# What does CDG mean for us?

When CDG is suspected, clinical tests will be carried out to confirm a diagnosis. The first is a simple blood test: clinicians want to assess the levels of glycosylation in the blood, as low levels of glycosylation indicate that there is an error in this pathway. When the clinicians have taken a blood sample they are particularly interested in analysing the glycosylation status of a protein in the blood called transferrin. Under normal circumstances, glycans (sugar chains) are attached to transferrin, however in CDG patients the level can be much lower.

Any abnormal transferrin patterns can be detected by separating the molecules with specialised techniques. This test is useful to identify any defect in:

- N-linked glycosylation (type I CDG)
- O-linked glycosylation (type II CDG)

(N means the sugar chain is attached to a nitrogen atom and O means an oxygen atom).

Analysis of the blood test is not 100% accurate and further tests, such as an MRI scan on the brain, may be needed.

CDG is commonly diagnosed during infancy and children with CDG often have significant medical problems during the first few years of their lives. The type, symptoms and severity of CDG vary from patient to patient, and some of the symptoms become more prominent at different ages, and some of them won't ever be a problem at all. Ideally, there will be one clinician coordinating the care of all medical issues, and making referrals to the correct specialists. CDG is a multisystem disorder, as glycosylation is essential to the function of many proteins in the body, so here are the main clinical issues for CDG patients, along with their causes and effects, and who the primary specialist is, for these issues:[1]

## 1. Neurological issues (the brain)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Ataxia | Atrophy (shrinkage) of the brain, especially the cerebellum | Lack of coordination in movement and posture, delay in motor development, tremor | Physiotherapist, Occupational Therapist |
| Seizures | Abnormal electrical activity in the brain | Possible involuntary movements and loss of consciousness | Neurologist |
| Stroke-like episodes | Temporary thickening of blood in the brain, possibly after an illness | Possible drowsiness, dullness, coma, loss of vision, paralysis on one side or both[i] | Neurologist |
| Peripheral neuropathy | Damage to peripheral nerves | Possible weakness, numbness and pain in hands and feet and other parts of the body | Neurologist |
| Cognitive dysfunction | Damage to the brain | Poor attention span and scholastic performance | Education specialist |

[i]This can be very frightening as a stroke-like episode has the appearance of a stroke. Anecdotal evidence suggests that most patients eventually make a full recovery.

## 2. Gastrointestinal issues (digestion)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Failure to thrive | Neurological symptoms and low muscle tone | Low weight and height, possible malnutrition | Gastroenterologist, Dietician |
| Gastro-oesophageal reflux | Low muscle tone | Possible involuntary movements and loss of consciousness | Gastroenterologist |
| Protein-losing enteropathy | Disorder in building cells | A decrease in protein levels of the plasma (in blood) | Gastroenterologist |
| Diarrhoea | Possible infection | Illness, low sugar levels | See GP faster than you would with a non-CDG patient |

## 3. Hepatology issues (liver)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Enlarged liver, fibrosis or liver connected blood vessels | Fluctuation of transaminases (enzymes in protein formation) | Liver damage | Hepatologist |

## 4. Urology (kidney and urinary tract)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Renal abnormalities | Problems on development | Abnormal kidney anatomy (rare), cysts on the kidney | Nephrologist, Urologist |
| Nephrotic syndrome | Underlying kidney problems | Abnormal loss of proteins in urine and kidney damage | Nephrologist, Urologist |

## 5. Haematology (the blood)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Deep vein thrombosis | Blood clotting | Pain and swelling in site of clot | Haematologist, Coagulation specialist |
| Blood disorders | Varying levels of blood factors (factor XI, anti thrombin III, protein C and protein S) | Before surgery or dentistry, platelet number and function, and coagulation factors should be checked | Haematologist |

## 6. Endocrinology (hormones)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Abnormal thyroid function | Abnormal glycosylation of the transporters of the thyroid hormone | Problems in growth and learning how to move | Endocrinologist |
| Delayed or absent puberty | Abnormal glycosylation of hormones or transporters of hormones | Limited pubertal development | Endocrinologist |
| Hypoglycaemia (low blood sugar levels) | Abnormal glycosylation of hormones or transporters of hormones, hyperinsulinism (high blood insulin) | Possible drowsiness or loss of consciousness, jitteriness or seizures | Endocrinologist |

## 7. Ophthalmic issues (the eyes)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Strabismus (eyes looking in different directions) | Muscle weakness and poor communication of coordination instructions from the cerebellum | Possible double vision, loss of depth perception, functional blindness in the diverging eye | Ophthalmologist |
| Retinitis pigmentosa (loss of vision) | Degeneration of the retina at the back of the eye | Possible night blindness, tunnel vision, blindness, bright light may cause irritation, cataracts | Ophthalmologist |
| Nystagmus (wobbly eyes) | Poor communication of coordination instructions from the cerebellum | Possible blurred vision, strange head position to minimise the wobbling | Ophthalmologist |
| Refractive errors | Refractive errors | Blurred vision | Ophthalmologist, Optician |

## 8. Orthopaedic issues (muscles and skeleton)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Scoliosis (curvature of the spine), or lordosis (curvature in the lower spine) | Low tone of the muscles of the spine and low bone density | Possible pain, respiratory problems, eating disorders | Orthopaedic doctor |
| Dysostosis multiplex (general skeleton abnormalities) | Skeletal changes, fibrosis (stiffness and scarring) of tendons, ligaments and soft tissue | Skull abnormalities, changes in ribs (such as inversion), and long bones | Orthopaedic doctor |
| Coxa valga (hip deformity) | Underdevelopment of muscles in the buttocks | Hip problems, possible dislocation | Orthopaedic doctor |
| Osteopenia (light bones) | Poor bone calcium, lack of standing or walking | Decrease in bone mineral density which may lead to osteoporosis | Orthopaedic doctor, Physiotherapist |

## 9. Cardiology (heart)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Pericardial effusion (fluid around the heart) | Possibly thyroid abnormalities, an infection, or kidney problems | No symptoms, but in rare cases pressure on the heart causing chest pain | Cardiologist |
| Cardiomyopathy (stretching, thickening or stiffening of heart muscles) | Possible abnormalities of the heart value | Possibly poor weight gain, fatigue, paleness, muscle weakness, irritability, difficulty breathing | Cardiologist |

## 10. Immunology (fighting infections)

| Problem | Cause | Effect | Specialist |
|---|---|---|---|
| Recurrent infections | Lack of protein/iron absorbed from diet | Possible pneumonia, ear infection, anaemia, throat infection, etc | See GP faster than you would with a non-CDG patient, Immunologist |
| Non-response to immunisations | Genetics, nutrition | Vaccine failure | Immunologist |

Please note: there is no reason why patients with CDG should not have their vaccinations as normal.

More recently there have been questions over a CDG patient's ability to sweat (hypohydrosis),[2] and therefore avoiding excessive heat and too much direct sunlight may be prudent.

## Urgent Hospital care

Donna Krasnewich, of the National Institute of Health in the US, recommends you show the following checklist to hospital doctors on admission.

- Check hydration
- Check for infection
- Do a liver function test (which may be high due to CDG)
- Check glucose levels (which may be low)
- Check for swelling (indicating fluid leaking from blood vessels)
- Check for stroke-like episode
- Check for DVT (pro- and anti-clotting factors are low in CDG)
- Check for pericardial effusion
- Use with caution medication that is broken down by the liver e.g. acetaminophen

## Daily life

Currently, there is no treatment or cure for the vast majority of CDGs. This means that medical interventions are adopted to help manage the varied clinical symptoms associated with disease. Here are some practical suggestions of how, and what, you should try and record in order to aid the healthcare professional looking after your child.

As a child with CDG commonly develops more slowly than a child without CDG, it is important to keep a record of common childhood milestones and at what age your child reaches them. This information is very valuable for both healthcare and educational professionals. A useful guide on things to look out for can be found in the Red Book your child was issued with at birth. Additionally, we recommend that you regularly record the height and weight of your child so that growth development can be tracked.

It is particularly important to monitor and record the weight of your child, as some children have issues with swallowing and feeding. If your child does not put on enough weight, they may need to be tube fed.

As your child grows, it may be necessary to visit speech and language therapists (SALT) to help your child practice swallowing and speaking.

Due to the effects of CDG on the brain (specifically the cerebellum), a child with CDG may have problems with coordination, so will need input from physiotherapists (PT) and occupational therapists (OT). Regular hearing and sight tests are also recommended.

CDG patients can suffer seizures or stroke like episodes. These can be scary to witness and require hospital stays. Getting a first aid certificate will help you feel more confident should this situation occur, and many of our families have a hospital bag packed and on standby in case of emergencies. Seizure medication may be required if seizures occur often. Our website gives more information about how to organise medical notes and what to take to hospital.

## The long term

The first year of life for a CDG patient is the riskiest, with infection, heart disease and liver problems potentially becoming life threatening, however, many patients are never hospitalised during infancy and live well into adulthood and some into middle age.

Therefore, in the long term, parents need to consider the best setting for schooling. A special school setting may be the best place for some children and for others a mainstream setting with some support may be more appropriate.

Social services can provide your family with a social worker, who can advise on local services and provision that you could access. For example, there may be a respite service to give parents a break, or sibling support days.

The psychological characteristics of CDG patients are not well researched but anecdotally, CDG patients have happy and fun personalities, however, behaviour such as stubbornness and tantrums can be a problem.

Specialist equipment can be expensive, so you may be able to apply for benefits in the UK, such as the Disability Living Allowance for children. There are charities listed on our resources pages on the CDG UK website that may also be able to give grants for specialist equipment such as car seats and bicycles. You may be able to access grants for home improvements too, if you need to make adaptations to your house.

## What about our other children?

A genetic counsellor will be able to explain to you why your child has CDG. It may be that both mum and dad are carriers of the gene, or it may be due to a spontaneous mutation in the DNA. You may wonder if your other children are affected by CDG, or are carriers of the gene, and your doctor and genetic counsellor will also be able to help here. Siblings in the UK can be tested for CDG if there is reason to suspect they may have it, but a sibling will need to be 16 years old before they can be tested to find out if they are carriers.

You may want to have more children in the future. The risk of another child having CDG is 1 in 3[3], so your doctor and genetic counsellor will be able to advise on the options available to you.

CDG UK family days happen once a year in the UK, so if you would like to meet other families to share issues and discuss life with CDG, please check our website for updates.


**References:**

1. Ferreira, V (2010) The Practical Guide to CDG Families. Downloadable at http://www.apcdg.com/uploads/4/1/1/9/41196831/the_practical_guide_to_cdg_families_fv.compressed.pdf
2. Ryman, D (2014) speaking at the second World CDG Conference in Lyon
3. Sparks, S and Krasnewich, D (2017) Congenital Disorders of N-Linked Glycosylation and Multiple Pathway Overview [Online] https://www.ncbi.nlm.nih.gov/books/NBK1332/ (accessed 2/4/2018)


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