Hit Early, Hit Hard?

The feds' long-awaited antiretroviral guidelines spark controversy

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POZ periodically publishes different standards of care, guides by which people with HIV and their care providers can make personal choices about health care regimens. HIV standards of care differ by region, treatment philosophy and patient population. The charts published below are drawn from the federal government's Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents (as simplified by Positively Aware, a Chicago-based HIV treatment periodical), released in June. The Guidelines were developed by a U.S. Public Health Service-sponsored panel that included HIV researchers (federal and private), clinicians, insurance representatives and community advocates. (But activists noted that the panel was stacked in favor of "hit early, hit hard" advocates and included no experts on nutrition or alternative medicine.) The Guidelines were based on the Report of the NIH Panel to Define Principles of Therapy of HIV Infection, developed by a similar panel sponsored by the Office of AIDS Research of the National Institutes of Health.

Any advice on treatments or tests is only as good as the science behind it. The Principles of Therapy offers the NIH panel's rendition of the current state of that science and what it means for antiretroviral therapy and viral-load testing. Among the points, some of them controversial, addressed by the Principles:

Combo therapy. Ongoing HIV replication leads to immune-system damage and disease progression and should be suppressed to undetectable levels, or to the greatest extent possible,by using effective antiretroviral combinations.

New drugs. If possible, this should include simultaneously beginning drugs with which the patient has not yet been treated and that are not cross-resistant with any others used in previous treatment -- with all drugs used according to optimal schedules and dosages. Due to cross-resistance and the limited number of antiretrovirals available, consideration should be given to the fact that therapy choices can limit future options.

Viral load. Regular periodic measurements of viral loads and CD4 counts are necessary to determine the risk of disease progression and todecide when to initiate or modify antiretroviral treatment regimens.

Pregnant women. Women should receive optimal antiretroviral therapy regardless of pregnancy

status (but see qualifying factors).

Children. The same principles apply to children and adults, though the treatment of children involves several unique considerations related to their immune function and response to medications.

New infections. During acute HIV infection (immediately after a person is infected), treatment with combination antiretroviral therapy should be given with the goal of suppressing the virus to undetectable levels.

Based on these principles, the other federal panel developed its guidelines about the best ways to use antiretroviral drugs and viral-load tests. The goal was to help health care providers nationwide standardize and improve care for all PWAs.

Many community advocates believe that the broad-ranging guidelines are sound, except in a few important respects. Martin Delaney, founding director of Project Inform, served on the panel and says: “These guidelines should go a long way toward clearing up many of the misconceptions currently affecting the treatment of people with HIV. They’re not perfect, but overall they’re the boldest strokes I’ve seen government make in HIV disease and should really make a difference for a lot of people.”

However, Delaney and other advocates argue that no clinical data supports the guidelines’ call for treatment during the acute infection stage. Although these activists acknowledge possible benefits -- limiting the virus’ spread throughout the body, lowering the overall viral levels and reducing the genetic diversity of the virus (which might make it easier to treat down the line) -- they fear that such early treatment could encourage development of drug resistance, limiting future therapy options. And some immunologists have expressed concern that using antiretrovirals during acute infection might even prevent development of a proper immune response to the virus. Activists also criticize the failure, in the widely quoted “treatment recommendations” chart -- as opposed to the much less- referred-to text -- to note the lack of evidence for long-term benefit from treatment of asymptomatic people with more than 500 CD4 cells or less than 20,000 viral load (measured by PCR).

Citing similar concerns, Mike Barr, editor of TAGLine, the newsletter of the Treatment Action Group, also criticizes the recommendation to offer treatment to asymptomatic HIV positive people with less than 500 CD4 cells or more than 20,000 viral load (PCR). “Until we have more long-term clinical experience, I think it wouldmake sense to hold off on using these drugs in asymptomatic HIV infection,” he says. Barr prefers the guidelines of the British HIV Association -- updated as of this April -- that call for no therapy in symptom-free infection until CD4 cells drop below 200-300 or viral load goes above 100,000 (PCR).

Meanwhile, advocates of complementary medicine are troubled by the guidelines, which offer no information on nutritional and herbal therapies that can reduce antiretrovirals’ liver-stressing toxicities and related side effects (using the herb milk thistle and antioxidants such as NAC and alpha-lipoic acid) as well as improve the drugs’ absorption (using the amino acid glutamine), thus

potentially slowing development of resistance.

Addressing these problems, they argue, may enable more PWAs to tolerate the drugs' effects over the long term. These advocates also say people should be informed of studies that have linked optimal nutrient levels with much slower disease progression. There are also hundreds of anecdotal reports that particular combinations of herbs and nutrients (along with any needed drug prophylaxes) have helped PWAs maintain good health and increased CD4 counts without antiretrovirals.

Yet another objection comes from women activists who note the guidelines fail to mention that virtually no dosing studies for women exist on any antiretrovirals, despite some research showing that blood levels of drugs are different in women than in men. Maxine Wolfe of ACT UP/New York says, "Women must have the option of using these drugs, but the guidelines must clearly state that these drugs have not been tested for dosing, efficacy or toxicity in women, and that women need this information to make treatment decisions."

However, in at least one important respect, the guidelines adopt the aggressive standard of care long recommended by many treatment activists. This includes -- for anyone who chooses to use drug treatment -- the simultaneous use of at least three antiretrovirals: One potent protease inhibitor (either indinavir, ritonavir or nelfinavir) combined with two nucleoside analogues known to work well together. Poorly absorbed saquinavir is not recommended except as a fallback treatment for those lacking better options.

Unfortunately, in the recent past many PWAs have had their chances for long-term viral suppression greatly diminished by physicians who continued to recommend suboptimal treatment. The result has been development of viral resistance that has left many people with few, if any, remaining drug options. (See "At the End of Your Rope?" for suggested treatments.)

The use of two-drug combos was judged by the panel to be suboptimal, and the use of single-drug treatment (mono-therapy) completely unacceptable -- except for pregnant women as a means for reducing the rate of mother-to-child transmission, under limited circumstances.

The latter advice has been denounced by some women activists, since months of use of a single therapy might lead to resistance that would limit a woman's future options.

They have also strongly criticized the guidelines' suggestion that clinicians delay initiation of, or interrupt, optimal antiretroviral therapy for the first trimester of pregnancy due to unknown but very real risks of birth defects or later problems in the children. Wolfe of ACT UP says, "The FDA should require drug companies to immediately complete research on risks to the fetus, but until that time, all women should be giventhe choice of optimal antiretroviral therapy for their own health, with full knowledge of the risks."

Overall, says Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), "the meat of these guidelines is to treat aggressively, to get the virus down to as low as possible for as long as possible," while building in flexibility. Marshall Glesby, MD, PhD, of

the Community Research Initiative on AIDS in New York City, concurs, saying, “All treatment decisions still have to be individualized. The clinical judgment of the medical provider and the preferences of the individual patient remain important components in the decision-making process.”

And so does access to the treatments. Whether the quality of care for most PWAs will actually improve depends on increased government funding to pay for what’s being recommended.

Few people can afford the $15,000-$25,000 annual cost of the recommended drug combos and viral-load tests. Kiyoshi Kuromiya, editor and publisher of Critical Path AIDS Project and a longtime treatment activist,says, “Now that we finally have a standard of care that matches what we know about AIDS treatment, we need an AIDS policy that paves the way for coverage of the earlier, more aggressive intervention that the guidelines recommend.” He continues: “For this to be real, the federal government’s AIDS definition -- used by insurance companies and federal and state programs to determine whose drug costs are covered -- will have to change. Right now, those who are relatively asymptomatic with mid-level or higher CD4 counts won’t generally get reimbursement even though their viral loads are elevated.”

So the new treatment guidelines could greatly improve the chances for slowing disease progression long-term -- but only if the recommended drugs and tests really end up in people’s hands. Show us the money.

Complete texts of both the Report of the NIH Panel and the Guidelines, which include recommendations on viral-load and CD4 testing and many other issues, are available from the CDC National AIDS Clearinghouse at 800.458.5231 or on the Web from Healthcare Communications Group at www.healthcg.com/NIHreport. Positively Aware can be reached at 773.472.6397 or through its website at www.tpan.com/.

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