

# Acute Transfusion Reactions

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# Objectives

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To develop an approach to the management of acute (within 24h) transfusion reactions

To discuss the most common transfusion related reactions categorized according to

Fever

Dyspnea

Allergy

# Frequency of Transfusion Reactions: **NOT UNCOMMON**

Reaction	Frequency
FNHTR	1/20 platelet pools, 1/300 RBC
Hives	1/100
TACO	1/700
Bacterial contamination	1/1000-10,000 platelet pools, 1/50,000 RBC
TRALI	1/10,000
Anaphylaxis	1/40,000

FEVER

# Approach to Acute Transfusion Reactions

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## For All Acute Reactions

1. **STOP** the Transfusion
2. Check patient ID with ID on component
3. Report to the Transfusion Medicine Laboratory
4. Return the unit

# Case 1

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41 year old male with lymphoma receiving chemotherapy,  
hemoglobin 60 g/L, neutrophil count  $1.5 \times 10^9/L$

Transfused 2 U RBCs

4 hours later, fever  $40^{\circ}C$ , chills, rigors

Hemoglobin 70 g/L

# The most likely diagnosis is

Acute hemolytic  
transfusion reaction

Hyperhemolytic  
transfusion reaction

Delayed hemolytic  
transfusion reaction

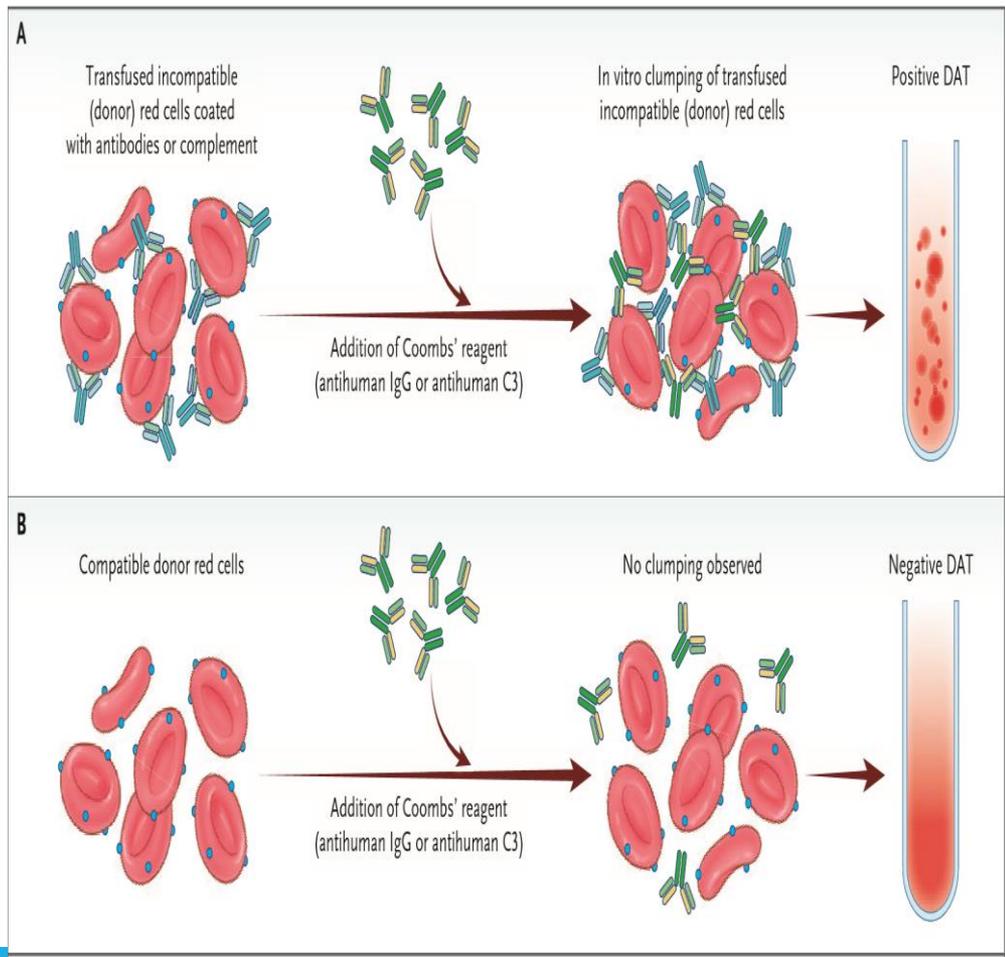
Bacterial sepsis  
secondary to transfusion

# Laboratory Tests for Acute Hemolytic Transfusion Reactions: Show the Incompatibility

To show an incompatibility between donor and recipient

Direct antiglobulin test (DAT) and Indirect antiglobulin test (IAT)

Group and screen



# Laboratory tests for acute hemolytic transfusion reactions: Show the effects of the incompatibility

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To determine the effects of the incompatibility, red cell destruction

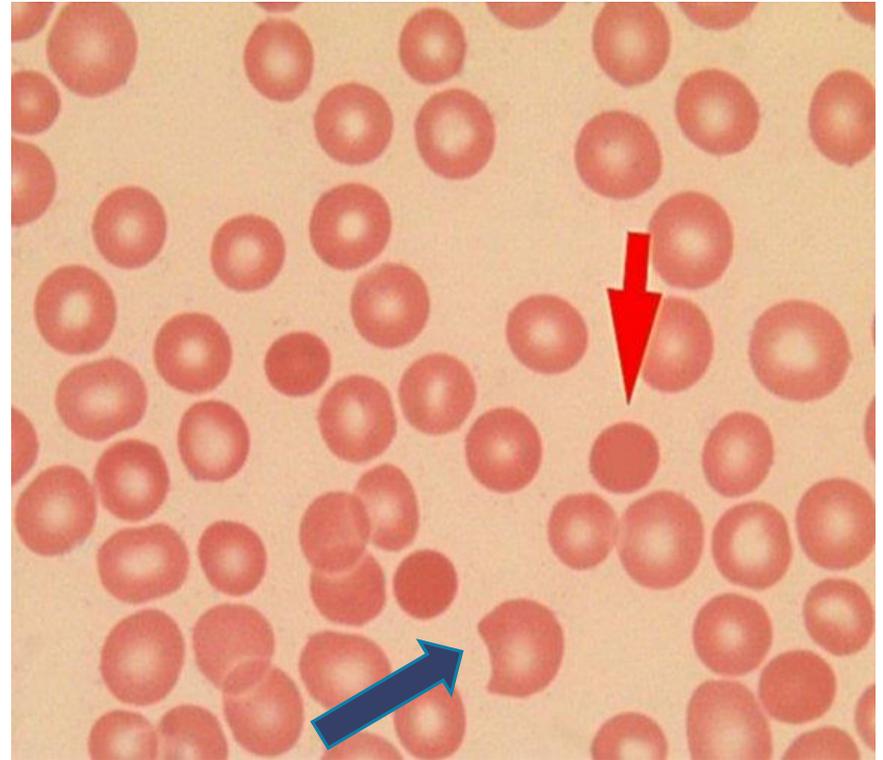
CBC (degree of anemia),  
peripheral smear (spherocytes,  
schistocytes)

Hemolytic screen

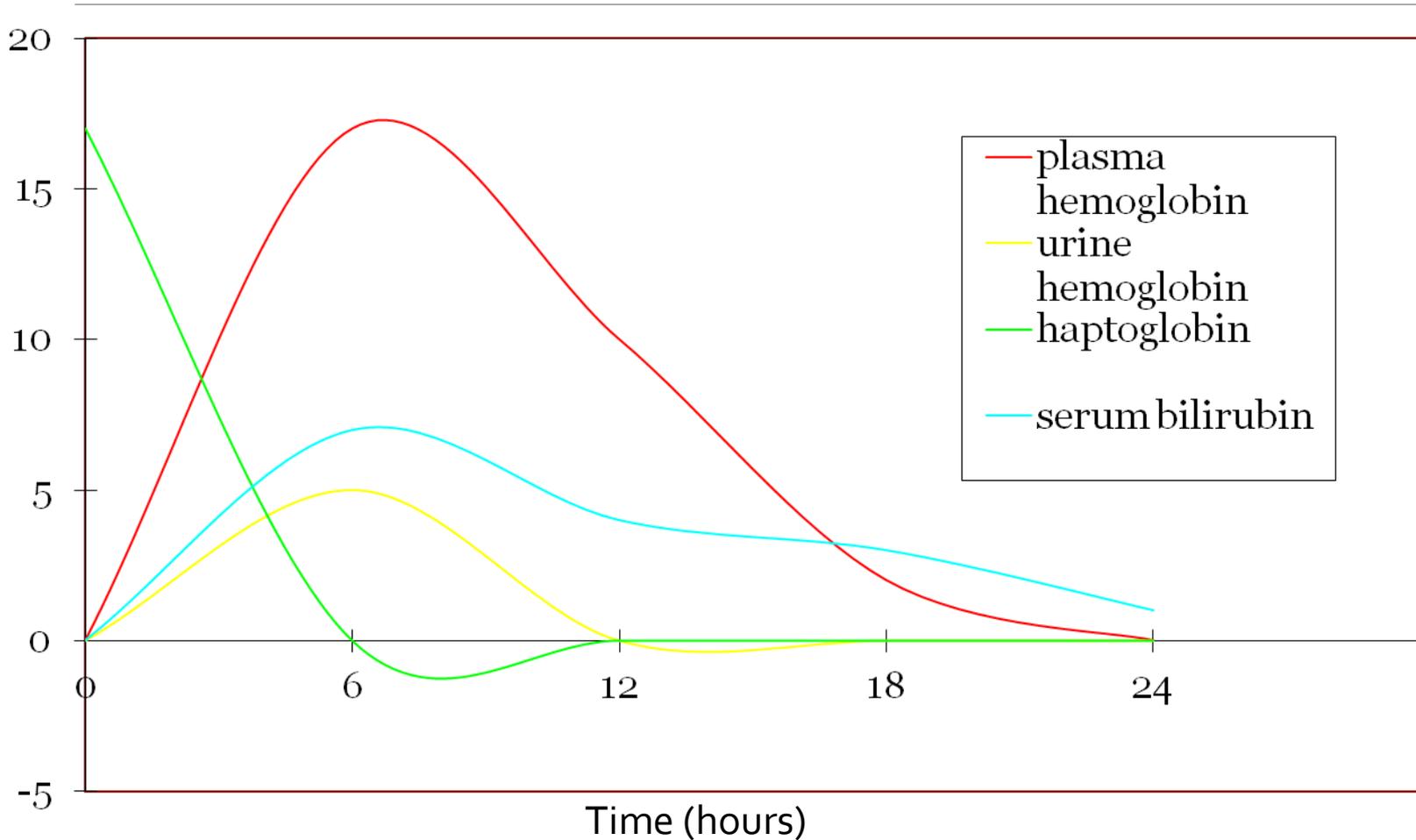
LDH, bilirubin, haptoglobin,  
reticulocytes

Coagulation screen (DIC)

Creatinine



# Hemolytic parameters with acute intravascular hemolysis



# Etiologies of hemolytic transfusion reactions

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## IMMUNE CAUSES

ABO incompatible hemolytic transfusion reaction

Transfusion error

Other red cell antigens: Kell, Duffy, Kidd

Emergent use of uncrossmatched RBCs

## NON-IMMUNE CAUSES

Osmotic stress –cryopreserved cells  
inappropriately washed

Thermal

Hypotonic solution

Conditions exacerbated by transfusion:  
Autoimmune hemolytic anemia and drug induced anemia

# Outcome of acute intravascular hemolysis secondary to ABO incompatibility

<10% are fatal

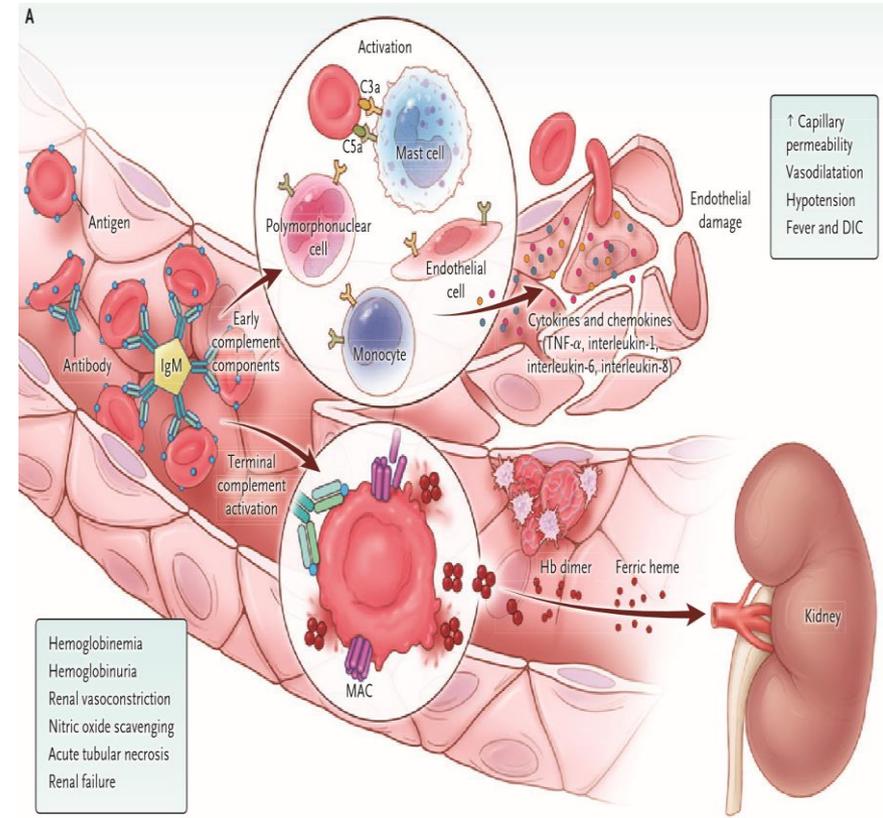
75% of all fatal hemolytic transfusion reactions are secondary to ABO

Dependant on the volume of blood

Most fatalities occur with  $\geq 200$  ml

Prevention

CSTM standards requires to G&S prior to transfusion



# Management summary of suspected hemolytic transfusion reactions

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Maintain urine output-crystalloids  $\pm$  diuretics  
100 mL/hour for approximately 24 hour to increase renal  
clearance, dialysis may be necessary

# Hyperhemolysis leads to an acute reduction in Hb < pretransfusion Hb

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Reticulocytopenia

May occur within 7 days: DAT may not be positive

After 7 days, DAT may be possible

A medical emergency as may be life threatening

Occurs in 1-19% of sickle cell disease, also other diseases

Further transfusion will exacerbate the hyperhemolysis

IVIg, corticosteroids, erythropoietin,

Eculizumab, rituxan are potential interventions

## Case 2

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18 year old female with AML admitted with febrile neutropenia

Treated with Piperacillin and gentamycin

3 days following admission she receives 1 adult unit of platelets  
for a platelet count of  $20 \times 10^9/L$

Immediately following transfusion, has a fever of  $39^{\circ}C$  and rigors

What is the likely diagnosis?

# What is the likely diagnosis?

Sepsis secondary  
to platelet  
transfusion

Sepsis

Acute hemolytic  
transfusion reaction

Unclear presently

# Bacteria in blood components may be from

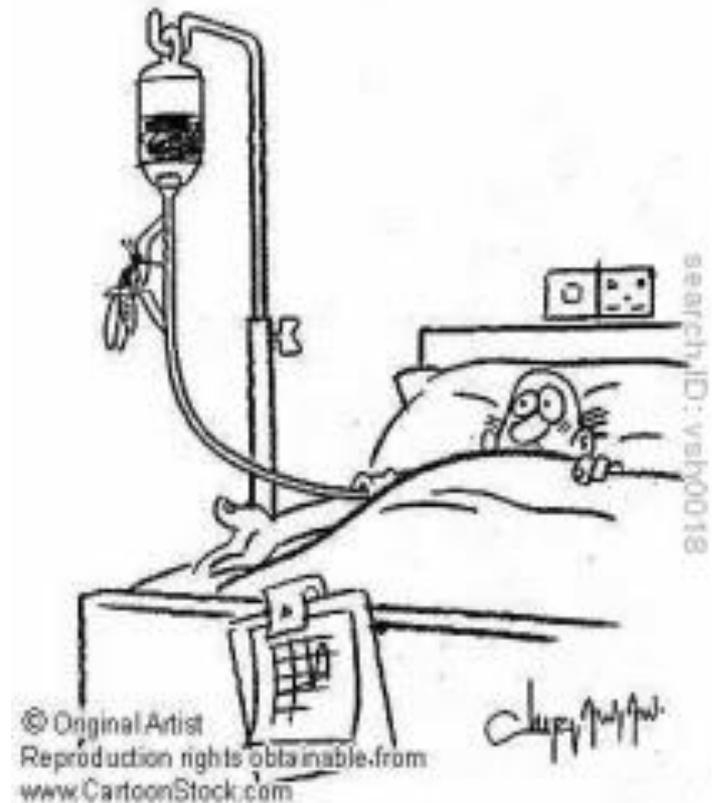
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Phlebotomy

Skin disinfection, donor  
skin plug

Donor bacteremia

Contamination from the  
environment



# Outcome of bacterially contaminated transfusion

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Immunosuppressed and older individuals with poor nutritional status are more susceptible to poorer outcomes

3-year-old girl with AML- platelet transfusion before a CT scan–guided drainage of pleural fluid

Treated with Meropenem

Within minutes of completing the transfusion-febrile, confused, and hypotensive

Died of multisystem organ failure 21 hours after transfusion

# The more common organisms causing bacterial sepsis...

Product	Organism
Red cells	Yersinia enterocolitica Pseudomonas spp Serratia spp
Platelets	Staphylococcus aureas and epidermidis Propionibacterium acnes Bacillus cereus

# Management of bacterial contamination/sepsis

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Supportive care-maintain IV access and infuse saline

Culture everything

Broad spectrum antibiotics

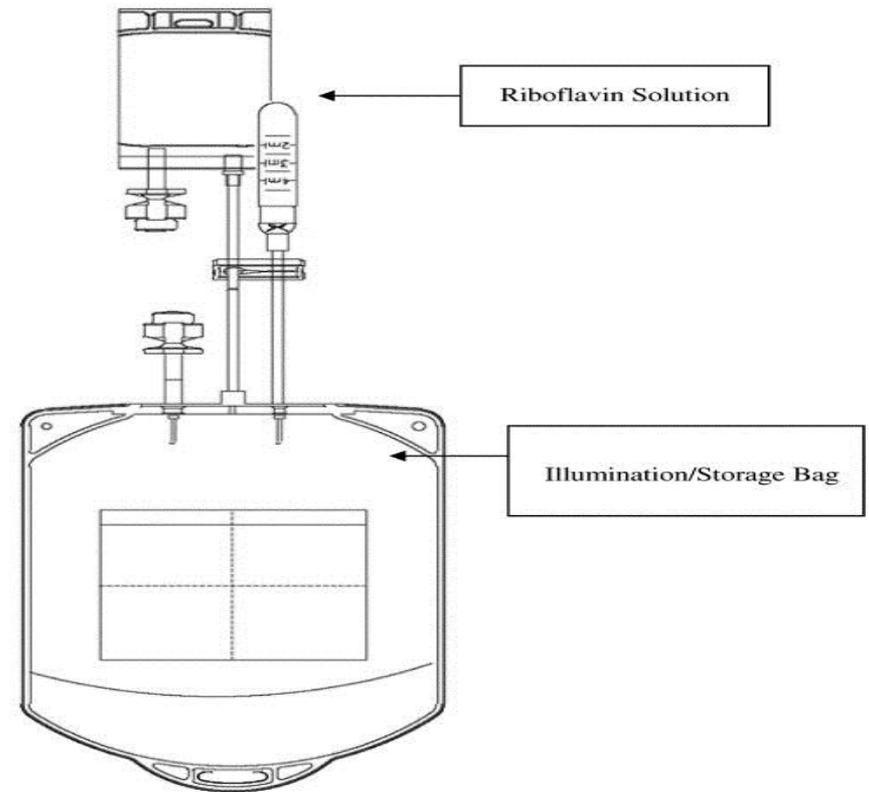
Do not wait for cultures to start antibiotics



# Pathogen inactivation reduces bacterial contamination in addition to culture of blood component

Photodynamic or photochemical method to the reduce viruses, bacteria, and protozoa

Mirasol system uses riboflavin and UV light to introduce irreparable lesions into nucleic acids inhibiting pathogens and leucocyte replication



# Febrile non Hemolytic Transfusion Reaction is a Diagnosis of Exclusion

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Type and screen: compatibility

DAT results: negative

Gram stain: negative

Culture: negative

CBC: unchanged

# Febrile non Hemolytic Transfusion Reactions

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Fever usually within 4 hours:  $>1^{\circ}\text{C}$  &  $> 38^{\circ}$

Symptoms may occur without fever and include

Rigors, pain, headache, nausea, vomiting

Hypertension

Tachycardia

Diarrhea

Cough

Anxiety

# Febrile non hemolytic transfusion reactions are mediated by

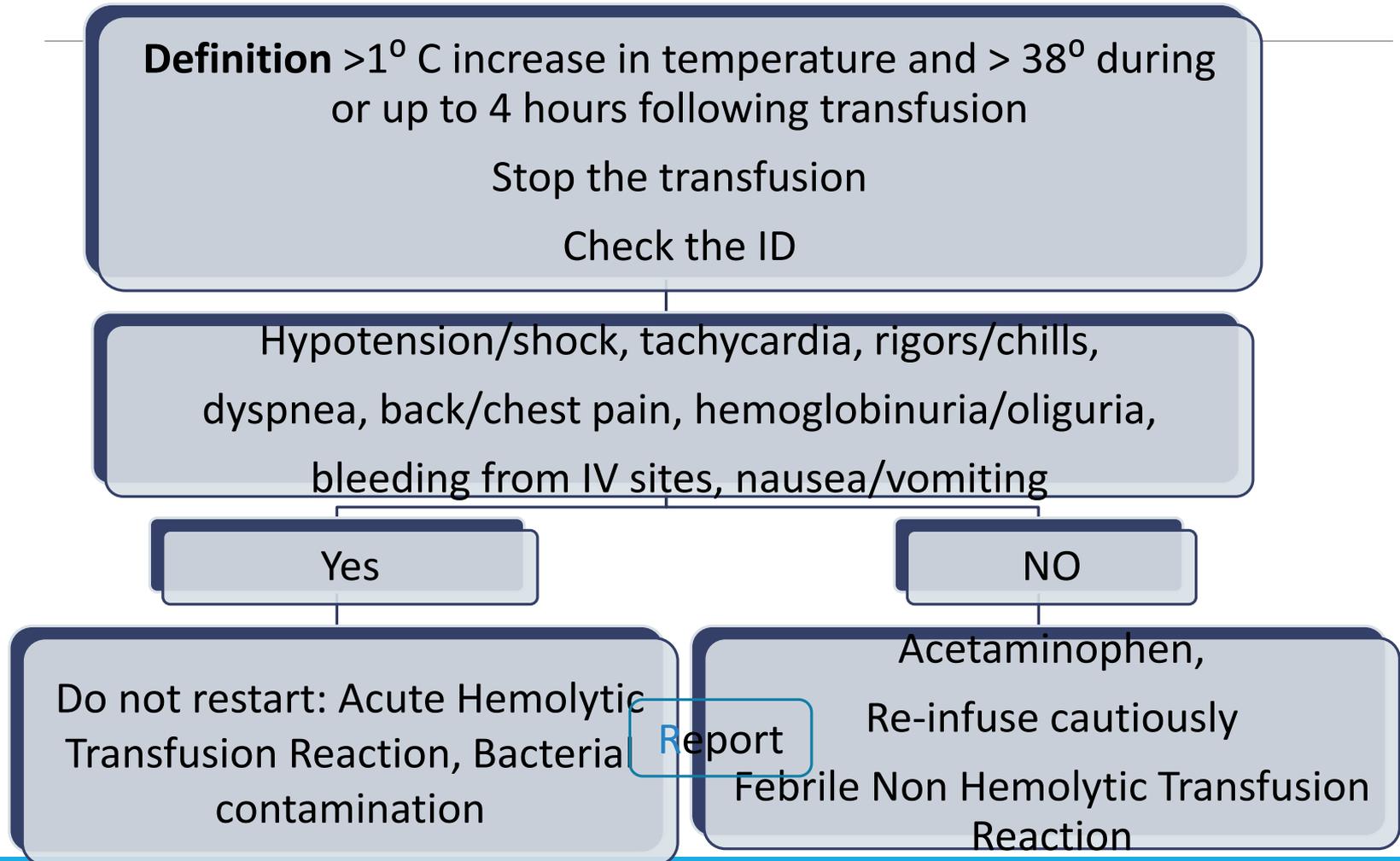
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Antileukocyte antibodies present in recipient plasma

Antileukocyte antibodies in recipients interact with residual donor WBCs to resulting in activation and release of mediators of fever and inflammation, e.g. TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 (cause of FNHTR secondary to red cells)

And/or biologic response modifiers that accumulate in blood products during storage e.g. release of cytokines, chemokines, and byproducts of the complement cascade during storage (cause of FNHTR from platelets)

# Summary: Management of Fever Secondary to Transfusion



DYSPNEA

## Case scenario

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40 year old male with AML, creatinine 150  $\mu\text{mol/L}$

Receives 4 units of plasma for an INR of 1.6 prior to a bone marrow biopsy

Following the transfusion acutely dyspneic, 10 mmHg drop in systolic blood pressure, chest x-ray shows bilateral chest infiltrates

# The most likely diagnosis is

Transfusion related acute  
lung injury (TRALI)

Transfusion associated  
circulatory overload (TACO)

Pneumonia

Transfusion associated  
anaphylaxis

# Transfusion Associated Circulatory Overload (TACO)

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“Pulmonary edema following blood transfusion is a frequently encountered and potentially avoidable clinical complication”

Occurs during or within 12 hours of transfusion

Risk factors for TACO:

- chronic renal failure

- a past history of heart failure

- hemorrhagic shock

- number of blood products transfused

- fluid balance

- respiratory disease

# Prevention of TACO

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AABB Standards for Transfusion Services and Blood Banks (30<sup>th</sup> edition) requires hospitals to have a policy for issuing blood for those at increased risk for TACO

Identify risks pre transfusion for volume overload

Optimize volume status prior to transfusion

Decrease the infusion rate

Diuretics pretransfusion halfway through or at the end of transfusion

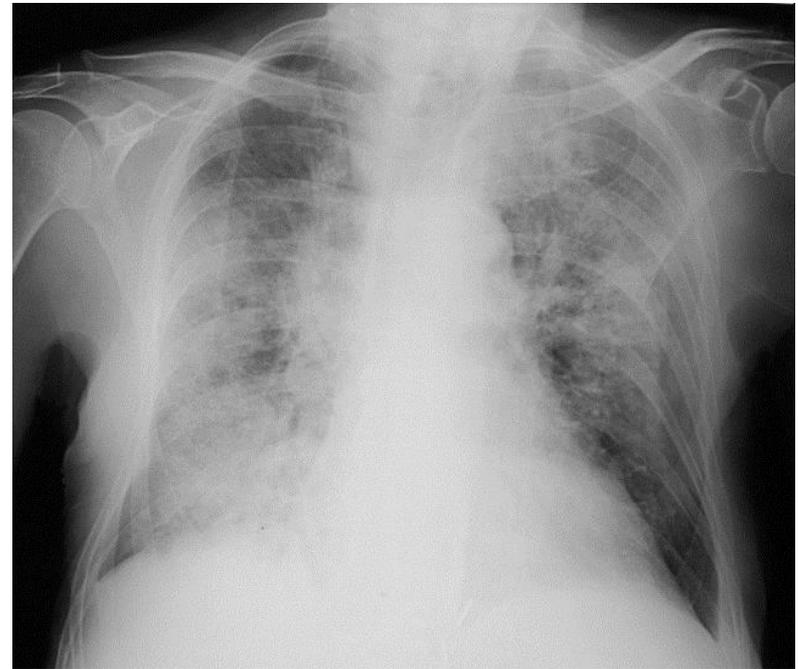
# Criteria for Transfusion Related Acute Lung Injury

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## Acute Lung Injury (ALI)

1. Acute onset
2. Hypoxemia:  $SpO_2 < 90$
3. Bilateral chest infiltrates

2<sup>o</sup> anti HLA and HNA antibodies in the donor to antigens in the recipient or an inflammatory response



# Criteria for Transfusion Related Acute Lung Injury

2. No preexisting ARDS
  3. During or within 6 hours of transfusion
  4. No temporal relationship to an alternative risk factor for ARDS
  5. No left atrial hypertension or if present not causative for hypoxemia
- If preexisting lung injury, lung injury is stable within last 12 hours
  - \* Reverse TRALI cases reported



# Characteristics to differentiate TRALI and TACO

	TRALI	TACO
Patient Characteristics	Frequently reported in hematology and surgical patients	All ages, but age > 70 yrs characteristic
Type of component	Usually plasma or platelets	Any
Speed of onset	During/within 6 hrs of transfusion	Within 12 hours of transfusion
Oxygen saturation/ BP/JVP/Temperature	Reduced/often reduced/normal/raised	Reduced/often raised/raised/unchanged
CXR	Normal heart size	Cardiomegaly
Echo/PCWP/BNP	Normal/low/normal	Abnormal/raised/raised
CBC	May have neutropenia followed by neutrophilia	No specific changes
Response to fluids/Lasix	Improves/Worsens	Worsens/Improves

# Treatment of TRALI vs TACO

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TRALI: Supportive care

Mild-oxygen

Severe- ventilatory support

Diuretics not recommended

Mortality for TRALI is estimated between 5% -25%

# TACO needs to be differentiated from TRALI

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To defer the implicated donor  
Antibody mediated TRALI

Male only plasma has reduced TRALI

Solvent detergent plasma may also reduce TRALI

# Transfusion Associated Dyspnea

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Respiratory distress within 24 hours of transfusion

Does not fulfill criteria for TRALI, TACO, allergy

# ALLERGIC REACTIONS

# Anaphylaxis secondary to transfusion may be due to

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Anti-IgA in an IgA deficient patient (<0.05mg/dl)

1/300 to 1/500

40-50% will have antibodies

Haptoglobin deficiency (1/1000 in Asians)

Passive transfer of IgE

Antibodies to proteins e.g. haptoglobin

Transfusing an allergen

Incidence higher with plasma containing components

# Symptoms suggestive of a severe allergic reaction include

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Dyspnea, hypotension, rash >2/3 body, tachycardia, nausea and vomiting

Do not restart the transfusion

Diphenhydramine/corticosteroids

# Transfusion associated hypotension occurs within 15 min of transfusion..

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A drop in blood pressure of  $>30$  mmHg

Resolves with discontinuing transfusion within 10 min

Increased bradykinin generation exacerbated with ACE inhibitors

ACE is a key enzyme in the bradykinin degradation

For patients requiring longterm transfusion-change of antihypertensive should be considered

# Summary

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Transfusion reactions do not occur

uncommonly after transfusion

Reporting of transfusion reactions assist

in identifying the correct diagnosis, and

preventative measures

