



Saskatchewan
Health Authority

NEWBORN SCREENING IN SASKATCHEWAN

INFORMATION FOR HEALTH CARE PROVIDERS

2020

Newborn Screening
Roy Romanow Provincial Laboratory
Regina, Saskatchewan

Newborn Screening: a healthy start leads to a healthier life

Since the mid-1960s, health care providers have offered newborn screening for phenylketonuria (PKU) to all infants born in Saskatchewan. Today, newborn screening has expanded to screen for at least 30 plus metabolic and endocrine disorders. Individually, these disorders are rare, but will, as a group, affect eight to 12 out of 16,000 newborns in the province each year.

Roy Romanow Provincial Laboratory (RRPL) in Regina conducts all testing for congenital disorders.

Early detection. Early treatment. Big benefits.

These babies appear normal at birth and, unless they are screened, might otherwise not be identified to have one of these disorders until irreversible damage has occurred. If not treated, these conditions are associated with recurrent illnesses and/or developmental disabilities and/or death. Early diagnosis and treatment can result in significantly improved or positive outcomes. In some, preventive 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 in making a definite diagnosis.

Informed parents make smart choices

It's important that you, as a health care provider, emphasize to parents that newborn screening is part of their baby's routine care and could save their baby's life and/or prevent serious health problems. The vast majority of parents agree to have their baby screened.

Should a parent refuse newborn screening, the decision should be documented in the baby's medical records and the parents will be required to sign a refusal form.

What health care providers need to do

A newborn screening specimen card should be completed between one day (24 hours) and seven days after the birth of the infant: ideally, between two days (48 hours) and three days (72 hours) after birth. If tested before 24 hours of age, the baby's health care provider should repeat the test within five days, at the first postnatal check-up.

Blood spots from infants are collected using the heel-prick method, which is detailed on the back of the specimen card. If you are providing care for an infant who is premature (i.e. less than 37 weeks gestation), ill, has been transfused, or has been on total parenteral nutrition (TPN) or antibiotics, please refer to the Special Considerations section on the next page.

Submitting cards: time is critical

It is critical that RRPL receives the newborn screening specimen card as soon as possible after the blood spots are collected. Therefore, the 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 can prevent this damage.

Screening test results: positive and negative

Once RRPL has received and analyzed the specimen card, one of the following will occur:

Negative

The infant under your care “screens negative” for all conditions. A report is issued by mail to both the referring hospital 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 will be contacted and asked to obtain another sample from the newborn as soon as possible and repeat the submission procedure.

Positive

The infant under your care “screens positive” for a disorder. A screen positive does not necessarily mean that the baby has a disorder, but that it needs further investigation. RRPL will immediately notify your regional treatment centre (the Metabolic Clinic in Saskatoon) about the screen positive result and the clinic will arrange with you or the infant’s parent(s) for confirmatory testing. If a diagnosis of a disorder is confirmed, the clinic will provide management, counselling and follow-up. A report is also issued by mail to the referring hospital and health care provider, and should be filed in the baby’s medical records.

The screening test: there are limitations

It’s important to remember that, as with all screening tests, there will be false positive and false negative results. False positives will 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.

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 sick should have their first specimen collected for newborn screening when they are 24 to 72 hours old. For infants born at 32 weeks or less, a second card should be collected after TPN has been discontinued for 7 days or prior to discharge. Premature infants will often have a high thyroid-stimulating hormone (TSH) level and may screen positive for congenital hypothyroidism. However, on repeat specimens, results can be differentiated into false and true 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

RRPL 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 card.

For additional information on newborn screening, visit <https://www.saskhealthauthority.ca/Services-Locations/RRPL/Pages/Screening-and-Reference-Services.aspx>

Transfusions

Infants who are affected with one of the disorders screened for by RRPL 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 completed before transfusion.

Disorders screened

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 cause serious health problems. 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 perfectly healthy at birth, but may become quite ill within the first few days of life, even before the results of the newborn screening are known. Treatment often involves a low-protein diet and/or a diet low in specific amino acids and/or dietary supplements (such as carnitine, biotin, riboflavin), medical foods or other medications. It is very important for affected individuals to avoid fasting. Included in the OAs for which Saskatchewan screens are isovaleric academia (IVA), glutaric academia type 1 (GA1), HMG-CoA lyase deficiency (HMG), multiple carboxylase deficiency (MCD), methylmalonic academia, 3-Methylcrotonyl-CoA carboxylase (MCC) deficiency, propionic academia (PROP), B-Ketothiolase (BKT) deficiency, and dienoyl CoA reductase deficiency.

Fatty Acid Oxidation Defects (FAODs)

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 nothing to eat for more than a few hours, for instance, during illness.

Fatty acids are transported into the cell and then into the mitochondria. Once in the mitochondria, the 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 causes hypoketotic hypoglycemia and tissue damage, especially liver, muscle, and heart disease. Lethargy, seizures, coma, and sudden death are also signs of FAODs. An undiagnosed FAOD can present as sudden infant death syndrome (SIDS). Dietary supplementation with carnitine and/or cornstarch may also be part of the treatment for FAODs. It is very important for affected individuals to avoid fasting.

Included in the FAODs for which Saskatchewan screens are medium chain and short chain acyl-CoA dehydrogenase (MCAD) and SCAD deficiency, very long chain acyl-CoA dehydrogenase (VLCAD) deficiency, long chain 3-Hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, trifunctional protein (TFP) deficiency, and carnitine uptake defect (CUD).

Amino acid disorders

These disorders occur when the body cannot either metabolize or produce certain amino acids, resulting in the toxic accumulation of some substances and the deficiency of other substances. Amino acids are derived from protein. 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 individuals to avoid fasting.

Examples:

Phenylketonuria (PKU) is a condition in which individuals cannot use phenylalanine properly so it builds up in the blood (hyperphenylalaninemia).

Without treatment, phenylalanine accumulation will cause severe and irreversible developmental disabilities, eczema, and other problems. Saskatchewan has screened for PKU since 1965.

Tyrosinemia (TYR) occurs when tyrosine cannot be properly metabolized, leading to an accumulation of this amino acid and its metabolites in the liver, kidneys, and the central nervous system, causing liver disease and other problems.

Homocystinuria (HCY) occurs when homocystine accumulates in the urine. It is caused most commonly by a deficiency in an enzyme called cystathionine beta-synthase (CBS). Affected babies can have developmental disabilities and failure to thrive. They may also develop eye problems, skeletal problems, and a high chance of developing blood clots.

Citrullinemia (CIT) and argininosuccinic acidemia (ASA) are urea cycle defects. The urea cycle is the body's system for excreting waste nitrogen and ammonia, and for synthesizing arginine and urea. Hyperammonemia results when one of the enzymes in the urea cycle functions improperly. Symptoms can include lethargy, vomiting, coma, seizures, liver disease, failure to thrive, and death.

Maple syrup urine disease (MSUD) occurs when the amino acids, leucine, isoleucine, and valine cannot be metabolized. Symptoms include poor feeding, lethargy, convulsions, and even death. The urine of an affected child can have the odour of burnt sugar or maple syrup, giving the disorder its name.

Other disorders:

Congenital hypothyroidism (CH) can cause developmental disabilities and failure to thrive if not recognized and treated. It is a relatively common condition and is the result of a thyroid hormone deficiency. Saskatchewan has screened for CH by measuring thyroid stimulating hormone (TSH) levels in blood since 1978. Thyroid hormone replacement is a very effective treatment.

Congenital adrenal hyperplasia (CAH) is an inherited defect in which the adrenal gland cannot make cortisol and overproduces male hormones. Without cortisol, infants may be unable to regulate salt and fluids, and can die. Some newborns with CAH can be symptomatic at birth with virilization of females. Replacement of deficient hormones is an effective means of preventing a salt-wasting crisis and preventing long-term complications.

Biotinidase deficiency (BIOT) - Biotinidase is 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.

Cystic fibrosis (CF) is an inherited disease that affects the lungs and digestive system. The body produces thick mucus that may interfere with lung function and/or digestion. Approximately one in 3600 children born in Canada has CF.

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, however, 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 RRPL screens may change over time. For the most current list, please check the Saskatchewan Health Authority website at www.saskhealthauthority.ca

Discussion guide

This discussion guide will help you to counsel your patients and answer their questions about newborn screening. The brochure Newborn Screening: A healthy start leads to a healthier life is also available to provide to your patient.

Health care providers offer newborn screening to all infants born in Saskatchewan. Although screening for phenylketonuria (PKU) and congenital hypothyroidism (CH) have been offered in Saskatchewan since 1965 and 1978, respectively, newborn screening expanded to cover 30 plus disorders.

Newborn screening is a strongly recommended part of neonatal care since babies affected with these disorders usually appear normal 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 and/or developmental disabilities and/or 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 strongly recommended for all babies born in Saskatchewan as part of neonatal care. Results are very accurate and cover 30 plus different conditions. These are disorders of metabolism and the endocrine system.

- **Discuss the benefits of testing**

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

- **Discuss how testing 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 RRPL.

- **Testing must be timely**

Optimal collection of the baby's blood sample is when they are between one (24 hours) and three (72 hours) days old. If a baby is tested before one day (24 hours) of age, the test should be repeated within five days, at the first postnatal check-up.

Babies with some of the disorders screened will start to become ill and may suffer irreversible damage right from birth. Rapid diagnosis and treatment can 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 blood sample should be taken as soon as possible.

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

A screening test determines if there is a high or low risk that a baby has a particular condition. Only a subsequent diagnostic test will determine with certainty if the baby is affected with a condition or not.

- **Discuss possible results of screening**

The baby screens negative for all disorders. A report is issued by mail to the health care provider/referring hospital. Over 99 per cent of babies who have the newborn screen will have a negative result.

The baby screens positive for one of the disorders. A screen positive does not necessarily mean that the baby has the condition but only that further investigation is required. RRPL will contact the Metabolic Clinic in Saskatoon, which will, in turn, immediately notify the baby's health care provider or parents about the screen positive result and arrange for confirmatory testing. If a diagnosis of a condition is confirmed, the clinic will provide management counselling and follow-up.

Resources

For more information on Saskatchewan's newborn screening and the conditions screened for by the test, please visit www.saskhealthauthority.ca/services-locations/RRPL/Documents/ or contact RRPL at (306) 787-3142.

Roy Romanow Provincial Laboratory
Saskatchewan Health Authority
5 Research Drive
Regina, Saskatchewan S4S 0A4

Other resources:

- 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

Used and adapted with permission from the Government of Ontario