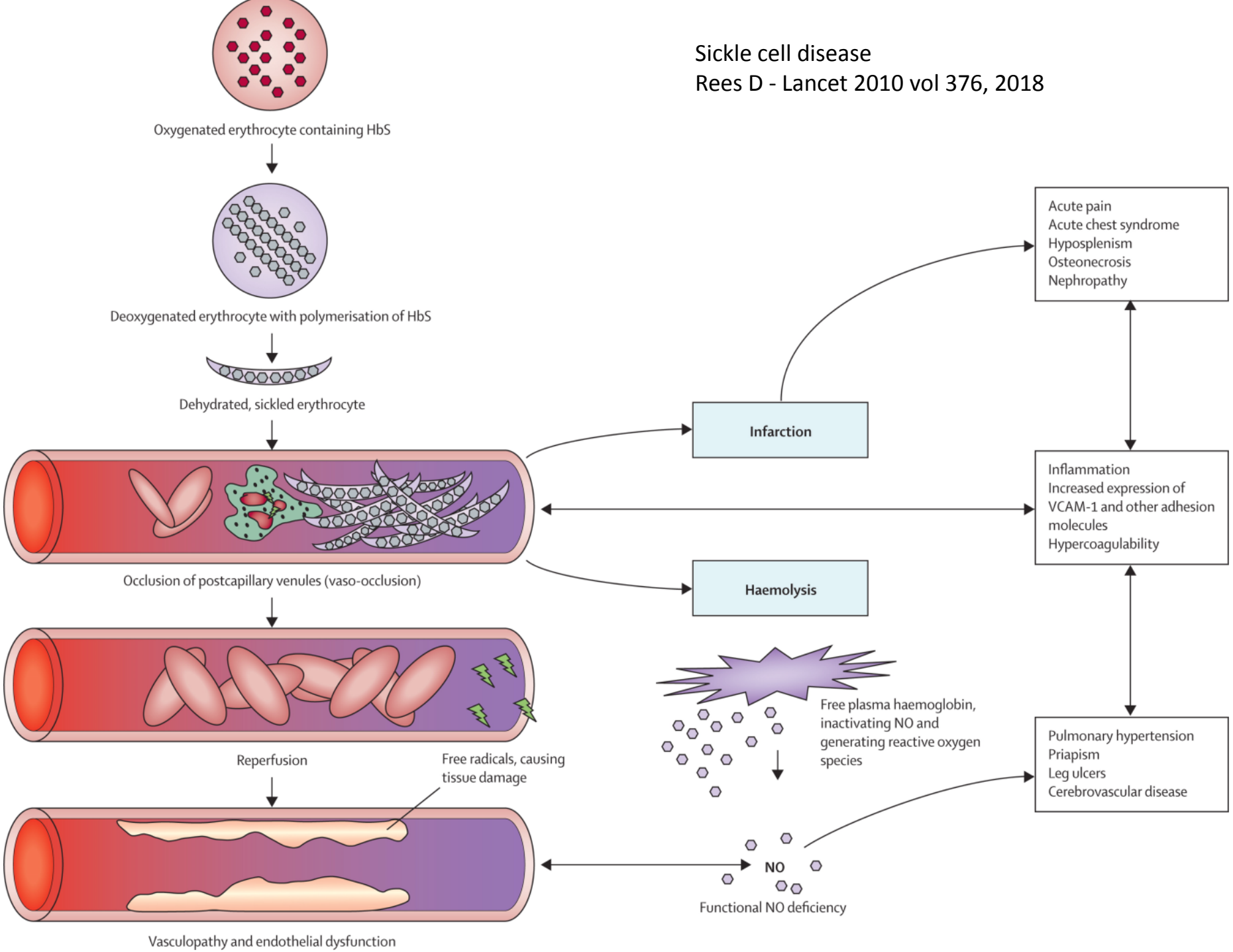
To be'e' or not to be'e'? – that is the question

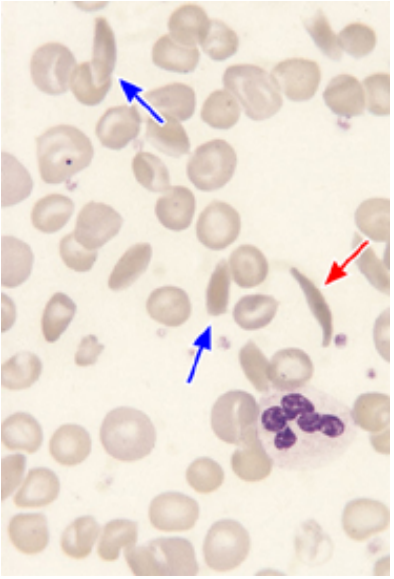
Dr Shubha Allard
Consultant Haematologist
Barts Health NHS Trust &
NHS Blood and Transplant

Case

- 17 year old female
- Sickle cell anaemia (HbSS)

Sickle cell disease
Rees D - Lancet 2010 vol 376, 2018





Sickle cell anaemia

Chronic anaemia
Acute exarcebation anaemia
- haemolysis
- Sequestration
- Aplastic

Painful crisis – dactilitis, acute painful bony crises

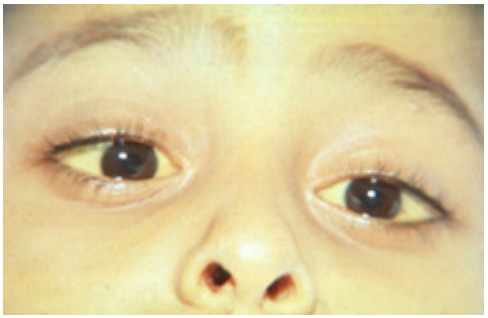
Acute chest syndrome

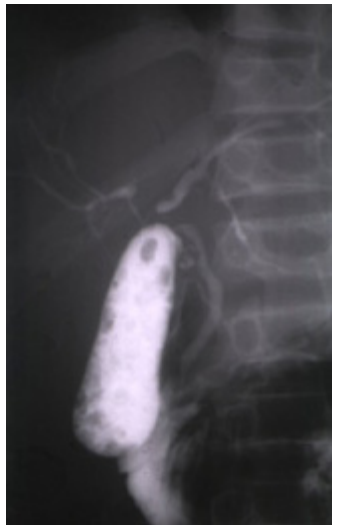
Stroke

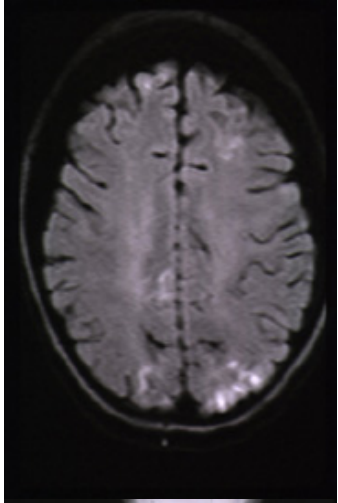
Infections
Hyposplenism
Priapism, Leg ulcers

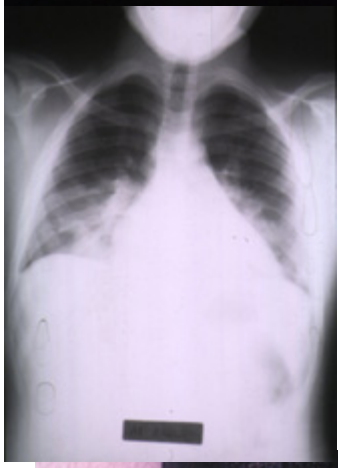
Pulmonary hypertension
Renal disease

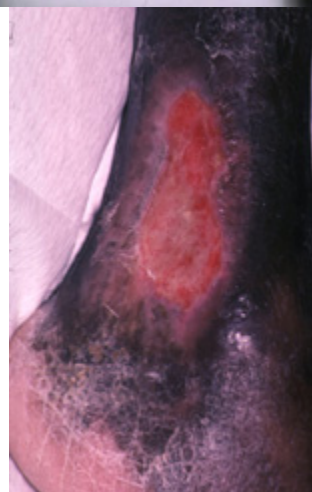
Pregnancy, surgery











SCD and neurological disease

- **Stroke Prevention Trial in Sickle Cell Anemia (STOP)**
  - in asymptomatic high-risk children with Transcranial doppler (TCD) velocities ≥200 cm/s regular blood transfusions resulted in 90% reduction in first stroke

- **Silent Infarct Study (SIT) NEJM 21st Aug 2014**
  - A third of children with SCD have silent infarcts on MRI
  - Randomised children aged 5 -15 years with silent infarct to standard therapy vs transfusion for 3 years
  - 58% reduction in stroke or recurrence silent infarct with transfusion

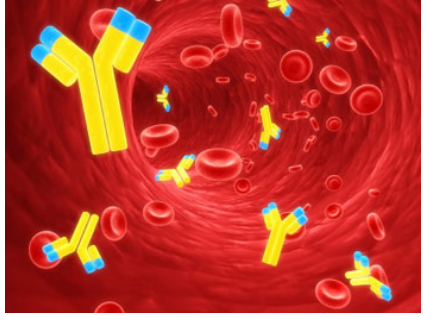
Case 17year old female

- Sickle cell anaemia (HbSS)
- Painful crises
- US – gallstones
- 2005 – CMV infection – anaemia needing Transfusion
- Penicillin and Folic Acid; Pneumovax
- For analgesia Paracetamol, Ibuprofen or Diclofenac, Codeine.

Progress

- Transcranial Dopplers from 2005: Standard Risk
  - due repeat early December 2009
- Dec 2009 - C/O pain R foot, problems with gait
- Repeat Transcranial Dopplers - now showed High risk velocities
- **MRI & MRA**
  - left frontal cortical ischaemia and left lentiform nucleur ischaemia, deep watershed ischemic lesions left and right hemispheres.
- **Commenced transfusion regime**
  - maintain sickle haemoglobin percentage <30%

Special requirements Haemoglobinopathy



- Alloimmunisation risk SCD reported 20–35% or higher
  - Risk haemolytic transfusion reactions
  - Multiple and complex antibodies can result in significant delays in sourcing appropriate red cells units
- Extended phenotyping prior to transfusion or genotyping if transfused
  - C, c, E, e, K, k, Jka, Jkb, Fya, Fyb, MNS
- Transfuse red cells matched for Rh (D, C, c, E, e) and K antigens
- Antigen negative for current or historical red cell antibodies that are clinically significant
- Age of blood
  - Top up <14 days; exchange (SCD) <7 days
  - HbS negative

Transfusion regime

- 13.01.10 Ab Screen Negative ARhD neg (r'r)
- Flag in Laboratory system special requirements
- A rr K negative units

- November 2011 - In-dwelling Portacath for venous access

- Aug 2012 Portacath frequently blocked

- 16.04.12 Ab Screen positive
- Initially just anti Kpa but then……

NHSBT report 2012

A RhD negative

DAT

PS	IgG	IgA	IgM	C3c	C3d	Control
	1+	0	0	0	0	0

Red Cell Antibody Results

Type	Specificity	Technique	Sample Type
Allo	Anti-K	IAT	Plasma
Allo	Anti-Kpa	IAT	Plasma
Auto	Anti-e	Polybrene technique	Plasma

These antibodies are clinically significant.
No additional alloantibodies were detected.
Select ABO compatible, (and HT-, if not ABO identical), D-, C-, E-, K-, Kp(a-) red cell units for crossmatching.
An eluate prepared from the patient's cells contained a pan-reactive autoantibody detected by IAT.
An antibody card for this patient is enclosed.

Joint case review - clinical and laboratory teams

- 2013 Poor increment in Hb and poor suppression of HbS level
- Further Red cell serology review
- Samples send to IBGRL

IBGRL results and commentary

- Ala85Gly mutation suggesting that she has an RHCE*ceAG gene.
- That is, that she is heterozygous for RHCE*ceAG and for a d(C)ces haplotype.
- RHCE*ceAG produces abnormal e and hrB antigens
- It is possible that this patient could be capable of making alloanti-e-like and an alloanti-Hr-like antibody.
- ‘but this does not help you very much with transfusing this patient’

- Chou et al British Journal of Haematology 2012159, 304-404
- Challenges of alloimmunisation in patients with haemoglobinopathies

Feb 2013

- Discussed hydroxyurea
- Transfusion stopped
- Overall well on hydroxyurea good HbF response

Feb 2014

- 1/52 hx gastro-intestinal illness following family party
- 1/7 history generalised pain

- O/E – unwell, jaundiced, tachycardia, tachypnea, hypotensive, pyrexial, bilateral reduced air entry, hepatomegaly

- Severe sepsis -requiring fluid resuscitation, HDU admission, IV antibiotics, noradrenaline

- Salmonella septicaemia confirmed

- Worsening respiratory failure, deranged LFT, renal impairment

Deterioration

- CXR – extensive bilateral consolidation
- ECHO – normal LV function; hyperdynamic LV circulation
- RR ~50 on CPAP; Hyperpyrexial; Hb dropping
- Portacath removed, exchange transfusion
  - Arr, Kneg, Kpa neg units, IVIG cover
- Intubated, ventilated, increasing PEEP required

Further deterioration

- Decision to transfer to Papworth for ECMO
- Transfusion discussion NHSBT RCI re selection of units
  - Arr Kneg, Kpa neg, IVIg cover

Improvement!

- D12 – Improved
- Repatriated to RLH; extubated, short trial on CPAP
- Rehabilitation on paediatric ward - Discharged home March 2014
- Further Progress
  - 2 further transfusions - Arr Kneg Kpa neg blood without IVIG cover
  - Venous access difficult
  - Transferred back onto Hydroxyurea
- Currently remains an outpatient on regular review

Discussion

- Hb SS - Increasing indications for transfusion
  - STOP study and now SIT Study (NEJM Aug 2014) for cerebro-vascular disease
- Special requirements for SCD patients in relation to Transfusion
- Risk of alloimmunisation in SCD
- Implications of ‘e’ variant to transfusion management
- Other challenges with transfusion in SCD patients – chelation, venous access

Acknowledgements

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