Saskatchewan Health Authority

Neonatal TSH Test Comment:

This is a fluoroimmunometric screening test for neonatal hypothyroidism that uses dried blood spot concentration of thyroid stimulating hormone (TSH) to identify screen positive neonates. Neonatal hypothyroidism is caused by an altered development of the thyroid gland or production of thyroid hormone and occurs in approximately 1 in 500 live births. This screening test measures the fluorescence emitted from the interaction between the TSH antigen in the patient sample and fluorescence-labeled antibody. The emitted fluorescence is directly proportional to the concentration of the TSH in the sample.

Neonatal TSH Test Disclaimer:

Positive results are presumptive and require appropriate follow-up procedures to establish the diagnosis of neonatal hypothyroidism. Consistent with other screening modalities, the results of this test should be used as a guide to other established standards of care and results interpreted in the context of the patient's clinical presentation and other available clinical information. The TSH concentration of the newborn, as determined by this test, could be affected if the mother is undergoing thyroid disease treatment. Some newborns' TSH surge will take longer than 24 hours for levels to decline. Samples collected on newborns before they reach 24 hours of age may have elevated TSH levels. Premature babies may have underdeveloped endocrine systems causing a delay in the rise of TSH. Inadequate sample volume because of a poorly spotted card could cause spurious results. This assay is prone to heterophilic antibody interference. The presence of EDTA and citrate in the sample may affect the results of this test.

Neonatal IRT Test Comment:

This is a fluoroimmunometric screening test for cystic fibrosis (CF) that utilizes dried blood spot concentration of neonatal human immunoreactive trypsinogen (IRT) to identify screen positive neonates. Cystic fibrosis is an autosomal recessive disorder with an incidence of 1 in 2500 live births in the Caucasian population. This screening test measures fluorescence emitted from the interaction between the IRT antigen in the sample and fluorescence-labeled antibody. The fluorescence is directly proportional to the concentration of IRT in the sample.

Neonatal IRT Test Disclaimer:

Positive results are presumptive and require an appropriate diagnostic procedure to establish the diagnosis of CF. Diagnostic modalities may include CF mutation analysis and sweat chloride test. Consistent with other screening modalities, the results of this test should be used as a guide to other established standards of care and results interpreted in the context of the patient's clinical presentation and other available clinical information. Critically ill and/or premature newborns may have stressed pancreases resulting in false-positive IRT results. Immunoreactive trypsinogen results from this test may not be reliable in patients with meconium ileus or bowel obstruction, and additional testing may be warranted. Inadequate sample volume because of a poorly spotted card could cause spurious results. This assay is prone to heterophilic antibody interference. The presence of EDTA and citrate in the sample may affect the results obtained from this test.

Neonatal GALT Test Comment:

This enzymatic test measures galactose-1-phosphate uridyl transferase (GALT) in dried blood spots as part of the newborn screening process for classic galactosemia caused by GALT deficiency. Galactosemia is an autosomal recessive inborn error of metabolism characterized by an altered metabolism of lactose to glucose and galactose. This screening test measures the florescent intermediate produced by the action of GALT on its metabolites.

Saskatchewan Health Authority

Neonatal GALT Test Disclaimer:

Positive results are presumptive and require an appropriate diagnostic procedure to establish the diagnosis of galactosemia. Confirmation of a positive screen may be done by measuring galactose-1-phosphate using the definitive mass spectrometry method. Consistent with other screening modalities, the results of this test should be used as a guide to other established standards of care and results interpreted in the context of the patient's clinical presentation and other available clinical information. Extreme heat and humidity during sample transportation could cause decreased enzyme activity. Inadequate sample volume because of a poorly spotted card could cause spurious results. Samples from patients with galactosemia that have undergone blood transfusion will appear normal due to the activity of the GALT enzyme in the donor blood.

Neonatal 17-OH Progesterone Test comment:

This fluoroimmunoassay measures the concentration of human 17-OH-progesterone (17-OHP) in dried blood spots and it is used for neonatal screening of congenital adrenal hyperplasia (CAH). Congenital adrenal hyperplasia is an autosomal recessive disorder with an incidence of 1 in 10,000-15,000 births. Congenital adrenal hyperplasia results from a deficiency in one of five enzymes involved in steroid biosynthesis with 90% of cases attributed to a defective 21α-hydroxylase enzyme. This causes blockage of the production of cortisol resulting in the accumulation of 17-OHP and androstenedione. Testing for elevated 17-OHP in the newborns allows infants with CAH that did not present at birth to be diagnosed before symptoms occur. This screening test is based on the competition between labeled 17-OHP and the17-OHP present in the patient's sample for a limited number of binding sites on specific polyclonal antibodies. A second antibody is used to separate the bound and free 17-OHP. The resulting fluorescence is measured and inversely proportional to the concentration of 17-OHP in the sample.

Neonatal 17-OH Progesterone Test Disclaimer:

Positive results are presumptive and require an appropriate diagnostic procedure to establish the diagnosis of CAH. Confirmation of a positive screen may be done by measuring17-OHP using definitive mass spectrometry. Consistent with other screening modalities, the results of this screening test should be used as a guide to other established standards of care and results interpreted in the context of the patient's clinical presentation and other available clinical information. Samples collected before the infant reaches 24 hours of age may result in false-positive 17-OHP screen results. Sickness, prematurity, or stress may cause spuriously elevated 17-OHP. Falsely elevated results may be caused by cross-reactivity of other hormones with the 17-OHP used in this immunoassay. Maternal steroid treatment (eg. prednisone) can suppress the fetus' adrenal function and may result in false-negative CAH screening results. Inadequate sample volume because of a poorly spotted card could cause spurious results. The presence of EDTA and citrate in the sample may affect the results obtained from this test.

Neonatal Biotinidase Test comment:

This is fluorometric test for the measurement of biotinidase activity in dried blood spots for the screening of neonatal biotinidase deficiency. Biotinidase deficiency is an autosomal recessive disorder caused by a deficiency of the enzyme biotinidase. Biotinidase is important in the metabolism of biotin. Incidence of biotinidase deficiency is 1:130,000 for profound deficiency (less than 10% of normal enzyme activity) and 1:110,000 for partial deficiency (10 – 30% of normal) for a combined incidence of 1:60,000. The reaction of the analyte in the sample with the reagent causes fluorescence. The resulting fluorescence is directly proportional to the biotinidase activity in the sample.

Saskatchewan Health Authority

Neonatal Biotinidase Test Disclaimer:

Positive results are presumptive and require an appropriate diagnostic procedure to establish the diagnosis of biotinidase deficiency. Consistent with other screening modalities, the results of this screening test should be used as a guide to other established standards of care and results interpreted in the context of the patient's clinical presentation and other available clinical information. This test should not be used to distinguish partial from profound biotinidase deficiency. Extreme heat and/or humidity during sample transportation can cause decreased biotinidase. Some antibiotics and elevated levels of albumin, gammaglobulin, triglyceride, and biotin have been known interfere with this method. Inadequate sample volume because of a poorly spotted card could cause spurious results.

Neonatal Amino Acids and Acylcarnitines Test Comment:

This is a screening test that utilizes electrospray tandem mass spectrometry to determine the concentrations of analytes that may be suggestive of metabolic disorders of amino acids, organic acids, and fatty acid metabolism using dried blood spots. This method does not require chromatographic separation and allows for simultaneous analysis of both amino acids and acylcarnitines on the same blood spot.

Neonatal Amino Acids and Acylcarnitines Test Disclaimers:

This is a broad-spectrum test that screens for all amino acids and acylcarnitines. Positive results are presumptive and require confirmation using targeted and specific mass spectrometry. Antibiotics and total parenteral nutrition are known to cause spurious results in this test.

Spinal Muscular Atrophy (SMA) Test Comments:

This is a screening test for SMA to detect homozygous SMN1 deletions. This is not a carrier screen and carriers of SMA with one copy of the SMN1 gene or no copies of SMN1 but with 5 or more copies of SMN2 will be reported only as SMA screen negative. Spinal muscular atrophy (SMA) is an autosomal recessive disorder caused by pathogenic variants in the SMN1 gene. The majority (>95%) of SMA patients are homozygous for a deletion of exon 7 and/or 8. SMA positive patients that will be missed by this screen are a compound heterozygotes with a single SMN1 deletion and a different pathogenic variant in the SMN1 gene. In approximately 2% of the cases, there is a de novo mutation in SMN1. Copy number of SMN2 is polymorphic within the population. SMN2 copy number affects the severity of the disease in individuals with no copies of SMN1 with <2 copies of SMN2 having a more severe phenotype than patients carrying 3 or 4 copies. Individuals having 5 or more copies of SMN2 have not been affected by SMA and will be considered screen negative with this test. Confirmation of the SMN1 and SMN2 copy numbers is performed through two methods; Multiplex Ligation-dependent Probe Amplification (MLPA - MRC Holland P021) and in vitro nucleic acid amplification (Asuragen SMA - A00055). All SMA screen positive results from a blood spot card must be confirmed with a fresh EDTA blood collection. Once confirmed, a clinical consultation with a pediatric neurologist will be arranged.

SMA Test Disclaimer (under test validation effective February 1, 2022):

Mutation analysis should be combined with phenotypic and pedigree data for the most accurate interpretation. Possible diagnostic errors include sample mix-ups and genotyping errors resulting from trace contamination of PCRs, and from rare polymorphisms, which interfere with analysis. Low level mosaicism may not be detectable by this method. Mistaken paternity may be inadvertently identified. Blood transfusions are known to affect some newborn screening results. If the bloodspot is not collected prior to a transfusion, arrangements should be made through the baby's physician / midwife, that two repeat cards be collected, one at three weeks (21 days) and one at four months (120 days) after the date of the transfusion. The SMA screen will be repeated for each collection.

Saskatchewan Health Authority

SCID Test Comments:

This screening test helps to identify newborns with very low or absent naïve T-cells due to severe combined immunodeficiency (SCID) or other congenital disorders causing severe T-cell lymphopenia including X-linked agammaglobulinemia (XLA). This screen encompasses the use of semi-quantitative determination of TREC (T-cell receptor excision circles) and KREC (Kappa-deleting recombination excision circles) by real-time PCR as well as variant specific tests in DNA from blood specimens dried on newborn screening cards. Variant specific tests by real-time PCR are included in the screen to detect some attributable deficiencies (but not all) in either the inhibitor of kappa light polypeptide gene enhancer in B-cells kinase beta (IKKβ) or zeta chain-associated protein kinase (ZAP70) genes. IKBKB-deficiency and ZAP-70-deficiency are forms of SCID in which T-cells mature and produce TRECs but have been rendered inactive when both copies of the gene are mutated. The specific variants included in the screen are NM_001556.3(IKBKB): c.1292dup p.(Gln432Profs*62) and NM_001079.3(ZAP70): c.1624-11G>A p.?. Homozygosity for either of these variants will be reported as SCID screen positive but carriers (i.e. heterozygotes) will not be reported.

SCID Test Disclaimer (under test validation effective February 1, 2022):

This test is not intended for use as a diagnostic test or for screening of SCID-like syndromes, such as DiGeorge Syndrome, or Omenn Syndrome. It is also not intended to screen for less acute SCID syndromes such as leaky-SCID or variant SCID, atypical XLA and XLA carriers. Possible diagnostic errors include sample mix-ups and genotyping errors resulting from trace contamination of PCRs, maternal cell contamination of fetal samples, and from rare polymorphisms, which interfere with analysis. Low level mosaicism may not be detectable by this method. Mistaken paternity may be inadvertently identified. Blood transfusions are known to affect some newborn screening results. If a blood transfusion is not collected prior to the transfusion this laboratory will request, through the baby's physician / midwife, that two repeat cards be collected, one at three weeks (21 days) and one at four months (120 days) after the date of the transfusion.

CMV Test comments:

The CMV screening test is designed to detect congenital Cytomegalovirus (cCMV). Vertical transmission from mother to fetus leads to cCMV infection in approximately 1 in 150 babies with up to 20% of these babies developing complications; most common late-onset sequelae are hearing loss and developmental delay. cCMV causes 10-25% of all sensorineural hearing loss in children. The CMV screen uses real-time PCR with targets unique to human Cytomegalovirus; Unique Long 55 (UL55), Unique Long 83 (UL83) genes and the human RnaseP gene as an internal quality control marker for adequate DNA collection.

CMV Test Disclaimer (under test validation effective February 1, 2022):

Screen positive CMV results in a bloodspot need to be confirmed by NAAT in a urine specimen. False positives from the bloodspot can occur. Possible diagnostic errors include sample mix-ups and genotyping errors resulting from trace contamination of PCRs, and from rare polymorphisms, which interfere with analysis.