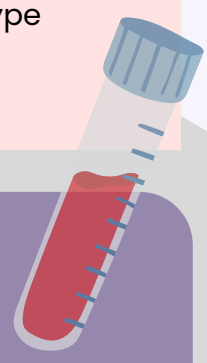
Genetic Carrier Screening in Canada: Hemoglobinopathies

Reviewed March 2023

Hemoglobinopathies are a group of inherited conditions where production of the hemoglobin molecule is abnormal. They may be the result of a pathogenic (*harmful*) variant in the alpha and/or beta globin genes. Examples include Sickle Cell Disease and thalassemias. Many provinces offer newborn screening for these conditions.

Condition	At-risk population/ethnicity	Screening recommendations
Alpha-thalassemia Beta-thalassemia Sickle Cell Disease	• African • South and East Asian • Mediterranean • Middle Eastern • Western Pacific • Caribbean • South American	Offer carrier screening to couples from ethnic backgrounds listed on the left WHEN red blood cell indices reveal a mean cellular volume (MCV) < 80 fl *OR* hemoglobinopathy testing reveals an abnormal hemoglobin type



Method of carrier screening:

- Complete blood count
- Hemoglobinopathy testing
  - laboratory methods vary on method used (e.g. Hemoglobin (Hb) electrophoresis (HE) or Hb high performance liquid chromatography (HHPLC))

- Refer for genetic consultation if both members of a couple are carriers of thalassemia OR a combination of thalassemia and a hemoglobin variant
- If consult to genetics not available, consider referral to hematology

Notes:

- Sickle Cell Disease carrier frequency among African Americans is~ 8-10% and in many regions of Africa it is as high as 25-35%
- The prevalence of alpha-thalassemia carriers in Hong Kong is 4-6% and in Laos and Thailand is 30-40%
- Those of Indigenous (First Nation, Métis and Inuit), Japanese, Korean, and Northern European ancestry are not at increased risk of hemoglobinopathies
- Check out the GECKO site for links to provincial newborn screening programs under Resources for Public and click Links to provincial programs

References and resources

- Wilson et al 2016 J Obstet Gynaecol PMID: 27638987
- Thalassemia Foundation of Canada
- The Sickle Cell Disease Association of Canada
- Sickle Cell Awareness Group of Ontario

Patient is of one of the following ancestries:

African
South and East Asian
Mediterranean
Middle Eastern
Western Pacific
Caribbean
South American

Yes

No

Arrange:
- Complete blood count
- Hemoglobinopathy testing

Clinical suspicion (e.g. family history mean cellular volume less than 80fl)

Yes

No

STOP

Abnormal results

Yes

No

STOP

For partner arrange:
- Complete blood count
- Hemoglobinopathy testing

Abnormal results

Yes

No

STOP

Refer to your local genetics center with results or hematology depending on resource availability

Remember to also take a family history targeting red flags that may suggest additional testing.

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POINT OF CARE TOOL

March 2023

If pregnant, consider arranging testing for both members of the couple concurrently to expedite results for the couple.

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POINT OF CARE TOOL

Reproductive genetic carrier screening in Canada

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All couples planning their families should have a three-generation family history taken, ideally in the preconception period. Attention should be paid to the red flags in the box below to assess risk to future offspring.

NOTE: Canadian guidelines (Wilson et al 2016 J Obstet Gynaecol PMID: 27638987) are currently under review by the Canadian College of Medical Geneticists, and a new publication is not yet available. We will update our content when new recommendations are released.

A personal or family history of:

- congenital anomaly e.g. congenital heart defect, neural tube defect
- intellectual disability or developmental delay
- genetic syndrome e.g. neurofibromatosis, Noonan syndrome
- chromosomal disorder e.g. Down syndrome (trisomy 21), familial translocation
- muscular disorder e.g. X-linked Duchenne and Becker muscular dystrophies
- bleeding disorder e.g. X-linked hemophilia A or B
- stillbirth
- sudden unexplained death
- other major health concerns such as cardiomyopathy, neurological disease, epilepsy, hearing loss, autism spectrum disorder, and psychiatric disorders
- consanguinity

A history of any of these red flags should prompt referral for genetic consultation. Individuals and their partners should be encouraged to make their best efforts to obtain confirmatory information such as medical records, genetic test results, even family photos.

One's ethnicity is an important piece of risk assessment as some populations are known to have a higher incidence of certain genetic conditions due to a founder effect. Founder effect confers reduced genetic diversity in a population descended from a small number of ancestors. A founder mutation refers to a specific pathogenic genomic variation in a specific population due to the presence of that genomic variation in a single or small number of ancestors.

Other considerations:

- There is a higher incidence of **hemoglobinopathies** in certain populations. Screening recommendations can be found here
- Canadian recommendation for reproductive carrier screening in individuals of **Ashkenazi Jewish** ethnicity are here, and those from **certain regions of Québec** can be found here
- Canadian carrier screening recommendations for **cystic fibrosis, fragile X syndrome and spinal muscular atrophy** can be found here.
- Individuals who are of **Cree ancestry** have a higher carrier frequency of Cree encephalitis (1/30-1/17) and Cree Leukoencephalopathy (~1/10). Screening programs have been developed in some regional communities. The CE-CLE Screening Program is offered to adults in the Awash clinics and to high school students.
- **Aboriginal Manitoba** populations have a higher incidence of cerebro-oculo-facio-skeletal syndrome
- **Newfoundland populations** have a higher incidence of Bardet-Biedl syndrome and neuronal ceroid lipofuscinosis.
- A maternal family history of **bleeding disorders** in male relatives (father, brother, and/or maternal uncles) should prompt referral for consideration of carrier screening of X-linked hemophilia.
- Families of **Amish, Mennonite, or Hutterite** background based on family history and/or geographic or religious settlement locality, in addition to a three-generation family history, should be offered referral for genetic consultation.

Expanded carrier testing is privately available genetic testing which screens an individual for more than just guideline/ethnicity-based conditions. See our Education Module for more information on this type of testing.