The Red Cell Network
Haemoglobinopathy Coordinating Centre

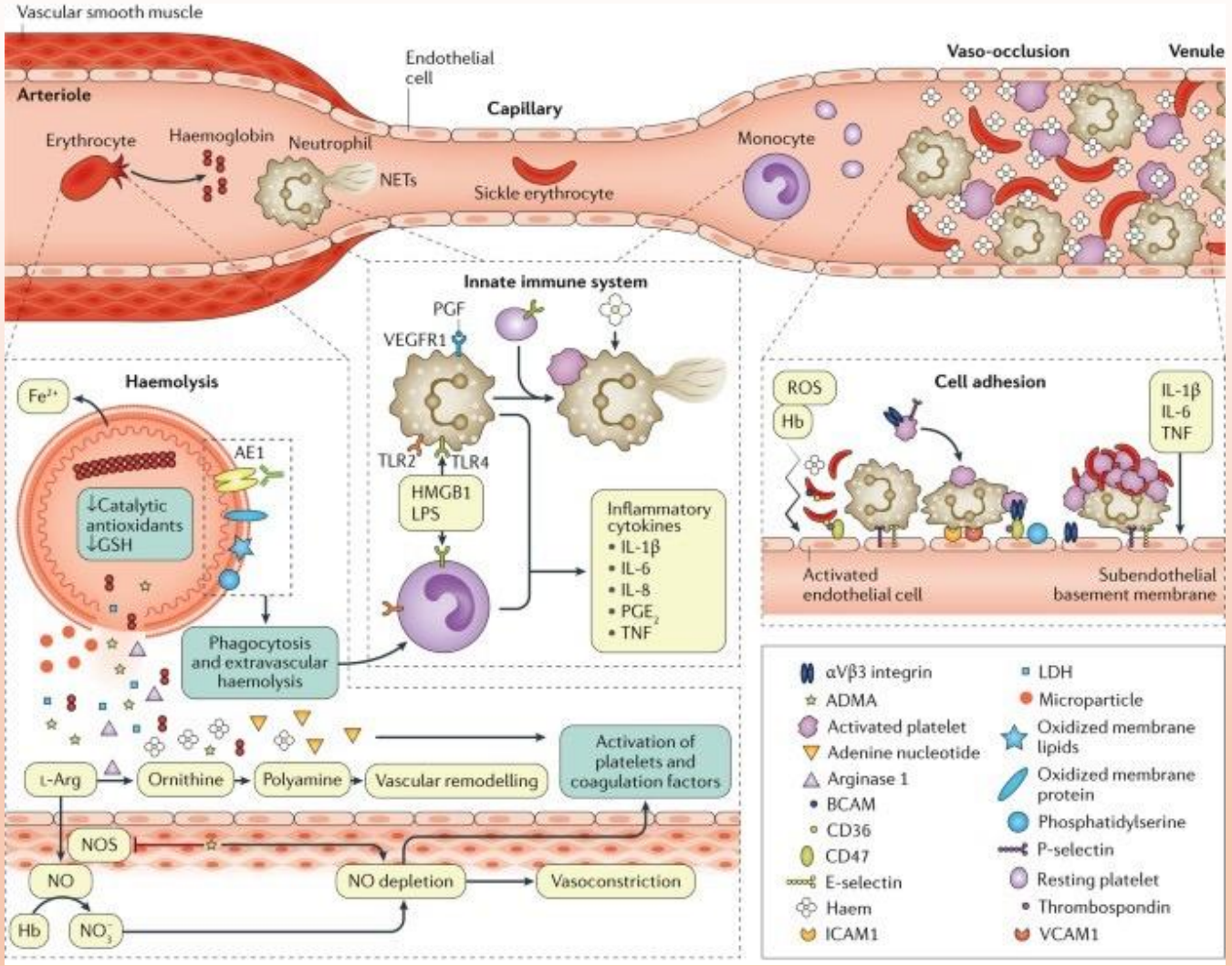
Clinical Aspects of Transfusion for Haemoglobinopathy Patients

Dr James Leveson
Haematology SpR (ST7)
Whittington Hospital, London

Objectives

- Explain the transfusion options in Sickle Cell Disorder
- Understand the risks of alloimmunisation
- Recognise haemolytic transfusion reactions
- Appreciate the treatment options for patients with haemolytic transfusion reactions

Pathophysiology

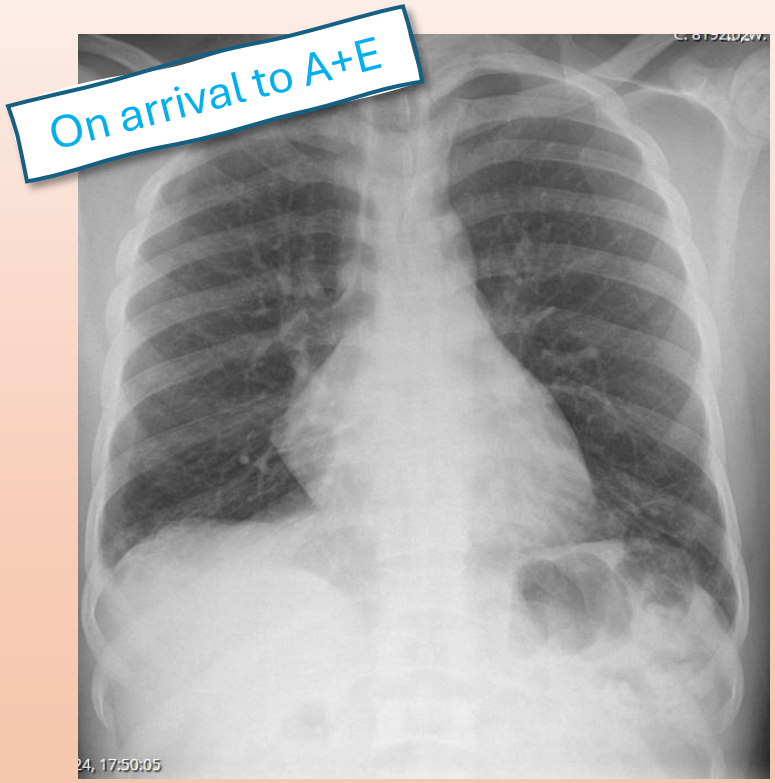


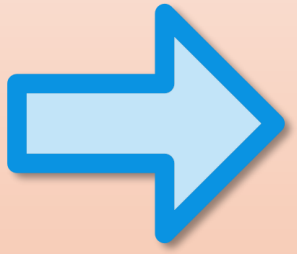
Transfusion in Sickle Cell Disorder

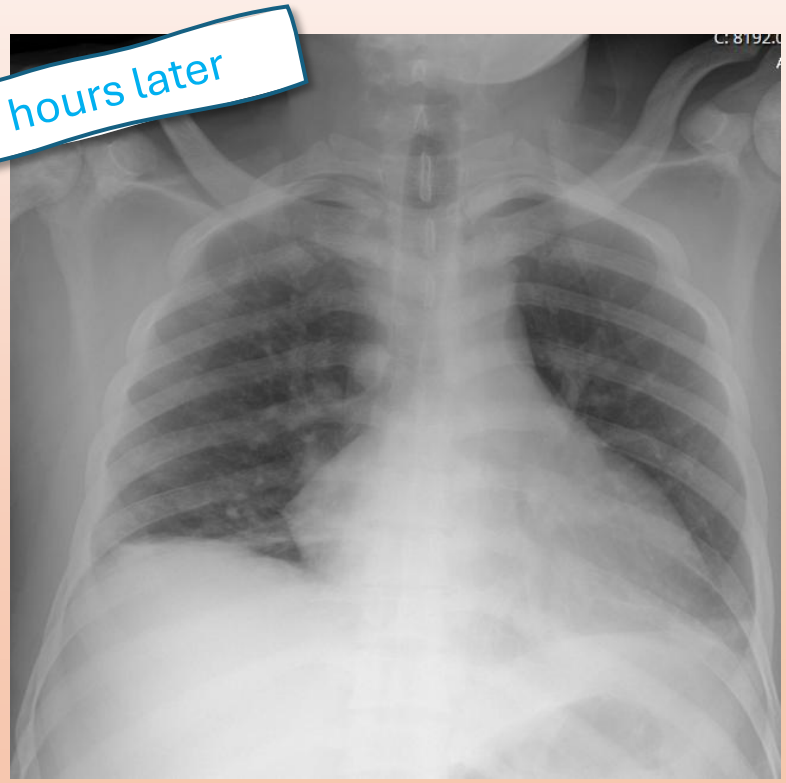
- Transfusion is sometimes indicated: acutely and chronically
  - Acute chest syndrome
  - Stroke treatment and prevention
  - Symptomatic anaemia (consider if <20g/l fall from baseline)
  - Planned surgery
  - Some pregnant women
- Modality depends on the patient and situation
- Exchange vs. top up

Case

- 24F with sickle cell disorder (HbSS)
- Attended A+E with chest pain and shortness of breath







Case

- Diagnosed by the clinical team as Acute Chest Syndrome
  - Variable findings on the CXR
- Hb 60, reticulocytes 500
- Team decides that the patient needs a transfusion…
  - **What are the options?**
  - **What information do you need to know prior to making this decision?**

Emergency transfusion

- This should not be given without haematological advice (risk of alloimmunisation)

Top-up transfusion

- If the Hb **less than** steady state level
- Examples:
  - Aplastic crisis
  - Splenic sequestration

Exchange transfusion

- When rapid reduction in sickle % is needed
- Examples:
  - Acute chest syndrome
  - Stroke
  - Prior to emergency surgery

Case

- Let's assume the Hb is below the steady state – **what are the pros and cons of arranging a top up for this patient?**

Pros

- Quicker to organise
- Less exposure to donor units
- May avoid exchange
- Often a good 'temporizing measure' whilst exchange is arranged

Cons

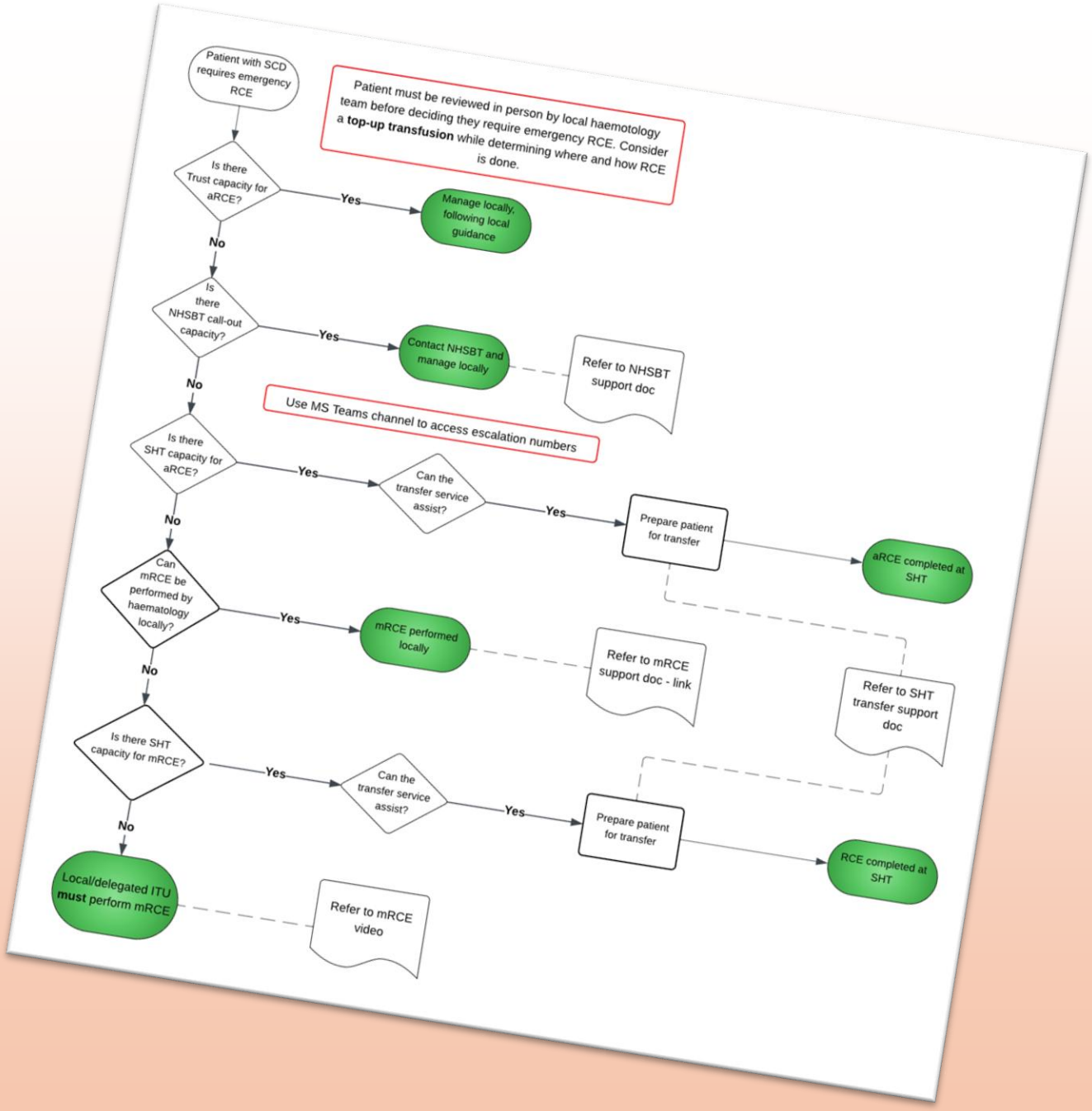
- Will not suppress S% by that much so may continue to sickle and get worse
- May waste precious units

Red cell exchange

- New flow chart for the Red Cell Network
- Discuss with a red cell consultant first

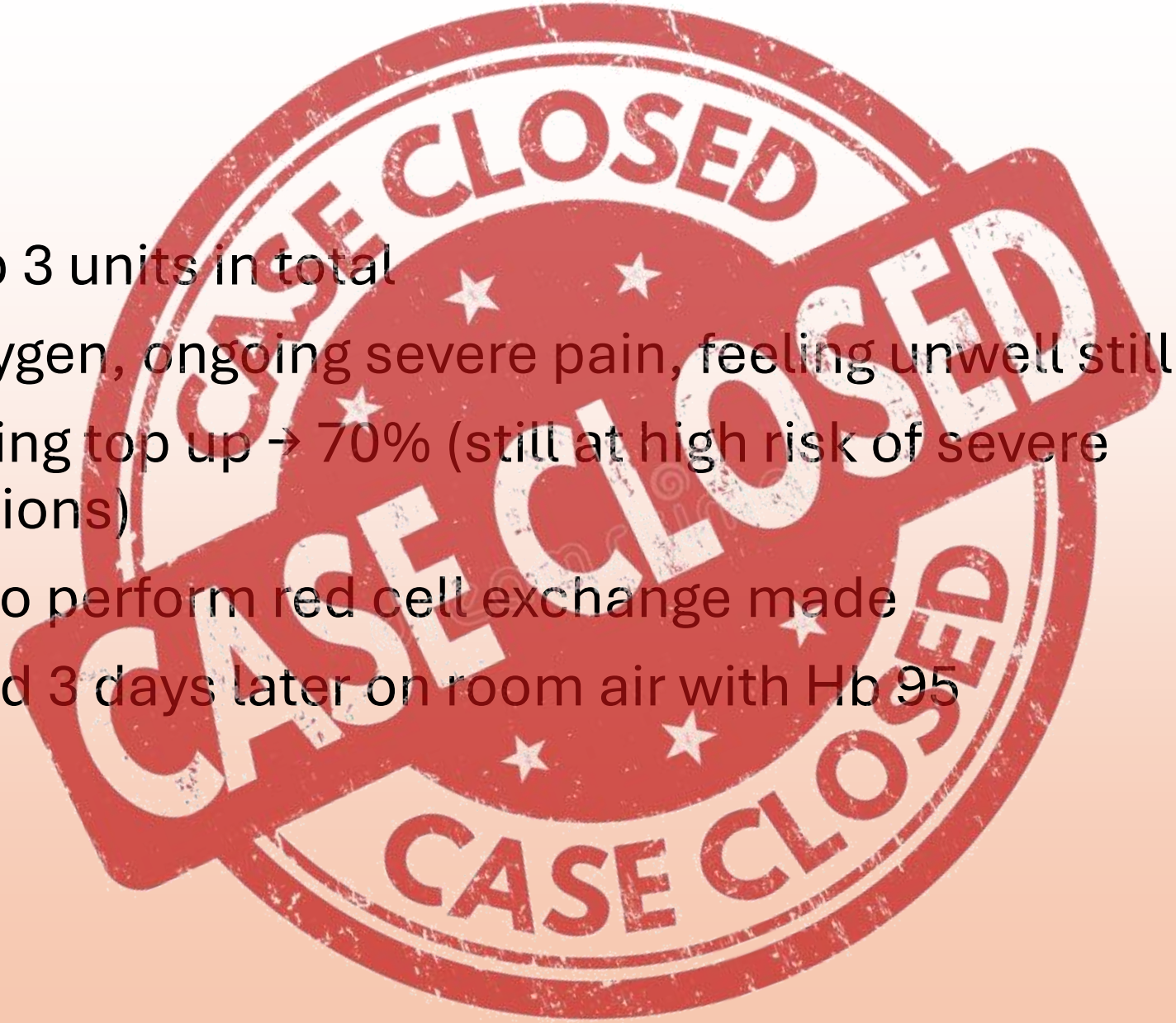
ABO compatible, Rh and Kell matched units
Any units should be negative for corresponding antigens of clinically significant red cell antibodies

Aiming for HbS% <30, Hb 90-100 – on-call consultant and apheresis team will help with targets and amount of blood that you need to order from blood bank



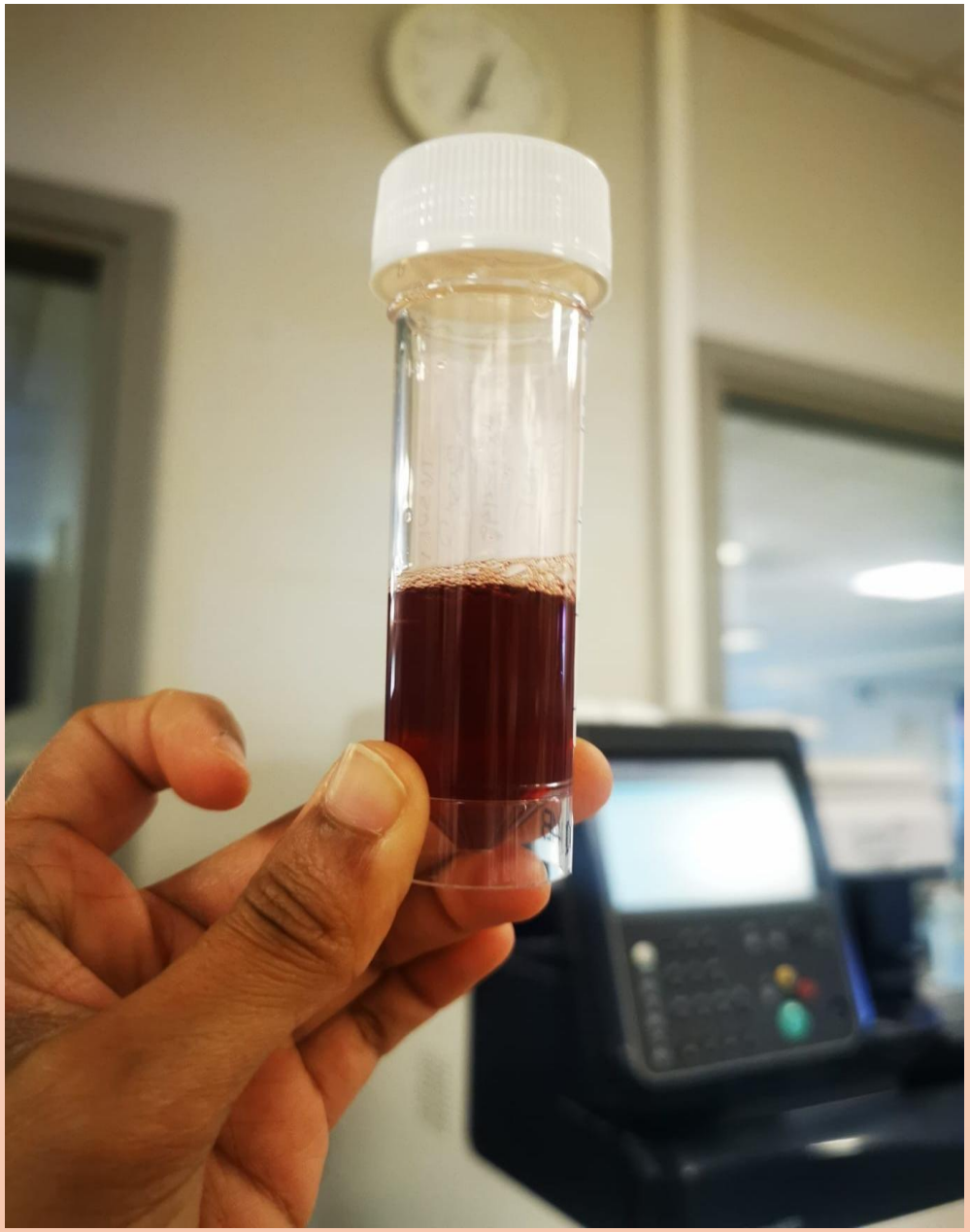
Case

- Topped up 3 units in total
- Still on oxygen, ongoing severe pain, feeling unwell still
- S% following top up → 70% (still at high risk of severe complications)
- Decision to perform red cell exchange made
- Discharged 3 days later on room air with Hb 95



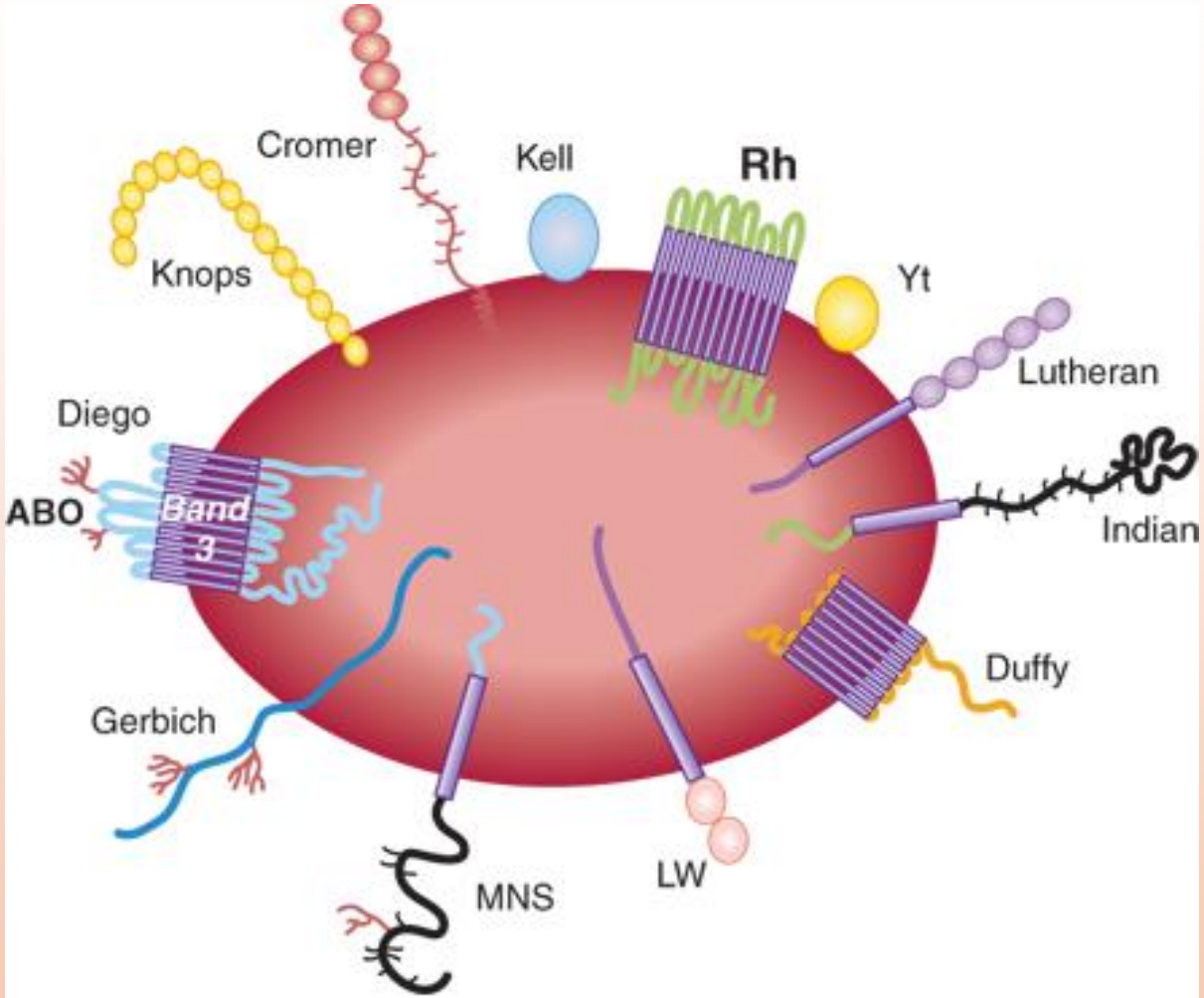
Case

- 3 days later…
- Flank pain and dark urine
- Hb now 62
- Bili 73 (baseline 30), LDH 1900, retics 179
- Unable to perform G+S and DAT due to haemolysis in tube
- **What's happened?**



Red cell antigens

- Any antigen the patient *lacks* can be recognised as foreign after transfusion, triggering alloimmunisation.
- Fully matching isn't feasible with donor supply, turnaround time, or testing constraints



Source: H. Franklin Bunn, Jon C. Aster: Pathophysiology of Blood Disorders
www.accessmedicine.com

Matching in Sickle Cell Disorder

- As we've heard already, SCD patients are a "perfect storm" for alloimmunisation
  - More likely to be transfused repeatedly
  - Often population-level differences in antigen frequencies between donor pools and recipients → chance of antigen mismatch is higher
- Rh - especially tricky due to variants

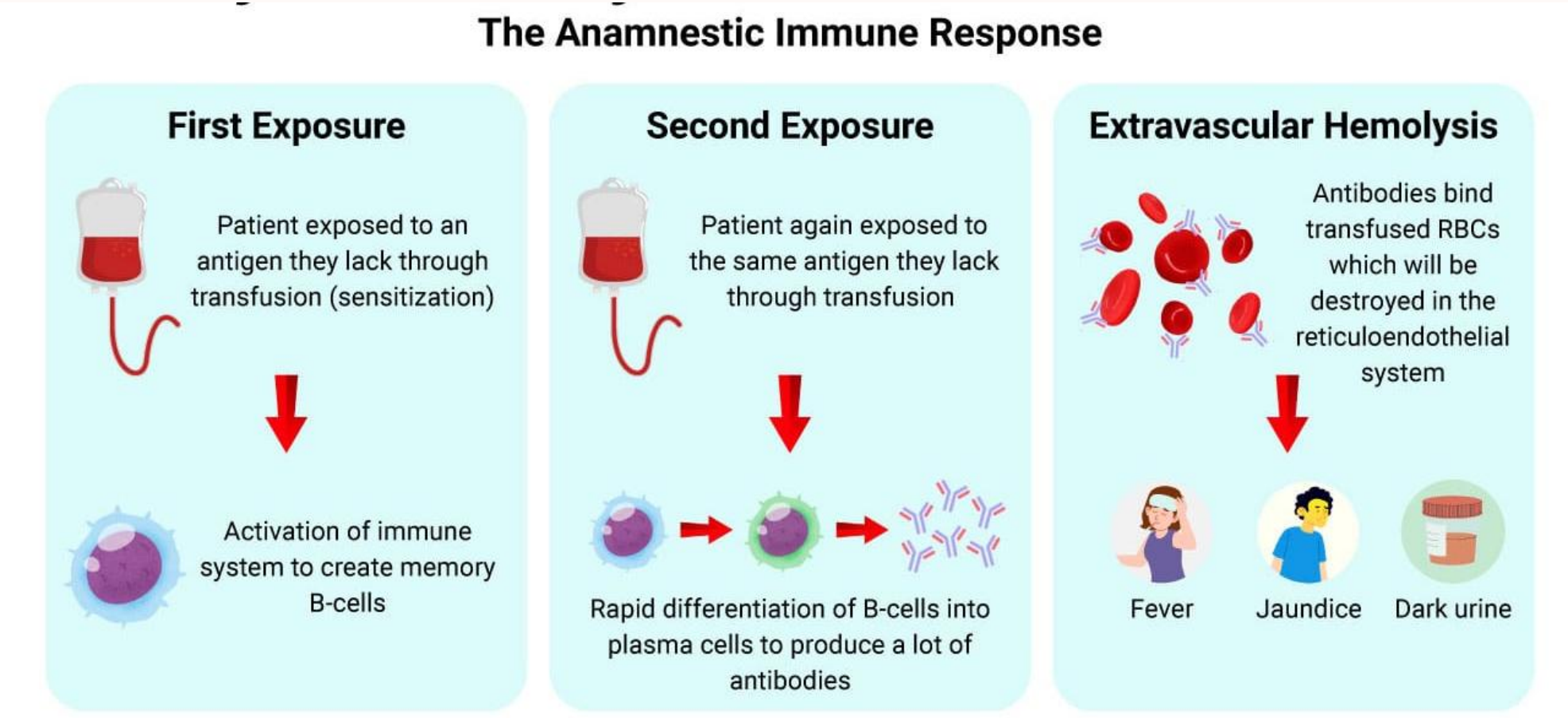
Delayed haemolytic transfusion reaction (DHTR)

- Significant **Hb drop** in absence of an alternative cause
- **Within 21 days** of transfusion
- Associated with 1 or more additional clinical criteria:
    1. New red cell alloantibody (or antibodies)
    2. Haemoglobinuria
    3. Hb level that decreases more rapidly than expected post transfusion
    4. Relative reticulocytopenia or reticulocytosis from baseline
    5. Significant rise in LDH from baseline

Hyperhaemolysis (HH)

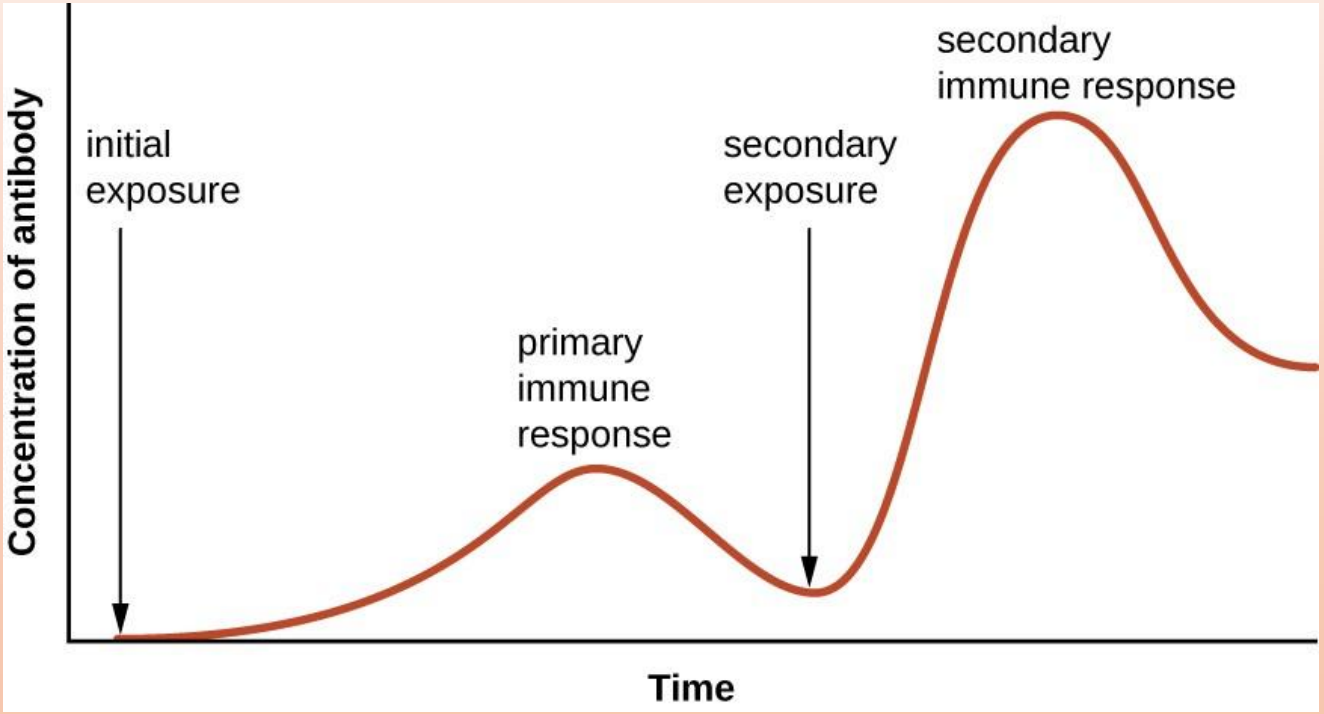
- Most severe type of DHTR associated with bystander haemolysis (so there is a rapid Hb decline below pre-transfusion Hb)
- Increased mortality
- Can occur in presence or absence of a detectable alloantibody
- Risk of recurrent HH with subsequent transfusions, even if several years later

Pathophysiology



Pathophysiology

- Previously formed and subsequently undetectable red call alloantibodies can cause DHTR - record keeping and communication with laboratory and clinical staff essential



Treatment

- **Admit** all suspected DHTR or HH
- Supportive management (hydration etc), minimise phlebotomy
- Start **erythropoietin** (EPO) in absence of CI, and significant anaemia (<20g/l below baseline or <70g/l)
- Optimise haematinics: folic acid, B12, IV iron
- **1st line = methylprednisolone IV + intravenous immunoglobulins (IVIG)**

Treatment

- 2nd line: Eculizumab if ongoing despite IVIG + steroids
  - ↓ complement activation
- 3rd line:
  - Blood transfusion – avoid if possible:
    - Only after discussion with a consultant experienced in SCD management + NHSBT
    - NHSBT might provide extended phenotype matched units
  - Rituxumab
- Need to **monitor** response to treatment with daily bloods inc transfusion investigations (DAT), HbS% etc

Follow up

- Report ALL cases of post transfusion hyperhaemolysis to SHOT
- Ensure documented cases/suspected cases are recorded locally and on Sp-ICE
- If you issue an antibody card at your Trust – update
- Secondary prevention:
  - Optimise Sickle care (HU)
  - Consider pre-treatment with IVIG + MP if requiring transfusion
  - If continue to haemolyse despite pre-treatment, then can give rituximab (following MDT discussion and appropriate viral screening)

Primary prevention

- Optimise care, e.g. hydroxycarbamide, to avoid transfusion
- Good communication between clinical and laboratory staff
- Good record keeping including on EPR
- Appropriate selection and matching of units
- Future precision transfusion medicine - patient and donor red cell genotype to ensure maximum compatibility

Case

- Admitted
- Received IVIG and steroids, started on EPO and haemtinic support
- No new alloantibodies detected
- Haemoglobin started to rise and patient discharged 9 days later
- DHTR documented in notes and on SpICE, given card
- Sickle care subsequently optimised in clinic

Objectives

- Explain the transfusion options in Sickle Cell Disorder
- Understand the risks of alloimmunisation
- Recognise haemolytic transfusion reactions
- Appreciate the treatment options for patients with haemolytic transfusion reactions

Any questions?