

Emergency department tests HIV screening strategy

Anne Paxton

July 2022—Thanks to more than two years' experience with SARS-CoV-2, perhaps at no point in U.S. history has the general public been as aware of antigen and PCR testing, and the difference between them, as it is now. SARS-CoV-2 has also raised the profile of emergency departments as critical access points to get patients with infectious diseases diagnosed and in treatment. Yet much remains to be learned about exactly how screening using PCR testing for infectious diseases can improve public health and what role the ED should play in ordering that testing.

Clinical research on nontargeted screening for HIV and HCV in the ED suggests that real-time PCR testing, ordered earlier in the standard screening algorithm for certain patients, can help EDs quickly identify people with those diseases and link them to care.

From May 2016 to February 2022, the ED at Tampa General Hospital, where Jason Wilson, MD, MA, is director of the ED's clinical decision unit, ran an HIV antigen/antibody test on 99,691 ED patients, of which 1,725 were reactive. That was followed by HIV-1/2 Ab confirmatory testing and, if the first antigen/antibody test was reactive, by an HIV RNA PCR viral load test. He and his team deviate from the currently recommended algorithm by ordering HIV RNA PCR on anyone who is reactive on the first screen, regardless of what the antibody test reveals. "The patient is in front of us, we can get blood if we need it, but also we know 13 percent of our [reactive] patients are equivocal, and of those, one-third are acute positives who have negative or undetectable antibody," Dr. Wilson explained at a conference this spring on "Advancing HIV, STI, and Viral Hepatitis Testing."

While the clinical encounter in the ED lasts on average four to six hours, the HIV RNA PCR test has a 72-hour turnaround time, which sometimes means lost opportunity for care. "We've really begun to recognize that there's a difference between screening for HIV or hepatitis C and testing for HIV or hepatitis C," said Dr. Wilson, associate professor of internal medicine at the University of South Florida Morsani College of Medicine.



Dr. Wilson

In a recent interview and in his presentation at the conference, sponsored by the CDC, Association of Public Health Laboratories, American Sexual Health Association, and American Sexually Transmitted Diseases Association, Dr. Wilson related his hospital's experience with having the ED play a more effective role in screening for HIV and HCV and getting infected patients into treatment. He and his colleagues have found that an alternative testing strategy, using real-time PCR testing and obtaining results in 91 minutes rather than 72 hours, could mean greater likelihood of success in meeting that goal.

The CDC in 2006 revised its algorithm for HIV screening to a public health model with a multistep approach. "That approach works just fine in the public health clinic or a public event where you're seeing lots of people and trying to screen as many as possible for a disease state," Dr. Wilson says. But there is a growing view that emergency departments should be doing public health HIV screening on their patients as well.

The CDC in 2007 funded a small group of 10 emergency departments to implement its algorithm in the ED setting. But as Dr. Wilson was trying to implement the 2006 guidelines in the ED at Tampa General Hospital, there were a few obstacles. "One was that we still had laws in Florida around written consent and pre- and post-test counseling that made it difficult to do this type of work in the ER."

The main problem was Florida's opt-in requirement for obtaining consent for HIV testing. When the ED uses a consent form requiring patients to opt in to HIV testing—rather than including HIV testing among the general medical consent tests unless patients opt out—it greatly affects the number of HIV screening tests performed, Dr. Wilson notes. "I would have had to go into the room with a consent form and say to the patient, 'I would like to test you for HIV. Here are the risks. Here are the benefits. Can you sign this form?'"

"It's not that we couldn't do that. But it creates a stigma, potentially, and it's time-consuming. It carves out HIV as different from testing your white blood cell count or testing your BUN and creatinine."

In Florida, opt-in was the law until 2015 when the state passed a statute dropping the requirement for separate written consent. After that, "We were able to move to notifying patients of an opt-out test and that's what we do with the signs that are in every patient room and in other areas that are publicly accessible in the emergency department."

Moving to opt-out testing was a game changer, Dr. Wilson says. "It allowed us to test for HIV as a nontargeted screening practice. We could start putting that strategy into our routine workflow."

"We went from doing zero HIV tests in the ER for screening to a handful—five or six a week—to now more than 1,100 HIV tests per month consistently since 2016." The ED conducts hepatitis C screening during the ED encounter along with HIV screening.

The ED integrated clinical decision support into its screening processes through its Epic EHR. "The way we got to nontargeted high-volume screening is we took the CDC algorithm and built it into the computer. So as that information is gathered during the patient's encounter and entered into Epic, once the patient meets the screening criteria and has not opted out, a test order will pop up for the provider and say, 'Please order the test.'"

Over time, the decision support has become more nuanced and more detailed, Dr. Wilson says. "For example, for the patient who has a nonconfirmatory antibody test for HIV, the viral load test order will automatically pop up as well. For a patient we identify as having IV drug use, we will want to order a hepatitis C RNA test because we have a number of patients who may have just acquired HCV and have no HCV antibodies but they do have detectable, quantifiable RNA, so we move right to RNA testing for them."

Within the first couple of weeks of broad high-volume HIV screening, however, ED clinicians encountered something surprising. "We had had a couple of patient scenarios where the HIV antigen/antibody test was reactive, but then in one of those patients early on there was no HIV virus in the RNA and in the other one there was. So we realized we're dealing here with clinically equivocal results during the clinical encounter."

"They can go two ways: Either the person is an acute seroconverter and it's important we intervene right now, or the person doesn't have HIV but has a potentially transient p24 reactivity." Over the past three or four years, Dr. Wilson says, "we thought about that population of people with reactive HIV antigen/antibody tests. Doing 1,100 tests a month, we have 1.73 percent seropositivity and 13.4 percent of those are equivocal." It is one in every eight patients with a reactive HIV Ag/Ab, he says. "These numbers add up pretty quickly."

Equivocal results can present a clinical dilemma for emergency medicine providers who see a patient for generally only a few hours. "Some people get admitted but we're not as worried about the people who are admitted because they're going to be sticking around," he says. For those not admitted, "we may have lost an opportunity if we don't know the true HIV status of that patient during the encounter." But the other 68 percent of patients—the majority—will be p24 antigen positive for some other reason. If I were to result those patients during the ED encounter, I would likely give them undue grief and worry and my colleagues may not be willing to do the testing."

He described a recent patient with a reactive HIV antigen/antibody result but a history and lack of risk factors that suggested she was not seropositive. "I would tell her we're at a coin toss as to whether you have HIV or not; we'll run the PCR and I'll get you the result in another two days. But we can easily lose that patient into the transition space as to whether or not she was acutely seroconverted. So it's a big game changer to know what the specific

true diagnosis clinically is for that patient.” For positive patients, Dr. Wilson says, “we have a very good linkage to treatment rate.” But “we worry about these equivocals because we’re not telling them much of anything” before the typical patient encounter is over.

For the past year, on an experimental basis “in the background,” Dr. Wilson’s ED started ordering a GeneXpert real-time RNA PCR test for HIV as soon as a reactive antigen/antibody test result is known. Then the research team measured concordance between the GeneXpert qualitative HIV assay (not FDA approved) and the standard-of-care Aptima HIV-1 Quant assay on the Panther; calculated and compared turnaround time on the GeneXpert to the standard of care; collected GeneXpert actual run time metrics; reviewed ED length of stay and laboratory TAT data for the standard-of-care test; and calculated differences between GeneXpert and the standard of care.

“So we took 20 samples of HIV and the research team found that the Cepheid GeneXpert HIV PCR test was concordant with the standard of care 100 percent of the time and the test decreased TAT by more than 2,000 minutes,” Dr. Wilson says, noting two equivocal samples with known standard-of-care HIV RNA results were included. The researchers found that the GeneXpert HIV PCR turnaround time and overall clinical encounter throughput time of about 465 minutes is reasonable for an ED encounter given that only 1.73 percent of patients in their ED have a reactive Ag/Ab screening result.

Based on concordance and throughput, they recommended that formal clinical trials considering real-time HIV RNA testing in the ED be completed, and depending on trial results, that alternative and/or enhanced algorithms be created for ED HIV screening and testing.

Dr. Wilson and colleagues chose to include HCV screening as well as HIV screening in their experiment because of the similarities between the two as public health threats.

“HCV is our other significant infectious disease epidemic and there are overlapping population characteristics around people who are at risk for HIV and people who are at risk for hepatitis C,” he says. When he started studying the role of the ED in this type of screening, there were not a lot of treatment options for HCV, unlike HIV. “Now you essentially have the direct-acting antivirals that are the equivalent of antiretroviral therapy for HCV and you’ll only have to take it for eight to 12 weeks.”

“That means that clinicians faced with a positive test can do something for the patient and decrease transmission rapidly. If we’re going to get out of these two disease states, the issues around linkage and testing and getting people into treatment are very similar,” he says.

It is still rare, however, to find many other EDs that are doing nontargeted screening, Dr. Wilson says. He estimates that only about 100 hospital emergency departments, or fewer than one percent of EDs in the country, are capable of doing high-volume HIV screening.

“Most of us are part of a group within the Society for Academic Emergency Medicine called the Emergency Medicine Transmissible Infectious Diseases and Epidemics Consortium,” a network that can rapidly and efficiently mobilize emergency departments for early detection and response to transmissible infectious disease threats. “That group is probably the only one even thinking about this or doing any HIV screening.” Only a subset of that group with the necessary testing equipment would be able to do real-time testing, Dr. Wilson says. “Right now, I think our colleagues are waiting for an ER that has been doing this for a while to disseminate how you can do it and not get confusion around results.” Even in an ED like his, “We’re still constantly process-improving all of our steps: When should we retest false-positives? When should we have the RNA test? Should we do the RNA right now for high-risk patients?”

There should probably be a screening algorithm separate from the testing algorithm for an acute encounter, Dr. Wilson says, “and right now we don’t have a differentiation of those two. I would feel more comfortable if we eventually would see a fever or a patient you’re concerned is high-risk symptomatic, and then go right to PCR-based testing. On the other hand, we’re starting to see enough variables where a patient might be excluded from that pathway. Pregnancy, lupus, prior vaccine trial for HIV—those should probably all exclude the patients from

even going through an HIV antigen/antibody reactivity test.”

More real-time nucleic acid-based testing should be performed in EDs, he says. “And as we get confidence with the test results, we’ll get to see clinicians taking action based on those test results, which might mean giving antiretroviral therapy, seeing higher linkage rates, or seeing better CD4 and viral load testing downstream. Then eventually we’ll see clear differentiation of the algorithms for screening in the acute environment and screening in the public health environment,” because it may not be necessary or cost-effective to move to PCR-based testing as the only modality available. “If I’m at a health fair and at low risk, a cheek swab may be perfectly appropriate. So we may just need to see carve-outs of those algorithms, and that will probably require some clinical trial work to get to each of those carve-outs.”

Right now, he says, “It’s hard for me to advocate to emergency medicine that we should be doing more testing, because I’m going to put a lot of people in a difficult situation given the current technology with 13 percent equivocal. I think most ERs can accomplish linkage to care, even a small community ER. But there are still more questions we need to answer to get emergency medicine to broadly buy into this or broadly make policy recommendations around not only what the academic ERs are doing but what the community ERs are going to do as well.”

For Dr. Wilson, a key message from this screening research is, “We took that CDC algorithm and put it to an acute ED space and learned that it doesn’t quite fit, and that in reality we’re probably a little behind on technology. We probably need to get the technology to match the acute encounter, and that technology is likely real-time nucleic acid-based technology.”

“We’re not there yet,” he adds. “But we’re getting closer based on the fact that the technology at least is existing and some of the companies out there are working on it too.”

Much progress in increasing the ED’s role in screening has been made to date, he says. When Tampa General Hospital’s ED started conducting HIV screening, “Just by doing the antigen test we essentially doubled the screening that was happening in the entire county. We are now doing 1,100 tests a month and that’s a lot of HIV testing. So we’re going to change the prevalence of the disease just because we’re picking up more of it by doing the test.”

Since one in eight people with HIV don’t know they have HIV (representing half of all new transmission), in places that are not doing testing like this, “the disease prevalence doesn’t change. Those are people you can’t get into treatment and you can’t change your transmission rate either. They are people who are ‘lost to care.’ We’ve seen big success with ERs doing nontargeted high-volume screening to identify people and relink people to care who have been lost to care.”

Many states and territories of the U.S. still have much higher than expected HIV rates, he says. “We know from the historical literature that people who know their status and people who start ART early are more likely to retain care and stay in care. Attempts to do this in the ED have been fraught and mixed with testing scenarios that have lots of steps but are not clear and streamlined. It makes it difficult to do this in the ED setting.”

“Where we would love to get to eventually is a place where we know we’ve got the linkage rates, we know the status, and we’ve started medication and can do it confidently.” That’s an achievable goal, in his view, and one to which the ED is well suited. In fact, Dr. Wilson says, COVID-19 reinforced that “we’re not going to solve the HIV crisis—or any highly transmissible infectious disease—without the emergency departments on the front lines.”

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