STEM CELL TRANSPLANT FOR SICKLE CELL DISORDERS

Dr Amy Cooper
Haemoglobinopathy QI Fellow

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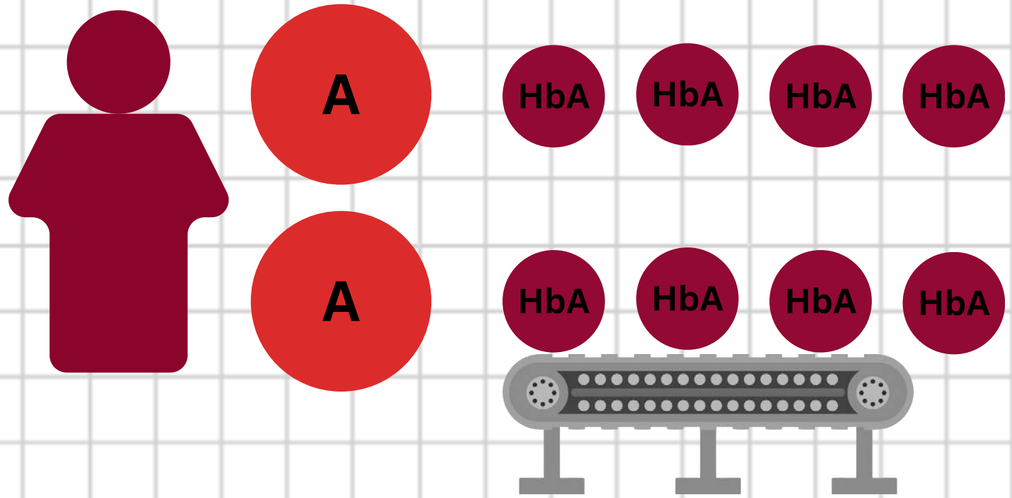
RED CELLS

- Red cells are blood cells which travel around the body in the blood stream
- They are filled with proteins called haemoglobin which carry the oxygen
- Haemoglobin is made by the two genes which are inherited - one from each parent
- Most people have the same kind of haemoglobin - HbA.



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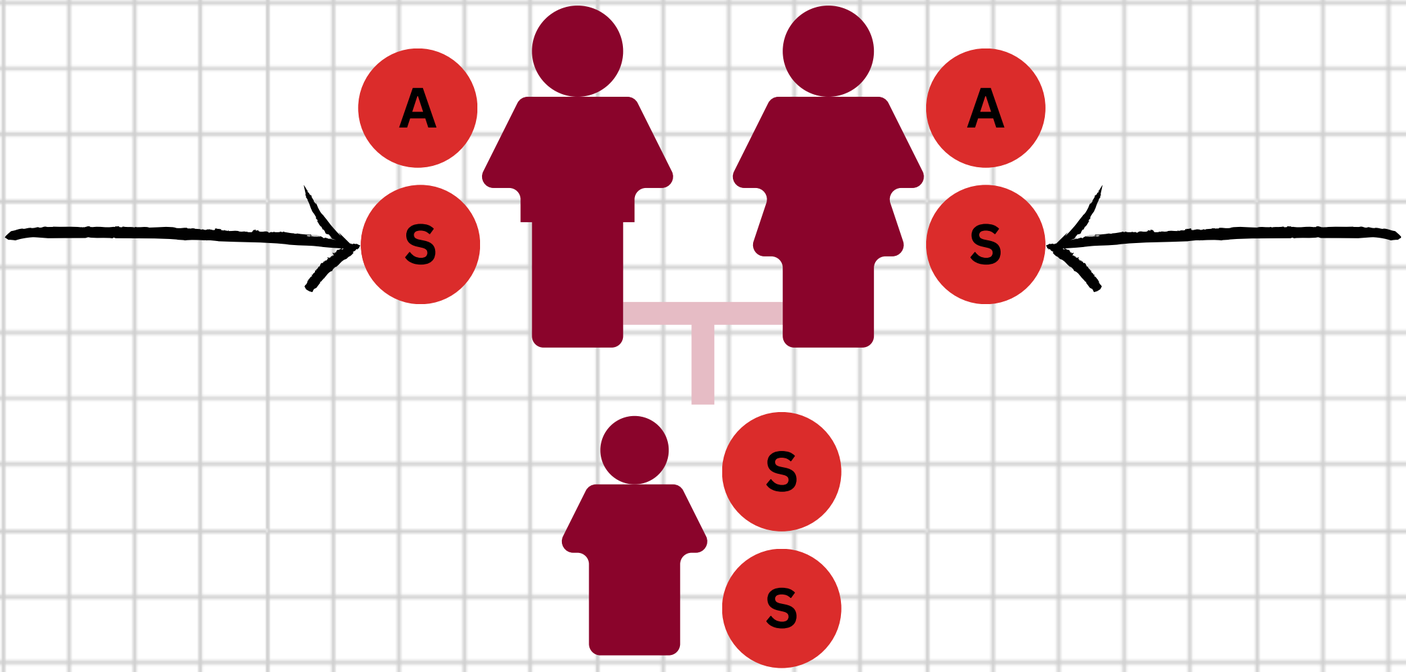
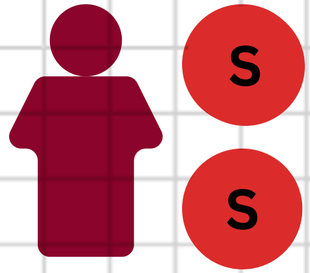
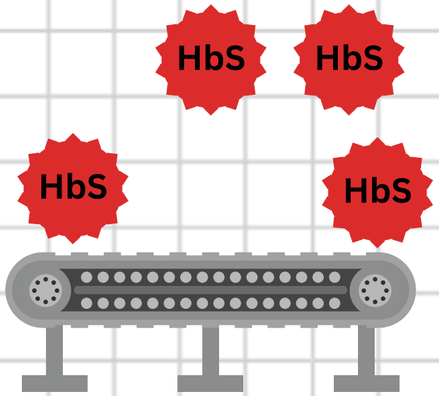
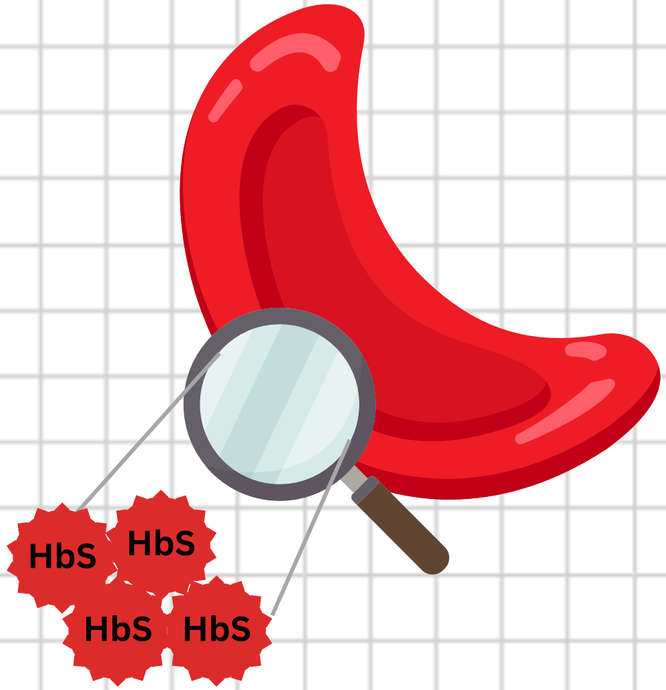
SICKLE CELL ANAEMIA









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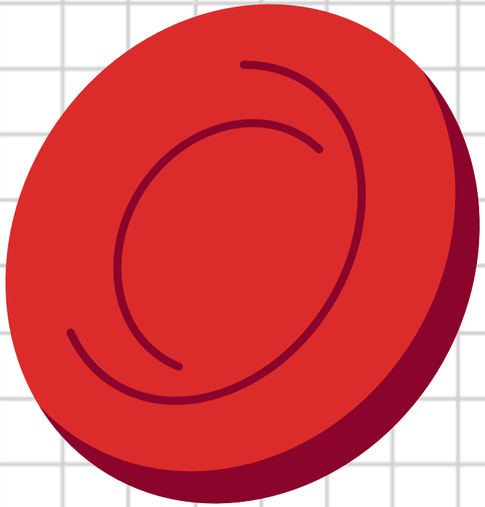
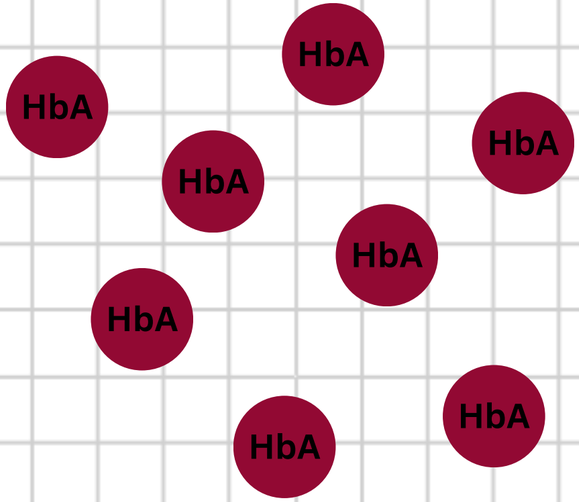
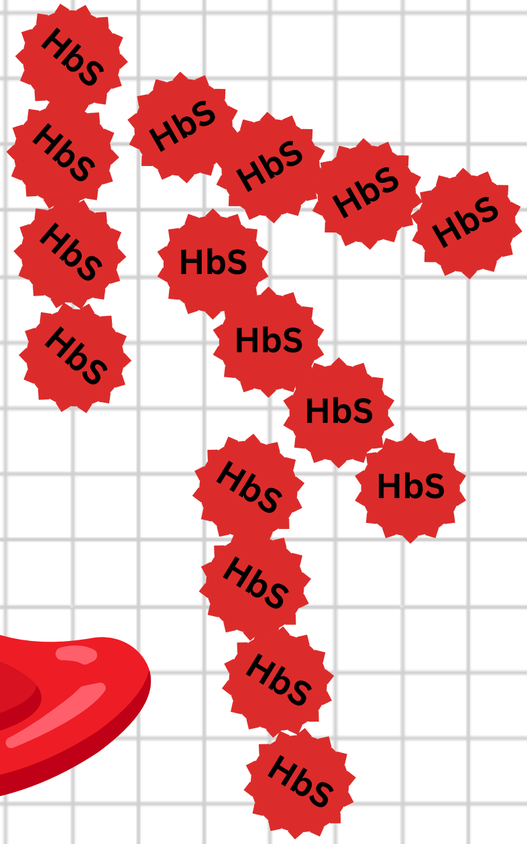
SICKLE CELL ANAEMIA

WHY DO CELLS SICKLE?







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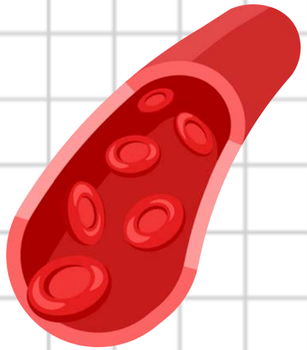
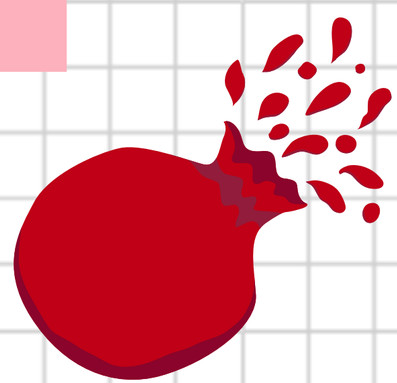
WHAT DO SICKLED CELLS DO IN THE BODY?



VESSEL BLOCKAGES

Sickle cells block small vessels, causing severe pain and background organ damage



CELL BREAKDOWN

Sickle cells are destroyed quickly by the body as it recognises them as abnormal.

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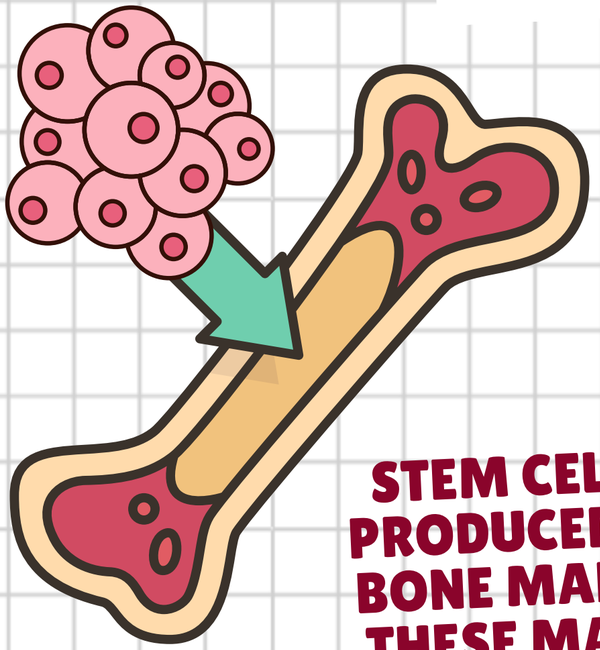
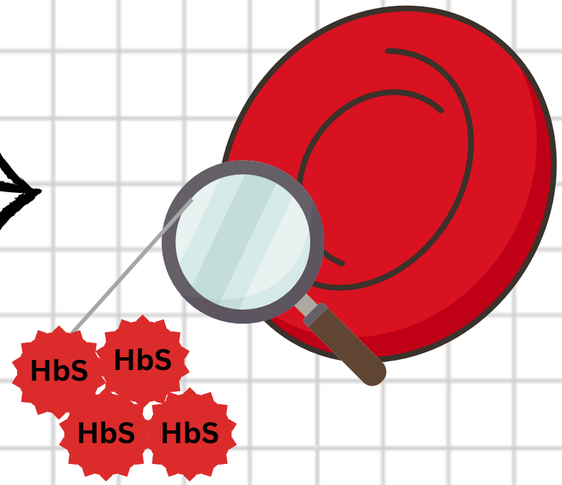
SICKLE CELL ANAEMIA

WHERE DO SICKLE CELLS COME FROM?



STEM CELLS ARE PRODUCED IN THE BONE MARROW – THESE MAKE RED CELLS, WHITE CELLS AND PLATELETS



RED CELLS ARE MADE – FILLED WITH SICKLE HAEMOGLOBIN

CELLS BECOME SICKLE SHAPED WITHIN 10 DAYS

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STEM CELL TRANSPLANT

1

Stem cell transplant has been available since 2020 in the UK for sickle cell disorders and is a potential cure

2

Patients need a 10/10 sibling match to be eligible to have a transplant on the NHS

3

The REDRESS trial is currently studying ‘half matched’ transplants in sickle cell disorders.

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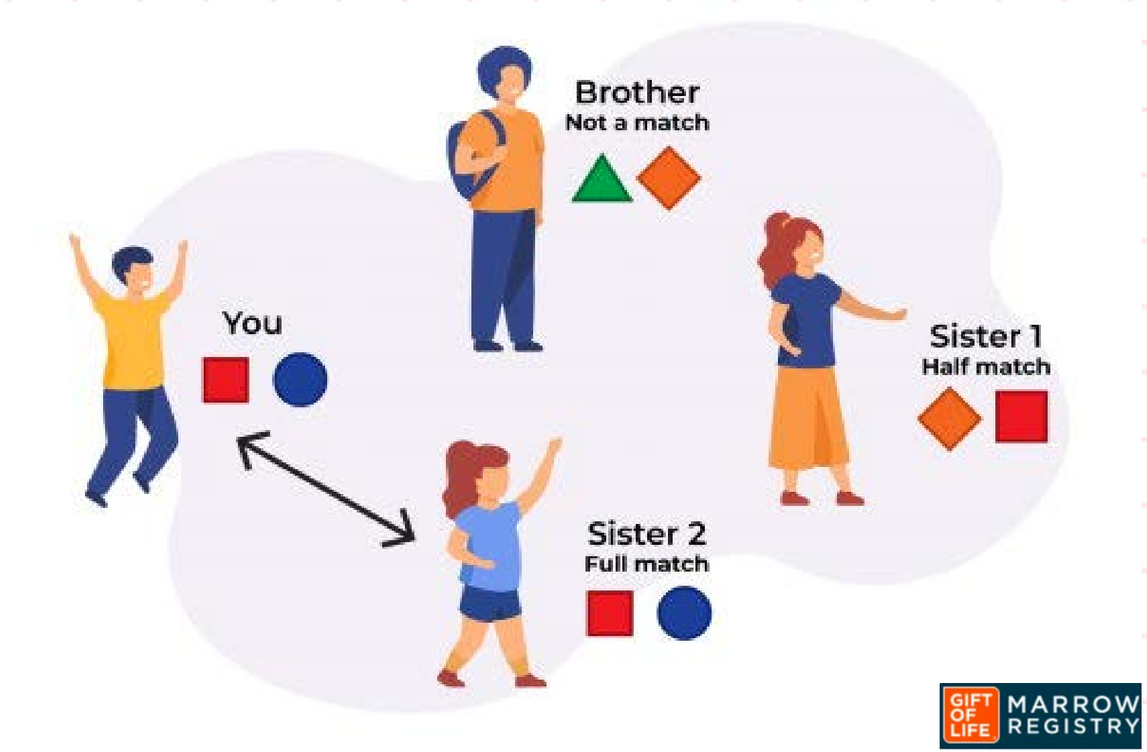
TYPES OF MATCH



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GIFT OF LIFE MARROW REGISTRY

WHY DO WE OFFER STEM CELL TRANSPLANT?

1

Sickle cell disorders cause serious acute illnesses, but also cause chronic background organ damage

2

Life expectancy remains shortened despite recent advances

3

Impacts of sickle cell disorders on wellbeing and quality of life are high

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WHO IS ELIGIBLE FOR TRANSPLANT?

1

Patients with organ damage related to sickle cell disease

2

Patients on regular red cell exchange transfusions

3

Patients who have severe complications such as acute chest syndrome and stroke

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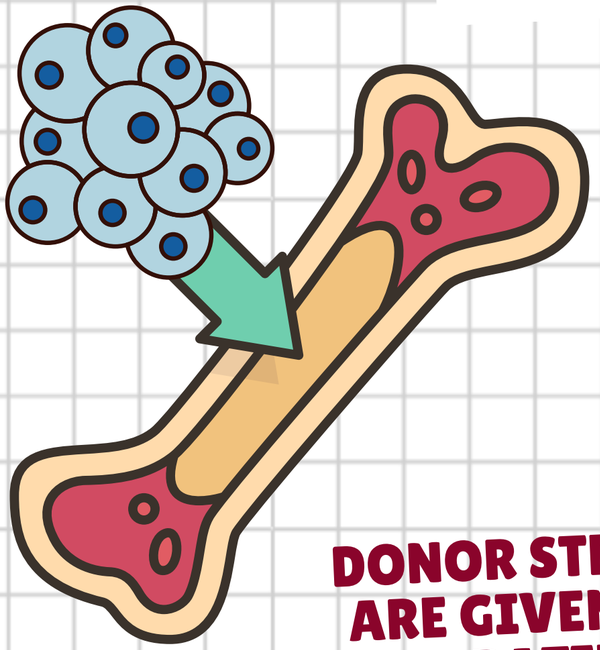
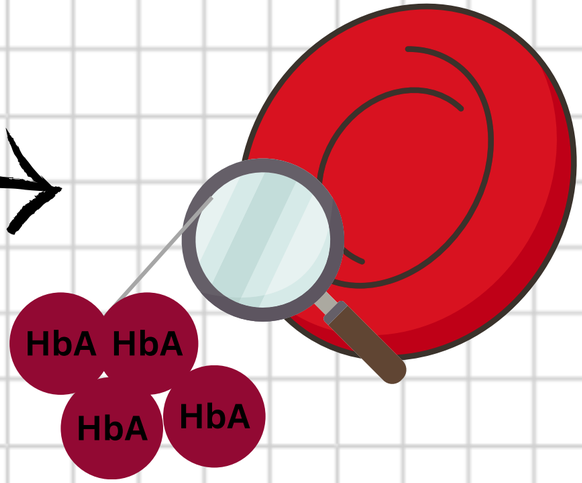
STEM CELL TRANSPLANT

HOW DOES IT WORK?



DONOR STEM CELLS ARE GIVEN TO THE PATIENT



RED CELLS NOW ONLY HAVE NORMAL HAEMOGLOBIN

CELLS CAN NO LONGER SICKLE AND LIVE FOR 120 DAYS

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THE TRANSPLANT PROCESS

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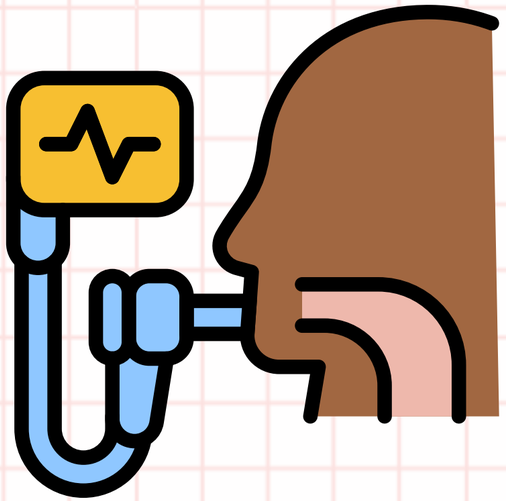
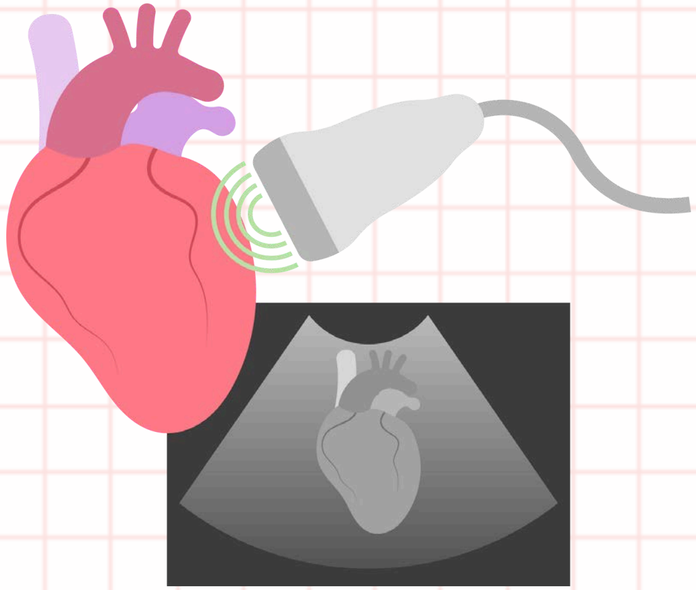
THE TRANSPLANT PROCESS



EXTENSIVE WORK UP IS REQUIRED TO DETERMINE A PATIENT'S FITNESS FOR THE PROCEDURE



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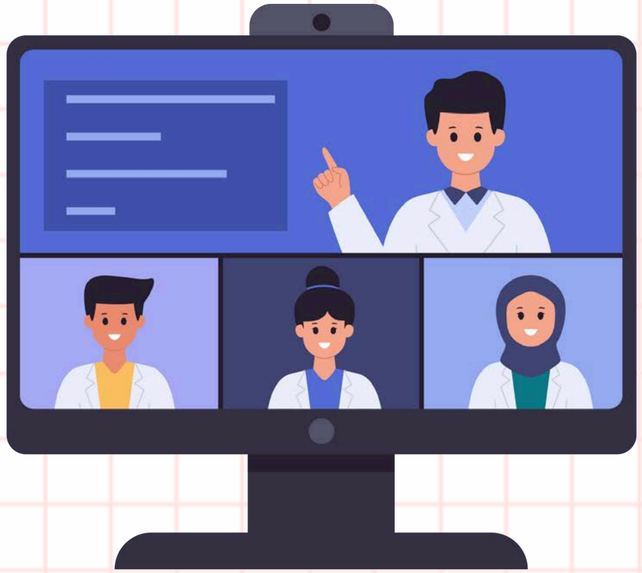
THE TRANSPLANT PROCESS



EACH CASE IS DISCUSSED WITH A NATIONAL PANEL OF EXPERTS BEFORE PROCEEDING

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THE TRANSPLANT PROCESS

THE PATIENT MEETS THE TRANSPLANT TEAM TO DISCUSS THE PROCESS IN EXTENSIVE DETAIL

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THE TRANSPLANT PROCESS

THE DONOR (RELATIVE) ATTENDS TO DONATE THEIR STEM CELLS

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THE TRANSPLANT PROCESS

ADMISSION TO HOSPITAL – AROUND 1 WEEK BEFORE THE STEM CELLS ARE GIVEN BACK

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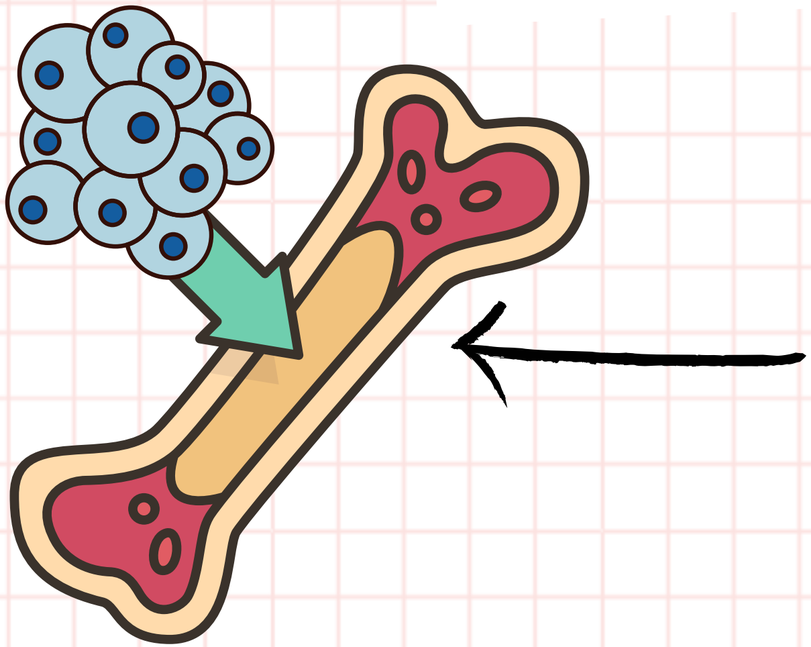
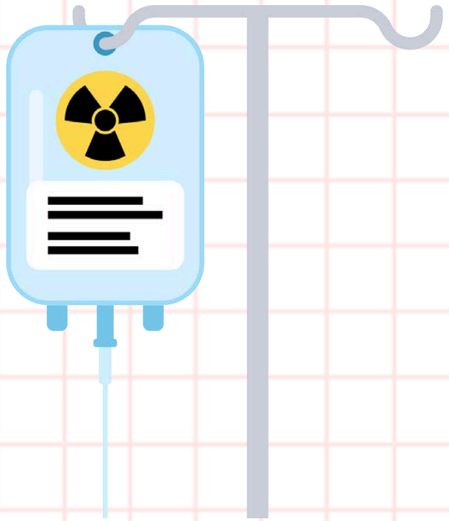
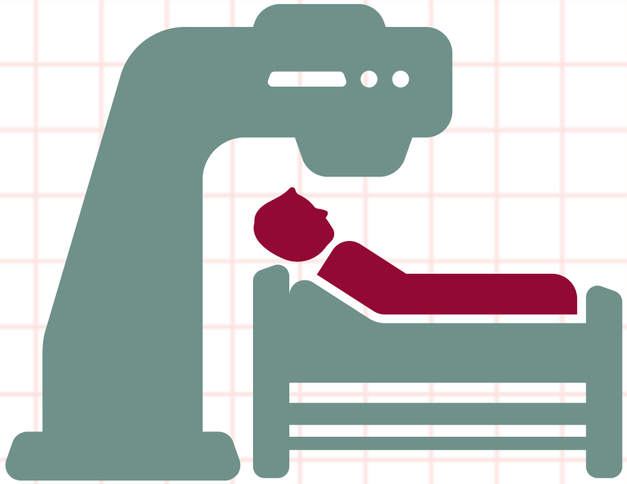
STEM CELL TRANSPLANT

HOW DOES IT WORK?





TO MAKE ROOM FOR THE DONOR STEM CELLS, THE NATIVE CELLS MUST BE ELIMINATED. TOXIC TREATMENTS (OFTEN STRONG CHEMOTHERAPIES OR TOTAL BODY IRRADIATION) ARE USED TO DO THIS



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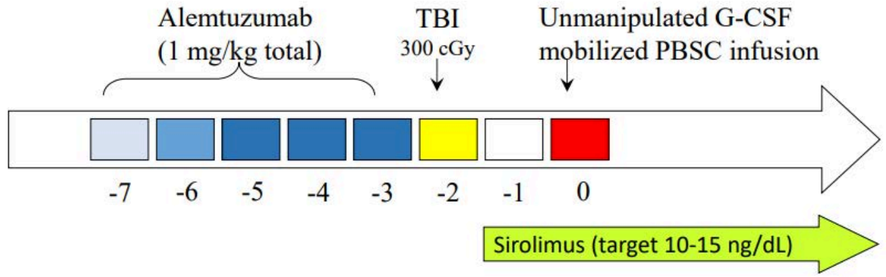
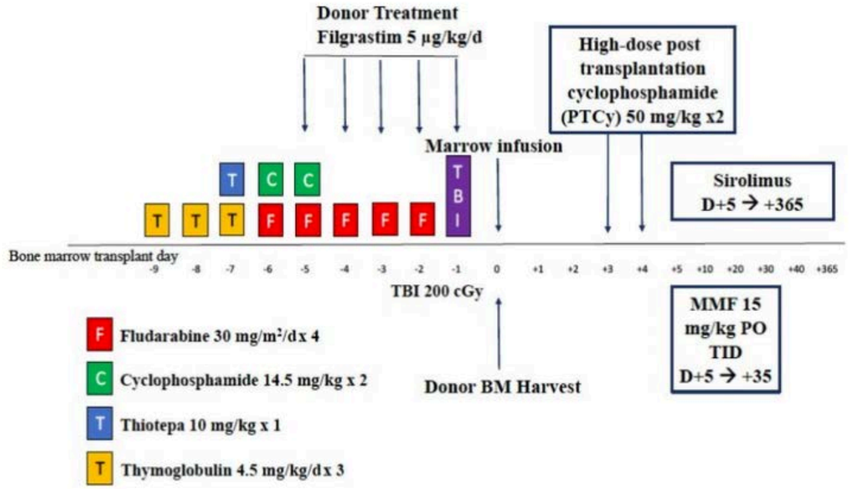
STEM CELL TRANSPLANT

CONDITIONING

MATCHED SIBLING TRANSPLANT:



HALF-MATCHED (HAPLOIDENTICAL) TRANSPLANT:



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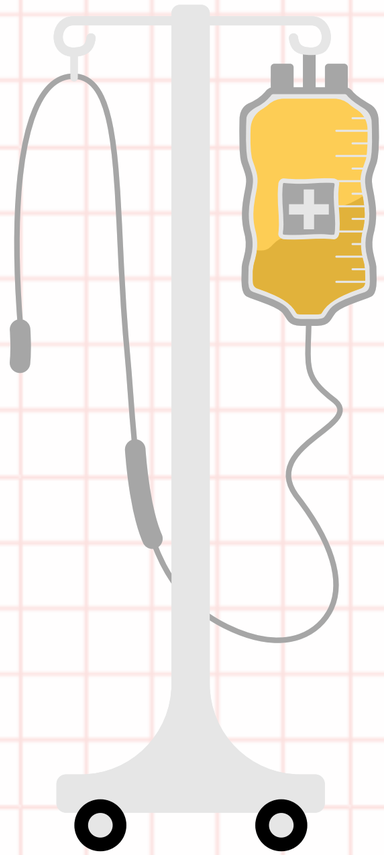
THE TRANSPLANT PROCESS



"DAY ZERO" – STEM CELLS ARE GIVEN TO THE PATIENT

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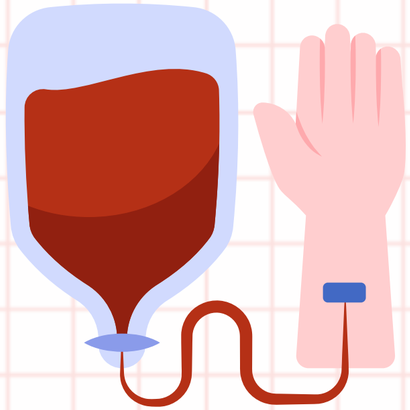
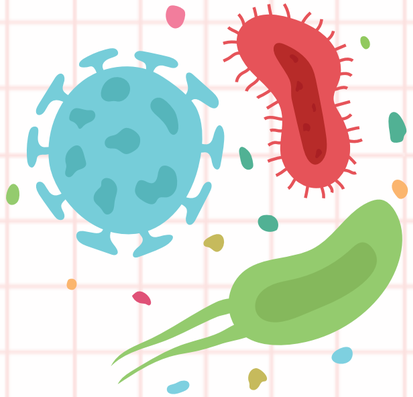
THE TRANSPLANT PROCESS





AFTER STEM CELLS ARE GIVEN, THEY NEED 2–3 WEEKS TO START WORKING. DURING THIS TIME, THE PATIENT HAS VERY LOW BLOOD COUNTS.

THEY WILL LIKELY REQUIRE TRANSFUSION AND ARE VERY SUSCEPTIBLE TO SERIOUS INFECTION.

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THE TRANSPLANT PROCESS

AROUND 2–4 WEEKS AFTER STEM CELLS ARE GIVEN, PATIENTS CAN BE DISCHARGED.

CLOSE FOLLOW UP AND IMMUNOSUPPRESSIVE MEDICATION IS REQUIRED

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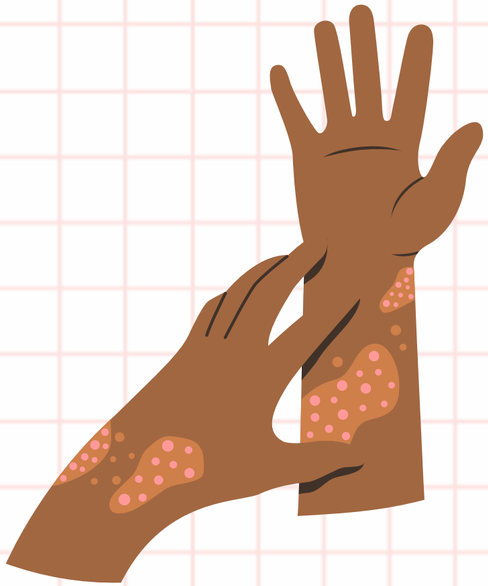
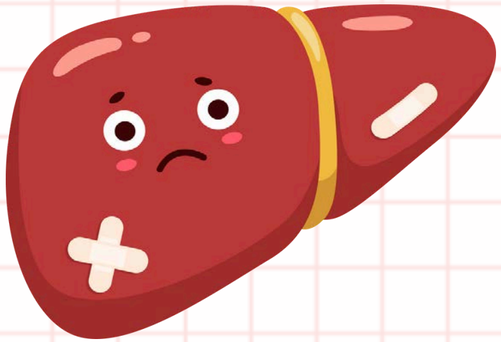
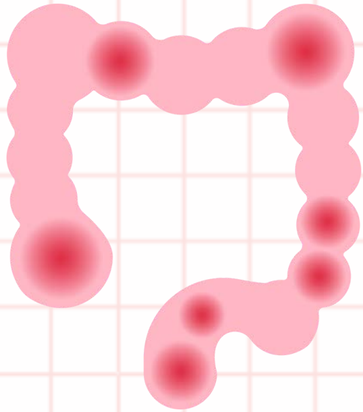
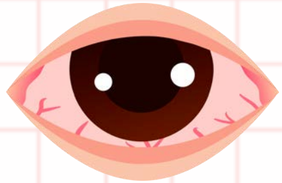
THE TRANSPLANT PROCESS







DURING AND AFTER THE TRANSPLANT, THERE IS A RISK OF GRAFT VERSUS HOST DISEASE



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GRAFT VS HOST DISEASE

RISK OF GVHD:

- MATCHED SIBLING TRANSPLANT:
  2% ACUTE, NO CHRONIC GVHD
- HAPLOIDENTICAL TRANSPLANT:
  10% ACUTE, 3% CHRONIC GVHD

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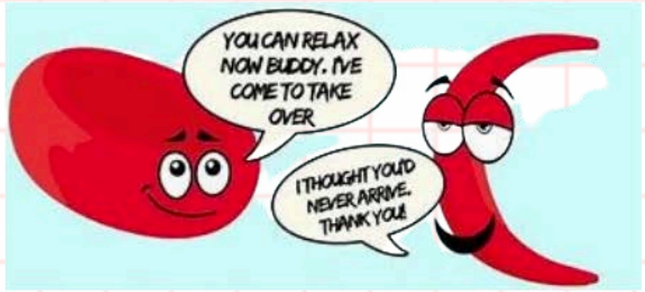
SIBLING TRANSPLANT

What are the outcomes of sibling transplant for sickle cell disease?

IN THE UK WE HAVE ADOPTED A NATIONAL PROTOCOL

This is that used by NIH which showed how safe transplant could be for adults



Median age 29 (10-65)
48% patients >30
17% patients >40

OS = 93%
Sickle free survival = 85%

GVHD rates are low
2% acute
No chronic GVHD

14 pregnancies (7 M, 7 F)

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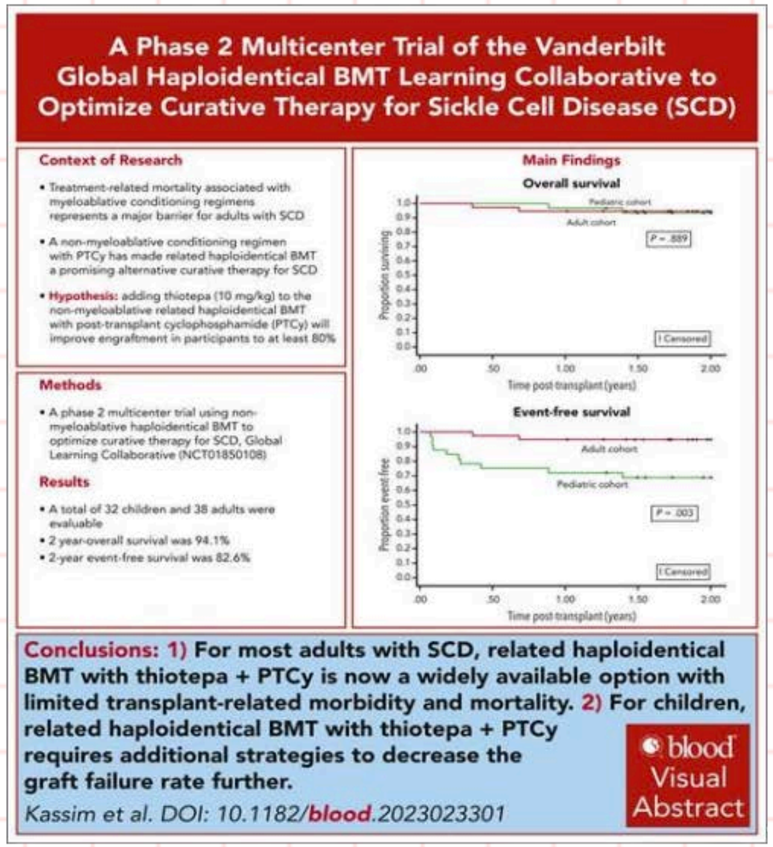
Adapted from REDRESS presentation slides

HAPLOIDENTICAL TRANSPLANT



A Phase 2 Multicenter Trial of the Vanderbilt Global Haploidentical BMT Learning Collaborative to Optimize Curative Therapy for Sickle Cell Disease (SCD)

Context of Research

- Treatment-related mortality associated with myeloablative conditioning regimens represents a major barrier for adults with SCD
- A non-myeloablative conditioning regimen with PTCy has made related haploidentical BMT a promising alternative curative therapy for SCD
- **Hypothesis:** adding thiotepa (10 mg/kg) to the non-myeloablative related haploidentical BMT with post-transplant cyclophosphamide (PTCy) will improve engraftment in participants to at least 80%

Methods

- A phase 2 multicenter trial using non-myeloablative haploidentical BMT to optimize curative therapy for SCD, Global Learning Collaborative (NCT01850108)

Results

- A total of 32 children and 38 adults were evaluable
- 2 year-overall survival was 94.1%
- 2-year event-free survival was 82.6%

Main Findings

Overall survival

Event-free survival

Conclusions: 1) For most adults with SCD, related haploidentical BMT with thiotepa + PTCy is now a widely available option with limited transplant-related morbidity and mortality. 2) For children, related haploidentical BMT with thiotepa + PTCy requires additional strategies to decrease the graft failure rate further.

*Kassim et al. DOI: 10.1182/**blood**.2023023301*

blood Visual Abstract

90% of patients screened has suitable haploidentical donors

Sickle free survival = 83%

Event free survival in adults was 94%

Acute GVHD 10%
Chronic GVHD 3%

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Adapted from REDRESS presentation slides

SUMMARY

Adapted from Anthony Nolan 'Sickle Cell Disease and stem cell transplant' page

Benefits

- A stem cell transplant can cure your sickle cell disease.
- You can expect your pain crises to stop but this may take some time. You might experience chronic pain due to the effects of your sickle cell disease.
- A stem cell transplant should prevent further complications caused by your sickle cell disease, like problems with your eyes and organ dysfunction.
- You can have a better quality of life.

Risks

- Any current complications you have from your sickle cell disease, like liver failure or heart conditions, could put you at risk during a stem cell transplant.
- Graft versus host disease (GvHD) is a potentially life-threatening side effect of a stem cell transplant.
- You will need to have conditioning therapy before your transplant. Currently, for people with sickle cell disease, this is made up of an immunosuppressive drug and low dose radiotherapy. Conditioning therapy prepares your body for your new stem cells and you're more at risk of infection during this time.