

wise words

Women, HIV and Depression

Having “The Blues” for a day or two is something we all feel occasionally. Depression is different. Depression can last weeks or months, or even years. It can change your body chemistry and, left untreated, can worsen or even cause other illnesses.

Many things can cause depression, including some HIV drugs (particularly efavirenz/Sustiva), medications for hepatitis C, vitamin deficiency and hormonal irregularities. Social factors and life stressors, like money problems or loneliness, can also contribute to depression.

Numerous studies have shown that HIV-positive women experience

higher rates of depression than HIV-negative women and men. This is probably partly due to hormonal changes and the increased burden and isolation experienced by many women living with HIV.

Depression makes you feel bad about yourself and your environment, and it can make you feel hopeless about the future. Fortunately, depression usually responds well to treatment.

Signs of Depression

Recognizing signs of depression is the first step to combating it. Many people associate prolonged sadness and thoughts of suicide as classic signs of depression. While some experience these symptoms, not everybody who is depressed does. Other common signs include fatigue and/or insomnia. Loss of appetite and/or sex drive are also signs, as is losing interest in family, friends, work and life.

Treating Depression

Talking, using medications (anti-depressants) and making lifestyle changes (like exercise and nutrition) are ways to treat depression. An approach that combines these strategies works better than choosing only one.

Connecting with Others

Talking is an essential part of beating depression. Talking to a therapist can be very effective. Increasingly, there are therapists who specialize in working with people living with HIV. Sometimes your doctor, local AIDS service organization or support group can refer you to such a therapist. Choosing one you feel comfortable with may take time. Health insurance, as through private insurance or Medicaid, sometimes covers these expenses.

Support groups are sometimes just as effective as talking with a professional therapist, and they're often free. Many experts recommend that all positive people seek some form of support. Few, if any of us, were taught all the skills needed to cope with a life-threatening illness. Also, many books can be bought or checked out at your local library with useful information on overcoming depression.

a word from wise

A sincere thanks for your generous responses to the Wise Words readers survey. So many of you not only told us what you wanted to read, but you shared your incredible life stories. Your feedback, ideas and experience will help us craft a better newsletter that is more reflective of your needs. To start, this issue covers some of the most frequently requested topics noted in the survey. We hope you like it.

The readers survey is posted on Project Inform's website. If you have Internet access, please take a few moments to fill it out. It's easy and your feedback is extremely helpful!

Again, thank you!

Angela Garcia

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WHAT'S INSIDE WISE

Women, HIV and Depression	1-2
Sex and Living with HIV	3
Telling Others About Your HIV	4
Nutrition and Weight Maintenance	5
What's on the New Drug Horizon?	6
New Guidelines Available	7
Fighting for the Cure	7-8

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Anti-Depressants

Anti-depressants have proven to make a big difference in the lives of many who suffer depression. These pills can be taken short- or long-term, depending on your need. A commonly used class of anti-depressants is called SSRIs (*serotonin specific re-uptake inhibitors*). These work on the brain chemical, *serotonin*. SSRIs like paroxetine (Paxil), sertraline (Zoloft) and fluoxetine (Prozac) are widely used in treating of HIV-related depression.

Other types of anti-depressants, like bupropion (Wellbutrin), and new treatments are in development. People respond to anti-depressants differently, and it might take time to find one that works well for you. Anti-depressants work best when coupled with some sort of talk therapy, be it with a trained professional or a support group.

An important consideration when talking to your doctor about choosing an anti-depressant is the potential for drug interactions, especially if you take HIV drugs. For example, ritonavir (Norvir) should not be used with bupropion: it can increase blood levels of SSRIs. Also, some anti-depressants increase or decrease blood levels of oral birth control; dose modifications of oral contraceptives may be necessary.

Again, talk to your doctor or pharmacist about possible drug interactions with anti-depressants and other therapies you take. (See Project Inform's *Drug Interactions* for more information.)

Despite the success of anti-depressant therapies, not all people benefit from them nor do the effects always last. It's common for people to start with one anti-depressant and then either switch to another or add others to their daily regimens. Some end up using two to four anti-depressants at the same time. Even then, the drugs can fail, especially when a person ignores her other forms of support.

Herbal Remedies

The herbal treatment most often used in hopes of combating depression is St. John's Wort. Caution is advised when using this herb for several reasons. First and foremost, the most recent controlled clinical study found little or no effectiveness when comparing St. John's Wort to a placebo (harmless sugar pill). Even its supporters claim it may only work in mild forms of depression.

The herb also has a significant interaction with indinavir (Crixivan). Indinavir blood levels were greatly decreased when they were used together, greatly reducing indinavir's anti-HIV activity. This can lead to developing resistance to indinavir.

St. John's Wort is also likely to greatly decrease blood levels of other protease inhibitors as well as non-nucleoside reverse transcriptase inhibitors. People who take these drugs are advised not to use St. John's Wort. Individuals who use complementary therapies should always discuss possible interactions with their doctors and pharmacists.

A final reason for using caution is because all herbal remedies are completely unregulated—there is no way of really knowing how much herb is actually present in a supplement, or even its quality. If you try St. John's Wort look for the active ingredients, hypericum at 0.3% and hyperforin at 6%, and seek advice as to which are the most reliable brands. Some nutritionists recommend trying 300 milligrams three times a day, but even this figure is uncertain. The kind of studies needed to determine proper dosing of a drug have not been done with St. John's Wort.



Lifestyle Changes



Because depression affects your daily routine, it's important to try to develop and maintain healthy sleeping, eating and exercise patterns.

Small changes—like eating regularly and well, sleeping enough but not too much, and getting out and moving your body—helps your body and mind tremendously!

When people are depressed they tend to skip their daily routines, missing meals and sleep and forgetting to take their meds. This only makes things worse.

Finally, never give up hope if you are depressed! Depression can be treated. There's a great deal of support out there to help you determine the best way to treat your depression. The sooner you tap into it, the faster you'll begin to feel better.

Sexual intimacy is essential to well being. All human beings need to touch and be touched. Yet people living with HIV are often denied touch because of other people's ignorance; or they themselves shy away from touch because of shame, pain or fear of HIV transmission. It shouldn't and doesn't have to be that way. Honest, informed and safe discussions (especially with yourself!) about desire, HIV and transmission are the keys to fulfilling sexual intimacy.

Testing positive for HIV forces many women to really think about, and talk about, sex for the first time. While this may feel hard, it's actually really good! It can get you in touch with your health, your history and your sexual desires. This is an incredible opportunity—one

that many women, positive and negative, simply miss.

Our desire for sexual intimacy changes over time depending on many factors, including our environment, our opportunities or where we are in our lives. Stress, illness, depression, low self-esteem, poor body image, hormonal changes, sickness and how we have been treated in relationships can diminish our interest in sex. HIV itself can be a deterrent for sex, as sex is often associated with getting HIV. Recognizing that sex needn't stop after an HIV diagnosis is an important part of facing and adapting to one's HIV status. This often takes time.

There are things that can rejuvenate our interest in sex, including the emotional healing, strong self-image, health and just missing physical intimacy. Becoming informed about safer sex and, if possible, having safe and open

discussions with your sexual partner(s), can enhance sex. This can be hard at first. But safer sex, with or without disclosure, is a necessary fact for *everybody*.

FOR MORE INFORMATION

... on safer sex, read the article in **Wise Words #4** entitled

"Sex and Transmission, A Continued Concern for HIV-Positive Women."



Enhancing your sex life

Here are some helpful tips for enhancing your sexual life. They may not be, or work, for everybody, but considering them can't hurt.

- **Talk to other positive women you know and trust about sex, be it a friend or a support group.** Knowing that other positive women worry about, miss or have fulfilling sex makes you feel less alone and, admit it, can be fun!
- **When you're ready, talk about your HIV status.** The more you learn to live with and talk about HIV, the more you'll be able to incorporate sex into your life again.
- **Explore your own sexual desires.** Start reading about sex. There are great books for women these days. Consider keeping a journal and writing down your thoughts, fears and interests.
- **Enhance your general health—physical, emotional and psychological.** Feeling fit in body and mind can help get you in touch with your desires—and be able to fulfill them.
- **Explore resources for women about sex.** If you have web access, check out www.chickpages.com/zinescene/dentata/. It's a website on sex for positive women and those who love them; and it's filled with inspiring stories, great questions and other cool stuff. Another great resource is Good Vibrations, a terrific women-owned store that has wonderful books and toys for women located in the San Francisco Bay Area. They have a free catalogue (they ship anywhere in the world!) and can be reached at www.goodvibes.com.



telling others you're living with HIV can be scary, painful and hard. In the long run, it's usually not as hard as the heavy burden of secrecy. One of the most frequent comments from readers responding to the *Wise Words* survey was that you wanted information on how to best disclose your HIV status to people in your lives. While there's no one best way, there are a few things to think about in advance that might help.

telling others about your hiv

Weighing the Pros and Cons

Common reasons why some people choose not to disclose is that others may find it hard to accept your HIV status; some may even discriminate against you because of it. Discrimination within one's family or friends can really hurt. Discrimination at work can hurt, too, but it is also illegal.

The pros may be that sharing your status can feel empowering and can foster a new sense of closeness among friends, family and loved ones. Not hiding your HIV status from doctors or other healthcare providers can help ensure that you get the most appropriate care, too. Disclosure can also reduce the risk of HIV transmission to others, and it can lead to better, healthier sexual relationships.

Who

Remember, you don't have to tell everybody, only those who *you* trust and want or need to tell. Give yourself time to determine who these people are and how you want to tell them.

Sometimes it's easiest to first disclose to someone who has been through it themselves, like a friend or family member living with HIV or members of support group or someone who has disclosed another serious illness.

If you don't know anyone living with HIV, or don't have access to a support group, calling an HIV hotline and telling an operator you have HIV can break the ice. They are used to these kinds of calls. They won't judge you; they will understand. They might even be willing to work with you, through role-play or just by

listening, to help you find the language and courage to tell others.

How

Blurting things out all at once is certainly one way of getting out the fact that you're positive. But healthy disclosure is a process that may require many discussions and contemplations.

Think of disclosing your HIV as the beginning of a new dialogue with the ones you most love and trust. Not only will they learn about you through this process, but you'll learn a lot about yourself as well. The starting point may be your saying "I have something to tell you—I have HIV." But chances are, that isn't going to be the final word.

Setting the stage for disclosure can make a big difference. Think about where you want to tell—a place where you feel comfortable and safe. If possible, line up some place safe for you to go after the initial disclosure, like a friend's house or a support group.

Consider bringing a few pamphlets about HIV or an HIV hotline card for the person you're telling. Not only might they use these resources later but having them helps that person know you're not alone, that there's support for you—and for them. Consider bringing someone who already knows you're living with HIV.

Remember that their first reaction is not going to be their last. Like you, those who you love need time to adjust to this new information. **Finally, be brave and proud of the decision you've made!**



Telling Children

If you have kids, telling your children about your or their HIV status can be even more challenging, but also rewarding. Like other touchy topics—such as bodies, puberty and sex—discussions about HIV, be it your own, their HIV or HIV in general, should be age appropriate. The National Pediatric HIV Resource Center has great information for parents who need guidance on disclosure. They can be reached at www.pedhivaid.org.

Telling Employers

You do not have to tell your employer you have HIV. Confidentiality of medical information is part of your right to privacy. The only situation in which an employee *may* need to reveal their status is on the application for Family and Medical Leave. Even then, the information must remain in a separate, private file to which only the director of human resources or you have access. *Legally, it cannot be shared with anyone else.* If it is, and discrimination results, the employee could sue the employer.

If you have any questions about disclosing for employee or benefits purposes (like insurance, disability or medical leave), contact an employee benefits counselor, HIV or legal advocate *before* disclosing.



g ood nutrition, combined with exercise, strengthens the body and mind. It relieves stress and optimizes the most out of HIV-related therapies. The building blocks of good nutrition include an appreciation of the basic food groups and principals of a well-balanced diet.

When making a nutrition and exercise plan, it's probably best to start with small improvements over what you already do. Do you eat three healthy meals a day? If not, try to incorporate that third (or even second) meal into your day. Do you exercise? If not routinely, then commit to walking around the block or stretching in your home each day.

Once you've made these small changes, then try another set of healthful new activities. The key to success is not to create unrealistic goals and expectations, but rather real and do-able goals that you find enjoyable and fit within your lifestyle. And like any basic program, periodically check and adapt your strategy to your changing needs.

Women, HIV and Weight Loss

Society's glamorizing of thin women might lead doctors—and some women with HIV—not to be alarmed by unplanned weight loss. Any weight loss that is unplanned and can't be explained should be cause for alarm. Your weight should be monitored with the same watchful eye as your lab results.

Malnutrition and weight loss are common problems with HIV disease. Malnutrition can result from loss of appetite and food intake due to depression, fatigue, illness or

nutrition and weight maintenance

side effects from therapy. Without monitoring, it can persist undetected for a long time.

Weight loss is an obvious sign of malnutrition. It can begin and become severe anywhere in the course of HIV infection, though it's an increasing threat when CD4+ cell counts fall below 100. *Wasting* is an extreme type of weight loss and is an unexplained loss of 10% or more of a person's normal weight.

Treat the Causes

HIV and related conditions can cause weight loss, fatigue, loss of muscle mass and chronic diarrhea. The gut, where your body absorbs nutrients, is a major reservoir of HIV infection. Also, many other infections grow unchecked there once the immune system is weakened. All these factors can contribute to weight loss and poor nutrition.

It is important to identify the cause of weight loss and diarrhea. Often, multiple causes occur at the same time. Also, some wasting is due to *malabsorption*, when the tissue and cells lining the intestines can no longer properly transfer nutrients.

Finding the cause(s) of weight loss and/or diarrhea is always critical to finding the right solution. Treating symptoms, without understanding the underlying causes, can sometimes do more harm than good.

A Final Word

When correcting nutrition and wasting problems, there's no guaranteed solution for every situation. What works for one person in one situation may not work for the next. The best solution is to form your own opinions after collecting as much information as possible.

Of all the options out there, enhancing and maintaining a well-balanced diet is likely the best cornerstone of a nutrition and weight maintenance program. For more information, read Project Inform's publications, *Nutrition and Weight Maintenance*, *Drug Interactions* and *Herbs, Supplements and HIV*, available from the hotline.

BROWN BAG IT!

A brown bag medical check-up is an important part of health monitoring. Each time you visit your doctor, put all the therapies you take into a bag. Include vitamins, herbs, nutritional supplements and all prescribed meds. Ask your doctor or pharmacist to review your therapies for their safety and instructions for use. This will help avoid drug, vitamin and herb interactions and may help diagnose symptoms caused by side effects of therapies.

Consider Supplements

Many people attempt to give their bodies an edge over HIV with vitamins and nutritional supplements. Although a healthy diet is the best source of most vitamins and nutrients, supplements may help correct minor deficiencies. Much research still needs to be done to document nutritional deficiencies of HIV disease and how supplements may correct them. Still, taking a reasonable level of supplements makes common sense.

For some people, supplements are often too expensive. Some counties and states have programs that help cover the cost of nutritional supplements. To find out if programs exist in your area, call your local health department.

However, supplements should not replace food. Whenever possible, increasing vitamins through better eating habits is preferable.

Lastly, the vitamins and supplements industry is entirely unregulated. This means that a product may not contain what the bottle label advertises, and there's no guarantee that it will do what its promoters say. One source that might be useful in evaluating different brands of vitamins is www.consumerlabs.com.



what's on the new drug horizon?

Today, advances in anti-HIV and anti-HCV research are few and far between. Only a handful of new drugs are in development that block HIV reproduction in new ways. Most in development are simply improved versions or new variations of those now available. Such drugs may only offer small improvements in potency, simpler dosing and reduced side effects. Some will claim to be effective against drug-resistant viruses based on lab tests, but it remains to be seen whether they will truly offer help for people with highly resistant virus. This article briefly reviews these new drugs.



New Protease Inhibitors

Tipranavir (PNU-140690): Results from a lab study shows that tipranavir is active against almost all the protease inhibitor-resistant viruses tested. In lab studies, it has been difficult to develop resistance to this drug. (This has been true for many other drugs only to later find that it can develop quite readily.)

Early formulations used up to 30 pills a day. A new capsule formulation has been created that allows for better absorption into the body. This new formulation should allow for twice-a-day dosing as well as fewer pills per day.

Tipranavir is also being studied together with ritonavir (Norvir), which greatly boosts its levels. It is hoped that this combination will be useful for people with protease inhibitor resistance. Its development was delayed due to the formulation problem and the fact that it was sold by its original owner, from Pharmacia & Upjohn to Boehringer Ingelheim. Wider access to the drug will probably occur in 2002.

BMS-232632: Bristol-Myers Squibb's first protease inhibitor is designed for once daily dosing. Lab studies suggest that it may remain sensitive to viruses resistant to other protease inhibitors, but it remains to be seen whether this will be the case in people.

One study shows that the drug is reasonably potent. About 60% of the participants achieved viral loads below 400 copies HIV RNA and 40% were below 50 copies after 16 weeks. The most common side effects seen so far are mild-to-moderate diarrhea and elevated bilirubin levels (a measure of liver function), which normalized after stopping or reducing the drug to the lowest dose studied.

New NNRTIs

Emivirine (Coactinon, MKC-442): The NNRTI furthest along in development is Triangle

Pharmaceuticals' emivirine. Studies show that it has the same resistance patterns as other NNRTIs, and most researchers believe it will not benefit people already resistant to other NNRTIs. Emivirine is dosed twice a day and is quite well tolerated. The most common side effects are gastrointestinal distress and rash, although at a much lower incidence than nevirapine (Viramune).

New NRTIs and NtRTIs

FTC (emtricitabine, Coviracil): Triangle Pharmaceuticals' FTC is very similar to 3TC (lamivudine, Epivir) and it has the same resistance profile. However, FTC appears to be more potent and is only dosed once a day. Like 3TC, FTC is also active against hepatitis B.

Tenofovir: Studies show that Gilead Sciences' tenofovir is significantly more potent against HIV than their other drug, adefovir. Tenofovir is also dosed once a day and lab studies suggest that it remains active against most NRTI-resistant viruses. Furthermore, studies show that there are few or no kidney side effects, a common problem with adefovir. Tenofovir is likely to be approved before the end of 2001. The drug is available free of charge under a limited expanded access program for people unable to make an effective combination without it. Call Project Inform's Hotline for more info.

Fusion Inhibitors

Pentafuside: One drug getting a lot of attention in the past year is pentafuside (T-20), being developed by Trimeris and Hoffman-La Roche. It belongs to a class of drugs called fusion inhibitors, which work by physically blocking HIV from attaching to CD4+ cells.

Studies show that T-20 is effective as third line therapy, even in people who are resistant to all current protease inhibitors. Getting a

long-lasting response, however, requires it to be paired with at least one other anti-HIV drug that the person still responds to. Pentafuside has to be given through injection under the skin (*subcutaneously*) twice a day.

The only significant side effects reported so far are problems at the injection site, ranging from minor discomfort to long-lasting bruises and sores. This can limit a person using the drug since there are only a few places where the injections can be given.

For information on how to participate in drug trials, call 1-800-TRIALS-A or go online at <http://hivinsite.ucsf.edu>.

Anti-HCV Therapies

Pegylated Interferon: The FDA recently approved Schering-Plough's pegylated interferon-alfa (Peg-Intron). This new formulation binds alfa-interferon to a chemical called *polyethylene glycol*, which makes it stay longer in the bloodstream than standard interferon-alfa.

The FDA approved using peg-interferon alone and not combined with ribavirin (Rebetol). One large study showed that Peg-Intron was about twice as effective in controlling HCV replication than standard interferon-alfa. However, more people developed mild bone marrow suppression.

The results of peg-interferon alone are comparable to those seen with standard HCV therapy (standard interferon-alfa and ribavirin, bundled as Rebetron). However, more recent results suggest that combining peg-interferon with ribavirin will be more effective. Dosed subcutaneously, peg-interferon is dosed only once a week while standard interferon-alfa is dosed three times. Another pegylated interferon-alfa (Pegasys) being developed by Hoffman-La Roche is expected to be approved before the end of 2001. This, too, will be dosed once a week.

prior to the availability of protease inhibitors and powerful three-drug combinations in 1996, it was common for people living with HIV and activists to talk about fighting for “The Cure.” Along with the new drugs came excited talk about the possibility of eradicating or completely eliminating HIV from the body. Together, the new drugs and the hope of eradication mistakenly led many people to believe that The Cure had either been achieved or was just around the corner. Activism for The Cure all but disappeared.

fighting for the cure

Over time, we learned more about the limits of currently available therapy, and each new scientific conference told us that the goal of “eradication” was several more years away. Best estimates today suggest that for most people, it would take more than 60 years of near-perfect suppression of HIV to completely eliminate the infection—a goal that few people see as attainable. In the meantime, people learned of the complex array of side effects that was the darker side of the new anti-HIV drugs, ranging from changes in body shape to heart disease.

The pendulum of expectations for The Cure rapidly swung from excessive hope to exaggerated despair, a cycle that has been repeated many times in the history of AIDS research and activism. With so much recent

attention devoted to drug side effects and development of resistance, the word “cure” seems to have fallen from our vocabulary.

Will science ever be able to “cure” HIV disease? Perhaps it all depends on the definition. If the only definition of “cure” requires eradicating all traces of HIV from the body, then most scientists would say a cure is unlikely in our current generation. We simply have no idea how to remove HIV from our cells once the virus’ genetic material becomes entangled with our own.

One alternative is to find a way to selectively kill all cells infected with HIV, but to date, these efforts have proven too toxic to use. A few researchers are still trying to pursue eradication with aggressive 4- and 5-drug therapies, and perhaps a few others hope that we will someday get a miracle drug that will safely root out every infected cell in the body. Most scientists, however, find these goals little more than wishful thinking. Several have argued since the earliest days of HIV that once the virus becomes integrated into our cells, we will never completely get rid of it. This is the sobering truth for a number of other viral illnesses as well.

Still, there is hope if we use another definition of cure. If we define “cure” as a treatment or strategy that will allow HIV-positive people to live out a normal lifespan, without a need for constant medication or threat of disease progression, then there may be several ways to achieve this goal. How do we know this is possible? Easy—because we have already seen it in nature.

A small percentage of people living with HIV have remained disease- and symptom-free now for more than two decades, without treatment and without suffering the loss of their immune systems. These are the so-

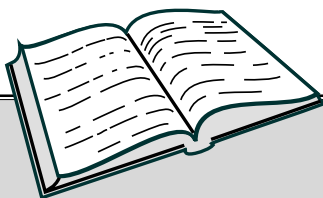
called “long-term non-progressors,” who make up somewhere around 3% of all HIV-positive people. While 3% sounds small, it might easily add up to 20,000-30,000 people in the US alone.

If we define “cure” as a treatment or strategy that will allow HIV-positive people to live out a normal lifespan, without a need for constant medication or threat of HIV disease progression, then there may be a number of possible ways to achieve this goal.

Earlier on, scientists thought such people might have a weakened form of the virus, but that has not proven to be the case. Nor has any study found some common, personal element among the people—the right diet, exercise, beliefs, etc. There’s evidence of unique genetic factors in some, but not all such people.

Scientists are gradually concluding that their experiences are due to a stronger and more effective kind of immune response against HIV itself. Why some people have it and others don’t is still a mystery, but if this is the mechanism that makes HIV disease all but irrelevant to their health, it gives us a profound clue about where future AIDS research must go. Other clues might exist in monkeys who can be infected by HIV but never become ill.

This pursuit of stronger HIV-specific immune responses is the goal behind some of the research into Structured Treatment Interruptions (see publications *Wise Words #7* and *PI Perspective 31* for more information). It is also the goal of recently



New Guidelines Available

Guide to the Clinical Care of Women with HIV is now available!

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www.hab.hrsa.gov

fighting for the cure

continued

renewed interest in using vaccines as a form of treatment for people already infected, called *therapeutic vaccination*.

The theory of using vaccines as therapy has been around for many years, but it's only now that we are beginning to see vaccines powerful enough to produce the desired effects. Improving the immune response against HIV itself is also the goal of many therapeutic strategies aimed at the immune system itself. Unfortunately, this field of research doesn't get nearly the amount of attention or funding as developing anti-HIV drugs.

One vision of future treatment strategy builds upon what is good about anti-HIV therapy, but then brings in new approaches to supplement and carry on for it. For example, a year's worth of strong antiviral treatment might be followed by a period off treatment coupled with the use of a therapeutic vaccine. The therapeutic vaccine might work best when viral load has first been suppressed by antiviral therapy. But the vaccine might have the additional advantage of causing long-term protection against the virus by the immune system itself. In contrast, the action of antiviral drugs stops rapidly once the drug is withdrawn.

Perhaps the immune response triggered by a potent vaccine might even be amplified by a drug like interleukin-2, which causes most types of CD4+ cells to aggressively multiply and appears to extend the life-span of these cells. If this effect occurs when viral levels are extremely low, and the anti-HIV immune response is being stimulated, it may be possible to trigger a condition

similar to that seen in long-term non-progressors.

This is but one possible scenario for upcoming research. But there is a growing sense that we have achieved all we can with anti-HIV approaches and that the next generation of research must seek to better harness the immune system. In effect, treatment will mean training the immune system to do a better job fighting HIV, just as we know it is capable of. If the outcome could be indefinitely long periods without a need for anti-HIV therapy, and thus without their side effects—perhaps boosted by periodic vaccinations—one reasonable definition of "The Cure" might be achieved.

How long will this take? It's just a guess, but perhaps within five to ten years we will know if since this strategy is taking us in the right direction. It may be that one or another of the elements of it—treatment interruption, therapeutic vaccination or direct immune based therapy—will prove useful, or that one or all will fail.

It's impossible to predict the future. Uncertainty is always present. But the general theory of modeling our search for a functional cure on the example of natural control of HIV infection is almost certainly a wise pursuit that seems far more likely to succeed than an endless series of slightly improved antiviral drugs.

Although a cure for HIV is not clearly in sight at the moment, we need to continue working toward it and remembering that it is, overall, our most important goal. And, as always, hope and positive thinking, along with well-targeted activism, will play a critical role in getting there.

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