



INFORMATION FOR PARENTS & CARERS

CONGENITAL HYPERINSULINISM

**This booklet aims to provide parents and
carers / families with information on the
Diagnosis and Management of Congenital Hyperinsulinism.**

What is Congenital Hyperinsulinism (CHI)?

Congenital Hyperinsulinism is a condition where there is an inappropriate secretion of high levels of insulin from the pancreas, which in turn causes persistently low/unstable blood glucose levels (hypoglycaemia) in the body. Hypoglycaemia due to CHI is relatively rare but potentially a serious condition occurring after birth. CHI has an estimated global prevalence of 1/50,000 live births.

What is Insulin and how does it work?

Insulin is a hormone, which helps control the level of glucose in the blood and it also stores glucose as glycogen in the liver. Insulin is released by specialised cells in the pancreas called beta-cells.

When food is eaten, the blood glucose level rises and the pancreas in turn releases insulin to keep the blood glucose level within a normal range (which is 3.5mmol to 6mmol). Glucose, which comes from the food you eat, moves through your bloodstream to help fuel your body.

If the blood glucose level is dropping (for example when fasting or asleep), the insulin secretion is slowed down or even switched off. This process allows stores of glycogen to be released from the liver into the bloodstream, which will help maintain a normal blood glucose level. When insulin secretion is switched off, protein and fat stores can be used instead of glucose as a source of fuel and energy.

What happens in CHI?

In CHI the close regulation of blood glucose and insulin secretion is lost. The pancreas continues to release insulin inappropriately despite the low blood glucose level.

As a result, the child develops severe hypoglycaemia and requires large and often continuous amounts of glucose to maintain a normal blood glucose level. The high insulin levels also suppress the release of alternative fuels like ketones (chemicals produced by the body from fats stores for energy). This means the brain is deprived of its most important fuels, both glucose and ketones. If the brain cells are deprived of these fuels for prolonged periods, they cannot make the energy they require to function.

Infants with CHI usually show symptoms within the first few days of life and these include:

- Floppiness
- Shakiness
- Poor feeding
- Sleepiness
- Irritability

These symptoms occur as a result of persistent hypoglycaemia and if not corrected this may result in seizures, prolonged unconsciousness and the possibility of permanent brain impairments, hence the importance of maintaining the blood glucose between 3.5mmol/l to 6mmol/l.

What causes CHI and the 2 different types of CHI

There are different forms of CHI. Some forms are considered transient (temporary) – sometimes requiring medication for a few days, weeks or months. Other forms arise from genetic defects and in rare circumstance can be permanent, requiring medication for life.



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There are defects in the genes that can lead to abnormalities in the insulin secretion from the pancreas, thereby causing CHI. Genetic testing will be needed in children who have persistent and severe CHI and who do not respond to first line medical therapy. Your Consultant Endocrinologist, will explain more depending on the course of the illness.

Transient CHI

Transient CHI means that the increased insulin production is only present for a short duration of time (weeks to months) and it is found in conditions such as:

- Babies with a low birth weight/born small for gestational age
- Infants of mothers with Type 1 / Type2 / gestational diabetes (not all on insulin)
- Babies stressed at the time of birth, a difficult or traumatic births

Transient CHI can also occur in infants with no predisposing factors such as those listed above, the reason for this is unclear. Some of the transient forms of CHI, will need treatment with medication for a period of time.

Persistent CHI

There are two main types of persistent CHI; focal and diffuse. In focal CHI, one particular area of the pancreas is affected with the abnormal cells. In diffuse CHI, the abnormal cells are spread throughout the pancreas. Children with either form of disease are identical in their presentation and behaviours. They tend to have significant number of hypoglycaemia events within the first few days of life and require large amounts of intravenous glucose to keep their blood glucose levels normal.

How is CHI diagnosed?

Once your child is stabilised, the endocrine team will confirm or out rule a diagnosis of CHI. CHI is usually diagnosed by detecting high levels of insulin in the blood during a hypoglycaemia episode, therefore the team will take a number of blood and urine samples to help determine the cause of the hypoglycaemia which is done in a controlled manner.

In the situation where the critical samples were not taken at the time of the hypoglycaemia event, the team may organise a controlled 'diagnostic fast' where your child's feeds and fluids will be stopped for a discussed period of time. This will cause your child's blood glucose levels to drop and then the appropriate blood and urine samples will be taken. Your child will then be given glucose and/or a feed in order to return their blood glucose to a normal level.

How is CHI treated?

The aim of treatment is keep the child's blood glucose stable and above 3.9mmol/l.

Initial Treatment Plan

The first line of treatment is to maintain normal blood glucose with Intravenous fluids containing high levels of dextrose (a type of sugary fluid). Your child will need an (IV line) intra venous cannula for this. Sometimes, a glucagon infusion (a medicine used to release stored glucose from the liver in the body) may be needed.

Your child will be established on breastfeed or formula feed when stable. They may require the insertion of a Nasogastric tube (NGT is a special feeding tube that is passed through the nose into the stomach) for milk feeds for a short period of time, to help maintain their blood glucose levels but where possible



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bottle/breast feeds will be encouraged. Your child may require high carbohydrate feeds so a dietician will be involved in their ongoing care to ensure adequate intake of calories and weight gain.

Long Term Treatment Plan

- The blood and urine samples taken during the diagnostic fast will be reviewed by an Endocrinologist and based on these results a diagnosis of CHI maybe confirmed and a definitive treatment plan can be commenced.
- Diazoxide is the first line treatment for CHI, this is an oral medication that is taken up to three times a day. It works by suppressing the production of insulin by the pancreas.
- Diazoxide can cause fluid retention, and for this reason a diuretic called Chlorothiazide is usually prescribed twice a day in conjunction with Diazoxide.
- A baseline ECHO (echocardiogram) of your child's heart, will be performed prior to commencing Diazoxide and repeated 5 to 7 days after commencing the medication. This is to ensure your child doesn't have or develop extra pressure on the heart and lungs as this can be a rare side effect of Diazoxide.
- The other main side effect is excessive hair growth, this can happen with more long term use of Diazoxide and does not occur in all children and resolves once the medication is discontinued.
- Once Diazoxide is commenced your child's blood glucose will be monitored closely on the ward by nursing staff to ensure the medication is working correctly. Their feeds will be increased gradually from continuous NGT feed to 3hourly bottle/breastfeeds if possible. Intravenous fluids will be discontinued if tolerating feeds. Bottle/breast feeds will be encouraged and Nasogastric tube removed if possible. This can be a slow process over a number of days or even weeks depending on the child.
- A safety fast will be performed once your child is established on Diazoxide and can tolerate full feeds while maintaining a normal blood glucose level and then plans for discharge home can be made.



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During the safety fast your child's feeds will be stopped for a certain amount of time depending on their age. The aim of the fast is to ensure your child is able to maintain their blood glucose within the normal range (3.9mmol to 6mmol/l) and that the current treatment plan is successful prior to discharge home.

Other Treatments

In some cases, the child may not respond to first line treatment (Diazoxide), further investigations will be needed and the endocrine team will discuss other treatment options with you (*see additional information leaflet on "Diazoxide unresponsive CHI"*).

Prior to discharge home and follow-up

- As mentioned above a 'safety fast' will be carried out to ensure your child can maintain normal blood glucose levels for an appropriate amount of time
- It is very important that once you go home that your child doesn't exceed the fasting times that the endocrine team have recommended
- It is also very important to make sure child doesn't miss any doses of Diazoxide
- The Endocrine Clinical Nurse Specialist, will teach you how to check the blood glucose level, and advise you what to do if your child's blood glucose goes below 3.5mmols
- You will be provided with a monitor that is used to measure the amount of glucose in the blood. This is done by performing a small prick on a finger or heel depending on the age of the child, which will give a single drop of blood to put on a blood glucose testing strip. The monitor will display the blood glucose level as a figure measured in mmol/litre
- The aim prior to discharge home is to have your child on full bottle or breast feeds but rarely some children may require the Nasogastric tube to remain in place for a longer period of time, the nurses will teach you how to pass and care for this tube at home if required
- The hospital pharmacists, will advise you on how to draw up and administer the medication. Once your child is ready for discharge you will be given a prescription for the medications and any required supplies.



- You will be given an appointment to return to the Endocrine department usually in 6 to 8 week for follow up with your Endocrinologist and Endocrine nurse specialist. During this appointment, another 'safety fast' may be carried out in order to extend fasting/ sleep times for your child at home.
- The dose of your child's medication may be adjusted by your Endocrinologist as they grow.
- The aim is to eventually wean your child off Diazoxide as many children grow out of CHI. The team will trial your child off Diazoxide for 5 days, while you monitor their blood glucose closely at home. If successful, a 'cure fast' may be carried out in the endocrine department to ensure your child can maintain blood glucose levels within normal range without any treatment
- Your endocrine consultant, may prescribe a glucagon injection (Glucagon works by triggering the liver to release stores of glucose in the body) for your child for use in the event of a severe hypoglycaemia at home. The Endocrine nurses will demonstrate how to give the injection if required.
- If your child is getting blood glucose readings of 6mmol/l and above consistently for a number of days than contact the Endocrine nurses as they may require a review of their Diazoxide dosing schedule

Checklist for discharge home

- Prescription for the following
 - Diazoxide
 - Chlorothiazide
 - Glucose gel
 - Glucagon (may be prescribed for your child)
 - Glucose testing Strips and Lancets for the blood glucose machine
- You have received a blood glucose machine that is in working order, along with an enough strips and lancets for a few days at home
- Education has been given on how to use the blood glucose monitor and that you are confident with the machine and interpreting the results correctly at home.
- Education and understanding on how to recognise and manage a hypoglycaemia at home



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Follow up appointment with The Endocrine team and contact details for Endocrine CNS

How to recognise and treat hypoglycaemia at home?

What is Hypoglycaemia?

Hypoglycaemia is a word used to describe low blood glucose. It is important that you can recognise the symptoms and know how to treat a low blood glucose level at home.

We aim to maintain blood glucose levels above 3.5mmol to 6mmol. Hypoglycaemia may be mild, moderate or severe and it can occur when your child has:

- Been fasting for a prolonged time
- Missed feeds
- Missed medication
- Vomiting/Diarrhoea

Steps to avoid hypoglycaemia

- If your child is unwell/off form always check their blood sugar more frequently and ensure adequate fluid intake day and night
- If concerned about your child contact the Endocrine team or get them reviewed by a medical professional if out of hours
- It is also important to be aware that not all children show symptoms of a hypoglycaemia. If you have any concerns check their blood glucose and act accordingly.
- Always ensure adequate supply of Diazoxide at home and let your local pharmacy know well in advance when you require refill as it can be difficult for local pharmacies to get a supply at short notice.

Glucagon Injection

Glucagon works by triggering the liver to release stored glucose back into your child's bloodstream to help raise their blood glucose levels. Glucagon is given as an Intramuscular injection into your child's thigh and your endocrine consultant may prescribe a glucagon injection for your child for use in the event of a severe hypoglycaemia at home. Your Endocrine nurse specialist will explain how to recognise a severe hypoglycaemia episode when at home and when glucagon may be required.

- **Works fast** – Glucagon begins to raise blood glucose levels within about 10 minutes after an injection is given
- **Storage:** Keep the medicine in a fridge and protect it from light. Make sure that it does not freeze. A pack carried for use may be kept at room temperature (no warmer than 25°C) for up to 18 months.

When you take the medicine out of the fridge, write the date on it and make sure you throw it away or give it to your pharmacist after 18 months, if you have not used it.

- **Picture instructions** - The instructions on the orange protective case to show family and friends how to give an injection if you suffer a severe hypoglycemic episode



When to give Glucagon?

Glucagon will be required in the event of a severe hypoglycaemia at home.

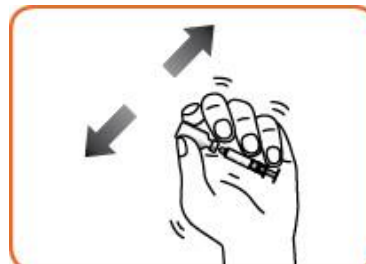
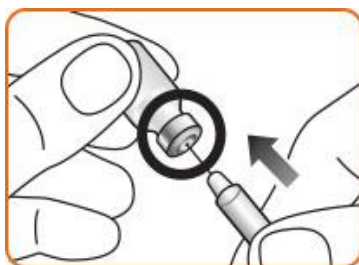
Symptoms of a severe hypoglycaemia include:

- Drowsiness
- Unconsciousness
- Seizure

Give glucagon if your child has any of the above symptoms. Put them into the recovery position and seek urgent medical help/call ambulance. **Don't give your child anything by mouth if unconscious.** Glucagon will raise blood sugar for a short period of time. Once your child is alert and able to swallow, give them something to eat and drink while waiting for medical attention.

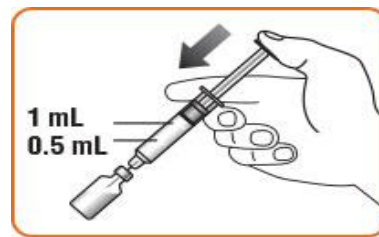
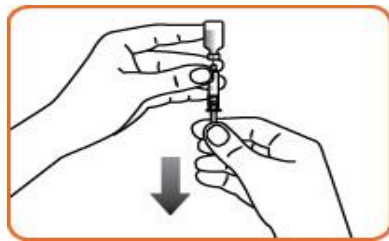
How to give Glucagon?

- Wash hands and check expiry date of medication.
- Remove protective cover from the vial of dry powder and inject the sterile water from the prefilled syringed into the vial via the rubber stopper in the centre.

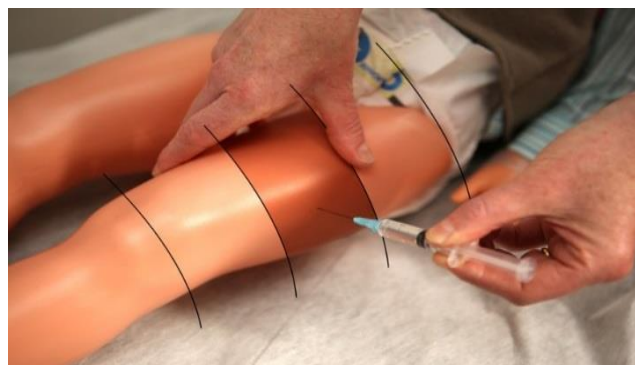


Firmly hold both the vial and syringe together in one hand with needle still in the vial, and gently shake until the powder is completely dissolved. Do not use if a gel has formed, or if you see particles in the solution.

- With the needle still inserted into the vial, gently pull down on the plunger and slowly withdraw all of the liquid into the syringe.



- Check the syringe for air bubbles. If you see bubbles, tip the syringe to point needle towards ceiling and gently tap side to dislodge any air bubbles to top of syringe, and then remove them by pushing plunger until the air has passed through the neck of the syringe.
- Gently push the plunger until it is at the desired mark on the syringe. Take the syringe and needle out of the vial when the correct dose is in the syringe. Your endocrine team will advise on the correct dose for your child based on their age and weight.



- Divide the thigh in 3 parts and inject the medication in the middle third, within the upper outer area (as per picture). Stretch skin tight using thumb and forefinger. Hold syringe like a pencil and keep straight, push the needle into the skin with a quick firm action and push down on the



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plunger of the syringe to give the medication. Inject medication slowly: 1-2 seconds. If possible, leave needle in place for 5-10seconds after injecting the medication

- Dispose of needle into sharps bin
- The medicine should take about 10 minutes to work; your child may feel nauseated or vomit after the glucagon injection. You do not need to worry if your child is sick, as the medicine will still work
- When your child has recovered and can swallow, give them a sugary snack (e.g. glucose gel, sweet biscuits) or a sweet drink or formula feed. This is to make sure that their blood sugar levels do not fall again when the effects of glucagon have started to wear off.

Signs and treatment of hypoglycaemia at home		
Mild Hypoglycaemia	Moderate Hypoglycaemia	Severe Hypoglycaemia
Symptoms		
<ul style="list-style-type: none"> • Sweating • Pallor • Jittery • Hunger • Irritability 	<ul style="list-style-type: none"> • Irritability • Hunger • Drowsiness • Pallor • Change in behaviour 	<ul style="list-style-type: none"> • Drowsy • Unconscious • Seizure
Treatment		



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<ul style="list-style-type: none"> • Check blood sugar • If blood sugar low (3.5mmol or below) feed straight away (formula for baby or sugary drink for older child) • Recheck blood sugar in ½ hour to ensure it has returned to normal • Check blood glucose more frequently for 24hours • If persistent, hypoglycaemia seek urgent medical attention 	<ul style="list-style-type: none"> • Check blood sugar • If blood sugar low (3.5mmol or below) and if your child is awake and alert, then feed • If unable to take feed but awake and alert, then massage glucose gel into their gum • Feed child once alert • Recheck blood sugar in 15minutes • If drowsy and not alert, then DO NOT give anything by mouth • If your Child's condition has not improved, seek urgent medical attention. 	<ul style="list-style-type: none"> • If your child is unconscious, put them into the recovery position (side lying position) • If you feel able, give Glucagon injection immediately into the thigh • Seek urgent medical help/call ambulance and stay with the child • Don't give your child anything by mouth if unconscious. • Glucagon will raise blood sugar for a short period of time. Once your child is alert give them something to eat and drink while waiting medical attention
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Please remember that persistent vomiting and/or hypoglycaemia always require medical treatment.

Useful Resources

<https://www.glucagenhypokit.com/content/glucagenhypokit/en/instructions.html>

Congenital Hyperinsulinism International: <https://congenitalhi.org/>

<https://www.qosh.nhs.uk/conditions-and-treatments/conditions-we-treat/hyperinsulinism>

Useful contact numbers:

Children's Health Ireland at Crumlin - Hospital Switch: 01 409 6000

Dr. _____ Ext _____

Dr. _____ Ext _____

Endocrine Clinic _____ Endocrine CNS _____ Bleep no: _____



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