Practice Guide for Sickle Cell Trait Identified in Newborn Screening

Objective

To provide guidance to health care providers when they receive notification a newborn in their care is a sickle cell trait carrier. Providers will be responsible for communicating results with the family and arranging necessary follow-up in accordance with this guide.

See algorithm in Appendix A.

Background

Sickle cell disease (SCD) is a clinically significant hemoglobinopathy that is inherited in an autosomal recessive manner. In patients with SCD, red blood cells can acquire a crescent or 'sickle' shape, which may cause pain and tissue damage. Individuals with SCD have two sickle cell gene variants, or one sickle cell gene variant alongside a second gene variant that impacts the quantity or quality of adult hemoglobin, such as beta thalassemia.

When an individual has only one sickle cell gene variant, they are said to carry **sickle cell trait (SCT)**. SCT occurs in all ethnic groups, but it is more common in certain populations such as African, Mediterranean, Middle Eastern and Asian groups. Carrier frequency is dependent on ethnic background. Worldwide, SCT affects an estimated 300 million people, with a prevalence ranging from 2% to 30% in more than 40 countries[1]. The incidence of SCT is approximately 1 in every 128 infants born in Alberta.

Considerations

Summary

There are no immediate health concerns for an infant who carries SCT. No urgent action is required and referral to a hematologist is generally not necessary. However, there may be implications for other family members. See Appendix B for frequently asked questions to help guide your discussions with the family.

Health Expectations for People with Sickle Cell Trait

Most people who carry SCT will not have associated health problems and they will not develop SCD. In rare cases, carriers may experience some health issues such as hematuria, proteinuria or chronic renal disease, see Centres for Disease Control and Prevention – Sickle Cell Trait Toolkit for additional information. People who carry SCT may also experience exertional health illness associated with extreme strenuous activities or during periods of significant dehydration.

While SCT is usually a benign condition that does not require referral to a hematologist, if you are concerned that your patient may have active clinical symptoms associated with SCD, please contact pediatric hematology, based on the family's location preference:

Edmonton

Stollery Children's Hospital
8440 – 112 Street
Edmonton, AB T6G 2B7
Phone: 780-248-5415
Fax: 1-888-775-9068

Calgary

Alberta Children's Hospital
28 Oki Dr. NW
Calgary, AB T3B 6A8
Phone: 403-955-7155
Fax: 403-955-7393

Implications for Other Family Members

When a child is found to carry SCT, at least one parent is also expected to carry SCT. Given how common SCT is, there is a chance that both parents carry SCT. These couples have a 1 in 4 probability of having a child with SCD (see Figure 1).

If the parents of an infant carrying SCT are planning more pregnancies, the following hemoglobinopathy investigations are recommended for each parent: hemoglobin electrophoresis, CBC and ferritin. Genetic counselling is recommended if both parents are found to be carriers for any thalassemia or other hemoglobinopathy.

If your patient's family is interested in reproductive genetic counselling, and both parents are carriers, please contact the Clinical & Metabolic Genetics Program, based on the family's location preference:

Edmonton

8-53 Medical Sciences Building
8440 – 112 Street
Edmonton, AB T6G 2H7
Phone: 780-407-7333
Fax: 780-407-6845

Calgary

Alberta Children's Hospital
28 Oki Dr. NW
Calgary, AB T3B 6A8
Phone: 403-955-7373
Fax: 403-476-8762

Resources for Healthcare Providers

- Centres for Disease Control and Prevention – Sickle Cell Trait Toolkit: https://www.cdc.gov/ncbddd/sicklecell/toolkit.html
- Alberta Health Services, Alberta Newborn Screening Program Provider Information Sheet – Sickle Cell Disease https://www.albertahealthservices.ca/info/Page9024.aspx under Condition Fact Sheets > Other Conditions

Resources for Patients and Families

- Sickle Cell Foundation of Alberta: www.ourscfa.org
- Sickle Cell Society: www.sicklecellsociety.org
- My Health Alberta: https://myhealth.alberta.ca

References

1. Naik, R. P., Smith-Whitley, K., Hassell, K. L., Umeh, N. I., de Montalembert, M., Sahota, P., et al. Clinical outcomes associated with sickle cell trait: a systematic review. Ann Intern Med [Internet]. 2018 November [cited 2019 March 19]; 169 (9), 619-627. Available from: https://annals.org/aim/article-abstract/2709819/clinical-outcomes-associated-sickle-cell-trait-systematic-review

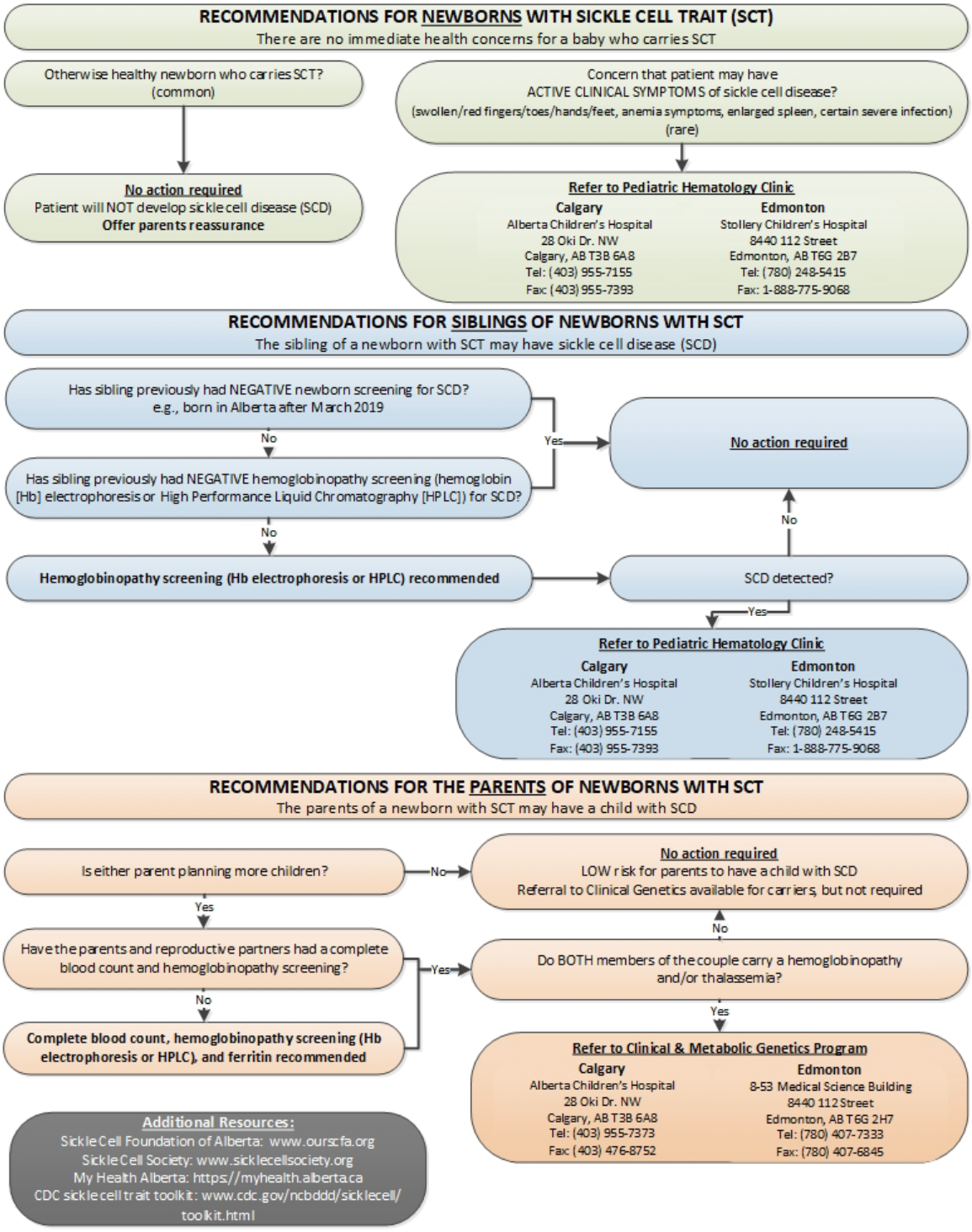
Sickle Cell Trait Development Committee

In 2019, a Sickle Cell Trait Development Committee was formed to develop resources to support physicians. The committee consisted of representatives from family medicine, medical genetics, genetic counsellors, pediatric hematology, screening programs and public health and preventive medicine.

Aisha Bruce, Stollery Children's Hospital, Edmonton, Alberta; Joseph Ojedokun, University of Alberta; Margaret Lilley, Ross Ridsdale, Alberta Precision Laboratories; Courtney Felker, Grace Johner, Huiming Yang, Kara Patterson, Screening Programs, Alberta Health Services; Michael T Leaker, Nicola Wright, Mary Ann Thomas, Sajid Merchant, Raechel Ferrier, Alberta Children's Hospital, Calgary, Alberta

Appendix A

Sickle Cell Trait Notification Algorithm



These recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

Appendix B

Sickle Cell Trait Frequently Asked Questions

This resource can be used by health care providers when talking with parents about their child's sickle cell trait status.

What is sickle cell trait?

Sickle cell trait (SCT) is not a disease, but an inherited blood condition. This occurs when a person inherits a sickle hemoglobin gene from one parent and a standard (fully working) hemoglobin gene from the other parent. Therefore, a person with one sickle hemoglobin gene is said to 'carry' SCT.

Hemoglobin is a protein in red blood cells that carries oxygen throughout the body.

What is the difference between SCT and Sickle Cell Disease (SCD)?

SCT is NOT a milder form of SCD. SCD results from the inheritance of <u>two</u> sickle hemoglobin genes, one from each parent, which causes normally round red blood cells to become curved or "sickle" shape. When the sickled red blood cells travel through small blood vessels, they are more likely to become stuck and clog the blood flow to organs in the body. Since individuals with SCT have only one sickle hemoglobin gene, they still make enough standard hemoglobin to prevent the cells from sickling. Without sickling, red blood cells are able to transport oxygen to tissues and organs in the body without becoming stuck in the small blood vessels. Individuals with SCT are at no higher risk for symptoms of SCD than anyone else.

Who is affected by SCT?

SCT can occur in any ethnic group, but it is more common in certain populations such as African, Mediterranean, Middle Eastern and Asian groups. Worldwide, an estimated 300 million people carry SCT, with a prevalence ranging from 2% to 30% in more than 40 countries (1). The incidence of SCT is approximately 1 in every 128 infants born in Alberta.

What health complications are associated with SCT?

Most people with SCT will rarely have any associated health problems as a result of being a carrier and will not develop SCD. However, people with SCT are at increased chance of experiencing blocked blood vessels should they become significantly dehydrated, particularly during times of extremely strenuous activity. In rare cases, people who carry SCT may have some health issues such as blood in the urine, presence of excess proteins in the urine, or chronic kidney disease.

Why is it important to know that my child has SCT?

Your child and their future partner may want to know this information before they plan to have children of their own. Should your child's partner also have SCT, then their children (your grandchildren) would be at an increased risk of having SCD (see Figure 1).

What does having a child with SCT mean for me, my partner and for future pregnancies?

If both members of a couple carry SCT, they can have a child who has SCD. Each child born to a couple where both parents carry SCT has a:

- 1 in 2 (50%) chance of carrying SCT.
- 1 in 4 (25%) chance of having SCD.
- 1 in 4 (25%) chance that they will neither have SCT or SCD.

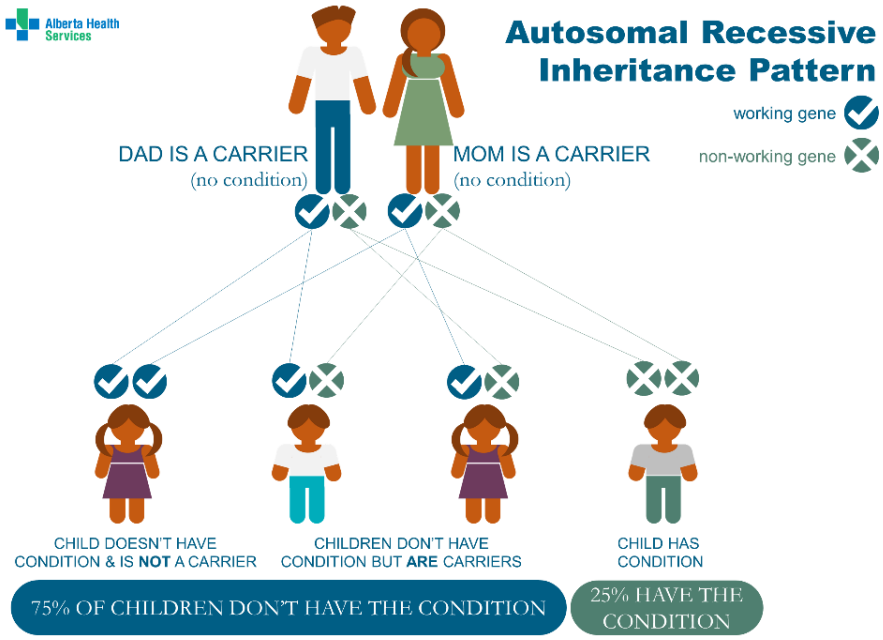


Figure 1: Autosomal Recessive Inheritance Pattern of SCT

If the parents of an infant with SCT are planning more pregnancies, carrier testing is recommended. Genetic counselling is also recommended if both parents are found to be carriers in order to review the different options available to the parents during pregnancy.

Should my other children be tested?

If your other children were born outside of Alberta, or within Alberta but before April 1, 2019 they may not have been screened for SCD. Therefore, we suggest you talk with your family doctor about additional screening for SCD.

References

1. Naik, R. P., Smith-Whitley, K., Hassell, K. L., Umeh, N. I., de Montalembert, M., Sahota, P., et al. Clinical outcomes associated with sickle cell trait: a systematic review. Ann Intern Med [Internet]. 2018 November [cited 2019 March 19]; 169 (9), 619-627. Available from: https://annals.org/aim/article-abstract/2709819/clinical-outcomes-associated-sickle-cell-trait-systematic-review