

Your Guide to Type 2 Gaucher Disease



What is Type 2 Gaucher Disease?

Type 2 Gaucher disease is a very rare, rapidly progressive form of Gaucher disease which affects the brain (central nervous system) as well as the spleen, liver, lungs and bones. It is characterised by severe neurological (brain) involvement in the first year of life. It is also called acute neuronopathic Gaucher disease.



*Above:
Ellie Carter*

*Front cover:
Summer Smith*

Fewer than 1 in 100,000 newborn babies have Type 2 disease and this form of the disease is not associated within any particular ethnic group.

Babies usually appear normal at birth but develop neurologic and other symptoms by the age of 3 to 6 months. Type 2 is almost always apparent by 6 months of age. Many children die in infancy and survival beyond 2 years is rare. In some exceptional cases, the disease course may be prolonged over a number of years.

Early signs and symptoms include slow development, squint (strabismus), poor feeding and slow weight gain. In the subsequent months, developmental milestones may be lost (regression), there may be rigidity of the neck and limbs (hypertonia), back arching, abnormal head posturing, and noisy breathing (stridor), swallowing problems and recurrent vomiting may become apparent. The abdomen may appear very swollen due to enlargement of the liver and spleen.

As the disease progresses, other difficulties such as throat (laryngeal) spasm, seizures, low blood counts, bleeding and a failure to shake off colds and other infections may complicate the course. The lungs may also be affected and the bones may show signs of disease.

In the later stages of the disease, the infant may show signs of pain and distress that may arise from spasms, seizures, choking, breathing difficulties, infections, bleeding and bone pain. It is very important to recognize and manage these symptoms with appropriate measures and pain relief in order to keep the child as comfortable as possible. Sudden death may occur, or in some cases the baby may eventually 'switch off', not reacting to parents or stimulus, for a period before death.

How is Type 2 diagnosed?

The diagnosis is usually made on the basis of the clinical features, enzyme analysis in blood and/or genetic (mutation) analysis.

Type 2 (also called acute neuronopathic) Gaucher disease is quite distinct from the chronic neuronopathic Gaucher disease (type 3) and non-neurological Gaucher disease (Type 1).

It is important that the infant is referred to one of the specialist centres for careful evaluation and initial assessment (see contact list at the end of this booklet).

What is the cause?

Gaucher disease is an inherited disorder. Children with Type 2 have a severe deficiency of an enzyme called glucocerebrosidase which is important in maintaining the structure and integrity of all cells in the body.

The enzyme deficiency results in the accumulation of fatty substances (glucocerebroside and related chemicals) which are normally produced during the recycling of cells in the body and are then broken down by the enzyme. Babies with Type 2 Gaucher disease are unable to break down glucocerebroside and related chemicals. Instead, these substances remain stored within cells of the body, preventing them from functioning normally and eventually leading to their destruction. The cells affected include those found in the bone marrow, spleen, liver, lungs and brain.

Is there a treatment?

No specific curative treatment for Type 2 Gaucher disease is available at present.

Although enzyme replacement therapy and substrate reduction therapy has been found to be effective for Type 1 and in some cases Type 3 Gaucher disease, these therapies have not worked in treating Type 2 infants.

Like in most conditions with brain involvement, once neurological damage has occurred, this cannot be reversed.

In type 2 Gaucher disease, brain damage starts while the baby is within the womb and to date, no treatment has been effective in preventing this.



Emma Hall

What are my options for symptom management and palliative care?

Professional help and support is available, whether the child is being looked after in hospital or at home. It is important to talk to the doctors and nursing staff especially if parents are finding it hard to deal with a particular issue.

It is worth considering support from a local hospice as they can offer respite and support for the whole family (please see contacts at the end of this booklet).

Although there is no cure for Gaucher disease type 2, the symptoms can be managed with appropriate measures and specific medications.

With help and support, parents can deal with many unfamiliar situations, in particular medical techniques to care for their child. Doctors will outline, at the time of diagnosis, how the disease will progress. It may be difficult at that time for parents to fully anticipate the practical difficulties which may arise, for which the medical team will give ongoing support.

Management of the symptoms and problems that arise as the disease progresses is important in order to ensure a good quality of life and may include:

- Poor feeding and weight gain
- Infections
- Seizures
- Spasms
- Pain
- Bleeding
- Excessive secretion
- Breathing difficulties

Measures such as nasogastric tube feeding, antibiotics, anticonvulsants, pain relief, regular suction and oxygen may be required. Some children develop spasm of the vocal cords (laryngospasm) that can result in choking and may require specialized assessment and management.

Input from a range of health professionals is usually necessary and it is important to have a coordinated approach to multidisciplinary assessment and day-to-day management.

This may include the GP, local paediatricians, specialized and community nursing, neurologists, dieticians, physiotherapists, speech and language therapists (SALT) and ear nose and throat (ENT) specialists.

One of the major contributions given by nursing staff is moral and emotional support – this cannot be under-estimated. Social workers can help by giving advice and information on financial allowances and benefits available for parents.

Relatives and friends can give invaluable support. If possible enlist their help in the everyday caring of the child. They often want to help and this can give parents a much needed break, even if just for the evening, or spending more time with another child.

Contacting parents who are, or have been, in a similar situation can also be useful – they alone can understand the pressures on parents who are caring for a sick child. See the contact list at the end of this leaflet.

Help is available and should be asked for.

Is Type 2 Gaucher Disease an inherited disorder?

Type 2 Gaucher disease is inherited. Both parents must be carriers of the disease in order for there to be a risk of them having an affected child.

For a couple who are both carriers, there is a 1 in 4 (25%) chance with each pregnancy that the child will have the disease, a 1 in 2 (50%) chance the child will be a carrier and a 1 in 4 (25%) chance that the child will neither be a carrier nor have the disease.

Much of a person's make-up is a result of what is inherited from each parent. Many characteristics, such as eye colour, blood groups and genetic conditions, are passed from parents to children through their genes. The genes for these characteristics are organised on 23 pairs of chromosomes, one of each pair coming from the mother and one from the father. Each chromosome carries thousands of genes.

The gene which instructs the body to make the enzyme glucocerebrosidase is also passed on from both parents to their children. In Gaucher disease, this pair of genes is defective. As a result, the enzyme produced from the defective pair of genes, one gene inherited from each parent, is unable to perform its normal function.

Gaucher disease is an autosomal recessive disorder. Autosomal describes the type of chromosome on which the gene is carried. Recessive refers to the fact that in order to develop the disease, a child must inherit two defective genes, one from each parent.

A person with one normal gene and one defective (Gaucher) gene is a carrier of Gaucher disease. Carriers are perfectly healthy and will not develop any symptoms of Gaucher disease. As long as one of the pair of genes is normal, enough enzyme can be produced to prevent abnormal chemicals from accumulating within the cells of the body.

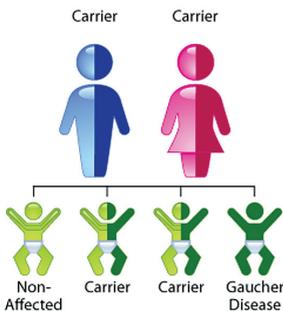
If only one parent is a carrier of Gaucher disease, none of the children will have Gaucher disease but there is a 1 in 2 chance (50%) of the child being a carrier.

It must be emphasised that the chances in each pregnancy, of the child inheriting Gaucher disease, are totally independent of whether or not a previous child has the disease. Having had one child with Gaucher disease does not mean that the next three children cannot inherit the disease.

Genetic counselling

In families where a baby with Gaucher disease Type 2 has been born, the parents and their close family may wish to be offered genetic counselling. Your paediatrician or GP can arrange this.

Pre-natal testing, carrier screening, which are described below, together with individual genetic counselling are available at several centres around the UK.



Prenatal testing

In families where a baby with Type 2 Gaucher disease has been born, pre-natal testing on subsequent pregnancies is available and can be discussed in advance of a pregnancy.

A chorionic villus sample (CVS) or amniocentesis can be performed to diagnose the disease early in pregnancy. A CVS is carried out at around 10 weeks of pregnancy and an amniocentesis around 16 weeks. In CVS, a sample of cells is taken from the developing placenta under ultrasound guidance and analysed. In amniocentesis, a needle is inserted through the mother's abdominal wall into the amniotic sac holding the baby. A sample of amniotic fluid removed, and cells are separated and tested. Results are usually available within a few days.

PGD

PGD (pre-implantation genetic diagnosis) is licensed by HFEA (Human Fertilisation and Embryology Authority) for use in couples who have a 1 in 4 risk of having an affected child (both partners are carriers of type 2 Gaucher disease). In PGD, the genes of embryos created by IVF (in vitro fertilisation) are checked for the condition before implantation. If you would like to know more please contact your GP.

Carrier screening

Close relatives of a family where a baby with Type 2 has been born and who are of reproductive age or younger may wish to be offered genetic counselling in order to discover if they are a carrier. Carrier screening may then be offered.

The chance of close family members being carriers exists but there is only a risk to their children if their partner is also a carrier of Gaucher disease. The chance of any one person in the general population, outside of an affected family, being a carrier of Type 2 is very small.

Specialist Paediatric Lysosomal Storage Disorder Centres in the UK

Birmingham Children's Hospital

Steelhouse Lane, Birmingham B4 6NH
Tel: 0121 333 9907/08 (Secretaries)
Fax: 0121 333 9998

Consultants:
Dr Suresh Vijay
Dr Si Santra

Great Ormond Street Hospital for Sick Children

Great Ormond Street
London WC1N 3JH
Tel: 020 7405 9200 (ext. 0075)
Fax: 020 7813 8258

Consultants:
Dr Anupam Chakrapani
Dr Maureen Cleary
Dr Lara Abulhoul
Prof Paul Gissen
Dr Stephanie Grunewald
Dr Emma Footitt

Royal Manchester Children's Hospital

St Mary's Hospital, Oxford Road
Manchester M13 9WL
Tel: 0161 701 2137/2138
Fax: 020 701 2303

Consultants:
Dr Simon Jones
Dr Beth Jameson
Dr Alex Broomfield
Dr Bernd Schwahn

University Hospital of Wales

Heath Park, Cardiff CF14 4XW
Tel: 02920 747 747

Consultant: Dr Graham Shortland

Organisations that can offer help and support to families:

The Gauchers Association

www.gaucher.org.uk

Evesham House Business Centre
48-52 Silver Street, Dursley
Gloucestershire GL11 4ND
Tel: 01453 549231

*Information on Gaucher disease.
Have a Patient and Family Support
Worker to help with non-clinical
support needs.*

Climb

www.climb.org.uk

176 Nantwich Road
Crewe CW2 6BG
Helpline: 0800 652 3181

*Offers information on metabolic
diseases, support and befrienders.*

Contact a Family

www.cafamily.org.uk

209-211 City Road, London EC1V 1JN
Free helpline: 0808 808 3555

*Supports families whatever the
disability or health condition. Offers
local support, resource library and
connects families.*

The Compassionate Friends

www.tcf.org.uk

53 North Street, Bristol BS3 1EN
Tel: 0845 123 2304

*Supporting bereaved parents and
siblings. Has a helpline, online
forums and offers local support.*

Child Bereavement UK

www.childbereavement.org.uk

Clare Charity Centre
Wycombe Road, Saunderton
Buckinghamshire HP14 4BF
Tel: 01494 568900

*Supporting families with
bereavement.*

Together for Short Lives

www.togetherforshortlives.org.uk

4th Floor, Bridge House
48-52 Baldwin Street, Bristol BS1 1QB
Tel: 0117 989 7820

*The UK voice for children and young
people who are not expected to
reach adulthood and their families.
Families can search for palliative
care services and children's
hospices in their local area.*

ARC (Antenatal Results and Choices)

www.arc-uk.org

345 City Road
London EC1V 1LR
Tel: 020 7713 7356
National Helpline: 0845 077 2290

*Supporting families through
antenatal testing.*

The logo for the Gauchers Association features the word "Gauchers" in a bold, green, sans-serif font, with "ASSOCIATION" in a smaller, green, sans-serif font directly below it. The text is positioned on a light green rectangular background that overlaps a darker green square on the left side.

Gauchers
ASSOCIATION

Contact us

For more information contact:

Gauchers Association Ltd.
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GL11 4ND

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