Reproductive Genetic Carrier Screening in Canada

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 Box 1 to assess risk to future offspring.

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, and psychiatric disorders
- consanguinity

Box 1. Personal and family history red flags that should prompt a referral for genetic consultation, ideally when individuals are planning a family (preconception).

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. Founder mutations refer to specific gene mutations observed at high frequency in a specific population due to the presence of that gene mutation in a single or small number of ancestors.

Other considerations:

- There is a higher incidence of **hemoglobinopathies** in certain populations see page 2 of this tool for more.
- Link to the Canadian recommendations for carrier screening in individuals of **Ashkenazi Jewish** ethnicity, those from certain **regions of Quebec** and those regarding **cystic fibrosis, fragile X syndrome** and **spinal muscular atrophy.** All point of care tools 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. In Quebec the CLE-CE program provides education, screening, and counselling services on a voluntary basis through local Community Miyupimaatisiiun Centres and high schools.
- **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 a woman's male relatives (father, brother, and/or maternal uncles) should prompt referral for consideration of carrier screening of X-linked hemophilia**.**
- Families **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 family history or guideline/ethnicity-based conditions. See our pre- and post-test Point of Care tools here.

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POINT OF CARE TOOL

Reproductive Genetic Carrier Screening in Canada: Hemoglobinopathies

Table 1. Canadian recommendations for reproductive carrier screening of hemoglobinopathies.

Condition	At-risk population/ethnicity	Screening recommendations
Hemoglobinopathies — α-thalassemia — β-thalassemia — Sickle cell disease	○ African ○ South and East Asian communities ○ Mediterranean ○ Middle East ○ Western Pacific ○ Caribbean ○ South American	Offer to couples from ethnic backgrounds listed in left box **WHEN** red blood cell indices reveal a mean cellular volume (MCV) < 80 fl OR electrophoresis reveals an abnormal hemoglobin type — *Preconception*: Begin with female member of the couple, IF her screening results are positive, then screen male partner — *Prenatal:* Screen both members of the couple concurrently Method of carrier screening: ✓ Complete blood count ✓ Hemoglobin (Hb) electrophoresis (HE) or Hb high performance liquid chromatography (HHPLC) ✓ Quantification of Hb alpha 2 and fetal Hb ✓ Serum ferritin/H bodies (blood smear stain using brilliant cresyl blue) if microcytosis (MCV < 80 fl) and/or hypochromia (mean cellular Hb < 27 pg) in the presence of a normal HE or HHPLC assessment — Refer for genetic consultation **if both members** of a couple are carries of thalassemia OR a combination of thalassemia and hemoglobin variant

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 α-thalassemia carriers in Hong Kong is 4-6% and in Laos and Thailand is 30-40%.*
- *Japanese, Koreans, Caucasians of Northern European ancestry, Native Americans (First Nations in Canada), and Inuit are not at increased risk of hemoglobinopathies*
- *Many Canadian provincial newborn screening programs screen for sickle cell disease, including Maritimes, Ontario, British Columbia, Yukon, Nunavut (Baffin) and to certain populations in Manitoba and Quebec*

References and Resources:

Wilson RD, De Bie I, Armour CM, et al. Joint SOGC-CCMG Opinion for Reproductive Genetic Carrier Screening: An Update for All Canadian Providers of Maternity and Reproductive Healthcare in the Era of Direct-to-Consumer Testing. J Obstet Gynaecol Can 2016;38(8):742-762.e3

Thalassemia Foundation of Canada https://www.thalassemia.ca/
The Sickle Cell Disease Association of Canada https://sicklecelldiseasecanada.com/

Reproductive Genetic Carrier Screening in Canada: Hemoglobinopathies

www.geneticseducation.ca/

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