# Transfusion Reactions in the Hospital Setting

## Definition and Epidemiology

Transfusions involve the administration of blood products (packed red blood cells [PRBCs], platelets, plasma, cryoprecipitate) to treat anemia, coagulopathy, or thrombocytopenia. Transfusion reactions are adverse events triggered by immune, allergic, or non-immune mechanisms during or after transfusion.

Prevalence ~10-15 million transfusions occur annually in the U.S.; reactions occur in 1-5% of transfusions (febrile non-hemolytic most common, ~1%). Severe reactions (e.g., TRALI, hemolytic) are rare (<0.1%).

Risk Factors Prior transfusions, pregnancy (alloimmunization), HLA mismatches, high transfusion volume.

Rare Demographics Sickle cell disease (alloantibody risk), transplant recipients (GVHD), IgA deficiency (anaphylactic reactions).

## Pathophysiology

- Mechanisms Transfusions restore oxygen delivery (PRBCs), clotting factors (plasma, cryoprecipitate), or platelet function. Reactions occur via immune (e.g., ABO mismatch, anti-HLA antibodies), allergic (e.g., IgE-mediated), or non-immune (e.g., volume overload) pathways.
- Effects Hemolytic reactions cause intravascular hemolysis, releasing free hemoglobin, leading to AKI and DIC. TRALI results from anti-HLA antibodies activating neutrophils, causing pulmonary edema. TACO overloads the heart, leading to hydrostatic pulmonary edema.
- Molecular Pathways In hemolytic reactions, IgM/IgG antibodies trigger complement (C3b, C5a), lysing RBCs. TRALI involves IL-8 and leukotriene B4, promoting alveolar damage. Allergic reactions involve mast cell degranulation (histamine, tryptase).
- Key Pathway Antigen-antibody interaction or cytokine release → Immune activation or fluid overload → Organ dysfunction (kidneys, lungs, heart).

## Causes

| Category | Common Reactions | Rare Reactions | Notes |
|---|---|---|---|
| Immune-Mediated | Acute hemolytic (ABO mismatch), febrile non-hemolytic | Delayed hemolytic, GVHD | ABO mismatch: Clerical error, 1:40,000 |
| Allergic | Urticarial, anaphylactic | Post-transfusion purpura | Anaphylaxis: IgA deficiency, anti-IgA |
| Non-Immune | TACO, transfusion-related sepsis | Iron overload, citrate toxicity | TACO: Common in CHF, elderly |
| Pulmonary | TRALI | Air embolism | TRALI: Anti-HLA/HNA antibodies |
| Infectious | Bacterial contamination | CMV, Babesia | Bacterial: Platelets > PRBCs |
| Metabolic | None | Hyperkalemia, hypocalcemia | High K+ in stored PRBCs |

## Clinical Presentation

### Symptoms

- Fever, chills (febrile, hemolytic, septic)
- Chest pain, dyspnea (TACO, TRALI, hemolytic)
- Urticaria, pruritus (allergic)
- Rare Jaundice (hemolytic), purpura (post-transfusion), rigors (anaphylaxis)

### Exam

- Tachycardia, hypotension (hemolytic, anaphylactic, septic)
- Pulmonary crackles, JVD (TACO)
- Rash, angioedema (allergic)
- Rare Flank pain (hemolytic), cyanosis (TRALI), bleeding (GVHD)
- Red Flags SBP <90 mmHg, SpO2 <90%, hemoglobinuria, respiratory failure

## Labs and Studies

### Labs

- Direct Coombs Test Positive in hemolytic reactions (IgG/C3d on RBCs)
- LDH, Haptoglobin Elevated LDH, low haptoglobin (hemolysis)
- CBC Hemoglobin drop (hemolysis), thrombocytopenia (post-transfusion purpura)

- CMP Bilirubin >2 mg/dL, Cr rise (AKI, hemolytic)
- Advanced Tryptase (anaphylaxis), HLA/HNA antibodies (TRALI), blood cultures (sepsis)

### Imaging

- CXR Pulmonary edema (TACO, TRALI), bilateral infiltrates (TRALI)
- Echocardiogram EF assessment in TACO, rule out CHF
- Advanced CT chest (TRALI vs. ARDS), PET-CT (GVHD tissue involvement)

### Other

- Urinalysis Hemoglobinuria (hemolytic), myoglobinuria (rhabdomyolysis mimic)
- Blood Bank Workup Clerical error check, crossmatch, antibody screen
- Advanced Flow cytometry (GVHD, T-cell chimerism), genetic testing (IgA deficiency)

## Diagnosis

- Criteria Adverse symptoms (fever, dyspnea, rash) during/within 6h of transfusion + lab/imaging evidence (e.g., Coombs, CXR) confirming reaction type.
- Differential MI, sepsis, ARDS, pulmonary edema (CHF), drug reaction.

### Flowsheet

- Step 1 Stop Transfusion Fever, hypotension, or dyspnea → Halt infusion, secure IV access
- Step 2 History/Exam Timing, symptoms (fever, rash, lungs), transfusion history
- Step 3 Labs Coombs, LDH, haptoglobin, bilirubin; blood cultures if septic
- Step 4 Imaging CXR (TACO, TRALI), echo (TACO)
- Step 5 Classify Reaction Hemolytic (Coombs+), TRALI (bilateral infiltrates), TACO (JVD, BNP)

## Treatment

General Principles Stop transfusion, stabilize patient, and treat specific reaction type while reporting to blood bank.

### Supportive Care

- IV Fluids NS 500 mL bolus for hypotension (avoid in TACO)
- Oxygen 2-6 L/min NC for SpO2 <92%; BiPAP/intubation for TRALI
- Monitoring Telemetry, urine output, serial labs (Hgb, Cr)

### Specific Therapies

- Acute Hemolytic Hydration (NS 100-200 mL/h), furosemide 20 mg IV (AKI prevention)
- Febrile Non-Hemolytic Acetaminophen 650 mg PO/IV, continue transfusion if mild
- Allergic Diphenhydramine 25-50 mg IV, epinephrine 0.3 mg IM (anaphylaxis)
- TACO Furosemide 20-40 mg IV, oxygen, upright positioning
- TRALI Supportive (O2, ventilation), avoid diuretics; report to blood bank
- Advanced IVIG (GVHD, post-transfusion purpura), plasmapheresis (refractory hemolytic)
- Rare Reactions Doxycycline 100 mg IV (sepsis), dantrolene (hyperkalemia-induced rigidity)

### Prevention

- Pre-transfusion ABO verification, leukoreduction (febrile, CMV)
- HLA-matched platelets (TRALI risk), washed RBCs (IgA deficiency)

### Monitoring

- Serial Hgb, LDH q4-6h (hemolytic)
- Daily CXR, BNP in TACO/TRALI
- Blood bank follow-up for antibody identification

## Complications

### Acute

- AKI Hemoglobin-induced tubular injury (20-30% of hemolytic reactions)
- ARDS TRALI, severe sepsis (5-10% mortality)
- DIC Hemolytic or septic reactions (rare, 1-2%)

### Long-Term

- Alloimmunization Anti-Rh/Kell antibodies, complicates future transfusions
- Iron Overload Chronic transfusions (e.g., sickle cell)

- Rare GVHD (1:1,000,000, immunocompromised), transfusion-associated microchimerism

## Clinical Scenarios

### Case 1 Acute Hemolytic Reaction

- Presentation 65 y/o F receiving PRBCs for anemia develops fever, flank pain 30 min into transfusion. Vitals BP 90/60, HR 110, SpO2 94%, RR 20. Exam Hemoglobinuria, tachycardia.
- Labs/Studies Coombs positive, LDH 800 U/L, haptoglobin <10 mg/dL, bilirubin 3 mg/dL.
- Interpretation Acute hemolytic reaction, likely ABO mismatch.
- Management Stop transfusion, NS 200 mL/h, furosemide 20 mg IV. Blood bank notified, crossmatch rechecked. AKI resolved by day 3.

### Case 2 TRALI

- Presentation 50 y/o M post-surgery receives plasma, develops dyspnea, hypoxia 2h later. Vitals BP 120/80, HR 100, SpO2 88%, RR 28. Exam Bilateral crackles, no JVD.
- Labs/Studies CXR Bilateral infiltrates, BNP normal. Anti-HLA antibodies detected.
- Interpretation TRALI, plasma-triggered.
- Management Stop transfusion, O2 10 L/min non-rebreather, BiPAP. Supportive care in ICU. Recovery by day 5, blood bank restricts donor.

### Case 3 Anaphylactic Reaction (Rare)

- Presentation 40 y/o F with IgA deficiency receives PRBCs, develops urticaria, wheezing 5 min into transfusion. Vitals BP 80/50, HR 120, SpO2 90%, RR 30. Exam Angioedema.
- Labs/Studies Tryptase 50 ng/mL, normal Coombs. IgA <7 mg/dL confirmed.
- Interpretation Anaphylactic reaction, IgA deficiency.
- Management Stop transfusion, epinephrine 0.3 mg IM, diphenhydramine 50 mg IV, hydrocortisone 100 mg IV. Washed RBCs for future transfusions. Stabilized by 6h.

## Expert Tips

- Verify ABO compatibility twice; clerical errors cause most hemolytic reactions
- Use leukoreduced blood to reduce febrile and CMV transmission risks

- Suspect TRALI in hypoxia within 6h of transfusion; CXR and BNP differentiate from TACO
- Administer epinephrine immediately for anaphylaxis; delay risks airway closure
- Monitor urine output in hemolytic reactions; early hydration prevents AKI
- Pitfall Missing TACO in elderly; JVD and BNP >500 pg/mL are clues
- Advanced HLA/HNA antibody testing post-TRALI; use solvent-detergent plasma to reduce risk

## Key Pearls

- Stop transfusion immediately for any reaction; assess ABCs
- Hemolytic reactions show Coombs positivity, hemoglobinuria
- TRALI causes bilateral infiltrates; TACO has JVD, elevated BNP
- Allergic reactions respond to antihistamines; anaphylaxis needs epinephrine
- Rare IgA deficiency requires washed or IgA-deficient blood products

## References


UpToDate “Transfusion Reactions: Diagnosis and Management” (2025)

AABB Guidelines “Standards for Blood Banks and Transfusion Services” (2023)

NEJM “Transfusion-Related Acute Lung Injury” (2024)

Blood “Management of Hemolytic Transfusion Reactions” (2024)

J Allergy Clin Immunol “Anaphylactic Transfusion Reactions” (2023)