

Newborn Screening in Manitoba

Information for
Health Care Providers



Newborn screening: a healthy start leads to a healthier life

Health care professionals have provided newborn screening for phenylketonuria (PKU) since 1964 and for congenital hypothyroidism (CH) since 1977 to all infants born in Manitoba. Today, newborn screening has expanded to screen for over 40 metabolic and endocrine disorders. Individually, these disorders are rare, but as a group, will be detected in 10-12 newborns each year, or approximately 0.07% of children born in Manitoba.

The Cadham Provincial Laboratory (CPL) in Winnipeg conducts all newborn screening for these disorders.

Early detection. Early treatment. Big benefits.

Babies affected with these conditions appear normal at birth and, unless they are screened, might not be diagnosed until irreversible damage has occurred. Most of these conditions are associated with recurrent illnesses, developmental disabilities and potentially infant death, if not treated. Early diagnosis and treatment can significantly improve outcomes. For some, preventative care can improve or maintain the quality of life of these babies. For babies who start to become ill soon after birth, newborn screening may save valuable time and resources by providing early and definite diagnosis.

Informed parents make smart choices

It is important that health care providers emphasize to parents that newborn screening is part of every baby's routine care and could save their baby's life or prevent serious health problems. The vast majority of parents are happy to have their baby screened. Should a parent refuse newborn screening, the decision should be documented in the baby's medical records, and on a Manitoba newborn screening card which should be sent to CPL.

Obtaining the sample

A newborn screening specimen card should be completed between one day (24 hours) and five days after the birth of the infant: ideally, between two days (48 hours) and three days (72 hours) after birth. If screened before 24 hours of age, the screening specimen should be **recollected and the screen repeated** within five days.

Blood spots from infants are collected using the heel-prick method, which is detailed on the back of the newborn screening specimen card and in greater detail in the online CPL Guide to Services. If you are providing care for an infant who is premature (i.e. less than 37 weeks gestation), ill, has been transfused, or is receiving total parenteral nutrition (TPN) or antibiotics, please refer to the Special Considerations section on page three of this booklet.

Submitting cards: time is critical

It is critical that CPL receives the newborn screening specimen cards as soon as possible after the blood spots are collected. Therefore, the completed cards should be sent no later than 24 hours after collection and, ideally, as soon as the blood spots are dry (four to six hours after collection). Babies with some of the conditions screened will start to become ill and may suffer irreversible damage soon after birth. Rapid diagnosis and treatment are therefore imperative.

Screening test results: positive and negative

Once CPL has received and analyzed the specimen card, one of the following reports will be made:

- **Screen Negative** – The infant under your care “screens negative” for all conditions.

A report is issued by fax or mail to the birth facility or the designated healthcare provider listed on the newborn screen card, and should be filed in the baby’s medical records.

- **Repeat Sample**

If the initial sample is insufficient or unacceptable, or if the results are equivocal, you may be contacted to obtain another sample from the newborn as soon as possible.

- **Screen Positive** – The infant under your care “screens positive” for a disorder.

A positive screen does not necessarily mean that the baby has a disorder, but that further investigation is required. CPL will immediately notify the Metabolic, Cystic Fibrosis or Endocrine Clinics as appropriate at Winnipeg Children’s Hospital at the Health Sciences Centre for critical, characteristic or persistently abnormal screen results. The clinic will contact you to help locate the infant and their parent(s) to arrange confirmatory testing for the condition. They will ask you to medically assess the infant or to make arrangements for the child to be assessed at the Winnipeg Children’s Hospital (WCH). If a diagnosis of a disorder is confirmed, the respective clinic will provide management, genetic counselling and follow-up for the affected newborn. A CPL report is issued by fax or mail to the designated health care provider at the birth facility, and should be filed in the baby’s medical records.

The screening test: there are limitations

It is important to remember that, as with all screening procedures, there will be false positive and false negative results. False positives temporarily increase parental anxiety, while false negatives will give a misleading sense of reassurance. If a baby in your care exhibits symptoms of a particular disorder, but the newborn screen was negative, the child should be investigated and managed appropriately and the relevant consultant specialist should be contacted immediately for further advice. Currently the Program does not provide screening for hemoglobinopathies such as sickle cell disease or thalassemias.

There is wide clinical variation in some of the disorders that the newborn screen detects. Therefore, there will be so-called “affected” individuals – babies who are confirmed by diagnostic testing to have a particular disorder – who will remain asymptomatic even without treatment or will only have very mild symptoms.

Special considerations

Prematurity or illness

Infants who are premature (i.e. less than 37 weeks gestation) or who are ill should have their first specimen collected for newborn screening when they are five to seven days old. Premature infants will often have a high thyroid-stimulating hormone (TSH) level and may screen positive for congenital hypothyroidism. However, with repeat testing, results can be differentiated into true and false positives. Prematurity or illness in an infant being screened should be clearly indicated on the newborn screening specimen card.

Total Parenteral Nutrition (TPN) and antibiotics

CPL can analyze heel-prick blood spots from infants who have had TPN (hyperalimentation) or antibiotics. However, levels of certain amino acids and organic acids can be elevated in these infants. In order to ensure the most accurate analysis, the administration of these therapies should be clearly indicated on the newborn screening specimen cards.

Transfusions

Infants affected with one of the disorders screened for by CPL may be missed if they have had a recent blood transfusion. Normal levels of newborn screening analytes may be found in these cases because of the donor blood. Ideally, a specimen card should be “spotted” and submitted before transfusion.

Birth trauma

Infants who experience even mild forms of birth trauma (e.g. forceps delivery) are more likely to screen positive for cystic fibrosis screening tests. Subsequent stages of testing will differentiate the false positive results produced by trauma.

Disorders screened

Amino Acid Disorders

Amino acid (AA) disorders occur when the body either cannot metabolize or produce certain amino acids, resulting in toxic accumulation of some substances and/or the deficiency of others. Amino acids are derived from protein, thus treatment often involves a low-protein diet and/or a diet low in specific amino acids. Specific medications and/or vitamins may also be prescribed, depending on the disorder. It is very important for affected infants to avoid fasting.

Included in the amino acid disorders that would be detected by newborn screening are:

- phenylketonuria (PKU)
- tyrosinemia (TYR)
- homocystinuria (HCY)
- citrullinemia (CIT)
- argininosuccinic acidemia (ASA)
- maple syrup urine disease (MSUD)

Organic Acid Disorders

Organic Acidemias (OA) are a class of inherited metabolic disorders that occur when the body cannot metabolize certain amino acids and fats. This leads to an accumulation of organic acids in the blood and urine, which can be serious. Clinical symptoms of OA may include acute encephalopathy, vomiting, metabolic acidosis, ketosis, dehydration or coma, hyperammonemia, lactic acidosis, hypoglycemia, failure to thrive, hypotonia, global developmental delay, sepsis, hematological disorders, and death. Newborns with OAs are healthy at birth, but may become quite ill within the first few days of life, sometimes even before the results of the newborn screening are known. Treatment often involves a special diet, which can be low-protein, low in specific amino acids and may include dietary supplements, medical foods or medications.

Organic acidemias which can be detected by newborn screening are:

- isovaleric acidemia (IVA)
- glutaric acidemia type 1 (GA1)
- 3-hydroxy-3-methylglutaryl-CoA lyase (HMG) deficiency
- multiple carboxylase deficiency (MCD)
- propionic acidemia (PA)
- methylmalonic acidemia (MMA)
- 3-methylcrotonyl-CoA carboxylase (3-MCC) deficiency
- β -Ketothiolase (BKT) deficiency
- 2,4-dienoyl-CoA reductase deficiency.

Fatty Acid Oxidation Defects (FAOD)

The breakdown of fatty acids in the mitochondria is an essential part of the body's ability to produce energy, especially if an infant has been fasting for more than a few hours, for instance, during illness. Fatty acids are transported into the cell and then into the mitochondria, where carbon chains or fatty acids are metabolized two at a time, using specific enzymes. If the transporter molecule(s) or any of the enzymes used to reduce the number of carbons in the chain are missing, an accumulation of fatty acids in the body occurs and may cause hypoketotic hypoglycemia and tissue damage, due to fatty acid accumulation, especially in the liver, muscle, brain, and heart. Symptoms include lethargy, seizures, coma, and sudden death. An undiagnosed FAOD can also present as sudden infant death syndrome (SIDS). Dietary supplementation with carnitine and/or cornstarch may be part of the treatment for FAODs. It is very important for affected individuals to avoid fasting.

Fatty acid oxidation defects which can be detected by newborn screening are:

- short chain acyl-CoA dehydrogenase (SCAD) deficiency
- medium chain acyl-CoA dehydrogenase (MCAD) deficiency
- very long chain acyl-CoA dehydrogenase (VLCAD) deficiency
- long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency
- trifunctional protein (TFP) deficiency
- carnitine uptake defect (CUD)

Other disorders that are screened for are:

- **Congenital hypothyroidism (CH)** can cause developmental disabilities and failure to thrive if not recognized and treated early. While still rare, it is a somewhat more common condition and is caused by a thyroid hormone deficiency. Manitoba has screened for CH by measuring thyroid stimulating hormone (TSH) levels in blood since 1977. Thyroid hormone replacement is a simple and effective treatment.
- **Congenital adrenal hyperplasia (CAH)** is an inherited disease in which the adrenal gland cannot make cortisol and over produces male hormones. Without cortisol, infants may be unable to maintain blood sugar and blood pressure or produce aldosterone to regulate salt and fluids. Some newborns with CAH can be symptomatic at birth with virilization in some females. Replacement of cortisol and aldosterone is an effective means of preventing dehydration, hemodynamic instabilities and long-term sequelae.
- **Cystic fibrosis (CF)** is an inherited chronic disease affecting the lungs and digestive system of children and young adults. Mutations in the chloride pump genes responsible for regulating the components of sweat, digestive juices, and mucous leads to the production of thick, sticky secretions. Affected infants often suffer from recurrent respiratory infections, constipation or meconium ileus and malnutrition. Treatment is directed at improving secretions, optimizing nutrition and protecting respiratory function.
- **Biotinidase deficiency (BIOT)** – Biotinidase is an enzyme essential for the recycling of the vitamin biotin, which, in turn, is an enzyme cofactor. These enzymes, the carboxylases, are important in the production of certain fats and carbohydrates and for the breakdown of proteins. Features of this disorder include neurological symptoms, such as developmental disabilities and seizures, and cutaneous symptoms, such as hair loss and skin rash, which can be effectively treated with biotin supplementation.
- **Galactosemia (GALT)** – Lactose is the main sugar in breast milk, cow's milk, and many infant formulas. This sugar is metabolized into glucose and galactose in the intestine. Individuals with galactosemia are not able to break down galactose. This can result in life-threatening complications including feeding problems, failure to thrive, liver damage, bleeding, and sepsis in untreated infants. A diet restricted in lactose is very effective in preventing these complications. Even with early treatment, children with galactosemia are at increased risk for developmental disabilities, speech problems, abnormalities of motor functions and, in females, premature ovarian failure.

Please note: The disorders for which the Cadham Provincial Laboratory screens may change over time. For the most current list, please check the current Cadham Provincial Laboratory Guide to Services at www.gov.mb.ca/health/publichealth/cpl/documents.html.

Discussion guide

This discussion guide will help you to counsel your patients and answer their questions about newborn screening. The English/French brochure **Newborn Screening in Manitoba: Helping Your Baby get a Healthy Start** is also available to provide to your patient and can be found online at www.gov.mb.ca/health/publichealth/cpl.

Health care providers offer newborn screening to all infants born in Manitoba. Although screening for phenylketonuria (PKU) and congenital hypothyroidism (CH) have been offered in Manitoba for over 30 years, newborn screening has expanded to cover more than 40 disorders.

Newborn screening is strongly recommended as part of routine neonatal care as babies affected with these disorders usually appear healthy at birth. Unless they undergo screening, they may not be identified as having a disorder until irreversible damage has occurred.

In many cases, preventive care can improve or maintain the quality of life of these babies and their families. For babies who start to become ill soon after birth, newborn screening may save valuable time and resources in making a definite diagnosis. These conditions, if not treated, are associated with recurrent illnesses, developmental disabilities and potentially death. Early diagnosis and treatment can result in a normal outcome. That's why it's so important to discuss newborn screening with your patients.

Points to discuss with expectant parents

- **Offer newborn screening**

Newborn screening is considered standard of care and is strongly recommended for all babies born in Manitoba. Results are accurate and screening covers more than 40 different conditions. The disorders identified are genetic, metabolic or endocrine disorders.

- **Discuss the benefits of screening**

Identifying a baby with one of the disorders is beneficial because early diagnosis and treatment can prevent consequences such as recurrent illnesses, developmental disabilities or even death.

- **Discuss how screening is done**

The blood sample is obtained by pricking the baby's heel. The blood is transferred to a special paper card and sent to the Cadham Provincial Laboratory.

- **Screening must be timely**

Acceptable samples can be taken between one day (24 hours) and five days after birth, however the best time to collect the blood sample is when the baby is between two days (48 hours) and three days (72 hours) old. If a baby is screened before one day (24 hours) of age, the screen should be **repeated** within five days.

Babies affected by some of the disorders screened become ill very soon after birth and may suffer irreversible damage if left untreated. Rapid diagnosis and treatment may prevent this damage.

- **A repeat sample is sometimes required**

It may be that the first sample was not taken properly, the amount of blood taken was not enough to complete the testing, or there was some other problem with the sample. If requested, a repeat bloodspot collection should be taken as soon as possible, or at the time indicated by CPL.

- **Discuss the difference between a screening and a diagnostic test**

A screening test determines if there is a high or low risk that a baby has a particular condition and therefore whether diagnostic testing is required. Only a diagnostic test will determine with certainty if the baby is actually affected with a condition or not.

- **Discuss possible results of screening**

If a baby screens **negative** for all disorders, a report is issued by fax or mail to the birth facility. Over 99 per cent of babies who have the newborn screen will have a negative result.

A positive screen **does not necessarily mean** that the baby has the condition but only that further investigation is required. When results are critical, characteristic or persistently abnormal, Cadham Provincial Laboratory will contact the Cystic Fibrosis, Metabolic and/or Endocrine Clinics as appropriate in Winnipeg. They will, in turn, immediately notify the baby's health care provider who will contact the parents about the positive result and help arrange for further testing. If a diagnosis of a condition is confirmed, the appropriate specialty clinic will provide management, counseling, and follow-up.

- **Storage of Newborn Blood Cards**

The baby's newborn screen card will be securely stored after the newborn screening is completed. It may be used for follow-up tests or quality control purposes. Sometimes newborn screen cards may also be used for research purposes, but only after full approval from the Research Ethics Board at the University of Manitoba is obtained and all identifying information is removed. (<http://www.umanitoba.ca/faculties/medicine/research/ethics>). Parents who know they do not want any research conducted with their child's bloodspot may contact CPL to have it excluded from any future research.

Resources

For more information on Manitoba's newborn screening and the conditions screened for, please visit www.gov.mb.ca/health/publichealth/cpl, or contact Cadham Provincial Laboratory at **(204) 945-7980**.

Cadham Provincial Laboratory
Provincial Programs and Services
Manitoba Health
750 William Avenue
P.O. Box 8450
Winnipeg MB R3C 3Y1

Other resources

- Screening, Technology and Research in Genetics (STAR-G) Project
www.newbornscreening.info/index.html
- Save Babies Through Screening Foundation
www.savebabies.org/
- American Academy of Pediatrics:
www.aap.org/healthtopics/newbornscreening.cfm
- OrphaNet (information about rare disorders):
www.orpha.net
- National Organization for Rare Disorders (NORD):
www.rarediseases.org/search/rdblist.html

