Transfusion Medicine

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Content

- Blood groups
- Cross-matching and pre-transfusion tests
- Blood components and blood products
- Complications of blood transfusion
- Blood transfusion in specific situations

Blood groups (血型)

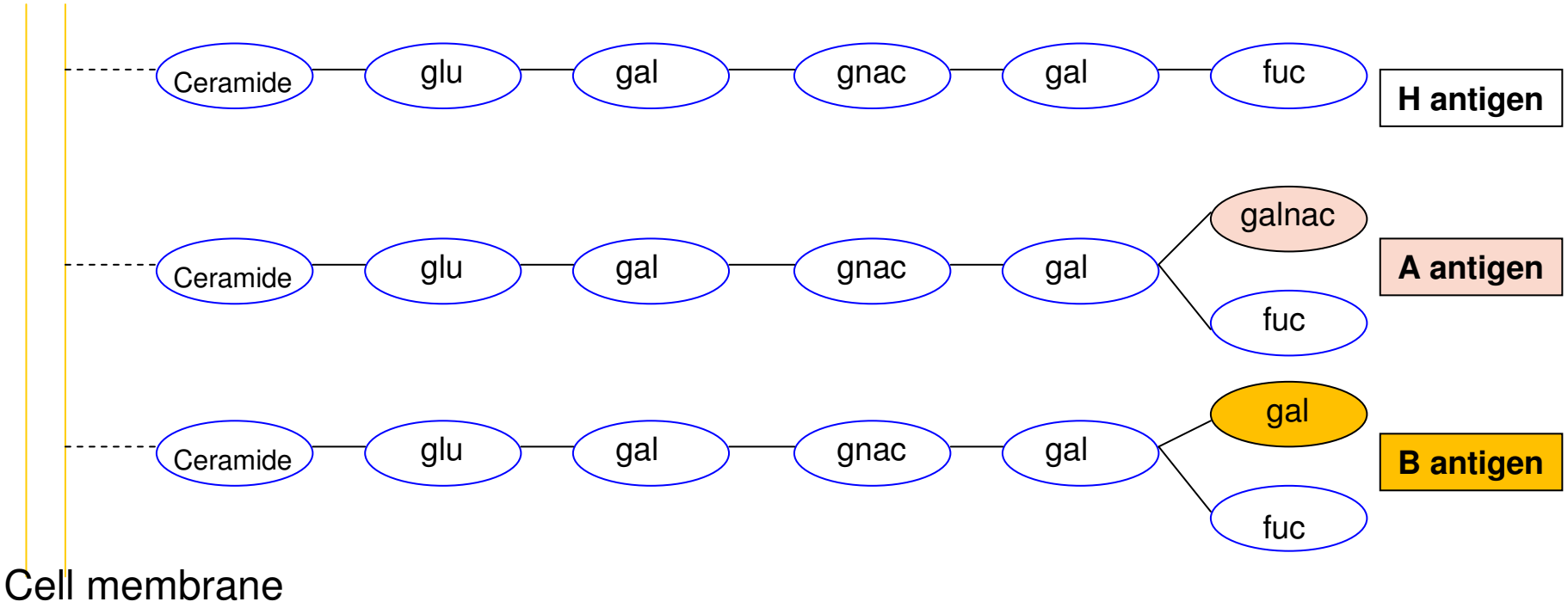
- Determined by the red cell antigens (紅血球抗原)
- About 400 red blood cell group antigens have been described
- Individual who lack a particular blood group antigen may produce antibodies (抗體) reacting with that antigen and may lead to a transfusion reaction (輸血反應)
- ABO and rhesus (獼因子) groups are the most clinically significant blood groups

Blood group antibodies

- Naturally occurring antibodies
  - occur in plasma of subjects who lack the corresponding antigen and who have not been transfused or been pregnant
  - Most important are anti-A and anti-B
- Immune antibodies
  - Develop in response to exposure to antigens by transfusion or by trans-placental passage during pregnancy
  - Most important is the Rhesus (Rh) antibody, anti-D

ABO blood group system

- Consists of 3 allelic genes: A, B and O
- A and B gene control the synthesis of specific enzymes which transform the H substance



ABO blood group system

Phenotype (表型)	Genotype (基因型)	Antigens	Naturally occurring antibodies
O	OO	O	Anti-A, anti-B
A	AA or AO	A	Anti-B
B	BB or BO	B	Anti-A
AB	AB	AB	None

- The O gene is an amorph (無效基因) and does not transform the H substance
- The A, B and H antigens are present on most body cells including platelets and white blood cells

Rhesus (Rh) blood group system

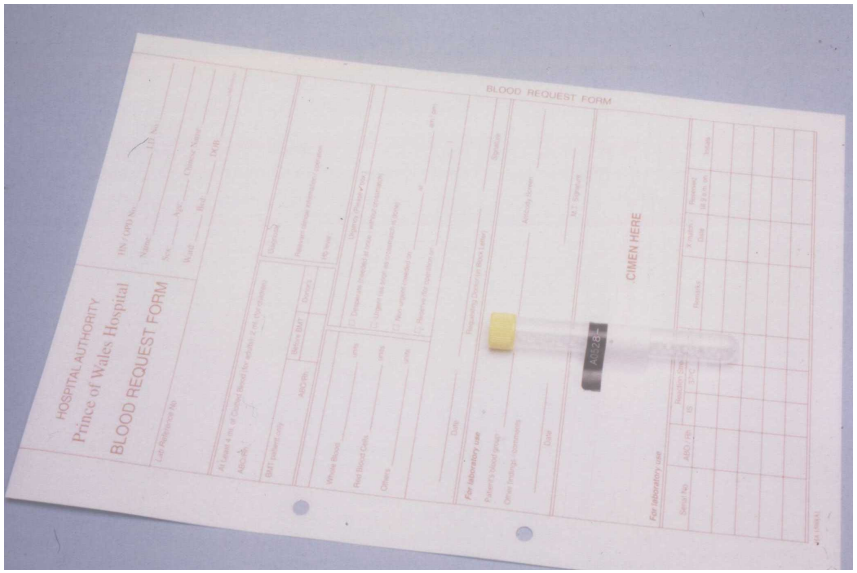
- Composed of 2 related structural genes, RhD and RhCE, which encode membrane proteins that carry the D, Ce and Ee antigens
- RhD gene may be present or absent, giving the Rh D+ or Rh D- phenotype
- Rh antibodies rarely occur naturally
- Most antibodies are immune (previous transfusion or pregnancy)
- Anti-D is responsible for most of the clinical problems associated with Rh system

Other blood group systems

Systems	Frequency of antibodies	Cause of haemolytic transfusion reaction	Cause of haemolytic disease of newborn
Kell	Occasional	Yes (occasional)	Yes
Duffy	Occasional	Yes (occasional)	Yes (occasional)
Kidd	Occasional	Yes (occasional)	Yes (occasional)
Lutheran	Rare	Yes (rare)	No
Lewis	Occasional	Yes (rare)	No
P	Occasional	Yes (rare)	Yes (rare)
MNS	Rare	Yes (rare)	Yes (rare)

Procedure for blood transfusion

- Blood sample taken from patient (recipient) and labeled with patient's information before send to blood bank



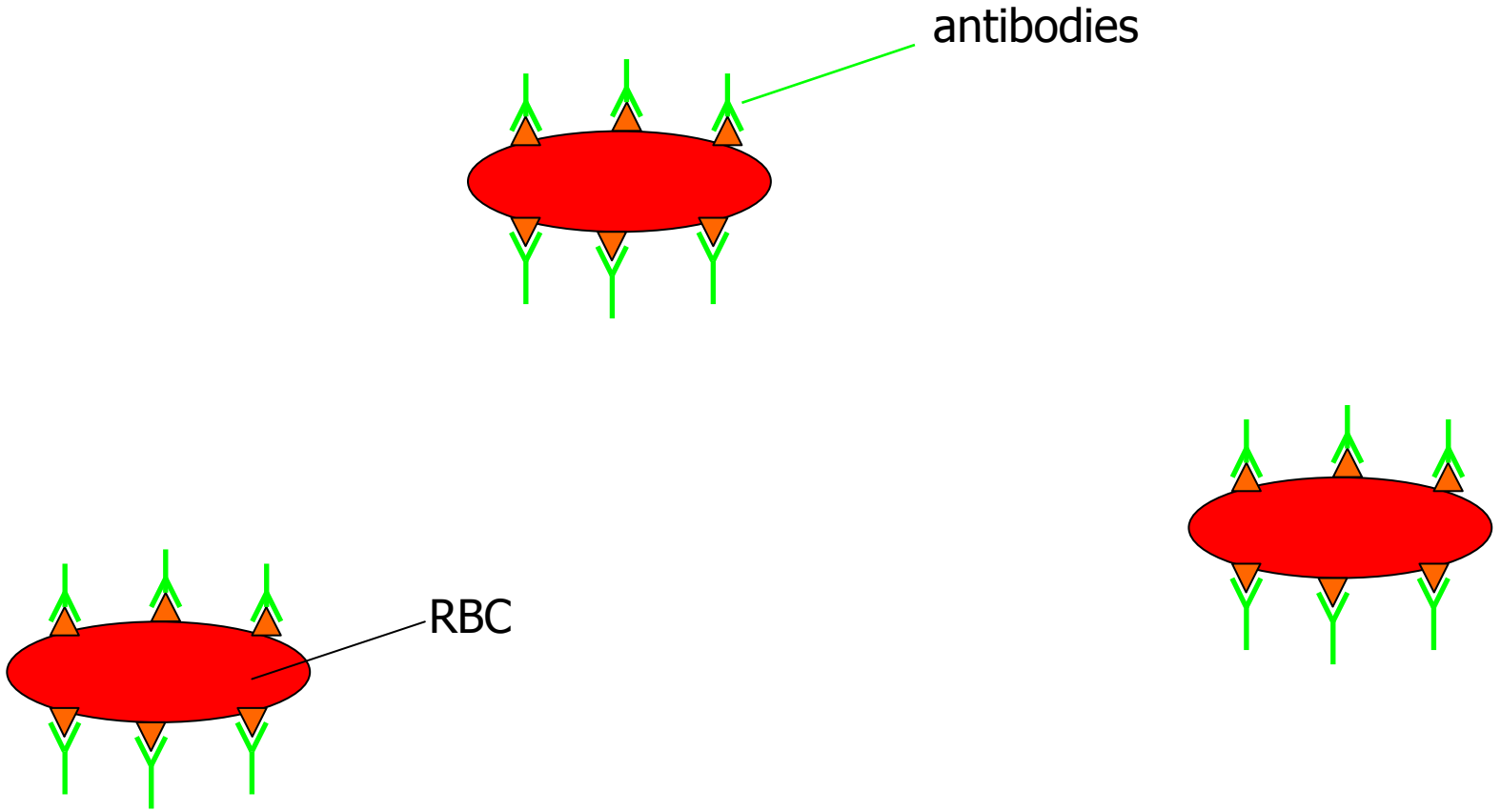
- Clerical error is the most common cause of transfusion error

- Technology such as bar-code scanning system has been developed to enhance checking of patient's identity

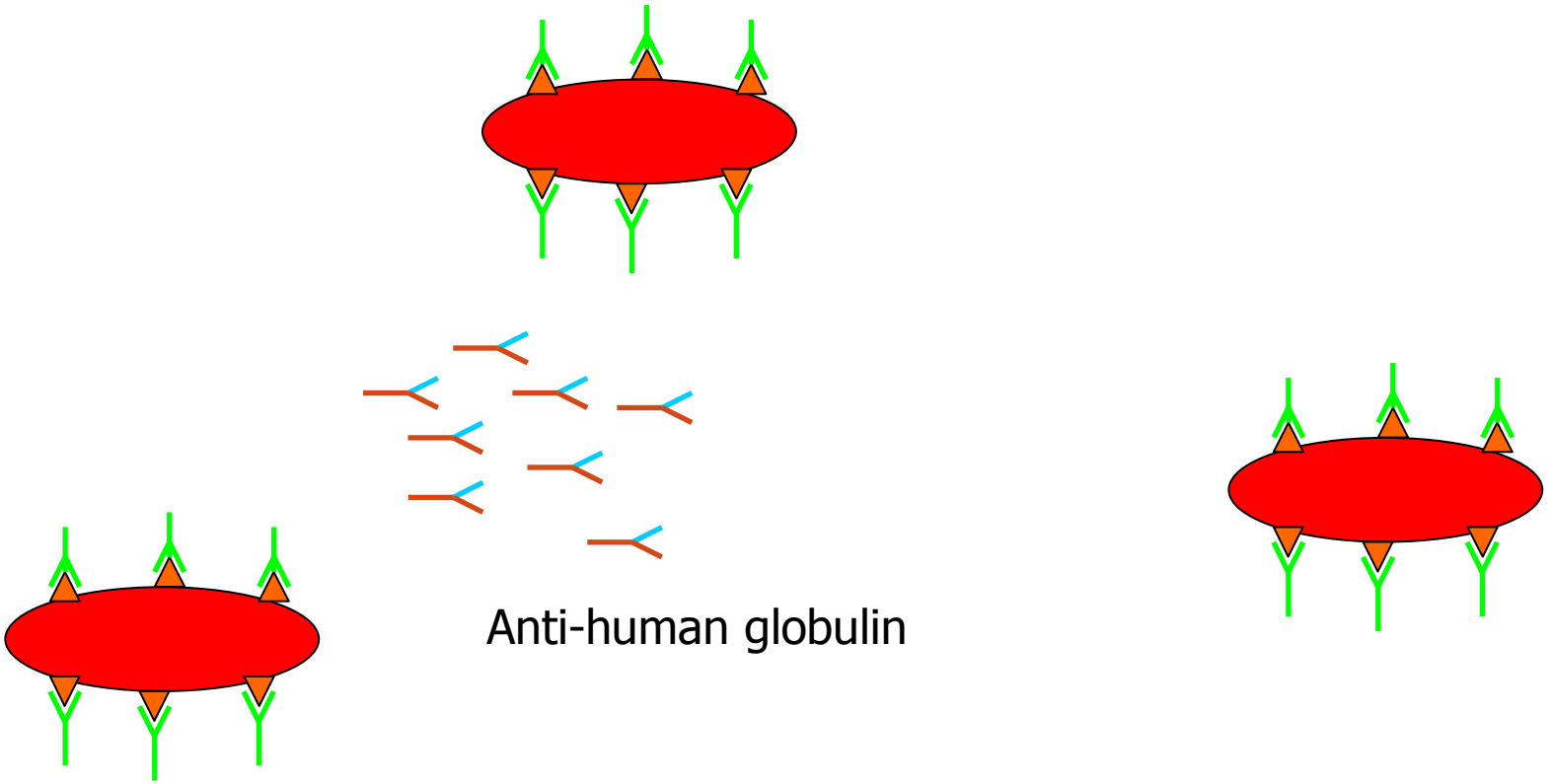
Cross-matching and Pre-transfusion tests

- “Type and Screen (血型與抗體篩檢)”
- The ABO and Rh blood group of the recipient (patient) is determined
- Serum of patient is screened for important antibodies by an indirect antiglobulin (抗球蛋白) test on a panel of antigenically-typed red cells
- If antibodies are detected in the patient’s serum, determine the specificity (專一性) of the antibodies and select the donor blood unit without the corresponding antigen

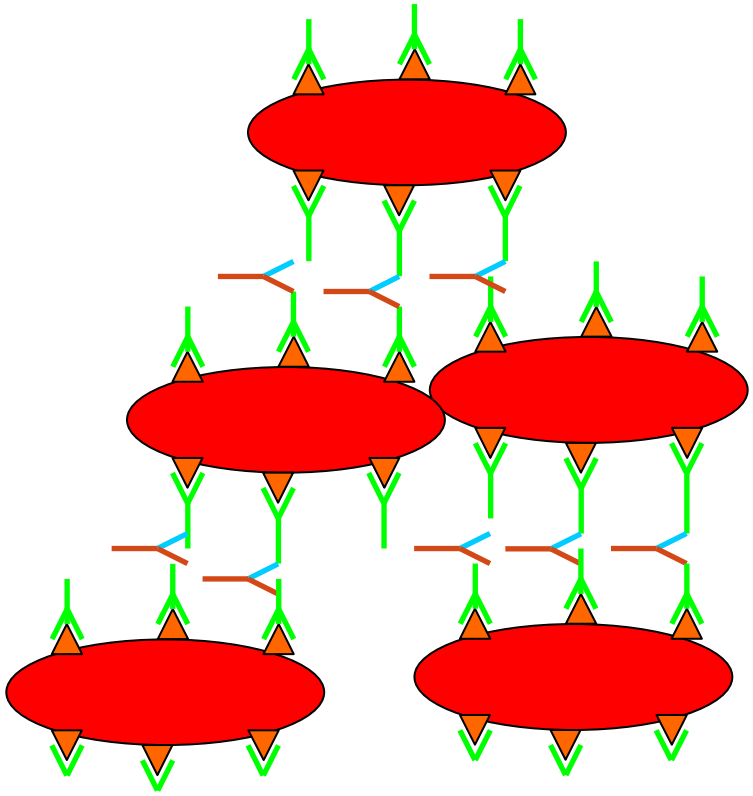
Direct Anti-globulin test (Direct Coomb's test)
直接抗球蛋白測試



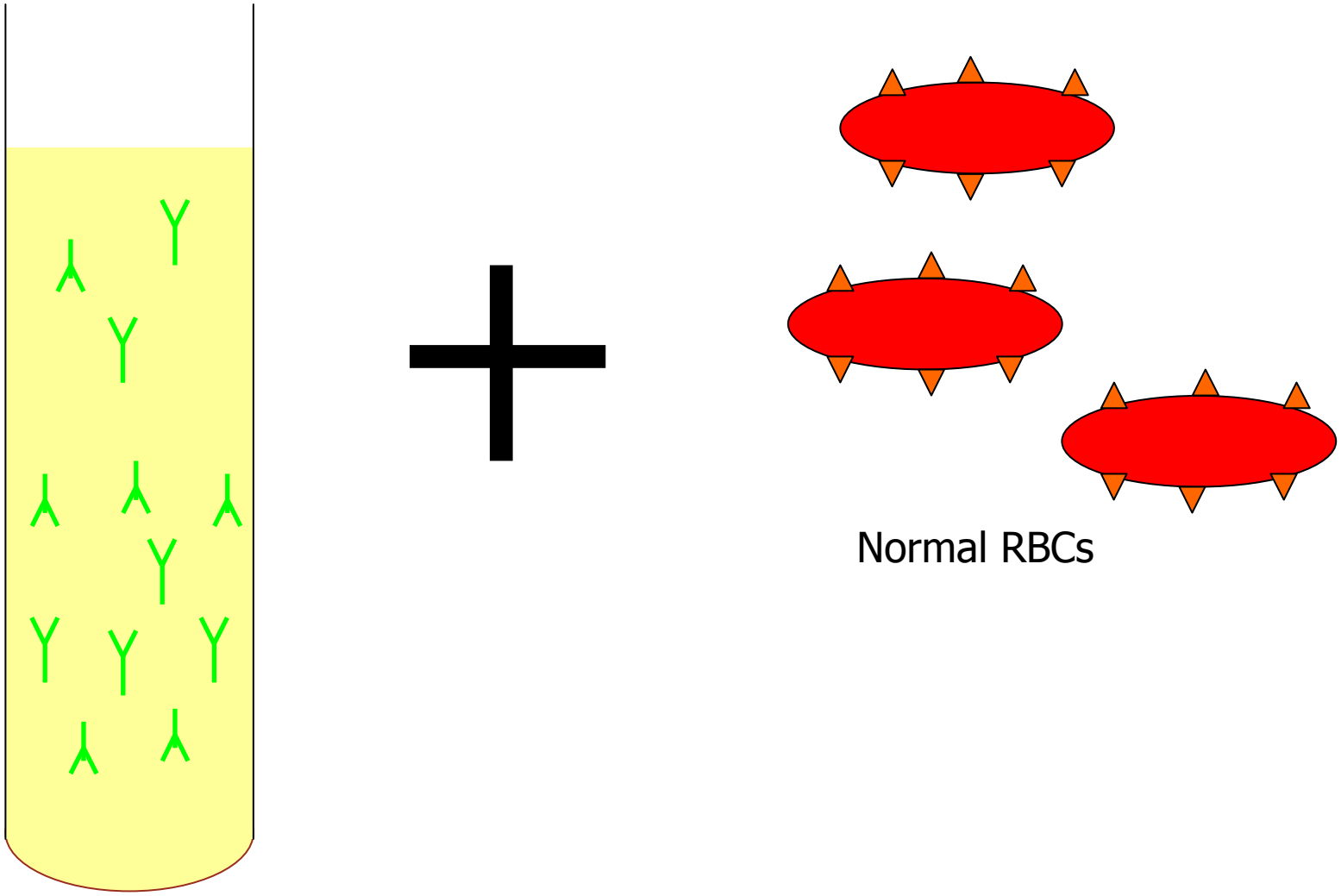
Direct Anti-globulin test (Direct Coomb's test)



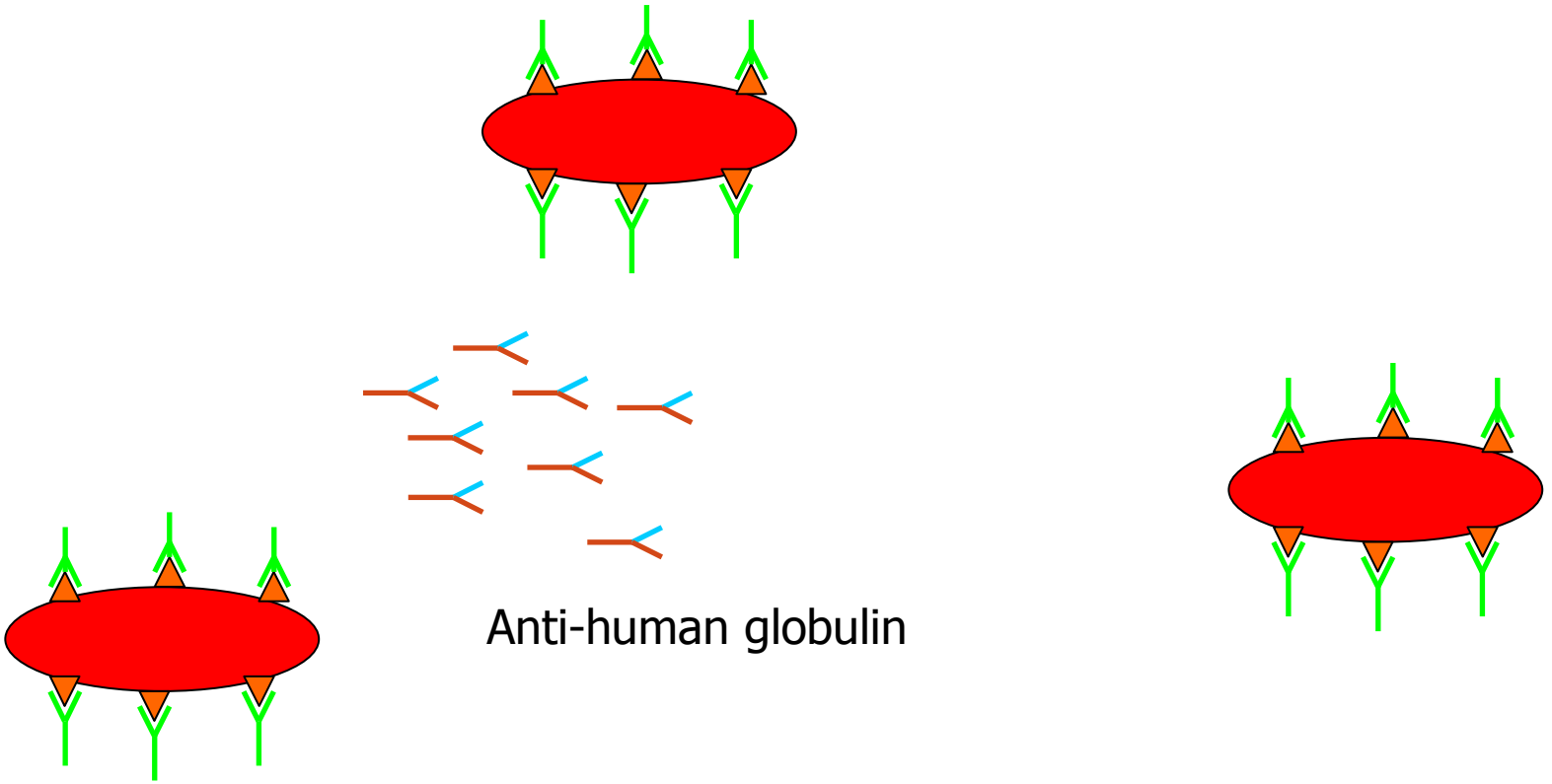
Direct Anti-globulin test (Direct Coomb's test)



Indirect Anti-globulin test (Indirect Coomb's test)
間接抗球蛋白測試



Indirect Anti-globulin test (Indirect Coomb's test)



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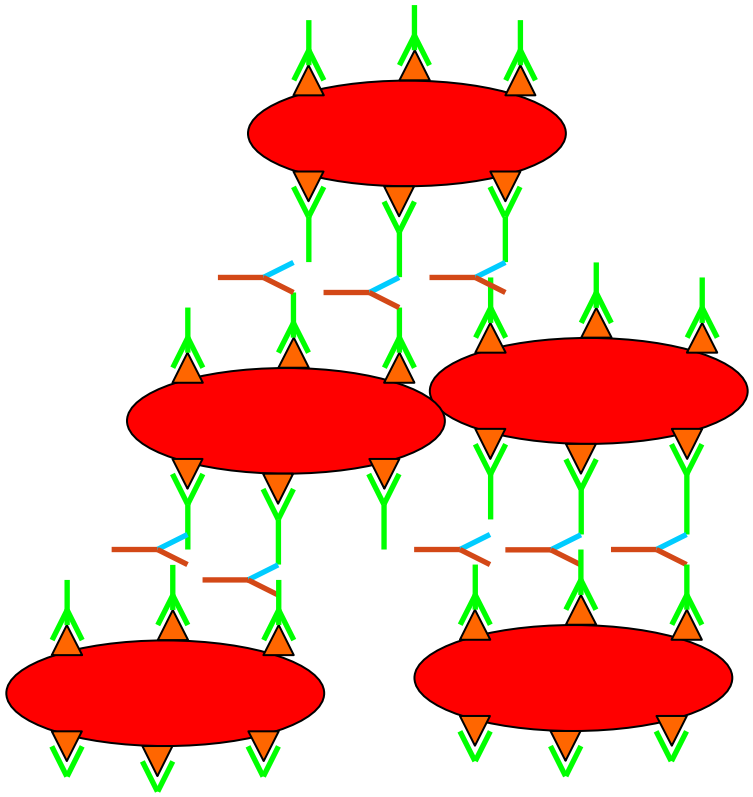


Blood group typing

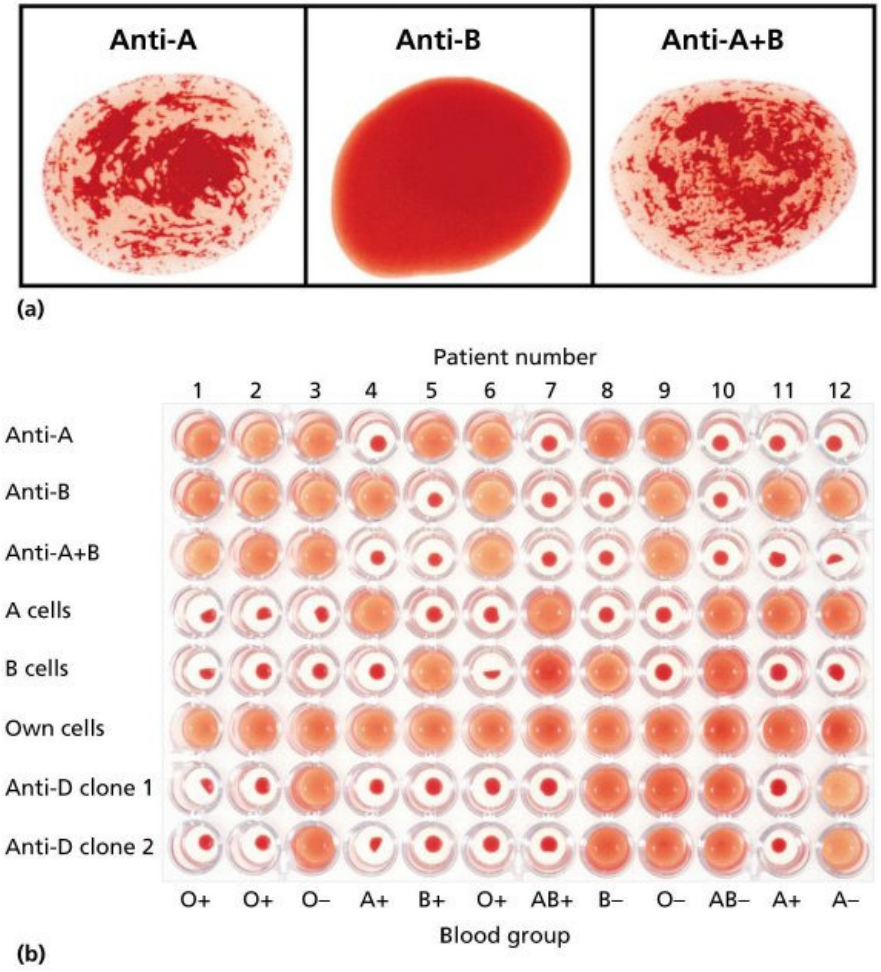


Figure 29.3 **(a)** The ABO grouping in a group A patient. The red cells suspended in saline agglutinate in the presence of anti-A or anti-A + B (serum from a group O patient). **(b)** Routine grouping in a 96-well microplate. Positive reactions show as sharp agglutinates; in negative reactions the cells are dispersed. Rows 1–3, patient cells against antisera; rows 4–6, patient sera against known cells; rows 7–8, anti-D against patient cells.

Antibody Screening

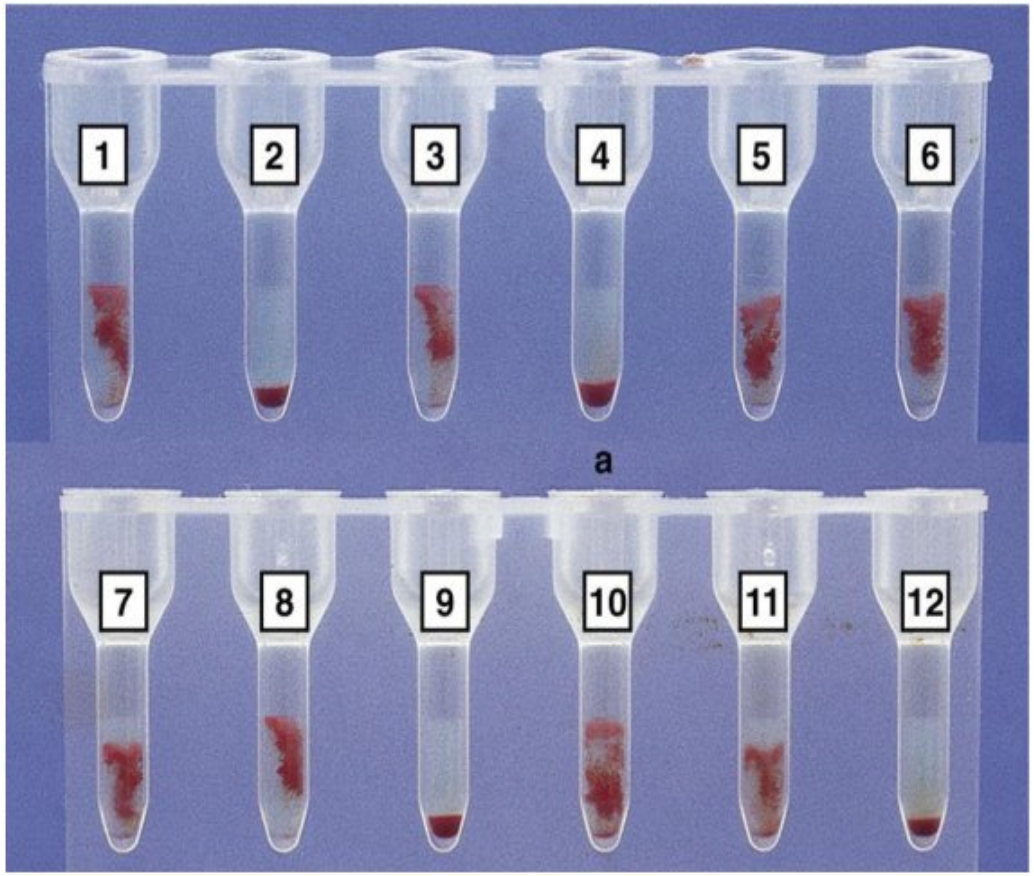


Figure 29.6 Patient antibody screening using the microcolumn (gel) system: 10 tests with two controls (tube 11 is the positive control and tube 12 the negative control) are shown. The patient's serum is tested against screening cells with known red cell phenotype. Tubes 1, 3, 5–8 and 10 show positive results. The patient's serum contained anti-Fy^{a}. (Courtesy of Mr G. Hazlehurst.)

Blood components and products

Whole Blood Units collected from donor

centrifugation (離心)

Packed red cells

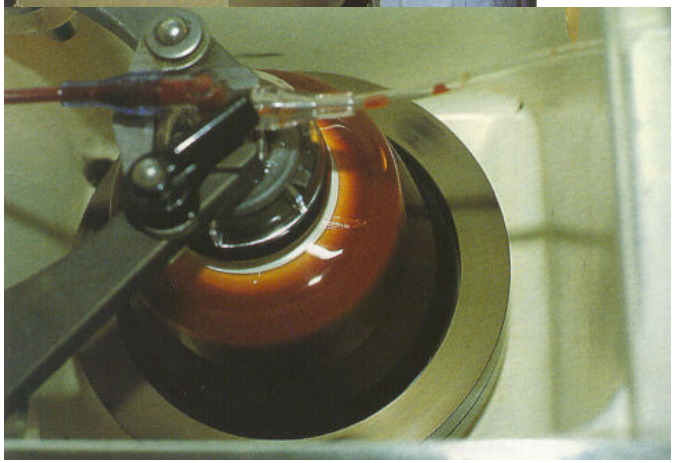
Plasma

Platelet concentrate

cryoprecipitate

Production of other blood products such as immunoglobulins (免疫球蛋白), clotting factors, albumin (白蛋白), etc.

Collection of blood components by apheresis



- Blood components separated by centrifugation in the apheresis (血液成分分離) machine
- Specific component can be collected and the rest re-infused into donor

Red blood cells

- Indications (適應症)
  - To increase hemoglobin level and oxygen carrying capacity in anaemic patients
  - No single haemoglobin value taken as transfusion trigger
  - Principles for consideration
    - Hb <7g/dL and assessment on the rate of ongoing blood loss
    - Hb 7-10 g/dL, often not justified
    - A higher Hb level may be required in patients who may tolerate anaemia poorly, e.g. elderly and patients with cardiovascular or respiratory disease
- Dose: In adult, one unit of red cell should raise the haemoglobin by about 1 g/dL.
- Administration: Through a blood giving set, at a rate determined by clinical condition, but each unit should be completed within 4 hours

Platelet Concentrate

Indications (prophylactic 預防性and therapeutic 治療性)

- Platelet < 10 x 10^9/L in stable patients (usually not indicated in ITP, SLE, TTP or HUS)
- Platelet < 20 x 10^9/L in patients with fever or sepsis
- Platelet < 50 x 10^9/L with diffuse microvascular/mucosal bleeding, major bleeding or before invasive procedure (e.g. liver biopsy, lumbar puncture, epidural anaesthesia, surgery, etc.)
- Platelet < 100 x 10^9/L with retinal or CNS bleeding/surgery, or with active bleeding in postcardiopulmonary bypass
- Platelet < 50 x 10^9/L in stable premature neonates or platelet < 100 x 10^9/L in sick premature neonates
- Suspected platelet dysfunction with active bleeding or before invasive procedure
- Suspected platelet deficiency with severe active bleeding or following massive transfusion

Platelet Concentrate

- Not indicated
  - ITP unless with major bleeding
  - Thrombotic thrombocytopenic purpura (TTP 血栓性血小板减少性紫癜)
  - For procedure where adequate external pressure can be applied to the puncture site to control bleeding, e.g. bone marrow biopsy
- Dose: 4 units of random donor units should raise the platelet count by 20-40 x 10^9/L for adults up to 70kg
- Administration: Transfuse as soon as possible and not longer than 6 hours after issue from blood bank

Fresh frozen plasma (FFP) 新鮮冰凍血漿

- Indications:
  - Clotting factor deficiencies where factor concentrate or cryoprecipitate is not appropriate
  - Correction of warfarin overdose in patients who bleed
  - Supportive therapy in acute disseminated intravascular coagulation (DIC) 彌散性血管內凝血
  - Thrombotic thrombocytopenic purpura (TTP) 血栓性血小板減少性紫癜
  - Hereditary angio-neurotic oedema 遺傳性血管神經性水腫 (C1 esterase inhibitor deficiency)

Fresh frozen plasma

- Must be ABO compatible to recipient's red cells

Recipient's blood group	Donor's blood group
O	O, A, B, AB
A	A, AB
B	B, AB
AB	AB

- Dose: depends on the clinical situation. The initial dose for factor replacement for an adult should be 12-15 ml/kg (approx. 2-4 units for adults)
- Administration: thraw at 30-37 ˚C and infuse as soon as possible through a blood giving set not greater than 10ml/min

Cryoprecipitate

- Contains fibrinogen, factor VIII, vWF, and small amount of XIII and fibronectin

- Indications:
  - von Willebrand's disease (if DDAVP or factor concentrate is inappropriate)
  - Fibrinogen deficiency or dysfunction
  - Factor XIII deficiency

Adverse Transfusion Reaction

Acute

- Haemolytic transfusion reaction
- Febrile non-haemolytic transfusion reaction
- Allergic reaction
- Septic reaction
- Circulatory overload
- Transfusion related acute lung injury (TRALI)

Delayed

- Delayed haemolytic reaction
- Transfusion associated graft-versus-host disease
- Post-transfusion purpura
- Transmission of infectious diseases
- Iron overload

Acute haemolytic transfusion reaction
急性溶血性輸血反應

- Estimated risk 1:250,000 to 1:1,000,000 units transfused
- Infusion of incompatible blood components
- Rapid destruction of red cells immediately or within 24 hours of transfusion
- 74% of all fatalities due to ABO incompatibility (不相容的)
- Most common cause is clerical error: ***misidentification of the patient***

Acute haemolytic transfusion reaction

Types of Clerical Errors

- Venipuncture of the wrong patient
- Failure to identify patient correctly
- Wrong name placed on sample
- Blood taken to the wrong patient
- Failure to properly identify the patient prior to transfusion

Acute haemolytic transfusion reaction

- Fever, chills and/or rigors
- Pain at the infusion site or localized to the loins, abdomen, chest or head
- Hypotension, tachycardia
- Agitation, distress and confusion; particularly in the elderly
- Nausea or vomiting
- Dyspnoea
- Flushing
- Haemoglobinuria (血紅蛋白尿)

Acute haemolytic transfusion reaction

Management (1)

- Stop transfusion immediately and spigot off the unit
- Save the blood units and blood giving set for investigation
- Use a new giving set and keep vein open with normal saline
- Clerical check for compatibility between recipient and blood unit(s) given
- Inform blood bank to return blood units for investigations. Take post transfusion blood sample for investigation as well

Acute haemolytic transfusion reaction

Management (2)

- Treat shock if present
- Maintain BP with IV colloid solutions
- Diuretics (mannitol 甘露糖醇 or frusemide 夫塞米) may be used to maintain adequate urine output
- Insert indwelling urinary catheter to monitor hourly urine output
- Patient may require dialysis if renal failure occurs

Delayed haemolytic transfusion reaction
延遲性溶血性輸血反應

- Estimated risk: 1 in 1000
- Destruction of transfused red cells by antibody not detectable during the pre-transfusion compatibility testing
- Rapid secondary boost in antibody level after transfusion: anamnestic response
- Typically cause jaundice at day 5 onwards
- Fever, haemoglobinuria
- Renal failure very rare

Delayed haemolytic transfusion reaction

- Most are asymptomatic and found to have a failure to have a predicted response from blood transfusion (Hb level does not increase or even drop after transfusion and blood loss is excluded)
- Management is in general supportive
- Investigate for the antibodies involved and reason for failure of detection in pre-transfusion testing
- Haemolysis may be severe in some enough to require active treatment

Febrile non-haemolytic transfusion reaction
非溶血性發熱輸血反應

- Frequent 1:100 with non-leukoreduced (非減除白血球) blood products
- Mainly occur with red cells and platelets
- Alloimmunization (同種異體免疫) to antigens on donor leukocytes or platelets
- Transfusion of cytokines (細胞因子) released from donor leukocytes during storage
- Symptoms usually occur about 30 min to 2 hour after starting a red cell transfusion. Even earlier after a platelet transfusion
- Flushing, fever, tachycardia, sometimes rigors
- Infected blood product should also be considered

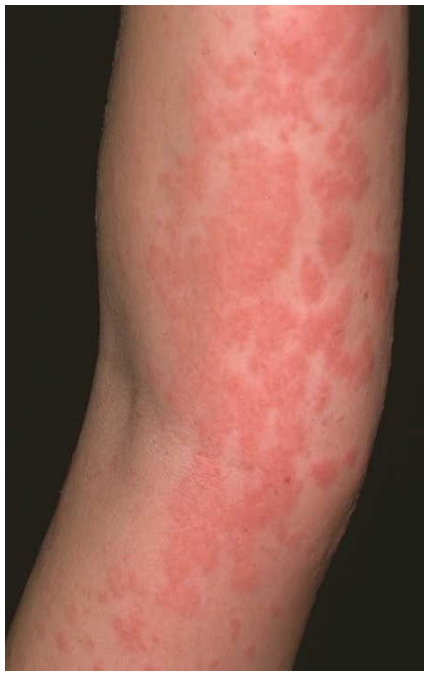
Febrile non-haemolytic transfusion reaction

Management

- Stop transfusion immediately, keep vein open
- Clerical check for compatibility between recipient and blood unit(s) given
- Antipyretic e.g. paracetamol can be given
- For mild febrile reaction and rapidly resolving symptoms, transfusion may be resumed slowly
- For severe febrile reaction (e.g. rise in temperature > 1.5°C), the same unit should not be restarted
- Haemolytic transfusion reaction and septic reaction should always be suspected and investigated and managed accordingly

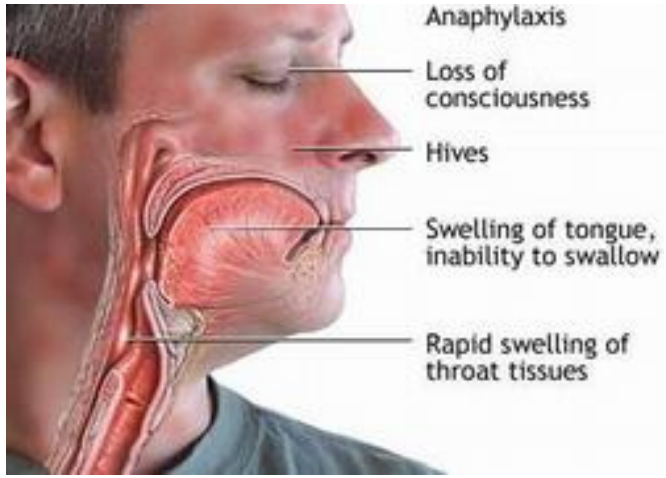
Allergic reaction 過敏反應

- Frequent, 1:100 to 1:300
- Usually mild, self-limiting
- Recipient is allergic to something in the donor (foodstuff, medication, protein)
- Rash (疹), urticaria (蕁麻疹，風疹)
- Pre-medication with antihistamine (抗組織胺劑) can prevents allergic reaction
- May need to use washed products



Anaphylactic reaction

- Dyspnoea, wheezing
- Laryngeal oedema, bronchospasm, shock
- Frequency 1:20,000 to 1:50,000
- Usually seen in IgA deficient subjects, form antibodies to donor IgA
- Need to use saline-washed red cells or IgA deficient products

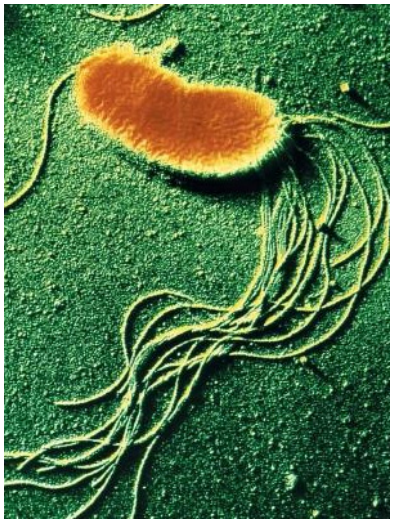


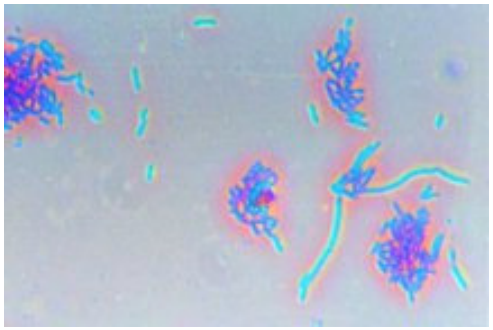
Management of allergic reaction

- Stop transfusion immediately and keep vein open
- Give antihistamine as directed
- Observe for anaphylaxis (鈍敏)
- For anaphylaxis, adrenaline injection may be required
- If urticaria are the only sign, the transfusion may sometimes continue at a slower rate

Septic reaction (細菌感染反應)

- Transfusion of bacterial contaminated blood or blood components
- Red cell 1:500,000, Platelet 1:10,000
- Rapid onset of chills and rigors
- High fever usually > 2°C
- Nausea, vomiting, diarrhoea
- Hypotension, DIC, intravascular haemolysis, renal failure





Septic reaction - Management

- Stop transfusion immediately, keep vein open
- Monitor patient closely for septicaemic shock (敗血性休克)
- Clerical check for compatibility between recipient and blood unit(s) given and exclude haemolytic transfusion reaction accordingly
- Obtain patient's blood for septic workup and send blood bags and administration set for culture
- Treat septicaemia with intravenous broad spectrum antibiotics with adequate anti-pseudomonas coverage

Transmission of Infection

- Bacteria
  - Transfusion of bacterially contaminated blood is very rare, more common in platelet concentrates
  - May present with circulatory collapse

- Virus
  - A wide variety of viruses may be transmitted by transfusion
  - Use of nucleic acid testing (NAT) by molecular technique in addition to serology test helps to shorten the “window period”

Emergency transfusion – What to use?

- If blood transfusion is needed immediately, use of "unmatched blood unit" may be required
- Only 0.27% of Hong Kong Chinese are D-negative, it is impossible to have enough supply to be used in all emergency transfusion
- Group O Rh D-positive blood units will be used in most cases
- Priority for Rh D-negative blood components:
  - Exchange or intrauterine transfusion for haemolytic disease of newborn (HDN) due to maternal anti-D
  - D-negative individuals with anti-D
  - D-negative females prior to menopause, without anti-D
  - D-negative male or female after menopause
  - Emergency resuscitation of Caucasian females with unknown D status in reproductive age or younger

Autologous donation and transfusion
自身捐血及輸血

- Anxiety over HIV and other infections has increased the demand for autologous transfusion
- 3 ways of autologous transfusion
  - Predeposit – 2-5 units collected weekly prior to elective surgery
  - Haemodilution – blood is removed immediately prior to surgery once the patient has been anaesthetized and then reinfused at the end of operation
  - Salvage – blood lost during the operation is collected during heavy blood loss and then reinfused