Transfusion and Cross-Matching

BY:

DR. FATMA AL-QAHTANI

LEARNING OBJECTIVES

- To identify the key elements in the current blood bank services.
- To appreciate the implemented measurements and standards for obtaining the highest quality in the blood bank services.
- To have a general idea about the donation process and main blood components.
- To understand the inheritance and significance of the ABO system.
- To understand the nature and significance of the Rh blood group system.
- To understand the cross-matching process, including the antiglobulin test.
- To have an overview about main hazards of blood transfusion.

Blood Bank Units

- Traditionally, two parts:
  - 1) **Donation services**: donor area, component separation, infectious testing, ABO typing and RhD screening, inventory.
  - 2) **Transfusion services**: inventory, Patient (recipient) ABO grouping, RhD and antibody identification screening, cross-match, component issuing.
- Currently in the major hospital, there is a **apheresis** unit (donation, therapeutic or prophylaxis).
- In many tertiary hospitals, stem cell unit, cord blood unit and tissue banking.

Table 30.1 Measures used to protect the donor and for donor selection.

Donor selection
Age 17–70 years (maximum 65 at first donation)
Weight above 50 kg (7 st 12 lb)
Haemoglobin >134 g/L for men, >120 g/L for women
Minimum donation interval of 12 weeks (16 weeks advised) and three donations per year maximum
Apheresis for platelets or plasma up to 24 times in 12 months
Pregnant and lactating women excluded because of high iron requirements; donation deferred for 9 months post pregnancy
Exclusion of those with: Known cardiovascular disease, including hypertension Significant respiratory disorders Epilepsy and other CNS disorders Gastrointestinal disorders with impaired absorption Previous blood transfusions in the UK Intravenous drug users Insulin-dependent diabetes Chronic renal disease Cancer Ongoing medical investigation or clinical trials

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Chronic renal disease
Cancer
Ongoing medical investigation or clinical trials

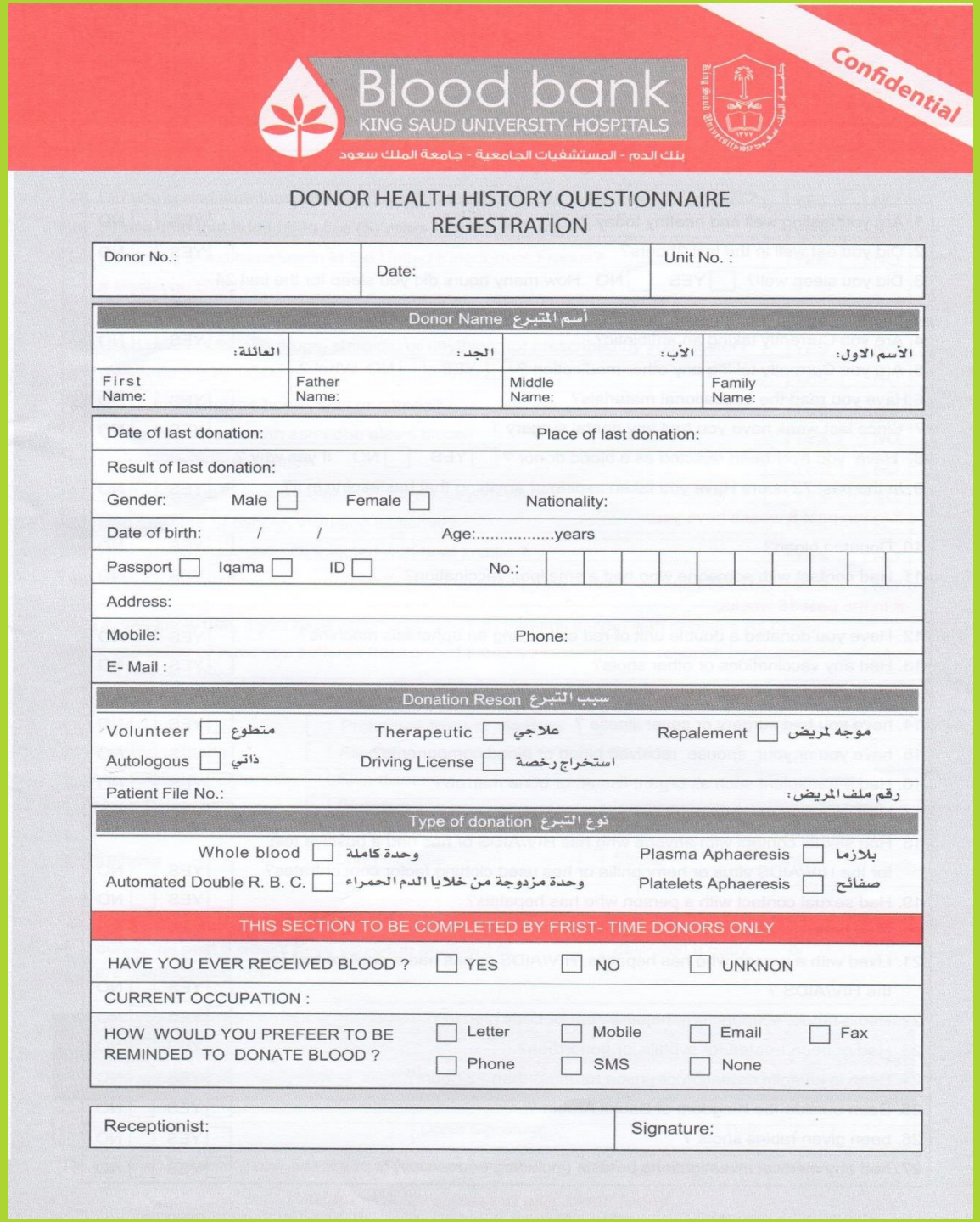
Exclusion of any donor returning to occupations such as driving bus, plane or train, heavy machine or crane operator, mining, scaffolding, etc. because delayed faint would be dangerous

Defer for 12 months after body piercing or tattoo, paid sex or homosexual sex, after acupuncture

Defer for 2 months after live vaccinations such as measles, mumps

Defer if travel history suggests risk of infection

Drugs



Blood bank
KING SAUD UNIVERSITY HOSPITALS
بنك الدم - المستشفيات الجامعية - جامعة الملك سعود

Confidential

DONOR HEALTH HISTORY QUESTIONNAIRE
REGESTRATION

Donor No.:	Date:	Unit No. :

Donor Name أسم المتبرع

الأسم الاول:	الأب:	الجد:	العائلة:
Family Name:	Middle Name:	Father Name:	First Name:

Date of last donation: Place of last donation:

Result of last donation:

Gender: Male ☐ Female ☐ Nationality:

Date of birth: / / Age:.....years

Passport ☐ Iqama ☐ ID ☐ No.:

Address:

Mobile: Phone:

E- Mail :

Donation Reson سبب التبرع

Volunteer ☐ متطوع Therapeutic ☐ علاجي Repalement ☐ موجه لمريض

Autologous ☐ ذاتي Driving License ☐ استخراج رخصة

Patient File No.: رقم ملف المريض:

Type of donation نوع التبرع

Whole blood ☐ وحدة كاملة Plasma Aphaeresis ☐ بلازما

Automated Double R. B. C. ☐ وحدة مزدوجة من خلايا الدم الحمراء Platelets Aphaeresis ☐ صفائح

THIS SECTION TO BE COMPLETED BY FRIST- TIME DONORS ONLY

HAVE YOU EVER RECEIVED BLOOD ? ☐ YES ☐ NO ☐ UNKNON

CURRENT OCCUPATION :

HOW WOULD YOU PREFEER TO BE REMINDED TO DONATE BLOOD ? ☐ Letter ☐ Mobile ☐ Email ☐ Fax ☐ Phone ☐ SMS ☐ None

Receptionist:	Signature:

- **Powerful tool for screening**
- **Identify high risk behaviors.**
- **Some issues can only be ruled out by systemic questionnaire.**

Infectious Testing

Table 30.2 Donor testing in England and Wales.

1 Blood group, Rh status (D,C,E,c,e), K

2 Screen for red cell alloantibodies

3 *Microbiological tests*

Human immunodeficiency virus (HIV) 1 and 2; antibody and RNA

Hepatitis B virus (HBV) – antibody and RNA

Hepatitis C virus (HCV) – antibody and RNA

Human T-cell leukaemia viruses (HTLV) – antibody

Cytomegalovirus (CMV) – antibody, for immunosuppressed recipients

Malaria – antibody screening of potentially exposed donors

Chagas' disease – antibody screening of potentially exposed donors

Bacteria – all donations tested for antibody to syphilis

N.B. At the current time there is no reliable test for detecting prions in blood products.

- **Extra testing (not in all cases); Sickle cell &G6PD level.**

Component Separation

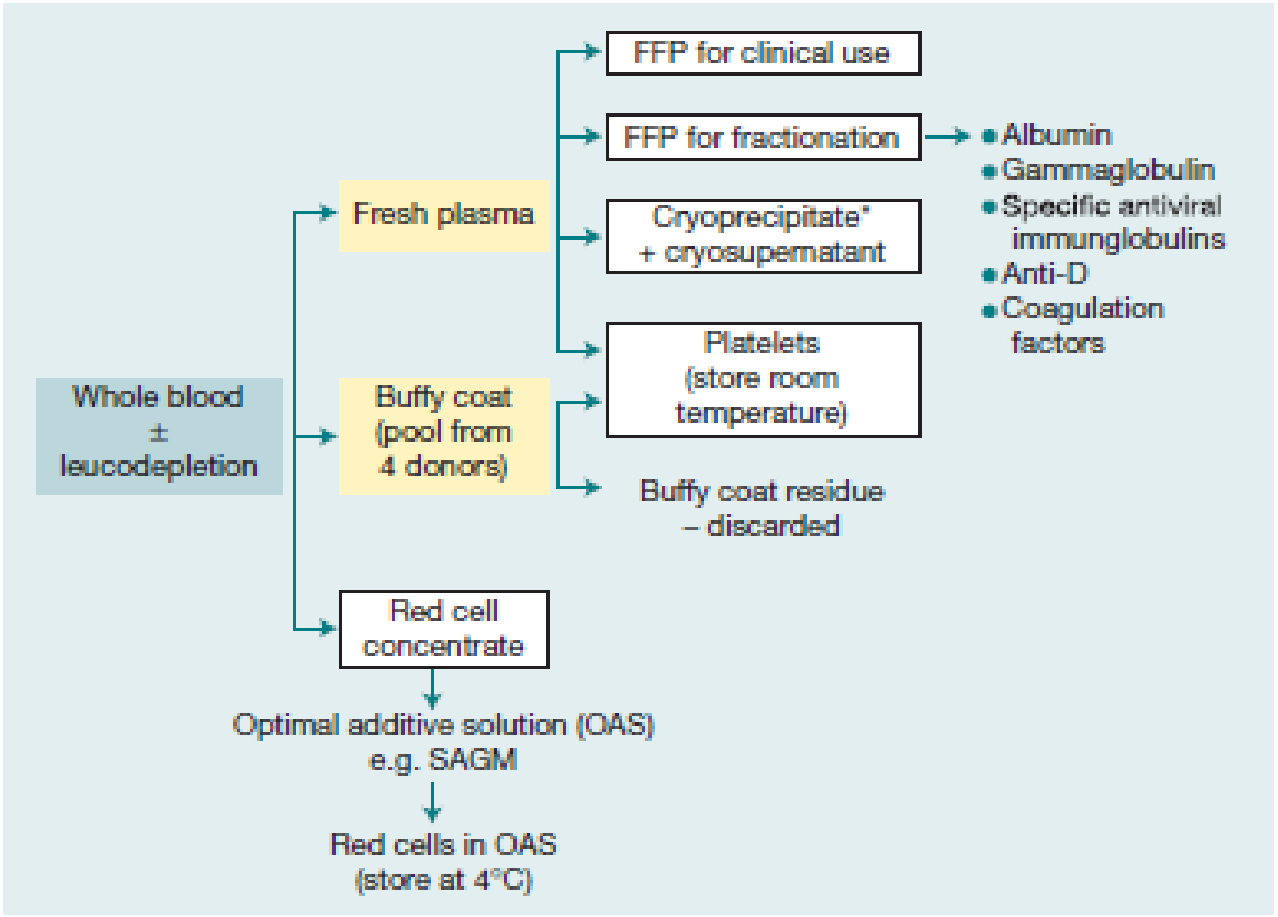
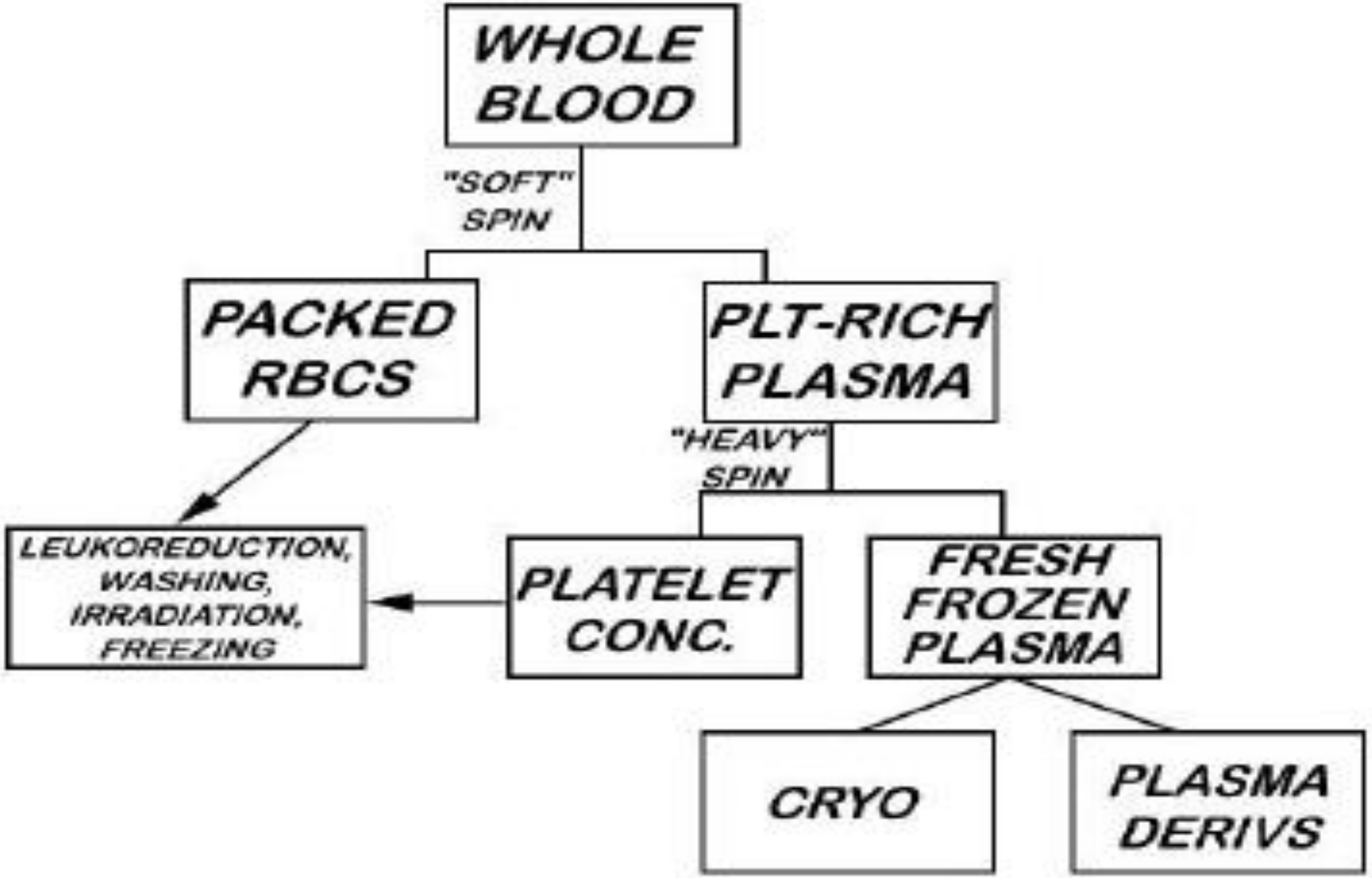


Figure 30.1 The preparation of blood components from whole blood. FFP, fresh frozen plasma; SAGM, saline-adenine-glucose-mannitol.
* Cryoprecipitate is mainly a source of fibrinogen. Cryosupernatant is used for plasma exchange in thrombotic thrombocytopenic purpura.
Leucodepletion – see text.


WHOLE BLOOD
"SOFT" SPIN
PACKED RBCS
PLT-RICH PLASMA
"HEAVY" SPIN
LEUKOREDUCTION, WASHING, IRRADIATION, FREEZING
PLATELET CONC.
FRESH FROZEN PLASMA
CRYO
PLASMA DERIVS

Component Storage

Table 1: Storage Details for Various Blood Products			
Product	**Storage**	**Product**	**Storage**
RBCs / Whole blood	35 days (CPDA-1) 42 days (Additives) 1-6 C	**Granu-locytes**	24 hours; 20-24 C (no agitation)
Frozen RBCs	10 years; –65 C; 24 hours after thaw	**Fresh Frozen Plasma**	1 year; –18 C OR 7 years, –65 C; 24 hours at 1-6 C after thaw
Washed RBCs	24 hours; 1-6 C		
Platelets	5 days; 20-24 C (gentle agitation); 4 hours if pooled	**CRYO**	1 year at –18 C 6 hours at 20-24 C after thaw (4 hours if pooled)

Whole blood

1. The original blood product!
2. Minimal availability in most blood banks today
3. Specifics:

Volume:	450-500 mL
Contents:	RBCs (200-250 mL)
	Plasma (250-300 mL)
	WBCs (10^9)
	Platelets
	Anticoagulant (63 or 70 mL)

Volume:	40-60 mL
Contents:	PLTs ($\geq 5.5 \times 10^{10}$ in 90%)
	Plasma (40-60 mL)
	WBCs (10^7)
	pH $\geq$ 6.2 (90%)

Whole blood donor (5-6 pooled)

Volume:	200-250 mL
Contents:	All coag factors
	- 400 mg fibrinogen
	- 1 IU/mL of all others
	Almost no viable WBCs
	NOTE: No QC testing

Fresh Frozen Plasma (FFP)

Specifics:

Packed RBC unit

Volume:	350 mL (incl. additive)
Contents:	RBCs (200-250 mL)
Without leukoreduction	Plasma ($\leq$ 50 mL)
	WBCs (10^9) and PLTs
	Anticoagulant (63 or 70 mL)
	Additive solution
	200-250 mg iron

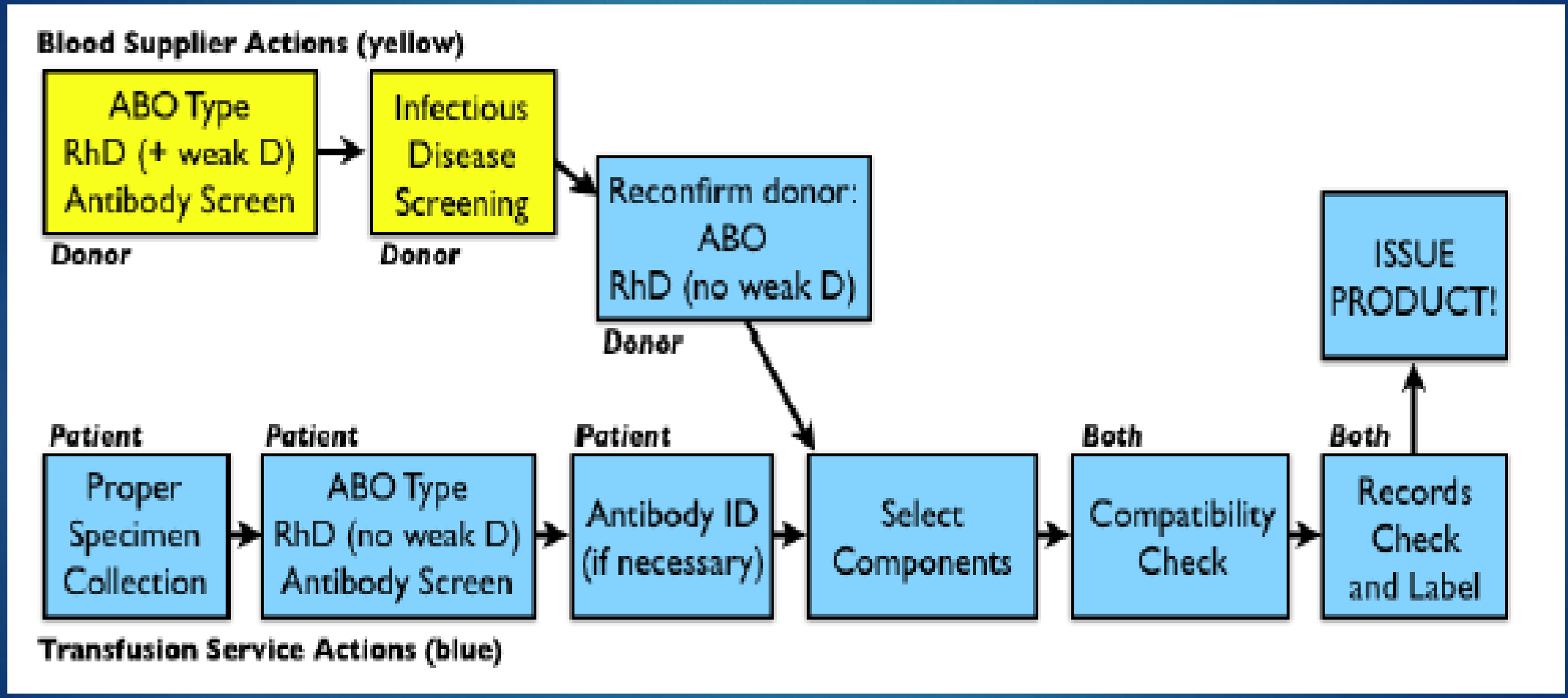
Single donor (apheresis) adult dose

Volume:	100-150 mL (or more)
Contents:	PLTs ($\geq 3.0 \times 10^{11}$ in 90%)
	Plasma (100-150 mL)
	WBCs ($< 5.0 \times 10^6$)
	pH $\geq$ 6.2 (90%)

Cryoprecipitate

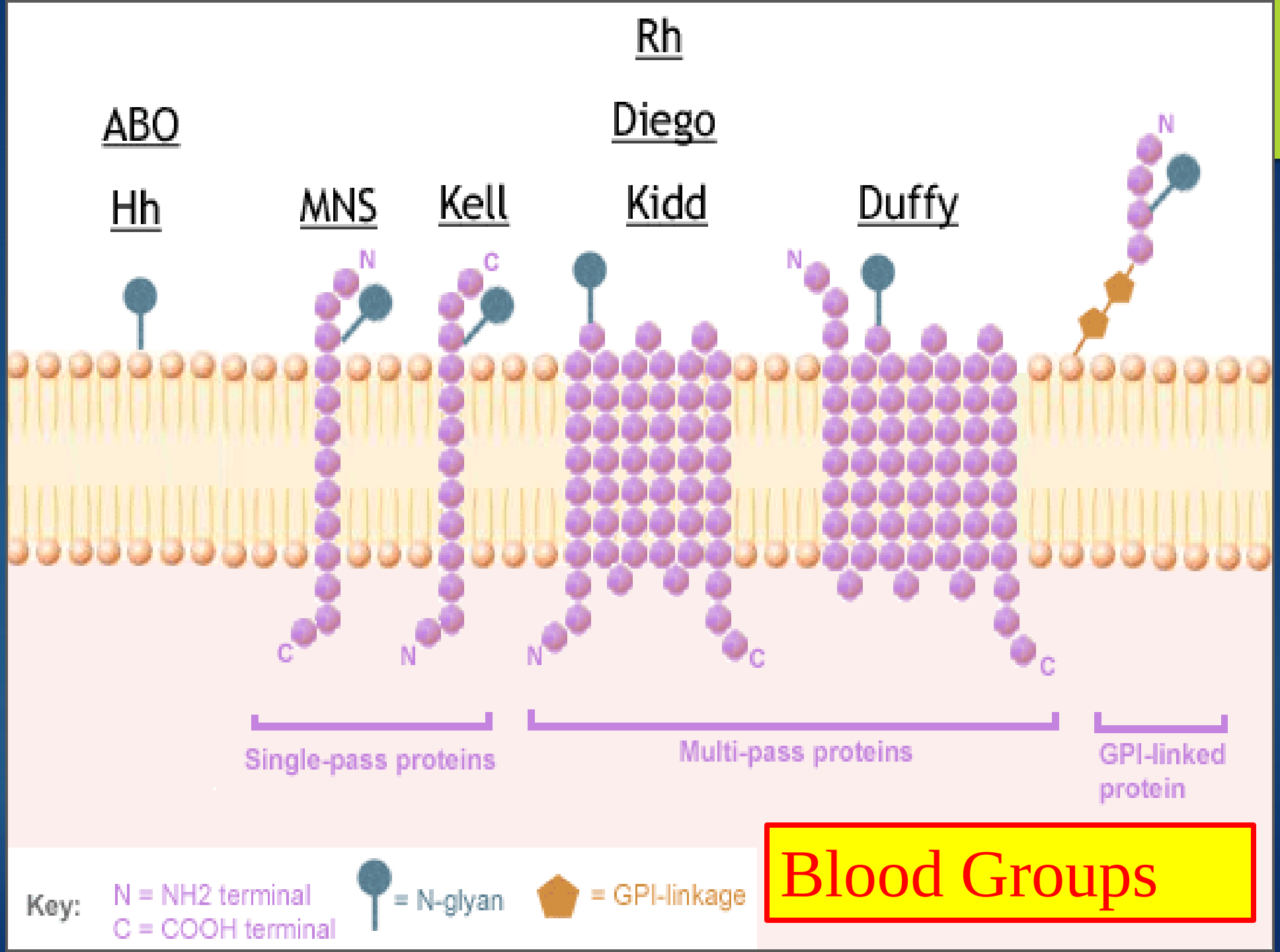
Volume:	15 mL
Contents:	$\geq$ 150 mg fibrinogen
	$\geq$ 80 IU Factor VIII
	80-120 IU vWF
	40-60 IU Factor XIII
	Fibronectin

II] Transfusion Unit



Blood Groups

- One of the main problems in the transfusion of blood is the avoidance of **immunological reactions** resulting from the differences between donor and recipient red cells.
- When the red cells of a donor are transfused into a recipient who lacks these **antigens**, they may induce an immunological response.
- There are at least 30 major blood group systems (e.g. the ABO group, Rh group).



Blood Groups

Table 30.3 Clinically important blood group systems.

Systems	Frequency of antibodies	Cause of haemolytic transfusion reaction	Cause of haemolytic disease of newborn
ABO	Almost universal	Yes (common)	Yes (usually mild)
Rh	Common	Yes (common)	Yes
Kell	Occasional	Yes (occasional)	Anaemia not haemolysis
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)
MN	Rare	Yes (rare)	Yes (rare)
Li	Rare	Unlikely	No

ABO system

- Practically all red cells have the **H antigen**, a carbohydrate group attached mainly to proteins on the cell membrane (FUT1, Ch19q).
- This H antigen is the basis for the ABO blood groups.
- The ABO locus is encoded on chromosome 9q, where one of three possible alleles may be found.
- The **A allele** encodes for a glycosyltransferase, which modifies the H antigen by adding ***N*-acetylgalactosamine** to it (thus forming the A antigen).

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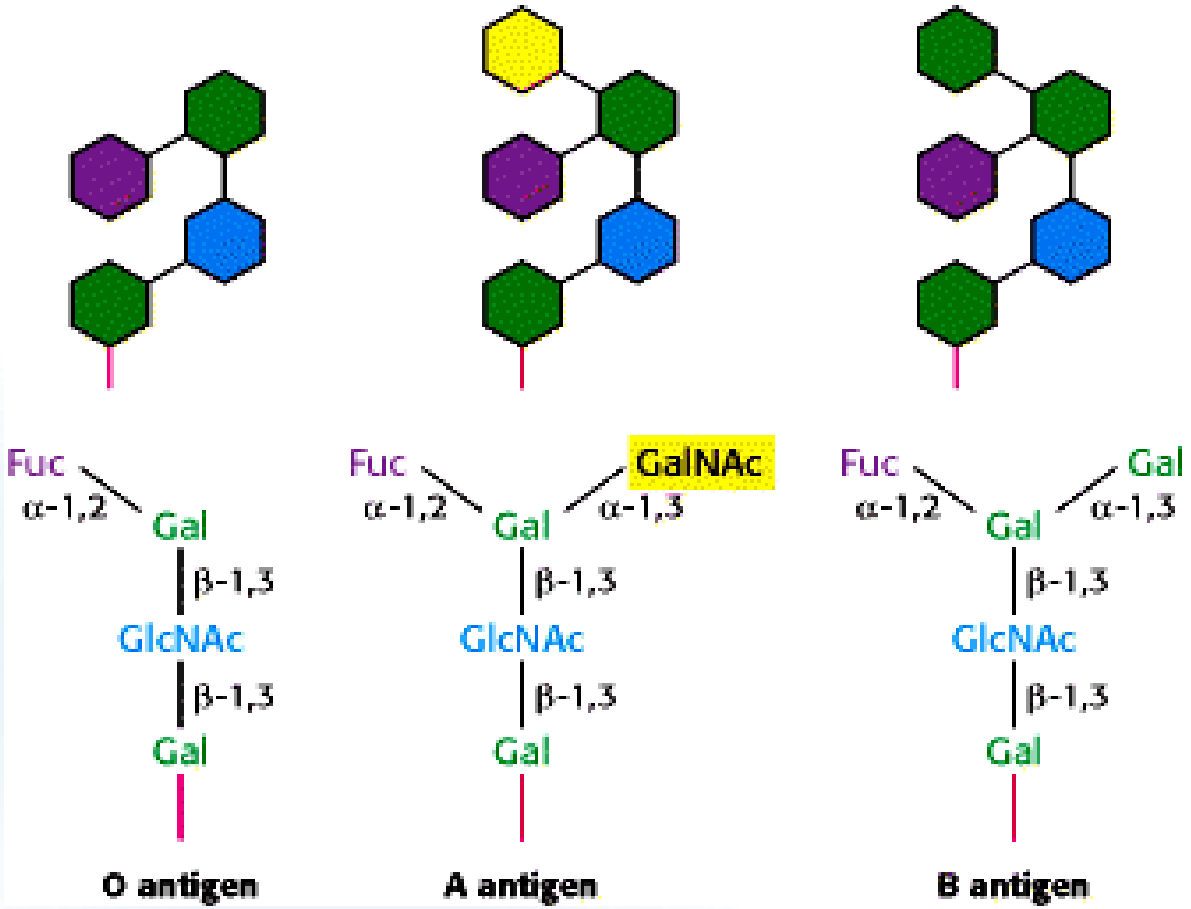
- The **B allele** of the ABO locus encodes an alternative glycosyltransferase that links **galactose** to the H antigen (thus converting it to the B antigen).

- The **O allele**, by contrast, encodes **no functional enzyme** at all, such that the H antigen remains unmodified.

- Hemolytic reactions will occur **immediately** in the event of incompatible transfusion, and may be fatal.



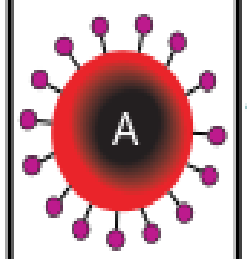
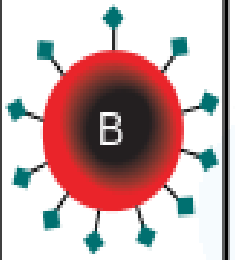
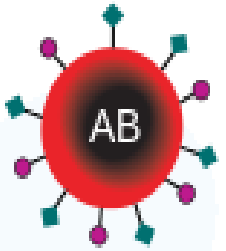
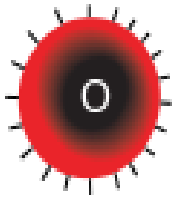
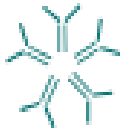
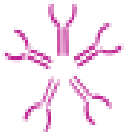
	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

Table 30.4 The ABO blood group system.

Phenotype	Genotype	Antigens	Naturally occurring antibodies	Frequency (UK) (%)
O	OO	O	Anti-A, anti-B	46
A	AA or AO	A	Anti-B	42
B	BB or BO	B	Anti-A	9
AB	AB	AB	None	3

Type	Whites	Blacks	Asians	Native Americans
O	45%	49%	40%	79%
A	40%	27%	28%	16%
B	11%	20%	27%	4%
AB	4%	4%	5%	<1%

Forward grouping

Backward grouping

RhD grouping

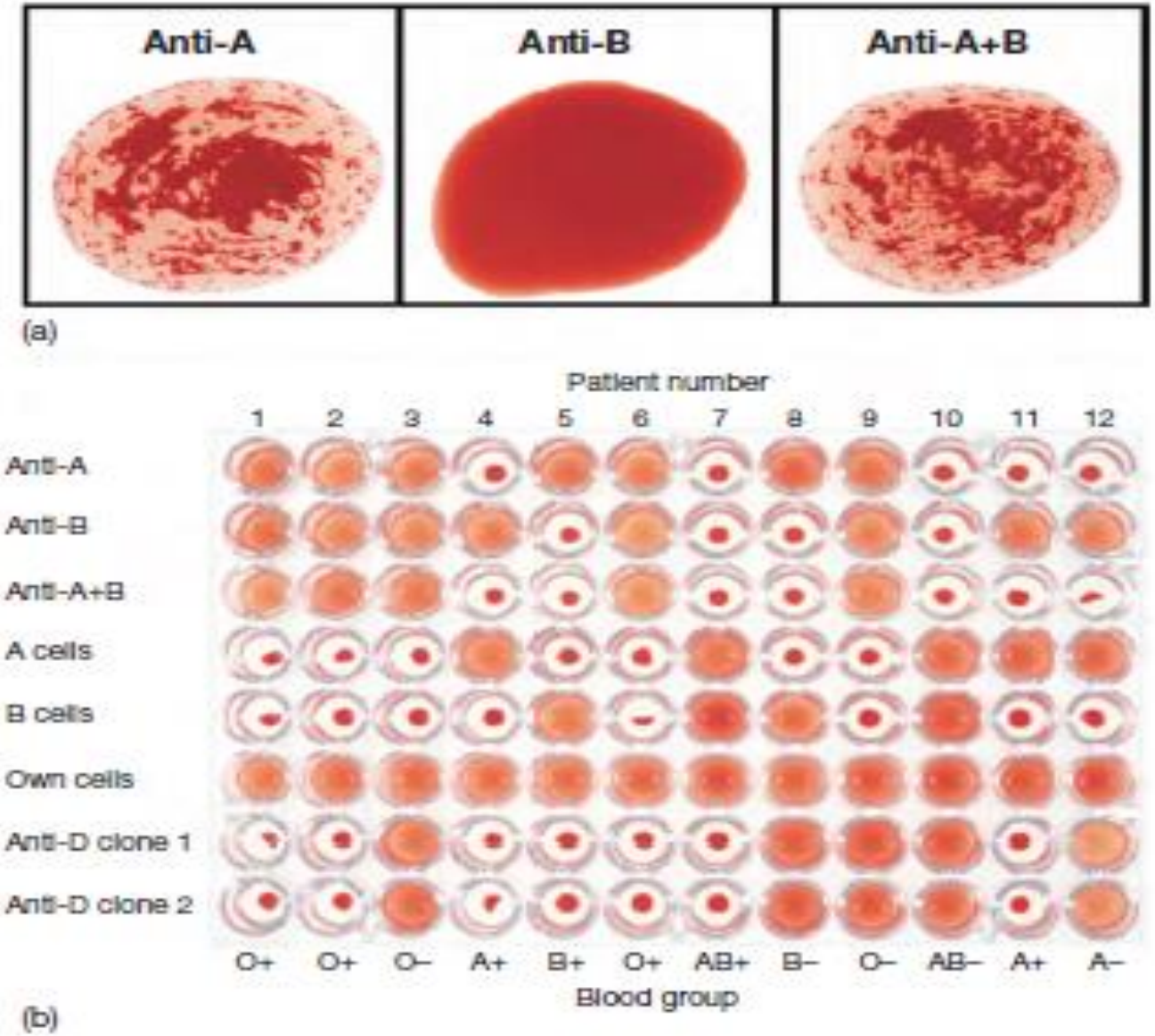


Figure 30.3 **(a)** The ABO grouping in a group A patient. The red cells suspended in saline agglutinate in the presence of anti-A or anti-A + B (serum from a group O patient). **(b)** Routine grouping in a 96-well microplate. Positive reactions show as sharp agglutinates; in negative reactions the cells 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.

Table 15.1 Appropriate blood groups for transfusion.

Recipient blood group	Donor red cells	Donor plasma
A	A or O	A or AB
AB	A, B or O	AB only
B	B or O	B or AB
O	O only	A, B or O

Note: This table does not take account of other blood group antigens, and assumes that high-titre/atypical antibodies have been excluded from the donor unit.

Rh system

- The Rh system is also of great importance and can cause problems with both transfusion and pregnancy. The inheritance of the Rh blood group system is slightly more complex than that of the ABO system.
- Two separate genetic loci on chromosome 1 encode for a total of five antigens.
- The first locus, *RHD*, has alleles D or d; D encodes a transmembrane protein featuring the D antigen, while the allele d encodes a variant that does not bear this antigen.
- *RHCE* is an adjacent locus that encodes a transmembrane ion channel bearing the antigens C (or its variant, c) and E (or its variant, e). Alleles at this locus may be described as CE, Ce, cE and ce, denoting the set of antigens they encode.
- A complete description of the Rh haplotype for a patient will include alleles at both *RHD* and RHCE loci. The commonest haplotypes are DCe, dce and DcE.

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- The D antigen is the most clinically important of the Rh group antigens, due to its high immunogenicity.
- An RhD-negative person (e.g. dce/dce) has over a 50% chance of developing anti-D antibodies after the transfusion of one unit of RhD-positive blood: it is therefore important that RhD-negative patients receive RhD-negative blood.

- Note that unlike the ABO system, Rh antibodies are not naturally occurring; they must be raised by exposure of an antigen-negative individual to the appropriate antigen, either through transfusion of incompatible blood or through pregnancy.
- After the exposure, IgG antibodies come to predominate, and hemolysis is generally extravascular (**major cause of HDFN/HDN**).

Management of mother and child

- Women who are negative for RhD are given routine antenatal anti-D prophylaxis at 28 weeks, 34 weeks and within 72 hours of delivery.

- This involves an intramuscular injection of anti-D immunoglobulin, which prevents active immunization in the case of red cell transfer across the placenta.

- Any potentially sensitizing event is also treated with additional anti-D administration: such events include abdominal trauma, threatened abortion, or any spontaneous abortion after 12 weeks.

Other blood group systems

- Other blood group antibodies, which are sometimes a problem during blood transfusion, include the following:
  - anti-K (Kell system),
  - anti-Fy^a (Duffy system),
  - anti-Jk^a (Kidd system) and
  - anti-S (part of the MNSs blood group system).
- These antigens are relatively poorly immunogenic.
- Their potency in stimulating antibody production is 10-1000 times less than that of RhD.
- Consequently, these antigens may not need be routinely assessed prior to transfusion.

Compatibility

- The purpose of **cross-matching** blood before transfusion is to ensure that there is no antibody present in the recipient's plasma that will react with any antigen on the donor's cells (major cross-match, IAT).

- The basic technique for detecting such antibodies relies on their ability to agglutinate red cells that bear the appropriate antigen.

Antiglobulin test

- Its purpose is to detect antibodies to red cell surface, either bound to the red cell surface or free in the serum.

- The antiglobulin test can be used in two ways:

  - First, the ***direct antiglobulin test (DAT)***, used in the diagnosis of autoimmune hemolytic anemia. it can be used to detect antibody already on the patient's cells *in vivo*. Red cells are washed to remove the free IgG in the plasma, which would otherwise react with and neutralize the antiglobulin. After washing, anti-human globin is added and, if the red cells are coated with antibody, agglutination takes place.

cont'd…

- Second, *the* ***indirect antiglobulin test (IAT)***, the test can be used to detect the presence of antibody in serum, as in the cross-matching of blood for transfusion. In this case, serum from the patient who requires transfusion is incubated with donor red cells. Any antibody present in the recipient's serum that has specificity for antigens on the donor's cells will interact with those cells. After washing, addition of anti-human globulin will bring about red cell agglutination.

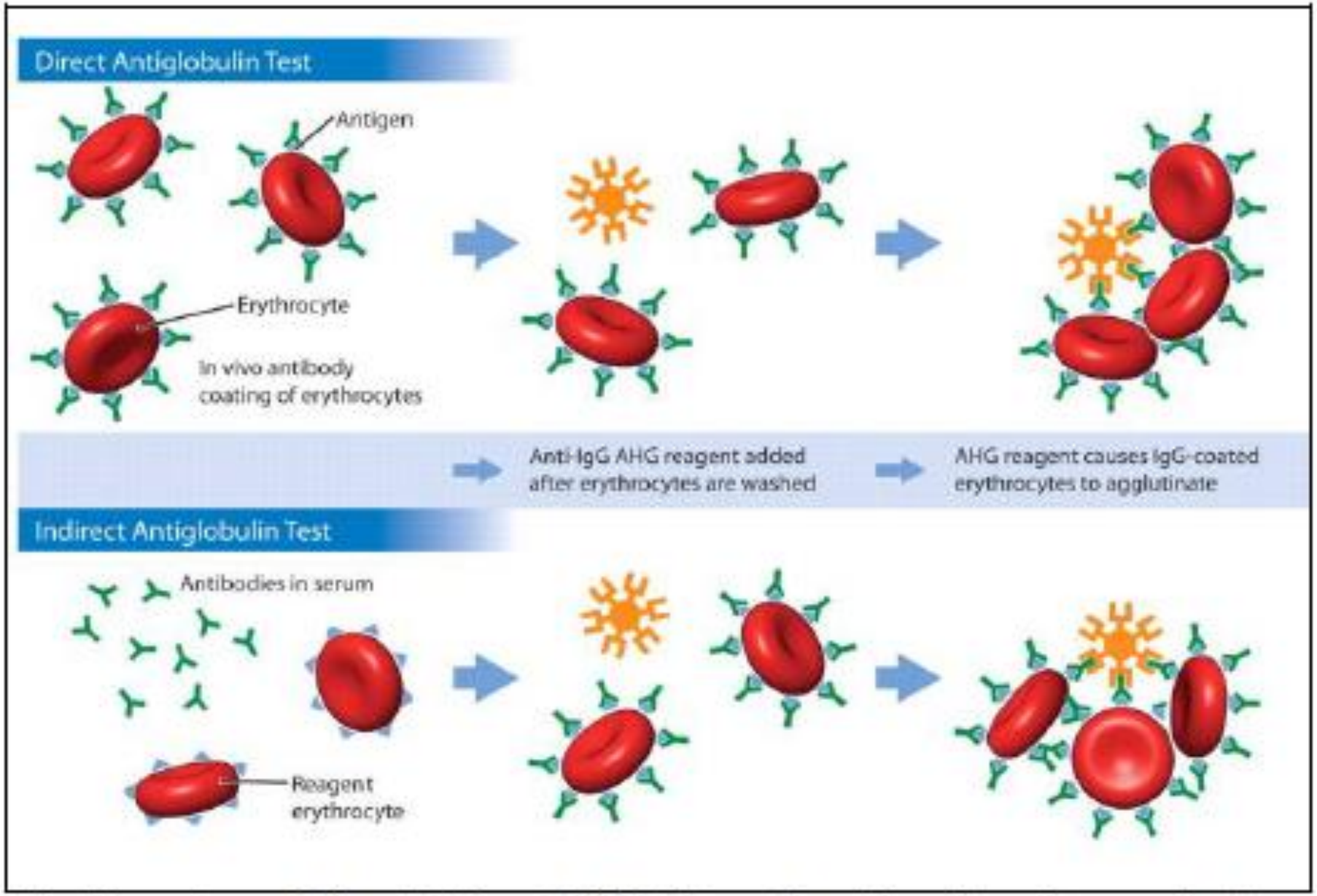

Image credit: Zarandona JM and Yazer MH. The role of the Coombs test in the evaluation of hemolysis in adults. Canadian Medical Association Journal 2006;174:305-307

Hazards of blood transfusion:

the Serious Hazards of Transfusion (SHOT) Committee, between 1996 and 2010.

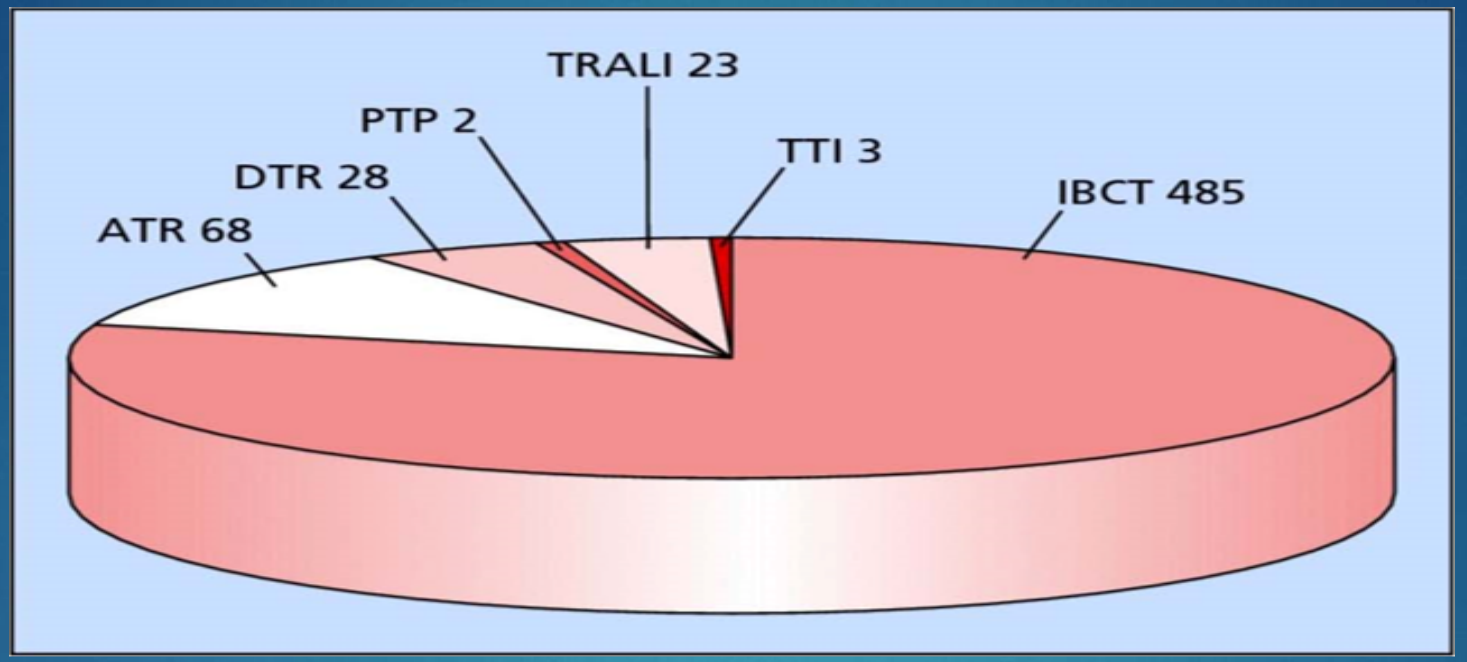

Figure 15.1 **Pie chart showing hazards of transfusion in the UK from 1996-2010 as reported to the SHOT Committee. *Notes:* TRALI - transfusion-associated acute lung injury; TTI - transfusion-transmitted infection; ATR - acute transfusion reaction; DTR - delayed transfusion reaction; PTP - post-transfusion purpura; IBCT - incorrect blood component transfused**

Source: UK SHOT Committee report 2010.

Table 30.6 Measures to protect recipient.
Donor selection (see Table 30.1)
Donor deferral/exclusion (see Table 30.1)
Stringent arm cleaning
Microbiological testing of donations (Table 30.2)
Immunohaematological testing of donations
Discarding the first 20–30 mL of blood collected
Leucodepletion of cellular products
Post-collection viral inactivation of FFP
Monitoring and testing for bacterial contamination
Pathogen inactivation of cellular components
Safest possible sources of donor for plasma products

FFP, fresh frozen plasma.

Early

Citrate toxicity
Hyperkalaemia
Hypocalcaemia(infants, massive transfusion)
Clotting abnormalities (after massive transfusion)
Transfusion-related acute lung injury (TRALI)
Post-transfusion purpura
Anaphylaxis (in IgA deficient subjects)

Table 30.9 Complications of blood transfusion.

Early	Late
Haemolytic reactions: immediate (IgM) or delayed (IgG)	Transmission of infection (see Table 30.7)
Reactions caused by infected blood	Transfusional iron overload (see Chapter 4)
Allergic reactions to white cells, platelets or proteins	Immune sensitization, e.g. to red cells, platelets or Rh D antigen
Pyrogenic reactions (to plasma proteins or caused by HLA antibodies)	Transfusion-associated graft-versus-host disease
Circulatory overload	
Bacterial contamination	
Air embolism	
Thrombophlebitis	

Solution: irradiation

Important Slide

Management of Transfusion Reactions

- The **first action is always to stop the transfusion** and clarify that the correct patient's details are on the component being transfused.
- Any suspicion of ABO incompatibility should lead to the institution of circulatory support with IV fluids, careful monitoring of pulse, blood pressure and urine output, and supportive management of any developing DIC.

- The component bag should be returned to the transfusion laboratory with a fresh cross-match sample from the patient.
- Samples should also be sent to assess for intravascular hemolysis - including a full blood count, serum haptoglobin, and hemoglobinuria.
- It is important to ensure that the possibility of bacterially contaminated units has been addressed through taking blood cultures.

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- If necessary, broad-spectrum antibiotics may be commenced empirically after cultures have been drawn.
- Severe allergic reaction should be treated initially by stopping the transfusion and returning the unit to the laboratory.

- Chlorpheniramine may help, but severe reactions are likely to require oxygen and nebulized salbutamol, plus intramuscular adrenaline in the case of circulatory collapse.
- With mild fevers only, simple interventions may suffice (e.g. giving an antipyretic and slowing the transfusion); similarly, if a mild allergic reaction is evident (e.g. urticaria), chlorpheniramine followed by a slower reinstatement of the transfusion may help.

- Appropriate investigations include a full blood count, a direct antiglobulin test, serum bilirubin and assessment of renal function.

Massive transfusion

- Patients with acute hemorrhage (i.e. loss of red cells and plasma) may need to be transfused with large quantities of packed red cells.
- Massive transfusion has been defined as the replacement of one blood volume over 24 hours, or as the replacement of 50% of circulating volume in 3 hours.

- With the transfusion of many units of packed red cells, the patient may become deficient in key plasma components such as clotting factors and may also become thrombocytopenic (even in the absence of DIC).

- The administration of one unit of FFP per unit of red cells may be effective in replacing clotting factors. Fibrinogen and platelets should also be replaced, with 2 pools of cryoprecipitate and 1 adult dose of platelets per 6-8 units of packed red cells.

Always Quality First;

Contents

Conclusion:

- The main goal of blood bank services is to provide a safe blood component in timely and cost-effectiveness manners.
- Different key dedicated areas in the blood bank serve in harmony to achieve the main goal.
- Always, there is a risk in transfusion. All implemented standards goal to minimize the risk.
- **Always, maintain the quality!**

Example MCQs

- **Q1) Which one of the following services is under the transfusion/cross-match services of the blood bank?**
  - A) Collection of whole blood unit.
  - B) Reconfirmation of donor blood group.
  - C) Component separation.
  - D) Infectious agents testing.

Example MCQs

- **Q2) Which one of the following potential complications of the blood transfusion is an acute/early complication?**
  - A) TRALI.
  - B) GvHD.
  - C) Allo-antibodies/immue sensitization.
  - D) Iron overload.

Example MCQs

- **Q3) Which one of the following step is critical for reducing the frequency of GvHD?**
  - A) Washing the transfused unit.
  - B) Stop the transfusion when you suspect a chronic GvHD.
  - C) Irradiation prior to transfusion.
  - D) Transfuse only fresh unit (<7 days).

Example MCQs

- **Q4) Which ONE of the following statements is TRUE about the indirect antiglobulin test?**
  - A) It may detect complement on the surface of red cells.
  - B) It is positive in hemolytic disease of the newborn because of Rh incompatibility.
  - C) It detects agglutination of antibody-coated red cells.
  - D) It is used for cross-matching recipient and donor blood.

Example MCQs

- **Q5) Which ONE of these infectious agents is usually identified by high risk behavior and NOT routinely tested for in blood products?**
  - A) Hepatitis C antibody.
  - B) Hepatitis B.
  - C) Gonorrhoea.
  - D) HIV.

Thank You!!!