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
- Canadian recommendation for reproductive carrier screening in individuals of Ashkenazi Jewish ethnicity 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 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 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 guideline/ethnicity-based conditions. See our Education Module for more information on this type of testing.
Table 1. Canadian recommendations for reproductive carrier screening of hemoglobinopathies.

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

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:


Thalassemia Foundation of Canada www.thalassemia.ca