

2- Blood transfusion = Haematology 435 =

إن أحسنا فمن الله عزوجل, وإن أخطأنا فمن أنفسنا والشيطان.
نظراً لشمولية العمل لمحاضرات الطلاب والطالبات بإمكانكم اعتماده كمصدر للمذاكرة

Objectives:

- To understand the inheritance and significance of the ABO system
- To understand the nature and significance of the Rh blood group system including RhD
- To know the principles involved in the selection of donor blood of suitable ABO and Rh groups for a recipient, and the principles of the cross-match, including the antiglobulin test
- To understand the hazards of blood transfusion
- To know how to investigate a patient suspected of receiving an incompatible transfusion
- To know the basis of blood fractionation and the rationale for the use of specific blood products
- To know the pathogenesis, clinical features and the principles underlying the treatment and prevention of haemolytic disease of the newborn (HDN) due to anti-D.

Color Codes:

- **Pink:** Girls' notes. **Blue:** Boys' notes. **Red:** Important Notes. Gray: Extra notes.
- **Purple:** Lecture notes & Pathoma notes.

References:

- Girls&Boys Doctors Slides and Notes.
- Lecture notes pathology (chapter 12)
- Pathoma (chapter 5)
- Team 434 & 433.

Revised by
خولة العماري & هشام الغفيلي

➤ **Correction File:** [\(HERE\)](#)

terms	The donors	
1-Voluntary donors	Outdoor donors	
	Hospital staff	
	Recruitment campaigns	
2-Involuntary donors	1-Relatives of patients admitted to hospital for elective surgery and normal deliveries. 2-relatives of pts who receive emergency blood transfusion	
	Person applying for driving licenses	
3-Autologous donations	<p>Patients for elective surgery can donate 4 units in one month before surgery (<u>one unit/week</u>)</p> <p>(this can be obtained by either 2 methods of combination of both methods)</p>	<p>Acute normovolaemic haemodilution: 2-3 units of blood can be obtained from the pt immediately <u>before surgery</u> (before anaesthesia) (target haematocrit 25-30-%)</p>
		<p>Salvage: heavy blood lost <u>during surgery</u> is collected with special blood salvage devices.</p>
4-Direct blood donations خلال العملية	From close relative of patient of their <u>requests</u> .	

-Volunteer donors provide nearly all blood used for transfusion in KSA

ناخذ منهم كل مكونات الدم زي RBC WBC platelets بس في ناس يتبرعوا بشي واحد بس.

-The donors body replenishes the fluid lost from donation in 24 hrs.

-The RBC's may take up to 2 months (8weeks)(56days) to replace the RBC's lost from donation (when donating **ONE** unit only)

And it takes up to 16 weeks when donating **TWO** units in a process called "red cells apheresis". (means you can donate one unit every 2 months and 2 units every 16 weeks)

-the whole blood can be donated once every 8 weeks (56 days)

❖ What is Apheresis?



Definition: Apheresis, an increasingly common procedure, is the process of removing a specific component of the blood, such as platelets, and returning the remaining components, such as red blood cells and plasma, to the donor.

Is performed to collect red blood cells, plasma (liquid part of the blood), and granulocytes (white blood cells).

Benefits: This process allows more of one particular part of the blood to be collected than could be separated from a unit of whole blood.

Durations: The apheresis donation procedure takes **longer** than that for whole blood donation.

A whole blood donation takes about **10 to 20 minutes** to collect the blood, while an apheresis donation may take about **one to two hours**.

❖ What are the criteria for accepting blood donation?

Healthy person and at least <u>16 years</u> of age (You must be at least 17 years old to donate to the general blood supply, or 16 years old with parental/guardian consent)	Must weight at least <u>110 pounds (50kg)</u> (You should know the weight in pounds and kg)
Donors must pass the physical and healthy history examination before donation.	Most blood banks have no upper age limit. (but its knows to be up to 70 years old)

What are the criteria for accepting blood donation?

❖ Who should not donate blood?

Who should not donate blood?

Donors temporary deferral

Active disease under treatment	Cold, flu, syphilis, infections, curable disease of heart, lungs, kidneys, liver and GIT. Who's on treatment with antibiotics.
For 3 years	-immigrant coming from malarial endemic area . -one who had diagnosis of malaria .
For one year	-Hepatitis B vaccine , Rabies vaccine , history of close contact with viral hepatitis pts. - Tattoo pts. -Contact with persons with high risk of AIDS .
For 2 months	- <u>Recent blood donation</u>
For six weeks	-Following delivery
For 1 month	- Rubella vaccination (German measles)

People cannot donate permanently

Any one who has:

Ever used **IV drugs (illegal)**

Men who have has sexual contact with other men

Ever received clotting factor concentrates

Positive test for **HIV (AIDS virus)**

Men and women who have sex for money

Hepatitis since his or her **ELEVENTH BIRTHDAY**

Had **babesiosis of changs diease**

Had **Zika virus infection**

Had **West Nile virus infection**.

Had any of the other **NEW VIRUSES** infection

EVER TAKEN Tegison for psoriasis.

Risk factor for **Crueutzfeldt-jakob disease (CJD)** or had an immediate family member with **vCJD**.

Spent 3 months or more in UK from 1980 through 1996 (applied in USA)

Spent 5 years in Europe from 1980 to the present (applied in USA)

EVER taken any of these medications, (check the medications list in the previous slide) *(Kindly check the medications list in the next slide)*

If the donor now taking or if he has EVER taking any on these medications:

-Some medications of **prostate gland enlargement**: Proscar (finasteride)
Avodart (dutasteride)

-Some medications for **baldness**: Propecia (finasteride)

-Some medications for **severe acne**: Accutane (amnesteem, claravis, sotert, isoteretinoin)

-Some medications for **severe prosriasis**: Tegison (**eterinate**)
Soriatane (acitretin)

-**Growth hormone** from human pituitary glands (used for delayed impaired growth)

-Medications that treat **diabetes**: insulin from Cows (bovine or beef, insulin)

-**Hepatitis B immunoglobulin** (given following to an exposure of **hepatitis B**)

NOTE: (this is different from hepatitis B vaccine which is a series of 3 injections given over a 6 months period to prevent future infection from exposures to hepatitis B)

-**unlicensed vaccine.**

Types of anticoagulants

types	Contains	Store RBCs for	Store platelets for	notes
ACD-A (NIH-A) solution <i>(not used anymore)</i>	Trisodium citrate Citric acid Dextrose water	21 days at 1-6 OC	-	67.5 ml of this solution (pH 5.0 – 5.1) are mixed with 450 ml of blood.
Citrate-phosphate dextrose (CPD)	The same of ACD-A but with <u>PHOSPHATE and water.</u>	28 days at 1-6 OC	3 days at 20-24 OC	63 ml of this solution (pH 5.0 – 5.1) are mixed with 450 ml of Blood
Anticoagulant citrate phosphate dextrose (CPDA-1)	The same of CPD but with <u>adenine</u>	35 days	<u>5 days</u>	63ml Anticoagulant Citrate Phosphate Dextrose Adenine Solution USP for collection of 450ml of blood
Optisol AS-5 (red cell preservation solution)	The same but With <u>mannitol</u>	42 days	-	<u>Caution:</u> Add Optisol solution to Red Blood Cells within 72 hours after Blood Collection.
Anticoagulant citrate phosphate dextrose (CPDA-2)+ Optisol for RBC <i>أحسن واحد</i>	All of the above	42 days	5 days	63ml Anticoagulant Citrate Phosphate Dextrose Solution USP for collection of 450ml of blood

❖ Blood Groups:

We have many blood groups but the most important ones are ABO system and Rh system (rare blood grouping include: Hh, MNS, Kell, Kidd, Duffy, Diego)

1-ABO system:

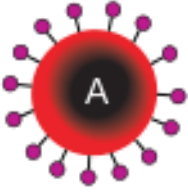
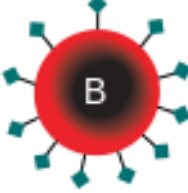
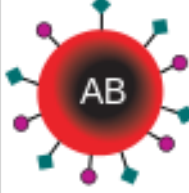







-Practically **all red cells have H antigen** (a carbohydrate group attached mainly to proteins on the cell membrane) **This antigen is the basis for the ABO blood groups.**

-The ABO locus is encoded on **chromosome 9q**, where one of these possible alleles may be found:

Allele A	H antigen + N-acetylgalactosamine = A antigen	By encoding for a glycosyltransferase .
Allele B	H antigen + galactose = B antigen	By encoding an alternative glycosyltransferase .
Allele O	The H antigen remains unmodified	Encode no functional enzyme at all.

6 Possible genotypes						4 Possible phenotypes			
AA	AO	BB	BO	AB	OO	A	AB	B	O

-Haemolytic 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

Blood groups

2-other blood group systems: (just read it)

-Other blood group antibodies, which are sometimes a problem during blood transfusion, include the following: **anti-K (Kell system)**, **anti-Fya (Duffy system)**, **anti-Jka (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 need not be routinely assessed prior to transfusion. Unless for patients who require multiple transfusion.

Blood types distribution

O+ Most common	O-	A+	A-	B+	B-	AB+	AB- Lest common
38%	7%	34%	6%	9%	2%	3%	1%

❖ ABO Blood Groups Inheritance:

ABO Genotype in the offspring		ABO alleles inherited from the Mother		
		<u>A</u>	<u>B</u>	<u>O</u>
ABO alleles inherited from the Father	<u>A</u>	A	AB	A
	<u>B</u>	AB	B	B
	<u>O</u>	A	B	O

❖ Blood Transfusion:

Blood compatibility testing (CROSSMATCH) "IMPORTANT"

<u>F</u> ront type	<u>B</u> ack type
Determines which antigens ("Flags") in the ABO blood group system are on the patient's Red Blood Cells as follows:	identifies the iso haemagglutinin (Naturally Occurring AntiBody) in the patient's serum and should correspond to the antigens found on the Red Blood Cells as follows:
B antigen only >> type B A and B antigens >> type AB Neither A or B >> type O	Anti-A >> type B Anti-B and anti-A >> type O Neither anti-A or Anti-B >> type AB

In addition, RBCs are Rh typed and identified as "D" positive or negative.

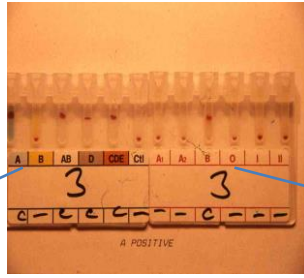
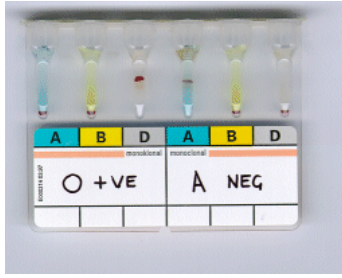
❖ If an Acute Transfusion Reaction occurs:

- 1-**Stop** blood component transfusion **immediately**.
- 2-**Verify** the correct unit was given to the correct patient.
- 3-**Maintain IV** access and ensure adequate urine output with an appropriate crystalloid or colloid solution.
- 4-**Maintain blood pressure, pulse.**
- 5-**Maintain adequate ventilation.**
- 6-Notify attending **physician** and **blood bank**.
- 7-**Obtain blood/urine** for transfusion reaction workup.
- 8-**Send blood bag** and administration set to blood transfusion service immediately

Blood bank performs workup of suspected transfusion reaction as follows:

- A. Check paper work to ensure correct blood component was transfused to the right patient.
- B. Evaluate plasma for hemoglobinemia.
- C. Perform direct antiglobulin test.
- D. Repeat other serologic testing as needed (ABO, Rh).

❖ BBC Gel cards:



antigens

antibodies

لازم نعرف كيف نقرأ الصور، إذا كان الخط مرتفع، إبدأ +، والعكس صحيح إذا كان منخفض. لو أخذنا الصورة اللي على اليمين كمثال، نلاقي إن الخط ارتفع عند A، ونلاقي ارتفع كمان عن D، إذا بلس وليس ماينس. بالتالي يكون الجواب: **A+**.

The specific tests performed on donated blood are listed

below: لما يجي شخص يتبرع بالدم يسون كل هذي الأشياء لدمه

- Hepatitis B surface antigen (**HBsAg**).
- Hepatitis B core antibody (**anti-HBc**)
- Hepatitis C virus antibody (**anti-HCV**).
- HIV-1 and HIV-2 antibody (**anti-HIV-1 and anti-HIV-2**).
- HTLV-1 and HTLV-II antibody (**anti-HTLV-I and anti-HTLV-II**).
- Serologic test** for syphilis, VDRL(**V**enereal **D**isease **R**esearch **L**aboratory), RPR(**R**apid **P**lasma **R**egain), TPHA (**T**reponema**P**allidum **H**aem**A**gglutination)
- N-ucleic acid amplification testing (**NAT**) for HIV-1 and HCV.
- NAT for WNV. (West Nile virus)
- G6PD**(Glucose-6-phosphate dehydrogenase) **test**.
- Sickle cell test**.

• Mandatory Tests on All Units of Blood:

1-ABO group and Rh Type	2-Screening for blood-group antibodies	3-Serologic test for syphilis	4-Serologic tests for human retroviruses	5-Serologic test for hepatitis
			<ul style="list-style-type: none"> - HIV-1 antibody, - HIV-2 antibody, - HIV p24 antigen, - HTLV I antibodies 	<ul style="list-style-type: none"> - Hepatitis B core antibody (HBcAb), - Hepatitis B surface antigen (HBsAg), - Hepatitis C antibody

❖ Compatibility Testing & Cross-Matching Laboratory Tests:

This test must be completed before transfusing blood or any of its products.

• The purpose of these tests include:

1. Determining the blood type with a crossmatch (**between patients serum and donor red cells**)
2. **Indirect Coomb's test***: Antibody screening on patients sera
3. **Direct Coomb's test***: done on donor's red cells and patients red cells
4. Screening for antibodies that may produce adverse effects if transfused
5. Screening for possible infectious agents that could be transmitted with transfusion

*For more information on Coomb's test ([Click Here](#)) ← it's a really simple one ^^

• Antiglobulin Test:

Its purpose is to detect antibodies to red cell surface constituents, either bound to the red cell surface or free in the serum. This test can be used to detect the antibodies in two ways:

<u>Antibodies already on the Patient's Cells in Vivo*</u>	<u>Antibodies in Serum (in the cross-matching of blood for transfusion)</u>
<p>1. First, red cells are washed to remove the free IgG in the plasma <i>Why? Because it will react with and neutralize the antiglobulin.</i></p> <p>2. After washing, anti-human globulin is added. <i>If the red cells are coated with the antibody, agglutination** takes place.</i></p> <p>This is the DIRECT antiglobulin test, which is used in the diagnosis of autoimmune haemolytic anaemia.</p>	<p>1. The serum of the patient who is in need of transfusion is incubated with the donor's red cells</p> <p>2. If the patient's serum has any antibodies that has a specificity for the antigens on the donor's cells, it will interact with them</p> <p>3. It will be washed, and after washing, anti-human globulin is added and will cause red cell agglutination.</p> <p>This is the INDIRECT antiglobulin test.</p>

*In Vivo: performed or taking place in a living organism.

**تكتل Clumping of particles.

Type and Cross Matching test: (A very important test):

This test determines the compatibility between patient serum and donor red blood cells.

- A full cross-match procedure takes about **45 minutes** to complete, and should not be shortened.
- **Units are refrigerated** until used.
- A unit of blood **MUST** be properly labeled and the label **MUST** be checked before use.
- Every unit cross matched is removed from the general inventory and reserved for the patient in need for **72 hours**.
- Units which are cross-matched unnecessarily will deplete Blood Bank inventories and can result in blood shortages, which can result in cancellation of elective surgical procedures.
- Blood will **NOT** be released for transfusion until compatibility testing is complete.

HOWEVER, during an **emergency**, blood products may be released without a cross-match (*if the patient is in danger of dying if transfusion is delayed*).

-In this case, if the patient's blood type is **UNKNOWN**, group **O Rh negative (O-)** blood can be released even **WITHOUT** compatibility testing.

-If the patient's blood type is **KNOWN**, then **type-specific blood** (RBCs of the same ABO and Rh group may be released)

زبدة الكلام: تخيلوا أحد راح يتبرع بالدم، وكان كل شيء عنده تمام وخالص الدكتور سحب منه وقال له الله يعطيك العافية. راح الدكتور يحط على الدم المسحوب بطاقة إبتو نوعه كذا وكذا ودخلها بالثلاجة. اليوم الثاني جاء مريض يحتاج نقل للدم. الدكتور راح لماكن حفظ الدماء وأخذ من الثلاجة نفس نوع دم المريض وعمل له اختبار التلاؤم اللي ياخذ ٤٥ دقيقة. نتيجة الاختبار إن دم المتبرع يتلاءم مع دم المريض، فقام المسؤول حجزها تحت اسم المريض لمدة ٧٢ ساعة، وإذا ما احتاجها (مثلا كان بعملية ونجحت بدون ما ينزف)، ترجع حقيبة الدم للثلاجة. ولكن، إذا كثرت الحجز وقلت الدم الموجود بالثلاجات، بيصير فيه نقص وأي عملية جراحية "اختيارية" تحتاج للدم راح تنلغي. أما بالحالات الطارئة: على طول ينقلون الدم من الثلاجة للمريض بدون اختبار التلاؤم، ويصير **(O-)** إذا كان دم المريض **مجهول**، أو يصير نفس نوع دم المريض إذا كان معروف. وفي كلتا الحالتين ما يسوون اختبار تلاؤم (Emergency situation)

❖ So, What is Compatibility?

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

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

اللي هي نفس فكرة الـ Anti-globulin test، إذا الدم ما تكتل (يعني ما تفاعل) يصير دم المتلقي والمناح للدم متلائمين

❖ Haemolytic Disease of the Newborn:

Haemolytic disease of the newborn (HDN): is a major example of the clinical significance of blood groups.

Causes: It arises as a consequence of fetus and mother having different blood group antigens.

How?

- Following the passage of fetal red cells across the placenta, there is immunization of the mother to fetal blood group antigens that she does not possess.
- The IgG antibodies produced are subsequently transferred back across the placenta, and react with the fetal red cells causing their destruction.

antigens IgG Antibodies انتقل دم الجنين عبر المشيمة إلى داخل الأم، نتيجة لذلك، الأم تسوي حق الجنين لأنه يعتبر "جسم غير معروف" مما يؤدي إلى تدمير خلايا الجنين. عشان نتجنب هذه الجنين بحيث إذا antigens الكارثة: نعطي الأم حقن بعد الولادة تمنع الجسم من صناعة مضادات لـ حملت مرة ثانية، ما يصير لها نفس المشكلة

❖ Introduction of treatment by exchange transfusion:



- Approximately **60%** of affected infants require an exchange transfusion.
- **(Prophylactic anti-D immunoglobulin injections)** were routinely introduced for RhD negative mothers in the hours immediately following labour, to prevent active immunization due to fetal RhD exposure.

HOW IS BLOOD STORED AND USED?

Each unit of whole blood normally separated into several components

Component	STORAGE DAYS	USES	NOTES
RBC	Stored under <u>refrigeration</u> for a maximum of <u>42 days</u> .	1-carry oxygen 2-to treat anemia.	Can be frozen for up to <u>10 years</u> .
Platelets	At room temperature with continuous agitation for <u>5 days</u> maximum	1-control bleeding 2-for patient with leukemia and other form of cancer	-
Plasma	Kept in a frozen state (<u>-70°C</u>) For usually up to a <u>one year</u>	1-control bleeding due to low level of some clotting factors.	-
Cryoprecipitate ** AHF (antihemophilic factor)	Stored frozen for up to <u>one year</u>	1-contain few clotting factors.	Made of fresh frozen plasma.
Granulocytes	Must be transfused within <u>24 hrs</u> of donation	to fight infection	Their efficacy is <u>NOT</u> well established
Others: 1-albumin. 2-Ig. 3-specific Ig. 4-clotting factors.	-	-	Commercial manufactures commonly produce these blood products

**an extract rich in a blood-clotting factor obtained as a residue when frozen blood plasma is thawed

❖ Complications of blood transfusion:

Immediate transfusion reactions	Delayed transfusion reactions
<ul style="list-style-type: none">➤ Hemolytic reactions➤ Allergic reactions➤ Febrile reactions➤ Transfusion related acute lung injury (TRALI)➤ Bacterial contamination➤ Circulatory overload citrate toxicity➤ Air embolism➤ Alloimmunization*:<ul style="list-style-type: none">-RBCs.-Platelets.	<ul style="list-style-type: none">➤ Graft versus host disease (GVHD)➤ Transfusion associated graft versus host disease (TAGVHD)➤ Post-transfusion purpura➤ Haemosiderosis➤ H.D.N (Hemolytic Disease of Newborn) <p><u>Transmitted diseases:</u></p> <ul style="list-style-type: none">• Hepatitis B and C• HIV• Cytomegalovirus (CMV)• HTLV-1 (human T-lymphotrophic virus)• kaposi's sarcoma and human herpes virus-8 (KS and HHV-8)• Malaria• Leishmaniasis <p><u>Others:</u></p> <ul style="list-style-type: none">• Babesiosis• Lyme disease• Chagas disease• CJD• Toxoplasmosis

***Alloimmunization** is defined as an immune response to foreign antigens after exposure to genetically different cells or tissues. Although **alloimmunization** is a natural event during pregnancy, frequently it is the undesirable outcome of a blood transfusion and/or transplant

❖ Massive Transfusion:

- **What is massive transfusion:** the replacement of one blood volume over **24 hours**, or as the replacement of **50%** of circulating volume in **3 hours**.
- **When to use it:** Patients with **acute hemorrhage** (i.e. loss of red cells and plasma) may need to be transfused with large quantities of packed red cells.
- **Complications:** 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 (Disseminated intravascular coagulation)).

Solution:

- 1- The administration of one unit of **FFP** (Fresh Frozen Plasma) per unit of red cells may be effective in replacing clotting factors.
- 2- **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.

❖ Signs and symptoms of Blood Loss “Not That Important”:

mL	%	Clinical Signs
500	10	-Vasovagal syncope in blood donors.
1000	20	-At Rest: No clinical evidence -Excise: Drop BP & tachycardia.
1500	30	-Neck veins flat when supine; postural hypotension.
2000	40	-At rest: air hunger, cold clammy skin, tachycardia.
2500	50	Signs of shock, tachycardia, hypotension, oliguria, drowsiness, or coma.

❖ Investigation of a Haemolytic Transfusion Reaction:

Only for you as a Doctor! Read it.

- Evidence of **Haemolysis**.
- Examine patient's plasma and urine for haemoglobin and its derivatives.
- Blood film may show **Spherocytosis**.
- Evidence of bacterial infection of donor blood
- Gram stain and culture donor blood.

➤ Evidence of incompatibility:

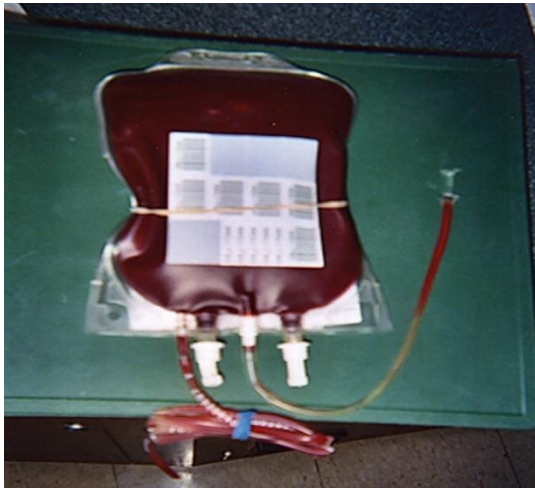
-Clerical checks: An identification error will indicate the type incompatibility.

-If no evidence of clerical error, proceed as follows:

(Repeat ABO and Rh D groups of , Use patient's pre-and post-transfusion samples, Repeat compatibility tests, using patient's pre-and post transfusion serum, Direct antiglobulin test)

❖ If intravascular hemolytic reaction is confirmed:

1. Monitor renal status (BUN, creatinine).
2. Initiate a diuresis.
3. Analyze urine for hemoglobinuria.
4. Monitor coagulation status (prothrombin time, partial thromboplastin time, fibrinogen, platelet count).
5. Monitor for signs of haemolysis (lactate dehydrogenase, bilirubin, haptoglobin, plasma hemoglobin).
- 6.. Repeat compatibility testing (crossmatch).
7. If sepsis is suspected, culture unit and patient, and treat as appropriate



Packed red cells may contain enough leukocytes and platelets to result in alloimmunization.



Platelet blood components may be stored for 5 days at room temperature without loss of function or viability

➤ Check your Understanding!
[\(HERE\)](#)



= Haematology 435 =

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