# HEALTHCARE PROFESSIONAL'S NEWBORN SCREENING UPDATE

Department of Health & Human Services
DHHS
NEBRASKA

Nebraska Newborn Screening Newsletter August 2014

## Severe Combined Immune Deficiency(s) (SCIDs) to be added to Nebraska's newborn screening panel

Screening for Severe Combined Immune Deficiency (SCID) will begin in Nebraska with blood spots received at the screening lab on October 4, 2014 Screening for SCID more familiarly known to the lay public as "bubble boy disease" is currently done in 19 states.

Following a National Insitute of Health//Centers for Disease Control sponsored pilot in which over one million babies were screened, incidence rates were found to be higher than formerly believed. Classic SCID incidence is about 1:68,000, SCID Variants 1:68,000 and SCID + SCID Variants about 1:34,000. Hispanics have been found to have a higher incidence at about 1:22,000. Including all related T-cell deficiencies that are being detected by the screen, the incidence is about 1:22,000. A report of 11 states' experience with SCID screening is expected to be published in JAMA in the coming months.

Newborn screening for SCID has provided the opportunity to initiate treatment prior to symptoms for more babies. For babies with classic SCID who will receive a transplant, outcome is much better if it is achieved prior to infections and before three and half months of age. Rapid follow up with confirmatory testing is necessary to allow the babies with SCID and other T-cell deficiencies to be treated quickly and to ensure the best possible outcomes.

Read inside to find out how Nebraska's Newborn Screening Program and pediatric specialists in immunology will help you talk to new parents about SCID, and support you in responding to positive results.

*" It is very exciting to have Nebraska start screening all newborns for this serious, but fortunately rare, genetic condition. Early detection is the key to successful therapy"*

*- Russell Hopp, DO*

*Pediatric Allergy/Immunologist*

## In This Issue


- SCID Screening Test
- Follow-up Steps
- Confirmatory Testing Recommendations

**Thanks to research resulting in successful treatment and therapies, and earlier identification via the screening test, more babies live lives free of isolation. Patients with classic SCID can reconstitute their immune system with hematopoietic bone marrow stem cell transplant.**

## SCREENING TEST

The screening test for SCID is a measurement of the number of TRECs (T-cell receptor excision circles) formed during the maturation of T-cells. Pieces of DNA are lost during the recombination of T-cell receptor genes. These leftover pieces of DNA form into circles known a TRECs. The number of TRECs reflects the number of naïve T-cells. Low copy numbers of TRECs indicate decreased T-cell production which can indicate SCID. Other conditions with low T-cell numbers may also be detected.

The screening test is done on a punch from the same dried blood spot specimen collected for the rest of the screening panel. Using Real-time Polymerase Chain Reaction (RT-PCR), the test detects copy numbers of TRECs. Zero or low TREC copy numbers are considered abnormal. When low TRECs are found, another test is run to determine adequacy of DNA amplification by running PCR on the sample for Beta Actin. If the results show low TRECs *and* low Beta Actin, it is considered **inconclusive** due to failure of the DNA to amplify and a repeat dried blood spot is requested. Zero or very low copy numbers of TRECs (with adequate amplification as verified by Beta Actin) are indicative of Classic SCID or another variant or T-cell lymphopenia and are reported as **positive**. Because of the risk of SCID, positive results on screening represent a **medical emergency**, as many will require transplant, enzyme therapy or gene therapy, and preventive steps should be followed to avoid exposure to sources of infection.

The screening test is **highly sensitive and specific** in the full-term newborn population. However the pre-term population tend to have more abnormal results because of the immaturity of the immune system and fewer T-cells being produced in the very early and early preterm births. We anticipate that most NICU admits with abnormal TRECs, will have normal results on the required repeat screens. This has been the experience of other programs. However we will be monitoring and tracking this as other states' repeat protocols may utilize different repeat screen time intervals.

Ebrahim Shakir, MD

Russell Hopp, DO

Pediatric Immunologists in Nebraska who will work with primary care providers who have patients with positive SCID screening results to assist with diagnosis and treatment.

## FOLLOW UP:

The Nebraska Newborn Screening Program (NNSP) in collaboration with the Advisory Committee and specialists have developed recommended follow-up activities for all probable situations including positive screens, inconclusive screens and situations where it appears the DNA failed to amplify. A newborn's physician will be provided with information including Parent Information (Fact sheets0, Physician Action (ACT) sheets, and recommendations for immediate next steps. For positive screens the baby's health care provider will be contacted by phone and connected with the Pediatric Immunologist on service that day. Nebraska's SCID Team has planned for rapid communication, confirmatory and diagnostic work up, and referral for transplant as needed.

**Since bone marrow stem cell transplant is so successful in newborns with Classic SCID who are transplanted *before the onset of any infection* and *by three and a half months of age*, rapid intervention to avoid exposure to sources of infection will be important when positive screen results are reported.** Recommendations and consultation with one of the Pediatric Immunologists from the SCID team will be available to advise on this. One family's circumstances may be suitable for in-home protective isolation of the newborn, while another newborn's family situation might make hospital admission and protective isolation a better choice.

## CONFIRMATORY TESTING:

Upon notification of a positive SCID result and consultation with the Pediatric Immunologist on call, the baby's primary healthcare provider should arrange the collection of blood for "Flow Cytometry, Immunodeficiency or SCID panel." Regional Pathology Services at the University of Nebraska Medical Center has developed this panel specifically for confirming newborns with positive SCID screen results. Testing is available Monday through Saturday, and specimens must be processed within 24 hours. Therefore **specimens should be collected *only* when they can be shipped to arrive the same day or overnight**. (i.e. don't collect confirmatory specimens for SCID on Saturdays).

## Resources For Your Patients' Parents

Immune Deficiency Foundation – www.primaryimmune.org

Angels for Life Foundation
- www.SCIDangelsforlife.com

American Academy of Allergy, Asthma and Immunology
- www.aaaai.org

Nebraska Newborn Screening Program
- www.dhhs.ne.gov/nsp

National Newborn Screening Clearinghouse
- www.babysfirsttest.org

## Nebraska's SCID Team

**Karen Eveans, MD** will be the primary Follow-up Specialist from the Newborn Screening Program from whom you will receive initial notification of abnormal results, as well as supportive educational materials both professional and parent oriented. She will advise the baby's primary healthcare provider on ordering the confirmatory testing. She will follow up with you and the SCID Team until diagnosis has been made and treatment or intervention as appropriate have been initiated. **Krystal Baumert, and Julie Luedtke** may also be contacting you. 402 471-0374

**Ebrahim Shakir, MD** 402 397-7400 or **Russell Hopp, DO** 402 354-4700 are the Pediatric Immunologists who will be the primary provider's first point of contact after hearing from the newborn screening program. They will consult on next steps and interpreting the flow cytometry. Referrals to these specialists may be in order after flow cytometry is complete for further diagnosis and treatment plan.

**James L. Harper, MD**, Pediatric Hematologist will work with the team to facilitate donor match and bone marrow stem cell transplant as needed.

**Samuel Pirruccello, MD**, UNMC Regional Pathology Services, has developed the Flow Cytometry, Immunodeficiency or SCID Panel including appropriate subspecies, specifically to help in the diagnosis of positive SCID screens.

**NEXT STEPS FOR POSITIVE RESULTS**:

- Expect a phone call and fax from the program for positive screens (Instruct clinic staff to quickly triage these faxes directly to the baby's physician/healthcare provider in your clinic).

- Consult with the Pediatric Immunologist on call.

- Contact the parents to explain the screening results, possible meaning, and next steps for obtaining the confirmatory test specimen, including the following:

  -Screening is NOT diagnostic.
  -Besides the possibility of SCID, a false positive result is possible, or another variant immune deficiency could be possible.
  -Many forms of immune deficiencies are treatable and some may even be cured.

- Advise the family about measures they should take to prevent exposure to sources of infection:

  -Discuss protective isolation at home vs. hospital,
  -Keep people with colds or signs of infection away,
  -Boil water used for formula feedings,
  -Interrupt breast feeding until mother's cytomegalovirus (CMV) status is established. (Mother can pump and store, and if CMV negative - may use the breast milk)
  -Do not give any live attenuated vaccine to the baby or household contacts (e.g. no rotovirus vaccine)

- Provide the family with the Parent Information Fact Sheet, and direct them to reliable web sites as listed on the sheet.

- Fax or enter electronic order for the confirmatory test to an outpatient laboratory for specimen collection (often the birth hospital for the newborn), and instruct the parents where to take the baby. Follow- p to be sure specimen is collected and sent.

## Contact Us

Give us a call for more information or questions about SCID or newborn screening.

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Visit us on the web at www.dhhs.ne.gov/nsp

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