



Getting testy:

Assays developed to predict antipsychotic drug response

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Nurses challenge the idea that only doctors can lead trials

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Point-of-care tests poised to alter course of HIV treatment

Testing for HIV does not simply end with the diagnosis that the virus is present in a patient; caregivers also need to track the disease's progress to adjust ongoing treatment. Yet tests for monitoring HIV infection require sophisticated instruments, well-trained clinicians and expensive lab ware. All those are in short supply on HIV's front line in places such as rural sub-Saharan Africa. "It's a problem not just of cost," explains hematologist Helen Lee of the University of Cambridge in the UK. "It's a problem of having access." In the last year, stripped-down standalone tests have appeared on the market, offering rural patients a cheaper, faster count of their CD4 immune cells. And in the coming months, a class of tests that measure viral load should enter routine point-of-care use, too, offering caregivers a choice of simple tools for measuring HIV infections.

At present, monitoring the virus in patients presents a logistical challenge, even in wealthy areas. In such places, an HIV-positive patient's blood may be drawn every six months by a trained nurse and stored in \$40 worth of reagents, refrigerated and sent to a laboratory where a skilled technician uses a laser-equipped machine costing around \$100,000 to count the CD4 immune cells in the patient's blood. If the count drops below certain thresholds, such as 350 cells per milliliter, implying damage from HIV, the patient's caregivers may initiate antiretroviral therapy or change to a new therapy if an existing one is no longer working. If treatment happens early enough, it can fend off the HIV infection before the patient's immune system is weak enough to allow an opportunistic infection such as tuberculosis. Follow-up tests can help caregivers decide whether the treatment is working and whether to switch to backup drugs.

In resource-poor settings, testing and monitoring the infection might involve a trip to a clinic many miles away. By the time an answer comes back from a far-off laboratory—sometimes as much as a month later—the patient may also be harder to track down and his infection tougher to fight.

The turnaround of results could shorten to hours, rather than weeks, thanks to recent arrivals on the point-of-care market, such as PointCare NOW, the Pima CD4 Analyser



Count it in: The Pima CD4 Analyser.

and the CyFlow™ CD4 miniPOC, which count a patient's CD4 immune system cells in a body fluid such as saliva or blood. These simple CD4 counters could improve survival rates and reduce infection in places with little infrastructure, says immunologist Steven Reid of Imperial College London, who managed a competition to develop a new CD4 point-of-care test. Zyomyx, a Fremont, California-based diagnostics company, won that competition and a round of development funding in 2008 and plans clinical trials of its CD4 test later this year.

Another type of test limited until now to laboratories may soon reach point of care, too. Viral-load tests detect and amplify the nucleic acid present in HIV and give a direct measure of the infection's extent. "CD4 counts drop more slowly than viral load rises," Reid explains, so some researchers favor viral-load testing to monitor the illness. Earlier this year, Lee, through

her spin-off company Diagnostics for the Real World in Sunnyvale, California, conducted a trial in rural Malawi testing a point-of-care HIV test called simple amplification-based assay, or SAMBA. Consistent with what Lee's team previously found with clinical samples in the lab (*J. Infect. Dis.* **201**, S65–S72, 2010), the field trial found a 96–98% agreement between the SAMBA test and a standard laboratory assay, prompting the Swiss-based global nonprofit Doctors Without Borders to plan routine implementation of SAMBA in Malawi by the end of this year. Three other viral-load point-of-care tests are already in advanced trials, and a recent report from UNITAID, a UN body, identifies eight more in the pipeline. This type of testing is currently used for monitoring antiretroviral treatment effectiveness, but it might also one day replace CD4 assays for deciding when to begin administering these drugs in the first place, argues Gottfried Hirschall, director of the World Health Organization's HIV/AIDS Department in Geneva.

For now, viral load testing technology is more expensive than CD4 tests. Yet Hirschall, a speaker at the 19th International AIDS Conference in Washington, DC, in July, is optimistic that competition among manufacturers will lower soon drive down those prices. CD4 will serve as a stepping-stone for POC viral load tests, he says: "The new [CD4] tests are competing with the big machines," he says, "ultimately this will be to the benefit of the patients."

Lucas Laursen

Select point-of-care HIV assays in the pipeline

Assay name	Company	Target measured
Daktari™ CD4 Counter	Daktari Diagnostics	CD4 cells
MBio™ Diagnostics CD4 System	MBio Diagnostics	CD4 cells
CD4 Point of Care Technology	BD Biosciences	CD4 cells
Zyomyx CD4 Test	Zyomyx	CD4 cells
Semi-quantitative CD4 Test	Burnet Institute	CD4 cells
NAT System	Alere	Viral load
Liat™ Analyser	IQuum	Viral load
SAMBA	Diagnostics for the Real World	Viral load
EOSCAPE-HIV™ HIV Rapid RNA Assay System	Wave 80 Biosciences	Viral load

Source: HIV/AIDS Diagnostic Technology Landscape, UNITAID (June 2012)