Sickle cell disease: Complications in adult patients

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Sickle cell and thalassaemia
Nurses, AHP and Junior Doctor Training Days
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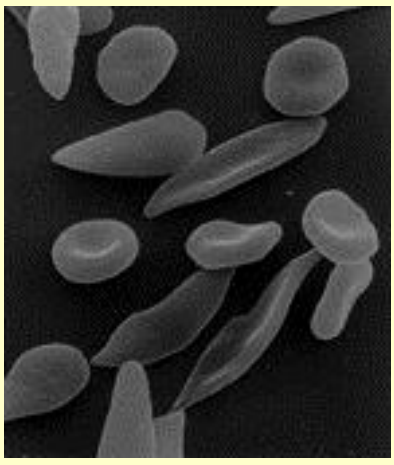
SCD is caused by a point mutation in the β-globin gene



- Life-long inherited disorder
- Rigid sickle-shaped red blood cells
- Symptoms rare before 3 months due to protective foetal haemoglobin (HbF)
- **HbSS (70%) severe**
- **HbSC (25%) less severe**
- Rarer combinations:
  - HbSβ^{o} thalassaemia
  - HbSβ^{+} thalassaemia
  - HbSD^{Punjab}, HbSO^{arab}
- Sickle cell trait (HbAS) and HbSHPFH rare symptoms

History

- **1870s** African literature
  - ***ogbanjes*** "children who come and go“
- **1904** Ernest Edward described **"peculiar elongated sickle-shaped"** cells in 20 year old Grenadian with "muscular rheumatism" and "bilious attacks“ who died aged 32
- **1949** Linus Pauling (Nobel Peace Prize)
  - SCD is due to **Hb molecule abnormality**
- **1984 Hydroxycarbamide** for SCD first reported - rapid increase in HbF cells

Mechanism of disease:

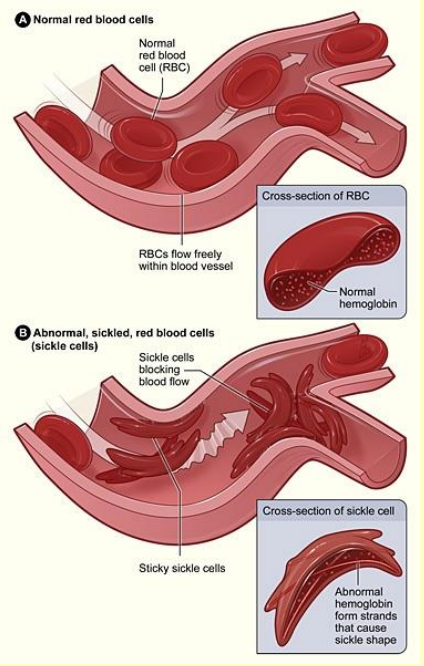
Hb polymerisation leads to red cell distortion (sickling)

Anaemia due to reduced life span (10-20 days) of sickled RBCs (normal 90-120 days)

Less elastic RBCs **block small blood vessels**

Lack of blood supply results in **hypoxia**, release of inflammatory chemicals, and activation of pain fibres

+/- organ damage



What can patients do to keep well?

- **2-3 litres of fluid/day** to avoid dehydration – reduced urine concentrating ability
- **Regular prescribed medications** e.g. hydroxycarbamide, antihypertensives
- **Avoid temperature extremes** – central heating, double glazing, thermal underwear etc.
- **Avoid infections (hyposplenic)** – food and general hygiene, vaccinations, penicillin V prophylaxis, malaria prophylaxis
- **Eat well, rest well, gentle exercise**
- **Manage pain** - analgesia, heat pads, skin rubs, psychological techniques, physiotherapy
- **Community specialist nurse support** – Yvonne Owusu-Sekyere

What do we do in clinic?

- **Care plan** and **review of medications** and **current problems**
- **Medications:** (Folic acid), penicillin V, HU, analgesia, vitamin D
- **Vaccinations**: 5 yearly pneumovax, hepatitis B
- **Blood pressure:** antihypertensives
- **Physical check:** Height, weight, pulse, oxygen saturations
- **Urine protein:creatinine screen:** ACE-inhibitor (e.g. ramipril)
- **Special tests:** echocardiogram, lung function, ophthalmology, ferriscan, hip and shoulder X rays, liver and gall bladder ultrasound
- **Psychological** assessment and support
- **Specialist nursing support** – dedicated Sickle CNS team

Painful crisis

- Varies in frequency, severity, site, duration (5-7 days)
- Caused by:
  - **Low oxygen levels (exertion, anaesthetic)**
  - **Dehydration**
  - **Infection**
- Treat with:
  - **Hydration (IV or oral)**
  - **Analgesia +/- broad spectrum antibiotics**
  - **Oxygen if saturations <95%**
- Severe crises may require opiates (morphine/oxycodone)
- **Incentive spirometry** reduces risk of chest complications

Don't forget…

- **Adjuvants**
  - **Analgesia**: Paracetamol, ibuprofen
  - **Laxative**: Lactulose/movicol, senna
  - **VTE prophylaxis**: Clexane injections daily
  - **Anti-pruritic**: Hydroxyzine
  - **Anti-emetic**: cyclizine (avoid IV bolus), metoclopramide
  - **Anxiolytic**: Haloperidol
- **Empathy**
  - Patients report **fear**, discrimination, long waits for analgesia, insinuations of drug dependency
- **Pain assessment**

Standard Pain Assessment Tool

Queen Elizabeth Hospital

Sickle Cell Disease Pain scoring tool

0	1	2	3	4	5	6	7	8	9	10
No pain ☺					Moderate pain 😐					Unbearable pain ☹

Assess effect of pain relief every 30 minutes until satisfactory, then every 4 hours, asking:

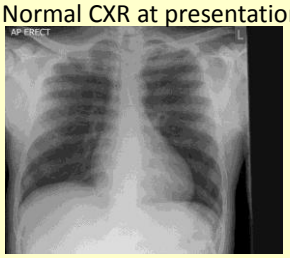
'How well did that last painkiller work?'

'Do you need more pain relief?'

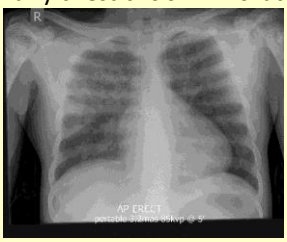
Acute chest syndrome

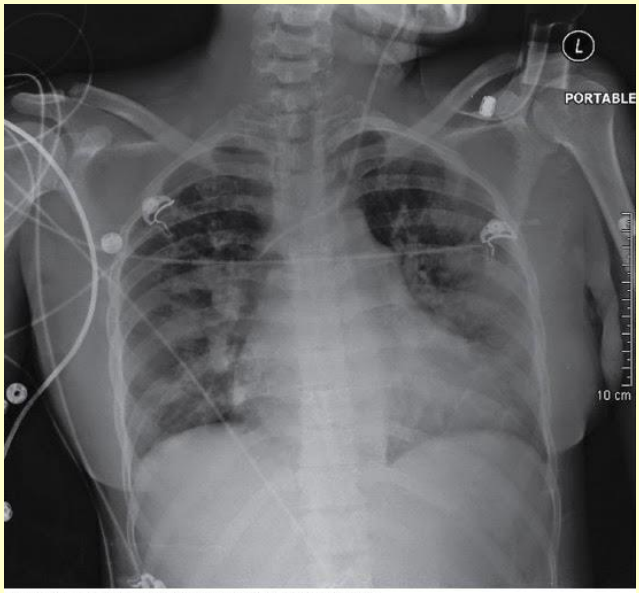
- Fever, chest pain, SOB, bilateral lung opacities
- Precipitated by painful crisis, chest infection, poor chest expansion, opiates, and surgery
- Treat with **Urgent exchange transfusion** and **supportive care** (oxygen, IV fluids, antibiotics, analgesia)
- **Act fast to prevent death**

- Normal CXR at presentation



- Early chest crisis 17 hrs later





Aplastic crises

- Anaemia with **low reticulocyte count**
- Caused by **Parvovirus B19**, stops red cell production for 4-8 days
- Short RBC life span in SCD results in severe anaemia
- **Blood transfusion** usually required
- Usually develop life-long immunity after one episode

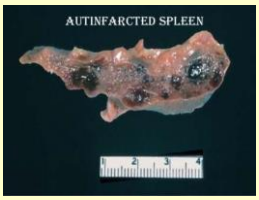
Parvovirus B19

Overwhelming infection

- Spleen usually infarcted during childhood
- Lack of spleen increases infection risk from **encapsulated organisms**
- **Twice daily penicillin V** gives some protection
- Use **broad spectrum antibiotics** if pyrexial
- Vaccinations provide further protection
  - **Pneumococcal C vaccine (pneumovax II) every 5 yrs**
  - **Conjugated Meningococcal C, single dose**
  - **Haemophilus influenzae type b, single dose**
  - **Meningococcal ACWY if travelling to high risk areas**
  - **Annual influenza vaccination**

Life sized spleens!

Autoinfacted spleen



Normal spleen

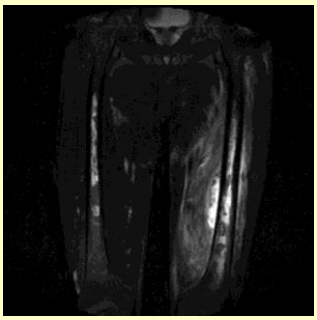
Acute cholangitis and cholecystitis

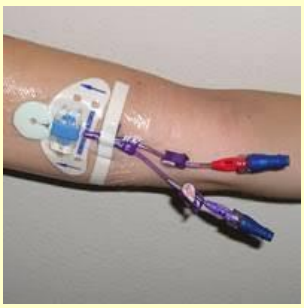
- Gall bladder complications due to excessive bilirubin due to RBC breakdown, leading to gall stones

- Cholecystectomy - most common surgical procedure in SCD
- Complications such as gall bladder perforation, abscess

Osteomyelitis

- **Bone infection** +/- collection
- May need surgery to drain a collection or remove a sequestrum
- Unusual organisms (e.g. salmonella)
- 6 weeks of antibiotics – often need PICC line



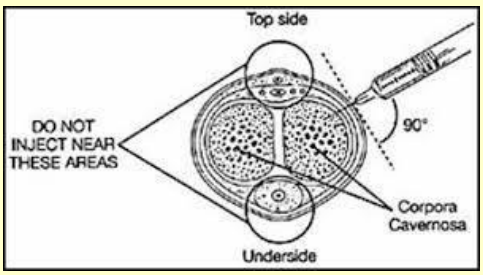


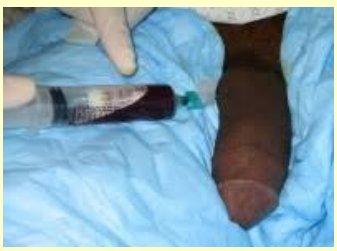
Priapism and erectile dysfunction

- Potentially devastating, **often concealed**
- 20-30% in SCD by age 20
- Treat first with simple measures: empty bladder, warm bath, fluids and analgesia, mild exercise
- **Medical management**
  - **Alpha agonists** (etilefrine) +/- prophylactically at night
  - **Aspiration** of corpora cavernosa
  - **Anti-androgens** (cyproterone acetate)
  - Sludging of sickle cells in anoxic corpora cavernosum, change in regulation of cGMP/NO synthesis pathway critical for sinusoidal smooth muscle relaxation in corpora –**sidenafil?**

Priapism treatment –

aspiration of the corpora cavernosa



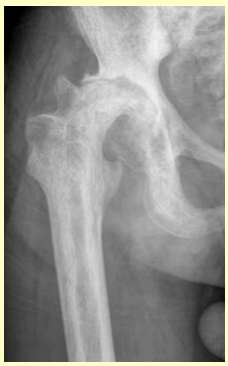


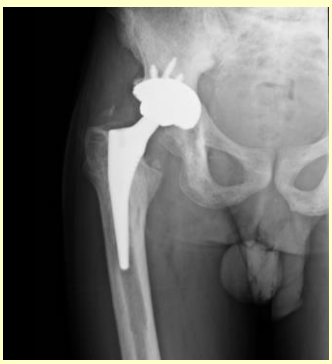
Chronic sickle complications:

- **Avascular necrosis of hip and shoulder**
- **Leg Ulcers**
- **Sickle eye disease**
- **Pulmonary hypertension**
- **CRF and proteinuria**
- **Chronic pain/opioid tolerance/dependence**

Avascular Necrosis (AVN)

Hip and shoulder joint replacement surgery



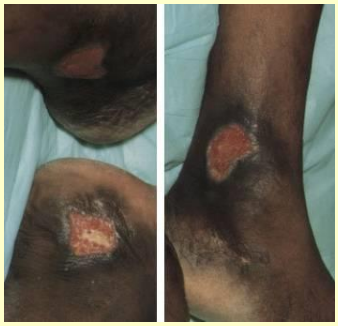


AVN of femoral head is a common complication in SCD and collapse of femoral head occurs in 90% of patients within five years of the diagnosis of osteonecrosis

Treatment is total hip replacement (pre-operative exchange transfusion)

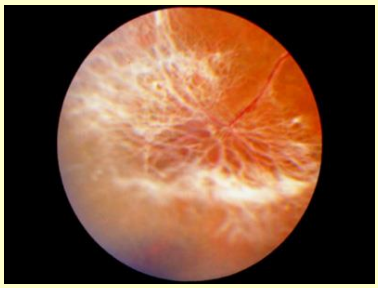
Leg Ulcers

- Rare < 10 years
- Most common in HbSS
- Caused by: anaemia, decreased NO bioavailability, arteriovenous shunting, trauma, infection and inflammation, interrupted microcirculation
- Leg ulcers occur in areas with less subcutaneous fat, thin skin, and decreased blood flow
- commonest sites are medial and lateral malleoli (ankles)



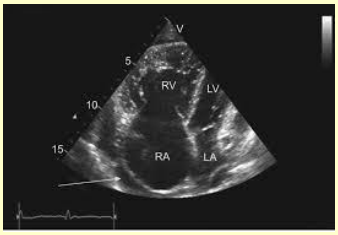
Sickle eye disease

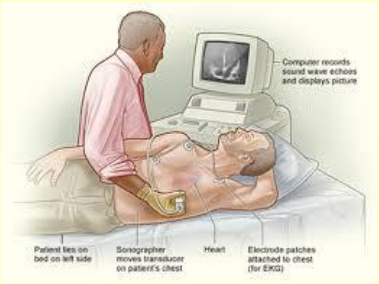
- Due to vascular occlusion in conjunctiva, iris, retina, and choroid
- Rule out other causes of occlusion, including central retinal vein occlusion and retinopathy secondary to diabetes
- Treatment to prevent vision loss from vitreous haemorrhage, retinal detachment



Pulmonary hypertension

- Early diagnosis by screening echocardiogram
- Indication for red cell exchange program or HU
- Main echo findings are
  - Right ventricular enlargement
  - Right ventricular hypertrophy
  - Right atrial enlargement
  - Functional tricuspid regurgitation with high velocity regurgitant jet (TR jet)





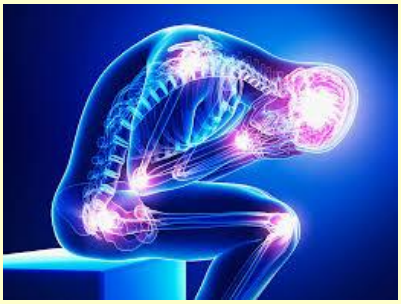
Proteinuria and chronic renal failure

- Urine protein:creatinine ratio measured at least yearly
- If >50 on 2 consecutive tests consider starting an ACE inhibitor

  (e.g. Ramipril)
- Careful avoidance of further renal injury – i.e. no NSAIDs

Proportion of patients will go on to need renal replacement therapy
e.g. haemodialysis

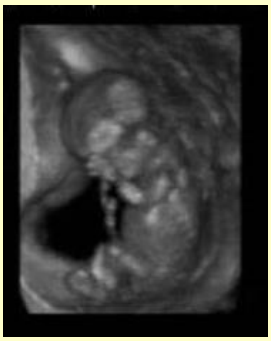
Chronic pain/opioid tolerance/dependence



By adulthood, some patients will have chronic pain with no pain-free days and need regular opiates (e.g. oxycodone SR bd with IR when required), NSAIDs, heat therapy, psychosocial support etc.

Pregnancy in SCD

- Increased risk to mother (3% mortality) and infant (6% mortality)
- IUGR, premature labour, VTE, miscarriage, pre-eclampsia
- Regular clinic and growth scans
- **Blood transfusion** if
  - previous pregnancy problems
  - haemoglobin <6og/l
  - sickle cell complications
  - Trial of exchange transfusion from 14/40
- **Folic acid, aspirin, LMWH**, urgent treatment of infections and crises



Sickle cell disease in childhood

- Painful crises
- Infection
- Dactylitis
- Splenic sequestration
- Aplastic anaemia
- Haemolytic crises

Stroke

- Previously affected 1 in 10 children
- Assess risk by **transcranial Doppler**
- Prevent with **transfusion program** to maintain HbS<30-50%

Summary

- Sickle cell is an inherited **multisystem disorder**
- Life expectancy and QOL are improving
- Complications can affect most organs
- Effective treatments and preventative strategies are often available
- Some will develop multi-organ damage and chronic pain and need effective multidisciplinary support