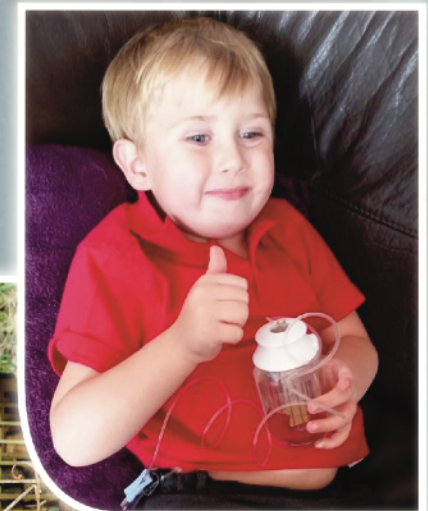


Produced in collaboration with Lead Specialist
Nurse Elizabeth Morris from
Addenbrooke's Hospital, Cambridge.

This booklet was supported with unrestricted grants
by Sanofi Genzyme and Shire



information



Images on front cover, Tommy Whittaker & Blake Mackinnon

Registered charity number: 1095657
www.gaucher.org.uk

type 1 Gaucher disease

contact details

Addenbrooke's Hospital

Hills Road, Cambridge CB2 0QQ

Tel: 01223 336864

Fax: 01223 336846

National Helpline: 01223 216295

Consultants: Prof Timothy Cox, Dr Patrick Deegan,

Dr Chong Yew Tan

<http://www.cuh.org.uk>

Birmingham Children's Hospital

Steelhouse Lane, Birmingham, B4 6NH

Tel: 0121 3339907/08 (secretaries)

Fax: 0121 3339998

Consultants: Dr Saikat Santra, Dr Suresh Vijay, Dr Julian

Raiman, Dr Srividya Sreekantam

<http://www.bch.nhs.uk/>

Great Ormond Street Hospital for Sick Children

Great Ormond Street, London, WC1N 3JH

Tel: 020 74059200 (ext. 0075)

Fax: 020 78138258

Consultants: Dr S Batzios,

Dr M Cleary, Dr A Chakrapani, Dr J Davison, Dr E

Footitt, Prof P Gissen, Dr S Grunewald, Prof S Rahman

<http://www.gosh.nhs.uk/>

National Hospital, London

Charles Dent Metabolic Unit, Box 92, National Hospital
for Neurology

and Neurosurgery, Queen Square, London, WC1N 3BG

Tel: 020 34484778 (secretaries)

Tel: 020 34483606 (direct line)

Fax: 020 72092146

Consultants: Dr Robin Lachmann, Dr Elaine Murphy

[http://www.uclh.nhs.uk/OurServices/](http://www.uclh.nhs.uk/OurServices/OurHospitals/NHNN/Pages/Home.aspx)

[OurHospitals/NHNN/Pages/Home.aspx](http://www.uclh.nhs.uk/OurServices/OurHospitals/NHNN/Pages/Home.aspx)

New Queen Elizabeth Hospital

Inherited Metabolic Disorder Unit, Department of
Endocrinology, Room 27, Ground Floor, North Block,
Queen Elizabeth Hospital, Birmingham, B15 2TH

Tel: 0121 3712000 (ext. 5922)

Consultants: Dr Tarek Hiwot,

Liz McAlister - I MD Co-ordinator

<https://www.uhb.nhs.uk/new-hospital.htm>

Royal Free Hospital

Pond Street, London, NW3 2QG

Tel: 020 74726409

Fax: 020 78302313

Consultants: Prof Atul Mehta, Dr Derralynn Hughes,

Dr Uma Ramaswami

<https://www.royalfree.nhs.uk/>

Royal Manchester Children's Hospital

St Mary's Hospital, Oxford Road, Manchester, M1 9WL

Tel: 0161 7012137 / 2138

Fax: 0161 7012303

Consultants: Dr Simon Jones, Dr Beth Jameson,

Dr Alex Broomfield, Dr Bernd Schwann

<http://www.cmft.nhs.uk/childrens-hospitals>

Salford Royal Hospital

The Mark Holland Metabolic Unit, NW2, 2nd Floor,

Ladywell Building, Salford Royal NHS Foundation Trust,

Stott Lane, Salford, M6 8HD

Tel: 0161 2064365 / 1899

Fax: 0161 2064036

Consultants: Dr Mark Roberts, Dr Reena Sharma,

Dr Ana Jovanovic, Prof. Chris Hendricksz,

Dr Gisela Wilcox

<http://www.srft.nhs.uk/>

University Hospital of Wales

Heath Park, Cardiff, CF14 4XW

Tel: 02920 747747

Consultants: Dr Graham Shortland, Dr Duncan Cole

<http://www.cardiffandvaleuhb.wales.nhs.uk/our-hospitals>

type 1 Gaucher disease

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Adele Rawcliffe & Willow

Welcome to the Gauchers Association information booklet on Type I Gaucher disease. In 2016 The Gauchers Association undertook a survey amongst their members to understand what information they would like to see in an information booklet.

Following on from the analysis of this survey the information in this booklet, along with additional inserts is to help you understand and answer questions on Gaucher disease, from, what it is, how is it inherited, how will it affect your life and the latest clinical research.

We hope you find it informative and useful, whether you have been living with Gaucher disease for many years, or you or a family member have just been diagnosed or you work within the Gaucher community.

If you have any unanswered medical questions please refer back to your Specialist medical team or if you have any unmet non-medical needs contact the Gauchers Association's Patient & Family Support Service on 01453 549231.



Further information on neuronopathic Gaucher disease is available on the Gauchers Association website at www.gaucher.org.uk

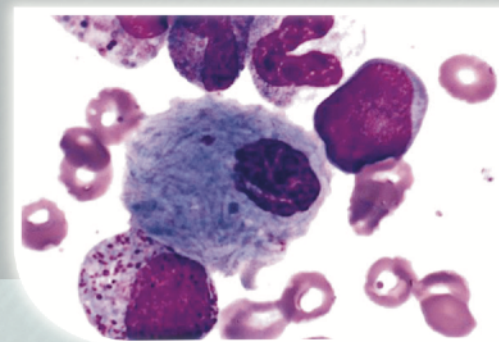
Andrew Bloom

Gaucher disease is a rare inherited (genetic), enzyme deficiency disorder. Symptoms range from mild to severe and can appear at any time, from infancy to old age. They may include anaemia (low haemoglobin), tiredness (fatigue), easy bruising and a tendency to bleed. An enlarged spleen and liver with a protruding stomach may also occur as well as bone pain, loss of bone strength and density with an increased risk of fractures.

People with Gaucher disease lack sufficient activity levels of an enzyme called glucocerebrosidase. This enzyme helps the body break down worn-out cells and as a result, a fatty substance called glucocerebroside accumulates usually in the spleen, liver, bone marrow, rarely in the lungs and in some types of Gaucher disease in the central nervous system.

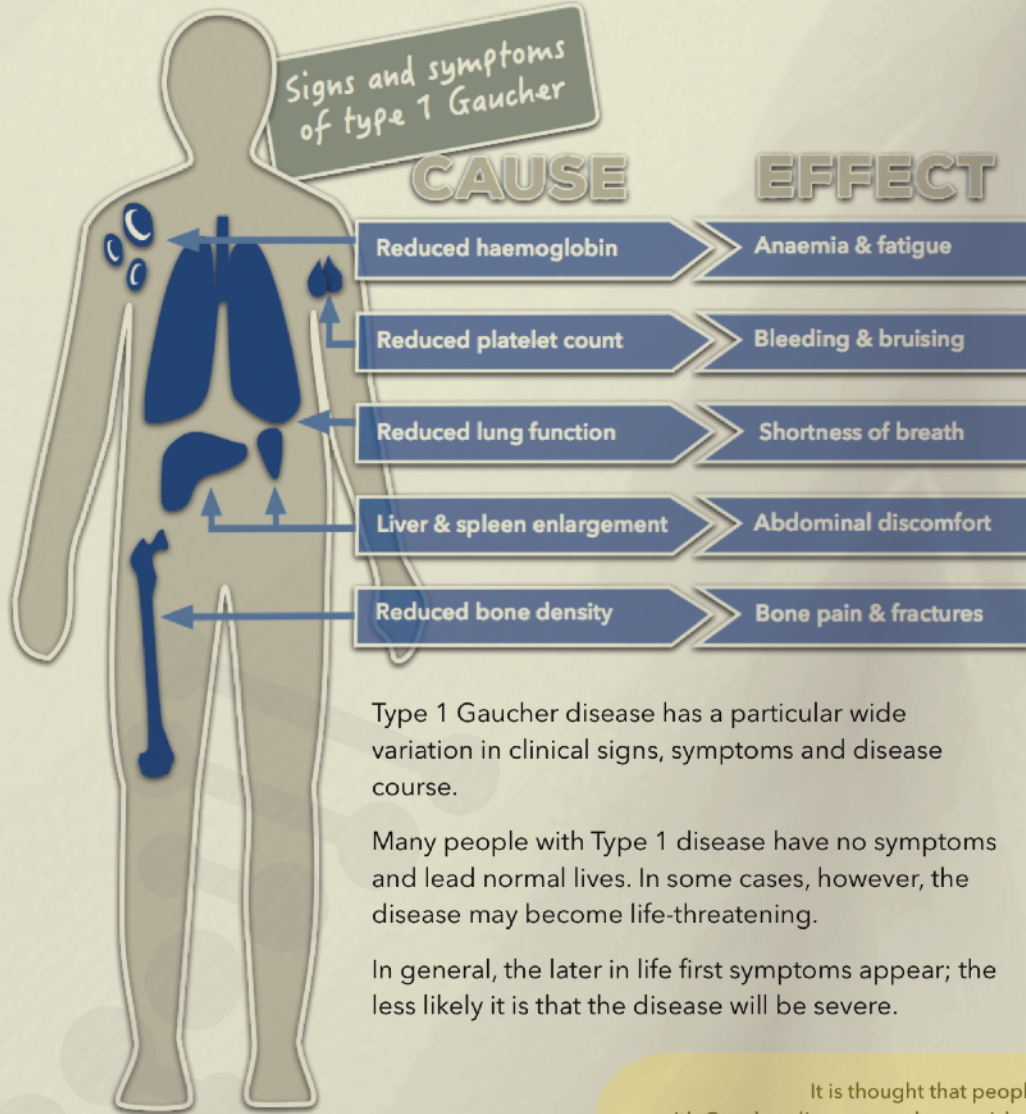
The most common form of Gaucher Disease (Type 1) affects 1 in 100,000 of the general population but 1 in 850 of Jewish (Ashkenazi) descent, although not all those who inherit the mutated genes for this disorder will show symptoms.

In the rare Neuronopathic (Types 2 and 3) Gaucher Disease, neurological symptoms occur which include an eye movement disorder (oculomotor apraxia), unsteadiness (ataxia), fits (seizures), loss of skills and sometimes a degree of learning difficulty (central auditory processing disorder). Children with Type 2 Gaucher disease usually die within the first few years of life.



Gaucher cell

Type 1 Gaucher disease, the most common form, is often but misleadingly referred to as Adult Gaucher disease. Individuals of all ages can be affected. This form of Gaucher disease does not generally affect the nervous system, it is sometimes referred to as non-neuronopathic Gaucher disease.



Type 1 Gaucher disease has a particular wide variation in clinical signs, symptoms and disease course.

Many people with Type 1 disease have no symptoms and lead normal lives. In some cases, however, the disease may become life-threatening.

In general, the later in life first symptoms appear; the less likely it is that the disease will be severe.

It is thought that people with Gaucher disease may have a risk of developing other conditions later in life including Parkinson's disease and Multiple Myeloma (cancer of the white blood cells). This is an ongoing area of research; see additional leaflet at back of booklet for more information.

Signs and symptoms of Type 1 Gaucher disease:

General symptoms

Generalised fatigue
Lack of energy and stamina

Abdomen

Enlarged liver and spleen

Digestive

Loss of appetite

Skeletal system

Growth retardation in children
Bone pain
Reduced bone density
Widening of bones above the knee joint
Spontaneous fractures
Acute bone infarctions - "bone crisis" eg severe pain
Bone necrosis (death of tissue)

Delayed onset of puberty

Respiratory

Shortness of breath

Blood

Increased bleeding tendency such as nosebleeds and bruising
Low levels of:

- Blood platelets (thrombocytopenia)
- Red blood cells (anaemia)
- White blood cells (neutropenia)
- Elevated levels of biomarkers including chitotriosidase, PARC / CCL18

Perhaps the most common sign of Type 1 Gaucher disease is an enlargement of the spleen and/or liver.

Over activity of the enlarged spleen may result in an increased tendency for bleeding due to decreased platelets, related clotting disorder or fatigue related to anaemia. Spleen enlargement is often the most frequent initial finding and may be first recognised from as young as 6 months of age. The spleen may become sufficiently enlarged to affect the child's mobility and to attract attention.

A child with severe disease may be shorter than average and may adopt a swayback posture to support the weight of an enlarged abdomen.

Skeletal symptoms of bone involvement can occur at any time in life: in children as young as 2 years of age, or in adults as old as 70. In more than half of the people with Type 1 Gaucher disease, x-rays reveal a characteristic deformity called the "Erlenmeyer flask deformity" in the thigh bones.

The thigh bones have a flaring at the knee (resembling a Erlenmeyer flask), instead of having a normal round shape. Reduction in bone density increases the risk of fracture and is important to be aware of in later life.



Lucy, Tommy, Mackenzie & Billie

how is Gaucher disease inherited?

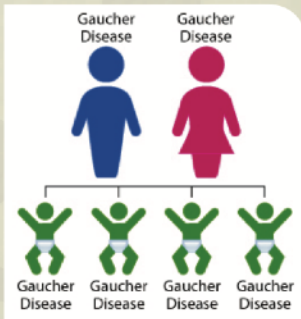
An individual inherits two copies of every gene; one from each parent. In the case of Gaucher disease, the gene for the production of the enzyme glucocerebrosidase is unable to function normally.

To develop Gaucher disease a person must have two copies of that abnormal gene (often referred to as a 'mutation'). A person with one normal and one mutated gene is a "carrier" of Gaucher disease and will not have the condition, but there is a 50% chance that they will pass the "Gaucher gene" onto their offspring.

Many of the mutations of the gene for Gaucher disease have been identified; therefore, carrier testing is possible in affected families.

If you are interested discuss this with your specialist centre.

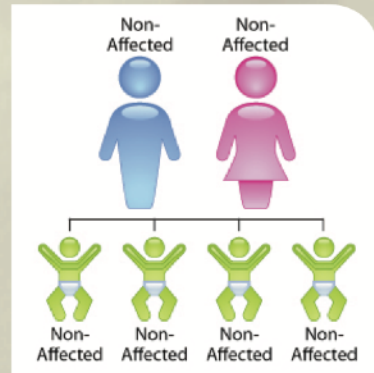
If both parents have normal genes for glucocerebrosidase, each child will inherit two normal genes, one from each parent, and will neither have Gaucher disease nor be a carrier.



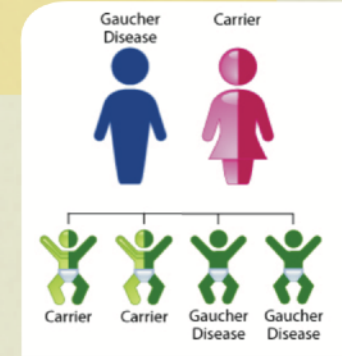
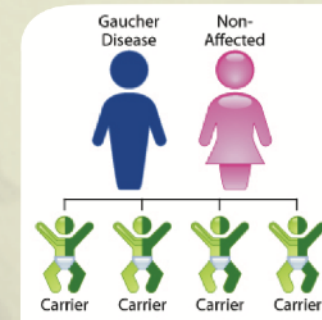
If both parents have Gaucher disease, all of their children will inherit two Gaucher genes and will have the disease as well.

The possibilities of passing on the mutated Gaucher gene:

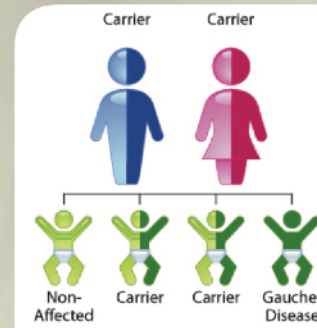
Both parents have Gaucher disease. All their children inherit two Gaucher genes - one from each parent, therefore all children have Gaucher disease.



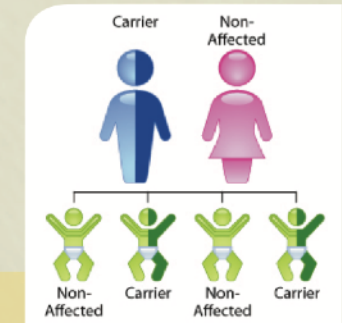
One parent has Gaucher disease and the other parent is a carrier. Their children will have a 50% chance of having Gaucher disease and a 50% chance of being a carrier.



One parent has Gaucher disease and the other parent is not affected. All the children will inherit the Gaucher gene from the affected parent and become carriers, but none of the children will have Gaucher disease.



Both parents are Gaucher carriers. Their children have a 50% chance of being a carrier and a 25% chance of having Gaucher disease and 25% of being neither.



One parent is a Gaucher carrier (one mutated gene and one normal), and the other parent has two normal genes and is therefore not affected. Their children have a 50% chance of being a carrier but none of their children will have the disease.

how is Gaucher disease diagnosed?

The process of diagnosing many diseases, and especially Gaucher disease, is not always straightforward.

Often, the patient initially visits their doctor for another problem such as the flu, for nonspecific pain, or for a routine check-up. Although making a diagnosis of Gaucher disease is not difficult, some symptoms may resemble other diseases. The doctor may first perform other tests to eliminate from consideration more common disorders. For example, in cases where patients have low platelet counts, doctors may first test for leukaemia. If a patient complains of joint pain, the doctor may first suspect arthritis. Sometimes specialists at a genetics unit, a haematologist or metabolic physician, may be helpful in distinguishing the symptoms of Gaucher disease from other diseases with similar symptoms.



DNA strand



Gaucher disease might be suspected in a person who has an unexplained enlargement of the spleen, tendency toward bleeding, bone, joint pains or spontaneous fractures.

A paediatrician might make the diagnosis in a child complaining of abdominal discomfort or of frequent nosebleeds.

A haematologist might make the diagnosis in a person with low blood or platelet counts.

An orthopaedic doctor might diagnose Gaucher disease in the course of treating someone suffering with frequent unexplained fractures.

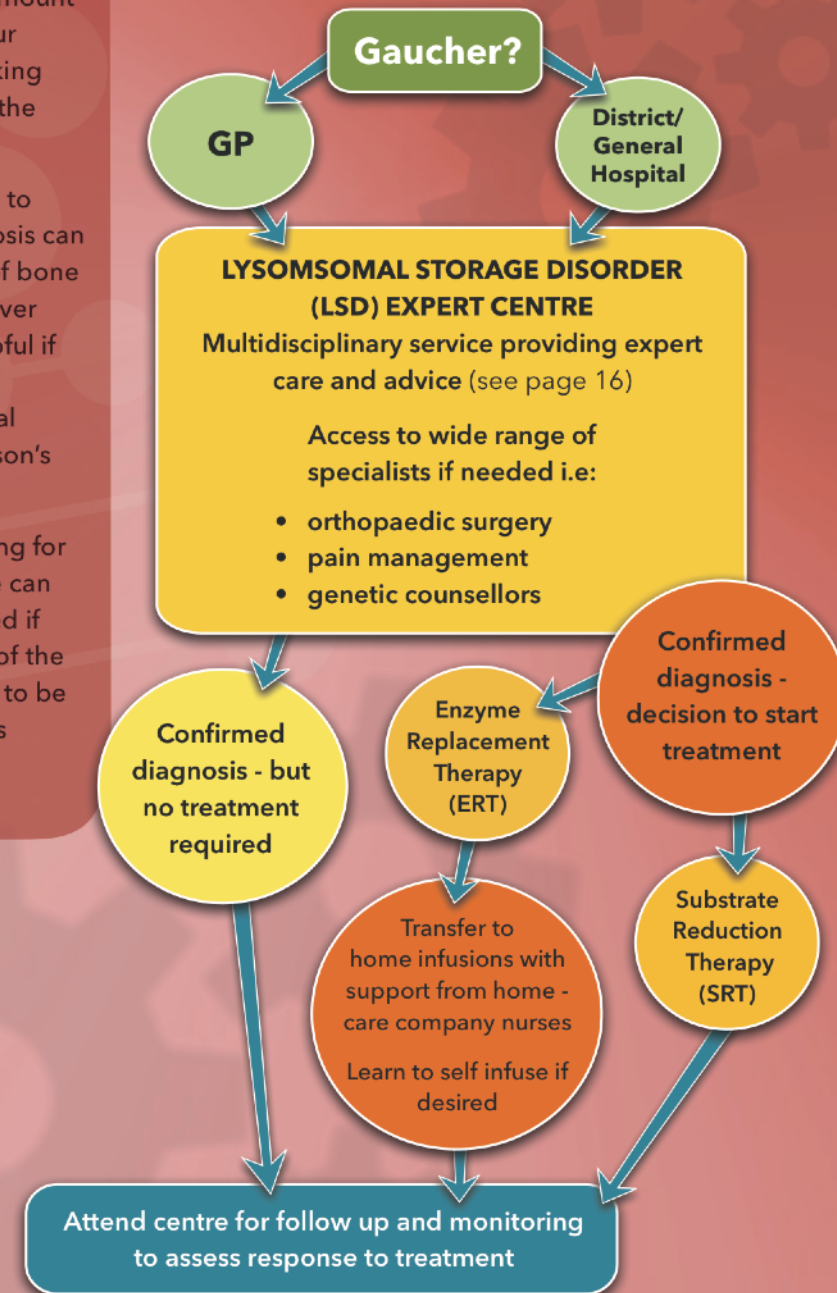
Gaucher disease would be particularly suspected in people with family members who are known to have the disease. See page 3.

Gaucher disease can be diagnosed by a simple blood test - by measuring the amount of enzyme in your blood and checking for mutations in the Gaucher gene.

Other tests used to make the diagnosis can include biopsy of bone marrow and or liver and may be helpful if there are multiple potential causes for a person's symptoms.

Sometimes testing for Gaucher disease can be recommended if other members of the family are found to be affected with this disorder.

route to a Gaucher centre



is there a cure?

There is currently no cure for Gaucher disease, but different therapies are available which can help to treat many of the major symptoms. With treatment, people with type I Gaucher may lead full lives and may be able to carry out many of their normal daily activities.

Some people with type I Gaucher disease have no clinical symptoms and do not need treatment.

For those that do require treatment, the options are:

Enzyme replacement therapy (ERT)

People with Gaucher disease are deficient in the enzyme glucocerebrosidase, the recommended treatment is enzyme replacement therapy; which has to be infused directly into a vein at regular intervals throughout the individual's life. As such, enzyme replacement therapy (ERT) is an effective therapy, rather than a cure. There are two licensed enzyme replacement therapies on the market in Europe, Cerezyme® (immiglucerase - Genzyme Therapeutics) and VPRIV® (velaglucerase - Shire Human Genetics) licensed to treat Type I Gaucher disease.

Substrate reduction therapy (SRT)

This treatment reduces the amount of fatty substances in our cells and therefore helps to reduce their build up. SRT is an oral therapy, with two products licenced for use in Europe - Zavesca® (miglustat Acetelion Pharmaceuticals) Cerdelga® (eliglustat Genzyme). These products are not suitable for everybody and your specialist doctor will advise if they are right for you.



Bisphosphonate

For patients with Gaucher disease who have low bone density and fractures, the bisphosphonate group of drugs (e.g. oral alendronate or IV zoledranate) are often prescribed to help combat osteoporosis and bone disease.

Gaucher Disease Specific Therapies:

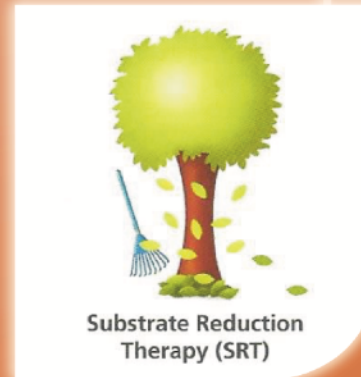


In Gaucher disease, it is as if there are too many leaves to be dealt with by one rake, so a leaf pile accumulates.



Enzyme Therapy (ERT)

With ERT, it is as if more rakes are made available, so you are able to get rid of the leaves.



Substrate Reduction Therapy (SRT)

With SRT, it is as if fewer leaves fall from the tree, so the rake available is adequate to get rid of the leaves.

Imagine that the substance glucocerebrosidase is represented as leaves, and that the enzyme that breaks down this substance, glucocerebrosidase, is represented as rakes.

Other treatments

For those people who have had their spleen removed long term antibiotic therapy and up to date vaccinations are essential.

Bone Pain

If you experience bone pain, talk to your doctor about pain management it may be helpful if you keep a pain diary. If it is necessary for you to undergo orthopaedic surgery it is essential that this is planned in conjunction with your specialist centre.

For an update on clinical trials currently being undertaken in patients with Gaucher disease, see the Gauchers Association website at: www.gaucher.org.uk for up to date information.

Emotional wellbeing

People with Gaucher disease, their spouses, and friends may face a wide variety of emotional and social challenges in addition to the physical limitations or complications posed directly by the disease.

Which issues have to be dealt with, and to what degree will depend directly on the severity of the disease in each individual. People with Gaucher disease may find that over time they experience some, none, or many of the following challenges:

However, these difficulties sometimes add to the development of **exceptional inner strength** that many people with chronic illnesses often possess, enabling them to live **full and active lives**.

If you are affected by any of these symptoms getting help is important and available. This could be psychology, counselling, mental health services. The Association can put Gaucher patients in contact with others.

- Feelings of isolation
- Lack of knowledge of the disease, both for those affected by the disease and their local healthcare professionals
- Delayed diagnosis; as a rare disease it can be a significant amount of time before a diagnosis is made
- Uncertainty about disease progress; symptoms and their severity may vary widely and may occur at any time. Some people remain symptom-free for many years, while others may begin having symptoms very early in life. This can sometimes make it difficult in making short and long term plans.
- Anxiety about relationships and having a family
- Anxiety & depression; being affected by a chronic disease can lead to anxiety and depression. If this affects you discuss with your healthcare team who can help you to access services available
- Accepting the diagnosis; long term denial can be dangerous particular if this prevents or delays medical help.

Diet

It is important for everyone to maintain a healthy balanced diet, whether they have Gaucher or not.

If your calcium and vitamin D levels are low, you may be advised to increase your calcium intake and possibly take supplements, as these nutrients are important to help strengthen your bones. The main dietary sources of calcium are dairy products, some fish, spinach, broccoli, nuts and seeds.

If you have anaemia, your healthcare professional may advise that you take iron tablets or increase the iron content in your diet. Foods that are high in iron include spinach, wholegrain cereals, pulses such as lentils and kidney beans and some dried fruits.

If you have an enlarged liver or spleen, you may find that you feel full more quickly. You may, therefore, need to consume food that is energy rich.

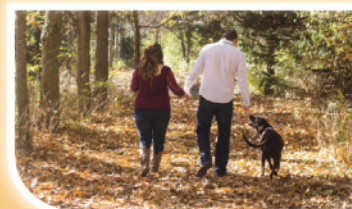
Other lifestyle

Limiting your alcohol intake and not smoking can help to improve your overall health and maintain bone health.

Exercise

Physical activity - It is important to try and stay physically active.

- Regular exercise can help to strengthen your bones and muscles
- If you bruise easily, you should probably avoid contact sports
- Your healthcare professional will be able to advise on what type of exercise is right for you



Work and school

It may be helpful that your school or workplace fully understands your condition and the impact of the symptoms you are experiencing, particularly as they have probably never heard of Gaucher disease.

When you talk to them it may be helpful to show them information in this pack which can help you to explain the condition in more detail.

Managing tiredness

Pace yourself, plan accordingly and get a good night's sleep.

The Gauchers Association was formed in 1991 and is the only registered UK charity providing support to individuals and families affected by Gaucher Disease, acting as the centre point for the Gaucher community working alongside medical professionals, scientists and the pharmaceutical industry to meet our aims;

- To **support** those individuals and their families affected by Gaucher disease through our patient and family advocacy service
- To provide **information** to patients and families regarding all aspects of Gaucher disease
- To **advocate** on behalf of patients and families to ensure access to appropriate treatment and specialised care through the Centres of Excellence in the UK
- To raise **awareness** and promote **education** in the medical profession of Gaucher disease to improve diagnosis and the impact of the condition on patients and families lives.

The Gauchers Association is managed by a Board of Directors consisting of Gaucher patients, parents and relatives. The Directors and Executive members volunteer their time to achieve the above aims and objectives. The Association has a Chief Executive who manages the day to day activities of the charity.

Funding

The Group relies solely on membership fees, voluntary donations, fundraising events and charitable grants for its income. The Gauchers Association receives financial contributions in the forms of unrestricted grants towards its patient support programme from pharmaceutical companies.



Jan, Jessie & David Thompson
(left)
Gaucher Association Walk
(far left)



Andrew Bloom



Susan Lewis Memorial Award

Susan Lewis (1945-2007) was a founder member of both the UK Gauchers Association and the European Gaucher Alliance (EGA). The constant focus of all of Susan's activities was to help Gaucher patients and their families.

In 2008 the Gauchers Association launched the Susan Lewis Memorial Fund in memory of Susan after she passed away in 2007. The fund was supported by donations from family, friends, Association members and the pharmaceutical and homecare companies involved in Gaucher disease.



The Gauchers Association is:

- A Registered UK Charity, Registered Charity Number: 1095657
- A Registered Company Limited by Guarantee in England and Wales Number 446823
- The Registered Office
8 Silver Street, Dursley,
Gloucestershire, GL11 4ND
- Telephone: 00 (44) 1453 549231
Email: ga@gaucher.org.uk

The purpose of the fund was to provide grants and bursaries to doctors and other healthcare professionals from developing countries to allow them to travel to the UK Centres of Excellence to undertake mentoring and educational programmes in the treatment and management of Gaucher disease.

Following on from the success of the award it was agreed to expand the scope of the fund to provide support in other areas of education including bursaries for post-doctoral students to attend conferences; UK specialists to visit overseas clinics to provide support and guidance to doctors in developing countries; specialists involved in the LSD field to travel to educational lectures and conferences and medical students to do their electives overseas.

Anaemia: A condition defined by reduced haemoglobin in the blood. This reduces the amount of oxygen delivered to the body and which can make a person feel tired and look pale

Biomarker: Something in the body that can be measured to indicate the presence of a particular disease, a particular biological process or a response to therapy

Bone crisis: An episode of severe pain in the bone, which is accompanied by local swelling, redness, tenderness and increased temperature at the site of pain

Bone marrow: The soft substance found at the core of bones, especially the long bones of the arms and legs, breastbone, spine, ribs, skull, and pelvic bones. Bone marrow contains the stem cells that make blood cells (red blood cells, white blood cells and platelets)

Bone mineral density (BMD): A measurement of mineral levels in the bones. A measure of BMD can show how strong bones are

Bone pain: Non-specific pain in the bones

Carrier (relating to inheritance of disease): A person who has one faulty gene (for example, a faulty gene for glucocerebrosidase) and one healthy gene

Cell: The basic independently replicating structural and functional unit of all known living organisms

Chromosome: A thread like structure of DNA (see below) and associated proteins containing many genes (see below)

Diagnosis: The process of determining the presence of a particular disease or condition

DNA: An abbreviation for 'deoxyribonucleic acid' – the material that carries all the inherited information that defines the growth and development of an individual

Enzyme: A substance (a protein) that causes specific biochemical reactions in the body to occur. The names of enzymes usually end in 'ase', for example, glucocerebrosidase.

ERT: Abbreviation for enzyme replacement therapy, a treatment where healthy enzyme is introduced into the body to supplement the activity of a deficient enzyme

Gaucher cell: Cells (usually macrophages) that contain excessive amounts of glucocerebroside, causing them to enlarge. Gaucher cells are characteristic of Gaucher disease

Gaucher disease: A rare lysosomal storage disorder that is characterised by a deficiency of the enzyme glucocerebrosidase and which leads to the accumulation of glucocerebroside in cells, particularly macrophages

Gene: A unit of DNA that codes for a certain inheritable characteristic

Gene therapy: An investigational therapy approach that is aimed at correcting genetic disorders by introducing healthy genes into cells of the body

Glucocerebrosidase: the enzyme that breaks down glucocerebroside, and which is deficient in Gaucher disease

Glucocerebroside: a fatty substance (a lipid) composed of a ceramide and glucose that accumulates in the tissues of patients with Gaucher disease

Haemoglobin: The iron containing protein in red blood cells. Haemoglobin gives red blood cells their colour. Its function is to bind (pick up) oxygen from the air in the lungs and to deliver it to cells in the body

Immune system: The system of organs, tissues and cells (such as the spleen, thymus, appendix, lymph glands, tonsils and white blood cells) that work together to protect the body from unwanted particles and substances such as bacteria, viruses, toxins, parasites, fungi

Infusion (relating to enzyme infusion): The introduction of enzyme replacement therapy into a person's blood stream through a vein

Lysosomal storage disorder / LSD: A group of rare diseases characterised by deficiencies in the activity of specific lysosomal enzymes

Neuropathic/neuropathic/neuropathy: A disease process characterised by damage to nerves

Orthopaedic: Relating to the prevention or correction of bone injuries

Osteoporosis: A bone condition where the bones have low bone mineral density, become weaker and more likely to break

Spleen: An organ situated to the left of the stomach below the diaphragm. It acts to break down and recycle old blood cells and filter unwanted substances from the blood

Substrate reduction therapy: A therapy that inhibits the production of a substrate (for example, glucocerebroside in Gaucher disease) to help stop the substrate from accumulating in cells

