ANAEMIA: INTERPRETING THE FBC LIKE A HAEMATOLOGIST

Red cell disorders with a focus on haemoglobinopathies

Dr Amy Cooper, Haemoglobinopathy Quality Improvement Fellow

LET'S TEST CANVA LIVE

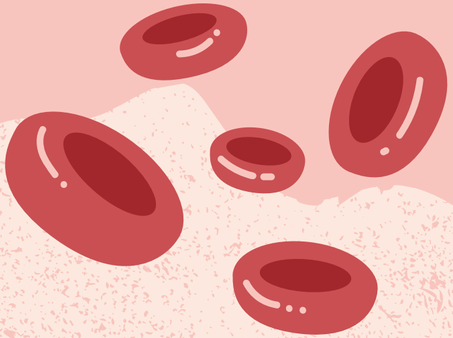
WHAT IS THE BEST MEDICAL SPECIALTY?

Put your answer in the chat.

Scan the QR code

TODAY, YOU WILL...

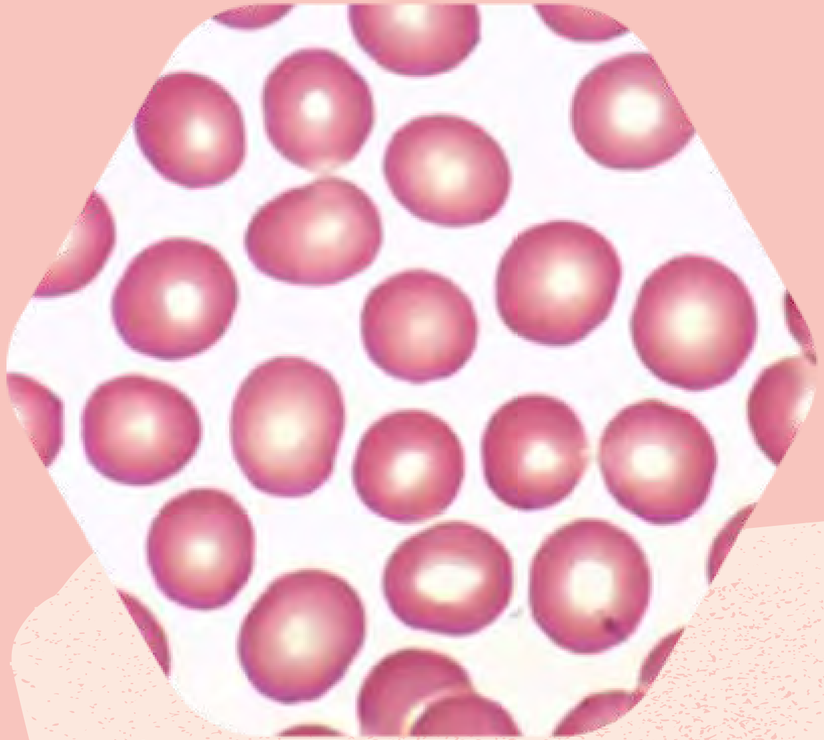
Learn what the FBC represents and how to interpret it.



Understand the main red cell disorders and how to distinguish them.

ALL ABOUT RED CELLS: A REMINDER

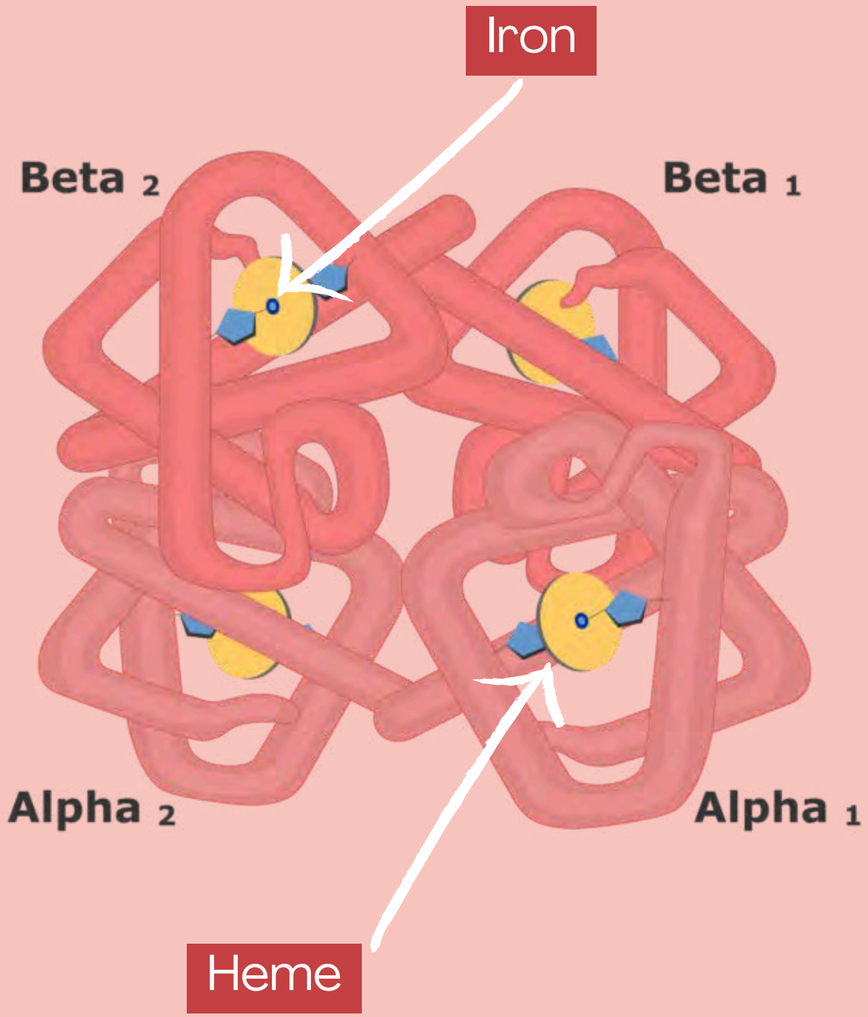
- Biconcave disc (to increase surface area) without a nucleus
- Should be uniform in size
- Normal red cells are flexible and deformable
- Normal lifespan - 120 days
- Cell membrane maintained by a cytoskeleton filled with specialist proteins
- Cytoplasm contains no organelles - only haemoglobin



HAEMOGLOBIN

- Consists of two alpha and two beta globin chains
- Heme sits inside the globin chain and holds one iron molecule (4 per haemoglobin)
- The iron molecule reversibly binds oxygen (allowing it to carry and give up the O2 molecule)

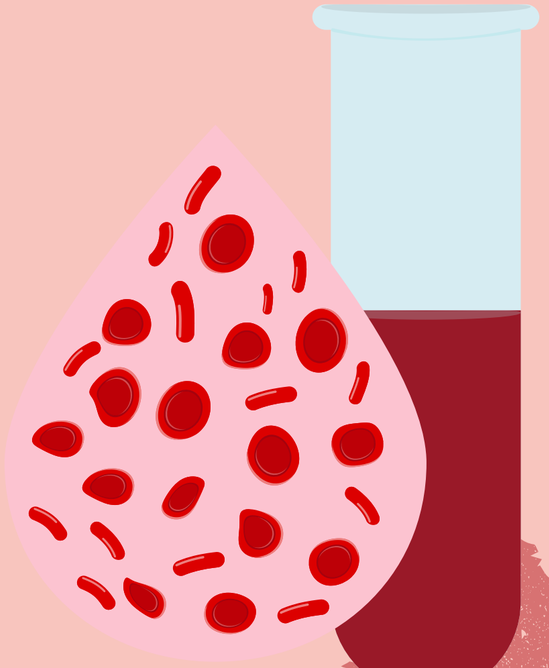
Reminder - this is what Hb measures!



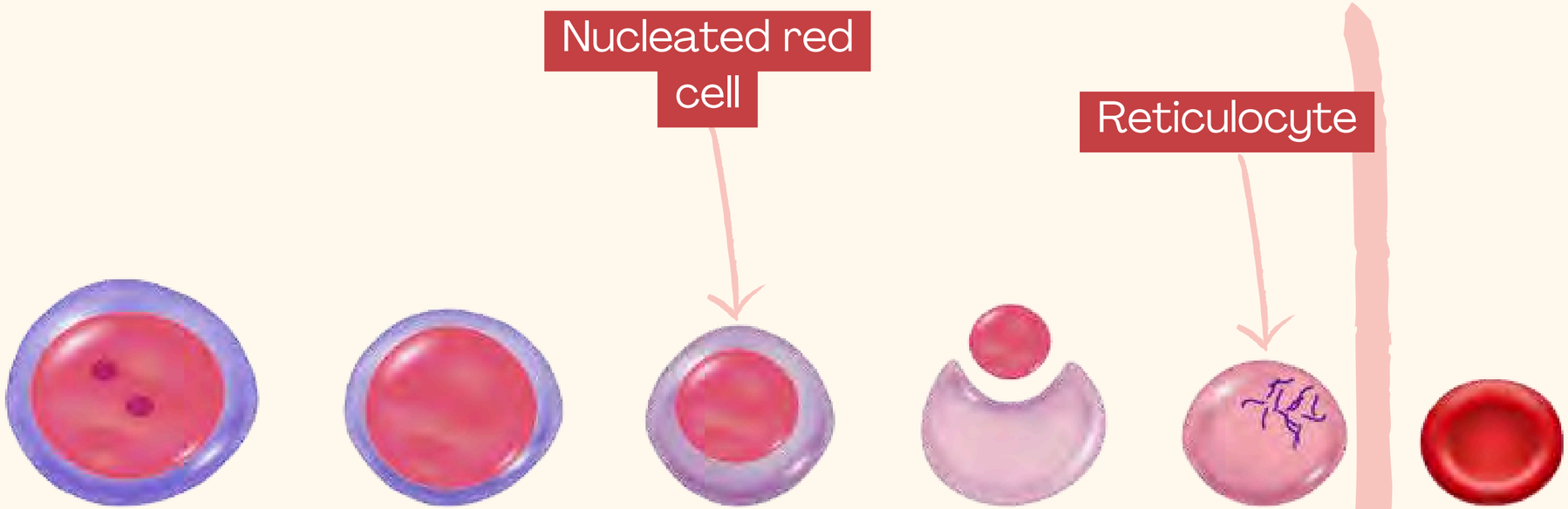
DEFINITION OF ANAEMIA

WHO definition

Anaemia is defined as a **haemoglobin** concentration below a specified cut-off point; that cut-off point depends on the age, gender, physiological status, smoking habits and altitude at which the population being assessed lives



HOW ARE RED CELLS MADE?



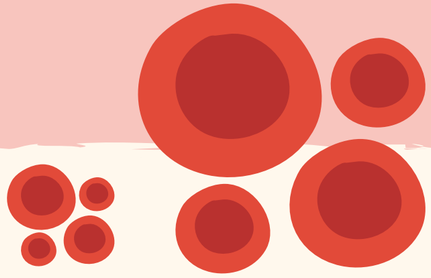
HOW CAN WE MEASURE WHETHER RED CELLS ARE BEING MADE?

Reticulocytes are released into the blood stream in small, predictable and constant numbers in normal health.

High reticulocytes - more red cells are being pushed out of the bone marrow

Low reticulocytes - red cells production is reduced

WHAT CAN GO WRONG WITH RED CELLS?



Size

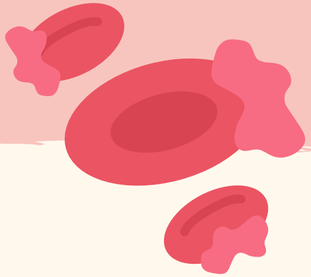
Unusually small or large cells can be caused by vitamin deficiency or haemoglobin abnormalities.

Varying sizes is called anisocytosis.

Shape

Red cells can be misshapen for lots of reasons (poikilocytosis).

Haemoglobinopathies are problems with the haemoglobin molecule which result in deformed and misshapen red cells.



Structure

If the proteins in the red cell membrane don't work properly, this causes a problem with how the red cell survives.

These are called membranopathies.

THE NORMAL FULL BLOOD COUNT (FROM A RED CELL PERSPECTIVE)

RBC: Number of red cells

RBC		5.03	10^{12}/L
Haemoglobin		149	g/L
Haematocrit		0.431	L/L
MCV		85.6	fL
MCH		29.6	pg
MCHC		346	g/L
RDW		11.9	

Haematocrit: Percentage of blood which is made up of red cells (e.g. this would be 43%)

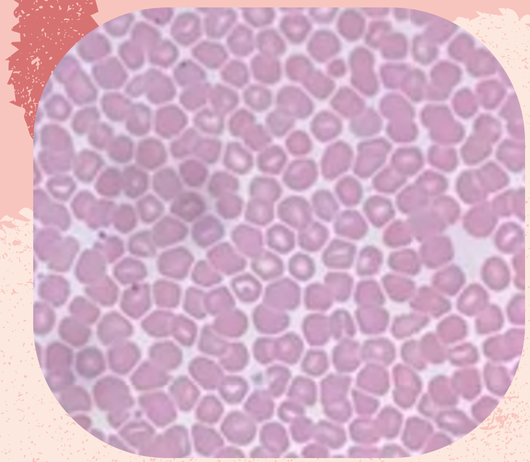
Mean cell volume: the mean size of the red cells. Small = microcytic Large = macrocytic

Red cell distribution width: The size difference between the circulating red cells

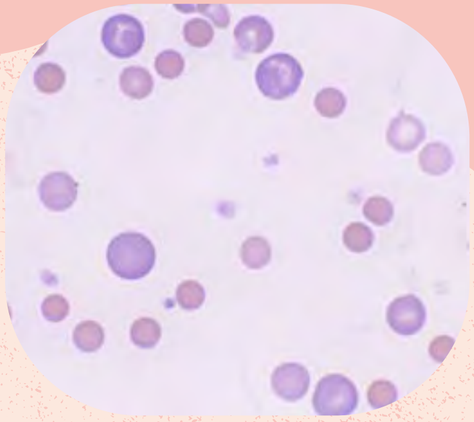
MCH (**mean cell haemoglobin**): how much haemoglobin there is per cell. Low = **hypochromic**

MCHC (**mean cell haemglobin concentration**): how much haemoglobin there is per red cell, but taking into account the size

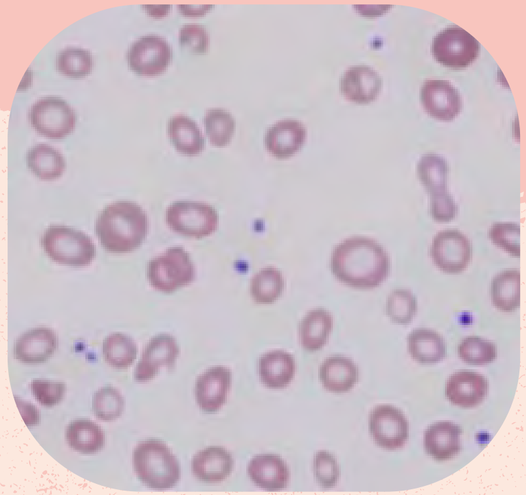
VISUAL EXAMPLES



High haematocrit



Wide red cell distribution width



Low MCV and low MCH (hypochromic and microcytic)

TYPES OF ANAEMIA (SIMPLIFIED!)

Low reticulocytes

Bone marrow suppression related to:

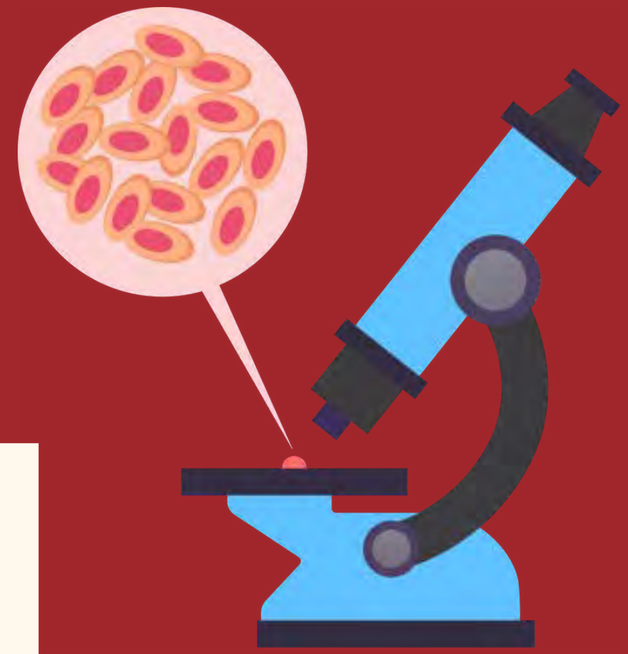
- The bone marrow filling up with abnormal cells and reducing production (bone marrow infiltration)
- Not enough building blocks (haematinic deficiency - can be low or normal)
- Toxic effects on the bone marrow (drugs, poison, sepsis etc).

High reticulocytes

Bone marrow working hard to make cells in:

- Haemolytic anaemia (replacement of destroyed red cells)
- Haemoglobinopathies like sickle cell disease and thalassaemia
- Bleeding

LET'S INTERPRET SOME FBCS!



CASE ONE:

17 year old female seen in ED

We've not yet taken a history but the bloods from triage are back.

Value	Result	Normal range
Haemoglobin	**83**	120 - 160
Haematocrit	**0.289**	0.36 - 0.46
MCV	**62.8**	83 - 100
MCH	**18.1**	27.0 - 32.0
MCHC	**289**	310 - 350
Platelets	**681**	150 - 400
RDW	**34.0**	11.5 - 15.5

CASE ONE:

17 year old female seen in ED

We've not yet taken a history but the bloods from triage are back.

What single test will be most useful to make a diagnosis?

Scan the QR code

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Low haemoglobin

Very small cells with low haemoglobin concentrations

Wide variation in cell size

CASE ONE:

Diagnosis: Iron deficiency anaemia

Microcytic and hypochromic indices
Also - high platelet count

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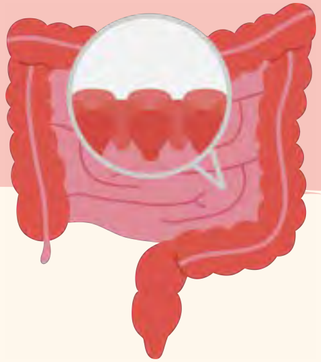
CAUSES OF IRON DEFICIENCY

Poor intake

Very unlikely, but possible in vegetarians/vegans.

More likely in children



Malabsorption

Examples include:

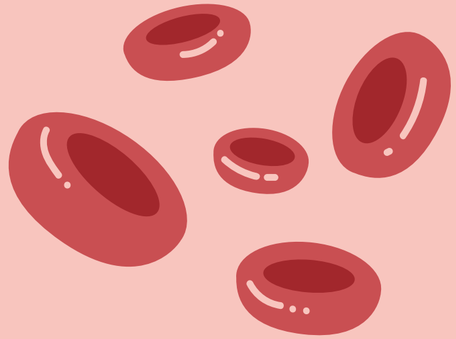
- Coeliac disease
- Crohn's disease
- Post gastric bypass

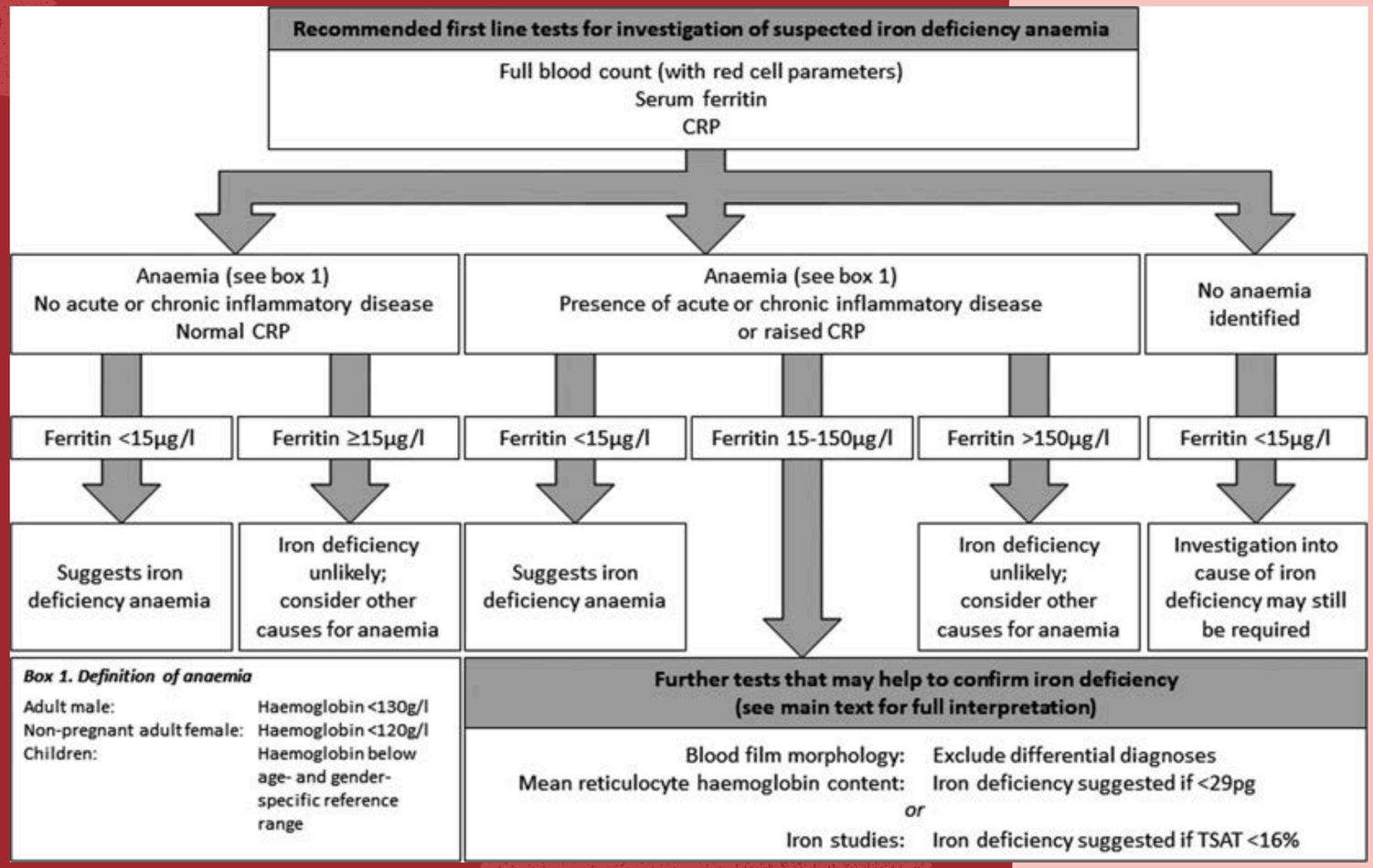
Blood loss

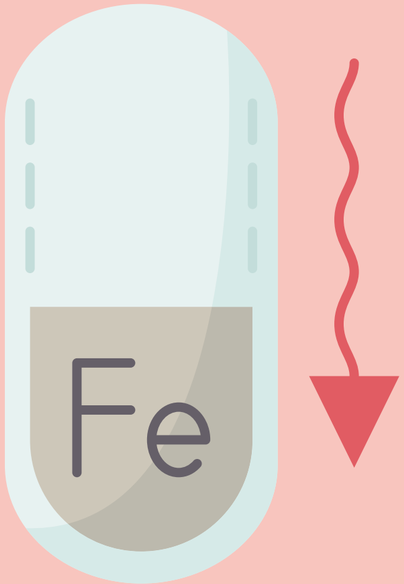
Most common!

- Menstruation
- GI blood loss
- Other blood loss including nose bleeds, urinary tract
- Pregnancy/childbirth
- Trauma

DIAGNOSIS OF IRON DEFICIENCY







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MANAGEMENT OF IRON DEFICIENCY

Iron replacement

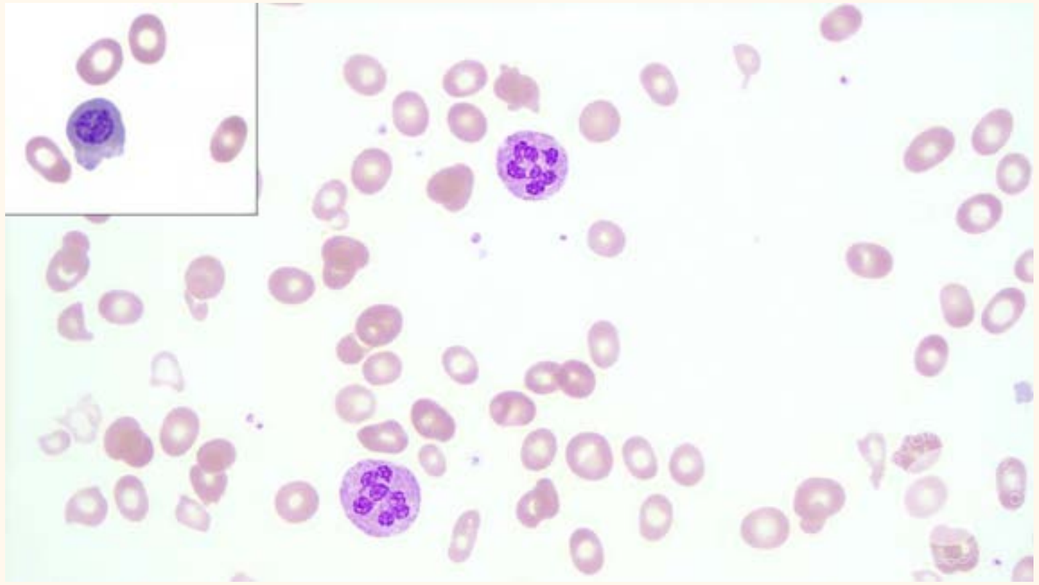
Oral or IV depending on clinical scenario

Identification of underlying problem

Full history and examination is crucial

! Blood transfusion is not the usual management !

OTHER HAEMATINIC DEFICIENCIES



- **B12** deficiency is most common in vegans or intrinsic factor deficiency. **Folate** deficiency is more common in diets low in leafy greens.
- B12 and folate deficiency cause a macrocytic anaemia (high MCV, low Hb). Also known as megaloblastic anaemia
- If deficient in both - start B12 first then folate (work in alphabetical order!)

CASE TWO:

17 year old female

Presenting to emergency department with intense pain.

Thoughts?

Scan the QR code

Value	Result	Normal range
RBC	**2.15**	3.80 - 5.30
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Reticulocyte count	**343**	50 - 100

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Low amount of red cells

Normal cell size (normocytic)

Normal amounts of haemoglobin per cell

BLOOD FILM

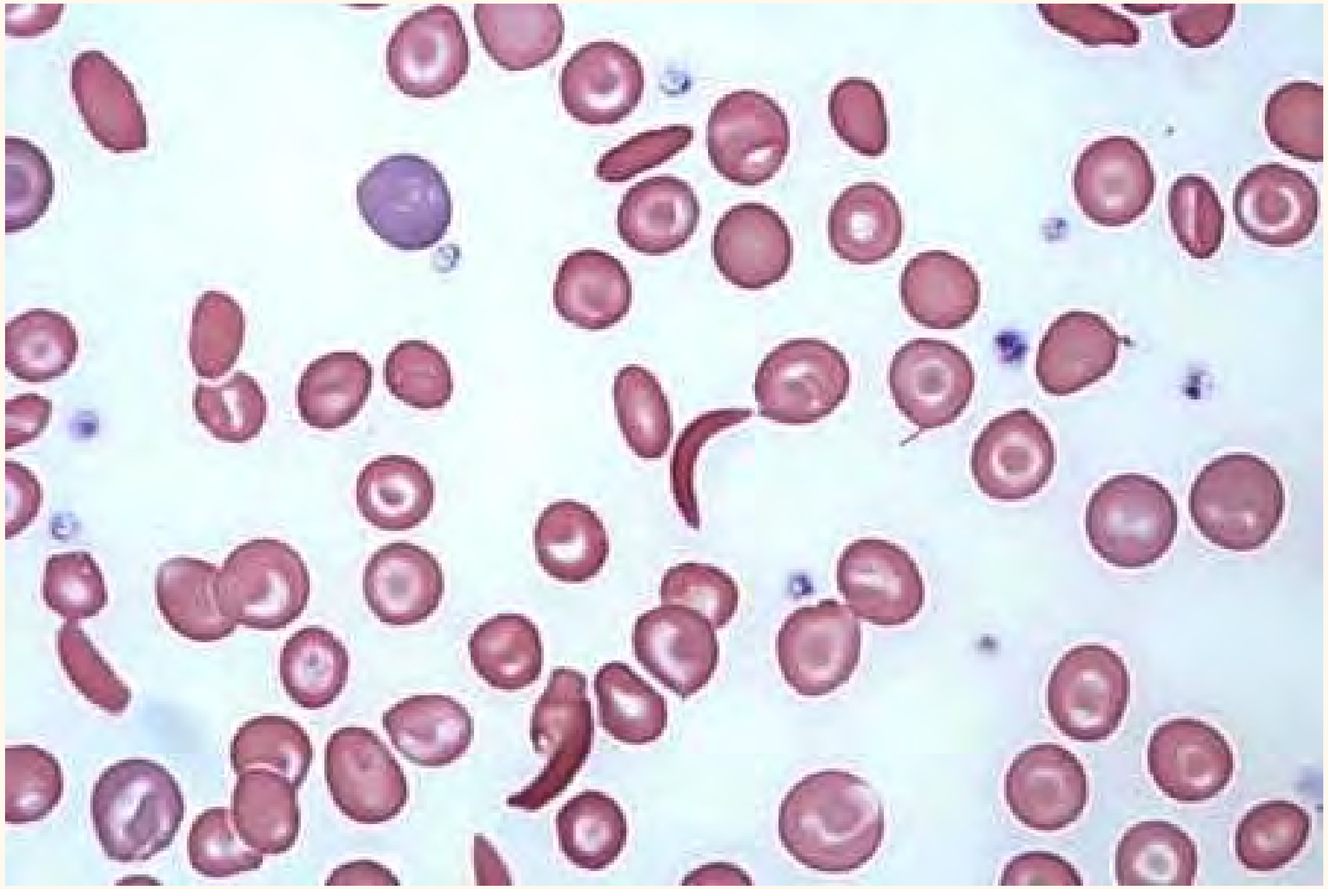

Image credit: Berjaoui, Zeina & Youness, Mohamad & Matar, Jad & Ariss, Abdel. (2016). PREVALENCE OF SICKLE CELL TRAIT IN THE SUBURBS OF BEIRUT, LEBANON. Mediterranean Journal of Hematology and Infectious Diseases. 8. e2016015. 10.4084/mjhid.2016.015.

CASE TWO:

Diagnosis: **sickle cell disease**

Cells have normal amounts of haemoglobin, but the abnormal structure of the haemoglobin causes the cells to be destroyed

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RBC	**2.15**	3.80 - 5.30
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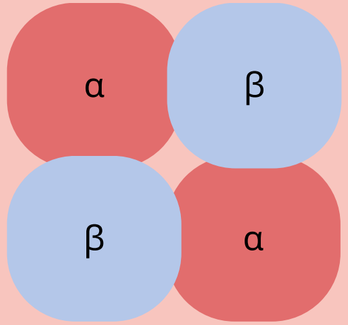
WHAT IS SICKLE CELL DISEASE?

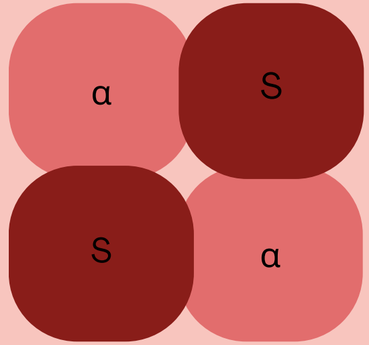
Sickle cell disease is a **haemoglobinopathy.**

Beta globin chains are abnormal due to a single gene mutation on chromosome 11.

This makes a type of abnormal haemoglobin called S, rather than the normal ‘A’ haemoglobin.



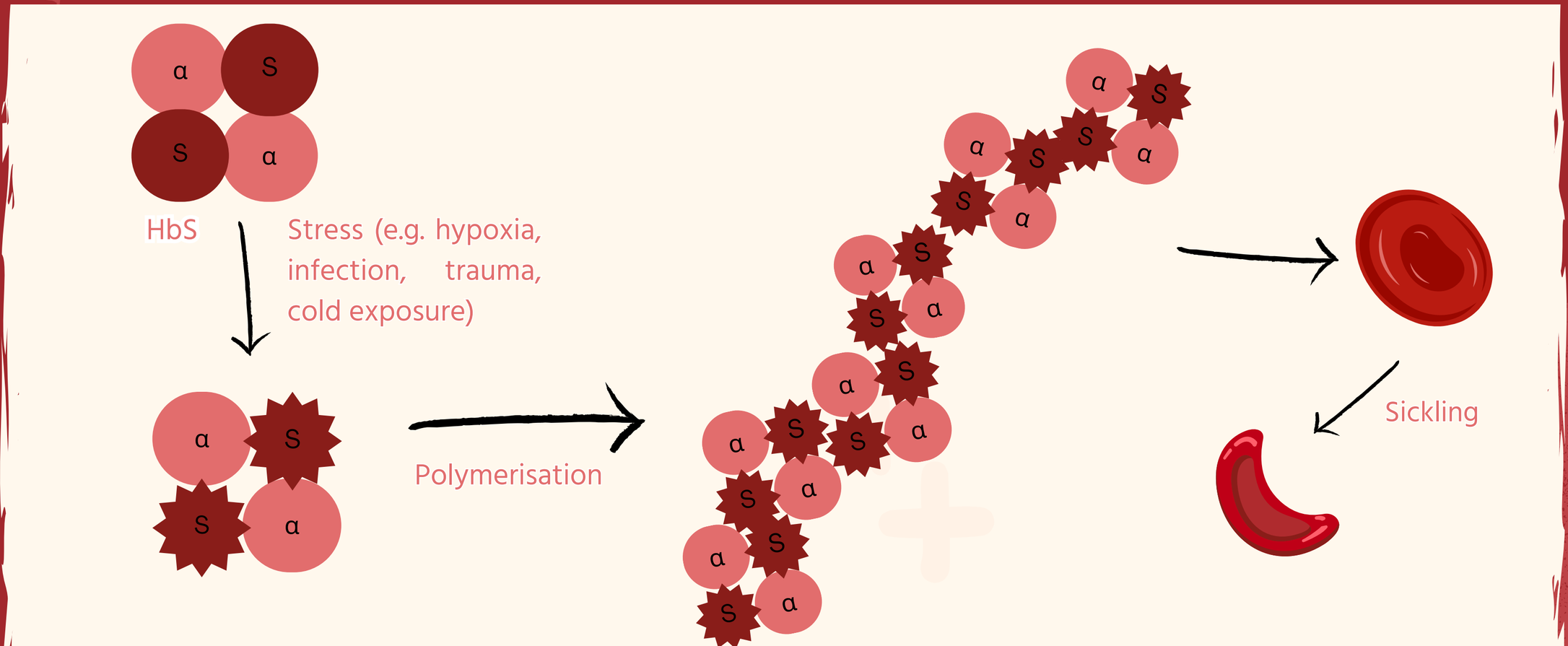
HbA - normal haemoglobin



HbS - sickle haemoglobin

WHY IS HBS A PROBLEM?

In perfect conditions, HbS exists in the same form as HbA.
However if any of the following adverse conditions occur:
- Dehydration - Stress (e.g. infection, trauma) - Cold weather - Hypoxia
HbS stacks (polymerises) and causes the red cell to deform into a sickle shape.



WHAT DO SICKLED CELLS DO IN THE BODY?

Vaso-occlusion

Sickled cells are rigid and non-deformable. They can get stuck in small vessels leading to ischaemia, organ damage and pain

Haemolysis

The abnormal sickled cells are destroyed through intravascular haemolysis. The lifespan of a sickle cell is around 10 days. Haemolysis causes local vascular damage and promotes systemic inflammation

WHAT ARE THE CONSEQUENCES OF SICKLE CELL DISEASE?

Acute

- Pain crisis
- Acute chest syndrome
- Stroke
- Priapism

Chronic

- Renal disease
- Pulmonary hypertension
- Retinopathy
- Liver disease

SMALL GROUP CASES

15 minutes to look through cases within your small group then 5 minutes each to feedback

Googling is encouraged! :)

ACUTE COMPLICATIONS

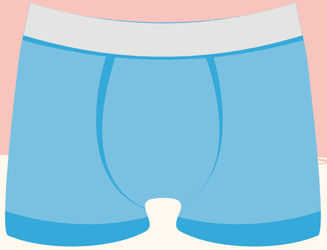
Occur when an insult prompts significant sickling of red cells

Acute painful crisis

- Usually occurs in limbs or back, but can occur anywhere
- Excruciating pain. Be aware that patients may not show their pain as you expect
- Early management with opioid analgesia within 30 minutes
- Close monitoring of observations and sedation score required
- **Always contact haematology team if patient seen in hospital**

Acute chest syndrome

- Cycle of sickling --> hypoxia --> sickling --> hypoxia....
- This cycle can be triggered by **any** lung or ribcage pathology
- Risk of rapidly escalating oxygen requirements related to lung damage
- **Always call haematology if a sickle patient has an oxygen requirement or sats <95% on room air**



Priapism

- Unwanted and painful erection caused by vaso-occlusion of venous drainage
- Can lead to ischaemia and potential need for amputation if not managed quickly
- **Urgent referral to urology and haematology**
- Managed initially with needle aspiration

HOW ARE ACUTE COMPLICATIONS MANAGED?

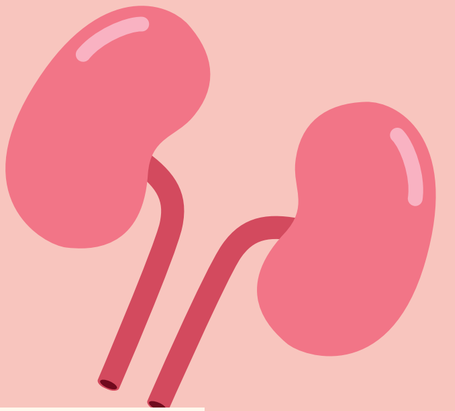
Good supportive care

Sickle Cell Crisis – every second counts

A NALGESIA	**Give analgesia within 30 minutes**, in line with NICE guidance. **Regular assessment of pain score** every 30 minutes until controlled and then every 4 hours. Refer to individualised care plan.
C OMPASSION	**Be compassionate**, Kind, Actively listen, Provide reassurance and keep the patient informed
T EST/TRIGGER	Tests: including transfusion history/previous transfusion reactions. Blood tests (FBC, reticulocyte count, group and save, routine renal, liver & bone biochemistry, CRP), other tests as suggested by history e.g. CXR, MSU. Trigger – what has precipitated the crisis? e.g. infection, dehydration, hypoxia, travel, pregnancy, stress, cold exposure. **Consider IV fluids & antibiotics to treat infection and dehydration.**
N OTIFY	**Notify Specialist Haematology Team** Notify Next of Kin or advocate (when requested or in individual care plan)
O XYGEN	**Offer oxygen supplementation if saturations <95% in room air**; regularly monitor oxygen saturations, including on room air, hourly for the first 6 hours and then 4 hourly if stable as per NICE guidance.
W ATCH	**Watch and keep warm** – regular observations of BP, pulse, respiratory rate, SpO2, temperature. Assess pain every 30 minutes until controlled. **Escalate promptly** (use local scoring e.g. NEWS2 for adults). **Encourage fluids.**

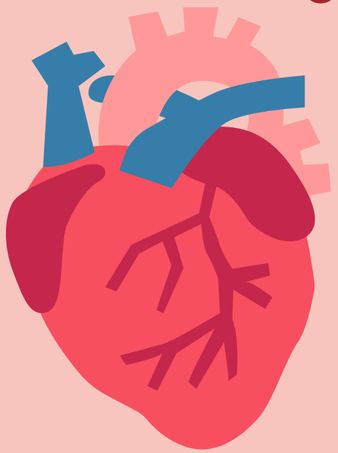
Blood transfusion - top up or exchange

****Never transfuse without haematology advice****

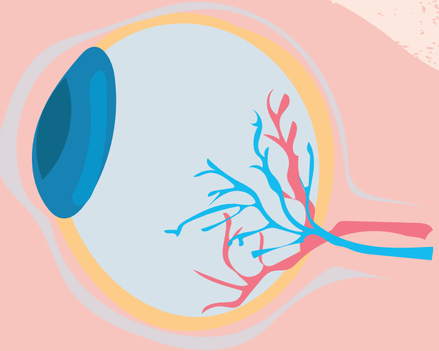


CHRONIC COMPLICATIONS OF SICKLE CELL DISEASE

Chronic vaso-occlusion and haemolysis in end organs can cause long term damage and lead to organ failure.



Hydroxycarbamide is protective.



CASE TWO:

Diagnosis: **sickle cell disease**

...but there is one extra detail that we haven't discussed

Value	Result	Normal range
RBC	**2.15**	3.80 - 5.30
Haemoglobin	**64**	120 - 160
Haematocrit	**0.203**	0.36 - 0.46
MCV	94.3	83 - 100
MCH	29.8	27.0 - 32.0
MCHC	316	310 - 350
Platelets	**1160**	150 - 400
RDW	**16.5**	11.5 - 15.5
Reticulocyte count	**343**	50 - 100

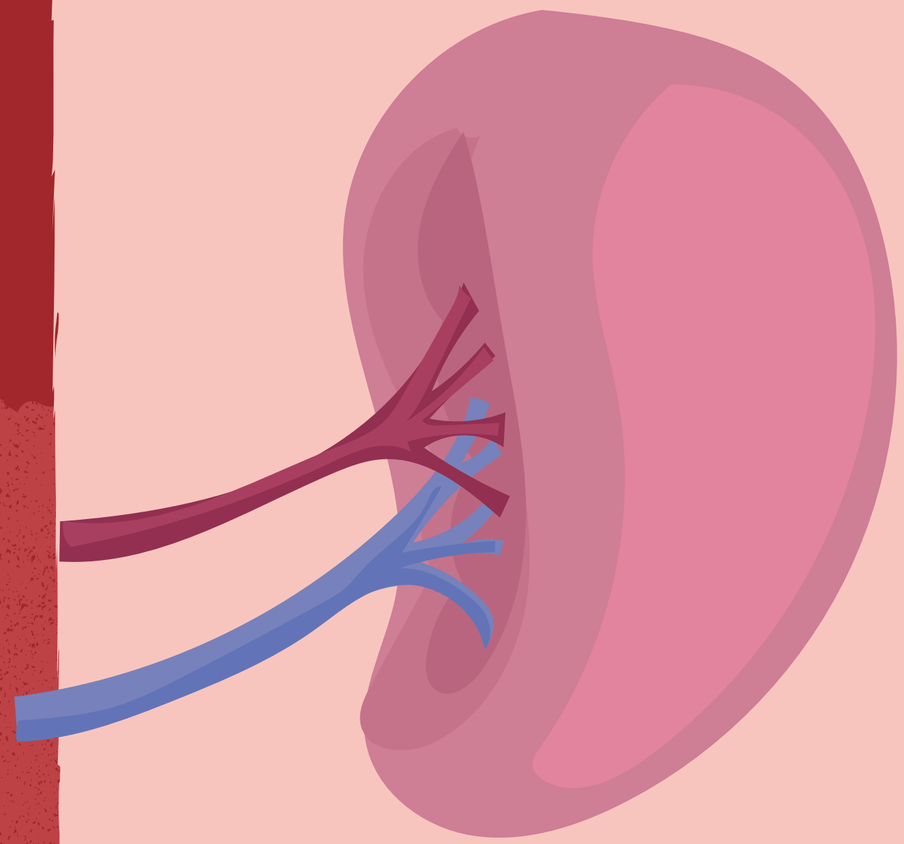
THE SPLEEN

The spleen usually functions to:

- Protect from encapsulated organisms
- Store or remove platelets
- Extra-vascular haemolysis

Patients with sickle cell disease are asplenic. **Without a spleen:**

- Vulnerable to encapsulated organisms such as meningococcus, pneumococcus
- Higher platelet count
- Mainly intravascular haemolysis



CASE THREE:

41 year old man with pneumonia is found to be anaemic.

Appears **jaundiced** on examination.

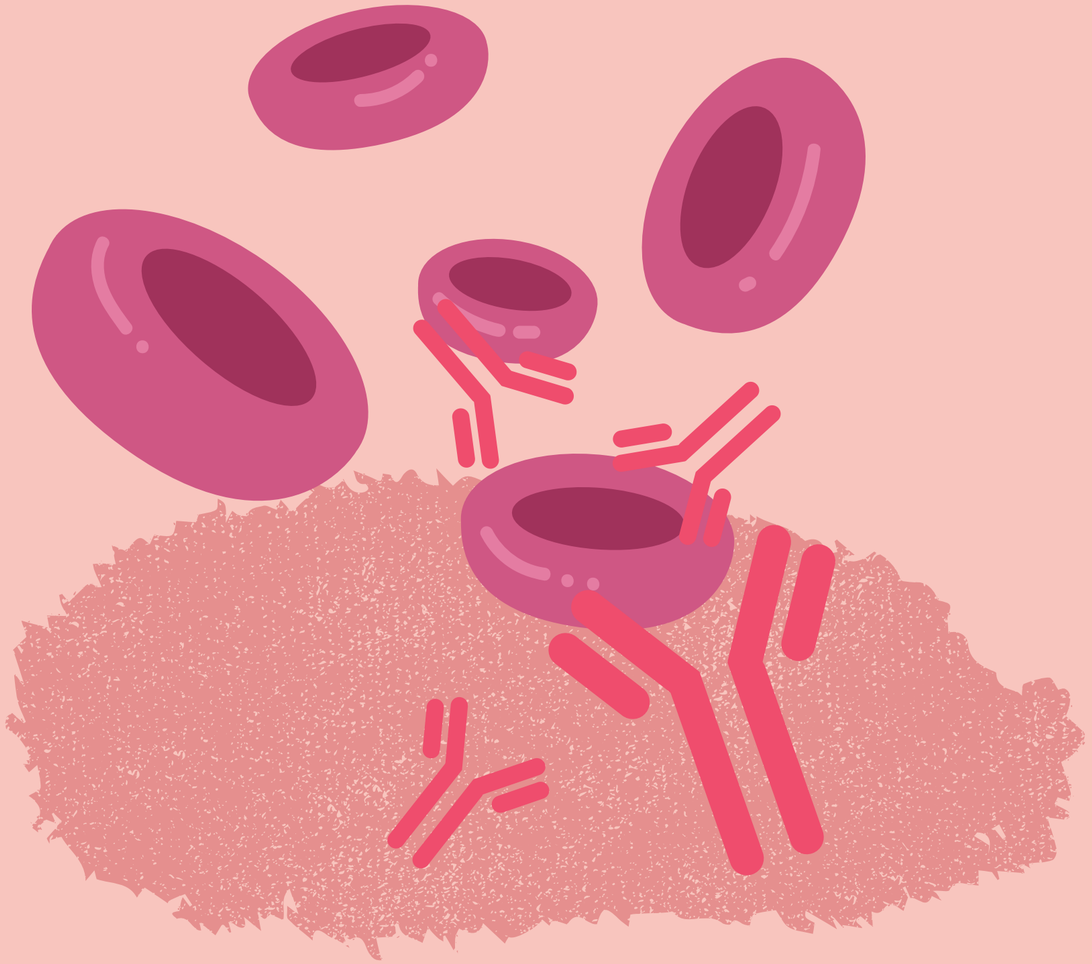
Thoughts?

Scan the QR code

Value	Result	Normal range
RBC	**2.20**	3.80 - 5.30
Haemoglobin	**69**	120 - 160
Haematocrit	**0.202**	0.36 - 0.46
MCV	92.1	83 - 100
MCH	31.6	27.0 - 32.0
MCHC	343	310 - 350
Platelets	293	150 - 400
RDW	**19.0**	11.5 - 15.5

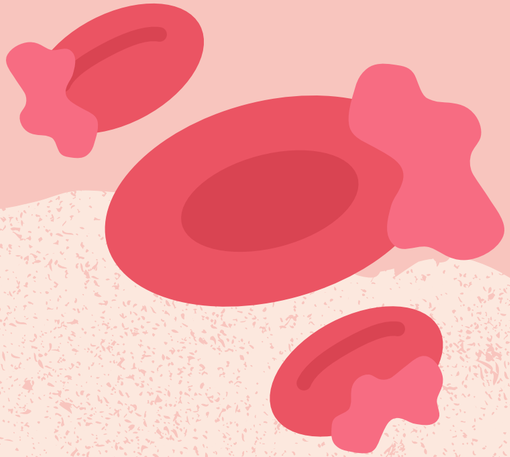
HAEMOLYTIC ANAEMIA

Cells are destroyed inside the body before they reach their normal lifespan by a variety of mechanisms.



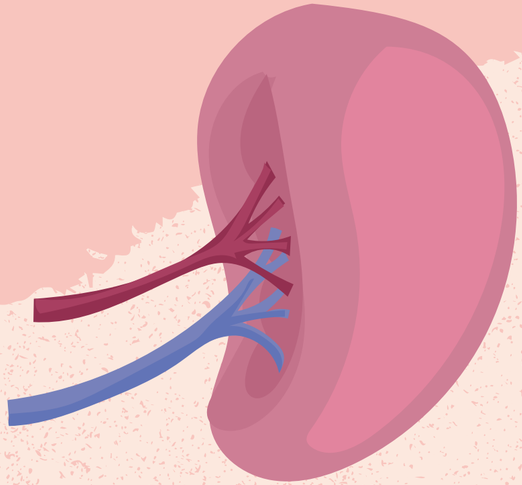
HAEMOLYSIS CAN BE...

Autoimmune (AIHA)
Red cells are abnormally flagged for destruction by the immune system



Non-immune
Red cells are destroyed for other reasons

CELL DESTRUCTION IS EITHER...



Extravascular
Red cells are flagged for destruction and removed by the spleen

Intravascular
Cells are destroyed in the blood vessels

HOW DO WE TEST FOR HAEMOLYSIS?

DAT

Measures whether there is an antibody on the outside of the red cells.

Bilirubin

Released as red cells breakdown.

Specifically **indirect**/**unconjugated** bilirubin

LDH

Released as red cells break down.

A marker of cell turnover

Blood film

Can tell us whether cells appear abnormal in shape (e.g. spherocytes) or being sheared in the blood vessels (fragments)

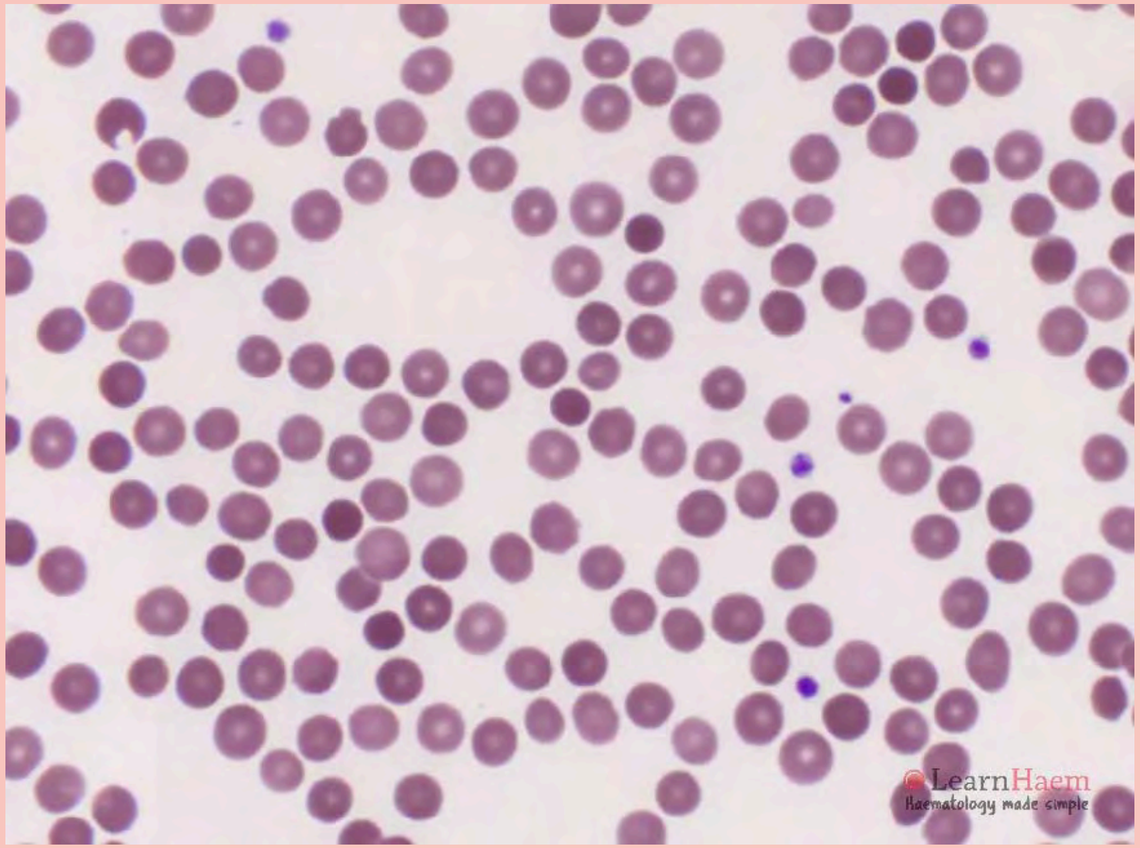
Reticulocytes

Young red cells released into the circulation to compensate for anaemia

Haptoglobin

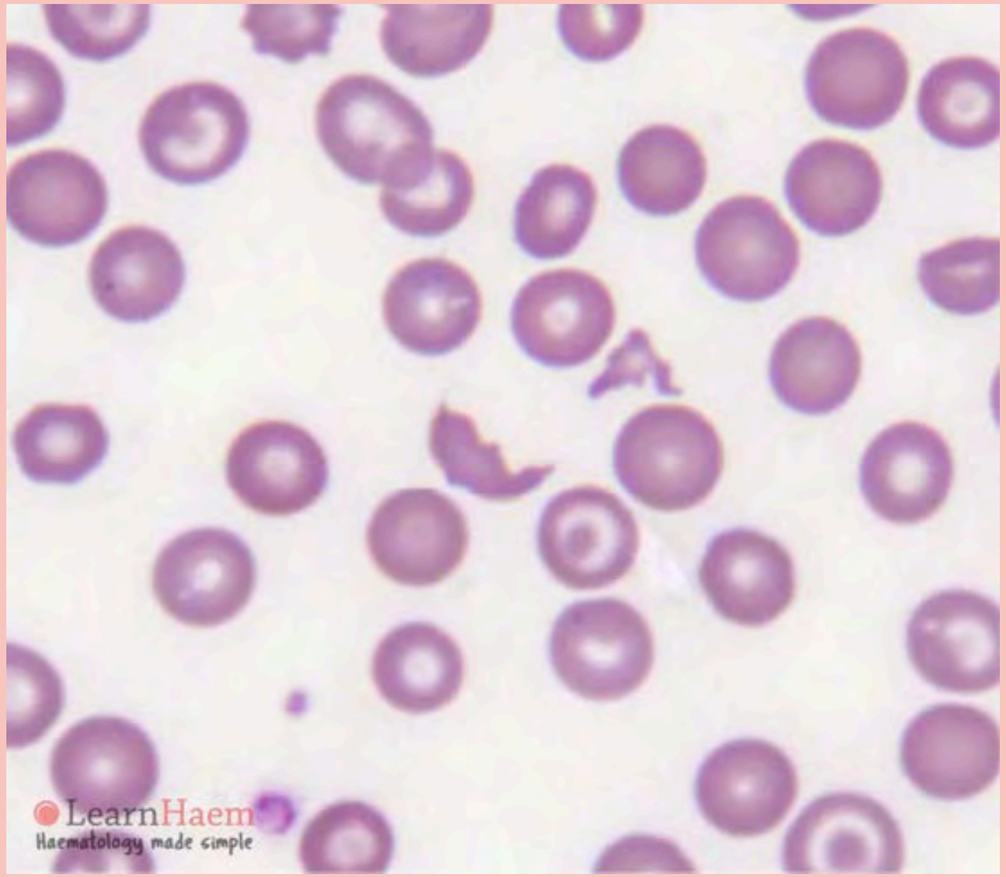
Normal protein created by the liver which gets mopped up when red cells are broken down.

Haptoglobin is usually undetectable in haemolysis



Spherocytes

Red cell fragments



CAUSES OF HAEMOLYSIS

DAT+ (immune - antibodies on outside of red cells)

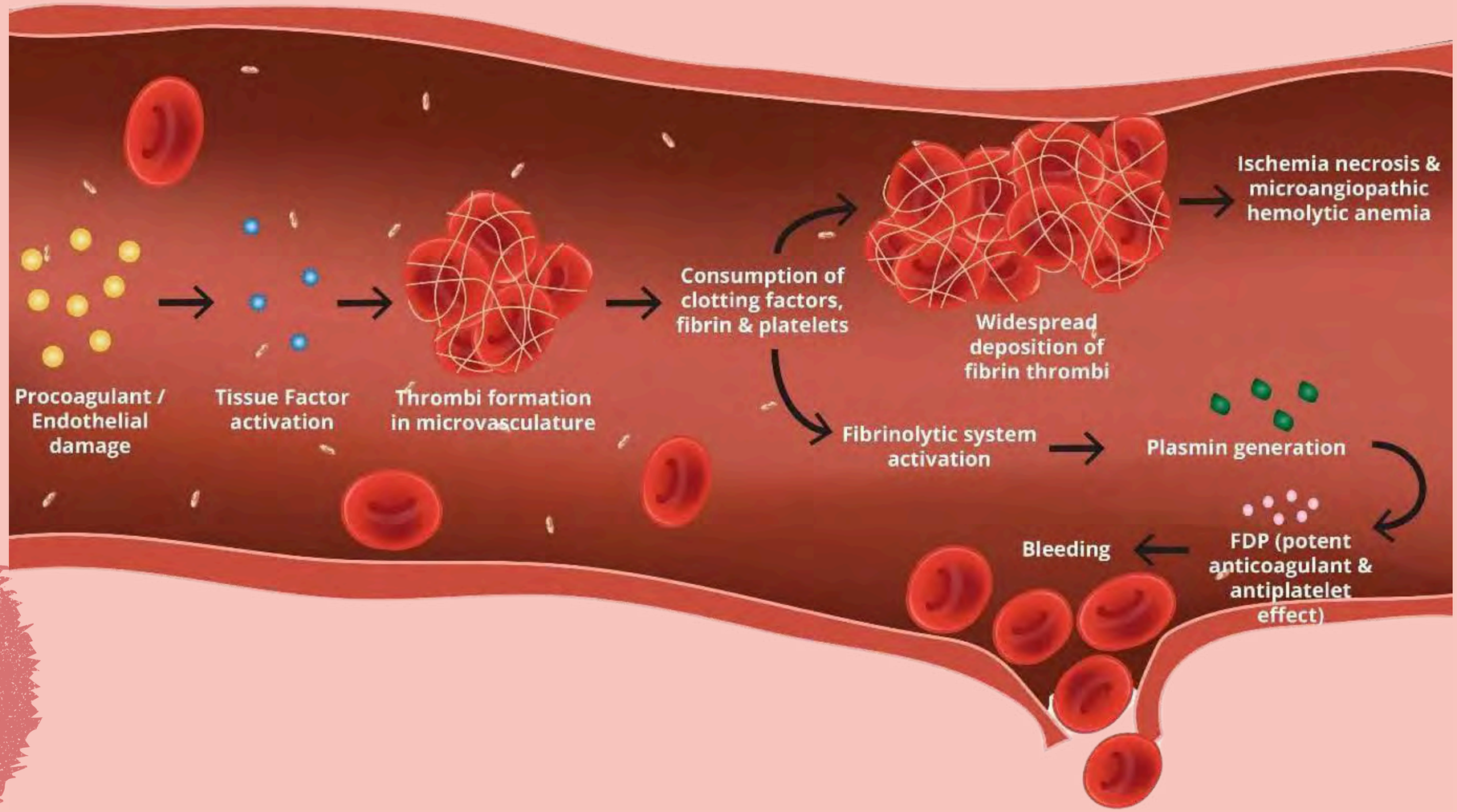
- Idiopathic
- Malignancy
- Drug induced
- Lymphoma
- Infection:
  - EBV
  - Mycoplasma infection

Transfusion reaction can also give DAT +

DAT- (non-immune - destroyed for other reasons)

- Sickle cell disease
- Membranopathies
- TTP
- Malaria
- DIC

DISSEMINATED INTRAVASCULAR COAGULATION – EXAMPLE OF NON-IMMUNE HAEMOLYSIS



CASE THREE:

41 year old man with pneumonia is found to be anaemic.

Appears jaundiced on examination.

Value	Result	Normal range
Anti-IgG	**POSITIVE (1+)**	
Anti-C3d	**POSITIVE (4+)**	
Haptoglobin	**<0.15**	0.4 - 1.6
Lactate dehydrogenase	**1589**	<250
Reticulocyte count	**148**	50 - 100

CASE FOUR:

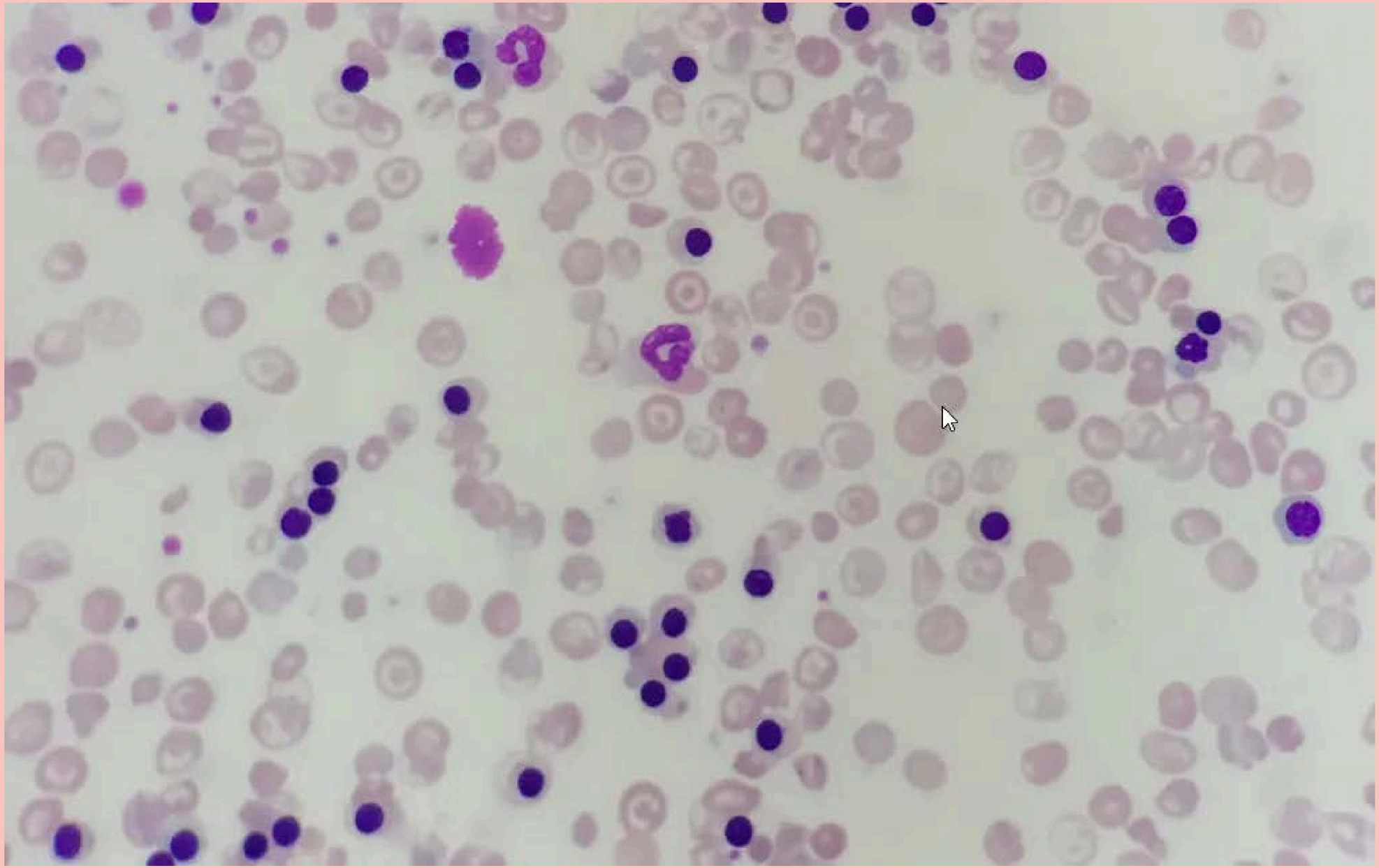
32 year old lady attends for a blood transfusion.

Her routine bloods prior to the appointment are below.

Thoughts?

Scan the QR code

Value	Result	Normal range
RBC	**2.80**	3.80 - 5.30
Haemoglobin	**70**	120 - 160
Haematocrit	**0.259**	0.36 - 0.46
MCV	**81.2**	83 - 100
MCH	**21.9**	27.0 - 32.0
MCHC	**270**	310 - 350
Platelets	**459**	150 - 400
RDW	**32.7**	11.5 - 15.5

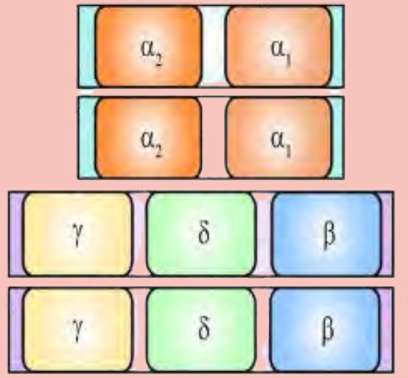


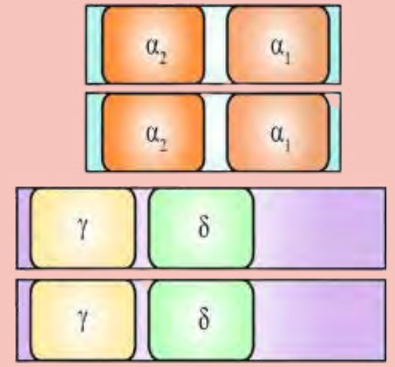
THALASSAEMIA

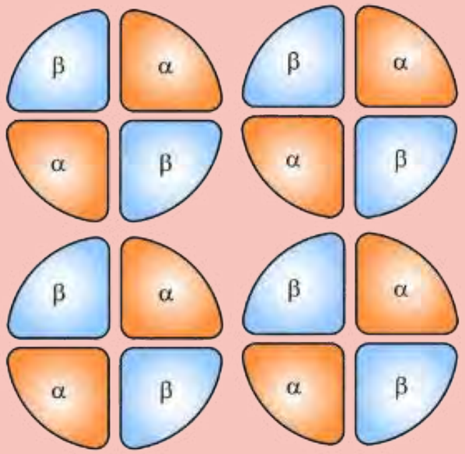
Thalassaemia is a haemoglobinopathy.

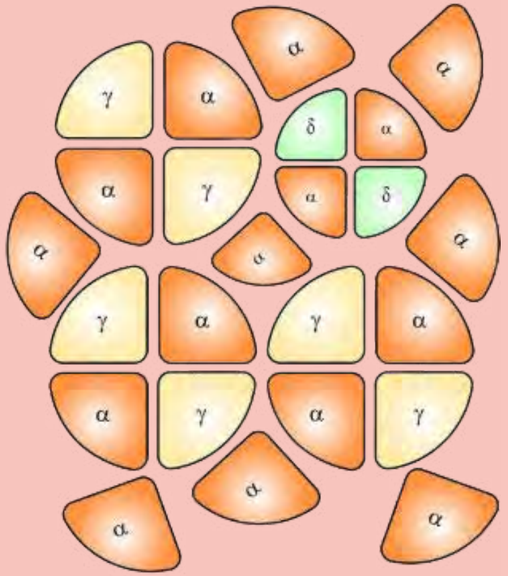
Refers to a difficulty or inability in making globin chains due to a genetic problem.

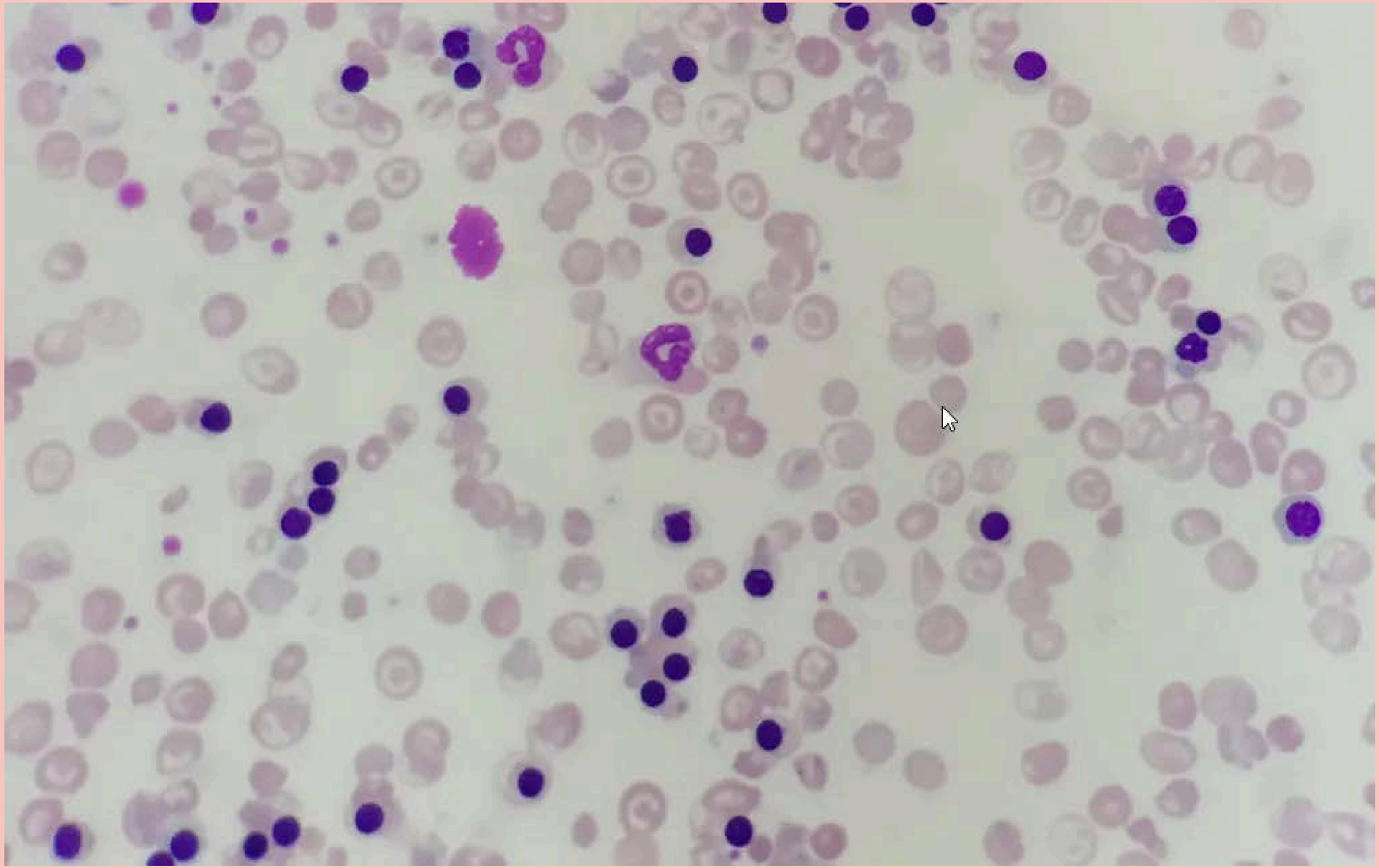
Alpha thalassaemia - alpha chains
Beta thalassaemia - beta chains



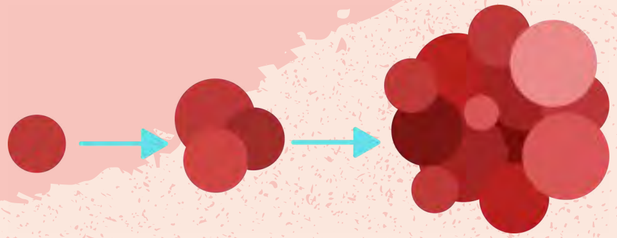








WHAT HAPPENS IN THALASSAEMIA?



Extramedullary haematopoesis ensues to try to improve anaemia

The body desperately tries to compensate for the anaemia by absorbing more iron, leading to **iron overload.**

TREATMENT OF THALASSAEMIA

Transfusion is the mainstay of treatment, aiming for a haemoglobin of over 100.

As this introduces more iron, all patients will require **iron chelation.**

Iron overload can cause many issues including faltering growth, endocrine dysfunction and cardiac failure if not managed.

SUMMARY

- Anaemia can be related to having a low number of red cells or a problem creating haemoglobin
- Haemoglobinopathies are genetic conditions which cause significant morbidity and mortality
- Haemolysis can happen for immune and non-immune reasons
- Hopefully you are now confident in interpreting a FBC! :)