Medical Ethics and the Rights of People With HIV Under Assault

April 28, 2010 By Sean Strub

Sorry for having such a long initial blog post. Thanks to Dr. Joseph Sonnabend for his continued leadership, mentorship and friendship. I could not have written the article below without his guidance and assistance. --- Sean

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Antiretroviral Treatment as HIV Prevention?

The approach to prevention and treatment of HIV in the U.S. has undergone a radical and dangerous shift over the past few months.

The new concept, called “Test and Treat” (TNT) or “Testing with Linkage to Care” (TLC) will dramatically increase HIV testing, identify more people with HIV and “link” them to care. Those are worthy objectives.

The danger is that some policy leaders driving these ideas are more interested in “treatment as prevention”, meaning getting people with HIV on antiretroviral treatment, than they are in providing the best possible healthcare for them. Because antiretroviral treatment makes one less likely to transmit HIV, they believe treating all people with HIV is a good prevention strategy.

Neither the state of the science or government guidelines support antiretroviral treatment for every person with HIV, but advocates, public health officials and pharmaceutical companies are promoting the idea.

There are also plenty of TNT/TLC proponents, aware of the ethical issues, who rightly recognize that treatment should be recommended only within government-established guidelines supported by conclusive science.

But when important public health officials announce publicly that they seek to put everyone with HIV on treatment, it is cause for concern and ethically unacceptable without informed consent.

Belmont Commission

The beloved and enormously respected former president of the National Council of Negro Women, Dorothy Height, recently a leading advocate for HIV prevention in African-American communities, died recently. She lived a remarkable life spanning nearly a century, dying at the age of 98.

In her decades of public service, one of her most important roles was as a member of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, called the Belmont Commission. Formed in the 1970s, in the aftermath of the Tuskegee Experiment scandal, it was the first public national body to shape bioethics policy in the U.S.

The beginning of the Belmont Report addresses the boundary between medical practice and medical research: "...'practice' refers to interventions that are designed solely to enhance the well-being of an individual patient or client... By contrast, the term"research" designates an activity designed to test an hypothesis... if there is any element of research in an activity, that activity should undergo review for the protection of human subjects..."

The purpose of the guidelines in the Belmont Report, it should be noted, is to avoid unethical experimentation on human subjects, like what happened at Tuskegee. This is relevant, because the discussion concerning TNT/TLC and "treatment as prevention" has often confused medical practice and medical research.

It is clear that the health of people with HIV has become, for some, secondary to HIV prevention. Those of us with HIV are now viewed by much of the public health establishment primarily as potential infectors, "viral vectors of disease".

There are few precedents, in recent history, where drugs are given to people for any reason other than for the patient's benefit.

The occasions that come to mind are when drugs are administered as part of a clinical trial--and subject to ethical review and protections by an Institutional Review Board--or when they are administered as punishment, like with sex offenders forced to undergo chemical castration.

"Treat everyone" advocates propose to, for the first time outside of a research or punitive context, give pharmaceutical treatment to people for whom it is not been demonstrated to be of benefit.

This is an important precedent with extraordinarily significant ramifications far beyond the HIV epidemic. Where are the ethicists? Are HIV positive lives of so little value that something as monumentally unjust as this can happen and not be worthy of notice?

TNT/TLC Sounds Simple

The seeming simplicity of preventing new infections through the TNT/TLC approach is appealing. But that simplicity hides deeply disturbing truths, including that many people coerced into unnecessary treatment will suffer side effects and treatment-induced diseases. Today's treatment regimens are certainly better than what was available years ago, but they remain intense chemotherapeutic regimens to which one must make a lifetime commitment.

Testing people at risk and treating those who need to be treated should be an urgent priority. Too many people with HIV--especially people of color--don't know they have HIV until they show up in an emergency room with a severely-compromised immune system.

Spending precious resources on treatment for those who do not need it, and for whom it is not indicated as appropriate by government guidelines, while there are others in desperate need who cannot get care, or are dying while on AIDS Drug Assistance Program waiting lists, is outrageous.

There is no empirical basis to support TNT/TLC as an HIV prevention strategy. It is an experiment based on a mathematical model predicated on two assumptions, both based on inconclusive evidence. The first assumption is that treatment for everyone with HIV is the best medical strategy, and the second is that suppression of the “community viral load” is an effective HIV prevention strategy.

It is as though a decision has been made to redirect the country’s public health response to AIDS from proven behavioral interventions, like condoms and prevention education, to the use of anti-retroviral medications.

Public health officials’ focus on treatment as prevention and the pharmaceutical industry’s incentive to expand markets are now in dangerously perfect alignment.

Dr. Fauci Changes His Tune

In 2000, at the International AIDS Conference in Durban, Dr. Anthony Fauci, the director of the National Institute of Allergies and Infectious Diseases, questioned the viability of lifetime antiretroviral treatment. He said “...prolonged courses of continuous HAART are not an option for most HIV-infected individuals...With current drugs, it is almost certainly not feasible to have people on therapy for an indefinite period of time.”

But now Fauci--the most powerful AIDS official in the U.S.--is pursuing TNT/TLC research and programs to put all who have HIV on lifetime antiviral therapy. NIH press releases and documents frequently refer “immediate treatment” for all who test positive, “early treatment” or “universal treatment”. The NIH rarely references the possibility that some people with HIV may not need, or be helped by antiretroviral treatment, or that they could be harmed or killed by it.

Dr. Carl Diffenbach, appointed by Fauci as director of the NAID’s AIDS division, posted an article in March (http://blog.aids.gov/2010/03/putting-tlc-to-the-test.html) that makes no reference to the complex ethical issues and is offensive in his patronizing attitude towards people with HIV, whom he represents solely as potential infectors:

He writes “Yet these individuals can continue to spread the virus in their communities until we entice them to step through the door, whether it’s giving them a pat on the back or offering financial incentives...It seems like the hardest aspect of the experiment is getting those who test positive to report for treatment.”

Press releases for an NIH-funded program underway in Washington reference a pilot program to study the “...test-and-treat concept aimed at stemming new cases of HIV infection.” That is different than a program aimed at improving the health of the individual patient.

San Francisco Leads TNT/TLC/“Treatment as Prevention”

San Francisco’s department of public health has pioneered the “treat everyone” approach. On April 2, the New York Times reported “In a major shift of HIV treatment policy, San Francisco public health doctors have begun to advise patients to start taking antiviral medicines as soon as they are found to be infected, rather than waiting -- sometimes years -- for signs that their immune systems have started to fail.”

The SF director of public health, Dr. Mitchell Katz, told the Bay Area Reporter, “…we believe all HIV-infected persons should be treated with antiretroviral therapy unless there is a strong reason not to…” Katz is disingenuous in implying the prevention aspect of TNT is a coincidental, secondary aspect: “I do anticipate it will drive down the rates of new infections. It’s a nice, secondary benefit of this new policy.”

Katz’s decision to use an unproven strategy risks the health of some people with HIV in his city in order to try and slow the spread of the virus. This does little to address one of the major factors for HIV transmission in his city, acute infection, when someone is especially infectious and HIV tests are least likely to be accurate.

The possibility that he truly believes treatment is appropriate for all people with HIV only supports labeling his approach “faith-based medicine”.

At the same time, he has also proposed radical budget cuts for traditional behavior-based HIV prevention strategies. As goes San Francisco on HIV prevention, so may go the nation, further jeopardizing condom promotion and behavioral-based prevention strategies in favor of test and treat.

Project Inform’s View

Project Inform, an important AIDS treatment advocacy group also based in San Francisco, has changed its position on when to commence treatment. In January they updated a sensible paper that said “There’s no definitive answer on the best time to start. Some people choose to put off taking meds for as long as safely possible. Others decide to start earlier in the course of their disease. Both strategies have merit and both are supported by some research.”

But a few days ago, they made an about face, unsupported by conclusive science, which advocates treatment for all: “Project Inform believes that the long-term damage from untreated HIV is greater than the potential damage caused by long-term use of HIV medications…”

Project Inform now suggests starting antiretroviral treatment before one’s CD4 count (a marker for the strength of one’s immune function) falls below 500; the U.S. government recommends treatment after one’s CD4 cell count falls below 500; most other countries around the world don’t recommend treatment until one’s CD4 count falls below 350.

What happened between January and April that caused such a change in their position?

Pharma Funding Promotes Treatment as Prevention

This has been a boon to pharmaceutical companies looking to increase their potential markets. They have been glad to promote the “treatment as prevention” bandwagon.

Recent promotional literature for a pharma-funded continuing education “Best Practices” symposium for doctors makes it clear the purpose of the training is for HIV prevention, not the care of the individual patient: “Enhanced Test-and-Treat approach for the Prevention of HIV Transmission”.

“The goal of this activity is to provide the skill set for clinicians to implement state of the art strategies and technology on universal testing followed by early universal treatment in an effort to get patients enrolled into care earlier and to maximize prevention opportunities.”

The statement of purpose doesn’t say anything about improving patient health outcomes, as that isn’t the point. The point is to get people on antiretroviral treatment and neutralize them as potential infectors.

New York’s Albert Einstein College of Medicine and the Jacobi Medical Center, who are sponsoring the event, ought to be institutionally ashamed of themselves.

The Great Unanswered Question: When To Start Treatment?

An indisputable truth nearly 30 years into the epidemic, 25 years after the first anti-HIV drug and 15 years after discovery of the combination therapy that has saved so many lives, is that we still do not know the best point in the course of the disease for one to start treatment.

The most common marker of HIV disease progression is a type of white blood cell called CD4 that combats infection. A healthy HIV negative person might have a CD4 count of 600, 800, 1000 or more. For people with HIV, the lower the CD4 count, the greater the likelihood of opportunistic infections and AIDS-defining illnesses. A CD4 count below 200 is one marker for an AIDS diagnosis, even in the absence of any opportunistic infections.

Last December, in a controversial vote, a government advisory panel issued guidelines recommending treatment for all people with HIV whose CD4 count is below 500. Previously, the recommended treatment commencement point was 350, which remains the standard in most countries around the world.

The “when to start” question has vexed the epidemic since the 1986 introduction of zidovudine (then popularly known as AZT) and which was the first antiretroviral approved for use against HIV. For some at late stages of the disease zidovudine was a miracle treatment, bringing them from the brink of death back to life. But resistance to zidovudine developed within weeks or months and severely immune-compromised patients then usually resumed a rapid decline to death.

For many with higher CD4 counts, the toxicities of zidovudine--then administered at a higher dose than today, when it is used as part of a drug combination--proved to outweigh potential benefits.

Resistance remains a problem today, which raises an important question for those who advocate putting everyone with HIV on treatment. What will they tell those who are put on treatment unnecessarily and develop resistance when they get sick? Starting treatment too early limits options that may be needed later in the course of the disease.

Some argue for “hit hard, hit early”, meaning treat aggressively as soon as a person was diagnosed with HIV. There are valid arguments in favor of this approach, especially in the days and weeks immediately following infection.

Others, including some of the most well-respected researchers, scientists and clinicians, advocate caution, believing it makes more sense, in the absence of conclusive evidence in favor of early treatment, to wait until there is clinical manifestation of disease or one’s CD4 count falls below a certain level.

Why Wait To Start Antiretrovial Treatment?

Antiretroviral therapy creates a reservoir of potentially dangerous toxicities that cause serious and sometimes deadly side effects, the extent and severity of which have usually not been discovered until long after they are introduced into the marketplace. While it is life-saving for those who need it, antiretroviral therapy is a lifetime commitment to serious chemotherapeutic agents and should not be undertaken lightly.

From infection to the point where one’s CD4 count falls below 500, when the government advises starting antiretroviral treatment, often takes years, but it varies dramatically from one person to the next, depending on co-factors, genetics, access to care and other factors. Some people with HIV are known as “slow progressors” and a few long-term non-progressors may never need antiretroviral therapy.

The longer people with HIV take the drugs, the more we learn about toxicities and side effects. Fat redistribution causing facial and bodily disfigurement, including what is known as “protease paunch”, “buffalo hump” and “chipmunk cheeks”; dramatically increased risk of heart attacks and stroke; bone demineralization causing increased fracture risk; premature aging; kidney failure; all these are risks of antiretroviral HIV treatments.

Individuals whose health status falls outside the categories recommended for treatment may choose to take antiretroviral therapy anyway, because they and their physician believe they need it, or perhaps to make themselves less infectious to partners. Those choices should be respected.

It is unethical and irresponsible to coerce or encourage people who are not recommended for treatment under the guidelines to start therapy without fully informing them of the risks.

For those of us who were very ill and credit our survival to antiretroviral treatment, there is no question the reward of treatment greatly exceeded the risk. Importantly, many of us consider our survival to be as much about having known when not to take antiretroviral treatment as it is about having access to those treatments when we chose or needed to start them.

Our experience with HIV has consistently taught us how information, even “conventional wisdoms” about HIV treatment and prevention, change frequently over time. It is vital this lesson not be forgotten, because it is no different today than it was years ago. Too many statements, including the new one from Project Inform about starting treatment, do not adequately acknowledge this reality.

Some TNT/TLC advocates suggest side effects are less of a concern today because treatments have improved and we know more about them. But one of the most important things we have learned is how HIV drug toxicities accumulate over time. Even if a drug has been in the marketplace for many years, it does not mean that all of the long-term side effects are known.

For example, two common HIV drugs that have been prescribed for nearly 20 years were recently found to produce a metabolic abnormality called hyperhomocysteinemia. This is a condition associated with vascular abnormalities, including a greatly higher risk of heart attacks.

TNT/TLC Could Jeopardize START Trial

A definitive answer to the “when to treat” question might come from the START trial, now taking place at 90 sites in 30 countries, with an ultimate enrollment of 4,500 participants. It is vital research that we have demanded for years.

But statements by policy leaders that all people with HIV “ought” to be on treatment risk suppressing enrollment in START and jeopardizing its chance for completion. The International Network of Strategic Initiatives in Global HIV Trials has circulated a sign-on letter to raise the alarm and support enrollment in START. Their letter also questions last year’s decision to raise the U.S. treatment guidelines’ threshold from 350 CD4 cells to 500 CD4 cells:

“When to start antiretroviral treatment is one of the most important outstanding questions for people with HIV and their clinicians...We are concerned that some may interpret the new [US] recommendations as implying that the deferral group of this trial is no longer ethical. Such an interpretation would endanger the future of the trial in the [US].”

"We ... do not believe that there is convincing evidence to conclude that deferral of initiation of ART to a CD4 count of [350 cells/mm3] causes net harm, particularly in terms of mortality, compared with starting at any higher level... The available evidence is insufficient to determine if the adherence challenges and long-term side-effects of early antiretroviral treatment are outweighed by reduced risk of illness conferred by these medicines. Only a randomized controlled trial, such as START, can determine this. (underscoring added) ...We too are concerned that the new US recommendation:

1. raises theoretical concerns about continued enrolment of patients in the US, a substantial source of patients, and
2. is based on poor evidence and therefore might not be in the best interests of patients;
3. previous recommendations to use earlier treatment failed to recognize the negative impact of resistance and side effects, and
4. A minority of individuals has normal CD4 counts between 350-500 and would therefore be using treatment prior to any significant immune damage. It is worth noting that evidence that treatment above a CD4 count of 350 is not warranted would cost the pharmaceutical industry billions of dollars."

Volunteering to be Criminalized

TNT/TLC is closely linked to a campaign over the past several years to increase the number of people who get tested for HIV. That is an admirable objective; especially if it provides access to treatment for those who need it. The CDC estimates the number of untested HIV-positive people in the U.S. at 235,000.

Physicians should raise the subject and encourage their patients to get tested; too often, patients are left undiagnosed because they did not feel they were at risk, they were not willing to admit risky behavior, or their physician never suggested getting tested.

The CDC, NIH and others support “routinizing” HIV testing by eliminating requirements for written consent and testing patients routinely at annual check-ups, emergency rooms, etc. Pharmaceutical companies fund lobbying efforts in state legislatures, as Gilead is right now in Massachusetts, to repeal this important educational and privacy safeguard.

The single biggest obstacle to getting tested is stigma. A smarter strategy to get more people tested would be to combat stigma and discrimination against people with HIV. That should start with eliminating

HIV criminalization statutes that imprison people for behaviors that pose no or little risk of HIV transmission or for the failure to disclose their HIV positive status prior to intimate contact.

Codifying discrimination in the law, as has occurred with HIV, is the most extreme manifestation of stigma. These laws often result in extraordinarily harsh punishments and treat HIV differently from human papilloma and other viruses that are more casually transmitted and that can also lead to death.

They are terrible public health policy because ignorance of one’s HIV status is the best legal defense. “Take the test and risk arrest” is the message many at risk, who need to get tested, will ultimately hear.

“Routinizing” HIV testing means the person getting tested will likely not understand the potential legal jeopardy or the risks they could face once their name is on a government list as a person with HIV.

Will all the new people tested through TNT/TLC be informed, in advance, that if they test positive, their name is put on a government list? Or that health departments use those lists to target individuals for “behavioral interventions” and potentially for criminal prosecution?

Leadership from federal officials, public health leaders and AIDS organizations is urgently needed to support efforts to repeal these statutes. Yet most of these leaders have remained silent or uninvolved, even as they promote policies that will greatly exacerbate the problem of HIV criminalization.

Project Inform’s statement acknowledges concerns about privacy and discrimination against people with HIV, but they minimize those concerns by noting: “However, important federal and state laws prohibit both the disclosure of medical information and discrimination against people living with HIV/AIDS.” They would better serve their constituents if they also pointed out that statutory protection against discrimination is no guarantee they will not be subject to it.

Informed Consent and Voluntary Treatment

Informed consent prior to voluntary commencement of antiretroviral treatment ought to happen as a matter of course. But while most TNT/TLC advocates take pains to reiterate their intent for treatment to be voluntary, there has not been adequate discussion as to how they will get informed consent from patients recommended for treatment who do not meet the established treatment guidelines.

Will persons with high CD4 counts be told it is not certain treatment will help them? Will they be told about the likelihood of suffering side effects over time? Will they be told that respected experts advocate that people with HIV wait until their CD4 cells fall below 350 before starting treatment?

Will they be told that the recommendation that they start treatment immediately is driven in part in pursuit of a societal benefit, rather than what is best for the individual patient or proven by science?

What We Need From TNT/TLC Advocates

It is tragic that public health policy, coupled with the trend towards growing criminalization of HIV, is institutionalizing the view of people with HIV as primarily a potential threat to society--the very thing AIDS activists and leaders like the late Dorothy Height fought most passionately against.

That some AIDS advocates and organizations borne of the blood, pain and struggle of the epidemic have become partners and cheerleaders for this approach is cause for disappointment, concern and, yes, anger. We need them to reconsider their approach.

To avoid having TNT/TLC turn into a shameful episode in the epidemic, it is vital that its supporters in government, academia, medicine and the AIDS community step to the forefront as leaders in at least six areas:

- Make sure truly informed consent is a non-negotiable, integral part of any TNT/TLC program and consistent with the Belmont Report guidelines
- Advocate for research--including full enrollment in the START trial--to definitively answer the “when to start treatment” question.
- Speak out against criminalization and demand federal leadership on the issue.
- Advocate that pharmaceutical companies withdraw from lobbying for the elimination of patient informed consent protections.
- Support a renewed commitment to behavioral-based HIV prevention programs
- Implement meaningful participation of people with HIV, including those with diverse opinions and perspectives, in the development, design and implementation of TNT/TLC programs.

Absent such a commitment, TNT/TLC risks harming some people with HIV, preventing or greatly delaying the research necessary to determine the best point to start therapy, increasing criminalization prosecutions and creating unnecessary new HIV infections by undercutting non-pharmaceutical, HIV prevention strategies that have been proven effective.

And if you’ve made it this far, you’re my kind of reader. Further posts won’t be so long, I promise.
Thanks, SOS