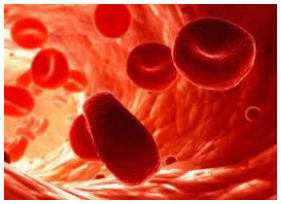
BLOOD LECTURE 2



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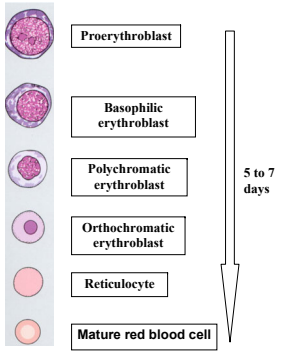
Objectives of this lecture

- Describe the developmental stages of the red blood cell
- Describe the control of erythropoiesis and the role of erythropoietin
- Understand the nutritional requirements for red cell production
- Describe some of the different types of anaemias
- Understand the basis of ABO blood groups and the reasons for incompatibilities
- Understand the basis of Rhesus blood groups and the repercussions of incompatibilities

DEVELOPMENTAL STAGES OF THE ERYTHROCYTE (ERYTHROPOIESIS)



CONTROL OF ERYTHROPOIESIS

The state of tissue oxygenation is the basic regulator of red cell production. Any condition that causes the quantity of oxygen transported to the tissues to decrease will increase the production of red blood cells.

<u>Factors that decrease oxygenation</u>

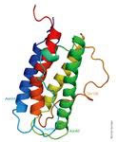
1. Haemorrhage
2. Destruction of bone marrow
3. High altitudes due to low atmospheric oxygen
4. Diseases of the circulation eg cardiac failure
5. Pulmonary disease

ERYTHROPOIETIN (EPO)

EPO (hormone) stimulates erythropoiesis.

- ± 90% of EPO formed in kidneys, rest in the liver
- EPO stimulates production of proerythroblasts from myeloid committed stem cells in bone marrow
- EPO also causes these cells to pass more rapidly through the different erythroblastic stages so production of new cells is sped up
- production of cells continues as long as person remains hypoxic or until enough red blood cells are produced
- testosterone increases the basal rate of erythropoiesis by raising the level of EPO secretion

Schematic of human EPO



NUTRITIONAL REQUIREMENTS FOR RED CELL MATURATION

- rate of reproduction & maturation affected by nutritional status
- vitamins B_{12} (cobalamin) & folic acid essential for DNA production in red cells
- folic acid – found in leafy plants, yeast & liver – easily destroyed by cooking
- B_{12} - water soluble, only in animal products
  - only absorbed from intestine bound to intrinsic factor- a glycoprotein released by cells in stomach
  - once absorbed, stored in large quantities in liver
  - then slowly released as needed to bone marrow & other tissues
  - minimum amount of B_{12} required each day – 1-3µg
  - normal store about 1000x this amount.

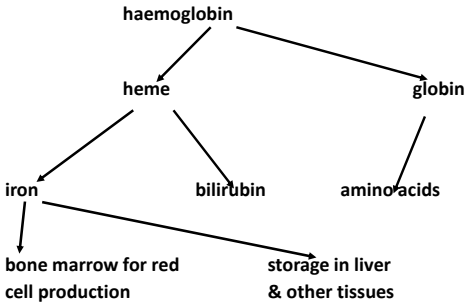
IRON

- Iron is also required for haemoglobin synthesis
- total quantity of iron in body 4-5 grams
  - 65% haemoglobin
  - 4% myoglobin
  - 15 to 30% stored, mainly in the liver
- ±10% of ingested iron is absorbed into blood
- Fe^{2+} ions (ferrous) are absorbed much more easily than ferric or Fe^{3+} ions
- vitamin C (ascorbic acid) increases iron absorption by reducing ferric ions to ferrous ions
- phosphate & oxalate form insoluble compounds with ingested iron that can't be absorbed

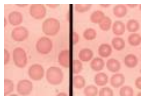
- free iron & certain iron-containing compounds bind with apotransferrin (secreted by liver) to form transferrin which is absorbed into epithelial cells & released into blood capillaries
- iron is loosely bound - easily released to any tissue
- excess iron in blood deposited in all cells but especially in the liver and bone marrow
- in receiving cell cytoplasm, iron combines mainly with protein apoferritin, to form ferritin- storage form of iron
- if supply of iron in diet drops, stored iron is released from ferritin, binds to transferrin & carried in plasma to wherever it's required.

DESTRUCTION OF ERYTHROCYTES

- aged erythrocytes are destroyed mainly by macrophages in the spleen
- haemoglobin is catabolised



ANAEMIAS



anaemia = deficiency of haemoglobin

- **nutritional anaemia** –
  - Fe deficiency – microcytic anaemia
  - Insufficient folic acid slows red cell reproduction & those produced are large, odd shaped, megaloblasts, fragile membranes, rupture easily = megaloblastic anaemia
- **pernicious anaemia** - gastric mucosa of stomach fails to produce intrinsic factor, vitamin B_{12} not adequately absorbed → megaloblastic anaemia
- **haemorrhagic anaemia** - after rapid haemorrhage, plasma volume is replaced within one or two days, leaving a low concentration of red cells
- **aplastic anaemia** - lack of functional bone marrow – due to exposure to radiation, x-rays, chemicals, drugs
- **haemolytic anaemia** - hereditary abnormalities of red cells that make the cells fragile.
  - spherocytosis – very small spherical cells
  - sickle cell – abnormal haemoglobin
  - thalassaemia – absent or abnormal globin chains

BLOOD GROUPS

Erythrocytes have plasma membrane proteins & carbohydrates that can function as antigens when exposed to another person's blood

> 300 erythrocyte antigens but ABO system is most important for transfusion reactions.

4 possible ABO blood groups depending on presence or absence of two antigens, the A & B antigen

Only type A antigen – blood group A
Only type B antigen – blood group B
Neither antigen – blood group O
A and B antigens – blood group AB

Two genes, one on each of 2 paired chromosomes, determine the ABO blood group.

These genes can be of 3 types - A, B or O.

O gene – practically functionless, causes no significant O antigen – recessive

A and B genes – cause strong antigens – are co-dominant

Genetic possibilities					
Homozygous	Heterozygous	Antigen on RBC	Blood Group	Antibody in Plasma	Freq*
AA	AO	A	A	Anti-B	38%
BB	BO	B	B	Anti-A	10%
-	AB	A and B	AB	Neither	3%
OO	-	Neither	O	Both	49%

- Frequency of blood groups in Australian population – Australian Red Cross Blood Service

- Type A antigens <u>not</u> present → anti-A antibodies develop in plasma.
- Type B antigens <u>not</u> present → anti-B antibodies develop in plasma.
- Both A and B antigen are present → no antibodies develop in plasma.
- Group O - neither A or B antigens produces both Anti-A & Anti-B antibodies.

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens present	 A antigen	 B antigen	 A and B antigens	None

Why does a blood group A person who doesn't have the B antigen, develop antibodies to the B antigen?

Small amounts of group A & B antigens enter the body in food, bacteria & other ways & initiate development of antibodies. Newborn babies have almost no Anti-A or Anti-B in their plasma. These develop after birth.

Type A recipient and type B donor

- donor's Anti-A reacts with recipient's A antigen - little consequence because donated antibodies are diluted in recipient's plasma.
- recipient's Anti-B reacts with donor's B antigen - reaction is severe because recipient's antibodies can cause the donated red cells to clump together = agglutination. These clumps plug small blood vessels throughout the circulatory system. Physical distortion of cells or attack by phagocytic white blood cells → destruction of agglutinated cells → release of haemoglobin into plasma = transfusion reaction.

Blood group AB – no antibodies so can accept any blood type = universal recipients

Blood group O – no antigens – can give blood to anyone = universal donors

RHESUS (Rh) BLOOD TYPES

- Rh +ve person (81% of Australians) has Rh antigen
- Rh -ve person does not have Rh antigen
- genetically determined
- Rh –ve person does not develop antibodies to Rh factor until exposed to Rh antigen, usually by transfusion of blood or by a mother having a baby who has the antigen (that is an Rh negative mother who conceives an Rh positive child)
- red blood cells containing Rh antigen injected into person whose blood does not contain the factor, will cause antibodies to develop over several months
- first transfusion may cause no immediate reaction, but the recipient is 'sensitised' to the antigen & further transfusions cause severe reactions

ERYTHROBLASTOSIS FETALIS
(Haemolytic Disease of the Newborn)

- disease of fetus & newborn (Rh +ve baby, Rh –ve mother)
- characterised by agglutination & phagocytosis of baby's red blood cells
- usually mother is Rh –ve & father is Rh +ve
- baby inherits Rh antigen from father & mother has developed Rh antibodies from exposure to baby's antigen
- mother's antibodies diffuse through the placenta into fetus to cause red blood cell agglutination.
- first Rh +ve child – mother doesn't usually develop enough antibodies to cause any harm.
- 3% of second babies affected
- about 10% of third babies

- **babies - anaemic at birth & jaundiced (bilirubin from red cell destruction)**
- **liver & spleen enlarged - haemopoietic tissues attempt to replace damaged red blood cells**
- **severe anaemia is usual cause of death**
- **children who survive the anaemia may have permanent brain damage because of precipitation of bilirubin in neuronal cells which causes their destruction**

- **Prevention**

  - flood mother's blood stream with Rh antibodies just after each child is delivered

  - injected Rh antibodies destroy any fetal cells that may have entered the mother's blood before they can initiate a response from the mother's own immune system that would affect subsequent Rh+ve babies.