BLOOD TRANSFUSION

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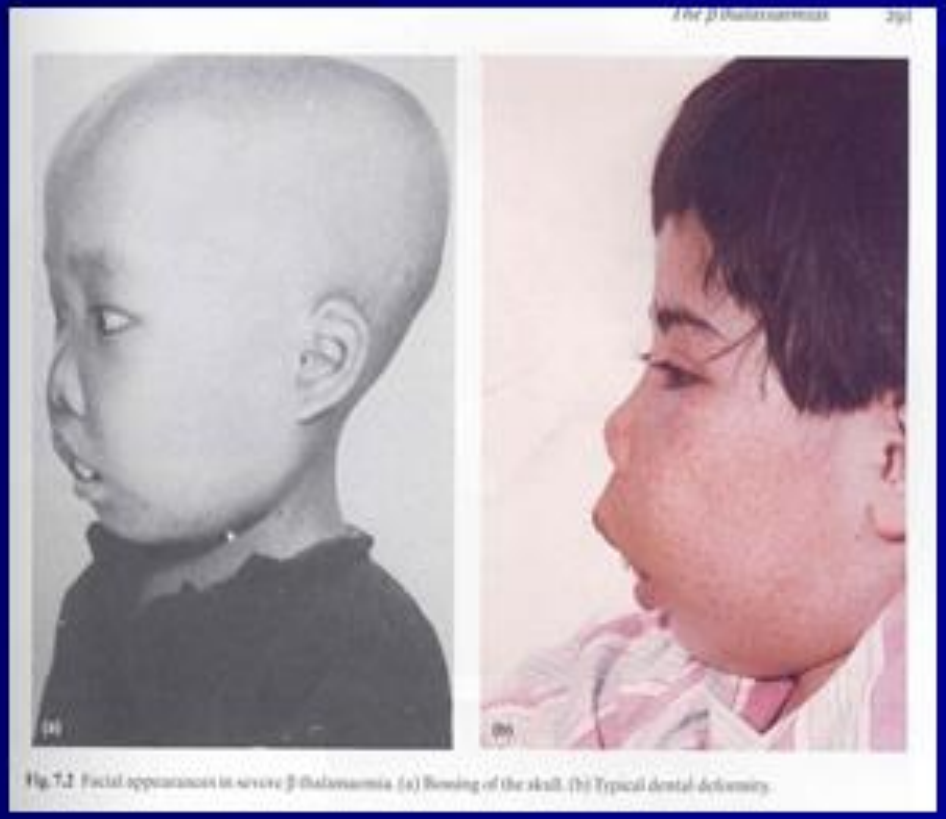
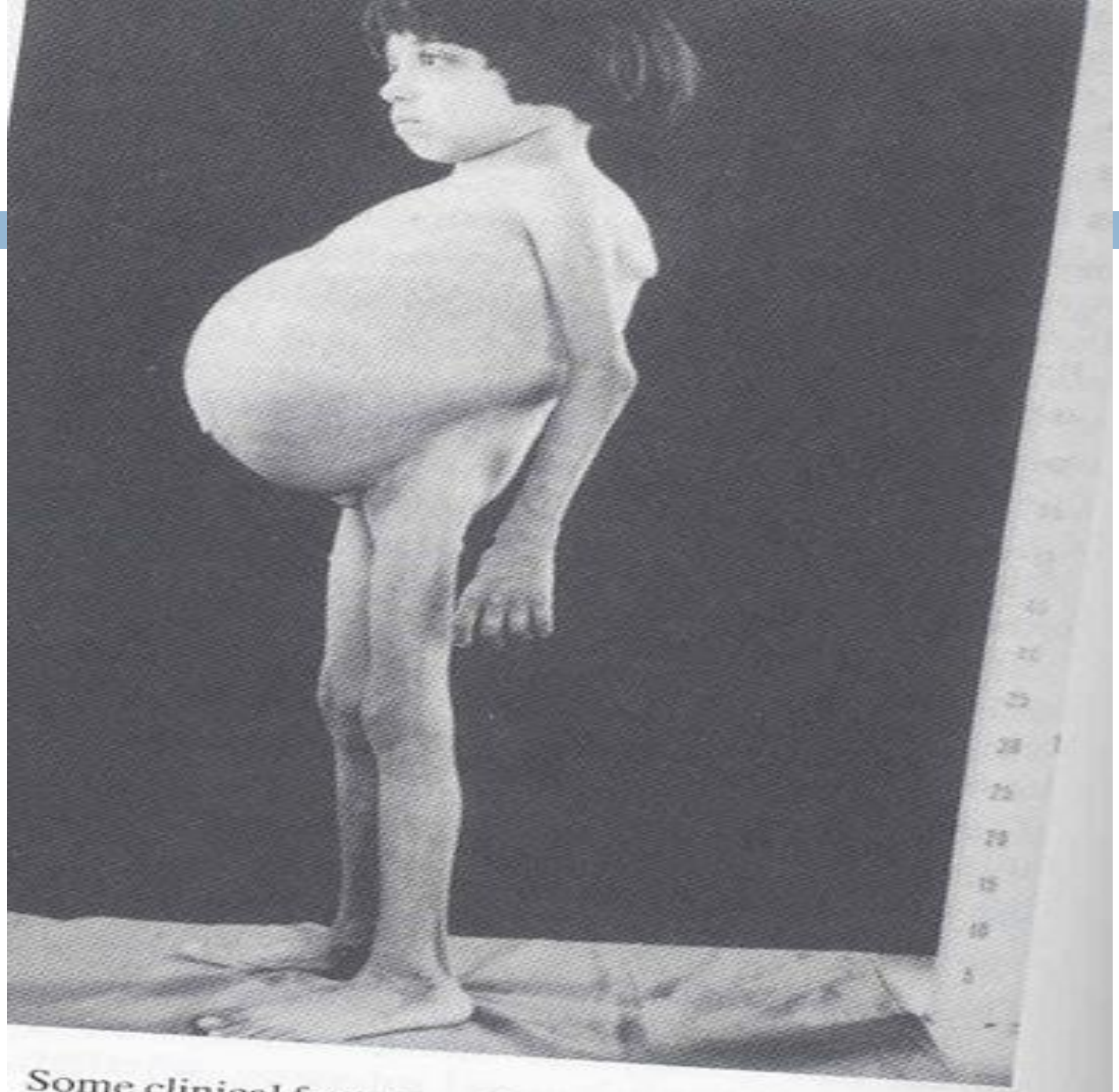
Blood transfusion

- Aims of blood transfusion
- Hemovigilance
- Blood Donation
- Blood component specification
- Compatibility testing and alloimmunization
- Criteria for initiating transfusion therapy
- Transfusion thresholds and frequency
- Volume to be transfused
- Transfusion and the spleen
- Adverse reactions

Aim of blood transfusion

- Is to deliver a safe and effective transfusion regimen whilst minimizing the burden of transfusion
- Effective transfusion regimen will result in:
  - Good growth and development
  - Good energy levels
  - Suppression of intra/ extramedullary haematopoiesis





Some clinical features of severe β thalassaemi
ld has massive

Aim of blood transfusion

A safe transfusion regimen will:

- Use a product that is collected, tested, selected, issued and administered adherent to established quality and safety regulations and guidance
- Be administered by staff trained in blood transfusion
- Involve informed patient consent
- Be performed in a system with good hemovigilance structure

Hemovigilance

- "Hemovigilance is the set of surveillance procedures covering the entire blood transfusion chain, from the donation and processing of blood and its components, through to their provision and transfusion to patients, and including their follow-up

Hemovigilance

- It includes the monitoring, reporting, investigation and analysis of adverse events related to the donation, processing and transfusion of blood, and taking action to prevent their occurrence or recurrence.
- The reporting systems play a fundamental role in enhancing patient safety by learning from failures and then putting in place system changes to prevent them in future.

Hemovigilance

- This system should involve all players and should be coordinated between the blood transfusion service, hospital staff and transfusion laboratories, hospital transfusion committees, the national regulatory agency and health authorities
- The resulting modifications to transfusion policies, standards and guidelines, as well as transfusion practices in hospitals, lead to improved patient safety"
- Good hemovigilance is key to the delivery of safe and effective transfusion in any setting such as those with thalassaemia

Blood donation

- To safeguard the health of patients with thalassaemia, blood should be obtained from carefully selected voluntary, donors and should be collected, processed, stored and distributed, by dedicated blood transfusion centres with established quality assurance systems
- With consideration of national needs, resources and prevalence of infectious agents, should safeguard the quality of blood transfusion services particularly to prevent transfusion transmitted infections (TTI).

Blood donation

- Patients who have repeated donor exposure are at greater risk of such infection.
- Blood donation guidelines, donor selection (e.g., through questionnaires) and specific product screening for hepatitis B, hepatitis C, HIV, syphilis and, in some countries, other infectious diseases such as HTLV I/ II, malaria, toxoplasma, Hepatitis A, Hepatitis E, West Nile virus and Chagas disease constitute some of the most important strategies that contribute to the safety and adequacy of blood

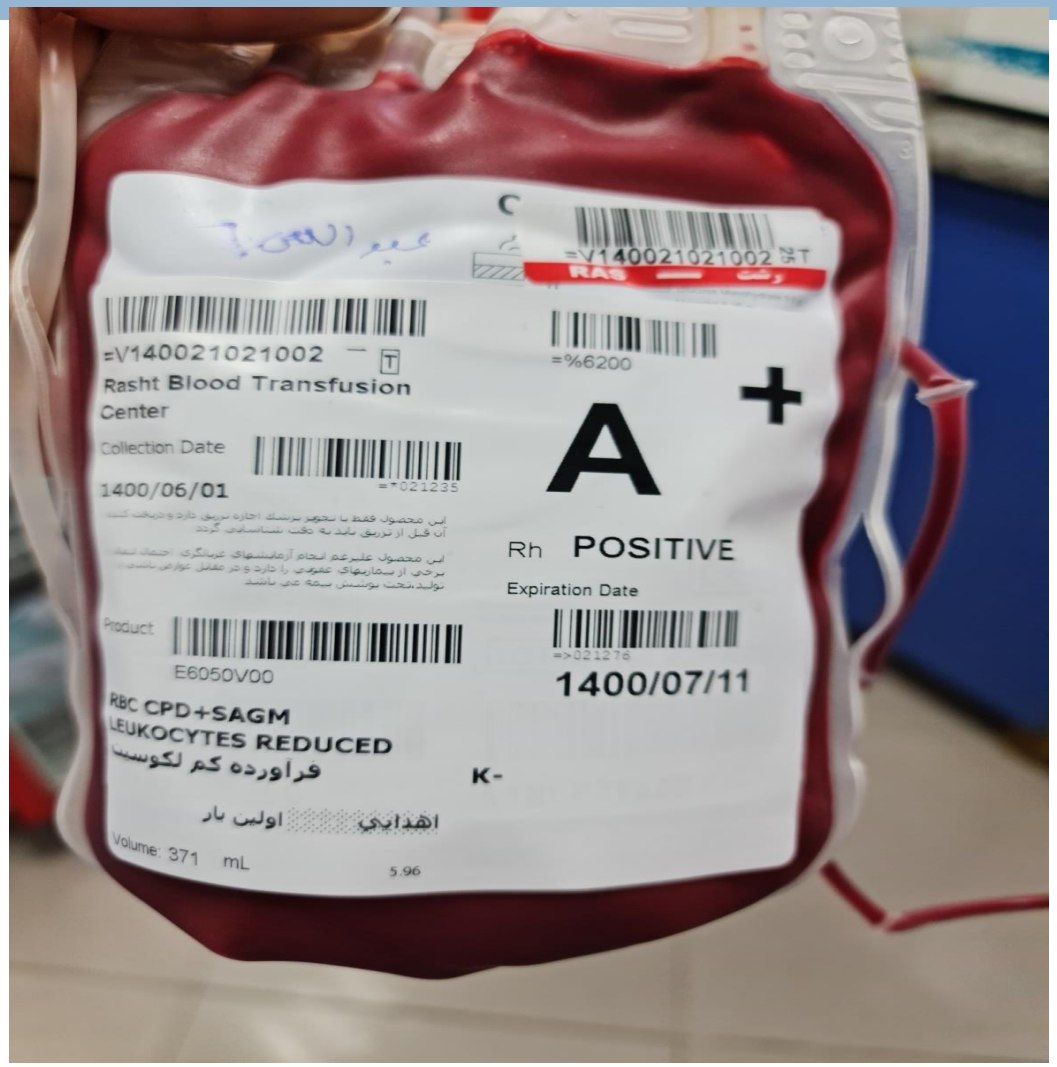
Blood component specification

Leucodepletion

- Reduction to 1 X 10^6/l or less WBC/unit is considered the critical threshold for eliminating adverse reactions attributed to WBC
- In countries where variant Creutzfeld Jakob Disease was prevalent (e.g. UK), it is universally used for all cellular products to decrease the risk of transmission through blood product

Blood component specification

- Pre-storage filtration of whole blood is the preferred method for leuco-reduction
  - This method of leucocyte removal offers high efficiency filtration and provides consistently low residual leucocytes.
  - Packed red cells are obtained by centrifugation of the leucodepleted whole blood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Product
E6050V00
RBC CPD+SAGM
LEUKOCYTES REDUCED
فرآورده کم لکوسیت
K-
اهدایی اولین بار
Volume: 371 mL
5.96

Blood component specification

- Pre-transfusion, laboratory filtration refers to the filtration at the blood bank laboratory of packed red cells, prepared from donor whole blood.
- Bedside filtration refers to the packed red cell unit that is filtered at the bedside at the time of transfusion. This method may not allow optimal quality control because the techniques used for bedside filtration may be highly variable

Blood component specification

Blood Washed red cells

- may be beneficial for patients who have:
- repeated severe allergic transfusion reactions
- or for patients with IgA deficiency,
- in which the recipient's antibody to IgA may result in an anaphylactic reaction.
- Washing of the donor product removes plasma proteins that constitute the target of antibodies in the recipient.
- Washing may be accomplished using manual or automated techniques

Blood component specification

Blood Washed red cells, continued

- Washed red cells that are not suspended in storage solution must be transfused within 24 hours, and creates the possibility of wastage if patients are not available for transfusion at the time the blood is prepared.
- Suspension in SAGM after washing allows for shelf life as long as 14 days if a closed circuit is used.

Blood component specification

- Washing alone usually does not result in adequate leucocyte reduction and should not be used as a substitute for leuco-reduction.
- Instead, washing should be used in conjunction with filtration.
- In addition, washing of red cell units removes some erythrocytes from the transfusion product, and it is therefore valuable to monitor post-transfusion haemoglobin levels to ensure attainment of the targeted haemoglobin level.

Blood component specification

Cryopreserved (frozen) red cells

- is the component derived from whole blood in which red cells are frozen, preferably within 7 days of collection , and can be stored at –60°C to –80°C in an electrical freezer, when a high-glycerol method is used or alternatively at –140°C to –150°C if stored in vapour phase liquid nitrogen, when a low-glycerol method is used.

Blood component specification

- This product is used to maintain a supply of rare donor units for patients who have unusual red cell antibodies or who are missing common red cell antigens.
- Approximately 20% of the donor cells are lost in the washing after the freezing process.
- There is no good evidence about how long these can be stored though in NHS Blood and Transplant they are now kept for 30 years.

Blood component specification

Red cells obtained by donor apheresis

- Refers to the collection of two units of red cells from the same donor for transfusion of one patient.
- The reduction of donor exposures may decrease the risk of transmission of infections and developing alloantibodies and other transfusion-related complications.

Blood component specification

- This approach creates significant logistical problems as the donors need higher hematocrits, can attend less regularly for donation and the collections are performed using more invasive apheresis techniques.
- In addition, the collection of two separate bags may create an organizational challenge in ensuring that both units go to the same donor

Blood component specification

- **Neocyte** transfusions may modestly reduce blood requirements by using only the younger fraction of red cells form the donor units .
- However, patients are exposed to a higher number of donors, with a consequent increase in cost, risk of transmission of infections, and risk of developing alloantibodies

Blood component specification

Additional selection or processing of products may be necessary in certain clinical situations :

- CMV negative products for pregnant women
- Irradiation if issues with T-cell function e.g. Hodgkin Lymphoma

Storage of Donor Red Cell Units

- The anticoagulant preservative solutions used in blood collection have been developed to prevent coagulation and to permit storage of RBC without loss of metabolic integrity.
- All of these solutions contain sodium citrate, citric acid and glucose, and some of them also contain adenine, guanosine and phosphate (e.g., CPD-A).
- The introduction of additives such as AS-1, AS-3 and AS-5 permits storage of red cells for up to 42 days

Types of preservatives

Solution type	Shelf-Life (days)
CPD	21
CP2D	21
CPDA-1	35
CPD, CP2D or CPDA-1 with AS-1 (Adsol), AS-3 (Nutricell), AS-5	35-42

Storage of Donor Red Cell Units

- In TDT, decreased recovery and a shortened red cell half-life may increase transfusion requirements and hence the rate of iron overload;
- The current practice is to use red cells stored in additive solutions for less than two weeks where this is available

Compatibility Testing

- Development of red cell antibodies (alloimmunization) is an important complication of chronic transfusion therapy
- The prevalence of alloantibodies varies widely and may be related to the homogeneity of the population, strategies for antigen matching and ….
- It is important to monitor patients carefully for the development of new antibodies
- Anti-E, anti-C and anti-Kell alloantibodies are the most common
- 5-10% of patients develop antibodies against other antigens

Table 3. Age and alloimmunisation in thalassaemia.

AGE AT FIRST TRANSFUSION (YRS)	ALLOIMMUNISATION RATE (%)	REFERENCE
<1	7.7	(Michail-Merianou et al., 1987)
<1	27.9	
<3	20.9	(Spanos et al., 1990)
<3	47.5	

Compatibility Testing

- Before initiation of transfusion therapy, patients should have extended red cell antigen typing that includes at least A, B, O, C, c, D, E, e, and Kell, (& preferably a full RBC phenotype)
- If the patient is already transfused, antigen typing can be performed using molecular rather than serological testing.
- All patients with thalassaemia should be transfused with ABO and Rh (C, c, D, E, e) and Kell compatible blood to avoid alloimmunisation against these antigens.

Compatibility Testing

- There should be a valid group and antibody screen available prior to transfusion being administered
- Most blood banks currently perform a screen for new antibodies and an IAT (indirect antiglobulin test) crossmatch before each transfusion.

Compatibility Testing

- A complete and detailed record of antigen typing, current and historical red cell antibodies and transfusion reactions should be maintained for each patient, and should be readily available if the patient is transfused at a different centre.
- Transfusion of blood from first-degree relatives should be avoided because of the risk of developing antibodies that might adversely affect the outcome of a later stem cell transplant and the risks of transfusion associated graft versus host disease.

Criteria for initiating transfusion therapy

- **Confirmed** diagnosis of thalassaemia. **&**
- Laboratory criteria: - Hemoglobin level <7, 2 weeks apart (excluding all other contributory causes such as infections) **AND/OR**
- Clinical criteria irrespective of hemoglobin level

> Significant symptoms of anemia

> Poor growth / failure to thrive

> Complications from excessive intramedullary hematopoiesis such as pathological fractures and facial changes

> Clinically significant extramedullary hematopoiesis

Criteria for initiating transfusion therapy

- The decision to initiate a long-term transfusion regimen should be based on a definitive diagnosis of TDT
- It must be established that the severity of anemia is not transient to issues such an infection, in which case a one-off transfusion may be sufficient.

Criteria for initiating transfusion therapy

- The initiation of regular transfusion therapy for TDT usually occurs in the first two years of life
- Some patients with milder forms of thalassemia who only need sporadic transfusions in the first two decades of life may later need regular transfusions because of a falling hemoglobin level or the development of serious complications

Transfusion thresholds and frequency

- The recommended treatment for TDT is lifelong regular blood transfusions,
- Usually administered every 2-5 weeks, to maintain the pre-transfusion hemoglobin level 95-105 g/l
- This transfusion regimen promotes normal growth, allows normal physical activities, suppresses bone marrow activity , and minimizes iron accumulation

Transfusion thresholds and frequency

- A higher target pre-transfusion haemoglobin level of 11-12 g/dl may be appropriate for patients with heart disease, significant extramedullary hematopoeisis, and for those who do not achieve adequate suppression of bone marrow activity at the lower haemoglobin level.
- Sometimes back pain occurs prior to blood transfusion and may respond to a higher pre-transfusion hemoglobin level
- Although shorter intervals between transfusions may reduce overall blood requirements, the choice of interval must consider other factors such as the patient's school or work schedule and other lifestyle issues

Volume to be transfused

- It is difficult to make clear recommendations regarding the volume of blood to be infused
- These relate to the acceptable hematocrit of the donors, the volume collected at donation, whether it is whole or packed red cells and the type of anticoagulant used
- To limit donor exposure, a certain number of units (e.g. one or two) rather than volume of blood is ordered

Volume to be transfused

		HAEMATOCRIT OF DONOR RED CELLS			
		50%	60%	75%	80%
Target increase in haemoglobin level	20 g/l	12 ml/kg	10 ml/kg	8 ml/kg	7.5 ml/kg
	30 g/l	18 ml/kg	15 ml/kg	12 ml/kg	11.2 ml/kg
	40 g/l	24 ml/kg	20 ml/kg	16 ml/kg	15 ml/kg

Volume to be transfused

- For children or for others who may need a specific volume, the following calculations is used: (Desired – actual Hb (g/l)) x weight (kg) x 0.3 = ml to be transfused assuming the HCT of the unit is 0.58
- Post transfusion hemoglobin can be measured for evaluating the effects of changes in transfusion regimen, the degree of hypersplenism, or unexplained changes in response to transfusion

Volume to be transfused

- To achieve pre-transfusion hemoglobin of 9-10.5 g/dl it is often usual to aim for a post transfusion hemoglobin of 13-15g/dl.
- This approach to transfusion has been shown to promote normal growth, to allow normal physical activities, to adequately suppress bone marrow activity and to minimize iron accumulation

Rate of transfusion

- **The rate** of transfusion has not been prospectively studied
- British Society of Hematology Guidelines state that for adults, a unit of blood can be infused over 90 minutes
- Another study suggests that in carefully selected adults >45kg, free of cardiac disease and receiving up to 3 units of mean volume of 260ml can be administered at the rate of one unit per hour
- Particular caution should be taken with smaller patients, particularly children, patients with cardiac failure or very low initial haemoglobin levels

Transfusion and the spleen

- The transfusion requirements in unsplenectomized patients are generally higher than splenectomized patients.
- In a study, splenectomy decreased the annual iron loading by an average of 39% .
- Average transfusion requirements are about 30% higher in unsplenectomised than splenectomised thalassaemia major patients
- With modern chelation regimes, this is seldom a justification for splenectomy unless blood transfusion rates increase into unmanageable ranges, in the context of an enlarging spleen.

Transfusion and the spleen

- Hypertransfusion decreases the rate of splenic enlargement
- Introduction of a hypertransfusion regimen may diminish the extent to which the spleen contributes to an increased blood transfusion requirement. thus preventing the need for a splenectomy.
- Potential reduction in transfusional iron loading after splenectomy must be weighed against the long-term consequences of asplenia including sepsis, thrombosis and pulmonary hypertension.

Transfusion and the spleen

- With access and tolerance to good chelation regimens, splenectomy is not often needed for iron control
- Nevertheless, as the annual transfusion requirements rise above 200 ml/kg/year of pure red cells, splenectomy may be considered as one of several strategies to reduce transfusion requirements

Adverse Reactions

- Blood transfusion exposes the patient to a variety of risks and adverse event.
- Thus, it is vital to continue to improve blood safety and to find ways of reducing transfusion requirements and the number of donor exposures
- Adverse events reporting should be embedded within the hemovigilance system

Adverse Reactions

- Allergic reactions
- Non-hemolytic febrile transfusion reactions
- Acute hemolytic reactions
- Alloimmunization
- Delayed transfusion reactions
- Autoimmune hemolytic anaemia
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated graft versus host disease (TA-GVHD)
- Transfusion-associated circulatory overload (TACO)
- Transfusion transmitted infections (TTI)

Summary and Recommendations

- Confirm the diagnosis of thalassemia and appropriate clinical and laboratory assessment for transfusion
- Blood transfusion requires informed consent
- Hemovigilance and adverse events reporting are key to the safety of blood transfusion.
- Use careful donor selection and screening, favoring voluntary, regular, non-remunerated blood donors

Summary and Recommendations

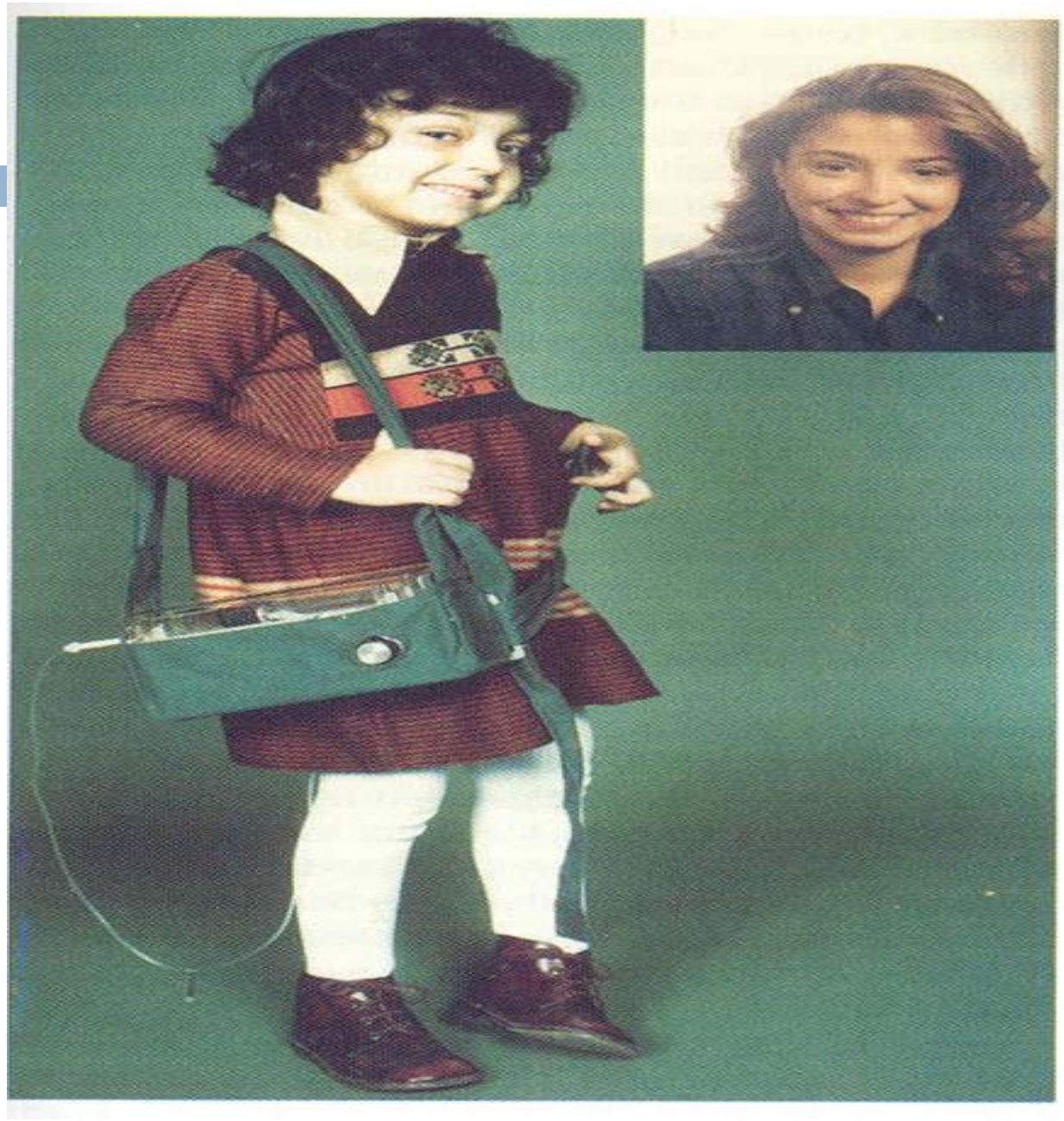
- Before first transfusion, perform extended RBC antigen typing of patients at least for D, C,e, E,e and Kell and if available a full red cell pheno/genotype
- At each transfusion, give ABO, Rh(D) compatible PC
- Choosing units compatible units for ABO, C,c, E,e and Kell antigens is highly recommended
- Before each transfusion, perform a screen for new antibodies and an IAT cross- match

Summary and Recommendations

- Use leukoreduced packed RBC.
  - Pre-storage filtration is strongly recommended, but blood bank pre-transfusion filtration is acceptable.
  - Bedside filtration is only acceptable if there is no capacity for pre-storage filtration or blood bank pre-transfusion filtration
- Use washed RBC for patients who have severe allergic reactions

Summary and Recommendations

- Transfuse red cells stored in CPD-A within one week of collection and red cells stored in additive solutions within less than two weeks of collection
- Transfuse every 2-5 weeks,
- Maintaining pre-transfusion hemoglobin above 9-10.5 g/ dl or up to 11-12 g/dl for patients with cardiac complications
- Keep a record of red cell antibodies, transfusion reactions and annual transfusion requirements
- Keep the post-transfusion hemoglobin below 14-15 g/dl



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