**HAEMATOLOGY 3  
BLOOD TRANSFUSION, DONOR SELECTION, TESTING OF DONATIONS AND PRE-TRANSFUSION TESTING**

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**Objectives**

* To be able to describe the major significant blood groups and their importance clinically
* To be able to describe the screening of blood donors undertaken and reasons why
* To be able to describe the various blood components used and the potential side effects of blood transfusion

# TESTING PATIENT SAMPLES

Blood Group Systems

1. **The ABO system:** is important because people have naturally occurring antibodies that are IgM, reactive at 37ºC and capable of activating complement. They are, therefore, able to cause potentially fatal haemolysis if incompatible blood is transfused.

|  |  |  |  |
| --- | --- | --- | --- |
| **Frequency in population (UK)** | **Blood group** | **Antigens** | **Antibodies** |
| 46% | O | nil | anti-A and anti-B |
| 43% | A | A | anti-B |
| 8% | B | B | anti-A |
| 3% | AB | A and B | nil |

**Genes:** O, A, B - O is *'recessive'* to others

**e.g.** Group O = OO Group A = AO or AA  
Group AB = AB Group B = BO or BB

1. **The** **Rh system:** the most important antigen is D

D positive = RhD positive = Rh positive

D negative = RhD negative = Rh negative

|  |  |  |  |
| --- | --- | --- | --- |
| **Frequency in population (UK)** | **Blood group** | **Antigens** | **Antibodies** |
| 85% | RhD positive | D | - |
| 15% | RhD negative | nil | after exposure to RhD pos blood from transfusion or fetus, patient can make anti-D |

**Genes:** D is dominant

*d* is recessive (no actual antigen)

**e.g.** Group RhD neg = dd  
Group RhD pos = DD or Dd

1. **Other red cell antigens:**

It is impossible to provide *'identical'* or fully matched red cells for transfusion. In practice, only two blood group systems are taken into account - ABO and RhD.

In order to provide ABO and Rh compatible blood, it is necessary to test the blood groups (or *'group'*) the recipient. An antibody screen should be performed at the same time as grouping, on the plasma of all patients due to be transfused (*'group & screen'*).

It is relatively common for a D-negative woman to become sensitised through exposure to fetal D pos red cells during pregnancy, as her partner is likely to be D-positive (fetomaternal leakage of red cells across the placenta occurs commonly at the time of delivery, but also silent bleeds are not uncommon and may occur during late pregnancy). If an RhD-negative woman develops anti-D antibodies, then in the next pregnancy, the IgG antibodies can cross the placenta and destroy fetal red cells - causing hydrops fetalis or haemolytic disease of the new-born (hdn). It is therefore important **not** to sensitise RhD negative girls or women of child bearing age, by transfusing RhD positive blood.

**Blood Grouping**

Red cells are grouped for ABO and RhD by taking the patient's red cells, incubating with antibodies of known specificity, and observing for agglutination – indicating the patient has the corresponding antigen.

**Selection of Blood:** blood selected for transfusion should be ABO and RhD compatible; plus the purpose of compatibility testing is to ensure that the recipient does not have antibodies against blood group antigens present in donor blood selected for transfusion, which could cause haemolysis.

***'Antibody screen'*** of recipient plasma to exclude **any** clinically significant immune antibodies. Recipient plasma is incubated with 2 or 3 different fully typed *'screening'* red cells, which are known to possess all the blood group antigens which matter clinically. If the screen is negative, any donor blood which is ABO (and D) compatible can be given. If positive, the antibody must be identified with the use of a large panel of red cells; donor units that lack the corresponding blood group antigen are then chosen for cross matching with the recipient's plasma prior to transfusion.

**Compatibility test** done between donor red cells and recipient plasma = ***'cross-match'***.

**BLOOD DONORS**

**Careful Donor Selection**

Blood is collected in the UK only from volunteer, unpaid donors, who are between 17-70 years of age. Donors are excluded if they have any disease that might make blood donation hazardous, e.g. cardiovascular/ neurological disease, or if their blood would be hazardous for the recipient (risk of viral, bacterial or parasitic infections, certain diseases or drugs). Donor education and self-exclusion of individuals who are at high risk of having contracted blood-borne infectious diseases are essential to ensure that subjects who are in an early infectious stage, but who have not sero-converted (they have not yet developed antibodies, i.e. in the *'window period'*) are not accepted as blood donors.

**Common causes of donor exclusion:**

1. High risk groups:
2. Men or women who are infected with HIV, hepatitis B or C
3. Men or women who have injected illegal or non-prescribed drugs, including body-building drugs, at any time
4. Men or women who have ever been given money or drugs for sex
5. Men or women who have had sex in the last 12 months with:
6. anyone in the above groups
7. a man or woman who may have ever had sex in parts of the world where HIV/AIDS is very common (this includes most African countries except those bordering the Mediterranean)
8. Men who have had oral or anal sex with another man with or without a condom or other form of protection
9. Women who have had sex in the last 12 months with a man who has had oral or anal sex with another man with or without a condom or other form of protection

**Tests Undertaken on Blood Donations**

*1. Group & screening:*

Every blood donation has the ABO and RhD blood group determined. Also, the other Rh blood groups, namely, C, c, E, e and the K blood group are determined on most donations in the UK.

Every donation is tested to ensure that no strong clinically significant red cell antibodies are present in the donor's plasma, so that any transfusions containing plasma will only contain ABO antibodies.

*2. Infection testing:*

**NB:** The most important step in maintaining a safe blood supply is rigorous donor selection and self-exclusion of subjects at high risk of transmitting blood-borne agents. Testing donations for the relevant agents adds to safety, but no test can pick up all infections, especially early ones. The tests done on every blood donation are shown in table below. In addition, giving blood only to patients who really need it reduces the risk to patients.

Tests performed on donated blood in UK

\*Ab=antibody: Ag=antigen

|  |  |
| --- | --- |
| **Infections** | **Tests done** |
| HIV  hepatitis B  hepatitis C  HTLV  Syphilis | anti-HIV 1+2 Ab; PCR  HBsAg  anti-HCV Ab; PCR  anti-HTLV Ab  TPHA (Ab test) |
| Plus some donations:  CMV (cytomegalovirus) T.Cruzii Malaria | anti-CMV Ab  anti-T. cruzii Ab  anti-Malarial Ab |

**Prion Disease: -** Prion proteins have been found in membranes of lymphocytes and platelets and the prions of variant Creutzfeldt-Jacob disease (CJD) are found in lymphoreticular tissues. There have been 4 cases in the UK of variant CJD transmitted by transfusion of blood or blood products in humans, where donors who were entirely well, donated then years later developed vCJD. A blood test to exclude any donor with vCJD is not yet available

**BLOOD COMPONENTS AND PRODUCTS**

450ml blood is collected from a donor into a sterile plastic bag containing anti-coagulant. Over the last 25 years, the emphasis in blood transfusion has changed. It is no longer the aim to provide unseparated whole blood, because very few patients require all the components in blood. With improved diagnosis of coagulation factor deficiencies, modern aggressive chemotherapy regimes, bone marrow transplantation, and improved technology, it has become routine to treat patients only with those components which are required - for example platelets, red cells, factor VIII, etc. Component therapy enables more efficient use of blood donations, and less waste of valuable resources. Also mainly due to the publicity given to transfusion-transmitted infections, clinicians are starting to become more conscious than ever that blood should be prescribed only when there is no safer alternative therapy, e.g. iron therapy, intraoperative salvage, etc.

To reduce the risk of vCJD through transfusion in the UK:

(i) Plasma from UK donors is no longer used for fractionation

(ii) All blood products are **LEUCODEPLETED** to remove white blood cells

**1 UNIT = WHOLE BLOOD OR BLOOD PRODUCTS DERIVED FROM ONE SINGLE BLOOD DONATION**



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Storage (°C)** | **Shelf life** | **Dose** | **Outcome** |
| **Red cells** | 2-6° | 35 days | 1 unit | Hb rise 1g/dl in adult |
| **Platelets** | keep room temperature agitated | 5 days | 1 pool | >10x109/l increase  - check platelet count after |
| **FFP** | frozen | 2 years | 12-15ml/kg | Response to FFP transfusions should be measured clinically and by post-transfusion coagulation tests |
| **Cryoprecipitate** | frozen | 2 years | 10 donors | Test coagulation function |

**A) Red cells** - less than 1% of blood is used as *'whole'* blood in the UK; it is deficient in labile clotting factors and functional granulocytes and platelets. Most blood is given as *'SAG-M’,* where red cells are more concentrated after plasma removal, so that plasma can be used for other purposes, plus this avoids fluid-overloading patients during transfusion.

**B) Platelet Concentrates** - available in two forms.

1. Pooled platelets - platelets from 4 donations pooled to constitute a single adult dose. (Commonest)

2. Or from a single donor by cell separator machine, equivalent to 4 single donations of platelets.

**Indications:**

***i) Preventative:***

1. Prophylaxis due to thrombocytopenia (with decreased platelet production e.g. chemotherapy, bone marrow transplant, aplastic anaemia) or defective platelet function
2. Bleeding becomes likely when platelet count is less than 10x109/L, but can occur at higher levels when there is fever, infection, platelet dysfunction (e.g. post cardiac bypass).

***ii) Therapeutic****: for treatment of bleeding due to thrombocytopenia or dysfunction*

1. Massive blood transfusion (dilutional thrombocytopenia)
2. Platelet dysfunction of cardiac bypass, aspirin

***NB: Autoimmune Thrombocytopenia (AITP):*** platelet transfusions are rarely indicated because there is rapid destruction of all platelets by the autoantibody. In this disease, platelets are required only for life-threatening bleeds.

Important to monitor clinical response (not just rise in platelet count).

**White Cells -** very rarely used except when severe infections occur in neutropaenic patients not responding to antibiotics/ antifungal drugs

1. **Fresh Frozen Plasma – FFP**

**Plasma -** contains clotting factors/ albumin/ immunoglobulins, water, electrolytes

1. Once thawed (at 30-37ºC) - deterioration of clotting factors - use ASAP
2. Use ABO compatible, as plasma contains anti-ABO group antibodies

**Indications** - very few definite indications. Should be given only in patients who are bleeding actively and have abnormal clotting tests or are receiving anticoagulant therapy and need urgent surgery.

**D) Cryoprecipitate**: separated from other plasma constituents by freezing fresh plasma and then allowing it to thaw at 4º-8ºC overnight. Approximately 3% of the FFP forms a residue - fails to redissolve = cryoprecipitate. Contains factor VIII and fibrinogen. Stored frozen in a small vol of plasma (approximately 15ml). When thawed quickly for use, it redissolves in plasma.

**Indications:** (i) treatment of DIC, together with other blood components  
 (ii) fibrinogen deficiency

## E) Blood Products - by fractionation of plasma

1. **Albumin** - human albumin solution (HAS) 4.5%. A safe product that is pasteurised and has never been implicated in the transmission of infections.

Clinical uses: - very few; a highly overused product  
 - hypoproteinaemia, burns, extensive surgery and plasma exchange

2. **Factor VIII Concentrate** - Large pools of plasma (2,000->5,000 donations) subjected to fractionation and heat treated to eliminate viral transmission.

Clinical uses: - treatment of haemophilia A (prophylaxis and acute bleeding)  
 - von Willebrands' disease

NB: Recombinant factor VIII is now given to all new haemophiliacs in the UK.

3. **Factor IX Concentrate**

Clinical uses: - treatment of Christmas disease or Haemophilia B (again, recombinant IX available)

4. **Normal Human Immunoglobulin:** prepared from pooled normal human plasma and contains a mixture of immunoglobulins present in the healthy adult population.   
Available as IM or IV preparations.

Indications for use: (a) mostly by IV route - as replacement in immunodeficiency states, ITP or autoimmune haemolytic anaemia. (b) by IM route - prevention of certain infections (by providing broad antibody cover from normal population) e.g. hepatitis A, measles, rubella.

5. **Specific Immunoglobulins:** fractionated from plasma from selected donors who have a high titre of a specific antibody (from hyperimmune donors) e.g. anti-D Ig, hepatitis B Ig, varicella zoster Ig, rabies Ig, tetanus Ig, CMV Ig.