



HIV-1 Strain Surveillance in Canada

At a Glance

- The Canadian HIV Strain and Drug Resistance Surveillance Program (SDR program) monitors and assesses HIV strains and the transmission of drug resistance among individuals with newly diagnosed and not yet treated HIV infection in Canada.
- Although HIV-1 strain B continues to predominate in Canada (89.4% of the cumulative samples analyzed), a wide variety of different non-B strains have also been identified.
- On the basis of results from the SDR program, the likelihood of a non-B strain infection in Canada is greater among individuals of African/Caribbean origin than Caucasians and greater among those whose primary risk exposure is heterosexual sex than among those with male-to-male sex as the primary risk exposure.

Introduction

HIV is classified into types, groups, subtypes and sub-subtypes according to its genetic variability. Two types of HIV have been characterized in humans, HIV type 1 (HIV-1) and HIV type 2 (HIV-2). Both HIV-1 and HIV-2 lead to AIDS, and differences in their transmission and biologic characteristics are well documented.¹ HIV-2 is less common than HIV-1 and is found mainly in West Africa. HIV-1, which is the predominant type and primarily responsible for the AIDS pandemic, can be further divided into three genetic groups: “M” (major or main), “O” (outlier) and “N” (new or non-M, non-O).² HIV-1 infections are almost exclusively caused by group M viruses. Group M viruses are further classified into subtypes (A-D, F-H, J and K) and over 40 circulating recombinant forms or CRFs (e.g. AB, CRF01_AE).³⁻¹⁰

HIV-1 subtypes are not distributed uniformly across the globe. Many studies have been conducted to estimate the regional and global distribution of HIV-1 subtypes and CRFs.^{11,12} According to the WHO-UNAIDS Network for HIV Isolation and Characterization, approximately 50% of diagnosed infections worldwide were due to HIV-1 subtype C in 2004.¹¹ This subtype predominates in India, southern Africa and Ethiopia. HIV-1 subtype A accounted for 12% of infections worldwide. HIV-1 subtype A predominates in Eastern Europe, Central Asia, and East and Central Africa. Overall, HIV-1 subtype B was responsible for 10% of diagnosed infections worldwide and is the dominant subtype in Canada, the United States, Western Europe, Australia and some Asian countries. The other main subtypes such as G and D were responsible for 6% and 3% of HIV-1 diagnosed infections respectively. The two major recombinant forms of HIV-1, CRF01_AE and CRF02_AG, are found in West and Central Africa and Southeast Asia respectively, and each represents 5% of the burden of HIV-1 globally.

The global distribution of HIV-1 strains is continuously evolving. Through increased travel and migration, infections with non-B subtypes are increasingly being reported in other parts of the world, and additional subtypes and recombinant forms are constantly being discovered.¹³ Moreover, the proportion of non-B subtypes is increasing in areas where subtype B infection has traditionally predominated, such as North America and Europe.¹⁴⁻²⁰

This *Epi Update* describes the rationale for the surveillance of HIV strains and provides a summary of the prevalence of the different HIV strains in Canada identified through the SDR program. Additional information will be available in the next edition of the report entitled *HIV-1 Strain and Primary Drug Resistance in Canada* (with anticipated publication in the fall of 2010).

HIV Strain Surveillance in Canada

The SDR program was initiated as an integrated group of projects aimed at enhancing the national surveillance of HIV; it is a collaboration between the provinces and the Surveillance and Risk Assessment Division and the National HIV and Retroviral Laboratories, Public Health Agency of Canada (PHAC). Laboratory samples (serum from treatment-naïve individuals with newly diagnosed HIV infection) and corresponding epidemiologic data are sent from the provincial health laboratories to PHAC for HIV strain and drug resistance testing. The results are then shared with provincial and other stakeholders. One of the central goals of this program is to conduct the systematic surveillance of HIV subtypes in Canada to meet the following four main objectives.

1. Improve HIV diagnostic and screening strategies

The broad genetic diversity of HIV has important implications for screening of donated blood, the ability of diagnostic tests to reliably detect circulating HIV strains, and patient monitoring. The sentinel arm of the SDR program, through the reference services of the National HIV and Retrovirology Laboratories, addresses this goal by testing samples with atypical test results. Using knowledge of the circulating HIV strains, modifications can be made to current tests to ensure that testing accurately detects all HIV-positive individuals. This is also relevant to the safety of the blood supply, since the tests used for screening donated blood would be able to detect circulating HIV variants.

2. Inform vaccine development

The genetic diversity of HIV-1 is a major challenge to vaccine development. Information on the distribution of the viral subtypes can be used to target vaccine development and testing, since the efficacy and effectiveness of any vaccine that is developed would likely be subtype specific.^{21,22}

3. Assess HIV transmission patterns

Although genetic analyses have been used to assess the spread of HIV globally, there is little consensus on whether differences in HIV subtype affect the transmissibility of the virus in sexual²³⁻²⁵ or maternal exposures.²⁶⁻²⁹ Some studies have noted differences in the biological properties of HIV-1 subtypes,^{25,28,30} though the

meaning of these differences has yet to be determined. Knowing the distribution of HIV variants in Canada, along with corresponding epidemiologic factors, will help to assess the implications of any differences in transmissibility. The public health implications of such findings, including prevention and treatment strategies, are of special interest.

4. Assess HIV pathogenesis and progression of HIV-related diseases

Several prospective, observational studies have examined the role that genetic subtypes may play in disease progression. Some studies have suggested that viral subtype is a contributing factor to progression rates,³⁰⁻³⁴ whereas others studies indicate that disease progression does not differ according to HIV-1 subtype.^{35,36} Note that a caveat to all these studies is that it was difficult to control for the many other variables that may affect disease progression, such as access to medical care, nutritional status, host genetic factors, plasma HIV-1 RNA level and CD4 T cell count.³⁷⁻³⁹

Recent evidence suggests that currently available antiretroviral drugs are equally effective in patients infected with different HIV-1 subtypes but that certain subtypes may develop different resistance patterns against specific antiretroviral drugs.⁴⁰⁻⁴³

Distribution of HIV-1 Subtypes in Canada

HIV-1 subtype A was first reported in Canada in 1995 from an individual of African origin⁴⁴ and HIV-2 was detected in Canada as early as 1988.⁴⁵

Cumulative results from the available data of the SDR program show that HIV-1 subtype B predominates, at 89.4%, with only 10.6% of the sampled population ($n = 4,598$) infected with non-B subtypes (see Table 1 for detailed subtype distribution).

Results from the available data of the SDR program suggest that individuals infected with non-B HIV-1 subtype are more likely to be female, younger in age at initial diagnosis, of African/Caribbean background (compared with Caucasian and other backgrounds) and to report heterosexual sex as their primary HIV risk factor (compared with male-to-male sex) (see Tables 2 to 5 for subtype distribution by sex, age group, ethnicity and exposure category).

Table 1. Distribution of HIV-1 subtypes in samples submitted to the SDR program (1985-Dec. 31, 2008)⁴⁶

HIV-1 subtype	Frequency	Percentage
B	4,109	89.4
C	258	5.6
A	81	1.8
AG	39	0.9
AE*	34	0.7
D	22	0.5
AD	12	0.3
G	7	0.15
BD	4	0.09
AB	2	0.04
BC	2	0.04
F	2	0.04
AC	1	0.02
B/AG	1	0.02
B/A	1	0.02
H	1	0.02
K	1	0.02
K/AE	1	0.02
K/AG	1	0.02
CRF01_AE**	11	0.24
CRF02_AG	5	0.11
CRF06_cpx	3	0.07
TOTAL	4,598	100

* The circulating recombinant form AE has also been referred to as subtype E.

** CRF = circulating recombinant form

Note: 1- Included in the analysis, data from participating provinces in the SDR program: BC, AB, SK, MB, ON and NS.

2- Quebec strain surveillance data are not included in the analysis but will be included in the fall report to be published later in 2010.

Table 2. Number and distribution of HIV-1 subtypes by sex

Gender	HIV-1 subtype		Total <i>n</i>
	B* <i>n</i> (%)	Non-B** <i>n</i> (%)	
Male	3198 (93.05)	239 (6.95)	3437
Female	894 (78.2)	249 (21.8)	1143
TOTAL	4109 (89.4)	489 (10.6)	4598

*Gender was unknown for 17 individuals with HIV-1 subtype B infection.

**Gender was unknown for 1 individual with HIV-1 non- subtype B infection.

Table 3. Number and distribution of HIV-1 subtypes by age group

Age group	HIV-1 subtype		Total <i>n</i>
	B* <i>n</i> (%)	Non-B** <i>n</i> (%)	
< 15	12 (40.0)	18 (60.0)	30
15-19	69 (89.6)	8 (10.4)	77
20-29	732 (86.4)	115 (13.6)	847
30-39	1310 (87.7)	184 (12.3)	1494
40-49	1092 (94.3)	66 (5.7)	1158
50-59	395 (91.9)	35 (8.1)	430
60+	158 (89.8)	18 (10.2)	176
TOTAL	4109 (89.4)	489 (10.6)	4598

*Age at diagnosis was unknown for 341 individuals with HIV-1 subtype B infection.

**Age at diagnosis was unknown for 45 individuals with HIV-1 non-subtype B.

Table 4. Number and distribution of HIV-1 subtypes by race/ethnicity

Ethnicity	HIV-1 subtype		Total <i>n</i>
	B* <i>n</i> (%)	Non-B** <i>n</i> (%)	
Caucasian	2431 (96.6)	85 (3.4)	2516
African/Caribbean	83 (23.9)	264 (76.1)	347
Asian/Arabic	146 (87.4)	21 (12.6)	167
Aboriginal (combined)	869 (94.9)	47 (5.1)	916
South Asian	59 (66.3)	30 (33.7)	89
Latin American	118 (96.7)	4 (3.3)	122
60+	23 (85.2)	4 (14.8)	27
TOTAL	4109 (89.4)	489 (10.6)	4598

*Ethnicity was unknown for 380 individuals with HIV-1 subtype B infection.

**Ethnicity was unknown for 34 individuals with HIV-1 non-subtype B infection.

Table 5. Number and distribution of HIV-1 subtypes by exposure category

Exposure category	HIV-1 subtype		Total <i>n</i>
	B* <i>n</i> (%)	Non-B** <i>n</i> (%)	
MSM	1452 (98.2)	27 (1.8)	1497
MSM/IDU	136 (95.1)	7 (4.9)	143
IDU	1257 (97.4)	33 (2.6)	1290
Heterosexual/Endemic	20 (10.8)	166 (89.2)	186
Heterosexual/Non-endemic	851 (81.6)	192 (18.4)	1043
Other	70 (69.3)	31 (30.7)	101
TOTAL	4109 (89.4)	489 (10.6)	4598

*Risk exposure was not identified in 323 individuals infected with HIV-1 subtype B infection.

**Risk exposure was not identified in 33 individuals infected with HIV-1 non-subtype B infection.

MSM: men who have sex with men; IDU: injecting drug users; Heterosexual/endemic: origin in a country where HIV is endemic (where heterosexual sex is the main mode of transmission and HIV prevalence is high, mainly countries in sub-Saharan Africa and the Caribbean); Heterosexual/non-endemic: heterosexual contact with a person who is either HIV infected or at risk of HIV or heterosexual contact as the only identified risk; Other: recipients of blood transfusion or clotting factor, perinatal and occupational transmission.

Comment

The introduction of new variant HIV strains into Canada is most likely related to travel and migration patterns from regions of the world where non-B HIV-1 strains predominate. The potential for increasing diversity of HIV-1 subtypes in Canada has implications for HIV diagnosis and vaccine development. The approval of HIV diagnostic kits in Canada is in part based on their ability to detect diverse pure and recombinant subtypes, and the potential utility in Canada of any vaccines that may be developed will need to take this subtype diversity into consideration. HIV-1 subtype surveillance creates the foundation for examining subtype-specific differences in transmissibility, pathogenicity and treatment. To address the challenges posed by these aspects of HIV strain diversity, it is therefore important to continue the systematic collection and analysis of information related to the dynamic change in HIV subtypes in Canada.

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For more information, please contact:

Surveillance and Risk Assessment Division
 Centre for Communicable Diseases and Infection Control
 Public Health Agency of Canada
 Tunney's Pasture
 Postal locator: 0602B
 Ottawa, ON K1A 0K9
 Tel: (613) 954-5169
 Fax: (613) 957-2842
www.phac-aspc.gc.ca

Mission

To promote and protect the health of Canadians through leadership, partnership, innovation and action in public health.

Public Health Agency of Canada

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