Severe Combined Immunodeficiency (SCID) and Newborn Screening in Missouri

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Newborn Screening

Background

- Refers to screenings performed on newborns shortly after birth to protect them from the dangerous effects of disorders that may not be detected for several days, months, or even years.
  - Newborn Bloodspot Screen
  - Newborn Hearing Screen
  - Critical Congenital Heart Disease (CCHD) Screening

- Missouri law requires all babies born in the state to be tested.
Newborn Screening

Background

- **1959** – Robert Guthrie began working on a method to screen for Phenylketonuria (PKU).

- **1961** – Guthrie developed his bioassay for PKU using dried blood collected on filter paper.

- **1965** – Legislation was passed in Missouri to start screening newborns for PKU.

- **1979-present** – In addition to PKU, over 70 disorders have been added to MO’s newborn screening panel.
What is SCID?

- Severe Combined Immunodeficiency (SCID), pronounced “skid”.
- Sometimes in the past called “Bubble Boy Disease”, referring to David Vetter who was born with SCID in 1971.
- New York Times Article
- “The Boy in the Plastic Bubble” movie
What is SCID?

- A serious and potentially fatal primary immunodeficiency.
- There are at least 15 different gene defects that can cause SCID. These defects result in:
  - Absence of T-cells
  - Absence or decreased function of B-cells
  - In many cases decreased non-killer cell function
X-linked Recessive Inheritance - Carrier Mother

ADA SCID

Forms of SCID

- Deficiency of the Alpha Chain of the IL-7 Receptor
- Deficiency of Janus Kinase 3
- Deficiencies of CD3 Chains
- Deficiency of CD45
- Other Causes
Symptoms

• Babies appear normal and healthy at birth.
• Infants begin developing infections early in life as their mother’s immunity wears off.
• Symptoms include, but are not limited to, recurrent bouts of diarrhea, pneumonia, ear infections, thrush, and bronchitis that do not respond to usual therapies.
• Untreated children develop life-threatening infections from bacteria, viruses, and fungi.
• Without treatment, children with SCID will die before their first or second birthday.
Incidence

- The estimated annual incidence of SCID is one case per 40,000-100,000 live births.
  - Approximately 40-100 new cases among infants in the United States each year.
  - Based on newborn screening evidence, incidence may be more like one case in 58,000 births.
  - The incidence for all types of immunodeficiency may be closer to one in every 15,000 births.
Treatment

- **Bone marrow transplant (BMT)** is the most effective treatment for SCID
  - 96% likelihood of cure if transplanted within the first 3.5 months of life, before serious infections have occurred.

- **Immunoglobulin Replacement Therapy (IRT)**
  - Although immunoglobulin therapy will not restore the function of the deficient T-cells, it does replace the missing antibodies resulting from the B-cell defect.

- **Isolation**
  - Avoid public places, large crowds, contact with pets, contact with anyone who may be sick, live vaccines, and limit contact with relatives.
Newborn Screening (NBS) and SCID

- Criteria to be added to newborn screening panel
  - There must be a screening test available that works well on dried bloodspots.
    - More than one available methodology to test for SCID
  - There should be a treatment available that greatly improves the prospect for the child.
    - BMT has 96% successful cure rate
  - An appropriate disorder should be one that can be caught and treated in the newborn period to prevent illness or death.
    - Early intervention is crucial for SCID survival
Newborn Screening (NBS) and SCID

• In 2008, Wisconsin became the first state to test for SCID on their newborn screen.
• SCID was added to the Recommended Uniform Screening Panel (RUSP) in 2010.
• House Bill No. 1682 was passed in 2016 requiring that all newborns in Missouri should be screened for SCID by January 1, 2017.
• A SCID Task Force was formed in 2016 to provide assistance and guidance in implementation of newborn screening for SCID.
• Full-population pilot SCID testing began on the first working day of the year, January 3, 2017.
**LABORATORY REPORT**

**Submitter:** COX MEDICAL CENTER BRANSON  
**Address:** 545 BRANSON LANDING BLVD  
**BRANSON, MO 65615**

**Specimen Type:** Initial  
**Date Collected:** 02/19/2016 at 17:35  
**Date Received:** 02/19/2016  
**Date Reported:** 02/19/2016  
**Copy Printed:** 02/19/2016

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<td>Lysosomal Storage Disorders</td>
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</tr>
</tbody>
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SCID Newborn Screening: Current Status of Implementation Map

42 States Currently Screening for SCID - 88% of all newborns in the U.S. are receiving SCID screening

*As of October 1, 2016

Immune Deficiency Foundation
www.primaryimmune.org
Newborn Screening (NBS) and SCID

• Testing is accomplished through the dried bloodspot specimens that are already being collected.

• Samples are tested for the presence of T-cell Receptor Excision Circles (TREC)s.
  o TREC are circular DNA molecules formed from developing T-cells
  o Babies with SCID have no TREC s

• Low values of TREC s are associated with other T-cell lymphopenia.
  o DiGeorge Syndrome
  o Trisomy 21
  o CHARGE Syndrome
  o Many other lymphopenias
Screen-Positive SCID Result

- Screen-positive results are called from the State Public Health Laboratory to the designated SCID follow-up nurse.
- The follow-up nurse will contact the Primary Care Provider (PCP) with the results. If the PCP is unable to be located, the family will be directly contacted.
- SCID information sheets will be provided to both the PCP and the families.
- Immunology specialist contact information will be provided in order to make an appointment for the child.
  - St. Louis Children’s Hospital
  - Cardinal Glennon Children’s Hospital
  - Children’s Mercy Hospital
Severe Combined Immunodeficiency (SCID)
Screen-positive Follow-up Guidelines

Newborn Screening
The newborn screen for this infant revealed an abnormal result for severe combined immunodeficiency (SCID). The screening test for T cell receptor excision circles (TRECs), a byproduct of normal T cell development, identifies SCID as well as certain related conditions with low T cells. The interpretation of this result is consistent with "possible" severe combined immune deficiency. If newborn screening results indicate low levels of TRECs, referral to an immunology specialist for flow cytometry should be made. In cases that are inconclusive a second newborn screening may be necessary for testing.

Description
Severe Combined Immunodeficiency (SCID) includes a group of rare but serious and potentially fatal, inherited immune disorders in which T lymphocytes fail to develop and B lymphocytes are either absent or compromised. Impairment of both B and T cells leads to the term “combined.” Newborns with SCID normally appear healthy and may not have a family history of immunodeficiencies. Early symptoms include, but are not limited to, frequently recurring bouts of ear infections, thrush, bronchitis, pneumonia, and diarrhea that do not respond to usual therapies. Untreated patients develop life-threatening infections due to bacteria, viruses and fungi. Without early detection and treatment, children affected by SCID will die before their first or second birthday. Treatment with bone marrow transplant within the first few months of life, before infection has occurred, can cure SCID in most cases.

You should take the following actions
- Contact an immunology specialist from the list provided and make an appointment for the newborn within 7 days.
- Contact the parent guardian today with test results and to check on the health of the infant. Point out that additional testing is needed to determine if the newborn actually has SCID or any other immune deficiency.
- Examine the infant in person within 1-2 days for signs of infection, congenital heart disease, and congenital abnormalities.
  - Use proper isolation precautions when evaluating the newborn in the clinic.
    - Take the infant directly to exam room, avoiding waiting areas and contact with other sick children.
    - Clinic staff should wear proper protective equipment, including masks, gowns, and gloves when in contact with child.
  - Please take the following precautions:
    - Monitor the newborn for any signs of infection.
    - If blood products are needed, they must be leukodepleted, irradiated, and CMV negative.
- No live virus vaccines for the newborn or family members. Vaccines to avoid include:
  - Rotavirus
  - Varicella (chickenpox)
  - Zostavax (shingles)
  - Measles, Mumps, Rubella (MMR)
  - Flu Mist
  - Yellow Fever
  - Typhoid
  - Small Pox
- Please instruct parents to:
  - Avoid contact with anyone including immediate family members with vomiting, diarrhea, fever, cough, and viral infections such as cold sores or shingles, etc.
  - Avoid crowded areas or child care facilities.
  - Use boiled water (not well water) to mix the infant’s formula.
  - Practice good hand hygiene.
  - All pets should be avoided. Practice good hand hygiene after handling pets.
- For any further questions contact the Missouri Newborn Screening Program at 573-751-6266.

Additional Resources
http://health.moe.gov/newbornscreening
http://primaryimmune.org
https://www.scid.net/
Immunology Specialist Contact Information

Cardinal Glennon Children’s Hospital
Dr. Alan P. Knutson, M.D.
Pediatric Allergy & Immunology
Contact Name: Theresa Forsythe
Clinic Number: 314-268-4014, choose option 4 to speak to Theresa

Children’s Mercy Hospital & Clinics
Dr. Nikita Raje, M.D.
Pediatric Allergy & Immunology
Contact Name: Connie Freeman
Contact Number: 816-560-2972
Clinic Number: 816-960-8885
After Hours: 816-334-3380, ask for the On-Call Immunologist

St. Louis Children’s Hospital
Dr. Caroline Horner, M.D.
Pediatric Immunology
Contact Name: Dawn Helfrich, RN, MSN, PNP
Dawn’s Number: 314-362-9062
Clinic Number: 314-454-2694
After Hours: 314-454-6000, ask for the On-Call Immunologist
Severe Combined Immunodeficiency (SCID) Parent Information Sheet

What is Newborn Screening?
A day or two after your baby was born, a small blood sample was taken from your baby’s heel to test for certain medical disorders. This sample is what’s known as a newborn bloodspot screen. The goal of the screening is to find conditions which, if caught early, can be treated and improve the health of babies.

Your Baby’s Test Results
One of the tests included in the newborn screen is for a disorder called Severe Combined Immunodeficiency (SCID), pronounced “skid.” Your baby’s test showed “possible” SCID. This does not mean your baby has SCID. More testing will need to be done to determine if your baby has this disorder.

What is Severe Combined Immunodeficiency?
SCID is a rare, but very serious genetic condition characterized by extremely low counts of T-cells, which are a specific type of white blood cell. White blood cells are responsible for your immune system’s ability to fight off infection. When the immune system is not working properly, your baby is at a very high risk of serious, life-threatening infections.

What Now?
Your baby’s doctor has been contacted and given a copy of the newborn screening results. He or she will recommend getting another blood sample and make an appointment with a specialist that cares for babies with SCID. It will take a few days before the other test results are back, so in the meantime, these are some things you and your family should do:

- Call your baby’s doctor if your baby shows any signs of infection such as:
  - High or low temperature
  - Poor feedings
  - Very sleepy and not waking up to eat
  - Irritability
  - Pale or grayish skin color
  - Faster than normal breathing
- Use good handwashing practices
- Avoid crowded areas and child care facilities.
- Avoid anyone who is sick or thinks they may be sick, including members of your immediate family. Anybody that has symptoms such as vomiting, diarrhea, fever, cough, or viral infections like cold sore or shingles should not be in contact with your baby.
- Avoid all contact with pets and use good handwashing practices after handling pets.

- No live virus vaccines for your baby or family members. Vaccines to avoid include:
  - Rotavirus
  - Varicella (chickenpox)
  - Zostavax (shingles)
  - Mumps, Mumps, Rubella (MMR)
  - FluMist
  - Yellow Fever
  - Typhoid
  - Small Pox
- Use boiled water (no well water) to mix your baby’s formula.
- If your baby were to need blood products, please be sure to inform the doctors that all products must be leukodepleted, irradiated, and CMV negative.

Additional Information
If you have any further questions or concerns about the information you have been given, please discuss your concerns with your baby’s doctor. You may also contact the Missouri Newborn Screening Program at 573-751-6266.

Other Resources
http://health.mo.gov/newbornscreening
http://primaryimmune.org
https://www.scid.net
Confirmatory Testing

- Flow Cytometry
- CBC with Manual Differential
- Gene Sequencing
Prognosis

- **SCID is one of the few NBS disorders that has a cure!**
  - 96% likelihood of cure if treated with BMT before 3.5 months of age
  - BMT transplant after 3.5 months leads to 60-70% chance of success
  - Untreated children rarely live past their 2nd birthday

- **Early detection and intervention is KEY!**
Timeliness

- Screens collected at 24-48 hours of age
  - No longer needs to be 24 hours from first feeding
- Holiday courier pick up
- Sunday courier pick up
- Saturday and holiday testing
- Lab Report Access Portal
NBS Sample Transit Time Improvements

Percentage of Samples

Days from Sample Collection to Testing of Sample by MSPHL

- All of 2013
- All of 2014
- Jan thru June of 2015
- July thru Sept 2015

Collection Date Not Provided - Transit Time Unknown
Education and Awareness

For more information:
- Missouri Department of Health and Senior Services
  [http://health.mo.gov/newbornscreening](http://health.mo.gov/newbornscreening)
- Immune Deficiency Foundation
  [http://primaryimmune.org/](http://primaryimmune.org/)
- SCID.net
  [http://www.scid.net/](http://www.scid.net/)
- Baby’s First Test

Front line staff
Newborn Screening Newsletter in 2017
References

http://www.babysfirsttest.org/newborn-screening/conditions/severe-combined-immunodeficiency-scid
https://www.aacc.org/publications/cln/articles/2013/november/scid
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5922a3.htm
http://www.newbornscreening.info/Parents/otherdisorders/SCID.html
Thank You!

Contact Information:
Amber Bryant, R.N.
amber.bryant@health.mo.gov
573-751-6266