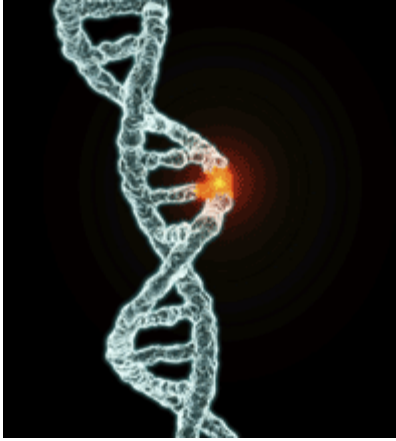


Genetics in Special Education Series

January 2011



Genetic disorders presented in this issue:

- [Porphyria](#)
 - [Wilson Disease](#)
-

Porphyria

What is Tuberous Porphyria?

The porphyrias are a group of different diseases, each caused by a specific abnormality in the heme production process. Heme is a chemical compound that contains iron and gives blood its red color. The essential functions of heme depend on its ability to bind oxygen. Heme is incorporated into hemoglobin, a protein that enables red blood cells to carry oxygen from the lungs to all parts of the body. Heme also plays a role in the liver where it assists in breaking down chemicals (including some drugs and hormones) so that they are easily removed from the body.

Heme is produced in the bone marrow and liver through a complex process controlled by eight different enzymes. As this production process of heme progresses, several different intermediate compounds (heme precursors) are created and modified. If one of the essential enzymes in heme production is deficient, certain precursors may accumulate in tissues (especially in the bone marrow or liver), appear in excess in the blood, and get excreted in the urine or stool. The specific precursors that accumulate depend on which enzyme is deficient. Porphyria results in a deficiency or inactivity of a specific enzyme in the heme production process, with resulting accumulation of heme precursors.

What are the signs and symptoms of porphyria?

The signs and symptoms of porphyria vary among types. Some types of porphyria (called cutaneous porphyria) cause the skin to become overly sensitive to sunlight. Areas of the skin exposed to the sun develop redness, blistering and often scarring.

The symptoms of other types of porphyria (called acute porphyrias) affect the nervous system. These symptoms include chest and abdominal pain, emotional and mental disorders, seizures and muscle weakness. These symptoms often appear quickly and last from days to weeks. Some porphyrias have a combination of acute symptoms and symptoms that affect the skin.

Environmental factors can trigger the signs and symptoms of porphyria. These include:

- Alcohol
- Smoking
- Certain drugs, hormones
- Exposure to sunlight
- Stress
- Dieting and fasting

How is porphyria diagnosed?

Porphyria is diagnosed through blood, urine, and stool tests, especially at or near the time of symptoms. Diagnosis may be difficult because the range of symptoms is common to many disorders and interpretation of the tests may be complex. A large number of tests are available, however, but results among laboratories are not always reliable.

How is porphyria treated?

Each form of porphyria is treated differently. Treatment may involve treating with heme, giving medicines to relieve the symptoms, or drawing blood. People who have severe attacks may need to be hospitalized.

What do we know about porphyria and heredity?

Most of the porphyrias are inherited conditions. The genes for all the enzymes in the heme pathway have been identified. Some forms of porphyria result from inheriting one altered gene from one parent (autosomal dominant). Other forms result from inheriting two altered genes, one from each parent (autosomal recessive). Each type of porphyria carries a different risk that individuals in an affected family will have the disease or transmit it to their children.

Porphyria cutanea tarda (PCT) is a type of porphyria that is most often not inherited. Eighty percent of individuals with PCT have an acquired disease that becomes active when factors such as iron, alcohol, hepatitis C virus (HCV), HIV, estrogens (such as those used in oral contraceptives and prostate cancer treatment), and possibly smoking, combine to cause an enzyme deficiency in the liver. Hemochromatosis, an iron overload disorder, can also predispose individuals to PCT. Twenty percent of individuals with PCT have an inherited form of the disease. Many individuals with the inherited form of PCT never develop symptoms.

If you or someone you know has porphyria, we recommend that you contact a genetics clinic to discuss this information with a genetics professional. To find a genetics clinic near you, contact your primary doctor for a referral.

What triggers a porphyria attack?

Porphyria can be triggered by drugs (barbiturates, tranquilizers, birth control pills, sedatives), chemicals, fasting, smoking, drinking alcohol, infections, emotional and physical stress, menstrual hormones, and exposure to the sun. Attacks of porphyria can develop over hours or days and last for days or weeks.

How is porphyria classified?

The porphyrias have several different classification systems. The most accurate classification is by the specific enzyme deficiency. Another classification system distinguishes porphyrias that cause neurologic symptoms (acute porphyrias) from those that cause photosensitivity (cutaneous porphyrias). A third classification system is based on whether the excess precursors originate primarily in the liver (hepatic porphyrias) or primarily in the bone marrow (erythropoietic porphyrias). Some porphyrias are classified as more than one of these categories.

What are the cutaneous porphyrias?

The cutaneous porphyrias affect the skin. People with cutaneous porphyria develop blisters, itching, and swelling of their skin when it is exposed to sunlight. The cutaneous porphyrias include the following types:

- **Congenital erythropoietic porphyria** [ghr.nlm.nih.gov]
Also called congenital porphyria. This is a rare disorder that mainly affects the skin. It results from low levels of the enzyme responsible for the fourth step in heme production. It is inherited in an autosomal recessive pattern.
 - Gene: UROS [ghr.nlm.nih.gov]
- **Erythropoietic protoporphyria** [ghr.nlm.nih.gov]
An uncommon disorder that mainly affects the skin. It results from reduced levels of the enzyme responsible for the eighth and final step in heme production. The inheritance of this condition is not fully understood. Most cases are probably inherited in an autosomal dominant pattern, however, it shows autosomal recessive inheritance in a small number of families.
 - Gene: FECH [ghr.nlm.nih.gov]
- **Hepatoerythropoietic porphyria** [ghr.nlm.nih.gov]
A rare disorder that mainly affects the skin. It results from very low levels of the enzyme responsible for the fifth step in heme production. It is inherited in an autosomal recessive pattern.
 - Gene: UROD [ghr.nlm.nih.gov]
- **Hereditary coproporphyria** [ghr.nlm.nih.gov]
A rare disorder that can have symptoms of acute porphyria and symptoms that affect the skin. It results from low levels of the enzyme responsible for the sixth step in heme production. It is inherited in an autosomal dominant pattern.
 - Gene: CPOX [ghr.nlm.nih.gov]

- **Porphyria cutanea tarda** [ghr.nlm.nih.gov]
The most common type of porphyria. It occurs in an estimated 1 in 25,000 people, including both inherited and sporadic (noninherited) cases. An estimated 80 percent of porphyria cutanea tarda cases are sporadic. It results from low levels of the enzyme responsible for the fifth step in heme production. When this condition is inherited, it occurs in an autosomal dominant pattern.
 - o Gene: UROD [ghr.nlm.nih.gov]
 - o Gene: HFE [ghr.nlm.nih.gov]
- **Variegate porphyria** [ghr.nlm.nih.gov]
A disorder that can have symptoms of acute porphyria and symptoms that affect the skin. It results from low levels of the enzyme responsible for the seventh step in heme production. It is inherited in an autosomal dominant pattern.

What are the acute porphyrias?

The acute porphyrias affect the nervous system. Symptoms of acute porphyria include pain in the chest, abdomen, limbs, or back; muscle numbness, tingling, paralysis, or cramping; vomiting; constipation; and personality changes or mental disorders. These symptoms appear intermittently. The acute porphyrias include the following types:

- **Acute intermittent porphyria** [ghr.nlm.nih.gov]
This is probably the most common porphyria with acute (severe but usually not long-lasting) symptoms. It results from low levels of the enzyme responsible for the third step in heme production. It is inherited in an autosomal dominant pattern.
- **ALAD deficiency porphyria** [ghr.nlm.nih.gov]
A very rare disorder that results from low levels of the enzyme responsible for the second step in heme production. It is inherited in an autosomal recessive pattern.

[To top](#)

Wilson Disease

What is Wilson Disease?

Wilson disease is a rare genetic condition that affects about one in 30,000 people. Wilson disease causes a person's body to store too much of the mineral copper. Many foods contain copper, and it is important for people to have a small amount of copper in the body. However, high levels of copper can damage organs in the body.

In Wilson disease, copper builds up in the liver, brain, eyes and other organs. Over time, the extra copper can lead to organ damage that may cause death.

Other names for Wilson disease include copper storage disease, hepatolenticular degeneration syndrome, WD and Wilson's disease.

What are the symptoms of Wilson disease?

Wilson disease may affect several of the body's systems.

Either the liver or the brain can be harmed first, with signs as early as 4 years, or as late as 70 years of age. **Symptoms of liver disease include:**

- Jaundice, which is when the skin or the white part of the eye turns yellow
- Fatigue
- Loss of appetite
- Swelling in the abdomen
- Easy bruising

Nervous system or mental health problems can develop in children or young adults who have Wilson disease. **These problems include:**

- Clumsiness
- Trembling
- Difficulty walking
- Problems with speech
- Problems with school work
- Depression
- Anxiety
- Mood swings

Eye changes and vision problems may also occur. These include:

- Kayser-Fleischer rings, which are green-to-brownish rings around the iris of the eye
- Difficulties with eye movement, particularly in looking upwards

In addition, people who have Wilson disease may experience:

- A low level of red blood cells, which is called anemia
- Low levels of white blood cells
- Low levels of clotting factors called platelets

- Slow clotting of blood
- High levels of protein, amino acids and uric acid in the urine
- Early onset of arthritis and bone loss

How is Wilson disease diagnosed?

Doctors diagnose Wilson disease through a physical exam and laboratory tests. The physical examination focuses on signs of liver disease as well as neurologic function.

The exam includes the use of a special light, called a slit lamp, to look for Kayser-Fleischer rings in a person's eyes. Kayser-Fleischer rings are found in almost all people with Wilson disease who show signs of neurologic damage. They are found in about half of people who have only signs of liver damage. Kayser-Fleischer rings do not harm a person's vision.

Doctors also order lab tests to measure the amount of copper in the blood and urine. Most people with Wilson disease will have lower-than-normal levels of copper in the blood, as well as lower blood levels of a protein called ceruloplasmin, a protein which contains copper. However, in people with acute liver failure caused by Wilson disease, copper levels in the blood are often higher than normal. Urine is collected over a 24 hour period to look for increased copper levels typical of Wilson disease.

In addition, a special procedure called a liver biopsy using a needle is done to remove a small piece of a person's liver. The liver sample is then examined under a microscope to look for damage found in Wilson disease. Copper content of the liver is also measured.

Genetic testing is frequently used to help diagnose Wilson disease in some people and is important for reliable early diagnosis of brothers and sisters of a patient with Wilson disease.

How is Wilson disease treated?

When Wilson disease is diagnosed early and treated effectively, people with the condition usually can have good health. However, for patients who have severe cirrhosis, acute liver failure or other serious liver disorders, a liver transplant may be the only option for treatment.

People who have Wilson disease must be treated throughout their lives to lower and control the amount of copper in their bodies. When Wilson disease is diagnosed early and treated effectively, people with the condition usually can enjoy good health.

The first steps in treatment of Wilson disease involve:

- Removing the excess copper from the body.
- Reducing intake of foods that are rich in copper.
- Treating any liver or central nervous system damage.

Doctors currently use two drugs to treat Wilson disease: D-penicillamine (Cuprimine) and trientine (Syprine). These drugs help remove copper from organs and release it into the bloodstream. Once the copper enters the bloodstream, it is filtered out by the kidneys and excreted in urine.

Both drugs carry the possibility of major side effects. The drugs can worsen neurologic symptoms because the copper released into the bloodstream may sometimes be taken back up by the central nervous system. In addition, about one-quarter to one-third of people treated with D-penicillamine will experience other reactions to the medication, such as fever, rash and effects on the kidneys and bone marrow. The risks associated with trientine appear to be lower.

If they are pregnant, women with Wilson disease are given lower doses of these drugs to reduce the risk of having a baby with birth defects. Lower doses also improve the body's ability to heal if surgery is done during childbirth.

Zinc is another therapy for Wilson disease. Given in the form of zinc salts, such as zinc acetate (Galzin), it keeps the digestive tract from absorbing copper. Because zinc removes copper rather slowly, it usually is given as maintenance therapy for Wilson disease. It appears safe to use a full dose of zinc during pregnancy.

Once the symptoms of Wilson disease have improved and tests show that a person's copper levels have been lowered to a safe level, maintenance treatment begins. This can be with D-penicillamine or trientine or zinc. Blood and urine are routinely tested to make sure that copper remains at a safe level.

Doctors often recommend that people with Wilson disease reduce the amount of copper in their diets. Specifically, they are instructed to avoid liver or shellfish, which may contain high levels of copper. During initial treatment, patients may also be told not to eat other copper-rich foods, such as mushrooms, nuts, and chocolate. Once people begin maintenance treatment, they may be able to eat these foods in moderation. In addition, people with Wilson disease should avoid multivitamins that contain copper and have their drinking water checked for copper content.

Is Wilson disease inherited?

Yes. Wilson disease is inherited in what doctors call an autosomal (not on the X chromosome) recessive pattern. In this pattern of inheritance, a person needs to inherit two altered (mutated) copies of a gene - one from each parent - to develop the disease. The parents of a person with Wilson disease each carry one mutated copy of the gene and one normal copy of the gene, so they do not show signs or symptoms of the disease. Doctors refer to such people as "carriers."

With each pregnancy, couples who are carriers of the gene for Wilson disease face a 25 percent chance of having a child who will develop Wilson disease. Such a couple also has a 50 percent chance of having a child who is a carrier for Wilson disease and a 25 percent chance of having an unaffected child with two normal copies of the gene.

[To top](#)