Staying Put?

Sticking with an HIV combo that doesn't fully suppress the virus may still help maintain your health.

July 1, 2008 By David Evans and Ben Munisteri

Since testing positive in 1989, jim has dealt with one failed HIV regimen after another. His CD4 count once hit an all-time low of 18, and his viral load has never been undetectable since tests became available, in 1996. Yet Jim, who asks that his last name be withheld, has endured all this—along with a chronically upset stomach and painful tingling in his feet—with a steady optimism.

A few years ago Jim's CD4s tanked again, signaling yet another treatment failure. There was only one new HIV med available at that time, so switching to a completely different combo wasn't an option. Even Jim's upbeat attitude couldn't keep him from wondering, "Why should I keep taking these meds—and dealing with side effects—when they don't seem to be helping me?" And what if sticking to the failing combo caused harm—such as massive resistance to HIV drugs? People in countries where even second-line HIV treatments are scarce might ask the same thing: Why continue treatment if it doesn't offer the Holy Grail of reducing your viral load to an undetectable level?

Now studies are beginning to offer a persuasive answer: A failing regimen may not only be harmless—it may help. According to this research, "failure" isn't necessarily all-or-nothing, and meds that fail to make HIV undetectable may still offer tangible health benefits. Recent research provides some clues about how this happens.

Results of one study question the assumption that continuing a failing regimen will lead to massive resistance and health problems. The study, led by Tejal Gandhi, MD, of the University of Michigan Health System, followed 47 people whose HIV meds were no longer keeping their virus in check and who, like Jim, had no new-combo option. They stayed on their regimens. Nearly four years later, viral loads were still rising in only 22 percent, and CD4 counts had dropped significantly in less than half. Although more than half the participants had developed at least one new drug-resistance mutation, the majority did not get sick. Resistance isn't a good thing, but this study suggests that it may not develop as easily or as quickly as previously thought—nor spell disaster.

Another study found that a failing regimen may still protect against potential brain problems. HIV reproduction and immune activation are often different in certain areas—such as the brain, eyes

and genitals—than in the rest of the body. So Elizabeth Sinclair, PhD, of the University of California San Francisco analyzed the blood and spinal fluids of 123 HIV-positive people. She found that when blood tests showed that a combo had stopped working, HIV often remained undetectable in the spinal fluid (reflecting HIV levels in the brain). Even when meds aren't working perfectly, Sinclair says, they still reduce HIV-related inflammation; that, in turn, slows viral replication and shields the central nervous system.

Paul Bellman, MD, a New York City HIV doctor, has long embraced the stay-the-course strategy. Bellman says, "unless the clinical situation is dire" or side effects intolerable, he'd choose to keep someone on a virologically failing regimen until several new HIV drugs likely to suppress their virus became available. "Unfortunately," says Bellman, "many patients have been given ineffective salvage regimens using one or two new drugs as they became available." It's far better, he says, not to waste the potential power of a new drug by adding it to a failing regimen. Instead, wait for other new meds with which to create a new combo.

While that's likely to be a satisfactory solution for a person with access to HIV meds, what about people in parts of the world where just a handful of drugs are available, and where a growing number of first regimens for HIV are failing?

A solution is to expand the list of drugs available in every country, and activists are fighting for that. In the meantime, however, it may be difficult for people to know just how long they're going to have to wait for new options.

In all cases, new research shows, it's important to distinguish between virologic failure—HIV becomes and remains detectable on lab tests—and clinical failure, in which a person becomes physically ill. Andrew Phillips of the London's Royal Free and University College examined the difference, using computer modeling. His findings: Waiting for symptoms to appear before switching meds offered nearly the same survival benefit as switching at the first sign of uncontrolled virus or falling CD4s. This finding may be especially welcome in places where lab tests are hard to come by—and it may provide some comfort to people in Jim's situation.

Indeed, staying the course seems to have paid off for Jim. Today, three new HIV meds are available, and his virus is most likely sensitive to them. So he's begun talking with his doctor about a new regimen. He isn't getting sicker, but his ever-present virus recently climbed from 18,000 to more than 80,000. How has he managed to keep the faith these last three years, despite his chronically detectable virus? "I believed that something was working," Jim says. "I didn't know what it was." Now he knows.

THE WAITING ROOM

Health
Diet, exercise and other techniques can help keep you healthy. Get tips for positive people by searching "nutrition," "supplements" and "exercise" at poz.com.

Tolerance
Failing regimens can still cause side effects. Get help from AIDSmeds.com lessons on managing them. (Serious side effects may make an intermediate switch necessary.)

Timing
Check on clinical trials (which make new meds available to participants or in expanded access) at AIDSinfo.nih.gov or acria.org/clinical. This will also help you judge how long it may be until new med choices are available for you.

Activism
In developing nations, check on the progress of widening treatment options and partner with other activists at healthgap.org.

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