

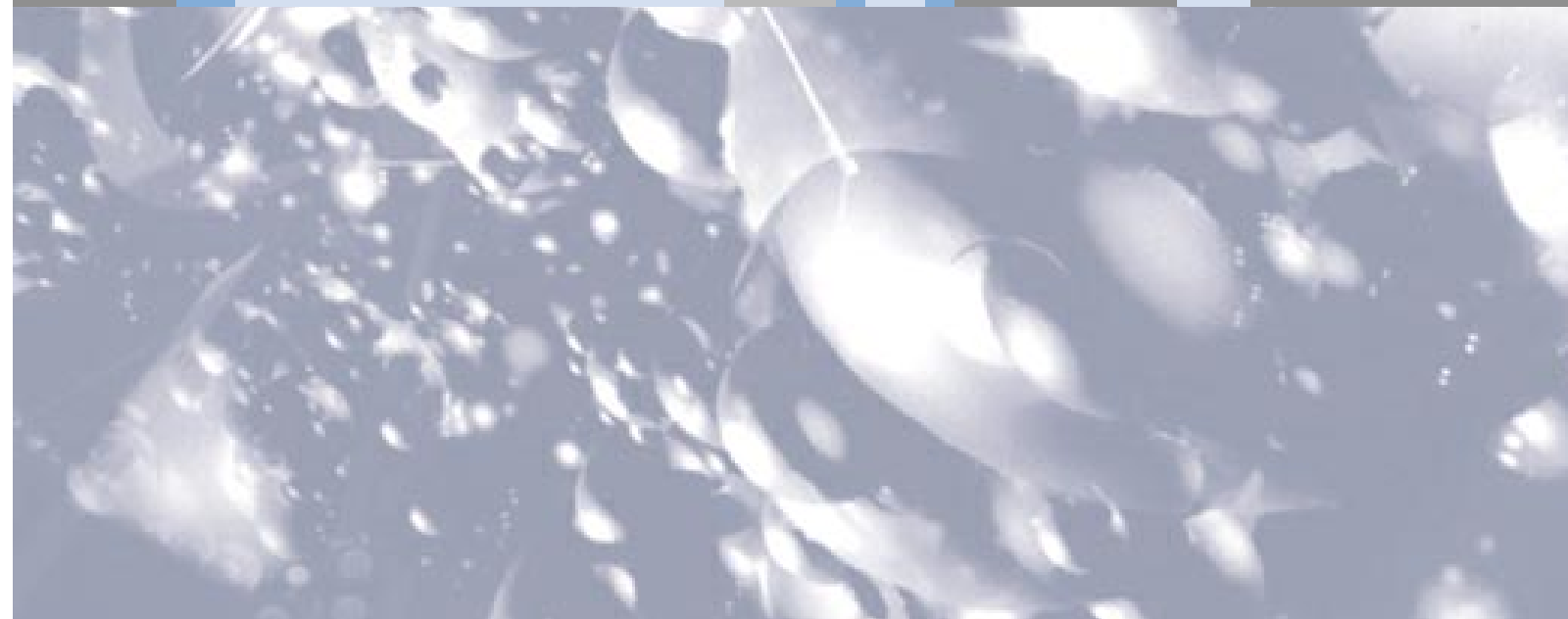
A-Z OF GAUCHER DISEASE

Patient Information Booklet

This booklet aims to help patients discuss Gaucher disease and the treatment options available with doctors and other healthcare professionals.

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Introduction

Whether you have just learnt that you or someone you care about has Gaucher disease, or you have been living with the condition for some time, this booklet aims to help you to understand Gaucher disease and how to treat it.

Improvements in treatment have been rapid in recent decades and most people with Gaucher can lead full and active lives. However, it is a complex condition and this booklet aims to answer any questions that may arise, but if it does not it should point you in the direction of more information. It is intended as an overview of the condition and its management. However, there are different aspects of the condition and each individual's response to the condition is different. Individual queries regarding treatment should therefore always be addressed to a specialist Gaucher doctor. You can also get in touch with the Gaucher Association, who provide an excellent source of support, advice and encouragement to those who are affected by the condition.

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Understanding Gaucher Disease

What is Gaucher?

Gaucher disease (pronounced go-shay disease) is a rare condition that is named after Philippe Gaucher, the French doctor who first described it more than one hundred years ago. The condition affects the body's ability to breakdown certain fats from the body's cells. This causes certain cells in the body to swell and leads to various symptoms.

The Disease Mechanism of Gaucher

Gaucher occurs when specific fats known as lipids that make up part of the cell membrane are not properly broken down by the body. These lipids mostly come from old red blood cells and are normally broken down into simple molecules that can be recycled easily by the body. They are broken down by a molecule called a protein, (specifically an enzyme), that is stored within special 'house-keeping' cells called macrophages in a compartment called the lysosome (this can be thought of as the 'recycling' unit of the macrophage).

In people with Gaucher a specific enzyme called glucocerebrosidase doesn't work properly. When this enzyme functions normally, it breaks down a specific lipid (called glucosylceramide) and when this doesn't happen - as in Gaucher - the lipid is not digested and is simply stored in the lysosomes (recycling units).

This unwanted storage causes the macrophage cells to swell and it is these enlarged cells, containing undigested glucosylceramide, that are called Gaucher cells. This is illustrated in the diagram below:

Genetics and Gaucher

Gaucher is an inherited, or genetic, condition. Everyone's body is made up of cells, each of which contains your DNA. You could say this is the body's instruction manual. This instruction manual controls every aspect of the human body, from very complex bodily systems to simple things like the colour of someone's hair. Everyone has

23 pairs of chromosomes in their body which are in each of their cells and are like chapters in the manual. These chapters are then divided up into parts called genes, which can be likened to pages of the manual. It is these small parts of DNA - the genes - that are responsible for individual processes in the body, including the making of proteins, for example the glucocerebrosidase enzyme, which are essential for the body to work properly.

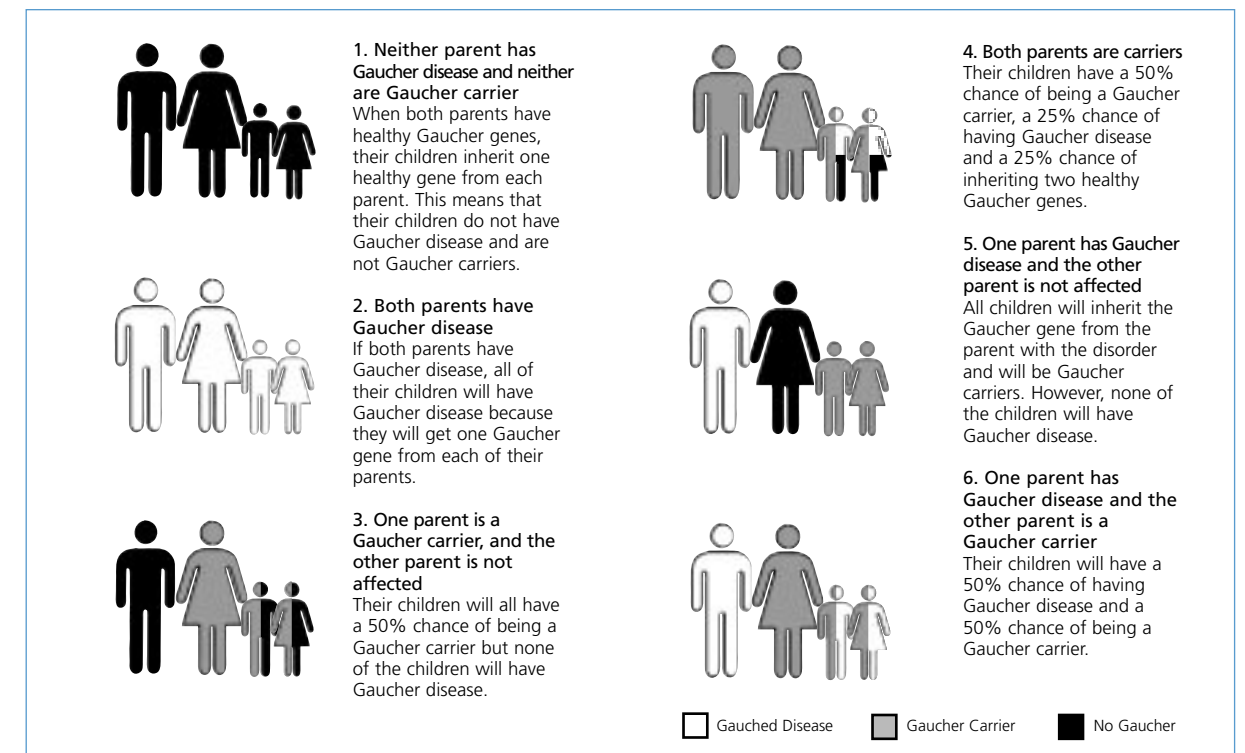
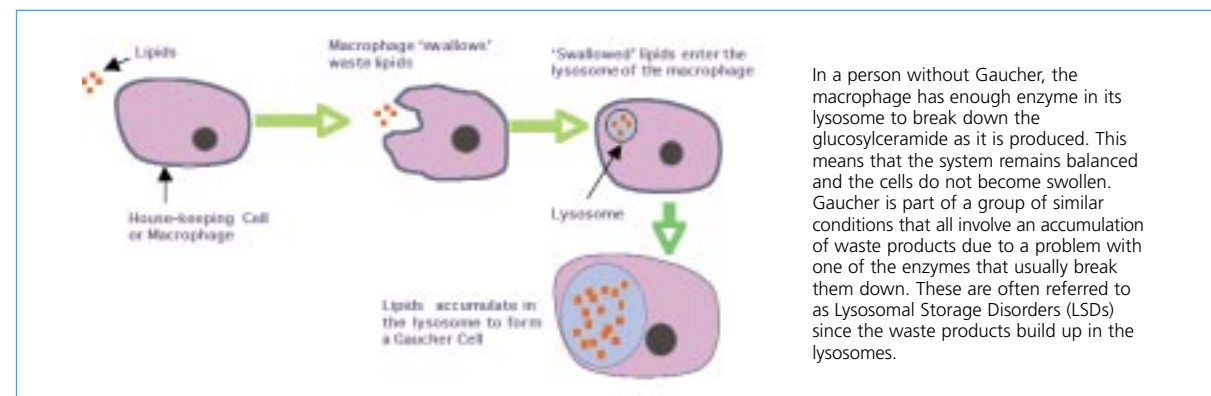
A child inherits one half of its chromosomes from each parent, which means the child gets one copy of each gene from each parent. In Gaucher, the instructions for making the glucocerebrosidase enzyme are faulty and, as a result, the glucocerebrosidase produced doesn't perform its normal function.

Gaucher Carriers and Inheritance

Of the 23 pairs of chromosomes in the body only one pair determines the sex of the person. The other 22 are called autosomes and copies of genes from these chromosomes are passed on to both males and females. Gaucher is what is known as an 'autosomal recessive condition'. It is 'autosomal' because the gene for glucocerebrosidase is on one of the autosomal chromosomes and can be passed on to both males and females. It is 'recessive' because, in order to develop the condition, an individual must inherit two faulty copies of the gene, one from each parent. However, it is important to remember that even if someone has two faulty genes they can sometimes have very little or no symptoms of Gaucher.

A person with just one faulty gene is called a 'carrier' of Gaucher and does not develop symptoms because their one working gene allows glucosylceramide to be broken down and no build up occurs. Nevertheless, there is still a chance that this gene will be passed to any children that they may have.

The diagram right helps to illustrate the likelihood of having a child who has Gaucher or is a Gaucher carrier, however it is important to remember that the chances of a child inheriting Gaucher are the same whether or not a previous child has the condition.



The Gaucher Spectrum

Everyone with Gaucher has low levels of glucocerebrosidase enzyme activity. However, there are many ways in which the genetic instructions for making glucocerebrosidase can be faulty and the modified instructions for making the enzyme will be different from individual to individual. This means that the precise amount of enzyme activity can vary greatly from person to person and, as a result, so do the symptoms they experience.

Gaucher is a condition with symptoms that vary from very mild to very severe and this range of symptoms is often referred to as a spectrum. To aid with identifying appropriate treatment regimens for each person, Gaucher specialists divide the condition into three classifications, depending on the symptoms and the timing of the development of these symptoms.

The three types of Gaucher are referred to as Type 1, 2 and 3. Most people with Gaucher have Type 1, where symptoms vary greatly; some people have no symptoms and can lead totally normal lives, whilst others may experience symptoms that cause them great discomfort.

Types 2 and 3 Gaucher are even rarer conditions, affecting less than 1% of all Gaucher patients, and are often referred to as neuronopathic Gaucher. In Type 2 or 3, untreated patients can have the same or worse symptoms in the liver, spleen and blood as Type 1, but their condition also has pronounced effects on the nervous system and brain function. The effect on the nervous system and brain in Type 2 is more severe than in Type

3. (see signs and symptoms section page 4).

A child who has Type 2 Gaucher does not usually live beyond two years old, because the condition severely affects the nervous system and the rapid accumulation of glucosylceramide in the cells begins before the child is even born. There are currently no treatments that can address this rapid build-up within the brain and nervous system. In Type 3 Gaucher, neurological symptoms mainly appear in early to late childhood. This neurological accumulation is often initially seen in children as problems with moving the eyes correctly, learning difficulties at school or auditory problems (problems with hearing) and eventually may lead to difficulty with movement and balance. Further information on neuronopathic Gaucher can be found in other booklets listed in the Support section of this booklet (page 14) or through the Gaucher Association.

How Common is Gaucher?

The number of people suffering with Gaucher disease is usually grouped into the different 'Types'. For Type 1 Gaucher, around one in 40,000-60,000 of the general population is thought to inherit a Gaucher gene from both parents (although not all will show symptoms). Type 1 Gaucher is more common within the Ashkenazi Jewish community, with one in 850 believed to inherit the condition.

Those Types associated with neuronopathic symptoms are much rarer. For Type 2 Gaucher, the incidence in the UK is as low as one or two births per year and for Type 3 Gaucher the incidence is similar at around two or three births per year.

Diagnosis

Diagnosing a rare condition is not always straightforward as many of the initial symptoms can be similar to those of other 'more common' conditions. It is likely that the doctor will have first performed tests to eliminate some of the other more common complaints before suspecting Gaucher, including arthritis (due to joint pain) or leukaemia, (due to low platelet counts).

However, a doctor may suspect Gaucher if symptoms such as excessive bruising and bleeding, a swollen abdomen or bone pain are seen. In particular the doctor may suspect the presence of Gaucher if there is a known family history, and it is worth noting that symptoms may appear at any time of life, from early childhood to adulthood, depending on the severity of the condition in each individual. If this is the case a GP should refer the individual to a specialist centre for further tests and for a diagnosis to be confirmed. In England there are currently six specialist centres designated for the diagnosis, monitoring and treatment of LSDs such as Gaucher and these are detailed later in the booklet, on page 14. There are also useful fact sheets available from the Institute of Child Health, a link for which can be found at the back of this booklet on page 14.

Gaucher is formally diagnosed by measuring the amount of glucocerebrosidase enzyme in white blood cells or in special skin cells called 'fibroblasts'.

Since Gaucher is a genetic condition, the diagnosis should be confirmed by DNA analysis (called genotyping). The DNA test allows doctors to obtain more information about the specific genetic type of Gaucher and helps them to understand how best to manage the condition.

Signs and Symptoms

The symptoms of Gaucher depend on where the Gaucher cells accumulate. In general, Gaucher cells tend to build up mostly in the liver, spleen and bone but they also collect in other organs including the lungs and brain as well as, in some cases, the central nervous system. These parts of the body are highlighted in the diagram right.

However, this does not mean that a person with Gaucher will get all of the symptoms detailed below. Each person's response to Gaucher is unique with some patients being severely affected whilst others are affected so mildly that the symptoms might not be detected until very late in life or sometimes they might never have symptoms. The information in this booklet may help you to discuss your own situation more fully with doctors and others involved in your care.

Spleen

The spleen is involved in blood cell production. When Gaucher cells build up in the spleen they cause it to grow bigger (splenomegaly), and may cause the abdomen to

swell, making someone look overweight or pregnant when they are not.

When the spleen is functioning correctly it breaks down old blood cells at the same rate that new ones are produced in the bone marrow. However, if the spleen is enlarged it often breaks down red blood cells too quickly and this means that there are not enough red blood cells to carry oxygen from the lungs around the body. This is called anaemia and it means that due to a lack of oxygen that is used to create energy powering the muscles, people whose Gaucher has affected their spleen often become easily tired.

In addition, they may also have a reduced number of blood platelets (a condition called thrombocytopenia). Platelets are important in forming blood clots and therefore a lack of them means that it is easier for people to bleed and bruise. Because of this, people with Gaucher may suffer from heavy nosebleeds and bleeding gums and extensive bruising may sometimes occur with only a slight knock. For women, menstruation may also be heavier and last longer.

Liver

When Gaucher cells build up in the liver, it becomes enlarged (a condition known as hepatomegaly), which causes pain or discomfort in the abdomen. Gaucher cell accumulation in the liver can cause scarring of the liver (cirrhosis) or, in the most severe cases, stop the liver from working properly. Gaucher patients also tend to have gallstones more often than other people.

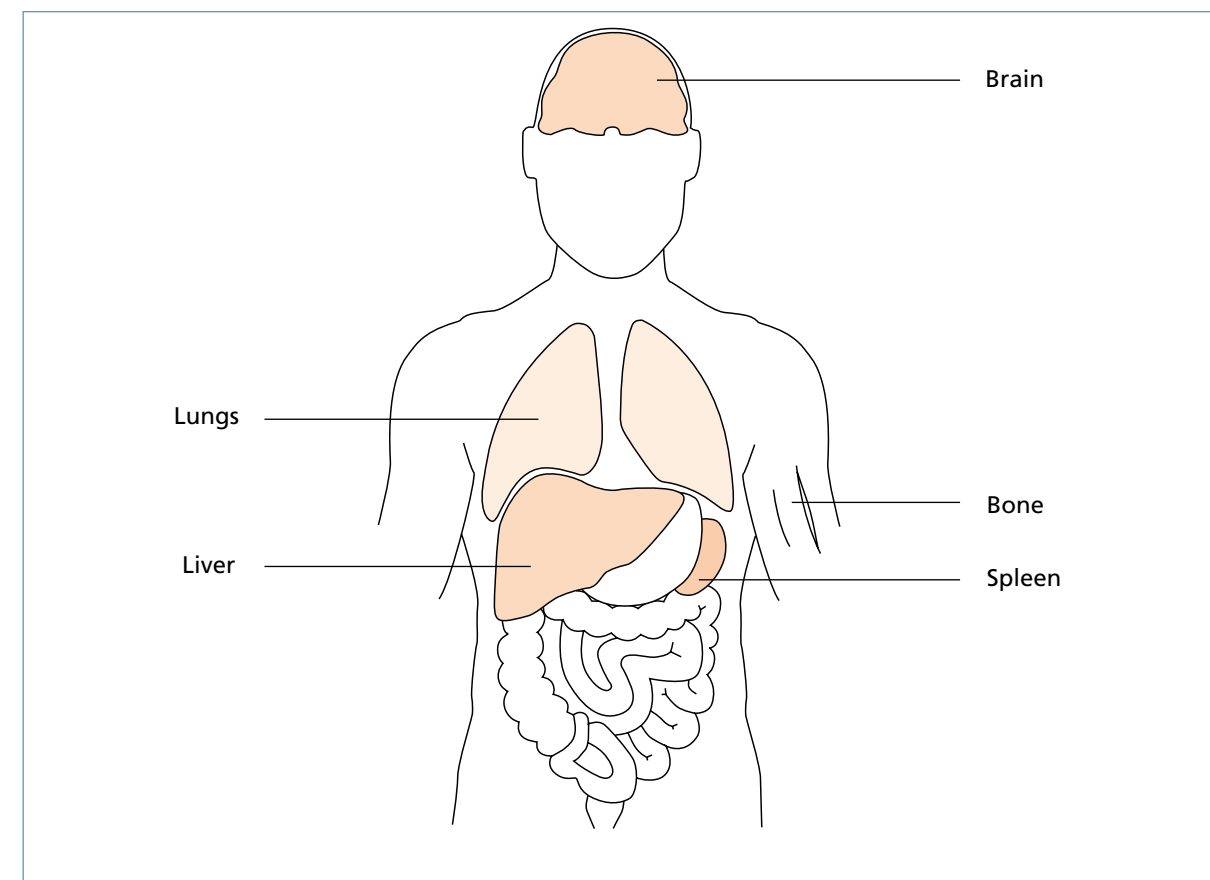
Bone Marrow

Bone Marrow is the primary site of blood cell production and Gaucher cell build-up within the marrow can interfere with this process, compounding the problems associated with Gaucher cells in the spleen.

Bone

Gaucher cells collecting within the bone, inside the bone marrow itself, is one of the main problems of the condition. In fact, general bone and joint pains are a common complaint of people with Gaucher and this pain is usually attributed to inflammation in the skeletal system caused by the presence of Gaucher cells. Gaucher cells in the bone marrow can also damage bone in several other ways:

- The end of the thigh bone may have a flattened shape, sometimes referred to as an 'Erlenmeyer flask deformity' by doctors because the bone shape resembles that of a glass instrument used by scientists. This shape is a sign that Gaucher cells are present in the bone marrow and they are causing new bone to form incorrectly.



- Gaucher cells may cause the bones to become thinner or weaker than normal (osteopenia) which means that they may break more easily.
- Gaucher cells can prevent blood flow in the bone, which harms bone tissue (aseptic necrosis), and this can lead to permanent mobility problems.
- Sometimes the swelling caused by Gaucher cells in bones which stops blood flow, causes a sudden lack of oxygen to bone cells. This causes an episode of severe pain that may last for hours or days and is called a bone crisis. In addition, the affected bone may swell, become shiny and red and feel warm to the touch.

Lung

Occasionally, people with Gaucher experience problems with their lung function and become breathless - a complication called pulmonary hypertension. This complication is most likely to occur in patients who have had their spleen removed, a procedure which is no longer recommended. In severe forms of the condition, lung disease, which is thought to be due to the presence of Gaucher cells in the lungs,

is more common and can cause breathing problems, a troublesome cough and chest infections.

Neurological and Central Nervous System

As mentioned on page 3, some individuals with Gaucher (those classified with Type 2 or Type 3 Gaucher) have pronounced neurological symptoms that include the following:

- Problems with quick eye movements (horizontal is usually affected first).
- Difficulty in processing sounds and distinguishing background noise.
- Problems with posture and movement including floppiness, rigidity, twitches, tremors and difficulty with balancing.

Treatment

History

Bone Marrow Transplantation

Bone marrow transplantation was used before ERT became available. Approximately 20-25 transplants have been carried out on people with Gaucher, mostly in Sweden and the UK. There is some evidence that their outcome has been better than that of untreated people. However, at present, the procedure is not recommended.

Splenectomy

The surgical removal or reduction in size of the swollen spleen was carried out on many patients in the pre-ERT era. Although useful in alleviating some of the problems in Gaucher, splenectomy may increase the likelihood of bone problems and other complications, hence it is now only carried out very rarely.

Enzyme Replacement Therapy (ERT)

Enzyme Replacement Therapy (ERT) was introduced in 1991. Currently, imiglucerase (Cerezyme®), a recombinant (generally engineered) man-made form of the enzyme glucocerebrosidase, is injected into the blood stream so that there is enough enzyme within the body to break down the accumulated glucosylceramide. ERT is given by an intravenous infusion, which takes 1-2 hours or more and is usually given every two weeks. Some people taking ERT may require a small, permanent tube to be inserted into their vein to make the infusions easier. Over time, ERT reduces the build up in the Gaucher cells and reduces many of the symptoms of Gaucher. Since its introduction, ERT has been able to help many patients to live with their condition more comfortably, increasing their quality of life and life expectancy, and it is currently the most widely used therapy for Gaucher.

ERT can be prescribed by doctors to treat people with Type 1 or Type 3 Gaucher. Unfortunately, due to the relatively large size of the molecules, ERT has not been shown to cross the blood-brain-barrier (a barrier between the brain and the blood that prevents unwanted chemicals getting into the brain) or get into the central nervous system. This means that there is no evidence that ERT has any effect on the neurological symptoms of Gaucher.

The side effect profile of imiglucerase is generally good. Some patients may experience hypersensitivity to treatment and, very rarely, severe allergic reaction has been reported (although pre-treatment with antihistamines and/or corticosteroids and reduced rate of infusion generally allow continued use of ERT in most instances). As with many intravenous treatments there

are also some reactions related to the route of administration including discomfort, itching, burning or swelling at the site of infusion.

Some patients may also develop an IgG antibody which recognizes the infused enzyme and usually occurs within the first year of treatment. This antibody can limit the effectiveness of the treatment and Gaucher patients with IgG antibodies who receive ERT often experience diminished response to treatment or deterioration of their condition. However the antibody will often resolve spontaneously and, if it does not, then the individual can undergo something called tolerisation therapy which involves increasing the dose of ERT. In addition, patients may find that they gain weight when they are on ERT, although some of these patients will have been underweight before they began treatment.

Substrate Reduction Therapy (SRT)

The alternative treatment for Gaucher is known as substrate reduction therapy, currently in the form of miglustat (Zavesca®). Miglustat is an oral treatment taken in tablet form, usually three times a day. Miglustat works in a totally different way to ERT as it reduces the rate at which the glucosylceramide is made, thereby slowing down the swelling of the Gaucher cells. It aims to reduce the amount of undigested glucosylceramide to a level that can be cleared naturally by the body, despite its reduced ability to do so.

Doctors can currently prescribe miglustat tablets for adults with mild or moderate Type 1 Gaucher if the patients are unsuitable for ERT treatment. This means people with Type 1 Gaucher who are unable or unwilling to have ERT. For example, an individual may not want to have infusions due to a fear of needles or because they do not have easily accessible veins, which leads them to have persistent difficulties with infusions. However, it can also be because they travel frequently with their job and find it difficult to fit regular infusions into their schedule. Miglustat can be taken by both newly diagnosed patients and patients who have previously been on ERT for a long time.

Due to its small size, shape and chemical properties, miglustat has been shown to enter the brain by crossing the blood-brain-barrier. Scientists are therefore hopeful that it might help to relieve some of the problems associated with the accumulation of Gaucher cells in the nervous system. There is a clinical trial under way to see whether miglustat might benefit Type 3 patients, and it is also being trialed in both adult and juvenile patients with other LSDs.

The majority of miglustat's side effects are mild to moderate in intensity and/or are resolved spontaneously. The most common adverse events include diarrhoea, weight loss and sometimes it an effect on your appetite. The diarrhoea can usually be alleviated with loperamide (an anti-diarrhoea tablet) or sometimes with a slight temporary alteration in diet. There have also been reports of tremors and in clinical trials there were two reported cases of Type 1 Gaucher patients experiencing peripheral neuropathy. However, more recently there have been reports of peripheral neuropathy in Type 1 patients who have never received SRT treatment. These new reports highlight the fact there are still many unknown aspects of the 'natural history' (development) of Gaucher in the longer term. However, introducing treatment early on in life is believed to prevent some of the complications of Gaucher disease from developing into severe symptoms.

On the Horizon

The outlook for most Gaucher patients has dramatically improved since the introduction of ERT in the early nineties and more recently with miglustat, and research into the condition continues. There are currently ongoing trials into the use of miglustat in Type 3 Gaucher patients, adult and juvenile with other LSDs and in those individuals with Type 1 Gaucher whose symptoms have been stabilised with ERT and who have then switched to miglustat for long-term maintenance in addition, there is other research underway and this includes a new form of ERT currently known as GA-GCB another recombinant form of enzyme currently known as prGCD (ongoing updates on continuing research can be found on the Gaucher Association's website, please see page 14).

Chaperone Therapy

Chaperone therapy is a new concept of treatment that will begin trials in Gaucher in 2006. A small molecule is used to stabilise the existing enzyme so that it can work more effectively to break down the glucosylceramide which would otherwise build up in the cells.

Gene therapy

Researchers are also looking for a cure for Gaucher using gene therapy. Gene therapy would involve introducing normal Gaucher genes into the cells of someone with Gaucher. Ideally, these cells would then cure the condition. Research is underway, although, a great deal more work is required before a treatment suitable for patients is available.

Monitoring Tests

To monitor the effect of treatment and/or the progress of the condition there are a number of tests a doctor is likely to recommend:

- Blood tests to show abnormalities such as low platelet counts, or red blood cell counts.
- X-rays, magnetic resonance imaging (MRI), or computerised tomography (CT or 'cat' scan) to show abnormalities in bone.
- MRI or CT (to measure the size of the liver and spleen).
- Tests to examine nerve functions, such as eye movement tests and hearing (audiology) tests, most usually carried out to investigate Type 3, however they are also becoming increasingly common for those with Type 1 Gaucher.

Bone tests

People with Gaucher may have regular tests to assess their bones. These tests include an MRI, which is now considered to be the best way to monitor bones in Gaucher. In addition, an X-ray of the thighbone, or an X-ray of the spine, every one to two years is likely to be carried out, often with a special form of X-ray called DEXA that measures Bone Mineral Density (BMD). BMD is a good indicator of the health of bones as it is more precise and allows the specialist to better assess the risks of fractures or other problems in the future.

Liver and or spleen tests

The size of the spleen and liver may be measured every one to two years by MRI or CT scanning to monitor the progression of the condition or effects of treatments. Ultrasound tests (similar to those used in pregnancy) may also be used.

Blood abnormalities

Red blood cell and platelet counts help measure the progression of Gaucher and the effect of treatment. The blood also contains what are called 'biomarkers', chemicals such as acid phosphatase and chitotriosidase. The concentration of these biomarkers varies depending on the number of Gaucher cells in the body and this provides a useful way of monitoring the progression of the condition and the effectiveness of therapy.

Quality of life

As an adult you may be asked to fill in a short form (called "SF-36"), which measures the impact of Gaucher on your life. There are different forms that are used to measure the quality of life of children (called "CHQ").

Bone Complications

Many people with Gaucher suffer from bone disease and this is often associated with considerable pain, mobility impairment and, as such, may have a very negative impact on a patient's quality of life. Where there is a decrease in mobility the use of ambulatory aids, such as a wheelchair, crutches, cane, or walker, may be helpful. The pain associated with bone disease, which can also cause a raised temperature, can be;

- **acute** - as occurs in a bone crisis, causes intense pain for up to a few days.
- **chronic** - long-term pain of variable severity and cause, generally treated with pain-relieving drugs and gentle exercise.

There is growing evidence that ERT and SRT have an effect on bone mineral density (BMD). However, bone turnover is slow and some of the changes may be irreversible. The BMD response to ERT is slower than that of the other signs of Gaucher. For example in one study 52% of patients experiencing bone pain prior to treatment were pain free after two years of ERT therapy.

Specific Treatment of Bone Complications

There are various other treatments available to treat bone complications in Gaucher. These include exercise such as swimming, vitamin D, analgesics (for pain), orthopaedic procedures (bone surgery) including hip replacements, bisphosphonates and growth hormone. Of those options, pain relief accompanied by bisphosphonates is currently the most common, although it should be remembered that appropriate treatment depends on the individual and should always be discussed with a Gaucher specialist.

In general, treatment with a bisphosphonate drug reduces the breakdown of bone and enhances the growth of new bone. It is effective in various bone conditions, including osteopenia and osteoporosis, and produces an increase in BMD and a reduction in fractures. However, there are side effects associated with bisphosphonates especially if it is not taken correctly, including irritation of the oesophagus (the tube that goes from your mouth to your stomach), stomach upset, and muscle or bone discomfort. Recently it has also been shown that long term bisphosphonate use can very rarely increase the risk of a serious jaw complication (speak to your Gaucher specialist if you would like to discuss this).

Surgery for Bone Complications

For some bone complications, including difficult fractures or areas where the bone is not healing or is infected, surgery may be necessary. Hip replacement, as well as shoulder and knee replacement, may sometimes be required in cases where there is severe deterioration in the condition of the bone. This needs special care due to the risk of infection (especially if the patient has no spleen), bleeding (if the patient has low platelet count) or fragile bones. Surgery should preferably take place at one of the specialist centres under the supervision of a specialist Gaucher doctor.

Pain Management

The pain associated with Gaucher can vary widely and, if the pain does become severe, coping with it can present a challenge. However, there are many things that you can do to overcome this challenge. The pain is usually related to enlarged organs or affected bones and may resolve within a couple of weeks, although it can last longer. Medication may be necessary to control the pain during these episodes.

Those individuals in whom pain related to their Gaucher disease is a problem should work with their Gaucher specialist to develop a management regime that may include pain relief medication or pain relieving techniques. The specialist centre may also have a pain management clinic run jointly by professionals from a number of disciplines and patients can be asked to be referred to such a service if pain is a continuing problem.

It is important not to underestimate the effect chronic pain can present in daily life. For example not being able to go out with friends or play with your children, or even do relatively simple things like household chores, can be frustrating and upsetting. Pain management programmes usually focus on helping develop skills to manage pain more effectively. Programmes can include the development of a wide range of skills including identifying realistic ways of achieving personal goals, learning to pace activities, reducing muscle tension and managing stress.

Self Monitoring - Keeping a Pain Diary

Chronic pain often becomes part of everyday life and is sometimes overlooked or under-reported, despite the fact that it has a large impact on an individual's quality of life. In order to hold a detailed discussion about the level of pain you experience with your Gaucher specialist it can be helpful to monitor what pain you are feeling.

It is likely that your doctor will be aware that you are in pain, but it may be difficult for them to tell how much. However, talking about pain is complicated, particularly if you only have a check up every few months as it can be difficult to remember what has happened since your last appointment, particularly if you have not been in too much pain in the weeks before an appointment.

Keeping a pain diary can help you and your doctor to see clearly how pain is impacting on your life. If you are able to record specific details about the pain then it is more likely that trends or patterns can be identified that will give some insight into how your pain can be best managed. In addition, by recording what you have done to relieve any pain and how successful it was, will help you to adapt your management regimen to increase its effectiveness.

If you want to keep a pain diary you will find an example that you can photocopy on page 16 of this booklet. You may find it useful to record the following:

- Where pain is felt?
- When it occurs?
- How it feels? e.g. aching, stabbing, shooting, etc.
- How severe the pain is on a scale of 0 (no pain) to 10? (the worst pain imaginable)
- How often the pain is felt? e.g. every couple of minutes/hours, constant

How severe is your pain today? Place a vertical mark on the line below to indicate how bad you feel your pain is today.

No pain _____ Very severe pain

In addition, there are other more simple scales that can be used by children to indicate their pain, such as the smiley faces shown below:



- How long the pain lasts? e.g. minutes/hours, constant?
- Does anything seem to trigger it or make it worse e.g. temperature, stress, movement?
- Does anything make it better e.g. resting, heat/cold, bathing, medication?
- What impact it has on your life e.g. restricts physical movement, depression, etc.
- How you have tried to relieve it e.g. painkillers (and their doses), complementary therapy, etc.

Further help

If you experience continuous pain it can be difficult to record this in a meaningful way and it is not always easy to label it as mild, moderate or severe pain. In this instance, a Visual Analogue Scale (VAS), a simple measurement tool, may help. Quite simply, a VAS is usually a drawn horizontal line, 100mm in length, anchored by word descriptors at each end, such as no pain and very severe pain. (See example below.) It enables patients to mark on the line the point that they feel represents their current state of pain. This simple scale will help you and your Gaucher specialist assess how your pain has changed over time. This type of scale is often used by pain clinics.

Healthcare Environment

Specialist Centres and National Funding

Until recently, in the UK, a group called the National Specialist Commissioning Advisory Group (NSCAG) named and funded services at four Gaucher centres to supply diagnosis and manage treatment for Gaucher alone. Treatment was initiated through the patient's local doctor or through their Gaucher centre doctor and payment for an individual patient's treatment came from the Primary Care Trust (PCT) where they lived. However, this meant that final funding decisions on treatment were subject to the 'lottery' of separate PCT decisions.

From April 2005 there was a shift in the funding responsibility in England from the patient's local PCT to NSCAG. NSCAG began to fund both services and treatment on a national scale via six named centres. In addition, the coverage of these centres was extended to LSDs as a group. The six centres created by this change diagnose, manage, prescribe and deliver treatment to all existing and new LSD patients. The funding available covers both conventional therapy with intravenous ERT and the oral SRT (see page 7 for further details). The national funding system means that Gaucher specialist doctors simply have to notify NSCAG of the start of, or change to, treatment.

The six centres currently designated as LSD specialist centres are listed below and the contact details along with the names of their lead doctors are given on page 14.

- Addenbrookes Hospital - Cambridge
- Central Manchester and Manchester Children's Hospital - Manchester
- Great Ormond Street Hospital - London
- The Hope Hospital - Salford
- The Royal Free Hospital - London
- University College Hospital (Queens Square) - London

In addition to the centres listed above it is expected that other centres in the UK may receive LSD specialist status in the near future.

For patients, this system gives equal access to appropriate treatment with existing therapies and ensures that all specialist centres work to a tight common Service Standard and common Clinical Protocols. It is important to note that funding for treatment is only reimbursed through NSCAG via designated LSD centres. An additional benefit to patients of national funding is that they are free to attend the specialist centre of their choice, subject to referral.

However although we have one NHS there are differences within the UK for support of LSD patients. The funding system described above is only used in England and there are different funding systems in place in Scotland, Wales and Northern Ireland which the Gaucher Association can give you more information about.

Healthcare Professionals - Who's Who

There are a wide range of healthcare professionals involved in the care of your Gaucher. The doctor at the specialist centre will be closely supported by a team of specialist nurses who are often the first port of call for individuals with Gaucher. Those at the specialist centres will also liaise closely with doctors and nurses in your local area, (both GPs and doctors at the local hospital) to ensure a consistent level of care when the individual is away from the specialist centre. In addition, there are other professionals including physiotherapists, dieticians and social workers who also have a role to play.

- **Gaucher Specialist** - this doctor will have a vast amount of experience in Gaucher and other LSDs. They will take a lead in your care, prescribe your treatment and monitor the progress of your condition through regular check-ups. This is also the person with whom you should raise any concerns about the progression of your condition or the nature of your treatment regime, see page x for some suggested questions to help you get the most from your consultation.
- **Specialist Nurses** - support the Gaucher specialist in the specialist centre and you are likely to have a lot of contact with them. They will often provide services such as education services to other healthcare professionals, workplaces and schools as well as providing practical advice on a whole host of topics from parenting and schooling to travelling and sport. In addition, the specialist nurse plays an important part in making sure that the Gaucher patient is well cared for away from the specialist centre by liaising with local healthcare providers and ensuring all notes are kept up-to-date.
- **Local Hospital Doctor and GP** - it is important that your local GP and a doctor at your local hospital has contact with your specialist Gaucher doctor and is familiar with your case and condition. This will enable them to provide appropriate care for your immediate healthcare needs when you are not at the specialist centre.
- **Hospital or District Nurses** - these more general nurses can give practical help on using and maintaining specialist equipment, which may be of relevance for those individuals with neuronopathic Gaucher.
- **Homecare or Home Delivery Nurse** - if you are receiving ERT treatment for your Gaucher you may (after an initial introductory period) begin to receive your regular infusions at home and it is the home care or home delivery nurses that will facilitate this for you, visiting your house at pre-arranged times to give you treatment.

- **Physiotherapists and Physical Therapists** - can play an important role in helping to maintain flexibility in those limbs affected by bone complications and can help to devise exercise regimens to build bone and muscle strength.
- **Dieticians** - can give advice about the most appropriate diet, particularly for those that are suffering from fatigue or weight gain or loss as a side effect of their treatment. In addition, in the case of the neuronopathic forms of Gaucher, they can help if the individual has difficulty swallowing.
- **Social workers** - can help to give advice on financial entitlements available to support individuals with Gaucher and their families.
- **Psychologists and/or Counsellors** - can provide additional support if required.

Making the Most of Consultations

Before you see your doctor, spend some time thinking about how your condition has impacted on your day to day activities - this will help make the most of the consultation time. For instance, have things improved, got worse or stabilised? Do you have any questions about your treatment regimen? It may be worth considering the following questions and writing some notes to take with you so that you don't forget anything. Some questions to consider include:

- How have you been feeling since your last consultation?
- Have any of your symptoms got any worse or better - did anything prompt this?
- How much pain have you been feeling? (please see page 9 and the inside back cover which should help you to monitor your level of pain)
- Have there been any developments in Gaucher treatment that you have heard about that might help to address any of your ongoing symptoms?
- Has there been, or is there likely to be, a change of circumstances or something new that you want to do? i.e. start a family or travel, If so, can your doctor give you any advice on what would be the best way to approach this and whether there is any additional support that they can offer?
- If you are considering starting a family discuss this with your Gaucher specialist. He/she will explore with you the best way to manage your pregnancy, which may or may not include adjustments to your treatment regime. There is no reason why you should not have a positive, trouble free pregnancy.

General Well-being

Fatigue

The fatigue associated with Gaucher (sometimes due to anaemia) means that individuals can lack the stamina and they can find it difficult to concentrate for lengthy periods. If fatigue is a concern, speak to the nurses at your specialist centre who should be able to advise you on practical ways to overcome this.

Diet

There are number of ways in which altering your diet can help with Gaucher and it is worth speaking to a specialist dietitian if you want advice about the problems given below, as they will be able to provide you with detailed eating plans or more general advice that can help to alleviate the problems you might be experiencing:

- **Symptomatic** - fatigue and loss of appetite can be helped by a high energy, low bulk diet that is still generally well balanced and varied
- **Treatment related**
 - weight gain due to ERT - your dietitian can advise you on low calorie diets
 - weight loss due to SRT - this can be alleviated with certain temporary adjustments to your diet

Keeping Fit

It is important to remember that being physically active is essential for a healthy life, whoever you are. In fact, exercise helps to strengthen bones and muscles, though the level of activity that is appropriate for an individual with Gaucher depends on the severity of their symptoms and any concerns should be discussed with your Gaucher specialist.

One of the most important reasons for an individual with Gaucher to exercise regularly is that weight bearing exercise is one way to help reduce bone loss as the body responds to it by increasing bone density, which can help with the osteoporotic effects of the condition. Exercise can also help prompt the release of endorphins, the body's natural 'feel good' chemicals and helps people to feel empowered and positive.

Regular exercise, designed around an individual's physical abilities and limitations, yields many benefits:

- Cardiovascular health improves.
- Blood pressure is lowered and there is an increase in 'good' cholesterol.
- Circulation improves reducing the risk of heart disease.
- Muscles around the joints get stronger reducing strain on the joints and helping to protect them.
- Flexibility is better for easing stiffness.
- Mental functions tend to improve. Math skills,

creativity, reaction time, imagination and other mental skills have been linked to aerobic exercise.

- There are other benefits including sleeping better at night, less fatigue, and more energy.

Top Tips

- Talk with your doctor before you begin any exercise programme.
- Those with enlarged spleens or those who have a tendency to bleed or who are at risk of fractures may be advised to avoid contact sports and should try things such as walking, cycling, tennis, other racquet sports, dancing or yoga.
- Swimming is an ideal exercise for many people as it strengthens muscles without putting pressure or stress on joints, although it should be remembered that swimming is not weight bearing and will not increase bone density.
- An individual that has had hip or knee replacement surgery should avoid exercises that jar joints, including jogging and skiing.
- An individual with low physical endurance because of breathing difficulties or anaemia should consider non-aerobic activities such as weight training.
- Before any exercise, warming-up and stretching is essential as is a cool down phase that lasts several minutes at the end of a session, this will help to prevent stiffness, pain and injury as well as increasing the likelihood of success. It is particularly important for individuals with bone complications.

Travel Advice

Going overseas, particularly to developing countries, may present some unique challenges. However, a list of treatment centres in the country being visited, plus a letter explaining your care in the language of that country, can be invaluable. Your specialist centre can help you to organise your trip, so it is wise to let them know your plans. For example, they can advise on the most appropriate treatment for your trip (this may depend on how long you plan to be away), provide details of a treatment centre abroad and even tell them when you are arriving, although this may limit your options if you need to rely on infusions. The Gaucher Association can offer guidance on what travel documentation will be useful to take, plus advise on appropriate travel insurance cover.

Gaucher patients should also consult their centre if they are travelling abroad about infectious diseases such as malaria, yellow fever and meningitis as this will help them decide what are the best preventative measures to take. This is all the more important for individuals who

have had their spleen removed. In this case, due to a lowered immunity it is advisable to avoid travelling to the tropics where malaria is common. However, should it be necessary to visit a malarial area, then scrupulous attention to avoiding exposure to mosquitoes by the use of insect repellents and mosquito netting is also advised.

Travel Tips for those on ERT

- It is important to try to avoid any interruptions in your ERT treatment.
- Most pharmacies do not stock ERT due to the relatively small Gaucher patient population and it can be tricky to travel with ERT as the drugs need special storage and improper handling may result in loss of enzyme activity. However, it is possible to arrange to travel with ERT following discussion with your Gaucher centre providing that your travel is well thought out and well planned and the enzyme is refrigerated.
- For longer trips it will be important to locate a specialist centre, infusion centre or home treatment company well in advance of your trip (usually at least a few months) and you should notify your Gaucher specialist who will be able to help you arrange for your treatment to be delivered and administered while you are away.
- For shorter trips you may need to re-organise your infusion schedule to ensure that you don't miss your treatment. For example, if you have fortnightly infusions and are going on holiday for three weeks, you may wish to consider receiving two infusions just one week apart before you travel, then another infusion immediately after you return and this should be discussed with your Gaucher specialist.
- If you are planning a longer trip or one that will see you travelling from place to place (for example a gap year), it is advisable to speak to your Gaucher specialist about the most appropriate way to manage your condition.

Travel Tips for those on miglustat

- The oral nature of the medication means that it is possible to take your treatment with you when or wherever you are travelling.
- It is important to always take the exact medication that is needed as it may not be available abroad or the cost of it may not be reimbursed, therefore it should be carried as hand luggage along with a copy of the doctor's letter.

Financial Support & Advice

There is a range of entitlements potentially available for people with Gaucher and their carers, such as the:

- Disability Living Allowance (under 65 years)
- Attendance Allowance (65 years and over)
- Carer's Allowance

Disability Living Allowance (DLA) consists of two components (care and mobility) and is not income related. It is available from the age of three months and to make a claim the individual should call 08457 123 456 and ask for a DLA pack. The care part of DLA relates to the amount of care and supervision a person requires as a result of their condition, whereas the mobility share of DLA relates to their ability to walk. If the mobility part of DLA is being claimed, they may also be entitled to a disabled parking badge (known as a Blue Badge). There is more information on how to apply from the Department for Transport on line (www.dft.gov.uk). Anyone with a Blue Badge can also apply for exemption from the congestion charge in London. An application form is available from Transport for London (www.cclondon.com), The exemption costs a nominal amount to register for a year, and is free to renew.

Attendance Allowance (AA) is effectively DLA for those over the age of 65 and is available to those who need help with personal care because of a physical or mental disability. There are two rates of AA and the amount you get depends on how much your disability affects your daily life.

Carer's Allowance can be potentially claimed by a parent caring for a child with long term condition. However there are certain criteria that the carer needs to fulfil in order to qualify:

- They must be over 16.
- They must be caring for someone with a disability for at least 35 hours per week.
- They must earn less than a set amount per week.
- They cannot be in full time education.

In addition the person being cared for also needs to be claiming the middle or higher rate care part of the DLA to be allowed to claim Carer's Allowance. To apply for Carer's Allowance contact the local social security office (also called the Department for Work and Pensions or DWP). A search engine for your local DWP office can be found at www.dwp.gov.uk or by calling the DWP Carer's Allowance Unit (01253 85 61 23).

The Gaucher Association is an excellent source of advice for those wishing to obtain extra support, providing guidance on which support you may be entitled to and how to fill out the appropriate forms. They can also provide information on the best insurance companies to approach for travel, health or life insurance cover.

Support

The Gauchers Association

The Gauchers Association was formed in 1991 to support those suffering from Gaucher and their loved ones. They provide information about Gaucher through their twice yearly newsletter and website and are active in promoting the availability of treatment for those that require it. They also help to put families in touch with one another and actively encourage continuing research into Gaucher.

Gauchers Association

3 Bull Pitch
Dursley
Gloucestershire GL11 4NG

Tel/Fax: 01453 549231
Website: www.gaucher.org.uk
E:Mail: ga@gaucher.org.uk

UK Specialist Centres

Prof T Cox
Gaucher Disease Service
Box 135, Addenbrookes Hospital
Hills Road
Cambridge CB2 2QQ
Tel: 01223 216295

Dr C Hendriksz
Inherited Metabolic Disorders Department
Birmingham Children's Hospital NHS Trust
Steelhouse Lane
Birmingham B4 6NH
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Dr JE Wraith
The Willink Biochemical Genetics Unit
Royal Manchester Children's Hospital
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Tel: 0161 727 2137
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Dr A Vellodi
Metabolic Unit
Great Ormond Street Hospital for Sick Children
Great Ormond Street
London WC1N 3JH
Tel: 020 7405 9200 ext 0075
Website:
http://www.ich.ucl.ac.uk/gosh/clinicalservices/Metabolic_medicine

Dr S Waldeck
Salford Royal Hospitals NHS Trust
Department of Lysosomal Storage Disorders
CSB 1st floor A block, Hope Hospital
Stott Lane, Salford
Manchester M6 8HD
Email address: steve.waldek@srht.nhs.uk

Dr A Mehta
Lysosomal Storage Disorders Unit
The Royal Free Hospital
Pond Street, London NW3 2QG
Telephone: 020 7472 6409
Website: www.royalfree.nhs.uk/LSDU

Dr Phil Lee
The Charles Dent Metabolic Unit
National Hospital for Neurology & Neurosurgery
Queen Square, London WC1N 3BG
Email address: philip.lee@uclh.org

Other Sources of Information

CLIMB
Climb Building
176 Nantwich Road
Crewe CW2 6BG
Telephone: 0800 652 3181
Website: www.climb.org.uk

Disease Specific Advice, Information or Support:

Family Services Manager:
Pam Davies: pam@climb.org.uk

Regional Development & Educational Services

Regional Development Manager:
Lesley Greene: lesley@climb.org.uk

Other Web Resources:

BBC Website - database of different medical conditions including Gaucher <http://www.bbc.co.uk/health/conditions>

European Gaucher Alliance - details of patient groups in the European Gaucher Alliance and latest news www.europeangaucheralliance.org

Gaucher Patient Website - Dutch patient talks about her experiences of Gaucher and SRT treatment www.gaucherpatient.com

Global Organisation for Lysosomal Diseases - International alliance dedicated to improving the lives of all patients with a lysosomal disease, the site includes educational information and discussion forums <http://www.goldinfo.org/>

Institute of Child Health - database of factsheets including Neuronopathic Gaucher and Neuronopathic Gaucher disease: Special education needs <http://www.ich.ucl.ac.uk/factsheets>

Glossary

Anaemia

Low red blood cell count

Aseptic necrosis

Bone tissue destroyed by restricted blood flow

Cirrhosis

Scarring of the liver

Enzyme

Protein produced within the human body, which breaks down a specific substance in the cell

Femur

Thigh bone

Gaucher disease

Inherited Lysosomal Storage Disorder

Glucocerebrosidase

The enzyme deficient in Gaucher Disease, which breaks down Glucosylceramide

Glucosylceramide

Fatty substance arising from the membranes of worn-out red and white blood cells

Hepatomegaly

Enlargement of the liver

Lysosomal Storage Disorder

Accumulation (or storage) of fats or carbohydrates in lysosomes

Lysosomes

Cell compartments

Oedema

Accumulation of excessive amount of watery fluid

Obstetric

Branch of medical care concerned with looking after pregnant women through to child birth and for a short while after the birth

Osteopenia

A condition of reduced bone mass or density

Platelets

Cells responsible for blood clotting

Pulmonary Hypertension

A condition which causes difficulty in breathing

Splenectomy

A surgical procedure to remove the spleen

Splenomegaly

Enlargement of the spleen

Thrombocytopenia

A condition where the number of blood platelets is reduced

Recombinant

A virtual replica of a compound produced naturally by the body that is made using genetic engineering

Pain Diary

A pain diary may help you identify activities that cause you pain and what makes the pain better or worse. The following is an example of a pain diary and the items you may want to keep track of to help you talk things through when you visit your Gaucher specialist. You can use the guidance on page 10 of the Living with Gaucher Booklet to help you fill it in or record the answers in your own diary

Questions	Daily Observations						
	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Where is pain felt?							
When does pain occur?							
How does the pain feel?							
How severe the pain is on a scale of 0 to 10? How often the pain is felt?							
How long does the pain last?							
Does anything seem to trigger the pain or make it worse?							
Does anything make the pain better?							
What impact does pain have on your day?							
What have you tried to							