

Transfusion Reactions

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Complications of transfusion

- **Acute hemolytic transfusion reaction**= rapid destruction of red cells immediately or within 24 hours of transfusion
- Most common cause is clerical error: ***misidentification of the patient***
- Hypotension, shock, consumptive coagulopathy & acute renal failure
- High mortality rate

Acute hemolytic transfusion reaction

- Rate 1 in 12,000 to 1 in 35,000 reactions per units transfused
- Fatal 1 in 100,000 to 1 in 600,000 units transfused
- ***74% of all fatalities are due to ABO incompatibility***
- Reported rates may underestimate actual occurrences

Conditions that destroy donor red cells

- Naturally occurring antibodies (ABO)
- Stimulated alloantibodies (anti-K, Jk^a)
- Autoantibodies
- Drug-induced antibodies
- Bacterial contamination
- Mechanical trauma associated with infusion
- Thermal trauma (heat or cold)
- Reconstitution of red blood cells with hypotonic solutions
- Equipment that damages blood cells extracorporeally

Conditions that destroy recipient red cells

- ABO incompatible plasma, cryoprecipitate, or plasma-derived products
 - (including platelet products which contain plasma)
- Infusion of large amounts of hypotonic solutions
- Mechanical trauma
 - (mechanical heart valves, microangiopathic syndromes)

Signs & Symptoms of Acute Hemolytic TR

- Fever
- Chills/ rigors
- Anxiety, feeling of dread
- Facial flushing
- Chest pain
- Abdominal pain
- Back & flank pain
- Nausea
- Vomiting
- Diarrhea
- Dyspnea
- Hypotension
- Hemoglobinuria
- Hemoglobinemia
- Pallor
- Icterus
- Oliguria/anuria
- Pain at transfusion site
- Diffuse bleeding
- Jaundice

Management of AHTR

1. Stop transfusion & maintain venous access
2. Rapid assessment of pt & requirements for basic & advanced support
3. Notify transfusion service, collect transfused units & tubing and return to BB
4. Reconfirm identity of blood units & pt
5. Collect appropriate patient blood specimens
6. Supportive approaches→

Management of AHTR

1. Maintain ***IV fluids*** at 3000 ml/M²/day with administration of sodium bicarbonate to keep pH >7.0
2. Diuretics:
 - ***Mannitol*** (20%) 100ml/ M² given over 30-60 min, then 30 ml/M²/hr for next 12 hrs.
 - ***Furosemide*** : Adults: 20-80 mg. / Infants & children: 1-2 mg/kg up to an adult dose
3. ***Dopamine***, low dose: 1-5 mcg/kg/min
4. Replacement of ***coagulation factors*** and ***platelets***
5. ***Heparin*** (controversial in severe DIC) enhances anti-thrombin III

Additional Transfusion Reactions

1. Delayed hemolytic TR (DHTR)
2. Febrile nonhemolytic (FNHTR)
3. Uncomplicated allergic (urticaria)
4. Anaphylactoid
5. Anaphylactic (ie. IgA-deficiency)
6. TRALI (Transfusion-Related Acute Lung Injury)
7. TACO (Transfusion-Associated Circulatory overload)
8. Septic Reaction
9. Post-transfusion purpura (profound thrombocytopenia
1-2 wks post-transfusion, rare)
10. Iron overload

Delayed Hemolytic Transfusion Reactions

- Antibody not detected at the time of XM
- Rapid secondary boost in antibody level after transfusion: Anamnestic response
- 1:2500 to 1:6000 transfusions

- Typically cause jaundice at day 5 onwards
- May cause hemoglobinuria
- Renal failure very rare
- Probably under-reported

Febrile Non-Hemolytic Transfusion Reaction

- Due to cytokines/bioactive proteins in donor plasma or
- Released after WBC antibody in recipient reacts with WBC antigen in product.
- Stop transfusion to clinically assess:
 - Consider acute hemolytic, and bacterial sepsis as part of differential
 - Report TR to lab, send bag and samples to lab for work up
 - Treat symptoms with antipyretic (acetaminophen)

Febrile nonhemolytic reactions

- Frequent 1: 650 – 1000*
- Mainly occur with red cells and platelets
- Usually start within 30 minutes
- Patient feels cold, shaking, rigors
- Temperature rises
- Diastolic BP rises
- Infected blood should also be considered when this type of reaction occurs

**Transfusion 2004; 44: 1-4*

Allergic reaction

- **Frequent 1 in 250**
- **Usually mild, self-limited**
- **Urticaria**
 - Antihistamine prevents**
- **Patient is allergic to something in the donor (foodstuff, medication, protein) or or in the pack (Latex)**
- **May need to use washed products**
- **If Donor is atopic**
 - Should not be allowed to donate**

Anaphylactic reaction

- **Severe anaphylaxis**
- **Bronchospasm, shock**
- **1:20,000 to 1: 50,000**
- **Usually seen in IgA deficient subjects**
- **They form antibodies to donor IgA**
- **They must receive IgA deficient products**

TRALI: Transfusion Related Acute Lung Injury

- **Severe and potentially fatal reaction to transfusion**
- **Associated with infused granulocyte antibodies and anti-HLA antibodies from donor**
- **Usually donor is multiparous female**

TRALI

- Chills, fever, dyspnea, non-productive cough, hypotension, 4-6 hours after transfusion
- Causes severe respiratory distress and hypoxemia
- CXR shows bilateral nodular infiltrates with no cardiac enlargement
- Pulmonary wedge pressure is normal

TRALI

- **Symptoms clear in 24 hrs**
- **CXR clears in 4 days**
- **Estimated frequency 1: 5,000 transfusions**
- **Underdiagnosed, often occurs in patients with other reasons for ARDS and is overlooked**

TRALI

- Donor antibodies activate Pt's WBC's which cause damage to blood vessels in lung tissue
- Then fluids and proteins leak into alveolar space/interstitium
- Mechanism similar to ARDS

TRALI

- **Management**
- Steroids
- Aggressive ventilatory support
- Hemodynamic support

TRALI

■ Prevention:

- Hemovigilance: Reporting reactions in order to screen involved donor for HLA and neutrophil antibodies
- UK: all male donor plasma
- ARC: moving in the direction of all male donor plasma

TACO: Transfusion-Associated Circulatory Overload

- **Cause:**
- **Iatrogenic** – physician induced rxn
- Fluid(s) administered faster than Pt circulation can accommodate volume load
- Some at risk types of pt.'s: congestive heart failure, renal failure, hepatic cirrhosis, normovolemic anemia

TACO

- **Signs & Symptoms**
- Cough
- Dyspnea
- Pulmonary congestion
- Headache
- Hypertension
- Tachycardia
- Distended neck veins

TACO

- **Management:**
- Place Pt in upright position, if possible, with feet in dependent position
- Diuretics
- Oxygen
- Morphine (if necessary)

TACO

■ Prevention

- Adjust transfusion flow rate based on Pt size and clinical status
- Consider dividing unit(s) into smaller aliquot(s) to better space apart blood component(s) pace of transfusion

Septic Reaction

■ Signs & Symptoms:

- Rapid onset of chills & fever
- Vomiting, Diarrhea
- Profound hypotension, Shock

■ Cause:

- Transfusion of bacterially contaminated blood components
- Common problem for platelet concentrates stored at room temp.

Septic Reaction

- **Management**
- Obtain blood cultures from Pt
- Return blood component bag(s) to blood bank for further laboratory work-up
- Treat septicemia with antibiotics
- Treat shock with fluids & vasopressors

Septic Reaction

■ Prevention

- Collect, process, store, transport, and transfuse blood components according to contemporary standards of practice (e.g. for FDA standards adhere to cGMP's – current good manufacturing practices – found in Code of Federal Regulations)
- Transfuse blood components within 1 to 2 hrs – do not exceed 4 hrs

Complications of Transfusion

- Immunomodulation
- Post-operative infections
- Transfusion transmitted infections
- Graft vs host disease

Transfusion Associated Graft Vs Host Disease (TA-GVHD)

Symptoms and signs:

- Skin rash trunk to extremities day 4 to 30**
- Fever day 4 to 23**
- Leukopenia day 11 to 30**
- Hepatitis**
- Secondary bacterial / fungal infections**
- Death day 12 to 65**

TA-GVHD

- **Cause / culprit: transfused lymphocytes**
- **May occur in immunosuppressed or immunocompetent persons**
- **In the immunosuppressed, leukemia and BMT patients are most at risk**
- **In immunocompetent persons:**
 - Donor is a homozygote for HLA haplotype carried by patient

TA-GVHD

- **In the non-immunosuppressed:**
 - **Areas with high rate of HLA homozygosity**
 - **Japan (1 in 400)**
 - **Open heart surgery patients**
 - **Cases where fresher blood is used**
 - **Those receiving blood from close family members (directed donations)**

TA-GVHD

- **Often missed or misdiagnosed**
- **Occurs in patients with other pathology**
- **Preventable by irradiation of cellular blood products: prevents the transfused lymphocytes (Graft) from attacking recipient (Host)**

TA-GVHD

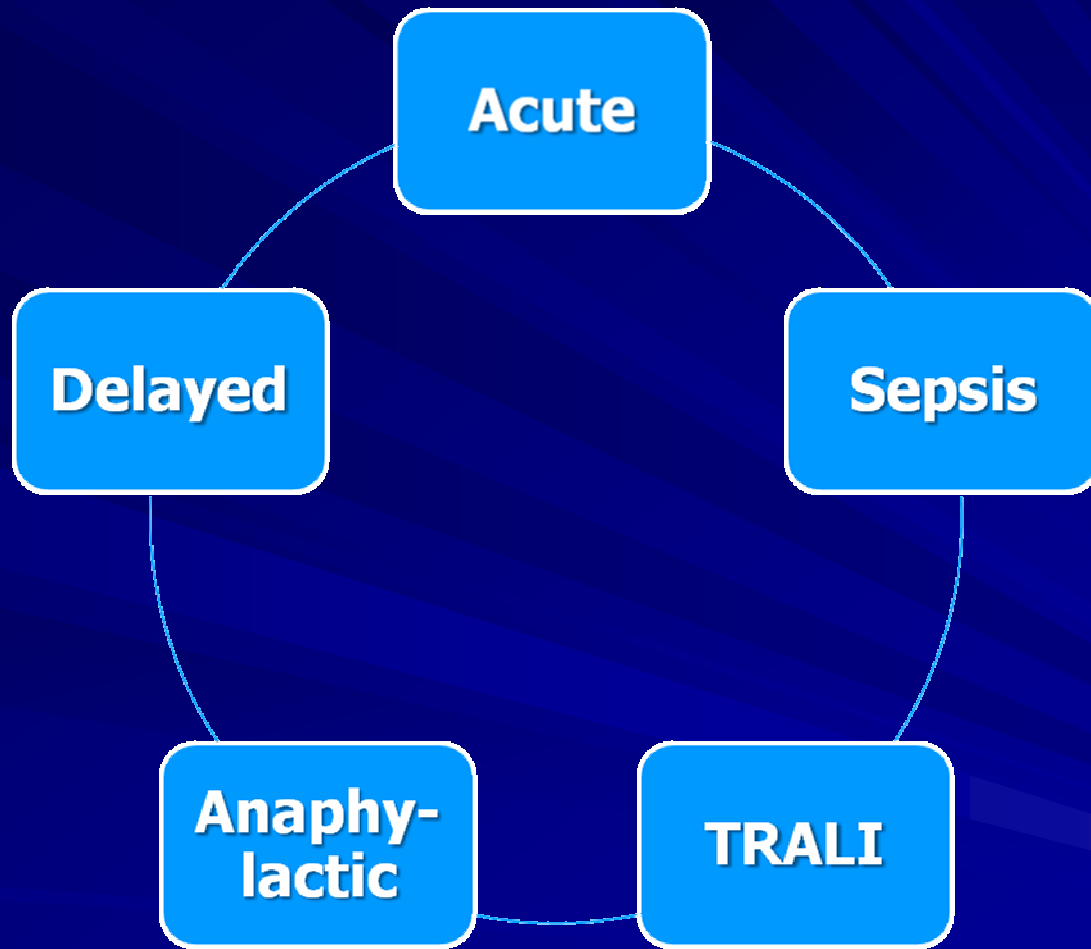
- Gamma irradiation virtually 100% effective in preventing transfusion-associated GVHD
- Irradiate all cellular products transfused to pts at risk
- Crosslinks DNA, prevents proliferation of lymphocytes
 - 25Gy to midplane of the blood container,
min 15Gy to any point of the irradiated field;
max dose not to exceed 50Gy

TA-GVHD

- Clear risk
 - Congenital immunodeficiency
 - Hodgkin's disease
 - CLL treated with fludarabine
 - Newborns with erythroblastosis fetalis
 - Directed donations (relatives)
 - Recipients of HLA matched platelets
- Probable risk
 - Other hematologic malignancies
 - Solid tumors treated with cytotoxic agents
 - Genetically homogeneous populations
 - Premature and possibly full-term neonates
- No defined risk
 - AIDS pts
 - Immunosuppressive medications

Laboratory Investigation of Transfusion Reactions

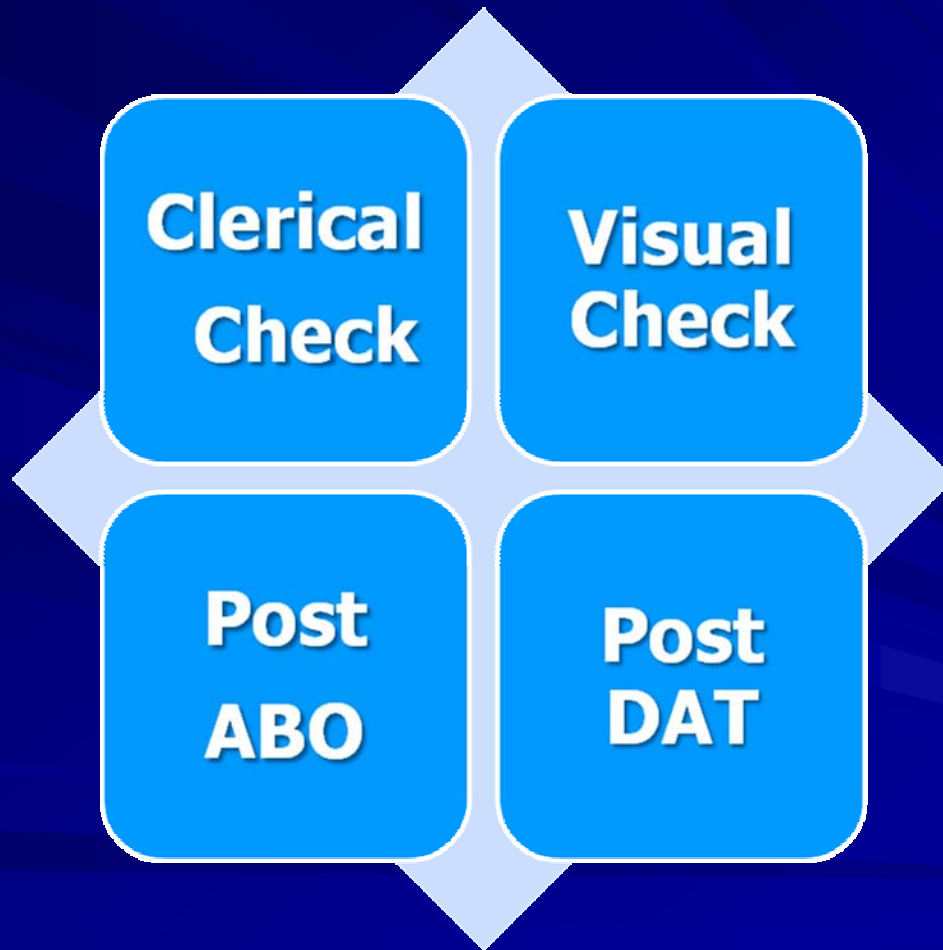
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October 24, 2008



Acute Reaction

1	Stop transfusion; keep line open - saline
2	Contact physician for instructions
3	Perform clerical check of patient and blood
4	Notify blood bank
5	Return blood unit, IV solution and tubing
6	Collect post-transfusion sample STAT
7	Complete transfusion reaction form

Standard Investigation



Why Do a Clerical Check?

- 🔴 Detect labeling errors
- 🔴 Detect patient identification errors
- 🔴 Treat patient for ABO incompatibilities
- 🔴 Prevent companion errors with another patient or another blood unit

Clerical Check - Bedside

At the bedside compare

- 🔴 Patient identification
- 🔴 Labels on blood unit

Clerical Check – Blood Bank

Compare post-transfusion sample/record

- 🔴 Pre-transfusion sample
- 🔴 Pre-transfusion test results
- 🔴 Blood unit labels
- 🔴 Inspect blood unit for color change
- 🔴 Confirm IV fluid is saline

Why Do a Visual Check?

Hemolysis in patient plasma may be a sign of an acute hemolytic reaction

- 🔴 Antibodies bind to antigens on transfused RBCs
- 🔴 Complement system activated
- 🔴 RBCs are destroyed
- 🔴 Free hemoglobin is released into the plasma

Destruction of 5mL of red cells may be visible

Visual Check for Hemolysis

- Observe **pink** or **red** color in plasma of post-transfusion sample
- Compare with pre-transfusion sample

Visual Check Problems

Hemolysis observed in plasma may be

- 🔴 **Myoglobinemia in trauma**
- 🔴 **Hemolysis in the donor unit**
- 🔴 **Underlying condition: AIHA, G6PD**
- 🔴 **Traumatic draw**

Collect second sample if hemolysis present

Why Repeat the ABO?

Sample	Wrong label
	Wrong patient
Lab	Double sample labels
	Specimen mix up
	Switched blood tags
Recipient ID	Wrong patient
	Wrong unit

Repeat Rh for additional confirmation

Post ABO Result

- 🔴 Compare to pre-transfusion ABO
- 🔴 Repeat pre-transfusion ABO if different
- 🔴 Explain mixed field agglutination

WBITs

Wrong Blood In Tube

- 🔴 Discovered by transfusion reaction
- 🔴 Not discovered if companion sample is same blood type
- 🔴 Missed during pre-transfusion testing when patient has no historical record

CAP TRM.30575

Does the facility have a plan to implement a system to reduce the risk of mistransfusion for non-emergent red cell transfusions?

Among the risk reduction options are:

- *Documenting the ABO group of the intended recipient on a second sample collected at a separate phlebotomy*
- *Utilizing a mechanical barrier system or an electronic identification verification system that ensures that the patient from whom the pretransfusion specimen was collected is the same patient who is about to be transfused.*

The use of a second manual banding system, while acceptable, is probably not as effective as the above two options.

Never Events

Never should have happened

- ❖ Incompatible blood transfusions are preventable
- ❖ Medicare and other insurers will stop paying for added costs of treatment
- ❖ Patients cannot be charged for error costs

Why Do a DAT?

Detect incompatibility

- 🔴 Patient antibodies coat transfused RBCs
- 🔴 Undetected antibodies
- 🔴 Donor antibodies coat patient RBC antigens

Key DAT Points

- 🔥 Wash EDTA cells thoroughly
- 🔥 2-5% cell suspension
- 🔥 Polyspecific, IgG, Complement AHG
- 🔥 Saline control
- 🔥 Centrifugation
- 🔥 Grade/record agglutination immediately
- 🔥 Incubate complement, if directed
- 🔥 IgG and Complement check cells
- 🔥 If post DAT positive, perform pre DAT

DAT Best Practice

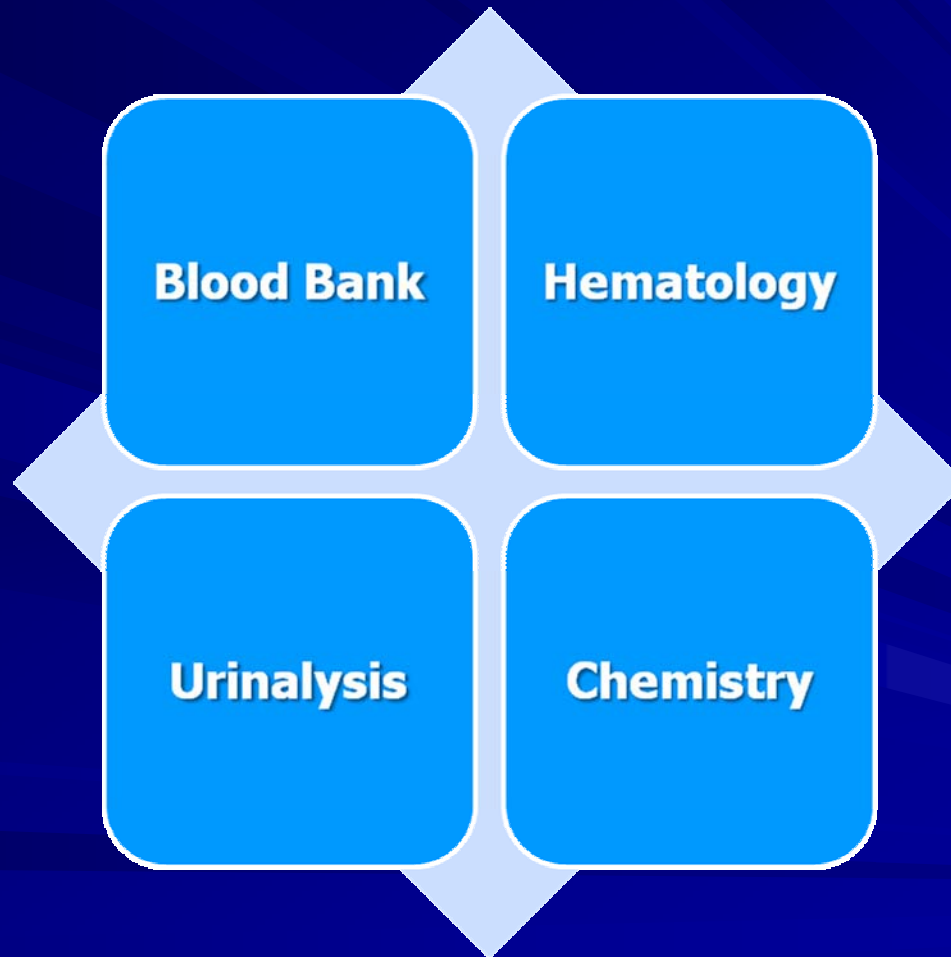
No delays start to finish!

- 🔴 Fresh cell suspension prevents IgG disassociation
- 🔴 Immediate centrifuging/reading prevents weakened agglutination

Post DAT Problems

- Positive before transfusion
- Invalid due to spontaneous agglutination
- Negative if transfused red cells are destroyed
- Negative with low levels of attached globulins

Positive Investigation



Urinalysis

- 🔴 Red or dark urine is observed
- 🔴 Visual check shows hemolysis
- 🔴 Additional test for intravascular hemolysis

Urinalysis Results

If blood is detected, exam microscopically

- 🔥 Hemoglobinuria= RBC absent (Hemolysis)
- 🔥 Hematuria = RBC present (R/O hemolysis)
- 🔥 Compare to pretransfusion results

Further Testing: Blood Bank

- 🔥 Post-transfusion DAT positive:
 - 🔥 **Elution**
 - 🔥 **Include ABO cells if indicated**
- 🔥 Antibody screen pre and post
- 🔥 AHG crossmatch pre and post
- 🔥 Antibody studies
- 🔥 Antibody enhancement studies

Acute Reaction Antibodies

ABO

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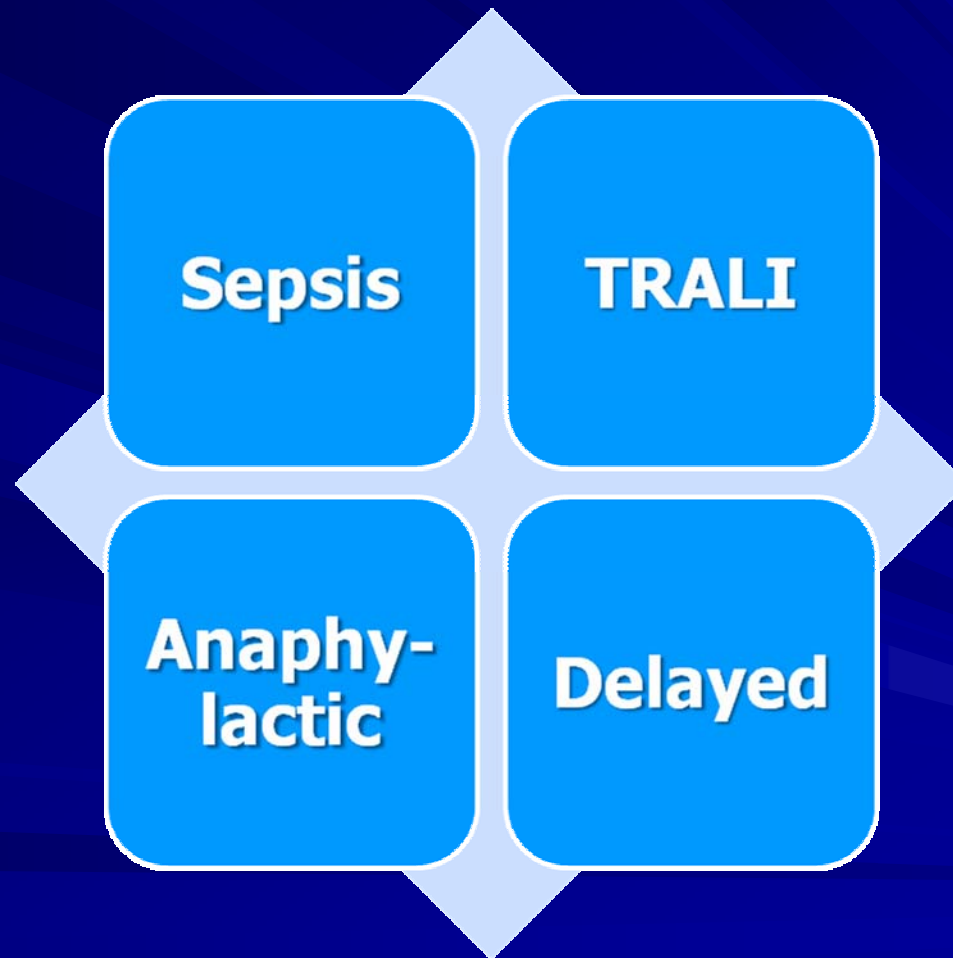
Rh

Others

Other Lab Testing

- 🔥 LDH increased
- 🔥 Bilirubin increased (5-7 hours)
- 🔥 Haptoglobin decreased
- 🔥 CBC, platelet count
- 🔥 Coagulation studies for DIC
- 🔥 BUN, creatinine, urine output

Other Investigations



Sepsis

Brown/purple/frothiness/bubbles observed in unit
Gram's stain and culture blood unit and patient

Problems:

Little or no blood left in bag

Contamination during sample collection

- 🔴 Gram negative organisms (*Yersinia enterocolitica*)
- 🔴 Coagulase- negative Staphylococcus
- 🔴 Others

TRALI

Test pre-transfusion and post-transfusion samples

- 🔴 BNP not increased
- 🔴 CBC may show decreased WBCs

Suspected TRALI

- 🔴 Report to blood center
- 🔴 Test patient for HLA and granulocyte antibodies/antigens
- 🔴 Test donor for HLA and granulocyte antibodies

Anaphylactic

- IgA deficient
- Track as special needs patient
- Special order IgA deficient products
- Washed RBCs and platelets may be given

Delayed Reactions

- Positive antibody screen
- New antibody
- Anamnestic or primary response
- Autocontrol/DAT may be + or -
 - Eluate if transfused < 2 weeks ago
- Antigen type pre-transfusion sample and donor segments

Delayed Testing

- Antibody identification studies
- Bilirubin may increase at 5 days
- CBC may show decreased Hgb
- Urinalysis may show hemoglobinuria

Abbreviated Investigation

Simple allergic

- 🔥 Few hives early in transfusion
- 🔥 Clerical check
- 🔥 Visual check
- 🔥 Omit repeat ABO and DAT

Reporting

FDA

- 🔥 Fatalities
- 🔥 BPDR for manufacturing errors

Supplier

- 🔥 Bacterially contaminated units
- 🔥 TRALI

Physician

- 🔥 All investigation reports
- 🔥 Includes delayed reaction reports

Questions?