkamp O, Europ. J. Pediat. 125,227--234(1977)

Thank You for Your Patience

Additional informational slides if needed.

Maximum Flow Rates

TABLE 1. Flow Rates of Tested Catheters with Normal Saline Solution Under Gravity

Catheter	Length (inches)	Mean Flow Rate (ml/min)*	Range (ml/min)
Angiocath®†			
14 gauge	2	93	92–94
16 gauge	2	75	74–75
16 gauge	5 1/4	64	63–65
18 gauge	1 1/4	55	—
20 gauge	1 1/4	38	37–39
22 gauge	1	24	—
24 gauge	3/4	14	—
Quik Cath®‡			
22 gauge	1	24	23–24
24 gauge	5/8	15	—
Medicut®§			
14 gauge	2	92	90–94
16 gauge	2	81	80–82
18 gauge	2	62	61–63
20 gauge	2	42	41–42
22 gauge	1	26	—
Desilets-Hoffman Sheath®‖			
16 gauge	3 1/2	77	76–78
CVP®‖			
18 gauge	4 3/4	28	28–29
20 gauge	2 3/4	26	26–27
Intramedicut®§			
16 gauge	8	31	—
18 gauge	8	13	—
20 gauge	8	5	4–5

* Rounded to the nearest ml.
† Deseret Medical, Inc., Sandy, Utah.
‡ Travenol Laboratories, Inc., Deerfield, Illinois.
§ Argyle-Sherwood Medical Industries, St. Louis, Missouri.
‖ Cook, Inc., Bloomington, Indiana.

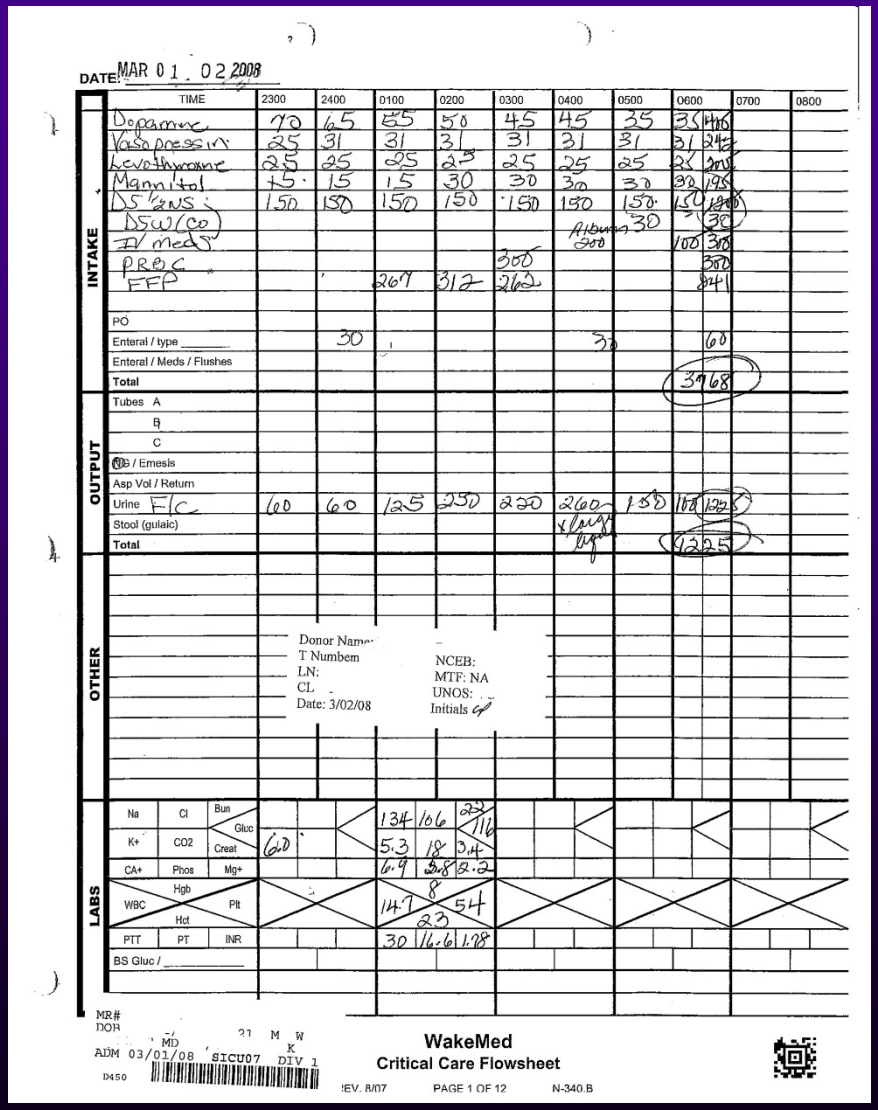
TABLE 2. Flow Rates of Tested Catheters with Normal Saline Solution at 300 mm Hg Pressure

Catheter	Length*	Mean Flow Rate (ml/min)†	Range (ml/min)
Angiocath®‡			
14 gauge	2 in	301	296–310
16 gauge	2 in	248	244–250
16 gauge	5 1/4 in	199	194–206
18 gauge	1 1/4 in	164	157–168
20 gauge	1 1/4 in	103	100–106
22 gauge	1 in	65	62–68
24 gauge	3/4 in	42	42–43
Quik Cath®§			
22 gauge	1 in	68	67–70
24 gauge	5/8 in	47	46–48
Medicut®‖			
14 gauge	2 in	319	304–328
16 gauge	2 in	280	268–284
18 gauge	2 in	214	210–216
20 gauge	2 in	126	116–130
22 gauge	1 in	77	74–78
Desilets-Hoffman Sheath®**			
16 gauge	3 1/2 in	228	212–240
CVP®**			
18 gauge	4 3/4 in	81	—
20 gauge	2 3/4 in	87	83–90
Intramedicut®‖			
16 gauge	20 cm	97	94–100
18 gauge	20 cm	51	50–52
20 gauge	20 cm	16	—

* For length, in = inches, cm = centimeters.
† Rounded to the nearest ml.
‡ Deseret Medical, Inc., Sandy, Utah.
§ Travenol Laboratories, Inc., Deerfield, Illinois.
‖ Argyle-Sherwood Medical Industries, St. Louis, Missouri.
** Cook, Inc., Bloomington, Indiana.

Hodge D. *Am J Emer Med*. 1985;3:403-407

ICU Flowsheet



DATE: MAR 01 . 02 2008

	TIME	2300	2400	0100	0200	0300	0400	0500	0600	0700	0800
INTAKE	Dopamine	70	45	55	50	45	45	35	35		
	Vasopressin	25	31	31	31	31	31	31	31		
	Levothyroxine	25	25	25	25	25	25	25	25		
	Mannitol	15	15	15	30	30	30	30	30		
	DS 1/2NS	150	150	150	150	150	150	150	150		
	D5W (CO IV meds)						Albumin 30		100		
	PROC					300			300		
	FFP			269	312	262			843		
	PO										
	Enteral / type		30				30		60		
	Enteral / Meds / Flushes										
	Total								3968		
OUTPUT	Tubes A										
	B										
	C										
	NG / Emesis										
	Asp Vol / Return										
	Urine F/C	60	60	125	250	220	260	150	1225		
	Stool (guiac)										
	Total								1225		
OTHER											
LABS	Na / Cl / Bun / Gluc			134 / 106 / 22					116		
	K+ / CO2 / Creat	6.0		5.3 / 18 / 3.4							
	CA+ / Phos / Mg+			6.9 / 3.8 / 2.2							
	WBC / Hgb / Hct / Plt			14.7 / 8 / 23 / 54							
	PTT / PT / INR			30 / 16.6 / 1.38							
	BS Gluc /										

Donor Name
T Numbem
LN:
CL
Date: 3/02/08

NCEB:
MTF: NA
UNOS:
Initials

MR#
DOB -/ 21 M W
MD K
ADM 03/01/08 SICU07 DIV 1
D450

WakeMed
Critical Care Flowsheet

REV. 8/07 PAGE 1 OF 12 N-340.B

Transfusion Record

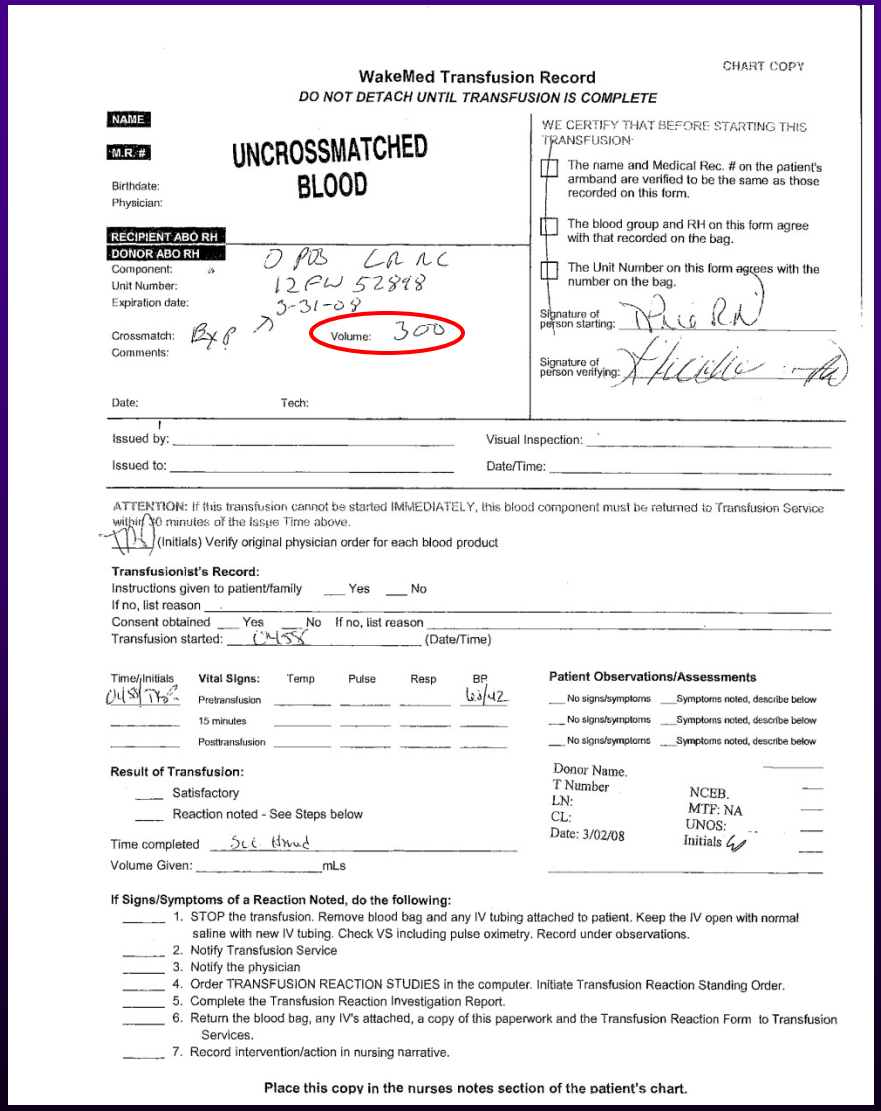


CHART COPY

WakeMed Transfusion Record

DO NOT DETACH UNTIL TRANSFUSION IS COMPLETE

NAME

M.R.#

UNCROSSMATCHED BLOOD

Birthdate:
Physician:

RECIPIENT ABO RH
DONOR ABO RH
Component: O PRB LR 1C
Unit Number: 12PW 52898
Expiration date: 3-31-08
Crossmatch: Bxp
Comments:
Volume: 300

Date: Tech:

WE CERTIFY THAT BEFORE STARTING THIS TRANSFUSION:

- ☐ The name and Medical Rec. # on the patient's armband are verified to be the same as those recorded on this form.
- ☐ The blood group and RH on this form agree with that recorded on the bag.
- ☐ The Unit Number on this form agrees with the number on the bag.

Signature of person starting: RN
Signature of person verifying:

Issued by: _____ Visual Inspection: _____

Issued to: _____ Date/Time: _____

ATTENTION: If this transfusion cannot be started IMMEDIATELY, this blood component must be returned to Transfusion Service within 30 minutes of the issue Time above.

(Initials) Verify original physician order for each blood product

Transfusionist's Record:

Instructions given to patient/family ___ Yes ___ No
If no, list reason _____
Consent obtained ___ Yes ___ No If no, list reason _____
Transfusion started: _____ (Date/Time)

Time/Initials	Vital Signs:	Temp	Pulse	Resp	BP
	Pretransfusion				68/42
	15 minutes				
	Posttransfusion				

Patient Observations/Assessments

___ No signs/symptoms ___ Symptoms noted, describe below
___ No signs/symptoms ___ Symptoms noted, describe below
___ No signs/symptoms ___ Symptoms noted, describe below

Result of Transfusion:

___ Satisfactory
___ Reaction noted - See Steps below

Time completed 5cc Hmd
Volume Given: _____ mLs

Donor Name.
T Number
LN:
CL:
Date: 3/02/08

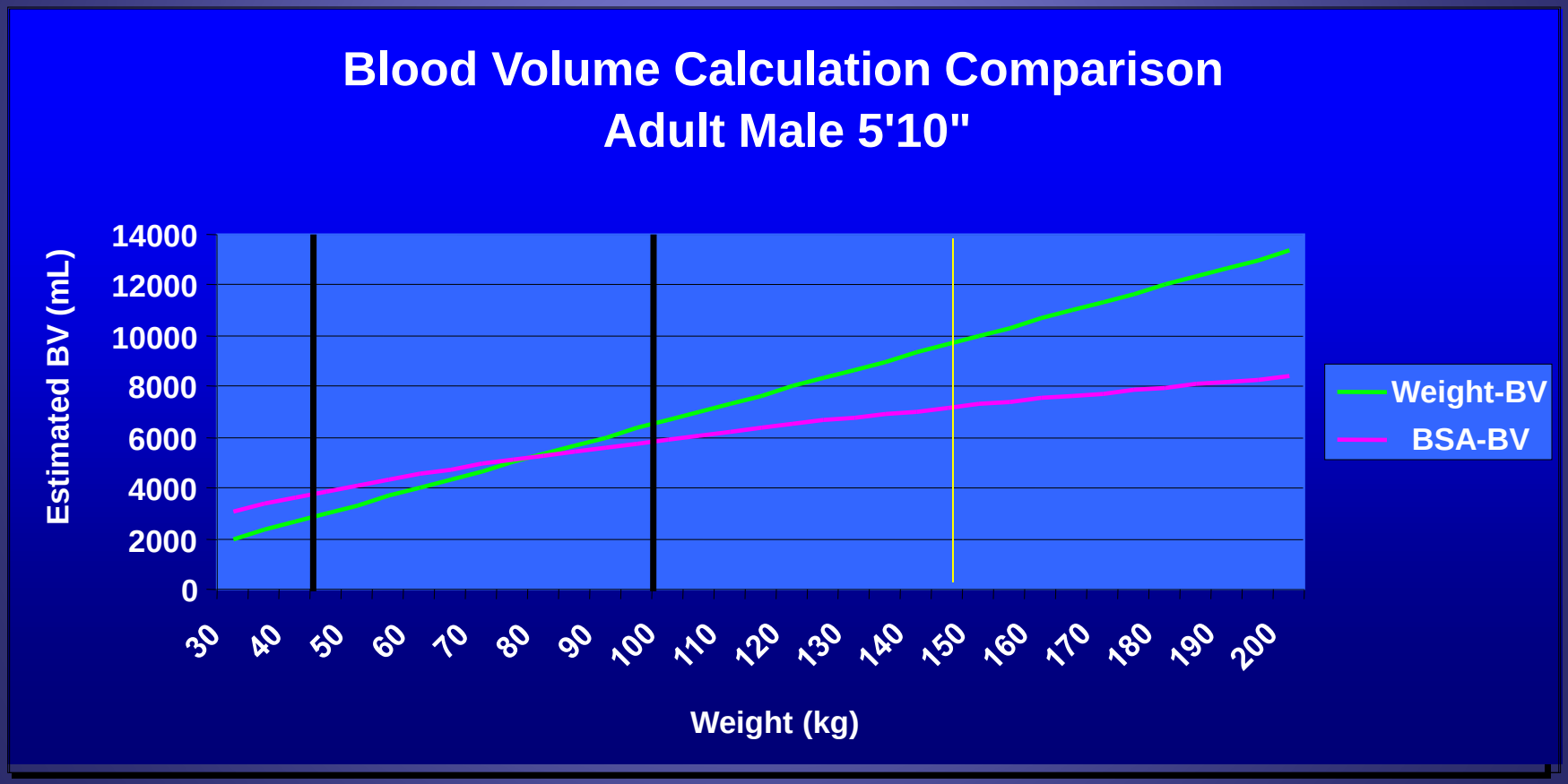
NCEB.
MTF: NA
UNOS:
Initials

If Signs/Symptoms of a Reaction Noted, do the following:

1. STOP the transfusion. Remove blood bag and any IV tubing attached to patient. Keep the IV open with normal saline with new IV tubing. Check VS including pulse oximetry. Record under observations.
2. Notify Transfusion Service
3. Notify the physician
4. Order TRANSFUSION REACTION STUDIES in the computer. Initiate Transfusion Reaction Standing Order.
5. Complete the Transfusion Reaction Investigation Report.
6. Return the blood bag, any IV's attached, a copy of this paperwork and the Transfusion Reaction Form to Transfusion Services.
7. Record intervention/action in nursing narrative.

Place this copy in the nurses notes section of the patient's chart.

Blood Volume
Weight vs. Body Surface Area



1271 DE Guidance Document Section V (F)

3. Other Clinical Situations

- A donor who has previously had blood loss, stabilizes, then expires, but has received fluids in the 48 hours before sampling;
- A donor who is obese;
- A donor who in the absence of bleeding may have received large amounts of infusions which the medical director or designee believes may affect test results;
- A donor who weighs less than 45 kilograms or more than 100 kilograms.