



IDAHO DEPARTMENT OF
HEALTH & WELFARE

Disease Bulletin

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Notice to Providers: new HIV testing algorithms approved

Many healthcare providers are familiar with the most common screening algorithm for HIV infection, involving an enzyme immunoassay (EIA) followed by a Western blot for confirmation of the presence of HIV antibody. Developments in HIV testing technologies over the last few years have necessitated assessment of testing algorithms that do not rely on traditional confirmatory tests such as Western blot or IFA (immunofluorescent antibody) assays. Healthcare providers are beginning to receive laboratory results for HIV tests using these new algorithms from some laboratories, which could be difficult to interpret. A new algorithm is already in use by the Idaho Bureau of Laboratories, Idaho's public health laboratory, and LabCorp, a commercial laboratory; we have not yet seen changes in other laboratories' HIV testing algorithms. The two main benefits of the new algorithms—earlier detection of acute HIV infection and determination of HIV-1 or HIV-2 subtype—are described below.

Background

CDC and the Association of Public Health Laboratories collaborated several years ago to assess the need to change HIV testing algorithms because of advancing testing technologies. The result was a report which "...describes a menu of HIV testing algorithms that have the potential to augment and provide alternatives to the algorithm currently used to diagnose HIV infection..." and detailed key data needs for advancing the algorithms evaluated.¹

This effort led to the publication of approved guidelines for six algorithms by the Clinical and Laboratories Standards Institute (CLSI) in July 2011.² Although further guidance on use of such algorithms is expected from CDC next year, the CLSI guidelines allow clinical laboratories to change their HIV diagnostic testing practices. The

change in the HIV testing algorithm does not apply to rapid tests performed in health clinics or in the field, as confirmation of HIV infection cannot be made at the point-of-care using Clinical Laboratory Improvement Amendments (CLIA)-waived tests. The guideline does not address organ or tissue donation, or screening the blood supply.

The most important new HIV testing algorithm outlines an HIV-1/HIV-2 antigen/antibody (Ag/Ab) combination immunoassay as the initial screening test, followed by HIV-1/HIV-2 Ab differentiation immunoassay, with an HIV nucleic acid amplification test (NAAT) to resolve discrepant results from the first two steps^{3,4} (Figure). This algorithm provides earlier detection of HIV infection and HIV-1 or HIV-2 subtype determination, and identification of acute HIV infection in the absence of detectable antibody. One other algorithm in the CLSI guidelines will offer similar benefits, with an HIV-1/HIV-2 Ag/Ab differentiation immunoassay when the test becomes available; the remaining four algorithms do not provide acute HIV infection detection or do not determine subtype. For more information about approved HIV diagnostic testing algorithms, see the CLSI guidelines document.

Earlier detection of newly infected persons

Enhancements to the HIV EIAs over time have resulted in better detection of IgG to HIV in 2nd generation immunoassays and the ability to detect IgM to HIV in 3rd generation immunoassays, shortening the "window period" — the time between HIV infection and the ability to detect HIV antibody. The availability of Ag/Ab combination immunoassays (sometimes referred to as 4th generation EIAs) which will give a positive result if p24 (a component of the capsid surrounding the HIV RNA strand) is detected or if HIV antibody



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is detected, shorten the window period even more.

The difference is remarkable. Estimated average time between infection and detection is now 2–3 weeks with newer Ag/Ab combination immunoassays or as little as 6–12 days for HIV NAATs, compared with the 5–6 week average window period using Western blot for confirmation.⁵

Additionally, these tests can assist in diagnosing acute HIV infection when antigen or HIV nucleic acid is detected, but antibody is not. Acute HIV infection precludes the use of Western blot for confirmation because the ability to detect antigen typically occurs before the ability to detect antibody. Individuals with acute HIV infection have been shown to have higher HIV viral load and consequently an increased risk of transmitting HIV to others if exposed.⁶ Counseling about HIV risk reduction, partner notification, and immediate referral and initiation of HIV medical care are important to preventing transmission during acute HIV infection.

Distinguishing HIV-1 from HIV-2 infection

The ability to distinguish both acute HIV and HIV-1 or HIV-2 infection provides an opportunity for providers to discuss exposures and treatment with patients at initial diagnosis. HIV-2 infection has been largely confined to persons in or from West Africa. Although both HIV-1 and HIV-2 share the same routes of transmission and both can cause AIDS, HIV-2 infection is less likely to cause AIDS and clinical management of HIV-2 is different because of differences in intrinsic and acquired resistance in HIV-2. For example, HIV-2 appears intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to enfuvirtide. HIV-2 also differs in virologic response to common treatment regimens.⁷

In summary, clinical and laboratory use of new diagnostic algorithms for HIV testing can identify acute HIV infection earlier and determine HIV type, allowing clinicians to provide

earlier diagnosis and counseling of acutely infected patients, and referral for type-specific HIV medical care.

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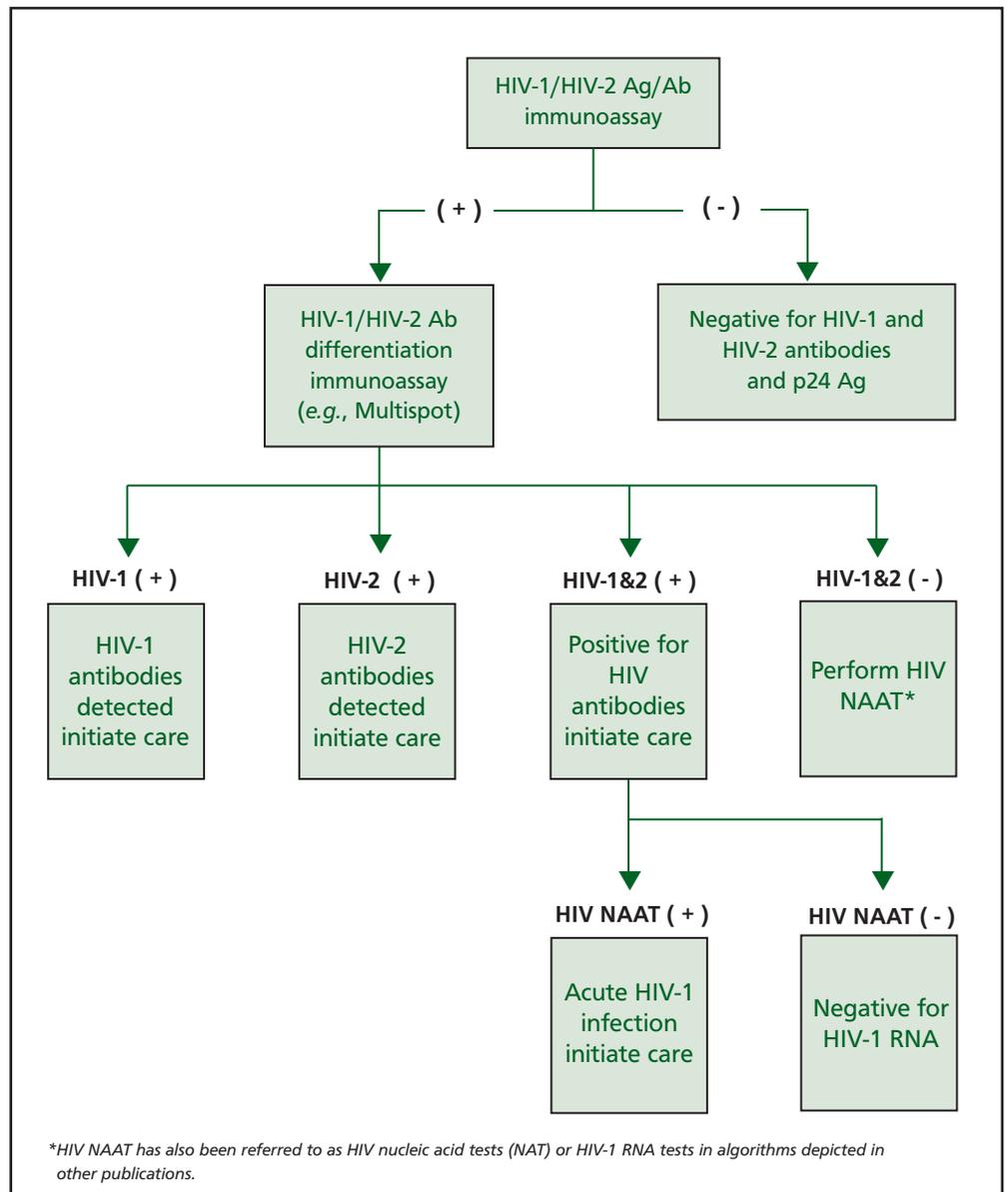
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Figure. Example of a new diagnostic algorithm for HIV diagnosis (now in use at the Idaho Bureau of Laboratories)



*HIV NAAT has also been referred to as HIV nucleic acid tests (NAT) or HIV-1 RNA tests in algorithms depicted in other publications.

Adapted from: Clinical and Laboratory Standards Institute. Criteria for laboratory testing and diagnosis of human immunodeficiency virus infection; approved guideline. CSLI document M53-A. Wayne, PA: CSLI. 2011 and Branson BM. Establishing the diagnosis of HIV infection: new tests and a new algorithm for the United States. *J Clin Virol* 52S (2011) S3-S4.



Elevated MICs Relegate Cefixime to Alternative Gonorrhea Treatment

CDC has updated its treatment guidelines for gonococcal infection in response to increasing proportions of gonococcal isolates with elevated minimum inhibitory concentrations (MICs) to cefixime in the United States during 2006–2011. CDC no longer recommends cefixime at any dose as a first-line regimen for treatment of gonococcal infections.¹ If cefixime or other alternative regimens are used, CDC recommends performing a test-of-cure at the site of infection at one week post-treatment (Figure). Although no documented treatment failures have been reported in the United States, an increasing number of cefixime treatment failures have been reported from other countries.¹ Treatment recommendations were updated in anticipation of declining effectiveness of cefixime and aim to slow the emergence of drug resistance to ceftriaxone.

Ceftriaxone (250 mg IM in a single dose) is the only cephalosporin recommended for inclusion in dual-therapy regimen for gonococcal infection (Figure). Cefixime can be used in an alternative regimen when ceftriaxone is not available; azithromycin can be used as an alternative for patients having a severe allergy to cephalosporins. Neither alternative is recommended for gonococcal infections of the pharynx. Culture for test-of-cure is preferred, but nucleic acid-based methods can be used if culture is not available. There is concern about using nucleic acid amplification tests (NAATs) as a test-of-cure because the test can detect residual

gonococcal nucleic acid even if no viable gonococcal bacteria are present. CDC is confident the NAAT for *Neisseria gonorrhoeae* will be negative one week after treatment unless there are intervening exposures or treatment failure. However, due to the body's slower clearance of chlamydia nucleic acid, a one week test-of-cure using a NAAT that tests for both chlamydia and gonorrhea will likely result in a false positive chlamydia result. The patient should not be retreated for chlamydia, but should be instructed to return for a chlamydia rescreen in 3–4 months per current recommendations.² Patients with persistent or recurrent

symptoms of gonorrhea shortly after treatment with the recommended combination therapy and without intervening exposures should also have a new sample collected for testing by culture; isolates should be submitted for antimicrobial susceptibility testing.

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Figure. Updated gonorrhea treatment guidelines

Recommended regimen (uncomplicated gonococcal infections of the cervix, urethra, rectum, and pharynx* ¹)	Alternative regimen 1 (uncomplicated gonococcal infections of the cervix, urethra, and rectum*)	Alternative regimen 2 (uncomplicated gonococcal infections of the cervix, urethra, and rectum*) (if the patient is severely cephalosporin-allergic)
Ceftriaxone 250 mg IM in a single dose PLUS Azithromycin 1 g orally in a single dose [‡] OR Doxycycline 100 mg orally twice daily for 7 days [§]	Cefixime 400 mg orally in a single dose PLUS Azithromycin 1 g orally in a single dose [‡] OR Doxycycline 100 mg orally twice daily for 7 days [§] PLUS Test-of-cure in 1 week	Azithromycin 2g orally in a single dose PLUS Test-of-cure in 1 week
<p>*Dual antibiotic treatment should be given regardless of any chlamydia test result. ¹Dual treatment with ceftriaxone is the only recommended treatment for pharyngeal infection. [‡]Azithromycin is preferred over doxycycline for dual antibiotic treatment due to high rates of co-existing tetracycline resistance among gonococcal isolates with elevated cefixime minimum inhibitory concentrations (MICs)³. [§]Pregnant women should not be treated with quinolones or tetracyclines.</p>		

First Reported Idaho Human Metapneumovirus Outbreak

On February 8, 2012, Southwest District Health was notified of a cluster of pneumonia among residents of a long-term care facility (LTCF). Public health district epidemiologists conducted a public health investigation, with assistance from facility staff and the Idaho Division of Public Health, to determine the extent and etiology of the outbreak. A case was defined as new cough onset in a facility resident during January 31–February 29. Patient medical records, including prior laboratory results, were reviewed. Cases were identified

in 29 (36%) of 80 residents; 2 (40%) of 5 hospitalized residents died. Eleven of approximately 100 facility staff also reported respiratory illness during this time, but no laboratory testing was done.

Illness among residents was characterized mainly by lower respiratory tract symptoms; 10 had physician-diagnosed pneumonia. Median duration of illness among 26 residents was 4.5 days (range: 1–4.5 days). Eighteen (62%) of 29 cases in residents were treated empirically with antibiotics. Physician-ordered diagnostic tests,

including rapid influenza antigen, rapid respiratory syncytial virus (RSV), *Legionella* urinary antigen, *Streptococcus pneumoniae* urinary antigen, and bacterial cultures on sputum and blood collected up to seven days after illness onset were all negative; however, in two of five patients, blood was collected for bacterial culture four days after antibiotic therapy was initiated.

Because both influenza and pneumococcal vaccines might reduce risk of respiratory infection or complications, we collected information about influenza and

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pneumococcal vaccinations for ill residents from patient medical records. Although long-stay resident influenza and pneumococcal vaccination coverage >90% was reported by the facility to the Centers for Medicaid and Medicare Services, documentation in patient charts was often difficult to find and residents might have been vaccinated elsewhere.

Nasopharyngeal (NP) specimens from nine non-hospitalized resident cases were collected within four days of illness onset for respiratory virus testing at the Idaho Bureau of Laboratories (IBL). Rhinovirus/enterovirus was detected in one NP specimen. Human metapneumovirus (hMPV) was detected by qualitative nucleic acid multiplex assay or reverse transcription polymerase chain reaction (PCR) in 5 (56%) of 9 NP specimens and in a bronchoalveolar lavage specimen from one patient who died. No other viruses were detected by viral culture, qualitative nucleic acid multiplex assay, or PCR.

First detected in 2001 in the Netherlands¹, hMPV is a paramyxovirus closely related to RSV. Clinical manifestations of disease range from mild upper

respiratory symptoms to bronchiolitis and pneumonia and are indistinguishable from those caused by RSV. Infants and young children are most at risk for severe disease; advanced age and underlying cardiopulmonary disease are risk factors for severe disease among adults. Serologic evidence suggests that most people have been infected by five years of age, so infection in older children and adults likely represents reinfection. Although hMPV has been detected in communities and causes outbreaks in LTCFs throughout the year, peak activity for hMPV is generally in the late winter and spring in temperate climates.² Outbreaks caused by hMPV reported elsewhere from community hospitals, and pediatric and adult LTCFs typically resulted in attack proportions of 18%–35% and case fatality proportions of 7–12%.^{3,4} No specific treatment other than supportive care is recommended for hMPV.

Viral testing by IBL in this outbreak of respiratory illness at an LTCF enabled public health to identify the first outbreak caused by hMPV reported in Idaho. Prompt reporting of clusters of influenza-like illness (ILI) in congregate settings to your local public health district can help facilitate

identification of outbreak etiology and implementation of appropriate infection control measures, treatment, or chemoprophylaxis. To assist in tracking vaccination status among LTCF residents, LTCFs could consider using Idaho's Immunization Reminder Information System (IRIS) to record up-to-date immunization information that would be available to all of a resident's medical providers who use IRIS.

General guidance for infection control in the long-term care setting can be found at www.cdc.gov/HAI/settings/ltc_settings.html. Additional guidance related to influenza and ILI outbreak management can be found at www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm.

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