ADVERSE EFFECTS OF BLOOD TRANSFUSION

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OUTLINES

- Introduction
- Acute transfusion reactions
- Delayed transfusion reactions

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INTRODUCTION

CLASSIFICATION

- Acute transfusion reactions
  - Immune vs nonimmune
  - Infectious vs noninfectious
- Delayed transfusion reactions
  - Immune vs nonimmune
  - Infectious vs noninfectious

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ACUTE TRANSFUSION REACTIONS

- Signs and symptoms present within 24 hours of transfusion.

- Adverse events
  - Acute hemolytic transfusion reaction (AHTR)
  - Transfusion-associated sepsis (TAS)
  - Febrile-nonhemolytic transfusion reaction (FNHTR)
  - Allergic transfusion reactions (ALTR)
  - Transfusion-related acute lung injury (TRALI)
  - Transfusion-associated circulatory overload (TACO)

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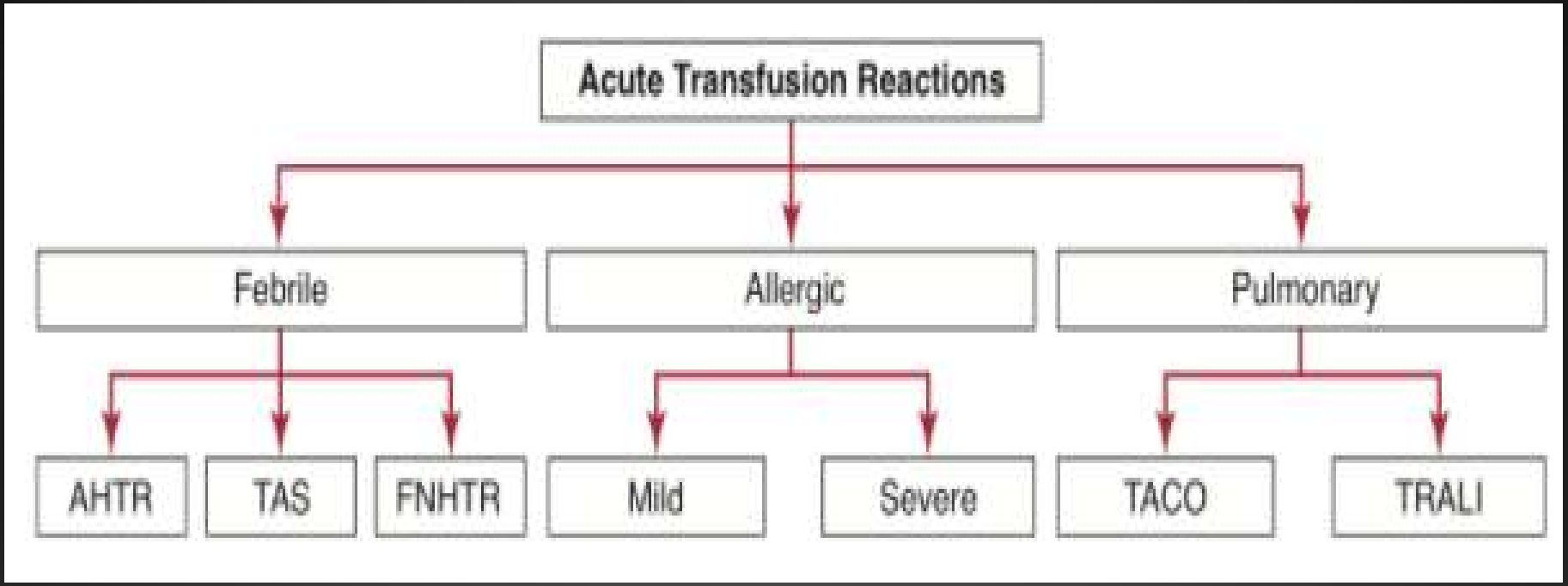

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DELAYED TRANSFUSION REACTIONS

- Signs and symptoms present after 24 hours of transfusion.

- Adverse events
  - Delayed hemolytic transfusion reaction (DHTR)
  - Transfusion-associated graft-versus-host disease (TA-GVHD)
  - Post-transfusion purpura (PTP)

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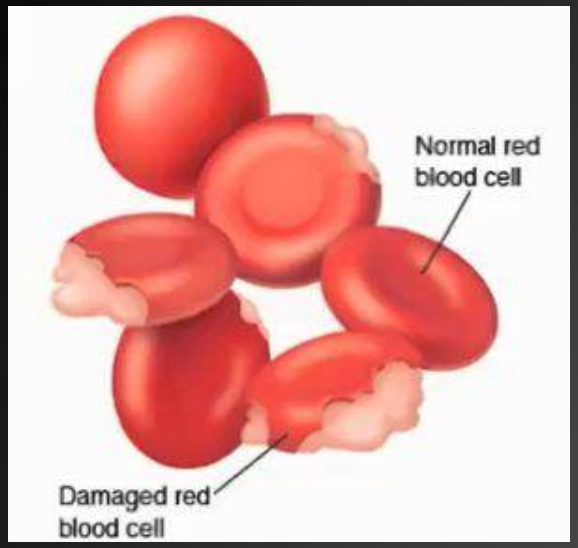
ACUTE TRANSFUSION REACTIONS



ACUTE HEMOLYTIC TRANSFUSION REACTION (AHTR)

ACUTE HEMOLYTIC TRANSFUSION REACTION (AHTR)

- Acute hemolysis within 24 hours of transfusion.

- Etiology
  - Immune-mediated
  - Nonimmune

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IMMUNE MEDIATED ACUTE HEMOLYTIC TRANSFUSION REACTION

- Signs and symptoms
  - Abdominal pain
  - Chest pain
  - Flank pain
  - Back pain
  - Pain at infusion site
  - Hemoglobinemia
  - Hemoglobinuria
  - Hypotension
- Renal failure
- Shock
- DIC
- Diffuse oozing (anesthetized patient)

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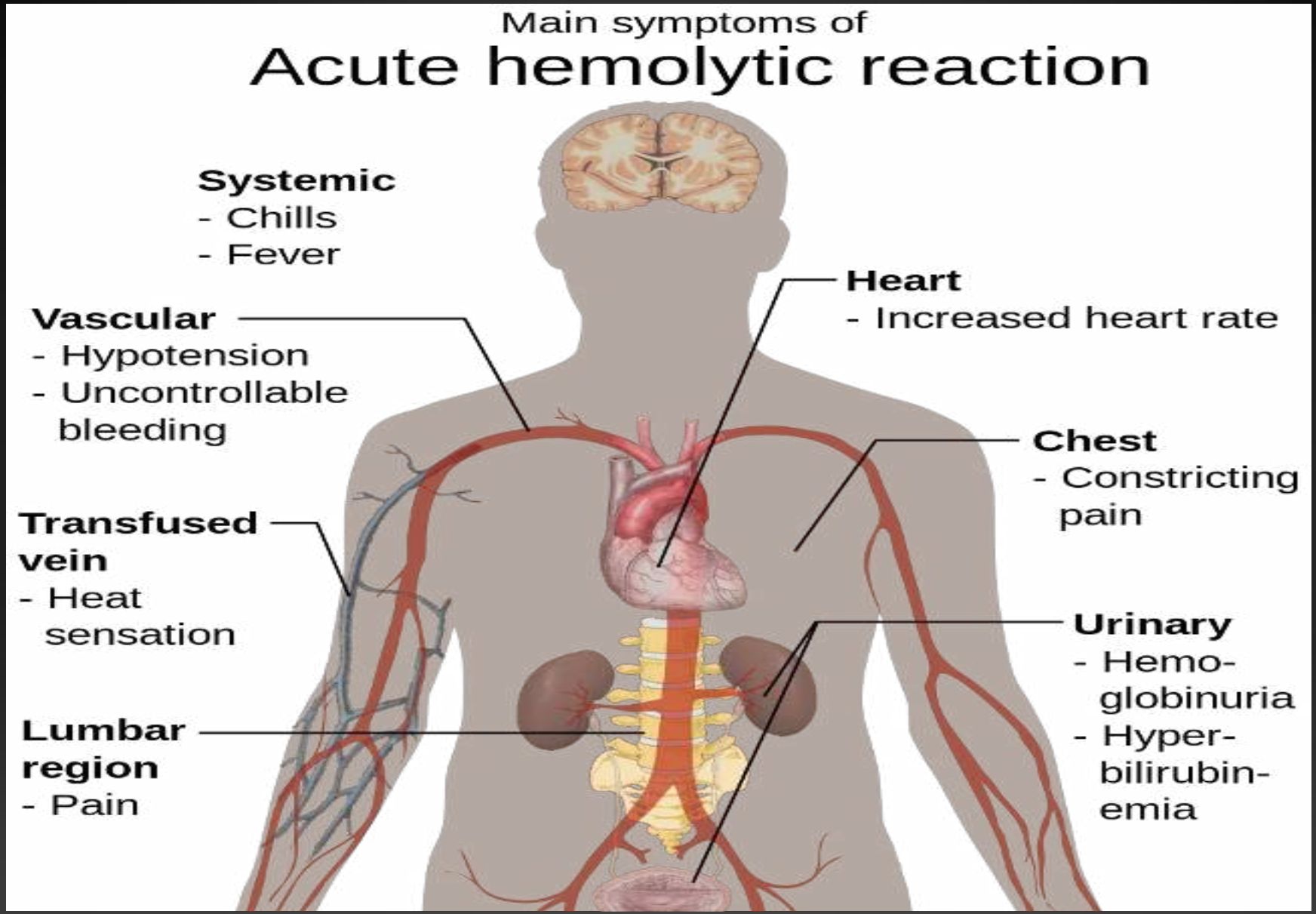

https://commons.m.wikimedia.org/wiki/File:Main_symptoms_of_acute_hemolytic_reaction.png

IMMUNE MEDIATED ACUTE HEMOLYTIC TRANSFUSION REACTION

- Pathophysiology – interaction of preformed antibodies in recipient with donor red cell antigen.
- Severity of symptoms related to amount and rate of incompatible blood transfused.
- Most severe reaction – ABO incompatibility.

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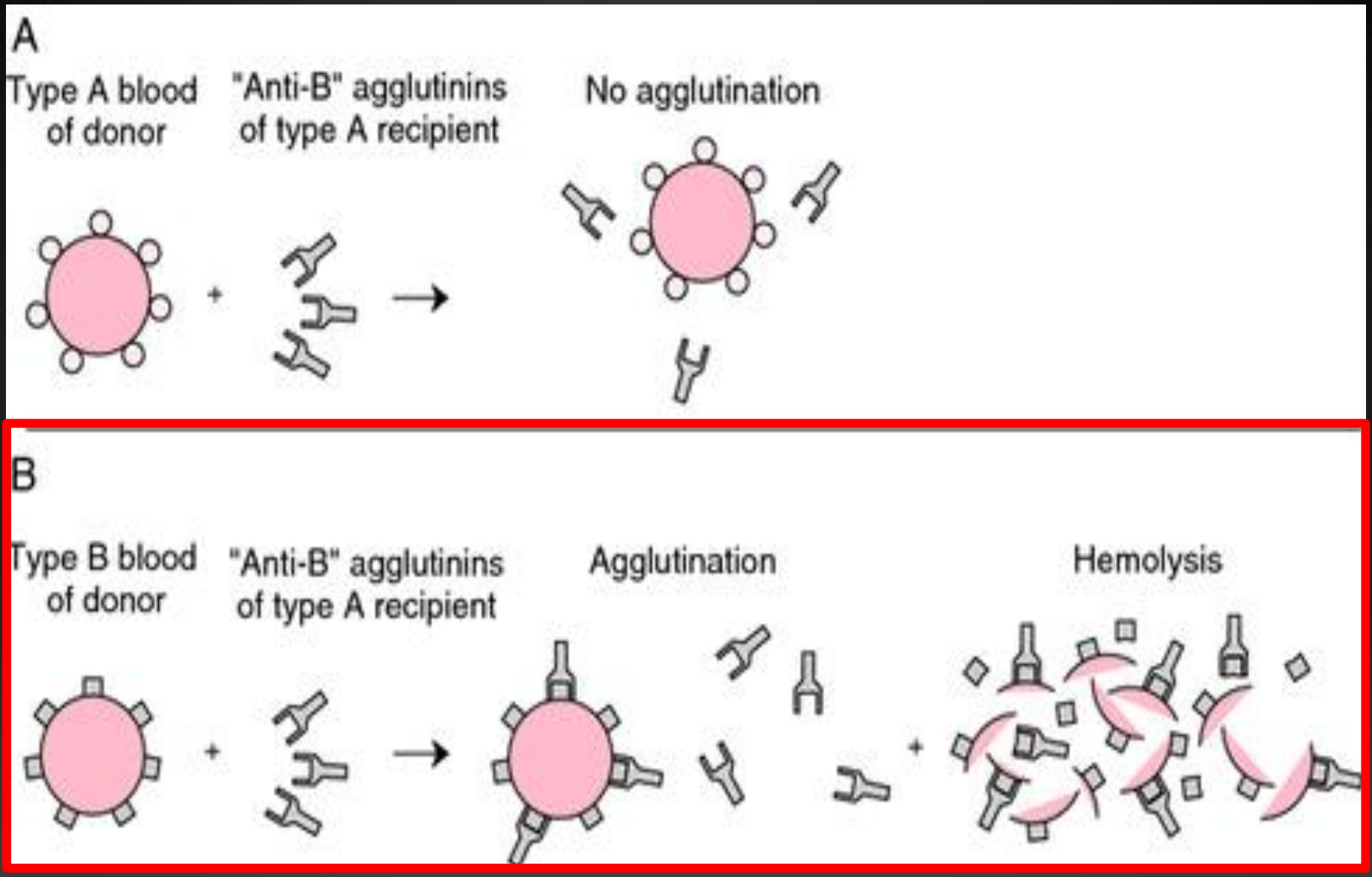

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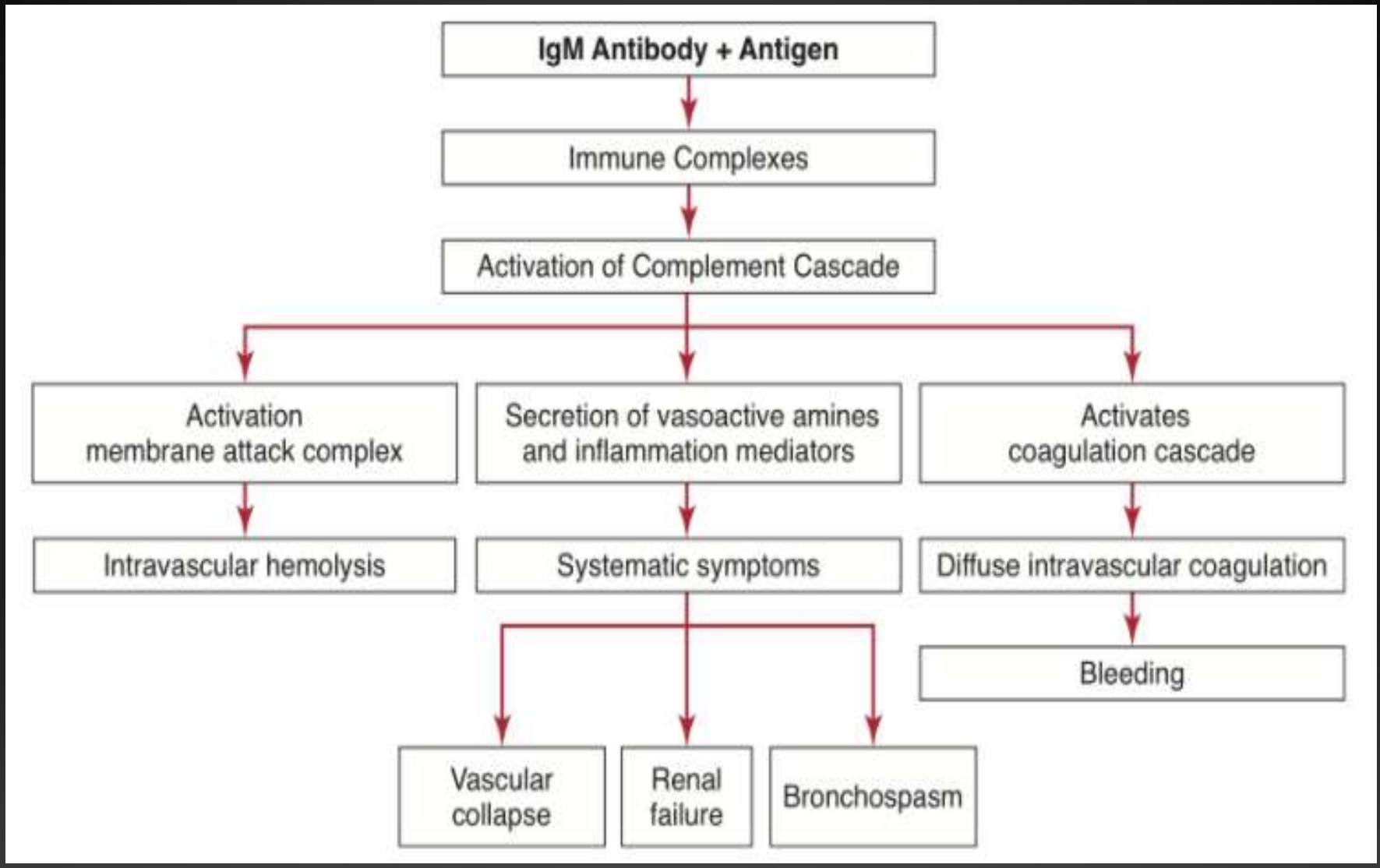

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NONIMMUNE HEMOLYSIS

- Signs and symptoms
  - Asymptomatic hemoglobinuria – most presentation.
  - Renal dysfunction – occasionally.
  - Death – rare.

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NONIMMUNE HEMOLYSIS

- Pathophysiology
  - Chemical & mechanical damage
    - Improper storage temperatures.
    - Inappropriately small bore sized needles used for transfusion.
    - Rapid pressure infuser/roller pumps.
    - Improper use of blood warmers.

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INVESTIGATIONS

- Plasma hemoglobin
- LDH ↑
- Total and indirect bilirubin ↑
- Haptoglobin ↓
- Urine hemoglobin

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INVESTIGATIONS

- Laboratory testing for pre-transfusion and post-transfusion blood samples
  - ABO, Rh(D)
  - DAT
  - Antibody screening
  - Crossmatches
- Laboratory testing for blood unit
  - ABO, Rh(D)
  - Crossmatches

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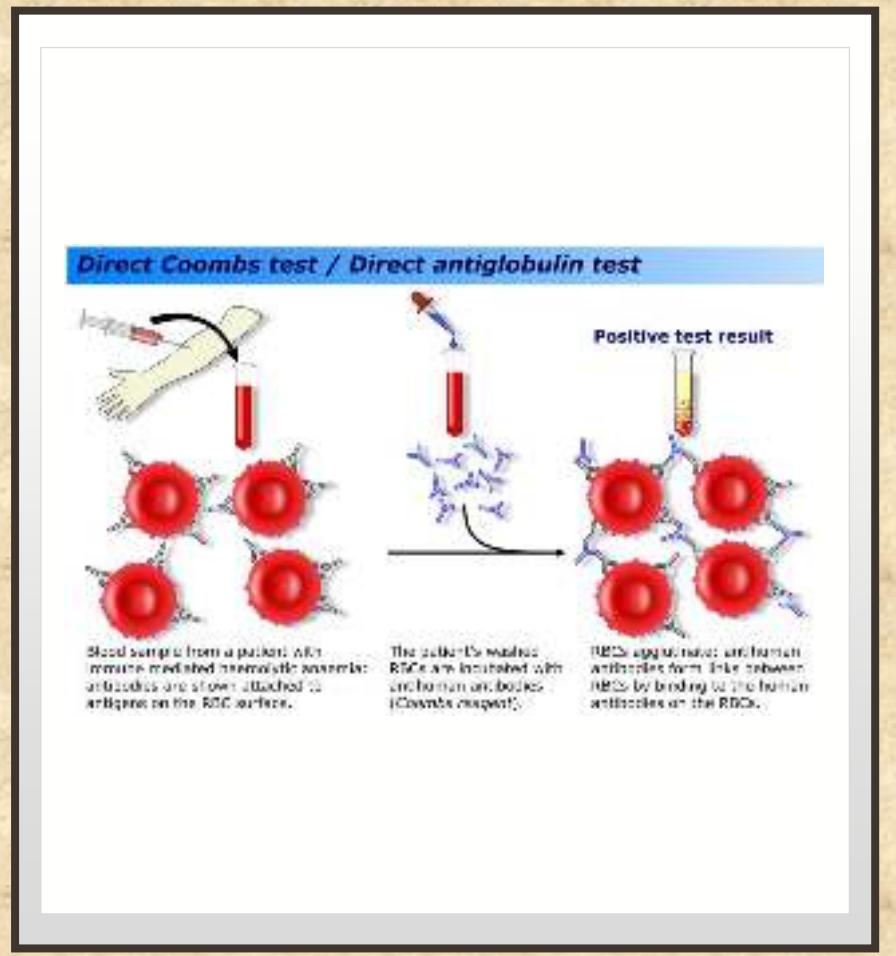
DIAGNOSIS

- Positive DAT in postreaction sample = suspected presence of incompatible transfused red blood cells.

- Negative DAT → not exclude immune hemolysis
  - All DAT positive cells are hemolyzed.



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MANAGEMENT

- Discontinue transfusion immediately
- Clerical verification
- Notify transfusion service
- Supportive therapy
  - Intravenous access for crystalloid/colloid (10-20 ml/kg)
  - Maintain adequate blood pressure (low dose dopamine 1-5 μg/kg/min)
  - Diuretics to maintain adequate urine output (>1 ml/kg/hr)

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http://www.pathologyoutlines.com/topic/transfusionmedacutehemolytic.html

MANAGEMENT

- If discrepancy identified → determine if another patient is involved in discrepancy to prevent another adverse event!

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PREVENTIONS

- Identify patient properly
  - Strict adherence to pre-transfusion bedside patient's identification procedures
  - Innovation of new technology to reduce human error
    - Barcoding blood component
    - Patient identification systems

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CASE

CLINICAL PRESENTATION

- 53 year-old female
- Underlying HT
- Admit ICU 26/3/60 due to alteration of consciousness with community acquired pneumonia with sever ARDS

- CBC

Factors	Value	Unit
Hb	11.4	g/dL
Hct	34.1	%
WBC	24,900	/µL
Neutrophils	93	%
Lymphocytes	2	%
Basophils	0	%
Eosinophils	0	%
Platelets	510,000	/µL
MCV	86.5	fl
RDW	14.2	%

INVESTIGATION

- Hemoculture – no growth x II
- Sputum culture – no growth
- Rapid test for influenza – negative

- Impression : suspected IPF with ARDS
- Management
  - Ceftriaxone + azithromycin + oseltamivir
  - On ECMO

- Clinical worsening with hypothermia
- Management;
  - Switch antibiotics to meropenem + vancomycin

- Clinical ARDS improvd
- Management;
  - Off ETT

4-7/4/60

- Blood oozing at ECMO insertion site
- EBL ~ 400-600 ml/day
- Plan : RBC transfusion

- CBC

Factors	29/3/60	4/4/60	6/4/60	7/4/60 (pre-transfusion)
Hb (g/dL)	11.4	11.2	8	6.9
Hct (%)	34.1	36.4	26.3	20.4
WBC (/μL)	24,900	29,100	27,700	20,700
Neutrophils (%)	93	91	94	86.8
Lymphocytes (%)	2	1	0	5.7
Basophils (%)	0	0	0	0
Eosinophils (%)	0	0	0	0
Platelets (/μL)	510,000	199,000	105,000	106,000
MCV (fl)	86.5	90.3	91.6	86.1
RDW (%)	14.2	16.5	18	18.3

7/4/60

- Developed shortness of breath after transfused LDPRC 1 hour (200 ml), shivering, no rash, no fever, no dark urine (on Foley's catheter)
- On physical examination;
  - BT = 37.5 °C (baseline ~36-37 °C)
  - BP = 60/40 mmHg (baseline ~ 100/60 mmHg)
  - P = 140 BPM (baseline ~ 120 BPM)
  - RR = 40 /min (baseline ~ 18-20 /min)
  - Pulse oximeter = 95% RA

7/4/60

- On physical examination;
  - Good consciousness, response to command
  - Heart : tachycardia, regular rhythms, no murmur
  - Lungs : clear, no adventitious sound
  - Abdomen : soft, no guarding, normoactive bowel sound
  - Liver & spleen : impalpable, liver span 8 cm, not increased splenic dullness
  - Extremities : no rash, no edema
  - Neurological : intact

DIFFERENTIAL DIAGNOSIS

- Transfusion-associated sepsis
- Acute hemolytic transfusion reaction
- Anaphylaxis

MANGEMENT

- Stop transfusion
- Levophed 96 microgram/ml rate 26 ml/hr
- Adrenaline (1:10) rate 10 ml/hr
- Continue empirical broad spectrum antibiotics
  - Meropenem + vancomycin
- Clerical verification
  - Patient blood group A, Rh positive
  - LDPRC group A, Rh positive, No. 1006006585, expired date 18/4/60

INVESTIGATION

- Pre-transfusion sample
  - ABO blood group = A
  - Rh = positive
  - DAT = negative
  - Ab screen = negative
  - Crossmatch = compatible

INVESTIGATION

- Post-transfusion sample
  - ABO blood group = A
  - Rh = positive
  - DAT = negative
  - Ab screen = negative
  - Crossmatch = not done

INVESTIGATION

- LDPRC, No. 1006006585
  - ABO blood group = A
  - Rh = positive

INVESTIGATION

- CBC (post-transfusioin)

Factors	Value	Unit
Hb	8	g/dL
Hct	25.4	%
WBC	51,200	/μL
Neutrophils	89	%
Lymphocytes	1	%
Basophils	0	%
Eosinophils	0	%
Platelets	108,000	/μL
MCV	92.4	fl
RDW	18.1	%
Reticulocyte	2.9(1.63)	%

INVESTIGATION

- Liver function test

Factors	Value	Unit
Albumin	3.7	g/dL
Globulin	1.8	g/dL
Total bilirubin	8.1	mg/dL
Direct bilirubin	5.4	mg/dL
Indirect bilirubin	2.7	mg/dL
AST	168	U/L
ALT	229	U/L
AP	212	U/L

INVESTIGATION

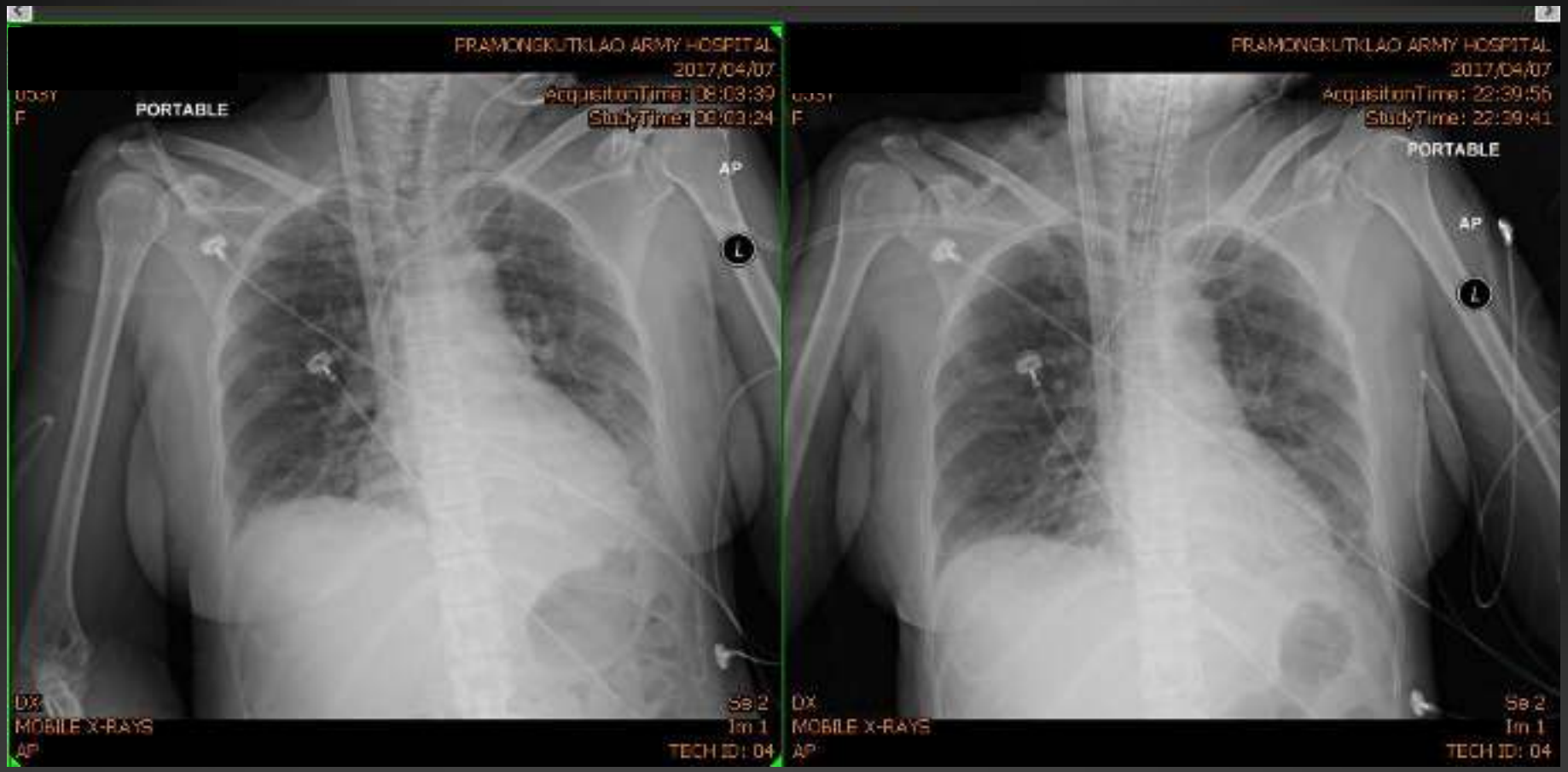
- Blood chemistry

Factors	Value	Unit
Na	140	mEq/L
K	4.37	mEq/L
Cl	101	mEq/L
CO_2	23.7	mEq/L
BUN	19.3	mg/dL
Cr	0.42	mg/dL
GFR	117.4	mL/min/1.73m^2
Lactate	59.1	mg/dL

INVESTIGATION

- Hemoculture from post-transfusion sample (peripheral)
  - Klebsiella pneumoniae (ESBL, CRE)
- Hemoculture from post-transfusion sample (central catheter)
  - Klebsiella pneumoniae (ESBL, CRE)
- Hemoculture from LDPRC, No. 1006006585
  - Klebsiella pneumoniae (ESBL)

INVESTIGATION

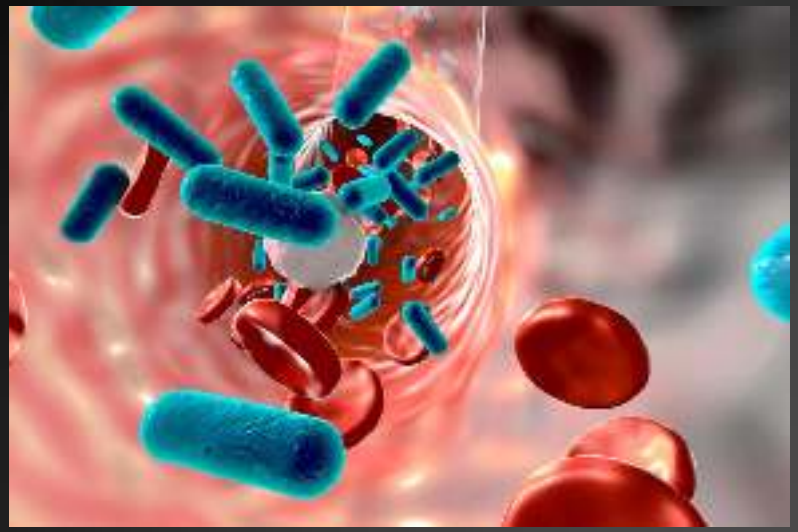


DIAGNOSIS

- Transfusion associated sepsis

MANAGEMENT

- Continue meropenem + vancomycin



TRANSFUSION-ASSOCIATED SEPSIS (TAS)

TRANSFUSION-ASSOCIATED SEPSIS (TAS)

- Transfused by bacterial-contaminated blood component.
- Signs and symptoms usually present shortly after transfusion begins.
- Clinical presentation may be similar to AHTR.

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SIGNS AND SYMPTOMS

- Increase in body temperature ≥ 2 °C or body temperature ≥ 39 °C
- Rigors
- Hypotension

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SOURCES OF BACTERIAL CONTAMINATIONS

- Sources of bacterial contamination;
  - Skin flora
  - Gut flora associated with transient bacteremia in asymptomatic donor.

- Bacterial endotoxin generated during storage → related to morbidity and mortality.

- Platelets – most frequent component causing TAS, due to room temperature storage.

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Bacterial Organisms Associated with Transfusion-Associated Sepsis (TAS)

GRAM STAIN	BACTERIA IDENTIFICATION	TAS RISK	SOURCE
Gram-positive	• *Staphylococcus* species • *Streptococcus* species • *Bacillus* species	Red Blood Cells • Risk: 1:500,000 • Mortality: 1:10,000,000 Platelets • Risk: 1:75,000 • Mortality: 1:500,000	• Skin flora • Natural environment
Gram-negative	• *Serratia* species • *Yersinia* species • *Acinetobacter* species • *Escherichia* species • *Pseudomonas* species • *Providencia* species	Red Blood Cells • Risk: 1:500,000 • Mortality: 1:10,000,000 Platelets • Risk: 1:75,000 • Mortality: 1:500,000	• Bloodstream • Natural environment

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INVESTIGATIONS

- Laboratory testing for pre-transfusion and post-transfusion blood samples;
  - ABO, Rh(D)
  - DAT
  - Antibody screening
  - Crossmatches
- Laboratory testing for blood unit;
  - ABO, Rh(D)
  - Crossmatches

Rule out hemolysis

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INVESTIGATIONS

- Gram stain
- Blood culture

} Blood unit & recipient

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DIAGNOSIS

- Isolation of the same organism in both patient's blood and blood unit.

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MANAGEMENT

- Discontinue transfusion immediately
- Initiate broad-spectrum antibiotics

- Adjust to more specific coverage based on organism identified and antimicrobial susceptibility.

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PREVENTION

- Interventions used to detect bacterial overgrowth prior to storage.
  - More sensitive, delay distribution of platelets for clinical use.
- Interventions used to detect bacterial overgrowth at time of transfusion.
  - More rapid, less sensitive.
- Single donor platelets > whole blood-derived platelets (single venipuncture used for collection).

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Interventions to Prevent Transfusion-Associated Sepsis

At Collection

- Donor history
- Proper phlebotomy technique
- Single arm collection technique
- Diversion pouch

Prior to Storage

- Prestorage leukoreduction
- Pathogen inactivation
- Automated culture

At Time of Transfusion

- Visual inspection
- Biochemical markers
- Microscopy/stains
- Immunoassays

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FEBRILE NONHEMOLYTIC TRANSFUSION REACTION (FNHTR)

SIGNS AND SYMPTOMS

- Increase ≥ 1 °C in body temperature – resolve within 2-3 hours.
- Chills
- Nausea/vomiting
- Tachycardia
- Hypertension
- tachypnea

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PATHOPHYSIOLOGY

- Two white cell-related mechanisms;
  1. Immune mediated = presence of preformed antibodies + specific white cell antigens in blood component → release endogenous **pyrogens**

  2. Related to platelet storage changes = white cells in blood component during storage → produce & release active **cytokines**

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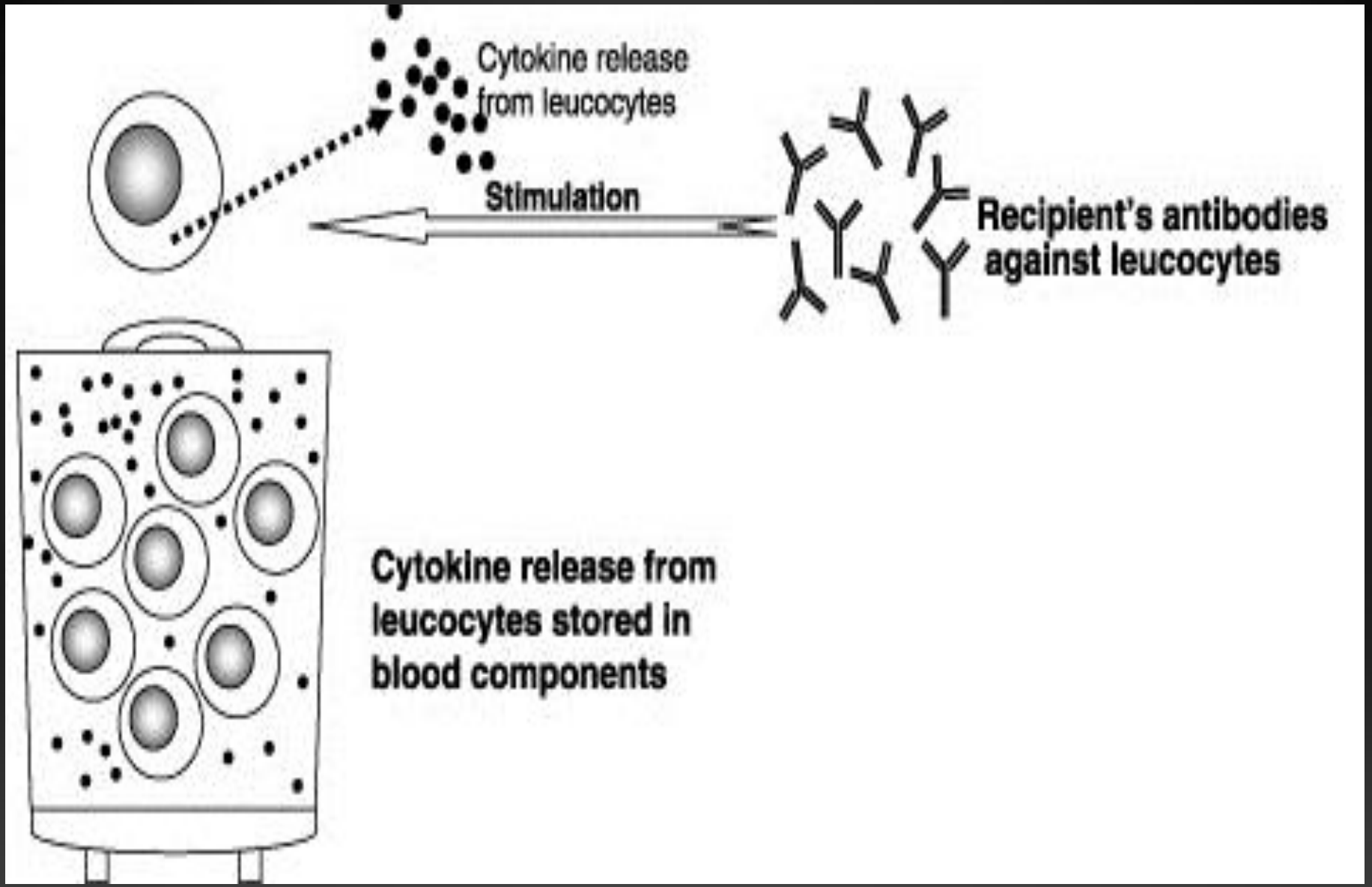
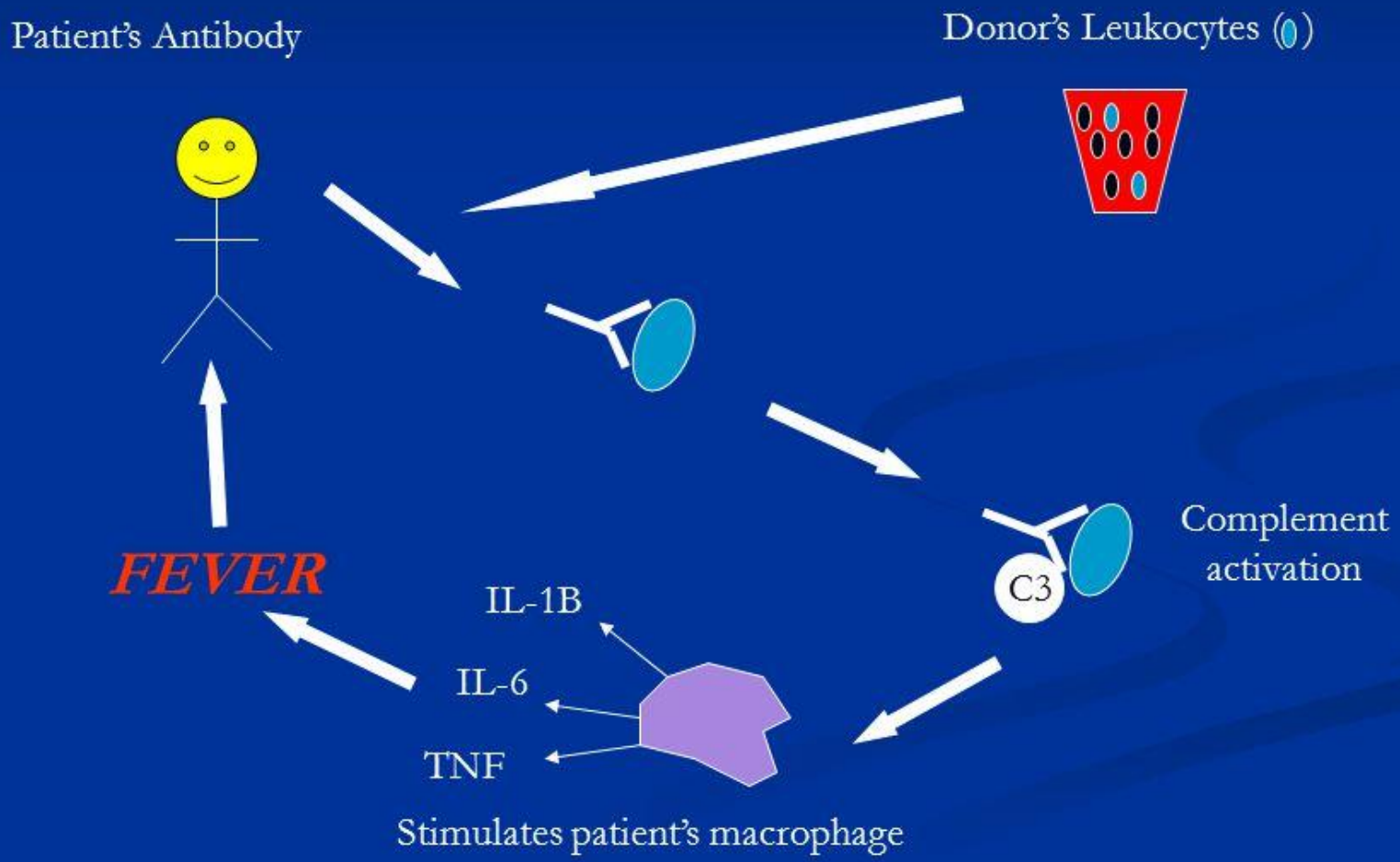


https://www.researchgate.net/publication/227999306/figure/fig3/AS:295494367629324@1447462756236/Figure-1-Pathophysiology-of-febrile-non-haemolytic-transfusion-reactions-FNHTR-three.png

Mechanism of FNHTR

(HLA, platelet, or granulocyte antibodies in recipients plasma interact with transfused antigens, e.g., donor WBCs)



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MANAGEMENT

- Self-limited → may not require treatment
- Supportive treatment – antipyretic, antihistamine
- Rigors → not response to antipyretic but **meperidine**

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PREVENTION

- Use of prestorage leukocyte reduction blood component = most effective

- Premedications – antipyretic, antihistamine.

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CASE

CLINICAL PRESENTATION

- 74 year-old female
- Known case
  - Papillary thyroid carcinoma
  - HBV cirrhosis Child B
  - Situs inversus with dextrocardia
  - Immune cytopenia from carcinoma
- Admit ENT 16/5/60 for total thyroidectomy

PREOPERATIVE LABORATORY

- CBC

Factors	16/5/60
Hb (g/dL)	10.6
Hct (%)	31.9
WBC (/µL)	2,100
Neutrophils (%)	71
Lymphocytes (%)	16
Basophils (%)	1
Eosinophils (%)	2
Platelets (/µL)	64,000
MCV (fl)	108.9
RDW (%)	15.3

PREOPERATIVE LABORATORY

- Coagulogram
  - APTT = 31.1 sec (22.6-31)
  - APTT ratio = 1.17
  - PT = 17.4 sec (12.1-14.1)
  - INR = 1.33
  - TT = 11.7 sec (11.1-13.9)
  - TT ratio = 1.18

MANAGEMENT

- Plan set OR on call for total thyroidectomy on 16/5/60
- FFP & platelet transfusion
  - Keep platelet ≥ 100,000
  - Keep INR ≤ 1.2

16/5/60

- Developed shortness of breath & chest tightness after 10 minutes of FFP transfusion, no rash, no abdominal pain, no flank pain, no fever
- On physical examination
  - BT = 36 °C
  - BP = 120/70 mmHg
  - PR = 100 BPM
  - RR = 24 /min
  - Pulse oximeter = 76% RA

16/5/60

- On physical examination
  - Good consciousness
  - Heart : normal S1S2, regular rhythms, no S3 gallop
  - Lungs : wheezing both lungs
  - Abdomen : soft, not tender, normoactive bowel sound
  - Extremities : no rash, no edema

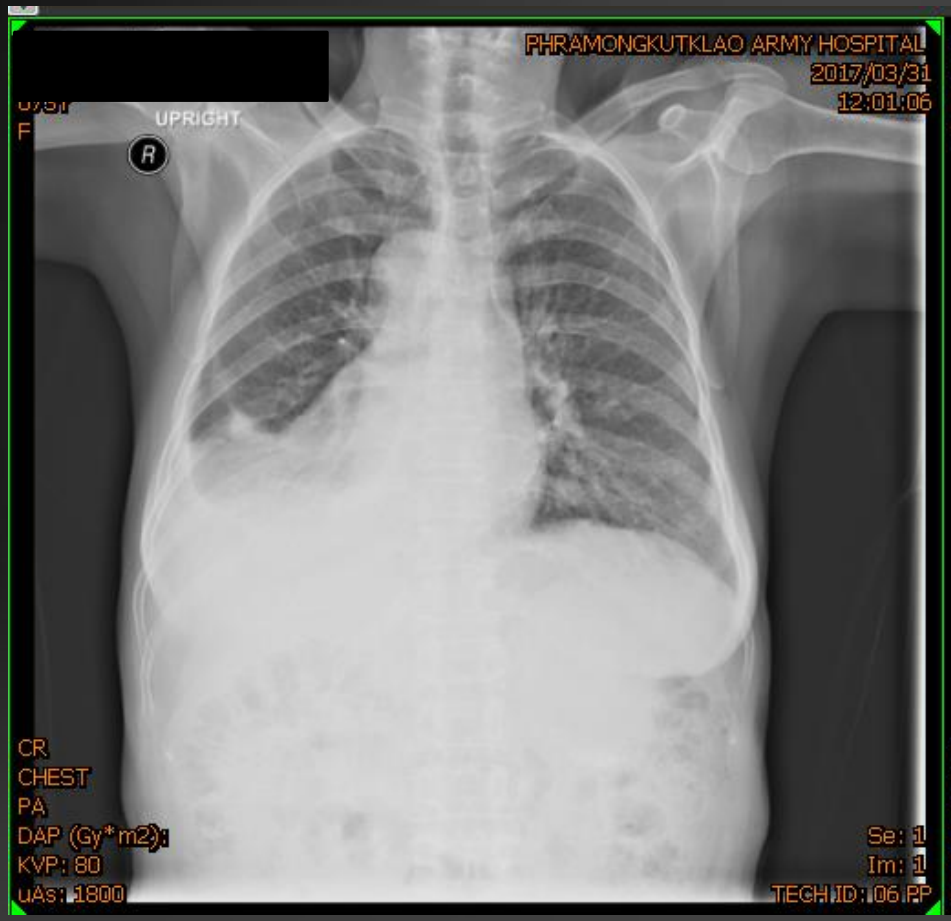
IMPRESSION

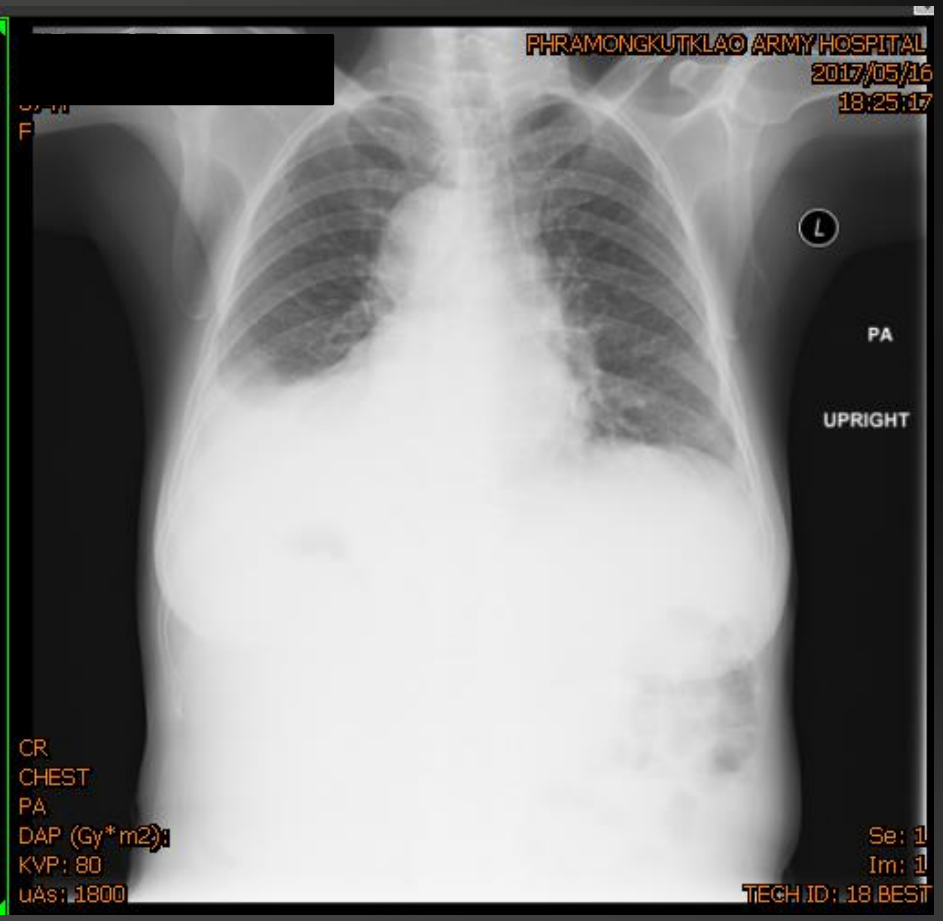
- Severe allergic transfusion reaction

MANAGEMENT

- Strop transfusion
- Adrenaline (1:1000) 0.5 ml IM stat
- Chlorpheniramine 10 mg IV stat
- Dexamethasone 10 mg IV stat
- Ventolin 1 nebule via nebulizer stat
- Clerical verification
  - Patient blood group B, Rh positive
  - FFP group B, Rh positive, No. 16960302977

INVESTIGATION





INVESTIGATION

- CBC

Factors	16/5/60	17/5/60 (pre-transfusion)
Hb (g/dL)	10.6	9.4
Hct (%)	31.9	25.1
WBC (/µL)	2,100	1,400
Neutrophils (%)	71	98
Lymphocytes (%)	16	2
Basophils (%)	1	0
Eosinophils (%)	2	0
Platelets (/µL)	64,000	50,000
MCV (fl)	108.9	107
RDW (%)	15.3	16.3

INVESTIGATION

- Coagulogram
  - APTT = 28.7 sec (22.6-31)
  - APTT ratio = 1.08
  - PT = 18.2 sec (12.1-14.1)
  - INR = 1.39
  - TT = 11.4 sec (11.1-13.9)
  - TT ratio = 1.15

INVESTIGATION

- Serum tryptase = 4.09 ng/mL (1.9-13.5)
- Serum IgA level = 1,156 mg/dL (70-400)

DIAGNOSIS

- Severe allergic reaction from non-IgA plasma protein.

ALLERGIC TRANSFUSION REACTION (ALTR)

ALLERGIC TRANSFUSION REACTION (ALTR)

- Acute, immune complications

- Variety of symptoms;
  - Mild – minor urticaria
  - Severe – anaphylactic shock & death

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SIGNS AND SYMPTOMS

- **Mild allergic reaction** – present at anytime during or after transfusion.
  - Wheals, hives, erythema, pruritus

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SIGNS AND SYMPTOMS

- Severe allergic reaction (anaphylactoid, anaphylaxis) – present shortly after transfusion started & minimal volume transfused.
  - Bronchoconstriction – wheeze
  - Angioedema – periorbital edema, tongue swelling
  - Gastrointestinal symptoms – diarrhea
  - Cardiovascular instability – hypotension, cardiac arrhythmia, loss of consciousness, shock, cardiac arrest.

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DIAGNOSIS

Criteria for diagnosing anaphylaxis.

1. *Acute onset of disease (minutes or hours) with involvement of skin, mucosa, or both (for instance, generalized nettle-rash, pruritus or facial erythema, lips-tongue-uvula edema).*

And at least one of the following items:

a) Respiratory impairment (dyspnea, wheezing-bronchospasm, stridor, decreased peak expiratory flow, hypoxia).

b) Low blood pressure or symptoms associated with organic dysfunction (for instance, hypotonia [collapse], syncope, incontinence).

2. *Two or more of the following symptoms occurring shortly after exposure to a likely allergen for that patient (minutes to hours)*

a) Involvement of skin-mucosa (for instance, generalized nettle-rash, pruritus or facial erythema, lips-tongue-uvula edema).

b) Respiratory impairment (dyspnea, wheezing-bronchospasm, stridor, decreased peak expiratory flow, hypoxia).

c) Drop in blood pressure or symptoms associated with organic dysfunction (for instance, hypotonia [collapse], syncope, incontinence).

d) Persistent gastrointestinal symptoms (for instance, persistent abdominal colic, vomiting).

3. *Drop in blood pressure after exposure to a known allergen for that patient (minutes to hours):*

a) infants and young children: low systolic arterial pressure (age-specific) or a drop in the systolic arterial pressure > 30%

b) Adults: systolic arterial pressure less than 90 mmHg or drop > 30% in basal systolic arterial pressure

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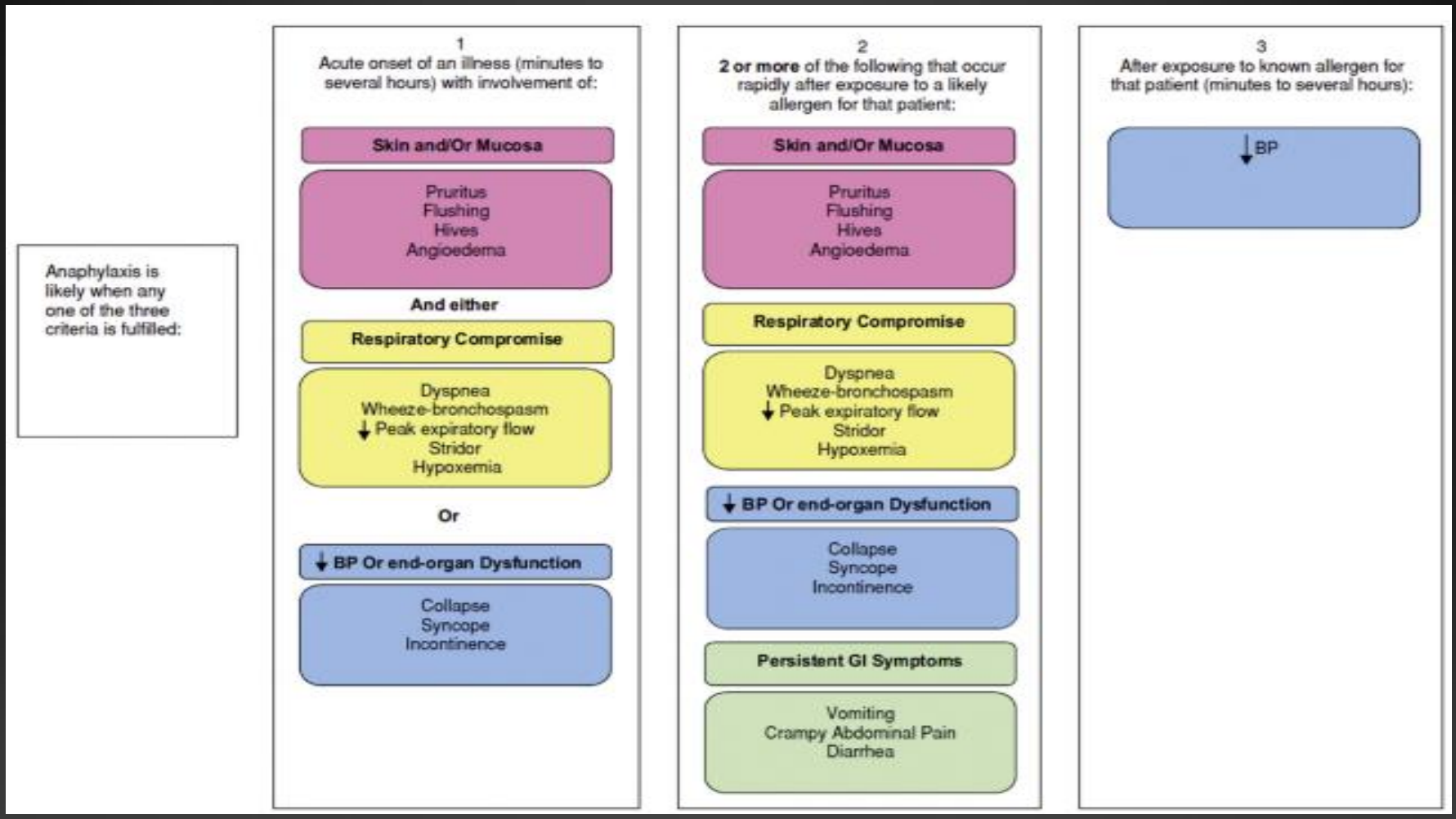
DIAGNOSIS



https://openi.nlm.nih.gov/imgs/512/320/2672985/PMC2672985_12245_2009_93_Fig1_HTML.png?keywords=anaphylaxis,food+allergies,infectious+disease

PATHOPHYSIOLOGY

- Allergen in plasma of blood component

- Preformed IgE antibodies in recipient interact with donor allergen

- IgE bound to mast cell in recipient

- Release histamine & other granule contents.

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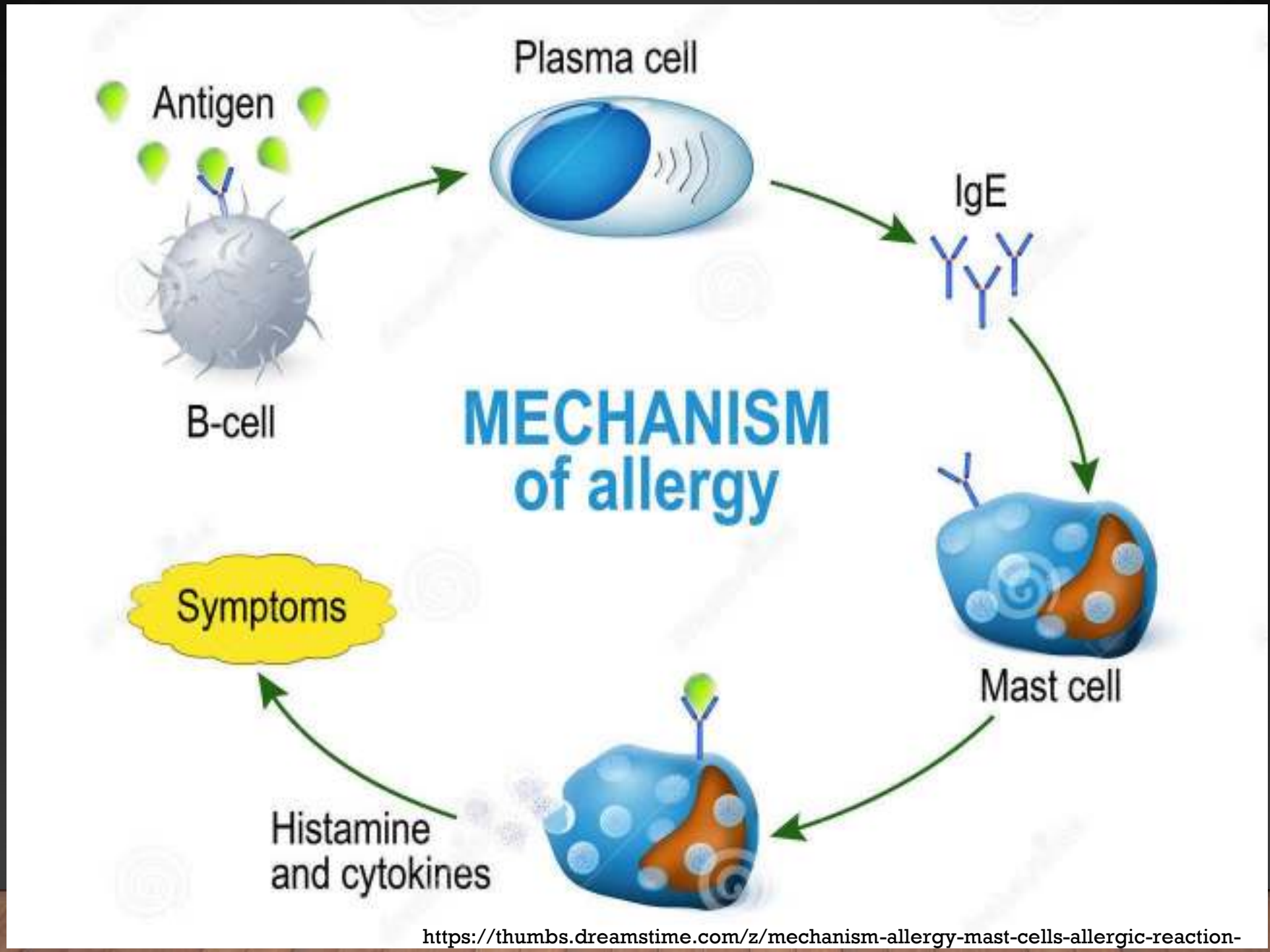

https://thumbs.dreamstime.com/z/mechanism-allergy-mast-cells-allergic-reaction-b-cell-exposed-to-allergen-plasma-will-initiate-overproduction-83295404.jpg

TRIGGERING FACTORS

- Triggering factor for severe ALTR = IgA-deficiency
  - Absolute IgA deficiency = IgA level < 0.05 mg/dL
    - 1:700 individuals of European descent
    - 40% form anti-IgA antibodies
    - Anti-IgA antibodies = natural occurring → their presence cannot be predicted
  - Haptoglobin deficiency
    - Similar type of reaction as absolute IgA deficiency
    - In Japanese population

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MANAGEMENT

- Mild ALTR
  - Discontinuation of transfusion
  - Restart of transfusion if antihistamine improves symptoms
  - Laboratory work up – not required

- Anaphylactic symptoms
  - Oxygenation supplement
  - Epinephrine
    - Dose 0.5 mg IM/SC (=500 µg = 0.5 mL of 1:1000) repeated every 5-10 minutes according to response or relapse
  - Antihistamine
  - Systemic corticostreroid

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https://www.resus.org.uk/_resources/assets/attachment/full/0/824.pdf

PREVENTION

- Patients with proven absolute IgA deficiency → work up for anti-IgA → if anti-IgA antibodies present;
  - Must receive blood component deficiency in IgA
  - May receive washed red blood cells & platelets
  - Plasma & cryoprecipitate → obtained from IgA deficiency donors

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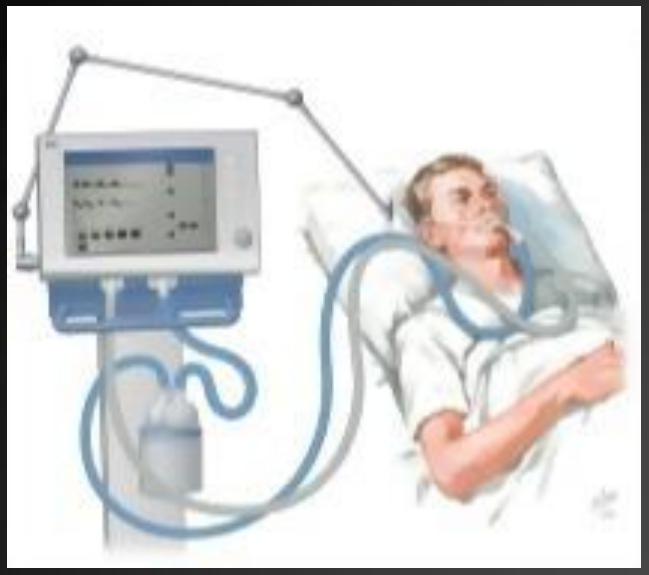

TRANSFUSION-RELATED ACUTE LUNG INJURY (TRALI)

SIGNS AND SYMPTOMS

- Respiratory distress
- Severe hypoxemia
- Fever
- Hypotension
- Occur during or within 6 hours of transfusion

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SIGNS AND SYMPTOMS

- Absence of other causes of acute lung injury
  - Aspiration
  - Pneumonia
  - Toxic inhalation
  - Lung contusion
  - Near drowning
  - Severe sepsis
  - Shock
  - Multiple trauma
- Burn injury
- Acute pancreatitis
- Cardiopulmonary bypass
- Drug overdose

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PATHOPHYSIOLOGY

- Antibodies against class II HLA, anti-HLA-A2(antibodies against class I HLA), anti-HNA-3a(antibodies against HNA) = associated with severe & fatal cases

- Rare incidence (6%) – Ab presence in recipient → react with donor leukocytes.

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PATHOPHYSIOLOGY

- **“Two-hit event”**

- Risk depends on patient’s predisposition to TRALI

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PATHOPHYSIOLOGY

- First hit = patient's predisposition (i.e., lung trauma, lung infection, inflammatory disease)
  - Proinflammatory priming event of patient's endothelium → prime patient's neutrophils

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PATHOPHYSIOLOGY

- Second hit – active substance accumulated during blood storage
  - Cause activation of primed neutrophils
  - ⬇
  - Cause endothelial damage
  - ⬇
  - Pulmonary capillary permeability
  - ⬇
  - Noncardiogenic pulmonary edema

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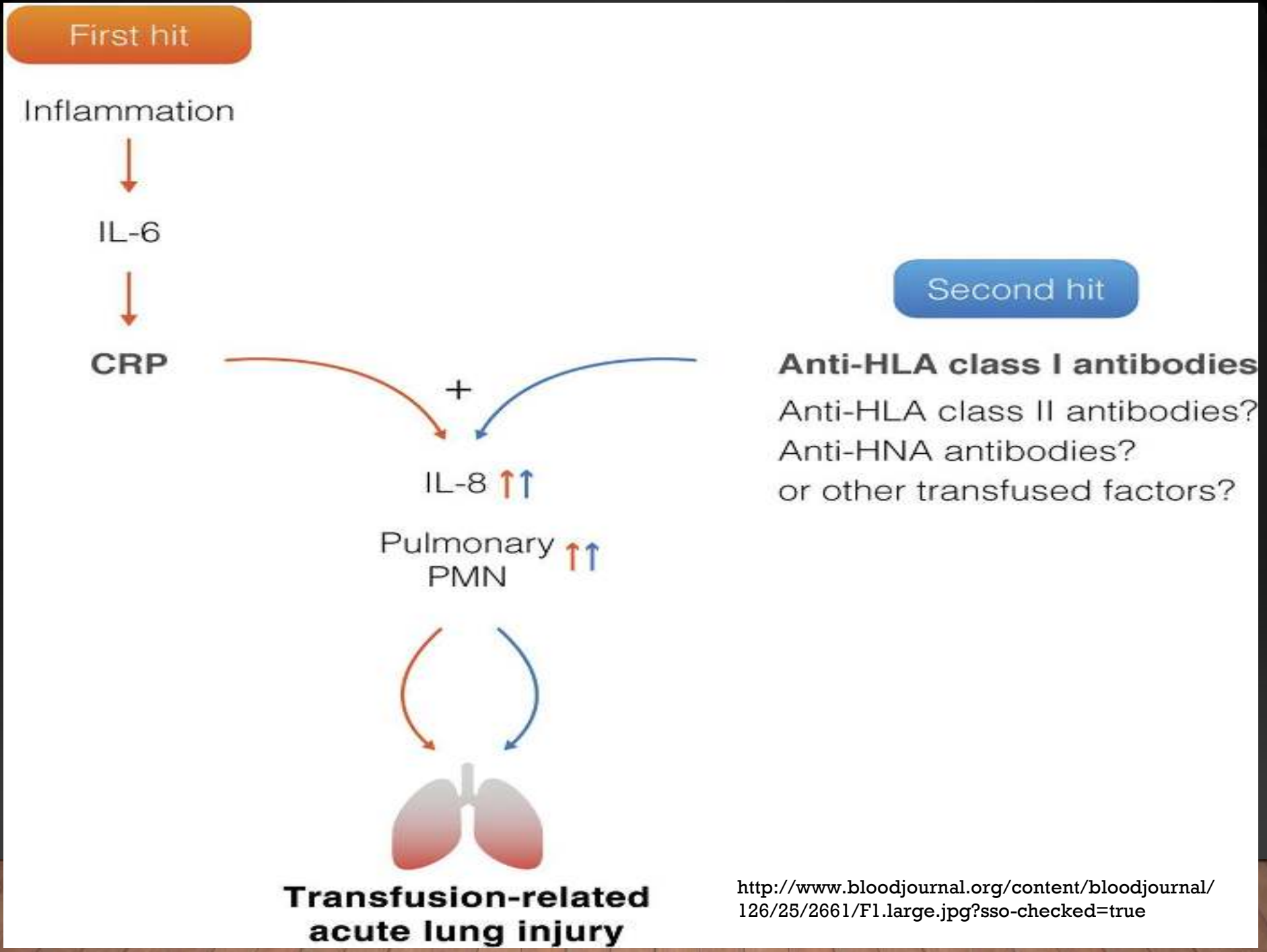

http://www.bloodjournal.org/content/bloodjournal/126/25/2661/F1.large.jpg?sso-checked=true

RISK FACTORS FOR TRAIL (RECIPIENT)

- Lung trauma
- Lung infection
- Inflammatory diseases

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RISK FACTORS FOR TRAIL (DONOR)

- Blood component donated by multiparous females
- Large volumes of plasma
- Presence of anti-HNA-3a

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DIAGNOSIS

Criteria for the Diagnosis of TRALI

Onset

Within 6 hours of transfusion

Oxygenation

$PAO_2/FiO_2 \leq 300$ mm Hg regardless of positive end-expiratory pressure level
or
Oxygenation saturation of $\leq 90\%$ on room air.

Chest X-ray

Bilateral infiltrates on frontal chest radiography

Blood Pressure

Pulmonary artery occlusion pressure ≤ 18 mm Hg when measured
or
No evidence of left atrial hypertension

FiO_2 = fraction of inspired oxygen; mm Hg = millimeters of mercury; PAO_2 = partial pressure of arterial oxygen; TRALI = transfusion-related acute lung injury
Data from Popovsky, MA: Transfusion associated circulatory overload: The plot thickens. Transfusion 49:2–4, 2009.

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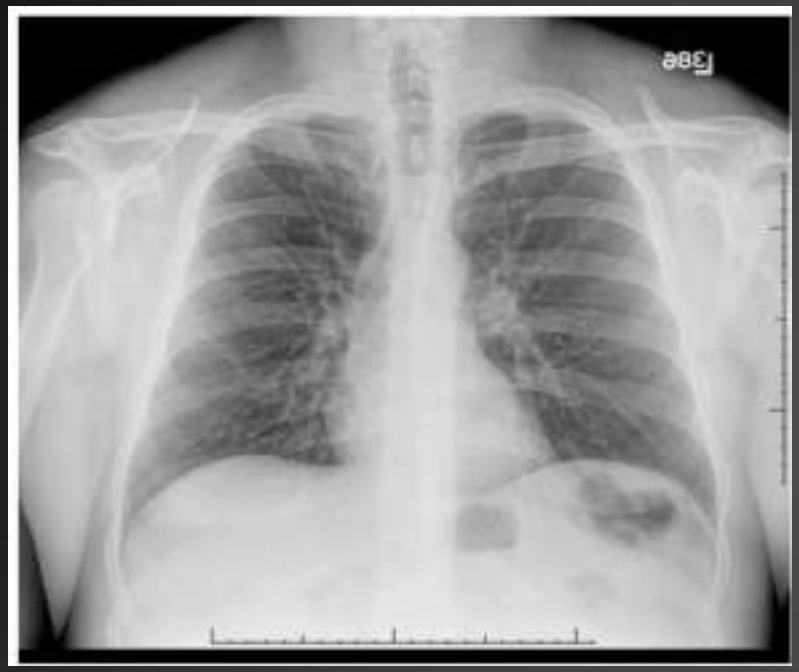
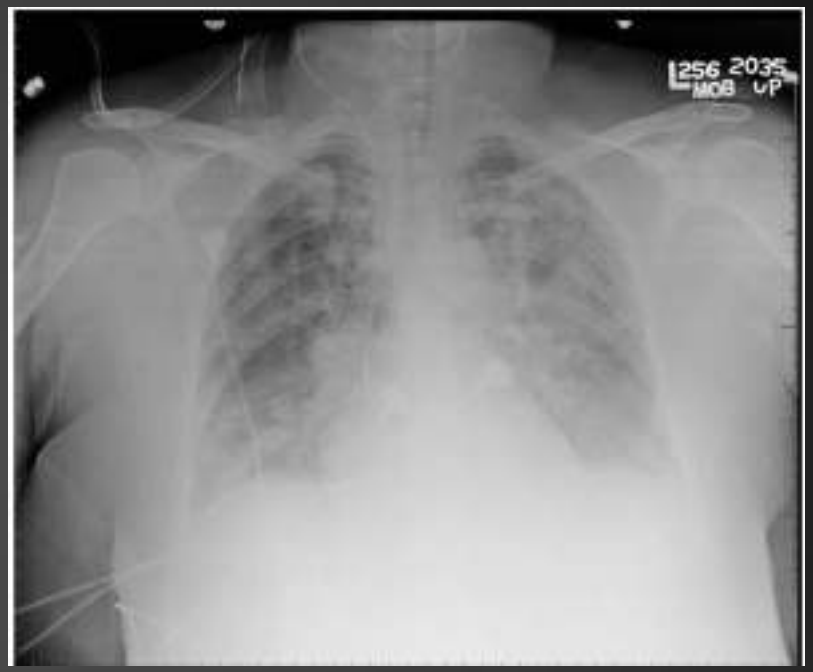


Normal



TRALI

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DIAGNOSIS

- Definite TRALI = no other risk factor for acute lung injury

- Possible TRALI = with other risk factor for acute lung injury

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https://professionaleducation.blood.ca/en/transfusion/publications/transfusion-related-acute-lung-injury-trali

RISK FACTORS FOR ACUTE LUNG INJURY

- Direct lung injury
  - Aspiration
  - Pneumonia
  - Toxic inhalation
  - Lung contusion
  - Near drowning

https://professionaleducation.blood.ca/en/transfusion/publications/transfusion-related-acute-lung-injury-trali

RISK FACTORS FOR ACUTE LUNG INJURY

- Indirect lung injury
  - Severe sepsis
  - Shock
  - Multiple trauma
  - Burn
  - Acute pancreatitis
  - Cardiopulmonary bypass

https://professionaleducation.blood.ca/en/transfusion/publications/transfusion-related-acute-lung-injury-trali

INVESTIGATIONS

- HLA/HNA antibodies – both recipient & donor

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MANAGEMENT

- Supportive therapy;
  - Oxygen support – 72% required mechanical ventilatory support
  - Not respond to diuresis
  - Typically improve within 48 hours – some persist for a week
  - Fatality 6-20%

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PREVENTIONS

- "Predominantly male plasma policy" in some countries
  - Obtain plasma from male donors
  - Nulliparous female donors
  - Multiparous but leukocyte antibody-negative female donors
  - Obtain platelets from male donors
  - Removing plasma contents from platelets → resuspending platelets in platelet additive solution

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PREVENTIONS

- Impact of the policy in the U.S.;
  - 50% reduction in units of whole blood for plasma manufacturing.
  - 37.1% loss of all apheresis platelet donations

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TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO)

SIGNS AND SYMPTOMS

- Onset during or after transfusion
  - Respiratory distress
  - Hypoxemia
  - Cough
  - Hypertension
  - Jugular vein distension
  - Elevated central venous pressure
  - Elevated pulmonary wedge pressure

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INVESTIGATION

- Chest radiograph
  - Pulmonary edema
  - Cardiomegaly
  - Distended pulmonary artery

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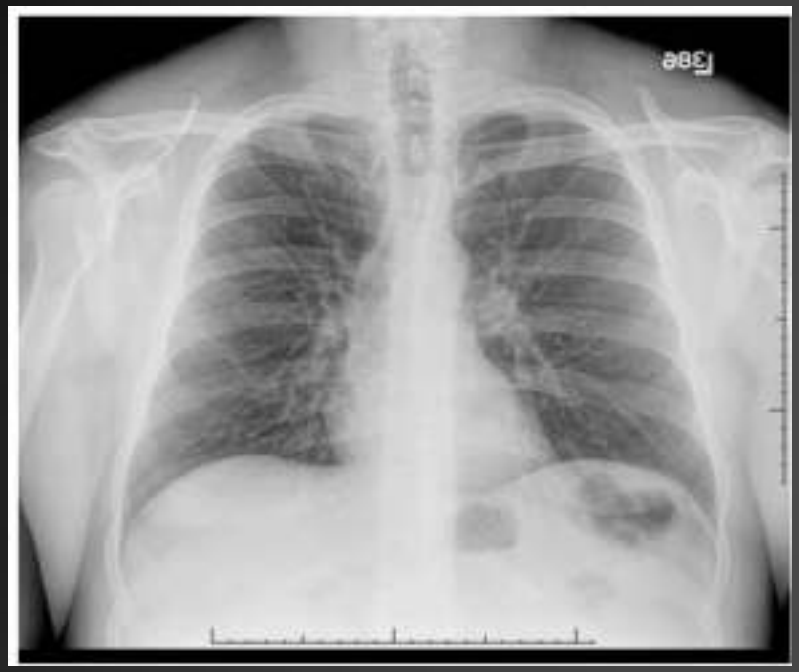

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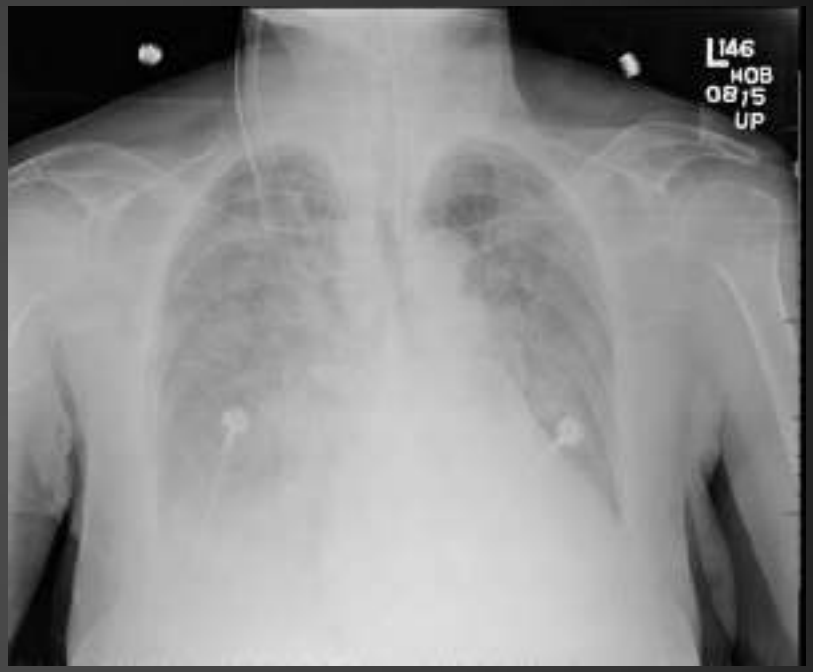

TACO

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INVESTIGATION

- Post-transfusion to pre-transfusion BNP ratio ≥ 1.5

- Post-transfusion BNP ≥ 100 picograms per milliliter – 81% sensitivity, 89% specificity

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RISK FACTORS

- Patients with diminish cardiac reserve
- Chronic anemia
- Very young patients
- Very old patients

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MANAGEMENT

- Oxygenation supplement
- diuresis

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PREVENTION

- In general
  - Transfusion rate not more than 3 ml/kg/hr
- For patient at risk of developing TACO;
  - Slow transfusion rate;
    - Not more than 1 ml/kg/hr
    - Diuretic before blood transfusion.
  - Divide blood component into smaller aliquots.

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สมชาย พัฒนอางกูล และ คณะ. Complications of blood transfusion. Review in internal medicine. โรงพยาบาลพระมงกุฎเกล้า. 2561; ครั้งที่ 2: 143-151.

Table 16–5 Summary: Acute Transfusion Reactions

	SYMPTOMS	DIAGNOSIS	TREATMENT	PREVENTION
AIHTR	Fever/chills Back pain Hemoglobinemia Hemoglobinuria Hypotension, renal failure Shock DIC	DAT positive ↓ Hemoglobin ↑ LDH ↑ Bilirubin ↓ Haptoglobin	Discontinue transfusion Maintain vascular access Maintain blood pressure Maintain renal blood flow Treat DIC if present	Follow standard operating procedures for identification of the patient
ANIHTR	Asymptomatic Hemoglobinuria	DAT negative	Discontinue transfusion Maintain vascular access Maintain renal blood flow	Follow standard operating procedures for equipment operation
TAS	Fever/chills Hypotension Shock	DAT negative Gram stain blood bag Culture blood bag Culture patient	Discontinue transfusion Maintain vascular access Consider initial broad-spectrum antibiotic coverage	Follow standard operating procedures for collection Implement bacterial detection intervention prior to transfusion
FNHTR	Fever/chills Nausea/vomiting Tachycardia Tachypnea ↑ Blood pressure	DAT negative	Treat with antipyretics For rigors, treat with meperidine	Prestorage leukoreduction of PRBC and platelets

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Table 16–5 Summary: Acute Transfusion Reactions

	SYMPTOMS	DIAGNOSIS	TREATMENT	PREVENTION
Allergic Mild	Erythema Pruritus	Clinical diagnosis DAT not required	Temporary discontinue transfusion Treat with antihistamines If symptoms improve restart transfusion	For repeated reactions, consider premedication with antihistamines
Allergic Severe	Angioedema Wheezing Hypotension Anaphylaxis	DAT negative IgA deficiency workup when indicated	Discontinue transfusion Maintain vascular access Treat with subcutaneous epinephrine Maintain blood pressure Provide respiratory support	For IgA absolute deficient patients provide IgA deficient blood components
TRALI	Severe hypoxemia No evidence of left atrial hypertension	CXR: bilateral infiltrates Donor test for HLA/HNA antibodies Recipient test for HLA/HNA antigens	Discontinue transfusion Maintain vascular access Supplemental oxygen Mechanical ventilation	Use male only plasma Exclude or screen female platelet donors
TACO	Severe hypoxemia ↑ Blood pressure Jugular vein distension ↑ Central venous pressure	CXR: pulmonary edema, cardiomegaly, distended pulmonary artery BNP	Upright posture Supplemental oxygen Diuresis	Slower transfusion rate Transfuse in smaller volumes

AIHTR = acute immune hemolytic transfusion reaction; ANIHTR = acute nonimmune hemolytic transfusion reaction; DAT = direct antiglobulin test; DIC = diffuse intravascular coagulopathy; FNHTR = febrile nonhemolytic transfusion reaction; LDH = lactic dehydrogenase; PRBC = packed red blood cell; TAS = transfusion-associated sepsis

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DELAYED TRANSFUSION REACTIONS

DELAYED HEMOLYTIC TRANSFUSION REACTION

DELAYED HEMOLYTIC TRANSFUSION REACTION

- Immune reaction
- Detection of "new" red cell antibodies after 24 hours of transfusion

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CLINICAL PRESENTATION

- Hemoglobin levels lower than expected for transfusion interval with or without jaundice

- Unexplained/unexpected drop in hemoglobin with increased requirement in transfusion frequency in absence of active bleeding

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PATHOPHYSIOLOGY

- Transfusion – expose to non-ABO Ag → develop IgM Ab in recipient → switch to IgG production
  - Detect within weeks – months after transfusion → diminish to undetectable level with time

- Subsequent exposure to incompatible red cells → rapid production of IgG
  - Detect between 2 days – 2 weeks after reexposure

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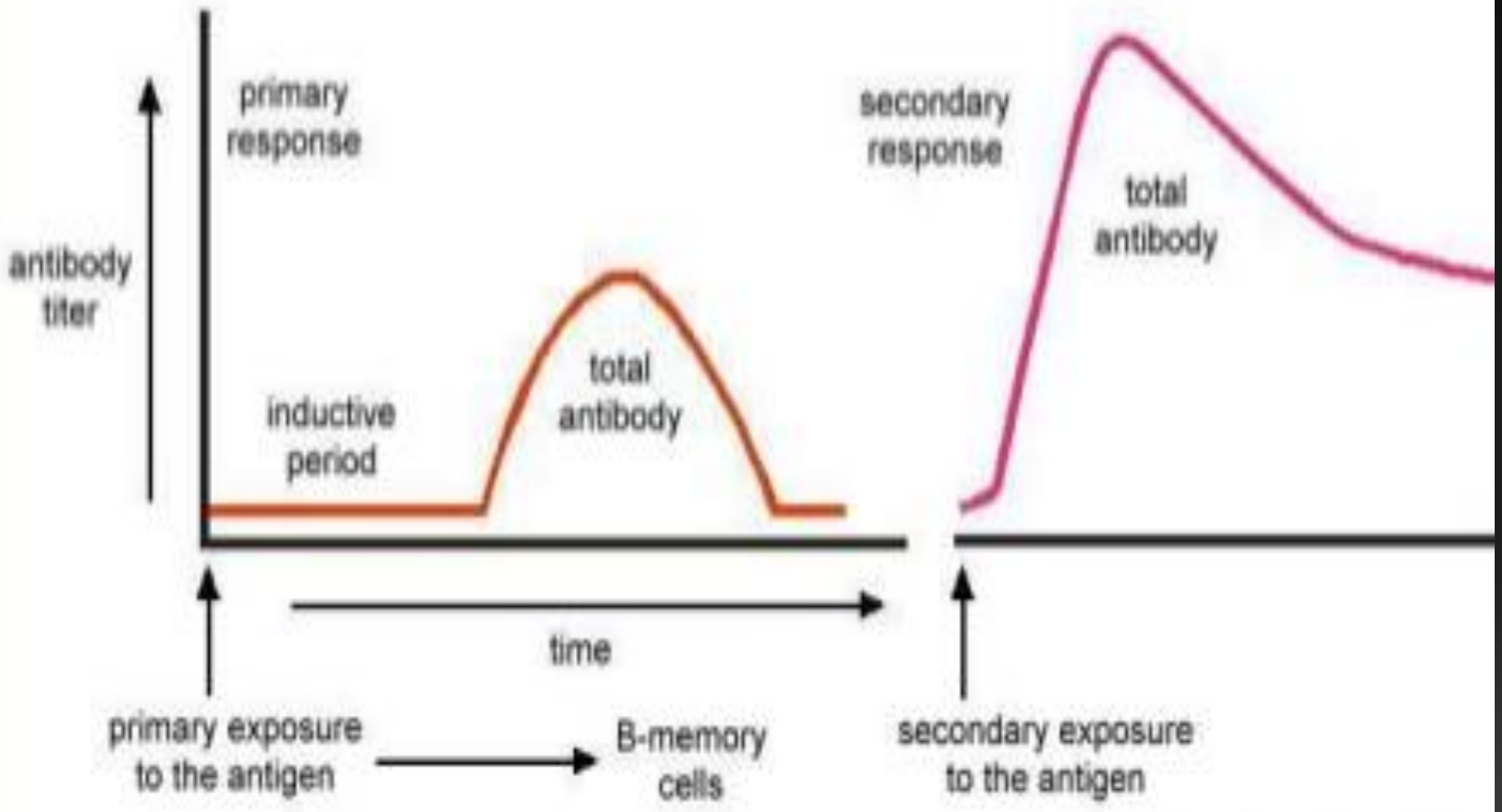

https://www.slideshare.net/mobile/bloodbankhawaii/common-transfusion-reactions-by-randal-covin-md-fcap

INVESTIGATION

- ABO, Rh(D)
- Antibody screen
- DAT
- Antigen typing of unit recently transfused
- Hemoglobin ↓
- Total & indirect bilirubin ↑
- LDH ↑
- haptoglobin ↓

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MANAGEMENT

- Only careful monitoring – due to generally mild symptoms

- Red cell exchange – if antigen typing suggest large burden of Ag-positive cells + on going hemolysis.

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PREVENTION

- Use of partially or fully phenotypically matched red cell units – to decrease alloimmunization

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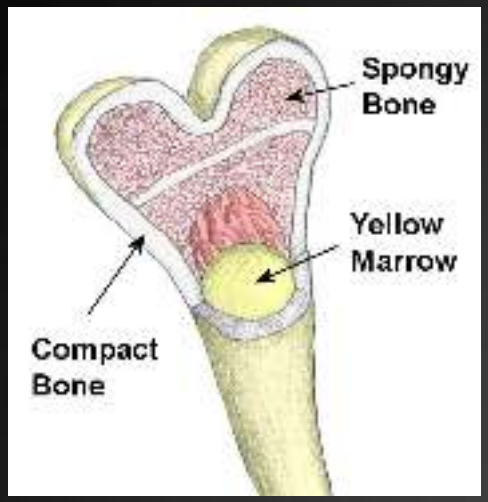

TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE (TA-GVHD)

TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE (TA-GVHD)

- Immune reaction
- Onset between 3-30 days post-transfusion
- Mortality rate ≥ 90% - death within 1-3 weeks after first symptoms

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CLINICAL PRESENTATION

- Fever
- MP rash – pruritic, start centrally extend to extremities
- Watery diarrhea & abdominal pain
- Elevated liver enzymes
- Pancytopenia – marrow aplasia

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PATHOPHYSIOLOGY

- 3 conditions must exist
  - HLA antigen difference between donor & recipient
  - Presence of donor immunocompetent cells in blood component
  - Recipient incapable to reject donor immunocompetent cells

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PATHOPHYSIOLOGY

- Recipient's immune system unable to eliminate donor viable lymphocytes
- Presentation of recipient Ag to donor lymphocytes
- Donor lymphocyte activated & proliferation
- Donor effector cells damage host tissue

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INVESTIGATION

- Skin biopsy – superficial perivascular lymphocyte infiltrate, necrotic keratinocytes, bullae formation

- Bone marrow examination – hypocellular/aplastic marrow

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INVESTIGATION

- Liver biopsy – degeneration & eosinophilic necrosis of small bile ducts, intense periportal inflammation, lymphocytic infiltration.

- Molecular studies – patient's buccal swab/skin fibroblast → distinguish between recipient & donor cells

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DIAGNOSIS

- Identify donor-derived lymphocytes in recipient circulation/tissues & presence of clinical symptoms.
  - Donor DNA → obtained from blood or affected tissue of recipient.
  - Recipient DNA may be difficult to obtain because of aplasia in the host. → use buccal swab or skin fibroblast to detect recipient DNA

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MANAGEMENT

- Stem cell transplantation – only curative option
  - Mostly unavailable due to urgent need for intervention.

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PREVENTION

- Gamma irradiation of cellular blood component in patient at risk of TA-GVHD
  - Minimum dose of 25 Gy

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Indications for the Transfusion of Irradiated Cellular Blood Components

Immunocompromised State (Indicated by Patient Condition)

- Intrauterine transfusions
- Low birth weight infants
- Neonates receiving a whole blood exchange
- Neonates undergoing extracorporeal membrane oxygenation
- Congenital immunodeficiencies
- Hematopoietic progenitor cell transplantation
- Solid organ transplantation
- Acute leukemia
- Hodgkin's disease
- Patients with B-cell malignancies
- Patients receiving fludarabine

Immunocompetent State (Indicated by Origin of Blood Component to Be Transfused)

- Directed donations from blood relatives
- HLA-matched platelets or granulocytes
- Crossmatched platelets or granulocytes
- Granulocyte components

HLA = human leukocyte antigen

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POST-TRANSFUSION PURPURA (PTP)

POST-TRANSFUSION PURPURA (PTP)

- Immune reaction
- Clinical presentation
  - Thrombocytopenia
    - <10,000 /L in 80% of case
  - Bleeding
    - Mucous membrane, GI, GU

7-10 days after blood transfusion

- 13% mortality related to intracranial hemorrhage

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PATHOPHYSIOLOGY

- <<Uncertain mechanism>>
- Previously sensitized to human platelet antigens (HPA) by pregnancy/transfusion

- Developed antibodies to HPA

- Reexposed HPA via platelet transfusion + microparticles of donor platelets coated on patient's platelets

- Immune response destroy both transfused and autologous platelet

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COMMON HPA ANTIBODIES

- HPA-1a = 60%
- HPA-1b
- HPA-2b
- HPA-3a
- HPA-5a
- HPA-5b
- Glycoprotein IV

Less frequency

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INVESTIGATION

- Detection of platelet antibodies
  - Platelet immunofluorescence assay (PIF)
  - Mixed passive hemagglutination assay (MPHA)

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DIAGNOSIS

- Presence of Ab in patient's plasma against HPA

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MANAGEMENT

- Intravenous immunoglobulin (IVIg)
  - Dose 0.5 – 1 gm/kg/day over 2-10 days
  - 85% response rate
  - Response time = 4 days after start therapy

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PREVENTION

- Receive antigen-negative blood product if documented history of PIP

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Summary of Delayed Transfusion Reactions

	SYMPTOMS	DIAGNOSIS	TREATMENT	PREVENTION
DSHTR	Asymptomatic Fatigue	+ Antibody screen/DAT ↓ Hemoglobin	As needed Transfuse antigen negative, AHG crossmatched compatible PRBC	Accurate record-keeping Obtain transfusion history Limit transfusions
DHTR	Flulike symptoms Pallor Jaundice	↓ Hemoglobin ↑ Total bilirubin	As needed Transfuse antigen negative, AHG crossmatched compatible PRBC	Accurate record-keeping Obtain transfusion history Limit transfusions
TA-GVHD	Rash Fever Diarrhea	Pancytopenia Identify donor engraftment	Not available	Gamma irradiation of cellular blood components as indicated
PTP	Bleeding	Thrombocytopenia HPA antibodies	Intravenous immunoglobulin	Limit transfusions
Iron overload	Multiorgan failure	High ferritin levels	Use of iron-chelating agents	Prophylactic use of iron-chelating agents Red cell exchange

AHG = antihuman globulin; DAT = direct antiglobulin test; DHTR = delayed hemolytic transfusion reaction; DSHTR = delayed serologic/hemolytic transfusion reaction; HPA = human platelet antigen; PRBC = packed red blood cells; PTP = post-transfusion purpura; TA-GVHD = transfusion-associated graft-versus-host disease

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THANK YOU