HIV Type 2 in New York City, 2000–2008

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Background. Antibody cross-reactivity complicates differential diagnosis of human immunodeficiency virus (HIV) type 2 (HIV-2) using standard serologic screening and confirmatory tests for HIV. HIV type 1 (HIV-1) viral load testing does not detect HIV-2. Although HIV-2 is, in general, less pathogenic than HIV-1, it can lead to immunosuppression and clinical AIDS, and there are important differences in the selection of antiretroviral therapy for HIV-2–related immunosuppression that make it imperative to differentiate between the 2 viruses. The New York City Department of Health (New York, NY) seeks to facilitate accurate diagnosis and surveillance of HIV-2 infection in the city.

Methods. We used routine HIV-1–2+O screening and a comprehensive algorithm to differentiate between HIV-1 and HIV-2 infection, universal HIV-related laboratory test reporting, population-based surveillance of HIV infection, and active communication with clinicians.

Results. Between 1 June 2000 and 31 December 2008, 62 persons received a diagnosis of confirmed or probable HIV-2 infection. The majority (60 [96.8%] of 62 individuals) were foreign-born (96.7% were born in Africa) and of black race/ethnicity (93.5%). At the time of initial diagnosis, 17.7% of patients with HIV-2 infection had AIDS. Forty (64.5%) of the patients received an initial diagnosis of HIV-1 infection. Among these patients, the median lag between initial diagnosis of HIV-1 infection and identification of HIV-2 as the infecting organism was 487.5 days.

Conclusion. HIV-2 should be ruled out in persons presenting for HIV testing who originate in or travel to West Africa and other areas in which HIV-2 is endemic, particularly those who have negative or indeterminate results on HIV-1 Western blot testing or have atypical banding patterns and/or present with clinical signs of HIV infection or unexplained immunosuppression.

Human immunodeficiency virus (HIV) type 1 (HIV-1) is responsible for the majority of cases of HIV infection and AIDS in the United States and throughout the world. A related but distinct virus, HIV type 2 (HIV-2), was first isolated in 1985 from sex workers and patients with AIDS from West Africa [1, 2]. HIV-2 is endemic in West Africa and, since its discovery, has been diagnosed in most of the countries in that region, including the Gambia, Guinea, Ghana, Guinea-Bissau, Cote d'Ivoire, Liberia, Senegal, and Niger [3]. It has also been found in France, Portugal, and their former colonies (Mozambique and Angola, India, and Brazil) [4].

HIV-2 is less transmissible than HIV-1, both heterosexually and vertically [5–10]. HIV-2 infection progresses more slowly than does HIV-1 infection [4, 11, 12], and many individuals do not experience disease progression at all [13–16]. Low viral loads and preserved $CD4^+$ cell counts and cell function are characteristic [17–19]. Rates of viral evolution are generally low, in contrast to the rate of viral evolution associated with HIV-1 [20], and are consistent with the low replication rate of HIV-2 in vivo [21, 22], low peripheral blood RNA levels [23, 24], and low rates of transmission [12]. Nevertheless, HIV-2 can cause immunosuppression and progression to AIDS in the absence of a detectable HIV-1 viral load and sometimes in the absence of a positive HIV-1 antibody test result. Moreover, antiretroviral therapy (ART) for HIV-2 infection differs

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Laboratory criteria for diagnosis

- The presence of antibodies to gp36 and at least one additional envelope protein of high molecular weight (gp105, gp125, or gp140) upon HIV-2 specific Western Blot testing

OR

- Detection of HIV-2 proviral DNA on PCR testing

OR

- Sequencing of the HIV-2 integrase gene

Case Classification

Suspect:

A person of west African origin who has no detectable HIV-1 viral load, **AND**

A physician diagnosis of HIV-2, **OR**

A positive antibody response to HIV-2 gp36 with no report or evidence of reactivity at gp105, gp125 or gp140

Probable:

A case that meets the suspect case classification, **AND**

Has multispot reactivity equal to 2 or higher in the HIV-2 test spot and reactivity to 0 on each gp41 peptide in the last dilution performed, **OR**

Is epidemiologically linked to another probable or confirmed HIV-2 case

Confirmed:

A case that meets the laboratory criteria for diagnosis

Figure 1. Laboratory criteria for diagnosis and case classification of human immunodeficiency virus type 2 (HIV-2) infection. PCR, polymerase chain reaction.

in important ways from ART for HIV-1, and clinical monitoring is challenging, because there are no commercially available HIV-2 viral load assays. Thus, correct diagnosis of HIV-2 infection has important implications for clinical management, as well as for surveillance and epidemiology.

During the past 2 decades African immigrants have accounted for a growing proportion of the foreign-born population in New York City (NYC) and, during the early 2000s, a growing proportion of new diagnoses of HIV infection [25–27]. To estimate the prevalence of HIV-2 infection and to aid in formulating future testing policy, the NYC Public Health Laboratory (PHL) tested 2 waves of specimens using a dual peptide-based HIV-2 enzyme-linked immunosorbent assay (EIA) algorithm: (1) HIV-1–inconclusive specimens submitted during the period 1988–1992, and (2) specimens from persons born in Africa submitted for HIV testing during 1993–1995. Of the 8579 HIV-1–inconclusive specimens, 13 (0.15%) were positive for HIV-2; the earliest blood specimens were drawn in 1988 [28]. Of the specimens obtained from individuals with an African country of birth, 19 (67.9%) of 28 that were positive for HIV-2 were initially misidentified as being positive for HIV-1 [29]. On the basis of these data, the PHL then began to conduct HIV-2 testing for all persons whose laboratory requisitions noted an African country of birth. Routine screening of all specimens for HIV-1 and HIV-2 was introduced in 1998; 6 cases of HIV-2–associated AIDS were diagnosed as a result of these combined efforts. As of 1 June 2000, when HIV infection became reportable by law, diagnostic test results positive for HIV-2 have been routinely reported to surveillance [30]. In addition, the NYC Department of Health and Mental Hygiene (DOHMH) reaches out to and routinely receives calls from clinicians wishing assistance with differential diagnosis of cases that are serologically, virologically, and/or clinically problematic. We used routinely reported laboratory data, new cases based on our public health laboratory diagnostic algorithm, and active case-finding to report the number of new HIV-2 infections diagnosed during the first 8 years of named HIV

Assay Type	Trade Name	Manufacturer
HIV-1-2+O EIA	GS HIV-1/HIV-2 PLUS O EIA	Bio-Rad Laboratories, Redmond, WA
HIV-1-2 EIA	GS HIV-1/HIV-2 EIA	Bio-Rad Laboratories
HIV-1 EIA	GS rLAV HIV-1 EIA	Bio-Rad Laboratories
HIV-1 WB	GS HIV-1 Western Blot	Bio-Rad Laboratories
HIV-2 EIA	GS HIV-2 EIA	Bio-Rad Laboratories
Multispot EIA	Multispot HIV-1/HIV-2 Rapid Test	Bio-Rad Laboratories
HIV-2 WB	In-house HIV-2 Western Blot assay	California Department of Health Services, Richmond, CA
HIV-2 DNA PCR	HIV-2 Lightcycler High Pure Viral Nucleic Acid Kit	Roche Molecular Systems, Belleville, NJ
HIV-1 RNA PCR	Aptima HIV-1 RNA Qualitative Assay	Gen-Probe, Inc., San Diego, CA

Figure 2. Assays for the detection of human immunodeficiency virus (HIV) type 1 and type 2. EIA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction; WB, Western blot.

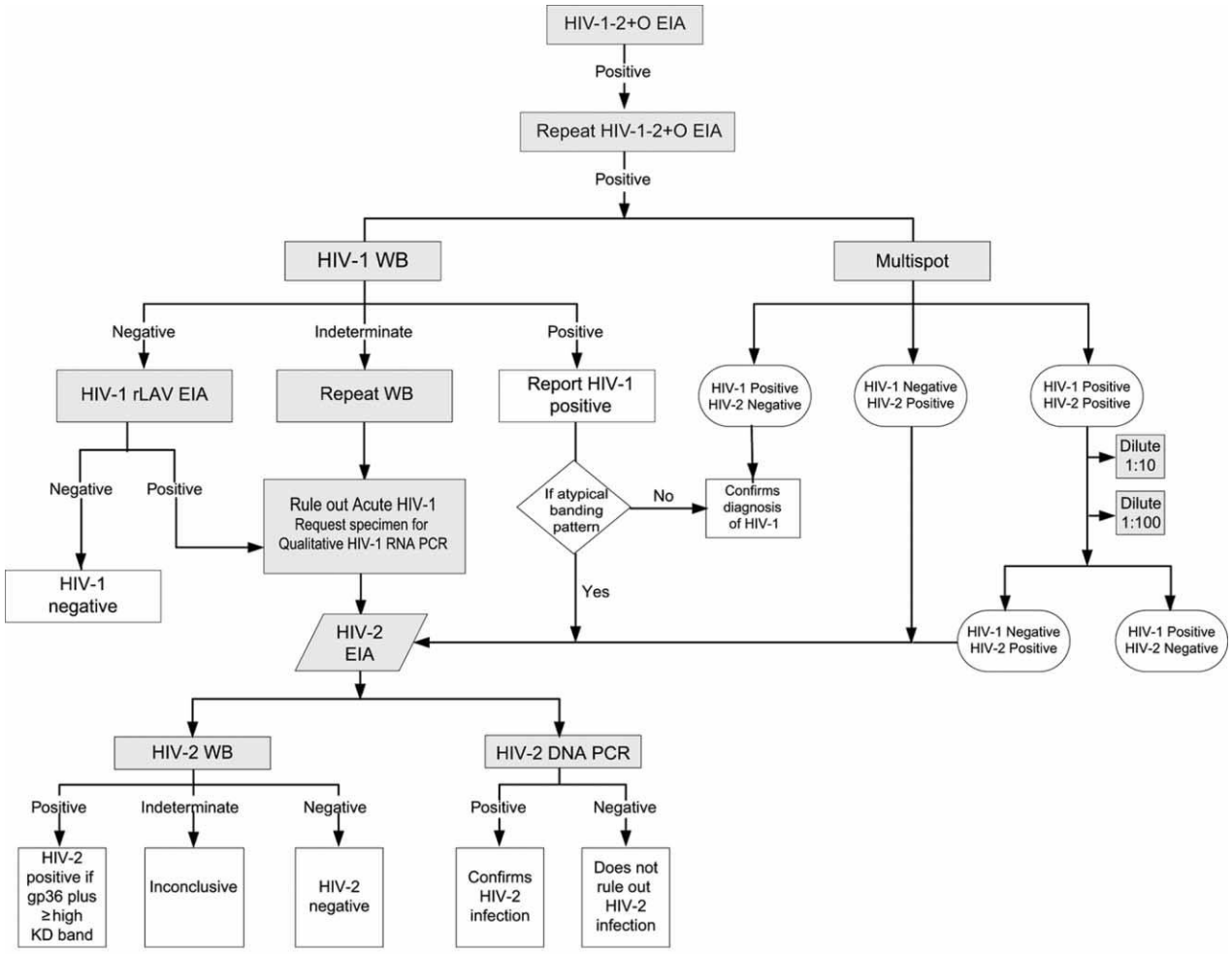

Figure 3. Algorithm for the diagnosis of human immunodeficiency virus (HIV) infection and differentiation of HIV type 1 and type 2. EIA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction; rLAV, recombinant lymphadenopathy-associated virus; WB, Western blot.

reporting in NYC, and we describe the challenges associated with diagnosis and surveillance.

METHODS

Data source. New York State requires named reporting of all diagnoses of HIV infection and AIDS, all HIV-related illness, all Western blot (WB) test results positive for HIV, all viral load and $CD4^+$ cell count values, all positive results on qualitative viral testing, and all HIV genotypes. Electronic laboratory reporting of all positive HIV-2 WB, polymerase chain reaction (PCR), and genetic sequence results is required under this law. Health care providers who diagnose HIV-2 infection are also required to report the diagnosis on the standard New York State Provider Report Form, just as they routinely report diagnoses of HIV-1 infection.

All data were obtained from the NYC HIV/AIDS Reporting System (HARS) as of 30 September 2009. HARS is a population-based registry that has existed since 1981 and is continuously updated with new, de-duplicated diagnoses and laboratory results. Incoming diagnostic WB and viral load reports from providers and laboratories that cannot be matched to an existing registry record initiate a field investigation to confirm the case, date, and disposition of diagnosis and collect other data required for surveillance. HARS also obtains data through regular matches with other disease registries, the NYC Vital Statistics Registry, the National Death Index, and the Social Security Death Master File.

Diagnoses of HIV-2 infection are reported to surveillance through 3 main routes. The first is routine surveillance, which involves laboratory reporting of confirmatory testing for HIV-2 (such as WB test results positive for HIV-2 antibody, positive PCR test results for HIV-2 proviral DNA, and sequencing of the HIV-2 integrase gene) and active surveillance conducted at testing and care sites. The second route begins with direct clinician contact, generally after the clinician has puzzled over an equivocal or contradictory laboratory picture that may include

Table 1. Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) Infection Diagnoses among New York City Residents with African Countries of Birth

	No. (%) of patients		
Country of birth	HIV-1 infection (n = 1236)	HIV-2 infection (n = 58)	Total (n = 1288)
Cote d'Ivoire	168 (93.3)	12 (6.7)	180
Ghana	173 (96.1)	7 (3.9)	180
Guinea	95 (94.1)	6 (5.9)	101
Mali	70 (90.9)	7 (9.1)	77
Senegal	56 (91.8)	5 (8.2)	61
South Africa	55 (98.2)	1 (1.8)	56
Gambia	48 (88.9)	6 (11.1)	54
Togo	43 (97.7)	1 (2.3)	44
Burkina Faso	30 (96.8)	1 (3.2)	31
Sierra Leone	23 (95.8)	1 (4.2)	24
Mauritania	13 (86.7)	2 (13.3)	15
Rwanda	8 (80.0)	2 (20.0)	10
Swaziland	0 (0.0)	1 (100.0)	1
Unknown African COB	…	6	–

tests for HIV antibody, viral load, and $CD4^+$ cells that are not consistent with the clinical status of the patient. The clinician notifies the Health Department, and the case is reviewed. Clinical status, previous test results and medical history, risk factors, and country of origin are ascertained, and, if appropriate, a decision is made to activate the diagnostic testing algorithm for laboratory confirmation of HIV-2 infection at the DOHMH Public Health Laboratory. Clinicians receive instructions on specimen collection and handling, and arrangements are made for DOHMH personnel to pick up the specimens and transport them back to the laboratory for accessioning and testing. A third route is triggered by routine laboratory reporting of HIV-2 reactivity in a person previously unknown to the registry. If the WB banding pattern or a positive nucleic acid test result is not available in the report, we contact the clinician to request activation of the Public Health Laboratory testing algorithm.

Population. This analysis includes all persons who received a diagnosis of confirmed or probable HIV-2 infection that was reported to HARS from 1 June 2000 (the date of implementation of named HIV reporting in New York State) through 31 December 2008.

Case definition. Surveillance uses the NYC Public Health Laboratory diagnostic algorithm combined with information obtained from medical record review to classify HIV-2 infections as confirmed, probable, or suspect. The specific criteria required to meet each level of the case definition are provided in Figure 1. Our case classification requirements begin with the testing that occurs after initial screening by HIV-1–2+O EIA, HIV-1 WB, and, in cases of indeterminate HIV-1 WB result and/or suggestive clinical signs and symptoms, HIV-1 nucleic acid testing to rule out acute HIV-1 infection.

Diagnostic testing. The NYC Public Health Laboratory and the majority of commercial laboratories serving the NYC area screen specimens submitted for HIV testing using an EIA that detects antibody to HIV-1, HIV-2, and Group O (Figure 2). Specimens that repeatedly have positive screening results are then tested by HIV-1 WB. If the HIV-1 WB result is positive, HIV-1 infection is diagnosed and reported. If the HIV-1 WB result is negative, indeterminate, or atypical (ie, incomplete); if an African country of birth is designated on the laboratory requisition; or if there is a special clinician request, additional testing is performed to rule out acute HIV-1 infection or HIV-2 infection.

The Public Health Laboratory has a comprehensive algorithm for diagnosis of HIV infection and differentiation between HIV-1 and HIV-2 (Figure 3). The standard initial tests include HIV 1–2+O EIA, HIV-1 WB, and—in cases where the HIV-1 WB is negative, indeterminate, or atypical and/or clinical signs and symptoms of seroconversion are present—HIV-1 nucleic acid testing to rule out acute HIV-1 infection. Supplemental HIV-2 testing includes a US Food and Drug Administration (FDA)–approved EIA that differentiates between HIV-1 and HIV-2, HIV-2–specific EIA, HIV-1 qualitative DNA PCR, and HIV-2 qualitative DNA PCR. Commercial and hospital laboratories generally stop testing after performing HIV-2 WB, and some report a positive result based exclusively on reactivity to gp36, which is highly cross-reactive with the corresponding HIV-1 transmembrane gp41. We do not consider

Table 2. Demographic and Clinical Characteristics of Individuals with Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) Infection Diagnoses among New York City Residents

Variable	HIV-2 diagnoses[a] (n = 62)	All HIV-1 diagnoses (n = 40,238)	P	All Africans with HIV-1 (n = 1634)	P	All West Africans with HIV-1 (n = 894)	P
Sex			.006[b]		.808[b]		.756[b]
Male	33 (53.2)	27,952 (69.5)		844 (51.7)		494 (55.3)	
Female	29 (46.8)	12,286 (30.5)		790 (48.3)		400 (44.7)	
Race/ethnicity			<.001[b]		.423[c]		.146[c]
Black	58 (93.5)	20,733 (51.5)		1,566 (95.8)		876 (98.0)	
Hispanic	2 (3.2)	11,981 (29.8)		17 (1.0)		7 (0.8)	
White	1 (1.6)	6,499 (16.2)		32 (2.0)		4 (0.4)	
Asian/Pacific Islander	0 (0.0)	874 (2.2)		15 (0.9)		6 (0.7)	
Native American	0 (0.0)	69 (0.2)		2 (0.1)		0 (0.0)	
Other/unknown	1 (1.6)	82 (0.2)		2 (0.1)		1 (0.1)	
Age group at diagnosis			.030[b]		<.001[c]		<.001[c]
0–12 Years	0 (0.0)	326 (0.8)		17 (1.0)		8 (0.9)	
13–19 Years	0 (0.0)	1412 (3.5)		36 (2.2)		22 (2.5)	
20–29 Years	7 (11.3)	8597 (21.4)		347 (21.2)		181 (20.2)	
30–39 Years	23 (37.1)	13,004 (32.3)		676 (41.4)		352 (39.4)	
40–49 Years	26 (41.9)	10,774 (26.8)		406 (24.8)		237 (26.5)	
50–59 Years	6 (9.7)	4533 (11.3)		126 (7.7)		80 (8.9)	
⩾60 Years	0 (0.0)	1592 (4.0)		26 (1.6)		14 (1.6)	
Age at diagnosis			.160[d]		.005[d]		.102[d]
Mean years (±SD)	40 ± 8	38 ± 12		36 ± 10		37 ± 10	
Median years	40	37		36		36	
Borough of residence			<.001[b]		.290[b]		.435[c]
Manhattan	19 (30.6)	11,158 (27.7)		386 (23.6)		205 (22.9)	
Brooklyn	7 (11.3)	10,822 (26.9)		265 (16.2)		154 (17.2)	
Bronx	30 (48.4)	9201 (22.9)		676 (41.4)		409 (45.7)	
Queens	4 (6.5)	5819 (14.5)		174 (10.6)		58 (6.5)	
Staten Island	0 (0.0)	729 (1.8)		51 (3.1)		33 (3.7)	
Unknown or outside NYC	2 (3.2)	2509 (6.2)		82 (5.0)		35 (3.9)	
Place of birth			<.001[b]				
US born	2 (3.2)	31,132 (77.4)		0 (0.0)		0 (0.0)	
Foreign born	60 (96.8)	9106 (22.6)		1634 (100.0)		894 (100.0)	
Africa	58 (96.7)	1634 (17.9)		1634 (100.0)		894 (100.0)	
Asia	0 (0.0)	474 (5.2)		0 (0.0)		0 (0.0)	
Central America	2 (3.3)	1325 (14.6)		0 (0.0)		0 (0.0)	
Caribbean	0 (0.0)	3554 (39.0)		0 (0.0)		0 (0.0)	
Europe	0 (0.0)	453 (5.0)		0 (0.0)		0 (0.0)	
Middle East	0 (0.0)	78 (0.9)		0 (0.0)		0 (0.0)	
Not specified	0 (0.0)	71 (0.8)		0 (0.0)		0 (0.0)	
Other or unknown region	0 (0.0)	71 (0.8)		0 (0.0)		0 (0.0)	
South America	0 (0.0)	1446 (15.9)		0 (0.0)		0 (0.0)	
Transmission risk factor			<.001[b]		<.001[c]		<.001[c]
Heterosexual[e]	36 (58.1)	8950 (22.2)		653 (40.0)		327 (36.6)	
Men who have sex with men	0 (0.0)	13,662 (34.0)		132 (8.1)		58 (6.5)	
Injection drug use	2 (3.2)	4518 (11.2)		23 (1.4)		14 (1.6)	
Other risk	0 (0.0)	346 (0.9)		17 (1.0)		8 (0.9)	
Unknown[f]	24 (38.7)	12,762 (31.7)		809 (49.5)		487 (54.5)	
Clinical status at diagnosis			.383[b]		.056[b]		.036[b]
HIV infection only	51 (82.3)	31,329 (77.9)		1162 (71.1)		623 (69.7)	
HIV/AIDS	11 (17.7)	8999 (22.4)		472 (28.9)		271 (30.3)	
First $CD4^+$ cell count			.002[b]		<.001[b]		<.001[b]
<200 cells/mL	20 (37.7)	11,649 (34.4)		566 (41.9)		313 (42.1)	
200–349 cells/mL	6 (11.3)	7167 (21.2)		324 (24.0)		179 (24.1)	
350–499 cells/mL	7 (13.2)	8449 (25.0)		267 (19.8)		152 (20.4)	
⩾500 cells/mL	20 (37.7)	6539 (19.3)		193 (14.3)		99 (13.3)	
Missing data	9	6434		284		151	

Table 2. ***(Continued.)***

Variable	HIV-2 diagnoses[a] (n = 62)	All HIV-1 diagnoses (n = 40,238)	P	All Africans with HIV-1 (n = 1634)	P	All West Africans with HIV-1 (n = 894)	P
First CD4+ cell count			<.001[b]		<.001[b]		<.001[b]
<500 cells/mL	33 (62.3)	27,265 (80.6)		1,157 (85.7)		644 (86.7)	
⩾500 cells/mL	20 (37.7)	6539 (19.4)		193 (14.3)		99 (13.3)	
Missing data	9	6434		284		151	

NOTE. Data are no. (%) of patients, unless otherwise indicated. Based on data reported to New York City Department of Health and Mental Hygiene as of 30 September 2009. NYC, New York City; SD, standard deviation.

[a] This column contains all probable and confirmed diagnoses of HIV-2 infection from 1 June 2000 through 31 December 2008 reported to the New York City Department of Health and Mental Hygiene.

[b] By χ^2 test.

[c] By Fisher's exact test.

[d] By pooled t test.

[e] Includes New York City Department of Health and Mental Hygiene presumed heterosexuals (ie, women with no injection drug history who have had sex with men).

[f] Most patients with HIV-2 infection with unknown transmission risk are presumed to have infection due to heterosexual transmission.

reactivity to gp36 alone to be confirmation of HIV-2 infection [31]. Other reasons for our conservative approach include the wide variation in the HIV-2 WB platforms used across laboratories, the absence of FDA approval of any HIV-2 WB, the failure of most laboratories to evaluate an HIV-2 WB side-by-side against an HIV-1 WB performed on the same specimen, and the failure of most laboratories to follow a positive HIV-2 WB result with a qualitative HIV-2 DNA PCR [32–37]. Therefore, we require that the WB contain at least 1 high molecular weight glycoprotein in addition to gp36 or a positive HIV-2 DNA PCR result to confirm HIV-2 infection. Commercial HIV-1 viral load assays do not detect HIV-2 and cannot be used to diagnose or rule out HIV-2 infection.

We take a similarly conservative approach to cases with laboratory data suggestive of dual HIV-1 and HIV-2 infection. Because there is no standardized diagnostic algorithm for dual infection, we did not classify any patient in our surveillance system as dually infected. Thus, all patients appearing in our tables have either confirmed or probable HIV-2 infection or confirmed HIV-1 infection.

Statistical analysis. Standard frequency distributions and cross-tabulations were conducted to enumerate and describe HIV-2 diagnoses according to the case definition. Pearson χ^2 statistics were used to ascertain statistically significant differences in demographic characteristics, risk factors, country of origin, and stage of illness at diagnosis for persons with HIV-2 infection vs persons with HIV-1 infection, Africans with HIV-1 infection, and West Africans with HIV-1 infection. SAS, version 9.1 (SAS Institute) was used to conduct the analyses.

RESULTS

Since the implementation of named HIV reporting on 1 June 2000, 52 confirmed and 10 probable cases of HIV-2 infection have been diagnosed and reported in NYC. The majority of diagnoses were made in persons born in Africa (58 [96.7%] of

Table 3. Test Results for Cases of Human Immunodeficiency Virus Type 2 (HIV-2) Infection Diagnosed from 1 June 2000 through 31 December 2008 in New York City

Variable	HIV 1-2+O EIA[a]	HIV-1 EIA	HIV-1 WB	HIV-2 EIA	HIV-2 WB	HIV-2 DNA PCR	HIV-2 integrase[b]	Multispot HIV-2 result
Patients with HIV-2 tested	35	39	58	41	55	49	2	42
No. of tests performed	41	54	182	54	85	66	3	55
Proportion (%) of patients with positive test results	31/35 (89)	36/39 (92)	54/58 (93)	41/41 (100)	54/55 (98)	41/49 (84)	2/2 (100)	40/42 (95)
Proportion (%) of tests performed with positive results	35/41 (85)	48/54 (89)	158/182 (87)	52/54 (96)	84/85 (99)	51/66 (77)	3/3 (100)	48/55 (87)
Positive WB result with bands reported	…	…	5	…	21	…	…	…
Positive WB results without bands reported	…	…	153	…	63	…	…	…
Proportion (%) of tests with negative results[c]	6/41 (15)	5/54 (9)	2/182 (1)	2/54 (4)[d]	1/85 (1)	13/66 (20)	0/3 (0)	5/55 (9)
Proportion (%) of tests with indeterminate results[d]	0/41 (0)	1/54 (2)	25/182 (14)	0/54 (0)	0/85 (0%)	2/66 (3)	0/3 (0)	2/55 (4)

NOTE. EIA, enzyme-linked immunosorbent immunoassay; PCR, polymerase chain reaction; WB, Western blot.

[a] HIV-1-2+O screening introduced 1 November 2003; HIV-1-2 peptide EIA used 1 June 2000–31 October 2003

[b] Total number of HIV-2 integrase sequencing tests performed is not available.

[c] EIAs and negative or indeterminate WB results are undercounted, because they are not reportable by New York State law.

[d] One patient had 2 negative and 1 positive HIV-2 EIA results reported.

62), especially in West African countries (48 [82.7%] of 58), including the Cote d'Ivoire ($n = 12$), Ghana ($n = 7$), Mali ($n = 7$), the Gambia ($n = 6$), Senegal ($n = 5$), Guinea ($n = 6$), Mauritania ($n = 2$), Burkina Faso ($n = 1$), Togo ($n = 1$), and Sierra Leone ($n = 1$). Two persons were born in Rwanda, and 1 each were born in Swaziland and South Africa (Table 1). The earliest known date of arrival in the United States is 1991.

There were significant differences in demographic characteristics, risk factors, borough and neighborhood of residence, and stage of illness at diagnosis between patients who received a diagnosis of HIV-2 and those who received a diagnosis of HIV-1 during the same time period (Table 2). HIV-2 represented a small proportion of all diagnoses of HIV infection, compared with HIV-1 (62 [0.15%] of 40,300 diagnoses vs 40,238 (99.8%) of 40,300 diagnoses). The overwhelming majority of patients with HIV-2 infection (60 [96.8%] of 62) were foreign-born, as opposed to 22.6% of persons who received a diagnosis of HIV-1 infection ($P < .001$). Africa was the region of birth for 93.5% of individuals with a diagnosis of HIV-2 infection and 4.1% of those with a diagnosis of HIV-1 infection. Of patients with HIV-2 infection, 46.8% were female and 93.5% were black; of patients with HIV-1 infection, 30.5% were female and 51.5% were black ($P = .002$ and $P < .001$, respectively). Median age at diagnosis of HIV-2 infection was 40 years (mean $\pm$ standard deviation [SD], 40 $\pm$ 8 years), in contrast to a median age at diagnosis of HIV-1 infection of 37 years (mean $\pm$ SD, 38 $\pm$ 12 years). Although HIV-2 cases have been diagnosed in all boroughs except Staten Island, the majority have been in upper Manhattan and the Bronx, where many recent West African immigrants have settled.

Risk factors were distributed differently between individuals with HIV-2 infection and those with HIV-1 infection ($P < .001$). More than one-half (58.1%) of HIV-2 infection diagnoses were the result of probable or confirmed [25] heterosexual transmission, whereas 22.2% of HIV-1 infection diagnoses were attributed to this risk. There were no cases of HIV-2 infection in men who have sex with men (MSM), whereas 34.0% of HIV-1 infection diagnoses were made in MSM. Similarly, there were 2 (3.2%) injection drug users (IDUs) among those with HIV-2 infection diagnoses and 4518 (11.2%) among those with HIV-1 infection diagnoses. Significantly more HIV-2 than HIV-1 infection diagnoses had no risk factor documented in their medical record (38.7% vs 31.7%; $P < .01$). Two maternal HIV-2 infections were first identified through positive results on newborn antibody screening tests performed by the NYS heelstick program. Subsequent seroreversion and serial negative PCR results ruled out HIV-2 infection in both infants. To date, no perinatal transmissions of HIV-2 have occurred in NYC.

Stage of illness at diagnosis differed between persons who received a diagnosis of HIV-1 infection and those who received a diagnosis of HIV-2 infection. Overall, 17.7% of patients who received a diagnosis of HIV-2 infection received a diagnosis of AIDS within 31 days of initial diagnosis of HIV infection (ie, concurrent HIV/AIDS). In contrast, 22.4% of persons who received a diagnosis of HIV-1 infection had a concurrent diagnosis of AIDS ($P = .005$). Fifty-one percent of those with HIV-2 infection and 55.7% of those with HIV-1 infection had an initial $CD4^+$ cell count <350 cells/mL, a difference that was not statistically significant ($P = .09$). Because of slower progression of HIV-2 infection, a $CD4^+$ cell count of <350 cells/mL likely represents longer-standing infection in a person with HIV-2 infection than it does in a person with HIV-1 infection.

The majority of cases reported here were first detected by screening at the Public Health Laboratory. Cases were confirmed by a variety of methods in accordance with our laboratory algorithm and case definition. HIV-2 proviral DNA was amplified for 77% of cases; 29% of patients had a positive WB result using our strict banding criteria, and the HIV-2 integrase gene was successfully sequenced for 8% of patients. Thirteen percent of cases were confirmed by multiple tests (Table 3).

The patients with HIV-2 infection who had complete testing histories exhibited considerable cross reactivity to the tests used to diagnose HIV-1 infection. Eighty-five percent of HIV-1 WB tests performed on patients with HIV-2 infection had positive results, as did 86% of HIV 1–2+O EIAs and 94% of HIV-1 "specific" EIAs. HIV-2 EIAs and WBs were positive in 96% and 99% of cases, respectively. Seventy-two percent of HIV-2 DNA PCR tests performed on specimens from patients with HIV-2 infection had positive results. Multispot, the only FDA-approved test for differentiation of HIV-1 and HIV-2, correctly identified HIV-2 for 90% of cases of HIV-2 infection. Although 100% of reported integrase tests had positive results, this test is performed on request by the CDC; we would not receive negative results of tests performed elsewhere.

DISCUSSION

Routine laboratory screening and enhanced vigilance by clinicians and surveillance personnel resulted in the testing, diagnosis, and reporting of 62 probable or confirmed HIV-2 infections over the first 8 years of named HIV reporting in NYC. We hope that improved outreach to health care providers through individual contacts, offering of laboratory services, and the issuing of a health advisory and "Frequently Asked Questions" on diagnosis of HIV-2 infection will result in increased inquiries and testing of possible cases [38]. City clinicians are increasingly aware of the need to include HIV-2 infection in the differential diagnosis of immigrants from Africa and other areas of endemicity who present for HIV testing and of the need to consider HIV-2 infection in a patient with AIDS who has an undetectable result on HIV-1 viral load testing. To our knowledge the NYC HIV/AIDS registry contains the largest

number of HIV-2 diagnoses in any single jurisdiction in the United States. Nevertheless, the true incidence and prevalence of HIV-2 infection in the city remains unknown.

For a number of reasons, it is likely that we have undercounted the number of HIV-2 infections in NYC. HIV-1–2+O screening followed by HIV-1 WB will not identify all patients with HIV-2 infection, because many HIV-1 cross-reactors will receive a diagnosis of HIV-1 infection; some HIV-1–negative or indeterminate specimens may not resolve; or the patient may be lost to follow-up. A patient who has erroneously received a diagnosis of HIV-1 infection or who is experiencing failure of therapy despite an undetectable HIV-1 viral load is more likely to receive an aggressive diagnostic work-up than is a more typical patient with HIV-2 infection who has normal $CD4^+$ cell counts and does not have signs and symptoms of disease. In one series, 30% of patients had previously received a diagnosis of HIV-1 infection and had laboratory testing for HIV-2 only after progressive immunodepletion occurred in the absence of detectable (HIV-1) viremia [13]. In our series, 40 (64.5%) of the 62 patients with HIV-2 infection initially received a diagnosis of HIV-1 infection. The true number of persons with a current diagnosis of HIV-1 infection who actually have HIV-2 infection is not known. Our surveillance system contains West African patients with deteriorating $CD4^+$ cell counts and persistently undetectable HIV-1 viral loads, but because it does not collect data on treatment history, it would not be reasonable to suggest that progressive HIV-2 infection might be the cause of their equivocal clinical picture. The test results presented in Table 1 show the challenges associated with differentiating HIV-1 and HIV-2 using commercially available antibody and viral testing.

In another scenario, negative WB test results may initially appear to rule out HIV infection. For example, late in 2007, 3 patients were admitted to 3 different NYC hospitals with central nervous system toxoplasmosis, $CD4^+$ cell counts <200 cells/mL, WB results negative for HIV-1, and undetectable HIV-1 viral loads. All were of West African origin. All ultimately received a diagnosis of HIV-2 infection after the DOHMH was contacted and the diagnostic algorithm activated. We cannot estimate the frequency of this scenario, because EIAs and negative or indeterminate WB results are not reportable in New York State. Overall, our experience and data suggest that patients with HIV-2 infection who are HIV-1 antibody nonreactors or cross-reactors will remain without a diagnosis or will be classified as having HIV-1 infection unless they experience disease progression and that few such cases will come to our attention, because few individuals with HIV-2 infection have progressive disease. Our approach and results support the increased implementation of testing algorithms that include type differentiation, as well as increased supplemental testing capacity at public health and other laboratories [39, 40].

Finally, we received laboratory results and obtained information from medical record review that suggests that an additional 10 HIV-infected patients met the case definition for suspected HIV-2 infection. However, because laboratory data sufficient to classify the person as having probable or confirmed HIV-2 infection were not available, these patients remain classified as having HIV-1 infection.

NYC is an immigration gateway. Among those who present for screening, supplemental testing to rule out HIV-2 infection should be performed for persons originating from or traveling to West Africa and other regions where HIV-2 infection is endemic, particularly those patients who have negative or indeterminate HIV-1 WB results or have atypical banding patterns and who present with risk factors for HIV infection and/or clinical signs suggestive of HIV infection or unexplained immunosuppression.

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