Acute Transfusion Reaction

High Institute For Education and Research on Transfusion Medicine

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Definition:

Any adverse change in clinical situation during or following transfusion

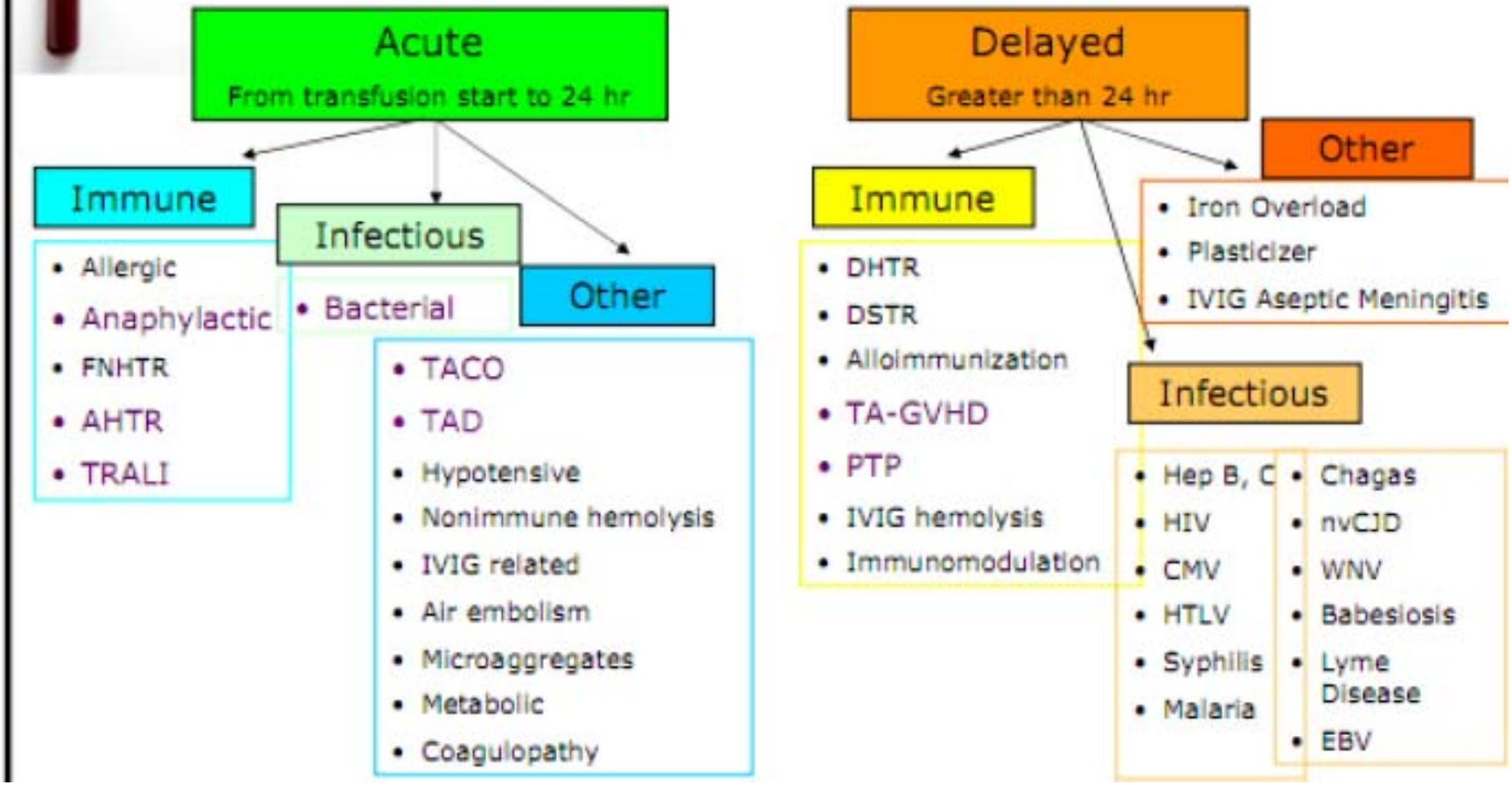
When can they occur?

- Usually during or immediately following transfusion but...
- Some may happen within 6 – 24 hours post transfusion
- A few are recognized 2 – 10 days post transfusion
- Many of the infectious hazards of transfusion are delayed - occurring weeks or months after transfusion *(we won't consider these further)*

How can we classify them?

- Acute
- Immune
- Infectious
- Common
- Mild
- Blood component related
- Delayed
- Non immune
- Non infectious
- Rare
- Severe
- Plasma protein related

Serious Transfusion Reaction Types – a Classification verview



Recognizing a Reaction?
... Almost any change...

Symptoms

- Fever
- Chills
- Itching
- Shortness of breath
- Chest tightness
- Pain at infusion site
- Anxiety

Signs

- Hypotension
- Hypertension
- Rigors
- Tachypnea
- Hypoxia
- Tachycardia
- Rash
- Red or dark urine

Recognizing a reaction

- You won't identify, treat or develop prevention strategies if you can't recognize a reaction

- Training for providers administering blood

- Patients should be informed
  - *a benefit of the informed consent process*

Pre transfusion assessment

- Provides a baseline clinical status for comparison
- May inform transfusion rate and patient monitoring

- Temperature
- Pulse
- Respiratory rate
- Blood pressure
- oxygen saturation

Differential diagnosis

- Minor or isolated initial symptoms can evolve into a severe reaction
- For each of the key transfusion related symptoms or signs, consider the differential diagnosis
  - "unrelated" to transfusion… or related to the underlying diagnosis or condition is always a possible explanation
  - Also consider concomitant therapies and their possible contributions

First things first…

- STOP the transfusion
- Maintain IV access
- Do a Clerical Identification check
  - Right patient? Right blood group? Right Unit?
- Inspect the blood component
  - Color, clots, hemolysis?
- Repeat vital signs assessment
- Provide symptomatic care

Fever &/or Rash

- Isolated symptom?
- Mild increase in temperature?
- Mild itching or minimal localized rash?
- Any progression of symptoms?

Treatment of mild isolated fever or fever and rash

- Oral antipyretic and/or antihistamine
- Cautious re initiation of transfusion or...
- **Continue with a new compatible component**

For all reactions other than mild and isolated rash, itching or fever – remaining component should be sent to transfusion service for possible further investigation

Severe or progressive fever

≥39° C or associated symptoms

- Hemolytic transfusion reaction
- Bacterial contamination

- Consider early antibiotic therapy
- Manage DIC and blood pressure
- Treat symptoms

Investigations

- Blood Bank testing
- Microbiology
- Additional investigations
  - CBC
  - coagulation studies
  - Urine sample

Hypotension

> 30mmHg drop in systolic or diastolic blood pressure

- Acute hemolytic transfusion reaction
- Sepsis
- TRALI
- **Anaphylaxis**
- Bradykinin mediated

- Consider Epinephrine if allergic symptoms (adrenaline)
- Urgent assessment for respiratory support
- Supportive care

Investigations

- Clinical assessment for:
  - Dyspnea, cough, tachycardia generalized flushing or anxiety, widespread rash

- After initial support consider IgA testing or other plasma proteins (haptoglobin)
- Many are idiosyncratic (patient and donor history may be informative)

Respiratory Distress

Oxygen saturation <90%

- **TACO**
- **TRALI**
- Anaphylaxis

- Oxygen
- Consider diuresis
- Supportive care including ventilator support

Investigations

- Oxygen saturation/arterial blood gas assessment
- JVP, orthopnea, cyanosis tachycardia
- Chest X ray
- echocardiography, BNP
- CBC

Respiratory Distress

TACO

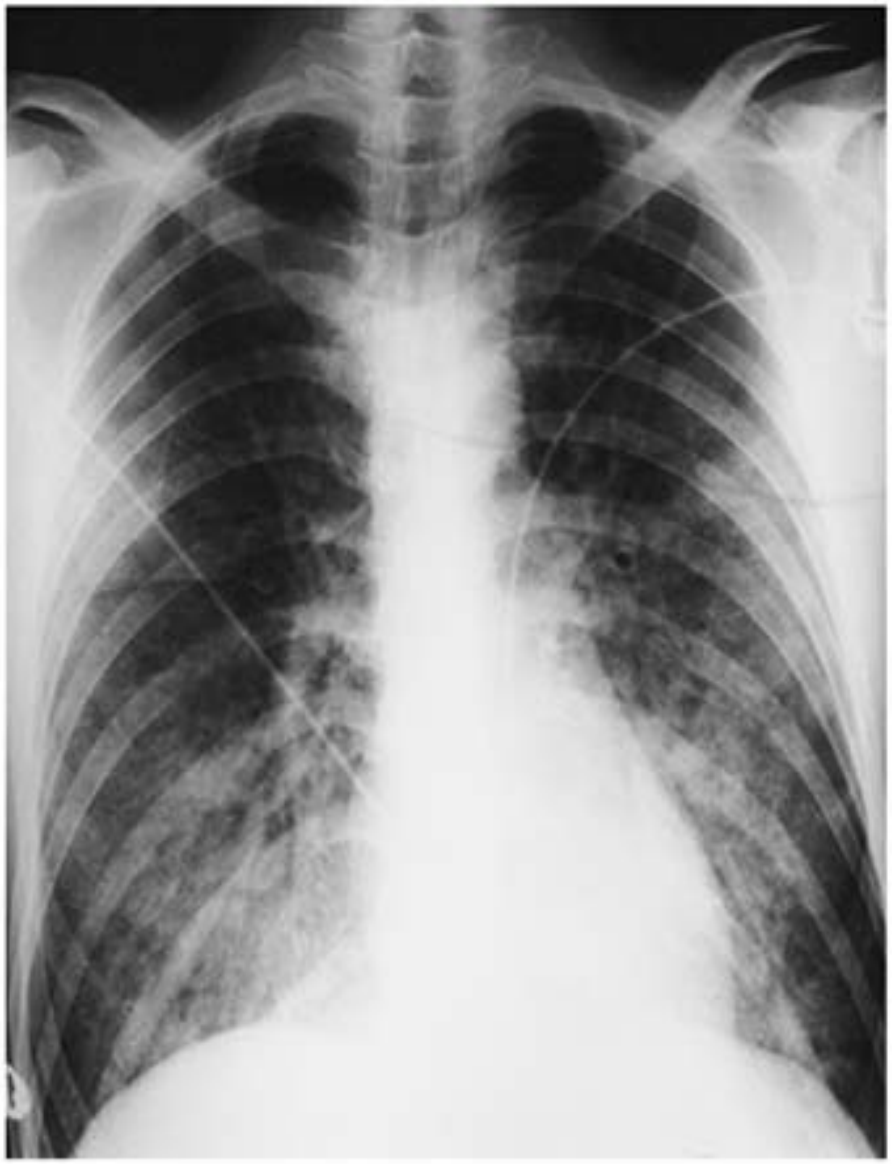
- Dyspnea, with tachycardia and increased venous pressure
- high risk patients or high volume & rapid transfusions

- Transfuse small volumes
- Preemptive diuretics

TRALI

- Hypoxia within 6 hours of transfusion
- Bilateral lung infiltrates on CXR
- No evidence of circulatory overload
- Patient HLA typing

- Reporting to supplier is critical for donor management



Considerations: Transfusion Reaction

- **Pulmonary Transfusion Reaction**
  - Transfusion-associated circulatory overload (TACO)
  - Transfusion-related acute lung injury (TRALI)
- **Transfusion Reaction with Pulmonary Symptoms**
  - Allergic (anaphylaxis)
  - Septic Transfusion Reaction

Other Considerations

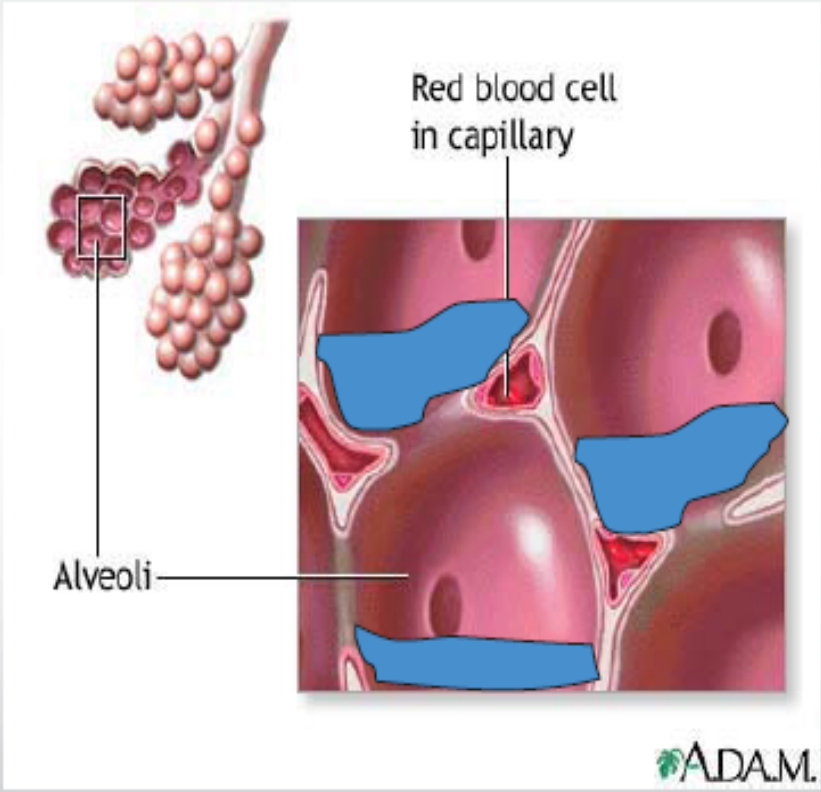
- Myocardial infarction
- Acute respiratory distress syndrome (ARDS)
- Sepsis
- Drug reaction
- Pneumonia

Pulmonary Edema

- **Cardiogenic (hydrostatic)**
  - TACO
  - Myocardial Infarction
- **Non-cardiogenic (permeability)**
  - TRALI
  - ARDS

Transfusion-Associated Circulatory Overload (TACO)

- Volume overload temporally associated with transfusion
- **Signs and Symptoms**
  - Shortness of breath
  - Increased respiratory rate
  - Hypoxemia
  - Increased left atrial pressure
  - Jugular venous distension
  - Elevated systolic blood pressure

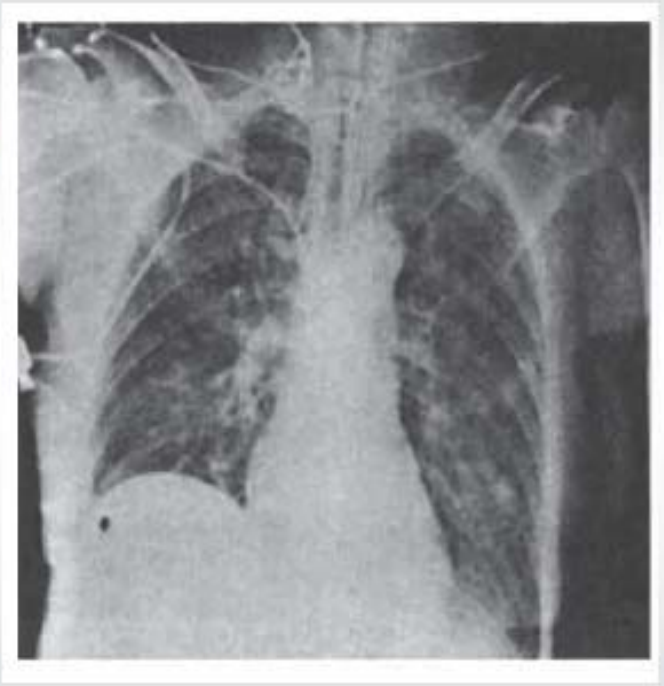


TRALI is a Diagnosis of Exclusion

We must rule out all other possible etiologies before rendering a diagnosis of TRALI

TACO vs. TRALI
Diagnostic Tools: Chest X-ray

- Pros:
  - Identify pulmonary edema
  - Identify pleural effusions (more consistent with TACO)
  - See evidence of other pulmonary disease
- Cons:
  - Does not show specific mechanism of edema
  - Radiology reports are often vague
- Suggested to measure vascular pedicle width and cardiothoracic ratio to improve specificity (never seen this)



Cytopenias

Anemia or thrombocytopenia

- Delayed hemolytic transfusion reaction
  - Immunohematology
  - hemolysis
  - Treatment: supportive
- Post Transfusion Purpura
  - HPA mismatch
  - Severe thrombocytopenia
  - Treat with IVIG(steroids or plasma exchange)
  - Subsequent transfusions from antigen negative donors (or washed cellular products?)

Pancytopenia

- TA-GVHD
  - immune deficiency; HLA similarity
- Rash, fever, abdominal pain and abnormal LFT with evolving pancytopenia
- Diagnosis with biopsy; identify donor lymphocytes
- Prevent with irradiation of cellular blood components

Summary of Initial Clinical Investigation

- Vital signs
  - Important that vital signs be assessed routinely pre transfusion
  - Post transfusion *and* post reaction
  - Compare with prior status
- Underlying diagnosis and specific indication for transfusion
- History & Physical examination
  - Rash, hives, edema, breath sounds, heart rate, pain, venous pressures

Summary of follow up

Depending on presentation

- CXR
- Urine Hb
- CBC, retic
- Culture/Gram Stain; D& R
- IgA
- HLA typing
- Blood smear
- Hemolysis indicators

Serological investigation

- Hemolysis inspection
- DAT
- Repeat the BG
- Ag Screening
- Cross Match

Treatment

- Supportive care:
  - Fluid and/or pressor support for hypotension
  - Antipyretics for fever
  - Antibiotics for suspected infection
  - Analgesics for pain
  - Antihistamines for hives
  - Epinephrine for anaphylaxis
  - Diuresis for volume overload
  - Oxygen for dyspnea with hypoxia

Prevention

- Premedication… or not?
  - Repeated reactions… or not?
  - The evidence for efficacy of premedication is lacking
  - Do antipyretics mask a fever?

- Review transfusion process
  - Are there local or system changes that would limit reactions?
  - Transfusion reactions as an element of routine review in your quality system

Haemovigilance...what do the data tell us about adverse events?

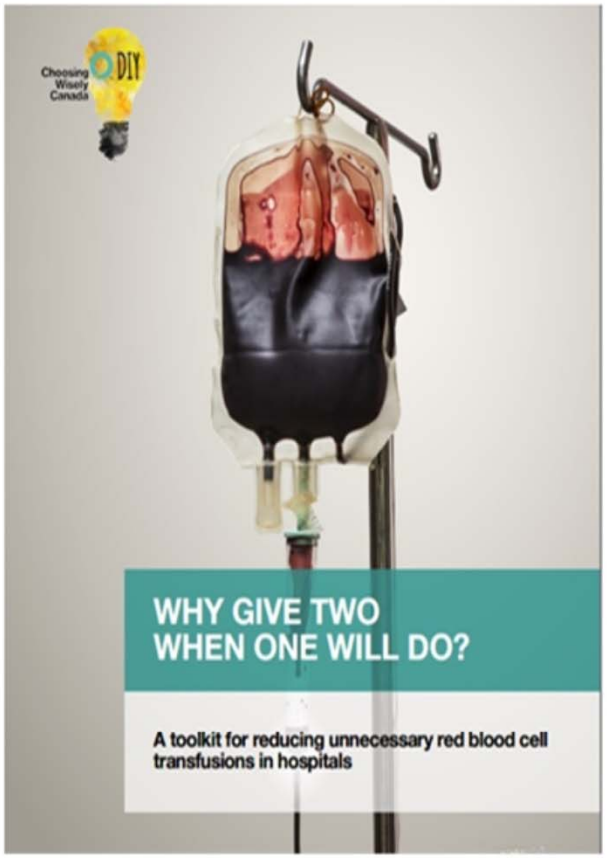
- Blood transfusion is a very common procedure.
- Transfusion reactions are also very common:
  - *Up to 1 reaction per 100 transfusions (Lancet)*
- Haemovigilance helps inform:
  - What is common
  - What is serious
  - What is "emerging"
  - What is "operational" vs "biological"

Process changes leading to safer transfusion

- Two blood groups (or mechanical barriers) to prevent mis transfusion
- TRALI mitigation by limiting plasma containing products to those without anti HLA antibodies
- Pre transfusion culture of platelets
- Additive solutions
- Leukoreduction

Transfusion Safety/Transfusion Risk

- Transfusions are very safe; but there is always risk
- Informed consent is important
- A valid indication for transfusion is equally important



http://www.choosingwiselycanada.org/

DHTR

Tx-Associated Graft Versus-Host Disease (TAGVHD)

- Tx immunologically competent graft cells e.g (T-cells, CD8) to immuno-incompetent host incapable rejecting the cells
- **Types**

1. Acute:

Occur 2–30 days post Tx of graft cells

2. Chronic:

Occur 100 days post Tx of graft cells

Graft-vs-host disease (GVHD)

- Transfusion-associated GVHD is usually caused by transfusion of products containing immunocompetent lymphocytes to an immunocompromised host.
- The donor lymphocytes attack host tissues.
- GVHD can occur occasionally in immunocompetent patients

- Symptoms and signs include fever, skin rash (centrifugally spreading rash becoming erythroderma with bullae),
- vomiting, watery and bloody diarrhea, lymphadenopathy, and pancytopenia due to bone marrow aplasia.
- Jaundice and elevated liver enzymes are also common. GVHD occurs 4 to 30 days after transfusion and is diagnosed based on clinical suspicion and skin and bone marrow biopsies.
- GVHD has > 90% mortality because no specific treatment is available

Transfusion-associated Graft-versus-Host Disease (TA-GVHD)

Patient at risk:

- **Bone marrow transplantation**
- **Chemotherapy**
- **Radiation treatment**
- **Newborn**

Transfusion-associated Graft-versus-Host Disease (TA-GVHD)

Pathophysiology

Infusion of Immunocompetent Cells (Lymphocyte)

↓

Patient at risk

↓

proliferation of donor T lymphocytes

↓

attack against patient tissue

Graft-versus-Host Reaction

Signs & Symptoms

- Onset ~ 3 to 30 days after transfusion
- Clinical significant – pancytopenia
- Other effects include fever, liver enzyme, copious watery diarrhea, erythematous skin ⟶ erythroderma and desquamation

Graft-versus-Host Reaction

Therapy

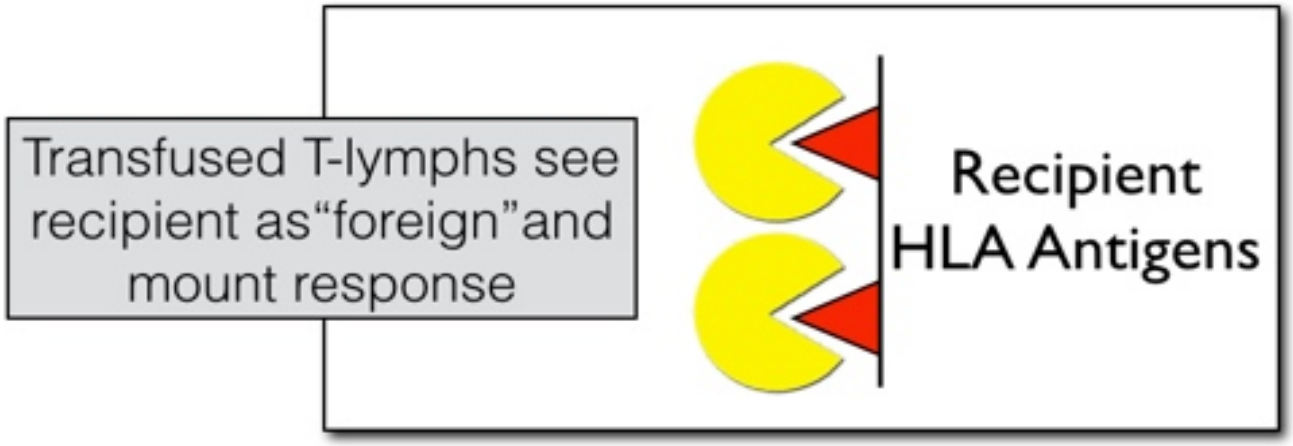
Drugs :- corticosteroids, methotrexate, azathioprine, antithymocyte globulin

But no adequate therapy

Prevention

Irradiation of Blood Components

Normal Events



Attack!

TA.GVHD

- Homozygous haplotype → heterozygous haplotype
- Recommendation:
  - Gammairradiation - 2500 cGY

GVHD pathology

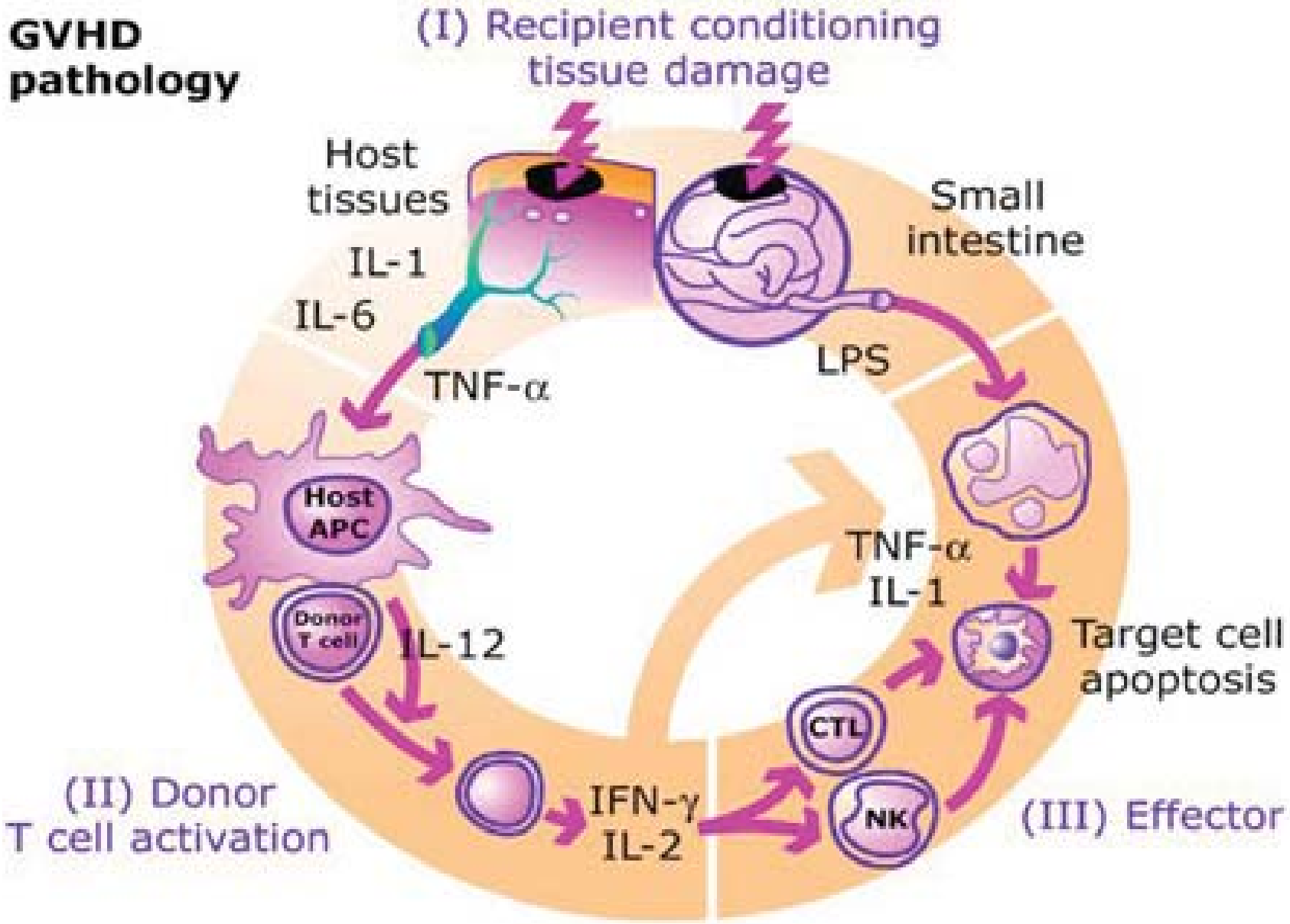
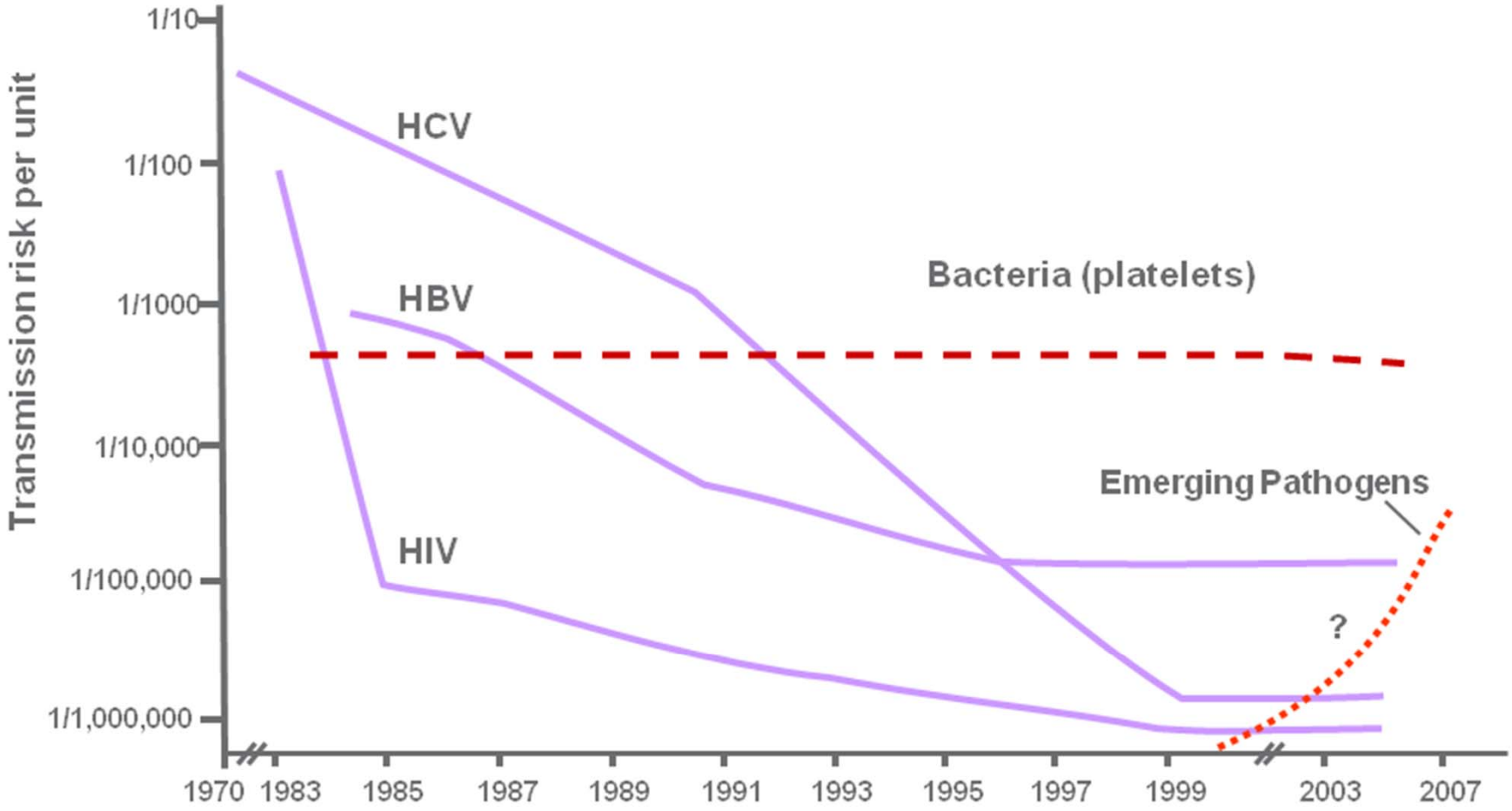


Table 1: Estimated residual risk during the period in which each screening test was in use

Virus; test	Window period, d (range)	No. of incident cases	No. of person-years	Incidence rate per 100 000 person-years	Residual risk per million donations (95% CI)
HIV					
Anti-HIV-1 / anti-HIV-2	22 (6–38)[6,7,20]	13	2 034 394	0.64	0.38 (0.05–1.03)
Anti-HIV-1 / anti-HIV-2 with p24 antigen	16 (8–24)[6,7]	7	1 284 391	0.55	0.24 (0.03–0.62)
HCV					
Anti-HCV EIA-2	82 (54–192)[7,21]	25	1 294 422	1.93	4.34 (1.93–15.04)
Anti-HCV EIA-3	66 (38–94)[7,22]	23	994 164	2.31	4.18 (1.60–8.97)
Anti-HCV EIA-3 with HCV NAT	19 (10–29)[23]	3	222 169	1.35	0.70 (0.08–3.13)
HBV					
HBsAg	59 (37–87)[7,22]	113	3 318 742	5.27	8.52 (4.44–15.11)
HTLV					
Anti-HTLV-I / anti-HTLV-II	51 (36–72)[7,24]	16	3 318 784	0.48	0.67 (0.24–1.42)

Infectious Disease Risks from Transfusion



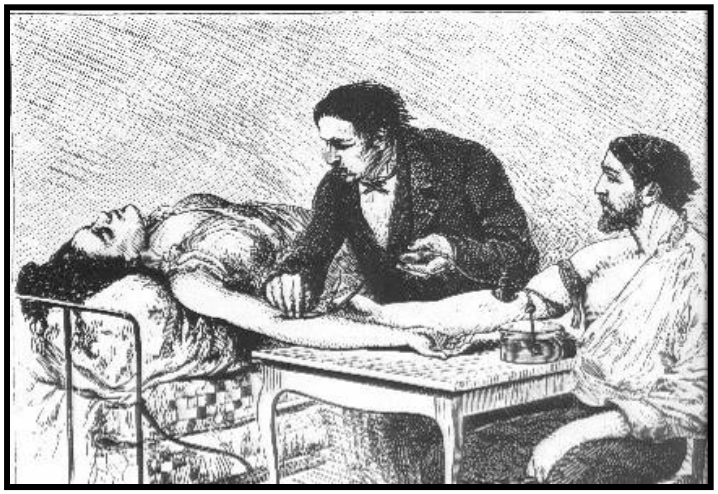
American Red Cross

H. Klein, Transfusion 2007

SUMMARY

"Blood transfusion is like marriage: it should not be entered upon lightly, unadvisedly or wantonly or more often than is absolutely necessary."

R. Beal
ISBT

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