

## Objectives

- The goals of intraoperative fluid and blood administration are to maintain adequate oxygen delivery, normal electrolyte concentrations, and normoglycemia. Research data from the past decade has led to refined knowledge of the physiology of fluid management.
- The focus of this session is two-fold: to present a surgical case in which massive volume resuscitation was required, and to examine these complex issues and discuss evidence that can be employed to optimize patient outcomes.

Learning objectives

- Review the physiology of massive volume resuscitation
- Review the clinical and theoretical evidence concerning the sequelae of fluid and blood administration

## Case Presentation

**OR Schedule**

- Aorto-carotid bypass, TEVAR, Possible CABG

**70 year old male**

- Wt. 94 kg; Ht. 168 cm

**Medical History**

- 6.5 cm thoracic aneurysm
- HTN
- Colon CA w/ chemotherapy (1996)
- Smoking
- Chronic low back pain

**Surgical History**

- s/p open AAA repair
- Multiple bowel surgeries
- Ventral hernia repair

## Case Presentation

**Medications**

- Cozaar, pravastatin, lolmel, advair, losapro, seroquel

**Diagnostic Studies**

- Echocardiogram revealed the aneurysm was located in the aortic arch extending distally to the left subclavian artery, severe global hypokinesis, and ejection fraction of 25%
- Chest X-ray-small bilateral lower lobe infiltrates
- EKG-sinus tachycardia

**Labs**

- Hgb 15.2
- Hct 48.2
- WBC 9.4
- Pt 181
- BG 114

- BUN 14
- Creat 1.1
- Na 138
- K 3.9

## Anatomy

Right common carotid artery, Left common carotid artery, Right subclavian artery, Left subclavian artery, Brachiocephalic trunk, Aortic arch, Ascending aorta, Descending aorta, Thoracoabdominal aortic aneurysm.

## Procedure Explanation

Procedure – Median sternotomy, aorto-left common carotid bypass, aorto-right innominate bypass, aorto-left axillary bypass, TEVAR

A Gore-Tex graft was constructed with one large aortic port, and 3 smaller, longer ports

The TEVAR was then completed through the third port of the Gore-Tex graft

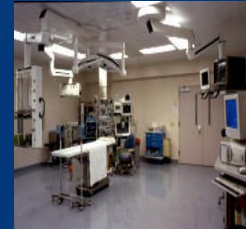
## Anesthetic Plan

GETA; TIVA with sufentanil infusion was utilized  
 Standard monitors and cerebral oximetry  
 16 gauge IV  
 Right radial a-line  
 Right femoral cordis  
 Left femoral a-line  
 Under body warming mattress  
 #8 HiLo ETT  
 Foley  
 Cell Saver



## OR Team

2 Cardiothoracic Surgeons  
 2 Vascular Surgeons  
 Perfusionist  
 Cardiac Anesthesiologist  
 Cardiac CRNA  
 SRNA  
 Anesthesia Tech  
 Circulating and scrub team



## Anesthetic Management

Pre-medication  
 • 3 mg midazolam  
 Induction  
 • 15 mcg sufentanil, 120 mg propofol, 100 mg succinylcholine  
 • Smooth induction with ETT placement  
 Maintenance  
 • propofol infusion 75-100 mcg/kg/min  
 • sufentanil infusion 1 mcg/kg/min  
 • 10 mg pancuronium  
 • 10 mg vecuronium after return of TOF  
 • cefazolin 2G/ redosed q4 hr  
 • phenylephrine infusion maintained for pressor support



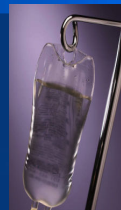
## Anesthetic Management

Heparin administered (13000 U)  
 • Prior to aortic clamp (17 min)  
 • Re-administered for subsequent clamping including partial innominate clamping (15 min) and left common carotid clamping (10 min)  
 Electrolytes  
 • Calcium chloride (2G)  
 • Magnesium sulfate (16.24 mEq)  
 • Potassium chloride (40 mEq)  
 Nicardipine (0.6 mg)  
 • Given to decrease pressure in increments at surgeon's request



## Anesthetic Management

Vasopressin (2U)  
 • For increasing BP rapidly, after grafts were completed  
 Epinephrine (2mcg/min)  
 • Inotropic support  
 Protamine / Calcium chloride (125 mg)  
 • Administered as an infusion for reversal of heparin



## Intake and Output Chart

Intake	Total Amount
Crystalloid	9000 ml
Cell Saver	5800 ml
Platelets	480 ml
PRBCs	1400 ml
FFP	1600 ml

Output	Total Amount
Blood	1000 ml
Urine	1700 ml



## Lab Values

Labs were monitored throughout the procedure

Time	Values
0900	Hgb 13.2, K 3.2
1030	Hgb 12, K3.8
1400	Hgb 11.2, K 3.8
1430	Hgb 11, K 4.7



## Post – op Follow-up

### POD 1

- Following commands intermittently
- Agitation requiring sedation
- Unable to meet extubation criteria
- OHU insulin protocol started
- Continued weaning from epinephrine infusion

### POD 2/3

- Weaned from ventilator
- Re-intubated within 6 hours after developing respiratory insufficiency
- Developed acute renal failure



## Post-op Follow-up

### POD 4

- Mechanical ventilation continues
- Developed atrial fibrillation
- Unsuccessful cardioversion X 2
- Amiodarone infusion initiated
- Cardizem infusion, insulin infusion and maintenance fluids continued

### POD 7

- Weaning from ventilator continues
- Hemodynamics more stable
- Lab values improving

### POD 8

- Extubated, pt transported to TOHU



## Surgical Fluid Balance

All anesthetics may blunt the normal physiologic responses to hypovolemia and stress response

- Regional anesthesia
- Inhalational and Intravenous anesthetics
  - Depress myocardium
  - ↓ Venous return
  - ↓ Blood pressure

Stress response to surgery causes increased production of anti-diuretic hormone (ADH)

Mechanical ventilation increases secretion of ADH



## Surgical Fluid Balance

Third space losses do not contribute to

- Intravascular volume
- Oxygen delivery
- Waste removal

Cellular damage caused by

- Occlusion of the capillary networks from edema

The anesthesiologist plays a vital role to ensure adequate fluid administration in the intra-operative as well as post-operative periods



## Intravascular Volume Expansion

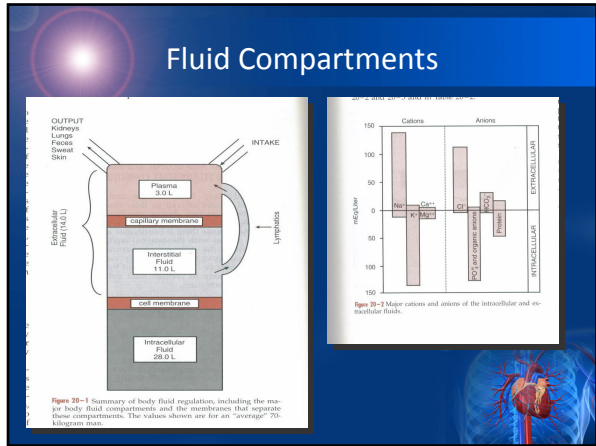
Three main purposes of fluid administration

1. Provision of maintenance fluid
2. Replacement of fluid lost due to surgery and anesthesia
3. Correction of electrolyte disturbances

Goals of fluid therapy

- Sustain oxygen delivery in relation to oxygen demand
  - Hemoglobin concentration
  - Oxygen tension
  - Organ perfusion pressure
    - systemic arterial pressure (CO and SVR)
    - organ venous pressure
  - Organ vascular resistance





## Fluid Compartments: Intracellular

40% (2/3) of the total body's fluid volume

Membrane bound adenosine triphosphatase (ATPase)-driven sodium-potassium pump (Na K-ATPase pump) exchanges Na for K (3:2 ratio)

- Highly permeable to water, but not most of the electrolytes in the body

Potassium (K) is the most important determinant of intracellular osmotic pressure

Characterized by high concentrations of potassium, phosphorus, and magnesium

Large amounts of protein – 4x plasma

## Fluid Compartments: Extracellular

Two compartments (20% or 14 liters)

- Interstitial fluid
- Intravascular fluid (plasma)

Plasma protein-impermeable membrane

- relatively the same composition of electrolytes
- Proteins have higher concentration in the plasma (albumin)

Sodium (Na) is the most important extracellular cation and the major determinant of extracellular osmotic pressure and volume

Interstitial compartment may act as an overflow reservoir for the intravascular compartment

## Starling Forces

The anesthetist has access to the intravascular space, which is the focus of fluid therapy

Starling Forces – govern fluid dynamics in the microcirculation

- Capillary pressure
- Interstitial fluid (ISF) pressure
- ISF colloid osmotic pressure
- Plasma osmotic pressure\*

The diagram shows a capillary bed with an arterial end and a venous end. It labels various pressures: Capillary hydrostatic pressure, Interstitial hydrostatic pressure, Interstitial colloid osmotic pressure, Plasma colloid osmotic pressure, and Na<sup>+</sup>. It also shows a cell with its own membrane.

## Plasma Oncotic Pressure

Force that is determined by the protein component in intravascular fluid

- Maintains circulating fluid volume within a space

Two important basics surround changes in intracellular and extracellular movement of fluids

- Aid in determining the effects of fluid volumes and osmolarities

- water moves rapidly across a cell membrane
- the cell membrane is almost completely impermeable to many solutes

## Crystalloids

Grouped as isotonic, hypotonic and hypertonic salt solutions

Fluids containing water and electrolytes; used to expand intravascular fluid

Replacement requirements are three-fold to four-fold the volume of blood lost

The distribution ratio is 1:4, and that is similar to ECF

- 20% should remain in the intravascular space

## Crystalloids

### Dextrose containing fluids

- Prevent hypoglycemia and limit protein catabolism
- Used in infants or with insulin infusions
- Iatrogenic hyperglycemia can limit effectiveness of fluid resuscitation
- Shown to aggravate ischemic or traumatic neurologic injury

### Balanced salt solutions - Hypotonic

- Electrolyte composition similar to ECF
- Lactated ringer's, Plasma-Lyte, Normosol

## Crystalloids

### Normal saline

- Isotonic and iso-osmotic
- Contains more chloride than ECF
- Large volumes → hyperchloremia (metabolic acidosis)
- Preferred solution for: brain injury, hypochloremic metabolic acidosis, hyponatremia, hyperkalemia, renal failure

### Hypertonic salt solutions

- Na concentrations range from 250-1200 mEq/L
- Less volume administered
- Osmotic forces move water from intravascular space to extracellular space.
- Reduced volume administered → "↓ edema"

## Crystalloid vs. Colloid

Controversy exists concerning crystalloid and colloid solutions and fluid administration techniques

Crystalloid administration dilute → plasma proteins → ↓ plasma oncotic pressure → edema

Colloid administration → additional albumin being cleared by the lymphatics and ultimately returning to the systemic circulation

Argument of cost/benefit ratio

Considerations of coagulopathy that studies have demonstrated to be present in trauma patients receiving massive amounts of fluid and blood

## Crystalloid vs. Colloid

Colloids produce ↑ in capillary pressure, often for a greater duration than crystalloids

In disease states associated with ↑ alveolar capillary permeability, infusion of colloid may aggravate pulmonary edema

- Sepsis
- Adult Respiratory Distress Syndrome (ARDS)

In the absence of an oncotic pressure gradient, either crystalloid or colloid administration may precipitate pulmonary edema

- Valvular heart disease
- Maintain low pulmonary artery occlusion pressure (PAOP)

## Colloids

Volumes equivalent to volume of blood lost

Initial volume of distribution is equivalent to the plasma volume

Synthetic colloids, processed albumin, and protein fractions have minimal to zero risk of infection

Restore intravascular blood volume temporarily

### 5% Albumin

- Half life of albumin is normally 16 hours
- Plasma protein fractions
- Peritonitis or extensive burns

### 25% Albumin

- Potential to expand plasma volume by up to 5x
- Plasma volume diminished, with an acceptable BP

## Colloids

### Hydroxyethyl Starch (Hetastarch)

- Synthetic colloid with molecular mass of 80%
- 6% in NS – Hespan
- Stored in reticulo-endothelium and excreted renally
- Dilutional effects and decrease in factor VII:C and vWF levels by 50-80% with prolongation of PTT
- Can interfere with platelet adhesion

### Hextend

- New form approved - 6% hetastarch is a solution that approaches physiologic concentrations of major electrolytes
- Study results illustrate patients receiving Hextend to have no major changes in thromboelastogram profiles

## Colloids

### Six percent Dextran 70

- Available as dextran 40 or 70 referring to molecular mass.
- Water soluble glucose polymers synthesized from certain bacteria from sucrose
- Dextran 70 is administered for same indications as 5% albumin
- Dextran 40 is used in vascular surgery to prevent thrombosis and is rarely used as a volume expander.
- Anaphylactic/anaphylactoid reactions
- Increase bleeding time, decrease platelet adhesion
- Interference with cross matching
- Toxic effect on pulmonary capillaries → non-cardiogenic pulmonary edema



## Patient with Heart Failure

Fluid management is aimed at optimizing

- Cardiac preload
- Avoid over administration of Na
- Diminish edema
- Correct electrolyte abnormalities

Maintaining ideal cardiac preload during fluid shifts

- Facilitated with direct and indirect measurements:
  - Central venous pressure (CVP)      Echocardiography
  - Thermodilution cardiac output      PAOP
  - End diastolic volume      Left atrial pressure

Cardiac contractile function measured by

- SV
- EF
- Stroke work



## Patient with heart failure

O2 on room air – 92%

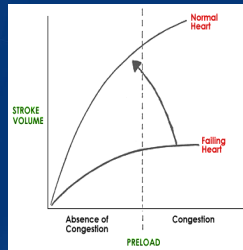
BP - 145-155 systolic

80-109 diastolic

Sinus tach – 100

Hgb – 15.2 (smoking hx)

Oxygen Supply	Oxygen Demand
Patency of coronary arteries	Heart rate
Autoregulation of coronary vascular resistance	Contractility
Diastolic perfusion gradient*	Preload
Diastolic time interval	Afterload



## Goals of transfusion therapy

- To restore intravascular volume, cardiac output, and organ perfusion to normal levels
- Increasing oxygen-carrying capacity is the only real indication for blood transfusions
- The elusive “transfusion trigger” remains a prominent part of the debates in anesthesia and medicine



## Practice guidelines

American Society of Anesthesiologists, (ASA), 2006

1. Transfusion is rarely indicated when the hemoglobin concentration is greater than 10 g/dL and is almost always indicated when it is less than 6 g/dL, especially when the anemia is acute.
2. The determination of whether intermediate hemoglobin concentrations (6 to 10 g/dL) justify or require RBC transfusion should be based on the patient's risk for complications of inadequate oxygenation.



## Practice guidelines

3. The use of a single hemoglobin “trigger” for all patients and other approaches that fail to consider all important physiologic and surgical factors affecting oxygenation is not recommended.
4. When appropriate, preoperative autologous blood donation, intraoperative and postoperative blood recovery, acute normovolemic hemodilution, and measures to decrease blood loss (i.e., deliberate hypotension and pharmacologic agents) may be beneficial.



## Practice guidelines

5. The indications for transfusion of autologous RBCs may be more liberal than those for allogeneic RBCs because of less frequent (but still significant) risks associated with the former.



## Transfusion practices

- Dramatic changes – a result of the knowledge that human immunodeficiency virus (HIV) is transmissible by blood
- Transfusion risk related to HIV is vanishingly small
- There remains numerous other hazards associated with blood products
- Complete understanding of risk and benefits prior to blood product administration is required



## Blood product administration Risks

- From 2004 to 2006, three of the four most common causes of transfusion-related deaths
- hemolytic transfusion reactions
  - septic transfusions (e.g., bacterial contamination)
  - transfusion-related acute lung injury (TRALI)



## Blood product administration Risks

- Etiologies – Infectious vs. non-infectious
- Viral infections – high profile
- Non-viral – greater morbidity and mortality



## Blood product administration Infectious risks

- Viral infectivity – rate has decreased dramatically in the last two decades
- Hepatitis B virus (HBV) – greatest risk
- Current estimated risk in the U.S. – 1 HBV infection per 350,000 donor exposures



## Blood product administration Infectious risks

- Bacterial contamination – occurs at a much higher frequency
- Associated with substantial mortality
- Estimated fatalities occur at a rate of between 1: 1-6,000,000 transfused units



## Blood product administration Infectious risks

- Rate is substantially greater with platelets than RBCs
- Platelets stored at room temperature, involves pools of 6 to 10 units

Bacterial sepsis/endotoxin reaction per donor exposure

- RBC – 1/30,000
- Platelets – 1/2,000



## Contaminated blood transfusion

Signs and symptoms – rapid onset of some combination of the following

- Fever
- Chills
- Tachycardia
- Emesis
- Shock
- Disseminated intravascular coagulation (DIC)
- Acute renal failure (ARF)



## Blood product administration Noninfectious risks

The majority are immunologically mediated

- Acute hemolytic transfusion reaction against foreign RBCs – hemolysis of the donor RBCs often leads to ARF, DIC, and death
- Incidence is 1 per 12,000 units transfused
- Hazardous process – clerical error



## Hemolytic reaction

- Incompatible blood is given → antibodies and complement in recipient plasma attack the corresponding antigens on the donor RBCs → hemolysis
- May occur in the intravascular space and/or extravascularly in the endoplasmic reticulum



## Hemolytic reaction

- Antigen-antibody complexes activate Hageman factor (XII) → kinin system → bradykinin
- Bradykinin ↑ capillary permeability and dilates arterioles → hypotension
- Mast cells release histamine and serotonin → bronchospasm
- DIC develops in 30% to 50% of patients



## Hemolytic reaction

- Hemolysis releases hemoglobin into the blood
- It binds to haptoglobin and albumin until binding sites are saturated
- Then it circulates unbound in the blood until it is excreted by the kidneys
- Renal damage occurs for several reasons



## Hemolytic reaction – renal damage

Reduced blood flow to the kidneys

- Systemic hypotension
- Renal vasoconstriction

Mechanical obstruction resulting from

- Free hemoglobin precipitate in the renal tubules
- Antigen – antibody complexes in the glomeruli
- Fibrin thrombi in the renal vasculature (with DIC)



## Hemolytic transfusion reaction Signs and symptoms

- Fever, chills
- Nausea, vomiting
- Diarrhea
- Rigors
- Hypotension
- Tachycardia
- Flushed
- Dyspnea
- Chest, back pain
- Restless, sense of doom
- Headache
- Hemoglobinuria
- Diffuse bleeding (DIC)
- During general anesthesia, many of the signs are masked
- Only clues may be
- Hypotension
- Hemoglobinuria
- Diffuse bleeding
- A reasonable index of suspicion should be maintained during administration of RBCs to anesthetized patients in order to avoid critical delay in diagnosis



## Hemolytic reaction - treatment

Three objectives

- Maintain systemic blood pressure
- Preserve renal function
- Prevent DIC



## Hemolytic reaction - treatment

1. STOP THE TRANSFUSION
2. Maintain the urine output at a minimum of 75 to 100 mL/hr by the following methods
  - a. Generously administer fluids intravenously and possibly mannitol (12.5 to 50 g, given over 5 to 15 minutes)
  - b. If intravenously administered fluids and mannitol are ineffective, administer furosemide (20 to 40 mg) intravenously



## Hemolytic reaction - treatment

3. Alkalinize the urine; because bicarbonate is preferentially excreted in the urine, only 40 to 70 mEq of sodium bicarbonate per 70 kg of body weight is usually required to raise the urine pH to 8, whereupon repeat urine pH determinations indicate the need for additional bicarbonate.



## Hemolytic reaction - treatment

4. Assay urine and plasma hemoglobin concentrations.
5. Determine platelet count, partial thromboplastin time, and serum fibrinogen level.
6. Return unused blood to blood bank for repeat crossmatch.
7. Send patient's blood and urine sample to blood bank for examination.
8. Prevent hypotension to ensure adequate renal blood flow.



## Transfusion-related acute lung injury (TRALI)

- A noncardiogenic form of pulmonary edema
- Has been associated with the administration of all blood components
- Occurs most frequently with PRBCs, FFP, and platelets
- Incidence 1:5,000 units transfused
- Mortality 5 to 8%



## Transfusion-related acute lung injury (TRALI)

### Mechanism of action

- Antileukocyte antibodies in donor plasma activate leukocytes in the host
- It is thought that biologically active lipids initiate the pulmonary insult
- Lipids thought to be derived from the breakdown of the membranes of cellular elements in stored blood products



## Clinical appearance/treatment of TRALI

- Symptoms begin within 6 hours of transfusion
- Dyspnea, chills, fever, noncardiogenic pulmonary edema
- Chest X-ray – bilateral infiltrates
- Treatment is supportive – oxygen and ventilatory support with low tidal volumes
- Treatment goal – to protect the lungs



## Massive transfusion

- The replacement by transfusion of more than 50 percent of a patient's blood volume in 12 to 24 hours
- Each unit of packed cells (300 mL) contains 200 mL of red cells
- In adults, will raise the hematocrit by 3 to 4%



## Massive transfusion

Consequences are due to the following properties

- The blood
- The preservatives and anticoagulants
- Biochemical reactions that occur during storage



## Hazards associated with massive transfusion

- Metabolic acidosis
- Hyperkalemia
- Citrate intoxication
- Microaggregate delivery
- Reduced O<sub>2</sub> carrying capacity (decreased 2, 3-DPG)
- Hypothermia
- Volume overload
- Dilutional coagulopathy



## Metabolic acidosis

pH of stored blood decreases (7.40 → 7.0 – 7.1) due to the following

- Addition of CPD to freshly drawn blood
- Ongoing metabolism of glucose to lactate

After 21 days, pH may be as low as 6.9



## Metabolic acidosis

1. Does rapid infusion of acidic banked blood lead to metabolic acidosis?
  2. Should sodium bicarbonate be administered empirically?
- Acid base balance is self-correcting as citrate from CDP is metabolized to endogenous bicarbonate



## Metabolic acidosis

Clinically patient will show signs of

- Hypotension
- Poor tissue perfusion
- Inadequate oxygenation

Is the metabolic acidosis due to

- Rapid transfusion?
- Lactic acidosis?



## Correcting metabolic acidosis

Arterial blood gas

- Base excess – best measure of metabolic acidosis
- Calculate bicarbonate dose from the volume to be treated (30% of body weight) and the base excess
- $0.3 \times \text{weight} \times \text{BE}$



## Hyperkalemia & stored blood

During storage

- $K^+$  moves out of RBCs to maintain electrochemical neutrality
- $H^+$  ions generated during storage redistribute

Rapid transfusion of PRBCs (> 90 – 120 mL/min) associated with  $\uparrow K^+$

What is the mechanism?



## Hyperkalemia & transfusion

Why does this cause hyperkalemia?

- One unit of PRBCs contains 20 – 60 mL of plasma

$K^+$  concentration in plasma varies:

- 19-35 mEq/L at 21 days

With rapid transfusion devices: 500 – 1000 mL of blood can be given in one minute

This scenario causes critical hyperkalemia, cardiac arrests have been documented



## Hyperkalemia – clinical signs

Electrocardiogram (ECG) changes

- Peaked T waves
- Prolonged PR interval
- Widened QRS complex

If ECG changes are observed

- Stop transfusion
- Administer IV calcium
- IV bicarbonate, insulin, and dextrose may be appropriate



## Citrate intoxication

- Leads to hypocalcemia

Clinical signs

- Hypotension
- Narrow pulse pressure
- ↑ intraventricular end-diastolic pressure
- ↑ CVP
- Prolonged QT interval
- Widened QRS complex
- Flattened T wave



## Blood preservatives and hypocalcemia

1. Citrate-phosphate-dextrose adenine (CPDA)
2. Additive Solution (AS) preservative – contains less citrate than CPDA

Citrate anticoagulates by chelation of ionized calcium

During massive transfusion most of the citrate administered is in fresh frozen plasma (FFP) rather than RBCs



## Blood preservatives and hypocalcemia

At normal transfusion rates – citrate is metabolized efficiently by the liver

Rapid administration of blood – temporarily ↓ ionized calcium levels

- Rapid transfusion is > 1 mL/kg/min
- 1 unit PRBCs / 5 minutes – in an adult



## Microaggregate delivery

With storage, aggregates form in the blood

- 2<sup>nd</sup> to 5<sup>th</sup> days – platelets
- After 10 days – fibrin, degenerated white cells, platelets, and macroaggregates of RBCs develop
- Microaggregates – implicated in the development of ARDS and the pathogenesis of pulmonary insufficiency
- Standard 170 micron filters remove larger “clots”
- 40-micron filters – efficiency is uncertain



## Microaggregate delivery

- Pulmonary injury and the development of ARDS are more often related to type and severity of injury versus the volume of blood transfused
- Hypotension and sepsis – greater role in ARDS than microaggregate delivery
- Microaggregates may be more closely related to TRALI



## Blood filters 170- vs. 40-micron

- Using a 170-micron standard set – may clog with repeated units
- Many clinicians use a micropore filter (40-micron) between the blood unit and administration set – this can be changed after 4 units of blood are administered



## Oxygen carrying capacity

- Diminished oxygenation due to inadequate oxygen-carrying capacity can have serious clinical implications
- Ischemic effects on the myocardium and brain
- Advanced hemodynamic monitoring and arterial blood gases allows calculation of oxygen delivery to tissues



## Oxygen delivery index (DO<sub>2</sub>I)

$$DO_2I \text{ (mL/min/m}^2\text{)} = CI \times 13.4 \times Hb \times SaO_2$$

CI = cardiac index

Hb = hemoglobin concentration

SaO<sub>2</sub> = arterial oxygen saturation

- DO<sub>2</sub>I may help estimate a deficit in oxygen supply
- Several studies show an improved outcome when supranormal DO<sub>2</sub>I levels >600 mL/min/m<sup>2</sup> have been achieved during resuscitation

*Miller et al, p 2796*



## Decreased 2, 3, DPG

- With storage → a progressive ↓ in 2, 3-diphosphoglycerate and intracellular ATP
- The oxyhemoglobin dissociation curve – shifts to the left → ↓ O<sub>2</sub> carrying capacity
- Transfusing 2, 3-DPG depleted blood while increasing the patient's hemoglobin value → less efficient oxygen delivery than would occur with native hemoglobin at the same hematocrit
- Levels return toward normal after 12 – 24 hours



## Acute normovolemic anemia

Hemoglobin 7 g/dL - most individuals

- Oxygen delivery adequate

Hematocrit 18% - 25% - healthy normovolemic individuals

- tissue oxygenation is maintained
- anemia tolerated



## Acute normovolemic anemia

Hemoglobin as low as 6 g/dL

- Myocardial lactate flux does not appear to be affected

Hematocrit 15% - 20%

- Heart produces lactic acid

Hematocrit 10%

- Heart failure occurs



## Hypothermia

Should be carefully avoided and aggressively corrected during massive transfusion

Has been associated with

- ↑ morbidity and mortality
- ↑ rates of infection

With ↓ body temperature

- Cardiac output declines
- Vasoconstriction and a left shift of the oxyhemoglobin dissociation curve → impaired tissue perfusion

- Metabolic acidosis may occur

Shivering ↑ O<sub>2</sub> consumption by 400%



## Volume overload

Circulatory volume overload occurs when blood or fluid is transfused too rapidly for compensatory fluid redistribution to take place

Permissive hypotension

- 1 – 2 liters of a balanced salt solution
- Systolic Blood pressure 80 – 100 mmHg

Minimizes

- Rates of additional blood loss
- Hypothermia
- Dilution of hemoglobin and plasma coagulation factors



## Coagulopathy

- Major trauma and/or blood loss initiates a cascade of coagulation abnormalities
- Includes a consumptive coagulopathy from tissue hypoperfusion → ↑ protein C levels
- The addition of a large amount of blood (6 – 10 units PRBCs) augments this coagulopathy



## Coagulopathy

Most important factors causing coagulopathy

- Volume of blood given
- Duration of hypotension/hypoperfusion

Well perfused, not hypotensive for long periods (e.g. 1 hour) → can tolerate multiple units of blood without coagulopathy



## Coagulopathy

Hypotensive patient who received many units of blood →

- coagulopathy resembling disseminated intravascular coagulopathy (DIC)
- Dilution of coagulation factors from stored banked blood



## Coagulopathy

### Differential diagnosis and clinical signs

Bleeding patient, with no preoperative coagulopathy

- Dilutional thrombocytopenia
- Low levels of factors V and VIII
- DIC - like syndrome
- Hemolytic transfusion reaction

Clinical signs

- Oozing into the surgical field
- Gingival bleeding
- Petechial bleeding – venipuncture sites
- Ecchymoses



## Dilutional thrombocytopenia

Independent of whether whole blood or PRBCs were given, few viable platelets exist when storage has been for > 24 hours

- After 6 hours of storage – 50% to 70% of the original in vivo activity
- After 24 hours – 10% of normal activity
- After 48 hours – 5% of normal activity



## Dilutional thrombocytopenia

- A platelet count of  $< 75,000 \text{ mm}^3$  → a hemorrhagic diathesis is likely to occur
- Although major emphasis has been placed on monitoring platelet count, the role of dilutional thrombocytopenia in the coagulopathy of massively transfused patients has been questioned



## Dilutional thrombocytopenia

Findings – platelet count rarely decreases to as low a level as would be predicted from dilution alone

Why?

- Platelets are released into the circulation from the spleen and bone marrow
- The presence of nonfunctional platelets

*Miller, 7<sup>th</sup> ed*



## Dilutional thrombocytopenia

- Platelets should not be given to treat laboratory evidence of thrombocytopenia unless clinical coagulopathy is also present
- Platelet count  $< 50,000$  to  $75,000 \text{ mm}^3$  - bleeding problem is likely and is probably a combination of dilutional thrombocytopenia and DIC
- Platelet therapy – appropriate in this situation



## Low levels Factor V and Factor VIII

- Most clotting factors are stable in stored blood, with two exceptions – factors V and VIII

In whole blood, after 21 days of storage –

- Factor V ↓ to 15% of normal
- Factor VIII ↓ to 50% of normal

Administration of fresh frozen plasma (FFP) has been recommended on a prophylactic or therapeutic basis



## Low levels Factor V and Factor VIII

This practice is of questionable benefit  
During surgery only

- 5% to 20% of factor V
  - 30% of factor VIII
- are needed for adequate hemostasis

- In massive transfusion factors V and VIII rarely decrease below levels required for adequate hemostasis



## NIH recommendations FFP administration

1985, National Institutes of Health,  
consensus conference

- There is little or no scientific evidence for the administration of FFP as part of the therapy for coagulopathy induced by multiple blood transfusions

JAMA, 1985



## NIH recommendations FFP administration

The following criteria should be used

- Generalized bleeding that cannot be controlled with surgical sutures or cautery
- Partial thromboplastin time at least 1.5 times normal
- Platelet count greater than 70,000 mm<sup>3</sup> (to ensure that thrombocytopenia is not the cause of bleeding)

JAMA, 1985



## Coagulation system

Clotting and fibrinolytic mechanisms  
Function of

- Clotting – prevent excessive blood loss
- Fibrinolysis – to ensure circulation within the vasculature



## Disseminated intravascular coagulation–like syndrome (DIC)

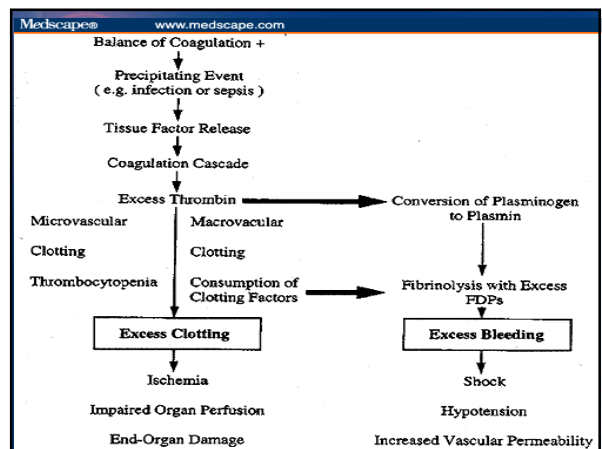
- Clotting system is deranged → disseminated fibrin deposition → the fluid blood is unclottable
- Microcirculation is altered → ischemic necrosis in various organs, particularly the kidney
- Unclottable blood → severe hemorrhagic diathesis



## DIC syndrome

- Specific reasons for its development usually not known
- Hypoxic acidotic tissues with stagnant blood flow probably releases tissue thromboplastin directly or through liberation of some toxin as possibly modulated through the protein C pathway
- The release of tissue plasminogen activator from damaged tissue may cause fibrinolysis

Brahi et al., 2007



## Bloodless medicine

Existing and emerging clinical strategies for medical care without allogenic blood transfusion

Developed in response to

1. Potential threat to the safety of donated blood
2. Rising costs related to blood and blood products
3. Blood supply shortage

*Shander & Rijhwani, 2005, p.193*



## Bloodless medicine Appropriate for all ages

Pharmacologic

- Desmopressin
- Epsilon aminocaproic acid
- Erythropoietin

Non-pharmacologic

- Intra- and post-operative cell salvage devices
- Pre-donation of autologous blood



## Multi-modal blood conservation

1. Preoperative optimizing of hemoglobin
2. Intraoperative acute normovolemia hemodilution (ANH)
3. Autotransfusion
4. Tolerance of anemia
5. Meticulous surgical techniques



## Multi-modal blood conservation

6. Endovascular vein grafting
7. On-site coagulation monitoring (thromboelastography and heparin concentration determination)
8. Targeted pharmacotherapy

*(Shander & Rijhwani, 2005, p. 197)*



## In summary

- Transfusions of blood and blood products, and crystalloid and colloid solutions have the potential for improving clinical outcomes in the perioperative setting
- Transfusion therapy is a practice surrounded by complex and controversial issues



## In summary

- Future research will no doubt lead to exciting discoveries that will continue to shape its practice
- Nurse anesthetists are uniquely situated to become experts on the implications and complications associated with transfusion therapy



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