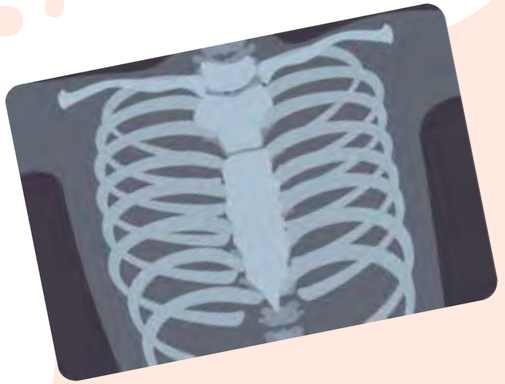
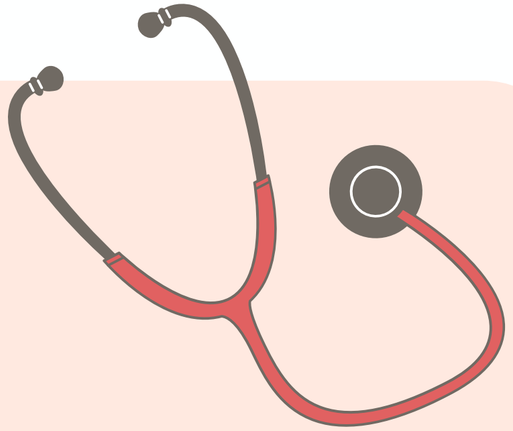
HAEMOGLOBINOPATHY EMERGENCIES FOR PAEDIATRICS



Dr Amy Cooper - Haemoglobinopathy QI Fellow
Dr Jemma Say - Paediatric Consultant



Today we will cover

What are haemoglobinopathies?

- Basic science underlying conditions
- How to apply this knowledge in understanding the management of the conditions

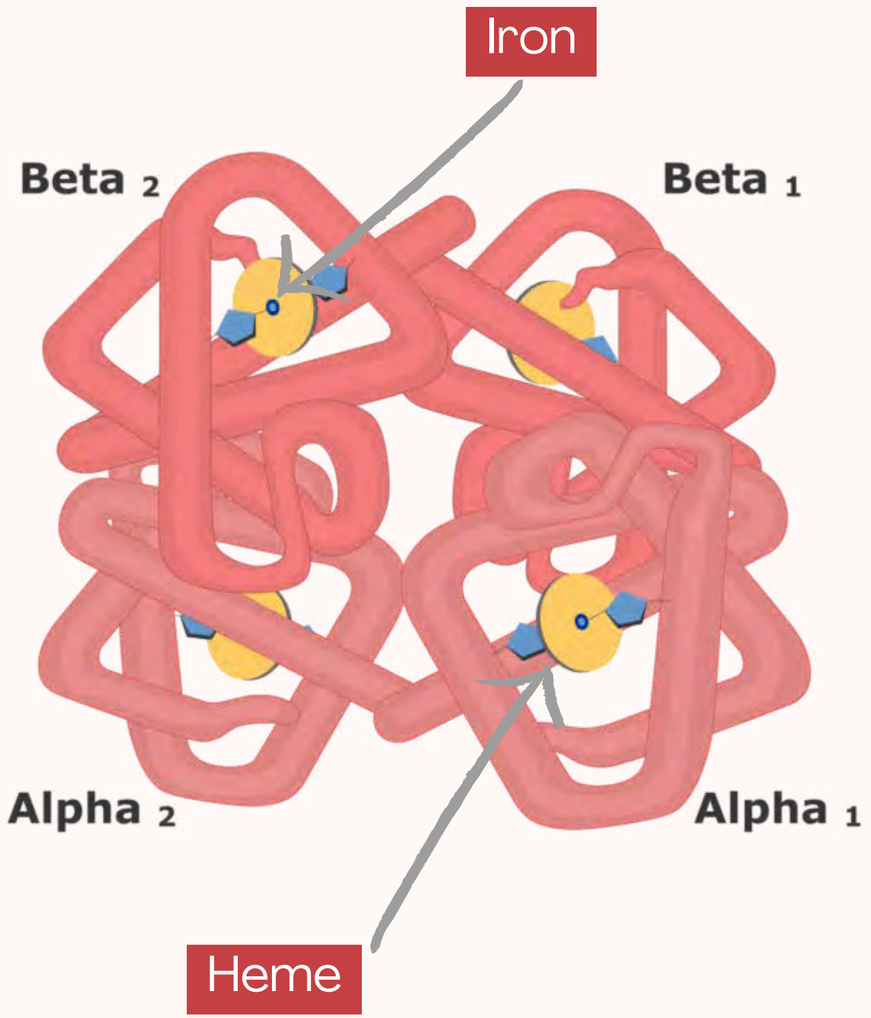
What complications of haemoglobinopathies can you see in the emergency department?

- Sickle cell disease
- Thalassaemia

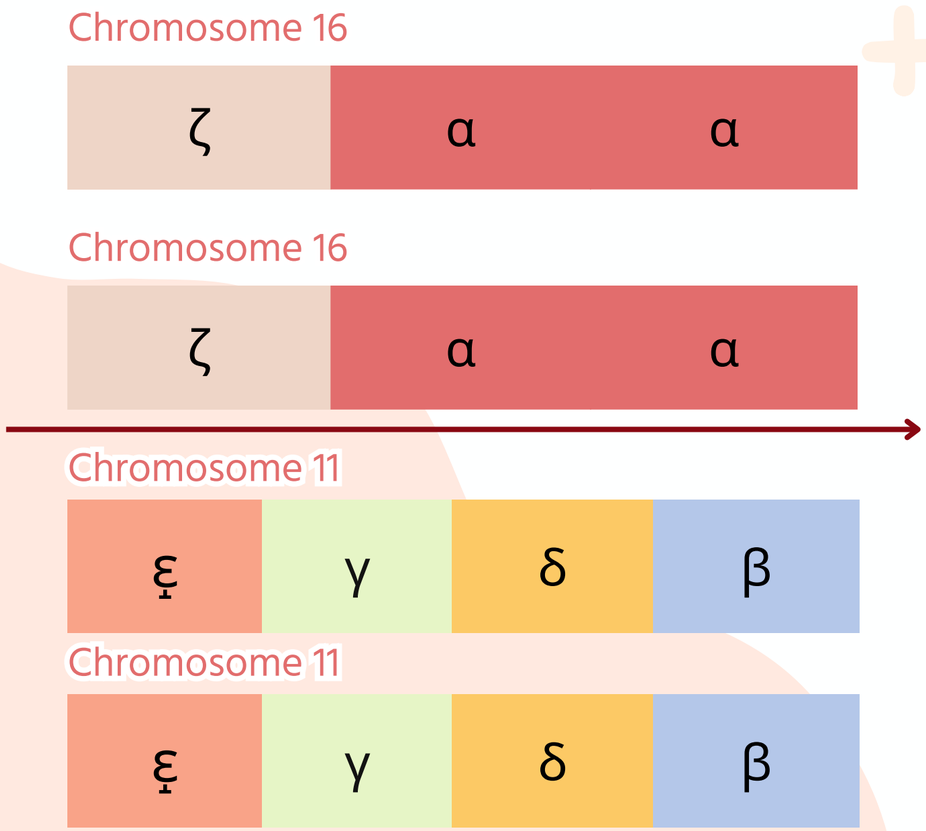
HAEMOGLOBIN

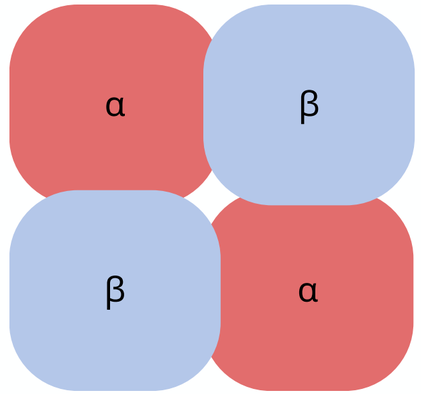
- Consists of two alpha and two beta globin chains
- Heme sits inside the globin chain and holds one iron molecule (4 per haemoglobin)
- The iron molecule reversibly binds oxygen (allowing it to carry and give up the O2 molecule)

Reminder - this is what Hb measures!

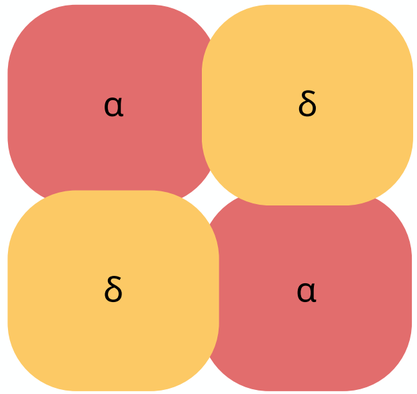


NORMAL HAEMOGLOBIN SYNTHESIS

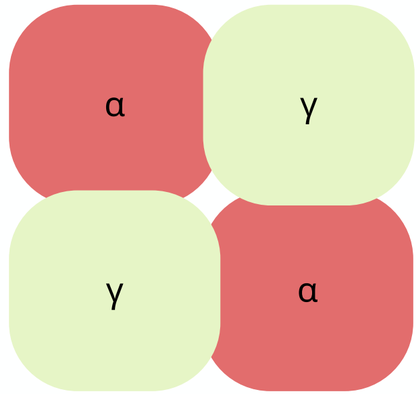




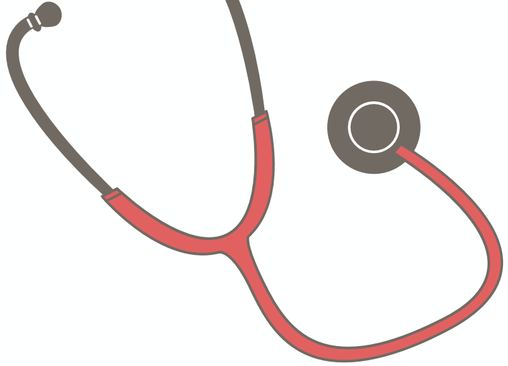
HbA



HbA2



HbF



HOW CAN HAEMOGLOBIN SYNTHESIS GO WRONG

Structural abnormalities

Haemoglobin is made, but the structure is different to normal haemoglobin due to a genetic mutation (usually affecting the beta gene). Examples include:

- HbS
- HbC

Abnormalities in haemoglobin production

Mutations in alpha or beta genes reduce the production in alpha or beta chains. This reduces the amount of normal haemoglobin. These conditions are called thalassaemias.

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HBSS SICKLE CELL DISEASE

Chromosome 16

ζ	α	α

Chromosome 16

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Chromosome 11

ε	γ	δ	βS

Chromosome 11

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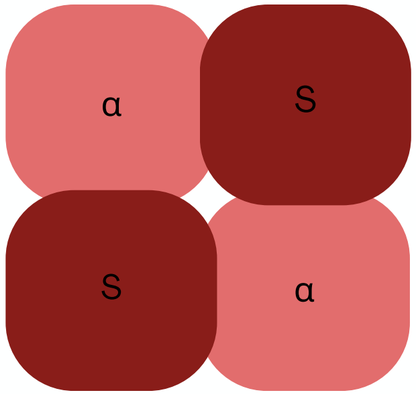
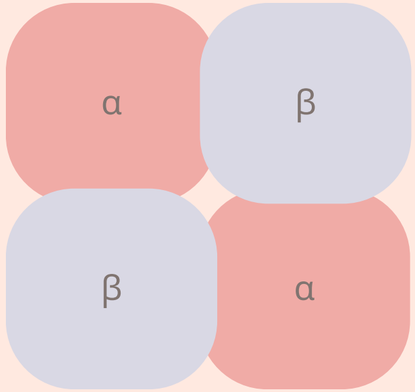
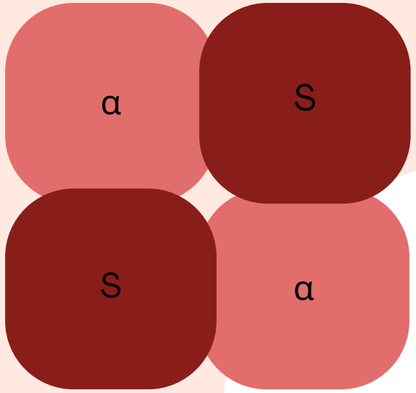


HbS

SICKLE CELL DISEASE (HBSS)

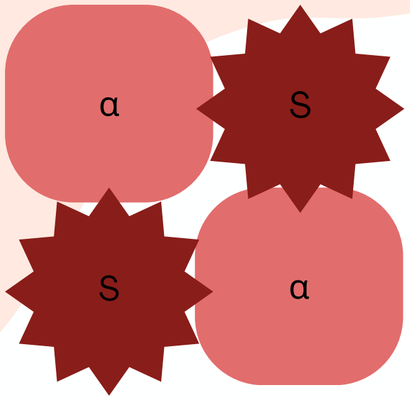


HbA

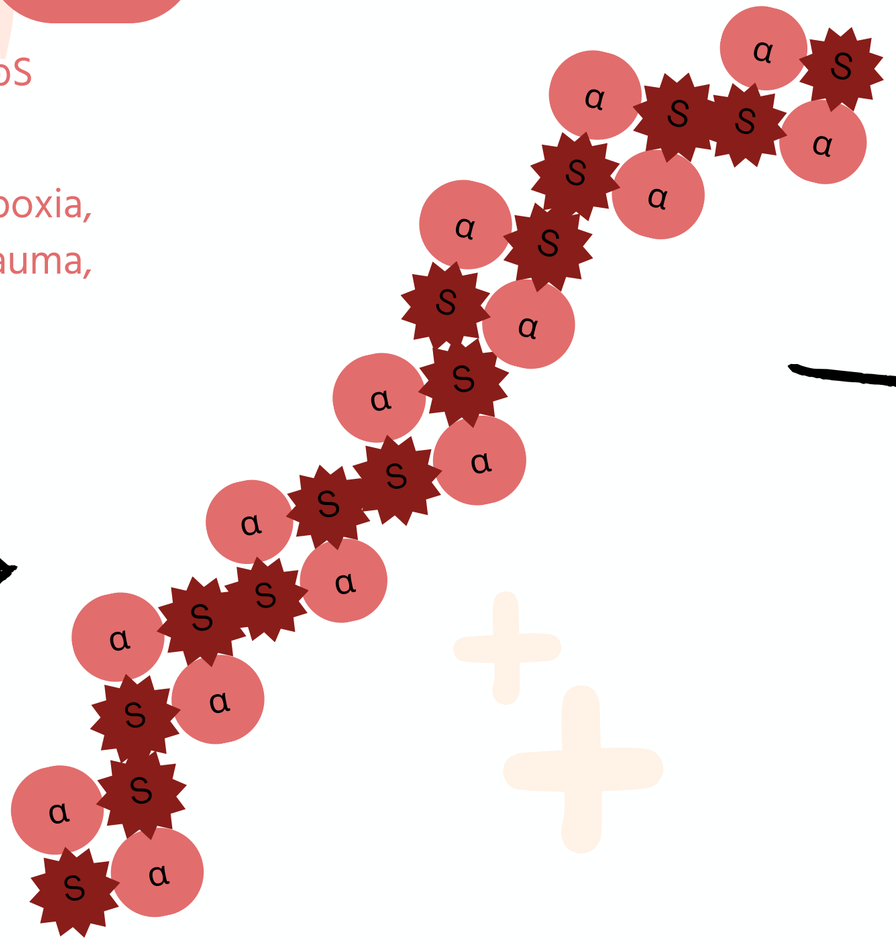


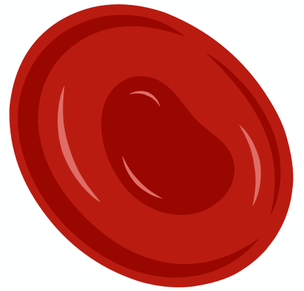
HbS

Stress (e.g. hypoxia, infection, trauma, cold exposure)

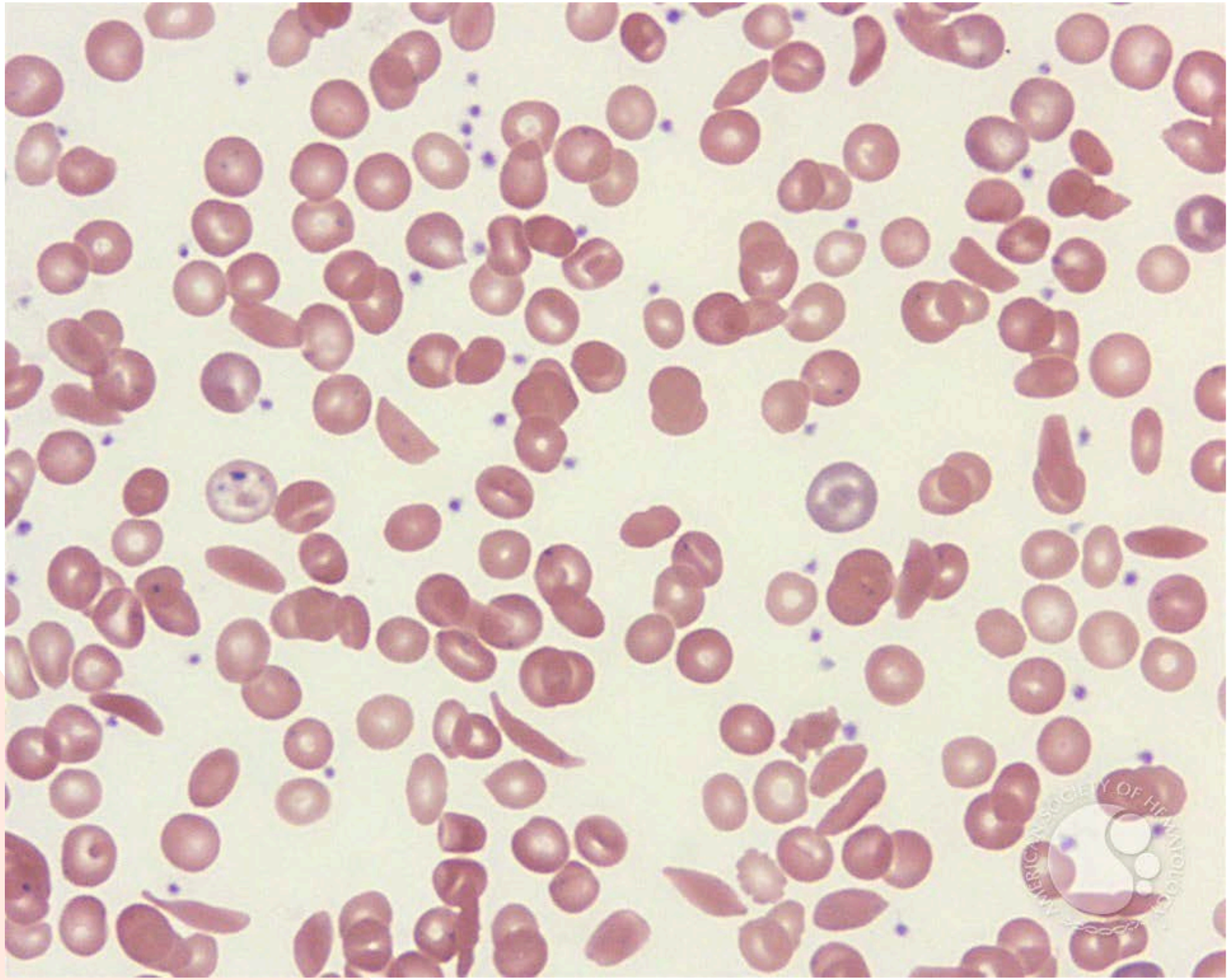


Polymerisation

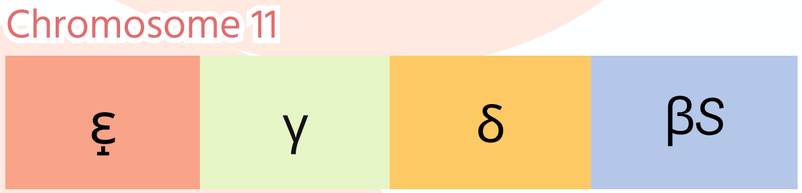


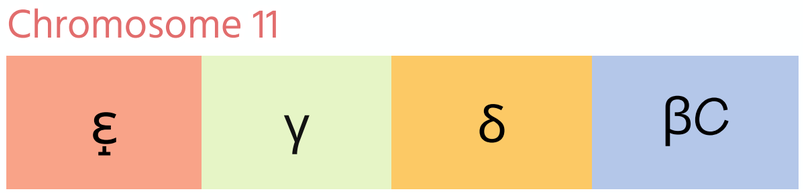


Sickling

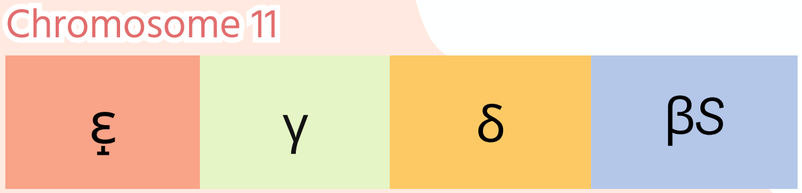


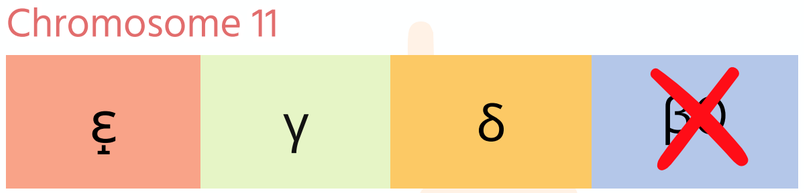
OTHER TYPES OF SICKLE CELL DISEASE





= HbSC disease





= HbS/beta thalassaemia

WHAT DO SICKLED CELLS DO IN THE BODY?

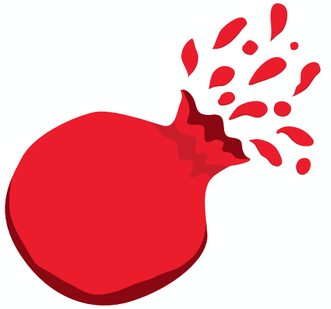
Vaso-occlusion

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.

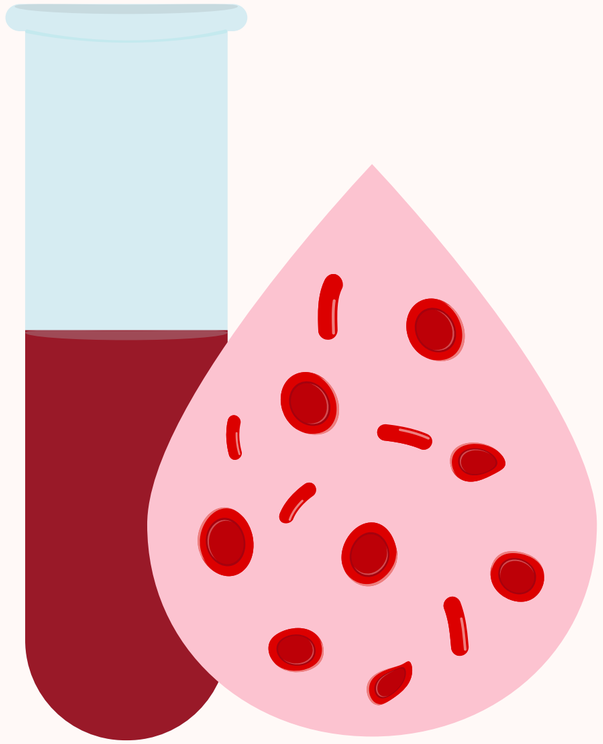
Haemolysis causes local vascular damage and promotes systemic inflammation

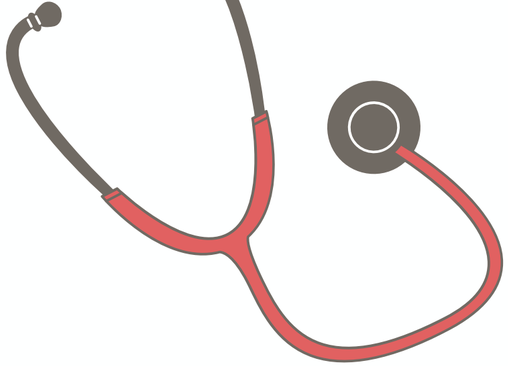


A NOTE ON ANAEMIA

- Patients with sickle cell disease have been anaemic since birth
- Able to tolerate anaemia with minimal side effects
- Usual Hb can range from 50-90 with HbSS, and 90-120 with HbSC

Anaemia without symptoms does not usually require blood transfusion





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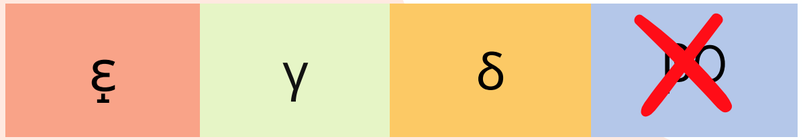
BETA THALASSAEMIA MAJOR

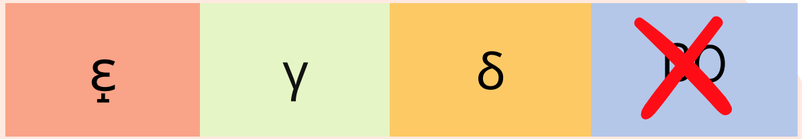
Chromosome 16

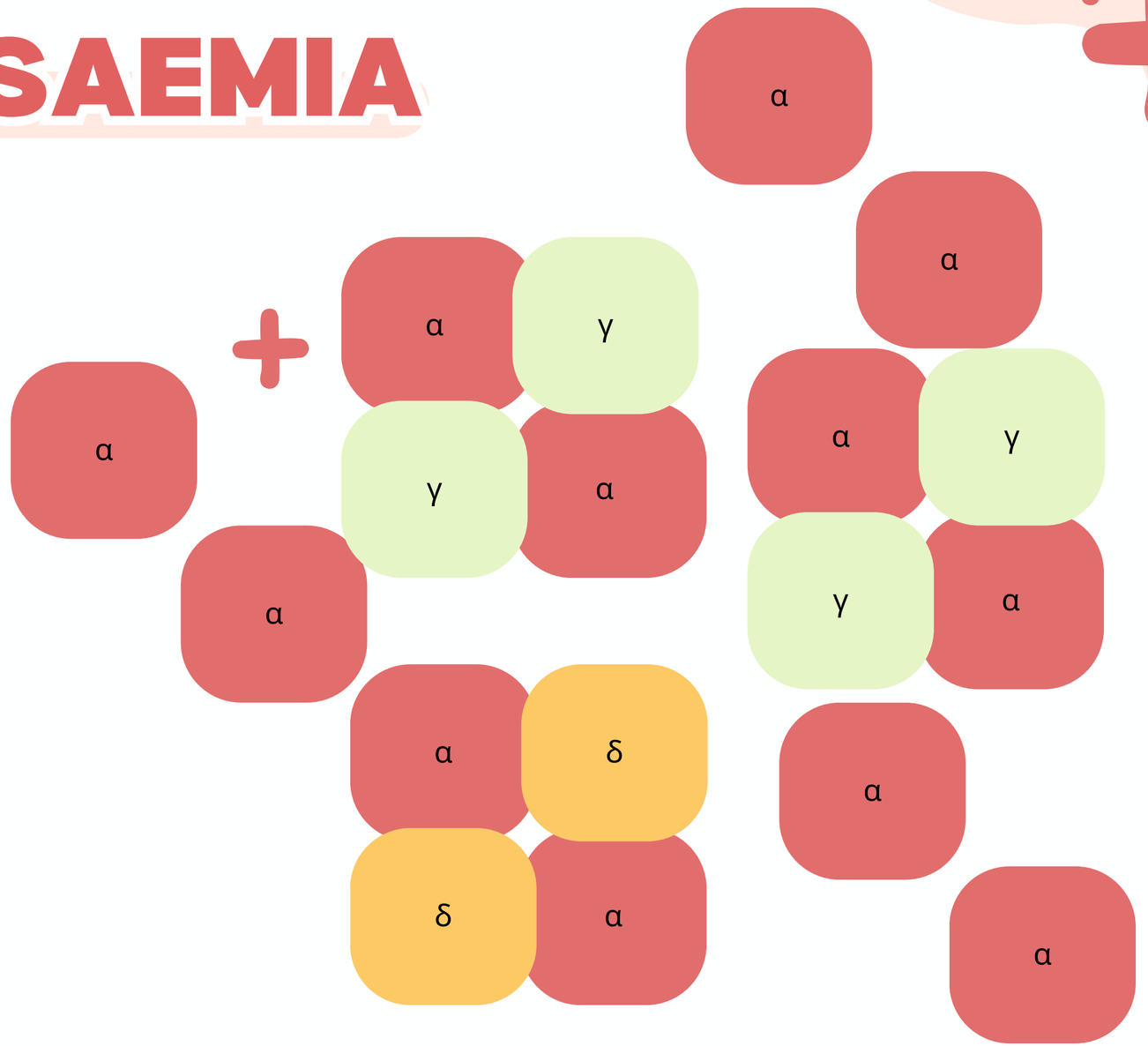
Chromosome 16

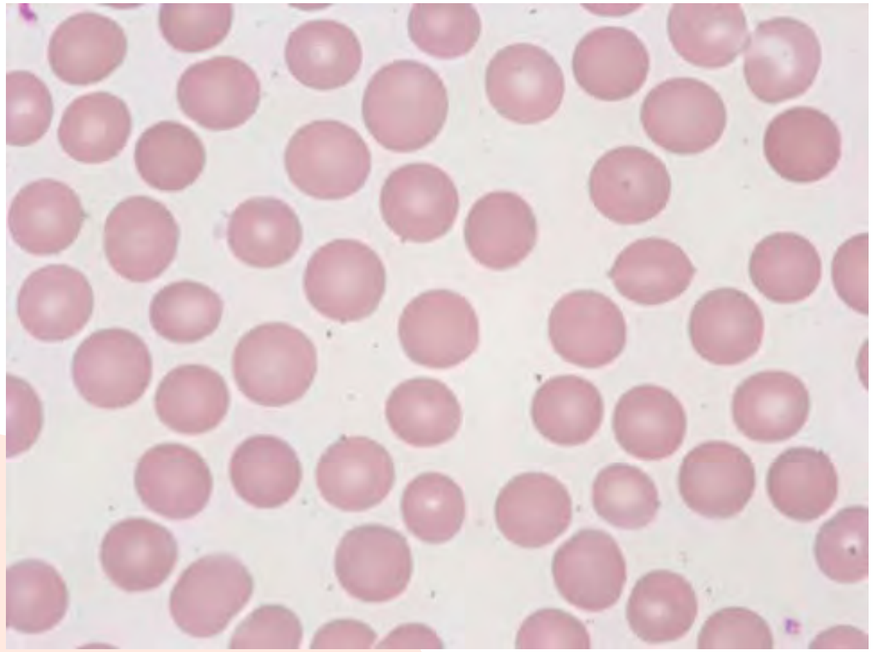
Chromosome 11



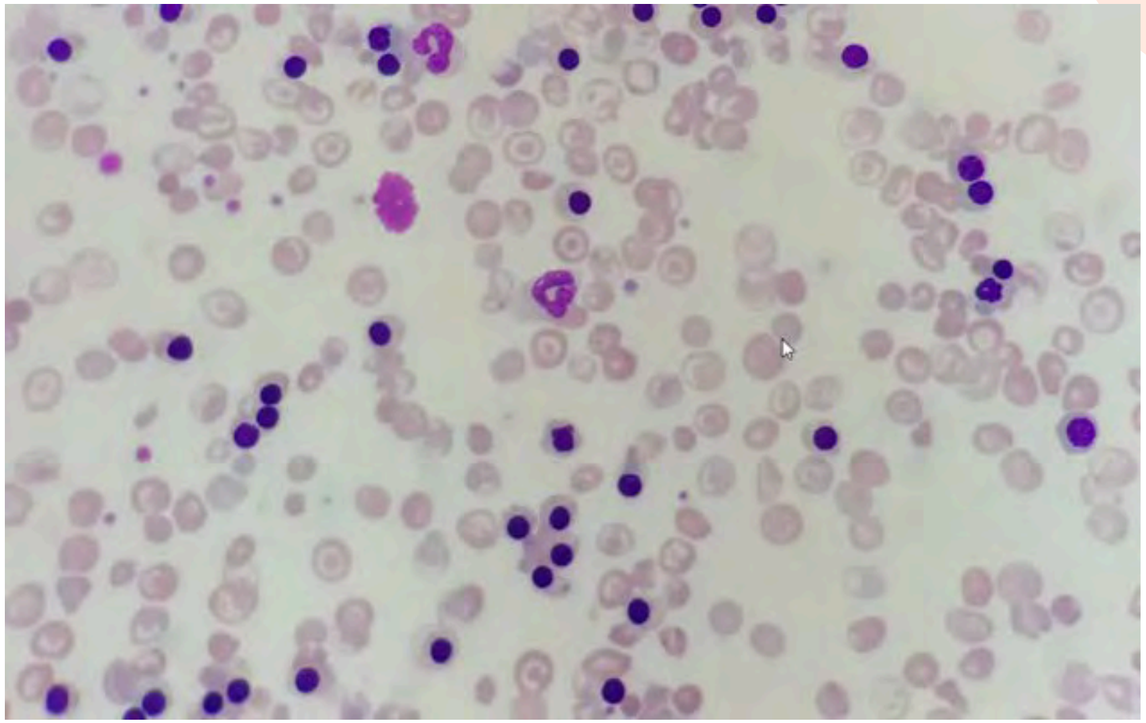
Chromosome 11





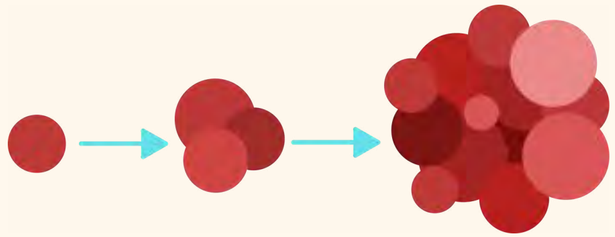


Normal



Thalassaemia major

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 is with regular blood transfusion and iron chelation

HBSS SICKLE CELL DISEASE

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ζ	α	α

Chromosome 16

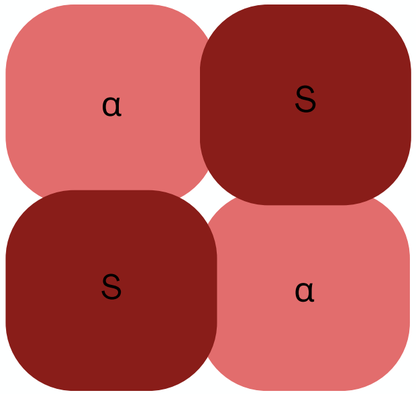
ζ	α	α

Chromosome 11

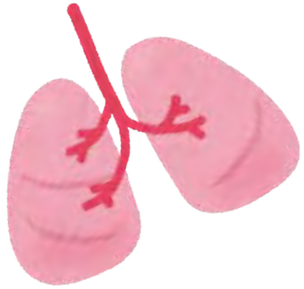
ε	γ	δ	βS

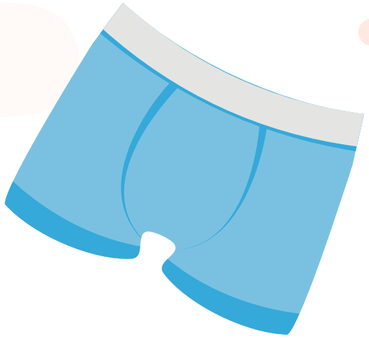
Chromosome 11

ε	γ	δ	βS

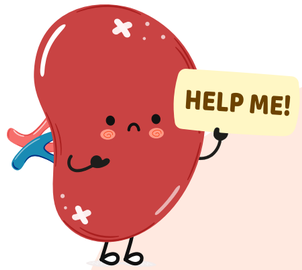


HbS





ACUTE COMPLICATIONS



This teenage girl with sickle cell disease has arrived to ED saying he has 8/10 pain in his right leg after playing netball in school yesterday.

What's going on?

ACUTE PAINFUL CRISIS

Mechanism

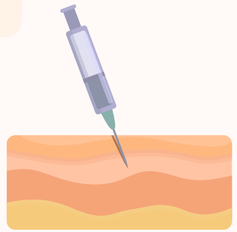
An acute insult (e.g. cold, infection, hypoxia, trauma) prompts red cells to sickle and cause vaso-occlusion. This leads to ischaemia and acute **severe** pain.

Most common sites

Can happen in any bone, but most common in limbs, back, ribcage/sternum.

Type of pain

Pain is related to acute ischaemia and is excruciatingly painful. Listen to your patient and treat appropriately. Patients may not show their pain as you would expect.



Parenteral or intranasal analgesia **within 15 minutes** of presentation for moderate to severe pain

Closely monitor observations, early warning score and pain score

Monitor for sedation while using opiates

Early discussion with paediatric haematology team (can discuss with BRCH if necessary)

ANALGESIA CHOICE

Analgesic Ladder

Paracetamol/ Ibuprofen (if not already administered)

↓

Tramadol + Paracetamol + Ibuprofen

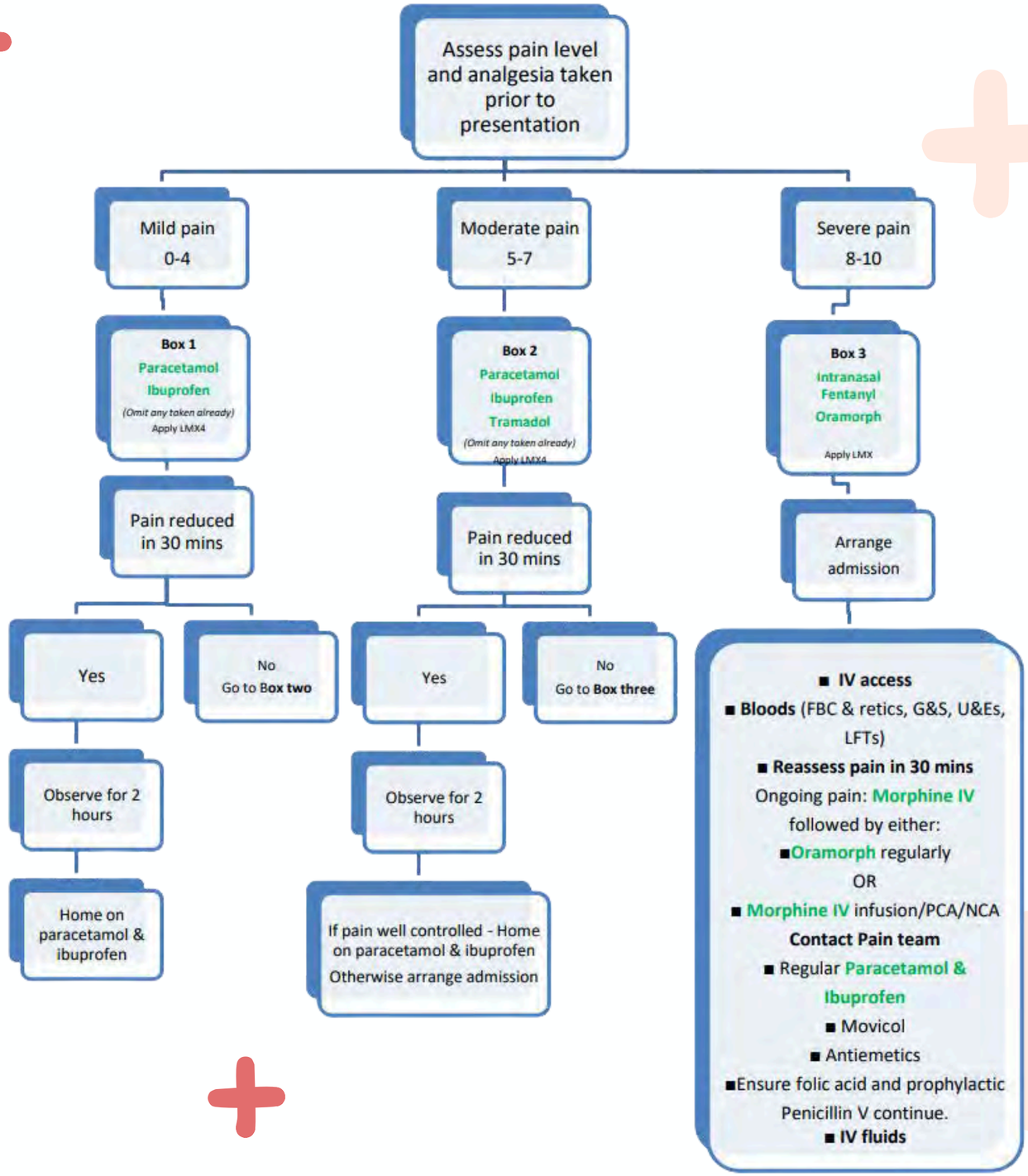
↓

Morphine (oral or intravenous) + Paracetamol + Ibuprofen

Severe Pain

The **drug of choice is MORPHINE**, given either orally or, if oral route not possible (vomiting, refusal, severe pain), intravenously by patient controlled analgesia (PCA). As per the analgesic ladder, this is given regularly in addition to Paracetamol and Ibuprofen.

If pain is severe, whilst establishing intravenous access give **intranasal fentanyl**.



SUPPORTIVE MEDICATION

Antiemetics

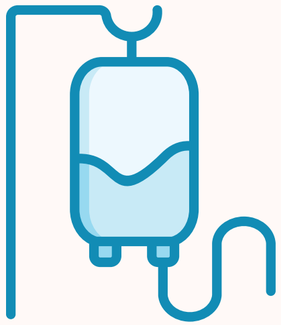
Laxatives

Prophylactic medications

Antipruritic

Naloxone

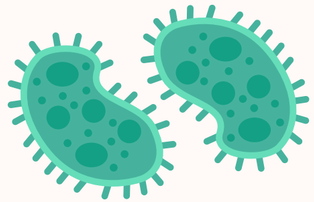
OTHER CONSIDERATIONS



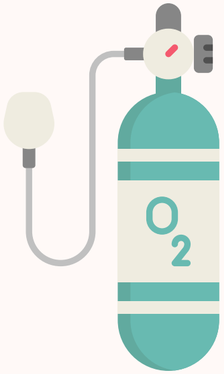
IV fluids and input/output monitoring

Look for dactylitis

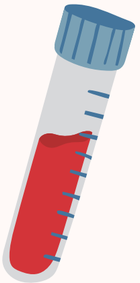
CXR if chest pain or O2 requirement



Low threshold for antibiotics to cover encapsulated/atypical organisms and septic screen



Give supplementary oxygen if O2 sats <95%



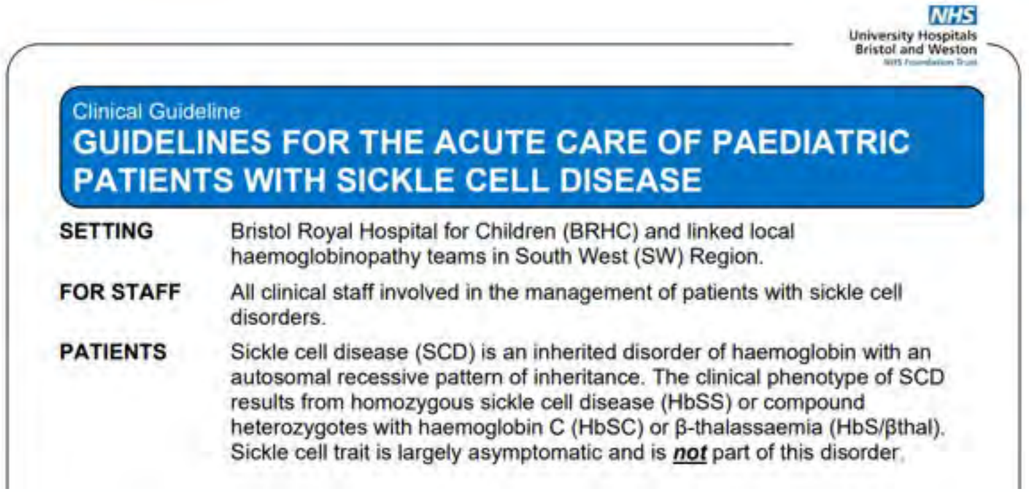
Send bloods including group and screen and haemoglobinopathy screen

OTHER CONSIDERATIONS

“Should I X-ray the painful limb?”

- Not really helpful in diagnosing simple pain crisis
- Consider if clear non-sickle related indication e.g. concern for fracture
- If persistent pain despite analgesia and fever/raised CRP - consider X-ray (but MRI better for osteomyelitis)

ACUTE MANAGEMENT GUIDELINES

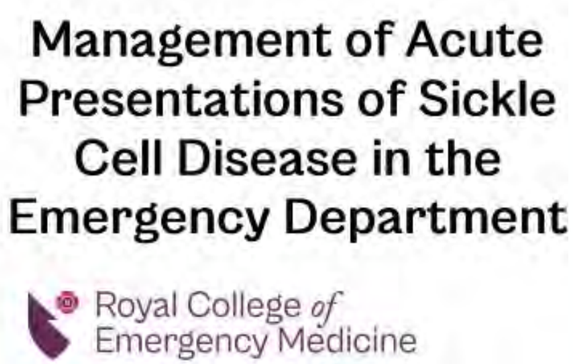


NHS
University Hospitals Bristol and Weston
NHS Foundation Trust

Clinical Guideline

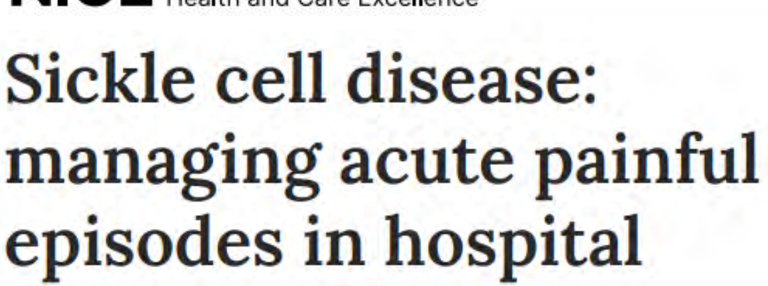
GUIDELINES FOR THE ACUTE CARE OF PAEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

SETTING	Bristol Royal Hospital for Children (BRHC) and linked local haemoglobinopathy teams in South West (SW) Region.
FOR STAFF	All clinical staff involved in the management of patients with sickle cell disorders.
PATIENTS	Sickle cell disease (SCD) is an inherited disorder of haemoglobin with an autosomal recessive pattern of inheritance. The clinical phenotype of SCD results from homozygous sickle cell disease (HbSS) or compound heterozygotes with haemoglobin C (HbSC) or β-thalassaemia (HbS/βthal). Sickle cell trait is largely asymptomatic and is ***not*** part of this disorder.



Management of Acute Presentations of Sickle Cell Disease in the Emergency Department

Royal College *of* Emergency Medicine



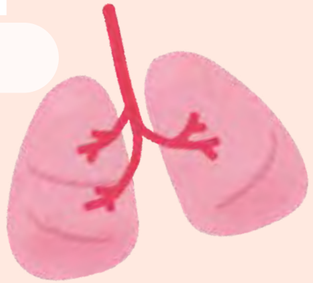
NICE National Institute for Health and Care Excellence

Sickle cell disease: managing acute painful episodes in hospital

My patient with sickle cell disease has been an inpatient for 2 days, unwell with fevers and all over body and chest pain. Their sats have deteriorated to 91% on room air and they have a fever.

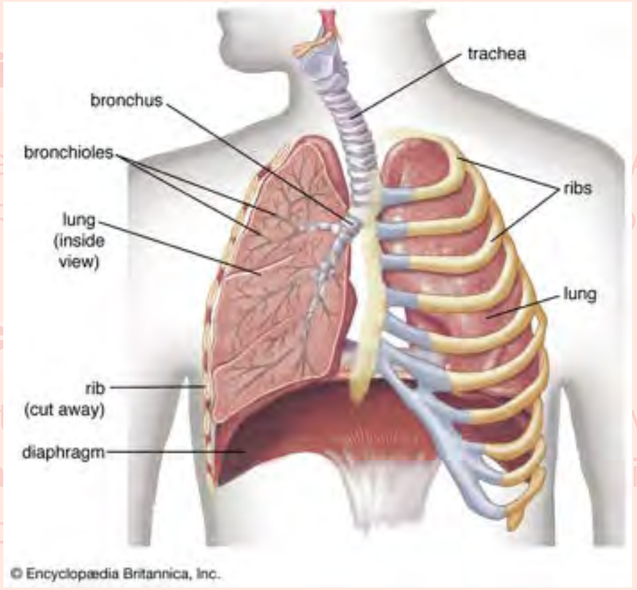
What could this be?

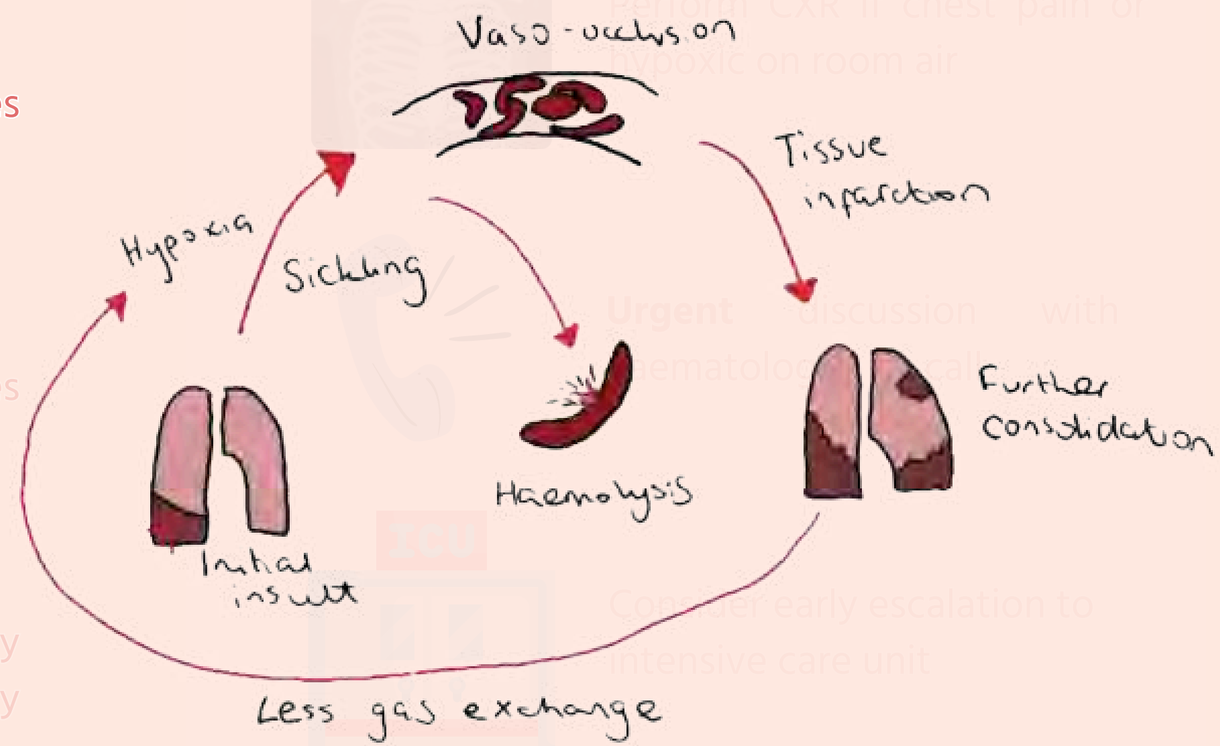
ACUTE CHEST SYNDROME



Mechanism

An acute insult on the lung prompts hypoxia, which causes sickling, which leads to more hypoxia, which leads to sickling...





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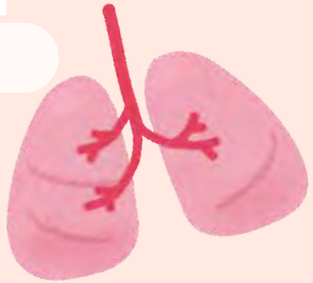

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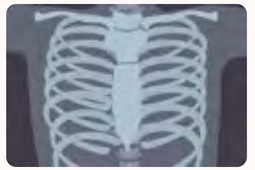
Definition

The definition of acute chest syndrome (ACS) is new infiltrates on CXR with fever and/or respiratory symptoms.

Clinical presentation

Patients may appear well at first but have an escalating early warning score, oxygen requirement or pain. Potential to rapidly deteriorate

Give supplementary oxygen if oxygen saturations are <95% on air



Perform or repeat CXR if chest pain or hypoxic on room air

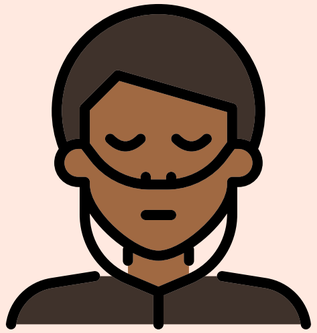
Urgent discussion with paediatric haematologist on call at BRCH

Consider early escalation to PICU and early transfer to Bristol

ACUTE CHEST SYNDROME - THE USUAL STORY

Day 1

Attended ED with back, leg and chest pain
Sats 99% on room air
CXR - clear
Looks very well



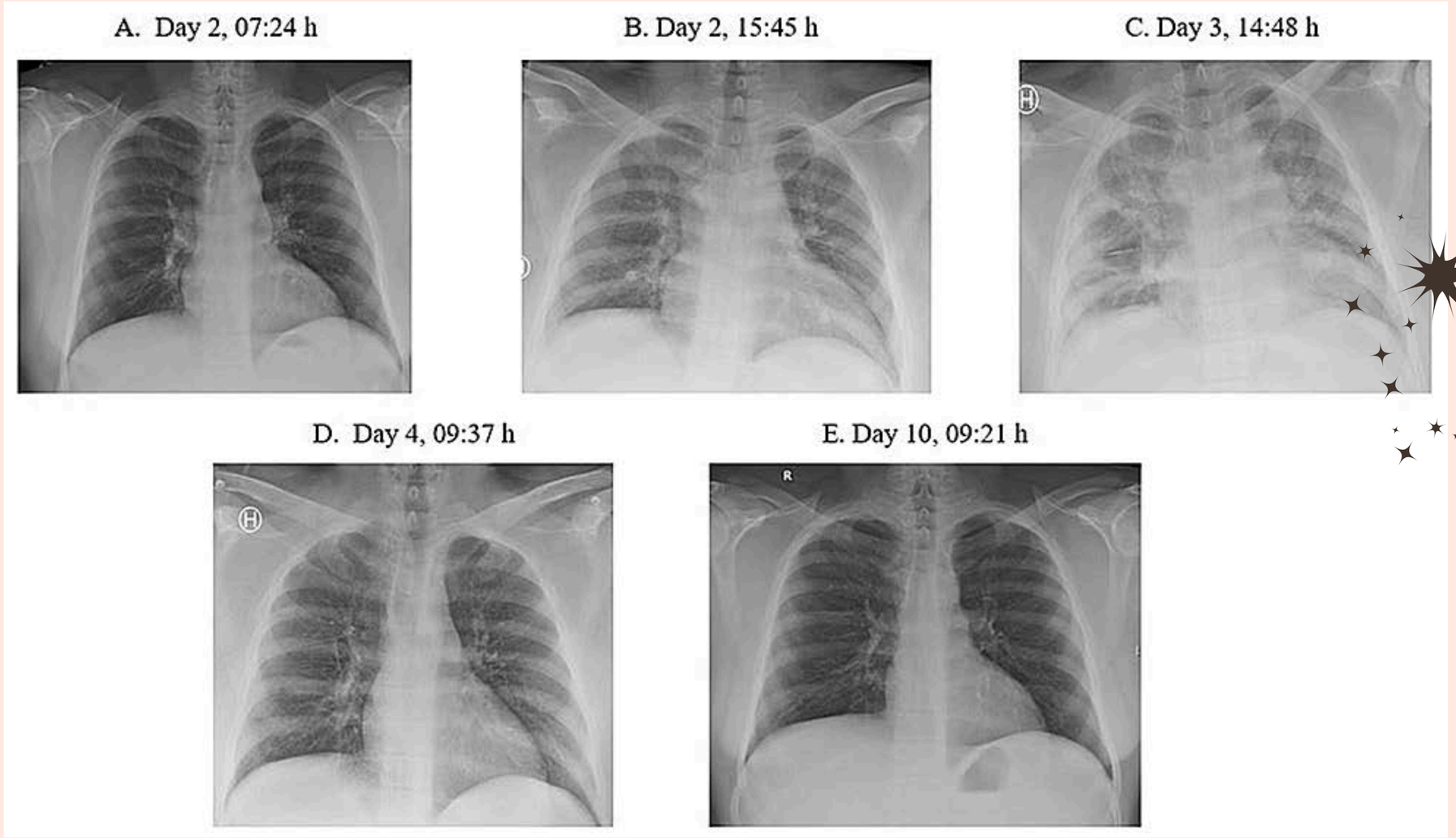
Day 2

New O2 requirement - 4L face mask
Chest pain settling slightly
New mild cough
Sats 91% on room air, 99% on 4L
CXR - bibasal atelectasis

Day 3

Found with dropped GCS next morning
Sats 85% on 4L O2 - put on 15L non-rebreathe
Transferred to PICU
CXR - left basal consolidation

ACUTE CHEST SYNDROME - THE USUAL STORY



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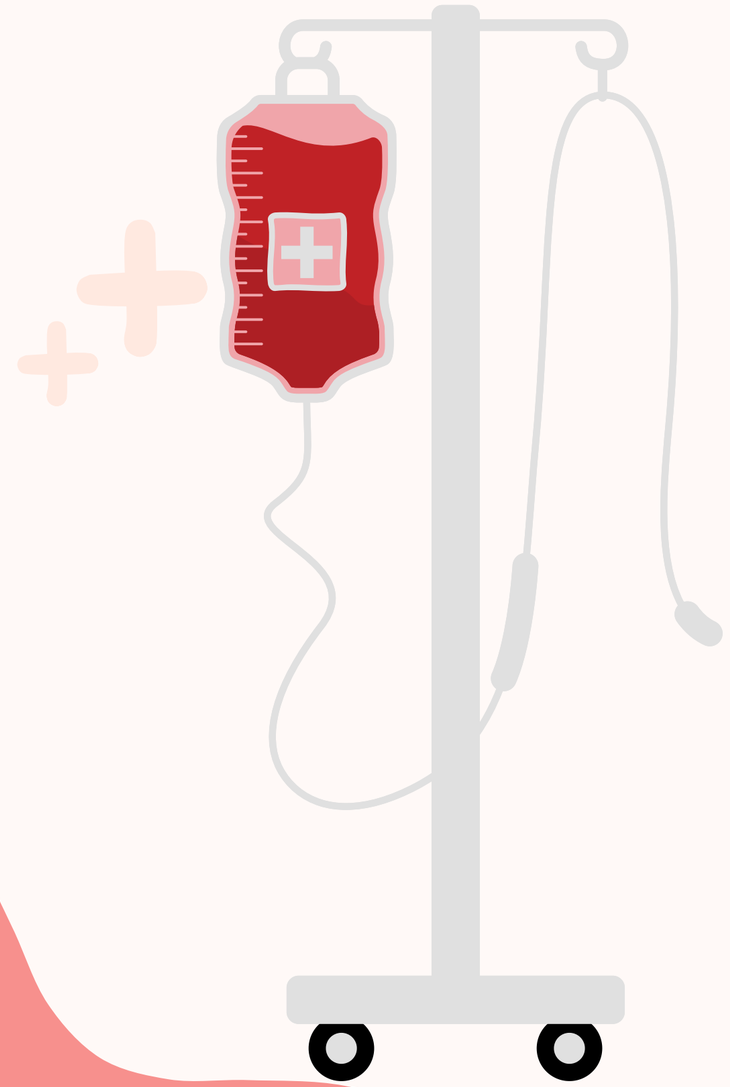

MANAGEMENT OF ACUTE CHEST SYNDROME

Initially:

- Supplementary oxygen
- Adequate analgesia but avoiding sedation
- Incentive spirometry/bubble PEP
- Treatment of underlying cause (e.g. antibiotics)

If deteriorating or very unwell:

- Likely to consider blood transfusion - top up or exchange
  - This is a **PAEDIATRIC HAEMATOLOGY CONSULTANT DECISION**

PRIAPISM

Mechanism

The venous drainage from the penis becomes dysfunctional due to nitric oxide depletion and sickling. Trapped blood causes pain like compartment syndrome. This is a very common complication in adolescent and young adult males.

Types of priapism

Stuttering priapism: recurrent episodes last for less than 4 hours and self-resolve. Penis may not be fully erect. Can precede fulminant priapism

Fulminant priapism: Fully erect penis with soft glans. Severely painful and lasting >4 hours.

Aims of treatment

Treatment aims to preserve erectile function. Significant damage can start to occur at around 6 hours.

Patient will have already tried conservative measures - warm bath, exercise, simple analgesia

Urgent discussion with both haematology and **urology** teams

Hyper-hydration can be helpful as a conservative measure

Needle drainage may be required to achieve resolution

SICKLE CELL SOCIETY

PRIAPISM
A SIMPLE GUIDE

Boston Scientific
Advancing science for life™

*supported by a non-conditional educational grant from Boston Scientific

NHS
Guy's and St Thomas'
NHS Foundation Trust

NHS
University Hospitals Bristol and Weston
NHS Foundation Trust

Patient information service
Bristol Royal Hospital for Children

Priapism associated with sickle cell disease

How do patients manage their priapism at home?

Many patients have developed different strategies for dealing with their own priapism.

Helpful strategies for dealing with priapism include drinking water, taking painkillers, heat packs and the application of warm water to the penis.

Exercise such as doing squats, jogging, cycling or running up and down stairs can resolve a priapism attack.

Emptying the bladder during the night to avoid early morning erections has been reported as a beneficial preventative measure in some cases.

Patients often report that the normal painkillers they use to treat their sickle cell crisis are not as effective in controlling the pain of priapism.

Before trying a strategy for managing your own priapism it might be helpful to discuss it with your sickle cell nurse or haematologist.

Treat a priapism as you would a normal sickle cell crisis including:

- Empty your bladder at night and immediately on waking to help you avoid early morning erections that might trigger your priapism.
- Try gentle exercise such as a walk. This may improve circulation blood and can help resolve your priapism.
- A warm bath or shower may help.

NHS
University Hospitals Bristol and Weston
NHS Foundation Trust

Patient information service
Bristol Royal Hospital for Children

Priapism in younger children with sickle cell disease

How can I help my child with their priapism attack?

- Your child should drink lots of extra fluid.
- Your child should do light exercises, such as running up and down stairs or squatting.
- If the priapism continues for more than 30 minutes please speak to the team or call the out of hours/children's emergency department on: 0117 342 8666. They may advise you to take paracetamol.
- A warm bath or shower may help.
- Don't apply ice or cold water to the penis as it may make it worse.
- Your child should empty their bladder at night and as soon as they wake up to help avoid early morning erections that might trigger priapism.
- If the penis remains erect for more than 2 hours **go to the emergency department immediately**

PRIAPISM

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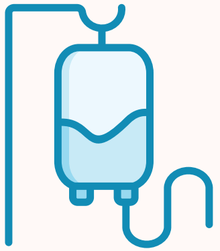

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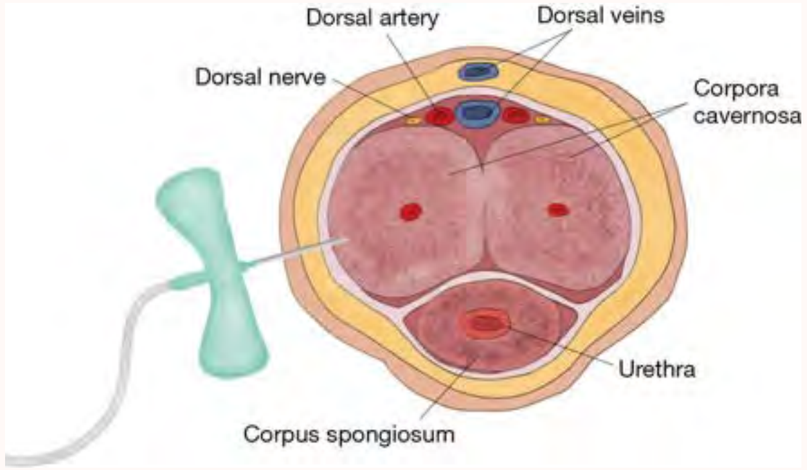
PRIAPISM - MANAGEMENT

Medical management



Needle aspiration +/- irrigation

T shunt procedure

My patient with sickle cell disease has presented with a history of new onset headache and ataxia this morning.

What do I need to do?

STROKE

Pathophysiology

Haemolysis causes local inflammation, increased endothelial adhesion, vasoconstriction, hypoxia, sickling and eventually ischaemic stroke

The odds are high

- 24% of patients with sickle cell disease have a stroke by age 45
- Children with SCD are 333 times more likely to develop a stroke
- Around half of patients with stroke will get a recurrent episode within 1-2 years without appropriate management

Ischaemic vs haemorrhagic

- Majority of strokes are ischaemic in children.
- Transcranial doppler (TCD) aims to identify those at risk early and prevent a stroke from occurring.
- Haemorrhagic stroke becomes more likely in late teenage years - Moya moya

Urgent discussion with haematologist and stroke/neurology clinician on call

Urgent MRI imaging (or CT to assess for haemorrhagic stroke if MRI not available) - keep NBM

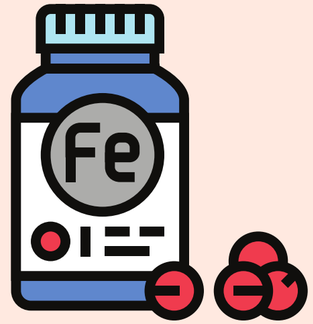
Red cell exchange transfusion can terminate the episode

Ensure other causes for stroke are considered within the differential diagnosis

ACUTE (ON CHRONIC) ANAEMIA

What should we look for?

ACUTE (ON CHRONIC) ANAEMIA

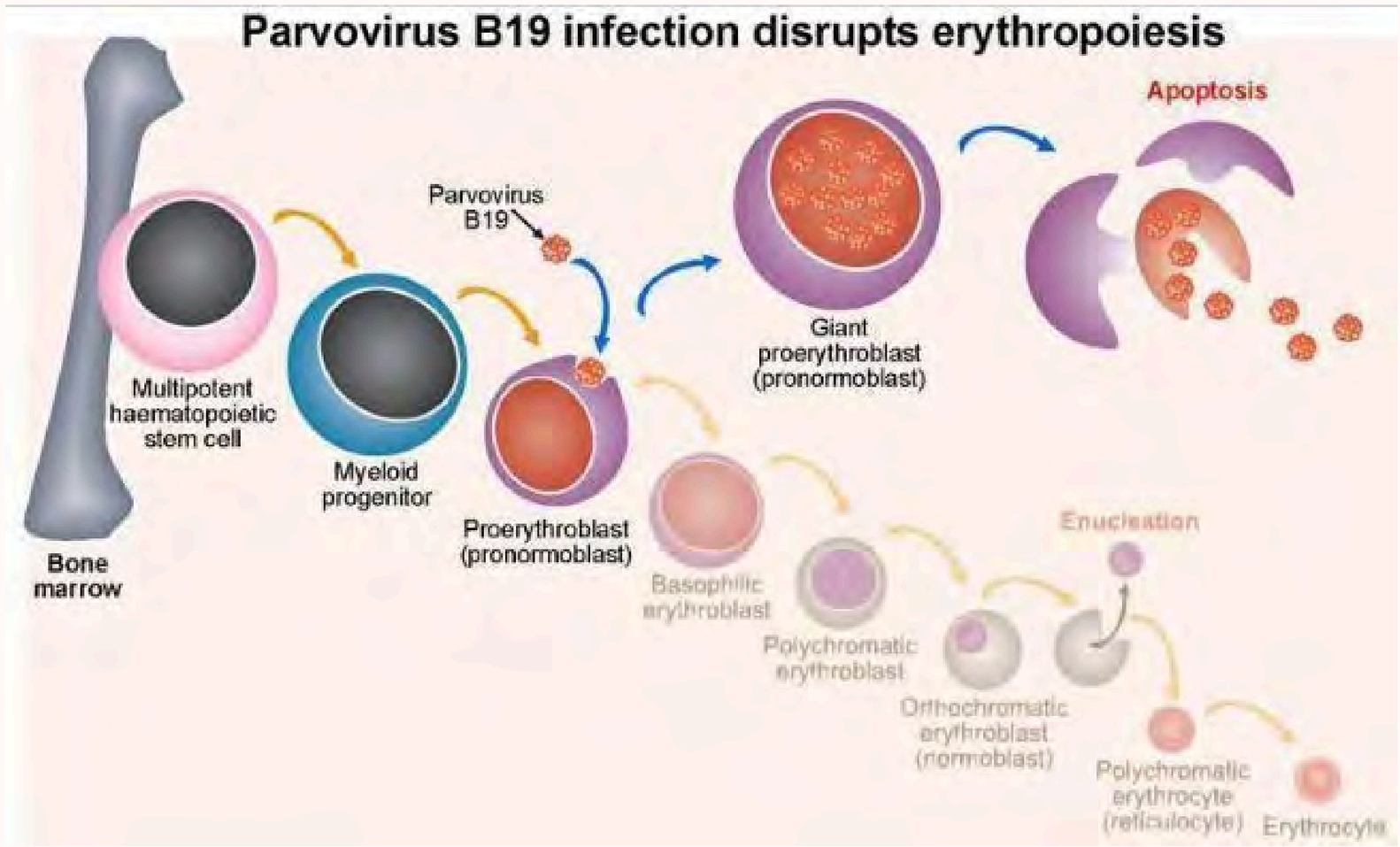


Shall I think of the usual culprits?

ACUTE (ON CHRONIC) ANAEMIA

Yes... but we also need to think outside of the box!

APLASTIC CRISIS - PARVOVIRUS



APLASTIC CRISIS - PARVOVIRUS

Fever

Respiratory symptoms

Headache

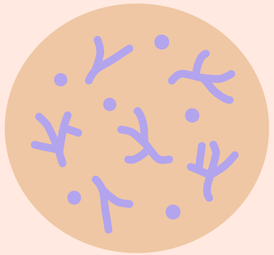
Classic ‘slapped cheek’ syndrome is uncommon

RBC	*	0.53	10^{12}/L	3.90 - 5.30
Haemoglobin	*	14	g/L	115 - 140
Haematocrit	*	0.048	L/L	0.34 - 0.40

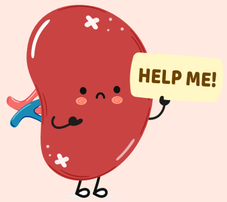
Reticulocyte count

On admission:	30
Baseline:	*257

Check the **reticulocyte count**!



Management - transfusion (on haematology advice)



SPLENIC SEQUESTRATION

Mechanism

The splenic sinusoids are a very hypoxic area. This makes red cells prone to sickling, which in turn can lead to a block in venous outflow and lead to blood being trapped (sequestered).

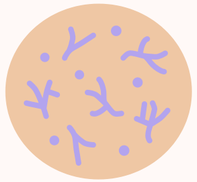
Presenting symptoms

Abdominal pain and a palpable spleen are the most common symptoms. Can present as shock/circulatory collapse given the reduction in circulating volume

Differentials

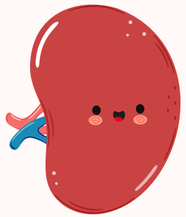
Other causes for abdominal pain include mesenteric syndrome, hepatic sequestration, gallstones. Don't forget common causes such as UTI or constipation

Urgent discussion with paediatric haematology team



Check reticulocyte count - would expect this to be raised

Cautious transfusion to steady state haemoglobin - **AVOID OVER-TRANSFUSION**



Monitor spleen size during inpatient stay - can teach family to look for signs of enlargement

INFECTION

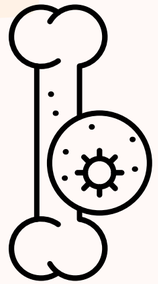
Mechanism

Patients with sickle cell disease become functionally asplenic in the first year of life, before becoming radiologically asplenic. This increases the risk of encapsulated organisms

Prevention

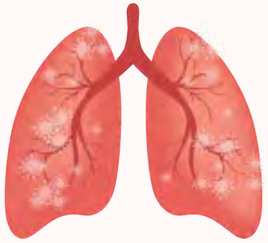
Patients are offered **lifelong penicillin V prophylaxis** and recommended to keep up to date with vaccinations plus additional vaccinations (influenza, meningitis ACWY and B, pneumococcal vaccination) as per Green Book recommendations.

Penicillin V most important before age 5, but recommended lifelong.



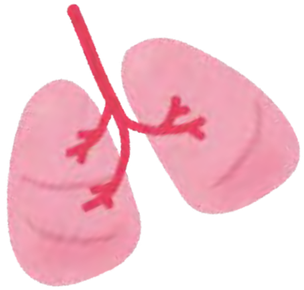
Risk of osteomyelitis caused by encapsulated organisms

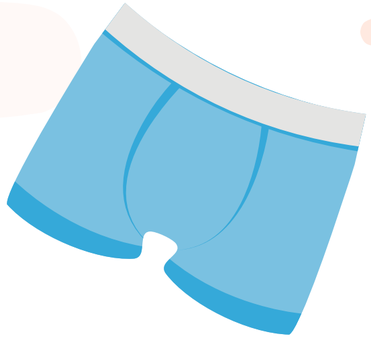
Pneumococcus or haemophilus infection



Consider malaria if appropriate travel history

Yersinia enterocolitica if on iron chelation therapy





THANK YOU!