

# ASK THE EXPERTS

Get answers to your treatment questions

## Time to Start?



**The decision to start treatment is a joint one made by you and your doctor. You likely look to your doctor for expert medical advice. Doctors, in turn, rely on their training and experience and on HIV treatment guidelines. Here, four medical doctors discuss how last year's changes to the U.S.-based DHHS guidelines—the granddaddy of such guidelines—have affected their thinking about the best time to start antiretroviral therapy.**

INTERVIEWS BY JENNIFER MCPHEE

### **JEAN-GUY BARIL, MD**

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When effective therapies first appeared in the mid-1990s, HIV doctors followed a “treat early and treat hard” approach. However, as we used these early anti-HIV drugs, we learned that they caused many short- and

long-term side effects. To minimize these effects, physicians and people with HIV/AIDS (PHAs) began delaying treatment for as long as possible, generally until CD4 counts fell to 200 cells.

As drugs have improved, however, the pendulum has swung back toward earlier treatment. Since 2008, HIV treatment guidelines have recommended

starting therapy at the 350-cell mark, and most experts agree that evidence from cohort trials supports this recommendation.

Based on growing evidence that, even at high CD4 cell counts, not being on treatment can increase the risk of certain diseases, such as heart or kidney disease, the U.S.-based DHHS (Department of Human and Health Services) guidelines moved in 2009 to recommend even earlier treatment by also recommending therapy when CD4 counts are between 500 and 350 cells. The DHHS experts did not reach a consensus: 55 percent strongly recommended this change, while 45 percent gave it a moderate recommendation. *[For a summary of the changes, check out TreatmentUpdate 176, available online at [www.catie.ca/tu.nsf](http://www.catie.ca/tu.nsf).]*

Half the panel also recommended treatment above the 500-cell mark, which essentially means they recommend therapy for everyone with HIV. The remaining panel members felt that therapy at such a high cell count should be optional.

No national HIV guidelines exist in Canada, but Quebec and British Columbia both publish provincial guidelines. I am chair of the advisory board that approves Quebec's guidelines. In our latest guidelines, we continue to recommend treatment at the 350-cell mark, and we recommend even earlier treatment for certain categories of PHAs: those with viral loads above 100,000 copies; those with a CD4 decline of more than 100 cells per year; people co-infected with hepatitis B or C; pregnant women; and anyone with HIV symptoms. Currently, however, we feel that insufficient evidence exists to support recommending treating everyone with HIV.

### **DARRELL TAN, MD**

Toronto General Hospital and  
St. Michael's Hospital, Toronto

The data supporting an earlier start to treatment comes mostly from two observational cohort studies. In these studies, researchers tracked a group of people with HIV and observed that people who started treatment between

500 and 350 cells were less likely to get or die of AIDS-related illness.

Observational studies are useful for generating hypotheses to prove in more rigorous clinical studies called randomized controlled interventional trials. However, observational studies do not prove cause and effect because they cannot account for other factors that may explain the real reason these particular early-starters had better outcomes.

For this reason, I still generally wait until a person's CD4 count dips to around 350 cells before I recommend treatment. However, I begin talking to my patients about treatment as soon as I meet them. I start the conversation by explaining that they have a lifelong incurable infection that can jeopardize their health and even their life and that they will almost certainly require daily treatment someday. But I also stress that treatment is not something to fear. After all, treatment is what will allow them to continue living long, fulfilling lives.

Some people become very worried about side effects. I try to help them overcome this and other fears by giving them good information. For instance, I explain that even the most common side effects don't happen to most people. More often than not, side effects are temporary or we can find a way to minimize or solve the problem. I also help put their concerns in perspective by reminding them that treatment prevents them from experiencing much more serious health problems.

### JOHN GILL, MB ChB, MSc

Southern Alberta HIV Clinic, Calgary

Debating whether people with HIV should begin treatment at the 350 or 500 CD4-cell mark is a nice academic exercise, but it's largely irrelevant in the real world. Like most other HIV care programs in the developed world, we struggle with the huge problem of people presenting late for care. Too often people arrive at their first appointment with CD4 counts so low that everyone would agree they need to be on

treatment. I would like to see more sexually active people undergo HIV testing during their annual medical exams because, right now, too many people aren't diagnosed soon enough.

It's also important to point out that the DHHS guidelines (and any other guidelines) are not rules. Equally wise experts have created other sets of guidelines and reached slightly different conclusions based on the same science. Personally, I feel that 350 is still the best threshold for starting treatment because the evidence used to support an even higher threshold is still somewhat speculative.

All this said, I keep all the various HIV guidelines in mind as I work with my HIV-positive patients on when to

start and what to take. The drug combination we most commonly prescribe consists of two nukes combined with either a non-nuke (usually efavirenz [Sustiva and in Atripla]) or a ritonavir (Norvir)-boosted protease inhibitor.

Of course, one size doesn't fit all, and my patients and I take other various factors into consideration, including drug resistance patterns, abacavir hypersensitivity tests and their underlying health. For example, one of my patients suffers from night terrors—a sleep disorder that causes him to awaken from sleep in a terrified state—so I would not suggest any drug that might make his condition worse.

### WALTER SCHLECH, MD

Queen Elizabeth II Health Sciences Centre, Halifax

Current HIV therapies cause fewer side effects, and evidence does suggest that starting treatment at the 500- to 350-cell mark prolongs life. However, the DHHS experts were clearly divided in their opinions, and I suspect some of them were also influenced by new observational trial data that suggest that PHAs taking HIV treatment are less likely to pass on the virus during sex. [See the sidebar for more on the idea of treatment as prevention.]

The physicians at my clinic always reach a consensus about when we will encourage each PHA to start treatment. For now, we've agreed to recommend that our patients start treatment at the 350-cell mark. However, we may encourage people to consider beginning sooner if they have consistently high viral loads or if their CD4 count rapidly declines over several months.

We inform people about the medical evidence and debate surrounding the best time to start treatment. If someone wanted to start early, we would all discuss it and likely move forward with treatment. But this request is rare. Most people realize that treatment is a lifelong commitment and prefer to wait as long as possible. +

## TREATMENT AS PREVENTION

Treatment as prevention is the idea that anti-HIV therapy may be able to reduce the risk of transmitting HIV. It's a debated topic right now because many experts find that the evidence supporting the idea is not yet convincing. The issue is made more contentious by the possible implications for PHAs, namely the possibility of starting treatment simply for the greater good, not for personal medical necessity.

The observational trials that have looked at this question are not able to prove that being on treatment actually causes a reduction in the risk of passing the virus. As well, it is not yet clear by how much the risk is lowered for heterosexual and homosexual sex—it might be different due to the differences between the two kinds of sex. A clinical trial currently underway will give us better answers to these questions. Results are expected in a few years.

To gain more perspective on the issue, here are some other readings:

- "Treatment as prevention: We've all heard about it but what does it really mean?" in the Winter 2010 issue of *Prevention in Focus*, available at [www.catie.ca](http://www.catie.ca).
- "Sex, Drugs and Viral Load" in the Winter 2008 *Positive Side*, at [www.positiveside.ca](http://www.positiveside.ca).