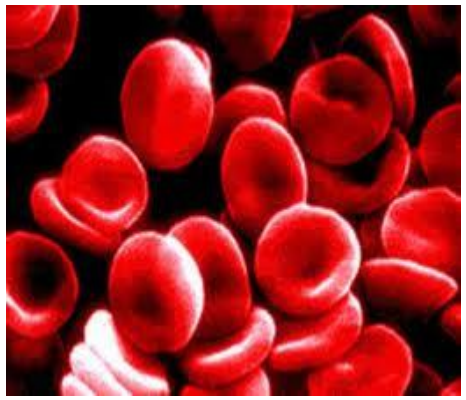
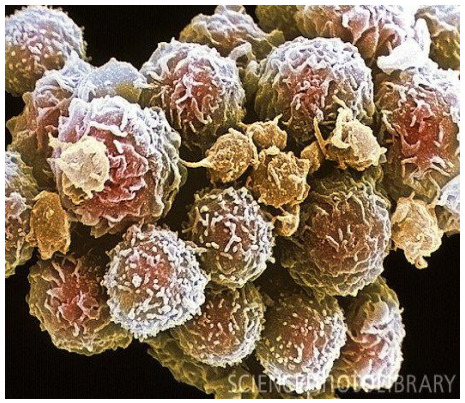
BLOOD TRANSFUSION GUIDELINES

rational and safe practices

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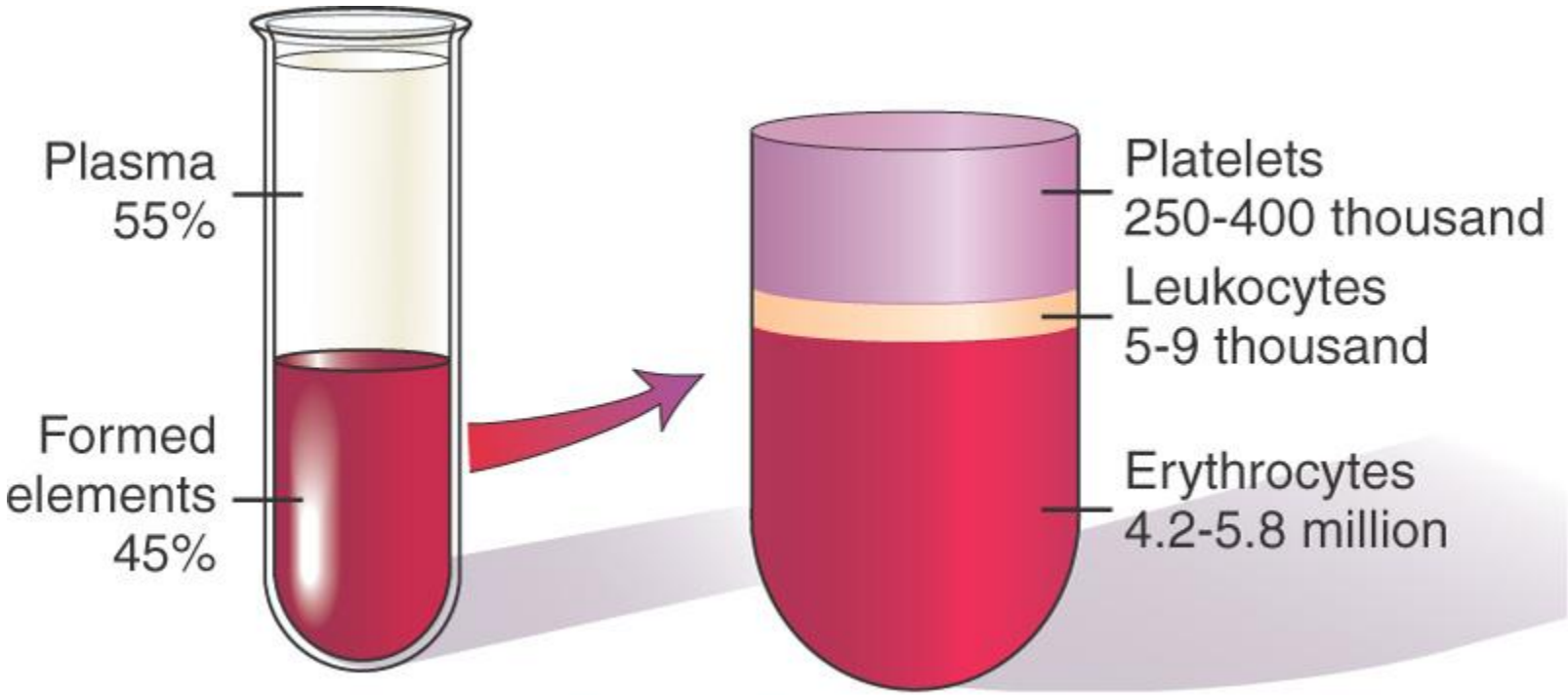
TOPICS

- Selection and preparation of blood product
- Indication, Dosing, and Response
- Safety procedure
- Case illustrations on The Challenges of Blood Transfusion in Certain Clinical Condition

PREPARING of BLOOD PRODUCTS



WHOLE BLOOD COLLECTION

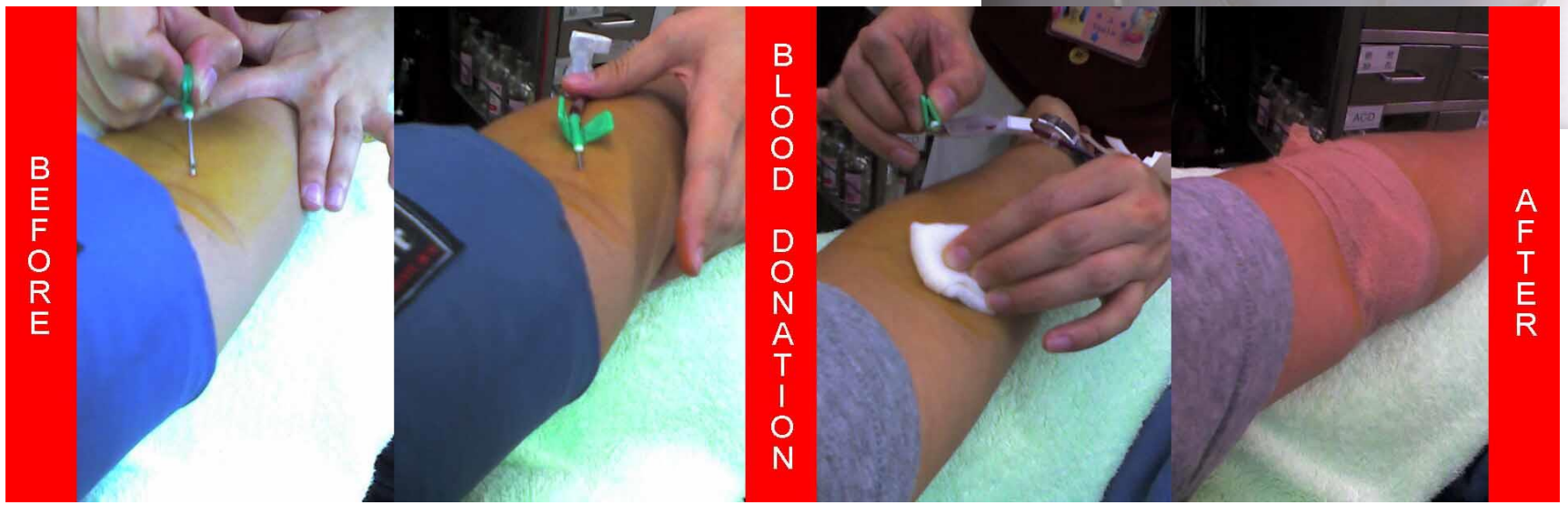
DONOR REQUIREMENT

- Up to 15% of donor's BV can be removed without physiologic signs or symptoms
- The maximum allowable intravascular volume deficit in single donation is 10.5 ml/kg
- To reduce the risk of anemia, allogenic donor should have Hg level > 12.5 g/ dL
- Limited to donating once every 8 weeks

Donor test samples: infectious disease marker, ABO, Rh, red cell alloantibodies

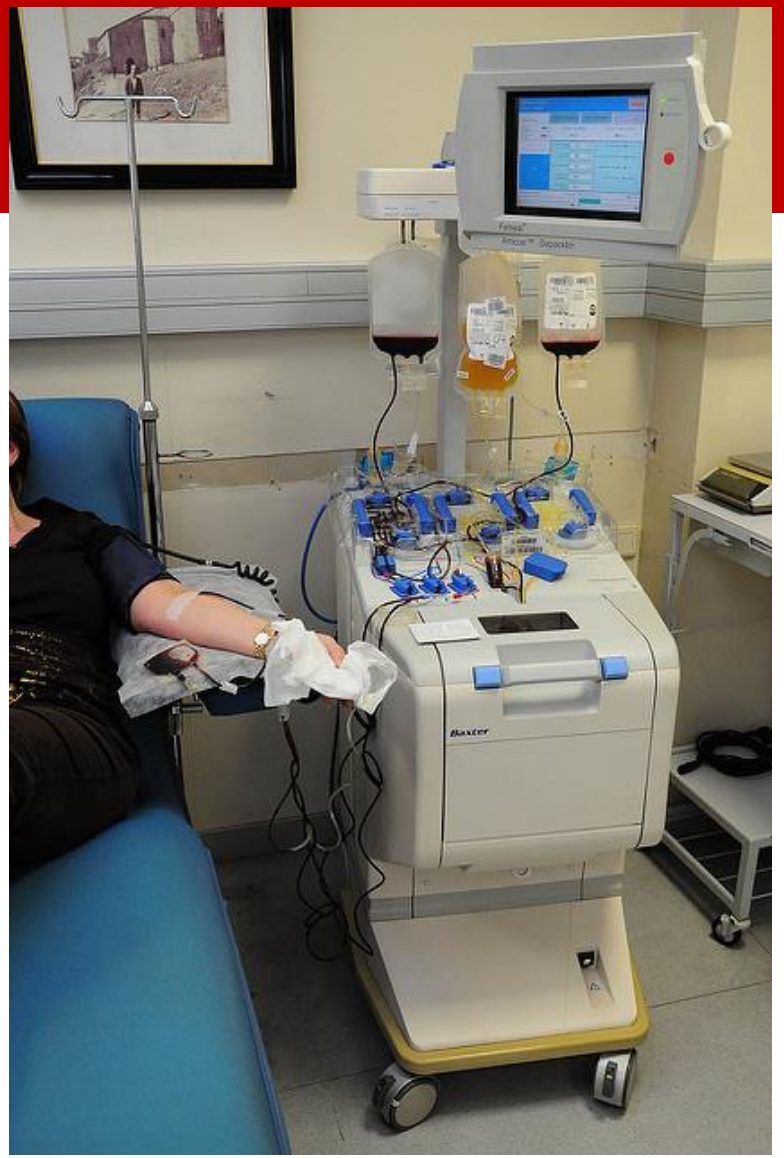
Collection procedure

- Phlebotomy with integral donor needle supplied with steril collection and storage kit
- Adequate blood flow, in 10 minutes



Apharesis Donation

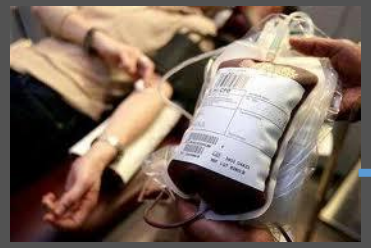
- Blood is drawn
- Blood is separated into component by a centrifuge
- Needed component are collected into steril bags
- Unused components are returned back to the donor



Whole Blood Sample

Sample Placed in Centrifuge

Blood Sample That Has Been Centrifuged



PRP method

Buffy coat method

Soft spin

Red cell

PRP

Hard spin

plasma

PRP
platelet concentrate

Hard spin

Red cell

BC

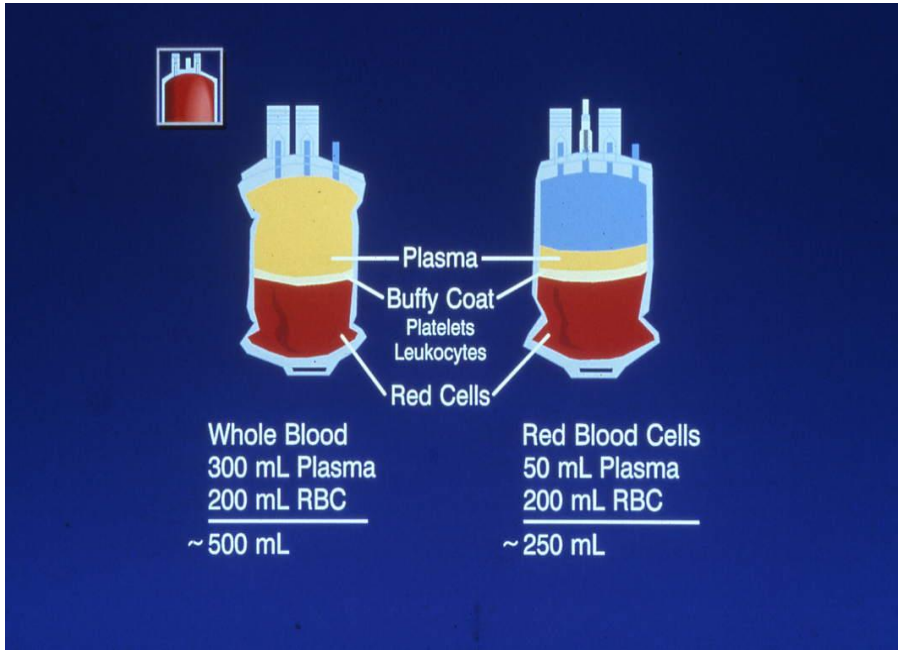
Plasma

Soft spin

BC
Platelet concentrate

Residual
white cells

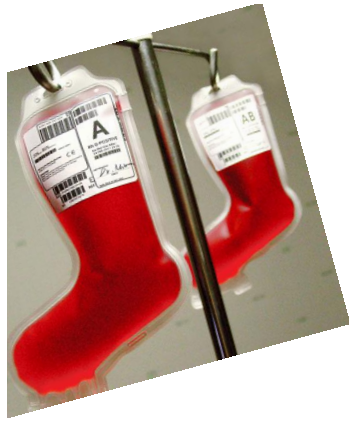
Hilyer et al. Blood Banking and Transfusion Medicine



Australian Red Cross Blood Services

Australian Red Cross Blood Services

Blood component therapy should only be given when the expected benefits to the patient are likely to outweigh the potential hazards



WHO PRINCIPLES
for the Clinical Use of Blood Component

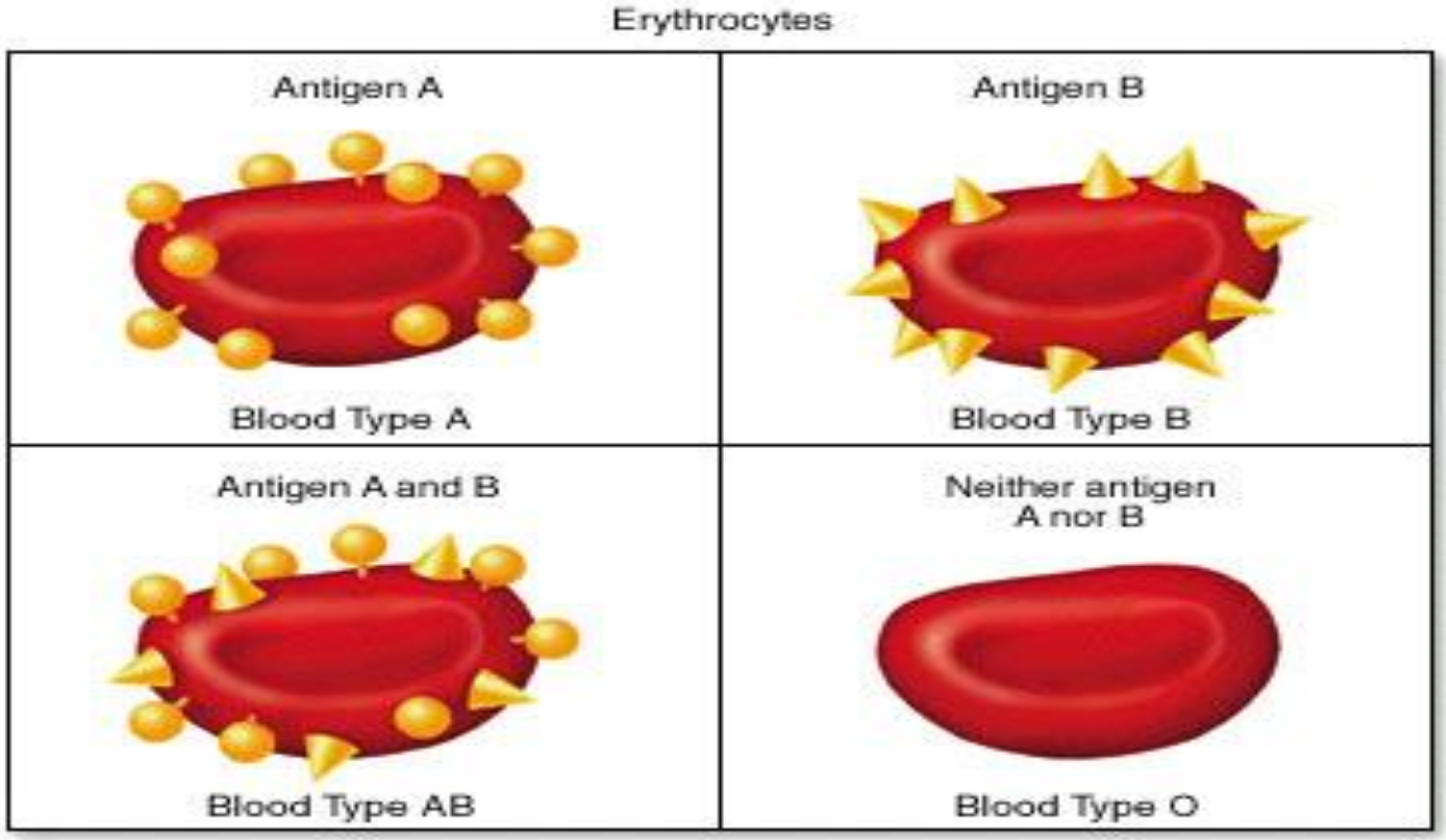
- Transfusion is only one element of patients management
- Prescribing decisions should be based on the national guidelines on the clinical use of blood components, taking individual patient needs into account.

WHO 1998

- Blood loss should be minimized
- Patients with blood loss should be rescucitated, while transfusion need is being assessed
- Aware the risk for transfusion
- Benefits outweigh the risks
- Clinician should record the reason for transfusion
- A trained person should monitor transfusion

Selection and preparation

- RBC must be compatible with antibodies in the serum of recipient
- CROSSMATCHED to detect compatibility of ABO and other antibodies



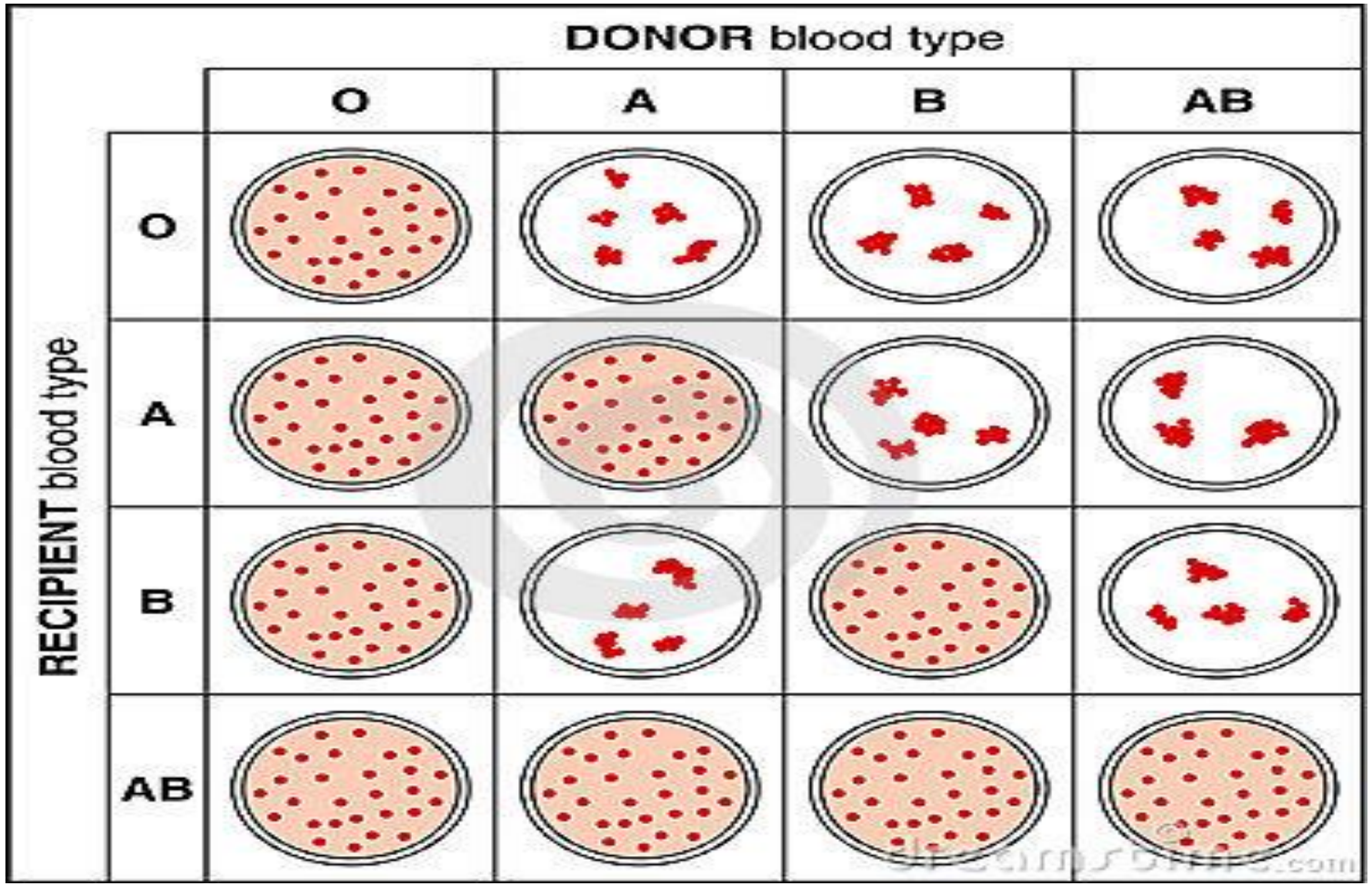
BLOOD TYPING

Erythro-cytes	Antigen A 	Antigen B 	Antigen A and B 	Neither antigen A nor B 
Plasma	Antibody B 	Antibody A 	Neither antibody A nor B	Antibody A and B 
	Type A Erythrocytes with type A surface antigens and plasma with type B antibodies	**Type B** Erythrocytes with type B surface antigens and plasma with type A antibodies	**Type AB** Erythrocytes with both type A and type B surface antigens, and neither type A nor type B plasma antibodies	**Type O** Erythrocytes with no ABO surface antigens, but both A and B plasma antibodies

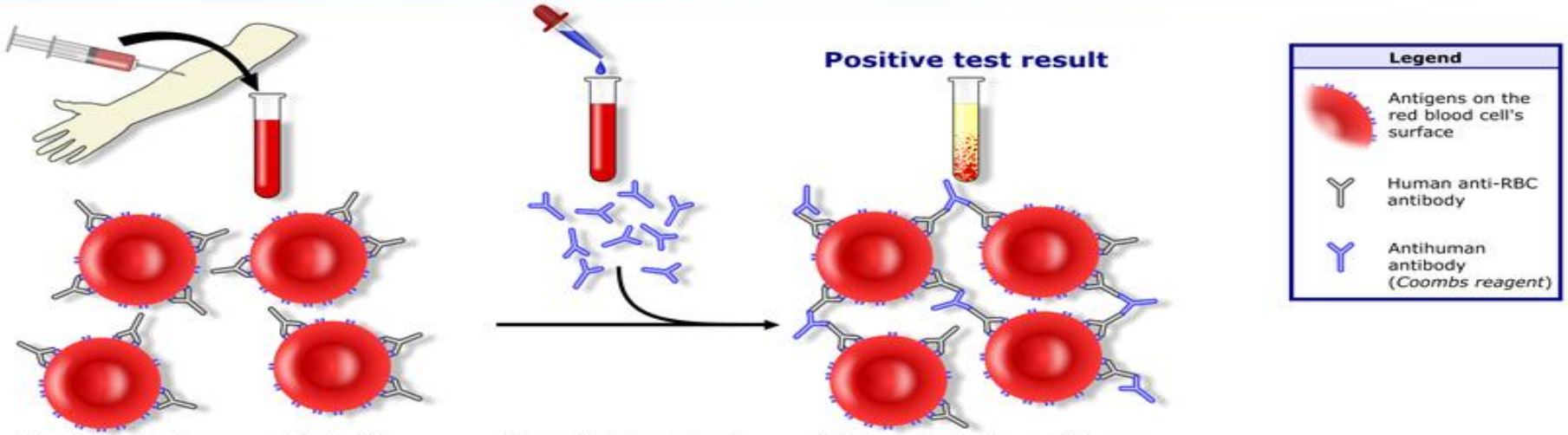
BLOOD GROUPS SYSTEMS

Name	Symbol	Number of Antigens	Gene Name	Chromosome
ABO	ABO	4	ABO	9
MNS	MNS	43	GYPA, GYPB, GYPE	4
P	P1	1	P1	22
Rhesus	Rh	49	RhD, RhCE	1
Lutheran	LU	20	LU	19
Kell	KEL	25	KELL	7
Lewis	LE	6	FUT3	19
Duffy	FY	6	FY	1
Kidd	Jk	3	SLC14A1	18

CROSS MATCH



Direct Coombs test / Direct antiglobulin test

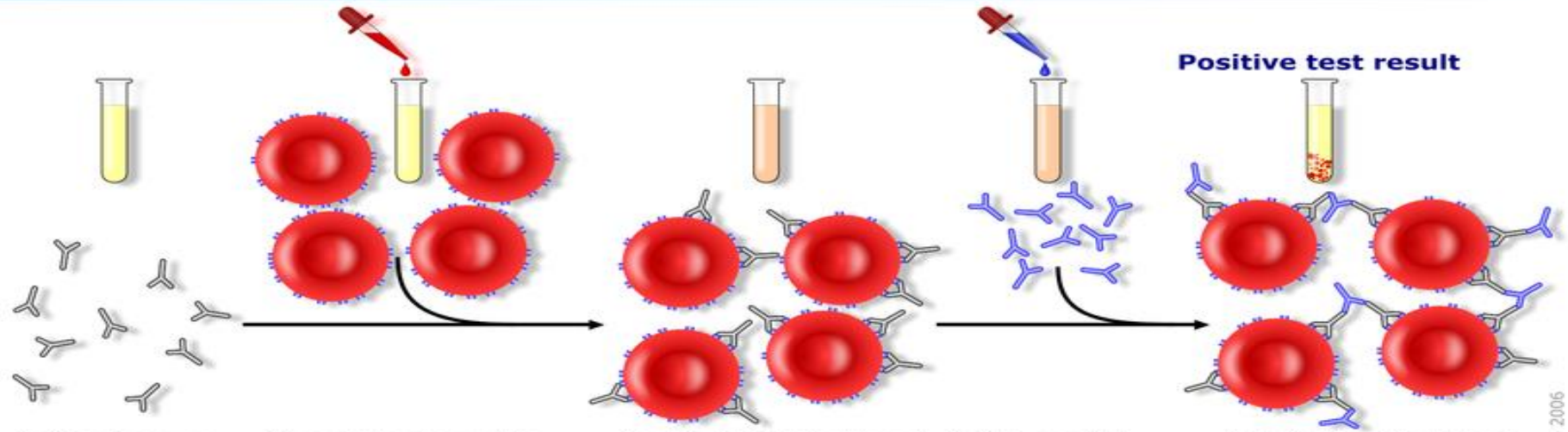


Blood sample from a patient with immune mediated haemolytic anaemia: antibodies are shown attached to antigens on the RBC surface.

The patient's washed RBCs are incubated with antihuman antibodies (*Coombs reagent*).

RBCs agglutinate: antihuman antibodies form links between RBCs by binding to the human antibodies on the RBCs.

Indirect Coombs test / Indirect antiglobulin test



Recipient's serum is obtained, containing antibodies (Ig's).

Donor's blood sample is added to the tube with serum.

Recipient's Ig's that target the donor's red blood cells form antibody-antigen complexes.

Anti-human Ig's (*Coombs antibodies*) are added to the solution.

Agglutination of red blood cells occurs, because human Ig's are attached to red blood cells.

Guidelines for Red Blood Cell Transfusion

- The decision to transfuse red blood cells should be based on clinical assessment of the patient and his or her response to any previous transfusion as well as the haemoglobin level.
- **Use of red blood cells is likely to be inappropriate when Hb > 100g/L**

  (level I evidence).

  If red blood cells are given at this haemoglobin level, reasons should be well documented.
- **Use of red blood cells may be appropriate when Hb is in the range 70–100g/ L** (level IV evidence).

  In such cases, the decision to transfuse should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.
- **Use of red blood cells is likely to be appropriate when Hb<70g/L**

  (level IV evidence)

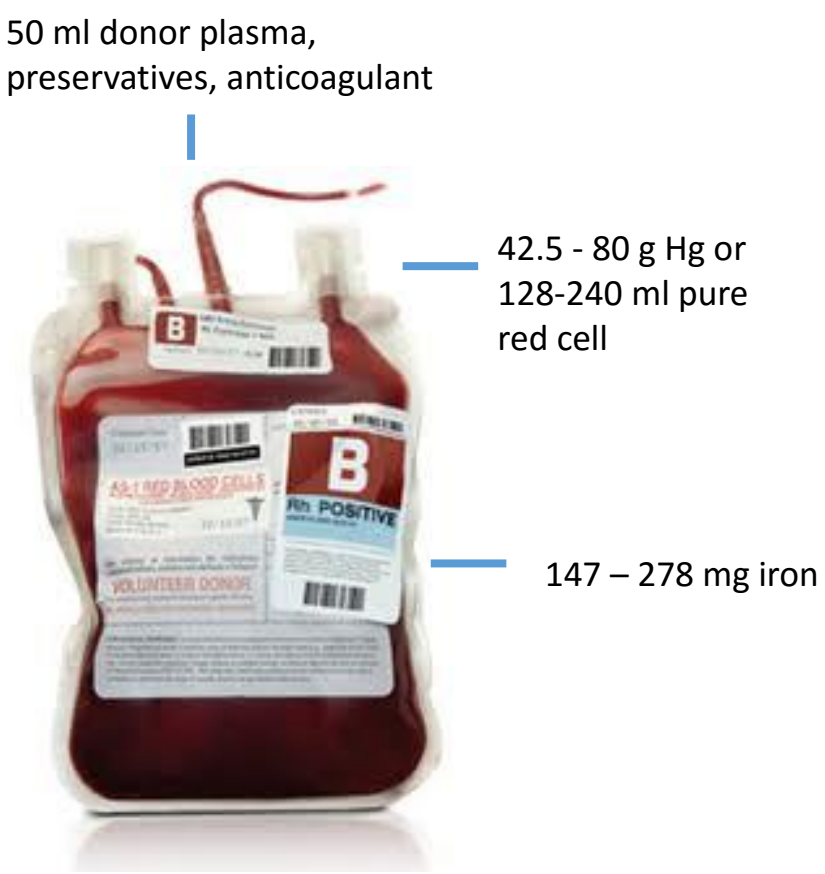
  In some patients who are asymptomatic and/or where specific therapy is available, lower threshold levels may be acceptable.

British Commitee Society of Hematology 2009 Clinical Practice Guideline on the Use of Blood Component 2001

RED BLOOD CELL

- Packed red cell

  Preparation :
- Red Blood Cells (Adenine-Saline Added);
- Red Blood Cells Leukocytes Reduced (LR-RBC);
- Red Blood Cells Apheresis;
- Red Blood Cells Deglycerolized;
- Red Blood Cells Irradiated;
- Red Blood Cells, Low Volume;
- Red Blood Cells Washed



Practice Guidelines for Transfusion. American Red Cross
Brecher M, ed. Technical manual. 15th ed. Bethesda, MD: AABB press, 2005

Red Cell Transfusion

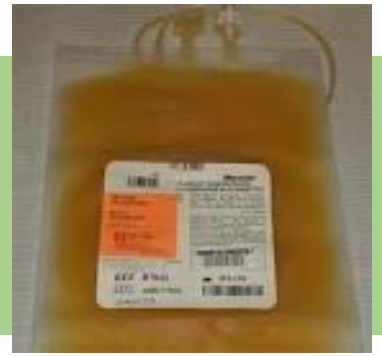
- Storage: designated temperature controlled refrigerator 4 ±2 oC
- Shelf life: 35 days
- Dose: 4ml/kg (equivalent to 1 unit per 70kg adult) typically raises Hb concentration by about 10g/l
- All red cell units should be transfused within 4 hours of removal from designated temperature controlled storage

Red Cell Transfusion

- For routine administration, there is extensive experience of safely administering a red cell unit over 90-120 minutes per unit
- Patients less tolerant of increased blood volume should be transfused more slowly with careful haemodynamic monitoring. For some patients it may be appropriate to give a diuretic (furosemide 20 to 40mg orally), though this is not necessary as a routine

  During major haemorrhage, rapid infusion (1 unit over 5-10 minutes) may be required (with monitoring)

Platelet Transfusion



- Indication : prevent and treatment of haemorrhage due to thrombocytopenia or platelet dysfunction
- Stable patients who do not have serious bleeding, the threshold for prophylactic platelet transfusion is < 10 x 10^9/L
- Bone marrow disease, septic, or unstable patients with active bleeding associated with thrombocytopenia threshold 15-20 x 10^9/L
- Patients with Life-threatening bleeding in the chest or head are transfused at 30-50 x 10^9/L
- Prophylactic for surgery: 25x 10^9/L for insertion of multi lumen cathether and 50 x 10^9/L for major surgery (grade B, III)

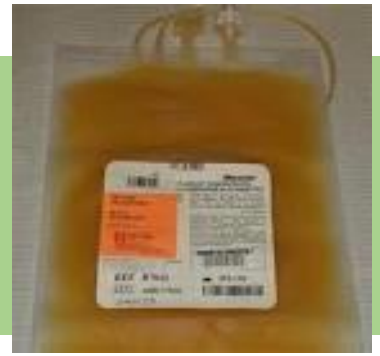
Bone Marrow aspiration can be performed without transfusion (grade C, IV)

Invasive procedure : 50x 10^9/L

Surgery in critical sites:

100 X 10^9/L (GRADE C, IV)

Platelet Transfusion



- DIC:

  in chronic DIC without active bleeding no indication for transfusion

  acute DIC: maintain Plt > 50 x 10^9/L

  (grade C, IV)

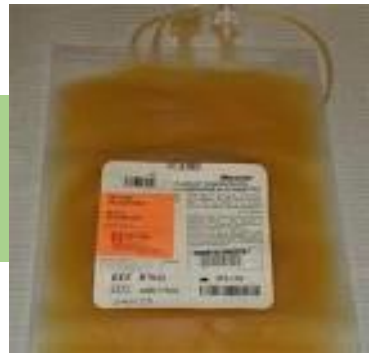
- ITP:

  Platelet transfusion should be reserved for patient with life threatening bleeding from gi tract, gu, and cns

  other treatment such as methylprednisolon, IVIG should be initiated

  (grade C, IV)

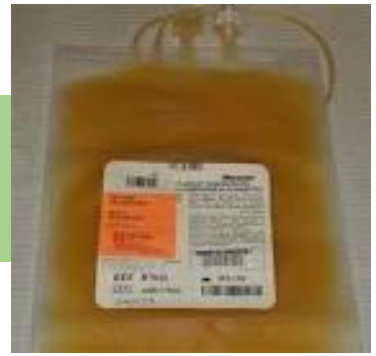
Platelet transfusion



- Storage: temperature controlled 22 ±2 ^{o}C – with continuous gentle agitation
- Platelets must not be refrigerated
- Shelf life: 5 days (In certain controlled circumstances 7 day platelets may be supplied)
- Dose: 1 adult therapeutic dose (ATD) typically increase the platelet count by at least 20-40x10^{9}/l
- Platelet concentrates should not be transfused through administration sets which have already been used to administer other blood components
- The infusion should be commenced as soon as possible after the component arrives in the clinical area
- Typically administered over 30-60 minutes per adult therapeutic dose (ATD)
- The dose can be calculated : PI x BV x 0.67^{-1}

  40 x 5 x 0.67^{-1} = 300 x 10^{9}/l

FRESH FROZEN PLASMA



- 1 unit of FFP contains all coagulant factors
- Indication : patient with a coagulopathy who are bleeding or at risk of bleeding AND where specific therapy is not appropriate
- massive transfusion, cardiac bypass, liver disease, acute DIC
- Warfarin overdose, where PCCs are not available
- Thrombotic Thrombocytopenic Purpura
- Dosage : 10-15 ml/kg per dose

Transfusion Practices

Overview of transfusion medicine

Administration of blood components

Informed consent

Patient identification

Documentation & traceability

Requests for transfusions

Pretransfusion blood samples

Monitoring & observation

Updated on 08 December 2011

Australian Red Cross Blood Service 2011

CASE ILLUSTRATION

Case Illustration

- Woman 73 year old, fatigue, shortness of breath, dark urine, inability to maintain activity daily living for the last week
- She looks pale, jaundice, and moderate performance status
- No lymphnodes enlargement, hepatomegaly, or splenomegaly
- Lab result: Hg: 5,4 g/dL; Hmt 16,3%, MCV 108 fl/cell, MCH 36 pg/cell, MCHC 33 g/dL, WBC 11 x 10^9/L, PLT 235 x 10^9/L,reticulocyte count 3%, Bil5 Dir 3 Indirek 2 LDH 429.
- She often receives prednison and cyclosporin for treating her anemia

Peripheral Blood Smear

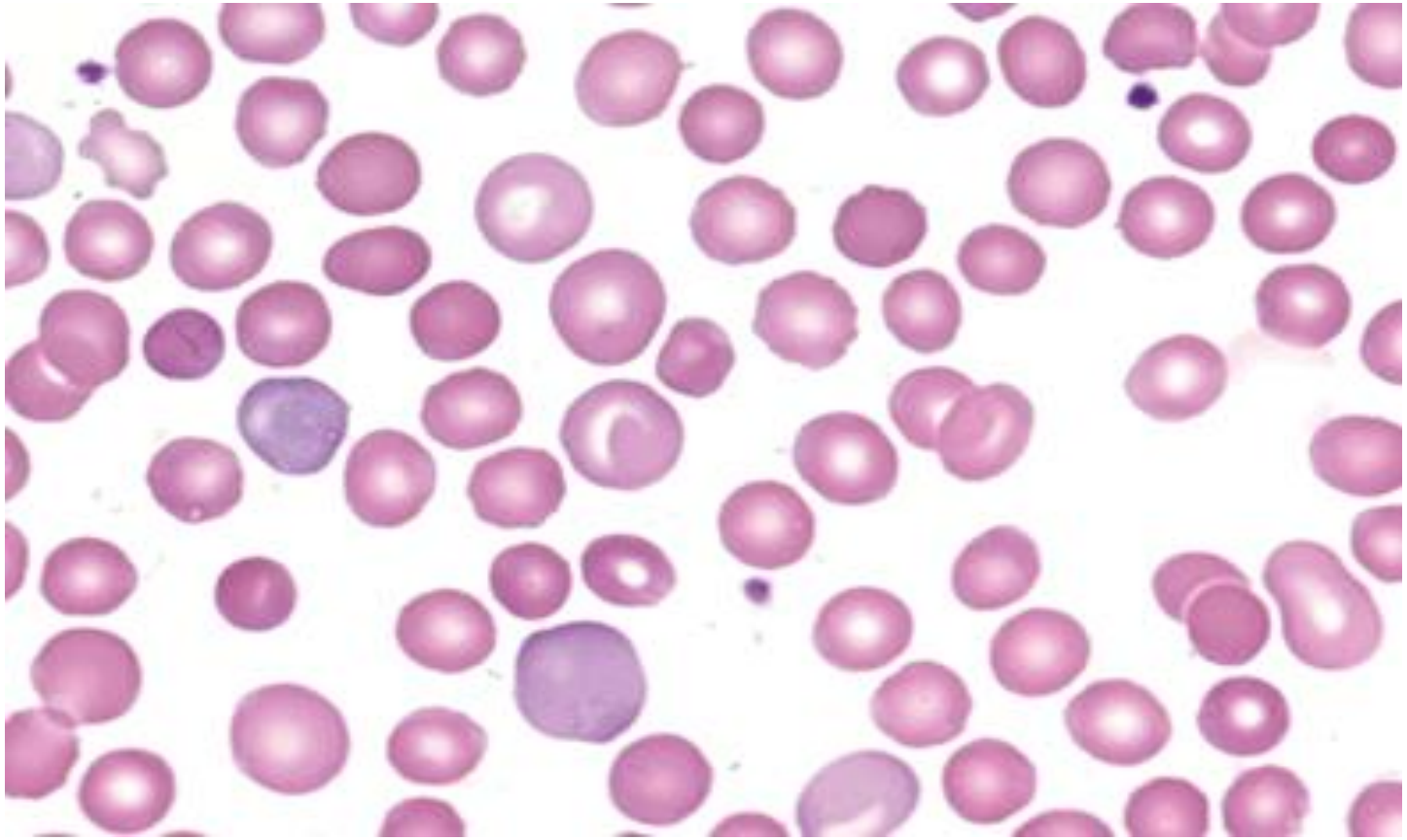
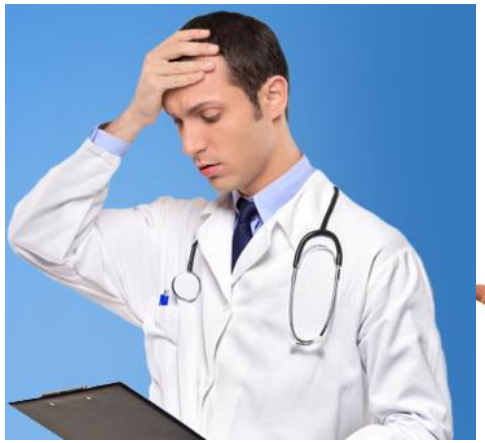
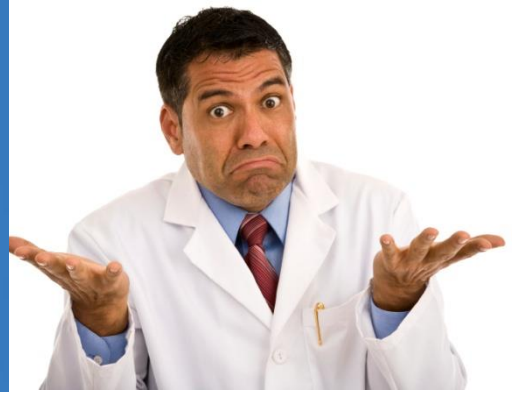


Figure is taken from Diagnosing and Managing Autoimmune Hemolytic Anemia. David Robert and John Burthem

- Due to incompatible blood test, her attending physician did not want to give her transfusion to avoid excessive hemolytic
- She was then reffered to tertiary hospital and received blood transfusion without significant adverse event / transfusion related hemolytic reaction





Mrs. JS, 57 yo admitted due to weakness, palpitation, palor, and shortness of breath. No history of bleeding. Previous transfusions were reported, and yet she could not maintain her normal hemoglobin level soon after blood transfusion procedures

Two week ago her hemoglobin level was 6 gram/dl, therefore she received 4 bags of PRC. Her Hg became 8 gram/dl and within 1 week Hg dropped to 4.5 g/dL.

No bleeding was detected

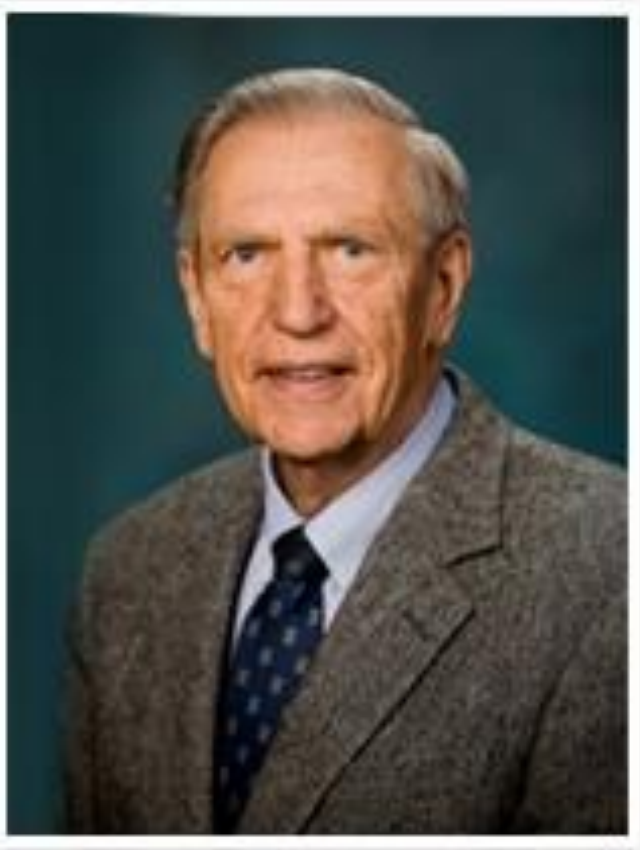
- Hg : 4.6 g/d; MCV: 110.2 fl; MCH: 33.8 pg MCHC 30.3 g/dL; corrected reticulocyte 5.9 %; LDH 434, bilirubin 1.5 mg/dl indirect 0.9 direct 0,5
- MDT :anisocytosis, poikilocytosis, spherocytosis, burr-cell
- Warm type antibody
- Coomb’s test direct and indirect : strong positive
- Cross test : O type RH+, major positive 3, minor positive 3, auto-control positive 3+

AUTOIMMUNE HEMOLYTIC ANEMIA

- When is transfusion needed ?
- Concerning major incompatibility test
- Should we performed additional screening test for compatibility test
- how to minimize the risk of hemolysis

Emergency Transfusion Guideline for Autoimmune Hemolytic Anemia

- Indication for transfusion
- Evaluation AIHA patients for transfusion : clinical and laboratory evaluation
- Specialized Procedures for detecting alloantibodies in Patients with autoantibodies
- Communication between transfusion services and clinicians



Lawrence D Petz, MD.
StemCyte International Cord blood Centre Arcadia CA

Indication for Transfusion in AIHA

- As long as compatibility procedure are performed to detect and identify RBC alloantibodies the indication to transfuse AIHA patients is not different than from non AIHA
- Most common mistake : Reluctant to transfuse to avoid hemolysis reaction due to incompatibility test

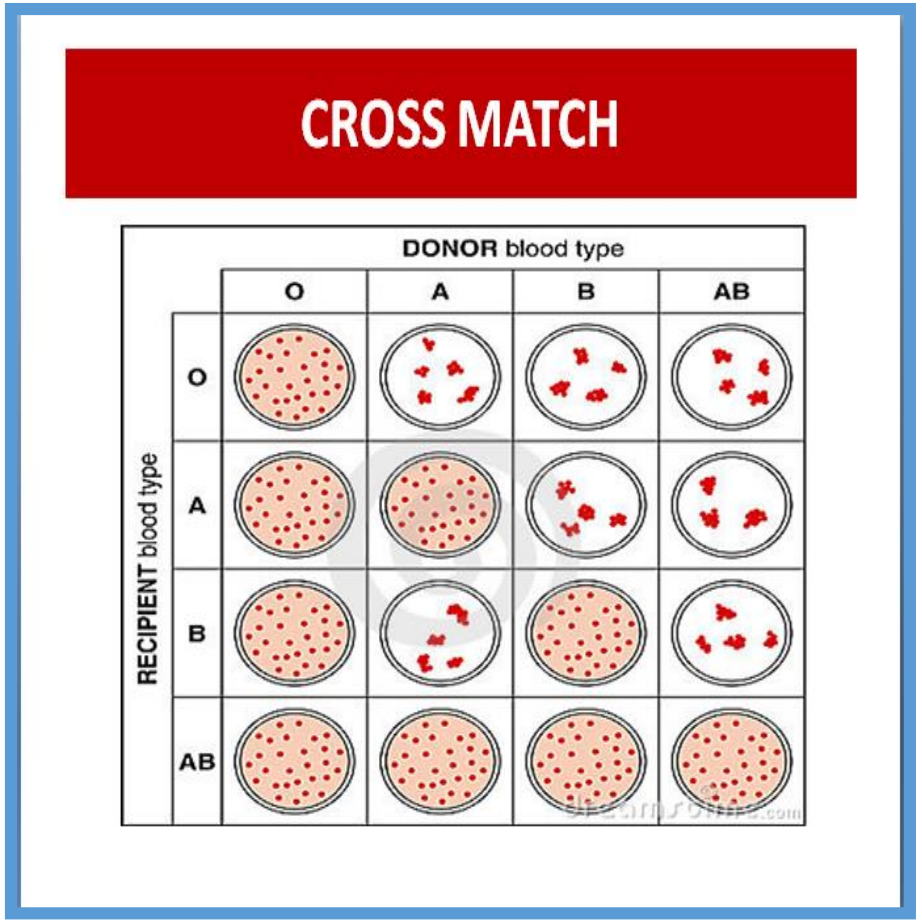
British journal of Hematology 2004: 124; 712-716

Laboratory value to guide necessity for transfusion

Hg > 10 g/ dL	Hg 8-10 g/dL	Hg 5-8 g/dl	Hg < 5 g/dL

Principles of Compatibily Test

- To detect and identify antibodies (alloantibodies) that have the potential to cause a hemolytic transfusion reaction

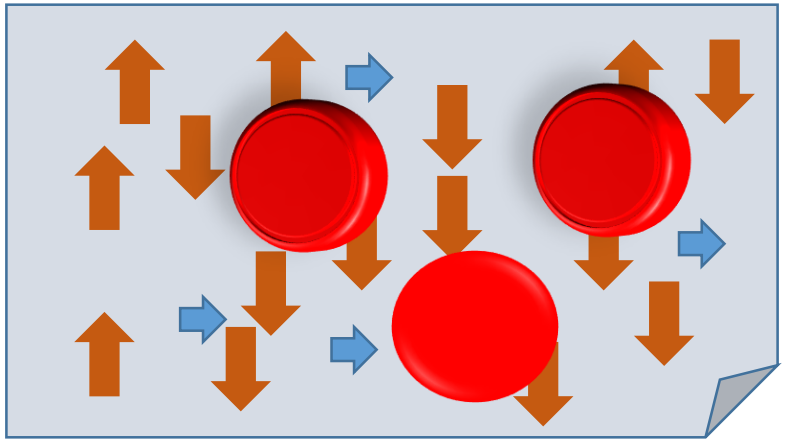


Compatibility test in AIHA

- The most important technical problem faced by the transfusion service regarding patients with AIHA :

  the detection of red cell alloantibodies in patients with a broadly reactive autoantibody

- Alloantibodies are directed against antigen of a number of blood group systems
- Allo antibodies are detected in 32% of patients with AIHA



Branch & Petz. Transfusion 1999: 39; 6-10

BEST MATCHED PROCEDURES

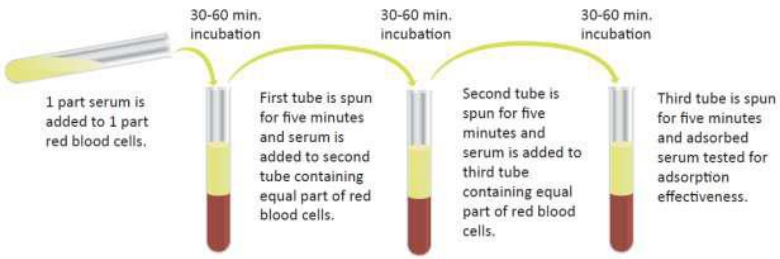
- Minimum investigation like direct antiglobulin test (D antibody screening and autocontrol)
- Best matched procedures should be done by all transfusion services
- Find the least incompatible blood donors / best matches donor

- 12-40% of transfused patients develop clinically significant alloantibodies inducing rapid hemolysis and causing hemolytic transfusion reactions.

Asian J Transfus Sci. 2014 Jul-Dec; 8(2): 105–108

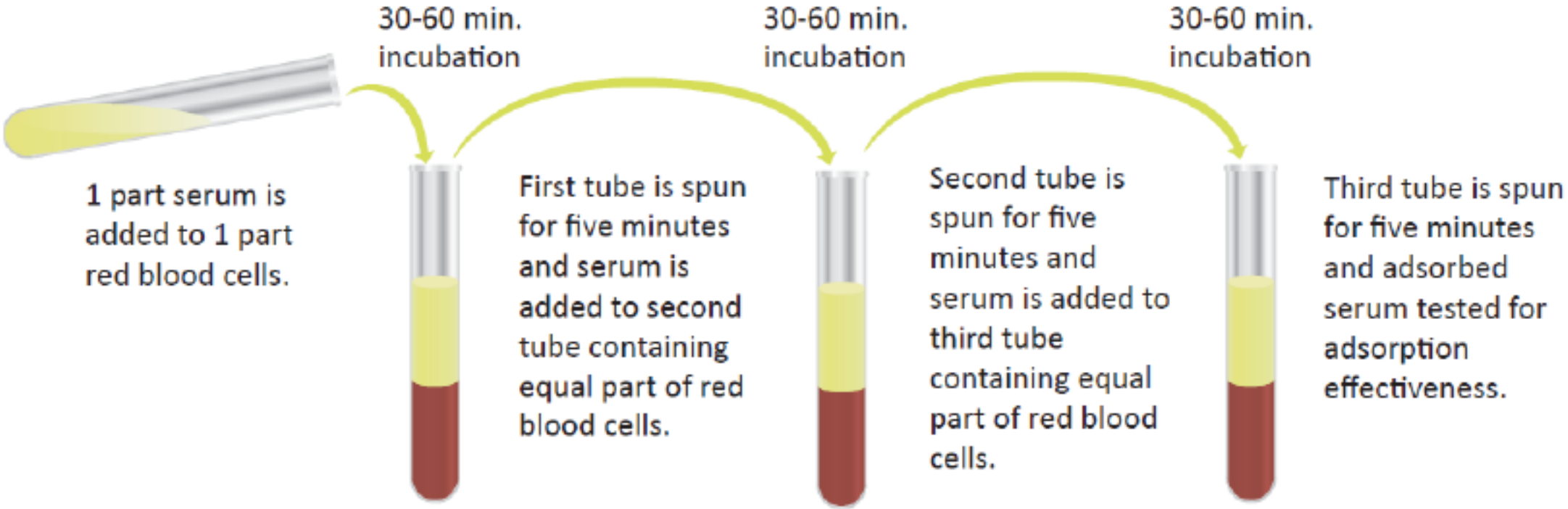
Specialized procedures for detection of alloantibodies in patients with autoantibodies

- ADSORPSION TEST



- EXTENDED RBC PHENOTYPING OF THE PATIENTS AND DONOR UNITS
- TESTING PATIENT'S SERUM AGAINST RED CELL PANEL AND DILUTING PATIENT'S SERUM BEFORE DOING COMPATIBILITY TESTING

British journal of Hematology 2004: 124; 712-716



Time per procedure = 105-195 min.

Summary of Assays used in the Diagnosis and Management of AIHA

Test	Purpose	Comment
DAT or direct Coombs test	Determine the presence of IgG and/or C3 on the RBC surface	Positive in almost 100% of cases of AIHA; amount of IgG and/or C3 correlates with risk of hemolysis
Elution	Characterize the specificity of the RBC-bound IgG	If DAT is only weakly positive for IgG, eluate may not react with panel cells; very important in patients who have received transfusions recently
Antibody screen or indirect Coombs test	Assess for the presence of autoantibody and/or alloantibody in the patient's serum	May be negative if all autoantibody is bound to RBCs
Autoadsorption	Remove excess autoantibody from the patient's serum and determine the presence of alloantibody	If patient has received transfusion during last 90 d, adsorption also may remove alloantibody
Alloadsorption	Remove excess autoantibody from the patient's serum and determine the presence of alloantibody	Useful for patients who have received transfusion and patients with severe anemia from whom an adequate specimen for autoadsorption cannot be obtained

Am J Clin Pathol 2006;125(Suppl 1):S71-S77

Communication between the clinicians and the transfusion services

Responsibility of the Clinician

- A discussion should take place as soon as it is evident that a patient with AIHA is being considered for transfusion
- Indicate the urgency of the transfusion
- Discuss the time required for more detailed serologic test
- Discuss the compatibility test as a guide to pretransfusion testing

Responsibilities of the transfusion service

- to initiate the communication since the diagnosis of AIHA may first be made during compatibility testing for a requested transfusion.

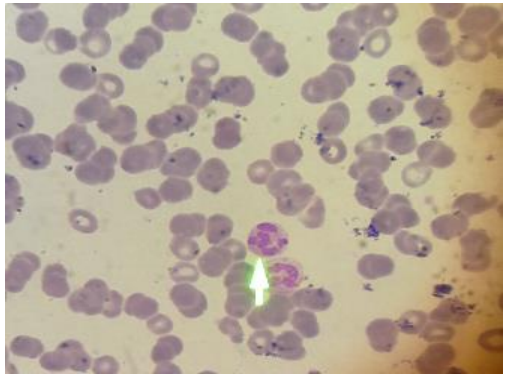
- Give information to clinician about compatibility test procedure performed

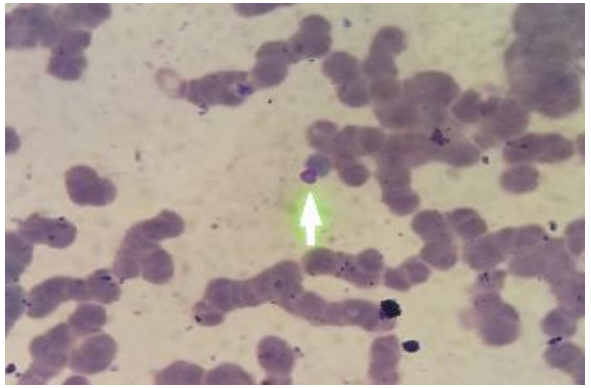
- the clinician should be assured that transfused RBCs are unlikely to cause an acute haemolytic transfusion reaction.

SUMMARY

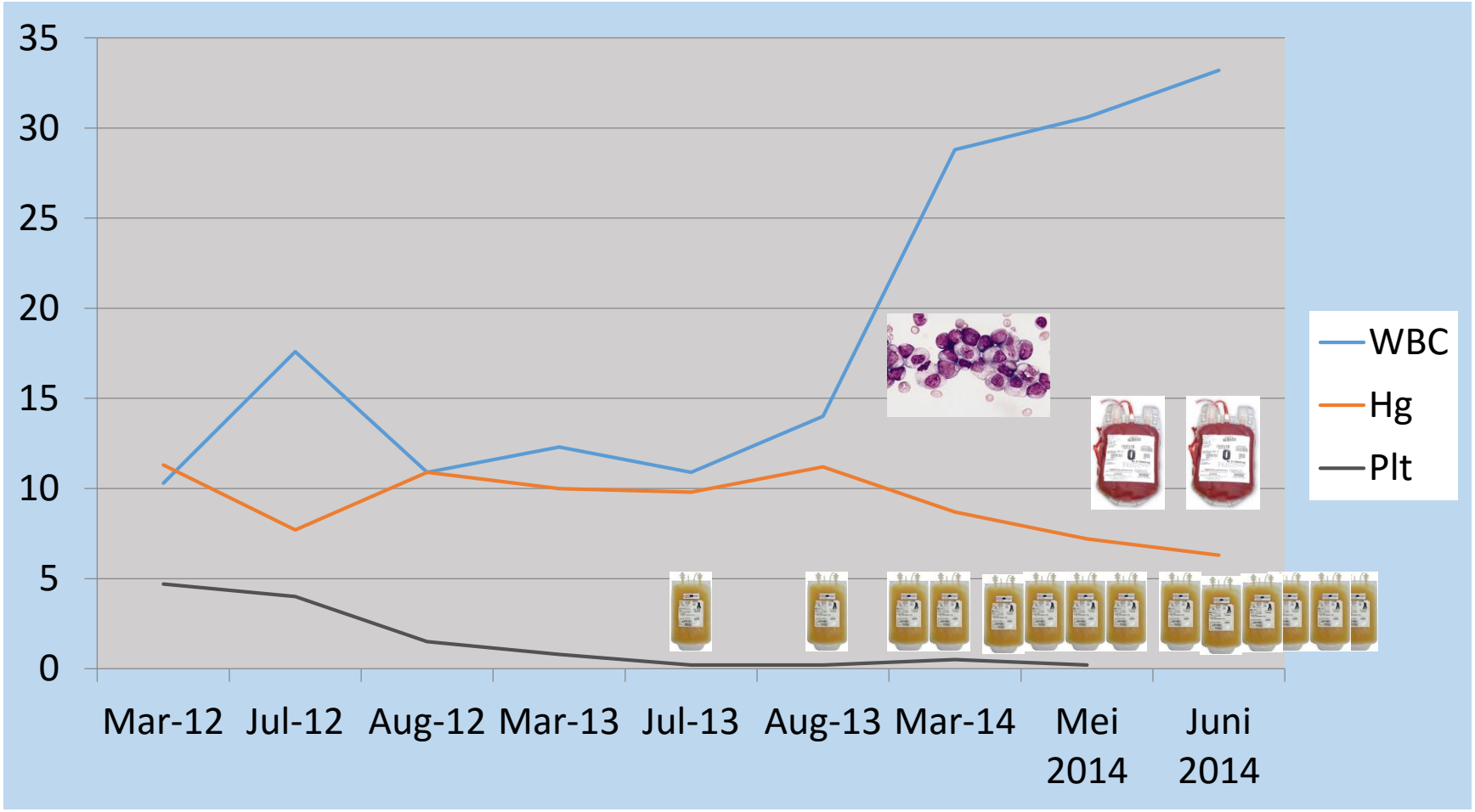
- Transfusion in patients with autoimmune hemolytic anemia presents a potential problem
- Patients have a broadly reactive autoantibodies making all units of RBS are incompatible
- The management of those patients become a responsibility of transfusion service and clinician

- A woman 74 year-old, was sent to the hospital in 2012 due to anorexia, fatigue, and pale, and easy bruising. During the last 4 month she only took 5 full spoons meal per day. No fever. She got weight loss 5 kg since the last 4 month. She is diabetic since 3 years ago. No significant co-morbidity was reported in her medical report. Height : 150 cm weight : 38 kg
- She was diagnosed with Myelodisplasia Syndrome multilineage dysplasia



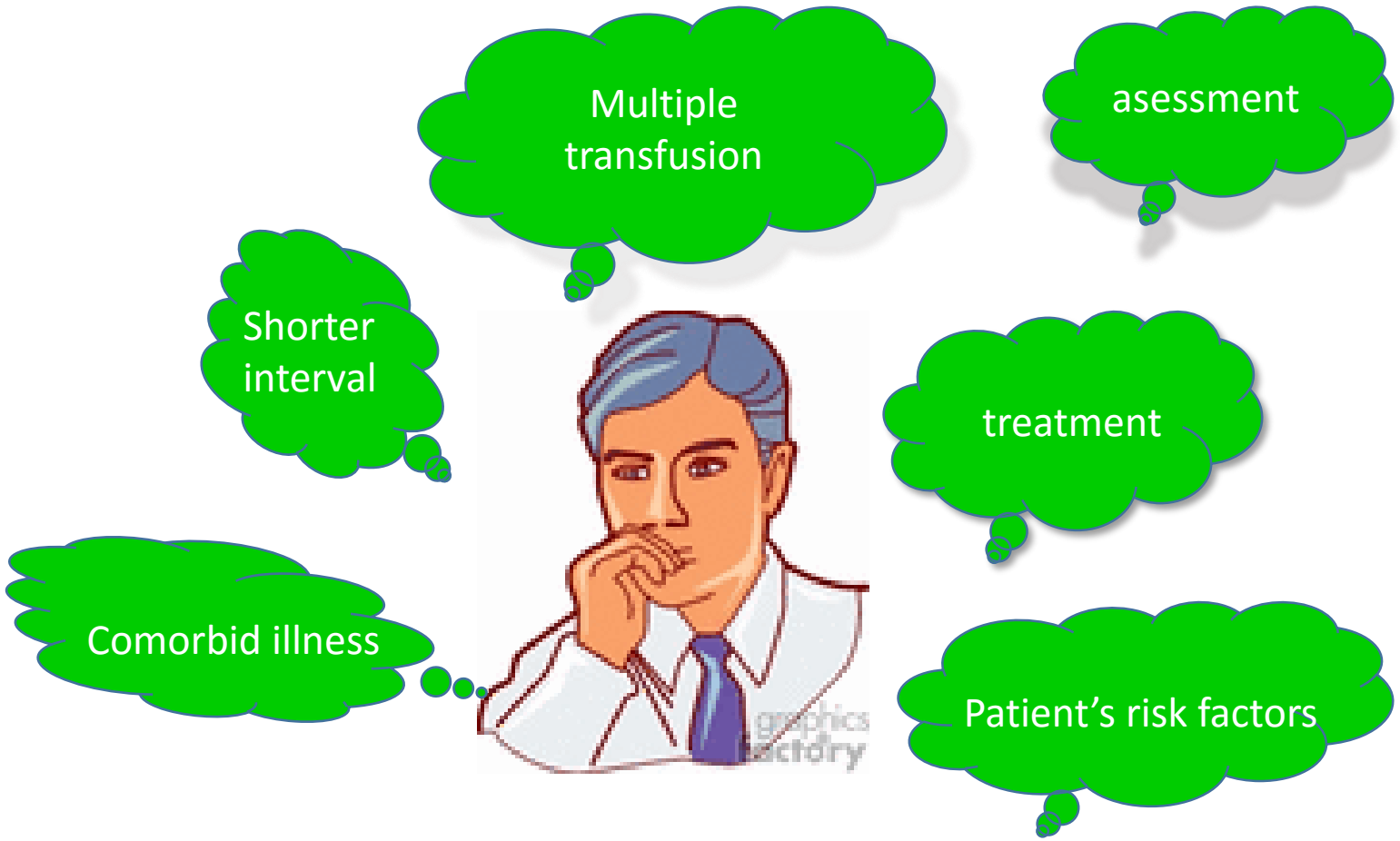


Disease transformation and progression



At 16th of June 2014 patients got melena, and bronchopneumonia
T= 100/80 mmHg, HR 120 x/min t: 38 C

date	PLT count	Transfusion	1h Post transfusion	24 h Post transfusion
13 june 2014	15,000/uL	Plt apharesis	48,000/uL	29,000/uL
16 june 2014	2,000/uL	Platelet apharesis 1	7,000/uL	3,000/uL
17 June 2014	3,000/uL	Platelet apharesis 1	1,000/uL	2,000/uL

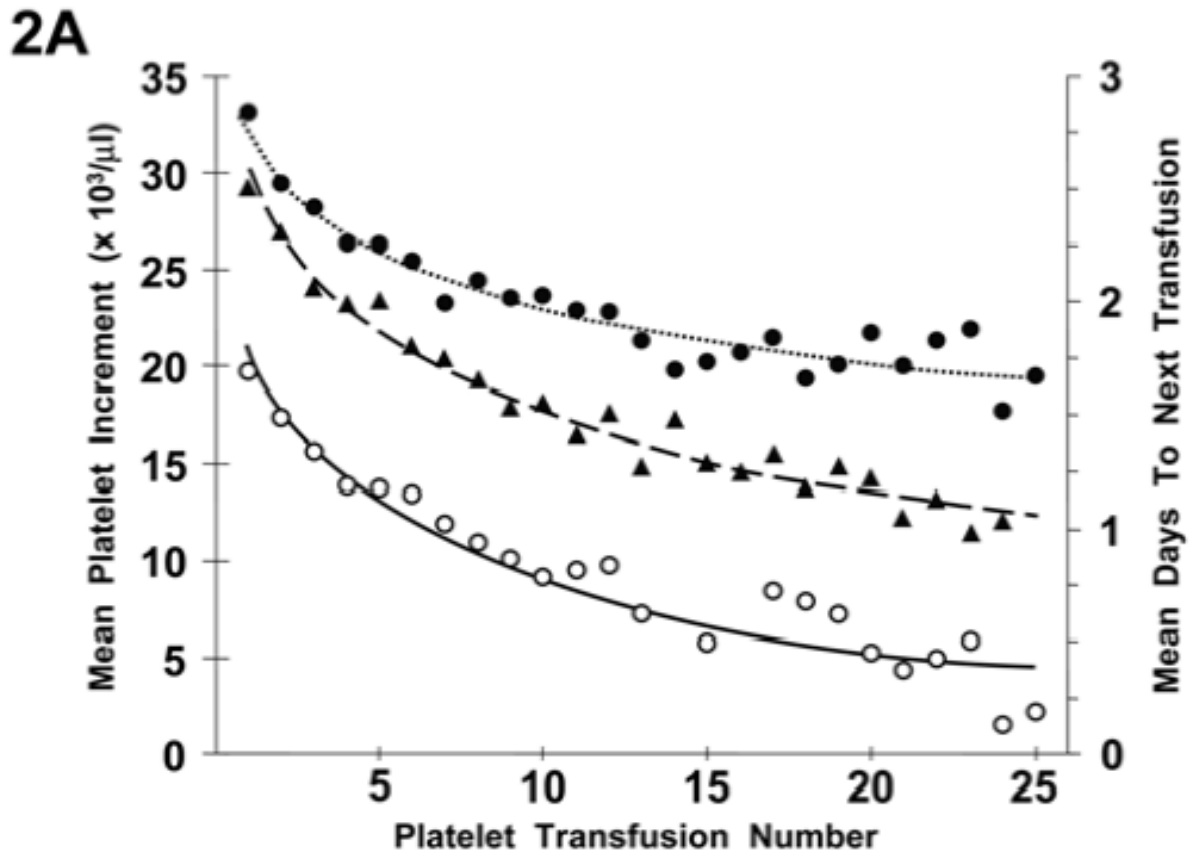


Platelet Transfusion Refractoriness ????

Platelets transfusion refractoriness

- **Platelet transfusion refractoriness** is defined as a less-than-expected increase (usually less than 10,000/mm3) in a patient's platelet count on at two occasion performed 1 hour after the transfusions.
- This is a common occurrence in thrombocytopenic patients that have had multiple transfusions (incidence of 20-70% in highly transfused patient populations) especially with non-leukoreduced blood components.

Relationship between number of platelet (plt) transfusions and plt increments at 1 hour and 18 to 24 hours after transfusion and days-to-next transfusion



Slichter et al. Blood 2005;105:4106

Common causes of platelet refractoriness

Non immune	immune
Disseminated Intravascular Coagulation Sepsis Fever Bleeding Sequestration Drugs (including amphothericin B)	Alloantibodies to HLA antigens Alloantibodies to specific platelets antigen Autoantibodies Drug (heparin).

Blood Review 1990:4, 16-24

How to prevent alloimmunization ?

Optimal platelet support for patients likely to receive multiple platelet transfusion?
Use leucocyte poor red cell or platelet concentrate, UV irradiated Type patients for HLA –A,B typing Use random donor for the initial platelet transfusion Screen patients' sera for HLA antibodies at regular intervals If refractoriness occurs, include non-immune platelet consumption and confirm the presence of HLA –antibodies before using HLA-matched platelet transfusion If no improvement occurs with HLA-matched transfusions, use platelet cross matching to identify the cause of the problem and select compatible donors

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