

TESTING ORAL FLUID FOR THE PRESENCE OF HIV ANTIBODIES

2013 STATUS REPORT

HIV testing is primarily done using blood-based specimens (fingerstick or venous whole blood, plasma, or serum). However, testing of oral fluid for the presence of HIV antibodies is another option that is commonly used. Reasons for choosing oral fluid over blood include testing of individuals averse to having their blood drawn and the reduction of risk from biohazards. This report evaluates the current status of testing oral fluid for the presence of HIV antibodies.

BACKGROUND

HIV tests that make use of an oral fluid specimen detect HIV antibodies in oral mucosal transudate (OMT). Oral fluid is often incorrectly considered synonymous with saliva. This is an important distinction, since the concentration of antibodies in saliva (produced by the salivary glands) is significantly lower than that in OMT (crevicular fluid, or plasma leaching from the gums).

Testing for HIV using oral fluid specimens was enabled by a number of products approved by the FDA. The OraSure® HIV-1 Oral Specimen Collection Device (approved 1994) is an oral fluid specimen collection device for use with a laboratory-based immunoassay (IA) screening test, the Oral Fluid Vironostika® HIV-1 Microelisa System (approved 1994) (currently marketed as the Avioq HIV-1 Microelisa System¹ – see below). Oral fluid specimens collected using the OraSure® HIV-1 Oral Specimen Collection Device that are repeatedly reactive on the oral fluid IA can be tested with the OraSure® HIV-1 Western Blot, which was approved in 1996 as an additional, more specific test for detection of HIV-1 antibodies. A rapid HIV test for testing using oral fluid specimens, the OraQuick® ADVANCE Rapid HIV-1/2

Antibody Test, was approved in 2004 for use with oral fluid and received Clinical Laboratory Improvement Amendments (CLIA) waiver status in June 2004. In July 2012, the same device was repackaged in a test system approved as an over-the-counter home-use test as the OraQuick® In-Home HIV Test.² The test detects antibodies against both HIV-1 and HIV-2. Most recently in December 2012, Chembio Diagnostics, Inc. announced the approval of the Dual Path Platform® HIV-1/2 point-of-care test that utilizes all blood matrices and oral fluid as specimens.³

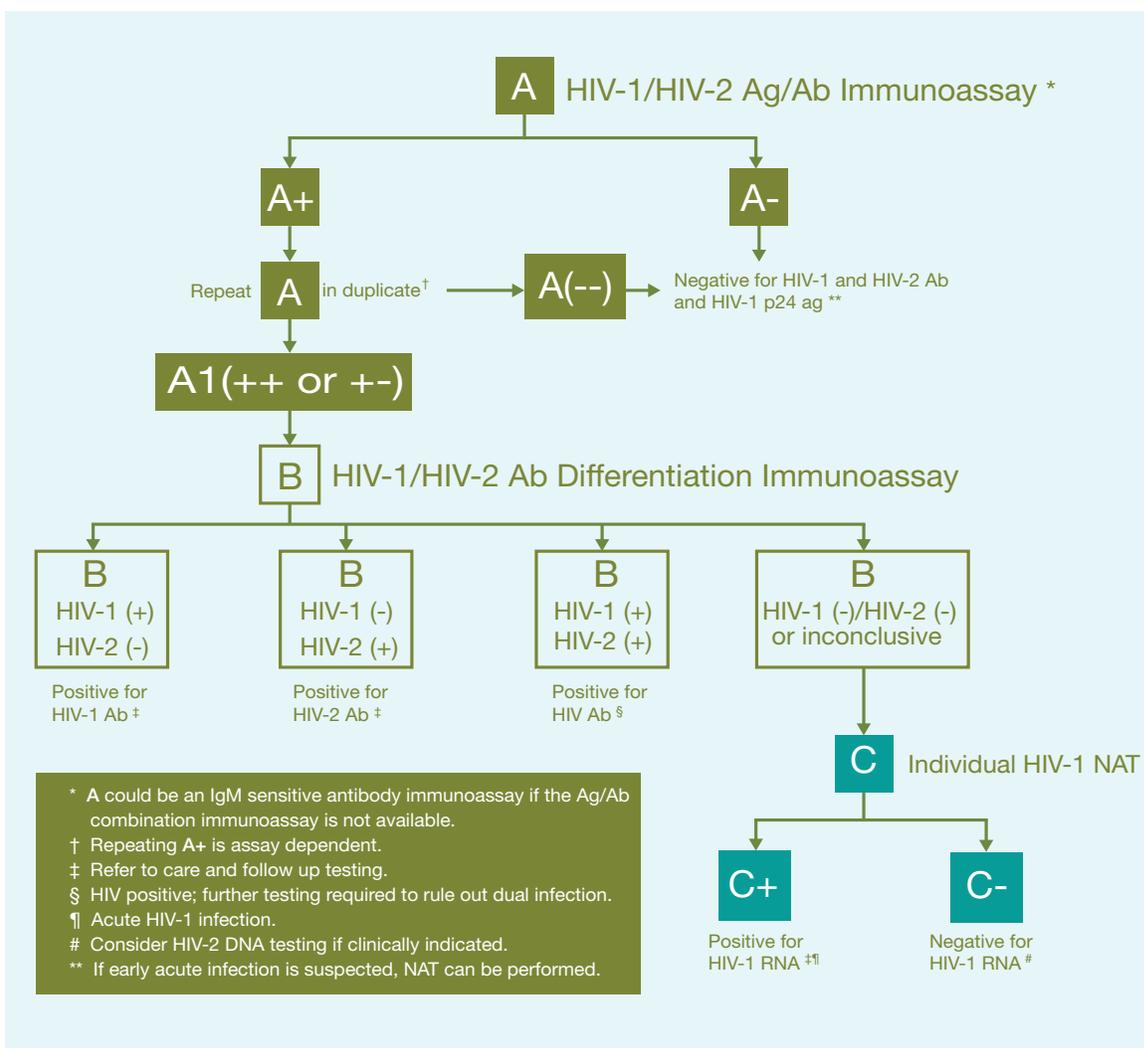
In contrast to tests used to detect HIV antibodies in oral fluid, over the past decade, IAs for diagnosis of HIV infection using blood samples have evolved considerably, resulting in assays with improved sensitivity for early infections and specificity and the ability to detect HIV subtypes. The newest IAs, 4th generation tests that detect both HIV antibodies and p24 antigen, have shortened the diagnostic period and allowed for earlier detection of HIV infection. These advanced IAs can detect HIV infection up to three weeks earlier than the traditional serum Western blot.^{4,5}

With the emergence of improved HIV diagnostic tests and the limitations of the Western blot, a new HIV diagnostic algorithm has been promulgated (Figure 1), which makes use of the HIV-1/2 Ag/Ab serum or plasma IAs, an HIV-1/HIV-2 antibody differentiation assay, and nucleic acid amplification tests (NAT), with the goal of identifying infections earlier and differentiating HIV-1 from HIV-2 infections. This algorithm has the potential to decrease costs, improve turnaround time, and reduce indeterminate results.

Tests approved for use with oral fluid do not detect HIV infections as early as other contemporary IAs that make use of a blood-based specimen,^{4,6} even when used with a serum specimen (which has an 800-1000-fold higher antibody concentration than oral fluid).⁷ Detecting early infections is especially important because of the increased likelihood of transmission during the early phase of

infection.⁸ The sensitivity standard listed in HIV test package inserts is typically the Western blot, which does not detect early infections. Tests which appear to have high sensitivity may detect established infections accurately, but may not detect early infections. It is necessary to rely on data from seroconversion panels to assess how tests perform during early infection and, currently, there is extremely limited data on oral fluid from seroconversion panels. In one recent study, oral fluid and plasma detection were compared in a Nigerian seroconverter cohort and it was found that there are significant delays in detection with oral fluid in some seroconverting individuals.⁶ In addition, because of the lower sensitivity and specificity of FDA-approved oral fluid tests⁴ relative to blood-based tests, and because there are no HIV-1/HIV-2 differentiation IAs or NAT available for use with oral fluid, oral fluid specimens are unsuitable for use with the new HIV-1/2 diagnostic algorithm.

Figure 1. HIV Diagnostic Testing Algorithm



Note: This algorithm was introduced at the 2010 HIV Diagnostics Conference⁹ and is the same as Algorithm 1 in the CLSI M53-A Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection guideline.¹⁰

CURRENT LABORATORY ISSUES

The Oral Fluid Vironostika® HIV-1 Microelisa System was withdrawn from the market in 2007. At that time, laboratories that screened for HIV-1 antibodies in oral fluid specimens had to validate a serum IA for that purpose, because no FDA-approved test was available for use with oral fluid (personal communication from the Centers for Medicare & Medicaid Services, 2007). Since the Avioq HIV-1 Microelisa system was approved by the FDA in September 2009 for use with oral fluid specimens, public health laboratories must perform oral fluid testing with the FDA-approved IA or validate use of oral fluid in a serum IA to meet CLIA requirements.

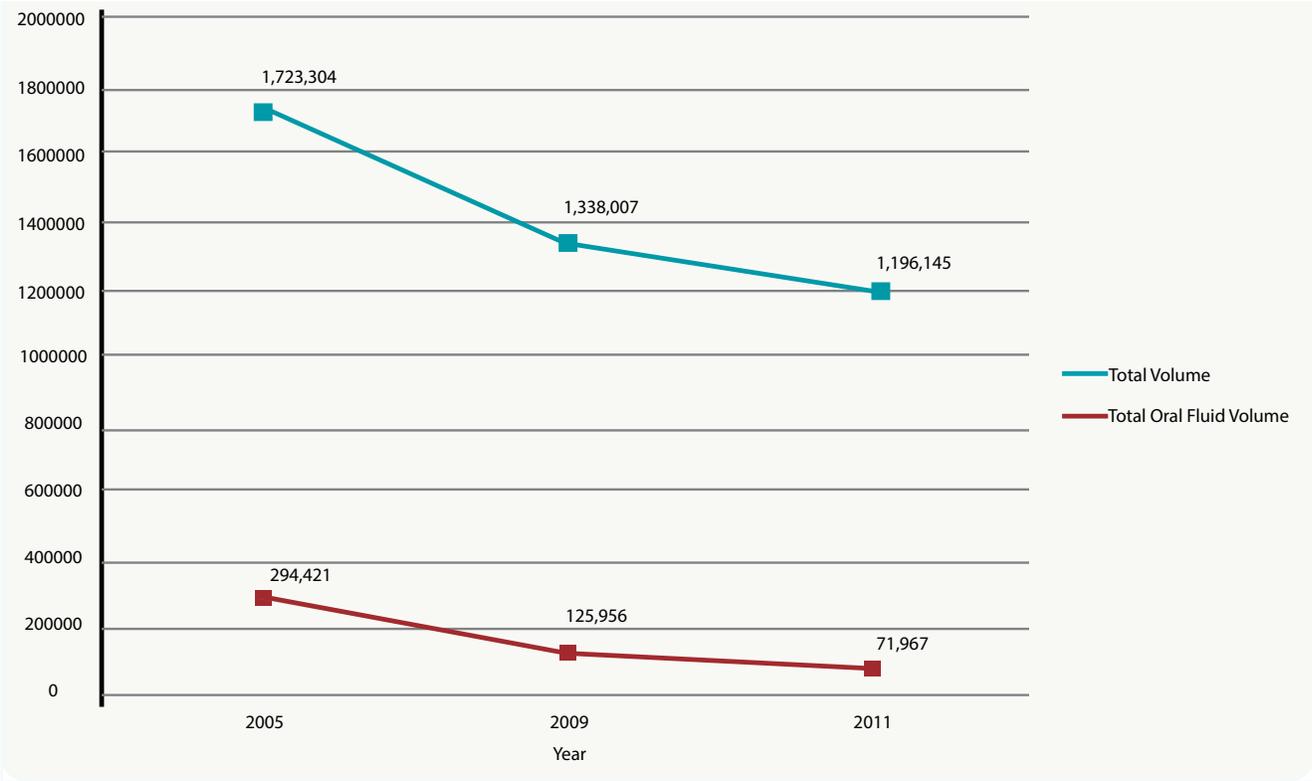
It is important to note that both sensitivity and specificity of the Avioq HIV-1 Microelisa System and Oral Fluid Vironostika® HIV-1 Microelisa System were lower when using oral fluid specimens compared with blood specimens in low and high risk subjects.¹ In addition, the Avioq HIV-1 IA does not incorporate specific antigens for HIV-2 antibody detection. In post-marketing surveillance, supplemental testing for confirmation of reactive rapid test results with serum specimens was found to yield better sensitivity than with oral fluid specimens.¹¹ In a study testing specimens from known HIV-infected persons with positive serum Western blot results, 99.4% of the oral fluid specimens tested positive using an oral fluid Western blot assay.¹²

CURRENT PROGRAM ISSUES

Oral fluid testing has been an important tool in public health HIV prevention efforts. In 2011, health departments reported conducting 3,324,689 HIV tests, of which 1,396,369 (42%) were conventional laboratory tests and 1,928,320 (58%) were rapid tests. Of the conventional tests, 98,379 (7%) were performed on oral fluid, representing 3% of all tests. Of the rapid tests, 747,227 (39%) were performed on oral fluid, representing 23% of all tests performed in 2011 (personal communication from the National Alliance of State & Territorial AIDS Directors). However, a recent survey conducted by the Association of Public Health Laboratories of its members on their HIV diagnostics testing capabilities, capacities and practices showed a decrease in oral fluid specimens tested in public health laboratories.¹³ Of the laboratories who responded to the survey, there has been a 76% drop in oral fluid specimens tested in public health laboratories since 2005 (Figure 2).

However, contemporary HIV blood-based IAs improve our ability to diagnose HIV infections earlier and facilitate earlier entry into care and treatment. Thus, public health programs and laboratories should carefully weigh the expected benefits of oral fluid testing relative to the drawbacks (summarized in Table 1), the needs of communities, and the capacities of testing providers. There might be situations in which oral fluid testing is appropriate, such as when clients would not otherwise be tested for HIV. In most circumstances, testing blood specimens yields more accurate results.¹⁴ Testing with blood specimens also enables the use of more advanced laboratory-based testing algorithms in populations in which acute and early infection are likely or when there is a need to discriminate between HIV-1 and HIV-2 infection.

Figure 2. HIV Testing Volume Trends for PHL System, 2005-2011



Note: Comparison of total and oral fluid specimens submitted for testing for 42 laboratories that completed the 2006, 2009, and 2011 APHL HIV surveys.

Table 1. HIV Prevention and Technology Aspects of Oral Fluid Testing

Benefits	Drawbacks
Decreased risk of occupational exposure to staff obtaining samples or performing testing.	Decreased sensitivity for acute and early infections, which are associated with increased potential for transmission.
Permits HIV testing in non-clinical settings where obtaining blood samples is not feasible and adherence to blood-borne pathogen requirements is not possible.	Decreased sensitivity and specificity compared to serum and plasma specimens.
Screening and supplemental assay performance acceptable for established infections.	Higher cost associated with proprietary specimen collection device cost.
Does not require a trained/certified phlebotomist to collect specimens.	Lack of automated screening.
May facilitate testing if clients would not be tested if venipuncture or finger stick sample collection were required.	Western blot is the only supplemental test available for confirmation.
	Does not incorporate specific antigens to detect HIV-2 antibody; unable to differentiate HIV-1 from HIV-2 infections.
	Increased indeterminate Western blot results in infected individuals.
	Fewer laboratories will conduct oral fluid testing.

CONCLUSION

HIV prevention programs and public health laboratories should work together to clearly identify the technologies and approaches that will most efficiently and effectively address program priorities, respond to the needs of communities, and address the capacity of a range of local providers of HIV testing services.

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