# Adverse Transfusion Outcomes

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## Transfusion Safety

- **Complications of transfusion occur in less than 3% of transfusions.**
- **Mortality: annually, 30-35 transfusion-related deaths are reported to the FDA[1]**
- **Human error (ABO incompatible transfusions) caused 45% of transfusion fatalities[1]. How?**
  - **Misidentified sample**
  - **Lab error**
  - **Failure to identity of patient before transfusing**

**1. Sazama K, Transfusion 1990; 30:583-590**

## Serious Hazards of Transfusion Initiative (Great Britain)

- **Documents all deaths or major complications from transfusion**
- **Of 366 total reports, 191 (52%) involved incorrect blood transfused, and 55 (15%) were acute hemolytic reactions. Thus, in 67% of all the reports human error was the major issue.**
- **In only 12 of the reports (3%), transfusion-transmitted infection was the complication**

**from Williamson, et al. BMJ 1999; 319:16-19.**

## Where Do ABO errors occur?

- Patient's blood sample for crossmatch had wrong identifying information written on the label at sample collection time.
- Wrong unit of red cells transfused (failure to check blood recipient's identity).
- Laboratory testing error is least likely cause.

## Prevention of ABO errors

**Identification procedures performed properly are the single most important way to prevent deaths.**

## Transfusion: Adverse Outcomes

- Immune reactions
- Transfusion-transmitted infection
- Physiological/metabolic overload

## Immune Transfusion Reactions

| TYPE | RISK | MORTALITY |
|---|---|---|
| • Acute hemolysis | 1:12,100 | 21-40% |
| • Delayed hemolysis | 1:2,500? | Low |
| • Acute lung injury | 1:10,000 | 5% |
| • Allergic reaction | | |
| urticaria | 1:1,000 | 0 |
| anaphylaxis | 1:150,000 | 20% |
| • Febrile, non-hemolytic | 1:200 | Low |
| • GVHD | Rare | 100% |

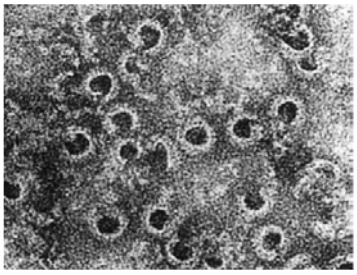
## Acute Hemolytic Reaction

- **Mechanism: Classical Complement cascade activation by IgM or IgG binding to red cell surface antigens.**
  - **Assembly of multiple copies of the "final attack complex" perforating the membrane.**
  - **Soluble complement fragments, C3a and C5a, affect smooth muscle, mast cells, endothelial, and phagocytic cells.**
  - **Activation of high molecular weight kininogen.**

## Acute Hemolysis Effects

- **Rapid onset of red cell destruction, within minutes after the start of transfusion.**
- **Nearby red cells which LACK the offending antigen may also be lysed as "innocent bystanders" due to the non-specific binding of C3b.**

## Complement Lesions



## Acute Hemolysis Effects 2

- Acute hemolysis rapidly releases $K^+$, hemoglobin, activated complement fragments, and membrane phospholipid into the entire vascular space, damaging organs "downstream."
- Complement may activate clotting , the kininogen system (bradykinin produced), and the fibrinolytic pathway.
- Release of cytokine IL-8 is triggered

## Clinical Presentation

- Onset: within minutes to a few hours
- Possible symptoms and signs
  - fever almost always present, but chills and rigors also occur frequently
  - flank pain, dark brown or red urine
  - shortness of breath, chest pain, cyanosis
  - abdominal pain, nausea, emesis, diarrhea
  - flushing, diaphoresis

## Acute Hemolysis Lab Effects

- **Most common laboratory findings:**
  - **positive direct antiglobulin test,**
  - **low serum haptoglobin,**
  - **sometimes visible plasma hemoglobin.**

## Acute Hemolysis Outcomes

- **Possible Consequences**
  - **Shock due to high levels of bradykinin or histamine.**
  - **Direct glomerular damage due to immune complexes/stroma deposited in glomerulus**
  - **Renal tubular damage secondary to shock**
  - **Direct cardiac effects of hyperkalemia**
  - **DIC**
  - **Death**

## Acute Hemolytic Reaction

**Fever (>2 degrees F.) in 100% of patients**
**Hypotension in 25% (subsequent excessive bleeding in 2/3 )**
**Oliguria (34% of patients)**
**Anuria (13%) with 83% mortality**
**Death in 21-40%**

## Clinical Management of Acute Hemolysis

- **Shock: correct volume deficits, use dopamine infusion to raise pressure**
- **Renal damage:**
  - **immediate: push output with fluids and furosemide diuresis: monitor output!**
  - **oliguric/anuric: limit fluids, watch $K^+$ level very closely--if elevated, start dialysis ASAP**

## Delayed Hemolysis

- **Hemolysis is gradual (days to weeks).**
- **Minimal signs and symptoms.... usually.**
- **Signs and symptoms may be severe in a susceptible patient (as in hemolytic disease of the newborn).**

## Delayed Hemolysis 2

- **Mechanism: IgG antibody binds to its target antigen exposing a phagocyte receptor binding site on the IgG molecule.**
- **Phagocytic cells destroy the red cell in an intracellular vacuole.**

## Delayed Hemolysis Effects

- Gradually increasing anemia, and slight (if any) elevations in bilirubin.
- Systemic complications are rare.
- Most common findings: mild fever, mild anemia, positive DAT.
- Complications: usually none
  - if complement activation occurs (very rare) then complications will be those of acute hemolysis.

## Delayed Hemolysis 3

- Frequency: 1:2,500 transfusions.
- This reaction is usually not clinically detected, but is found by hospital lab during subsequent testing.

## Febrile, Non-Hemolytic Reaction

- Two mechanisms:
  - Recipient anti-leukocyte antibodies triggering pyrogen release from blood donor WBC's in the transfused product.
  - Pyrogenic response due to cytokines (especially IL-6 and $TNF_{\alpha}$) elaborated in storage by leukocytes. 60% of febrile reactions.

## Febrile, Non-Hemolytic Reaction 2

- Frequency: 1:200 transfusions (most common form of transfusion reaction)
- Most common findings: Fever, chills, muscle pain.
- Less commonly: tachycardia, shortness of breath, blood pressure changes.
- Complications: usually none, but can be dangerous in elderly patients.

## Management of Febrile Reactions

- Administration of anti-pyretics
- Leukocyte-reduction filters will be effective for prevention in some patients
- For severe symptoms in the elderly, a small dose (100 mg ) of hydrocortisone I.V. may stop the reaction

## Allergic Reactions

- Mechanism: Poorly understood. Most likely donor protein-recipient protein interaction triggering tissue mast cells to release histamine, either localized in skin (urticaria) or systemic (anaphylaxis).

## Allergic Reactions 2

- **Frequency: Urticaria= 1:1000 transfusions. Anaphylaxis=1:150,000 transfusions.**
- **Most common findings: Urticaria , but very rarely, anaphylaxis (laryngeal spasm, dyspnea, hypotension) can occur.**
- **Outcomes: urticaria = none; anaphylaxis can be fatal.**

## Management of Anaphylaxis

- **I.V. (preferred) or subcutaneous epinephrine ASAP**
- **Oxygen by mask**
- **Antihistamine I.V. or orally**
- **Pressor agents if BP fails to respond**

## Acute Lung Injury

- **Mechanism: Uncertain--? activation of the alternate pathway of complement by donor leukoagglutinating antibodies.**
- **Recipient granulocytes adhere to each other in masses.**
- **Aggregates lodge in lungs causing severe hypoxia. $pO_2$ and $O_2$ saturation are low.**

## Acute Lung Injury 2

- Frequency: 1:10,000 transfusions.
- Signs/symptoms:
  - abrupt (minutes to several hours) onset of cyanosis, rapid breathing, rapid pulse (NO sign of airway obstruction)
  - hypotension occurs in severe cases
  - fever may or may not be present
- Complications: Respiratory distress syndrome, death.

## Clinical Management of Acute Lung Injury

- Oxygen, high percentage via mask, or if needed, intubate and respiratory support with PEEP
- Monitor BP and $O_2$ saturation
- I.V. bolus high-dose steroids (1-2 grams methylprednisolone) ASAP
- Pressor agents if needed

## Acute Post-transfusion Graft versus Host Disease

- Mechanism: donor lymphocytes engraft in a recipient that is unable to reject them, usually because of some underlying immune deficiency state (congenital, bone marrow transplant).
- Cytotoxic rejection response which affects skin, gut, liver, and bone marrow.
- Most common findings: skin rash, liver damage, diarrhea, pancytopenia.

## Acute Post-transfusion Graft versus Host Disease 2

- **Frequency: unknown, but extremely rare in the U.S.**
- **Complications: death. Post-transfusion GvH disease, unlike marrow transplant-associated GvHD, is almost always fatal.**
- **Prevention: Gamma Irradiation of components. 2500 centiGray dose**

## Questions?