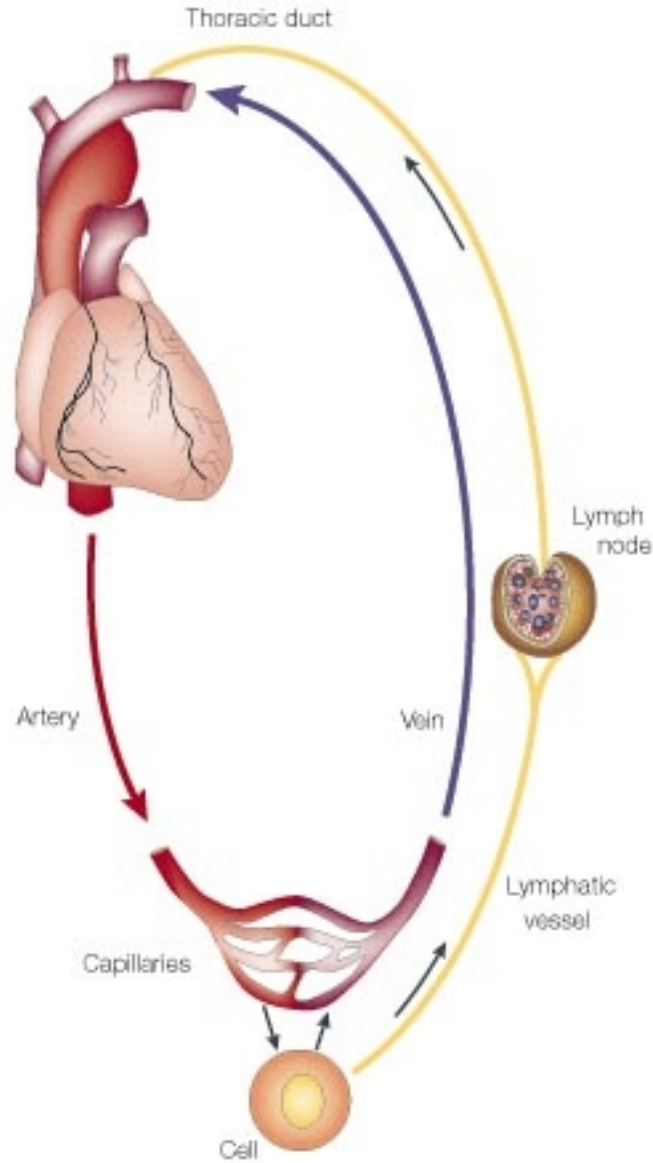


# Blood and Lymph Diseases



The cardiovascular system consists of the heart as well as blood vessels (arteries, veins and capillaries) and lymphatic vessels. Arteries deliver oxygenated blood (red) to the capillaries where bidirectional exchange occurs between blood and tissues. Veins collect deoxygenated blood (blue) from the microvascular bed and carry it back to the heart. Lymphatic vessels (yellow) collect extravasated tissue fluid, filter it through lymph nodes and return it to the circulation through the thoracic and lymphatic ducts and the lymphaticovenous anastomoses (not shown). The lymphatic vascular system is not continuous like the blood vascular system. (Figure and legend reproduced from: Jones, N., et al. (2001) Tie receptors: new modulators of angiogenic and lymphangiogenic responses. *Nat. Rev. Mol. Cell Biol.* 2; 257-267, with permission.)

As most of the cells in the human body are not in direct contact with the external environment, the circulatory system acts as a transport system for these cells. Two distinct fluids move through the circulatory system: blood and lymph. Blood carries oxygen and nutrients to the body's cells, and carries waste materials away. Blood also carries hormones, which control body processes, and antibodies, to fight invading germs. The heart is the pump that keeps this transport system moving. Together, the blood, heart, and blood vessels form the circulatory system.

The lymphatic system (lymph, lymph nodes and lymph vessels) supports the circulatory system by draining excess fluids and proteins from tissues back into the bloodstream, thereby preventing tissue swelling. It also serves as a defense system for the body, filtering out organisms that cause disease, producing white blood cells, and generating antibodies.

The biochemical make up of lymph — the fluid found in the lymphatic vessels — varies with the site of origin. For example, lymph from bone marrow, spleen, and thymus have high concentrations of white blood cells for fighting infection, while lymph from intestines is high in fat that has been absorbed during digestion. Damage to the lymphatic and circulatory systems leaves the body more susceptible to sickness and infection, as well as to serious conditions such as cancer.

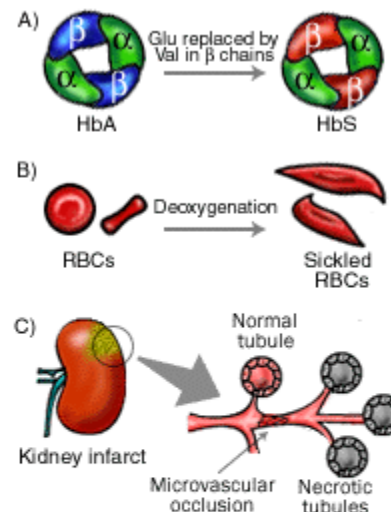
## Anemia, sickle cell

Sickle cell anemia is the most common inherited blood disorder in the United States, affecting about 72,000 Americans or 1 in 500 African Americans. SCA is characterized by episodes of pain, chronic hemolytic anemia and severe infections, usually beginning in early childhood.

SCA is an autosomal recessive disease caused by a point mutation in the *hemoglobin beta gene* (*HBB*) found on chromosome 11p15.4. Carrier frequency of *HBB* varies significantly around the world, with high rates associated with zones of high malaria incidence, since carriers are somewhat protected against malaria. About 8% of the African American population are carriers. A mutation in *HBB* results in the production of a structurally abnormal hemoglobin (Hb), called HbS. Hb is an oxygen carrying protein that gives red blood cells (RBC) their characteristic color. Under certain conditions, like low oxygen levels or high hemoglobin concentrations, in individuals who are homozygous for HbS, the abnormal HbS clusters together, distorting the RBCs into sickled shapes. These deformed and rigid RBCs become trapped within small blood vessels and block them, producing pain and eventually damaging organs.

Though, as yet, there is no cure for SCA, a combination of fluids, painkillers, antibiotics and transfusions are used to treat symptoms and com-

plications. Hydroxyurea, an antitumor drug, has been shown to be effective in preventing painful crises. Hydroxyurea induces the formation of fetal Hb (HbF)—a Hb normally found in the fetus or newborn—which, when present in individuals with SCA, prevents sickling. A mouse model of SCA has been developed and is being used to evaluate the effectiveness of potential new therapies for SCA.



**A)** Hemoglobin is made up of 4 chains: 2  $\alpha$  and 2  $\beta$ . In SCA, a point mutation causes the amino acid glutamine (Glu) to be replaced by valine (Val) in the  $\beta$  chains of HbA, resulting in the abnormal HbS. **B)** Under certain conditions, such as low oxygen levels, RBCs with HbS distort into sickled shapes. **C)** These sickled cells can block small vessels producing microvascular occlusions which may cause necrosis (death) of the tissue.

### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=sickle+cell+anemia&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=sickle+cell+anemia&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4504349&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4504349&org=1)] related sequences in different organisms

#### The literature

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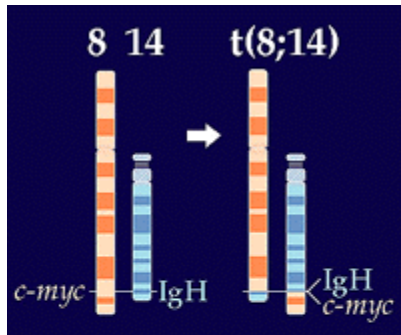
OMIM [[www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=603903](http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=603903)] catalog of human genes and disorders

#### Websites

Fact Sheet [[www.nhlbi.nih.gov/health/public/blood/sickle/sca\\_fact.pdf](http://www.nhlbi.nih.gov/health/public/blood/sickle/sca_fact.pdf)] from the National Heart, Lung and Blood Institute, NIH

SCDAA [[www.sicklecelldisease.org](http://www.sicklecelldisease.org)] Sickle Cell Disease Association of America

## Burkitt lymphoma



In Burkitt lymphoma, *Myc*, which is normally found on chromosome 8, is transferred to chromosome 14. This is known as chromosome translocation and can be characteristic of a cancer type. [image credit: Gregory Schuler, NCBI, NLM, NIH.]

Burkitt lymphoma is a rare form of cancer predominantly affecting young children in Central Africa, but the disease has also been reported in other areas. The form seen in Africa seems to be associated with infection by the Epstein–Barr virus, although the pathogenic mechanism is unclear.

Burkitt lymphoma results from chromosome translocations that involve the *Myc* gene. A chromosome translocation means that a chromosome is broken, which allows it to associate with parts of other chromosomes. The classic chromosome translocation in Burkitt lymphoma involves chromosome 8, the site of the *Myc* gene. This changes the pattern of *Myc*'s expression, thereby disrupting its usual function in controlling cell growth and proliferation.

We are still not sure what causes chromosome translocation. However, research in model organisms such as mice is leading us toward a better understanding of how translocations occur and, hopefully, how this process contributes to Burkitt lymphoma and other cancers such as leukemia.

### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=burkitt%20lymphoma&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=burkitt%20lymphoma&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=12962935&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=12962935&org=1)] related sequences in different organisms

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#### Websites

CancerNet [[cancernet.nci.nih.gov/](http://cancernet.nci.nih.gov/)] from the National Cancer Institute, NIH

American Cancer Society [[www.cancer.org/](http://www.cancer.org/)] research and patient support

Oncolink [[oncolink.upenn.edu/](http://oncolink.upenn.edu/)] comprehensive cancer information from the University of Pennsylvania

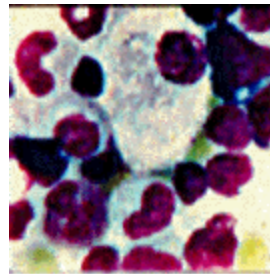
## Gaucher disease

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Gaucher (pronounced "go-SHAY") disease is an inherited illness caused by a gene mutation. Normally, this gene is responsible for an enzyme called glucocerebrosidase that the body needs to break down a particular kind of fat called glucocerebroside. In people with Gaucher disease, the body is not able to properly produce this enzyme, and the fat can not be broken down. It then accumulates, mostly in the liver, spleen, and bone marrow. Gaucher disease can result in pain, fatigue, jaundice, bone damage, anemia, and even death.

Gaucher disease is considerably more common in the descendants of Jewish people from Eastern Europe (Ashkenazi), although individuals from any ethnic group may be affected. Among the Ashkenazi Jewish population, Gaucher disease is the most common genetic disorder, with an incidence of approximately 1 in 450 persons. In the general public, Gaucher disease affects approximately 1 in 100,000 persons. According to the National Gaucher Foundation, 2500 Americans suffer from Gaucher disease.

In 1991, enzyme replacement therapy became available as the first effective treatment for Gaucher disease. The treatment consists of a modified form of the glucocerebrosidase enzyme given intravenously. Performed on an outpatient basis, the treatment takes about 1–2 h and is given every 2 weeks. Enzyme replacement therapy can stop and often reverse the symptoms of Gaucher disease, allowing patients to enjoy a better quality of life.



Gaucher cells. [Image credit: E. Beutler, Scripps Research Institute, La Jolla, CA, USA.]

## Important Links

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### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=Gaucher&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=Gaucher&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4503935&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4503935&org=1)] related sequences in different organisms

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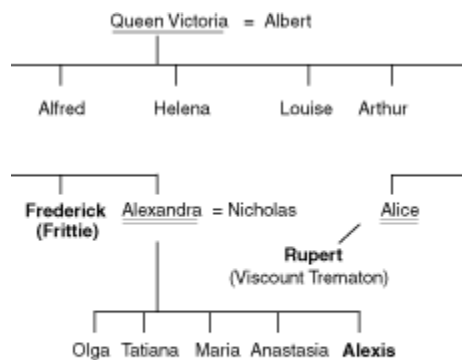
Books online books section

OMIM [[www.ncbi.nlm.nih.gov/entrez/dispmim.cgi?id=230800](http://www.ncbi.nlm.nih.gov/entrez/dispmim.cgi?id=230800)] catalog of human genes and disorders

### Websites

National Gaucher Foundation [[neuro-www2.mgh.harvard.edu/gaucher/ngfusa.html](http://neuro-www2.mgh.harvard.edu/gaucher/ngfusa.html)] supporting research into the causes of Gaucher disease

# Hemophilia A



Click on the figure to view the full chart in a pop-up window.

Hemophilia A is a hereditary blood disorder, primarily affecting males, characterized by a deficiency of the blood clotting protein known as Factor VIII that results in abnormal bleeding. Babylonian Jews first described hemophilia more than 1700 years ago; the disease first drew widespread public attention when Queen Victoria transmitted it to several European royal families. Mutation of the *HEMA* gene on the X chromosome causes Hemophilia A. Normally, females have two X chromosomes, whereas males have one X and one Y chromosome. Since males have only a single copy of any gene located on the X chromosome, they cannot offset damage to that gene with an additional copy

as can females. Consequently, X-linked disorders such as Hemophilia A are far more common in males. The *HEMA* gene codes for Factor VIII, which is synthesized mainly in the liver, and is one of many factors involved in blood coagulation; its loss alone is enough to cause Hemophilia A even if all the other coagulation factors are still present.

Treatment of Hemophilia A has progressed rapidly since the middle of the last century when patients were infused with plasma or processed plasma products to replace Factor VIII. HIV contamination of human blood supplies and the consequent HIV infection of most hemophiliacs in the mid-1980s forced the development of alternate Factor VIII sources for replacement therapy, including monoclonal antibody purified Factor VIII and recombinant Factor VIII, both of which are used in replacement therapies today.

Development of a gene replacement therapy for Hemophilia A has reached the clinical trial stage, and results so far have been encouraging. Investigators are still evaluating the long-term safety of these therapies, and it is hoped that a genetic cure for hemophilia will be generally available in the future.

## Important Links

### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=hemophilia&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=hemophilia&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4503647&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4503647&org=1)] related sequences in different organisms

### The literature

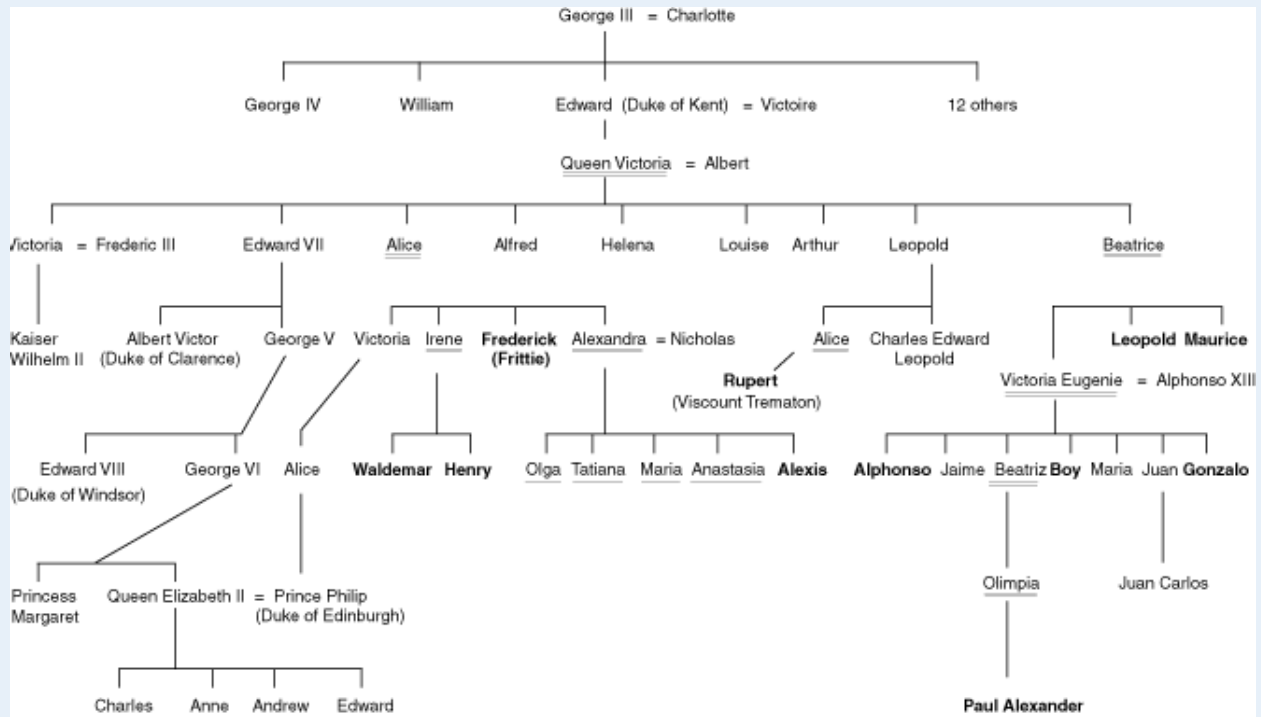
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### Websites

National Hemophilia Foundation [[www.hemophilia.org/](http://www.hemophilia.org/)] a nonprofit organization dedicated to finding cures for inherited bleeding disorders



**European royal family pedigree indicating instances of hemophilia.** Bold denotes hemophiliac male. Double underline denotes hemophilia carrier female. Single underline denotes possible hemophilia carrier female. [Reproduced from Stevens, RF. (1999) *British Journal of Haematology* 105:25-32., with permission.]

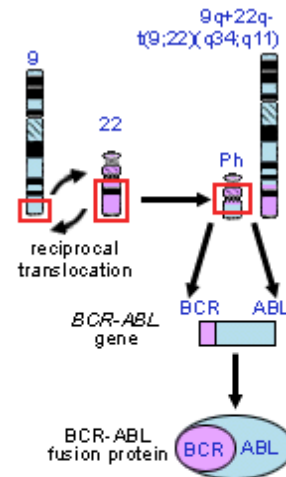
## Leukemia, chronic myeloid

Chronic myeloid leukemia (CML) is a cancer of blood cells, characterized by replacement of the bone marrow with malignant, leukemic cells. Many of these leukemic cells can be found circulating in the blood and can cause enlargement of the spleen, liver, and other organs.

CML is usually diagnosed by finding a specific chromosomal abnormality called the Philadelphia (Ph) chromosome (see figure), named after the city where it was first recorded. The Ph chromosome is the result of a translocation—or exchange of genetic material—between the long arms of chromosomes 9 and 22. This exchange brings together two genes: the *BCR* (breakpoint cluster region) gene on chromosome 22 and the proto-oncogene *ABL* (Ablason leukemia virus) on chromosome 9. The resulting hybrid gene *BCR-ABL* codes for a fusion protein with tyrosine kinase activity, which activates signal transduction pathways, leading to uncontrolled cell growth.

A mouse model has been created that develops a CML-like disease when given bone marrow cells infected with a virus containing the *BCR-ABL* gene. In other animal models, the fusion proteins have been shown to transform normal blood precursor

cells to malignant cells. To research the human disease, antisense oligomers (short DNA segments) that block *BCR-ABL* were developed that specifically suppressed the formation of leukemic cells while not affecting the normal bone marrow cell development. These and other experimental techniques may lead to future treatments for CML.



Leukemic white blood cells in CML contain a Philadelphia (Ph) chromosome, the result of a translocation between the long arms of chromosomes 9 and 22. The resulting fusion gene (*BCR-ABL*) produces an altered protein believed to play a key role in the development of CML.

### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=BCR%20OR%20ABLa&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=BCR%20OR%20ABLa&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=11038639&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=11038639&org=1)] related sequences in different organisms

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#### Websites

CancerNet [[cancernet.nci.nih.gov/wyntk\\_pubs/leukemia.htm](http://cancernet.nci.nih.gov/wyntk_pubs/leukemia.htm)] from the National Cancer Institute, NIH



## Niemann–Pick disease

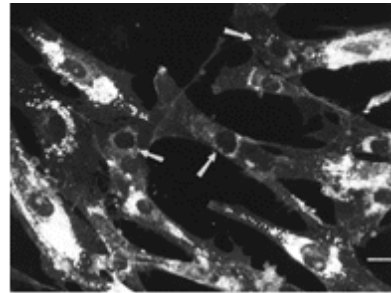
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In 1914, German pediatrician Albert Niemann described a young child with brain and nervous system impairment. Later, in the 1920's, Luddwick Pick studied tissues after the death of such children and provided evidence of a new disorder, distinct from those storage disorders previously described.

Today, there are three separate diseases that carry the name Niemann–Pick: Type A is the acute infantile form, Type B is a less common, chronic, non-neurological form, while Type C is a biochemically and genetically distinct form of the disease. Recently, the major locus responsible for Niemann–Pick type C (NP-C) was cloned from chromosome 18, and found to be similar to proteins that play a role in cholesterol homeostasis.

Usually, cellular cholesterol is imported into lysosomes—'bags of enzymes' in the cell—for processing, after which it is released. Cells taken from NP-C patients have been shown to be defective in

releasing cholesterol from lysosomes. This leads to an excessive build-up of cholesterol inside lysosomes, causing processing errors. NPC1 was found to have known sterol-sensing regions similar to those in other proteins, which suggests it plays a role in regulating cholesterol traffic.



Cells stained to show unesterified cholesterol in NP-C cells (white). The arrows show cell normalized by transfection with NPC1 DNA. [Reproduced with permission from Carstea et al. (1997) *Science* 277, 228-231.]

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### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=Niemann-Pick&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=Niemann-Pick&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4557803&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4557803&org=1)] related sequences in different organisms

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OMIM [[www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=257200](http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=257200)] catalog of human genes and disorders

#### Websites

Fact sheet [[www.ninds.nih.gov/health\\_and\\_medical/disorders/niemann.doc.htm](http://www.ninds.nih.gov/health_and_medical/disorders/niemann.doc.htm)] from the National Institute of Neurological Disorders and Stroke, NIH

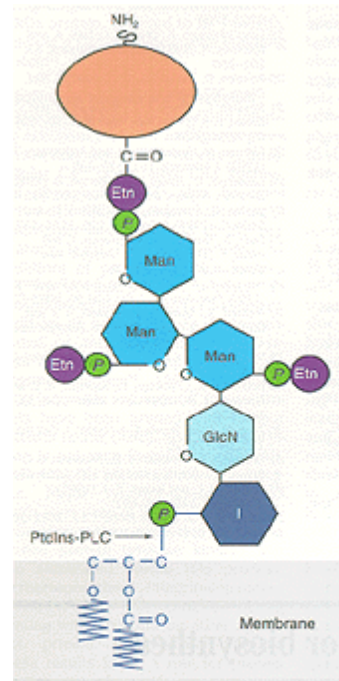
National Niemann-Pick Disease Foundation [[www.nnpdf.org](http://www.nnpdf.org)] an educational, support and fund-raising organization

## Paroxysmal nocturnal hemoglobinuria

The distinct and rather peculiar characteristics of paroxysmal nocturnal hemoglobinuria (PNH) have puzzled hematologists for more than a century. PNH is characterized by a decreased number of red blood cells (anemia), and the presence of blood in the urine (hemoglobinuria) and plasma (hemoglobinemia), which is evident after sleeping. PNH is associated with a high risk of major thrombotic events, most commonly thrombosis of large intra-abdominal veins. Most patients who die of their disease die of thrombosis.

PNH blood cells are deficient in an enzyme known as PIG-A, which is required for the biosynthesis of cellular anchors. Proteins that are partly on the outside of cells are often attached to the cell membrane by a glycosylphosphatidylinositol (GPI) anchor, and PIG-A is required for the synthesis of a key anchor component. If PIG-A is defective, surface proteins that protect the cell from destructive components in the blood (complement) are not anchored and therefore absent, so the blood cells are broken down.

The PIG-A gene is found on the X chromosome. Although not an inherited disease, PNH is a genetic disorder, known as an acquired genetic disorder. The affected blood cell clone passes the altered PIG-A to all its descendants—red cells, leukocytes (including lymphocytes), and platelets. The proportion of abnormal red blood cells in the blood determines the severity of the disease.



A glycosylphosphatidylinositol (GPI) anchor - people with paroxysmal nocturnal hemoglobinuria (PNH) have a mutation in the first enzyme in the GPI anchor synthesis pathway. [Reproduced with permission from Takeda, J. and Kinoshita, T. (1995) *Trends Biochem. Sci.* 20, 367-371.]

### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=paroxysmal+nocturnal+hemoglobinuria&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=paroxysmal+nocturnal+hemoglobinuria&ORG=Hs&V=0)] collection of gene-related information

BLink [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=11863130&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=11863130&org=1)] related sequences in different organisms

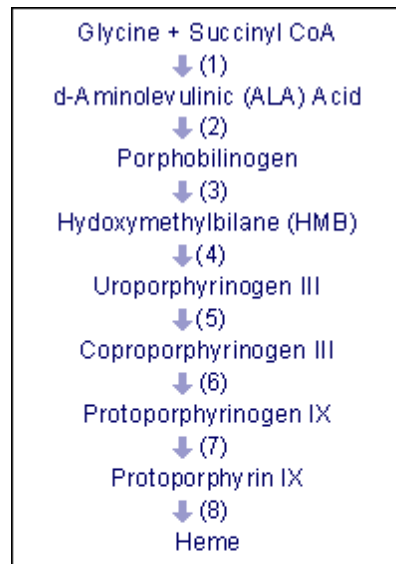
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# Porphyria



There are eight steps in making heme from glycine and succinyl CoA. Each step is helped by an enzyme. A problem in this pathway causes porphyria.

Click on the image for further information.

Porphyria is a diverse group of diseases in which production of heme is disrupted. Porphyria is derived from the Greek word “porphyra”, which means purple. When heme production is faulty, porphyrins are overproduced and lend a reddish-purple color to urine.

Heme is composed of porphyrin, a large circular molecule made from four rings linked together with an iron atom at its center. Heme is the oxygen-binding part of hemoglobin, giving red blood cells their color. It is also a component of several vital enzymes in the liver including the group known as

cytochrome P450. This enzyme family is important in converting potentially harmful substances such as drugs to inactive products destined for excretion.

Heme synthesis takes place in several steps, each of which requires a specific enzyme of which there are 8 in total. The genes that encode these enzymes are located on different chromosomes, and mutations of these genes can be inherited in either an autosomal dominant or autosomal recessive fashion, depending on the gene concerned. Affected individuals are unable to complete heme synthesis, and intermediate products, porphyrin or its precursors, accumulate.

Environmental triggers are important in many attacks of porphyria. Example triggers include certain medications, fasting, or hormonal changes. Genetic carriers who avoid a triggering exposure may never experience symptoms.

The cutaneous porphyrias cause sun sensitivity, with blistering typically on the face, back of the hands, and other sun-exposed areas. The most common of these is porphyria cutanea tarda (PCT). Triggering factors are alcohol use, estrogen, iron, and liver disease, particularly hepatitis C.

The acute porphyrias typically cause abdominal pain and nausea. Some patients have personality changes and seizures at the outset. With time the illness can involve weakness in many different muscles.

The cutaneous and acute forms are treated differently. Cure of these genetic diseases awaits the results of ongoing research on the safest and most effective means of gene transfer or correction.

## Important Links

### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=porphyria&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=porphyria&ORG=Hs&V=0)] collection of gene-related information

BLink for PCT [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=9845522&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=9845522&org=1)] related sequences in different organisms

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### Websites

Fact sheet [<http://www.niddk.nih.gov/health/digest/summary/porphria/porphria.htm>] from National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH

MedlinePlus [<http://www.nlm.nih.gov/medlineplus/ency/article/001208.htm>] a medical encyclopedia from the National Library of Medicine, NIH

Step in Pathway	Enzyme	Disease caused by enzyme deficiency
1	ALA synthase	
2	ALA dehydratase	ALAD porphyria
3	HMB synthase	Acute intermittent porphyria
4	Uroporphyrinogen synthase (UROS)	Congenital erythropoietic porphyria
5	Uroporphyrinogen decarboxylase (UROD)	Porphyria cutanea tarda
6	Coproporphyrinogen oxidase	Hereditary coproporphyrinemia
7	Protoporphyrinogen oxidase	Variegate porphyria
8	Ferrochelatase	Erythropoietic protoporphyria

## Thalassemia

Thalassemia is an inherited disease of faulty synthesis of hemoglobin. The name is derived from the Greek word "thalassa" meaning "the sea" because the condition was first described in populations living near the Mediterranean Sea; however, the disease is also prevalent in Africa, the Middle East, and Asia.

Thalassemia consists of a group of disorders that may range from a barely detectable abnormality of blood, to severe or fatal anemia. Adult hemoglobin is composed of two alpha ( $\alpha$ ) and two beta ( $\beta$ ) polypeptide chains. There are two copies of the hemoglobin alpha gene (*HBA1* and *HBA2*), which each encode an  $\alpha$ -chain, and both genes are located on chromosome 16. The hemoglobin beta gene (*HBB*) encodes the  $\beta$ -chain and is located on chromosome 11.

In  $\alpha$ -thalassemia, there is deficient synthesis of  $\alpha$ -chains. The resulting excess of  $\beta$ -chains bind oxygen poorly, leading to a low concentration of oxygen in tissues (hypoxemia). Similarly, in  $\beta$ -thalassemia there is a lack of  $\beta$ -chains. However, the excess  $\alpha$ -chains can form insoluble aggregates inside red blood cells. These aggregates cause the death of red blood cells and their precursors, causing a very severe anemia. The spleen becomes enlarged as it removes damaged red blood cells from the circulation.

Deletions of *HBA1* and/or *HBA2* tend to underlie most cases of  $\alpha$ -thalassemia. The severity of symptoms depends on how many of these genes

are lost. Loss of one or two genes is usually asymptomatic, whereas deletion of all four genes is fatal to the unborn child.

In contrast, over 100 types of mutations affect *HBB*, and deletion mutations are rare. Splice mutations and mutations that occur in the *HBB* gene promoter region tend to cause a reduction, rather than a complete absence, of  $\beta$ -globin chains and so result in milder disease. Nonsense mutations and frameshift mutations tend to not produce any  $\beta$ -globin chains leading to severe disease.

Currently, severe thalassemia is treated by blood transfusions, and a minority of patients are cured by bone marrow transplantation. Mouse models are proving to be useful in assessing the potential of gene therapy.



Adult hemoglobin (HbA) contains two alpha chains and two beta chains. In thalassemia, there is deficient synthesis of either the alpha chains or the beta chains. Symptoms are a result of not only low levels of HbA, but also the relatively high levels of the chain that is synthesized.

### Important Links

#### Gene sequence

Genome view see gene locations

LocusLink [[www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=thalassemia&ORG=Hs&V=0](http://www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=thalassemia&ORG=Hs&V=0)] collection of gene-related information

BLink  $\alpha$ -chain [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=122412&org=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=122412&org=1)]

BLink  $\beta$ -chain [[www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4504349&all=1](http://www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4504349&all=1)] related sequences in different organisms

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OMIM [[www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=604131](http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=604131)] catalog of human genes and disorders

Websites

Cooley's Anemia Foundation [[www.cooleysanemia.org/](http://www.cooleysanemia.org/)] Further information for patients and families

Thalassemia.Com [[www.thalassemia.com/home.shtml](http://www.thalassemia.com/home.shtml)] Further information for patients and health care workers