

As we head into 2004, it's a great time to be talking about strategies—both strategies for health as well as political strategies for preserving the programs that serve the healthcare and treatment access needs of people living with HIV. This *PI Perspective* is a slight departure from the usual. Each article is a strategy discussion—examining big picture issues to consider when approaching various aspects of HIV treatment and health.

A Call to Action: Strategies for Effective Advocacy in Challenging Times

When President Bush took office almost three years ago, there was considerable anxiety about how people with HIV/AIDS would fare. His record on AIDS issues as governor of Texas was not impressive, and he spoke little about what he would do to fight the disease during his campaign.

Little did we know how bad it would be.

Looking back, there were clearly disappointments for people living with HIV under past administrations. Even President Clinton failed in many ways in the fight against AIDS. His funding requests for AIDS programs always fell far short of what was needed. The HIV immigration ban was codified under his watch. He failed to lift the ban on federal funding for needle exchange programs—something he now regrets.

However, our challenges have multiplied and dramatically changed under the Bush Administration. President Bush has not only shown little to no leadership in fighting the epidemic, but his administration has shown itself to be experts in “bait and switch” tactics. They promise productive action while

actively pursuing an agenda that will reverse gains made in the fight against HIV disease.

The President has shown no leadership in providing adequate funding for the programs people depend on. For the first time since the federal government started funding AIDS programs, President Bush proposed flat funding—resulting in no increases for HIV care and treatment programs in his first two budgets.

He also began promising increased commitment for certain programs but then failed to deliver. For example, he proposed a \$100 million increase for the AIDS Drug Assistance Program (ADAP) in the 2004 budget, but then failed to insist that Congress include that funding in its appropriations

bill. Meanwhile the ADAP crisis rolls on, with many states forced by lack of funding to implement limits to treatment access, including waiting lists.

Even the President's highly publicized promises on the global AIDS pandemic have proven to be little more than rhetoric. He has neglected to use his influence in Congress to make the funds he requested in his initiative a reality. In the meantime, millions are dying in developing countries for lack of access to treatment.

And the challenges run even deeper than these broken promises. The Bush Administration enacted tax cuts at the same time they are leading the country into war. These cuts cripple our country's ability to fund the safety net healthcare and support programs that serve low-income, vulnerable and senior Americans. In addition, the billions of dollars requested for the war in Iraq means that even less money is available for essential healthcare and other domestic programs. This administration appears to be leading the U.S. government out of the business of healthcare, particularly for poor and low-income people, and working toward dismantling or disabling programs like Medicaid and Medicare.

This year the Bush Administration proposed harmful changes to Medicaid, the largest payer of healthcare for people with HIV. The proposal—which fortunately

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stalled in controversy for this year—would have ended the program's entitlement status (meaning everyone who qualifies for the program receives services) and turned this vital safety net program into a block grant. A block grant will cap the federal money that funds Medicaid and, if the money ran out or if some new disease or epidemic struck, services would have to be limited and in some cases even eliminated.

The Administration also has made much of its support for a prescription drug benefit for Medicare, the insurance system that serves seniors and some disabled people. However, their proposed benefit would be of little help for disabled people, including those with AIDS, or seniors who rely on several and/or high cost drugs. Their proposal leaves a large gap in drug coverage that most people couldn't pay out of their own pockets.

President Bush's philosophy on the role of government is dangerous to people living with HIV. He has shown little interest in ensuring that vulnerable populations have access to essential healthcare. He is willing to break promises made to people living with HIV and vulnerable Americans by underfunding the Ryan White CARE Act and threatening the entitlement programs they rely on, such as Medicaid and Medicare.

Unfortunately, the new challenges posed by the Bush Administration come at a time when the AIDS policy advocacy movement is facing its own troubles. Funding for policy staff at AIDS organizations has started to dry up, resulting in far fewer people available to advocate with Congress and the Administration. There are also few staff

left to run grassroots networks necessary to ensure that those most affected by HIV get the information they need and communicate with their elected representatives. Individual activists not associated with an organization find it challenging to get support for their work.

However, recently, this has started to change for the better. Recognizing that the best chance of being effective is by working together, policy advocates began forming coalitions around specific challenges. These included defending HIV prevention programs, successfully defeating the President's Medicaid proposal, and fighting for adequate funding for HIV/AIDS internationally. Activist groups such as ACT UP/Philadelphia and HealthGAP are working closely with policy organizations on shared strategies and community mobilization.

Local and statewide coalitions are forming, such as the North Carolina AIDS Action Network in response to the ADAP crisis in their state and the lack of adequate funding for other essential programs. In some cases, individuals have started to fill in gaps on their own by forming their own groups.

One such example is the AIDS Treatment Activists Coalition's "SAVE ADAP" committee. This was established by people who experienced the ADAP crisis locally and wanted to create a grassroots campaign to get adequate funding from the federal government. As SAVE ADAP grew, policy advocates associated with organizations joined the effort. The result is a highly effective coalition of individuals and organizations working together for a common goal.

While all of these are positive changes, we will only be as successful as the collective efforts of everyone who gets involved. That's where you come in. Our battles right now are so important that everyone who is affected and/or infected must be a part of the solution. Our elected officials are affected by what they hear from their constituents with regards to HIV policy and funding. In other words, the best chance we have of securing adequate funding for AIDS programs is to make sure that elected officials hear the demands directly from their own constituents.

Similar to developing a strategy around

treatment decisions, ensuring effective policy requires a combination of strategies. Policy advocates and activists are changing their strategies to meet the new challenges. However, one of the most effective ways to make change is your involvement as a citizen advocate, a person living with HIV or who cares for someone with the disease or a community at risk. It will also be important for you to develop and use the best strategies to build relationships with the elected officials who make the decisions that affect your life.

Below you'll find some strategies that might help you take action:

Educate yourself:

Take some time to learn more about policy issues and what role you can play as an advocate. While you don't have to be an expert on the issues or the legislative process to be effective, it does help to understand the basics. For example, it is helpful to know what decisions are made at the federal, state, and local levels so that you can target your advocacy with the right elected officials. It's also a good idea to pick one or two issues that you want to focus on so that you don't get overwhelmed.

You can find many good resources on Project Inform's public policy resource guide at www.projectinform.org/org/presources.html. You will find a host of national, state, and local organizations that engage in AIDS advocacy on a variety of issues. Many of them have websites with fact sheets on key domestic and international policy issues. Several maintain grassroots networks, organize visits with legislators, and send action alerts. Remember, you can ask local, regional, and national community based organizations for assistance and tips on how to start developing a relationship with your elected officials.

Join an advocacy coalition:

If you have time to get more involved in advocacy, you might consider being part of a local, state, or national advocacy coalition. These groups go beyond communicating with their own elected representatives and design campaigns to achieve a particular policy goal and/or to mobilize grassroots

In Memory Of . . .

We dedicate this issue of the
PI Perspective to:

Joel Martinez
Carlton Hogan

Their memory lives on in the
work that lies ahead of us all.

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support. Even if you don't have experience with this type of advocacy, you bring expertise based on your own life experience.

Most groups are happy to provide training or mentorship in advocacy work. The most useful members in a coalition are those willing to learn and take on work. You might contact some of the organizations in your area on Project Inform's resource guide and ask what coalitions you can join.

While many national coalitions are composed of organizations, recently several new groups have formed with individuals as members. The AIDS Treatment Activists Coalition (ATAC) is a national coalition of new and longtime treatment activists that is working to advance the AIDS research agenda. You can find more information at www.atac-usa.org. SAVE ADAP is a committee of ATAC and is a national group of policy advocates and treatment activists focused on grassroots strategies to get adequate funding for ADAP. For more information about this group, email rclary@projectinform.org.

Another new coalition is the HIV Medicaid and Medicare Working Group, which originally came together to fight the harmful proposed Medicaid reforms. The coalition now advocates to protect and expand Medicaid and is also working to influence the debate on a prescription drug benefit for Medicare beneficiaries, focusing on the needs of people with AIDS. New advocates are always welcome to this group. For more information, contact Lei Chou at theaccess-project@aol.com.

Prepare for 2004 election:

One of the most important ways you can get involved in AIDS advocacy is by getting involved in the 2004 election. If we elect the right leaders, fighting for adequate funding and protecting safety net programs like Medicaid would be much easier. In November of 2004, not only will we decide who should lead the country for another four years, but all House Representatives and one-third of the Senate are up for re-election. This provides an excellent opportunity not only to elect new representatives but to educate candidates as they campaign.

One way you can get involved is by joining Project Inform's Treatment Action Network (TAN). In 2004, we will send TAN members a fact sheet with tips on getting involved in the election process, including a listing of resources and suggested questions to ask candidates when they come looking for your vote. To join TAN, go to <http://projinf.fauldhouse.com/tanlist/tanlist.php4>, or send an email to tan@projectinform.org with "subscribe" in the subject field.

The political environment has shifted dramatically in recent years. The programs that support people living with HIV and those at risk of infection are suffering. Scientific research is being affected by advisory boards driven by ideology rather than science. Healthcare programs are threatened by inadequate funding. Entitlement programs are increasingly under subtle and overt attack as the government pulls away from its "commitments". The advocacy groups acting on behalf of people living with HIV continue to work but with fewer resources, less access, and reduced influence.

Elected officials do listen to voting constituents. Your help and action are essential to making a difference in this environment. Whether it's writing to your elected representatives for the first time, challenging candidates about their vision for fighting AIDS, or joining a coalition and organizing your own community, you can be part of the solution.

After all, if not you ... then who? ⁿ

General Health Maintenance Strategies

Have you ever heard someone say, “I don’t want HIV to take over my life. My life is more than my HIV status?” Perhaps you’ve had similar feelings or felt overwhelmed with trying to manage your health. This article provides a different way of thinking about health than what many people may experience at a doctor’s office. The goal is to offer a framework for thinking about a big picture of well-being and provide a path for developing a long-term strategy to promote and maintain overall general health.

Studies have looked at similarities among people who are long-term survivors of HIV and other life-threatening conditions. People who have spontaneous remissions from serious conditions or improving outcomes over time are people who are most likely to proactively address health on all fronts. This doesn’t contradict findings that people who see an HIV-experienced doctor are more likely to live longer and healthier lives with HIV infection. Nor does it disregard that some people might not progress to AIDS as quickly due to genetic factors, the virulence of the virus they were initially infected with and other factors. Yes, sometimes outcomes in HIV infection might just come down to luck. In the biggest picture, however, people who proactively address health on all fronts have a tendency to do better than people who do not.

What is health?

What is health and how does someone address health on all fronts? Is it possible to come up with strategies to address health on all fronts without it becoming a full time job? Sometimes health crises arise and managing them can take over a large part of a person’s life. Part of the goal of a general health maintenance strategy, however, is finding the right balance. It’s not about health maintenance interfering with life—it’s about healthy living.

Project Inform ascribes to a model of health as it concerns the whole being—a biopsychosocial model of health. This includes physical (biological), mental (psychological), spiritual and social health and assumes that each of these areas of health impacts the others.

At the biological level, health is freedom

from disease or injury and any limitations these might impose. Merely avoiding disease; having healthy bones, skin and teeth; and staying out of harms way doesn’t reflect the complexity of our lives. We are more than the sum of our parts and we can be healthy without being perfect. As the definition of health expands to include how our whole body is functioning, a picture of health that includes a mind-body connection emerges. It doesn’t stop there. Health includes a state of mind, a peace and harmony with ourselves and our physical and social environments.

Developing a strategy: building a strong foundation

A general health maintenance strategy addresses the mind, body, spiritual and social connections of who we are and how we live. By viewing health this way, the idea of a general health maintenance strategy being something that overwhelms one’s life begins to fade away. Through both action and inaction people make choices daily about their health. You likely have general health strategies that you are implementing all the time. Taking a moment to look at what those strategies are, name them, refine them and explore ways to improve them is the very foundation of health.

No single strategy works best for everyone. Rather, the best answers are those that fit you best. There are resources, tools and some basic principals to consider.

A good strategy includes goals you can achieve, is tailored to your needs, fits into your life and makes you feel better as you implement it. That doesn’t mean that your strategy is failing if you come down with the common cold or if you have a bad day. A general health strategy is not something one achieves or completes, it’s an ongoing process that needs to be revisited periodically and adjusted as your life changes—as you change.

Biological health

Your basic biological health is something that a doctor can help you to understand and develop tailored strategies for promoting and improving. While people living with HIV often see a doctor four times each year, many times both HIV specialists and patients can forget about basic health screening and maintenance. This includes physical examinations, vaccinations, other preventive health measures as needed and age appropriate health screening.

For information on what is looked for in a routine physical examination, what’s meant by age appropriate screening, general recommendations on vaccinations and a list of special health considerations, call the Project Inform hotline. Also available is information on standard tests, vaccines and issues to deal with during a first visit to a doctor after finding out that you’re living with HIV.

Taking care of your biological health includes more than seeing a doctor. The following are a few examples:

Nutrition: The body needs nutrients in order to work effectively. Often when people are really hungry they’ll get a headache, feel dizzy or may find themselves in a bad mood. How often and what do you typically eat in a day? What does good nutrition mean to you and what can you do to improve your nutrition? Realistic nutritional goals that fit with your life and lifestyle are key to success. What this often means is incremental improvements. For example, if a normal breakfast for you is a cup of coffee and a pastry on your way out the door, is it possible also to add a glass of juice? While it’s great to consult with a nutritionist (especially one who specializes in HIV), there are probably

ways you can improve on your general nutrition now. For some this means eating more, for others eating less and for others it's about eating different foods. For more information on these publications, *Nutrition and Weight Maintenance* and *Food Safety*, call the Project Inform hotline.

Exercise: A few pounds of muscle mass (lean body mass) can make a difference in whether someone recovers from a severe life-threatening infection. There are many reasons why exercise is good for us, from helping muscles and bones remain strong to improving the function of our heart and lungs. Are there ways you can improve how you exercise or the amount of exercise you

People who have spontaneous remissions from serious conditions or improving outcomes over time are people who are most likely to proactively address health on all fronts.

get each day? Some people love to go to the gym and workout; others wouldn't set foot in a gym if someone paid them. If you typically don't set aside any time for exercise, consider taking a walk for twenty minutes each morning and/or at the end of the day. Perhaps you'll never go to the gym, but you may enjoy going for a hike, bike riding or simply taking the stairs in your building. What can you do to improve the kind or quality of exercise you get each day?

Sleep: When we sleep, our bodies heal. In general it's recommended that people get eight hours of sleep each night. The amount of sleep needed differs to some degree between individuals and can also vary based on other things going on in a person's life. When someone is depressed they might sleep more or have trouble sleeping. Often when someone is fighting an infection their body demands more rest. Do you get enough sleep each night? If you are sleeping too much it is important to figure out why—are you depressed, fighting an infec-

tion, do you have low red blood cell counts (anemia)? If you are sleeping too little it's also important to figure out why—are you depressed, drinking coffee or other caffeinated beverages too late at night, or is something else going on? If you find your life is just too busy to find time for sleep, strive for incremental improvements. If you're sleeping only five hours a night, is it possible to make time for five and a half or six hours?

Relax! Chemicals produced by the body when people experience stress can weaken the immune system, leaving cells more susceptible to infection and crippling the ability of the immune system to rebuild itself. It's virtually impossible to completely avoid stress, but efforts to minimize and manage stress are important to our physical and mental health. Can you identify things that cause you stress that you could eliminate from your life? When the things that cause you stress are unavoidable, are there things you can do to minimize or manage that stress better? Some find that exercise decreases stress levels. Getting a massage, taking a hot tub, talking with friends, laughing, getting out of the house and going to a movie, spending time with people you love, reading a good book, finding a good support group and/or finding a good therapist are all possible ways to decrease and better manage stress. Keep trying different methods until you find what works best for you and then find ways to incorporate it into a daily, weekly or monthly routine.

Psychological (mental) health

Each of the issues discussed above, nutrition, exercise, rest and relaxation can affect mental health. By highlighting this, perhaps it's easier to see how health is more than just healthy bones, teeth and skin, and how it is that our physical, social, spiritual and mental health are connected. It's great to seek counsel and guidance from a therapist who is experienced in dealing with HIV issues. General mental health ranges from self esteem to addiction issues, from your emotional outlook to the relationships you have with other people. The paths to examining these issues and developing strategies that are right for each individual are varied.

Addiction: Is addiction a mental or a

biological health issue? Some people are genetically predisposed to alcoholism and other forms of addiction, because of the way that their body processes (or doesn't process) certain chemicals. Regardless of genetic predisposition to alcohol addiction, there is evidence of chemical changes in the brain that leaves people alcohol-dependent after consuming alcohol for a long period of time over days, months and/or years. Addiction comes in many forms. Alcohol and drug addiction are perhaps the most commonly spoken of. There are also people with addiction to food, sex, the internet, video games, gambling, nicotine, shopping and the list goes on and on. Whatever the case, anyone with an addiction who is speaking candidly about it can tell you how the addiction interferes with their life, their relationships and their health. Depending on the addiction there may be medical interventions, twelve-step programs, one-on-one therapy options, inpatient programs and harm reduction programs to explore. In many instances the first step is recognizing that you have an addiction and then seeking support, guidance and expert advice on plotting a course of action.

Depression: Studies show that the most common psychiatric diagnosis among people living with HIV is depression. As in the general population, some studies suggest that it is most common among women. Depression can be caused by chemical imbalances and it can be a side effect of some medications used to treat HIV and related conditions. Depression can be caused by HIV infection itself, HIV-related conditions and even changes in the body (such as menopause and/or decreases in testosterone production). The key to successful treatment of depression is identifying the possible causes. Another step is recognizing depression in the first place. When someone is depressed they may experience extreme fatigue, sleep disturbances, changes in appetite, and generally lose an interest and enjoyment in participating in life. Some of these conditions are interrelated as extreme fatigue can cause depression, sleep disturbances can also cause fatigue and depression, not eating well can impact mental and

biological health and be associated with fatigue. Especially when you're depressed, finding the strength to pay attention to sleep, nutrition and exercise is important to avoiding a cycle of ever-worsening problems. If you experience depression, seeking strategies to deal with it is critical. For some this might include anti-depressant medication and for others this might simply involve spending time with people who they love or doing things they enjoy.

Self esteem and emotional outlook: Another common theme that unites many people who are long-term survivors with HIV disease is that they have a philosophy of well-being. Often they believe that what they are doing today will make a difference for their tomorrow. They have a hopeful approach to the future. The road each of us must travel to believe in ourselves and the value of our voices and choices is unique. For some, a strategy to improve self esteem and emotional outlook might include seeking a therapist. For others it might include spiritual soul searching. For still others it might include going to the gym to improve body image. For those who feel like they

General mental health ranges from self esteem to addiction issues, from your emotional outlook to the relationships you have with other people.

have a positive outlook and good self esteem, what are you doing to maintain that? A philosophy of well-being doesn't mean that when you feel bad you ignore it or that when you're angry, depressed or upset that you're supposed to think positively. It's about experiencing those feelings, working through them and finding a way to embrace them as part of the picture, but not the whole picture.

Spiritual health

Defining what spirituality means to most people is nearly impossible because it means

something different to every person. For those who embrace forms of spirituality in their lives, most would contend a discussion of health without a discussion of spirituality is incomplete. Others, particularly those who have had negative feelings about spirituality and religion may be offended by any discussion.

Each person's path to exploring spiritual health is unique and very personal. Spirituality is not necessarily religion. A few examples: for some spirituality is the religion they were raised with, for others spirituality is founded on a harmony with nature, a notion of a Higher Power, The Goddess and/or a balance with the energies of the universe. Spiritual health involves exploring your spiritual beliefs and examining your life, your actions and inactions, accordingly. What matters isn't what your personal spiritual choices are, but that you're living your life consistent with your beliefs.

Social health

Social health is not only having healthy personal relationships with others, but also includes one's relationship to their communities and the health of the community.

While some people enjoy and are energized by social and group activities, others are not. Social health doesn't always mean participating in large group activities or even attending large-scale social events. It does mean, however, cultivating deep, rewarding and meaningful relationships and includes contributing to and participating in community. Social health is about giving and receiving support from community and loved ones.

The paths to promoting and maintaining social health are varied. Sometimes it starts with simply sitting down and thinking about personal relationships, identifying which relationships are most meaningful and why. Are you happy with your friendships and what might you do to strengthen those you have and/or cultivate new ones? Are you being the kind of friend you want to be and do you have the kinds of people in your life who support you? What kinds of things can you do to participate in community? Volunteer to help teach children to read? Write a letter

to an elected official advocating for an issue of importance to your community? Help your neighbor with his or her groceries?

Medications treat specific biologic conditions, health is an experience and healing is a process. Medications have their place in an overall strategy for health, but they are merely one piece of a much larger puzzle.

Discussion

Developing a strategy for good general health provides a strong foundation upon which to build strategies for dealing with HIV disease. There is a difference between medications, health and healing. Medications treat specific biologic conditions, health is an experience and healing is a process. Medications have their place in an overall strategy for health, but they are merely one piece of a much larger puzzle. ⁿ

Starting Anti-HIV Therapy

Deciding when to start anti-HIV therapy and what treatments to start with can leave many people feeling overwhelmed with choices. The discussion following, however, will demonstrate that the choices may be fewer and simpler than they appear at first. Charting your course of therapy options up front, outlining what therapies you will start with when you're ready and what you will switch to if that option doesn't work out, is the hallmark of long-term planning. You can then proceed to the next combination with confidence rather than being overwhelmed by the fact that your first choice didn't work out as you had expected.

Most strategic decision-making processes begin by formulating a list of questions to con-

sider. Some of the answers can only come from you; others your doctor can help answer. Several important questions about starting anti-HIV therapy are included here.

When to start

Periodically the Federal Guidelines committee (comprised of researchers, doctors, people living with HIV and their advocates) updates a set of guidelines for the use of anti-HIV medications. Often referred to as the "Federal Guidelines" or simply the "Guidelines," the excerpts presented on page 8 are for adults and adolescents starting anti-HIV treatment.

Starting anti-HIV therapy in women and women who are pregnant

The basic Guidelines for when to start therapy are largely the same for women who are pregnant or trying to get pregnant as for other adults. If a woman is pregnant and has a low CD4+ cell count and a high viral load, she must make decisions about protecting her health as well as the health of her developing baby. Some doctors recommend that women wait to begin treatment until the second trimester (13th week of pregnancy). The first trimester (first 12 weeks of pregnancy) is when the baby's major organs are developing and the potential for birth defects from medications are most likely to occur during this period. Some anti-HIV

medications should NOT be taken during pregnancy. For a more thorough discussion, read Project Inform's publication, *Pregnancy and HIV*.

Some anti-HIV drugs interact with oral contraceptives (i.e. The Pill). More detailed information on these interactions may be found in Project Inform's publication, *Drug Interactions*. It may be necessary to adjust the dose of the contraceptives or use other methods for birth control.

What is the best combination for people starting anti-HIV therapy?

The question of what combination of anti-HIV drugs a person should use as first line therapy can appear confusing at first. There are, however, only a few factors to consider and these effectively narrow the range of choices for first line therapy. These include:

- the potency of the combination,
- the ease of use and number of pills, and
- the potential for short- and long-term side effects.

If you have determined that you are ready to start anti-HIV therapy, there are some clear guidelines that can help you make an informed decision about which medications to use.

Remember the goals of anti-HIV therapy

An effective combination should lower your viral load as low as possible (preferably to undetectable), and increase your CD4+ cell count, without causing debilitating side effects or negatively affecting your quality of life. It should also be easy enough to take, given your schedule, that you are able to take every dose as prescribed (i.e. adhere well). The issue of adherence to medications cannot be stressed enough. A number of different studies have found that an inability to maintain a high level of adherence is the most common reason that a combination stops working. Project Inform's publication, *Adherence: Keeping Up with Your Meds*, can help you prepare for and maintain good adherence.

There are four different classes of anti-HIV drugs approved for use. These are:

- 1 Nucleoside Analog Reverse Transcriptase Inhibitors (NRTIs) and Nucleotide Analog Reverse Transcriptase Inhibitors (NtRTIs)
- 2 Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Questions to help you build your HIV treatment strategy

- What is your current CD4+ cell count?
- What is your current viral load?
- How is your general health?
- Are you ready and willing to commit to using therapy?
- Are you aware of how therapy may impact your quality of life?
- Are you aware of the potential side effects of the therapies?
- Do you know which therapies may preserve more options for later?

Federal Guidelines' Recommendations for When to Start Anti HIV Therapy

Symptoms	CD4+ Cell Count	Viral Load (Plasma HIV RNA)	Recommendation
Severe symptoms, AIDS defining illnesses	Can be any number	Can be any number	Strong recommendation to treat with anti-HIV therapy.
Either severe symptoms or no symptoms at all	Less than 200	Can be any number	Strong recommendation to treat with anti-HIV therapy.
No symptoms	More than 200, but less than 350	Can be any number	Treatment should be offered, though some controversy exists.
No symptoms	350 or more	More than 55,000	Although up to 30% of people in this category may have disease progression if left untreated, there are not yet data to prove conclusively that treating now is beneficial in the long term.
No symptoms or acute retroviral syndrome	350 or more	Less than 55,000	Most would not recommend anti-HIV therapy, as the risk of progression (15%) is low.
No symptoms	More than 200	Can be any number—can go as high as millions of copies	Primary HIV Infection (detectable viral load, but HIV antibodies are negative or indeterminate): Treatment may be offered, but benefits of treating now are still theoretical—no data exist to prove long term clinical benefit

3 Protease Inhibitors, sometimes called PIs; and,

4 Entry Inhibitors

The November 2003 Federal Guidelines list the following two combinations as “preferred” first line regimens, because they are believed to have good potency and are easy to take:

- Combivir* + efavirenz; and
- Combivir** + Kaletra.

[*d4T + 3TC or tenofovir + 3TC may be used in place of Combivir.]

[**d4T + 3TC may be used in place of Combivir.]

The Guidelines also list more than a dozen other alternative combinations that may be less potent, carry a somewhat higher side effect profile, have to be taken more often or that require taking more pills.

Not all “alternative” combinations, however, are equal. In fact, several are likely to be better than others and may be nearly equal to the “preferred” regimens. These include using:

- nevirapine instead of efavirenz
- FTC instead of 3TC
- atazanavir instead of Kaletra
- other ritonavir-boosted protease inhibitors instead of Kaletra.

Nucleoside analog reverse transcriptase inhibitors (NRTIs) and Nucleotide analog reverse transcriptase inhibitors (NtRTIs)

NRTIs are almost always used as part of anti-HIV regimens. Usually two NRTIs are combined with another class of drugs. Sometimes three NRTIs are used together as a complete first line combination. Although there are a number of different drugs in this class, there are few combinations that are considered for first line treatment. This is because most of the drugs other than AZT, 3TC, d4T and tenofovir are either seen as less potent, have too many side effects or are difficult to use. Even with d4T, there are growing concerns about its potential for causing long-term side effects.

FTC is a newly approved drug, likely to be interchangeable with 3TC. Tenofovir is also a newer drug. Since it works against most NRTI resistant virus, some recommend saving it for use in second and third line combinations.

Trizivir (AZT+3TC+ABV) is the only approved triple nucleoside combination available in one pill. This combination can be taken alone, without combining it with drugs of any other class. There is concern, however, that Trizivir may not be as potent for first line therapy as other combinations, particularly in people whose viral load is very high (more than 100,000). Since future combinations may depend on at least one or two of these three drugs in order to work effectively, using Trizivir as first line therapy can significantly impact future available options. For these reasons, Trizivir may only be an appropriate first line option in situations where a person requires an extremely simple regimen or cannot tolerate NNRTIs or PIs.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

As part of first-line therapy, NNRTIs are invariably used in combination with two NRTI drugs. Efavirenz-based combinations have consistently proven both potent and durable when compared to a number of other combinations. Efavirenz has been selected by the Federal Guidelines panel as a preferred drug for first line therapy.

While the Guidelines recommend efavirenz over nevirapine, there are occasions where nevirapine may be a more attractive

choice. This is particularly true for people who wish to save protease inhibitors for later, but who are concerned about the neurological (brain-related) side effects of efavirenz. Pregnant women and women trying to get pregnant should avoid efavirenz and may consider nevirapine a better option. Women in general shouldn't feel a particular benefit to choosing nevirapine over efavirenz, but women who are pregnant or trying to conceive need to be aware of the risks of efavirenz use during pregnancy.

All of the NNRTIs are highly cross resistant with one another, meaning that when the virus becomes resistant to one it will likely be resistant to the others, making them less useful. Of the three drugs in this class, delavirdine is used least often. This is because it must be taken three times per day and has interactions with a number of other medications.

Protease Inhibitors (PIs)

Kaletra (lopinavir+ritonavir) was likely selected as a preferred drug as it is a potent drug and simple to take. Atazanavir also appears to be potent, when boosted with ritonavir. It has some of the lowest potential for side effects of all the PIs and as a once-a-day drug it is easy to use.

Other protease inhibitor combinations may be used as first line therapy, but most require that a low dose of ritonavir be added as a booster so that they become more potent and are able to be taken less frequently and at lower doses. Aside from Kaletra, other ritonavir-boosted PIs have not been well studied for first line therapy use.

Entry inhibitors (EIs)

Although enfuvirtide has many positive attributes, it is not able to be taken in pill form and has to be given through injection. For this reason, it is unlikely that enfuvirtide will ever be considered a desirable first line therapy and it is currently approved for use only in situations where other combinations have already failed.

What to start first: NNRTIs, protease inhibitors, or neither?

Researchers have reported on dozens of different first line treatment regimens, but no large study has been completed that demonstrates which is best to start with. We know that when viral load remains under 50 for at least one year on therapy, virus will usually remain suppressed for *at least* another two years, assuming good adherence. Combinations containing efavirenz or Kaletra have been most likely to achieve this result in studies.

Some data show that when a person starts anti-HIV therapy using a protease

Drug Identification Chart

Abbreviation/ Nickname	Generic Name	Brand Name
Nucleoside Analog Reverse Transcriptase Inhibitors (NRTIs) & Nucleotide Analog Reverse Transcriptase Inhibitors (NtRTIs)		
ABV	abacavir	Ziagen
AZT	zidovudine	Retrovir
ddC	zalcitabine	Hivid
ddl	didanosine	Videx
ddl EC	didanosine enteric-coated	Videx EC
d4T	stavudine	Zerit
d4T XR	stavudine extended release	Zerit XR
FTC	emtricitabine	Emtriva
3TC	lamivudine	Epivir
TNV	tenofovir-disoproxil fumarate	Viread
NRTIs bundled together		
CBV	AZT + 3TC	Combivir
TZV	AZT + 3TC + abacavir	Trizivir
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
DLV	delavirdine	Rescriptor
EFV	efavirenz	Sustiva
NVP	nevirapine	Viramune
Protease inhibitors (PIs)		
APV	amprenavir	Agenerase
ATV	atazanavir	Reyataz
FPV	fosamprenavir	Lexiva
IDV	indinavir	Crixivan
LPV	lopinavir + ritonavir	Kaletra
NFV	nelfinavir	Viracept
RTV	ritonavir	Norvir
SQV-HG	saquinavir-hard gel capsule	Invirase
SQV-SG	saquinavir-soft gel capsule	Fortovase
Entry inhibitors		
T20	enfuvirtide	Fuzeon

inhibitor, they will likely be able to use efavirenz successfully as second line therapy. There are less data on the reverse scenario. There are even fewer data showing the long-term therapy implications of starting a combination with three NRTIs together, like Trizivir. Developing a longer-term treatment strategy requires weighing the theoretical risks and benefits.

When a person's virus develops a high level of resistance to one drug in a specific class, it will generally have at least some resistance to the other drugs in that class. This is called cross resistance. When resistance occurs, it causes the drug to be less potent. Thus, even with more than twenty approved drugs, it is only possible to come

*Whichever choice you make,
it's probably wisest to have a good fall
back strategy if your
first combination doesn't work
as well as you hoped.*

up with two or possibly three highly potent combinations in a row.

Some believe that the best first line strategy is to take whatever is most potent. Studies so far indicate that the most powerful and durable effects come from a person's first combination. The longer a person can stay on his or her first combination without significant side effects or resistance developing, the better. If a person can go five years or longer, the hope is that more new drugs will have been approved in the meantime, which will allow a greater number of second and third line therapy options. Kaletra is considered the most potent and durable first line anti-HIV medication.

Others feel that saving potent and longer lasting medications for second line therapy is the better strategy. Starting with a combination containing an NNRTI or only NRTIs is likely to work well for many people and spares protease inhibitors for later. It is hoped that the NNRTI and NRTIs will have fewer long-term side effects. The theory has

merit, but there are no studies to prove that this is the superior long-term strategy.

Whichever choice you make, it's probably wisest to have a good fall back strategy if your first combination doesn't work as well as you hoped. Decide in advance what your definition of treatment failure is and what your next combination will be.

Your doctor may have strong opinions about when to start therapy or which combination they think will be best for you. Your opinion and your concerns count too. Share them with your doctor so that he or she can help you build the best treatment strategy for you. Project Inform's publication, *Building a Cooperative Doctor/Patient Relationship*, offers a number of tips for building a relationship with your doctor that works best for you.

Because it is your life and your body that will be affected, only you can ultimately decide how you wish to balance the need to keep your virus in control with potential risks for HIV disease progression and side effects of medications. Remember to ask questions: of yourself, your doctor, other people living with HIV and information sources like Project Inform. Take your time, be prepared and then enjoy life to the fullest, knowing you have made the best decision you possible could have. ⁿ

The Basic Message

- Learn about HIV testing options and choose one that fits your needs! Be sure your privacy is protected!
- If you're positive, don't panic. If you make your health a priority, chances are you will be reasonably healthy for many years.
- Learn about your healthcare options and local support services.
- Get a complete physical and blood tests for CD4+ cell count and HIV level. Repeat quarterly and watch for trends. Women should get GYN exams and Pap tests every six months, more often if abnormal.
- Work with a doctor to develop a long-term strategy for managing HIV disease.
- If the CD4+ cell count is below 350 or falling rapidly, consider starting anti-HIV therapy. Test at least twice before taking action.
- If anti-HIV therapy fails to reduce your HIV level below the "limit of detection" or below 5,000 copies within 3–6 months, consider a different or more aggressive therapy.
- If the CD4+ count trend stays below 300, consider treatment for preventing PCP. If it stays below 200, start treatment for preventing PCP (if you haven't already done so) and reconsider anti-HIV therapy if not on one. Learn about drug interactions and preventive treatments for opportunistic infections.
- If you started preventive therapies and your CD4+ cell count rises in response to anti-HIV therapy, ask your doctor whether it might be safe to stop certain preventive therapies.
- If your CD4+ cell count stays below 75, consider more frequent blood work—perhaps monthly. Consider therapies for preventing MAC/MAI and CMV.
- Regularly seek support for your personal, spiritual and emotional needs. It takes more than medicines to keep you well.

Opportunistic Infection Strategy

The human immunodeficiency virus (HIV) infects immune cells, impairing their function and eventually destroying cells over time. This gradually weakens the immune system and the body loses the ability to fight disease. While HIV is the culprit, most people who die of AIDS do not die of HIV, per se, but from the numerous infections that the body can no longer control due to the collapse of the immune system. Relatively common infections, which may cause little or no harm in a healthy person, take the opportunity provided by weakened immune defenses to cause disease. This is why they are called opportunistic infections (OIs).

A strategy to deal with OIs is an important part of a comprehensive, long-term strategy for

managing HIV. The basics of an OI strategy include:

- understanding what an OI is,
- preventing infections by organisms that cause OIs,
- using appropriate preventive treatment (sometimes called prophylaxis) against OIs,
- treating infections as they occur and using appropriate maintenance therapy to prevent recurrence of OIs.

What is an opportunistic infection?

As noted above, an opportunistic infection is any infection or condition that takes the opportunity of a weakened immune system to cause disease. The Center for Disease Control (CDC) has developed a list of serious and life-threatening diseases, listed in the chart on pages 12–13, that in the presence of HIV infection are called Acquired Immune Deficiency Syndrome (AIDS)-defining OIs. In the presence of HIV infection, any one of these conditions results in a diagnosis of AIDS. Measures of immune health suggesting that a person is at serious risk for developing life-threatening conditions (i.e. when CD4+ cell counts are below 200 or CD4 percentages less than 14%), in the presence of HIV infection, also results in an AIDS diagnosis.

OIs can be relatively common infec-

tions, such as genital herpes. Not everyone with HIV who is having a herpes outbreak is deemed to have AIDS, however. To the contrary, herpes is deemed an opportunistic infection when it takes advantage of a severely weakened immune state to become more aggressive, persistent and less responsive to treatment. Therefore, having HIV and genital herpes isn't automatically considered AIDS, but having HIV and a herpes outbreak that persists for a month despite treatment is considered AIDS.

While there is a discrete list of AIDS-defining OIs, it's important to note that virtually any condition or disease can become opportunistic in the face of a weakened immune system. People living with HIV are not the only people at risk for OIs. Anyone with a severely weakened immune system, regardless of the cause, is at risk for OIs. For an OI to be the cause for an AIDS diagnosis, however, it must be one of the CDC AIDS-defining diseases occurring in the presence of HIV infection. People with HIV can get any number of worsening conditions that behave opportunistically and not all are on the CDC's list. Occasionally the CDC revisits this list, and over the years there have been several expansions. It's still possible, however, for people with HIV to develop opportunistic infections that are not on that list. Hepatitis C-associated disease is not AIDS-defining, though increas-

ingly data show that people with HIV are at higher risk for more aggressive HCV-related liver disease. Most importantly virtually any condition or disease can behave in an opportunistic manner and the first line of defense is prevention.

Preventing infections in the first place

OIs are often caused by infections and some of them are preventable. For people never exposed to herpes, for example, practicing safer sex reduces the risk of genital herpes infection. If you are not infected with herpes simplex virus, there is no worry of herpes becoming opportunistic or life threatening. Project Inform has a publication called *Sex and Prevention Concerns for Positive People*. This publication contains information on how you can prevent infections by many of the organisms that can cause opportunistic infections. Some of these are sexually transmitted, and you can reduce your risk of infection by practicing safer sex. Others are preventable with vaccines. Still others can be avoided through safer food handling and preparation and/or by being aware of and avoiding (when possible) disease-causing organisms. This might include being aware of diseases that birds carry and not handling birds, even those kept as pets. It may also in-

PCP remains the leading cause of death of people with AIDS in the United States and is largely preventable.

clude using gloves when changing cat litter boxes, or even better, having someone else deal with the cat litter box and/or keeping only indoor cats.

Recently there have been outbreaks of drug-resistant staph skin infections. The infection can be spread through casual contact, and some speculate that in urban areas staph infections may be spread through something as simple as sharing equipment at the gym. Because the organisms are drug resistant, treatment might require intrave-

CDC AIDS Defining OIs

Opportunistic Infections	What causes it, things to know
Candidiasis (thrush) of the throat (esophagus, trachea) or lungs	Fungal infection. Most people have candida in their body; generally the body keeps it under control. Sugars (including alcohol) are food for candida. There may be ways to adjust diet to help prevent candida from becoming problematic.
Cervical cancer, invasive and/or recurrent	Cancer/Viral infection. Often caused by human papilloma virus (HPV), the virus that causes anal and genital warts. Safer sex might help to reduce the risk of HPV infection, but many women are infected with HPV, even though they may have never had genital warts. Regular GYN exams are important for monitoring for cervical cancer.
Coccidioidomycosis occurring outside the lungs and/or throughout the body	Fungal infection: Found in soil in the Southwestern US. Likely transmitted airborne/windborne, in dust/dirt, but not from person-to-person. A fairly large outbreak followed the Northridge earthquake in Southern California and was likely do to dirt/dust in the air following the quake. Most problematic in Kern and Tulare counties and San Joaquin Valley in California.
Cryptococcosis, occurring outside the lungs	Fungal infection. Found in soil, associated with bird droppings in the soil. Transmitted likely airborne/windborne, not person-to-person. Avoid handling birds, even as pets, and avoid areas with lots of bird droppings.
Cryptosporidiosis with diarrhea persisting longer than on month	Parasite. Found in feces of many species, may contaminate drinking water. Prevent infection from humans by avoiding feces (diapers, sex with direct oral/anal contact.) Often exposure from animals occurs from fecal contamination of water. Avoid drinking from rivers/streams. When appropriate, drink bottled water and or use water filters on tap water capable of filtering our crypto oocysts.
Cytomegalovirus (CMV) disease of an organ other than liver, spleen, or lymph nodes, including CMV retinitis (in the eye)	Viral infection. Most (50-85%) people likely infected already. CMV is transmitted through close contact (sex, saliva, urine and other body fluids) and mother-to-child (during pregnancy and breast feeding.) If not infected, safer sex may help prevent infection.
Herpes simplex virus (HSV) outbreak persisting longer than 1 month; or HSV infections in the lungs or throat	Viral infection. Genital herpes transmitted sexually. Safer sex can decrease risk of infection. Oral to genital spread of herpes possible.
Histoplasmosis occurring outside the lungs and/or throughout the body	Fungal infection. Found in soil in Eastern and Central US. Grows in soil contaminated with bat or bird droppings. Becomes airborne when contaminated soil is disturbed—such as might be in the case in cave exploration (spelunking). Not transmitted person-to-person.
HIV encephalopathy (also called “HIV dementia” or “AIDS dementia”)	Viral infection. Caused by HIV itself. Possibly preventable with the use of anti-HIV medications that are known to cross the blood-brain barrier.
HIV wasting syndrome	Viral infection. Caused by HIV, inflammation and/or a consequence of OIs. Possibly preventable, to some degree, with nutrition and dietary intervention.
Isosporiasis with diarrhea persisting greater than one month	Parasite. Found in feces, may contaminate food or drinking water. Most common in tropical and subtropical region in the US. Prevent infection from humans by avoiding feces (diapers, sex with direct oral/anal contact.) Often exposure from animals occurs from fecal contamination of water. Avoid drinking from rivers/streams. When appropriate, drink bottled water or use water filters on tap water. Cook food thoroughly.
Kaposi’s sarcoma (KS)	Cancer/viral infection: Caused by human herpes virus 8 (also called HHV8 or KSHV.) Mode of transmission unknown, but believed to be transmitted through close sexual contact and from mother-to-child. Practicing safer sex might help to avoid HHV8 infection.
Lymphoma of the brain	Cancer. Unknown cause but Epstein Barr Virus (EBV) may play role in risk for lymphoma.
Lymphoma – Burkitt or non-Burkitt type	Cancer. Unknown cause.
Lymphoma – immunoblastic type	Cancer. Unknown cause.
	Cancer. Unknown cause.

Opportunistic Infections	What causes it, things to know
M. tuberculosis (TB) disease	Bacterial infection. Airborne infection, can be transmitted person-to-person via close contact, kissing, saliva. Transmission may occur very casually, especially in closed in spaces (e.g. low income hotel/housing facilities, shelters, other institutionalized settings with close quarter living.)
Mycobacterium avium complex (MAC) or M. kansasii disease occurring outside the lungs and/or throughout the body	Bacterial infection. Found everywhere in the environment—soil, food, animals. Avoid handling soil, practice careful food handling and preparation. Difficult, perhaps impossible, to prevent exposure to this bacteria as it's in so many places in our environment.
Mycobacterium disease of unknown type occurring outside the lungs and/or throughout the body	Bacterial infections. Likely found in soil, food, animals. May be difficult to prevent exposure.
Pneumocystis carinii pneumonia (PCP)	Likely caused by a fungus <i>Pneumocystis jiroveci</i> , found in many places in the environment. Likely not preventable except with therapy when risk for OI increases.
Pneumonia, current	Bacterial infections. Likely caused by blood exposure to bacteria. Most common in injection drug users. May be airborne and exposure may occur through casual contact/saliva.
Progressive multifocal leukoencephalopathy (PML)	Viral infection. Caused by the JC virus. Most people likely infected with the JC virus. Causes disease in about 1% of people with HIV. Cause for disease in some and not others not well understood. Possibly transmitted through sexual contact, mother-to-child, etc.
Salmonella septicemia, recurrent	Parasite. Some forms likely transmitted through contaminated poultry chicken. Also found in water, soil, kitchen surfaces, animal feces, raw eggs, raw meat (particularly chicken/poultry, pig and fish) and on certain animals (reptiles.)
Toxoplasmosis of the brain in people older than one month of age	Parasite. Cats and birds are major source of infection. Indoor cats less of risk, but toxo-negative cats that go outside can carry it back in. Cat feces should be avoided (use gloves to change litter box.) Avoid handling birds. Toxo also found in undercooked meats.

nous therapy. Doing something as simple as putting a towel down on shared gym equipment before use, and not using that towel to wipe sweat from your body, might help to prevent staph infection.

Preventing exposure to organisms is a great way to reduce your risk of particular OIs. In some cases, however, the organisms that can cause OIs are in our environment, unavoidable and/or exposures may have already occurred. People living with HIV should receive screening for many OIs upon first finding out that they are HIV-positive, as part of early lab screenings. This allows people to know, in some instances, if they are already exposed to an organism and enables people to learn about prevention for infections they don't already have. For more information on what's generally looked for on these lab tests, call the Project Inform hotline. In the case of *Pneumocystis carinii*

pneumonia (PCP), however, it's simply not known how the organism is spread and it is assumed that most people are infected with it. In that case, preventive treatment is routinely used as the immune system weakens and the risk for PCP increases. PCP remains the leading cause of death of people with AIDS in the United States and is largely preventable.

Preventive treatment for OIs

OIs are generally not a problem for people whose CD4+ cell counts remain stable above 200. It is extremely rare for a person living with HIV to die of AIDS when CD4+ cell counts are above 200. As CD4+ cell counts decline, however, a person's risk for developing opportunistic conditions increases. Perhaps the best strategy for preventing OIs is to not let CD4+ cell counts fall close to the 200 threshold. Therefore the Federal Guidelines for the use of anti-HIV therapy

recommend that people consider starting anti-HIV therapy when CD4+ cell counts are 350 or below. Moreover the Guidelines strongly recommend treatment for anyone experiencing symptoms of HIV disease (re-

... treating infections as they occur is critical not only to dealing with the infection, but also curbing further destruction of the immune system by HIV.

ardless of CD4+ cell counts) and for anyone with CD4+ cell counts of 200 or below. This is because anti-HIV therapy has been shown to stop the destruction of immune cells by HIV, preventing the further decline

in immune defenses.

There are Federal Guidelines for the prevention and treatment of HIV-related opportunistic infections. A summary of these guidelines is available in Project Inform's *Opportunistic Infections Chart*.

In general, if CD4+ cell counts fall to 200 or below (or CD4 percentage falls below

Any time a new treatment is being added to your regimen an assessment should be done to make sure it's safe to use with the other medications you are taking and to make any necessary dose adjustments to compensate for drug interactions.

14), people are at increased risk for PCP and preventive therapy is indicated. For people experiencing other symptoms of HIV infection, particularly recurrent fungal (candida) infections, PCP preventive therapy is often initiated when CD4+ cell counts are higher, around 300. If CD4+ cell counts fall to between 150 and 100, preventive therapy for toxoplasmosis is recommended for people who are toxo-positive. If CD4+ cell counts fall to 50 or below, preventive therapy for MAC and CMV is recommended. For people who have suspected exposure to tuberculosis, preventive therapy is warranted.

Treating infections as they occur

As noted previously, Project Inform's *OI Chart* summarizes Federal Guidelines for the treatment of the major OIs. Because HIV replicates more when the immune system is actively battling an infection, treating infections as they occur is critical not only to dealing with the infection, but also curbing further destruction of the immune system by HIV. This is true whether or not the infection is an opportunistic infection. When it comes to OIs, however, and many issues in later-stage HIV disease, diagnosing some

infections can be difficult.

One of the biggest challenges of OI treatment is early diagnosis, before it has been able to take hold in many different organ systems (e.g. the lungs, colon, brain, bone marrow, etc.). The earlier something is diagnosed and treated, the more likely treatment will be successful and result in full recovery. This means regular monitoring by a doctor (at least quarterly) and talking to a doctor about symptoms. If you experience any new or unusual symptoms and are between doctor visits, make an appointment—don't wait for three months to have something looked at. Keep a health journal or diary, or merely write on a calendar when a new or unusual symptom occurs and record how long the symptom remains. This might help a doctor figure out if a symptom is a drug side effect, sign of an OI or something else.

Many OIs have the same symptoms and some infections may be masking others—thus initial treatment may deal with part of a problem, but not the whole problem. Dealing successfully with multiple infections may take diligence and persistence when dealing with multiple doctors and specialists. It's ideal to have your primary doctor leading the charge, talking with all of your other doctors and specialists and making sure that they're talking to one another. The most difficult part of dealing with multiple conditions is that doctors often aren't very good about talking to each other. It easily can become a full time job trying to juggle doctor appointments and many different doctors ordering many different laboratory tests. It's your primary doctor's job to coordinate all of this, even when they're busy. Especially in cases where many problems may be rearing their heads at once, preparing for your appointments, writing down your questions beforehand and having an advocate with you to record answers to your questions is strongly encouraged.

Once a condition is diagnosed, following a course of recommended treatment through to completion is vital. Drugs to treat some opportunistic infections may interact with anti-HIV medications. Any time a new treatment is being added to your regimen an assessment should be done to make sure it's safe to use with the other medications

you are taking and to make any necessary dose adjustments to compensate for drug interactions.

Maintenance therapy

After treating an OI, sometimes life-long medications are required to prevent the recurrence of the disease. This is called maintenance therapy. In some instances maintenance therapy may be stopped if a person is able to see sufficient and sustained immune recovery and control of HIV with the use of anti-HIV therapy. The guidelines around maintenance therapy, and stopping maintenance therapy, are outlined in Project Inform's *OI chart*.

Some people with recurrent herpes infections will take long-term anti-herpes therapies to prevent recurrences. Similarly, some people who have had trouble with recurrent fungal infections will take long-term anti-fungal drugs to prevent recurrences. In both of these cases, maintenance therapy is somewhat controversial. This is because the organisms can develop resistance to the drugs, leaving few viable options for treat-

While there is a discrete list of AIDS-defining OIs, it's important to note that virtually any condition or disease can become opportunistic in the face of a weakened immune system.

ment if or when a serious infection occurs. When herpes or fungal infections become recurrent, however, it may come down to a quality of life issue and long-term therapy may be the only viable option for a person. Weighing the risks and benefits of these approaches carefully is critical to making the right choice. Some will choose to risk losing viable treatment options to alleviate the problems of recurrent infections. Others will choose to simply treat the recurrent infections when they happen in hopes of preserving the benefits of therapy.

Discussion

Regardless of where someone is at in the spectrum of HIV disease, there are things that can be done to prevent and/or treat opportunistic infections. Prevention of OIs is relevant to people at all stages of HIV infection. Prevention includes:

- maintaining good immune health,
- using anti-HIV therapies as appropriate to preserve the immune system from destruction by HIV and allow for immune recovery,
- preventing infections by the organisms that can cause OIs when possible,
- using treatments to prevent OIs when indicated, and
- using treatments to prevent recurrences of OIs when indicated.

A plan for treating OIs includes:

- Seeing a doctor regularly (generally quarterly, but it might be twice annually for people who have good measures of immune health or monthly for people dealing with complications from HIV or medications) who specializes in HIV disease, is informed about HIV and has treated other people living with HIV. (An experienced doctor is better able to recognize symptoms of OIs and will be more familiar with preventive OI medicine and how to treat OIs.)
- Telling your doctor about all symptoms you are experiencing so that they can diagnose problems early.
- Treating infections as they occur, aggressively, following through on

a course of treatment to completion and using maintenance therapy as indicated. This might include the need for life-long maintenance therapy to prevent recurrence. ⁿ

When to use therapy: the decision is yours to make!

Walking your way through making a treatment decision

When making these decisions, you should always consult with your doctor. This information is intended to help you understand the options and the risks of each. It is not intended to replace your doctor's advice. The information is for informational purposes only and is not intended to be used as a substitute for professional medical advice.

- 1** The medicine and what it does
- 2** What you want
- 3** What your doctor says
- 4** What about side effects?
- 5** What about the cost?
- 6** What about the time?
- 7** What about the risk?
- 8** What about the benefits?
- 9** What about the future?

Drug Information: [Text describing drug information]

OAI Classification: [Text describing OAI classification]

For a copy of this along with personal tracking charts, contact **1-800-822-7422** or www.projectinform.org.

What are STIs and What are the Goals of STIs?

STIs (Structured Treatment Interruptions) involve going off anti-HIV therapy for periods of time in a structured and strategic fashion, typically guided by increased lab and health monitoring. In all, more than two dozen studies of STIs of varying types have been conducted since 1998. It is important to note that interpreting the results of STI research can be challenging. Some of the assumptions about HIV disease that led researchers to investigate treatment interruptions in the first place have yet to be proven conclusively. At least some of the research on STIs, however, has been promising and other research has made clear those areas where interrupting therapy is neither safe nor effective.

The discussion that follows will explore what is known about the following STI-related strategies where the goals were:

- Interrupting anti-HIV therapy to reinvigorate the immune response,
- Interrupting anti-HIV therapy in people experiencing treatment fatigue,
- Interrupting anti-HIV therapy in people to reduce the costs and side effects of therapy, and
- Interrupting anti-HIV therapy before starting a third line or salvage therapy regimen.

Interrupting anti-HIV therapy to reinvigorate the immune response

The primary rationale for studies of STIs to reinvigorate immune responses came from observations suggesting that HIV disease progression might be linked to the loss of a specific type of immune cell, called an HIV-specific cytotoxic lymphocyte (CTL). HIV-specific CTLs are cells that seek out and destroy other HIV-infected cells. Some findings indicate that long-term non-progressors—those who remain well for many years despite HIV infection, without the use

of anti-HIV therapy—manage to maintain potent HIV-specific CTLs while people who progress more rapidly do not. Not all research supports that the loss of HIV-specific CTLs is responsible for HIV disease progression. Nevertheless, a number of studies including treatment during acute infection followed by STIs, or STIs combined with therapeutic vaccines to enhance immune responses against HIV, were planned or initiated.

The goal of this research is to enhance HIV-specific immune responses and thus improve the body's own ability to control HIV infection for the longer-term, preferably without anti-HIV therapy. In this context, anti-HIV therapy (with or without the use of an experimental therapeutic vaccine against HIV) was used to curb the destruction of cells by HIV. By starting and stopping therapy periodically, it was hoped that with each successive treatment interruption the immune system would demonstrate increasing ability to control HIV on its own. This approach is sometimes called autoimmunization, where it's hoped that modulating a person's exposure to virus can induce a more potent and effective response against the virus.

Ultimately the goal of this approach is

to enhance and preserve HIV-specific immune responses in people with very, very early HIV infection, such that a person's immune system would better control HIV on its own for longer, perhaps indefinitely, without anti-HIV therapy. Or, for people with established HIV infection, the goal is to enhance or restore HIV-specific immune responses, such that those who have lost these responses might regain them and thus hopefully do better in the long-term.

The results of this research, however, were exactly the opposite of what was expected. People who had been infected longest were actually the most likely to carry a broader and more potent HIV specific CTL response. Those who had initiated anti-HIV therapy during primary infection had a fairly narrow and weak CTL response that could be boosted somewhat during a treatment interruption, but then tapered again back to lower levels after reinitiating treatment. Similar results have been found in several other studies of STIs in people with chronic, established HIV infection.

More recently, several studies began to combine STIs with immune modulating therapies such as IL-2 (Interleukin-2) or therapeutic vaccines. The hope is that these therapies, used in conjunction with an STI may provide the additional lift necessary to orchestrate a stronger immune response to HIV. Although several studies are still ongoing, the results reported so far have not been

People who wish to go off of their medications, however, should only do so with the full knowledge and assistance of their doctors.

promising. As such, people who are hoping to “boost” their immune response to HIV should not look to STIs as a proven course.

There are, however, data that show it may be safe for people who started anti-HIV therapy early to go off of treatment safely.

Many people who initially went on anti-HIV therapy early now wish to try going without it. The decision to simply stop anti-HIV therapy and then reinstate therapy according to current Federal Guidelines is not an STI, per se. There have, however, been STI studies conducted in people who initiated treatment in the “hit it hard, hit it early” era of treatment. People in this population have been among the most likely to be able to discontinue anti-HIV therapy. On average, roughly one third to one half of people treated early in HIV disease who have participated in STI research have been able to go off of treatment and stay off for months at a time without virus levels climbing again. Some were able to achieve virologic control during the first treatment interruption; others required two or three treatment interruptions. The results of STIs in people who initiated treatment somewhat later (six months to several years after primary infection) have been less promising and consistent. Generally, however, people whose viral load was low and whose CD4+ cell

Perhaps the most hopeful data to emerge from the various STI studies is that some people can successfully take a break from treatment without developing drug resistance, treatment failure or symptoms of HIV disease progression.

counts were high before starting anti-HIV therapy are also the most likely to achieve long-term suppression of virus following an interruption.

For individuals who were treated early in HIV disease and who wish to attempt going off HIV medications, there are indications that it may be possible to do so safely. As reported in studies, however, treatment interruptions carry the risk even in people treated during primary infection of leading

to loss of control of the virus. There is no particular STI protocol in this population that can be recommended over another. People who wish to go off their medications, should only do so with the full knowledge and assistance of their doctors. It is important to monitor CD4+ cell counts and viral load following a treatment interruption and to resume anti-HIV therapy in accordance with the Federal Guidelines (*Starting Anti-HIV Therapy* on page 7). Most doctors would recommend reinitiating anti-HIV therapy if CD4+ cells drop below 200 or viral load climbs and remains over 55,000. It is also important to remember that some people experience symptoms of acute infection in the first weeks following a treatment interruption. These symptoms are flu-like in nature and can include a fever, muscle aches, swollen lymph nodes, and a rash.

Interrupting anti-HIV therapy in people experiencing treatment fatigue

Treatment fatigue is when a person is simply “tired” of taking anti-HIV medicines. For people who wish to discontinue anti-HIV therapy due to treatment fatigue the data are somewhat conflicting. Perhaps the most hopeful data to emerge from the various STI studies is that some people can successfully take a break from treatment without developing drug resistance, treatment failure or symptoms of HIV disease progression. Moreover, several factors have emerged that help predict when a person may have a poorer outcome during their time off of treatment. These are:

- a low CD4+ count (less than 200) prior to starting anti-HIV therapy
- a high viral load (greater than 55,000) prior to starting anti-HIV therapy
- poorer control of virus while on therapy or other signs of developing drug resistance
- a previous opportunistic infection

There is a significant difference between studies looking at a single treatment interruption versus multiple treatment interrup-

tions. There have been several studies that used CD4+ cell counts and viral load as a guide for when to restart therapy following a single treatment interruption. Nearly all of these studies were conducted in people who had achieved undetectable viral loads for at least the past twelve months and a CD4+ cell count above 350 for the past six months. In most studies, at least one third of volunteers were able to remain off of therapy for at least one year. The median time off therapy for the remainder of the study participants ranged from eight to twelve weeks.

It should be noted, however, that people who interrupted treatment had significant drops in their CD4+ cell counts (on average dropping 50%) compared to people who remained on treatment. Without appropriate preventive medicine against opportunistic infection, these CD4+ cell count decreases could be dangerous for people whose counts drop below 200 during an interruption. Also, the majority of the studies were unable to consistently measure significant or meaningful improvements in cholesterol and triglycerides in people taking an STI versus people on continuous therapy. Study dropout rates also tended to be higher among those taking STIs compared to those who received continuous therapy in most of these trials, indicating that treatment interruptions may actually be more difficult to manage than taking pills every day.

For people with treatment fatigue, who wish to take a break from anti-HIV therapy, there are certain guidelines that may be followed. Because of the risks for disease progression and opportunistic infections, careful monitoring by your doctor is critical. People should check their healthcare benefits (whether through private insurance or public assistance) to ensure that additional viral load and CD4+ cell counts will be covered if needed. In situations where additional tests are not covered, it can be argued that the cost of additional tests will be far less than the costs associated with remaining on most anti-HIV therapy regimens.

A viral load test and CD4+ cell count should be taken before interrupting therapy and at least three months following the

interruption. You and your doctor should decide in advance what factors will indicate that you should resume anti-HIV therapy. At minimum, most people would recommend using the Federal Guidelines for anti-HIV treatment (i.e. CD4+ cell counts that drop below 200 and/or a viral load count that settles above 55,000) as a basis for reinitiating therapy.

Your doctor may also wish to check your CD4+ cell count sooner if your counts were near 200 before stopping therapy, you had less than 200 cells before starting your last regimen or you have previously had an opportunistic infection. Federal Guidelines for preventing and treating opportunistic infections should absolutely be followed. Whenever CD4+ cell counts drop below 200, preventive treatment for opportunistic infections is highly recommended.

Interrupting anti-HIV therapy in people to reduce the costs and side effects of therapy

Another form of STIs studied were those designed primarily to reduce the amount of time a person spent on treatment. The first attempt, which directed volunteers to go on and off therapy every fourteen days, resulted in several people in the study developing drug-resistant virus and losing control of their viral load. Another small study of continuous cycles of seven days on and then seven days off therapy resulted in improvements in side effects and quality of life issues for people attempting STIs versus people on uninterrupted therapy. As well, virus levels were well controlled. A larger study in the U.S. is ongoing. A similar study in Thailand had conflicting results, however, so it is impossible to state conclusively whether STIs of this type are likely to work.

Interrupting anti-HIV therapy before starting a third line regimen

When a person is attempting to construct a new regimen that may contain specific medications that had previously failed, the combination is often referred to as a third

line or salvage regimen. Because salvage also means, “to save,” others sometimes call salvage regimens, “rescue therapy”. For the purposes of this article, the term *third line therapy* will be used to describe a new regimen that typically contains four or more different anti-HIV drugs, some of which a person’s virus may carry resistance for.

The theory behind treatment interruptions in settings where a person wishes to start a third line regimen is the hope that time spent off therapy may enhance the virus’ susceptibility to treatments to which it had previously become resistant. Studies conducted in the early days of anti-HIV treatment found that when a person goes off a therapy to which the virus has become resistant, the newly emerging virus will rapidly revert to what is called wild-type. Wild-type virus is one of the many strains of HIV that exist in the bodies of people living with HIV. It is the strain of virus that reproduces most easily and is sensitive to anti-HIV therapy. The earlier studies found that when the wild-type virus takes over as the dominant form existing in the body, a therapy that had stopped working could sometimes regain some of its earlier potency.

For this reason, several studies have now been conducted examining the impact of treatment interruptions in third line settings. One study from Barcelona found that a three-month treatment interruption did not provide any additional advantages before starting a third line regimen compared to starting immediately. The GIGHAART study from France, which used a shorter interruption, did show that people taking a treatment interruption had larger reductions in virus when they started their next regimen than those who started their next regimen immediately. More recently, researchers in San Francisco conducted a similar study comparing a group of patients who were given a four-month treatment interruption before starting a salvage regimen to another group who started the new regimen immediately. Unfortunately there were no benefits in viral response to treatment in the group who underwent the treatment interruption.

In fact, people who had interrupted treatment for four months were more likely than the other group to develop an opportunistic infection or die. Although the authors of this study concluded that treatment interruptions should not be attempted in people with lower CD4+ counts and drug-resistant virus, it may be fairer to say that they should certainly not be attempted in this population without proper medication and follow-up to prevent the development of opportunistic infections. It may also be that four months is too long to wait before resuming anti-HIV therapy.

It is critical for people to be monitored closely by their doctors when attempting a treatment interruption in this setting. Guidelines for preventing opportunistic infections are a must. Additionally, expert guidance in interpreting the results of drug resistance tests should be sought in constructing a third line regimen (see *Third Line Anti-HIV Therapy Strategies* on page 19).

Treatment interruptions: a final word

While the results of the STI studies conducted so far have not been what anyone might have hoped, they are also not a reason to be discouraged. Based on what has been learned from the various studies, there may still emerge a new strategy that will successfully allow people to spend more time off treatment without problems. The prospect of time off treatment and the chance for a reduction in side effects have been tantalizing enough that a number of people living with HIV are still eager to enroll in STI trials or to attempt them on their own. There simply isn’t sufficient data to say that any trial conducted so far or currently ongoing will offer a benefit to those attempting an STI. We do, however, know now that it is safe for at least some people to take a break from treatment for awhile. We also more clearly understand the conditions wherein breaks from treatment can result in problems. As stated in the lead article of *PI Perspective* #36, there are reasons to remain hopeful and to examine every piece of new information as the possible thread that will lead us one day to a cure. ⁿ

Third Line Anti-HIV Therapy Options

Third line therapy, sometimes called salvage or rescue therapy, is a term describing treatment regimens for people who have few or limited anti-HIV drug options. This includes people who have failed at least two previous anti-HIV regimens and/or people with evidence of HIV resistance to at least one drug in each of three major classes (NRTIs, NNRTIs and PIs, see the Drug ID chart on page 9 for more information on the drugs in each class). True salvage or deep salvage therapy is when a person has literally no viable treatment options. Treatment failure is a general term that encompasses a number of reasons that a regimen is deemed to be not working. The specific reasons for failure determines if or how the individual drugs in a regimen might be used again as part of a future combination.

Virologic failure

In general, a treatment regimen is considered to have failed virologically if:

- viral load does not drop by at least 90% within the first six months on a regimen, and
- viral load becomes and remains (on at least two consecutive tests) detectable again after being undetectable on a regimen.

Virologic failure and the development of drug resistance

When HIV that can reproduce in the presence of drugs emerges, the drugs can no longer block HIV as effectively. This is called drug resistance. Cross resistance is when the virus that can continue to produce in the presence of one drug is also capable of reproducing in the presence of other drugs. The development of drug resistance and cross resistance can severely limit effective anti-HIV drug options.

There are two different kinds of tests that can help determine whether virus has become resistant to anti-HIV drugs. Both require that you have a viral load of at least 1,000 in order to provide useful information. Both tests can fail to detect drug re-

sistance, because drug resistant virus may not be present in the blood sample being tested. The two tests, one called a genotype and the other a phenotype test, are used to determine which drugs your virus has become resistant to, and possibly the degree of resistance. Resistance tests provide the most meaningful results when they are conducted while a person is taking anti-HIV therapy and the information is likely most relevant to the drugs they are taking at the time of the test. Your history of anti-HIV drug use and your experiences with previous regimens will be critical to consider when choosing the “best” drugs to combine for your next regimen.

Expert guidance

When constructing a new regimen it is helpful to have expert guidance. In general, people who see an HIV-experienced doctor are less likely to experience HIV disease progression than people who see doctors with less experience treating HIV. It may be especially important to have experienced help in therapy choices and monitoring when making complex third line therapy decisions.

Not everyone has access to highly experienced doctors. In such cases a regional AIDS Education and Training Center (AETC) site may be able to provide expert consultation to your doctor. You may reach these centers on the internet at www.aids-ed.org or by having your doctor call 800-933-3413. The AETC Consultation Warm line is available only to doctors and other healthcare providers and does not give out treatment information directly to people living with HIV. Lastly, the online American Academy of HIV Medicine (www.aahivm.org) can guide doctors and patients to other doctors who have been certified as HIV specialists.

Constructing your next anti-HIV therapy regimen

The most ideal regimen contains at least two potent drugs for which you carry no drug-resistant virus, preferably drugs you've never used before. Numerous studies show that people who start a combination containing at least two new drugs will have a much greater degree and duration of viral suppression than people who start only one new drug.

For some people, the recently approved drugs, tenofovir, atazanavir and enfuvirtide, will be enough to construct a regimen containing two new drugs. For others, the advent of new drugs will only offer one viable drug. They will be dependent on expanded access programs or studies to access other new drugs. Activists are working with the pharmaceutical companies to increase the number of third line therapy studies and to enable people to use more than one expanded access program at a time to develop a more effective regimens. There are several new options that may be available through expanded access programs or studies. These include the following.

- Tipranavir is a protease inhibitor in large studies. It is taken twice daily boosted by small doses of ritonavir, and may have activity against virus that is resistant to other protease inhibitors.
- Fosamprenavir (GW-433908) is a new version of the approved protease

inhibitor, amprenavir, and should be approved by the end of 2003. It is expected to have similar side effects and degree of cross resistance to other protease inhibitors as amprenavir.

- T-1249 is a fusion inhibitor similar to enfuvirtide (T-20). It is in large studies and has activity against virus resistant to enfuvirtide.
- Elvucitabine (ACH-126,443) is an NRTI nearing larger phases of study. It has activity against virus that carries the M184V mutation, which is a hallmark of 3TC and FTC resistance.

Therapy options after multiple treatment failures

It is possible to find successful therapy options even when a person cannot construct a new regimen that will contain two new drugs. The success of these strategies may not be equal to that of a completely new regimen, but they have produced favorable results in at least some people in studies reported to date. These strategies often require expert guidance and monitoring and may come with additional risks of side effects and disease progression. They include:

- staying on a regimen when it has failed virologically, but CD4+ cell counts are stable;
- interrupting therapy before starting a new regimen; and,
- constructing a new regimen, with expert guidance, that includes five or more drugs (sometimes called MegaHAART or GigaHAART).

Sticking with a “failing” regimen

When the virus changes and becomes resistant to some anti-HIV therapies, it sometimes reproduces less well. This has been shown to be particularly true with protease inhibitors, and with some NRTIs that cause the virus to develop what is called the M184V mutation. Some researchers refer to these changes in virus as a reduction in viral fitness or replication capacity. Reducing the ability of virus to replicate in people whose CD4+ counts remain high and stable may allow them to stay on regimens, with some degree of continued benefit, as they wait for

new treatment options to become available.

One potential risk of remaining on therapy is the development of virus that carries multiple mutations conferring increasing resistance. This can further decrease the chance that other drugs will work. Also, several studies in treatment-experienced people

The most ideal regimen contains at least two potent drugs for which you carry no drug resistant virus, preferably drugs you've never used before.

have shown that allowing viral load to climb above 100,000 may lower the chance that the next regimen will work as well. Therefore, although the practice of remaining on a virologically failing regimen is becoming more common in third line therapy situations, it is far from ideal. Nevertheless, this strategy may be useful for some people awaiting new treatment options.

Interrupting therapy

Increasing benefits of previously used medications by interrupting therapy for a period of time before making a switch to a new (or recycled) regimen is under study. It is hoped that drug-resistant virus will fade into the background during the time when a person is not on treatment, allowing wild-type virus that is sensitive to the drugs to take over, giving people a more powerful and beneficial response to the new regimen.

The studies in this area are mixed, with one study showing a benefit to interrupting treatment before starting a next regimen and others showing no benefit. In each study, those interrupting therapy had a significant increase in viral load and a steep drop in CD4+ cell counts during the interruption. The main danger of treatment interruptions in third line settings is the risk for disease progression. In all studies conducted, people who attempt treatment interruptions typically lose at least 50% of their CD4+ cell count. For more information on treatment

interruptions, see the article on page 16.

Treating with five or more drugs

A number of studies have looked at the potential benefits of multiple drug combinations following treatment failure. Although one study did look at a combination containing two NNRTIs (efavirenz and nevirapine), the majority include using at least two and possibly three protease inhibitors along with NRTI drugs. Up to four NRTIs are sometimes used. The challenges of such a strategy are obvious. The more drugs used the higher the risk for side effects and the greater the impact on quality of life. Thus far, such strategies have achieved only modest benefits in most cases.

Discussion

The first step in developing a third line therapy strategy is understanding the reasons why your current treatment regimen is no longer working and why other previous regimens have been deemed failures. This provides clarity on what options truly are available. Resistance testing is warranted to

Adherence

One factor that can lead to the development of resistance is adherence. Several studies show that people are far more likely to achieve and maintain undetectable viral loads when they are able to take more than 95% of their doses as prescribed. Identifying the reasons that adherence has been challenging and doing something about it is important. The Project Inform publication, *Adherence: Keeping up with Your Meds*, has helpful tips for identifying and overcoming adherence challenges. Even when adherence is nearly perfect, however, virologic failure can occur. A recent study found that drug resistant-virus could be found even in people who were adherent most of the time.

guide treatment decision-making.

Ideally, with the use of resistance testing, expert guidance and newly available treatments, a regimen that contains at least two drugs that are active against HIV is feasible. When this is not possible, expanded access programs and studies may offer alternatives. Some people may continue to receive health benefits from their current regimens even

Reducing the ability of virus to replicate in people whose CD4+ counts remain high and stable may allow them to stay on regimens, with some degree of continued benefit, as they wait for new treatment options to become available.

when viral load is increasing. Therefore, those who can safely wait for new drugs to become available in order to build a regimen with two active drugs may wish to do so. However, waiting until viral load climbs to 100,000 or higher, may cause future regimens to work less well.

There continue to be glimmers of hope in the data on third line therapy studies and Project Inform will continue to push for the needs of treatment-experienced people. ⁿ

Immune Strategy

AIDS is a disease of primary immune dysfunction caused by HIV. To date, all of the approved and proven strategies for treating HIV disease focus on crippling the virus' ability to infect and/or destroy these cells. There are no approved treatments directed toward the immune deficits and dysfunctions caused by HIV. The good news is that when HIV replication is slowed through the use of anti-HIV drugs, the immune system begins to repair itself and there is evidence of a degree of immune restoration when HIV is controlled over time.

When HIV infects the body, it infects important cells, including CD4+ T cells, which it uses as a host to reproduce. When a cell is infected, its function is decreased and when HIV reproduces it can destroy the cell. CD4+ cells are central for directing other cells to perform tasks and control infection and disease. HIV doesn't only infect and affect CD4+ cells, but these are key cells in controlling disease. CD4+ cell counts are measured as part of routine lab work to monitor for immune health. When enough CD4+ cells are infected and destroyed, the body gradually loses the ability to fight disease and a person increasingly becomes at risk for serious life-threatening conditions.

A comprehensive strategy for managing HIV infection should include a strategy to preserve and promote immune health. While in theory this is true, in practice it's much more difficult to figure out how to do this.

What immune strategies are available today?

There are several approaches to improving our immune health that are available today and can be readily incorporated into a comprehensive strategy for managing HIV for the long-term. These include good nutrition, a sound exercise plan, stress reduction/management, getting eight hours of sleep each night and drinking at least eight cups of water daily. All of these have been shown to preserve and promote immune health. A discussion of each can be found in Project

Inform's material on *General Health Maintenance*, available through the hotline and website.

Other approaches, which some people might not think of readily when pondering immune health, also include skin and oral healthcare and preventive health measures.

Skin is the body's first defense against infection—it's a physical barrier that keeps infections out. Eating well, drinking lots of water, getting rest and reducing and managing stress are all great ways to promote skin health. Diagnosing and treating skin conditions promptly is also important.

Infections often enter our body through all of the places we have openings to the outside world—our nose, mouth and genitals to name a few. For women, when level of acidity (pH balance) in the gynecological (GYN) tract gets out of whack, the cell walls are compromised and infections are more likely. GYN conditions that increase in frequency and severity are often the first symptoms of immune compromise in women. Routine GYN care to monitor for (and treat) GYN conditions preserves and promotes immune health. Also, studies have shown that people with gum disease (gingivitis) are at higher risk for heart disease. The bacteria build up in the mouth/gums are breathed into the lungs and can compromise the heart. Regular brushing, flossing and good dental care has been shown to prevent certain kinds of heart disease. Maintaining the health of the mucosa (vaginal, anal, oral

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Saturday: 10am - 4pm (PST)

membranes) reduces risks of infection and disease which can further compromise the immune system.

One way to preserve, promote and maintain good immune health, especially in the setting of HIV infection, is to maintain

The most readily available treatment shown to improve immune health is potent combination anti-HIV therapy.

good preventive health measures. This not only includes routine health screening, age-appropriate health screening and vaccines as appropriate, but also includes following safer sex guidelines and safer food handling guidelines. For more information on each of these topics, call the Project Inform hotline.

HIV becomes active (starts reproducing) when the immune system becomes active in fighting infections and disease. HIV more easily infects activated immune cells. One way to prevent the destruction of the immune system by HIV is to prevent and treat infections promptly and aggressively. This means avoiding getting the flu each year by getting a flu shot (if appropriate); avoiding new sexually transmitted infections (e.g. herpes, syphilis, bacterial infections, hepatitis viruses, etc.) by practicing safer sex; and avoiding infections that can be transmitted more casually, through food handling and preparation, drinking water, or close contact, when possible. Avoiding more casually transmitted infections can be difficult, but there are tips and guidelines available to reduce risks. This ranges from using gloves when changing cat litter if you have a pet (to prevent infection with toxoplasmosis) to getting a water filter for your sink or drinking filtered/bottled water (to help prevent the risk of cryptosporidium).

Are there immune-based therapies available?

The most readily available treatment shown to improve immune health is potent com-

ination anti-HIV therapy. Studies show that the use of potent and effective anti-HIV therapy can increase CD4+ cell count, decrease immune activation that has been associated with HIV disease progression and improve the ability of the immune system to control serious life-threatening infections. It's theorized that potent anti-HIV therapy does this by slowing the destruction of the immune system by HIV, allowing the immune system to naturally repair and strengthen itself. Increasingly anti-HIV therapy is being used later in the course of HIV infection, once significant damage to the immune system has already occurred. The primary reason for initiating anti-HIV therapy later is because of side effect concerns. Some people do opt, however, to initiate anti-HIV therapy earlier in hopes of preventing the destruction of the immune system. This is a reasonable approach, but there may be a price to pay in terms of side effects, concerns about drug resistance over time and the impact of taking medications for a very long time, perhaps ten, twenty, thirty years or more, on quality of life.

Other immune-based therapies that are not proven, but are being studied, include interleukin-2 (IL-2, Proleukin), human growth hormone (HGH, Serostim) and a variety of therapeutic HIV vaccines. This

... "boosting" the immune system could worsen the problems caused by over activation and inflammation.

list is not exhaustive, nor does it include the varied and many immune-based therapy approaches that have been tested over time. For more information on immune-based therapies under study, call the Project Inform hotline and ask for information on Project Immune Restoration.

Interleukin-2 is perhaps the most widely available immune-based therapy in studies for HIV. Two large international studies are underway to determine if IL-2 can improve

life and extend quality of life in people with HIV. IL-2 is a naturally occurring immune chemical that potently increases the reproduction of CD4+ cells, increasing CD4+ cell counts in people using anti-HIV therapy. There is some evidence to suggest that it might also extend the lifespan of CD4+ cells. For more information on IL-2, call the Project Inform hotline.

Human Growth Hormone (HGH, Serostim) is currently approved for the treatment of HIV-associated wasting syndrome/weight loss. Recent observations that growth hormone may enhance the size and possibly the function of a very important immune organ, called the thymus, has led to a study of growth hormone for immune reconstitution in people with HIV. The thymus is an organ that lives behind the breast bone and in front of the heart. CD4+ T cells originate in bone marrow and gravitate to the thymus where they mature. (This is why they are called T cells, the T stands for thymus, or thymocyte.) The thymus is a very important

wise words



Wise Words is the publication of **Project Wise**, Project Inform's program focused on HIV/AIDS treatment information and advocacy for women. Each issue provides women with important tools for making HIV treatment decisions, covering topics such as anti-HIV therapy, prevention and treatment of infections, management of side effects and more.

Recent issues include:

- HPV and HIV
- Hepatitis C and HIV
- Treatment Advocacy Issues

If you would like to be added to the mailing list for *Wise Words*, call Project Inform's National HIV/AIDS Treatment Hotline at 1-800-822-7422 or email support@projectinform.org.

organ for new T cell development. Without a properly functioning thymus, it's doubtful that a person with a severely compromised immune system could realize full immune restoration.

Therapeutic Vaccines: There are a number of different therapeutic vaccine products

Many if not most immune-based therapies are tested in combination with anti-HIV therapy to decrease these potential risks.

in studies—a therapeutic vaccine is used for treating someone with HIV as opposed to preventing HIV. The goal of an HIV vaccine is to teach the immune system to better recognize and destroy HIV. By offering HIV vaccines to people who are already living with HIV, researchers hope to train the immune system to better control the virus. Currently all therapeutic vaccines are being studied in conjunction with the use of anti-HIV therapy.

What about complementary or alternative medicine (CAMs)?

The most commonly used CAMs are what are called non-pharmacologic therapies. These include energy healing, Reiki, acupuncture, acupressure, meditation, prayer, massage and guided visualization (hypnotherapy). These types of CAMs are likely not harmful and may have benefits in reducing or managing stress and improving overall well being.

Pharmacologic therapies, like vitamins, herbs and other nutritional health products are less well understood. Some may have interactions with drugs used to treat HIV infection and some may cause unwanted side effects. There are many nutritional health products which claim to have immune boosting effects, though it's unclear how they boost the immune system and if this is beneficial or harmful in the context of HIV infection. There is not a lot of research on nutritional health products in the setting of HIV infection. For more information on

Herbs, Vitamins and HIV, call the Project Inform hotline.

Discussion

It's been difficult to devise strategies for treating the deficits in immunity as well as the immune dysfunctions that are caused by HIV infection. While HIV infects and destroys immune cells, it also seems to lead to an over activation of the immune system, which causes its own set of problems. Therefore "boosting" the immune system could worsen the problems caused by over activation and inflammation. As noted, HIV preferentially infects activated cells and boosting the immune system to a further state of activation could increase HIV reproduction and worsen the situation. Researchers in the field of immune-based therapies are therefore extremely cautious when testing new approaches to monitor for immune activation, negative impacts on HIV replication and how a given approach might be causing harm. Many if not most immune-based therapies are tested in combination with anti-HIV therapy to decrease these potential risks.

Immune-based therapies under study might seem counterintuitive to some people. For example, there have been several studies of immune suppressive therapies for treating HIV infection. If AIDS is a disease of immune deficiency, why would you suppress the immune system in order to treat it? Part of the reason that immune cells might not work so well in HIV disease is because they are over active. Like a group of school children who ate too much sugar, it's difficult for the cells to focus and be effective in the presence of all this activation. By calming or suppressing the activation it might be possible to improve immune function, even if overall numbers of cells don't increase. Also, because HIV takes over the inner working of cells in order to reproduce, by suppressing certain factors inside the cell it might be possible to cripple the ability of HIV to use the cell as a factory. It's sort of like blocking a car from using the gasoline in its tank so it won't be able to run. The delicate trick here is to figure how to do this without causing



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Since the beginning of the AIDS epidemic, grassroots advocacy has been the heart of many political victories. In the current political environment, your involvement is needed more than ever. Join over 2,000 Treatment Action Network members and become an influential advocate for AIDS care, treatment and research funding and policies!

If you would like to sign up to be a part of the Treatment Action Network, call Project Inform at 415-558-8669, FAX to TAN Coordinator at 415-558-0684, or email TAN@projectinform.org.

harm. Suppressing factors that HIV might need in order to reproduce can also keep the cell from functioning properly.

More is being learned about the immune system daily as new research tools are devised, but it's a slow process of learning. While information emerges the task becomes trying to understand what the information means, what to do with it and how to turn it into studies of therapeutic interventions. ▢

This issue of the *PI Perspective* has been dedicated to discussions about advocacy, health and treatment strategies. As new data become available from studies, this information refines strategies and guidelines for managing your health. Project Inform has many resources to help keep you apprised of advances in HIV treatment and strategies to manage HIV for the long-term.

These include the *PI Perspective*, *Wise Words* and *TAN Alerts*. The *PI Perspective* offers timely updates and highlights of new information about treatment, health and policy issues. *Wise Words* is Project Inform's women's publication, wholly dedicated to covering topics and issues that are of particular importance and concern to women living with HIV. *TAN Alerts* are periodic public policy updates, including calls to action on public policy issues affecting people living with HIV. All are available free of charge through our hotline at 1-800-822-7422 and website at www.projectinform.org.

In addition to the discussions found in this *PI Perspective*, Project Inform has other strategy publications, including:

- Adherence: Keeping Up with Your Meds
- Anti-HIV Therapy Strategies
- Building a Cooperative Doctor/Patient Relationship
- Day One: After You've Tested Positive
- Making Decision About Therapy
- Personal Tracking Charts
- Sex and Prevention Concerns
- Weight Maintenance and Nutrition

These publications are excellent tools to assist you when con-

sidering your health and treatment options. They're also great tools to use if you're a case manager or peer educator working one-on-one with HIV-positive people. We're currently developing interactive tools for people living with HIV and their health educators as they walk through treatment decisions and develop long-term plans. Check the website regularly as we update these resources!

Project Inform also provides tools to assist people in accessing services and to advocate for themselves. These include resource guides for care and treatment as well as a variety of resources for those who want to become more involved in advocacy. Project Inform's Project Access helps people overcome barriers by providing guidance on negotiating healthcare systems, referrals for HIV case managers and services in their areas and assistance with drug access problems. Some of the publications available to help people become involved in advocacy include *Grassroots Advocacy 101*, a *Legislative Directory* and *TAN Alerts*.

In addition to these publications and services, Project Inform participates in many educational opportunities throughout the country. These range from presenting at conferences to educational Town Meeting events. We also have a vibrant program for educating non-medical service providers who provide support to people living with HIV—such as case managers, peer educators and other non-medical health professionals. If you want to put together an HIV educational program in your community and are looking for advice or technical assistance about how to do this, Project Inform's Outreach and Education Department staff can help.

Yes, I want to help Project Inform remain at the forefront of HIV treatment information!

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(\$40 or more per month for a year entitles you to Partners In Hope membership)

Enclosed is my **donation**: \$35 \$50 \$100 \$250 Other \$ _____

Enclosed is my **Partners in Hope donation**: \$500 \$1,000 \$2,500 Other \$ _____

In Honor of / In Memory of: (circle one) _____

I want to receive information on making a bequest or planned gift.

Omit my name from public listings of donors.

ADDRESS

Mr. / Ms. / Mrs.

Mr. / Ms. / Mrs.

Address

This is a new address.

City

State

Zip

Email

Fax

PAYMENT

Circle One: CHECK    

Credit Card #

Exp. Date

Print Name Shown on Card

Phone Number

Signature

(4120) N04AB