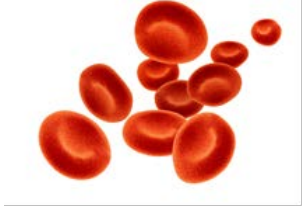

NHS Blood and Transplant

The use of red cell genotyping in the management of sickle cell disease

Dr Sara Trompeter – Consultant Haematologist

UCLH and NHSBT

Dr Keir Pickard– Core Medical Trainee

UCLH

British Blood Transfusion Society Annual Conference

22 September 2016

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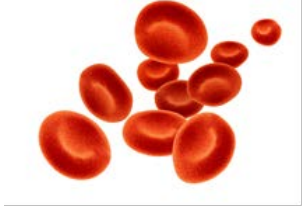

NHS Blood and Transplant

Content

- What is sickle cell disease?
- What is the role of blood transfusion in sickle cell disease?
- Why should we genotype recipients?
- Why should we genotype donors?
- Audit
- Summary

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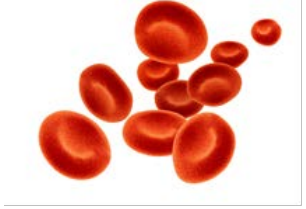

NHS Blood and Transplant

What is sickle cell disease?

- A group of autosomal recessive disorders
- Mostly in people of African/Arab/South Asian/Southern Mediterranean descent
- Can present early in life
- Red cells will sickle and become activated and activate other cells and the endothelium
- The rate can increase – these are called crises

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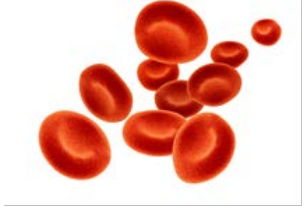
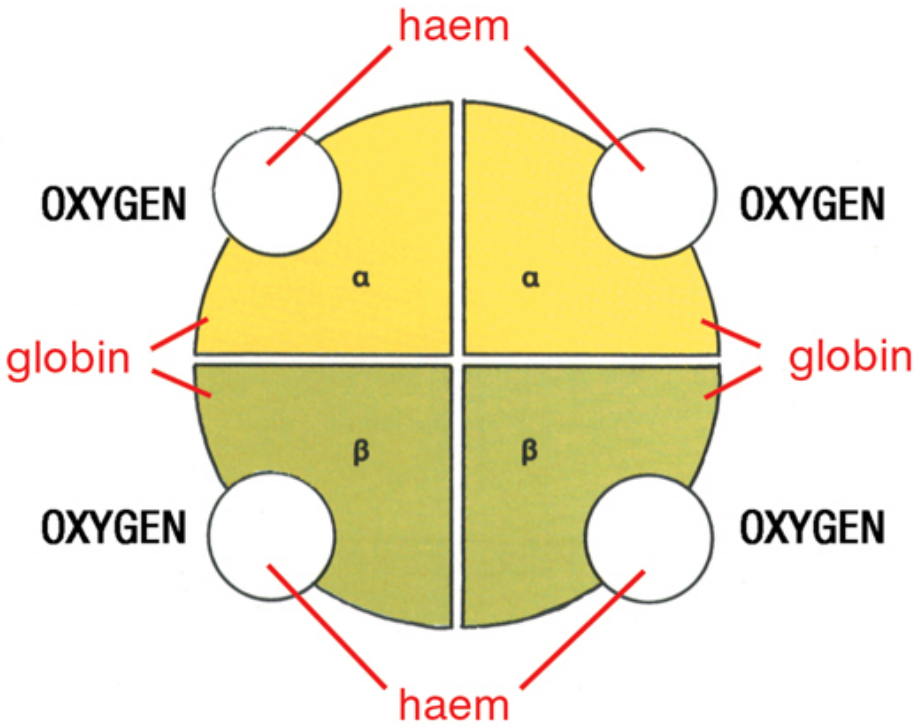


NHS Blood and Transplant

What is sickle cell disease?



- HbSS
- HbSC
- HbSD
- HbSHPFH
- HbSO Arab
- HbSβ^{+} thalassaemia.
- HbSβ^{0} thalassaemia.

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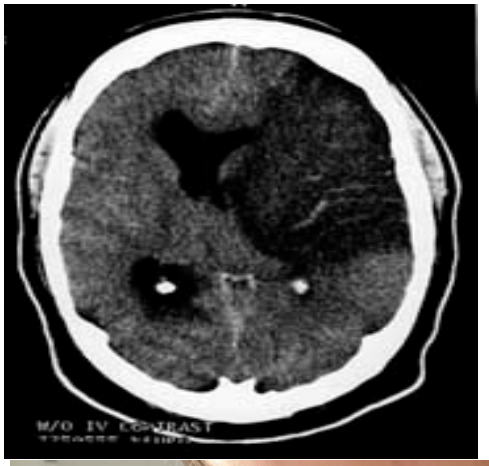
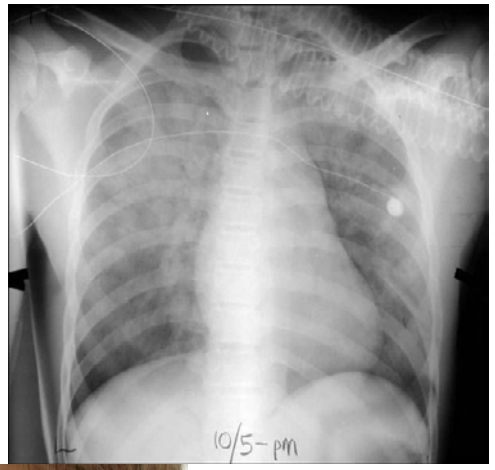
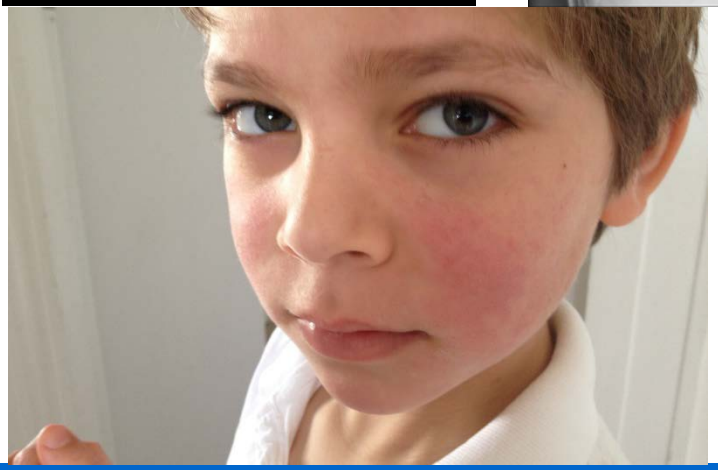
NHS Blood and Transplant

What is sickle cell disease?

- Acute problems:
  - Infection, sequestration, worsening anaemia, vaso-occlusion (stroke, pain, priapism)







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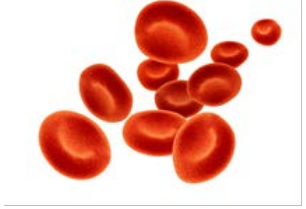

NHS Blood and Transplant

What is sickle cell disease?

- Long term problems:
  - Any organ damage
    - Renal
    - Pulmonary hypertension
    - Hepatic
    - bone

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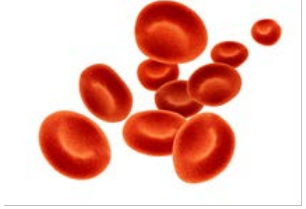

NHS Blood and Transplant

What is the role of blood transfusion in sickle cell disease?

- To correct a severe or sudden anaemia
- To reduce the proportion of sickle containing cells to either:
  - Treat a complication
  - Prevent a complication
- >90% of adults with SCD have had a transfusion at some point

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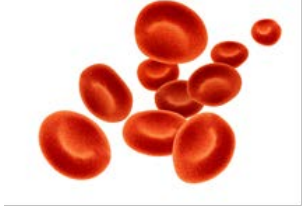

How is blood given in sickle cell disease?

NHS Blood and Transplant

- Simple top up transfusion
  - Common in childhood
  - Easy to give but leads to iron loading if given long term

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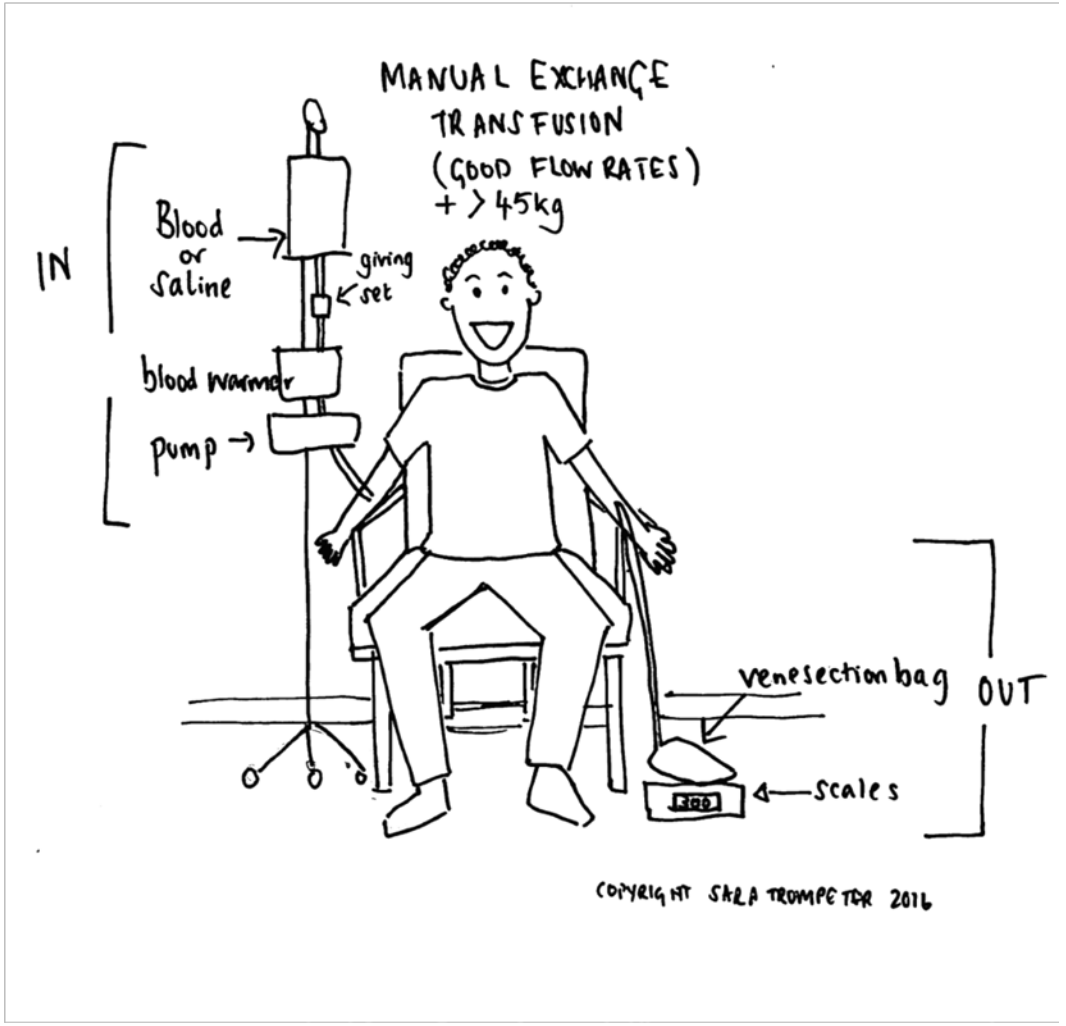
NHS
Blood and Transplant

Manual exchange

Rarely given but good in an emergency as not many resources needed and can reduce sickle percentage relatively simply, some iron loading if long term



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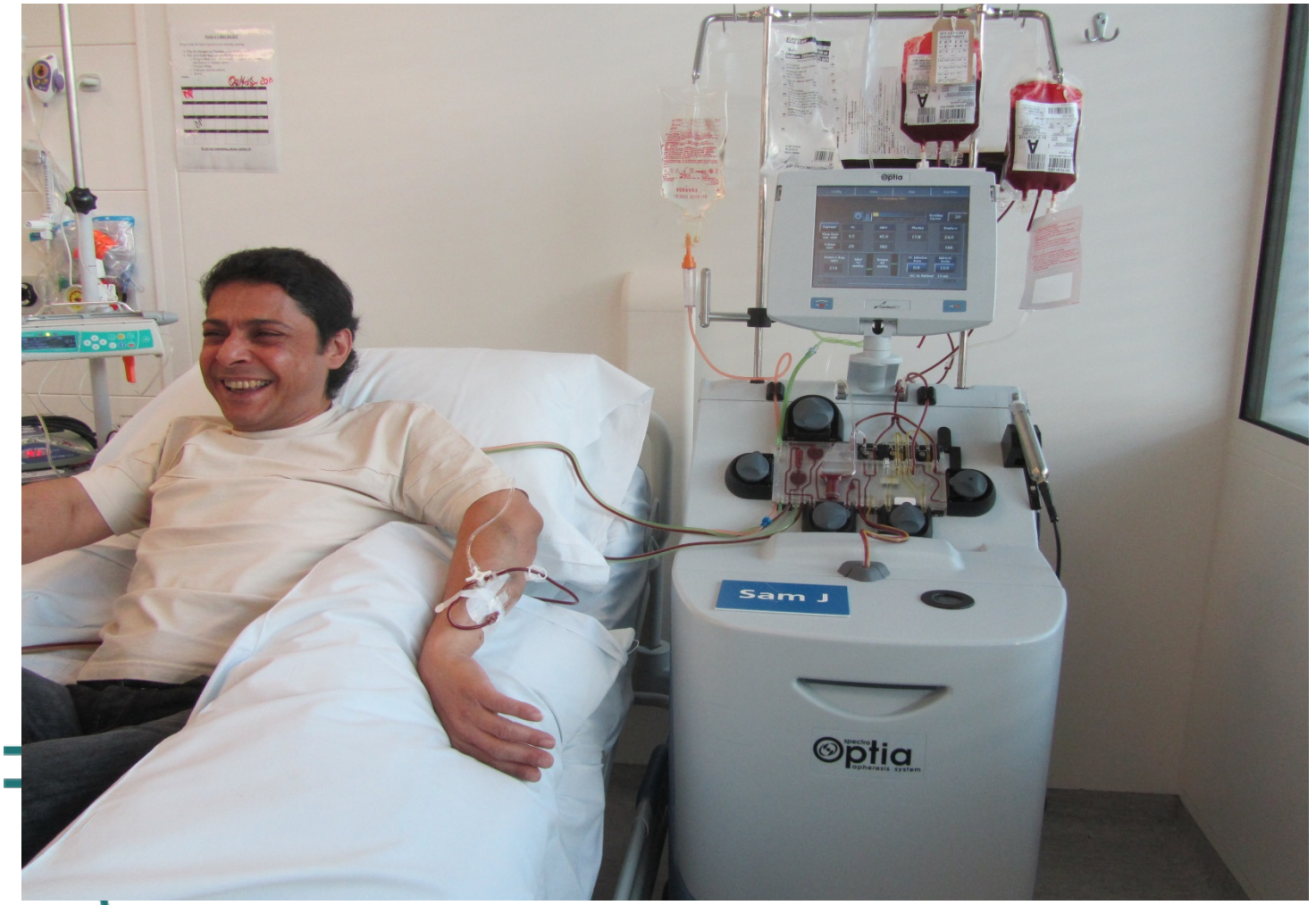
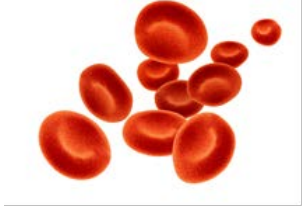


Automated exchange

- Quick, efficient, controlled, kit expensive and skills needed but less iron loading

NHS
Blood and Transplant

Automated exchange



NHS Blood and Transplant

Why genotype patients

- Why do we need to know all the red cell antigens anyway?
- What does genotyping offer over phenotyping?

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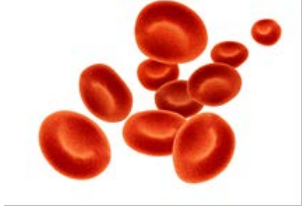

NHS Blood and Transplant

Why do we need to know the antigen status?

- Guidelines recommend
  - matching for full Rh and Kell- can reduced alloimmunisation by 90%
  - Testing full red cell pheno/genotype up front at diagnosis
- Rh groups of patients differ from the donor cohort significantly
- Alloimmunisation common
- Blood may be needed in an emergency

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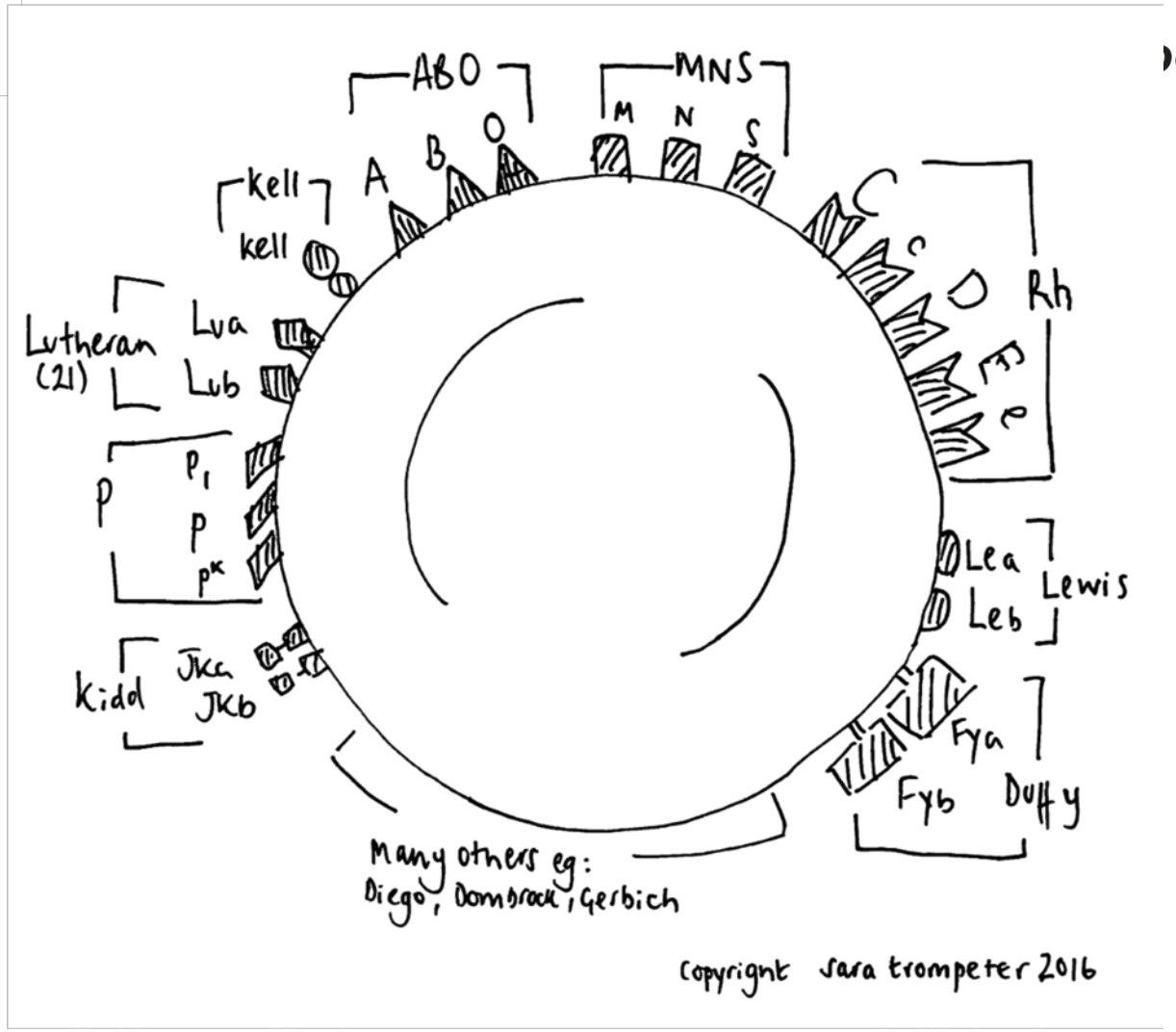
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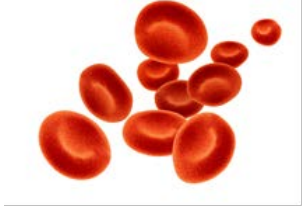

NHS Blood and Transplant

Why do we need to know the antigen status

- Patients often transfused out of hours by non haematologists in hospitals that don't know them
- SHOT reports highlight the catastrophic nature of alloimmunisation in this cohort
- Having a central resource with antigen status fully known is a good thing

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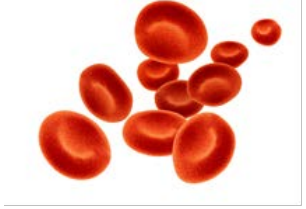
blood

2013 122: 1062-1071
Prepublished online May 30, 2013;
doi:10.1182/blood-2013-03-490623

High prevalence of red blood cell alloimmunization in sickle cell disease despite transfusion from Rh-matched minority donors

Stella T. Chou, Tannoa Jackson, Sunitha Vege, Kim Smith-Whitley, David F. Friedman and Connie M. Westhoff



NHS Blood and Transplant

What does genotyping offer over phenotyping?

- Can test for Rh variants
- Can be done if recently transfused
- Can test for unusual antigens if little antibody available
- Data kept centrally on Haematos and accessed through SpiCE

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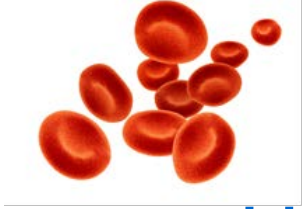

NHS Blood and Transplant

Haemoglobinopathy Genotyping Project – NHSBT 2015-16

- Completely innovative initiative
- Free red cell genotyping for all haemoglobinopathy patients including variants
- Shared on haemotos so can be seen when taken to other hospitals/move centre of care
- >4000 patients had their blood tested

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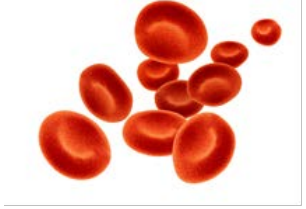

NHS Blood and Transplant

What about the donors?
Efficient accurate and timely provision of blood

– Current mechanism of blood ordering
– Ability of Pulse to filter orders
– OTIF (on time in full)

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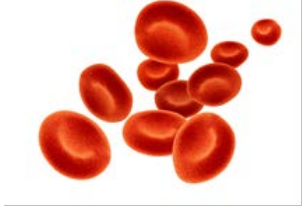
OTIF and Ro improvement project

- Initial work at UCLH 2013 orders on OBOS for sickle and thalassaemia patients

Substitution Flag	Total no. of units	%
N	30210	78.5
Y	8278	21.5
Grand Total	38488	

- Ro improvement project – Helen Mugridge and the wider NHSBT team



NHS Blood and Transplant

What about donors?: Cost

- RCI staff time
  - Have to locate units that may be a match and then offer extended testing at that stage on a unit
- Manual rather than automated process

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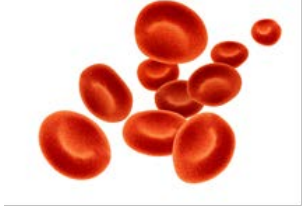

What about donors?: Meeting demand

NHS Blood and Transplant

- National Haemoglobinopathy Registry
  - 9000 patients registered (estimated 14000 in total)
  - 80% in London
  - Large expanding paediatric cohort
- Data from NCA shows
  - 1/3 of those regularly transfused are children
  - 15% of those regularly transfused have been so for >10 years
- Newborn screening programme
  - >300 children pa born with scd
  - >70% are HbSS
- Haemoglobinopathy survey
  - Adults on exchange get 10 units 6 weekly, on top up or manual exchange get 3 units 3 weekly.

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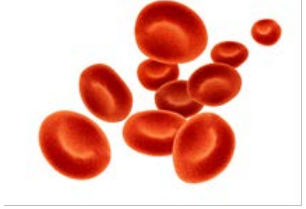

NHS Blood and Transplant

Audit – Dr Keir Pickard

- 30 patients
- 15 patients with Rh variants on the automated red cell exchange programme at UCLH
- 15 adult age and sex matched patients on the same programme who did not have red cell variants
- 6 month retrospective data for all patients

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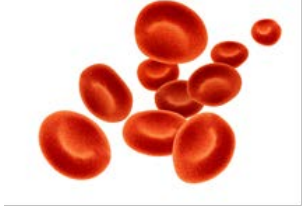

NHS Blood and Transplant

Summary data

- 2/3 men equally distributed between groups
- Mean age 43 years
- 67% of patients had any type of antibody
- 57% alloimmunised
- 10% had an antibody to a variant

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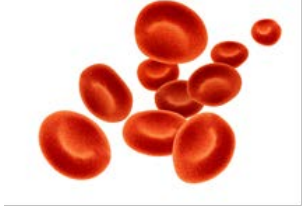

NHS Blood and Transplant

Parameters measured

- Measures of blood use
  - Total no. of units, average no. of units per episode, no of transfusion episodes
- Measures of haemolysis
  - Bilirubin and reticulocytes
- How well the targets are met: Hb and HbS pre/post exchange
- Iron loading
  - Ferritin
- Auto/allo antibodies
- Rh phenotype
- Demographics

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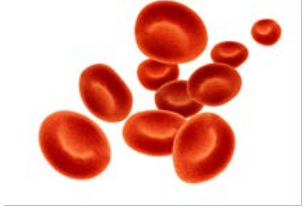

NHS Blood and Transplant

Grouping: 3 groups analysed

- Those with Rh variants vs. those without
- Those with antibodies to Rh variants vs. those without
- Those with antibodies to Rh variants and/or autoantibodies vs. those without

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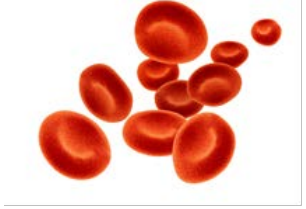

NHS Blood and Transplant

Statistical Analysis

- IBM SPSS v.24.0
- Independent t-test for most analyses
- Cross tabs / chi squared for non-parametric data

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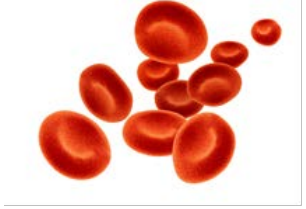

NHS Blood and Transplant

1. Variants vs. no variants

- 15 in each group
- No statistical difference in any parameter

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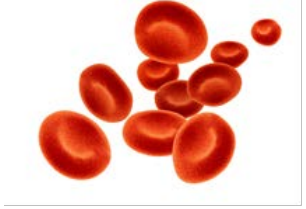

NHS Blood and Transplant

2. Variants with antibodies to variants vs. those without

- 3 with variants and antibodies to those variants, 27 not
- Only significance was that of bilirubin where mean 120 vs 48mmol/l p=0.036

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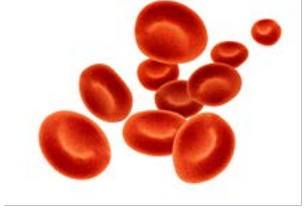

NHS Blood and Transplant

3.Variants with antibodies and/or those with autoantibodies vs. not

- 8 with auto/or alloantibodies to variants ie. 8/30 patients being transfused with blood that may be antigen positive for their antibody
- No statistical significance in any analysis

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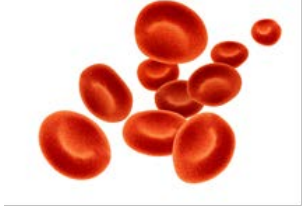

NHS Blood and Transplant

Limitations

- Cohort too small and therefore would not be able to detect clinically important differences
- Follow up period short
- Included those with poor compliance

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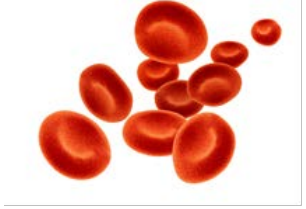

NHS Blood and Transplant

Plans

- To do a within patient analysis with those who are getting antigen negative blood for their Rh variants.
- Expand the cohort to use other sites for both between and within patient analysis

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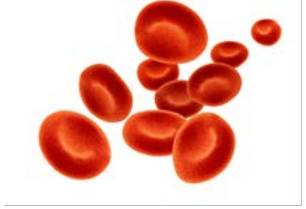

NHS Blood and Transplant

Summary

- Genotyping patients is of proven use in single complicated patients or in those who are recently transfused
- Patients need a red cell phenotype/genotype available centrally
- Genotyping donors would allow a more expedited issuing of results

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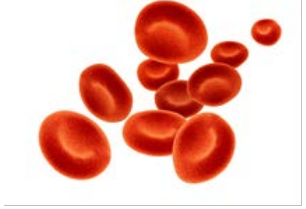

NHS Blood and Transplant

Acknowledgements

- Wendy Etheridge, Kirstin Finning, Andrew Hadley, Fiona Regan and all those on the HGP initiative
- Helen Mugridge, Kirk Beard and all those on the Ro improvement project
- Those throughout NHSBT who continue to support the transfusion care of SCD patients
- UCLH apheresis team especially Sr Nancy Huntley and David Leverett

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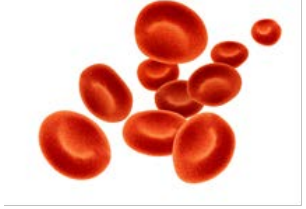

NHS Blood and Transplant

Thank you

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