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, screening recommendations can be found here
- Canadian recommendation for reproductive carrier screening in individuals of **Ashkenazi Jewish** ethnicity are on page 2, and those from certain **regions of Quebec** 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 regions or 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 a woman's male relatives (father, brother, and/or maternal uncles) should prompt referral for consideration of carrier screening of **X-linked hemophilia.**
- Families with **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.

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Reproductive Genetic Carrier Screening in Canada: Ashkenazi Jewish

Table 1. Canadian recommendations for reproductive carrier screening of individuals who are of Ashkenazi Jewish (AJ) ethnicity. Ashkenazi Jews are descendants of the Jewish communities of Germany, Poland, Austria and Eastern Europe. For genetics purposes, an individual with one biological grandparent of Ashkenazi Jewish heritage is considered a candidate for carrier screening.

Condition	Carrier frequency	Screening recommendations
Tay-Sachs disease	1/30	DNA-based mutation analysis is recommended for: ✓ all at-risk couples
Canavan disease	1/37-1/53	DNA-based mutation analysis is recommended for: ✓ all at-risk couples
Familial dysautonomia	1/32	DNA-based mutation analysis is recommended for: ✓ all at-risk couples
When only one member of a couple is of AJ ethnicity, the non-AJ partner should be screened for Tay-Sachs disease, using biochemical hexosaminidase enzyme activity since available DNA testing targets specific mutations found in AJ populations (founder mutations). No screening for Canavan Disease and Familial Dysautonomia is recommended as both are very rare in the general population.		
Some provinces offer carrier screening panels that include more than the three conditions above. See here for more on testing in your province. Screening for other genetic disorders where common founder mutations are known can also be considered, particularly when there is a positive family history, for example:		
Condition	**Carrier frequency**	**Screening recommendations**
Gaucher disease	1/18	If there is a positive family history, consider screening by DNA-based targeted mutation analysis (ideally for the familial gene mutation, although gene panels with common AJ mutations may be considered).
Cystic fibrosis (CF)	1/24	
Fanconi anemia group C	1/89	
Niemann-Pick type A	1/90	
Mucolipodosis type IV	1/100	
Bloom syndrome	1/104	
When only one member of a couple is of AJ ethnicity, the decision to screen the couple should consider the frequency of the condition and the availability of reliable screening in the non-AJ partner. E.g. Where there is a positive family history of CF and one member of a couple is of AJ ethnicity and the other member of the couple is of Northern European ethnicity; offering carrier screening for CF to this couple is reasonable. However offering screening for a family history of the rare Bloom syndrome would not be recommended as the carrier frequency and utility of screening in non-AJ individuals is unknown.		

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

The National Foundation for Jewish Genetic Diseases www.icahn.mssm.edu/research/programs/jewish-genetics-disease-center

Jewish Genetic Disease Consortium www.jewishgeneticdiseases.org/jewish-genetic-diseases/

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