



HHS Public Access

Author manuscript

Curr Opin HIV AIDS. Author manuscript; available in PMC 2024 August 01.

Published in final edited form as:

Curr Opin HIV AIDS. 2012 March ; 7(2): 125–130. doi:10.1097/COH.0b013e3283506613.

Testing for acute HIV infection: implications for treatment as prevention

S. Michele Owen

Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Abstract

Purpose of review—The aim of this study is to give an overview of the recent literature related to HIV testing with an emphasis on detecting acute HIV infection. Testing technology as well as implications for treatment as prevention will be discussed.

Recent findings—HIV testing technology continues to evolve. Advances include updated immunologic formats that detect both HIV antibody and antigen (4th generation assays), new nucleic acid amplification tests, and continued development of rapid assays that can be used in either clinical or nonclinical settings. Because of these advances there are proposed changes for HIV diagnostic algorithms to encourage detection of acute infection. These technologic advances have implications for HIV prevention as testing is a cornerstone for all HIV prevention strategies. There is considerable new research indicating that treatment may be an important aspect of HIV prevention. Data also suggest that detection of acute infection will be important for the success of these prevention strategies.

Summary—Continued improvements in technology and testing practice are vital for the success of HIV prevention. Detection of acute or early HIV infection will likely play a key role in the success of treatment as prevention, as well as play an important role in ongoing behavioral prevention strategies.

Keywords

acute infection; diagnostics; HIV; preexposure prophylaxis; prevention

INTRODUCTION

HIV testing plays an important role in HIV prevention in that knowledge of HIV status has both individual and public health benefits. The individual benefits of HIV testing are primarily associated with individuals accessing care and treatment. Individuals entering care and treatment have a substantial reduction in adverse health outcomes and increased

Correspondence to S.M. Owen, Centers for Disease Control and Prevention, 1600 Clifton Road N.E. MS A-25, Atlanta, GA 30333, USA.; fax: +1 404 639 4555; Mowen@cdc.gov.

Conflicts of interest

There are no conflicts of interest.

Disclaimer: the findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

life expectancy [1–4]. The primary public health benefit associated with testing and care is a reduction in virus transmission due to decreased risk behaviors in those aware of their infection [5–7], and a reduction of virus in plasma and genital secretions by use of and adherence to antiretroviral therapy. A recent article by Smith *et al.* [8] provides a substantial review of the literature regarding anti-retroviral therapy (ART) and decreased transmission. Testing technology and practices continue to improve and one of the major focuses is to detect individuals as soon as possible after infection [9,10–12].

This article will discuss acute HIV infection (AHI), highlight recent advances in HIV testing technology, testing practices and how improvements in testing interface with HIV prevention.

ACUTE HIV INFECTION: WHAT IS IT AND WHY IS IT IMPORTANT?

There are multiple definitions of acute HIV in the literature. The definitions are based on both clinical symptoms and measurable virologic markers such as p24 antigen and HIV nucleic acids. For example, it has been defined as a transient symptomatic illness associated with high-titer HIV-1 replication [13], the period from infection to complete seroconversion [14] and recently defined as the phase between the appearance of detectable p24 or HIV RNA and detectable antibodies [15]. Regardless of the definition, there is considerable evidence that this period is significant in terms of potential for HIV transmission. During this period, levels of infectious virus in plasma and genital secretions are very high [16,17,18]. Likely related to the high viral loads, persons with AHI may be more likely to transmit HIV. Wawer *et al.* [19] demonstrated that in a discordant couple cohort in Uganda individuals that were within 5 months of seroconversion were up to 10 times more likely to transmit HIV per sex act than individuals with chronic infection. In an additional study by Hollingsworth, in which a different statistical method was used, it was demonstrated that HIV-1 is 26 times more infectious during primary infection than during asymptomatic established infection [20]. Furthermore, it has been reported that persons with AHI often engage in sexual intercourse more frequently than those with later stages of infection [20]. A study by Brenner *et al.* [21] found that persons with recent infections (i.e. those infected <6 months following seroconversion) accounted for almost half of onward HIV transmission. Furthermore, a recent animal study using nonhuman primates and SIV indicates that viral strains that establish new infections may be up to 750 times more infectious than strains that predominate during established infections [22]. These findings if confirmed in humans further illustrate the importance of detecting HIV infection early. Several publications have illustrated that diagnosis during this period may have important implications for preventing further transmission [12,23,24,25].

TESTING TECHNOLOGY

The first HIV immunoassay was approved by the US Food and Drug Administration (FDA) in 1985. Since this time there have been major improvements in HIV diagnostics technology. First-generation immunoassays detect IgG antibodies to HIV using whole viral lysate as the antigen in a standard indirect immunoassay format. These assays detect HIV infection in the same time frame as the western blot, approximately 45–60 days following infection [26,27].

Second-generation immunoassays also detect IgG in an indirect format, but were designed to increase specificity by incorporating recombinant proteins or peptides as the antigens for detection. Second-generation immunoassays detect HIV infection approximately 5–7 days sooner than first-generation assays [28]. The next assays to come to the market (third-generation immunoassays) detect both IgG and IgM using peptides and recombinant proteins in an antigen sandwich format and improve detection of recent HIV infection. These assays generally detect infection within about 20–25 days after infection [27,28]. Most third-generation immunoassays marketed in the USA and around the world detect HIV-2 in addition to HIV-1 [28]. The latest laboratory immunoassays to come to the market, fourth-generation immunoassays assays, detect p24 antigen in addition to detecting anti HIV, IgM and IgG. Fourth-generation or combination antigen/antibody assays have been approved and used in many countries since the late 1990s [29–32,33[■]]. These assays detect p24 antigen at the level of 11–18 pg/ml [34], which is equivalent to approximately 30 000–50 000 copies/ml of HIV RNA [35]. Recently, two such assays (Abbott ARCHITECT HIV Ag/Ab Combo and Bio-Rad GS HIV Combo Ag/Ab EIA) have been approved for use in the USA. Several studies have been conducted with these assays and the data indicate they have similar performance characteristics as those marketed else-where [36,37[■],38[■]] and detect p24 approximately 5–7 days after the appearance of nucleic acid [39[■]]. Importantly, the data published to date indicate the assays available in the USA are capable of detecting AHI in greater than 80% of individuals that are nucleic acid amplification test (NAAT) positive but nonreactive or indeterminate in antibody only assays [36,37[■],38[■]].

Rapid HIV tests offer another option for HIV testing. Rapid tests are found in two types of formats, lateral flow and immune concentration [15[■]]. Many of the lateral flow tests do not require a laboratory and thus can be conducted in point-of-care (POC) settings. The ability to do testing in nonclinical settings has expanded the options for HIV testing [15[■],23[■]]. Rapid test results are typically available in 30 min or less and improve receipt of test results [40,41[■]]. Seven rapid HIV tests have been approved by FDA for use in the USA and there are multiple other rapid tests available for use in countries around the world [41[■]]. Current listings of available tests are maintained at the US FDA and the USAID web sites (<http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/UCM080466> and www.usaid.gov/our_work/global_health/aids/.../hiv_tests.xls). Most of these tests have performance characteristics comparable with first-generation and second-generation laboratory immunoassays [28,39[■],42]. However, there is one rapid test available in the US market that is based on the third-generation assay principle [43[■]]. Many rapid HIV tests detect both HIV-1 and HIV-2, and there is one approved for use in the USA that can differentiate HIV-1 from HIV-2 infection [37[■],39[■],44[■]]. Like laboratory-based tests, a negative rapid test result is considered to be conclusive for the absence of HIV antibody. However, as most of the tests currently available detect HIV infection in a similar manner as second-generation laboratory assays, they do not rule out the possibility of AHI [28,39[■],42,45]. Recently a fourth-generation Ag/Ab rapid HIV assay (Alere Determine HIV1/2 Ag/Ab combo) has become available commercially, but is not yet approved for use in the USA. Although this assay has the advantage of differentiating between antigen and antibody reactivity, data reported to date indicate that it does not detect HIV p24 antigen

at the same levels as laboratory-based fourth-generation assays and does not detect HIV infection as soon after infection as the laboratory assays [46[■],47[■]]. In addition to this commercial assay, there are several other rapid assays in the experimental pipeline that detect p24 antigen [48[■],49].

Quantitative NAAT detect HIV RNA approximately 10 days after infection and have typically been used to determine viral burden and monitor response to therapy [12[■],15[■],26]. To date none of these assays have been approved by FDA for diagnosis of HIV infection. In 2006, a qualitative NAAT (GenProbe APTIMA) was approved by FDA as a supplemental assay for diagnosing HIV infection. This assay allows detection of HIV infection prior to the appearance of HIV-specific antibody [28,39[■],45,50[■]]. The review by Cohen *et al.* [12[■]] gives a detailed review of the literature published to date regarding the use of NAAT to detect acute infection. However, the current NAATs (quantitative and qualitative) that are on the market have several limitations, including the need to draw blood, extraction of nucleic acid, cost, processing time and the technical skill required to perform the tests. To address some of the limitations associated with NAAT, there is considerable effort being spent to simplify NAAT and potentially make it feasible for POC testing [51[■]]. Many of these technologies rely on isothermal amplification techniques and include loop-mediated isothermal amplification [52], helicase-dependent amplification [53[■]], and a simplified amplification-based assay that incorporates a visual dipstick detection device [54[■]]. There is also considerable work being done to decrease the assay time for real-time polymerase chain reaction assays and package them so they can be used in point-of-contact settings [55[■],56,57]. Furthermore, although NAAT is ideal for detecting AHI, it has been demonstrated that there is a risk of false-negative NAAT results in individuals with established HIV infection, and this can be up to 3.7% [28,50[■]].

TESTING ALGORITHMS

The current algorithm for diagnosing HIV infection in the USA has been used for more than 20 years. This algorithm consists of confirming a repeatedly reactive HIV immunoassay with a western blot or immunofluorescence assay [58]. Given the large number of technological advances in HIV testing, CDC and the Association of Public Health Laboratories worked together to develop new potential algorithms for HIV diagnosis both in the laboratory and in POC settings. Based on data that were presented at the 2010 HIV Diagnostics Conference, a new algorithm for diagnosing HIV in the laboratory was proposed to take advantage of the progress in diagnostic technology to address challenges posed by AHI and HIV-2. The proposed algorithm calls for using the most sensitive serologic HIV assay possible (preferably a combination antigen/antibody assay) to screen for HIV. If the initial test is reactive (positive for the presence of HIV), it is followed by an HIV-1/HIV-2 antibody differentiation test. Specimens reactive in the second test would be considered positive for HIV antibody. In this algorithm specimens with positive results on the antigen/antibody assay, but with negative results on the second antibody only assay, would be tested for HIV-1 RNA to detect AHI [10[■],11[■]]. This algorithm is one of several testing algorithms contained in the recently published testing guidelines published by the Clinical Laboratory Standards Institute [15[■]]. Several recent studies have examined the performance of this proposed laboratory algorithm. In these studies it was shown that

the new algorithm had comparable or better performance in detecting HIV infection in individuals previously shown to be infected with HIV [59–62]. Furthermore, it was shown that detection of acute HIV-1 infection [39] and more accurate detection of HIV-2 was achieved using the proposed algorithm [61,62]. Thus, the proposed algorithm appears to accomplish many of the objectives that were identified for the algorithm, improved detection of AHI and more accurate diagnosis of HIV-2, without sacrificing any of the specificity of using a western blot or immunofluorescence assay (IFA). The algorithm appears to be a positive step forward for laboratory diagnosis of HIV in the USA. However, there are some challenges for implementation such as, state law restrictions for supplemental testing, compliance with regulatory requirements, sample handling requirements and staff training that will need to be addressed prior to this being implemented on a large scale.

TESTING IS AN INTEGRAL PART OF PREVENTION

HIV testing is an important component of HIV prevention. Individuals need to know their status in order to access care, treatment and prevention services. Because of this importance to public health, CDC updated the guidelines for HIV testing in clinical settings to encourage everyone to be tested at least once for HIV and to increase testing frequency by individuals at high risk for infection [63]. Given the apparent important contribution of AHI to sustaining the HIV epidemic, multiple groups have incorporated testing strategies that include NAAT to identify individuals that are in this highly infectious stage. This approach has been employed in the USA and in multiple countries with high HIV prevalence and the percentage of AHI found among infected individuals has ranged from around 1.8–10.5% [12,50,64–66]. Furthermore, it has been demonstrated that AHI constitutes a considerable proportion of the new diagnoses in high-risk populations, such as of young MSM in the USA [45,65,67,68].

Recently, several studies have directly addressed the use of ART either as pre-exposure prophylaxis (PrEP) or as treatment to prevent onward transmission and have shown these approaches to have great promise as tools for HIV prevention [8]. For example, there are now four studies that have shown that PrEP (either as a vaginal microbicide or orally) is efficacious at decreasing HIV acquisition [69,70,71]. In addition to PrEP, the recent HIV Prevention Trials Network Study 052, which evaluated the effect of immediate versus delayed initiation of ART on heterosexual transmission from HIV-infected persons to their HIV-uninfected partners, found that immediate initiation of ART resulted in a 96% reduction in sexual transmission of HIV in discordant couples [72]. Although these studies show great advancement in preventing HIV infection, neither of the approaches can work effectively without HIV testing. In the case of PrEP, testing that gives accurate HIV infection status is important so that only uninfected individuals are given this prevention tool. Detection of acute infection is important as demonstrated by results from the PrEP study. In this study, two individuals with undetected AHI were randomized to the PrEP arm of the study and developed drug resistance, highlighting the importance of accurate diagnoses when implementing PrEP [70]. In the case of treating infected individuals to prevent onward transmission (Test and treat), testing is the first step in the prevention effort. Based on data indicating a greater chance of transmission during AHI [17,19,21] and various

mathematical modeling studies [73–75], detection and rapid treatment of AHI is likely key to successfully implementing this prevention strategy.

CONCLUSION

There has been considerable progress in HIV testing technology and practice. Current diagnostic assays can detect infection much sooner after infection as compared with the assays that were first introduced for diagnosis in the 1980s. The introduction of HIV rapid tests has expanded HIV testing to nonclinical settings and improved receipt of test results. Furthermore, the implementation of updated testing algorithms, which take advantage of the latest diagnostic technology, offer the potential for continued improvements in HIV diagnosis in the USA and around the world. However, although there is reason to be optimistic, the optimism must be tempered somewhat. Even with the great advances that allow detection of infection within about 10 days of infection, we cannot completely close the HIV diagnostic window. There is currently no technology on the horizon that can detect HIV infection before the appearance of HIV nucleic acid. This period termed the ‘eclipse phase’ is approximately equal to the acute phase of infection using our most sensitive assays [15]. Because of this diagnostic gap (window) just after infection, we will likely continue to miss some individuals immediately after infection. A clear message about this potential should be given to anyone that tests for HIV to prevent a false sense of security and to illustrate the need for repeat testing at frequent intervals as long as high-risk behavior continues.

Even with its limitations, HIV testing will continue to play a major role in HIV prevention as knowledge of HIV status is the foundation for both behavioral and biomedical prevention efforts.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- ■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 205–206).

1. Detels R, Munoz A, McFarlane G, et al. Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. Multicenter AIDS cohort study investigators. *JAMA* 1998; 280:1497–1503. [PubMed: 9809730]
2. McNaghten AD, Hanson DL, Jones JL, et al. Effects of antiretroviral therapy and opportunistic illness primary chemoprophylaxis on survival after AIDS diagnosis. *AIDS* 1999; 13:1687–1695. [PubMed: 10509570]
3. Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. *Lancet* 1998; 352:1725–1730.
4. Walensky RP, Paltiel AD, Losina E, et al. The survival benefits of AIDS treatment in the United States. *J Infect Dis* 2006; 194:11–19. [PubMed: 16741877]

5. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. *J Acquir Immune Defic Syndr* 2005; 39:446–453. [PubMed: 16010168]
6. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS* 2006; 20:1447–1450. [PubMed: 16791020]
7. Metsch LR, Pereyra M, Messinger S, et al. HIV transmission risk behaviors among HIV-infected persons who are successfully linked to care. *Clin Infect Dis* 2008; 47:577–584. [PubMed: 18624629]
- 8■■■. Smith K, Powers KA, Kashuba AD, Cohen MS. HIV-1 treatment as prevention: the good, the bad, and the challenges. *Curr Opin HIV AIDS* 2011; 6:315–325. [PubMed: 21646878] This is an extensive review article on test and treat as an HIV prevention approach. It highlights the pros, cons and challenges for using treatment as prevention.
9. Parry JV, Mortimer PP, Perry KR, et al. Towards error-free HIV diagnosis: guidelines on laboratory practice. *Commun Dis Public Health* 2003; 6:334–350. [PubMed: 15067862]
- 10■■■. Branson BM. The future of HIV testing. *J Acquir Immune Defic Syndr* 2010; 55 (Suppl 2):S102–S105. [PubMed: 21406978] This article highlights current and future HIV testing technology and practices.
- 11■. Branson B. Conference wrap-up: unified laboratory algorithm 2010 HIV Diagnostics Conference; 24–26 March 2010; Orlando, FL. This is a meeting summary that highlights the key findings of the 2010 HIV diagnostics conference.
- 12■■■. Cohen MS, Gay CL, Busch MP, Hecht FM. The detection of acute HIV infection. *J Infect Dis* 2010; 202 (Suppl 2):S270–S277. [PubMed: 20846033] This is a comprehensive article that describes testing methodology and highlights the advantages for detecting AHIs.
13. Kahn JO, Walker BD. Acute human immunodeficiency virus type 1 infection. *N Engl J Med* 1998; 339:33–39. [PubMed: 9647878]
14. Hare CB, Kahn JO. Primary HIV Infection. *Curr Infect Dis Rep* 2004; 6:65–71. [PubMed: 14733851]
- 15■. Clinical and Laboratory Standards Institute (CLSI). Criteria for laboratory testing and diagnosis of human immunodeficiency virus infection; approved guideline; 2011. Document No. M53-A. This is a guideline document that explains the basic principles of HIV testing, as well as highlights the improved HIV testing algorithms for use in laboratory settings.
16. Daar ES, Moudgil T, Meyer RD, Ho DD. Transient high levels of viremia in patients with primary human immunodeficiency virus type 1 infection. *N Engl J Med* 1991; 324:961–964. [PubMed: 1823118]
17. Pilcher CD, Joaki G, Hoffman IF, et al. Amplified transmission of HIV-1: comparison of HIV-1 concentrations in semen and blood during acute and chronic infection. *AIDS* 2007; 21:1723–1730. [PubMed: 17690570]
- 18■. Morrison CS, Demers K, Kwok C, et al. Plasma and cervical viral loads among Ugandan and Zimbabwean women during acute and early HIV-1 infection. *AIDS* 2010; 24:573–582. [PubMed: 20154581] This article describes the viral loads found in plasma and cervical fluids during acute infection. The work highlights the potential for increased transmission during acute infection.
19. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005; 191:1403–1409. [PubMed: 15809897]
20. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. *J Infect Dis* 2008; 198:687–693. [PubMed: 18662132]
21. Brenner BG, Roger M, Routy JP, et al. High rates of forward transmission events after acute/early HIV-1 infection. *J Infect Dis* 2007; 195:951–959. [PubMed: 17330784]
22. Ma ZM, Stone M, Piatak M Jr, et al. High specific infectivity of plasma virus from the preramp-up and ramp-up stages of acute simian immunodeficiency virus infection. *J Virol* 2009; 83:3288–3297. [PubMed: 19129448]
- 23■. Pilcher CD, Christopoulos KA, Golden M. Public health rationale for rapid nucleic acid or p24 antigen tests for HIV. *J Infect Dis* 2010; 201 (Suppl 1): S7–S15. [PubMed: 20225950] This

article describes current rapid testing options and highlights the potential advantages for rapid HIV antigen assays.

- 24■■■. Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 Infection. *N Engl J Med* 2011; 364:1943–1954. [PubMed: 21591946] This is a comprehensive review of AHI. It describes virologic, immunologic and diagnostic aspects of AHI.
- 25■■■. Powers KA, Ghani AC, Miller WC, et al. The role of acute and early HIV infection in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: a modelling study. *Lancet* 2011; 378:256–268. [PubMed: 21684591] This is modeling study that predicts the value of detecting acute/early HIV infection as it relates to preventing further transmission.
26. Busch MP, Satten GA. Time course of viremia and antibody seroconversion following human immunodeficiency virus exposure. *Am J Med* 1997; 102 (5B):117–124; discussion 25–6. [PubMed: 9845513]
27. Fiebig EW, Wright DJ, Rawal BD, et al. Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. *AIDS* 2003; 17:1871–1879. [PubMed: 12960819]
28. Owen SM, Yang C, Spira T, et al. Alternative algorithms for human immunodeficiency virus infection diagnosis using tests that are licensed in the United States. *J Clin Microbiol* 2008; 46:1588–1595. [PubMed: 18322061]
29. Weber B, Gurtler L, Thorstensson R, et al. Multicenter evaluation of a new automated fourth-generation human immunodeficiency virus screening assay with a sensitive antigen detection module and high specificity. *J Clin Microbiol* 2002; 40:1938–1946. [PubMed: 12037046]
30. Ly TD, Martin L, Daghfal D, et al. Seven human immunodeficiency virus (HIV) antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. *J Clin Microbiol* 2001; 39:3122–3128. [PubMed: 11526139]
31. Ly TD, Laperche S, Brennan C, et al. Evaluation of the sensitivity and specificity of six HIV combined p24 antigen and antibody assays. *J Virol Methods* 2004; 122:185–194. [PubMed: 15542143]
32. Weber B Screening of HIV infection: role of molecular and immunological assays. *Expert Rev Mol Diagn* 2006; 6:399–411. [PubMed: 16706742]
- 33■■■. Murphy G, Aitken C. HIV testing—the perspective from across the pond. *J Clin Virol* 2011; 52, Supplement 1(0):S71–S76. This article describes the current HIV diagnostic testing methodology used in the United Kingdom and highlights the use of antigen/antibody assays as the initial (screening) HIV assay.
34. Ly TD, Ebel A, Faucher V, et al. Could the new HIV combined p24 antigen and antibody assays replace p24 antigen specific assays? *J Virol Methods* 2007; 143:86–94. [PubMed: 17395277]
35. Layne SP, Merges MJ, Dembo M, et al. Factors underlying spontaneous inactivation and susceptibility to neutralization of human immunodeficiency virus. *Virology* 1992; 189:695–714. [PubMed: 1386485]
36. Pandori MW, Hackett J Jr, Louie B, et al. Assessment of the Ability of a Fourth Generation Immunoassay for HIV Antibody and p24 Antigen to Detect both Acute and Recent HIV Infection in a High-Risk Setting. *J Clin Microbiol* 2009; 47:2639–2642. [PubMed: 19535523]
- 37■■■. Chavez P, Wesolowski L, Patel P, et al. Evaluation of the performance of the Abbott ARCHITECT HIV Ag/Ab Combo Assay. *J Clin Virol* 2011; 52, Supplement 1(0):S51–S55. This article describes the performance characteristics of the recently FDA approved Abbott Architect antigen/antibody assay.
- 38■■■. Bentsen C, McLaughlin L, Mitchell E, et al. Performance evaluation of the Bio-Rad Laboratories GS HIV Combo Ag/Ab EIA, a 4th generation HIV assay for the simultaneous detection of HIV p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum or plasma. *J Clin Virol* 2011; 52, Supplement 1(0):S57–S61. This article describes the performance characteristics of the recently FDA approved Bio-Rad antigen/antibody assay.
- 39■■■. Masciotra S, McDougal JS, Feldman J, et al. Evaluation of an alternative HIV diagnostic algorithm using specimens from seroconversion panels and persons with established HIV infections. *J Clin Virol* 2011; 52, Supplement 1(0):S17–S22. This article describes and evaluates

the recently proposed HIV laboratory-testing algorithm. Data in the study indicate that the proposed laboratory testing algorithm will detect a good proportion of AHIs.

40. Farnham PG, Hutchinson AB, Sansom SL, Branson BM. Comparing the costs of HIV screening strategies and technologies in health-care settings. *Public Health Rep* 2008; 123 (Suppl 3):51–62. [PubMed: 19166089]
- 41 ■■■. Heffelfinger J, Owen SM, Hendry RM, Lansky A. HIV testing: the cornerstone of HIV prevention efforts in the USA. *Future Virol* 2011; 6:1299–1317. This paper describes a very comprehensive review of HIV testing technology and testing practices. It highlights the importance of HIV testing in all HIV prevention efforts.
42. Stekler J, Wood RW, Swenson PD, Golden M. Negative rapid HIV antibody testing during early HIV infection. *Annals of internal medicine* 2007; 147: 147–148.
- 43 ■■■. Delaney KP, Branson BM, Uniyal A, et al. Evaluation of the performance characteristics of 6 rapid HIV antibody tests. *Clin Infect Dis* 2011; 52:257–263. [PubMed: 21288853] This article highlights the performance of the proposed laboratory HIV diagnostic testing algorithm and supports the implementation of the proposed testing algorithm.
- 44 ■■■. Nasrullah M, Ethridge SF, Delaney KP, et al. Comparison of alternative interpretive criteria for the HIV-1 Western blot and results of the Multispot HIV-1/HIV-2 Rapid Test for classifying HIV-1 and HIV-2 infections. *J clin virol* 2011; 52, Supplement 1(0):S23–S27. This article examines the performance characteristics of two assays that are potential components of the recently proposed laboratory HIV testing algorithm.
45. Stekler JD, Swenson PD, Coombs RW, et al. HIV testing in a high-incidence population: is antibody testing alone good enough? *Clin Infect Dis* 2009; 49:444–453. [PubMed: 19538088]
- 46 ■. Fox J, Dunn H, O’Shea S. Low rates of p24 antigen detection using a fourth-generation point of care HIV test. *Sex Transm Infect* 2011; 87:178–179. [PubMed: 21084439] A description of the performance characteristics of a rapid antigen/antibody is the primary focus of this article.
- 47 ■. Beelaert G, Franssen K. Evaluation of a rapid and simple fourth-generation HIV screening assay for qualitative detection of HIV p24 antigen and/or antibodies to HIV-1 and HIV-2. *J Virol Methods* 2010; 168 (1–2):218–222. [PubMed: 20561542] Like reference 46, this article describes the test procedure and performance characteristics of a rapid antigen/antibody assay.
- 48 ■. Parpia ZA, Elghanian R, Nabatiyan A, et al. p24 antigen rapid test for diagnosis of acute pediatric HIV infection. *J Acquir Immune Defic Syndr* 2010; 55:413–419. [PubMed: 20811289] This article describes the test procedure and performance characteristics of an experimental rapid antigen/antibody assay.
49. Workman S, Wells SK, Pau CP, et al. Rapid detection of HIV-1 p24 antigen using magnetic immuno-chromatography (MICT). *J Virol Methods* 2009; 160 (1–2):14–21. [PubMed: 19482361]
- 50 ■■■. Patel P, Mackellar D, Simmons P, et al. Detecting acute human immunodeficiency virus infection using 3 different screening immunoassays and nucleic acid amplification testing for human immunodeficiency virus RNA, 2006–2008. *Arch Intern Med* 2010; 170:66–74. [PubMed: 20065201] The data presented in this article illustrate the utility of using NAAT and or Ag/Ab assays for detecting acute HIV.
- 51 ■. Schito ML, D’Souza MP, Owen SM, Busch MP. Challenges for rapid molecular HIV diagnostics. *J Infect Dis* 2010; 201 (Suppl 1):S1–S6. The challenges for developing and validating rapid molecular HIV diagnostic tests are discussed in this article.
52. Curtis KA, Rudolph DL, Owen SM. Rapid detection of HIV-1 by reverse-transcription, loop-mediated isothermal amplification (RT-LAMP). *J Virol Methods* 2008; 151:264–270. [PubMed: 18524393]
- 53 ■. Tang W, Chow WH, Li Y, et al. Nucleic acid assay system for tier II laboratories and moderately complex clinics to detect HIV in low-resource settings. *J Infect Dis* 2010; 201 (Suppl 1):S46–S51. [PubMed: 20225946] This article describes an isothermal NAAT that could be performed in an area that does not have extensive laboratory equipment.
- 54 ■. Lee HH, Dineva MA, Chua YL, et al. Simple amplification-based assay: a nucleic acid-based point-of-care platform for HIV-1 testing. *J Infect Dis* 2010; 201 (Suppl 1):S65–S72. [PubMed: 20225949] This article describes an isothermal NAAT that has the potential to be used in POC settings to detect AHI.

- 55 ■■■. Tanriverdi S, Chen L, Chen S. A rapid and automated sample-to-result HIV load test for near-patient application. *J Infect Dis* 2010; 201 (Suppl 1):S52–S58. [PubMed: 20225947] This article describes a simple, rapid viral load test that would be useful for monitoring the efficacy of antiretroviral treatment.
56. Pau CP, Wells SK, Owen SM, Granade TC. Development of a simple, rapid and inexpensive method for the qualitative detection of HIV-1 RNA. Proceedings of the 2010 HIV Diagnostics Conference; 24–26 March 2010; Orlando, FL. <http://www.hivtestingconference.org/posters.html>.
57. Mazzola LT, Arsham AM, Pederson AM, et al. Innovative point-of-care HIV viral load detection in RLS. Proceedings of the 2010 HIV Diagnostics Conference; 2010; Orlando, FL. <http://www.hivtestingconference.org/posters.html>.
58. Centers for Disease Control and Prevention. Interpretation and use of the western blot assay for serodiagnosis of human immunodeficiency virus type 1 infections. *MMWR Morb Mortal Wkly Rep* 1989; 38 (Suppl 7):1–7. [PubMed: 2491906]
- 59 ■■■. Wesolowski LG, Delaney KP, Hart C, et al. Performance of an alternative laboratory-based algorithm for diagnosis of HIV infection utilizing a third generation immunoassay, a rapid HIV-1/HIV-2 differentiation test and a DNA or RNA-based nucleic acid amplification test in persons with established HIV-1 infection and blood donors. *J Clin Virol* 2011; 52, Supplement 1(0):S45–S49. This article shows that the performance of the recently proposed diagnostic algorithm is comparable with the current diagnostic algorithm that utilizes western blotting for a population of individuals with known established HIV infection.
- 60 ■■■. Delaney KP, Heffelfinger JD, Wesolowski LG, et al. Performance of an alternative laboratory-based algorithm for HIV diagnosis in a high-risk population. *J Clin Virol* 2011; 52, Supplement 1(0):S5–S10. The recently proposed diagnostic algorithm is examined in this body of work. The findings from this high-risk population indicate that the proposed algorithm functions well in high-risk populations.
- 61 ■■■. Torian LV, Forgione LA, Punsalang AE, et al. Comparison of Multispot EIA with Western blot for confirmatory serodiagnosis of HIV. *J Clin Virol* 2011; 52, Supplement 1(0):S41–S44. This is another article that examines the performance of two different assays in the proposed HIV laboratory diagnostic algorithm.
- 62 ■■■. Styer LM, Sullivan TJ, Parker MM. Evaluation of an alternative supplemental testing strategy for HIV diagnosis by retrospective analysis of clinical HIV testing data. *J Clin Virol* 2011; 52, Supplement 1(0):S35–S40. This work describes the performance of the proposed laboratory-testing algorithm in New York State and supports the implementation of the new laboratory testing algorithm.
63. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006; 55 (RR-14):1–17.
64. Fiscus SA, Pilcher CD, Miller WC, et al. Rapid, real-time detection of acute HIV infection in patients in Africa. *J Infect Dis* 2007; 195:416–424. [PubMed: 17205481]
65. Pilcher CD, Fiscus SA, Nguyen TQ, et al. Detection of acute infections during HIV testing in North Carolina. *N Engl J Med* 2005; 352:1873–1883. [PubMed: 15872202]
66. Priddy FH, Pilcher CD, Moore RH, et al. Detection of acute HIV infections in an urban HIV counseling and testing population in the United States. *J Acquir Immune Defic Syndr* 2007; 44:196–202. [PubMed: 17312561]
67. Patel P, Klausner JD, Bacon OM, et al. Detection of acute HIV infections in high-risk patients in California. *J Acquir Immune Defic Syndr* 2006; 42:75–79. [PubMed: 16763493]
68. Acute HIV infection: New York City, 2008. *Morb Mortal Wkly Rep* 2009; 58:1296–1299.
- 69 ■■■. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010; 329:1168–1174. [PubMed: 20643915] The performance of a gel that contains tenofovir as an HIV prevention tool is described in this article. The work is one of four studies that indicates that PrEP may be an effective prevention tool.
- 70 ■■■. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; 363:2587–2599. [PubMed: 21091279] Like

reference [69] this article describes the successful use of PrEP as an HIV prevention tool. In this study, oral PrEP was used in a population of MSM.

- 71. Conference Summary Report on the 6th IAS Conference on HIV pathogenesis, treatment and prevention (IAS 2011): research highlights and implications for policy and practice. Proceedings of the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; 17–20 July 2011; Rome Italy. http://www.iasociety.org/Web/WebContent/File/IAS2011_Conference_Report.pdf. This article is a meeting summary of the latest IAS meeting and, within the document, two of the most recent PrEP success stories are described.
- 72. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365:493–505. [PubMed: 21767103] This is a groundbreaking study that demonstrated that early retroviral treatment of infected individuals can serve as a tool for preventing onward transmission of HIV-1.
- 73. Cohen MS, Gay CL. Treatment to prevent transmission of HIV-1. *Clin Infect Dis* 2010; 50 (Suppl 3):S85–S95. [PubMed: 20397961]
- 74. Granich RM, Gilks CF, Dye C, et al. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009; 373:48–57. [PubMed: 19038438]
- 75. Walensky RP, Paltiel AD, Losina E, et al. Test and treat DC: forecasting the impact of a comprehensive HIV strategy in Washington DC. *Clin Infect Dis* 2010; 51:392–400. [PubMed: 20617921]

KEY POINTS

- HIV testing is the foundation for both behavioral and biomedical prevention efforts.
- Testing technology continues to evolve and with the latest technology we can detect HIV infection much sooner after infection than we could in the early days of the epidemic.
- Early identification of infection has both personal and public health benefits.
- The recent demonstration that early treatment of infected individuals is a potent prevention tool further strengthens the need for early and accurate diagnosis.