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Genetics Education Canada: Knowledge Organization
Centre d'éducation en génétique canadien: Connaissances organisées
POINT OF CARE TOOL

Reproductive genetic carrier screening in Canada

Reviewed March 2023

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.

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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 analysis is recommended for all at-risk couples
Canavan disease	1/37 - 1/53	
Familial dysautonomia	1/32	

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 pathogenic variants 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 page 2 for more on testing in your province.

Screening for other genetic conditions where common pathogenic variants 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 analysis (ideally for the familial pathogenic variant, although gene panels with common AJ pathogenic variants 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 et al 2016 J Obstet Gynaecol PMID: 27638987
- The National Council of Jewish Women of Canada
- Jewish Genetic Disease Consortium

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Ashkenazi Jewish Genetic Carrier Screening across Canada

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Province	How to order testing	Conditions screened
Alberta	• Testing is not available in province • Approval for out of province funding must first be obtained through the Genetic Resource Centre • Applications are reviewed on a case-by-case basis	o Tay-Sachs disease o Canavan disease o Familial dysautonomia
British Columbia & Yukon	• Instructions, requisitions and counselling information found here ◦ Molecular Genetics Laboratory at BC Children's and BC Women's Hospitals	o Tay-Sachs disease o Canavan disease o Familial dysautonomia o Fanconi anemia type C
Manitoba	• Requisition is available here through the Diagnostic Services of Manitoba ◦ Diagnostic Services of Manitoba	o Tay-Sachs disease o Canavan disease o Familial dysautonomia o Fanconi anemia type C
Maritimes (New Brunswick, Nova Scotia & Prince Edward Island)	Contact local genomics centre	o Tay-Sachs disease o Canavan disease o Familial dysautonomia o Fanconi anemia type C
Newfoundland and Labrador	Contact local genomics centre	
Ontario	Hospital for Sick Kids Department of Pediatric and Laboratory Medicine	o Tay-Sachs disease o Canavan disease o Familial dysautonomia o Fanconi anemia group C o Bloom syndrome o Mucolipidosis type IV o Niemann Pick disease
Québec	McGill University Health Centre Jewish Genetic Condition Screening Program Additional Québec resources	o Tay-Sachs disease o Canavan disease o Familial dysautonomia
Saskatchewan	Saskatchewan Health Authority Ashkenazi Jewish Genetic Panel Refer to Saskatoon Medical Genetics Centre	o Tay-Sachs disease o Canavan disease o Familial dysautonomia o Fanconi anemia group C o Bloom syndrome o Mucolipidosis type IV o Niemann Pick disease

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Canadian recommendations for reproductive carrier screening of French Canadian individuals

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Click here to see a map of Québec regions.

Recommendations for those who are from the Saguenay Lac-St-Jean (SLSJ) and Charlevoix regions

Condition	Carrier frequency	Screening recommendations
Cystic fibrosis	SLSJ 1/15 Charlevoix 1/20	DNA-based analysis is recommended for all at-risk couples For couples in Québec, see the provincial screening program site for steps to obtaining testing. For couples outside of Québec, consider contacting your local genetics centre for referral criteria or assistance ordering testing.
Tyrosinemia type I	1/19	
Leigh syndrome (French Canadian type)	1/23	
Agenesis of the corpus callosum with peripheral neuropathy	1/23	

For individuals from the SLSJ region, pay attention to family histories of myotonic dystrophy type I, congenital disorder of glycosylation type 1B, Tay-Sachs disease, and mucolipidosis II as testing for these conditions may also be considered.

Turnaround time for this testing can be lengthy and out-of-province approval may be necessary prior to ordering testing which can increase wait time for results. To maximize a couple's family planning options, these processes should be initiated as soon as possible.

Recommendations for those who are from Québec Bas-St-Laurent (Rimouski) and Gaspésie, adjoining New Brunswick

Condition	Carrier frequency	Screening recommendations
Tay-Sachs disease	1/14	If there is a positive family history, consider screening by DNA-based targeted analysis for the familial pathogenic variant

When only one member of a couple is of French Canadian ethnicity, the decision to screen the couple should take into consideration the frequency of the condition and the availability of reliable screening in non-French Canadian individuals.

References and resources

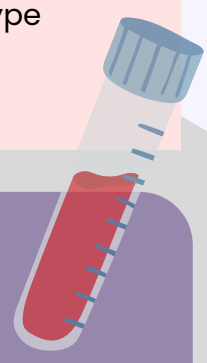
- Wilson et al 2016 J Obstet Gynaecol PMID: 27638987
- Dépistage et offre de tests de porteur en Québec:
  - Offre de tests de porteur pour quatre maladies héréditaires récessives chez les personnes originaires des régions du Saguenay–Lac-Saint-Jean, de Charlevoix et de la Haute-Côte-Nord

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	• 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
Beta-thalassemia		
Sickle Cell Disease		



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

Genetic Carrier Screening in Canada: Condition specific

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Current Canadian guidelines recommend against general population carrier screening for cystic fibrosis, Fragile X syndrome and spinal muscular atrophy. See the table below for current screening recommendations.

Condition	Screening recommendations
Cystic fibrosis (CF)	General population carrier screening for CF is not recommended. DNA-based analysis of the *CFTR* gene is recommended for: • Individuals with a personal or family history of CF • Both parents of a fetus with an ultrasound finding of echogenic bowel • All couples from the Saguenay Lac-St-Jean and Charlevoix regions in Québec, as the CF carrier frequencies are 1/15 and 1/20, respectively Newborn screening for CF is offered as part of most Canadian provincial screening programs.
Fragile X syndrome (FXS) and related conditions	General population carrier screening for FXS is not recommended. Offering FXS carrier screening is recommended for any person (46, XX) with a personal or family history of: • Fragile X syndrome or fragile X-related conditions • Unexplained intellectual disability or developmental delay • Autism spectrum disorder • Premature menopause i.e. ovarian insufficiency with elevated follicle stimulating hormone of unknown etiology under 40 years of age • History of male (46,XY) relatives with isolated cerebellar ataxia and tremor Due to the complexity of interpreting FXS carrier screening results, pre- and post-test genetic counselling is strongly recommended.
Spinal Muscular Atrophy (SMA)	General population carrier screening for SMA is not recommended. Any couple where one member has a family history of SMA should be offered referral for reproductive genetic counselling for consideration of carrier screening.

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

References and resources

- Wilson et al 2016 J Obstet Gynaecol PMID: 27638987
- Cystic Fibrosis Canada
- Fragile X Research Foundation of Canada
- Cure SMA Canada
- Muscular Dystrophy Canada

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

Both members of a couple are of AJ ethnicity

And
currently pregnant

Yes

- **Offer** AJ panel based carrier screening to both members concurrently
- Indicate ongoing pregnancy to expedite results

Both members are carriers of the **same** condition

Yes

Refer to your local genetics center with results

No

STOP

No, preconception

Offer AJ panel based carrier screening to **female** member first

Positive result

Yes

Offer the same AJ panel based carrier screening to male member

Both members are carriers of the **same** condition

Yes

Refer to your local genetics center with results

No

STOP

No

STOP

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One member of a couple is of AJ ancestry

And
currently pregnant

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Concurrently
rather than sequentially for prompt receipt of the couple's results

Offer AJ panel based carrier screening to AJ member only

Consider offering Tay-Sachs disease screening to the non-AJ member with biochemical analysis (vs genetic testing)

Indicate ongoing pregnancy to expedite results

Both members are carriers of Tay Sachs disease

Yes

Refer to your local genetics center with results

No

STOP

AJ member is positive for another condition

Pause

Consider the frequency of the condition and the availability of reliable screening in the non-AJ partner e.g. screening for familial dysautonomia or Canavan disease is not recommended in non-AJ individuals as the carrier frequency is low and testing/interpretation of genetic results is limited.

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

One member of a couple is of AJ ancestry

And not currently pregnant (preconception)

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Offer AJ panel based carrier testing to AJ member **only**

Positive result

Yes

Positive result for Tay Sachs disease

Yes

Offer Tay Sachs disease screening to partner with biochemical analysis (vs genetic testing)

Positive result

Yes

Refer to your local genetics center with results

No

STOP

No

STOP

No, positive for another condition

Pause

Consider the frequency of the condition and the availability of reliable screening in the non-AJ partner e.g. screening for familial dysautonomia or Canavan disease is not recommended in non-AJ individuals as the carrier frequency is low and testing/interpretation of genetic results is limited.

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

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