



CHAPTER 11 : CONSUMER FACT SHEETS

Family History (Fact Sheet from CDC) * Basic Genetic Information * Dominant and Recessive Genetic Diseases * X-linked Genetic Diseases * What is a Chromosome Abnormality? * Understanding Genetic Testing * Deciding Whether to Have a Genetic Test * Prenatal Diagnosis * Birth Defects & Congenital Disorders * Newborn Screening

Family History Is Important for Your Health

adopted from CDC's Family History Fact sheet

<http://www.cdc.gov/genomics/public/famhix/fs.htm>

Most of us know that we can reduce our risk of disease by eating a healthy diet, getting enough exercise, and not smoking. But did you know that your family history might be one of the strongest influences on your risk of developing heart disease, stroke, diabetes, or cancer? Even though you cannot change your genetic makeup, knowing your family history can help you reduce your risk of developing health problems.



Family members share their genes, as well as their environment, lifestyles, and habits. Everyone can recognize traits that run in their family, such as curly hair, dimples, leanness, or athletic ability. Risks for diseases such as asthma, diabetes, cancer, and heart disease also run in families. Everyone's family history of disease is different. The key features of a family history that may increase risk are:

- Diseases that occur at an earlier age than expected (10 to 20 years before most people get the disease);
- Disease in more than one close relative;
- Disease that does not usually affect a certain gender (for example, breast cancer in a male);
- Certain combinations of diseases within a family (for example, breast and ovarian cancer, or heart disease and diabetes).

If your family has one or more of these features, your family history may hold important clues about your risk for disease. People with a family history of disease may have the most to gain from lifestyle changes and screening tests. You can't change your genes, but you can change unhealthy behaviors, such as smoking, inactivity, and poor eating habits. In many cases, adopting a healthier lifestyle can reduce your risk for diseases that run in your family. Screening tests (such as mammograms and colorectal cancer screening) can detect diseases like cancers at an early stage when they are most treatable. Screening tests can also detect disease risk factors like high cholesterol and high blood pressure, which can be treated to reduce the chances of getting disease.



LEARNING ABOUT YOUR FAMILY HISTORY

To learn about your family history:

- ask questions,
- talk at family gatherings, and
- look at death certificates and family medical records, if possible.

Collect information about your grandparents, parents, aunts and uncles, nieces and nephews, siblings, and children. The type of information to collect includes:

- major medical conditions and causes of death,
- age of disease onset and age at death, and
- ethnic background.

Write down the information and share it with your doctor. Your doctor will:

- assess your disease risk based on your family history and other risk factors,
- recommend lifestyle changes to help prevent disease, and
- prescribe screening tests to detect disease early.

If your doctor notices a pattern of disease in your family, it may be a sign of an inherited form of disease that is passed on from generation to generation. Your doctor may refer you to a specialist who can help determine whether you have an inherited form of disease. Genetic testing may also help determine if you or your family members are at risk. Even with inherited forms of disease, steps can be taken to reduce your risk.

WHAT IF YOU HAVE NO FAMILY HISTORY?

Even if you don't have a history of a particular health problem in your family, you could still be at risk. This is because

- your lifestyle, personal medical history, and other factors influence your chances of getting a disease;
- you may be unaware of disease in some family members;
- you could have family members who died young, before they had a chance to develop chronic conditions such as heart disease, stroke, diabetes, or cancer.

Being aware of your family health history is an important part of a lifelong wellness plan.

WHERE YOU CAN FIND MORE INFORMATION

For more information on CDC's Office of Genomics and Disease Prevention, visit <http://www.cdc.gov/genomics>.

The following Web sites provide additional information on family history:

CDC's Family History Web site for the Public, <http://www.cdc.gov/genomics/public/fambhist.htm>

U.S. Surgeon General's Family History Initiative, <http://www.hhs.gov/familyhistory/>

National Society for Genetic Counselors, <http://www.nsgc.org/consumer/familytree/>

Basic Genetic Information

- Cells are the body's building blocks. Inside most cells is a nucleus—the center of the cell. The nucleus contains threadlike structures called chromosomes made up of smaller structures called genes.
- Genes direct the structure and function of your cells which make up all of your body's organs and tissues.
- Genes are inherited from your parents and determine how you will look.
- Genes come in pairs. One gene comes from your father and one from your mother. This is why you look like your parents.
- Genes also contain instructions for how you age, what diseases you are at risk for or may get in the future as you grow older, or what diseases you might pass down to your children.
- Some genes are stronger, or dominant, and they take over directing your body for that function.
- Some genes are weaker, or recessive, and need the presence of a like partner to become active and make a difference.
- Changes (also called mutations) can sometimes happen in a gene. Changes in a gene may cause cells or organs not to work correctly, leading to a disease. Changes in a gene may also lead to improvement in your body's ability to cope with disease. Changes in the genes can be inherited from your parents or happen due to the environment you live in—the chemicals you are exposed to, through the air you breathe, the food you eat, or the water you drink.
- Whether the specific set of genes you inherited from your parents—or any changes that occur to them during your lifetime—promote health or produce disease may depend on both environmental and behavioral factors. Proper exercise and nutrition can help delay or prevent disease, while smoking and lack of exercise can increase your chances of disease.
- You can take special tests—genetic tests—to see what specific genes are present in your body. These tests can sometimes tell you what diseases you might have or might develop later, and what diseases you might pass along to your children.
- Newborn babies also take genetic tests to look for diseases that might harm the baby or cause mental retardation if they are not treated immediately. These tests are done just after the baby is born so that interventions and treatment can be started immediately to protect the baby from these diseases. If a disease is found, a doctor will help you understand what treatment your baby needs. Sometimes you may be asked to see a genetic counselor.



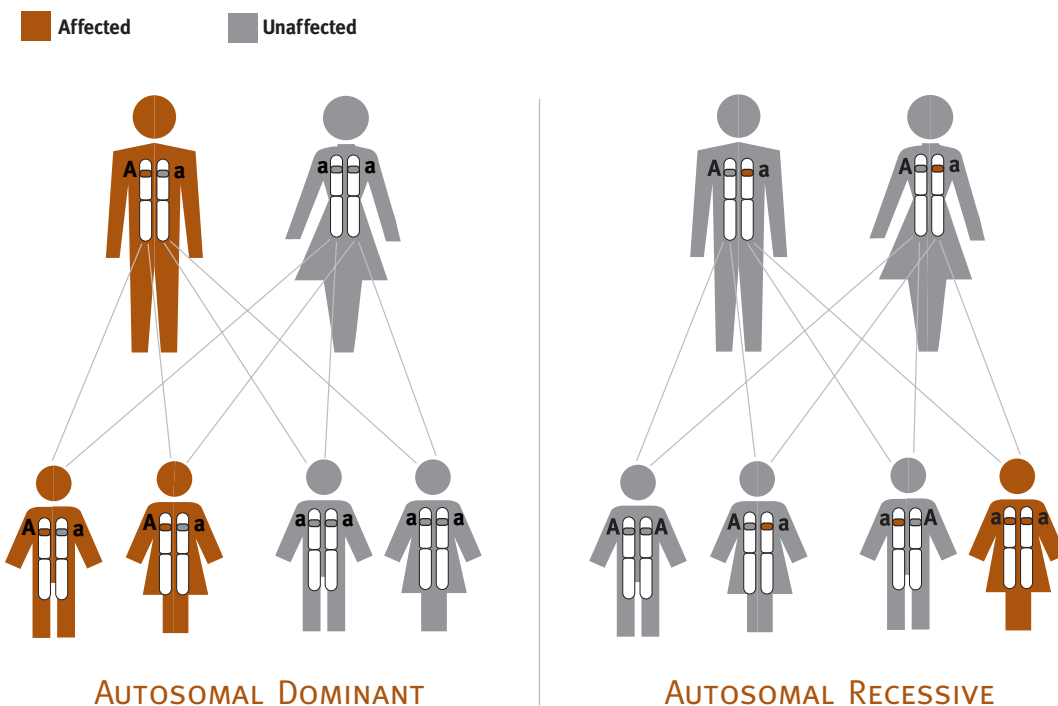
Dominant and Recessive Genetic Diseases

The basic laws of inheritance are important in order to understand how diseases are passed on in a family. For almost every gene, a person has two copies of each gene—one copy from your father and one copy from your mother. Changes to either copy of the gene or both copies of the gene can result in a wide range of effects. Some changes result in relatively minor or undetectable changes; these types of changes are often called single nucleotide polymorphisms (“snips”) or gene variations.

Other DNA changes in a gene can result in changes to the corresponding protein which can lead to disease. These changes are often known as mutations. Diseases caused by mutations in a single gene are usually inherited in a simple pattern, depending on the location of the gene and whether one or two normal copies of the gene are needed. For certain functions in the body, you need two copies of a gene to work normally. For other functions, only one copy is necessary.

There are two major modes of inheritance for single-gene diseases: recessive and dominant. When a person inherits a mutation in one of the two copies of a gene, disease may develop if both copies are required for normal function. In this case, the mutated gene is dominant and the person develops a genetic disease. Dominantly inherited genetic diseases tend to occur in every generation of a family. Each affected person usually has one affected parent.

If a person inherits a mutation in one copy of a gene, but does not develop a disease, the mutated gene is recessive. For a recessively inherited disease to develop, both copies of the gene must be mutated. This can happen when both the mother and father carry a copy of the mutated gene and pass each copy onto the child who will then have two copies of the mutated gene. Recessive genetic diseases are typically not seen in every generation of an affected family. The parents of an affected person are generally not affected.



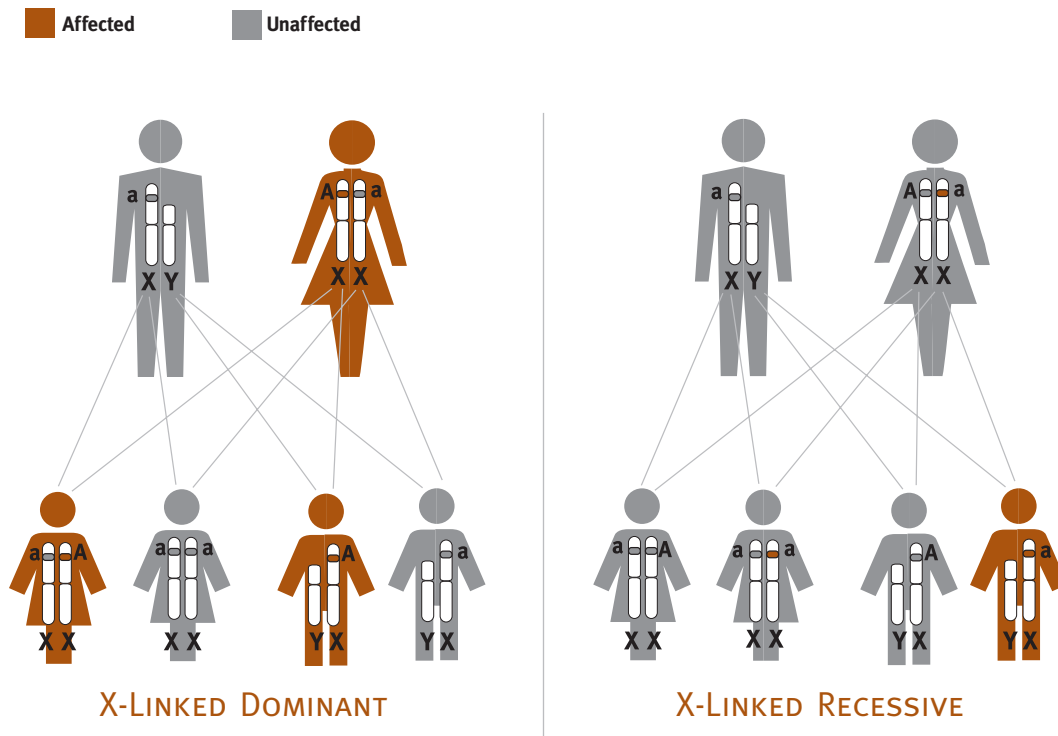
X-linked Genetic Diseases

For genes located on the sex chromosomes (X or Y), the inheritance patterns are slightly different than for genes located on the other chromosomes (1-22). This is due to the fact that females carry two X chromosomes (XX) and males carry a single X and Y chromosome each (XY). Therefore, females carry two copies of each X-linked gene similar to all other genes, but males carry only one copy of X-linked and Y-linked genes.

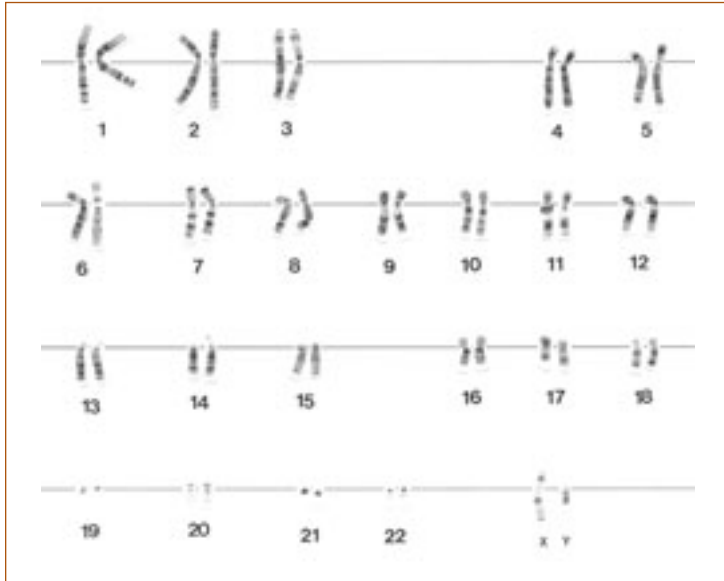
Since males only have one X chromosome, any mutated gene on the X chromosome will result in disease. But because females have two copies of X-linked genes, diseases caused by mutated genes located on the X chromosome can be inherited in either a dominant or recessive manner. For X-linked dominant diseases, a mutation in one copy of an X-linked gene will result in disease. Families with an X-linked dominant disorder often have both affected males and affected females in each generation.

For X-linked recessive diseases to occur, both copies of the gene must be mutated in order for disease to occur in females. Families with an X-linked recessive disorder often have affected males, but rarely affected females, in each generation.

A striking characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons since they only pass on the Y chromosome. In contrast, affected mothers can pass the mutated X-linked gene to either their son or daughter.



What is a Chromosome Abnormality?



Almost every cell in our body contains 23 pairs of chromosomes for a total of 46 chromosomes. Half of the chromosomes come from our mother and the other half come from our father. The first 22 pairs (called autosomes) are numbered according to size—the largest chromosome is chromosome 1. The 23rd pair are the sex chromosomes X and Y—females have 2 X chromosomes and males have an X and Y chromosome each. All of the information that the

body needs to work comes from the chromosomes. Each chromosome contains thousands of genes which direct the body's development, growth, and chemical reactions.

Although most everyone has a complete set of chromosomes, sometimes pieces of chromosomes can be switched or moved. In general, as long as all of the material is present, the majority of children with rearranged chromosomes do not develop any health problems. However, when sections of or entire chromosomes are missing or extra copies are present, miscarriage, infant death, or disease usually occurs. For example, an extra copy of chromosome 21 results in Down syndrome.

Chromosome abnormalities usually happen as a result of an error when cells grow and divide. Errors can occur when eggs or sperm are formed, resulting in either too many chromosomes or not enough chromosomes. Or, errors could occur during the early developmental stages of the fetus, also resulting in an abnormal number of chromosomes. The age of the mother and certain environmental factors can increase the risk of a chromosomal abnormality.

Testing can be performed to examine the chromosomes of the fetus. The two types of testing available are amniocentesis and chorionic villus sampling. In both cases, the cells from the baby are grown and processed in the laboratory so that the chromosomes can be studied. Pictures of the chromosomes viewed under a microscope are taken and the chromosomes are then arranged by size and paired together. The picture of the arranged chromosomes is known as a karyotype. The karyotype is evaluated for size and structure of the chromosomes.

Understanding Genetic Testing

Genetic testing involves examining a person's DNA found in blood or other tissues for some abnormality linked to a disease or condition. DNA is actually a chemical alphabet composed of four units that make up all of the genes or genetic material found inside our cells. Genes are important for our body's normal development and functioning. Each gene is unique due to the order of the four DNA units.

When a mistake happens affecting part or all of the gene, this can result in an abnormal function or change in our body leading to disease. The mistake can be fairly large or very small and different types of genetic tests are used to identify the specific gene abnormality. Genetic tests can be used to look for gene abnormalities in persons suspected of having a genetic disease based on symptoms the person may be having or because a close relative has a genetic disease.



The most common type of genetic testing is newborn screening. Almost every baby born in the United States has a blood sample tested for abnormal or missing genes or proteins. Early detection can allow the doctor to prescribe drugs or to place the baby on a specific diet in order to prevent or reduce the severity of a disease. Another type of testing known as carrier testing can help determine the risk of parents passing on a mutation to their child. And predictive gene testing can determine the risk of a healthy person developing a disease in the future.

Genetic testing is not always 100 percent accurate. Even when genetic testing positively detects a mutation, the test may or may not be able to determine when or what symptoms of the disease may show, which symptoms will occur first and how severe the disease will be, or how the disease will progress over time. If a test is negative, an individual may still be at risk for a disease. Therefore, it is important to speak to a health professional such as a genetic counselor to help you understand the benefits and risks of genetic testing and to answer any questions you may have before and after testing.



Deciding Whether to Have a Genetic Test

The decision to have a genetic test is a personal and sometimes difficult one. While a genetic test can determine the presence of a gene abnormality and/or identify an increased risk of disease, a genetic test cannot predict when a disease will develop or how severe the disease will be. Meeting with genetic health professionals can be extremely helpful in understanding and thinking through many of these issues.

Genetic counselors are trained health professionals in the areas of medical genetics and counseling. They work as members of a health care team, providing information and support to families who have members with birth defects or genetic disorders and to families who may be at risk for a variety of inherited conditions. Genetic counselors are trained to help persons as they consider testing, when they receive the results, and in the weeks and months afterward.

When deciding whether or not to have a genetic test for you or your child, several issues should be considered. In addition to the medical issues to be considered, genetic testing also raises some ethical and legal issues you should be aware of. Below is a list of some of the issues you should discuss with your physician or genetic counselor:

- What treatments are available for this genetic disease?
- What impact would the genetic test results have on your family?
- What happens if the results are uncertain or inconclusive?
- What are the risks for future pregnancies?
- What is the cost of the test and will my insurance cover it?
- Who will have access to the test results?
- What emotional support services are available?
- Do other family members have a right to know the test results?
- What is the risk of discrimination by my employer or insurer?

Prenatal Diagnosis

Prenatal diagnosis refers to testing performed during a pregnancy. Prenatal diagnosis is helpful for determining the outcome of the pregnancy, planning for possible complications during delivery, planning for problems that may occur in the newborn, deciding whether to continue the pregnancy, and finding conditions that may affect future pregnancies.

A common reason for prenatal diagnosis is the mother's age. According to professional guidelines, prenatal diagnosis should be offered to women who will be over the age of 35 years at the time of delivery because they have a higher risk of having a child with a genetic condition such as Down syndrome. Children with Down syndrome have a distinct facial appearance and mental retardation; however, the severity of the disease can vary greatly from child to child. The disease is caused by a chromosomal abnormality that can be detected through genetic testing, namely three copies of chromosome 21.

In addition, women who have had a previous child with a genetic condition, if the parents are carriers of a genetic mutation, or if there is a family history of a genetic condition would be eligible for prenatal diagnosis and should discuss the procedure with their doctor or a genetic counselor. Also, positive screening tests (triple screen, quadruple screen, first trimester screen) or abnormal findings on ultrasound are reasons for diagnostic testing.

Several types of prenatal diagnosis are available depending how far along the pregnancy is and what type of disorder is being tested. Chorionic villus sampling (CVS), amniocentesis, periumbilical blood sampling (PUBS), and fetoscopy are some examples of common procedures

used to obtain a sample from the baby for further testing.



Amniocentesis and chorionic villus sampling are both invasive procedures that carry a risk of miscarriage. Amniocentesis involves removing a sample of amniotic fluid from the uterine cavity by a syringe through the abdomen. The technique is generally performed at 15 to 20 weeks gestation. In CVS, the baby's cells are removed from an

area around the baby known as the chorion with a syringe inserted through the cervix or abdomen. CVS can be performed as early as nine week's gestation, but based on safety data, it is typically performed 10 to 13 weeks' gestation. This allows the results of any diagnostic assays to be available at an earlier stage of pregnancy. Both samples contain the baby's cells that can be grown in the laboratory for genetic testing.



Birth Defects/Congenital Abnormalities

A birth defect is a problem that happens while a baby is developing prior to birth. Congenital abnormalities refer to features or conditions that a baby is born with, as opposed to conditions that develop later in life. About one in 33 babies is born with a birth defect in the U.S.

A birth defect may cause physical or mental disabilities. It can affect almost any part of the body and can range from mild to severe. Some birth defects can be corrected by surgery or other medical treatments and children can lead normal lives. But some birth defects are very severe and can cause the baby to die. Some birth defects are easily detected, such as a club foot or cleft lip, but others such as heart defects or hearing loss may require x-rays and special tests.

Some of the most common birth defects to occur affect the heart. About one in every 200-300 babies is born with a heart defect. Depending on the type and severity of the heart defect, some can be corrected by surgery. Other common birth defects are called “neural tube” defects. Neural tube defects are due to abnormal development of the baby’s spine and brain. They affect about one in a 1,000 babies. These defects are often very severe, causing early death. Birth defects of the lip and the roof of the mouth are also common. They are referred to as cleft lip and cleft palate. They affect about one in 700-1,000 babies.

Many birth defects are caused by multiple factors—both genetic and environmental factors. For example, risk of neural tube defects is increased in families with a history of neural tube defects, but the risk can be reduced with folic acid supplementation. Uncontrolled medical conditions of the mother such as diabetes can also lead to birth defects such as heart defects. Some medicines such as Accutane are also known to cause birth defects.

To learn more about your risk of having a baby with a birth defect, please talk with your doctor or a genetic counselor. In particular, women should consult their doctor before becoming pregnant to begin multi-vitamin supplements containing folic acid, to get help with managing their medical conditions, decide which medications are safe to take, and to avoid exposure to alcohol, drugs, and smoking.

Newborn Screening (DC/Virginia/Maryland)

Each year, more than 95% of all children born in the United States (at least 4 million babies) are tested for a panel of diseases that, when detected and treated early, can lead to significant reduction in disease severity and possibly even prevention of the disease. About 3,000 newborns test positive for one of these severe disorders.

Within 48 hours of a child's birth, a sample of blood is obtained from a "heel stick," and the blood is analyzed for up to 35 treatable diseases, including phenylketonuria (PKU), sickle cell disease, and hypothyroidism. The sample, called a "blood spot," is tested at a state public health or other participating laboratory.

Newborn screening programs began in the U.S. in the 1960's with the work of Dr. Robert Guthrie, who developed a screening test for PKU. PKU is an inherited metabolic disease that is caused by a mutation in an enzyme responsible for metabolism of the amino acid phenylalanine. Children who are identified early can avoid foods with phenylalanine, thereby avoiding buildup of the amino acid which can lead to brain damage and mental retardation. When Dr. Guthrie also introduced a system for collection and transportation of blood samples on filter paper, cost effective wide scale genetic screening became possible.

In general, newborn screening is performed for conditions that, when detected and treated early, can lead to significant reduction in disease severity and possibly even prevention of the disease. The panel of newborn diseases screened for varies from state to state, and decisions for adding or deleting tests involve many complex social, ethical, and political issues. Usually, newborn population screening disorders are selected based on disease prevalence, detectability, treatment availability, outcome, and overall cost effectiveness. It is possible to screen for many disorders at birth and soon more will be possible. The American College of Medical Genetics and the March of Dimes recommends that all babies be screened for a core panel of 29 disorders. However, each state decides which disorders to include in its newborn screening panel.

OVERVIEW OF NEWBORN DISORDERS SCREENED IN DC, VA, AND MD

2,4-Dienoyl-CoA reductase deficiency—an autosomal recessive genetic disorder characterized by a deficiency of 2,4 Dienoyl-CoA Reductase necessary for the degradation of unsaturated fatty acids with an even number of double bonds. Symptoms include sepsis, hypotonia, decreased feeding, and intermittent vomiting. Low carnitine levels can be detected and respiratory acidosis may occur.

2-Methylbutryl-CoA dehydrogenase deficiency—an autosomal recessive genetic disorder resulting from a defect in the metabolism of the branched chain amino acid isoleucine. Symptoms include poor feeding, lethargy, hypoglycemia, and metabolic acidosis. Symptomatic patients display developmental delay, seizure disorders, and progressive muscle weakness in infancy and childhood.

3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)—a progressive autosomal recessive genetic disorder characterized by failure to thrive, hypotonia, muscle atrophy, seizures, mental retardation, and dermatological changes.



3-Methylglutaconyl-CoA hydratase deficiency—an autosomal recessive genetic disorder involving an enzyme in the metabolism of the amino acid leucine. Symptoms appear in a wide range of clinical severity and may include acute life-threatening cardiopulmonary symptoms soon after birth, psychomotor retardation, hypotonia, failure to thrive, microcephaly, seizures, and spasticity. Some patients may have acute episodes of vomiting, metabolic acidosis, and lethargy progressing to coma.

3-OH 3-CH₃ glutaric aciduria or 3-hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG)—an autosomal recessive genetic disorder. Symptoms may include metabolic acidosis, hypoglycemia, sensitivity to dietary leucine, carnitine deficiency, hepatomegaly, fever, somnolence, and coma. If this disorder is untreated, it is likely to result in death during childhood.

5-Oxoprolinuria (pyroglutamic aciduria)—a group of autosomal recessive genetic conditions including glutathione synthetase deficiency, glutamylcysteine synthetase deficiency, and 5-oxoprolinase deficiency caused by a deficiency of one (1) of three (3) enzymes in the gamma glutamyl cycle and characterized by metabolic acidosis, hemolytic anemia, electrolyte imbalance, and jaundice.

Argininemia—an autosomal recessive genetic condition that presents from two (2) months to four (4) years of age. Symptoms include progressive spastic paraplegia, failure to thrive, delayed milestones, hyperactivity, and irritability, with episodic vomiting, hyperammonemia, seizures, microcephaly, and cerebral atrophy resulting in mental retardation.

Argininosuccinic acidemia (ASA)—an autosomal recessive genetic disorder of the urea cycle. Symptoms are hyperammonemia accompanied by lack of appetite, vomiting, listlessness, seizures, and coma. Onset is usually at birth, but symptoms may not be noticeable for days or weeks. The build up in ASA, if too high, ultimately causes a build up in ammonia. Build up of ammonia is toxic and can cause brain damage. ASA is also characterized by excessive urinary excretion of argininosuccinic acid, epilepsy, ataxia, mental retardation, liver disease, and friable, tufted hair.

Beta-ketothiolase deficiency (BKT)—an autosomal recessive genetic disorder characterized by recurrent severe metabolic acidosis. Symptoms include increased plasma glycine level, metabolic acidosis, episodic ketosis, vomiting, dehydration, coma, and cardiomyopathy, with on average onset of five (5) to twenty-four (24) months.

Biotinidase deficiency (BIOT)—an autosomal recessive genetic disorder characterized by a lack of the enzyme biotinidase that can lead to seizures, developmental delay, eczema, and hearing loss that are treated with free biotin. Symptoms include hypotonia, ataxia, alopecia, seborrheic dermatitis, and optic nerve atrophy. Metabolic acidosis can result in coma and death.

Carbamoylphosphate synthetase deficiency (CPS def.)—an autosomal recessive genetic condition that presents within seventy-two (72) hours with symptoms of lethargy, vomiting, hypothermia, respiratory alkalosis, and seizures progressing to coma. Survivors of the newborn period have recurrent episodes of hyperammonemia associated with viral infections or increased dietary protein intake. Some patients have a later onset with less severe symptoms.

Carnitine uptake defect (CUD)—a class of autosomal recessive genetic disorders characterized by hypoketotic hypoglycemia, seizures, vomiting, lethargy progressing to coma, cardiomyopathy, and hepatomegaly. This disorder includes carnitine palmitoyl transferase deficiency type I and carnitine acylcarnitine translocase deficiency.

Citrullinemia (CITR)—an autosomal recessive genetic disorder characterized by a deficiency of argininosuccinic acid synthetase, hyperammonemia accompanied by lack of appetite, vomiting, listlessness, seizures, and coma. Onset is usually at birth, but symptoms may not be noticeable for days or weeks. When left untreated, brain damage, coma, and death will occur.

Congenital adrenal hyperplasia (CAH)—a set of inherited disorders that occurs in both males and females as a result of the excess production of male hormones and an underproduction of the enzyme 21-hydroxylase, severe acne, excess facial or body hair, early development of pubic hair, receding scalp hairline, menstrual disturbances in females, and infertility in males and females in its mild form and ambiguous genitalia in newborn girls and salt and hormonal imbalances in girls and boys in more severe forms. If not treated, CAH can cause heart failure and death within a few days from birth. CAH cannot be cured; however, it can be effectively treated.

Congenital hypothyroidism—is caused by a biochemical defect that reduces thyroid hormone secretion and consequently causes a deficiency in the circulating hormone thyroxine. This deficiency in thyroxine can result from the absence of a thyroid gland, incomplete gland development, thyroid inflammation resulting from autoimmune disorders, hereditary defects in thyroid hormone synthesis or an inability to synthesize thyroxine because of dietary iodine deficiency. Among infants and children, untreated hypothyroidism is usually characterized by slowed growth and development, decreased mental capacity, and a characteristic facial appearance. Mental retardation can be prevented, and these patients can be expected to develop normally if detected early through screening and treated with hormone replacement therapy.

Cystic fibrosis (CF)—an autosomal recessive genetic disorder characterized by progressive chronic damage to the respiratory system, chronic digestive system problems, and can affect other organs. CF affects mucus-producing glands producing thick mucus that can obstruct air passages in the lungs, affects sweat and salivary glands, and blocks enzymes secreted by the pancreatic duct. Cystic fibrosis can cause lung disease, failure to grow, clubbed fingers and toes, muscular weakness, and visual impairment.

Galactosemia—a rare inherited disorder that causes a certain kind of sugar to build up in the body. This sugar is called galactose. An infant with galactosemia is missing one of the enzymes that converts galactose into glucose. Most galactose comes from milk sugar in a form called lactose. Galactose builds up in the body and can cause damage to the brain, eyes, liver, and kidneys. Damage can be stopped by eliminating milk, breast milk, and other dairy products from the diet.

Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD)—G6PD is an inherited condition causing little or no G6PD in the red blood cells. G6PD deficiency does not cause growth problems or change ability to learn or participate in normal activities. Anemia can happen when a person with G6PD deficiency takes certain medicines or eats certain foods. The effects of G6PD can be avoided if certain foods and medicines that might change red blood cells are not consumed. After initial screening, additional blood studies are necessary to confirm the diagnosis between six to 12 months of age.



Glutaric acidemia type I (GA-I)—an autosomal recessive enzyme deficiency genetic disorder characterized by hypoglycemia, dystonia, and dyskinesia. After a period of apparently normal development, the disorder may appear suddenly and present as vomiting, metabolic acidosis, hypotonia, and central nervous system degeneration. It is not yet known how or why Glutaric acid causes brain damage, yet damage occurs when a crisis causes an acidic environment in the blood created by excess protein byproducts. Crises can be provoked by common childhood illnesses such as colds, flu, ear infections, stomach virus, fever, etc.

Hemoglobinopathy—a class of disorders caused by the presence of abnormal hemoglobin production in the blood, due to genetic variations that can result in production of hemoglobin with different structures or thalassemias and reduction in the amount of normal hemoglobin produced. This term includes the following hemoglobin variants: HbS, HbC, HbE, HbD, and alpha/beta thalassemias.

Homocystinuria—this metabolic disorder results from a deficiency of one of several enzymes needed by the brain for normal development. If untreated, it can lead to dislocated lenses of the eyes, mental retardation, skeletal abnormalities, and abnormal blood clotting. A special diet combined with dietary supplements may help prevent most of these problems.

Hyperammonemia, hyperornithinemia, homocitrullinemia syndrome (HHH)—an autosomal recessive genetic disorder that may present at birth or in later childhood. Newborns on high protein formulas or foods may vomit with feeding, refuse to eat, become lethargic, or develop hyperammonemic coma. Patients gravitate to diets low in milk and meat during childhood.

Hyperornithine with gyrate deficiency—an autosomal recessive genetic disorder characterized by slow progressive vision loss leading to blindness. Myopia and decreased night vision appear as early symptoms in the patient's teens and early twenties.

Isobutyryl-CoA dehydrogenase deficiency—an autosomal recessive genetic disorder involving the inability to metabolize valine with a highly variable presentation.

Isovaleric acidemia (IVA)—an autosomal recessive genetic disorder caused by a defect in the breakdown of the molecule isovaleryl-CoA that presents in acute or intermittent episodes. IVA can present as an acute episode of illness during the first few weeks of a newborn's life, or it may present chronically with intermittent episodes of illness throughout life. Both forms of IVA are caused by the same biochemical defect. Infants who survive an acute neonatal episode will go on to exhibit the chronic intermittent form. Symptoms of acute IVA are attacks of vomiting, lack of appetite, and listlessness; lethargy, neuromuscular irritability, and hypothermia are other characteristics. Episodes can be triggered by upper respiratory infections or by excessive consumption of high-protein foods. Early detection through newborn screening and good treatment of IVA generally leads to normal development. Permanent neurologic damage can occur if an acute episode is not prevented or is misdiagnosed.

Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHADD)—an autosomal recessive genetic disorder characterized by failure to oxidize fatty acids due to a missing or malfunctioning enzyme. Symptoms include hypoglycemia, lethargy, failure to thrive, cardiomyopathy, and developmental delay. Early identification and treatment can prevent life-threatening episodes.

Malonic aciduria—an autosomal recessive genetic disorder caused by a deficiency of malonyl-CoA decarboxylase (MCD) with a variable presentation ranging from acute neonatal onset to later in childhood. Symptoms include developmental delay, seizures, hypotonia, diarrhea, vomiting, metabolic acidosis, hypoglycemia, and ketosis.

Maple syrup urine disease (MSUD)—babies with MSUD are missing an enzyme needed to process three amino acids that are essential for the body's normal growth. When these are not processed properly, they can build up in the body, causing the urine to smell like maple syrup or sweet, burnt sugar. These babies usually have little appetite and are extremely irritable. If not detected and treated early, MSUD can cause mental retardation and physical disability. Protein foods containing those amino acids can prevent these outcomes.

Medium chain acyl-CoA dehydrogenase deficiency (MCADD)—an autosomal recessive genetic disorder characterized by inability to convert fat to energy. Fasting is not tolerated well in people with MCADD. Symptoms generally begin in infancy or early childhood, however, there are some with no apparent symptoms at birth. Low blood sugar, seizures, brain damage, cardiac arrest, and serious illness can occur very quickly in children who are not feeding well. Some experience recurrent episodes of metabolic acidosis, hypoglycemia, lethargy, and coma. If not detected and treated appropriately, MCADD can result in mental retardation and death. Those treated are expected to have normal life expectancy.

Methylmalonic acidemia—one of two variations of an autosomal recessive genetic disorder caused by an enzymatic defect in the oxidation of amino acids characterized by lethargy, failure to thrive, vomiting, dehydration, respiratory distress, hypotonia, and hepatomegaly. Acute episodes may include drowsiness, coma, and seizures, with subsequent developmental delays. This disorder includes methylmalonic acidemia CblA, methylmalonic acidemia CblB, and methylmalonic acidemia mutase deficiency.

Multiple acyl-CoA dehydrogenase deficiency (MADD)—an autosomal recessive genetic disorder, also known as glutaric acidemia type II, with three (3) different clinical presentations. Symptoms include hypotonia, hepatomegaly, severe nonketotic hypoglycemia, metabolic acidosis, and variable body odor of sweaty feet.

Multiple carboxylase deficiency (MCD)—an autosomal recessive genetic disorder characterized by a biotin deficiency. Symptoms include seizures, developmental delay, eczema, and hearing loss. Other symptoms are immune system impairment, skin rashes, hair loss and mental retardation that are treatable with oral biotin supplements.

Neonatal carnitine palmitoyl transferase deficiency-type II (CPT-II)—an autosomal recessive genetic disorder of mitochondrial fatty acid oxidation that presents in three (3) forms. The classic form has adult onset of exercise-induced muscle weakness, often with rhabdomyolysis and myoglobinuria that may be associated with renal failure. A second form that is often fatal between three (3) and eighteen (18) months of age with symptoms of hepatomegaly, non-ketotic hypoglycemia, cardiomyopathy, hypotonia, and muscle weakness. A severe form presents in newborns with non-ketotic hypoglycemia, cardiomyopathy, hypotonia, muscle weakness, and renal dysgenesis in some patients.



Phenylketonuria (PKU)—an autosomal recessive disorder that affects the way the body is able to use a part of all food proteins called phenylalanine which is an amino acid. The body uses amino acids as building blocks for body growth and repair. Unless found and treated early, PKU can cause the body to become overloaded with phenylalanine which can prevent the brain from developing as it should leading to severe mental retardation and other problems. When this disorder is detected early, feeding an infant a special formula low in phenylalanine can prevent mental retardation. A low-phenylalanine diet will need to be followed throughout childhood and adolescence and perhaps into adult life.

Propionic acidemia (PROP)—an autosomal recessive genetic disorder characterized by protein intolerance, vomiting, failure to thrive, lethargy, and profound metabolic acidosis. If not treated early, brain damage, coma, seizures and death can occur.

Short chain acyl-CoA dehydrogenase deficiency (SCAD)—an autosomal recessive genetic disorder of fatty acid beta oxidation with a usual clinical onset between the second (2nd) month and second (2nd) year of life, with some presenting within a few days of birth and some in adulthood. Symptoms include hypotonia, progressive muscle weakness, developmental delay, and seizures. Symptoms worsen with seemingly innocuous illness that may lead to lethargy, coma, apnea, cardiopulmonary arrest, or sudden unexplained death.

Short chain hydroxy acyl-CoA dehydrogenase deficiency (SCHAD)—an autosomal recessive genetic disorder of mitochondrial fatty acid beta oxidation for which a complete spectrum of presentation has not been defined. Most patients have hypoglycemia as the major symptom along with seizures, neurologic sequelae or death as the outcome. Several present in the first days or months of life with hypoglycemic seizures secondary to hyperinsulinism. Some patients present after one (1) year with acute onset of vomiting, lethargy, and hyponatremic seizures.

Trifunctional protein deficiency (TFP)—an autosomal recessive mitochondrial fatty acid oxidation genetic disorder characterized by an inability to break down long-chain fatty acids into an energy source. Metabolic crises can occur when fasting, as well as hypoglycemia, lethargy, hypotonia, myopathy, failure to thrive, cardiomyopathy, and neuropathy. Severe untreated cases may present as SIDS.

Tyrosinemia type I (TYRO-I)—an autosomal recessive genetic disorder that causes severe liver disease in infancy. Affected persons develop cirrhosis of the liver and eventually require liver transplantation. The most severe form causes symptoms within the first months of life. These infants experience poor weight gain, enlarged liver and spleen, swelling of the legs, increased tendency of bleeding. Even with therapy death frequently occurs within six (6) to nine (9) months of life for those with the severe form. Children with a less severe form also suffer from enlargement of the liver, spleen, poor weight gain, vomiting and diarrhea.

Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)—an autosomal recessive genetic disorder in which the body cannot oxidize fatty acids because of a missing or mal-functioning enzyme. Symptoms include hypoketotic hypoglycemia, hepatocellular disease, and cardiomyopathy. Fatal infantile encephalopathy may be the only indication of the condition.

