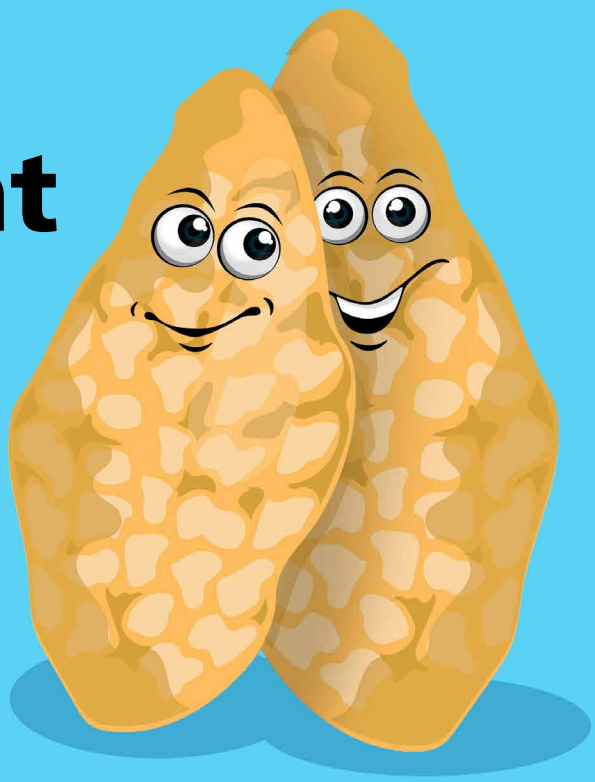
NHS
Great Ormond Street Hospital for Children
NHS Foundation Trust

Caleb
has a Thymus Transplant
at Great Ormond Street Hospital for Children

The European story of how and why children receive thymus transplantation for congenital athymia.



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Contributors: Thymus Transplantation Programme Team, GOSH and Thymus Transplantation Families

This story has been created with families, for families of children who will receive Thymus Transplantation at Great Ormond Street Hospital for Children, in London, England.

This story will provide helpful information about:

- Why the thymus is so important to fight infection
- What Thymus Transplantation is
- What will happen when your child receives this treatment
- How you can help protect your child

Throughout this story you will see **blue words** and **labeled pictures**. You can find out more about these at the end of the story in the glossary area. This information will help you to improve your understanding of the thymus transplantation journey.

You will also see in this story that we will call Great Ormond Street Hospital, **GOSH**, for short. Specialist Immunology doctors and nurses are available for further advice and support. You will find contact details at the end of the story.

This is Caleb and his family. Caleb is still a baby and has been in hospital a lot since he was born.

The doctors have said he has a condition called **DiGeorge Syndrome** which is causing some difficult health problems. Genetic investigations have shown he is missing a small piece of his **22q11 chromosome**.

They also say he has an **immunodeficiency** which is caused because Caleb did not grow a part of the body called a **thymus**. When this happens, we say children have ***complete* DiGeorge Syndrome**.

When children are born without a thymus we call this **congenital athymia**. At GOSH we can help Caleb and other children by giving them a **thymus transplant** to help recover their immune function.

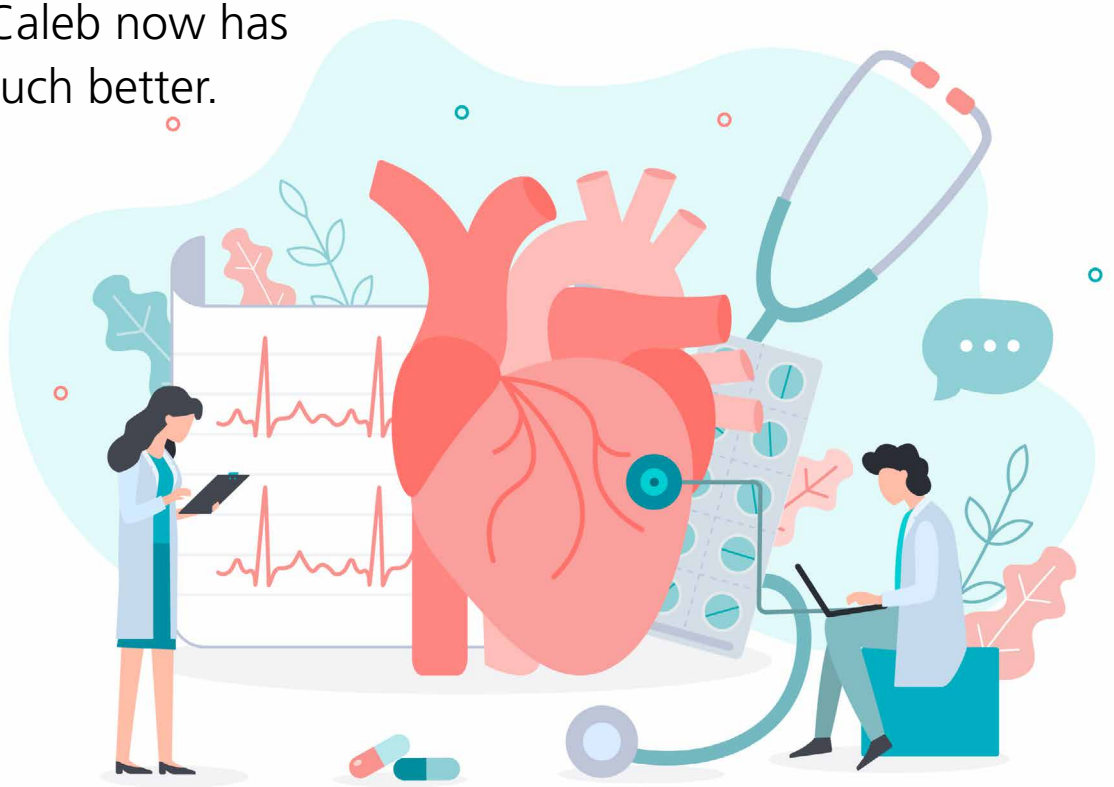
There can be different genetic and environmental causes for athymia. Some children can be born without a thymus caused by other **genetic conditions** such as CHARGE syndrome or PAX1 deficiency and for some children this may be caused by **environmental issues**.

Before Caleb can have his thymus transplant, he has some health problems which need immediate medical treatment.

Children like Caleb, with DiGeorge Syndrome, can often have problems balancing their **calcium** and **magnesium** levels and may need extra medications. Caleb's calcium level dropped so low that he had a seizure. This was very scary for him and his family. Caleb now has regular calcium medications and he feels much better.

Caleb's calcium levels still need to be monitored very carefully and he may need to take these medications for a long time.

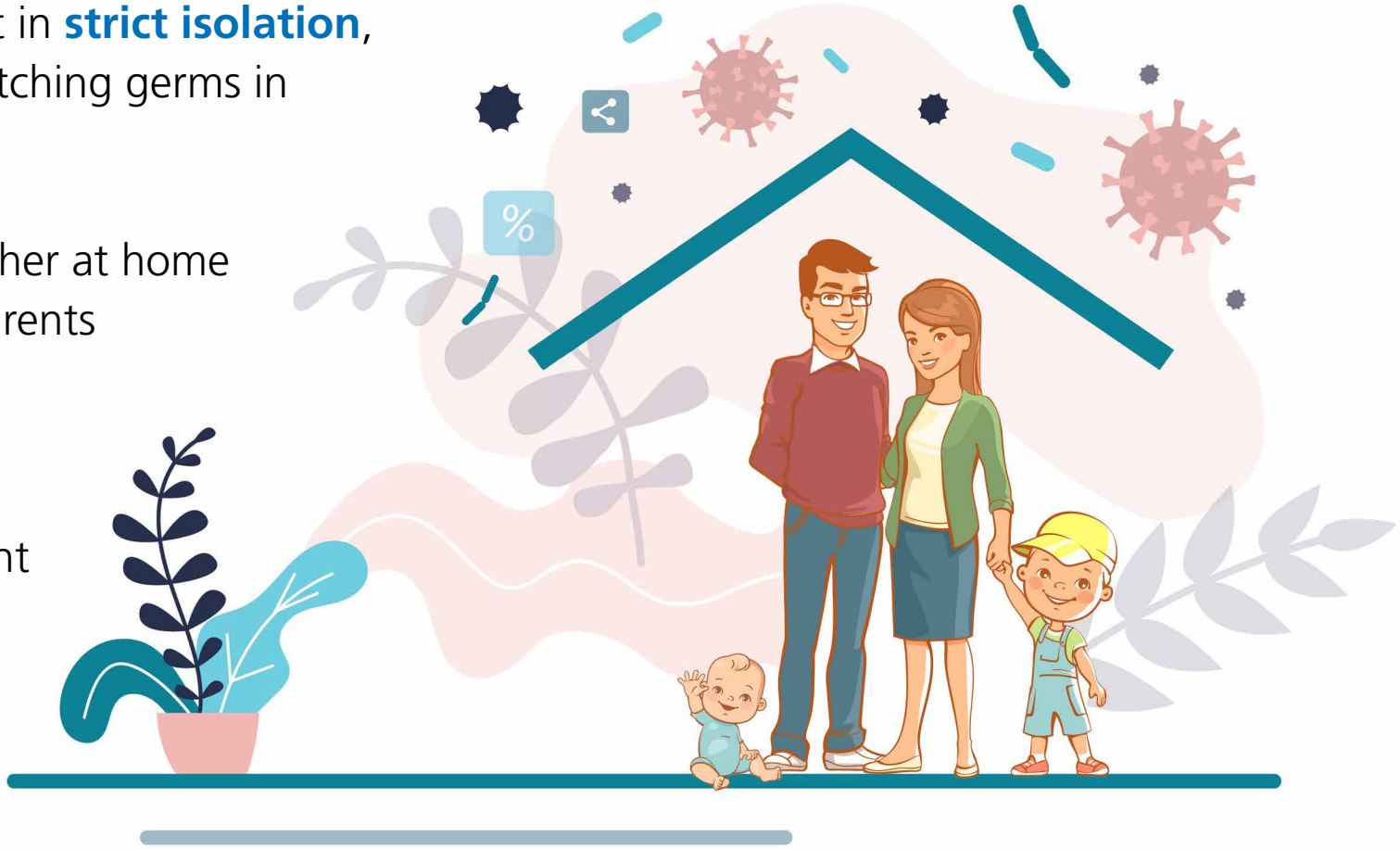
Caleb also has a problem with his **heart**. He will be having a surgery in his local hospital to help fix this. When his heart recovers, he can prepare to come to GOSH for his thymus transplant.



Caleb needs to be protected from infection while he is preparing for his thymus transplant. In order to do this, he needs to be kept in **strict isolation**, away from the risk of catching germs in public areas.

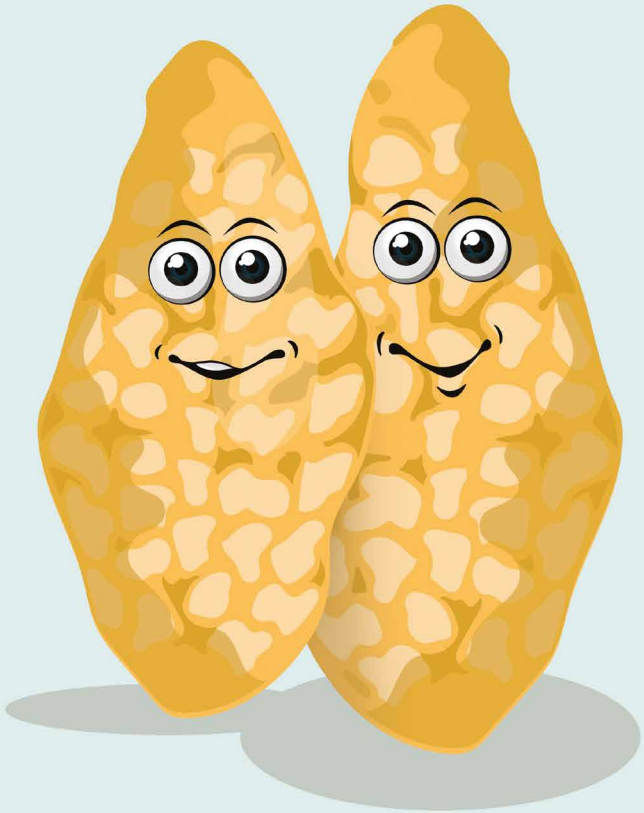
Caleb will be isolated either at home or in hospital with his parents or carer.

Protecting Caleb from infection is very important while he gets ready to come to GOSH for his thymus transplant.

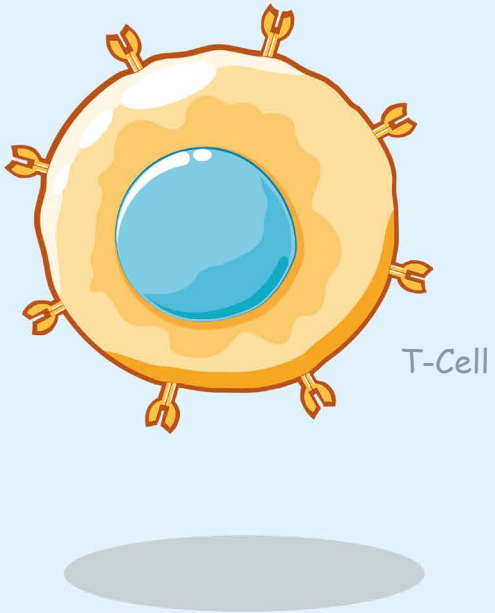


Caleb's family have been told he needs a thymus transplant because Caleb didn't grow his own **thymus**.

A thymus looks a lot like this, one organ with 2 lobes.



The thymus is important because it is like a school for the immune cells we call T cells.



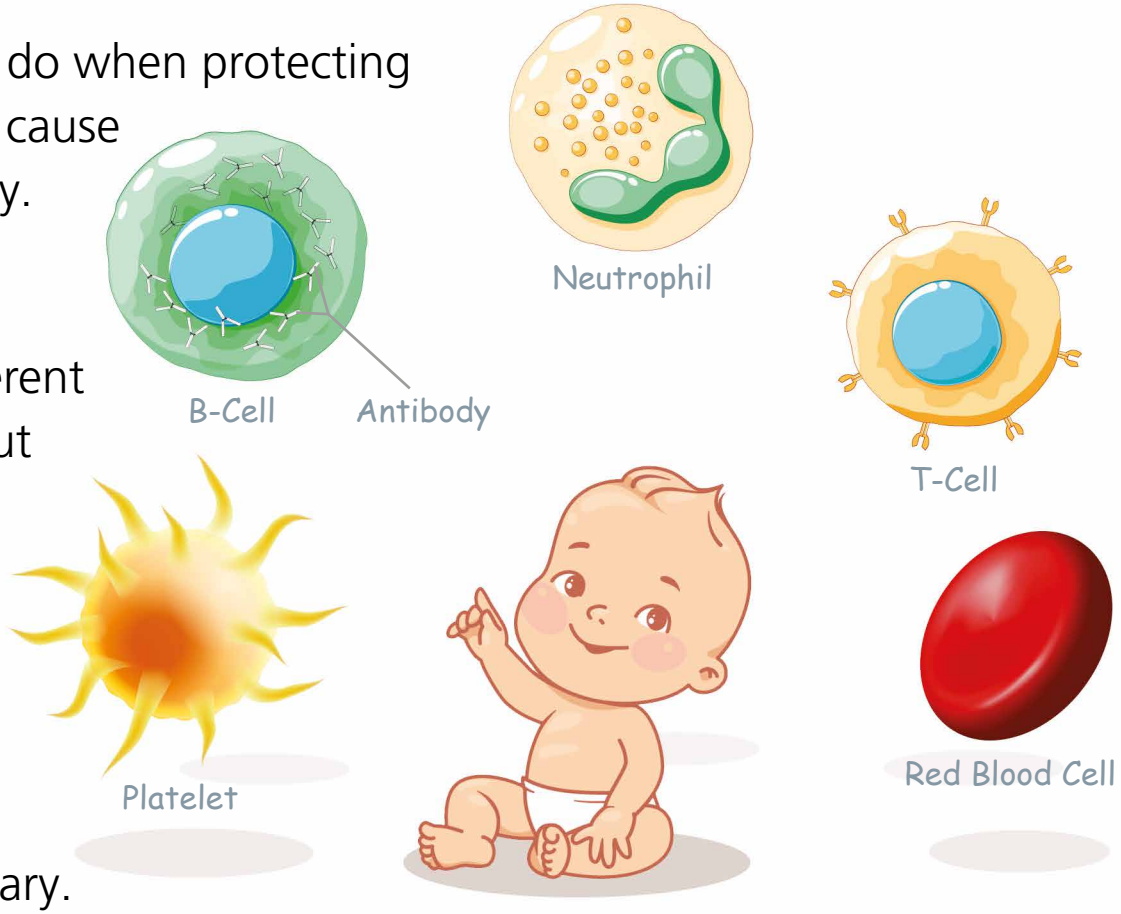
Caleb can make his own immune cells in his bone marrow. It is great that he can make them himself.

We have different types of white blood cells in our bodies and together, they make up our **immune cells**.

Each immune cell has a different job to do when protecting Caleb from harmful germs. **Germs** can cause infections, which can harm Caleb's body.

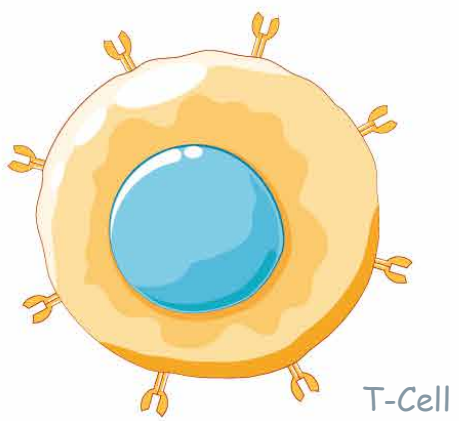
Unlike the other immune cells, T cells need to go to school to learn their different jobs. Their school is the thymus. Without a thymus to teach his T cells, Caleb cannot protect himself from the harmful germs. For this reason we say Caleb has an **immunodeficiency**.

Read more about the different immune cells at the end of the story in the glossary.



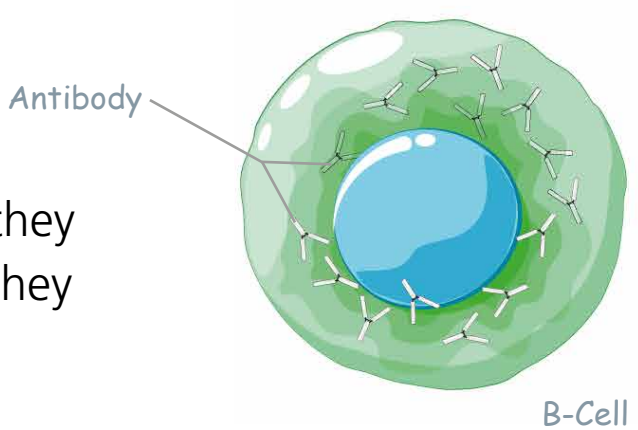
Our T cells have lots of different jobs to do in our immune system.

Some scan for and kill harmful germs. Some develop a memory to these germs for the next time they meet. Others help our bodies learn to know what is safe and what can be harmful when it gets inside our bodies.



T cells all learn these different jobs when they are developing inside the thymus.

T cells also have an important relationship with our B cells. They help B cells learn how to remember the harmful germs they have met, and how to build a team, ready to react quickly if they see the germ inside the body again in the future.

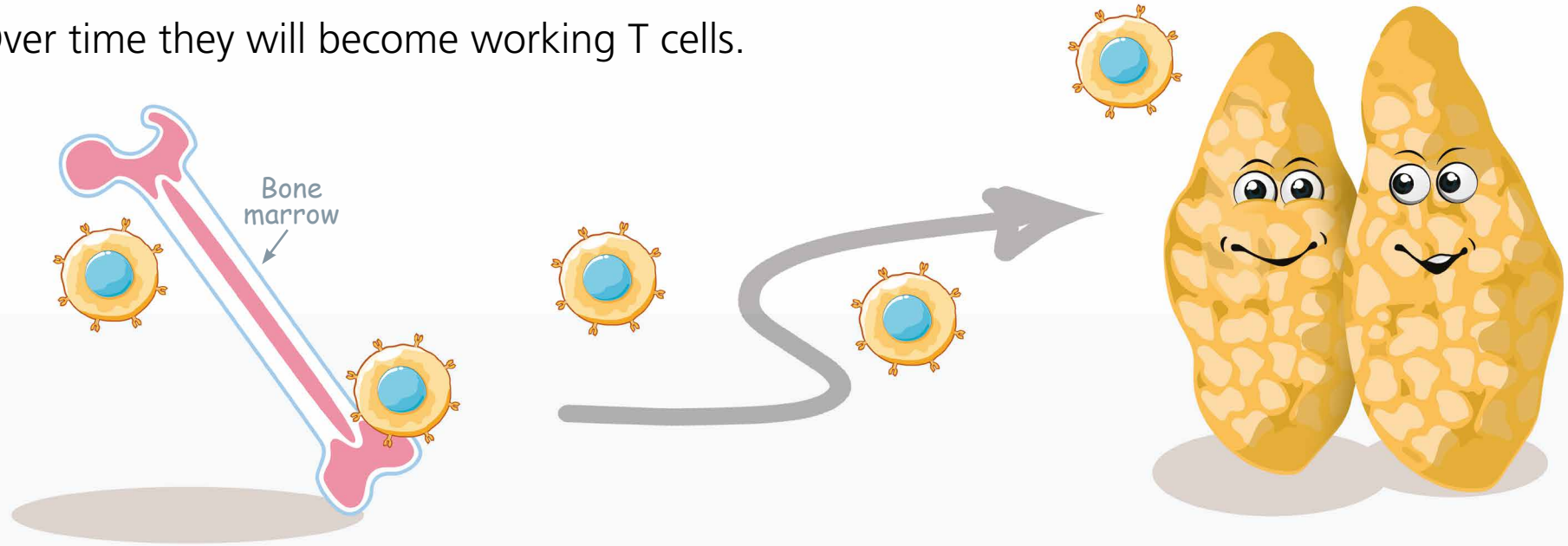


B cells make special proteins called **antibodies**, which help build the team.

B cells find it very difficult to work properly without instructions from T cells.

When Caleb receives his thymus transplant, we will give him new thymus tissue which can grow safely in his body. This means when Caleb's own T cells travel from his bone marrow, they will find the new thymus tissue. They will spend time here learning about their new jobs and how to communicate with other immune cells.

Over time they will become working T cells.



Until Caleb's T cells learn to do their jobs well, Caleb has a very high risk of becoming unwell from harmful germs, which can cause infection.

Some children can go home while they wait for their thymus transplant, but others might need more help and must stay in hospital in their local area. Caleb's Mum will stay with him at the hospital and other important carers can visit. When we find a thymus for Caleb, we will ask for him to make the journey to GOSH.

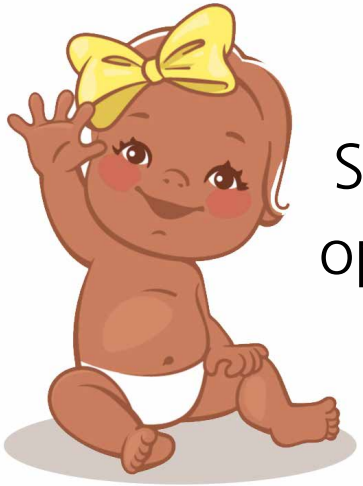
While we search for a donor thymus, Caleb must remain in strict isolation and take protective medications to protect him from possible infections. Learn more about the donor on the next page.

While in hospital Caleb's family will learn about the important medications Caleb will need to take regularly. One of these medications is called **Immunoglobulin**, and it will provide Caleb replacement antibodies until his own B cells are ready to make them. This will happen at a later stage, when his T cells are working well.

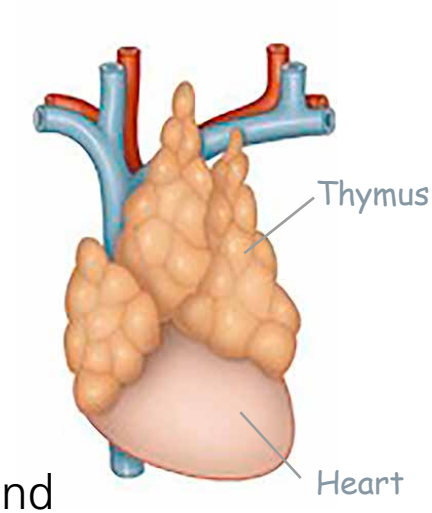
It is also important that Caleb does not receive any **vaccinations**. Some vaccines contain **live viruses** which can be harmful for children with no immune system.

Learn about the different types of **protective medication** Caleb needs to take and why, at the end of the story in the glossary.

This is Sarah.



Sarah is a baby too. She is having a heart operation at Great Ormond Street Hospital.



Part of the thymus is often removed during heart operations because it is very big when babies are young. Thymus tissue can sometimes get in the way when the surgeons are completing their operation and the surgeon needs to remove some of the thymus. It is usually discarded in theatre.

At GOSH, we have special permission to speak with Sarah's parents about **thymus donation**. This means if any tissue is removed, it can be collected and donated to be used for thymus transplantation. Thymus tissue can only be donated with the agreement of Sarah's parents. Caleb's Immunology team are going to speak with Sarah's parents to explain about the opportunity for thymus donation and what this means.

It's good news for Caleb and his family, Sarah's parents have agreed to donate her thymus tissue if any is removed during her heart operation. We call this agreement, *consent for thymus donation*.

Now the thymus tissue has been donated, it is taken to a special laboratory to be prepared for Caleb's thymus transplant.

Sarah's thymus tissue is called **donor thymus** from now on.

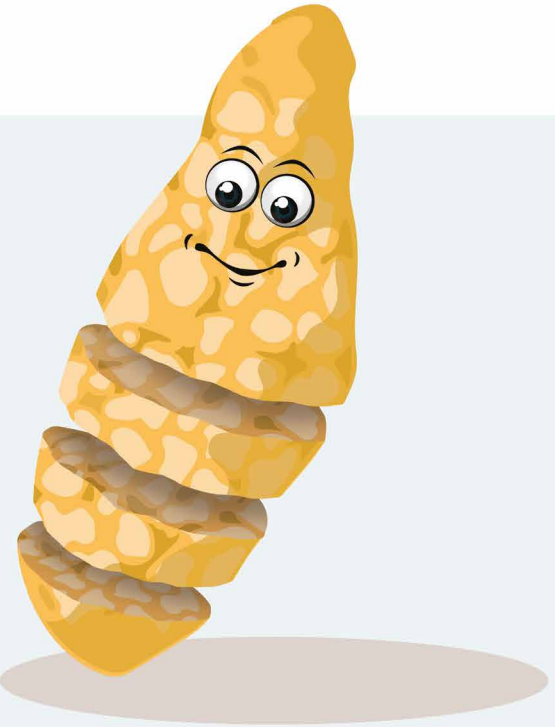
The donor thymus is looked after very carefully in a very clean, specially designed laboratory.

We start by checking that Sarah's blood group matches with Caleb's, so we know it is safe for him to receive.

Then the donor thymus will be checked for any infection risk to Caleb. We do this by carrying out blood and urine tests on Sarah and her Mum.

A specialist team in the **laboratory** will check on the donor thymus regularly over the next few weeks.

Before we can transplant the donor thymus, it needs to be sliced into small slices with special equipment and prepared in the laboratory ready for transplantation. Our laboratory team have specialist training to complete this very important step.



The donor thymus is kept in an incubator (a container which keeps the thymus in a safe and sterile (clean) environment). The thymus stays here for around 13-19 days before it can be used for transplantation.

If there are any concerns about the **safety** of the donor thymus, it will not be used for Caleb's transplant.

It is very rare for problems to occur with the donor thymus and we aim to prepare two donor thymus at the same time, so we have a back up thymus, just in case.

While Caleb has been getting ready to have his thymus transplant he has developed problems with his own T cells misbehaving – something we call **Omenn Syndrome**.

Omenn syndrome can happen to around half of the children we treat with athymia. Some of Caleb's own T cells have become unsettled waiting to go to school. We call these T cells, **rogue T cells**.

Rogue T cells have started travelling around Caleb's body looking for germs to fight and kill. Unfortunately, because they have not been educated by a thymus, these T cells do not know how to tell the difference between harmful germ cells and Caleb's own healthy cells. They have attacked Caleb's skin cells and tummy cells, causing a rash and symptoms of diarrhoea and vomiting.

We need to manage their behaviour quickly with a new medication called **Ciclosporin** and a new cream for his skin.

Caleb's rogue T cells have made his skin itchy, peeling and very dry.

The ciclosporin medication will help calm Caleb's rogue T cells. It will improve Caleb's skin condition and tummy symptoms, controlling the Omenn syndrome.

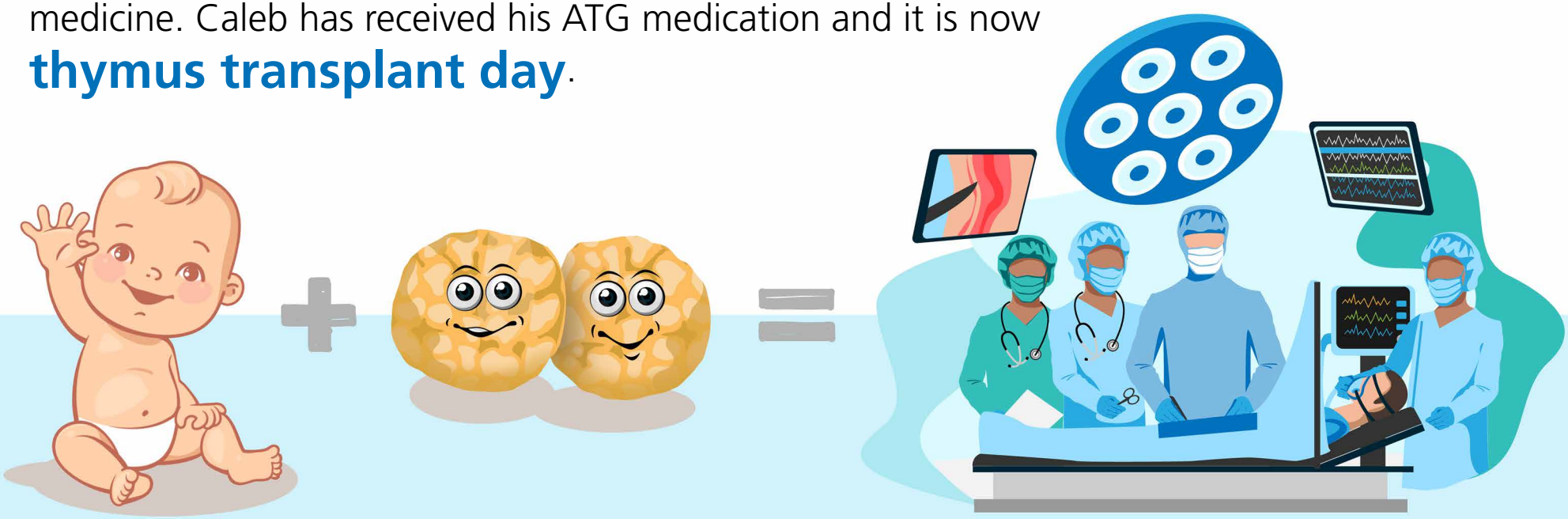
For Caleb and other children who experience Omenn syndrome, this will also mean they need another medication before their thymus transplant. This medication is called **ATG - Anti-Thymocyte Globulin**.

ATG is needed to completely kill the rogue T cells and to help protect the donor thymus when it is transplanted. Caleb will be given this medication at GOSH just before he receives his thymus transplant.

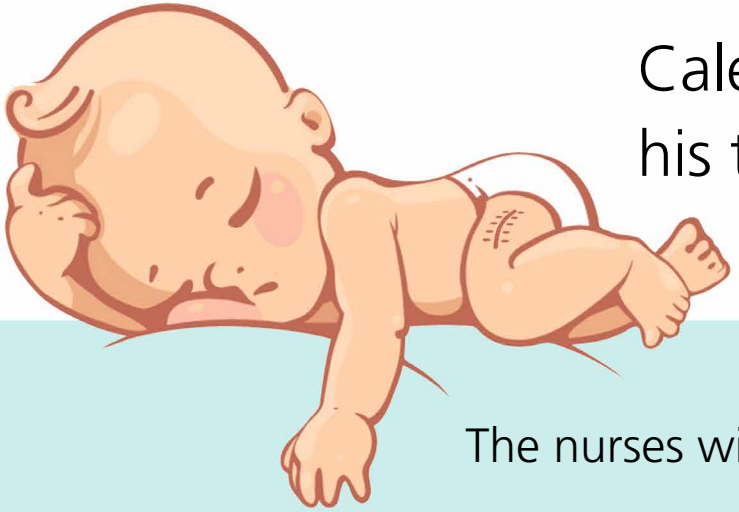
Remember, not all children will develop Omenn Syndrome, but you can look out for unusual skin rashes or ongoing symptoms of an upset tummy and speak to your child's doctor if they happen.

Caleb's donor thymus tissue has passed all the safety checks and is ready to be transplanted.

Caleb has arrived at GOSH and his skin condition has improved with his ciclosporin medicine. Caleb has received his ATG medication and it is now **thymus transplant day**.



The donor thymus pieces will be placed inside both of Caleb's thigh muscles.
The **thigh muscle** is chosen because it is a big muscle, with easy access, good blood flow and provides the best environment for the new thymus to grow and develop.



Caleb will go back to the children's ward after his thymus transplant. He will be very sleepy.

The nurses will look after Caleb by giving regular **pain medications**.

They will observe his surgical wounds through the clear dressings he will have on his thighs.

Caleb will continue to be isolated in his cubicle with his Mum.

Caleb's **wound** dressing will stay in place for about 7-10 days to let the thigh wounds heal.

Look at the end of the story to see real life **wounds** at different stages of healing

Caleb feels better already and after a couple of days, he is kicking his legs and playing with his Mum and the nurses.

Caleb will be able to leave GOSH soon, usually 2-3 weeks after his thymus transplant. He will go back to his local hospital for a little longer, so his other health needs can be monitored.

For children who do not have additional health needs, it is possible for them to go home from GOSH. They will still need to visit their local medical team regularly in clinic for monitoring. Local teams will agree a plan of care with families.

We will see Caleb again in London, after 3 months. This is for a short hospital stay when he will have a **thymus biopsy**.

We will speak with his local medical team regularly during this time.

Over the next few months Caleb will spend his time growing and developing as all babies do.

During this time Caleb's T cells will slowly begin to travel from his bone marrow to find his new thymus. Caleb's T cells will spend a lot of time in the thymus, going to school, and will learn all about their important jobs in Caleb's immune system.

T cell development is a slow process and their education will take several months.

It is important Caleb stays in **strict isolation** and continues to take all his **protective medications**.

It's time for Caleb to come to back to GOSH, for a short visit and a biopsy procedure. A biopsy is when the surgeon opens one of Caleb's old thigh muscle wounds and takes out small pieces of the transplanted donor thymus.

The thymus tissue collected during the biopsy is looked at through a **microscope** by another specialist team at GOSH.

The tissue collected during the biopsy provides important information, we cannot learn from blood tests. It tells us:

- The new donor thymus is growing well inside Caleb's muscles
- Caleb's own T cells have found the new thymus tissue and are being educated

This information helps us to carefully plan Caleb's future treatment, in particular in case of complications.

Do you remember Caleb had some T cells misbehaving before his thymus transplant and needed a medication called Ciclosporin?

It is also possible after thymus transplantation, that some children can have problems with T cells misbehaving. This can happen while the new thymus is settling into its new environment and T cells are still learning. It can also happen at later stages after the transplant.

We call these **autoimmune complications**. We can usually treat autoimmune complications with medicines mentioned before, like Caleb with ciclosporin or sometimes a medicine known as **steroids** or cortisol might be needed.

However, using steroids too soon after the transplant can be harmful to the new thymus. It is important that local teams and GOSH Immunology team have regular communication after transplantation and before steroids are given to children. This way we can keep giving advice and support. The biopsy results help us with these decisions.

Caleb's family will also watch for any unusual skin rashes, any new hair loss or continuous symptoms like diarrhoea. They will let the local team know straight away.

Caleb has recovered well from his biopsy procedure and is ready for **discharge**. We will share the results of Caleb's biopsy and recent blood tests with his local hospital team and his family.

Caleb's local hospital team are ready to look after him from now on, with regular communication with the GOSH team.

We will ask Caleb's local hospital team to send us blood samples every three months at first, to monitor his T cell development and progress.

It can take a long time, more than 6 months, for new T cells to begin to work really well. Caleb still needs to take his **protective medications** and remain **isolated** until his doctors tell his family it is safe to make changes.

The team at GOSH look forward to sharing Caleb's future care with his family and local team.

Here are some of the team you will meet at GOSH.

Professor Graham Davies
Founder of the European Thymus Transplantation Program at GOSH

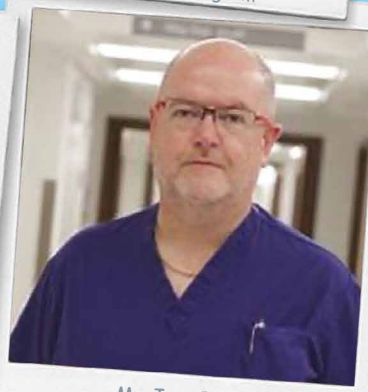
Dr Austen Worth
Consultant Paediatric Immunologist and Clinical Lead of European Thymus Transplantation Program

Dr Alexandra Kreins
Honorary Consultant
Immunology and Thymus Transplantation

Dr Zainab Golwala
Clinical Research Fellow in Thymus Transplantation

Evey Howley
Immunology Clinical Nurse Specialist in Thymus Transplantation

Cell Therapy Laboratory Team



Mr Joe Curry
Consultant Neonatal and Paediatric Surgeon

Mr Stavros Loukogeorgakis
Consultant Neonatal and Paediatric Surgeon

Mr Stefano Giuliani
Consultant Neonatal and Paediatric Surgeon

Children's ward nursing team

Helpful resources:

Contact us: Evey Howley Immunology Clinical Nurse Specialist – Thymus Transplantation
Evey.howley@gosh.nhs.uk Evey.howley@nhs.net

Great Ormond Street Hospital for Children NHS Foundation Trust
Main switchboard contact telephone number: Telephone: (+ 44) 0207 405 9200
Hospital address: Great Ormond Street Hospital, Great Ormond Street, LondonWC1N 3JH
https://www.gosh.nhs.uk

International and Private Care enquiries:
https://www.gosh.com.kw/

Patient stories:
https://www.immunodeficiencyuk.org/immunodeficiency/patient-stories/parent-and-children-stories/daniels-story-2/
https://www.immunodeficiencyuk.org/immunodeficiency/patient-stories/parent-and-children-stories/oscars-story/
https://www.gosh.com.kw/news-articles/50th-patient-treated-thymus-transplant-gosh

Helpful resources *continued*:

Immunodeficiency UK: Charity to support those affected by primary and secondary immunodeficiency in the UK
http://www.immunodeficiencyuk.org/

Max Appeal: UK based charity for families with diagnosis of 22q11 About Us — Max Appeal

Parathyroid UK: UK & Ireland based Charity for people living with parathyroid conditions
https://parathyroiduk.org/

IPOPI - International Patient Organisation for Primary Immunodeficiencies: https://ipopi.org/
National patient groups that represent the interests of primary immunodeficiencies patients:
https://ipopi.org/organisations/

Glossary of additional Information

Great Ormond Street Hospital will be shortened to **GOSH** throughout the glossary information.

A

ANTIBODIES

Antibodies help our immune system to develop a memory of harmful germs and help to remove them from our body. They are special proteins made by B cells to protect our body. If B cells see a harmful germ on more than one occasion, they react quickly to attack and release the special antibodies (see B cells). This action relies on working T cells (see T cells) to provide instructions to B cells before they know how to work properly.

Without the T cell communication for children with congenital athymia, B cells cannot carry out this important task. Children who do not have working B cells to produce antibodies, will be given a medication called Immunoglobulin, which can temporarily replace the missing antibody action (see Immunoglobulin).

ATG – Anti-Thymocyte Globulin

ATG is a special medicine given to children who develop symptoms of Omenns syndrome (See Omenn syndrome). The medicine works by finding uneducated, troublesome T cells which are moving around the child's immune system and destroys them. It does this without hurting any other cells in the body. ATG is given in 3 doses, once a day, for 3 days before children have a thymus transplant. This will happen while children are on the children's ward at GOSH.

ATG works just long enough for the new thymus to be transplanted and to have time to settle into its new home. This allows only new T cells leaving the bone marrow to populate the new thymus tissue.

IMPORTANT: If your child has experienced difficulties managing their calcium levels, like Caleb in the story, they will also be given extra calcium while in the hospital if they receive ATG. We do this because we know ATG has an effect of lowering calcium levels in this group of children. The extra calcium is a temporary treatment, and children will return to their usual calcium medication soon after the thymus transplantation. For some children it will be a few days, for others it might be a few weeks.

AUTOIMMUNE COMPLICATIONS

Do you remember about rogue (uneducated) T cells? The thymus is really important in educating T cells to know Caleb's own body tissues are different to harmful germs. If T cells are not educated properly they can cause problems and start attacking other blood cells, organs or a particular gland called the thyroid (see thyroid). When this happens after thymus transplantation, we call this autoimmune complications.

Doctors will monitor blood cell counts, like red blood cells, platelets and monitor the thyroid activity. They will watch carefully to see if children develop any signs of irritation on the skin, in the tummy or the liver. There are different medications that can be used if we see autoimmune complications and we will talk to families about these while they are at GOSH (see steroids).

B

B LYMPHOCTYE CELLS (say lim-fo-site)

We say B cells for short. B cells are one of our immune cells, made in our bone marrow. They make special proteins to protect our body called antibodies. Antibodies help to develop a memory of harmful germs and help to remove them from our body.

B cells need extra instructions from T cells before they can work in this way, otherwise they cannot make the antibodies and children are risk from the germs fighting against our bodies. Working T cells are important so they can learn how to talk to B cells and help them to do their job well (see T cells).

BIOPSY
A thymus biopsy is when the specialist surgeon opens one of the transplant thigh wounds and takes out small pieces of the transplanted donor thymus. A special team at GOSH will look through a microscope (a special magnifying glass) to look closely at the tissue. This allows us to see the new thymus very closely and to check the thymus tissue is working as expected.

The biopsy procedure happens 3 months after the thymus transplant at GOSH. Children will only need to be in London for a short time when the biopsy happens.

The biopsy results help us to plan care for the future.

C

CALCIUM
Calcium is an important mineral that helps support our bone and muscle development. It is important that we have stable levels of calcium in our body. Children with DiGeorge Syndrome can have low blood calcium levels and we call this hypocalcaemia (hypo meaning less than normal). Children who experience hypocalcaemia can shows signs of irritability, muscle pain and twitching, shaking hands, tiredness and sometimes when levels get very low, they can have seizures. Calcium supplements might be needed to help to maintain calcium levels. Children will need to be monitored regularly by their local hospital, by having regular blood tests (see hypoparathyroidism).

CHARGE SYNDROME
CHARGE Syndrome is a similar genetic condition to DiGeorge Syndrome, affecting several health systems. The word CHARGE is used to shorten the range of symptoms children can experience:
C - Coloboma of the eye
H – Heart defects
A – choanal Atresia (narrowing of the nasal passage)
R – growth Retardation
G - Genital abnormalities
E – Ear abnormalities
It is often diagnosed through the child's symptoms at birth and then through a genetic test where a change in the appearance of the CHD7 gene is found. Some children with CHARGE syndrome are also born without the thymus, meaning they also have congenital athymia and severe combined immunodeficiency (see SCID), and need a thymus transplant.

CICLOSPORIN
Ciclosporin is a special medication we give to children who start show signs of Omenn syndrome caused by uneducated T cells (see Omenn syndrome). Ciclosporin helps to control the T cells by reducing their ability to cause harm. We call this action suppression. Ciclosporin is known as an immunosuppressive medication, meaning to suppress the immune system activity. Children will need to have blood tests regularly to check there is an effective level of the medication in the child's blood system. If levels go too high children can have problems with their kidneys and their blood pressure, some children have had seizures. If levels are too low, it will not control harmful T cell activity.

Children like Caleb in the story who need this medication, will stay on this medicine for many months. This will be needed until the T cells begin to show signs of education.

complete DIGEORGE SYNDROME
complete DiGeorge is considered the most severe kind of DiGeorge syndrome (see DiGeorge Syndrome). This is because children will be born with a range of health conditions and without a thymus, known as congenital athymia. Congenital athymia creates the immunodeficiency known as **S**evere **C**ombined **I**mmuno**d**eficiency, shortened to be called SCID (see SCID).

CONGENITAL ATHYMIA (say A-thigh-me-a)
Congenital athymia means a child has been born without a thymus or if the child does have some thymus tissue it is not working normally. We shorten this to athymia, and it is a medical term you will hear the doctor's use a lot. Athymia causes the severe immunodeficiency we call SCID (see SCID). This is because without a thymus, our immune cells called T cells do not have the education system they need to function properly (see thymus). We know athymia can be successfully treated with thymus transplantation.

CYTOMEGALOVIRUS known as CMV
CMV is a particular virus we worry about for children with athymia. Healthy people can carry this virus with minor problems to their immune system, but for children with no thymus, it can be very harmful. CMV is a virus that can be passed from mother to baby via the breastmilk. Therefore, mothers of children with no thymus, will be checked for the virus. When mothers are known to carry CMV, they are asked to stop breastfeeding their baby, so they do not pass the virus on. Your local doctor will explain more to you about this virus if they are worried.

D

DIGEORGE SYNDROME

The DiGeorge condition has a range of symptoms and seriousness. It is most often due to a defect in the genetic development of a child. A small part of the chromosome 22 is missing, called 22q11.

DiGeorge syndrome is often diagnosed after birth. Other genetic conditions might be called DiGeorge syndrome, because of similar symptoms but different chromosomes can be affected, like CHARGE syndrome (see CHARGE syndrome).

The range of symptoms are unique for each child, but it usually affects several health systems of the body. The most serious problems for children with DiGeorge syndrome are:

- Heart problems
- Problems with calcium levels, known as hypoparathyroidism
- Immunodeficiencies

But also...

- Feeding difficulties
- Different facial features
- Hearing difficulties
- Kidney development
- Physical growth and
- Learning difficulties

The children who are most severely affected, with a poorly functioning immune system and are said to have *complete* DiGeorge Syndrome.

DISCHARGE

When children are discharged from GOSH, families must continue the isolation precautions. Children need to be isolated from the general public and public areas, to protect them from coming into contact with germs that can cause infection. Children must continue to take all protective medications.

T cell development is a slow process, so these protective measures are required for several months after the transplant.

If children are well enough and allowed to go home, the family must isolate their child at home by minimising visitors to the home. Only visitors who are helping the family care for their child should visit. If children need to stay in the hospital, like Caleb, they will be isolated in a cubicle with one of their parents / carers. At GOSH, a second parent / carer can visit and take turns when staying with their child. Siblings can go to school normally, however, family and school must communicate carefully, to highlight if there have been cases of contagious diseases like chicken pox or measles.

E

ENVIRONMENTAL

Some children may develop congenital athymia due to environmental issues, thought to have interrupted thymus development during early pregnancy. This includes mothers who have had hard to control diabetes or sometimes due to a build-up of toxins. This interruption in thymus development causes athymia and the same immunodeficiency of SCID.

These groups of children have also been successfully treated with thymus transplantation for congenital athymia, but often there is no no genetic diagnosis.

F

FOXN1

Another condition known to be successfully treated with thymus transplantation, is known as FOXN1. Children are born with different symptoms, such as nail deformity and alopecia (no hair on the head or body) and they are also born without a thymus, therefore congenital athymia and SCID. FOXN1 is another genetic diagnosis.

FOLLOW UP

After discharge from GOSH we will ask for blood samples to be sent to GOSH for special immune tests. At first, we ask for samples regularly, usually every 3 months. We look to see if new T cells are beginning their travels around the child's immune system. It is **unusual** to see working T cells before 6 months after the transplant. Each child is different, and children will educate their T cells slower or faster than others.

We will continue to ask for regular samples to check over time that the thymus tissue is working properly and developing all the different types of T cells that children need to be able to protect themselves from harmful germs. Once we see continued increase in T cell numbers over many months, we will discuss stopping any immunosuppression medications and some of the protective medications.

Immunoglobulin antibody replacement will continue for approx. 2 years post transplantation. This is because the communication between T cells and B cells takes a bit longer to happen (see immunoglobulin).

G

GENETICS

There are many children who have been successfully treated with thymus transplantation for congenital athymia and are given a genetic diagnosis, like 22q11 or CHD7. There are also groups of children who have the same symptoms and an immunodeficiency due to faulty thymus development, but a genetic diagnosis is not found. We say they are undefined, but the correct treatment is still with a thymus transplant. We will talk with you more about this at the time of admission to GOSH if this applies to your child.

GERMS

Germs include bacteria, viruses and fungi. Germs can be present in the air, in our foods, on hard surfaces and in our environment. They can enter the body through touch, by mouth or breathing. When germs enter the body and make us unwell, and we say we have an infection. In healthy people, the immune system fights the germs and removes them from our bodies, sometimes we may also need help with medications like anti-biotics. For children with immunodeficiencies, germs are more harmful and can make them very unwell (see immunodeficiency). It is important if children with immunodeficiencies are unwell, they see a doctor for assessment early. Your medical team will discuss with how to make early contact with them.

H

HEART

Children with DiGeorge syndrome, and similar conditions, can have difficulties with the development of their heart and some children (not all) require operations to fix these difficulties. Heart operations are completed by a specialist team in the child's home country/ local hospital. Children who need urgent heart operations, will need to have them before they travel to GOSH for their thymus transplantation. It is important the heart is healthy before any further treatment is started.

HYPOPARATHYROIDISM

Children with DiGeorge syndrome and similar conditions, often have a condition called hypoparathyroidism, meaning the parathyroid gland does not work properly. Our parathyroid gland makes a hormone called parathyroid hormone and this is responsible for maintaining a steady level of calcium and magnesium in our bodies.

Hypo = less than normal. So, when children have hypoparathyroidism, this means they produce too little parathyroid hormone, and this affects their ability to maintain calcium and magnesium levels (see calcium and magnesium).

I

IMMUNE CELLS

Immune cells are also known as white blood cells and help to make up our immune system. These include T cells, B cells and Neutrophils. Immune cells have different jobs to help protect us from infection and to fight germs.

IMMUNISATIONS see VACCINATIONS

IMMUNODEFICIENCY

An immunodeficiency is when the health system responsible for protecting us from harmful germs is faulty or completely missing. This system is called our immune system. Children can be diagnosed with immunodeficiencies for different reasons, depending on the different kinds of immune cells that do not work properly.

When children meet harmful germs and do not have an immune system, they develop what we call infections and they can become very sick, very quickly. Children with immunodeficiencies often have repeated infections. They need to see doctors more often for antibiotic treatment to help fight the infection, as they have no natural defences.

The most severe form of an immunodeficiency is called **S**evere **C**ombined **I**mmuno**d**eficiency, shortened to be called SCID. This is the immunodeficiency children without a thymus are diagnosed with (see SCID). They must be isolated immediately (see isolation precautions).

IMMUNOGLOBULIN

All children with congenital athymia will be given a medication we call Immunoglobulin. It is given to replace the faulty B cells, by providing replacement antibodies (see antibodies). Remember B cells need working T cells to communicate instructions before they can work well. This medication helps to protect children from many common viruses and bacteria.

Sometimes Immunoglobulin is called **IV**Ig, meaning the medication is given via a tube into the vein - intravenous. Sometimes it is called **SC**Ig, meaning it is given via a needle into the fatty tissue - subcutaneous. Children receive this medication for approx. 2 years after the thymus transplantation.

SCIg can be administered by parents at home, when they receive the correct education.

ISOLATION PRECAUTIONS

When Caleb was diagnosed with his immunodeficiency his family were asked to socially isolate. This is needed for all children diagnosed with an immunodeficiency (see above). This means they must be protected from the general public and public areas, to protect them from coming into contact with harmful germs that can cause infection.

If children need to stay in the hospital, like Caleb in the story, they will be isolated in a cubicle with one of their parents /carers. At GOSH, a second parent or carer can visit and take turns when staying with their child.

For children with no immediate health conditions that need medical attention, they are allowed to go home. They will be isolated at home with their family/ carers. Household members can go to school and work, but only visitors who are helping the family care for their child should visit. Family and school must communicate carefully, to highlight if there have been cases of contagious diseases like chicken pox or measles. Your local team will talk to you more about how to isolate with your child safely.

L

LABORATORY

We have several specialist teams of laboratory scientists. Some who prepare and care for the donor tissue, in a special sterile (very clean) environment to make sure it stays healthy right up to the day of surgery. Others complete special tests on the transplanted tissue collected at the time of biopsy, to check it is working as expected.

We also have specialist laboratory scientists who look at the blood samples we receive and help us to understand the T and B cell activity.

LIVE VACCINES

These include the seasonal Influenza vaccine, the BCG vaccine, the Rotavirus vaccines and later the MMR vaccine and the Varicella vaccine.

The seasonal (every autumn/ winter) Influenza vaccine helps protect against the flu virus. There are two forms of the vaccine. The live virus is usually given to children via a nasal spray – children with immunodeficiencies should not receive this form of the vaccine. The second form is given by an injection into a large muscle (usually the thigh muscle). This is what we call a 'killed' virus and is safe for children with immunodeficiencies.

BCG a live vaccine against the disease tuberculosis - it stands for Bacillus Calmette-Guerin after the scientists who discovered it. This vaccine is offered in many countries at or near birth. It should not be given to children with immunodeficiencies.

Rotavirus is a common virus in infants. It causes the symptoms of diarrhoea and can be very persistent in children with an immunodeficiency. A live vaccine is routinely offered at birth in many countries. It should not be given to children with immunodeficiencies.

MMR vaccine a live vaccine against Measles, Mumps, and Rubella (German Measles). This vaccine is given routinely at around one year of age. This vaccine is not to be given to children with immunodeficiencies. Once children begin to develop their own immunity and the time is right, doctors will tell families when their child is ready to receive the MMR vaccine. In the meantime, children with athymia will have some protection from the immunoglobulin medication they receive.

The Varicella vaccine is given to protect from the chicken pox virus. It is a live vaccine. Chickenpox is usually mild, but it can be more serious when people have a weakened immune system. This vaccine is not to be given for children with immunodeficiencies. Once children begin to develop their own immunity and the time is right, doctors will tell families when their child is ready to receive the chicken pox vaccine. In the meantime, children with athymia will have some protection from the immunoglobulin medication they receive.

It is rare, but the Polio vaccine is given by mouth (oral) in some countries. This also contains a live virus. This oral vaccine is not to be given for children with immunodeficiencies.

Children with congenital athymia and immunodeficiencies should not receive live vaccines. When it is safe for children to receive live vaccines, the medical team will talk to you about this. For children who receive thymus transplantation, this usually happens after around 2 years after transplant. If you have any questions about vaccinations, please speak to your medical team.

LYMPHOCYTES (say lim-fo-site)

Lymphocytes are a collection of different types of white blood cells, and they help to make up our immune system (see also T cells and B cells).

M

MAGNESIUM

Magnesium is another important mineral that helps support our bone development and our heart function. Children with conditions like DiGeorge Syndrome can often have problems balancing their magnesium levels. Often when calcium levels are low, we also see low magnesium levels, and this is treated with magnesium supplements (see hypoparathyroidism).

MICROSCOPE

Looking through a microscope (a special magnifying glass) allows us to see the human tissues very closely. The laboratory team at GOSH complete special tests on the new thymus tissue which is collected at biopsy. The team use microscopes to check the tissue is working how we expect 3 months after transplantation.

N

NEUTROPHILS (say new-trow-fills)

Neutrophils are another type of immune cell that provide early responses to help ease the symptoms of infections.

O

OMENN SYNDROME

Another important job of the thymus is to teach T cells to be able to know the difference between our own body tissues and harmful germs (see T cell). It is important that our own T cells do not attack and try to kill different parts of our own body. When uneducated T cells become unsettled, they become confused and can begin to attack our body tissues, usually the skin or our stomach area. We call these uneducated T cells Rogue T cells. The resulting symptoms are called Omenn Syndrome. It is a condition which can be treated with special medication called ciclosporin and is a temporary condition (see ciclosporin).

Children can show signs (symptoms) of:

- Skin rashes with peeling and itchy skin
- Hair loss
- Upset tummies, with loose stools (faeces) and this affects their ability to gain weight
- Glands in the neck or groin can swell (increase in size)
- Sometimes the spleen or liver can swell (increase in size)

These symptoms can happen before transplantation but also sometimes after transplantation while the new immune system is developing. Parents need to let their medical team know if their child develops any of these symptoms.

P

PAIN RELIEF

After the thymus transplant and biopsy procedures, all children will be given regular pain relief medication. After a few days this will likely reduce, and the team will continue to treat children in response to their individual pain levels. If you are worried your child is pain, you can speak with the nurses on the children's ward.

PALIVIZUMAB

Palivizumab is a medication given to children under 2 years, to protect against a virus called Respiratory Syncytial Virus or RSV for short. RSV is particularly harmful for this age group. Some people might call Palivizumab a vaccine, but actually it is a special antibody, and it is safe for children with immunodeficiencies.

PAX1

PAX1 is another example of a faulty gene that affects thymus development. Children with PAX1 deficiency can have difficulties with bone development, different facial features and learning difficulties. They can also be born with no thymus and therefore the same congenital athymia and immunodeficiency (see immunodeficiency and SCID).

PLATELETS

Platelets are a cell found in the blood and have the job of helping us to stop bleeding if our skin is cut or our body has an injury. When we bleed, our platelets stick together and fill the hole in the blood vessel that has been created. This helps to stop or slow the bleeding.

Sometimes, when children have faulty T cells, platelets can be attacked by the child's own T cells. This can happen before or after thymus transplantation. Doctors will monitor platelets regularly but if the family see an unusual rash on their child's skin (often like tiny red circles) they should ask a doctor to see their child.

PROTECTIVE MEDICATIONS also called **PROPHYLAXIS** (say pro-fil-lax-is)
Many germs live in our environment naturally. They do not cause infection in healthy individuals but can cause serious infection for children with congenital athymia when their immune system is having trouble working. Antibiotics and anti-fungal medicines will be needed to help provide extra protection against serious infection.

- One germ in particular is a fungus called Pneumocystis jirovecii pneumonia (PCP). Children are given extra protection against this fungus by taking a regular medication called Co-Trimoxazole.
- Another fungus is called Aspergillus. Your child will be given extra protection by taking a medication called Itraconazole or Fluconazole.
- Palivizumab is a protective antibody medication (see above)
- Immunoglobulin is a protective antibody medication (see immunoglobulin).

R

RED BLOOD CELLS

Our red blood cells help carry oxygen around our body, delivering it to our body's organs and tissues. Red blood cells also help to carry unwanted carbon dioxide to our lungs to be removed from our body. Sometimes, when children have faulty T cells, red blood cells can be attacked by the child's own T cells.

Children may show the following signs:

- Paleness
- Increased work of breathing
- Increased tiredness/ sleeping more
- Blood may be visible in the stools/ faeces
- Nosebleed

Doctors will monitor red blood cells regularly and if you are concerned about your child, you should ask to see a doctor.

S

SCID - Severe Combined Immunodeficiency

The most severe form of an immunodeficiency is called **S**evere **C**ombined **I**mmuno**d**eficiency, shortened to be called SCID. This is caused when the immune cells lymphocytes do not work properly. This can happen for many reasons.
For children with congenital athymia, the missing thymus tissue and lack of an education system for T lymphocytes creates this severe immunodeficiency (see lymphocytes, T cells and B cells).

SAFETY

During the time the donor thymus is in the laboratory, many safety checks take place. If our team see any problems with the donor tissue, we will not use it for transplantation. If there are safety concerns, we will speak with the family and talk about the next steps. Sometimes the tissue can be helpful for our research programme.

Safety is one of our priorities when planning care for your child.

STEROIDS

If children have serious problems with the uneducated T cells attacking the child's body (see autoimmune complications) a medication, called steroids (or cortisol) can be used to calm the harmful behaviour. However, steroids can also be harmful for the new thymus tissue. It is very important that local hospital teams and GOSH teams communicate regularly before steroids are started in children after thymus transplantation. If possible, steroids are best avoided in the first few months after transplantation and before the biopsy procedure. We will talk to you more about this when your child is at GOSH.

T

T LYMPHOCYTE CELL (say lim-fo-site)

We call them T cells for short. T cells are one of our immune cells which begin their life in the bone marrow alongside B cells. However, T cells need more time to develop, so they travel to the thymus for extra education. There are different kinds of T cells, with different jobs to do.

- Some scan for invading viruses and send out instructions to other immune cells
- Some kill the viruses and develop a memory of the germ, in preparation for future invasion
- Some T cells learn what is safe inside our bodies and what can be harmful. This is particularly important, so our immune system does not attack our own healthy bodily tissues by mistake (see autoimmune complications).

THIGH MUSCLE

Thigh muscles are used for the tissue transplantation because they are big muscles, are easy to get to and have a good oxygen supply which will help the new thymus grow and develop.

THYMUS

The thymus is a gland which sits between the chest bone and in front of the heart. It has two lobes, connected in the middle. The job of the thymus is to teach some of our immune cells, called T lymphocytes how to protect us from harmful germs (see T lymphocyte). When children do not develop a thymus is the normal way, we call this congenital athymia.

When a child is born without a working thymus, their immune system cannot provide the important lessons our immune cells need to protect the body from harmful germs, which cause infections. This leaves the children with no working immune system, which we call an immunodeficiency (see immunodeficiency). Children with immunodeficiencies can become unwell very quickly from the invading germs and need treatment to help fix the immunodeficiency early in life.

THYMUS DONATION

Families of infants having heart surgery at GOSH are approached to consider thymus donation, which can be used for thymus transplantation in children with congenital athymia. They are asked this because the position of the thymus in the body (see thymus) means the thymus can sometimes block the surgical view when surgeons are completing heart surgery. If this happens the thymus tissue needs to be removed to provide a clear space for the surgery. Families of these children are given the opportunity to donate any thymus tissue removed.

When parents agree for their child's thymus tissue to be donated for transplantation for another child, we call this agreement *consent*. This process is monitored through a research protocol with strict rules and ethical guidance. You will not know who the donor child is, and they will not know your child. Thymus donation is completely voluntary (meaning it is a family's choice).

Parents who consent to thymus donation often ask about the effect on their own child's immune system. Because the thymus gland works mainly before birth, the donor baby will already have developed working T cells. Removal of the thymus gland at this stage will not cause the problems of immunodeficiency. In fact, a small amount of thymus tissue is often left in place, and this may grow again after the surgery.

THYMUS DONOR TISSUE

The donor thymus tissue is prepared in a special laboratory, by specialist staff. They slice the thymus into several small pieces ready for the transplant. The donor thymus must pass many safety checks before we can say it is ready for transplantation into your child. It is checked for any harmful bacteria or viruses, to make sure no harmful germs can be passed onto to a child with an immunodeficiency. We also make sure the donor tissue is healthy and can educate T cells in the normal ways.

THYMUS TRANSPLANTATION

Thymus Transplantation means implanting (placing or inserting into the body) donor thymus tissue from an unrelated child into another child who has no thymus. This process allows the donor thymus to educate the child's own T cells and develop a working immune system.

On the morning of the thymus transplant, we will confirm to the family that the donor thymus has passed all safety checks and can be used for transplantation.

Children will be in the theatre for approx. 2 -3 hours. Parents /carers will be able to go to into the anaesthetic room with their child, where they will fall asleep.

The procedure is completed by surgeons who have developed specialist skills.

- The surgeon will carefully make a straight cut in the front of both of the thighs, down to the muscle.
- The surgeon will put around 15 pieces of the donor thymus tissue into little pockets in both of thigh muscles (the exact number and size of the pieces depends on the size of the child).
- The wounds will be carefully closed with stitches.

The wounds are then covered with paper steri-strips and a clear dressing, to allow observation of the wound healing (see wounds).

THYROID GLAND

The thyroid gland is not to be confused with the thymus.

The thyroid is a different gland which sits in the area of the neck. It is part of a different health system (the endocrine system) and releases hormones into the blood stream to help control our metabolism, meaning how our body uses naturally occurring chemicals to break down foods, to manage energy and growth.

These hormones are balanced in the thyroid. They have different jobs to do and help control our energy levels, our temperature, support for our heart rate and blood pressure and even our moods.

Some children with DiGeorge Syndrome and some children after thymus transplantation, develop a problem with their thyroid gland meaning they need to take a replacement medication to help balance these hormones. After thymus transplantation we call this an autoimmune complication (see autoimmune).

V

VACCINATIONS also called IMMUNISATIONS

On the rare occasion, some early infant vaccinations may have been given to children before they are diagnosed with congenital athymia and an immunodeficiency. Most of these vaccines are completely safe and do not cause any problems because they are what we call 'killed' vaccines.

However, it is very important that children with an immunodeficiency are not given live vaccines.

No vaccines are needed until children with athymia begin to develop their own immune function. When the time is right, doctors will tell families to stop immunoglobulin treatment and routine vaccinations can be given. Before this, immunoglobulin will provide the protection children need.

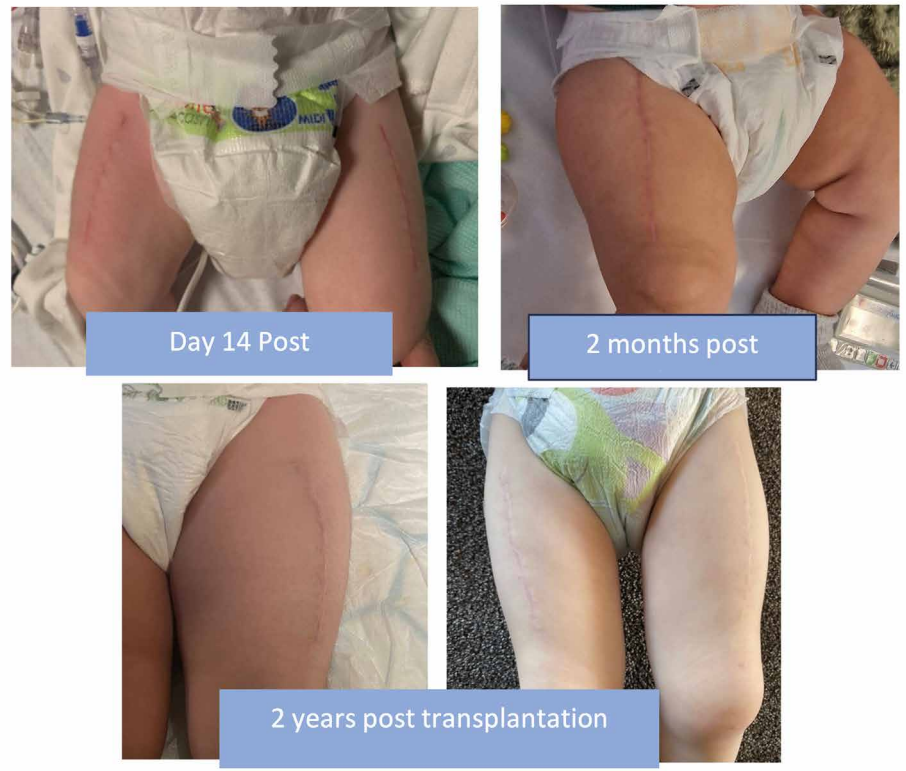
W

WOUNDS

The transplant wounds are covered with paper steri-strips and a clear dressing after the operation. After 7 days the edges of this wound dressing will start to come away from the skin naturally. We usually let the dressing fall off when it is ready. If it is still in place after this time, we can give it a gentle helping hand with gentle baths and special adhesive removal liquid.

If we are worried the wound is not healing or is showing signs of an infection, we will ask the surgeon to visit and check on it. It is rare to have wound complications.

See the pictures below, showing wound healing at different stages.



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