Childbirth International®

Newborn Screening Tests

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Biotinidase Deficiency

Biotinidase Fast Facts	
Incidence	1 in 60,000-126,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	The highest incidence is seen in Caucasians, particularly French Canadians. There have been several cases of African-Americans, Hispanic and Japanese racial groups.

Description of condition

Biotinidase deficiency is an inherited metabolic disorder in which the body cannot process the vitamin biotin normally. It is a treatable condition. Biotinidase is the enzyme in your body that separates the biotin from proteins in the food you eat. This biotin can then be used in your body. Biotinidase also recycles biotin so you can use it over and over again and you do not need to consume large amounts in your diet. Your body uses biotin to help metabolize fats, carbohydrates and proteins. If there is not enough biotinidase the result is for harmful byproducts to build up in the body and cause damage.

Symptoms

Common symptoms that result from untreated biotinidase deficiency are listed in below:

Affecting more than 50% of patients

- Hair loss
- Developmental delays
- Poor muscle tone
- Ketolactic aciduria
- Seizures (fits)
- Skin rash & skin infection

Affecting 25-50% of patients

- Poor coordination
- Conjunctivitis
- Hearing loss
- Drowsiness
- Hyperammonemia
- Breathing problems
- Eye problems

Affecting 10-25% of patients

- Coma
- Feeding difficulties
- Vomiting & diarrhea
- Fungal infections

Affecting less than 10% of patients

- Enlarged liver
- Speech problems
- Enlarged spleen

Symptoms usually appear between three and six months of age, but may start as early as one week of age or as late as ten years.

Treatment

Treatment will be given in the form of biotin supplements. If symptoms appear before treatment is started the child will generally improve and many symptoms will reverse. If treatment is given before symptoms appear the child does not usually develop any symptoms. The treatment would be continued for life. The optimal dosage of biotin is not known nor are any side effects of treatment known. The cost of treatment is low (approx US$25 to US$100 per year).

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the activity of biotinidase activity in the sample. The optimal timing for testing is not known although the deficiency has been seen in cord blood. It is therefore believed that any specimen taken after the birth is adequate. The false-negative and false-positive rates are not known although thought to be rare. Feeding the baby does not affect the results of this test.

Maple Syrup Urine Disease

Maple Syrup Urine Disease Fast Facts	
Incidence	1 in 170,000-400,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	The highest rate appears in the Mennonite population (1 in 760 babies). The incidence may be higher in African-American and Asian populations.

Description of condition

Maple Syrup Urine Disease is an inherited metabolic disorder, which causes mental retardation, physical disabilities and death if it is not treated. The name of the disorder comes from the smell that the urine has when a child is affected by this disease -- a sweet, burnt sugar, or maple syrup smell. The disorder affects the way the body metabolizes three amino acids in proteins -- leucine, isoleucine, and valine. The amino acids build up in the blood and cause a toxicity that then affects the way the brain functions.

Symptoms

Symptoms usually appear in the first week of life and include a lack of appetite, irritability, and the characteristic smell of the urine. Within days these babies lose their sucking reflex, have a high-pitched cry, and become floppy with periods of rigidity. If the condition is not diagnosed and treated the baby will rapidly progress to seizures (fits), coma, and eventually death. The earlier a baby is diagnosed and treated the less risk of permanent damage.

Treatment

The sooner treatment is started the better the outcomes for the baby. Treatment involves providing a special diet and close monitoring of protein intake. The diet is a synthetic formula, which provides nutrients and amino acids excluding the three that are causing the problems. These are added to the diet in controlled amounts to ensure normal growth and healthy development without exceeding the amounts the child can tolerate.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of leucine in the sample. As symptoms occur early the results should be available within the first two weeks of life so dietary changes can be made as quickly as possible if the baby has the condition. Babies with the condition have been found to have increased leucine levels from 4 to 14 hours after their birth regardless of how much protein they have consumed. However, leucine screening may not be sensitive if the sample is taken before 12 hours of age with optimum detection occurring at 24-48 hours of age. The false-negative and false-positive rates are not known although thought to be low and dependent on the age that the sample is taken at.

Congenital Adrenal Hyperplasia

Congenital Adrenal Hyperplasia Fast Facts	
Incidence	1 in 12,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	Caucasian incidence is 1 in 12,880, Japanese is 1 in 15,000, Yupik Eskimo is 1 in 680 and Italian is 1 in 5,500 to 1 in 10,000.

Description of the condition

Congenital Adrenal Hyperplasia (CAH) is a defect of the adrenal glands that affects the way the corticosteroids are produced. In its most common form, CAH is caused by a deficiency of the enzyme 21 hydroxylase -- an enzyme the body uses to produce cortisol and aldosterone. CAH results in a lack of cortisol and aldosterone, and an excess of androgen. Cortisol is used when the body responds to illness or injury by altering the blood sugar levels and the blood pressure. Aldosterone maintains the correct amount of salt in your body and affects the amount of urine excreted. Androgen is a male sex hormone and affects sexual development. In baby girls that are affected by CAH their external genitalia can appear more masculine than is normal. Their internal organs (vagina, uterus, ovaries) are normal.

Symptoms

Children with CAH are diagnosed as 'salt-losers' (80%) or 'non salt-losers' (20%). In girls the condition is usually diagnosed at birth since the clitoris is enlarged and the labia may be partially fused. In non salt-loser boys the condition may not be apparent until they are two-three years of age when their growth pattern appears to be far in advance of other children. In salt-losers, the enzyme deficiency is more severe and can result in excessive amounts of salt being lost in the urine. If this is not controlled, the following symptoms will appear: acute dehydration, very low blood pressure, nausea and repetitive vomiting, low sodium, chloride and sugar levels in the blood, increased blood potassium levels.

Treatment

There are no special dietary measures necessary for CAH children. The corticosteroids -- cortisol and aldosterone -- that they are missing are replaced in a tablet form. Surgery may be an option for girls as they grow older to restore the clitoris to a more normal appearance and to increase the vaginal opening. If undiagnosed a salt-losing condition can lead to severe illness and potentially death if an adrenal crisis occurs, particularly in a young baby. Due to the medication that is necessary, there may be concerns of height and weight. This is particularly the case for teenagers.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of 17-hydroxyprogesterone (17-OHP). Levels may be determined from cord blood, but the levels may be physiologically high at this time and not indicative of a problem. Immediately after the birth the levels of 17-OHP are usually elevated and then rapidly decline to normal levels by one-three weeks of age. Therefore if testing is done before 48 hours of age the false-positive rate may be increased. Premature babies may also have higher false-positive test results. The false-negative rate is low with 95% of 21-hydroxylase deficiency cases being detected. If testing is done before 24 hours of age, 3% of salt wasters may be missed. Feeding the baby does not affect the results of the test.

Congenital Hypothyroidism

Congenital Hypothyroidism Fast Facts	
Incidence	1 in 3,000-7,000 babies
Inheritance	Usually a non-genetic cause
Sex Ratio	2-3 Female: 1 Male
Racial & Ethnic Variability	Low incidence in African-American populations, more common in Hispanic populations (1 in 2,700) and Native Americans (1 in 700).

Description of the condition

Congenital hypothyroidism is a condition that occurs from birth. It is usually caused by a missing thyroid gland or a thyroid gland that is in an abnormal location. Not enough thyroid hormone ---- thyroxine or T4 -- is produced. This can result in abnormal growth and development and may also lead to poor mental development. There are a small number of children who have a temporary or transient congenital hypothyroidism for a period of time after their birth. The tests are not able to determine which babies have the transient condition and which have a lifetime condition so all will be offered treatment.

Symptoms

Many babies with this condition appear normal at birth, which is why the screening tests are considered to be important. Symptoms may include a puffy face and enlarged or swollen tongue, cold hands and feet, constipation that does not resolve, lethargy and tiredness, poor growth, poor feeding habits, a hoarse cry, prolonged jaundice, mottled and dry skin, a distended abdomen, umbilical hernia and poor muscle tone.

Treatment

To confirm the diagnosis the doctor may arrange for an x-ray of the baby's legs to be done. They will look at the ends of the bones, which would appear immature, to confirm the condition. A thyroid scan would also be done to identify where the thyroid gland is located or if in fact it is missing altogether. Once the diagnosis is confirmed the baby would be prescribed a tablet containing L-thyroxine (a synthetic version of the hormone). Parents should be advised not to give the baby soy milk since this can interfere with the absorption of the drug.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of T4 or TSH, or both. If the screening test is done within the first 24-48 hours after the birth there may be an increase in TSH and T4 levels. TSH levels increase significantly shortly after the birth and then gradually return to normal levels within 72 hours. If the sample is taken within this period there will be an increase in the false-positive rate. Premature babies may also show false readings. Approximately 10-15% of cases of congenital hypothyroidism will be missed on the first screening test and will only be identified at a second screening carried out between 2 to 6 weeks of age. The false-positive rate is dependent on whether the T4 test is done on its own or together with a TSH test. Feeding the baby does not affect the outcome of this test.

Cystic Fibrosis

Cystic Fibrosis Fast Facts	
Incidence	1 in 25 people are carriers of the mutated gene but are unaffected. If both parents are carriers the baby has a 1 in 4 chance of developing the disorder. Cystic Fibrosis affects about 1 in 2,500-4,500 babies.
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	Caucasians have the highest incidence of 1 in 3,300. Hispanics have a lower incidence of 1 in 8,000, Africans 1 in 15,000 and 1 in 32,000.

Description of the condition

Cystic Fibrosis is a genetic condition where a protein is missing from the cells of the lungs, pancreas and other organs. The cell is unable to move chloride ions in and out of the cell, resulting in a buildup of thick mucus and bacterial infections in the lungs. The disease would rarely cause any mental developmental problems. 10% of very young babies develop small bowel obstruction, which may lead to serious illness or death. There is a 13% mortality rate amongst newborn babies and infants resulting from malabsorption and malnutrition. The average life span of people with cystic fibrosis is mid-late 20's.

Symptoms

Symptoms include a persistent cough, poor weight gain, repeated chest infections and prolonged diarrhea. In addition to lung problems, people with cystic fibrosis have problems with digestion and malabsorption, which may result in malnutrition. One in ten babies born with cystic fibrosis will become ill within the first few days of life due to a bowel obstruction called meconium ileus. The meconium is so thick that it blocks the bowel and cannot pass through. An urgent operation is needed to clear the blockage.

Treatment

Treatment consists of physiotherapy to clear lung secretions, medication to help keep the lungs clear, enzyme medication, nutritional and mineral supplements.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of trypsin in the blood. The timing of the test is not critical, provided it is done in the first six weeks. The false positive rate for this test is 3-5%. Follow up testing of those babies that show positive should be done after 21 days to ensure no further false-positive results and before 60 days to ensure no false-negative results.

Phenylketonuria

Phenylketonuria Fast Facts	
Incidence	1 in 10,000-25,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	There is considerable variability in different racial and ethnic groups. Caucasians: 1 in 6,000 in Ireland & Scotland 1 in 8,000-10,000 in Germany 1 in 16,000 Italy 1 in 6,000 among Yemenite Jews 1 in 60000 among Ashkenazi Jews Less common in African-American and Asian families: China and Japan, 1 in 60,000.

Description of the condition

Phenylketonuria occurs when a baby is missing the enzyme necessary to break down phenylalanine -- an amino acid found in proteins. The phenylalanine builds up in the blood to toxic levels and can lead to severe mental retardation, seizures and autistic-like behavior.

Symptoms

Symptoms include hyperactivity, spasticity, seizures (fits), eczema, and autistic-like behavior. The built up toxins can cause an unusual mousey odor. Without screening the condition is unlikely to be identified before 6 months of age and then only after mental retardation has occurred.

Treatment

Without treatment 95% of affected individuals will develop severe mental retardation. Once diagnosis is confirmed, treatment should begin as soon as possible to prevent symptoms developing. The main treatment is restriction of dietary phenylalanine and ensuring there is no aspartame in the diet (artificial sweetener). This amino acid is necessary for healthy growth so its intake must be carefully controlled. Other essential amino acids, vitamins and iron can be given in special dietary supplements.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of tyrosine. Phenylalanine is usually converted to tyrosine when the condition does not exist and it is the levels of tyrosine that are checked in screening tests. Phenylalanine levels rise gradually after birth for the first 10 hours and return to the same levels at 24 hours of age as they were at one hour of age. If the test is carried out before 24 hours of age there will be a significantly high number of false positive rates. One study found that the false positive rate was 1.1% at 24 hours compared to 0.11 between 24-48 hours. The AAP recommend screening after 72 hours and before 7 days of age to maximize detection. It is believed that screening before 2 hours of age would have a detection rate of 84%, 97.8% between 2-48 hours, and 99.7% after 48 hours. The false negative rate appears to be 30% in babies tested in the first 12 hours of life.

Galactosemia

Galactosemia Fast Facts	
Incidence	1 in 60,000-80,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	None

Description of the condition

Galactosemia is an inherited disorder where there is a deficiency of one of three enzymes that process galactose. Galactose comes from lactose products such as breastmilk or formula milk. A baby with this condition is unable to digest the sugar found in milk. Untreated galactosemia leads to failure to thrive, vomiting, liver disease, cataracts, and mental retardation. This condition is usually fatal if untreated.

Symptoms

Symptoms generally occur within the first two weeks of life and include jaundice, vomiting, lethargy, enlarged liver and spleen, cataracts, and failure to thrive.

Treatment

If the condition is diagnosed early enough the diet can be changed to prevent the baby have any galactose and the outcomes is considered good. Babies who begin treatment before 10 days of age are likely to have a normal IQ. The galactose free diet must be continued throughout life. Despite treatment, 80% of females with galactosemia will have damage to their ovaries and speech or developmental delays are common.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for the levels of the deficient enzyme. False positive and false negative rates tend to be low. There is no need for the baby to have ingested milk before this test is done since it is the lack of the enzyme that is being tested rather than the buildup of galactose.

Homocystinuria

Homocystinuria Fast Facts	
Incidence	1 in 50,000-150,000 babies
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	The highest incidence appears to be in Caucasians and the lowest incidence in Japan.

Description of the condition

Homocystinuria is caused by a baby being deficient in the enzyme cystathionine beta-synthase. This enzyme metabolizes the amino acids homocysteine and methionine, found in proteins. If they are not metabolized, the levels of these amino acids build up in the blood and lead to mental retardation, seizures (fits) and usually death. Death is most commonly due to venous and arterial thromboses. If untreated, approximately 50% affected individuals will die by 25 years of age. Developmental delays are present in 65% to 80% of untreated individuals.

Symptoms

There are no symptoms in the newborn period. As the child grows older symptoms may occur including dislocated ocular (eye) lenses, stroke, intellectual delays, seizures, arachnodactyly, joint stiffness, osteoporosis, liver damage, connective tissue damage, psychiatric and emotional disorders. Children with this condition are more likely to have fair hair and skin.

Treatment

Treatment appears to reduce the risk of thrombotic events, the incidence of seizures and mental retardation. About 40% of the individuals with this disorder respond well to daily supplementation of high doses of vitamin B6. For the remainder, a diet that restricts methionine intake is prescribed. Supplementary medical foods are taken to provide necessary amino acids, vitamins, and minerals. Antiplatelet drugs such as aspirin may help prevent thromboembolic events.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for elevated levels of methionine. There is little increase in methionine in the first three days after birth due to the low protein intake. The AAP recommend that this condition be tested for at 2 to 4 weeks of age to be most effective. The false negative rate increases the earlier the test is carried out. The false positive rate is one true positive result for every 20 false positive results. Methionine levels can be temporarily elevated with no medical problems and is more common in premature babies. It can also be indicative of a liver problem.

Sickle Cell Disease & Sickle Cell Trait

Sickle Cell Disease & Sickle Cell Trait Fast Facts	
Incidence	Incidence is highly dependent on racial group
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	African-Americans: 1 in 375 Caucasians: 1 in 58,000 Hispanics from Eastern states: 1 in 1,100 Hispanics from Western states: 1 in 32,000 Asians: 1 in 11,500 Native Americans: 1 in 2,700

Description of the condition

These conditions are caused by abnormalities in the hemoglobin -- the red part of the red blood cell. With Sickle Cell Trait a person has both hemoglobin A (normal hemoglobin) and hemoglobin S. It rarely causes any significant health problems unless the person experiences low oxygen pressure as in an unpressurized airplane. A person with Sickle Cell Disease only has hemoglobin S. As the hemoglobin releases the oxygen to tissues around the body the cell changes to a sickle shape and it can become difficult for the cell to then move through the blood vessels.

Symptoms

Sickle cell disease is caused by abnormalities in the β (beta) globin chain of adult hemoglobin. Newborn babies have mostly fetal hemoglobin initially and so symptoms may not appear initially.

Treatment

The AAP recommend that all infants diagnosed should be given penicillin prophylaxis before 2 months of age to reduce the incidence of sepsis.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for abnormalities in the shape of the blood cells. The sample can be taken any time after birth and is not affected by the baby feeding. False positive rates are unknown, false negative rates are 1 in 3,000.

Thalassemia

Thalassemia Fast Facts	
Incidence	Incidence is highly dependent on racial group
Inheritance	Autosomal recessive
Sex Ratio	Female=Male
Racial & Ethnic Variability	Cypriot: 1 in 7 South Italian: 1 in 10 Turkish & Asian: 1 in 20 Indian: 1 in 7-20 Pakistani: 1 in 25 Greek: 1 in 12 English Caucasian: 1 in 1,100

Description of the condition

There are several different types of thalassemia: thalassemia trait, thalassemia intermedia and thalassemia major. If the person has thalassemia trait they are a carrier of the disease but not affected by it. In this handout we will discuss thalassemia major and its effects.

Thal-major are caused by abnormalities in the amount of hemoglobin produced -- the red part of the red blood cell. Because the affected person has a reduced amount of hemoglobin they are at increased risk of anemia.

Symptoms

During pregnancy the baby has fetal hemoglobin so is born appearing healthy. During the first six months of life their hemoglobin is gradually replaced with adult hemoglobin. They cannot make enough hemoglobin so become anemic. They tend to be very pale, have an enlarged spleen and become ill before two years of age.

As the anemia worsens the child's growth slows, the spleen gets bigger, and the stomach gets larger. The bone marrow attempts to make more red blood cells but they do not contain enough hemoglobin, and most die without ever leaving the bone marrow. The bones become weaker and change in shape. The cheekbones and the bones of the child's forehead bulge. Eventually the spleen begins to destroy red blood cells and progressively destroys other blood components as well.

Treatment

Thal-major is treated one of several ways. The traditional treatment is regular red-cell transfusions and medication to remove excess iron from the blood. If the spleen has become overactive it may be removed. If a donor is available the bone marrow transplant can be performed which provides a cure for the condition. Although no special diet is necessary it is recommended that iron rich foods be avoided to reduce work on the spleen and liver.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for abnormalities in the shape of the blood cells. The sample can be taken any time after birth and is not affected by the baby feeding. False positive rates are unknown, false negative rates are 1 in 3,000.

Tyrosinemia

Tyrosinemia Fast Facts	
Incidence	1 in 100,000 babies
Inheritance	Autosomal recessive in Type II and I. The inherited cause is unknown for neonatal tyrosinemia.
Sex Ratio	Female=Male
Racial & Ethnic Variability	Neonatal tyrosinemia is more commonly found in premature babies: 1 in 250 babies weighing less than 2.5 kg and 1 in 500 babies weighing more than 2.5 kg. The highest incidence is found amongst Canadian Inuit when they do not breastfeed their infants: 1 in 16. Type I tyrosinemia has an incidence of 1 in 120,000 in northern Europe with the highest incidence in the French-Canadian population of Quebec (1 in 12,500). The incidence of Type II is not known.

Description of the condition

This is an inherited condition where the baby is lacking the enzyme necessary to metabolize the tyrosine in proteins. There are three different types of Tyrosinemia -- all caused by disorders of tyrosine metabolism. Neonatal tyrosinemia is thought to be caused by a deficiency of deficiency of p-hydroxyphenylpyruvate. Tyrosinemia Type I is caused by a deficiency of fumarylacetoacetate hydrolase and results in severe liver and kidney failure and eventually death. Tyrosinemia Type II is caused by a deficiency of tyrosine aminotransferase. This results in eye and skin lesions, and neurological problems.

Symptoms

Symptoms depend on whether or not the baby has the acute or chronic form of the disease. Babies with the acute condition have poor weight gain, an enlarged liver and spleen, distended abdomen, swollen legs, and an increased tendency to bleed, particularly nose bleeds. There may be a cabbage like odor on the child. Despite therapy, death from liver failure usually occurs between three -- nine months of age unless a liver transplantation is performed. In the chronic form of the disease the onset is more gradual and the symptoms less severe. These children though will also eventually need a liver transplant.

Treatment

Dietary restriction of the amino acids phenylalanine, methionine and tyrosine should be followed to keep affected children as healthy. Eventually though the affected person will develop cirrhosis and will need a liver transplant.

Screening Test

The condition can be detected through infant screening tests. This involves taking a blood sample and testing it for elevated levels of tyrosine.