Early days, early detection, early treatment for HIV

May 2016—*In 1985, when the first test for HIV—then called human T-cell lymphotropic virus type III—became available, it was approved for screening blood products but not for diagnostic use. A diagnostic test for antibody to HIV-1 was soon approved. Over the subsequent 30-plus years, further iterations of HIV screening tests have been made, with increasing sensitivity and specificity and a shorter window to detection. Fifth-generation tests are now under review. CAP TODAY asked Eileen Burd, PhD, D(ABMM), to discuss the evolution of HIV diagnostics and algorithms for using them and to give a qualitative evaluation of the pending fifth-generation assay.*

Dr. Burd is director of clinical microbiology, Emory University Hospital, and associate professor, Emory University School of Medicine, Atlanta.

Dr. Eileen Burd of Emory says she finds it alarming that the rate of new infections in the United States has been holding steady for the past decade or so. “There are about 40,000 to 50,000 new HIV infections diagnosed each year and that is just too many.”

How have these assays and algorithms worked together with effective antiretroviral therapy to contain the HIV epidemic? What has been accomplished?

HIV has reached every corner of the globe and this virus continues to have a very serious impact on mortality rates and the economy in many developing countries. The majority of industrialized countries have been able to contain the epidemic because they have access to effective diagnostic tests and life-sustaining medications and have built programs that focus on preventive measures. A lot has been accomplished and transmission rates have declined dramatically, especially among injection drug users and mother-to-child.

With HIV largely under control, at least in developed countries, is there still a need for vigilance in detecting cases and detecting them ever earlier?

Even though there has been progress in controlling transmission, I find it alarming that the rate of new infections in the United States has not fallen further and has been holding steady for the past decade or so. There are about 40,000 to 50,000 new HIV infections diagnosed each year and that is just too many. There is definitely a need for vigilance in detecting new cases. About 12 percent of HIV-infected people in the United States do not know they

are infected and may unknowingly transmit the virus. We know that early treatment allows the infection to be managed better and the resultant reduction in viral load helps prevent transmission to others. In order for there to be early treatment, there has to be early detection.

What are the newest assays and algorithms?

Many laboratories are now using the fourth-generation combination immunoassays that detect both IgG and IgM antibodies against HIV-1 and HIV-2 as well as HIV-1 p24 antigen as the initial test in the diagnostic algorithm. Updated recommendations published by the CDC a few years ago called for supplemental testing of positive results from the initial test using an immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies, rather than using HIV-1 Western blot. When there are discrepant results between a positive initial combination immunoassay and a negative or indeterminate antibody differentiation test, the recommendations call for resolution using a nucleic acid amplification test.

The very newest tests are fifth-generation assays that detect HIV-1 and -2 antibodies, HIV-1 p24 antigen, and specifically identify whether it is the HIV-1 or HIV-2 component that is positive. Also, the antigen and antibody results are reported individually and can help distinguish between acute and established infection.

We will have an article on the performance of these new assays in an upcoming issue. But in general, how do they perform and how do they improve on past efforts?

The new assays perform very well. The biggest gains are in an improved ability to diagnose acute HIV-1 infections and also more accurately detect HIV-2 infections. Another gain is that the antibody differentiation test detects antibodies earlier and there are fewer indeterminate results compared with Western blot.

Does this improvement come at a higher financial price?

I don’t have specific numbers but my sense of it is that the improved tests and the new algorithm overall save the health care system money. Earlier diagnosis of cases allows for early access to treatment, which translates into prevention of opportunistic co-infections and progression to AIDS. Increased specificity of the tests in the algorithm prevents the need for repeat or additional testing.

The automation that comes with some of these assays can be expensive, but the immunoassay platforms have a broad testing menu and operate in a continuous-loading, random-access mode that allows for very efficient workflow. Western blot was an expensive test. The antibody differentiation test is somewhat less expensive, but low local Medicare reimbursement is a concern for us.

What assay and algorithm are you now using in your laboratory? Over the years, how difficult have you found it, from a laboratory director standpoint and from the view of technologists, to switch to new assays and algorithms?

We are using the updated algorithm recommended by the CDC. The Architect HIV Ag/Ab Combo assay (Abbott Diagnostics) is the initial test in our algorithm. Specimens with repeatedly reactive results are further tested with the Geenius HIV 1/2 Supplemental Assay (Bio-Rad Laboratories). In the rare case of discrepant results, our molecular diagnostics laboratory performs HIV-1 nucleic acid amplification testing, but because of special specimen handling needs, it is not an automatic reflex test and requires the clinician to order the test separately. We also use the Alere Determine HIV-1/2 Ag/Ab Combo test (Alere) at all of our hospitals as the initial rapid test available 24/7 for cases of needlestick injury or mucous membrane exposure and for pregnant women who enter the health care system with imminent delivery and lack of prenatal care.

Bringing new assays into a clinical laboratory always has some associated difficulties. From a laboratory director

standpoint, clinical justification was not difficult in this case because of the available data that show much improved sensitivity and specificity. Provider acceptance was also easy because of the data, and our infectious disease physicians were already aware of the newly recommended algorithm. We were able to bring in the HIV Ag/Ab Combo assay without budgetary constraints because we were already bringing the Architect instrument into the laboratory to improve workflow for a number of other tests. Our technologists were actually excited about the change and, after a short learning curve and fine-tuning the workflow, readily embraced the new technology. We had been sending Western blot tests to a reference laboratory and didn't change to the antibody differentiation test until recently. Bringing the test in-house did not really add at all to the workflow since it takes about as much time to perform the test as it did to get the repeatedly reactive samples to the referrals lab for shipment to the reference lab. A big advantage is that turnaround time is faster than when Western blot testing was part of the algorithm.

Do you plan to switch to a new assay and algorithm in the near future?

There are obvious advantages to the fifth-generation assay with much of the algorithm built into one test. Since there is currently only one manufacturer and we do not have the associated instrumentation, we will not be able to make a change at this point.

To take advantage of the newer assays' ability to turn positive earlier in infection, people need to come for testing as soon after a suspected exposure as possible. What efforts have been made to achieve this objective? How successful have these efforts been?

I am sure that I am not aware of everything that is being done to facilitate testing but I am aware that there are places where testing is free and confidential as well as some tests that the FDA has approved for use at home. I hope that people who suspect they could have been exposed to HIV would seek medical attention as soon as possible, not necessarily for testing but for prophylactic treatment even before antibody/antigen tests would be positive. I don't think the general population is aware that the newer tests are more sensitive and shorten the "window period."

Much HIV testing is done in public health laboratories. What is the role of the hospital laboratory in controlling the HIV epidemic?

Some hospital laboratories, especially in larger cities with higher prevalence, are beginning to offer 24/7 stat availability of either rapid manual or random-access, fully automated HIV tests to serve emergency departments and allow more people to have access to testing. The ELISA test is designed to be highly sensitive, that is, to miss as few HIV infections as possible. Approaches include targeted screening of at-risk individuals or non-targeted screening offered to all individuals, even those who are not at high risk. There are pros and cons to each approach. The downside to non-targeted screening is that the initial tests are designed to be highly sensitive and may produce a small number of false-positive results in a low-prevalence population due to the presence of other antibodies in an individual that the test mistakenly detects. The availability of post-test counseling is critical to the operation of these programs, especially since results of supplemental testing for initially positive specimens will most often not be available at the time the patient is being seen.