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Evelina London
Children's Hospital

Glycogen Storage Disease

A Parent/Carers' guide

Index

Introduction

Your child has been diagnosed with or suspected to have a **Glycogen Storage Disease (GSD)**.

There are a number of glycogen storage diseases but this booklet is going to focus on only **five** specific types.

TYPES:

I **ONE**
(Glucose -6 -phosphatase deficiency). This is further categorised into types **(a)** and **(b)**

III **THREE**
(Debrancher deficiency). This is further categorised into types **(a)** and **(b)**

VI **SIX**
(Liver glycogen phosphorylase deficiency)

IX **NINE**
(Phosphorylase kinase deficiency)

0 **ZERO**
(Glycogen synthase deficiency)

Blood results and symptoms will help to identify the type of GSD your child has. To confirm the diagnosis we will need to test your child's DNA to find the genetic alteration.

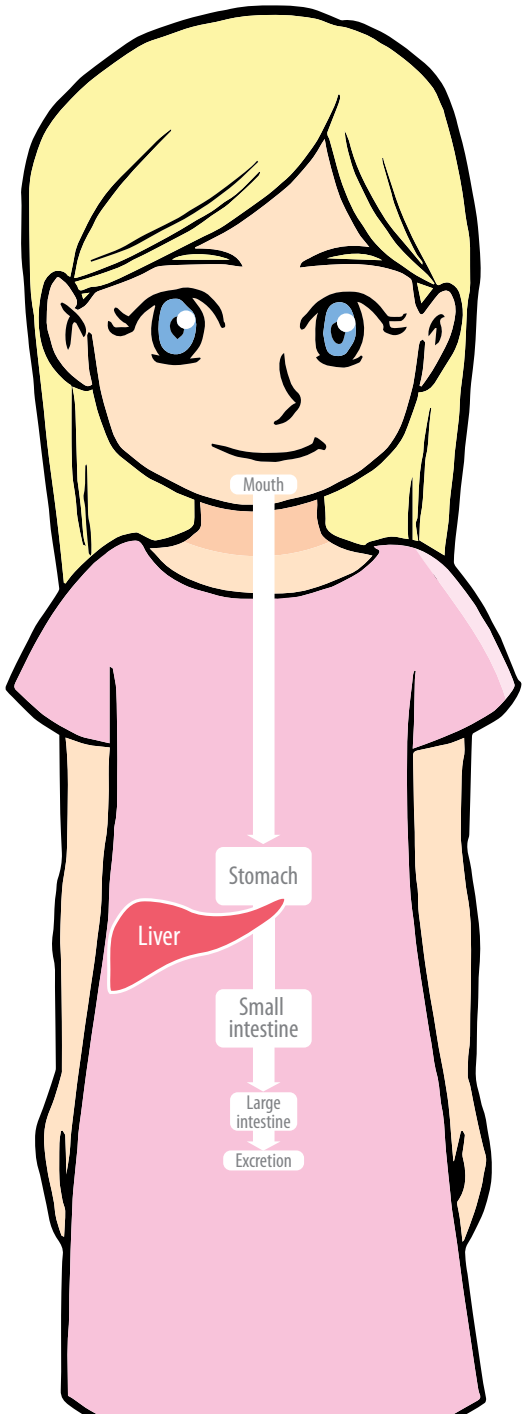
Please read this booklet and write down any questions you may have. Your specialist metabolic team can explain this further.

Metabolism

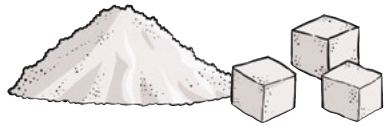
Glycogen Storage Diseases are known as **inborn errors of metabolism**.

What is metabolism?

To be a fit and healthy individual we must feed our body regularly with a variety of foods and water. Protein, fats and carbohydrates from the foods we eat are converted to energy and used for growth and repair. They are also stored for use between meals or disposed of as waste. Our body's main source of energy is glucose. This is all part of our normal metabolism.



Where does glucose come from?



Sugar

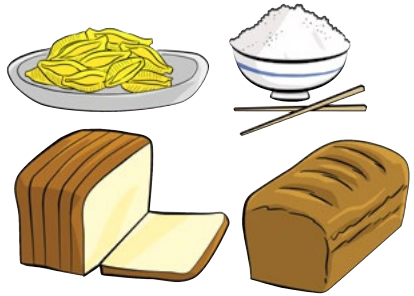
is sucrose that will be converted to glucose

Milk

the sugar part of milk is called lactose

Fruit

the sugar part of fruit is called fructose



Pasta, rice, bread and bread products

are starches that release glucose

Corn flour/corn starch

is starch that slowly breaks down to release glucose to be absorbed into the blood stream

How does the body normally regulate glucose?

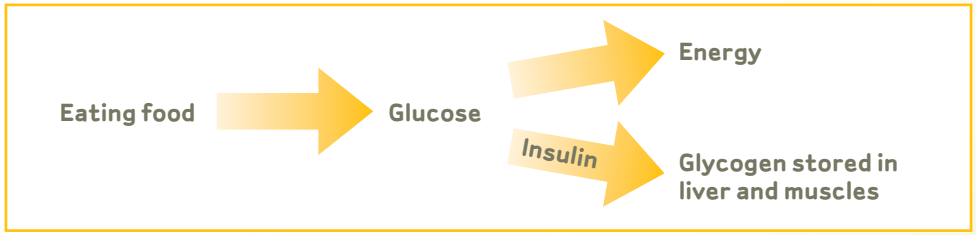
It is important that the body keeps the blood glucose level stable, between 4 and 7 millimoles per litre (mmol/l).

When we eat our blood glucose goes up, if it wasn't regulated it would go too high. If we don't eat for a long time our blood glucose would go too low. The body regulates blood glucose by storing any excess using the hormone insulin. It releases it from body stores using the hormone glucagon.

Enzymes help to carry out the hormones instructions to store or release glucose.

How do we store glucose?

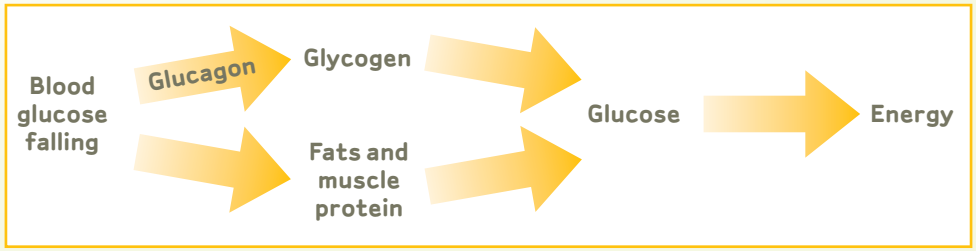
Once we eat we use some glucose for energy. The hormone insulin then instructs any glucose left over to be sent to the liver and stored as chains of glucose, known as glycogen. Glycogen can also be stored in muscles including the heart.



How do we release stored glucose?

When we haven't eaten for a while or when the blood glucose is low the hormone glucagon instructs the liver to breakdown glycogen and release glucose.

When the glycogen stores are getting too low the body starts to breakdown its stored fats and proteins to provide energy.



What are glycogen storage diseases?

Glycogen Storage Diseases (GSD's) are extremely rare, they are reported to affect approximately 1 child in every 100,000 born worldwide.

The underlying problem in all GSD's is the use or storage of glycogen, which is found in the liver and muscles.

Enzymes are involved in the many steps to store glucose as glycogen and to change glycogen back to glucose.

People affected with GSD have an inherited problem in one of these many enzymes.

Commons symptoms

Children with Glycogen Storage Diseases can have many different symptoms before treatment and during illness. Treatment aims to reduce the symptoms and promote growth and good health.

Enlarged liver (hepatomegaly)

Children with GSD can often have a large liver. From the outside this looks like a protruding round stomach, out of proportion to the rest of their body.

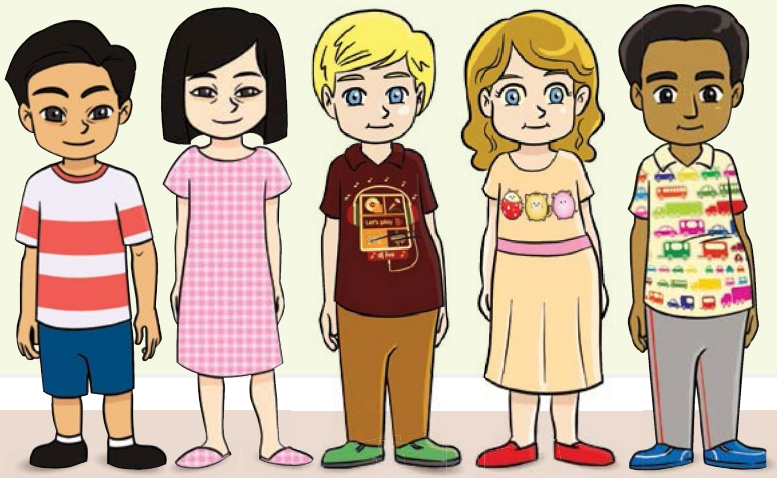
The glycogen builds up in the liver as it cannot be made into energy. Over time and with good treatment and control the liver should reduce in size.

The need to eat frequently

Children with GSD often cannot go for long without feeding or eating. This is because the body starts to run low on glucose. Without treatment babies may cry a lot in between feeds and demand to be fed more frequently. Older children may often need to eat more frequently to keep their blood glucose normal.

Short stature

To grow children need energy from foods, this includes glucose, fats and protein. In children with untreated GSD they use their body fat and protein from muscle as an alternative source of fuel to keep their blood glucose normal. The hormones released interfere with the normal action of the growth hormones and so the child does not grow properly.



GSD I (a and b) – Glucose- 6- phosphatase deficiency

Enzyme deficiency

Glycogen Storage Disease type I is further categorised to GSD type Ia and GSD type Ib. The unique differences are in the box below. Both are due to the deficiency of the action of the enzyme glucose -6-phosphatase. This is the most important step in providing glucose to the blood stream from the liver.

What happens if the enzyme is deficient?

If the enzyme is deficient the stored glycogen cannot be converted into glucose. They cannot use protein as an alternative as this also requires glucose-6-phosphatase for its conversion to glucose. The chemical changes in the liver, block the use of fat from the diet to make energy.

Alternative fuels

The glucose -6-phosphate (the part of glycogen that the enzyme cannot break down) builds up in the liver. Some of the glucose-6-phosphate is converted to other chemical sources of energy such as lactate and uric acid (urate). Urate in high levels is harmful to the kidneys and can cause kidney stones. Good dietary control to prevent low blood glucose is the most important part of the treatment. It also controls urate and lactate. Medication called Allopurinol can be used to reduce urate levels. Untreated children can present with high levels of lactate.

Fat stores are released for energy when the glucose is low, but the liver cannot use it as the excess glucose -6 phosphate blocks its use. This leads to high levels of fat in the blood (triglycerides) and the liver.

Those with GSD Ib have similar biochemistry to GSD Ia. Glucose-6-phosphate cannot be transported to the correct part of the cell where the enzyme (glucose-6-phosphatase) is located.

Features unique to GSD Ib

Neutropenia

Neutrophils are white blood cells that are important in fighting infection. Children with GSD Ib can have low levels in the blood (called **Neutropenia**).

- This can lead to gut and intestinal symptoms such as mouth ulcers or occasionally inflammatory bowel disease.

To help alleviate some of the symptoms of neutropenia those with GSD Ib should:

- Have good oral hygiene
- Go for regular dental check ups
- Have additional vitamin supplements
- If they have severe infections, see their specialist metabolic team for antibiotics or medicines to help increase the white blood cells.

GSD III- Debrancher deficiency

Glycogen Storage Disease type III is categorised further into GSD IIIa and GSD IIIb

Enzyme deficiency

Glucose is stored as branched chains in the liver and muscle. Amylo-1,6-glucosidase is the enzyme that allows the glucose branches to be broken off the main chain. This enzyme is important in the liver and muscle.

What happens if the enzyme is deficient?

If the enzyme is deficient, glucose is still converted to glycogen. However the glycogen stored is only partially broken down.

Alternative fuels

As limited glucose is available, fats stored around the body are broken down into ketones to be used for energy. Ketones are an alternative fuel used by the brain for energy when the glucose is low. Muscle protein is also used for energy. Untreated children can present with high levels of ketones.

Additional feature for GSD IIIa

Muscle weakness:

- The muscles cannot use energy from muscle glycogen due to the enzyme deficiency and this can lead to muscle weakness. Patients with GSD III may complain of leg pain, they may tire easily when walking long distances or tire during sports. Patients should be encouraged to take part in sport but they may require additional resting times.

Cardiomyopathy (Thickened heart muscle):

- The heart is large. Treatment and good control of GSD III aims to reduce any complications. This will be monitored with regular heart scans.

VI GSD VI - Liver glycogen phosphorylase deficiency

Enzyme deficiency

Liver glycogen phosphorylase is an enzyme that starts the process of breaking stored liver glycogen into glucose. This is then used for energy.

What happens if the enzyme is deficient?

In GSD VI one of the enzymes needed to breakdown glycogen into glucose is faulty. For most, the enzyme works slowly but it is still present. Those with GSD VI will therefore have some ability to release glucose from the liver.

Alternative fuels

As limited glucose is available, fats stored around the body are broken down into ketones to be used for energy. Ketones are an alternative fuel used by the brain and muscles for energy when the glucose is low. Muscle protein is also used for energy. Untreated children can present with high levels of ketones.

Additional information for GSD VI

GSD type VI may be milder than some of the other GSD's as there is still some ability to use stored glycogen. Poor growth and an enlarged liver may be the only sign of the disease. Management of this may not be as complex as others but it is equally important to adhere to your recommended treatment to improve growth and health.

GSD IX- Phosphorylase kinase deficiency IX

Enzyme deficiency

GSD type IX is a deficiency of the phosphorylase kinase enzyme.
This enzyme activates another enzyme (phosphorylase) that converts stored glycogen to glucose to be used for energy.

What happens if the enzyme is deficient?

If the enzyme is deficient glycogen builds up in the liver and the stored glycogen cannot be effectively converted to glucose for energy. This leads to low blood glucose.

Alternative fuels

As limited glucose is available, fats stored around the body are broken down into ketones to be used for energy. Ketones are an alternative fuel used by the brain and muscles for energy when the glucose is low. Muscle protein is also used for energy. Untreated children can present with high levels of ketones.

Additional feature for GSD IX

GSD IX is further categorised into 3 types:

- PHK (alpha) X-linked, affects males only
- PHK (beta), affects males and females
- PHK (gamma), affects males and females

The gene affected determines how it affects the body.

X –linked inheritance:

- Some GSD type IX (PHK1) are inherited in a different way to the other types of GSD. It is inherited in an X- linked pattern; this means it is carried by females but usually only males are affected.

GSD type IX is the most variable of the GSD's in the terms of severity. Some children have frequent low blood glucose but others may show only an enlarged liver and poor growth.

Enzyme deficiency

GSD type 0 has only recently been described in the literature. Glycogen synthase is the enzyme needed to convert glucose to glycogen for storage in the liver.

What happens if the enzyme is deficient?

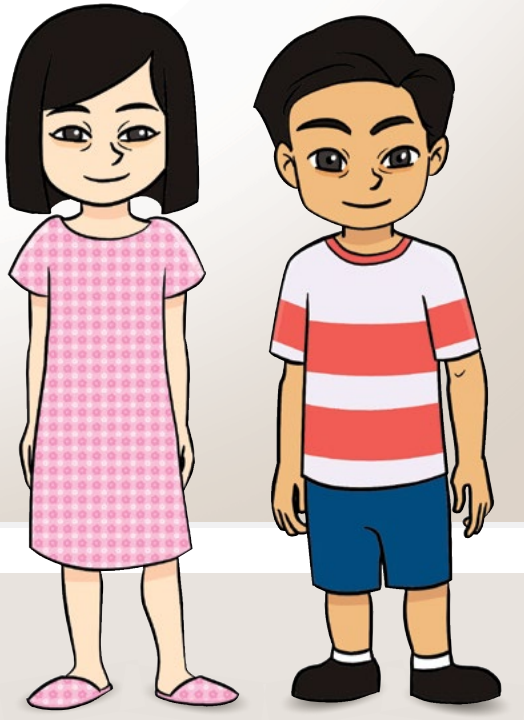
If the enzyme is deficient, those with type 0 are unable to store excess glucose as glycogen in the liver for later use. They will rely entirely on the glucose in their blood stream and when this is depleted it will lead to a low blood glucose.

Alternative fuels

As limited glucose is available, fats stored around the body are broken down into ketones to be used for energy. Ketones are an alternative fuel used by the brain and muscles for energy when the glucose is low. Muscle protein is also used for energy. Untreated patients can present with high levels of ketones.

Additional features for GSD 0

- **High blood sugars in between meals;**
  This is because glucose cannot be stored in the liver. It therefore remains in the blood waiting to be used up.
- **Normal sized liver;**
  Glycogen is not being stored in the liver and so the liver will remain a normal size.



Feeding and common questions

The main aim of management and treatment is to prevent hypoglycaemia (low blood glucose) and to stop the body using alternative fuels. Using these fuels can affect a child's growth. The treatment is regular feeds or meals during the day and possibly cornstarch. Some children may require overnight feed or overnight starch.

Your metabolic team will talk with you to create a regular feeding regimen (plan) for your child. It is important to follow this strictly to prevent low blood glucose levels, improve growth and overall health.

Why does my child need a continuous overnight feed?

Overnight is a long period of time and if your child has a reduced fasting time they will need to have sufficient glucose during this time. If the treatment for your child requires regular overnight feeding, e.g. every 2 hours, we would usually prefer for your child to receive this as a continuous feed. This enables them to sleep without interruptions.

What is in the overnight feed?

The overnight feeds will be a recipe that has been strictly calculated by your specialist metabolic team. It will provide your child with the correct volume of glucose to maintain a normal blood glucose and prevent them from using alternative fuels. It may also contain extra protein, vitamins and minerals.

How will my child receive their overnight continuous feed?

Initially this is through a nasogastric tube. This is a soft plastic tube that is passed through the nose into the stomach. It is a simple procedure that can be carried out at the bedside.

Once this treatment has been established your team may recommend a different type of feeding tube called a gastrostomy tube. This is inserted directly into the stomach and requires an operation.

Either type of tube is then attached to a feed pump that delivers the feed slowly overnight at a prescribed hourly rate.

You will be advised to give a prescribed amount of feed at the start and at the end of the overnight feed. This is called a pre or post feed bolus. This feeding regimen will be explained in detail by your specialist metabolic team.

Is there a risk with overnight feeding through a nasogastric tube?

Overnight feeding does carry a risk as a child may accidently disconnect their feed or the tube can become kinked or blocked. Feeding pumps will alarm if the tube is kinked or blocked but not if they are disconnected or removed. To alert you we will provide you with a body worn alarm for your child and/or a mat alert for the bed. These are activated by liquid from a disconnected feed. We recommend that you use one of these alarms during an overnight feed.

Will my child always need an overnight feed?

As your child's fasting tolerance increases we may be able to treat them with a slow release carbohydrate (starch) overnight. This will usually be used once your child is able to safely fast with starch for at least 6 hours overnight.

Will the regular feeding cause my child to become overweight?

Specialist metabolic dietitians will calculate the feeding regimen and regularly review this and your child's growth. It is important not to give extra food or snacks in between the feeding plan to prevent fluctuations in blood glucose levels and to maintain a normal weight gain.

Will a tube affect my child's eating and drinking?

Some children who have a nasogastric tube for a long time from a young age can have problems with eating and drinking. We recommend that you start weaning as normal to ensure that your child is used to eating and chewing food. If your child has any problems with this we can refer them to see a feeding specialist or a speech and language therapist.

How is starch used?

When you child is over 2 years old a slow release carbohydrate can be used, this is either cornstarch or Glycosade® (in rare circumstances it has been used before 2 years but it may not be well absorbed before this time). Your child will be prescribed a dose of starch at different times during the day, this may also be before bed.

What do I do if my child has vomiting and/or diarrhoea?

If your child has vomiting and/or diarrhoea extra treatment is needed. This is because they may not be able to fuel their body with sufficient energy.

For treatment during illness we recommend an 'Emergency Regimen' (ER). This is an emergency plan of care that can be used at home and in the hospital. Your specialist team will teach you what it is and how to use it.

As soon as your child is unwell we will advise you to give them a prescribed amount of a glucose polymer drink, e.g. S.O.S™ or Maxjul ™.

If your child cannot take this, or they are vomiting or refusing it, they will need to be admitted to their local hospital for a 10% dextrose (glucose) intravenous infusion (sometimes called a drip).

The Emergency Regimen will be given to your local hospital to ensure your child is seen quickly when unwell. Each hospital may have a different system and you will be advised where to take your child, e.g. the emergency department or the children's ward. Please take your copy of the Emergency Regimen with you if you have to attend hospital.

If your child has to start their Emergency Regimen or needs to go to hospital please inform your specialist metabolic team who can help you manage the illness.

How will I know if my child has symptoms of hypoglycaemia?

If your child does not have sufficient glucose they may behave differently to normal, they may also become sweaty or pale. This may be because they are unwell or that their feeding regimen needs to be reviewed.

We do not advise the use of blood glucose monitoring at home as it can give a false sense of security as well as not always being accurate at low levels. We would always advise that you act on your child's symptoms. Spending time checking a blood glucose level at home to see if it is low can be time wasted. If you think your child is unwell you should use your Emergency Regimen or feed your child straight away.

Treatment for symptoms of low blood sugar

Your specialist team will give you a prescribed amount of the Emergency Regimen to give to your child as a drink or to put down their nasogastric or gastrostomy tube. Once they are tolerating the drink, they should be encouraged to have a small snack. Please inform your specialist team if this happens regularly or is concerning you.

What is the treatment if your child is not responding to treatment or is very unwell?

A glucose gel (e.g. GlucoGel™) can be used when your child shows signs of severe hypoglycaemia or low blood sugar (floppy or not responding normally to voices). The gel is rubbed into the gums, it is a concentrated sugar that is rapidly absorbed. If your child is very unwell and needs this, you should give the gel and then call an ambulance to get further help. You should not give your child anything to swallow or into their nasogastric/ gastrostomy tube if they are unconscious. When they are more alert after using the gel give a feed or a glucose polymer. Please keep supplies of your glucose polymer with you at all times.

Please note

Normally when a child is unwell with suspected low blood glucose, Glucagon injections may be given to breakdown glycogen stores to produce glucose. A child with GSD has a problem with this step and therefore Glucagon injections are ineffective. You specialist team will provide you with a letter for ambulance crews asking them not to use Glucagon.

How has my child got this condition?

Glycogen Storage Diseases are genetic conditions. This means that they are not brought about by anything that you may have done during pregnancy.

In GSD I, III, VI , 0 and non x linked IX the mistake is inherited from both parents and is described as autosomal recessive.

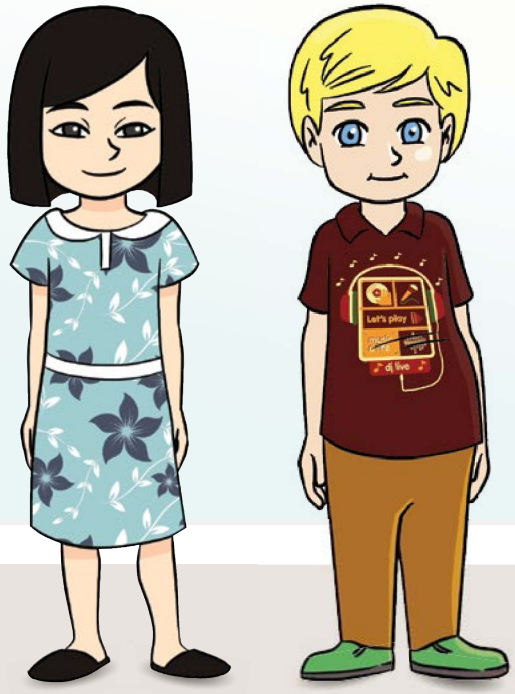
The instructions to make a baby are contained in our genes. For most characteristic in the body we have two copies of the gene, one inherited from our mother and one from our father. We only need one working copy of the gene to function normally.

We all have many mistakes (mutations) in our thousands of genes. However as we have one working copy of each gene then this is not a problem.

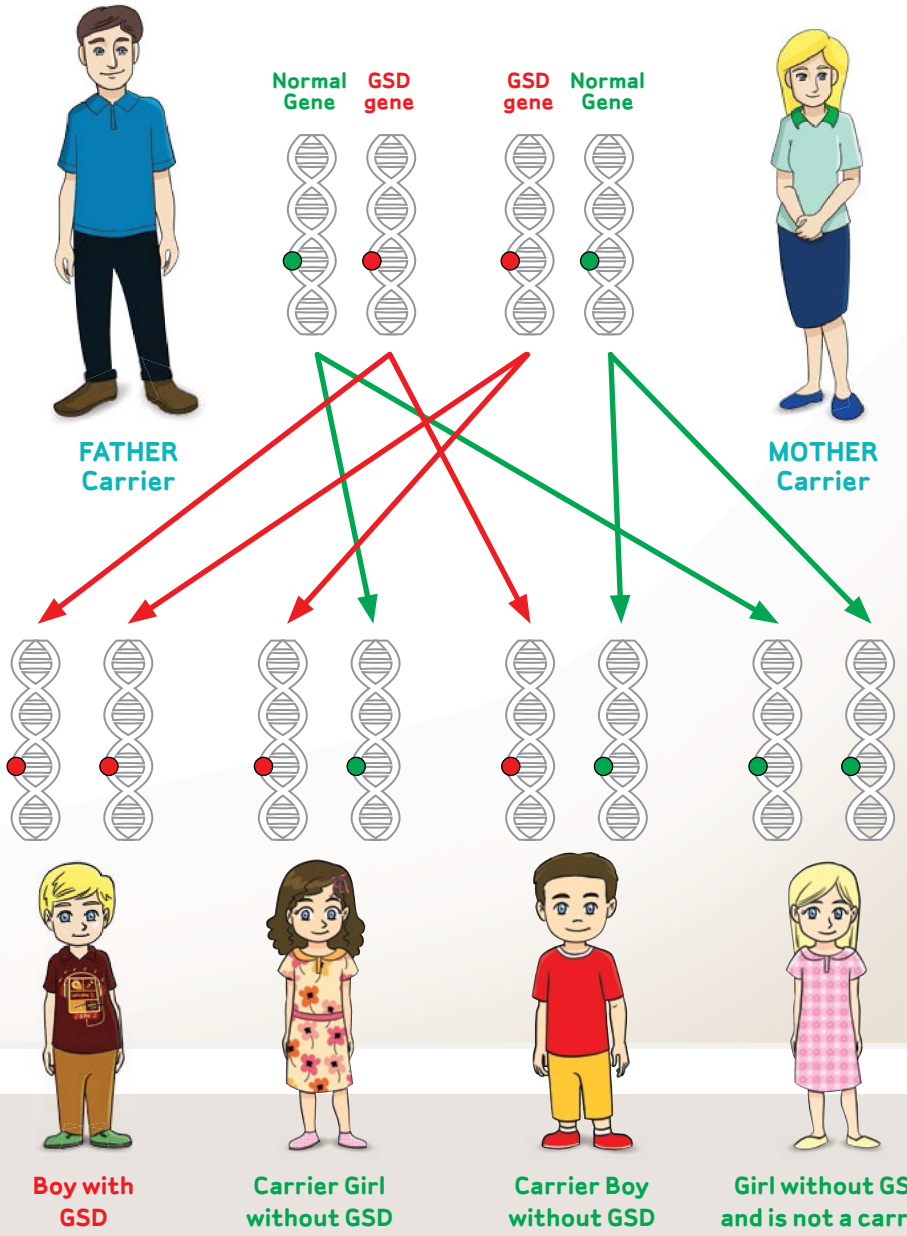
If you and your partner carry a mistake in the same gene there is a 1 in 4 chance with every pregnancy that these two genes with mistakes will come together. The baby will therefore have no working copy of that gene. This results in the enzyme being made incorrectly and the baby having the condition.

This condition is therefore life-long and at present there is no cure. Scientist and doctors are currently working together to design a genetic cure for GSD.

You will be offered the opportunity to meet with a geneticist to discuss genetics and future pregnancies further.

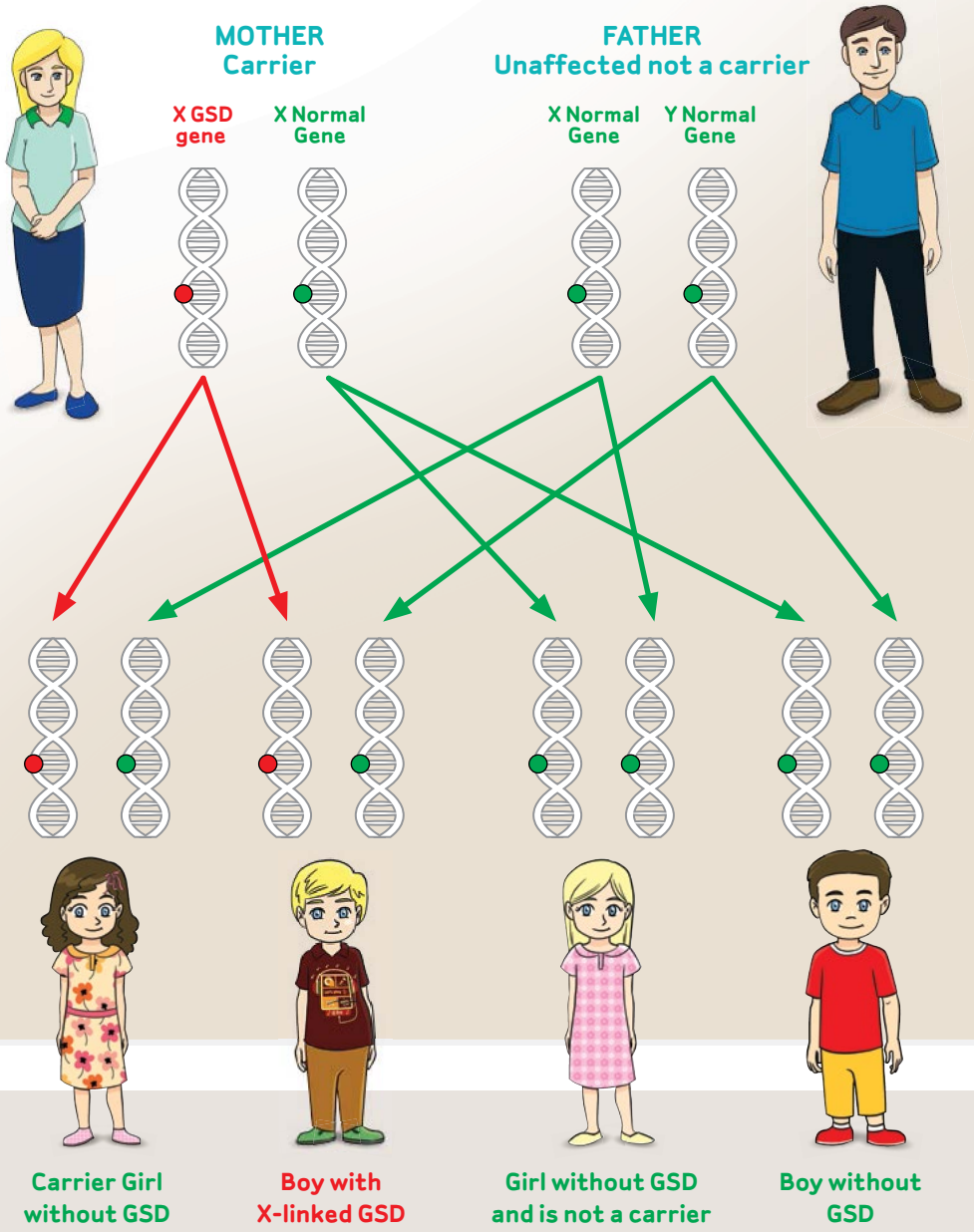


Genetics: Recessive Inheritance



When two people who are carriers of the same GSD gene conceive a child there is a 1 in 4 chance of that child having GSD.

Genetics: X-linked Inheritence (GSD IX)



Women have XX sex chromosomes and men have XY sex chromosomes.

If a woman carries an X-linked GSD gene and she has a boy, she has a 50:50 chance of that boy having an X-linked GSD.

The Future

Ongoing care

After your child's initial diagnosis you will be seen regularly by your specialist metabolic team. However, if you have any questions please contact your team in between these visits.

Your child will have regular blood profiles to ensure your child's glucose and ketones or lactate levels are within normal ranges on their current feeding regimen. Starch loads will be carried out to monitor safe fasting times when well. Your child's fasting tolerance should increase with age.

Depending on the type of GSD your child has, there are further regular monitoring scans. These include: ECHO (heart scan) and ECG's (heart electrical reading), liver ultrasound or MRI (Magnetic Resonance Imaging) and DEXA which looks at how strong your child's bones are.

Based on the results of these profiles and scans we may adjust the dietary regimen to ensure your child is receiving optimum treatment.

In addition to your specialist metabolic team, children's community nurses will also be involved to support you and help with tube feeding, the care of the tube and tube feeding supplies.

Sports

Being fit and healthy is important to us all whether we have GSD or not. Your specialist dietitian will help you to provide a balanced diet for your child.

We encourage children with GSD to take part in sports, however they may tire quicker than other children especially in swimming or endurance sports.

Contact sports such as rugby or karate should be avoided. This is because patients with GSD usually have a large liver and any significant blow to the liver can cause serious damage. It is usually acceptable if your child wishes to play 'tag rugby' as this is minimal contact and should not put the liver at risk. Please discuss sports and activity with your specialist team.

Travelling

Going on holiday should be no barrier to a child with GSD. It is a good idea to plan ahead should your child become ill whilst away. It is important to know what action to take and where to go for help. Some holiday destinations may be less suitable for a young child with GSD.

You should also:

- Inform your specialist metabolic team in advance of your holiday plans
- Obtain a customs letter for feeds and medical supplies
- Carry your information folder containing you ER, condition information etc.
- Ensure you have adequate feeds and equipment – this should be ordered in advance
- Divide your supplies between your hand luggage and hold luggage
- Carry a supply of your emergency regimen and spare feeds on board the plane if it is needed.

Please contact your specialist team for help with obtaining any of the above.

Pregnancy

Where possible all women with GSD should plan their pregnancies as extra care will be required.

During pregnancy your care should be shared between your specialist metabolic consultant and your local maternity team. This ensures that throughout pregnancy both mother and baby are provided with the maximum support available.

School

All children with GSD should be able to attend a mainstream school. Starting school or returning to school after a new diagnosis will require planning. Your specialist metabolic team will liaise with your child's school and help to plan for any extra care that may be needed. This is usually done through an educational health care plan.

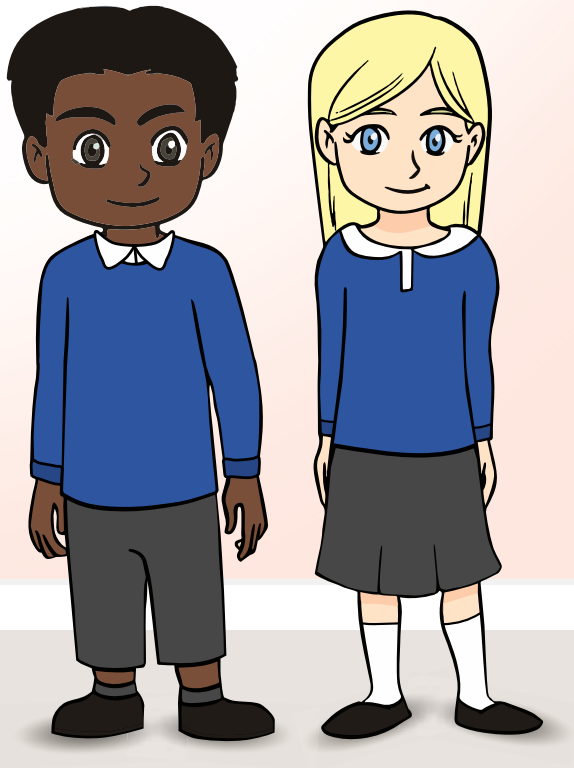
Your specialist team can contact the school and speak to the teachers to ensure that they are able to meet your child's needs during the school day.

The school will be required to:

- Be aware of your child's condition and how it affects them
- Be able to provide your child with their feed/meal plan on time (this may involve training someone to use a nasogastric tube or gastrostomy)
- Recognise signs of illness and what action needs to be taken if your child is unwell
- Know when and how to contact you for help and advice.

A plan of care should be in place before your child starts school. Training to use a nasogastric tube or gastrostomy is usually carried out by your local community nursing team, your specialist nurse can help with arranging this.

If your child is not yet in school please contact your specialist team as soon as you know which school your child will be attending. This will enable the specialist team to contact the school and put support in place as soon as possible and prevent any delays to starting school.



Support groups

Help and support for families living with GSD:

AGSD UK
Association for Glycogen Storage Disease

Old Hambledon Racecourse, Droxford, Southampton, SO32 3QY

Tel: 0300 123 2790

email: info@agsd.org.uk

www.agsd.org.uk

METABOLIC SUPPORT UK
Your rare condition. Our common fight.

5 Hilliards Court, Sandpiper Way, Chester Business Park, Chester, CH4 9QP.

Tel: 0845 241 2173

email: contact@metabolicsupportuk.org

www.metabolicsupportuk.org

Your specialist team contact details:

Your Consultant is: _____

Your Clinical Nurse Specialist is: _____

Your Specialist Dietitian is: _____