Transfusion reactions illustrated

Chapter 1
Transfusion practice

Procedure of transfusion practice

- In general, transfusion-associated incidents occur due to multiple errors, most of which occur in the clinical area. The most common errors in the clinical area are patient identification errors, which have led to serious results.

- However, some incidents are preventable if errors in the clinical area are discovered in the transfusion laboratory. Errors in the transfusion laboratory occur primarily due to inexperienced laboratory technologists.

- Transfusions in Japan have been conducted even in small hospitals. It is necessary to enforce the blood transfusion system at each hospital in accordance with the policies and guidelines of the Ministry of Health, Labour and Welfare of Japan: the appointment of a doctor responsible for blood transfusion, laboratory technicians, clinical nurse specialists; establishment of a department of blood transfusion to record blood consumption, disposal rate, and adverse events; and establishment of a transfusion committee in the hospital.

- It is recommended that a joint transfusion committee also established at the prefecture or county level in Japan.

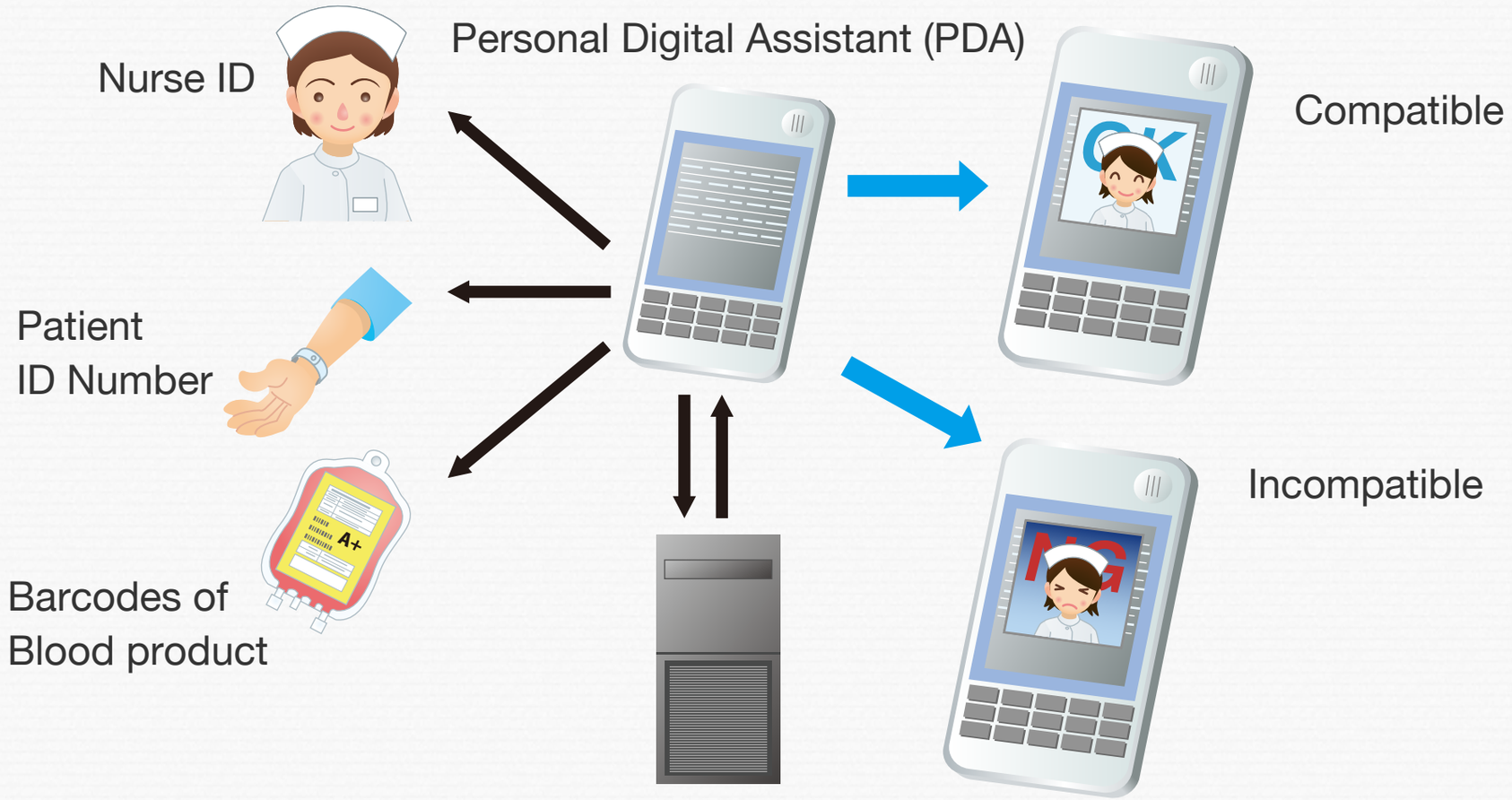


Figure 1-1-1 Electronic collation of blood product and patient at the bedside

The pre-transfusion check at the bedside is the most critical step in preventing mistransfusion. A bar code-based identification system is ideally suited to bedside check requirements. The label of blood products in Japan has a barcode showing ABO blood type and other information. The electronic collation of blood product and patient should collate the barcodes of the patient’ s wristband, the blood product, and operator identification number.

Blood components in Japan

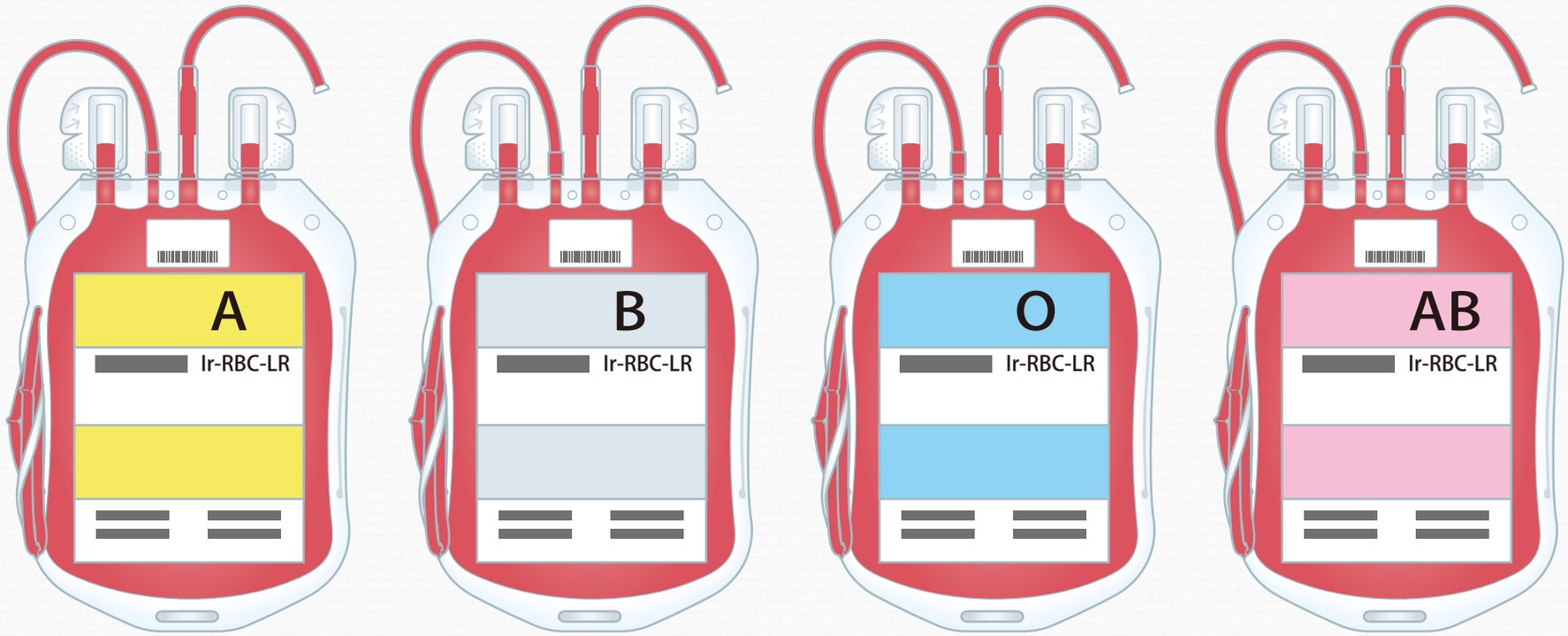


Figure 1-2-1 Colored labels for blood products

Blood products in Japan have colored labels according to ABO blood types. This might have some favorable effect for the prevention transfusion errors.

A bedside potassium adsorption filter

- Although extremely rare, some reports describe that the K+ ion, which exists in very low concentration in approximately 100 mL of MAP liquid, causes sudden hyperkalemia on red blood cell (RBC) transfusion.

- Therefore, a potassium adsorption filter has been developed by Kawasumi Laboratories, Inc. in 2002. This company makes a cation exchange resin using polystyrene sulfonate sodium, which exchanges an equivalent content of releasing sodium ion and adsorbing potassium ion. It received insurance coverage from 2012.

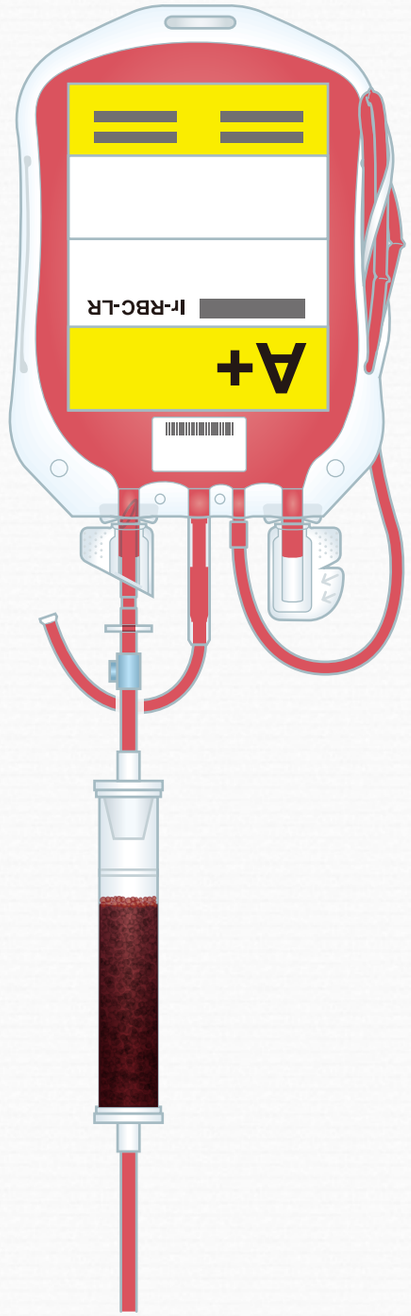


Figure 1-3-1 A bedside potassium adsorption filter

Chapter 2

Hemolytic transfusion reactions

ABO-incompatible blood transfusion

- Acute hemolytic transfusion reaction resulting from ABO-incompatible blood transfusion is usually due to the reaction of ABO antibodies in patient plasma with transfused red cells.

- Antibody-coated red cells activate the complement system and result in intravascular hemolysis. Following intravascular hemolysis, over production of cytokines, hypotension, renal failure, and disseminated intravascular coagulation (DIC) will appear.

- Patients transfused with more than 50 mL of incompatible blood are likely to have severe reactions.

- When ABO-incompatible transfusion occurs, it should be stopped immediately. A major mismatch(e.g., O recipient, A donor) can sometimes cause life-threatening side effects in the recipient. In severe reactions, vigorous treatment with pressure agents or diuretics, in addition to fluid resuscitation, should be carried out at intensive care units without delay to maintain systemic circulation and urine output.

- The cause of the ABO-incompatible transfusion must then be clarified in order to take measures to prevent similar errors in the future.

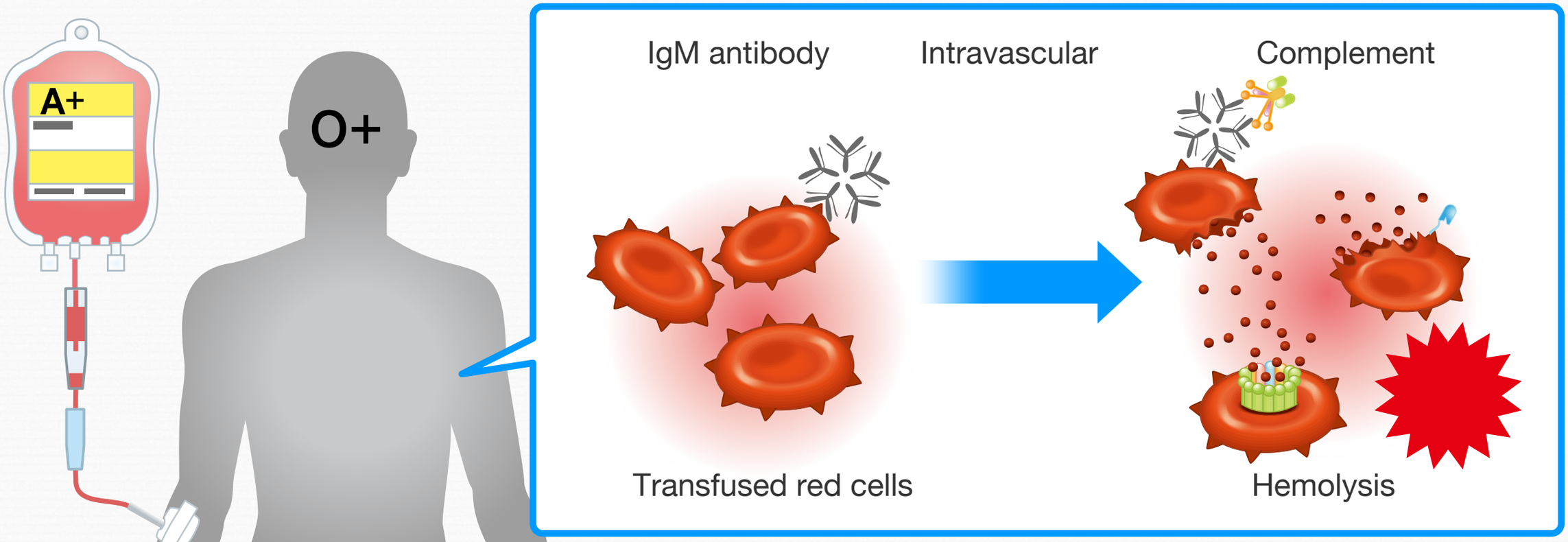


Figure 2-1-1 Pathophysiology of ABO-incompatible blood transfusion

Acute hemolytic transfusion reaction resulting from ABO-incompatible blood transfusion is usually due to the reaction of ABO antibodies with transfused red cells. Antibody-coated red cells activate the complement system, resulting in intravascular hemolysis. Subsequently, over production of cytokines, hypotension, renal failure, and disseminated intravascular coagulation will appear.

Delayed hemolytic reaction

- Virtually all delayed hemolytic transfusion reactions (DHTR) are due to secondary immune responses. Most commonly, the recipient has been immunized by one or more transfusions and/or pregnancies.

- The transfusion may provoke an anamnestic immune response so that, days to weeks after transfusion, there is a rapid increase in antibody concentration and rapid destruction of the transfused RBCs.

- The most constant clinical features of DHTR are a fall in Hb concentration and manifestation of fever. Other features which are often observed are jaundice and hemoglobinuria.

Table 11-2 Diagnosis of DHTR

1. Irregular antibody test and crossmatch test in the recipient's serum before and after transfusion（pretransfusion: －, posttransfusion: ＋）
2. Irregular antibody presence detected（one or more antibodies ）
3. Direct antigloburin test results become positive（ surviving transfused RBCs ）
4. Some instances of antibody elution test results become positive
5. Blood typing of transfused RBCs
6. Hemolitic clinical findings（fall in Hb concentration, increase in LDH, total-birilubin, hemoglobinuria, etc. ）
7. Test requisition or consult in blood center

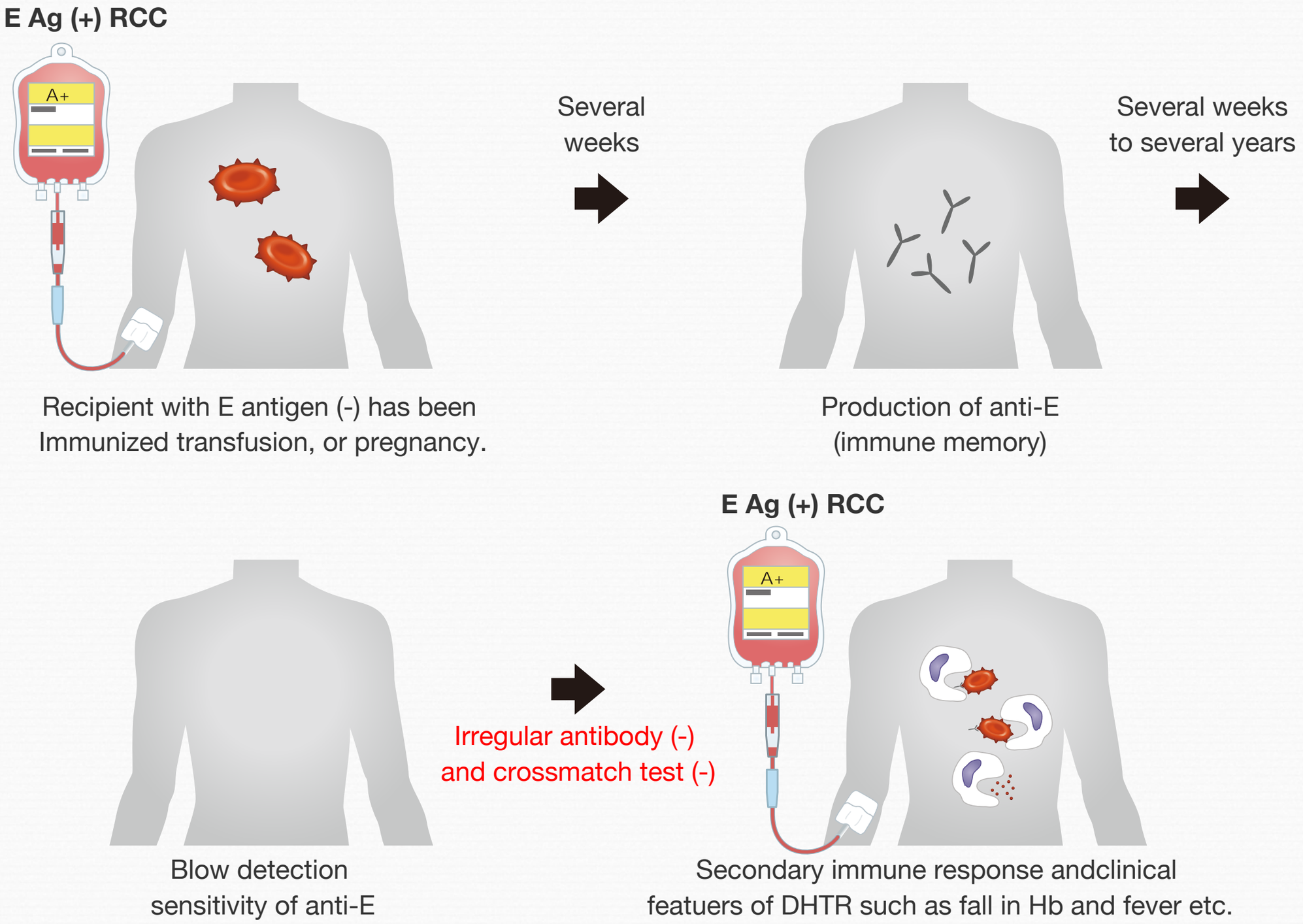


Figure 2-2-1 Pathogenesis of DHTR(e.g. : case of recipient with anti-E)

Chapter 3

Non-hemolytic transfusion reactions

Transfusion-related acute lung injury (TRALI)

- Transfusion-related acute lung injury (TRALI) is one of the most severe non-hemolytic adverse reactions. Although neither presence of antibodies in donors nor confirmation of cognate antigens in recipient is required for diagnosis, anti-HLA or anti-HNA is implicated as a cause of TRALI.

- Predominant use of male plasma has achieved a successful outcome for reducing TRALI cases.

- Circulatory overload should be ruled out for making a proper diagnosis of TRALI.

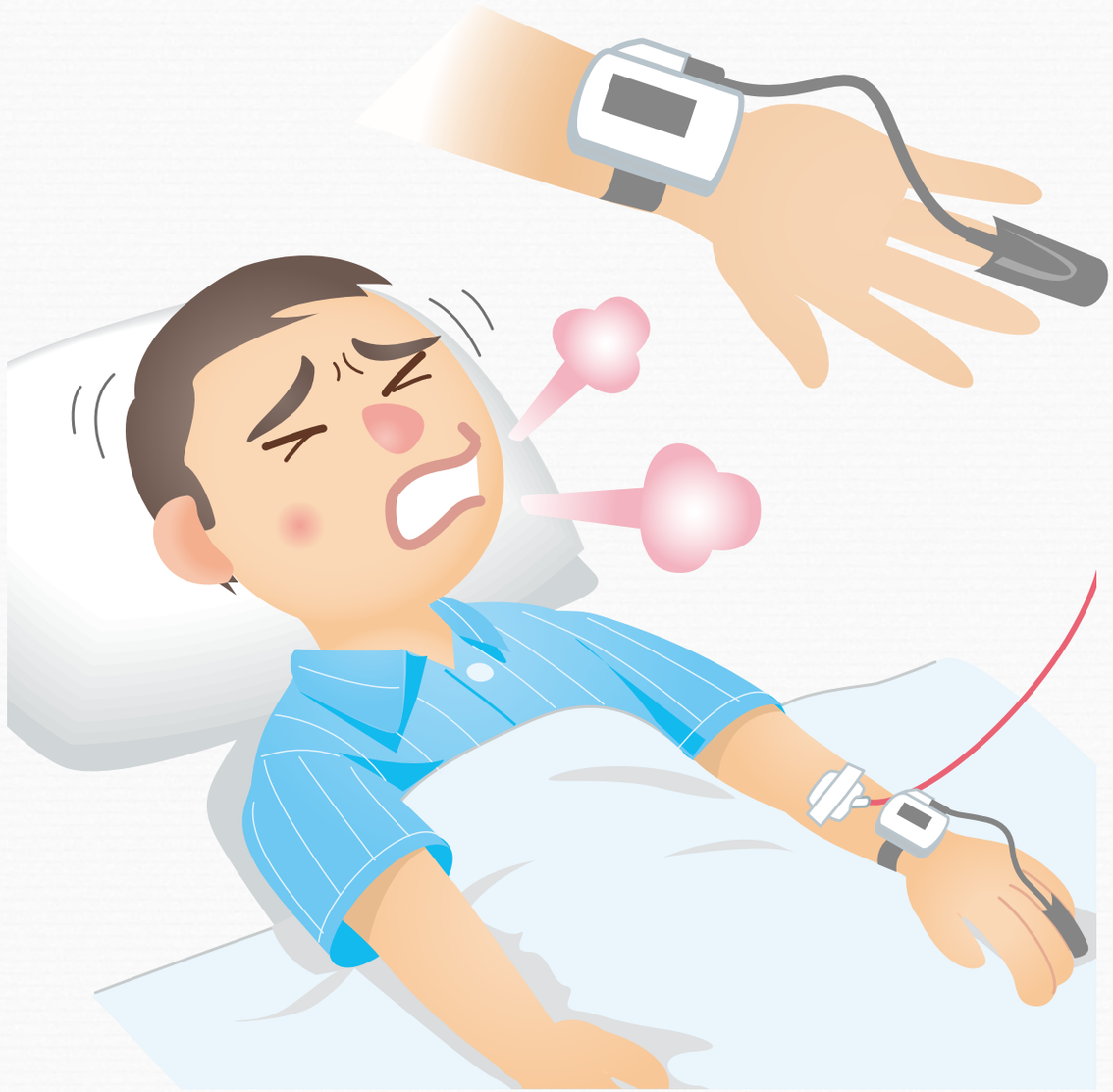


Figure 3-1-1 TRALI
- signs and symptoms: Dyspnea Hypoxemia

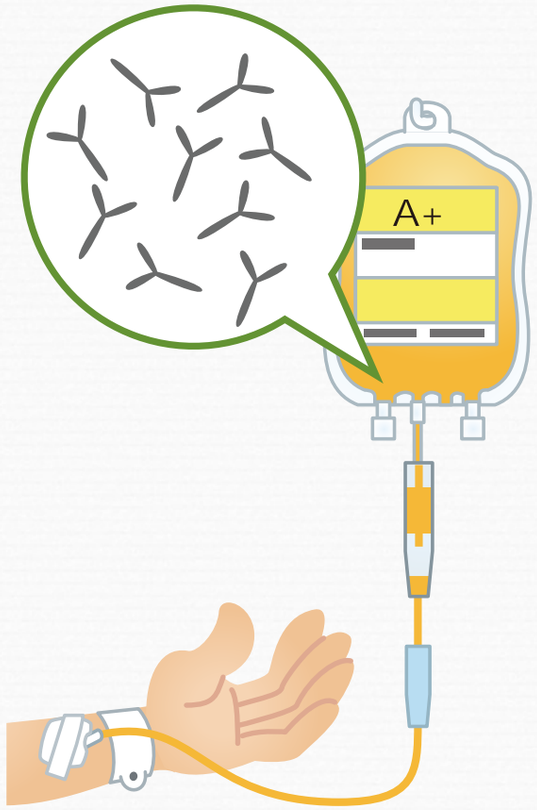


Figure 3-1-2 TRALI – causes
Anti-HLA or anti-HNA antibodies in donor blood

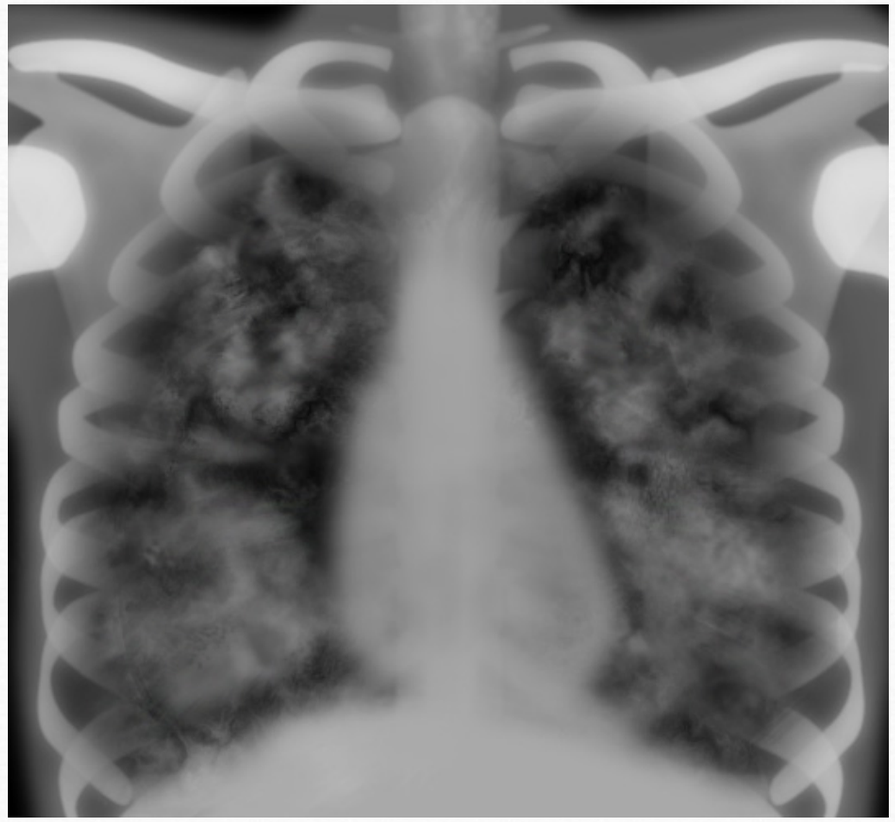
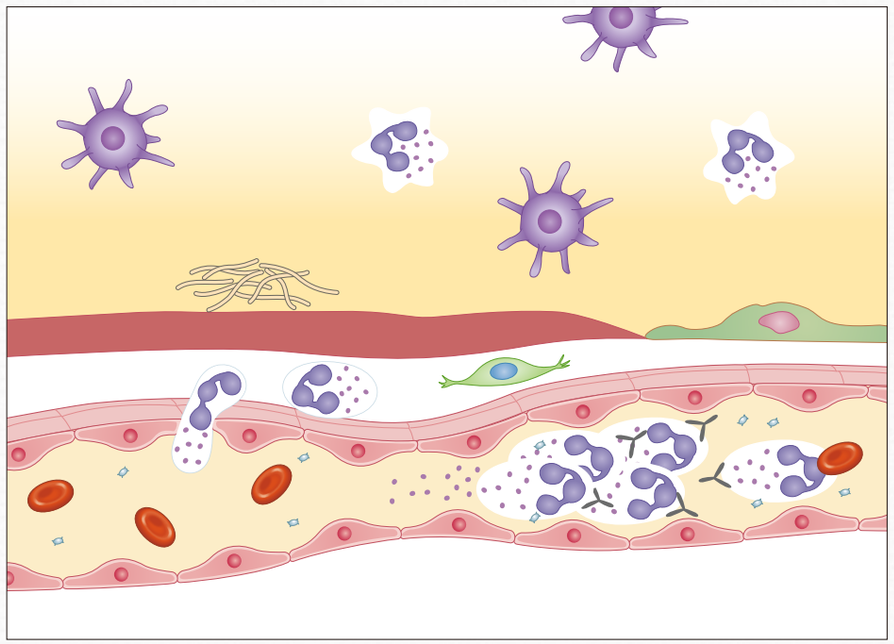


Figure 3-1-3 TRALI
– Chest radiograph
Bilateral infiltrates on frontal chest radiograph

Figure 3-1-4 TRALI – pathophysiology
The interaction between anti-HLA or anti-HNA antibodies in donors and cognate antigens in recipient result in the increase of permeability of lung microvasculature endothelial cells and the aggregation of neutrophils.



Transfusion-associated circulatory overload (TACO)

- Transfusion-associated circulatory overload (TACO) is one of the most severe complications of transfusion, which has been reported as early as 1940's. TACO has drawn much attention recently as a differential diagnosis of TRALI.

- TACO is basically a congestive heart failure with respiratory distress due to either volume overload or rapid infusion rate of blood products combined with underlying heart, renal or pulmonary disease.

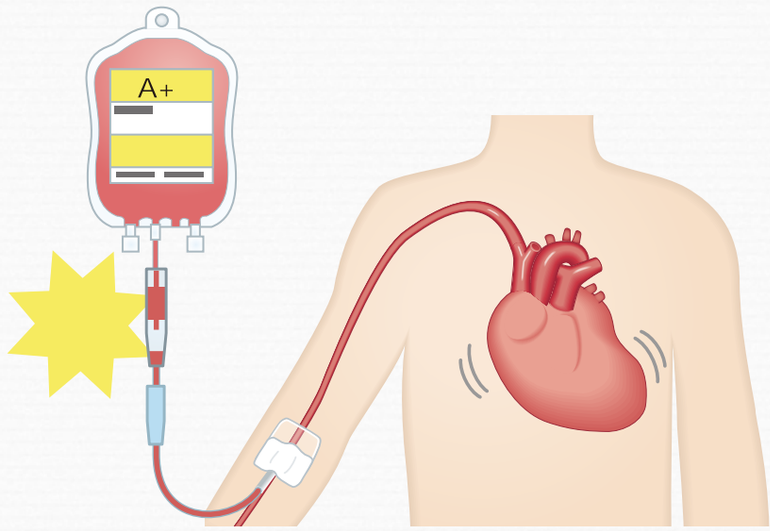


Figure 3-2-1 TACO – causes
TACO is a congestive heart failure due to circulatory overload of blood products.

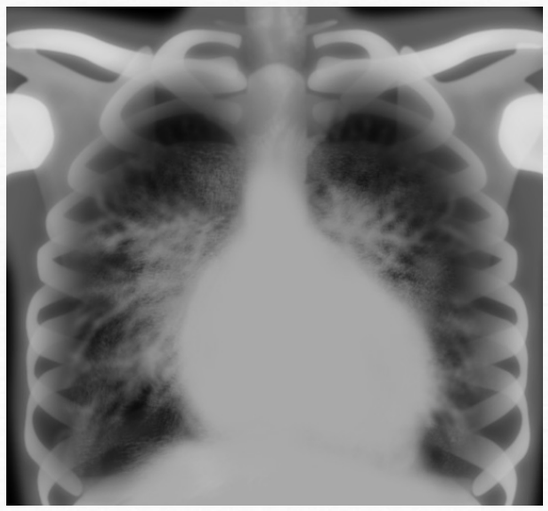


Figure 3-2-2
TACO – chest X-ray
Pulmonary congestion or edema on chest X-ray.

Allergic reaction

- Although serious allergic reactions are rare, allergic reactions are most common reactions among non-hemolytic transfusion reactions.

- An allergic reaction may present only with mucocutaneous signs and symptoms occurring during or within 4 hours of transfusion. An allergic reaction can also involve respiratory and/or cardiovascular systems and present like an anaphylactic reaction.

Figure 3-3-1 Allergic reactions
- symptoms Skin eruptions

- Elevation of serum tryptase level suggests a allergic transfusion reaction. However, exact mechanisms of allergic reaction are almost unknown.

- Allergens proven to elicit allergic reactions are plasma proteins such as IgA and haptoglobin. Introducing IgA and haptoglobin with transfused blood into patients who are deficient in these plasma proteins and who have specific IgE and/or IgG antibodies can cause immediate and serious reactions.

- Anti-histaminic is not effective in preventing allergic reactions, but effective to treat mild allergic reactions. In some cases washed red cells and platelets are used to prevent allergic reactions.

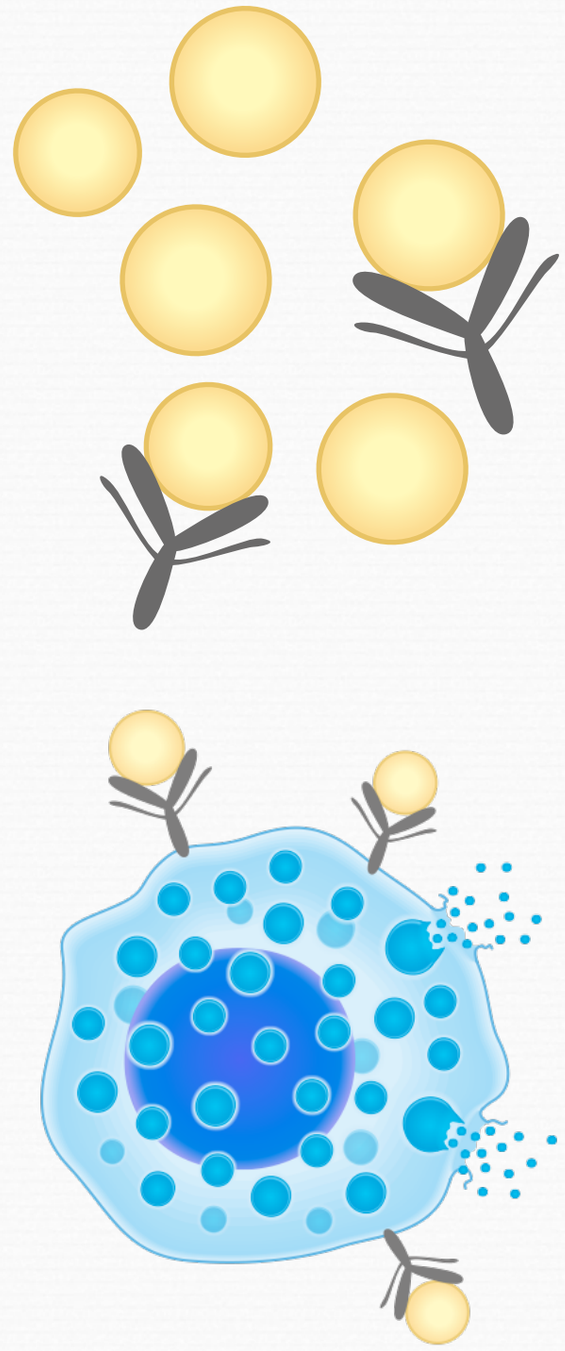


Figure 3-3-2 Allergic reactions – pathophysiology
Anti bodies to plasma proteins

Transfusion transmitted bacterial infection

- Bacterial infection is suspected when the recipient exhibits symptoms such as fever of 39°C or more and an increase or decrease in systolic blood pressure within four hours following the start of transfusion.

- If a transfusion-associated bacterial infection is suspected from clinical symptoms of the recipient, any transfusion in progress should be stopped, and the recipient should be treated for sepsis immediately.

Figure 3-4-1 Transfusion transmitted bacterial infection - signs and symptoms Fever > 39°C

- Culturing of the blood bag contents and the recipient's blood, as well as an endotoxin test should be done to confirm the presence of bacteria.

- The appearance of the unit should be checked before transfusion, and units with the obvious change in appearance should not be used.

- Currently Japanese Red Cross blood centers have implemented a universal leukocyte reduction and initial aliquot diversion system for all of blood and blood components.

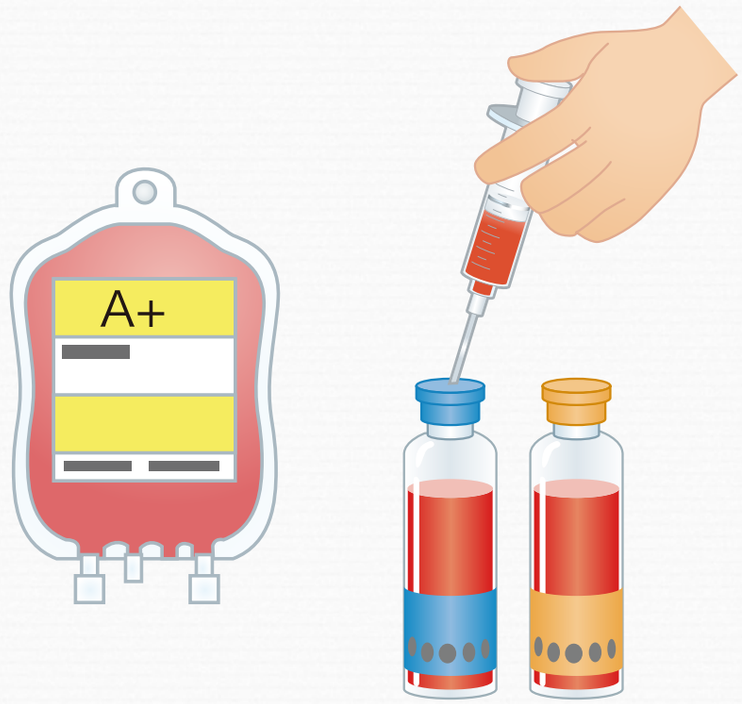


Figure 3-4-2 Transfusion transmitted bacterial infection Culturing of the blood bag contents

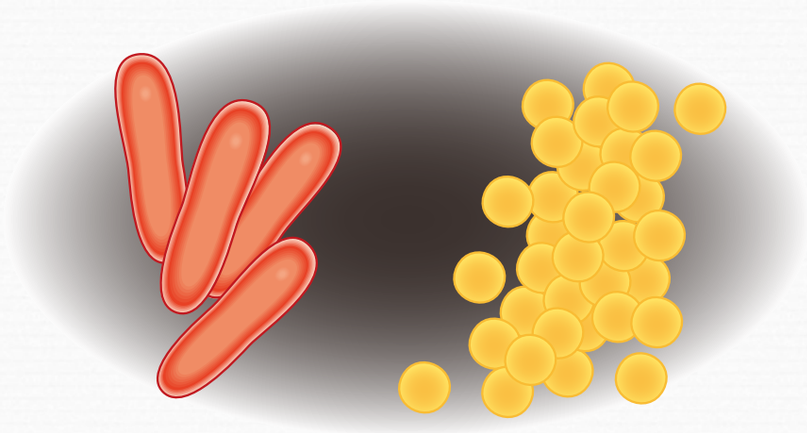


Figure 3-4-3 Transfusion transmitted bacterial infection
L: Yersinia enterocolitica
R: Staphylococcus aureus

Post-transfusion graft-versus-host disease

- Post-transfusion graft-versus-host disease (PT-GVHD) is a fatal transfusion reaction induced by blood donor lymphocytes. One or two weeks after transfusion, recipients show fever and erythema followed by liver dysfunction, diarrhea, melena, bone marrow aplasia, or multi-organ failure, and eventually dying a month after transfusion.

- Even an immunocompetent recipient may not be able to reject donor lymphocytes with HLA one-way match and may be suffered with PT-GVHD.

- Any effective treatments have not been established to cure PT-GVHD, and irradiation of blood before transfusion should be considered to prevent PT-GVHD.

- Japanese are known to be at higher risk of PT-GVHD, because there are few HLA haplotypes.

- The Japan Society of Transfusion Medicine and Cell Therapy (JSTMCT) organized a subcommittee for the prevention of PT-GVHD, and has issued five updates for the guidelines on irradiation of blood and blood components to prevent PT-GVHD.

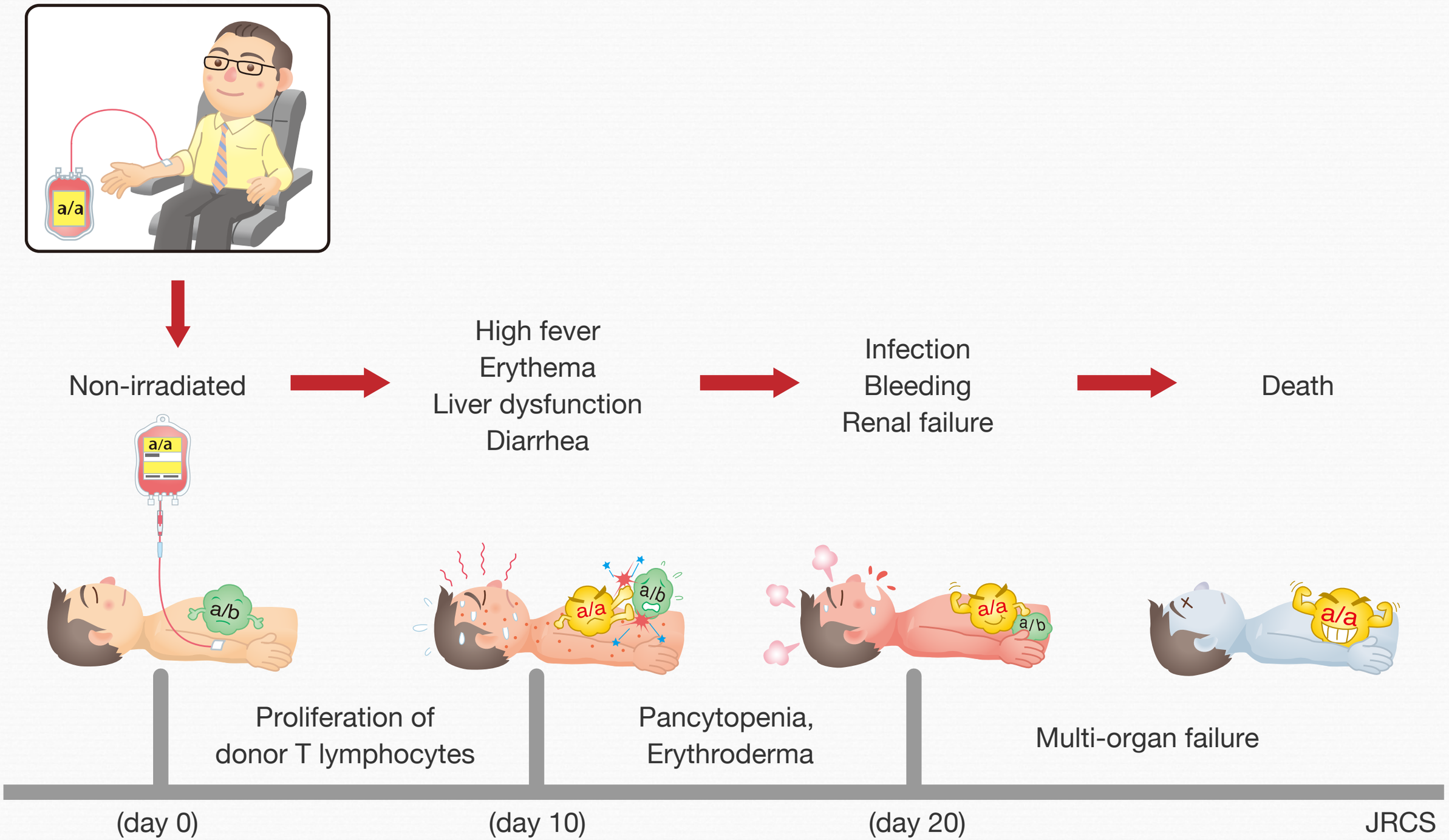


Figure 3-5-1 Post-transfusion graft-versus-host disease

PT-GVHD occurs when donor lymphocytes in transfused blood attack recipient organs and tissues recognizing recipient HLA and are not eliminated by host immunological defense.

Post-transfusional iron overload

- Many patients with severe aplastic anemia and myelodysplastic syndromes (MDS) often become transfusion-dependent. Excess transfusional iron deposited in the liver, heart, and other organs as free iron, can cause organ dysfunction and damage over time.

- Patients requiring chronic transfusion therapy should be screened for hyperferritinemia.

- Those with serial serum ferritin levels exceeding 1000 ng/mL or a total infused red blood cell volume of 100 mL/kg of body weight or more should be considered for treatment with iron chelation agents.

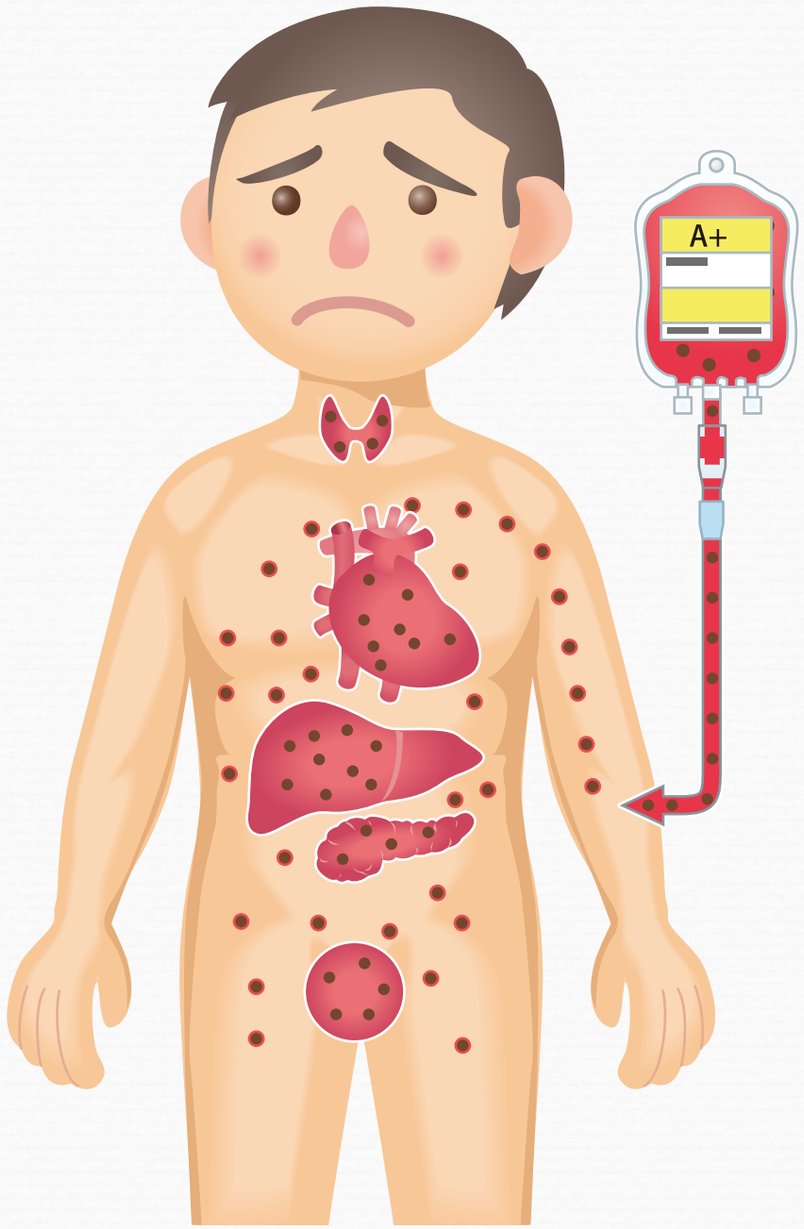


Figure 3-6-1 Pathophysiology of post-transfusional iron overload

Colophon

This eBook is published by a study group to establish guidelines to distinguish between TRALI and TACO (Japan Health and Labour Science Research Grant for Research on Regulatory Science of Pharmaceuticals and Medical Devices).

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Attribution

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- Figures 3-5-1 is modified from PT-GVHD Report in 1994 by JRCS.
- Summaries (page7, 9), and figures (1-1-1, 2-1-1, 3-1-1, 3-1-3, 3-2-2, 3-3-1, 3-3-2, 3-4-1, 3-4-2) are quoted from research reports in 2011 and 2012 of a study group concerning transfusion reactions granted by Japan Health and Labour Science Research Grant for Research on Regulatory Science of Pharmaceuticals and Medical Devices (study representative; Y Fujii).
- Figures (3-1-2, 3-1-4, 3-2-1) are quoted from research reports in 2014 of a study group to establish guidelines to distinguish between TRALI and TACO granted by Japan Health and Labour Science Research Grant for Research on Regulatory Science of Pharmaceuticals and Medical Devices (study representative; T Tasaki).