



☆ **Topic: Newborn Screening for Sickle Cell Anemia**

☆ **Summary:** Early identification of sickle cell anemia through newborn screening (NBS) enables antibiotic prophylaxis for *Streptococcus pneumoniae* which is one of the early life-threatening complications that can occur in untreated infants. Identification of newborns with sickle cell anemia also enables the provision of education to parents and caregivers about early treatment of crises and prevention of complications. Newborn screening may also detect children with other hemoglobin variants such as Hb C, Hb D, Hb E. However, NBS does not test reliably for other hemoglobinopathies like beta thalassemia or hemoglobin H disease. Hemoglobinopathy screening should also be offered to patients and their partners from high-risk ethnic backgrounds, ideally before pregnancy or early in a pregnancy.

☆ **Bottom line:** In some provinces, newborn screening is available which identifies children affected with sickle cell anemia so they can receive early interventions to prevent complications.

✓ **The Disease:**

- Sickle cell disease

✓ **The Gene**

- Adult hemoglobin (HbA) consists of 2 alpha globin and 2 beta globin polypeptide chains.
- Sickle cell anemia is caused by a mutation in the gene that makes the beta globin polypeptide chain.
- The mutation causes an abnormal beta globin protein to be formed and this causes the hemoglobin to become the characteristic 'sickle' shape when deoxygenated.
- Other mutations in the beta globin gene can cause hemoglobin variants such as Hemoglobin C, Hemoglobin E, Hemoglobin D, etc.
- These variants cause abnormal beta polypeptides that result in the formation of abnormal hemoglobin structures.
- Mutations that prevent the beta globin gene from producing beta polypeptide chains cause beta thalassemia.

✓ **Consequences of having a faulty gene**

- Carriers of beta thalassemia or beta variants have one normal beta gene and one that contains a mutation that prevents it from working normally.
- Carriers are healthy.
- Two carriers have a 25% chance of having a child with two abnormal beta genes and therefore a beta chain hemoglobinopathy.
- There are many possible combinations of beta gene variants: some combinations like Hb E/Hb E mutations do not lead to a significant hemoglobin disorder. Other combinations are rare and the clinical features have not been well documented.
- The following table includes some of the more common beta variant combinations.

At-risk couples	Possible disease in their children
2 Sickle cell carriers	Sickle cell anemia: <ul style="list-style-type: none"> ▪ anemia & painful crises that may require hospitalization ▪ higher risk for infections & often require prophylactic antibiotics
1 Sickle cell carrier & 1 beta thal carrier	Sickle/beta thalassemia: <ul style="list-style-type: none"> ▪ similar to sickle cell anemia, but severity is variable
1 Sickle cell carrier & 1 C trait	SC disease: <ul style="list-style-type: none"> ▪ similar to, but usually milder than sickle cell anemia

1 Sickle cell carrier & 1 HB D carrier	Sickle cell/Hb D disease: <ul style="list-style-type: none"> ▪ similar to sickle cell anemia
2 Beta thalassemia carriers	Beta thalassemia disease: <ul style="list-style-type: none"> ▪ severe anemia that requires lifelong regular blood transfusion & iron chelation therapy ▪ severity is related to the type of mutations the parents carry
1 Beta thalassemia carrier & 1 Hb E trait	Beta/E thalassemia: <ul style="list-style-type: none"> ▪ may have a severe anemia like beta thalassemia but severity varies

✓ Testing

- If a baby is identified as having sickle cell anemia through newborn screening then carrier testing for sickle cell anemia should be offered to the parents and other relatives. (See below under “benefits” section)
- Carrier screening for hemoglobinopathies should be offered to anyone whose ancestors come from Southern Europe, Asia, Africa and Middle East prior to starting a family or early in pregnancy. This includes people born in other areas where their ancestry likely originated from one of the high-risk regions (e.g. Caribbean, South America, etc).
- Carrier screening should include a CBC with an MCV and a hemoglobin electrophoresis. An MCV is considered low when it is less than 80. Iron deficiency can cause a low MCV, so ferritin testing is recommended when the MVC is low.

✓ Who should be offered referral for genetic counselling/testing?

- Couples who have a child who is found to have sickle cell anemia through newborn screening or couples who have been identified to be at risk of having a child with a hemoglobinopathy should be offered a referral for genetic counselling.
- Routine carrier screening for people from at risk populations should be ordered through their health care provider.

✓ Benefits of genetic testing

- Babies identified with sickle cell anemia through newborn screening are referred to pediatric hematologists in order to:
 - reduce one of the early life-threatening complications that can occur in untreated infants with sickle cell anemia by providing antibiotic prophylaxis for *Streptococcus pneumoniae*.¹
 - provide surveillance and education to parents and caregivers about early treatment of crises and prevention of complications.
- Some provinces are providing the child’s sickle cell carrier status from newborn screening testing upon parental request.
- Ideally, carrier screening is offered to couples prior to pregnancy because this allows couples at risk of having a child with a hemoglobinopathy the opportunity to have genetic counselling and to explore a number of reproductive planning options including preimplantation diagnosis, prenatal testing (chorionic villi sampling or amniocentesis) with the option of continuing or terminating the pregnancy, and postnatal testing for early detection and treatment. When a carrier is identified, other relatives are also at risk and can be offered testing.

✓ Harms/limitations of genetic testing

- Some carriers may experience anxiety because they believe that they have a disease. Historically, carriers of sickle cell anemia experienced discrimination by employers and insurers in the 1970s until legislation prohibited mandatory testing in the US. This led to increasing awareness of the potential misconceptions and/or dangers of labelling.

☆ **Web Resources:** genetics.kaiser.org/home/hemoglobinopathy.htm
www.genetests.org

☆ **References:**

1. Vichinsky E, Hurst D, Earles A, et al. Newborn screening for sickle cell disease: effect on mortality. *Pediatrics* 1988:749-755.

☆ **Review Article:**

Dumar KW, Boehm C, Eckman JR, et al. Practical Guide to the Diagnosis of Thalassemia. Council of Regional Networks for Genetic Services (CORN). *American Journal of Medical Genetics* 1996; 62:29-37.

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Dr Carroll is Principal Investigator of the GenetiKit Project and is the Sydney G Frankfort Chair in Family Medicine at Mount Sinai Hospital and an Associate Professor in the Department of Family Medicine at the University of Toronto.

In alphabetical order, other members of the GenetiKit Team are as follows: **Dr Allanson** is Chief of the Department of Genetics at the Children's Hospital of Eastern Ontario (CHEO) in Ottawa, Ontario and Full Professor in the Department of Pediatrics at the University of Ottawa. **Dr Blaine** is an Assistant Professor in the Department of Family and Community Medicine at the University of Toronto in Ontario and Lead Physician of the STAR Family Health Team in Stratford, Ontario. **Ms Cremin** is a Clinical Assistant Professor in the Department of Medical Genetics, University of British Columbia. **Ms Dorman** is a Genetic Counselor at the Sudbury Regional Hospital in Ontario. **Ms Gibbons** is a Genetic Counselor at the North York General Hospital in Ontario. **Dr Graham** is Vice-President of Knowledge Translation, Canadian Institutes of Health Research. **Dr Grimshaw** is a Professor in the Department of Medicine and Director of the Clinical Epidemiology Program at the Ottawa Health Research Institute. **Ms Honeywell** is an Assistant Professor in the Department of Pediatrics at the University of Ottawa and in the CHEO Departments of Genetics and Cardiology. **Dr Meschino** is a Clinical Geneticist at North York General Hospital and Assistant Professor in the Department of Paediatrics at the University of Toronto. **Ms Permaul** is a Research Associate in the Granovsky Gluskin Family Medicine Centre at Mount Sinai Hospital. **Dr Wilson** is an Associate Professor in the Department of Epidemiology and Community Medicine at the University of Ottawa.