

Monitoring Treatment: At What Cost?

In the past year, China, India, and Thailand each announced ambitious national programs to provide free anti-HIV drugs to people who need them most. Pharmaceutical companies in all three countries have followed Brazil's lead in producing generic versions of brand-name drugs, at a fraction of the cost. Now comes the hard part: figuring out how best to use the drugs.

Simply identifying patients and getting drugs to them will tax the resources of many countries. And it's no small task to educate patients about the side effects and the importance of taking all of their pills, notes Joep Lange, an AIDS researcher at the University of Amsterdam, the Netherlands, who will co-chair the upcoming international conference in Bangkok. But for clinicians, there's an additional hurdle: how to perform tests that are essential for effective treatment but are now prohibitively expensive.



Cash flow. The U.S. CDC lab in Bangkok has standard flow cytometers that many Asian labs cannot afford.

In wealthy countries, AIDS clinicians monitor an infected person's number of CD4 white blood cells—the critical lymphocytes that HIV slowly obliterates—and blood levels of the virus itself. Both measures help determine when to start treatment and indicate when treatment has failed. "The diagnostics are the major expense now," says Bruce Walker, director of the Partners AIDS Research Center in Charlestown, Massachusetts. So several investigators, Walker included, are developing cheap, easy-to-use diagnostics.

The most common CD4 test relies on flow cytometry, a technology that labels CD4 cells with fluorescent antibodies, shines a laser on the fluid, and counts the number of cells that light up. "It's just a fancy, advanced microscope with a fluid path," says Walker's co-worker William Rodriguez, who heads their project to develop a cheaper device. Popular flow cytometers made by Becton Dickinson and Beckman Coulter occupy the better part of a standard office-sized room and sell for \$65,000 and up. Each test costs up to \$40—and that's excluding labor and maintenance expenses.

With a grant from the Doris Duke Charitable Foundation, Rodriguez and Walker teamed up with chemist John McDevitt of the University of Texas, Austin, to develop a new, portable device that can measure CD4 counts for no more than \$3 per test. They expect the machine itself will sell for about \$2000. "It's really unbelievably cool," says Walker, who has projects in both China and South Africa (and does not intend to profit from the device). It blends digital camera technology with "the brains of a palm pilot," he says. Tests in Botswana have found that the machine's results match those from a flow cytometer 95% of the time.

The battery-powered device resembles a glucometer that measures blood sugar levels. Patients put a drop of blood on a stick that then slides into the machine. Reagents, kept inside a disposable cartridge the size of a credit card, tag CD4 cells with fluorescently labeled antibodies, and a cheap light-emitting diode takes the place of a laser. The machine then shoots a digital snapshot, and software does an inventory of the lit-up pixels, determining the CD4 count. Over the next 6 months, Rodriguez and Walker hope to shrink the device to the size of a small toaster weighing less than 4 kilos. "We set the specs so it had to work in a shantytown or a rural village," says Rodriguez. "And you can transport it on a jeep, a donkey, or whatever."

Labs in Indonesia and India have started trying out an even simpler CD4 test developed by Suzanne Crowe of the Macfarlane Burnet Centre for Medical Research and Public Health in Melbourne, Australia. "There's no equipment cost," says Crowe. The assay uses commercially available antibody-coated magnetic beads ("Dynabeads") to separate out CD4 lymphocytes, which a reagent then stains. A technician looks through a standard microscope and counts the cells. "It's only suitable for places where the volume of work is fairly low," cautions Crowe, who says each test costs about \$5.

At YRG CARE in Chennai, India, researchers are studying Crowe's test and a system made by Guava Technologies in Hayward, California. The Guava EasyCD4 machine, which sells for \$35,000, is a minia-

Cheaper CD4 Tests Under Development

Technology	Developers
Microchip with charge-coupled device	Mass General and Univ. of Texas
Microcapillary flow cytometry	Guava Technologies, Hayward, CA
Microlaser cytometry with antibody-conjugated colloidal gold particles	PointCare Technologies, Ashland, MA
Bench-top flow cytometer	NPE Systems, Pembroke Pines, FL
Bench-top flow cytometer	Partec, Münster, Germany
Immuno "Cytosphere" beads	Beckman Coulter, Fullerton, CA
Immunomagnetic "Dynabeads"	Dynal Biotech, Oslo, Norway

turized flow cytometer that uses vastly less reagent. YRG CARE's clinic director Suniti Solomon says it costs about \$2 to run a test, and she rates the system as "highly encouraging."

Many other academic labs and companies have entered the race with Beckman Coulter and Becton Dickinson to develop cheaper CD4 tests (see table). The Clinton Presidential Foundation, Médecins Sans Frontières, the Forum for Collaborative AIDS Research, Gay Men's Health Crisis, and the Bill and Melinda Gates Foundation all have become involved in pushing these cheaper technologies forward.

Several groups similarly want to develop less expensive viral load tests. At the moment, all are based on amplifying HIV's genetic material and typically cost \$50 to \$80 a test. Cheaper tests (\$5 to \$20) now being studied measure the HIV protein p24 or the reverse transcriptase enzyme that the virus uses to copy itself.

Clinicians primarily use viral load tests to determine whether a drug treatment has failed. If so, they switch patients to other drugs. But Walker and other researchers note that switching drugs won't be an option in many poor countries. For now, they argue, cheaper CD4 tests would pay bigger dividends. "In terms of global health," says Walker, "this is the one thing that can make the biggest difference." —J.C.