



**Nevada Newborn Screening Program
2009 Biennial Report
(2003-2007 Data)**

**Department of Health and Human Services
Nevada State Health Division
Bureau of Health Statistics, Planning, and Emergency Response
Office of Health Statistics and Surveillance**

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2009 Biennial Report**

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Nevada

Nevada Demographics

Nevada Demographics:

Nevada is the seventh largest state (geographically) in the nation and is comprised of 17 counties spread across 110,540 square miles. Nevada is a frontier state with a 2008 population estimate of 2.8 million (Nevada State Demographer) and is traditionally divided into three regions: Clark County (70.7% of the population), Washoe County (15.2% of the population), and the balance of the State (14.1% of the population). Approximately 83% of Nevada's land area is under the jurisdiction of the Bureau of Land Management; the remaining 17% is under private ownership or state and local jurisdiction. Nevada has 13 Indian colonies or reservations statewide and six military bases located in five counties.

Nevada was the fastest growing state in the nation for 19 straight years until surpassed by Arizona in 2006. In the ten-year period from 1998 to 2007 it is estimated that Nevada had a 46% increase in population, Clark County a 55% increase, Washoe County a 27% increase, and the balance of the State a 26% increase. Nevada's population growth is also reflected in birth rates which increased 44% in the ten-year period from 1998 to 2007.

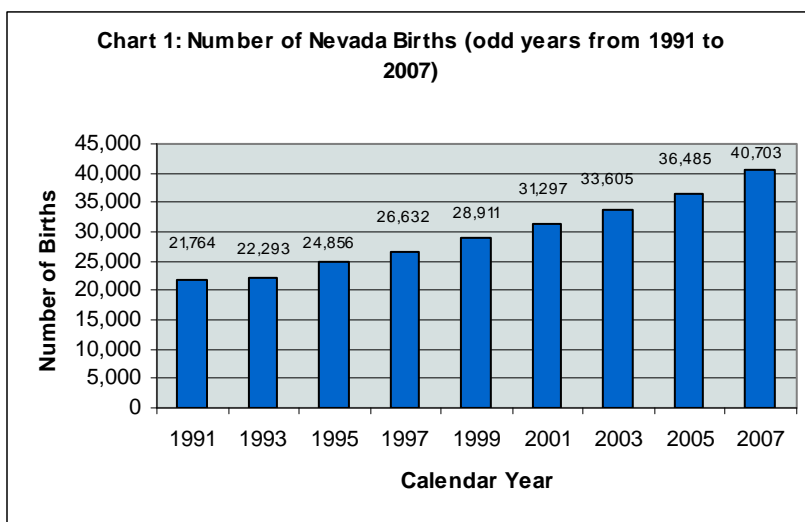
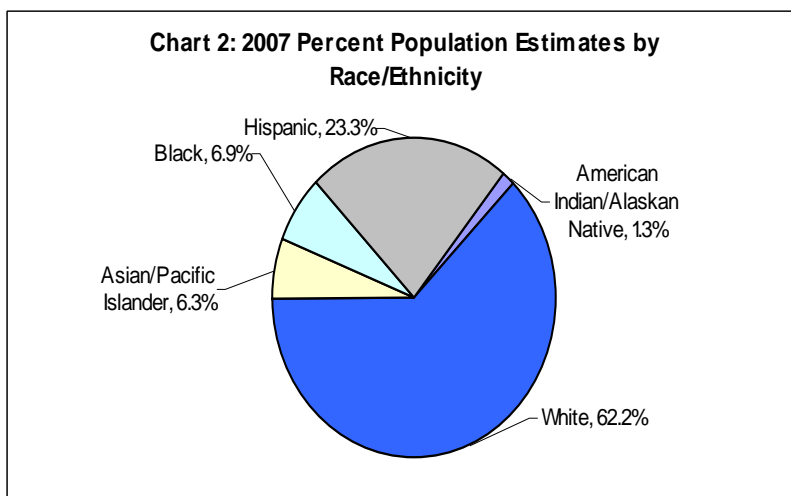


Chart 1 details the increase in Nevada birth rates from 1991 to 2007 (2007 estimates are preliminary). With the rapid increase in residents, Nevada's population is becoming more racially diverse.



The American Indian, Eskimo, or Aleut population increased 39% in the ten-year period from 1998 to 2007, the Asian/Pacific Islander population increased 80%, the African American population 48%, Hispanics 86% and whites 33%. The 2007 race/ethnicity breakdown estimate for Nevada is detailed in Chart 2.

Newborn Screening (NBS) for Inborn Errors of Metabolism and Inherited Disorders

Goal of Newborn Screening

The goal of newborn screening is the early identification of children at risk for selected metabolic and inherited disorders so treatment may commence before permanent neurological and developmental damage has occurred; thus, improving outcomes for the newborn. Newborn screening is recognized internationally as an essential, preventative public health program for early identification of disorders in newborns that can effect their long term health. Early identification and treatment of certain genetic, metabolic, or infectious congenital disorders can lead to significant reductions in death, disease, and associated disabilities.

History of Newborn Screening

In 1934, a Norwegian Doctor, Asbjorn Folling, studied two mentally handicapped children. He detected an unusual smell about them and being interested in diabetes he checked for the presence of ketones in their urine. When the sample turned blue-green instead of purple, he further determined that the color difference was due to phenylpyruvic acid. After finding high levels of phenylalanine in the children, he theorized that they could not metabolize phenylalanine. He suggested limiting protein intake, thus reducing amounts of phenylalanine in the diet, as a possible way to treat phenylketonuria, (PKU). In 1937, Dr. George Jarvis, the first doctor from the United States to study PKU, discovered that the normal breakdown of phenylketone to tyrosine did not take place in PKU patients because the gene containing the code for this enzyme had mutated.

In 1951, after persistent inquiries from a mother of a 17-month old girl with PKU, professor Horst Bickel, a German physician, and his colleagues developed a protein substitute drink for PKU patients. This protein drink in conjunction with a restricted diet had a positive effect on the child's condition and her behavior improved. Even though Horst Bickel made great gains in the development of effective treatment for PKU, the problem of early identification before brain damage occurred was still a problem. Dr. Willard Centerwall (Children's Hospital in Los Angeles) discovered the "Diaper Test"; by applying ferric chloride to a PKU baby's wet diaper a green color would be produced. Although this test was not effective until several weeks after birth, it was a step towards newborn screening programs implemented today. It wasn't until 1958 when Dr. Robert Guthrie developed the test for PKU, utilizing a dried blood spot, that early detection and treatment was possible. The blood spot was collected on filter paper from an infant at least twenty-four hours old. Today every state in the nation provides screening for PKU and other disorders.

With the development of the tandem mass spectrometer, and the ability to test for multiple disorders simultaneously, newborn screening panels have increased to include amino acid disorders, organic acid disorders, and fatty acid disorders. Currently, there is no standard state-wide newborn screening panel and each state's program differ. Many states, including Nevada, have increased their screening panel to include all tests recommended by the American College of Medical Genetics (ACMG). Nevada now screens for 31 disorders and began screening for cystic fibrosis in May of 2008.

Nevada's Newborn Screening Program

Funding

Nevada's Newborn Screening Program is funded through birth registration fees (NAC 440.210). Nevada's birthing facilities submit these fees monthly to the Nevada State Health Division for each child born at that facility. Birth registration fees are \$71.00 if paid on or before the 30th day after the date of birth of the child or \$73.00 if paid at a later date. These fees support 100% of the cost of the Newborn Screening Program. Including program staff and a contract with the Oregon Public Health Laboratory for blood spot testing, short-term follow up, and medical consultation to Nevada's primary care physicians. In addition, these fees fund specialty clinics for children with metabolic disorders.

Mandate

Newborn screening mandates are detailed in NAC 442.020 - 442.050. The birthing facility at which an infant is born must take an appropriate blood sample from the infant before the infant is discharged from the hospital. This sample must be taken no later than the seventh day of the infant's life regardless of the feeding status of the infant. If the infant is discharged before 48 hours of age, the blood sample must be taken as close as possible to the time of the infant's discharge. There is a chance that some disorders may show false negatives if taken prior to 48 hours of life. If an infant is transferred to another birthing facility during the first two days of life, the facility receiving the infant is required to take the first blood sample and if the infant is transferred after the first two days of life, the blood sample must be taken before the transfer. A second sample is to be taken between the 5th and 14th day of life if the first was taken within the first 48 hours of life, and between the 15th and 56th day of life if the first blood sample was taken between the 3rd and 7th day of life. A hospital that provides extended care to a newborn for more than 15 days is required to take the second sample before the infant is discharged.

Specimen Collection

Selected through the competitive process, Nevada contracts with the Oregon Public Health Laboratory (OPHL) to analyze newborn screening specimens. OPHL provides "double kits" with pre-addressed envelopes to birthing centers upon request. One part of the double kit is used to take the initial specimen in the hospital and the other is given to the mother for the second screen, usually taken about two weeks after birth. These two parts have identical laboratory numbers for easy matching by the OPHL. Each part of the kit has a filter paper portion on which to take the blood sample and a portion for patient information. It is important that the patient information is filled out completely and accurately for rapid follow-up in case of abnormal results. Single kits are also available in cases where the parent has misplaced or forgotten the second part of the kit. It is especially important that the information on these single kits is accurate so that results can be linked to the first specimen; the laboratory number of these single kits will not match the one on the initial screen done at the hospital. To collect the blood spot sample, the baby's heel is lanced and drops of blood are applied to the filter paper. It is important that this is done correctly and detailed instructions are available in the Nevada's Practitioner's Manual which will be available on the Health Division website early 2009. The Oregon Practitioner's Manual also has this collection information, and is available online at: <http://oregon.gov/DHS/ph/nbs/nbspract/manual.pdf>.

Nevada's Newborn Screening Program (continued)

Sample Analyses

Screening samples should be mailed as soon as they are dry and no later than 24 hours after collection. The OPHL initiates analysis of specimens within one day and completes the tests within 72 hours of receipt, unless a weekend or holiday occurs during that time period. The exception to this is the testing for congenital hypothyroidism which is conducted the day the specimen is received. Testing for hemaglobinopathies and cystic fibrosis is not done on the second sample unless positive results are obtained on the first. The Nevada Newborn Screening Panel currently includes 31 disorders plus cystic fibrosis. The complete battery is usually completed within 2 to 10 working days after receipt by the laboratory. A table of tests included in Nevada's Newborn Screening Panel is provided in Appendix A.

Results and Follow up

Normal results are mailed daily to hospitals and to the physician-of-record (the physician who appears on the newborn screening kit). Results considered urgent (significant abnormal results) are reported to OPHL medical consultants who contact the submitting hospital or practitioner with recommendations for further action. The primary care physician, in turn, contacts the newborn's parents. This is followed up by mail and fax confirmation. Nevada's Newborn Screening Program Staff are also notified by phone and fax. Program staff assist when difficulty arises locating a child or the child's primary care physician. It is the practitioner's responsibility to ensure that all infants with abnormal results receive follow-up testing. However, infants with abnormal results are tracked by the laboratory and/or medical consultants until a resolution of diagnosis is confirmed.

Quality Assurance

The laboratory provides program staff with monthly reports (Practice Profiles) for each birthing facility. These profiles detail inadequate specimens submitted from that facility during the specified month. Inadequacies include insufficient blood, uneven saturation, and contamination. In addition, samples taken from newborns older than seven days and samples that were over 5 days in transit are also noted. Incomplete data on the bloodspot kits is also included in this report.

Program staff are notified immediately by e-mail when the laboratory receives an inadequate sample and the birthing facility is notified by telephone and fax so they can contact the mother of the infant for retesting. In cases where the second screen is inadequate, the primary care physician is notified to retest the infant.

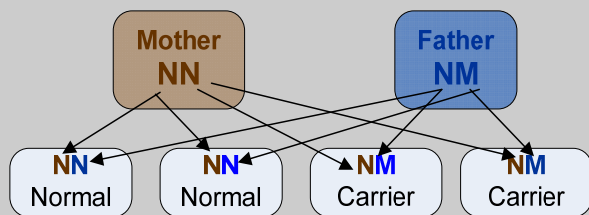
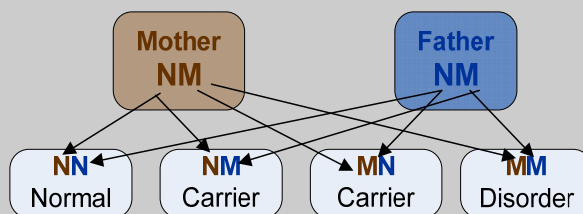
A nurse consultant is available to provide training to staff of facilities that frequently submit inadequate samples, or to provide refresher training upon request. Since steps have been taken to contact facilities concerning inadequate samples and refresher training has been conducted, inadequate samples submitted by Nevada birthing facilities have decreased from 40% to less than 10%.

Autosomal Recessive Disorders

Most inherited genetic disorders detected through newborn screening occur when a child inherits a pair of autosomal recessive genes - one donated by each parent. Autosomal genes are genes present on any chromosome except sex chromosomes; they are not linked to the sex genes (X or Y). Each autosomal gene has two copies (alleles) and one copy is inherited from each parent. When both alleles of a gene are the same, a person is said to be *homozygous* for that gene. When a person has one normal gene and one mutant gene that person is said to be *heterozygous*. The gene that gets passed down to the child is determined purely by chance. Autosomal recessive disorders are caused by a mutation in a gene. In order to have an autosomal recessive disorder, both copies of the gene (one inherited from each parent) must contain the mutation. In other words, the person must be homozygous for that gene. When only one mutant gene for an autosomal recessive disorder is inherited, the person does not have the disease and is known as a genetic carrier of the disease. In the diagrams below, "N" stands for a normal gene and "M" stands for a mutant gene. If both parents are carriers of the mutant gene (NM; heterozygous) there is a 25% chance that the child will have two normal genes, 50% chance of the child being a carrier, and a 25% chance that the child will have the disease (Figure 3:A). If one parent is a carrier (NM; heterozygous) and the other parent has two normal genes (NN; homozygous) then there is no chance that their child will have the disease, but a 50% chance that the child will be a carrier (Figure 3:B). If both parents are affected by the disorder (MM; homozygous) then all of their children will have the condition as well (Figure 3:C).

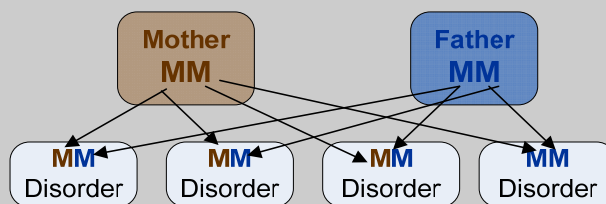
Chart 3: Parental Gene Combinations and the Chances of Offspring Inheriting Autosomal Recessive Disorders

A. Mother and Father, each heterozygous (one mutant and one normal gene NM) with a 25% chance of having a child with the disorder.



B. If one parent is homozygous for the normal gene (NN) and the other is heterozygous (NM) for the mutant gene, their child has a 50% chance of being a carrier but no chance of having the disorder.

C. If both parents are homozygous for the mutant gene (MM), then all offspring will most likely have the disorder.



Endocrine Disorders

Laboratory Testing

Endocrine disorders involve glands that secrete hormone substances into the blood stream. Newborns are screened for two endocrine disorders: congenital hypothyroidism (CH) and congenital adrenal hyperplasia (CAH). The Oregon Public Health Laboratory uses fluorometric analyses to identify these disorders in newborns. A low level of thyroxin (T4) and a high level of thyroid stimulating hormone (TSH) is indicative of CH. A high level of 17-hydroxyprogesterone (17-OHP) is indicative of CAH. False positives of CAH occur more frequently in premature, low birth weight infants.

Congenital Hypothyroidism

Congenital hypothyroidism or primary hypothyroidism is the inability of the thyroid gland (a small gland in the front of the neck) to make enough thyroid hormone (thyroxin), which acts as a chemical messenger to control the body's metabolism. CH occurs when the thyroid does not develop properly. In 80 to 85 percent of cases, the thyroid gland is absent, abnormally located, or severely reduced in size. Newborn screening is essential for CH because long before clinical symptoms appear the brain is damaged and mental retardation becomes the primary symptom. Other symptoms such as prolonged neonatal jaundice, constipation, lethargy, poor muscle tone, feeding problems, and delayed bone growth may also be manifested. Hypopituitary hypothyroidism, or secondary hypothyroidism, can also occur when the pituitary gland does not secrete enough thyroid stimulating hormone (TSH); thus, the thyroid gland produces insufficient amounts of thyroid hormone. Thyroxin is given once a day to infants with CH, who are closely monitored to normalize hormone levels. Normal mental outcome is expected with early treatment, but outcome depends on the severity of prenatal hypothyroidism, early and rapid normalization of thyroid levels, and compliance with therapy.

Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) occurs when the adrenal glands do not make enough cortisol resulting in the production of too much male hormone. About three-quarters of children with CAH also have problems keeping the right balance of salt (called salt wasting or classical CAH). In female fetuses, this causes varying degrees of virilization (the development of male secondary sexual characteristics) that is usually detected at birth. CAH leads to hypertension, elevated potassium levels, and a salt-losing crises within the first few weeks of life which can be fatal. About one-quarter of CAH cases are simple virilizing cases that do not demonstrate the salt wasting crises. CAH is treated with hydrocortisone and mineralocorticoids; surgical correction of virilized genitalia may be required. With proper treatment, an individual with CAH can experience normal development, growth and sexual maturation.

Incidence rate

The incidence rate of Primary Hypothyroidism in Nevada for the Years 2003 through 2007 was 4.62 cases per 10,000 live births. This translates to about 1 in 2,165 live births; the national estimate is 1 in 3,000 to 4,000 (9). The incidence rate of classical CAH in Nevada for the years 2003 through 2007 was 0.32 per 10,000 live births; this translates to about 1 in every 31,250 live births. A national estimate of the incident rate of classical CAH is about 1 in 19,000 newborns. These estimates

Endocrine Conditions (Continued)

vary but there is a general consensus that the incidence rate is greater than 1 in 25,000 newborns (1).

Table 1: Number of Infants Identified with Endocrine Disorders Through Nevada's Newborn Screening Program (2003-2007)

Endocrine Disorder	2003	2004	2005	2006	2007	Five-Year Total
CAH (salt-wasting)	0	0	3	1	2	6
CAH (Virilizing)	0	1	0	1	0	2
Primary Hypothyroidism	21	12	18	21	14	86
Hypopituitary Hypothyroidism	0	0	1	2	1	4
Total	21	13	22	25	17	98

Table 2: Incidence Rates for Infants with Endocrine Disorders Identified Through Nevada's Newborn Screening Program (2003-2007)

Endocrine Disorder	Total Cases (2003 - 2007)	*Estimated Incidence per 10,000 Live Births	95% Confidence Interval for Incidence	
			Low	High
Congenital Adrenal Hyperplasia (Salt-Wasting)	6	0.32	0.06	0.58
Congenital Adrenal Hyperplasia (Virilizing)	2	0.11	0.0	0.26
Primary Hypothyroidism	86	4.62	3.64	5.59
Hypopituitary Hypothyroidism	4	0.21	0.0	0.43
Total Incidence	98	5.26	4.22	6.30

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Hemoglobin Conditions

Laboratory Testing

The primary goal of hemoglobinopathy screening is diagnosis of significant sickle cell diseases (SCD) in the neonatal period before symptoms occur.

Sickle cell disease includes a group of red blood cell disorders. Newborn diagnosis of sickle cell disease, if coupled with family education and centralized comprehensive care, can significantly reduce symptoms and death from blood infections in most infants. One-hundred percent of sickle cell cases are identified on the first newborn screen (unless transfused). Therefore, hemoglobinopathy testing is not performed on the second newborn screen (taken about two weeks after birth) unless the infant was transfused or had a positive first screen. Initially, samples are screened using isoelectric focusing (IEF) in which proteins are separated on filter paper by charge in an electric field. If an abnormality is found the sample is reanalyzed by high pressure liquid chromatography (HPLC). In positive cases, the second sample is also tested by these two techniques. Thus, each hemoglobin abnormality is verified four times, using two different techniques on two different samples.

Sickle Cell Disease

Sickle cell disease is an inherited disease of red blood cells that produces abnormal hemoglobin, the protein found in red blood. Healthy red blood cells are round and carry oxygen to all parts of the body. In SCD the red blood cells become hard and sticky and look like a C-shaped farm tool called a "Sickle". Sickled cells die early, causing a constant shortage of red blood cells. They also may clog small vessels when traveling through the body, causing pain and serious problems.

A child with SCD receives a sickle cell gene from each parent; this is known as a "homozygous" condition (SS). Although newborn screening may identify several types of abnormal hemoglobin in newborns, the three clinically significant sickling disorders are sickle cell disease, sickle cell "C" disease, and hemoglobin beta thalassemia disease.

Sickle cell "C" disease occurs when a person inherits both a sickle cell hemoglobin "S" gene and a hemoglobin "C" gene (SC). A person will not have symptoms of anemia with a normal hemoglobin "A" and a hemoglobin "C" gene (AC). However, if the sickle cell gene, hemoglobin "S", is combined with hemoglobin "C" (SC), this causes some mild to moderate anemia. Individuals with sickle cell "C" disease often suffer some of the complications associated with sickle cell disease, but to a milder degree.

Hemoglobin S-beta-thalassemia is an inherited disorder that reduces the production of hemoglobin and is treated the same as sickle cell disease (SS). In *Thalassemia Minor* or *Thalassemia Trait* the lack of beta protein in the hemoglobin is not great enough to cause problems in normal hemoglobin functioning. In *Thalassemia Intermedia*, the lack of beta protein in the hemoglobin is great enough to cause a moderately severe anemia and significant health problems. *Thalassemia Major* or Cooley's Anemia is the most severe form of beta thalassemia. The complete lack of beta protein in the hemoglobin causes a life threatening anemia that requires regular blood transfusions and extensive ongoing medical care. From 2003 through 2007 Nevada's Newborn Screening Program identified two cases of hemoglobin S-beta-thalassemia.

Hemoglobin Conditions Continued

Sickle Cell Incidence

Sickle cell disease is one of the most common genetic diseases in the United States. All fifty states have newborn screening programs which test all newborns for sickle cell disease. Sickle cell disease is particularly common among people whose ancestors come from Sub-Saharan Africa, Spanish-speaking regions in the Western Hemisphere (South America, Cuba and Central America), Saudi Arabia, India, and Mediterranean countries such as Turkey, Greece, and Italy. In the United States, SCD affects around 72,000 people, most of whose ancestors came from Africa. In the five-year period from 2003 to 2007, there were 49 infants born with SCD in Nevada (Table 3).

Table 3: Number of Infants (Hispanic and African American) with Sickle Cell Disease Identified through Nevada's Newborn Screening Program (2003-2007)

Hemoglobinopathies	2003	2004	2005	2006	2007	Five-Year Total
Sickle Cell Disease (SS)	11	1	6	4	10	32
Sickle Cell Disease (SC)	3	3	7	2	2	17
Total SS and SC	14	4	13	6	12	49

Nationally, SCD occurs in about 1 in every 500 African-American births (2). Nevada's incidence rate of SCD for the African American population was 28.3 per 10,000 live births which translates to about 1.4 in every 500 births (Table 4). SCD is estimated to occur in one out of every 1,000 to 1,400 Hispanic-American births (10); however, the incidence rate in Nevada is much lower, at about one in every 12,000 births for the years 2003 through 2007.

Table 4: Incidence Rates for Infants with Sickle Cell Disease Identified through Nevada's Newborn Screening Program (2003-2007)

Race/Ethnicity	Total Sickle Cell Cases (2003 - 2007)	*Total Live Births by Race (2003 -2007)	Estimated Incidence Rates per 10,000 Live Births	95% Confidence Interval for Incidence Rates	
				Low	High
African American (SS)	28	15,193	18.43	11.60	25.26
African American (SC)	15	15,193	9.87	4.88	14.87
African American (SS & SC)	43	15,193	28.30	19.84	36.76
Hispanic (SS)	4	71,378	0.56	0.11	1.11
Hispanic (SC)	2	71,378	0.28	0.00	0.67
Hispanic (SS & SC)	6	71,378	0.84	0.17	1.51
Total	49	86,581	5.66	4.08	7.24

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Hemoglobin Conditions Continued

Sickle Cell Traits

Hemoglobin screening is the only newborn screening test that regularly identifies carriers (heterozygotes that have the sickle cell trait), as well as those affected by the disease. Although this report includes sickle cell disease data from 2003 through 2007, sickle cell trait data is only available for the years 2005 through 2007. People with sickle cell trait usually do not have any symptoms except rarely in extreme circumstances of high altitude flying, increased pressure (scuba diving), low oxygen (mountain climbing or extreme exercise), or dehydration. About two million Americans, or one in twelve African Americans, carry the sickle cell trait (2). The sickle cell trait is inherited when a child inherits one sickle cell gene from one parent and a normal gene from the other (page 5). The primary care physician receives a copy of the newborn screen laboratory report and the family is entitled to this private information. If both parents are African American, they should seek genetic counseling to determine if they are both carriers. If this is the case there is a 25% chance that subsequent offspring could have SCD.

Table 5: Number of Infants with Sickle Cell Trait Identified through Nevada's Newborn Screening Program (2005-2007)

Sickle Cell Trait	African American (SS/SC)	Hispanic (SS/SC)	Unknown (SS/SC)	Total Traits (SS and SC)
2005	178/52	93/12	72/16	423
2006	206/60	106/9	92/15	488
2007	192/62	121/14	77/20	486
Total	576/174	320/35	241/51	1,397

Table 6: Incidence Rate of Infants with Sickle Cell Trait Identified through Nevada's Newborn Screening Program (2005-2007)

Race/Ethnicity	Total Sickle Cell Cases (2005 - 2007)	Total Live Births by Race (2005 -2007)	Estimated Incidence per 10,000 Live Births	95% Confidence Interval for Prevalence	
				Low	High
African American					
SS	576	9,642	597.4	572.5	622.3
SC	174	9,642	180.5	166.8	205.4
Total (AS and AC)	750	9,642	777.8	722.2	833.5
Hispanic					
SS	320	45,535	70.3	66.3	74.2
SC	35	45,535	7.7	4.8	9.0
Total (AS and AC)	355	45,535	78.0	69.9	86.1

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Hemoglobin Conditions Continued

In the years 2005 through 2007, 1,397 Nevada newborns were identified as carriers of sickle cell disease or sickle cell "C" disease. Of these born with sickling traits, 54% were of African American descent, 25% were Hispanic, and 21% were of unknown race/ethnicity. The incidence rate for sickle cell trait was 778 per 10,000 live births in the African American population and 78 per 10,000 live births in the Hispanic population. This translates to about 1 in 13 African American births and about 1 in 128 Hispanic births. In actuality, these incidence rates will be slightly higher because there were 292 individuals born with sickle cell traits whose race/ethnicity was not known. The majority of these are most likely either African American or Hispanic, but they could not be used in the calculation of the incidence rate.

Sickle Cell Symptoms & Complications

People with sickle cell disease start to have symptoms during the first year of life, usually around five months of age. Symptoms and complications of sickle cell disease are different for each person and can range from mild to severe. When cells get stuck in small blood vessels and block blood flow, it can cause a pain "episode" or "crises" which is the most common reason for individuals with SCD to go to emergency rooms. This pain can start suddenly, be mild or severe, and can last for any length of time. Certain steps recommended by the Centers for Disease Control and Prevention that people with sickle cell disease can take to help prevent or reduce the number of pain crises are:

- Drink plenty of water
- Try not to get too cold or hot
- Try to avoid places with high altitudes (flying, cities located at high elevations)
- Try to avoid situations or places with low oxygen (mountain climbing or extreme exercise)
- If necessary, follow physician recommendations for medications to reduce the number of pain crises.

In addition to pain crises, individuals with sickle cell disease can experience swelling of the hands and feet (hand-foot syndrome) caused by blockage of small blood vessels. This is usually the first symptom of SCD. Individuals with SCD can also experience anemia; in severe cases transfusions are used to treat this.

People with SCD, especially infants and children, are more at risk for harmful infections. Pneumonia is the leading cause of death in infants and young children with SCD. Babies and children with SCD should have all their regular childhood vaccinations and a few others. Children with SCD are also given daily doses of penicillin to prevent infections. Adults with SCD should have a yearly flu vaccination. People with SCD can also have "acute chest syndrome" which should be treated in a hospital. It is similar to pneumonia and symptoms include chest pain, coughing, difficulty breathing and fever. Other complications include: vision loss; leg ulcers; strokes; damage to body organs, tissues or bones; gallstones and; enlarged spleen due to trapped blood cells (splenic sequestration), which should be treated in a hospital.

Metabolic Conditions: Amino Acid Disorders

Laboratory Testing

The Oregon Public Health Laboratory (OPHL) tests for amino acid disorders using tandem mass spectrometry. Table 7 lists the amino acid disorders that are currently on Nevada's Newborn Screening Panel. Although 90% of phenylketonuria cases are identified on the first newborn screen, other amino acid disorders, such as homocystinuria and tyrosinemias, are often identified on the second newborn screen due to the slow rise in metabolite levels of methionine and tyrosine respectively. Thus, before discharge from the hospital, mothers should be made aware of the importance of following through with the second newborn screen.

Table 7: Amino Acid Disorders Included in Nevada's Newborn Screening Panel

Amino Acid Disorders	
1.	Homocystinuria
2.	Hyperphenylalaninemia, including Phenylketonuria (PKU)
3.	Tyrosinemias
	Tyrosinemia, Type 1
	Tyrosinemia, Type 2

Amino Acid Disorders

Amino acid (AA) disorders cause the body to have problems breaking down certain proteins. As the body breaks down (metabolizes) food, the food is changed into nutrients the body can use and the body gets rid of chemicals it does not need. Individuals with amino acid disorders have problems processing certain amino acids, which are building blocks of proteins, because of the lack of or poor function of certain enzymes. Each enzyme deficiency causes a different AA disorder. The buildup of toxic chemicals in the body can be avoided with a special diet and medication. If left untreated, AA disorders can cause vomiting, eye problems, liver problems, mental retardation, and possibly coma or death. Amino acid disorders are inherited when both parents pass on an autosomal recessive gene to their child. Both parents are carriers of the defective gene, but do not experience any health related problems associated with the disorder. If both parents are carriers, their children will each have 25% chance of having the disorder.

There are eight different congenital enzymopathies characterized by the accumulation of phenylalanine and related metabolites in the body. Collectively these eight enzymopathies are referred as **hyperphenylalaninemia**. The most common, **phenylketonuria (PKU)** is the inability to break down the amino acid phenylalanine, which is found in protein. When phenylalanine builds up in the body, it becomes toxic. Infants may appear normal in the first few months of life, but left untreated, PKU can cause mental and motor retardation, microcephaly, poor growth rate, and seizures. PKU occurs in approximately one out of 15,000 infants in the United States. With a strict phenylalanine-free diet, infants with PKU should have normal growth and development. Untreated PKU can cause behavior problems and mental retardation.

Metabolic Conditions: Amino Acid Disorders (Continued)

Homocystinuria is caused by an enzyme deficiency resulting in the inability to breakdown the amino acid methionine. Homocystinuria is characterized by dislocation of the lens in the eye, an increased risk of abnormal blood clots, and skeletal abnormalities. In some cases problems with development and learning are also evident. Less common forms of homocystinuria are caused by the lack of other enzymes and can cause mental retardation, seizures, problems with movement, and blood disorders. It is estimated that homocystinuria affects one in 200,000 to 335,000 worldwide. Treatment may include a methionine-restricted and cystine-supplemented diet, as well as large doses of vitamin B6. Approximately 50% of patients are pyridoxine (vitamin B6) responsive and may not need additional treatment. Infants treated from birth with good biochemical control of methionine develop normally.

Hepatorenal Tyrosinemia (Type I) or fumarylacetoacetate hydrolase (FAH) deficiency is inherited and is the most severe form of Tyrosinemia. Tyrosinemia Type I results in the accumulation of tyrosine and its metabolites in the liver causing severe liver and renal disease with peripheral nerve damage. Symptoms include vomiting, lethargy, diarrhea and failure to thrive. If untreated, death in infancy or childhood from acute liver failure, neurological crises, and primary liver carcinoma is typical. Tyrosinemia Type I occurs in about one out of 100,000 births. With early treatment, a greater than 90% survival rate can be expected, along with normal growth. Individuals with Tyrosinemia Type I need a special diet and medications throughout life.

Oculocutaneous Tyrosinemia (Type II) is the deficiency of the enzyme tyrosine aminotransferase (TAT). Symptoms are manifested primarily in the eyes, skin, and the central nervous system. In the eyes, tyrosine crystals accumulate, resulting in painful corneal abrasions. Equally painful, plaques form on the undersurface of the feet, hands, and fingers. Symptoms usually develop in the first year of life, but can be present on the first day of life or may not occur until adulthood. A variable amount of retardation is present in about 50% of cases. TAT deficiency is very rare, although more infants may be identified as tandem mass spectroscopy continues to be implemented. If untreated, serious eye damage results and skin lesions become permanent making walking difficult. With treatment, eye symptoms are relieved within a week and skin lesions in a few months. Neurological problems should be avoided with treatment, but the number of patients treated before symptoms occur has been small.

Management of AA Disorders

Children with amino acid disorders should have a primary care doctor, a pediatric metabolic specialist, and a dietician. This panel of health professionals can provide comprehensive medical care and educate the family about the special diet that must be maintained. Families are taught to read labels carefully when shopping for groceries to avoid certain proteins associated with the disorder. Treatment for amino acid disorders is life-long and a child with an AA disorder should see a doctor on a regular basis; medications may help the body eliminate harmful toxins.

Metabolic Conditions: Amino Acid Disorders (Continued)

Incidence Rate

Table 8: Number of Infants with Amino Acid Disorders Identified through Nevada's Newborn Screening Program (2003-2007)

Amino Acid Disorder	2003	2004	2005	2006	2007	Five-Year Total
Hyperphenylalaninemia & Phenylketonuria (PKU)	0	1	1	3	3	8
Homocystinuria	0	0	2	2	0	4
Tyrosinemia (Type II)	0	0	0	1	0	1
Total	0	1	3	6	3	13

In the five-year period from 2003 through 2007, 13 newborns were identified with amino acid disorders. Over half of these cases were either hyperphenylalaninemia or phenylketonuria (Table 8), with an incidence rate of 0.43 per 10,000 live births (Table 9). This translates to about 1 in 23,256 live births, which is less than the national estimate of 1 in 15,000 live births (17). Literature estimates the incidence rate for the following disorders as:

- Homocystinuria - affects about 1 in 200,000 to 335,000 people worldwide, but appears to be more common in countries such as Ireland, Germany, Norway, and Qatar (9).
- Tyrosinemia Type I affects about 1 person in 100,000, but is much more common in Quebec, Canada (about 1 in 16,000) (9).
- Tyrosinemia Type II is much less common than Tyrosinemia Type I and affects fewer than 1 in 250,000 individuals (9).

The incidence rate for all Nevada amino acid disorders during this five-year period was 0.48 per 10,000 live births which translates to about one in every 20,833 live births.

Table 9: Incidence Rate of Infants with Amino Acid Disorders Identified through Nevada's Newborn Screening Program (2003-2007)

Amino Acid Disorder	Total Cases (2003 - 2007)	*Estimated Incidence per 10,000 Live Births	95% Confidence Interval for Incidence	
			Low	High
Hyperphenylalaninemia & Phenylketonuria (PKU)	8	0.43	0.13	0.73
Homocystinuria	4	0.21	0.00	0.43
Tyrosinemia Type II	1	0.05	0.00	0.16
Total Incidence	13	0.48	0.17	0.80

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Metabolic Conditions: Fatty Acid Oxidation Disorders (Continued)

Laboratory Testing

The Oregon Public Health Laboratory (OPHL) tests for fatty acid oxidation disorders (FAO) using tandem mass spectrometry. When fat is attached to carnitine it is called acylcarnitine. Acylcarnitines are identified by the size of the fat molecule attached to it. These are categorized as short, medium, long, and very long chain fats. Thus, FAO deficiencies are categorized as short-chain Acyl-CoA dehydrogenase deficiency, medium-chain Acyl-CoA dehydrogenase deficiency and so forth. As these compounds cannot be metabolized because the enzyme is lacking, they accumulate in the blood and tissues and become toxic. The tandem mass spectrometer determines the amounts of these substances in the blood. Once an abnormal amount of acylcarnitine is identified in an infant's newborn screen, the child's primary care physician is notified and further confirmatory testing is done. OPHL tests for the following FAO disorders:

Table 10: Fatty Acid Oxidation Disorders Included in Nevada's Newborn Screening Panel

1.	Carnitine Uptake/Transporter Defects
	A. Carnitine-Acylcarnitine Translocase Deficiency
	B. Carnitine Transporter Defect
	C. Carnitine Palmitoyl Transferase I Deficiency (CPTI)
	D. Carnitine Palmitoyl Transferase II Deficiency (CPTII)
2.	Other Fatty Acid Disorders
	A. Glutaric Aciduria, Type II (Multiple Acyl-CoA Dehydrogenase Deficiency: MADD)
	B. Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)
	C. Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)
	D. Short Chain Acyl-CoA Dehydrogenase Deficiency (SCADD)
	Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)

Fatty Acid Oxidation Disorders

Fatty acid oxidation (FAO) disorders are the absence of one or more enzymes (chemicals that assist with metabolism) needed to break down fat. When a person goes without eating for several hours the body relies on stored fat for energy, but an individual with FAO disease cannot utilize this stored energy. Therefore, eating often and getting immediate care for any illness can prevent problems caused by FAO disorders; glucose supplementation and hydration may be provided during times of illness. Fatty acid oxidation disorders are inherited autosomal recessive disorders (Page 5). This means both parents are carriers of an FAO disorder. Carriers do not usually experience any health problems related to FAO disorders. When two carriers have children, there is a one in four (25%) chance for each baby to have a FAO disorder.

Metabolic Conditions: Fatty Acid Oxidation Disorders (Continued)

Incidence of FAO

Medium-chain Acyl-CoA dehydrogenase deficiency (MCADD) has been diagnosed almost exclusively among individuals of northwestern European origin with frequencies ranging from 1 in 10,000 to 1 in 15,000 in United State's newborns. Other fatty acid oxidation disorders are rare and have an estimated incidence of greater than one in 75,000; however, there is a lack of consensus and the incidence rate varies from 1 in 40,000 to 100,000 in literature (1). Through newborn screening, eight newborns with fatty acid oxidation disorders were identified in Nevada from 2003 through 2007 (Table 11). Four were MCADD cases with an incident rate of 0.21 per 10,000 births which translates to about 1 in 47,600 births. Three were VLCAD cases with an incidence rate of 0.16 cases per 10,000 live births and one SCAD with an incidence rate of 0.05 cases per 10,000 live births. This translates to about 1 in 62,500 and 1 in 200,000 live births respectively. The total incidence rate for all FAO disorder from 2003 through 2007 was about 1 in 23,256 live births (Table 12).

Table 11: Number of Infants with Fatty Acid Oxidation Disorders Identified through Nevada's Newborn Screening Program (2003-2007)

Fatty Acid Disorders	2003	2004	2005	2006	2007	Five-Year Total
SCAD	1	0	0	0	0	1
MCAD	1	0	1	2	0	4
VLCAD	0	0	1	2	0	3
Total	2	0	2	4	0	8

Table 12: Incidence Rate of Infants with Fatty Acid Oxidation Disorders Identified through Nevada's Newborn Screening Program (2003-2007)

Fatty Acid Disorder	Total Cases (2003 - 2007)	*Estimate Incidence per 10,000 Live Births	95% Confidence Interval for Incidence	
			Low	High
Short Chain Acyl - CoA Dehydrogenase Deficiency (SCADD)	1	0.05	0.00	0.16
Medium Chain Acyl - CoA Dehydrogenase Deficiency (MCADD)	4	0.21	0.00	0.43
Very Long Chain Acyl - CoA Dehydrogenase Deficiency (VLCADD)	3	0.16	0.00	0.34
Total	8	0.43	0.13	0.72

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Metabolic Conditions: Fatty Acid Oxidation Disorders (Continued)

Management of FAO Disorders

Early diagnosis and treatment is essential for improved prognosis. If left untreated, an FAO disorder can cause vomiting, sleepiness, seizures, liver problems and possibly coma or death. With strict eating schedules, individuals with FAO disorders can live normal lives. Treatment regimes include the long-term monitoring of serum glucose, a low-fat/high-carbohydrate diet, supplemental carnitine, and avoidance of fasting. Aggressive medical management is essential during illness, especially if a child is vomiting or is not receiving adequate nutritional intake. A child with FAO disorder should have a primary care doctor, a pediatric metabolic specialist, and a dietician to provide medical care and educate the family. Treatment for FAO disorders is life-long and a child with an FAO disorder should see a doctor regularly. Before newborn screening was available, FAO disorders were fatal. Now, with immediate and ongoing treatment, many infants survive and live healthy lives with typical growth and development.

Metabolic Conditions: Organic Acid Disorders

Testing

Tandem mass spectrometry is used to identify organic acid (OA) disorders. Maple syrup urine disease is detected by an elevation of the amino acid leucine and an abnormal leucine/alanine ratio. All the other organic acid disorders are detected through elevations in acylcarnitines. When fat is attached to carnitine it is called acylcarnitine (see page 15: Fatty Acid Oxidation Disorders). Table 13 list the organic acid disorders included in Nevada's newborn screening panel.

Table 13: Organic Acid Disorders Included in Nevada's Newborn Screening Panel

Organic Acid Disorders	
1.	Beta-Ketothiolase Deficiency
2.	Glutaric Aciduria, Type I
3.	Isobutyryl CoA Dehydrogenase Deficiency
4.	Isovaleryl-CoA Dehydrogenase Deficiency (Isovaleric Acidemia)
5.	Malonic Aciduria
6.	Maple Syrup Urine Disease
7.	Methylmalonic Acidemia (MMA; 8 types)
	A. Methylmalonic Aciduria, Vitamin B-12 Responsive
	B. Methylmalonic Aciduria, Vitamin B-12 Nonresponsive
	C. Vitamin B-12 Metabolic Defect with Methylmalonic Acidemia and Homocystinuria
8.	Propionic Acidemia (PA)
9.	HMG-CoA Lyase Deficiency

Organic Acid Disorders

Organic acid disorders also called Organic Acidemias are a group of inherited metabolic conditions. All are inherited autosomal recessive gene disorders (page 5) and have an estimated collective incidence of about 1 in 25,000 live births (11). These metabolic disorders cause a buildup of toxic organic acid intermediates due to the body's inability to breakdown certain amino acids and odd-chain organic acids (organic acids with an odd number of carbon atoms in the chain). The enzyme deficiencies are farther down the metabolic pathways of amino acid metabolism, so there is not a buildup of amino acids, but rather their intermediate acid states. Each organic acid disorder is associated with a specific enzyme deficiency that causes the accumulation of organic acids in blood and urine. These accumulated compounds and their metabolites are toxic, resulting in clinical features of these disorders. The symptoms and treatment vary between different organic disorders and can also vary from person to person with the same disorder.

Metabolic Conditions: Organic Acid Disorders Continued

Incidence

Estimates of incidence vary widely for each organic disorder, and for many the actual incidence is not yet known. Most of these disorders may vary from 1 in 20,000 births to less than 1 in 200,000 births. In the five-year period of 2003 through 2007 eight infants were identified with organic acid disorders through Nevada's Newborn Screening Program (Table 14). The five-year (2003 - 2007) cumulative incidence for organic disorders in Nevada is 0.38 in 10,000 live births. This translates to about 1 in 26,316 newborns (Table 15). In the five-year period from 2003 through 2007, the Newborn Screening Program identified: two cases of methylmalonic acidemia (MMA) with an incidence rate of about 1 in 90,900 births; two cases of 2-methylbutyryl dehydrogenase deficiency (2MBC) with an incidence rate of about 1 in 90,900 live births; three cases of 3-methylcrotonyl CoA carboxylase deficiency (3MCC) with an incidence rate of 1 in 62,500 live births and; one case of glutaric acidemia type I (GAI) with a incidence rate of about one in 200,000 live births. National incidence rate estimates for these disorders from the Organic Acidemia Association are: MMA at 1 in about 80,000 live births (24), 2MBC is not known (21), 3MCC at 1 in about 50,000 live births (22), and GAI at about 1 in every

Table 14: Number of Newborns with Organic Acid Disorders Identified Through Nevada's Newborn Screening Program (2003-2007)

Organic Acid Disorders	2003	2004	2005	2006	2007	Five-Year Total
Methylmalonic Acidemia (MMA)	1	0	1	0	0	2
2-Methylbutyryl Dehydrogenase Deficiency (2MBC)	0	0	1	1	0	2
3-Methylcrotonyl CoA Carboxylase Deficiency (3MCC)	0	0	0	0	3	3
Glutaric Acidemia Type I (GAI)	0	0	0	1	0	1
Total	1	0	2	2	3	8

Table 15: Incidence Rate of Infants with Organic Acid Disorders Identified Through Nevada's Newborn Screening Program (2003-2007)

Organic Acid Disorder	Total Cases (2003 - 2007)	*Incidence per 10,000 Live Births	95% Confidence Interval for Incidence	
			Low	High
Methylmalonic Acidemia (MMA)	2	0.11	0.00	0.26
2-Methylbutyryl Dehydrogenase Deficiency (2MBC)	2	0.11	0.00	0.26
3-Methylcrotonyl CoA Carboxylase Deficiency (3MCC)	3	0.16	0.00	0.34
Glutaric Acidemia Type I (GAI)	1	0.05	0.00	0.16
Total	8	0.43	0.13	0.73

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Metabolic Conditions: Urea Cycle Disorders

Urea Cycle Disorders

The urea cycle is responsible for the detoxification of ammonia and for the synthesis of arginine and urea. The urea cycle processes excess nitrogen, a byproduct of protein metabolism, to make urea which is then excreted by the kidneys. When this process cannot proceed normally, nitrogen accumulates in the bloodstream in the form of ammonia (hyperammonemia). There are six enzymes in the urea cycle, each of which if missing, will result in excess ammonia and one of the six disorders of the urea cycle. The urea cycle is a sequence of reactions that occur in liver cells. Ammonia is especially damaging to the nervous system, so urea cycle disorders cause neurological problems, as well as eventual liver damage. Each of these disorders has genetic and clinical variability of mild to lethal. Only three urea cycle disorders can be detected by newborn screening. Nevada's Newborn Screening Panel includes these three which are:

- Arginase Deficiency
- Argininosuccinic Aciduria also called Argininosuccinate Lyase Deficiency (ASA)
- Citrullinemia (both Type I and Type II)

Infants with severe hyperammonemia may die in the first week to ten days if not diagnosed and treated. Infants with citrullinemia or ASA who survive a neonatal coma (caused by hyperammonemia) usually have a fair to poor outcome. Brain damage is common and the risk of hyperammonemia continues throughout life. Complications from arginase deficiency should be preventable with early and continuous treatment.

Incidence Rate

Argininosuccinate lyase (ASA) deficiency, also called argininosuccinate aciduria, causes ammonia to accumulate in the blood. While early diagnosis and treatment is lifesaving, neurologic damage is not usually prevented. The incidence rate of ASA is not known and estimates range from 1 in 70,000 to 180,000 live births (14). Treatment consists of a low protein diet, arginine supplementation to help complete the urea cycle, ammonia drugs in some cases, and supplemental carnitine if the patients have a secondary deficiency. During the five-year period of 2003 through 2007 the Newborn Screening Program identified three cases of ASA (Table 15) with an incidence rate of 0.16 per 10,000 live births, which translates to 1 in about 62,500 live births. There were no cases of citrullinemia or arginase deficiency reported during this period.

Table 16: Number and Incidence of Infants Identified with Urea Cycle Disorders Identified Through Nevada's Newborn Screening Program (2003-2007)

Urea Cycle Disorder	2003	2004	2005	2006	2007	Five -Year Total
Argininosuccinate Lyase Def.	0	0	1	1	1	3
Incidence Rate						
Urea Cycle Disorder	Total Cases (2003 - 2007)		*Estimated Incidence per 10,000 Live Births	95% Confidence Interval for Incidence		
Argininosuccinate Lyase Def.	3		0.16	0.00 - 0.34		

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Metabolic Conditions: Other metabolic Disorders

Biotinidase Deficiency

Biotinidase deficiency is caused by the lack of an enzyme called biotinidase. Biotinidase deficiency is an inherited disorder. Infants born with biotinidase deficiency appear normal at birth, but develop critical symptoms after the first weeks or months of life. Symptoms include excess sleep, failure of muscular coordination, seizures, hair loss, skin rash, hearing loss, and optic nerve atrophy. Individuals with less than 10% of normal biotinidase activity are considered to have profound biotinidase deficiency. People classified as having partial biotinidase deficiency have intermediate levels of biotinidase activity, 10 - 30% of normal. People with biotinidase deficiency are unable to use naturally occurring biotin in their diets and are unable to recycle biotin. Infants and children treated before symptoms appear rarely develop any symptoms. Untreated children with partial deficiency are usually healthy, although symptoms have occurred in some children when they are stressed from infection or poor diet. It is estimated that about 1 in 60,000 newborns are affected by profound or partial biotinidase deficiency.

Galactosemia

Galactosemia is an inherited disorder characterized by the inability to break down galactose (a sugar found in milk and milk products). As a result, galactose builds up in the body and becomes toxic; a special diet can prevent most problems. Galactosemia is different for each child and individuals treated for galactosemia may still have problems with speech, language, hearing, fine-motor coordination, eyes, stunted growth, tremors, reproduction, and learning disabilities. Treatment is life-long with a diet free of galactose and lactose. This includes cow's milk, goat's milk, human breast milk, and dairy products like butter, cheese and yogurt. Galactosemia occurs in about one out of every 60,000 live births. In the five-year period from 2003 through 2007, there were no cases of classical galactosemia identified through Nevada's Newborn Screening program.

In the five-year period from 2003 through 2007, Nevada's newborn screening program identified three cases of biotinidase deficiency and eight cases of partial biotinidase deficiency. This translates to about one in 62,000 live births and one in 23,280 live births respectively (Table 17).

Table 17 : Incidence Rate of Infants with Biotinidase Deficiency Identified through Nevada's Newborn Screening Program (2003-2007)

Biotinidase Deficiency	Total Cases (2003 - 2007)	*Estimated Incidence per 10,000 Live Births	95% Confi- dence Interval for Incidence	
			Low	High
Biotinidase Deficiency	3	0.16	0.00	0.34
Partial Biotinidase Deficiency	8	0.43	0.13	0.73
Total	11	0.59	0.24	0.94

* Estimated total live births in Nevada from 2003 through 2007 were 186,243.

Cystic Fibrosis

Cystic Fibrosis Testing

Cystic fibrosis (CF) was added to Nevada's Newborn Screening Panel on the first of May 2008 and is included in the contract with the Oregon Public Health Laboratory (OPHL). The identification of increased levels of immunoreactive trypsinogen (IRT) levels in the blood of infants with CF has made neonatal screening for CF possible. Trypsinogen is a secretory product of the pancreas and its level in the blood is a specific marker of pancreatic function. Detection of high levels of IRT in the newborn period place the infant at risk for CF. Although there is no cure, newborns can benefit from early diagnosis and treatment. All infants born in Nevada are tested for CF on the first screen. IRT levels are tested on the second screen only if the first screen is high. Newborn screening is not a definitive diagnostic test for CF. When an infant has high IRT levels on both the first and second screen, OPHL medical consultants contact the infants primary care physician to arrange for the infant to have confirmatory sweat chloride testing done.

Cystic Fibrosis

Forty-six states and the District of Columbia now include cystic fibrosis in their newborn screening panel. Of the remaining four states, one offers cystic fibrosis testing to a select population upon request, and the remaining three states are requiring cystic fibrosis testing but have not yet implemented testing (18). Cystic fibrosis is an autosomal recessive genetic disorder and it is estimated that ten (10) million Americans are symptomless carriers of the defective gene. The Cystic Fibrosis Foundation estimates the incidence of CF in United States at about 1 in 3,500 births with a prevalence of 30,000 individuals. According to the Cystic Fibrosis Foundation's 2007 Annual Report, Nevada has a current CF patient listing of 150 individuals (7).

Cystic fibrosis is a life-threatening disease that causes mucus to build up and clog some of the organs in the body, particularly in the lungs and pancreas. This thick mucus leads to chronic lung infections and difficulty digesting food and nutrients. The treatment for CF depends upon the severity of symptoms and the organs involved. Diagnosis through newborn screening and early treatment gives newborns with CF a better chance of improved health and longer life as detailed in the following bullets:

- Early diagnosis and treatment of CF have also shown to help individuals with CF improve lung function, reduce hospitalizations, have a significant delay in the onset of symptoms, and experience a better quality of life.
- Newborn screening has been associated with fewer hospitalizations and improved survival. In 1955, very few children with CF lived to see grammar school, but today the median age of survival for individuals with CF is 37.4 years old (7).
- According to the Centers for Disease Control and Prevention (CDC), the most convincing evidence of improved health outcomes with early detection and treatment of CF is in the area of nutrition and growth. In the absence of early treatment, infants and children with CF are subject to growth failure and prolonged vitamin deficiency measured by height, weight relative to height, and head circumference in infants.

Hearing Disorders

Newborn Hearing Screening

Hearing loss is the most common birth defect, affecting approximately three out of every thousand infants. Prior to the development of newborn hearing screening programs, the average age at which these children were identified with hearing loss in the United States was two and a half years, with milder hearing losses commonly remaining undetected until a child entered elementary school. Most developmental milestones for language occur within the first year of life, and if they pass without intervention, they will almost certainly result in life-long deficits in speech and language. In addition, infants who are not identified with hearing loss early will likely experience delays in other facets of life; including social and emotional development as well as cognitive and academic growth.

If children with hearing loss are identified early and have access to appropriate intervention, including amplification and speech therapy, the detrimental affects of hearing loss can be diminished or even eliminated. Research has shown that when a child with hearing loss is identified by three months of age and given appropriate services by six months of age their speech and language development can occur at a rate similar to that of their normal hearing peers. In addition, it is estimated by the National Centers for Hearing Assessment and Management (NCHAM) that statewide hearing screening programs would more than pay for themselves if an additional two percent of children with hearing loss could be placed in self-contained classrooms instead of residential programs.

In 2007, about 98.8 percent of newborns in Nevada were screened for hearing loss. The average percent screened in the four-year period from 2004 to 2007 was 97.1 percent. Referral outcomes are not available at this time. However, using the national estimate of three out of every 1,000 children born with a hearing loss, it is estimated that the Nevada's Newborn Hearing Screening Program identified 429 infants with hearing loss. Table 19 provides detailed information on the numbers of infants screened and referred for the years 2004 through 2007.

Table 18: Number and Percent of Newborns Screened for Hearing Disorders and the Estimated Number of Cases Identified (2004-2007)

Year	*Births Reported by Birthing Facilities	Number of Newborns Screened	Percent of Newborns Screened	Number of Infants Referred	Percent of Newborns Referred	**Estimated Hearing Loss Cases Identified
2004	33,000	31,815	96.4	819	2.5	95
2005	36,377	35,116	96.5	1,035	2.8	105
2006	38,951	37,648	96.7	832	2.1	113
2007	39,209	38,744	98.8	1,147	2.9	116
Total	147,537	143,323	97.1	3,833	2.7	429

* Number of Births are those reported by birthing facilities, thus there is some discrepancy between program Numbers and Birth Registry Data.

** Based on those screened, not births

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Appendix A: Disorders Included in Nevada's Newborn Screening Panel

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Appendix A: Disorders Included in Nevada's Newborn Screening Panel

Disorder		*Method of Testing
Endocrine Disorders		
1.	Congenital Adrenal Hyperplasia	Fluorometric
2.	Congenital Hypothyroidism	Fluorometric
Hemoglobin Disorders		
3.	Sickle Cell Disease and other Hemoglobinopathies	HPLC
Metabolic Disorders		
4.	Biotinidase Deficiency	Colorometric
5.	Galactosemia	Beutler & Hills
Amino Acid Disorders		
6.	Arginase Deficiency	TMS
7.	Argininosuccinate Lyase Deficiency (ASA)	TMS
8.	Citrullinemia	TMS
	A. Classic Citrullinemia	TMS
	B. Citrullinemia Type II	TMS
9.	Homocystinuria	TMS
10.	Hyperphenylalanemia, including Phenylketonuria	TMS
11.	Tyrosinemia	TMS
	A. Tyrosinemia, Type 1	TMS
	B. Tyrosinemia, Type 2	TMS
Organic Acid Disorders		
12.	Beta-Ketothiolase Deficiency	TMS
13.	Glutaric Aciduria, Type I (Glutaryl-CoA Dehydrogenase Deficiency)	TMS
14.	Isobutyryl CoA Dehydrogenase Deficiency	TMS
15.	Isovaleryl-CoA Dehydrogenase Deficiency (Isovaleric Acidemia)	TMS
16.	Malonic Aciduria	TMS
17.	Maple Syrup Urine Disease	TMS
18.	Methylmalonic Acidemia (MMA; 8 types)	TMS
	A. Methylmalonic Aciduria, Vitamin B-12 Responsive	TMS
	B. Methylmalonic Aciduria, Vitamin B-12 Nonresponsive	TMS
	C. Vitamin B12 Metabolic Defect with Methylmalonicacidemia and Homocystinuria	TMS
19.	Propionic Acidemia (PA)	TMS
20.	HMG-CoA Lyase Deficiency (3-hydroxy-3-methylglutaryl-CoA Lyase Deficiency)	TMS

*TMS = Tandem Mass Spectrophotometer
 HPLC = High Pressure Liquid Chromatography
 IRT = Immunotrypsinogen Testing

Appendix A: Disorders Included in Nevada's Newborn Screening Panel Continued

	Disorder	* Method of Testing
21.	2-Methyl-3-hydroxybutyryl CoA Dehydrogenase Deficiency	TMS
22.	2-Methylbutyryl CoA Dehydrogenase Deficiency	TMS
23.	3-methylcrotonyl-CoA Carboxylase Deficiency	TMS
24.	3-methylglutaconyl-CoA Hydratase Deficiency	TMS
	A. 3-methylglutaconyl-CoA Aciduria Type I	TMS
	B. 3-methylglutaconyl-CoA Aciduria Type II	TMS
	C. 3-methylglutaconyl-CoA Aciduria Type III	TMS
	D. 3-methylglutaconyl-CoA aciduria Type IV	TMS
25.	Multiple Carboxylase Deficiency	TMS
Fatty Acid Oxidation Disorders		
26.	Carnitine uUptake/Transporter Defects	TMS
	A. Carnitine-Acylcarnitine Translocase Deficiency	TMS
	B. Carnitine Transporter Defect	TMS
	C. Carnitine Palmitoyl Transferase I Deficiency (CPT I)	TMS
	D. Carnitine Palmitoyl Transferase II Deficiency (CPT II)	TMS
27.	Glutaric Aciduria, Type II (Multiple Acyl-CoA Dehydrogenase Deficiency (MADD))	TMS
28.	Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)	TMS
29.	Long Chain L-3 Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD)	TMS
30.	Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)	TMS
31.	Short Chain Acyl-CoA Dehydrogenase Deficiency (SCADD)	TMS
32.	Cystic Fibrosis	IRT

*TMS = Tandem Mass Spectrophotometer
 HPLC = High Pressure Liquid Chromatography
 IRT = Immunotrypsinogen Testing

Appendix B: Selected References

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