**Gaucher’s Disease**

*About the disease:*  
Gaucher’s disease (GD; pronounced as GO-SHEY) is a genetic disorder, in which a type of fat known as glucocerebroside is accumulated in various organs of the body. It occurs due to deficient activity of the enzyme glucocerebrosidase, which causes breakdown of glucocerebroside.

There are three types of GD – Type I, II and III. Type II and III in addition to liver, spleen and bone complications will have neurological complications as well. Type I is the most common treatable form of the disease while type II is the most severe form and is usually fatal by first year of life.

*Incidence:*  
Worldwide, the occurrence of GD is 1/57,000 to 1/75,000 births. According to certain studies, the incidence of GD is the highest among all the lysosomal storage disorders (LSD) seen in India.

*Signs and symptoms:*  
People suffering from GD show typical sings such as:  
- Anaemia (low number of red blood cells [RBCs])  
- Fatigue  
- Increased size of the liver and spleen (hepatosplenomegaly)  
- Easy bruising caused, in part, by a low level of platelets (thrombocytopenia) and bone disease (bone pain and fractures)  
- Neurological symptoms such as mental retardation, lack of coordination, difficulty in swallowing etc.

*Genetics and risk in the family:*  
GD is generally caused by a genetic mutation received from both parents (autosomal recessive inheritance), which leads to accumulation of the enzyme’s substrate glucocerebroside. It is caused by a recessive mutation in the gene GBA. An autosomal recessive disease, GD affects males and females alike. Both parents need to be carriers (or have the disease) for the child to have GD. This is more likely if the parents get married within a family. If both parents are carriers, there is a 25% chance that the child will be normal, or 50% chance that child will be carrier but not have disease, and 25% chance that the child will have GD.

*Diagnosis:*  
The diagnosis of GD is based on clinical symptoms and laboratory testing. A diagnosis of GD is suspected in individuals who have bone problems, enlarged liver and spleen (hepatosplenomegaly), changes in RBC levels, easy bleeding and bruising from low RBCs or signs of nervous system problems. The following tests may be done:  
- Blood test to look for Beta-Glucosidase enzyme activity  
- Magnetic resonance imaging scan (MRI)  
- Computed topography scan (CT)  
- X-ray of your skeleton  
- Genetic testing for mutation study of GBA gene

*Treatment:*  
Enzyme replacement therapy (ERT) is effective in treating individuals with symptoms of GD, which helps in stopping its progression. It involves injecting a modified form of the enzyme, glucocerebrosidase, by intravenous infusion once in 2 weeks. Other treatments that have been required include: removal of the spleen (splenectomy), blood transfusions, pain medications, and joint replacement surgery.

*Prevention:*  
Genetic counseling is recommended for prospective parents with a family history of GD. Testing can determine if the parents carry the gene that could pass on the GD. A prenatal test can also tell if a baby in the womb has GD. However, there is no known way to prevent GD.

*References:*  

*International Gaucher’s day is observed on July 26th worldwide, to honour the birth of PhilippeGaucher, the French dermatologist who discovered this disease.*
Tay-Sachs Disease

About the disease:
Tay-Sachs disease (TSD) is a rare neurodegenerative lysosomal storage disorder (LSD) in which the child has deficiency of an enzyme hexosaminidase A (Hex-A). This causes abnormal and excessive accumulation of sphingolipids known as gangliosides in the brain and nerve cells (neurons) causing dysfunction of the central nervous system and progressively destroys the neurons.

Prevalence:
TSD is very rare in the general population. The frequency of the condition is much higher in Ashkenazi Jews of Eastern European origin than in others. It affects males and females in equal numbers.

Genetic risk:
TSD results from changes (mutations) of the HEXA gene, which regulates production of the Hex-A enzyme.
TSD only occurs when both parents carry a defective copy of TSD gene and each parent transmits the defective gene to their child.
- A child who inherits the TSD genes from both parents produces defective Hex-A enzyme and will develop TSD
- A person with only one TSD gene will be perfectly healthy, but will act as a TSD carrier
- When both parents are carriers, there is a:
  - 25% chance, with every pregnancy, of having a child with TSD
  - 50% chance, with every pregnancy, of having a child who is a carrier
- When only one parent is a carrier, the child will be completely normal

Signs and symptoms:
A baby with TSD appears healthy at birth, but seems to be developing normally for a few months. Though the degradation of the CNS begins at the foetal stage, observations such as loss of peripheral vision and motor coordination are not seen until about 6 months of age. While symptoms vary from one child to the next, there is always a regression of development, hyperacusis and spasticity.

Diagnosis:
Diagnosis of TSD is confirmed by a thorough clinical evaluation and specialized tests, such as blood tests that measure the levels of Hex-A enzyme in the body. A blood test known as carrier screening identifies TSD carriers and non-carriers. Without carrier screening, it can remain hidden in a family for decades, surfacing unexpectedly in the child.

Treatment:
There is no specific treatment for TSD. Treatment is directed toward the specific symptoms that are apparent in each individual. Anticonvulsants may be used to treat seizures associated with some cases of TSD. Other supportive treatment includes proper nutrition and hydration. Genetic counseling may be of benefit for affected individuals and their families.

Prevention:
Couples who are both carriers of the disease should seek genetic counseling to understand the various choices available to them while planning a family. Prenatal diagnosis early in pregnancy will reveal the foetus has TSD. At-risk couples can choose from the following procedures: amniocentesis, done around the 16th week of pregnancy, and chorionic villus sampling (CVS), performed between the 10th to 13th weeks.

References:
Infantile Neuronal Ceroid Lipofuscinosis

Introduction:
Infantile neuronal ceroid-lipofuscinosis (INCL) is a rare genetic disorder, in which certain lipids i.e. ceroid and lipofuscin accumulate abnormally within the nerve cells (neurons) of the brain as well as other tissues of the body. This may result in the progressive breakdown of certain areas of the brain in addition to neurological impairment.

Prevalence:
All forms of NCL affect around 1 in 100,000 individuals worldwide. NCLs are more common in Finland, where approximately 1 in 12,500 individuals are affected.

Genetics and risk:
INCL is caused by the mutation in CLN1 (NCL1), the gene encoding the enzyme palmitoyl protein thioesterase 1 (PPT1). PPT1 removes certain long-chain fatty acids from proteins, which helps break down the proteins. Since INCL is an autosomal recessive disorder, the child needs to receive the abnormal gene from both parents in order to show any clinical symptoms.
- If an individual receives one normal gene and another gene for the disease, the person will only be a carrier for the disease
- The risk for both carrier parents to pass the defective gene and have an affected child is 25% with each pregnancy
- The risk to have a child who is a carrier like the parents is 50% with each pregnancy
- There is a 25% chance that a child will be completely normal
- The risk is the same for males and females.

Signs and symptoms:
Children develop normal motor skills during the 1st year, but the slowdown in head growth and decreased muscular tone are detectable after the age of 6 months. Loss in control of bodily movements and clumsiness develop along with irritability, sleep disturbance and visual failure, leading to a rapid developmental deterioration during the 2nd year.

Diagnosis:
Genetic testing may aid in the accurate diagnosis of the disorder and assist in prenatal diagnosis (before birth) as well as carrier determination. Both prenatal and post-natal diagnosis include the PPT enzyme assay (to detect the deficient activity of PPT enzyme) followed by DNA studies (to reveal the mutation). Prenatal diagnosis includes a method called chorionic villus sampling (use of placental tissues) and amniocentesis (use of the amniotic fluid).

Treatment:
There is no known specific treatment to halt or reverse the symptoms of INCL. Seizures (fits) can sometimes be reduced or controlled with anticonvulsant drugs, and other medical problems can be treated appropriately as they arise. Simultaneously, physical and occupational therapy may help patients retain their function as long as possible. Support and encouragement can help patients and families cope with the profound disability and dementia caused by NCLs. Often, support groups enable affected children, adults, and families to share common concerns and experiences.

Prevention:
Early diagnosis of INCL is important for counseling the affected families about future pregnancies.

References:
Late Infantile Neuronal Ceroid Lipofuscinosis

Introduction:
Discovered in 1998, late infantile neuronal ceroid lipofuscinosis (LINCL) or the Jansky-Bielschowsky disease manifests in a previously healthy child around the 3rd year of life. A deficiency of tripeptidyl-peptidase 1 (TPP1) results in abnormal storage of proteins and lipids in neurons and other cells. The cells cannot function as they should and symptoms develop. Originally, NCLs are defined by their age of onset and clinical symptoms.

Prevalence:
The prevalence of LINCL is unknown. All forms of NCL affect around 1 in 100,000 individuals worldwide. NCLs are more common in Finland, where approximately 1 in 12,500 individuals are affected.

Genetics and risk:
Classical late infantile NCL (NCL2) is caused by mutations in the CLN2 gene leading to deficiency of TPP1. Since LINCL is an autosomal recessive disorder, the child needs to receive the abnormal gene from both parents in order to show any clinical symptoms.
- If an individual receives one normal gene and one gene for the disease, the person will only be a carrier for the disease
- The risk for both carrier parents to pass the defective gene and have an affected child is 25% with each pregnancy
- The risk to have a child who is a carrier like the parents is 50% with each pregnancy
- The chance for a child to receive normal genes from both parents and be completely normal is 25%
The risk is the same for males and females

Signs and symptoms:
The signs and symptoms of this condition typically begin in late infancy or early childhood. The initial features usually include recurrent seizures (epilepsy) and difficulty in coordinating movements. Affected children also develop muscle twitches (myoclonus) and vision impairment. LINCL affects motor skills, such as sitting and walking, and speech development.

Diagnosis:
The diagnosis can be made by an enzyme study from leucocytes by TPP1 enzyme and molecular diagnosis can be made by TPP1 (NCL2) gene study. Prenatal diagnosis can be carried out at 11 weeks by chorionic villi study or at 16 weeks by amniotic fluid cultured cells for the enzyme or molecular study in case of known identified mutation in the gene.

Treatment:
Current disease management is primarily targeted at controlling the symptoms rather than "curing" the disease. Seizures can sometimes be reduced or controlled with anticonvulsant drugs, and other medical problems can be treated appropriately as they arise.

Prevention:
Early diagnosis of the disease is important for counseling the affected families about future pregnancies through prenatal diagnosis.

References: