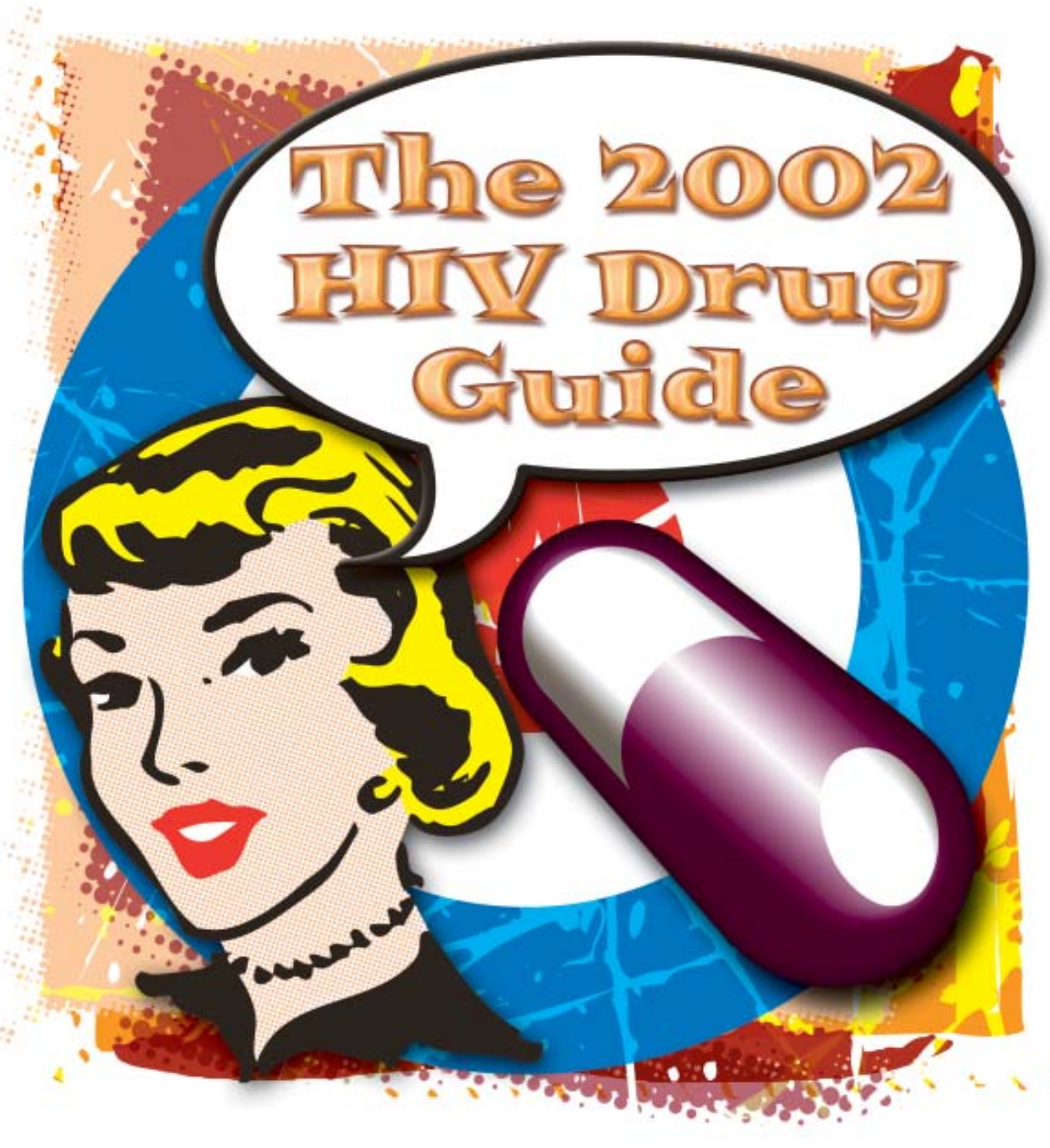
January / February 2002

Positively Aware

The Journal of Test Positive Aware Network



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A model, photograph, or author's HIV status should not be assumed based on their appearance in *Positively Aware*.

You can view these (and other stories from previous issues) online at http://www.tpan.com

Editor's Note

Keeping the faith

Photo by Russell McGonagle

Over the last few months I've come to realize a few things about the AIDS movement. There are many people in this struggle who are suffering from burnout. I was one of them. I also understand that there are lots of angry people out there. I'm still one of those. However, I've learned that when anger and fatigue are not processed properly they can be dangerous weapons. I've seen these weapons used viciously by Chicago's and the nation's "leading" HIV advocates. I've also recognized that my exhaustion and frustration stems from a belief that we—as an AIDS community—are feeding shamelessly on each other, rather than trying to address the real issues facing us.

During the last 20 years, seropositive and seronegative individuals have lived and worked together through one of the most difficult sexual and health challenges in the history of humankind. It is time to take stock of what we have achieved. AIDS has challenged our sexual mores in ways never again dreamed humanly possible. This struggle has not been easy. There have been many deaths. However, we have risen to the occasion and responded to the challenge. We struggled against stigmas and prejudices. We redefined sex and sexuality. We reconfigured notions of commitment and community. We fought government inaction. We confronted corporate greed. These accomplishments should be acknowledged and celebrated. Everyone should be applauded for fighting a good battle over the last 20 years.

However, the battle against AIDS is not over. There are new challenges on the horizon for all of us. We can not allow ourselves to become complacent and careless. We must have answers to the questions of how and why HIV manifests itself differently from one individual to another. We may not like the answers, but we must search for them regardless. We can not allow cutting-edge HIV prevention and treatment education programs to get lost among governmental red tape or irresponsible behaviors. We must recommit ourselves, seek out resources, and collaborate together in ways never previously thought necessary.

Race, sexuality, and HIV status… it doesn't matter. In the post-September 11, 2001 environment, we have to combine our resources and strategize together more than ever. Our over-arching challenge as a community seeking to stop AIDS is to work together, communicate with each other, to be as honest as possible about our needs, desires and behaviors. My challenge to you, as people living in the age of AIDS, is to closely re-examine your attitudes and your behaviors, because we are the only ones who will curb the spread of HIV. It will not be easy. And as the last 20 years demonstrate, there will be missteps. But we can do this, again. We have to. We can protect each other, as we protect ourselves.

As survivors of the last two decades of AIDS, we have a duty to those who have left this life, to our current lovers and partners, to our friends and families, and to ourselves to ensure that events of the early 1980s do not happen again. If you are HIV-positive, the challenge is to stay healthy. If you are HIV-negative, the challenge is to stay healthy. We are a living testament to the last 20 years. Be healthy. Stay alive.

Achieve. Survive.

Charles E. Clifton
Editor
Send comments and reactions to
posaware@aol.com

Sometimes the words that we most fear saying are the words that are most needed. When I wrote my last editorial I feared that I would be crucified. However, the feedback I've received from so many people has been food for my soul. Thanks to some good advice, I took some time off and spent some quality time with my partner, our dogs, and my family.

Test Positive Aware Network
5537 North Broadway
Chicago, IL 60640

phone: (773) 989-9400
fax: (773) 989-9494
e-mail: tpanet@aol.com
http://www.tpan.com

Editor Charles E. Clifton

Associate Editor Enid Vázquez

Advertising and Distribution Manager/ Editorial Assistant Jeff Berry

National Advertising Representative Rivendell Marketing 212-242-6863

Executive Director Dennis Hartke

Business Director Rick Bejlovec

Contributing Reporters Michael Barnett, Daniel S. Berger, M.D., Anthony Clark, Laura Jones, Jim Pickett, Glen Pietrandoni, R. Ph., Keith Waltrip, LPC

Art Direction Russell McGonagle

A new year—Reflections and continued hope

A new year. A time for renewal—new resolutions (which I swear I'll keep this year!), a new location for this agency, new commitment, new hope. It is also a time to reflect. A time to reflect on 2001, a year like no other for most of us. A time to reflect on our lives. A time to reflect on this continuing struggle with HIV and AIDS.

Positively Aware, January 1992, "Keeping Watch on HIV: Drugs vs. AIDS" (reprinted from Barrons, 12/16/91)—"The most intriguing ideas on attacking the AIDS virus, like preventive vaccines and more sophisticated genetic therapy approaches remain perhaps a decade or more away from fruition."… "We've just finished the first five years of a 30-year program…."

In January 1992 there were two approved drugs for combating HIV—AZT (approved since 1987) and ddI. The only drugs on the near-term horizon were of the same class—ddC, 3TC and d4T. The latest "breakthrough" was combination therapy using AZT and either ddI or ddC.

January 1994—List of FDA approved anti-HIV drugs has grown to 5—AZT, ddI, ddC, d4T, and 3TC. Drugs that are being tested and "show promise" include protease inhibitors from Abbott and Merck & Co. and Boehringer Ingelheim.

January 1996—FDA approved list of anti-HIV drugs is now six, with the accelerated approval of Hoffmann-La Roche's protease inhibitor (PI) saquinavir for use in combination with other drugs such as AZT, ddC, etc. Still in the testing phase are PIs such as Norvir, Crixivan, and Viracept.

January 1998—*Positively Aware's* annual drug guide lists 15 anti-HIV drugs that have received FDA approval or are in testing.

January 2002—Our annual drug guide lists more drugs than ever. Yet there is still no cure. Nor is there even realistic talk of a cure. Rather, attention continues to focus on drug resistance, treatment adherence and sustainability over many years, and when to start treatment (now in vogue: delay treatment and the possibility of structured treatment interruptions).

Ten years. Tens of thousands dead in this country; millions dead across the globe. Millions more infected.

But I remain hopeful. Despite the continued contraction of the pharmaceutical industry into fewer and bigger companies in which AIDS medications become less important to the bottom line. Despite the emergence of a "new wave" of HIV infection among young women and men. Despite the staggering number of infected humans in Africa and around the globe.

I remain hopeful because I am privileged to see a small slice of the large number of dedicated people who are fighting this disease on the streets, in the laboratories, and in doctors' offices. I remain hopeful because I see the tremendous progress that has been made in treatments over the last 10 years. I remain hopeful because I no longer go to funerals of friends and colleagues monthly. I remain hopeful because I continue to enjoy good health. I remain hopeful because the world AIDS crisis has finally received some attention.

I remain hopeful because the alternative is not one I want to embrace.

Dennis Hartke

Dennis Hartke
Executive Director
Thoughts, comments, reactions? Write me at tpaned@aol.com

Photo by Russell McGonagle

Readers' Forum

Positively Aware will treat all communications (letters, faxes, e-mail, etc.) as letters to the editor unless otherwise instructed. We reserve the right to edit for length, style or clarity.

Write to: Positively Aware,
5537 North Broadway
Chicago, IL 60640
Fax: (773) 989-9494
E-mail: posaware@aol.com

Communication

I read "It's All About Communication" in the July/August issue and it really hit home. I am 54 years old and my wife Sandy died from AIDS on December 2, 2000. Sandy and I had dated in high school in the '60s. We went different paths, married, had kids, and got divorced. I looked for her and we picked up like we were 18 again. We were so much in love. We married in 1993. In October of 1998 she developed non-Hodgkin's lymphoma. She then had three hospital stays in the next 14 months for pneumonia. We told her doctors about her two blood transfusions in the '80s but none of the four doctors ever suggested an HIV test. When she could barely breathe in November 2000, they did a bronchoscopy and said their findings indicated an HIV test. Ten days later she died.

I was destroyed by losing my soul mate, but I also did not know if I had brought this into my marriage. We were 45 years old and dumb not to have an HIV test before having sex. Her sister told me that Sandy tested positive in 1989 after a former boyfriend, an IV drug user, called to say he was positive. Sandy's best friend told me how Sandy had gone into herbal remedies for a poor platelet count and told her, "This is a miracle!" She said her blood had been cured. I don't know if the person I loved just blocked this all out because she was a single mother of three kids, struggling without a lot of hope and the social stigma was too much. I'll never have those answers in this life. I sit here and think all of this could have been prevented by her telling me up front. The second part of the "what if's" is why didn't four different doctors pick up on her symptoms? When I asked her cancer doctor, he said she was "white, middle-class, happily married and not doing an at-risk behavior." I asked about her transfusions and he said they just "blew it." There were so many opportunities to help her. This empty house and empty bed are so overwhelming. I feel like damaged goods. I have been married 31 of 33 years. I just cannot function alone. Thanks for listening.

Name withheld

We're tired

I was very touched by your Editor's Note, "The Past, The Present and The Future." I too am very tired. I have been fighting this disease 12 years and I'm tired, but I go on. I have one other option, and that isn't acceptable at this point in my life. Thank you for your wonderful column.

Carl Pinter,
via the Internet

After 20 years living with this illness, I am also tired. Thanks for saying it. My now-dead husband David and I exchanged vows on the beach under a full moon and before God. It was also October 8th. He died six years ago. You have, however, caught me at one of those rare moments where I have faith. Draw strength. Refresh yourself if you can. I care. You don't know me, but you do. Om.

Jim Hyde
Atlantic City, New Jersey

I too am tired of HIV/AIDS agencies that beg for money for people suffering from HIV/AIDS and they never see a dime. All the while agency staff are driving around in new vehicles and sport around in new clothes. These are the true barebackers. I'm tired of individuals who consider HIV/AIDS as a business rather than an illness. I'm tired of agencies that disguise their mission as a non-profit organization, when in all truth they are lining their pockets, and who claim to be crusaders in the name of eradication of HIV/AIDS. I'm tired of people being labeled gay, straight, bi, black, white, Hispanic or Asian. We are all in this together, and that means everyone on this planet. I'm so tired of being ill and when I can't hold my medications down. I'm so tired of losing muscle mass that my clothes won't fit me no more. I'm tired of politicians who can't look you directly in the eye and give you a straight but honest answer. Also, these are the same politicians who promise money and hack it to pieces before the agencies involved can even get a taste of it. All along it was a plan to win votes from the HIV/AIDS community. I'm tired of sitting for hours waiting for a doctor in the emergency room, especially when I'm so sick that I can't hold my head up. I'm tired of bloodwork, and the look of people in lab coats who go to extremes as to double glove. I'm tired of hospitals that stick big red biohazard signs on my door. I'm so tired of my friends who shared their journey with me suddenly swept away, and who are no longer with us. I'm tired of individuals who claim a commitment, and don't stick to their promises after they wedge their way into your life and privacy. I'm tired just because I am infected that this should be a reason for some people to try and dominate me and my household. I'm tired of people trying to convince me of their own simple, but ignorant ideologies. I'm tired from all the chaos in the world in which we live.

Darel McCauley
Little Rock, Arkansas

I read with great interest your Editor's Note in the Nov./Dec. issue. As an HIV/AIDS case manager who regularly reads *Positively Aware*, this was definitely the best letter I've seen yet. I appreciated the honesty and sadness reflected in the article. I noticed, however, that the article merely lists problems and frustrations without offering any solutions or ways to come to terms with the issues presented.

It is my hope that you follow up this Editor's Note with another letter that provides us with possible answers, with hope, and with a sense of wanting to go on. Without these elements, HIV has won—and I, for one, am not ready to throw in the towel yet.

Staci L. Benson, MSW
via the Internet

You must know or need to know that you are nowhere near alone in your feelings. AIDS burnout was a common theme at a recent CDC confab I went to last month. It has been spoke of even at the job. The interesting thing that helped me was watching the Electric Blanket at the CDC conference. A recent trip to Memphis this past weekend for a screening of Kevin's Room [TV show about black men and HIV] and the Faces of AIDS exhibit helped fuel my spirit. We often bitch about what we don't have. Take a trip south of Champagne, Illinois or near south like Tennessee or the dirty south like Mississippi and you'll see that we need not bitch but to continue the fight.

A break is sometimes needed because for the most part some of us do this for the passion and others for the glory (it is a billion dollar industry and we need to remember that).

I think the thing we need to bear in mind is, who are we grooming to take the torch? The other issues that you raised only compound the situation, especially if you're a man of color in this fight. Fighting to make sure there will be a race of African-Americans here in the U.S. We both know that the motherland is dying. If we won't fight for them who will? When we tire or expire, who'll take the torch and carry on with the struggle?

Hold your head up, baby! You're not alone in the struggle.

Sanford E. Gaylord
Chicago, Illinois

Don't forget that Rosa Parks was "just tired" when she sat down on that bus and ended up changing America.

Lee Magnuson
Washington, DC

I am an individual living with AIDS who has a viral load over 500,000, and a CD4 count of 77. I was recently in the hospital with a stroke, which my doctors say is a side effect of my meds, not to mention that I have just been diagnosed with hep C. I was extremely moved by your Editor's Note. If one person is saved from this nasty disease then you have done a wonderful thing.

Ty Hutt
Lake Worth, Florida

I wish to thank you for "taking the words right out of my heart" and printing them in your magazine for all to read. I could not have expressed my feelings any more eloquently had I written them myself. I have seen all that you have seen and heard all that you have heard and, like you, I am tired too. Having said that, I will use the message that I attained from your column and take some time to re-evaluate my life's journey in this fight. Again, thank you for your candor and I wish you peace in your life's journey, wherever that journey takes you.

Name withheld
via the Internet

Giving

Shortly after the events of September 11, I was named Executive Director of the AIDS service organization in a small, rural Pennsylvania community. In addition to homophobia and bigotry, September 11 was one of the biggest stumbling blocks in my attempts at fundraising.

I just finished reading your article, "Continued Giving Honors Their Memory," and was moved beyond words as you have so eloquently said what I have been struggling to say for a month.

Kirsten Felix
Williamsport, Pennsylvania

First encounter with your magazine

I have recently seen your magazine for the first time. It was brought to my attention by a case worker. He could not speak highly enough of your publication and I can see why he is impressed with it. The lobby of our office serves many who are either dealing with HIV or are concerned enough to get involved in our vaccine efforts. Staying current with information and being part of a larger community is important for all of these individuals. Recently I have found myself removing several free publications

from our lobby because of irresponsible and unprofessional articles. I would love to have your magazine available for everyone to see when in our lobby. Thank you for a great publication.

Richard Emerson
St. Louis University Vaccine Evaluation Unit

New-Fill

I read your article entitled, "New Facial Filling Treatment for Lipodystrophy," and found it very interesting. I suffer from facial wasting as a result of my treatment. It has become such so disturbing to me that I was ready to see a physician about collagen or fat injections. I found your article as I was doing some research. How would you compare the New-Fill treatment to collagen or fat injections? What is the cost for this procedure at NorthStar Healthcare? I live in Louisville, Kentucky, and Chicago would be the most feasible location for me to travel to if I wanted to have this procedure done. Any information you can give me would be greatly appreciated.

Name withheld
via the Internet

Narrow-minded

I just want to commend Enid Vázquez, J.P. Womble and *Positively Aware* for the rebuttals to the letter from the narrow-minded guy in Houston. I am a heterosexual woman, former IV drug user and current prisoner. I was diagnosed HIV-positive in 1988 in San Francisco. This was not a time when many heterosexuals were talking about HIV and AIDS. So I got my knowledge and support where I could, from the gay male community. Do you think I cared in the least that these wonderful men lived lifestyles other than my own? I will be forever grateful for the love and support I received and for the fact that no one judged me and dismissed me as worthless. All of us who are infected—gay, straight, male, female, old, young, black, white, Hispanic, incarcerated, free, American or from places around the world—are part of the HIV/AIDS community, and we need to stop focusing on the differences between us and start recognizing the ways in which we are the same. Human… deserving of love, support, knowledge, and empowerment. Thank you for facilitating all of this.

Judy Ricci, W69939, CCWF 512-12-IL,
P.O. Box 1508
Chowchilla, California 93610-1508

Divide and Conquer

I read with keen interest the Editor's Note on "Divide and Conquer" in the July/August issue of *Positively Aware*. The editor expressed the things we are watching on a daily basis, those of us who care to watch them. Maybe because HIV has overstayed as an epidemic and changes targets over the years, the people involved in addressing it all over the world are extremely exhausted.

From the community perspective of work to address HIV, from which I have the most exposure, the actors are indeed going for each other's throat. "Who can we trust?" Money has come onto the scene. Yes, the response to AIDS the world over is greatly under funded, but the little money there is, is a cause for scramble. Remember the scramble for Africa by colonialists? Everyone is out to bite the biggest chunk of the resources available, no matter that there is only the smallest bit that reaches the target populations, not only in the developing countries, but as I read, in the developed countries as well.

All having been shared, we have a bigger task. There are people who will continue to die as we struggle against each other. There are the young people who are growing and do not need a delay in educational information. There are resources that need to be gotten to the people, not to meetings and expensive travels.

M.K.
Kampala, Uganda

Journey with Reiki

I am writing in response to the article, in the November/December issue, "My Journey of Discovery with Reiki" by Kathy Harrison. First, and foremost, I want to compliment *Positively Aware* for addressing issues of complimentary health, of which Reiki is one such method.

I did, however have some concerns about the tone of Ms. Harrison's article. I have been a Reiki practitioner for two years, and while I agree with Ms. Harrison's view that Reiki is a channeling of Universal life Force Energy, I am concerned that some of her word choices may turn your readers off to the concept. I have found, in my journey with Reiki, that the terms "cosmic" and "Divine" cause people to view the topic as "too out there," "too religious," or as "New Age flakiness."

Reiki is an ancient healing form that exists right there with acupuncture, acupressure, and reflexology. While the specific methods of operation are very different, they very much reflect different facets of the same form of healing energy, and come from the same Source, if you will.

So, as a note to your readers, if you haven't tried Reiki, do so. You'd be amazed at how relaxing and healing it can be.

Thanks for your excellent work on *Positively Aware*!

Rick Bejlovec
Chicago, Illinois

ICAAC Update

by Enid Vázquez

Some news from the 41st annual Interscience Conference on Antimicrobial Agents and Chemotherapy, held in December in Chicago. Visit www.icaac.org.

Sustiva blood levels and side effects

Spanish researchers looked at people taking the standard dose of Sustiva who experienced long-lasting severe side effects and compared them to people who didn't. They found that the people with greater toxicity experienced higher blood levels of the drug. It is hoped that monitoring blood levels in the future can help curb side effects. Right now it's only done in the lab, not out in the real world.

Lasting HAART

How long can people stay on Highly Active Anti-retroviral Therapy (HAART)? The University of Alabama at Birmingham HIV clinic looked at the records of patients taking meds for the first time, who started after the introduction of protease inhibitors (the birth of the HAART era), in early 1996. After four years, nearly a third (27%) were still on their first regimen. But nearly half (45%) had taken four or more different antiviral combinations. There was no difference when taking into account age, race, gender or viral load at time of starting therapy. What did make a difference in having to change treatment was starting out with less than 200 T-cells or, more importantly, having a history of an OI (opportunistic infection, which occurs with weak immune systems).

Most lasting HAART

In Europe, researchers followed people whose HAART therapy was "failing" in terms of viral load going above detectable. They found that over a period of about a year, the viral load continued to increase slowly at the same rate as you would expect without therapy. However, T-cell counts stayed where they were, not going down. The 500 people with HIV had viral load between 1,000 and 10,000.

Trizivir in kids

In a group of 19 children taking Trizivir, four were switched to another HIV combo because their viral load went up above 5,000. (Children tend to have higher viral loads, so undetectable—under 400 or under 50—is not the standard for them.) Researchers reported that three of these four children had "adherence problems." Overall, Trizivir was safe and tolerated by the children. More children will need to be followed to judge the effectiveness of the med. Trizivir is three HIV drugs in one, taken as one pill twice a day.

Oh, baby

The World Health Organization recommends that in poor countries, a four-week course of Retrovir (AZT) be used at the end of pregnancy to prevent transmission to the child. (In wealthier countries, it's recommended that women use a triple combination throughout most of their pregnancy.) But even the shortened four-week treatment is expensive for poor countries. Researchers in Zimbabwe evaluated an "ultra-short" regimen. They gave women Retrovir every three hours starting with the beginning of labor. The newborns received Retrovir every six hours for the first three days of their life. Although the percent of children infected was about the same whether four weeks or ultra-short treatment was used (about 30% each), the ultra-short course won out because it's cheaper ($4 vs. $110). The researchers pointed out that it's probably also less likely to lead to drug resistance (when drugs can no long fight off the virus).

Researchers in Argentina looked at HIV-positive pregnant women taking different therapies. The mother-to-child transmission rate was 19.2% in the women who took no therapy, 4.8% for the women who took Retrovir, 2.1% for the women who took Retrovir/Epivir, and 2.8% for the women on Retrovir, Epivir and either Viramune or a protease inhibitor. The researchers reported that low birth weight was the only significant side effect associated with therapy, but noted that it came along with a great decrease in infection.

And in the U.S., a registry of pregnant women with HIV found no increased risk of birth defects in children whose mothers took antiviral meds during the first three months of pregnancy—especially if they took Retrovir (AZT) or Epivir. The first three months is when the greatest risk of drug toxicity exists for the fetus. However, the doctors reported that it's still too early too know about the risk of the other HIV medications for the first trimester. The registry phone is 1–800–258–4263.

Nice T-cells

What to do after one or two protease inhibitor combos fail? Researchers put 54 people on Sustiva, Ziagen and Videx, either with or without hydroxyurea (HU). The new combos worked well at knocking down viral load—about half of all people got to below 50 on the ultrasensitive test—but it didn't matter if they took HU or not. These are preliminary results from 24 weeks. Dr. Daniel S. Berger, who writes for *Positively Aware* and whose medical clinic patients participated in the trial, reported that the people who did not take HU saw a T-cell increase of 124 on average. "You don't see this kind of increase in people who've already been on PIs," he noted at his annual HIV update forum here in Chicago. (The people on HU dropped around 63 T-cells, to be expected with this drug. It's rarely taken nowadays because of toxicity and T-cell drops.)

News Briefs

by Enid Vázquez

Photo by Russell McGonagle

On-and-off trial

The National Institutes of Health has opened a study to compare a group of HIV-positive people receiving continuous HAART (highly active antiretroviral therapy) to a group using HAART on and off ("intermittent therapy"), with intervals of one week on/one week off. Participants must have a T-cell count of at least 175, no history of opportunistic infections, a viral load less than 500 for six months prior to enrollment, and a viral load less than 50 on screening. NIH will provide travel to the Clinical Center in Bethesda, Maryland. For more information, contact Diane Rock, RN, at 1-800-772-5464, ext. 58003. (*See page 27, "STI"*)

Stress and HIV

Stress "enables HIV to spread more quickly in infected persons and prevents antiretroviral drugs from restoring immune system function." So say researchers at the University of California, Los Angeles. In a press release, lead author Dr. Steve Cole says that, "Popular science has widely suspected that stress weakens the immune system. Now we've uncovered two reasons why." UCLA reported test tube results from the blood of 13 HIV-positive men. "When a person is under stress, the nervous system's 'fight or flight' syndrome kicks in. The body's nerves release the hormone norepinephrine into the lymph nodes, where the immune system's T-cells reside. The UCLA team recreated this scenario in the laboratory, exposing T-cells in culture to the same concentrations of norepinephrine released by the nerves during stress. They discovered that the hormone increased viral replication 10-fold via two molecular mechanisms. First, norepinephrine increases T-cells' vulnerability to infection fivefold by increasing levels of CCR5 and CXCR4—two co-receptor molecules that enable HIV to bind to the cell's surface and invade the T-cell. Second, the hormone increases HIV's rate of viral gene expression in the cells it has already infected. This allows the AIDS virus to spread five times more quickly." The university said this was the first report of molecular mechanisms linking stress and HIV. The UCLA researchers also looked at four health indicators of stress: blood pressure, skin moisture, heart rate and pulse rate at rest. Together, these four measures gave the level of a person's autonomic nervous system (ANS) activity. The researchers measured the ANS of a small group of 13 HIV-positive men before they went on HIV therapy for 11 months. "Even anti-HIV drugs prove more effective in people with low [ANS] activity," Cole said. The higher the stress level, the less response to the antiretroviral drugs. The average drop in viral load was more than 40 times for men with low ANS activity—yet less than 10 times for men with high ANS activity. "After several months on antiretroviral drugs, the viral loads of five of the seven men with low ANS activity plummeted to undetectable levels in their blood," said Cole. This happened to only one of the six men who exhibited high ANS activity. In addition, the men with low ANS activity on average showed the most striking cell-count increases. In comparison, men with high ANS activity displayed little increase in T-cell counts, or none at all. The study was published in the October 23 *Proceedings of the National Academy of Sciences*. Visit www.ucla.edu.

Hypocrisy

The World Trade Organization meeting in November in Doha, Qatar raised issues of drug patents. Many countries wanted poor nations to have the right to override pharmaceutical company drug patents in order to buy or produce inexpensive generic versions in health emergencies. This struggle is supremely important in the worldwide battle against AIDS, which threatens to destroy populations and economies of many nations. U.S. Trade Representative Robert Zoellick suggested an alternative that would give poor countries the right to override drug company patents until the year 2016 and stop the U.S. from taking actions against

sub-Saharan African countries for violations of drug patents held by companies in this country. AIDS activists disapproved of the proposal, preferring the unrestricted right to override patents to protect health. The Zoellick proposal was accepted, but many countries do not have the machinery to make their own medicines. Also, left open was a country's ability to exercise parallel importation, so that it can simply import generic meds from another country.

Activists pointed to the U.S. government's demand that the Bayer company cut the price of the antibiotic Cipro to treat inhalation anthrax infection in case of outbreaks, and threats to override the company's patent in order to acquire large quantities of the medicine at a steep discount. James Love of Consumer Project on Technology told the *San Francisco Chronicle*, "When the United States did not like the price of a medicine, we were very fast to say we might override patent rights. When Brazil did the same thing (for AIDS drugs), they were savaged." An editorial in the British medical journal *The Lancet* also noted the "stark contrast," and suggested that the U.S. government work to allow patent overrides. (Special thanks to the *Kaiser Daily HIV/AIDS Report* for its news round-up of early November 2001; visit www.kff.org.)

To tell or not to tell

People with HIV have a hard time telling casual sexual partners that they have the virus. Researchers talked with 269 people living with HIV, half of them men. Of people with a main sex partner, 74% disclosed their HIV status. For those who had been with a casual sex partner, however, only 25% had disclosed their HIV status. Still, a full 25% did not tell their main sex partner nearly three years (on average for the entire group) after their diagnosis. The researchers said their study shows that "few [people with HIV] disclose their status to a casual sex partner. Interventions to improve skills building for HIV disclosure are needed."

In another study, more than half of the self-identified gay men and bisexual men with HIV interviewed who had had sex with women as well as men in the previous six months also did not "always" disclose their positive status. A third of them had had unprotected anal or vaginal sex. Moreover, the people who did not tell their casual partners about their status were also less likely to use a condom. Researchers reported that, "Non-adherence to HIV medications, recreational drug use, tobacco use, and feeling the effects of drugs or alcohol during sex were significantly associated with sexual risk behaviors." The studies were reported at the 129th annual meeting of the American Public Health Association in October in Atlanta. Visit www.apha.org.

Conference News

Our annual HIV Drug Guide is a good time to round up some of the combination news from conferences during the past several months. Also check www.medscape.com and www.hivandhepatitis.com for more reports. See www.natap.org for detailed technical information about clinical trials and conference updates.

Once a day

After two years, the majority of people on a triple, once-a-day combo continued to be undetectable. Forty participants took Sustiva and once-a-day buffered Videx along with the experimental nucleoside analog emtricitabine (FTC). After 96 weeks, 34 (85%) had less than 400 viral load. Eighty percent had less than 50 (using an ultrasensitive viral load test). Moreover, of those people who started out with more than 100,000 viral load, 8/9 (89%) were under 400. Generally, HIV specialists believe in using a protease inhibitor combination for people with this high of a viral load. Half of all participants had a T-cell increase of greater than 272; the other half had an increase of less than this. Three people dropped out due to side effects. Serious side effects seen were high levels of triglycerides and transaminases (an indicator of liver function—an increase may indicate drug-induced hepatitis). Results are from 40 participants. (From the 8th European Conference on Clinical Aspects and Treatment of HIV Infection—ECCATHI—in Athens, Greece, in October.)

Switching back and forth

What would happen if you took a triple combination for three months and then switched to a different combo for the next three months? In a Barcelona study, participants who switched back and forth did better than people who stayed on the same regimen for 48 weeks. They took Zerit, Hivid and Sustiva for three months, followed by Retrovir, Epivir and Viracept, and then went back and forth. Seventy percent of the people who switched were undetectable (under 400 viral load), compared to 60% of the people who stayed on the same combo. All three groups gained about 70 T-cells. There were 160 participants total in the study, all of them taking HIV meds for the first time. The switchers had less severe side effects. The researchers said they believed these participants were prepared for the side effects and were therefore better able to deal with them. (From the 5th International Workshop on HIV Drug Resistance and Treatment Strategies, in June, in Scottsdale, Arizona.)

Trizivir vs. Crixivan

At 48 weeks—a scientifically significant amount of time—Trizivir, the triple therapy in one pill, was just as good as a Crixivan triple combination at lowering viral load (the amount of HIV in the blood). That's great, except that practically no one takes the original Crixivan dosing of every eight hours on a near-empty stomach that was used here. That dosing has long since given way to Crixivan taken twice a day with food with a mini-dose of Norvir. Still, it's an impressive result for one pill taken twice a day that's only made up of one of the three HIV drug classes out on the market. What about people who started the study with a viral load above 100,000? Previous results with Trizivir have been mixed for this group. In this study, the drop in viral load was also the same. All viral load decreases were good. T-cell increase was also the same. But Grade 3 or 4 lab abnormalities (considered serious) were two times greater in the people taking Crixivan,14% vs. 7%. A total of 342 people entered the study. (From the 1st International AIDS Society—IAS—Conference on HIV Pathogenesis and Treatment, in July, in Buenos Aires, Argentina.)

New PI

The experimental HIV protease inhibitor atazanavir, taken once a day, compared well to Viracept protease inhibitor. They were taken along with Zerit and Epivir. Results were from 48 weeks in almost 500 people. The study participants were taking HIV meds for the first time, so you would expect them to do well at lowering viral load and raising T-cells. Viral load for both groups dropped about 2.5 logs (for example, from about 40,000 to 400). T-cells increased by about 200. However, cholesterol and triglycercides did not increase as much in the atazanavir group (7% saw a marked rise vs. 25% for the Viracept group). Side effects included infection and headache in both groups. (ECCATHI)

Viread—and resistance—at two years

How does the newest HIV drug on the market do resistance-wise? It's an important question because HIV is a tricky character that mutates (changes) in order to resist any medication thrown at it. The search for resistance is still a new field, and one that's very complicated with lots of ups and downs.

In this study, a group of 189 people had a lot of previous treatment experience, which generally means they won't respond as well to new meds that they go on. Still, the people who took the 300 mg dose of Viread (tenofovir DF), that eventually became FDA approved dosage, had a half-log decrease in viral load at 24 weeks. The drop continued out for two years. That's not bad for heavily pre-treated people.

Here's where the resistance pattern comes in. Researchers reported that the resistance mutations people had when they started Viread—the primary Epivir mutation, Retrovir-associated mutations, plus non-nuke and protease inhibitor resistance mutations—did not stop them from lowering their viral load, as you would have expected. Moreover, the primary Viread resistance mutation, called K65R, developed in only 3% of the people taking the 300 mg dose, and it did not keep them from having a viral load drop, contrary to what you would have expected. It's a good start for the new drug. (IAS)

Switching from PIs to Ziagen

In a recent study, 87 people either continued their PI combo or switched over to one containing Ziagen, which is a nucleoside analog (nuke for short). After 24 weeks, the switch group was doing as well as the PI group in terms of viral load and T-cells. Although these are preliminary results, HIV specialist Stephen Becker had this to say in his report at HIVandHepatitis.com: "Unless they use a novel design, no further switch studies appear to be necessary. The accumulated weight of evidence from European and American studies suggests that a switch to a simplified regimen, replacing a PI with [Ziagen], [Sustiva], or [Viramune], is successful. Equally clear is that this switch strategy should not be used in those patients whose antiretroviral regimen included NRTI agents before their PI-based HAART [for example, Retrovir by itself or Retrovir/Hivid]. Tolerability, adherence, and quality of life can be expected to improve, while dysmorphic [body] changes are unlikely to show significant change." (39th Annual Meeting of the Infectious Diseases Society of America—IDSA, in October in San Francisco. Visit www.idsociety.org.)

Sparing the PIs

How about using a four-drug combo that has no protease inhibitor and is easy to take? One complaint about the PIs is that there are too many pills to pop. Standard of care calls for at least a three-drug combination, no matter what drug classes you choose to use. In a small study of only 29 people, good viral load drops were seen out to one year (a significant amount of time). These people had never used HIV meds before or had less than a week of therapy. Here they took a four-drug combo that consisted of Combivir (which is two drugs in one), Sustiva (taken once a day) and Ziagen (one pill twice a day). Altogether, that's "only" seven pills a day total, with pill-popping also only twice daily. The majority (63%) had less than 50 viral load (undetectable on an ultrasensitive test). In fact, using an even more ultrasensitive test (not available to the general public), researchers found that a full 59% of them (16 people) had a viral load of less than three. Half of them saw T-cell increases of more than 172, and the combo was well-tolerated. Moreover, looking at on-treatment analysis—only those people who actually stayed on the meds instead of dropping out of the study—100% had less than 400 viral load and 93% had less than 50. Additionally, people did well even if they started out with a viral load of 100,000. That's a group that would make most doctors reach for a protease inhibitor to prescribe. (IDSA)

Sustiva vs. Viramune

Although Sustiva has shown impressive results in almost every study it's been in, the question of how it compared to Viramune remained up in the air. Viramune is Sustiva's closest competitor, in a sense, because it's also been a long time favorite non-nuke. In this cohort study of 1,078 people taking HIV meds for the first time, 555 were on combination therapy including Sustiva and 523 took a Viramune combination. The people on Sustiva had a longer time to treatment failure (589 days) than did the people on Viramune (307 days). Treatment "failure" was defined as an HIV viral load of more than 400. Also, 51% of the Sustiva people were undetectable (under 400) at one year, compared to 45% of the people on Viramune (a statistically significant difference in this analysis). (ECCATHI)

Facial filling

French researchers reported good results using New-Fill polylactic acid in 50 people with facial lipoatrophy resulting from HIV therapy (loss of fat in the face that leads to a severe gaunt look, although most of the people are actually healthy). The group went from a median facial thickness of 2.1 mm to 9.5 mm after six months. The doctors aimed for an 8 mm thickness following a series shots with New-Fill during outpatient plastic surgery. Getting there took three sets of shots for four people, four sets for 29 people and five sets of shots for 17 people. The surgeons said all patients reported "good satisfaction" with their new appearance. New-Fill was pioneered in France for plastic surgery for about the last five years before its use in HIV lipoatrophy was discovered. A clinic for people with HIV opened in Tijuana, Mexico in the past year, but surgery in the U.S. was halted in the past few months. The Direct AIDS Alternative Information Resources buyers club in New York City (DAAIR) had started acquiring the product under special import law through the U.S. Food and Drug Administration, but the FDA has gone back to setting up road blocks for New-Fill, which is not approved in the U.S. Still, dozens of U.S. people with HIV who were able to have the surgery were quite happy with it. For updates, visit www.daair.org or call tollfree 1-888-951-5433. [*See "The Buzz."*](ECCATHI)

The 2002 HIV Drug Guide

The 2002 HIV Drug Guide was complied by Charles Clifton, Glen Pietrandoni, R.Ph. and Enid Vázquez.

Antiretroviral Therapy 2002

by Carlos H. Zambrano, M.D.

Antiretroviral therapy has been one of the major advances in the fight against Human Immunodeficiency Virus (HIV). HAART has improved morbidity and mortality, decreasing the risk of disease progression and prolonging life in HIV-infected patients (between 1996 and 1997, the number of AIDS-related deaths dropped 42 percent). Multiple studies have demonstrated virologic control and immune restoration (measured as an increase in CD4 count and antigen-specific response to opportunistic pathogens) with the advent of HAART. Clinical trials have shown durability of antiretroviral activity of up to 5 years. Combination therapies have also raised concerns about toxicities, tolerability, adherence and resistance. There are now 16 antiviral agents that have been formally licensed for the treatment of HIV infections.

We need to recognize the need for lifelong therapy. Drug cocktails have failed to eradicate the virus in chronically infected individuals. HIV/AIDS has become a chronic disease, comparable to hypertension or diabetes. It has become very difficult for patients to show perfect adherence to the regimens. However, a failure to do so could result in devastating complications, resulting in death. More convenient drug regimens are being developed (fewer number of pills, once or twice daily).

Another area of concern is drug resistance. Less than perfect adherence could cause resistance to current drugs. There is evidence of increased rates of Sexually Transmitted Diseases (STDs) in populations at risk, particularly young gay men and minorities. Some of these individuals may acquire drug-resistant HIV strains.

Reasons for the lack of adherence are the issues of toxicity and tolerability. It seems apparent that the choice of antiretroviral therapy must also be influenced by factors other than HIV (personal and family history). There is a strong clinical impression that ritonavir-boosted PI regimens are associated with significant increases in lipids. The potential atherogenic implications of such changes could be associated with an increased risk of cardiovascular disease. The management of hyperlipidemia in this population remains problematic. Other PI toxicities include insulin resistance, metabolic abnormalities, fat re-distribution and hepatotoxicity. Lactic acidemia (mitochondrial toxicity) was found to have an epidemiologic association with NRTI therapy. Other NRTI toxicities include lipoatrophy. In post-exposure prophylaxis, the use of nevirapine (NNRTI) is not recommended due to liver toxicity in otherwise healthy individuals.

Recently, the Department of Health and Human Services (DHHS), in collaboration with the Henry J. Kaiser Family Foundation, published major revisions in the HIV treatment guidelines. The new guidelines reflect a shift toward a more conservative view about the initiation of therapy (a CD4 threshold of 350 cells/mm3 instead of 500).

Newer drugs may be more convenient (simpler dosing schedules), and offer better tolerability as well as improved virological activity against resistant virus. Some of the new drugs in clinical trials are: NRTI: emtricitabine (FTC), diaminopurine dioxolane, and pronucleotides of d4T; Second generation NNRTIs: capravirine, emivirine (MKC-442), and quinoxaline; PIs: tipranavir, BMS-232632, and DMP 450. There are also newer classes of antiretrovirals such as the recently approved nucletotide analogue RTI tenofovir. Other potential targets in the HIV replicative cycle: a) viral absorption (polysulfates, zintevir), b) viral entry (AMD3100, T22, TAK-779), c) viral cell fusion (T-20 (pentafuside), T-1249), d) viral assembly and disassembly (DIBAs, azadicarbonamide), e) integrase inhibitors (L-731, 988), f) transcription inhibitors (fluoroquilone K-12, temacrazine, CGP64222).

Since 1987, more than 40 different AIDS vaccines have been tested. Only AIDSVAX has been thought promising enough to merit testing in humans in a large-scale study. A cure for HIV seems to be years away. Prevention and education projects are by far the best tools to stop the disease from spreading.

Carlos H. Zambrano, M.D. (Infectious Disease Specialist) is affiliated with the Erie Family Medical Center in Chicago, IL; with two centers located at: West Town, 1701 W. Superior, Chicago, IL 60622, (312) 666–3494 and Humboldt Park, 2750 W. North Avenue, Chicago, IL 60647, (773) 489–6060.

AIDS 2002: Still Room for Improvement

by Matt Sharp

2001 was not exactly a banner year for AIDS. June marked the 20th anniversary of the epidemic and provided an important perspective to where we are today with AIDS. Although there was incremental research progress in 2001, there are still many problems that have compounded as the epidemic has spread. A worldwide effort is taking shape but some say it has been too little, too late. AIDS continues to wreak havoc worldwide as the infection rate climbs and the world closes its eyes.

Some of the most significant contributions in medical history have been made in AIDS research in a relatively short time. In the U.S., in just 14 years, there are sixteen FDA approved anti-HIV drugs that slow disease progression. But treatments remain complex, less than perfect, and cause side effects, and AIDS is still with us. New formulations and simpler once-a-day dosages have been developed but there is still room for improvement. Several more drugs from new classes that target the virus differently are in the research pipeline, but beyond that there appears to be a lag in further promising development. A sizeable and growing percentage of people are drug resistant, meaning drugs are less effective. For these people, there is a pressing need for new treatments—either new, non-cross-resistant members of existing drug classes, or agents that work in different ways. The overall learning curve of HIV treatment has perhaps reached a critical peak; now the time for dealing with the longterm effects of the drugs and research into more effective drugs has come to pass.

With the dilemma of a pressing need for new therapies and drug companies cutting back on research and development, it makes sense that scientists need to concentrate on ways to improve immune function so that we do not have to rely as much on the mediocre, toxic antiviral drugs. There is some good, yet incomplete information on ways to bolster the immune system with immune modulators such as IL-2, that has been studied for years. Vaccine technology and structured treatment interruption are hopeful, yet inconclusive. More advocacy and research needs to be done in this area.

With the pressing need for new therapies and drug companies cutting back on research and development, it makes sense that scientists need to concentrate on ways to improve immune function...

New Drugs and Better Formulations

Most of us recognize that the majority of drug resistance is caused by poor adherence. One way to enhance adherence to antiviral therapy is to make drugs easier to take. AZT and 3TC have been combined to make Combivir, and AZT, 3TC and abacavir have been joined to make Trizivir. Both are one pill twice a day. ddI is now made in a once a day enteric coated formulation that will metabolize better. Newer versions of older drugs are also being developed to lower pill burden in order to improve adherence and improve bioavailability.

Viread was the only anti-HIV drug approved in 2001. The drug is looking good in resistant patients, and it only has to be taken once a day! T-20 is an exciting drug reaching a critical phase in development. A new open label study program will offer a small supply of the drug to the most advanced patients in the first part of 2002. Activists wouldn't stand for the company to call the program an expanded access program because of the limited number of slots.

The importance of developing drugs that will work against drug resistant strains cannot be overstated. A few novel nucleoside analogs, DAPD and dOTC, may have activity against some resistant strains. Emtricitabine is also in the pipeline as a once daily regimen but is not effective against 3TC resistant strains.

Second-generation NNRTIs that may retain activity against virus resistant to current agents include TMC120, that looks strong in early Phase I studies, and DPC 083, a cousin to Sustiva. Tipranavir is the leading new protease inhibitor in development that shows activity against many PI resistant strains. Several other protease inhibitors are in early stages of testing that may prove to be less toxic, easier to take, and not cross resistant to older PIs.

Inhibitors of fusion and entry are earlier in development, so it is too soon to know if they work. However, the drugs may perform well together and are encouraging because they won't be cross resistant to older drugs, possibly being more effective at lowering virus levels. Many of the co-receptor inhibitors have to be infused and there are various toxicity problems in early studies, so it is not yet clear just yet how these drugs will play out.

The Vaccine Front

The year holds more positive news on the vaccine front. For the second year there was a Vaccine Conference that didn't neces-

sarily provide dramatic news, but at least was a means to mobilize people working in the field. Most of the attention in prevention vaccines is currently focused on DNA vaccines with various viral vectors as boosters. A number of approaches are moving into production or are in very early safety trials. The Vaccine Trials Network and Walter Reed Army Institute are moving ahead with two other booster vaccines that could go into efficacy trials in 2002-3. Results from the VaxGen trials in gay men and IDUs will be available then too. It still is way too early to tell if any of these will be effective in preventing HIV, but it appears to be a good start. The world is watching and waiting.

In therapeutic vaccines, the most interest is with very early treated individuals and in structured treatment interruption, before chronic infection is established and HIV T-cell help is lost. Merck has initiated trials of its vaccines in HIV positive people and met with community representatives in December 2001 to report on its program.

Side Effects and Toxicities

It used to be that AIDS complications were mostly life threatening opportunistic infections. Today with at least partial viral control and some immune system repair, complications due to therapy have become more prevalent than OIs and malignancies. It is clear that in the longterm, HIV drugs are causing problems that are becoming more and more a serious problem. Liver toxicities are seen in 6-7% of people taking HIV medications. A major cause of death in HIV is liver failure. Hepatitis C and longterm antiviral use is the culprit. Metabolic complications remain a puzzling situation but there are more hints as to the cause. In the MAC cohort study 33% of participants reported body fat changes. Metformin, oxymetholone (a testosterone derivative), pioglitazone, and rosiglitazone are promising treatments for lipodystrophy. Serostim is helping with body fat accumulation as well. There seem to be less treatment interventions for lipoatraphy, or loss of body fat in the face and limbs.

Structured Treatment Interruption

Years ago, stopping HIV therapies might have seemed like suicide, but today with growing concern over longterm toxicity this new option is being studied. Therapy interruption is a protocol of stopping and starting HIV drugs in order to relieve the cumulative side effects and maybe kick start the immune system. There is growing evidence that in early infection the strategy may be effective in controlling HIV. However, in the chronically infected, STI appears to not work as well. One promising strategy is the NIH study of heavily treated patients on a 7 day on, 7 day off regimen. After 52 weeks there was no resistance seen. There were very low level blips in viral load in a few patients and complete control in the others. Significantly, drug toxicities appeared to be reduced. (*See "News Briefs."*)

It's clear that our government has put plans for prescription coverage for the elderly on the back burner, so any plan to fix our nation's pathetic health care system is not even in the picture.

Obviously, drug companies do not like the STI approach because in the end they lose. STI would undoubtedly save on prescription costs and be a godsend in developing countries. As with many areas of research that are new and controversial, researchers are divided over whether it is something to pursue. STI needs to be proven before people decide they can do it outside of the research setting.

Access Issues

Our health care infrastructure is ready to implode as the insurance industry is finding manipulative ways to not cover people who are sick. Quality care for the HIV patient today is complex and expensive. Co-payments and premiums are rising beyond the scope of most people's budget and drug coverage and diagnostics are covered less and less. HIV doctors have cut back in their practices and are closing because the companies will not pay for the specialized treatment required by people with HIV. Insurers are folding and merging, creating fewer options for coverage of quality care. Corporations and businesses have to find cheaper insurance plans that leave out people who need coverage the most. Most frustrating is the fact that AIDS drugs have set the precedent for high pricing seen by pharmaceutical companies, which is driving up the cost of health care. It's also clear that our government has put plans for prescription coverage for the elderly on the back burner, so any plan to fix our nation's pathetic health care system is not even in the picture.

The AIDS Drug Assistance Program (ADAP) is losing funds as interest with AIDS on Capitol Hill wanes. The feds identified $120 million for this year but that amount falls short since last year the budget began $50 million short of what was needed. Since state budgets complete the picture of ADAP funding, they will be pressured to come up with more funds. Given the murky past with some state ADAPs this news is not encouraging. New drugs are increasing the costs, especially high tech agents that are needed for treatment experienced folks.

The recent recession and war against terrorism have certainly changed American's "business as usual" attitude and therefore affected the way we think about AIDS. Now as I watch the AIDS drug pipeline, and the pathetic health care infrastructure, I worry that AIDS has become a thing of the past, only overshadowed by imminent problems.

Thanks to Bill Snow, Jeff Getty, Anne Donneley, and Martin Delaney for information provided for this article.

Matt Sharp is currently a member of two grassroots national groups, Coalition for Salvage Therapy and AIDS Treatment Activists Coalition. He has written extensively on AIDS treatment for the past seven years for the Bay Area Reporter *in San Francisco, and AIDS websites and newsletters all over the country. Recently transplanted from San Francisco where he was an AIDS treatment educator, activist and advocate, he now resides in Chicago with his partner.*

Brand Name:
Retrovir

Common Name:
zidovudine, AZT

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)

Standard dose: One 300 mg tablet twice a day (two 100 mg capsules three times a day also available), no food restrictions. Clear, strawberry-flavored liquid available for pediatric use. Take missed dose as soon as possible, but do not double dose.

Wholesale cost: $4,013/yr., $334/month

Patient assistance number: 1 (800) 722–9294, www.gsk.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Headaches, fever, chills, muscle soreness, fatigue, anemia, nausea, and fingernail discoloration. AZT has been associated with bone marrow suppression: anemia and/or neutropenia, particularly in people with advanced HIV. Potential for severe anemia requiring blood transfusion or hospitalization when used with hydroxyurea. Prolonged use of AZT has been associated with symptomatic myopathy (muscle damage). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions:

Biaxin (clarithromycin), Mycobutin (rifabutin), and rifampin (under various brand names, used for treating tuberculosis) may decrease AZT blood levels. Benemid (probenecid) may increase AZT blood levels and decrease AZT clearance. Methadone and ganciclovir (Cytovene and Vitrasert) increase AZT blood levels. Prescriber may need to adjust doses accordingly. AZT and Zerit shouldn't be used together due to evidence that one limits the other's bioavailability level in the test tube. Also, risk of bone marrow toxicity may increase with use of ganciclovir, amphotericin B, pentamidine (NebuPent, Pentam or Pentacarmat), dapsone, flucytosine, interferon-alpha ribavirin (Rebetol), and with other antineoplastics (anti-tumor treatment) such as hydroxyurea. Ribavirin and AZT may cancel each other out.

Tips:

Do not use with Hydrea (hydroxyurea). Retrovir has somewhat of a bad rep left over from its early years when the doses given were too high. Studies show that Retrovir crosses the blood-brain barrier to a useful degree, which may treat or prevent neurologic damage (such as dementia). Proven to significantly reduce mother-to-infant transmission. Also available in Combivir (one tablet twice a day, combined with Epivir) and in a triple combination in Trizivir (one tablet twice a day combined with both Epivir and Ziagen).

Manufacturer

FDA-approved in March 1987, Retrovir (AZT) was the first authorized antiretroviral AIDS drug. Together with 3TC, Retrovir is one of the most widely used anti-HIV drugs and has become a staple in many three-drug studies for the treatment of HIV/AIDS. Epivir and Retrovir are available together as a fixed dose combination tablet called Combivir. They are also combined with abacavir in a fixed dose combination tablet called Trizivir. The combination of 3TC and Retrovir was generally well tolerated in clinical trials. The most commonly reported adverse events consisted of headache, nausea, malaise and fatigue, runny nose and nasal congestion, diarrhea, low white blood cells and anemia. Its labeled dosing is one 300 mg tablet twice daily. Studies have shown Retrovir to be effective in significantly reducing the risk of transmission of HIV from an infected mother to her baby. Please refer to the full prescribing information for additional important safety information.

—GlaxoSmithKline

Doctor

FDA approved 3/19/87 for the treatment of adult AIDS or symptomatic HIV. Approved 9/28/89 in syrup formulation. Approved 2/2/90 in intravenous form. Approved 5/3/90 for pediatric HIV infection (ages 3 months to 12 years). Approved 8/8/94 for the prevention of perinatal transmission in HIV pregnant women and newborns. The first drug approved to treat AIDS, the well known zidovudine was created as a potential treatment for cancer. ZDV is metabolized to its active triphosphate metabolite (74% eliminated through the urine). There is cross-resistance between ZDV and other NRTIs. Its peak effectiveness is in treatment naïve patients as part of a combination regimen. Rash, nausea, headache, bone marrow toxicity (anemia), myopathy, lactic acidosis and hepatomegaly with steatosis have been reported. Concomitant nephrotoxic, cytotoxic or myelosuppressive drugs should be used with caution (e.g., amphothericin B, vincristine, gancyclovir).

—Carlos H. Zambrano, M.D.

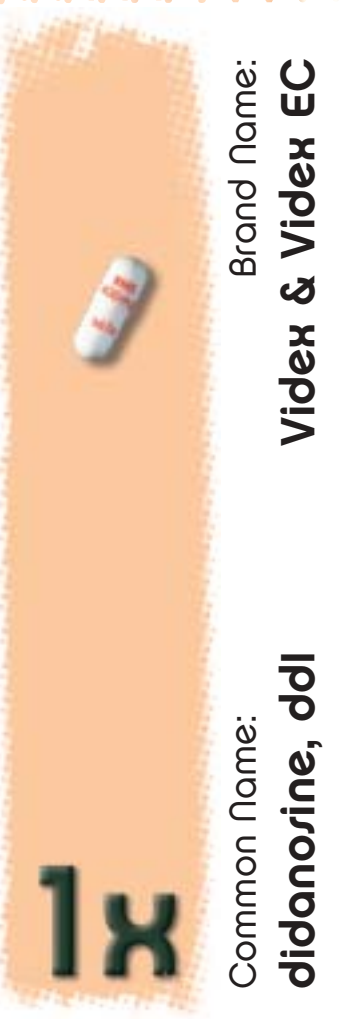
Activist

AZT (also known as Retrovir) was the first drug approved for AIDS in 1987; therefore, there is more experience with AZT than any other AIDS drug. It was initially dosed at 1200-1500 milligrams a day, the reason it has such a bad reputation. Later lower doses, 500-600 mg. a day, were found to be better tolerated and just as effective. Recognized as the standard of care for years, some doctors and patients have chosen to use other similar nucleoside analogs instead because AZT can cause nausea and headaches. Resistance tests should be performed in making initial treatment decisions because 10% of newly infected people are resistant to AZT.

Before use in HIV, AZT was shelved as a drug for cancer. After approval for HIV, ACT UP New York closed the New York Stock Exchange in a civil disobedience action over the high price of the drug. Two weeks later, the prices were lowered.

—Matt Sharp

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One 400 mg eneteric coated (EC) capsule once a day, with adjustments for weight. Older form (buffered tablets) must be taken at least two at a time for adequate absorption. Also, powder for oral solution. Strictly on an empty stomach (1/2 hour before or two hours after food or drink, except water). Adults with kidney dysfunction require dose adjustment. Take missed dose as soon as possible, but do not double dose.
Wholesale cost: $3,420/yr., $285/month
Patient assistance number: 1 (800) 426–7644, www.bms.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Retinal changes, optic neuritis and peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that is reversible but can be painful and permanently debilitating if not treated in time). Have periodic retinal exam. Headache, increased uric acid levels (indicating a number of disorders, including kidney damage and metabolic diseases), and insomnia are other potential side effects. People with a history of peripheral neuropathy, pancreatitis and heavy alcohol use should avoid Videx. Pancreatitis can be life-threatening and is indicated by increased amylase and lipase levels in lab reports and pain in the stomach and back, along with nausea, vomiting and blood in the urine—risk increases with higher doses, advanced HIV, and alcohol use. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions:
Consider increasing Videx dose when taken with methadone (which lowers Videx blood levels by 41%). Videx/Hivid combination is not recommended because of its higher incidence of peripheral neuropathy. Antineoplastics (anti-tumor treatment) such as AZT and hydroxyurea may increase risk of peripheral neuropathy. Alcohol, Cytovene, NebuPent, Zerit and hydroxyurea may increase risk of pancreatitis. Also, Cytovene raises Videx levels by up to 65 percent. Should not be taken with any prescription antibiotic containing any form of tetracycline. Videx tablets should be taken on an empty stomach two hours apart from protease inhibitors, Tagamet, Nizoral, Sporanox and dapsone, and one hour apart from Rescriptor, while Videx EC can be taken with them (still on an empty stomach).
Tips:
Study indicates Videx EC may lower risk of peripheral neuropathy. Swallow the new capsules whole (don't break open). Capsules eliminate awful texture of the tablets and the enteric coating eliminates diarrhea. Technically, twice-daily with the tablets is "preferred dose" according to the FDA. But that's based on a small registrational trial—other studies not counted indicate that once-daily tablets are just as potent. Because of complex dosing requirements (empty stomach) once-daily dosing was common long before FDA approval. Absorption can be decreased by as much as 50 percent when taken with food. If you have kidney dysfunction, you need regular tests to check how they're working with Videx. Notify your doctor immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare provider.



Manufacturer

In 1999 Videx was approved as the first once-daily nucleoside analogue. In October 2000, the FDA granted approval of Videx EC delayed release capsules, containing enteric-coated beadlets designed to protect the active ingredient in Videx from stomach acids, eliminating the need for buffer. Videx EC capsules are easy to swallow, with no chewing or dispersing of tablets. Fatal and nonfatal pancreatitis has occurred during therapy with Videx. Videx should be suspended in patients with suspected pancreatitis and discontinued in patients with confirmed pancreatitis. Lactic acidosis, hepatitis and liver failure have been reported with the use of nucleoside analogues, including Videx. Other important toxicities include retinal changes, optic neuritis, and peripheral neuropathy. Patients treated with Videx in combination with Zerit, with or without hydroxyurea, may be at increased risk for adverse events such as pancreatitis, peripheral neuropathy, and liver failure.
—Bristol-Myers Squibb

Doctor

FDA approved 10/31/01 for combination with other antiretroviral agents, as indicated for the treatment of HIV-1 infection in adults whose management requires once-daily administration of didanosine or an alternative didanosine formulation. The enteric-coated formulation consists of small beads coated with a methyl cellulose-based product that permits the drug to pass through the stomach and to be released in the upper portion of the small intestine. The enteric-coated formulation does not include buffering agents (less gastrointestinal side effects). Videx EC capsules dosed QD provide antiviral activity in a triple regimen similar to a reference triple regimen in treatment-naïve, HIV-infected subjects.
—Carlos H. Zambrano, M.D.

Activist

Bristol Myers/Squibb has worked hard to make the unpleasant ddI (Videx EC) pleasant. The old formulation was quite simply… yucky. It was a horse pill that had to be chewed or dissolved in water (yet another inconvenience) and it caused diarrhea. Now, given the competition in the market, the drug was first made into an orange flavor (yum!) then better yet, an enteric coated pill that only has to be taken once a day.
There are important drug interactions with other HIV drugs and with methadone. Neuropathy is a problem as it is with d4T and ddC (remember the "D" drugs cause neuropathy). There used to be excitement in adding hydroxyurea that may add to the effect of ddI. However, less hydroxyurea is being prescribed due to anemia and its effect on lowering T-cells. d4T and ddI together is a good way to go if you watch for pancreatitis and neuropathy.
—Matt Sharp

Brand Name: **Hivid**

Common Name: **zalcitabine, ddC**

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

Standard dose: One 0.75 mg tablet three times a day, no food restrictions. Liquid available through compassionate use program. Take missed dose as soon as possible, but do not double dose.

Wholesale cost: $2,808/yr., $234/month

Patient assistance number: 1 (800) 285–4484, www.rocheusa.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Headache, fever, skin eruptions, canker sores, general inflamation of the mouth, nausea, pancreatitis, malaise (general ill-feeling, as with the blahs, fatigue or a flu) and peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that is reversible but can be painful and permanently debilitating if not treated in time). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions:

Due to increased risks associated with peripheral neuropathy, according to the U.S. Department of Health and Human Services (HHS) HIV guidelines, whenever possible Hivid should not be taken with antiretroviral nucleoside analogues, Fungizone (amphotericin B), Chloromycetin (chloramphenicol), dapsone, Antabuse (disulfiram), Foscavir (foscarnet), isoniazid (for treating tuberculosis), Dilantin (phenytoin) and Benemid (probenecid). Antacids decrease Hivid levels by 25 percent. Tagamet (cimetidine), Maalox, Foscavir and Benemid may decrease Hivid levels. When used with Hivid, Pentamidine (NebuPent, Pentam or Pentacarinat, used for treating *Pneumocystis carinii* pneumonia, that is, PCP), may increase risk of pancreatitis, inflammation of the pancreas that can be life-threatening. Pancreatitis is indicated by increased amylase and lipase levels in lab reports and pain in the stomach and back, along with nausea, vomiting and blood in the urine. However, increased amylase levels may not occur until after pancreatitis does. The risk of pancreatitis increases with higher doses, more advanced HIV, and alcohol use. If you experience these symptoms, stop taking Hivid and seek medical attention immediately. If symptoms go away after stopping Hivid, you can consider starting Hivid again at a smaller dose.

Tips:

Dual use of Hivid and Videx is not recommended because of the association with a high incidence of peripheral neuropathy. Notify your doctor immediately if peripheral neuropathy is suspected, but do not stop medication unless directed to do so by your healthcare provider.

Manufacturer

Hivid (zalcitabine) is a nucleoside reverse transcriptase inhibitor (NRTI) used in combination with other antiretroviral agents for the treatment of HIV infection. Side effects associated with Hivid, when taken alone or in combination with AZT, are peripheral neuropathy and pancreatitis. Some patients also experience less serious side effects, including oral ulcers and rash.

—Roche, 2001

Manufacturer did not respond to request for updated statement.

Doctor

FDA approved 6/19/92 for combination use with AZT for the treatment of patients with advanced HIV disease. Approved 8/5/94 for monotherapy treatment of advanced HIV for those aged more than 13 years. The antiviral activity of zalcitabine depends on its intracellular conversion to ddCTP. AZT-resistant strains are still susceptible to zalcitabine and vice versa. Concomitant use of AZT and zalcitabine against HIV appears to be synergistic. Current recommendations generally advise a three-drug combination including a protease inhibitor, as a second line therapy. Zalcitabine caused peripheral neuropathy in 17%-31% of trial participants. Zalcitabine and ddI should not be combined due to increased risk of peripheral neuropathy. Rash, pharyngitis, oral and esophageal ulcers, flu-like symptoms, pancreatitis (potentially fatal), lactic acidosis and hepatomegaly with steatosis have been observed.

—Carlos H. Zambrano, M.D.

Activist

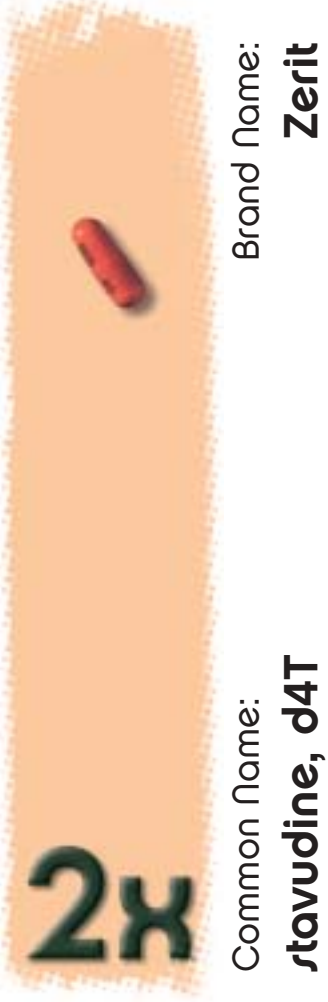
ddC (Hivid) has become the forgotten, least used nuke in today's armamentarium of AIDS drugs. It is the least effective nuke, not recommended for initial use in the DHHS guidelines in combinations or even as a second line therapy. ddC especially should not be used together with ddI because of it's ineffectiveness and overlapping toxicities such as neuropathy and pancreatitis. Ongoing studies of the drug are nonexistent, which show that there is little interest or promise for the future of this drug.

In the early days of the epidemic when AZT was the only therapy available, there was news that combination therapy was a better way to go so ddC became in demand. It was the only antiviral actually made on the underground and sold through buyers clubs by people with AIDS. Looking back it is unfortunate there was so much effort to provide this drug, but in those days people were desperate.

—Matt Sharp

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)
Standard dose: One 40 mg capsule twice a day for people weighing 132 pounds (60 kg) or more, or one 30 mg capsule twice a day for people weighing less; no food restrictions. Available in 15 mg, 20 mg, 30 mg and 40 mg capsules. Also powder for oral solution. Take missed dose as soon as possible, but do not double dose.
Wholesale cost: $3,960/yr., $330/month
Patient assistance number: 1 (800) 272–4878, www.bms.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Headache, chills/fever, malaise (overall ill feeling, as with fatigue or a flu), insomnia, anxiety, depression, rash, nausea, vomiting, diarrhea, abdominal pain and peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that can be reversible but could become permanent if not treated in time and that may be debilitating and painful). Symptoms may persist after stopping the drug. If symptoms go away after stopping Zerit, you can consider starting Zerit again at a smaller dose. Caregivers of young children should be instructed regarding noticing and reporting peripheral neuropathy. Adverse reactions and serious laboratory abnormalities in pediatric patients were similar in type and frequency to those seen in adults. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions:
Drugs such as Fungizone (amphotericin B), Foscavir (foscarnet), and dapsone may increase the risk of developing peripheral neuropathy. Cytovene and Vitrasert (ganciclovir) and intravenous Pentam (pentamidine) may increase the risk of pancreatitis. To be used with caution by people with pre-existing bone marrow suppression, renal insufficiency or peripheral neuropathy. When combined, Videx and hydroxyurea may increase risk of pancreatitis. AZT and Zerit shouldn't be used together due to evidence that one limits the other's bioavailability level in the test tube.
Tips:
A small sub-study examining the differentiating effects of Zerit and Retrovir (AZT) on both lipoatrophy and central fat accumulation showed that fat loss in the face, arms or legs after 30 months of therapy was twice as high in the group taking Zerit compared to the group taking AZT. One advocate noted this was seen from its FDA approval, long after Retrovir was on the market. Contact your doctor immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare provider. Stop taking Zerit immediately if experiencing symptoms of pancreatitis: pain in the stomach that sometimes extends to the chest and the back, along with nausea, vomiting or blood in the urine. Get immediate medical attention. Increased amylase levels indicate pancreatitis, but sometimes levels do not increase until after pancreatitis occurs. Studies show that Zerit crosses the blood-brain barrier to a useful degree, which may treat or prevent neurological damage (such as dementia).



Manufacturer

Zerit, approved in 1994, provides effective, long-term therapy, is generally well tolerated and may encourage adherence with an easy to swallow small capsule taken twice daily regardless of meals. An increase of lactic acid in the blood, an enlarged liver and liver failure, which can cause death have been reported in patients receiving NRTI-containing regimens. Fatal and non-fatal pancreatitis (inflammation of the pancreas) has occurred with Zerit taken in combination with didanosine and other HIV drugs. Zerit may cause numbness, tingling or pain in the hands or feet (neuropathy). This risk is increased in patients with advanced HIV disease or a history of neuropathy. If you are taking Zerit in combination with other medicines that may cause similar side effects, you may have a higher chance of developing these effects. Frequent side effects in triple combination regimens are nausea, headache, diarrhea, rash, vomiting and neuropathy.
—Bristol-Myers Squibb

Doctor

FDA approved 6/17/94 for the treatment of adults with advanced HIV infection. Approved in 1996 for adults and pediatrics who have undergone prolonged treatment with AZT. There is an antagonistic effect between stavudine and zidovudine. Extended release formulation has been found to be safe and effective. The major clinical toxicity of stavudine is peripheral neuropathy (up to 24%). All nucleoside analogues induce mitochondrial toxicity. Lactic acidosis and severe hepatomegaly with steatosis have been reported with stavudine use (possible risk factors include female gender, obesity, and prolonged nucleoside exposure). Lipoatrophy is of major concern in subjects with thymidine analogue (stavudine and zidovudine)-contaning regimens. Withdrawal of thymidine analogues in lipoatrophic patients on a PI-sparing regimen results in a significant improvement in peripheral fat stores, but is associated with loss of viralogical control.
—Carlos H. Zambrano, M.D.

Activist

In early studies d4T (Zerit) was shown to be as effective as AZT and less toxic, so doctors and patients thought it might be a better choice. It is approved as a first line therapy. However, using AZT before d4T has been shown to be more effective. It is also important to choose the dosage of d4T according to body weight: <132 lbs.: 30 mg, >132 lbs.: 40 mg. The company is working on a once a day pill rather than twice a day, but it is not yet approved.
Mitochondria, the "machinery" inside cells which may be linked to drug side effects, is decreased by 44% in people taking d4T. Also, d4T has long been known to cause serious neuropathy. Lactic acidosis and serious liver problems have also been reported in a small number of people using d4T. There appears to be safer nucleosides to choose from, especially if you are coinfected with hepatitis C.
—Matt Sharp

Brand Name:
Epivir

Common Name:
lamivudine, 3TC

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

Standard dose: One 150 mg tablet twice a day, with no food restrictions. Dose needs to be lowered for people who weigh less than 110 pounds (50kg), to 2 mg/kg (a kilogram equals 2.2 pounds). Strawberry/banana flavored liquid. Take missed dose as soon as possible, but do not double dose.

Wholesale cost: $3,435/yr., $286/month

Patient assistance number: 1 (800) 722–9294, www.gsk.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Headache, nausea, diarrhea, fatigue, hair loss, insomnia, malaise (overall ill feeling, as with the blahs, fatigue or a flu), nasal symptoms, cough and peripheral neuropathy. In children, may cause pancreatitis, a potentially fatal condition. Children should be monitored carefully for this condition. Symptoms include nausea, vomiting, clammy skin, and stomach pain that often extends to the back, along with increased amylase in the blood. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions:

No significant interactions.

Tips:

Is also the first oral therapy for treatment of hepatitis B virus (HBV), under the brand name Epivir HBV and used at a different dose. The once-daily dose for HBV may cause drug resistance (it may no longer work) for people with HIV. Also available combined with Retrovir (Combivir, one tablet twice a day) and in a triple combination with both Retrovir and Ziagen (Trizivir, one tablet twice a day). GSK is applying to the FDA for a 300 mg, once a day dose of Epivir.

Manufacturer

FDA-approved in November 1995, Epivir (3TC) has become a widely used antiviral in combination with (AZT). The two popular drugs, which are a foundation for many three-drug regimens, have been approved as Combivir, a fixed dose combination tablet. Lamivudine and zidovudine are also combined with abacavir in a fixed dose combination tablet called Trizivir. Data from a small number of patients suggest that Epivir may delay the development of viral resistance to Retrovir in patients with no previous treatment history. Epivir may reverse resistance to Retrovir in a small number of patients who have received extensive prior therapy with Retrovir. These resistance data continue to be studied. The most commonly reported adverse events consist of headache, nausea, malaise and fatigue, runny nose and nasal congestion, diarrhea, low white blood cells, and anemia.

—GlaxoSmithKline

Doctor

FDA approved 9/27/97 for combination use with AZT as a treatment option for HIV infection in adults and pediatric patients greater than or equal to 3 months old. The majority of lamivudine is eliminated unchanged in urine. Coadministration of lamivudine and zidovudine results in an increase in Cmax of zidovudine. Lamivudine may reverse resistance to zidovudine in zidovudine experienced patients (hypersensitivity). Coadministration of lamivudine and trimethoprim/sulfamethoxazole (TMP/SMX) results in an increase in lamivudine AUC. Lamivudine as once daily component of a triple combination has shown virological efficacy and safety. Lamivudine appears to be well tolerated. Paresthesia and peripheral neuropathies, pancreatitis, lactic acidosis and severe hepatomegaly with steatosis (including fatal cases), have been reported. Lamivudine has been approved for the treatment of hepatitis B virus infections.

—Carlos H. Zambrano, M.D.

Activist

Epivir, or 3TC, is one of my favorite nukes because it is the smallest pill, which makes it easy to swallow, and side effects are limited. 3TC is commonly taken with either AZT, d4T or less often, ddI, for first line regimens. Resistance develops quickly with 3TC. For this reason, GlaxoSmithKline has cleverly combined AZT and 3TC into Combivir, and another drug, Trizivir which is a combination of AZT, 3TC and abacavir. However, 3TC can be used without AZT or abacavir. It is also one of the most commonly used additions to combinations of non-nucleoside and protease inhibitor drugs and there are few interactions.

There may be benefits when recycling this drug with Viread. Three studies indicate that 3TC is also active against hepatitis B.

—Matt Sharp

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)
Standard dose: One 300 mg tablet twice a day, with or without food. Strawberry/banana flavored liquid. Take missed dose as soon as possible, but do not double dose.
Wholesale cost: $4,615/yr., $384/month
Patient assistance number: 1 (800) 513–3028, www.gsk.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Hypersensitivity (allergic reaction) can be fatal. People experiencing hypersensitivity must stop taking Ziagen and cannot take it again (called "rechallenging"), because of life-threatening, and in at least three cases, fatal reaction. Hypersensitivity usually occurs within six weeks of starting therapy, gets progressively worse and resolves quickly after permanent discontinuation. Approximately 5% of people taking Ziagen experienced hypersensitivity during clinical trials. The primary symptom is low-grade fever with multi-organ symptoms: muscle ache, nausea, vomiting or other gastrointestinal upset (including abdominal pain), malaise (run-down feeling, as with the blahs, fatigue or a flu), respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. Hypersensitivity might be confused with flu during flu season. The manufacturer recommends that people with symptoms of acute respiratory disease consider hypersensitivity even if other diagnosis such as pneumonia, bronchitis or flu is possible. If hypersensitivity is suspected, stop therapy and contact your doctor immediately. There should be no problem with this if you miss your doses for a few days and did not have an allergic reaction. Black box warning strengthened last year when hypersensitivity wasn't recognized and people went back on Ziagen, becoming seriously ill.

Other potential side effects include nausea, vomiting, diarrhea, fatigue, headache, fever, rash, anorexia (loss of appetite), high blood sugar and high triglyceride levels (fat in the blood). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions:
Alcohol increases Ziagen levels and might increase its side effects. The interaction between Ziagen and ethanol was studied in 24 HIV-positive men. No clinically significant interaction was observed. Females have not been studied.
Tips:
Ziagen has the potential to cross the blood-brain barrier, which may prevent or treat neurological damage (such as dementia).

Brand Name: **Ziagen**

Common Name: **abacavir sulfate**

Manufacturer

Ziagen (abacavir sulfate) is a one-tablet, twice daily nucleoside analogue reverse transcriptase inhibitor that is used in combination with other antiretrovirals. Results of one study suggest similar antiviral effects-at 48 weeks-of Ziagen + Combivir and Crixivan + Combivir on the proportion of patients with viral loads below 400 copies/ml. The most serious adverse event is a hypersensitivity reaction in approximately 5 percent of patients, generally characterized by signs and symptoms which include fever, skin rash, fatigue, nausea, vomiting, diarrhea, abdominal pain, cough, shortness of breath, or sore throat. Patients experiencing these symptoms must contact a physician immediately and suspend taking Ziagen. Ziagen and Trizivir should not be started again after a hypersensitivity reaction because you may experience life-threatening symptoms that may include lowering of your blood pressure or death.
—GlaxoSmithKline

Doctor

FDA approved 12/17/98 to treat HIV-1 in adults and children. Abacavir is a prodrug that is pharmacologically active only after conversion to carbovir triphosphate. Abacavir differs from other NRTIs in that it is a carbocyclic nucleoside rather than a dideoxynucleoside. Cross-resistance between abacavir and other NRTIs has been reported. Abacavir increases plasma concentrations of amprenavir (dosage adjustment not required). At 48 weeks, ABC/3TC and amprenavir (twice daily), showed to be potent and well-tolerated in therapy-naïve subjects. Abacavir is generally well tolerated. Potentially life threatening hypersensitivity reactions (usually within the first 6 weeks of treatment) have been reported in 5% of clinical trial patients in combination with lamivudine and zidovudine. Resolves within 2 days after discontinuation. Do not re-challenge. Lactic acidosis, hepatomegaly with steatosis and pancreatitis have also been reported.
—Carlos H. Zambrano, M.D.

Activist

Ziagen (abacavir) is one of the newest nucleosides approved. Head-to-head studies have not been done with other nukes. The DHHS guidelines do not recommend Ziagen as a first line therapy but the drug may be easier to take and less toxic than older drugs and be just as effective.
A serious life-threatening problem with abacavir is seen in approximately 5% of patients. It can cause a hypersensitivity reaction that can be life threatening. If the reaction occurs upon initial use, the drug should be discontinued. Restarting the drug can cause fatal symptoms of hypersensitivity. There was great hope in abacavir for the heavily treated patient. Activists initiated a boycott of Glaxo's Zantac to pressure them to provide Ziagen early in expanded access. The boycott forced an access program only to find the drug was not as good as activists had hoped.
—Matt Sharp

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Brand Name:
Combivir

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (150-mg lamivudine, 300-mg zidovudine), twice a day, with no food restrictions
Wholesale cost: $7,440/yr., $620/month
Patient assistance number: 1 (800) 513–3028, www.gsk.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects: See Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC).
Potential drug interactions: See Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC).
Tips: See Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC).

Manufacturer

Combivir brings together in one pill the two widely used antiretrovial medications: Epivir (lamivudine; 3TC) and Retrovir (zidovudine; AZT). Each Combivir tablet contains 300 mg Retrovir and 150 mg Epivir, which is only half the daily dose of each drug. By taking just one Combivir tablet in the morning and one at night, patients can receive the recommended daily doses for each drug. Combivir marks the first major step toward simplifying highly effective HIV combination drug regimens. Through availability of this simplified, alternative dosing option, it is hoped that adherence to multiple drug regimens containing Epivir and Retrovir may be encouraged. Please refer to the full prescribing information for additional important safety information.
—GlaxoSmithKline

Doctor

FDA approved 9/27/97 for the treatment of HIV infection in adults and adolescents greater than or equal to 12 years old. Combination of lamivudine and zidovudine has synergistic antiretroviral activity. In patients receiving combination therapy, mutations associated with zidovudine resistance develop more slowly and mutations associated with lamivudine resistance appeared to develop rapidly. Co-administration of other bone marrow suppressive or cytotoxic agents may increase the hematologic toxicity of zidovudine. Lamivudine plus zidovudine combination is recommended as part of a first line regimen. Combivir has been shown to be effective as part of PI and NNRTI-based regimens.
—Carlos H. Zambrano, M.D.

Activist

Combivir is simply a combination of AZT and 3TC in a one pill twice a day regimen. Glaxo found that since the drugs were used together and were effective together that maybe it would be a good marketing scheme to combine them and voila! an easier regimen for patients! Clever. Add a protease inhibitor and it's quite an easy regimen to adhere to. Remember that just because you are taking less pills does not mean there are less side effects. It is still a combination of AZT and 3TC.
—Matt Sharp

Brand Name: **Trizivir**

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (300-mg abacavir, 150-mg lamivudine, 300-mg zidovudine), twice a day, with no food restrictions
Wholesale cost: $12,060/yr., $1,005/month
Patient assistance number: 1 (800) 513–3028, www.gsk.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects: See Retrovir/zidovudine (AZT), Epivir/lamivudine (3TC) and Ziagen (abacavir).
Potential drug interactions: See Retrovir/zidovudine (AZT), Epivir/lamivudine (3TC) and Ziagen (abacavir).
Tips: For many individuals using HIV drugs for the first time and with a low-to-moderate viral load, Trizivir can be a good triple nuke regimen and easier to adhere to (one tablet twice a day), based on strong results at 48 weeks against 2NRTIs + PI regimen. The triple-nuke combo saves two classes of drugs for later if necessary. There are limited data on the use of this triple-combo regimen in people with viral loads greater then 100,000 copies/mL. (*See News Briefs.*)

Manufacturer

Trizivir, a product that combines three anti-HIV medicines abacavir sulfate (Ziagen), lamivudine (Epivir or 3TC), and zidovudine (Retrovir) into one tablet, taken twice a day, was approved by the FDA in November 2000. Trizivir is indicated alone or in combination with other antiretroviral agents for the treatment of HIV infection and it is intended only for patients whose regimen would otherwise include abacavir, lamivudine and zidovudine. Trizivir, which contains abacavir, must not be used by patients who have previously experienced a hypersensitivity reaction to abacavir because more severe symptoms will recur within hours and may include life-threatening hypotension and death. [see abacavir for severe reaction symptoms] Ziagen [abacavir] and Trizivir should not be started again after a hypersensitivity reaction because you may experience life-threatening symptoms that may include lowering of your blood pressure or death.

—GlaxoSmithKline

Doctor

FDA approved 11/14/00 for the treatment of HIV in adults and adolescents (not recommended for those who weigh less than 40 kilograms, fixed tablet). At 48 weeks, Trizivir was found to be a highly active antiretroviral regimen, generally well tolerated and comparable to indinavir/Combivir in HIV-infected naïve adults. At 48 weeks, Trizivir/efavirenz was found to be potent, generally well tolerated (with no adverse events other than those previously described with drugs in this regimen) and associated with good adherence (industry sponsored, 60% of patients were either black or American Hispanic, treatment naïve with advanced stage of the disease). ACTG 5095 comparing Trizivir vs. Trizivir/efavirenz vs. Combivir/efavirenz is underway.

—Carlos H. Zambrano, M.D.

Activist

I first heard about Trizivir in a data presentation at a conference before the drug became approved and thought it was a joke. First Combivir, a two-drug combination, then Trizivir, a three-drug combo? Given the three drugs (AZT, 3TC and abacavir) are made by GlaxoSmithKline, the combo ultimately makes more profit. Brilliant marketing, I must say.

But ultimately it is a good idea to make drugs easier to take by combining them. Hopefully the drug will be prescribed carefully, especially as a first line regimen. Doctors should know the patient's antiviral history before prescribing Trizivir.

It is easy to take, one pill in the morning, one at night. As with Combivir, people should be aware that Trizivir is a combination of three drugs and so the possibility for side effects and drug interactions is multiplied, in this case tripled.

—Matt Sharp

Brand Name: **Viread**

Common Name: **tenofovir disoproxil fumarate**

Class: nucleotide analog (also called nucleotide reverse transcriptase inhibitor—part of the nucleosides—NRTI, or nuke)

Standard dose: One 300 mg tablet once a day, with food

Wholesale cost: $4,896/yr., $408/month

Patient assistance number: 1 (800) GILEAD–5 (445–3235), www.viread.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Grade 3 or 4 (serious) increased creatine (a sign of kidney or muscle damage) and AST/ALT (liver function tests, a sign of liver damage) shown in lab reports. In one study, serious side effects ranged from 6 to 16%. Elevation of creatine phosphokinase (CPK). Also nausea, headache, diarrhea, vomiting, asthenia, flatulence, abdominal pain and anorexia. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back); lactic acidosis (seen mostly in women, especially obese women; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing); and enlarged, fatty liver (check for tenderness below ribs on right side).

Potential drug interactions:

No concomitant nephrototoxic drugs allowed for small compassionate access program. Such drugs include Crixivan, Viracept, Ziagen, Hydroxyurea, Zovirax, Cytovene, Mepron, and streptomycin (used rarely for tuberculosis). Until more studies are conducted caution is urged when using Viread with drugs causing renal toxicity, such as foscarnet, pentamidine and cidofovir.

Tips:

Pretty good results in treatment experienced individuals at 72 weeks. Adding once-a-day 300 mg Viread to a stable drug combination (called "intensification") quickly showed a significant viral load decrease in 92 heavily pretreated people, which was maintained after a year (drops of 0.6 and 0.7 log respectively). (A third of them also changed at least one drug halfway through the year.) T-cells did not go up significantly in trials, however. One doctor noted that you can see a greater drop (one log) in viral load when using a protease inhibitor for intensification, along with a good T-cell increase. But another noted Viread's potential in the growing number of people whose triple-class therapy is failing. To its credit, Viread was successful in showing viral load decrease in people with nuke resistance. Epivir resistance seems to reverse tenofovir resistance. Also, because it's in a new drug class, Viread is not expected to have cross-resistance with other HIV medicines, and no new mutations were seen with its use in clinical trials. Unlike the nucleosides, nucleotides can enter uninfected cells, and once there, protect against infection. The body clears 70–80% of the drug through the kidneys, so watch creatine levels. So far, serious kidney problems have been rare. Active against hepatitis B. Multi-nucleoside resistant HIV-1 with a T69S double insertion mutation in the reverse transcriptase showed reduced susceptibility to Viread *in vitro* (in the test tube). Less toxicity in the liver than the majority of NRTIs.

Doctors are talking about the once-a-day, "Vivitiva" regimen: Videx, Viread and Sustiva. Unfortunately, Viread significantly increases Videx intracellular levels and cases of pancreatitis are being seen when the two are combined, even in patients on long-term Videx.

Manufacturer

Viread is the first nucleotide analogue available for HIV treatment. In two studies of treatment-experienced patients, Viread demonstrated significant viral load reductions through 24 and 48 weeks. Studies were conducted in treatment-experienced adults with HIV viral replication despite ongoing antiretroviral therapy. The drug was well tolerated, most common side effects were mild to moderate events such as nausea, diarrhea, vomiting and flatulence. Additionally, Viread maintained activity against HIV expressing multiple resistance mutations at baseline.

Studies in antiretroviral-naive patients are ongoing; consequently, the risk-benefit has yet to be determined. There are no data demonstrating the effect of Viread on clinical progression of HIV. The use of Viread should be considered for treating adult patients with HIV strains that are expected to be susceptible to Viread as assessed by laboratory testing or treatment history.

—Gilead

Doctor

FDA approved 10/26/01 for treatment of HIV-1 infection in combination with other antiretroviral agents. Tenofovir DF is the first nucleotide analog approved for HIV-1 treatment. Tenofovir is active against HIV-1 and SIV. Chemically related to adefovir. No significant renal toxicity reported. At 96 weeks, adding tenofovir to existing antiretroviral therapy in highly treatment-experienced patients shows significant and durable HIV RNA reductions. There is an infrequent development of reverse transcriptase mutations associated with tenofovir. A regimen containing Kaletra, efavirenz, 3TC and tenofovir, is well-tolerated and more potent than standard HAART.

—Carlos H. Zambrano, M.D.

Activist

Viread (tenofovir DF) is an important drug today because of its effectiveness in treatment experienced patients, its safety profile and its simple once a day dosing. It is a different class of drug that targets the reverse transcriptase enzyme. Combination studies show it reduces viral load up to .6 log in people who have taken other anti-HIV drugs. Side effects are limited with Viread. Even though it is broken down by the kidney, there were no kidney problems as seen in adefovir, an earlier Gilead drug that was denied approval by the FDA. There isn't any liver toxicity as well. Damage to the cell's mitochondria is nonexistent with Viread. It should be taken with fatty foods. The drug costs about $4900 a year, twice as much as the new ddI formulation. But, after a painful history, Gilead finally appears to have come across with a decent drug.

—Matt Sharp

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: Two 200 mg tablets (smaller than the 100 mg) three times a day, no food restrictions. Take missed dose as soon as possible, but do not double dose.
Wholesale cost: $3,504/yr., $292/month
Manufacturer Contact: www.agouron.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Rash, headache, nausea, vomiting, diarrhea, fatigue and pruritus (itchy skin). Severe rash observed in NNRTI class can be life-threatening. Signs may include fever, blistering, oral lesions, conjunctivitis (pink eye, which if untreated may result in permanent loss of vision), swelling, muscle or joint aches, or general malaise (feeling unwell, as with a flu). Stop taking Rescriptor if these symptoms appear and seek immediate medical attention.
Potential drug interactions:
Do not use Zocor (simvastatin) or Mevacor (lovastatin) lipid lowering agents; suggested alternatives are Lipitor (atorvastatin), Lescol (fluvastatin), Baycol (cerivastatin), and Pravachol (pravastatin, the one that looks best on paper for people on protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Seldane (terfenadine), Hismanal (astemizole), Versed (midazolam) and Xanax (alprazolam) should not be used concurrently with Rescriptor. Potential toxicity when given with Biaxin (clarithromycin), dapsone, Mycobutin (rifabutin), ergot derivatives (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams), Procardia (nitedipine), Coumadin (warfarin) and quinidine. Tegretol (carbamazepine, an anti-seizure medication used to treat peripheral neuropathy), phenobarbital, Dilantin (phenytoin), Mycobutin (rifabutin) and rifampin (under various brand names, used to treat tuberculosis) are drugs that decrease Rescriptor levels. Certain amphetamines and antiarrhythmics drugs should not be used with Rescriptor. Use of Tagamet (cimetedine) and other drugs in that class is not recommended because they may reduce the absorption of Rescriptor. Rescriptor increases Crixivan, Fortovase, and Invirase levels. Absorption of Rescriptor is decreased with antacids, including Videx (because of its antacid buffer), so take one hour apart from these drugs. Prescriber may need to adjust doses of all these drugs accordingly.
Tips:
Rescriptor has demonstrated potential to boost protease inhibitor blood levels, research is ongoing. Using Rescriptor instead of Norvir to raise a protease inhibitor's blood levels would mean using three HIV drug classes and create the potential for cross-resistance to other non-nukes. Also, antacids and gastric achlorhydria (low stomach acid) decreases absorption. Take one hour before or after antacids and with acidic beverages such as orange or cranberry juice for achlorhydria. The drug level is increased 20% when the 100 mg tablets are given as a slurry (disintegrating drug in water; drink the rinse as well).

Brand Name: **Rescriptor**
Common Name: **delavirdine**

Manufacturer

Rescriptor is a potent NNRTI. Rescriptor has been studied in both "protease-sparing" and "protease-containing" regimens. Rescriptor is an inhibitor of the cytochrome P450 enzyme system and therefore has the ability to raise blood levels of saquinavir, indinavir, nelfinavir, ritonavir and amprenavir, which may allow for potential reduction of dosages (e.g., reduce indinavir dose to 600 mg TID as per package insert). Rescriptor's ability to increase blood levels of these protease inhibitors makes it unique among the NNRTIs. Rescriptor is now available in 200 mg tablets, as well as 100 mg tablets that can be easily dissolved in liquid (avoid grapefruit juice); taking the drug as a liquid suspension actually increases its bioavailability by 20%. Rescriptor may be taken with or without food. The most common side effect seen in patients using Rescriptor has been skin rash that usually lasts less then two weeks.
—Agouron Pharmaceuticals

Doctor

FDA approved 4/4/97 for use in combination with appropiate antiretrovirals for treatment of HIV infection. HIV-1 group O may not be inhibited by delavirdine. Delavirdine may confer cross-resistance to other NNRTIs. In clinical trials it has been used with Combivir or ddI, for initial management. Coadministration with ddI lowers the plasma levels of both drugs. Adding delavirdine to dual protease inhibitor salvage therapy decreases viral load. Delavirdine is a CYP3A4 inhibitor. Delavirdine increases indinavir, nelfinavir, ritonavir and saquinavir plasma levels (dose reduction). At 48 weeks, a triple regimen containing delavirdine and low dose indinavir demonstrated efficacy, in treatment naïve patients. Rash (18%), as with other NNRTIs, is the most significant side effect. Conjunctivitis, blisters, oral lesions, fever, muscle aches, neutropenia and transaminitis have been reported. A 600 mg twice daily dosing being studied.
—Carlos H. Zambrano, M.D.

Activist

Poor Rescriptor is the black sheep of the NNRTIs, but may actually find success by boosting levels of indinavir and saquinavir. This means taking lower doses of the PIs, perhaps reducing their side effects. Careful consideration should be taken if using the drug for its own antiviral benefits as well as a "booster," since effectiveness data is not that convincing and resistance develops very fast. Once resistant to Rescriptor you have knocked out all the other chances for other NNRTIs. As with neviripine, a rash is associated with its use. Some doctors suggest Rescriptor must be dissolved in water prior to taking it and then you have to drink the pepperminty sludge three times a day. Agouron bought Rescriptor from Pharmacia & Upjohn in 1999 because they had lost money on Rescriptor. It is not clear why Agouron made that decision.
—Matt Sharp

Brand Name: **Viramune**

Common Name: **nevirapine**

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI, or non-nuke)

Standard dose: One 200 mg tablet daily for two weeks, then full dose of one 200 mg twice daily from then on, with or without food. (If rash occurs in first two weeks, continue on one tablet a day until rash goes away before going on full dose.) Liquid formulation has pleasant taste. Take missed dose as soon as possible, but do not double dose.

Wholesale cost: $3,826/yr., $319/month

Patient assistance number: 1 (800) 274–8651, www.boehringer-ingelheim.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Rash, headache, nausea, vomiting, diarrhea, and fatigue. Abnormal liver function tests, including the development of hepatitis. May need to stop taking nevirapine until liver function returns to normal. Permanently discontinue if abnormalities return. Severe and life-threatening skin reactions and hepatotoxicity (liver damage), including fatal cases of each, have occurred. Symptoms of severe rash may include fever, blistering, oral lesions, conjunctivitis (pink eye, which if untreated may result in permanent loss of vision), swelling, muscle or joint aches, or general malaise (feeling unwell, as with a flu). Stop taking nevirapine and seek immediate medical attention. Do not increase dose if rash develops during dose escalation or if you develop any rash accompanied by the above listed conditions. Small studies found that 40–50 mg prednisone during induction period can lessen the risk. (People with hypertension or diabetes were not allowed to take prednisone.) Granulocytopenia (the loss of a specific type of white blood cell) is more common in children than in adults.

Potential drug interactions:

May cause methadone withdrawal. Viramune reduces levels of protease inhibitors and they should not be taken at the same time or the doses must be increased. Crixivan should be increased to 1,000 mg every eight hours. Kaletra should be increased to four capsules twice a day. Viramune interacts with rifampin requiring dose adjustment, but none with Mycobutin (rifabutin). The effectiveness of birth control pills may be decreased; use alternative contraception.

Tips:

Preliminary 32 weeks results in a small group (50 people) suggest equivalency to Crixivan, even in people with a high viral load (more than 100,000), plus greater T-cell increase (223 vs. 166). Other preliminary results (24 weeks in 142 people) suggest equivalency to Viracept, even in people with more than 100,000 viral load. Because of the high incidence of rash associated with Viramune, examine yourself thoroughly for the slightest sign of rash. Notify your doctor of any rash, even mild. Rash may be avoided by using dose escalation schedule. One analysis found more rash, and more severe rash, in women. Use of pretreatment, such as prednisone or Benadryl (diphenhydramine), a non-prescription oral antihistamine, may be used to minimize the risk of rash and to control itching. A topical (placed on the skin) hydrocortisone or an oatmeal-containing cream, such as Aveeno, may improve comfort. Topical antihistamine-containing products should be avoided since there have been reports of irritation and rashes spreading. Viramune given around the time of labor has shown effectiveness in preventing HIV transmission from a mother to her newborn. Studies suggest that Viramune crosses the blood-brain barrier to a useful degree. May cause abnormal liver funtion tests and clinical hepatitis. Monitor liver function tests during first six months.

Manufacturer

Available since 1996, Viramune is an NNRTI indicated for use in combination with other antiretrovirals (ARVs) for the treatment of HIV in adults and children. Viramune is available in 200 mg tablets and an oral suspension. Viramune in combination with other ARVs has been shown to reduce levels of HIV-RNA and increase CD4 counts. One study showed a Viramune combination suppressed HIV for up to one year in patients with advanced HIV disease and high baseline viral loads (BI1090). Findings from several studies demonstrate that patients taking a Viramune-based combination were observed to have an improved lipoprotein profile (FRAMS, LipART). Viramune has also been studied for prevention of mother-to-child transmission of HIV; however, it is not yet indicated for this use in the U.S. Side effects include hepatic events, rash, nausea and headache. Inform your doctor if you are experiencing a rash or other side effects.

—Boehringer Ingelheim

Doctor

FDA approved 6/24/96 for use in combination with nucleoside analogues for the treatment of HIV-infected adults. Nevirapine and ketoconazole should not be administered together. Nevirapine reduces indinavir, lopinavir and saquinavir-hard gel levels. Macrolides increase nevirapine. At 1 year, nevirapine plus Combivir had at least similar efficacy and acceptable tolerance than nelfinavir plus Combivir in HIV-infected naïve patients. Among NNRTIs, there is a high rate of hepatotoxicity, particularly with nevirapine and efavirenz, with high rates of discontinuation; some fulminant hepatic failure cases (including those from NVP-containing post-exposure prophylaxis regimens) have resulted in orthotopic liver transplant or death. Nevirapine should be targeted to persons with CD4 > 200 cells/mm3 and accompanied by liver function monitoring during the first 3 months of therapy. Once-daily dosing recommendation based on limited clinical data.

—Carlos H. Zambrano, M.D.

Activist

Viramune, also known as neviripine, is an interesting drug in that it has beneficial qualities, but also resistance can develop quickly if not taken properly. Cross resistance to other NNRTIs is common. Neviripine was the first of its class to be approved for HIV. It was approved based on its additive effect as a third in a combination of AZT and ddI.

It is one HIV drug that affects the absorption of many HIV drugs. Known for the rash it causes, it can be scaled up to the recommended dosage once started in order to prevent any reaction. Viramune can also cause serious liver toxicities. Talk with your doctor about the best way to approach neviripine in combination therapy because it may be important to use before protease inhibitors, saving them for down the road. Neviripine also works better than AZT in a single dose to mom and newborn baby in preventing HIV transmission.

—Matt Sharp

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)

Standard dose: Three 200 mg (600 mg) capsules once a day, preferably at bedtime, with no food restrictions (avoid high fat meals). Also available in smaller 50 mg and 100 mg capsules. Dose can be split up. Approved for children three years and older. Strawberry/mint flavored solution available to children under expanded access program. Take missed dose as soon as possible, but do not double dose.

Wholesale cost: $4,730/yr., $394/month

Patient assistance number: 1 (800) 334–4486, www.sustiva.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Central nervous system (CNS) symptoms (dizziness, headache, somnolence or hypnotic trance), psychiatric symptoms (confusion, insomnia, hallucinations, vivid dreams or nightmares, depression, euphoria or mania, agitation), rash, nausea, vomiting, diarrhea and increased liver enzymes. These symptoms occur early and generally resolve within two to four weeks. In a small number of patients, serious psychiatric symptoms have been reported. Rash is the most common adverse event. Rash is more common, and more severe, in children. Diarrhea, fever and low levels of neutrophils are also more common. Some people in recovery experience flashbacks. Women should not become pregnant because of the risk of birth defects.

Potential drug interactions:

May cause methadone withdrawal. When taken with Sustiva, Crixivan should be increased to 1,000 mg every eight hours. Kaletra should be increased to four capsules twice a day. Because Fortovase decreases 60%, it should be avoided. No interaction data available with Fortovase/Norvir—knowlegeable doctors double Fortovase to 800 mg twice a day. Sustiva and Norvir increase when used together and increase risk of liver damage and other potential side effects. Do not take with Hismanal (astemizole), Versed (midazolam), Halcion (triazolam), or ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams). Reduces Biaxin (clarithromyocin) dose by 37%. May affect Coumadin (warfarin) therapy. Back-up birth control method to the Pill is recommended because of potential for fetal deformaties.

Tips:

Received accelerated approval in 1998. Start taking Sustiva at bedtime to help reduce CNS symptoms (seen in half of all adults taking it), but can be taken at any time. Avoid driving or operating heavy machinery for a few hours after dose. Side effects may not go away soon. Some people have horror stories about Sustiva and others say it's "like taking candy." Some people can handle Sustiva better when taking Atavan or Ambien to sleep for the first few weeks. High-fat food as well as alcohol may increase risk of side effects. Strong preliminary results with Combivir (slightly better than Crixivan/Combivir) led to making Sustiva the first drug that's not a protease inhibitor to be added to US guidelines for first-line HIV therapy. Recently shown to penetrate lymphoid tissue, an HIV hiding place. May raise levels of triglycerides and cholesterol. Monitor liver enzymes. Second-generation Sustiva drug in development expected to be active against non-nuke resistance. Antihistamines or corticosteriods can hasten the resolution of rash. Severe rash can be life-threatening (see Viramune). Despite CNS side effects, Sustiva penetrates readily. Children have the same side effects as adults (primarily in the CNS), but experience more rash (40%), and also diarrhea/loose stools (39%), fever (26%), cough (25%) and nausea/vomiting (16%).

Brand Name: **Sustiva**

Common Name: **efavirenz**

Manufacturer

DHHS guidelines continue to list Sustiva as the only NNRTI "strongly recommended" for use in first-line combination HIV treatment. Data presented in 2001 indicate that a regimen containing Sustiva is superior to nevirapine in HIV treatment-naïve patients, in that patients treated with a Sustiva-containing regimen experienced lower rates of treatment failure (less than 400 copies/mL) over a longer duration of time when compared to a regimen containing nevirapine. Additionally, data from Study 006 demonstrate that patients taking Sustiva+AZT+3TC experienced greater and more durable viral suppression through three years of follow-up than combination therapy using a protease inhibitor. Sustiva was the first anti-HIV drug to be approved for use once-daily in combination regimens.

—Bristol-Myers Squibb

Doctor

FDA approved 9/17/98, efavirenz is the only NNRTI to be used in combination regimens as a first line therapy for naïve patients. In contrast to nevirapine and delavirdine, efavirenz appears to be effective in patients with high baseline viral loads (>100,000 copies). Efavirenz has been used successfully in PI-sparing regimens. Efavirenz plus Combivir demonstrated greater and more durable viral suppression than indinavir plus Combivir through 3 years of follow up. Addition of efavirenz to 2 NRTIs plus indinavir adds substantially to activity without significant change in tolerability. Efavirenz increases nelfinavir's levels and reduces amprenavir and lopinavir levels, but no dose adjustments are needed. Women should avoid becoming pregnant while taking efavirenz (birth defects seen in animals). Efavirenz is well tolerated. Most patients experience CNS side effects during the first 2 weeks of therapy (vivid dreams, nightmares, dizziness).

—Carlos H. Zambrano, M.D.

Activist

The first time I took Sustiva I was attending a meeting and the room was literally spinning. The drug's biggest misfortune is its "altered state" side effect and the fact that it will do you no good if you've been on the other NNRTIs. DuPont (now owned by Bristol-Myers) tried its best to pull out a winner with Sustiva. Its plot for approval and marketing was nothing short of appalling to many in the HIV community. For a while the drug looked as if it would be a promising candidate, as data for approval showed the first good data showing a combination with Sustiva looked better than the standard of care at that time, which was Crixivan, AZT and 3TC. It also only had to be taken once a day. The pills can be spread out throughout the day to lessen side effects that lessen over time. There are also drug interactions that should be discussed with your doctor.

—Matt Sharp

Brand Name: **Crixivan**

Common Name: **indinavir**

Class: HIV protease inhibitor (PI)

Standard dose: Strict schedule of two 400 mg capsules (800 mg) every 8 hours (q8h) on empty stomach (an hour before or two hours after eating) or with low-fat snack (call for food list). If you miss a dose, take the next dose as soon as possible. Do not double the next dose. 200 mg and 333 mg capsules available.

Wholesale cost: $6,280/yr., $523/month

Patient assistance number: 1 (888) CRIXIVAN, www.crixivan.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Headache, nausea and kidney stones, which may lead to more serious problems such as kidney failure. Signs include back pain, fever, abdominal tenderness, and painful urination. Call your doctor immediately if pain develops in the middle to lower stomach or the back, or if there is blood in the urine. Other potential side effects include hair loss, changed skin color, severe skin reactions (such as horribly dry skin), fatigue or weakness, malaise (feeling unwell, as with the blahs, fatigue or a flu), nausea, diarrhea, loss of appetite, ingrown toe nails (often requiring minor surgery), dry mouth, headache, taste changes, and liver toxicity. Increased uric acid indicates kidney damage. Symptoms include joint pain and arthritis. Hemolytic anemia, the premature destruction of red blood cells, is rare but dangerous: watch for unusual fatigue, jaundice (yellowing of eyes and skin), or reddish-brown urine, and monitor red blood cell counts. Watch out for other drugs also associated with this condition (such as Septra and dapsone). Protease inhibitors may cause high blood levels of cholesterol and triglycerides (fats) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.

Potential drug interactions:

Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Viracept increases levels of Crixivan but doses of both drugs remain standard. Increase Crixivan to 1,000 mg three times a day when taken with Viramune or Sustiva. Alcohol consumption may increase risk of stones. Reduce dosage if using Nizoral (600 mg every 8 hours). Do not take with Seldane, Hismanal, Halcion, Versed, ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams) and rifampin. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction.

Tips:

Full-dose Crixivan is a rarity these days, but combining with small doses of Norvir (100 or 200 mg) is popular. It avoids food restrictions and can be taken twice a day, at a smaller dose, but you need to drink even more water. Drink at least 48 oz fluids daily (about six 8-ounce glasses), preferably water or clear liquids (soda pop doesn't count!). Large amounts of coffee or alcohol can increase risk of stones. The pain of passing a kidney stone has been compared to that of giving birth to a baby. Stones may continue after stopping Crixivan. Grapefruit juice decreases Crixivan blood levels. Should be stored in original container. Hair loss due to Crixivan is mild and will grow back within 4 months when switched to another PI or NNRTI.

Manufacturer

Crixivan was one of the first protease inhibitors on the market and in combination therapy provides highly effective therapy for the treatment of HIV. Crixivan in combination with antiretroviral agents is a powerful protease inhibitor that fights HIV and is among the preferred treatments for HIV in federal healthcare guidelines.

Crixivan can help reduce chance of illnesses and death associated with HIV; Crixivan can also help lower the amount of HIV in the body and raise CD4 T-cell counts, as shown in studies over a one-year period. As with all products some patients may not experience these effects and Crixivan is not a cure for HIV or AIDS. Crixivan must be taken every eight hours and adults should drink at least 6 glasses of water per day.

—Merck and Co.

Doctor

FDA approved 3/14/96 for use alone or in combination with nucleoside analogues for the treatment of HIV infection in adults. Approved 12/17/98 new 333 mg capsule formulation. Indinavir, in combination with NRTIs (i.e.: AZT + 3TC), is recommended as first line therapy for HIV infected naïve patients. This regimen has demonstrated a reduction in the AIDS-defining illness or death and prolonged HIV-RNA suppression of up to 5 years. Ureteral obstruction and renal stone with hydronephrosis are adverse events prompting discontinuation of therapy (wks 160 and 171). Some strains of indinavir-resistant HIV are cross-resistant to ritonavir, but not all ritonavir-resistant strains are resistant to indinavir. Indinavir + saquinavir combination is antagonistic *in vitro* and difficult to dose.

—Carlos H. Zambrano, M.D.

Activist

Taking Crixivan is dependent on how regimented you can be. It must be taken on an empty stomach and with lots of water three times a day. That's a lot if you are working or raising a family. However, later information reveals that taking Crixivan with a low fat, light snack is OK. Other drugs such as ritonavir and delavirdine will boost the levels of Crixivan if taken together. Other data shows the positive effect of lowering viral load in the male genital tract, crossing the blood brain barrier, and cerebrospinal fluid. Overall, if you can handle the dry cracking skin, possible kidney stones and tough dosing schedule, this is a powerful drug. I was in one of the first clinical trials for Crixivan and was successful in taking my virus levels to the lowest they had ever been (still not undetectable). But unfortunately I developed resistance very quickly, probably because I had taken saquinavir first. Studies in HIV negatives show a decrease in insulin sensitivity, which is a marker for diabetes.—Matt Sharp

Class: HIV protease inhibitor (PI)
Standard dose: Six 100 mg (600 mg) soft gelatin capsules twice a day, preferably with food. Dose escalation is important to avoid side effects: 3 capsules twice a day for two or three days, then 4 capsules twice a day for two or three days, followed by 5 capsules twice a day for two or three days before beginning full dose. If you miss a dose, take the next dose as soon as possible. Do not double the next dose. Approved for children ages 3 and older. Liquid formula available, but tastes horrible.
Wholesale cost: $8,910/yr., $743/month
Patient assistance number: 1 (800) 637–2400, www.norvir.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Asthenia (weakness), nausea, diarrhea, vomiting, tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, headache, dizziness, pancreatitis (see nukes), and alcohol intolerance. Seen with all protease inhibitors are: high blood levels of cholesterol and triglycerides (fats) (especially with Norvir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs. Norvir has been shown to increase liver enzymes (AST, ALT and GGT), muscle enzyme (CPK), and uric acid.
Potential drug interactions:
May cause methadone withdrawal. Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Cannot be taken with Cordarone, ergot derivatives such as Cafergot (in any form—serious interactions seen with dilation during gynecological exams), Migranal, D.H.E. 45, Halcion, Hismanal, Orap, quinidine, Rythmol, Seldane, Tambocor, Vascor, and Versed. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. One report suggested Viagra should start at half that when taken by someone on Norvir. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. The street drug Ecstasy is greatly increased by Norvir, and at least one death has been attributed to the combination. GHB is also dangerous with Norvir. Tobacco and alcohol may lower blood levels of Norvir. Increases clarithromycin (Biaxin) levels by 80 percent. Rifampin decreases Norvir levels by 35 percent. Contains alcohol (but should not be enough to trigger relapse) and greatly hastens intoxication. Norvir should not be taken with Antabuse or Flagyl.
Tips:
Convenient twice-daily dosing with food is offset by high rate of side effects and early drop-out. Its real strength is in combination with other protease inhibitors, allowing for a lower dose of both. Take with fatty food with Fortovase or Viracept. Has also become popular to boost Crixivan levels. Capsules do not need refrigeration if stored below 77° F and used within 30 days. The capsules contain castor oil and have bitter taste. The liquid tastes foul and activates children's gag reflex. Taking it right before a meal may help. Taking with food—especially high fat such as peanut butter or avocado—may help prevent stomach upset. Watch for increased cholesterol and triglyceride levels, especially if heart disease runs in your family. Remember to get fasting levels. Keep in original container.

Manufacturer

Norvir, a protease inhibitor, was approved by the FDA in 1996 for early and advanced patients with HIV and is widely used in dual protease inhibitor therapy as well as to boost drug levels of other PIs. Norvir boosting increases the levels of other PIs, and gives patients the opportunity to reach undetectable viral levels without discontinuing their current PI or sacrificing adherence. By boosting drug levels, Norvir minimizes drug resistance and decreases the risk of viral rebound. Most commonly used to boost levels of other protease inhibitors like amprenavir, saquinavir and indinavir, this drug may be critical for patients on salvage regimens who cannot switch to a new protease inhibitor because of resistance.
Most widely used doses:

RTV/IDV	400/400 BID, 800/100 BID or 800/200 BID
RTV/SQV	400/400 BID
RTV/APV	600/100 BID

—Abbott Laboratories

Doctor

FDA approved 3/1/96 for use alone or in combination with nucleoside analogues for the treatment of HIV infection in adults and children between the ages of 2 and 16. Approved 6/29/99 soft gelatin, 100 mg capsule. The antiretroviral effects of ritonavir and other agents such as NRTIs are additive or synergistic against HIV-1. Ritonavir is metabolized by CYP-450 enzyme system and there is potential for pharmacokinetic interactions. Avoid changing from ritonavir to indinavir or vice versa for drug failure, since high level cross-resistance is likely. Ritonavir is commonly used as a PI-boosting agent resulting in improved pharmacokinetics and more effective regimens (e.g, amprenavir, saquinavir, indinavir and lopinavir). Ritonavir-boosted PI regimens are associated with significant increases in lipids. There are potential atherogenic implications of such changes. Elevated triglyceride, liver enzyme, CPK and uric acid levels have been reported with ritonavir use.
—Carlos H. Zambrano, M.D.

Activist

Ritonavir (Norvir) probably has one of the most interesting evolutions of all the PIs. It really made a name for itself because of the drug interactions discovered once the drug was already approved. Significant interactions are seen with calcium channel blockers, cholesterol-lowering agents, antiarrhythmics, sedative-hypnotics, Viagra, oral contraceptives, recreational substances, and others. Originally it had to be taken in a liquid form, then the pills came out and were discovered to be deficient, so for one year everyone who was on the pills had to switch to the nasty liquid formulation. Ritonavir is most useful as a booster to almost all the available PIs. So now it is mostly considered an addition to the other imperfect PIs, rather than a stand alone PI. Side effects include diarrhea (again!!) and an unusual numbness around the mouth. Ritonavir studies in HIV negatives show an increase in triglycerides and cholesterol.
—Matt Sharp

Brand Name: **Viracept**

Common Name: **nelfinavir**

Class: HIV protease inhibitor (PI)

Standard dose: Five 250 mg tablets (1250 mg) twice a day with food. Take a missed dose as soon as possible, but do not double the next dose. Also granular formula to mix in juice or water. 625 mg tablets (two twice a day) expected soon.

Wholesale cost: 8,381/yr., $698/month

Patient assistance number: 1 (888) VIRACEPT, www.viracept.com

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects:

Diarrhea, stomach pain, asthenia (weakness), nausea, flatulence (gas), and rash. Seen with all protease inhibitors are: high blood levels of cholesterol and triglycerides (fats) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.

Potential drug interactions:

Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Do not take with Seldane, Hismanal, Cordarone, quinidine, ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams), Halcion, or Versed. Blood levels of Viracept are reduced by rifampin and may be reduced by phenobarbital, phenytoin, and carbamazepine (Tegretol and others). Fortovase levels increase three- to five-fold, Crixivan increases 50% and Norvir levels are unchanged. Prescriber may need to adjust doses of any these drugs accordingly. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Mycobutin (rifabutin) dose must be decreased when used with Viracept. Rifampin and Viracept should not be used together. Reduces effectiveness of birth control pills; use alternative contraceptive.

Tips:

Data from a study of 92 treatment experienced people indicates that Viracept used in the correct combination may be a viable option for salvage therapy. Tablets are film-coated, which avoids the old tablets' habit of beginning to dissolve in your mouth—yucky. Do not leave the pharmacy without anti-diarrhea medication available without a prescription, such as Imodium. Take a change of clothes with you when you leave home for the first several weeks. Try Solgar oat bran tablets, psyllium husk fiber bars, calcium supplements (including Tums or Rolaids) and pancreatic enzymes (all with meals). First protease inhibitor choice for children who cannot swallow capsules or tablets, but solution tastes horrible and requires a large amount for mixing into food. It's preferable to crush adult tablets for use in children. Do not mix with acidic drinks because of bitter taste.

Manufacturer

Viracept, in combination with other antiretroviral agents, is indicated for the treatment of HIV infection. Viracept's potency, durability, and unique resistance profile make it an important first line treatment option for patients wanting to preserve their future treatment options. At 48 weeks of triple combination therapy, Viracept lowered the amount of HIV in the blood to levels below the limit of detection and substantially increased CD4 cell counts in the majority of people being studied. Viracept is well-tolerated; diarrhea is a common side effect, but manageable in most cases. Approved in March 1997, Viracept is currently available in film-coated tablets or powder formulation for the treatment of adults and children (ages 2–13 years). Twice daily dosing of Viracept was approved in November 1999. Viracept should be taken with a light meal or snack. For more information on Viracept, call toll-free 1–888–VIRACEPT (1–888–847–2237) or access the website at: http://www.viracept.com.

—Agouron Pharmaceuticals

Doctor

FDA approved 3/14/97 for the treatment of HIV infection when antiretroviral therapy is warranted in adults and pediatrics greater than or equal to 2 years old. Nelfinavir is metabolized, in part, by CYP3A. Concomitant administration of nelfinavir and delavirdine may affect the pharmacokinetics of both drugs. Nelfinavir is recommended as a first line therapy in ARV-naïve patients. When nelfinavir is used in combination with NRTIs, emergence of HIV variants resistant to nelfinavir is delayed. Although there is evidence that some degree of cross-resistance occurs among various HIV protease inhibitors, nelfinavir offers more options for salvage therapy. Loose stools are a common side effect. Moderate hypertension has also been observed. Nelfinavir has an acceptable tolerance.

—Carlos H. Zambrano, M.D.

Activist

I still think Agouron should provide free underwear to people who use the drug, especially since they have constantly raised the price to be the highest priced protease inhibitor. Viracept causes diarrhea and an unending supply of fresh skivvies. At least the drug can now be taken two times a day instead of three, the original dosage. Also, it is now film coated so that it slides down easier instead of blocking off your airways. Despite the constant trips to the bathroom, Viracept is not a bad drug and shows a sustained viralogical response as a first line therapy and may offer a chance at other PIs later on. There is evidence that it will work in the salvage setting if combined with the right drugs depending, of course, upon genotype analysis.

—Matt Sharp

Class: HIV protease inhibitor (PI)
Standard dose: Six 200 mg soft-gel capsules three times a day with food, or within two hours after a meal. If you miss a dose, take the next dose as soon as possible. Do not double the next dose.
Wholesale cost: $8,011/yr., $668/month
Patient assistance number: 1 (800) 910–4687, www.fortovase.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Diarrhea, nausea, abdominal discomfort or pain, flatulence (gas), indigestion, headaches, insomnia, fatigue, and taste alteration. Seen with all protease inhibitors are: high blood levels of cholesterol and triglycerides (fats) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor immediately) and increased bleeding in hemophiliacs.
Potential drug interactions:
Do not use Zocor or Mevacor lipid-lowering drugs; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Increased blood levels with Crixivan, Norvir and Viracept. Blood levels decreased significantly by Sustiva, but can be taken together if Norvir is included. Fortovase should not be taken with rifampin or Mycobutin. Other drugs that may also reduce Fortovase blood levels are Decadron and Tegretol, Dilantin, and phenobarbital. Do not take with Halcion, Versed, sedatives/hypnotics, ergot deviratives (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams), Seldane and Hismanal. High incidence of liver problems, and severe ones, when taken with Rescriptor. Protease inhibitors increase blood levels of Viagra (sildenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Mycobutin (rifabutin), phenobarbital, phenytoin dexamethasone and carbamazepine (Tegretol and others), Viramune and Sustiva decrease Fortovase levels (but the last two can be taken if Norvir is added). Rescriptor, Crixivan, Norvir and Viracept all significantly increase Fortovase plasma concentrations, but Crixivan may be antagonistic. The side effects of calcium channel blockers, clindamycin, dapsone and quinidine may be increased if taken with saquinavir.
Tips:
Must be taken with food or within two hours after a meal. Keep capsules at room temperature if they will be used up within three months. Zantac, Pepcid, Tagamet or antacids may be necessary to treat Fortovase heartburn (which is common). Refrigerated (36–46° F or 2–8° C) capsules remain stable until the expiration date printed on the label. Once brought to room temperature capsules should be used within 3 months. Avoid direct sunlight. Long popular when taken twice a day with Norvir (both 400 mg each). Potential for once a day dosing at 1600 mg with 100 mg Norvir, being studied. Older version of saquinavir, Invirase hard-gel capsules, is rarely used.

Brand Name: **Fortovase**

Common Name: **saquinavir soft-gel**

Manufacturer

Fortovase (saquinavir soft gel capusules), approved in November 1997, is a second-generation formulation of saquinavir that offers significantly improved efficacy over the original formulation, Invirase. Fortovase, when used in combination with other antiretroviral agents, slows the replication of HIV in the body to reduce viral load. Ongoing clinical trials are testing once-daily and twice-daily dosing of Fortovase in combination with a mini dose (100 mg) of the protease inhibitor ritonavir. Side effects associated with Fortovase include diarrhea, nausea and headaches. Additionally, an exacerbation of chronic liver dysfunction has been reported in patients taking Fortovase. Other side effects may include hyperglycemia or diabetes, and spontaneous bleeding in patients with hemophilia associated with the use of protease inhibitors.
—Roche, 2001
Manufacturer did not respond to request for updated statement.

Doctor

FDA approved 12/7/95 for combination use with nucleoside analogues for the treatment of advanced HIV infection. Metabolism by saquinavir is mediated by CYP3A4. Some studies have shown increased saquinavir concentration and improved antiviral activity for Fortovase compared to Invirase. Fortovase in combination with efavirenz should not be prescribed. Saquinavir appears to be well tolerated. Ritonavir increases saquinavir levels 3-fold or higher. Once-daily dosing of saquinavir with ritonavir is being studied. A SQV/RTV based-regimen is recommended as initial treatment of established HIV infection. All protease inhibitors could cause metabolic abnormalities, redistribution of body fat, new-onset diabetes or exacerbation of existing diabetes, hepatotoxicity and may increase the risk of spontaneous bleeding in patients with hemophilia.
—Carlos H. Zambrano, M.D.

Activist

Fortovase is a new name for an old drug called Invirase that was basically a failure in terms of effectiveness. Only 6% of saquinavir in its hard capsule formulation metabolized. So, Roche got smart and reformulated the drug into a soft-gel that got more of the drug into the blood stream. Still, Fortovase pills are enormous and you have to gag on six pills three times a day. However, combining ritonavir will increase the levels of saquinavir or Fortavase in combinations and only require a twice a day dose. Watch for multiple drug reactions of all agents you are combining. Use of saquinavir (or Fortovase) as an initial therapy may render resistance to subsequent protease regimens. I pity those who were subjected to saquinavir as initial therapy, then went on to develop resistance because of inadequate absorption, and consequently gave up options for other protease inhibitors.
—Matt Sharp

Brand Name:
Agenerase

Common Name:
amprenavir

Class: HIV protease inhibitor (PI)
Standard dose: Eight 150 mg (1200 mg) soft gelatin capsules twice a day, no food restrictions. Take a missed dose as soon as possible, but do not double the next dose. Approved for children ages 4 and older. Grape, bubblegum, peppermint flavored liquid. Adults should not use liquid if possible.
Wholesale cost: $7,994/yr., $666/month
Patient assistance number: 1 (800) 722–9294, www.agenerase.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Nausea, vomiting, abdominal pain, taste disorders, fatigue, headache, rash, anemia, colitis, bruising easily, prolonged bleeding, depressive or mood disorders, circumoral paresthesia (tingling or numbing around the mouth) and peripheral paresthesia. Gaseous symptoms are common and may be severe. Taking with food may help, but check for pancreatitis when there is severe stomach pain. Seen with all the other protease inhibitors are high blood levels of cholesterol and triglycerides (fats) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions:
Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Rescriptor and Viracept greatly increase Agenerase blood levels (and usually stomach discomfort) and prescriber may need to adjust dose accordingly. Sustiva has been shown to significantly reduce blood levels of Agenerase unless also taken with Norvir mini-dose. Interacts with several antihistamines, sedatives, and antifungal drugs. Do not use with rifampin. Dose reduction of Mycobutin is necessary. Increased blood levels and drug activity are seen with dapsone, erythromycin, Sporonox, Xanax, Tranxene, Valium, flurazepam, Cardene, Procardia or Adalat CC and Nimotop. Each capsule contains vitamin E, so avoid taking with other blood thinners, such as Coumadin (warfarin), clotting factor, vitamin K, and low-dose daily aspirin, as well as herbs such as ginger, garlic, feverfew, ginseng and gingko biloba. Ibuprofren (Advil) can also be problematic. Do not take extra vitamin E. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction.
Tips:
The huge number of horse pills is a major drawback. However, it can be reduced with Norvir (four Agenerase capsules [600 mg] with one capsule of Norvir [100 mg] twice a day equals the full Agenerase dose). Norvir significantly increased cholesterol and triglycerides. However, little data are available with Agenerase and Norvir. May also penetrate the lymph nodes, where virus can hide out. Severe rash can be life-threatening (grade 3 or 4, see Viramune). Avoid taking with food high in fat. Warning issued on Agenerase liquid solution. Should not be used by pregnant women, because the larger amount of propylene glycol in this formluation may be harmful to the fetus.

Manufacturer

Agenerase (amprenavir), approved April 1999, is an HIV protease inhibitor that, in clinical studies, has appeared to have significant antiviral activity when used in a variety of two-, three-, and four-drug combination regimens. Agenerase has been studied clinically in combination with numerous approved and investigational antiretroviral therapies, including nucleoside analogue reverse transcriptase inhibitors, non-nucleoside RTI's and protease inhibitors. In clinical trials to date, Agenerase appears to have an acceptable safety profile with few treatment-limiting adverse events. The most commonly reported adverse events in clinical studies have included nausea, diarrhea, headache, fatigue, vomiting, rash and perioral parasthesia. Please refer to the full prescribing information for additional important safety information.
—GlaxoSmithKline

Doctor

FDA approved 4/15/99 to treat HIV-1 infected adults and children. Amprenavir is usually well tolerated. Side effects: rash (20%), diarrhea, nausea. No serious adverse events or laboratory tests abnormalities are usually found. It is recommended as an alternative for initial treatment of established HIV infection. Usual dose: eight 150 mg (1,200 mg) capsules twice a day (pill burden). Ritonavir increases amprenavir levels significantly (once-daily dosing with ritonavir is being evaluated). Ritonavir/amprenavir based regimen has been of value in salvage therapy. It has been shown that amprenavir is little cross-resistant with other PIs in less-than-2 PI-experienced patients. Amprenavir plasma concentrations are dramatically decreased by the association with Kaletra. Amprenavir pro-drug shows promise in early clinical trials.
—Carlos H. Zambrano, M.D.

Activist

Increasing their AIDS portfolio, in 1999 GlaxoSmithKline developed Agenerase, a protease inhibitor to go along with their nucleosides. There was a considerable delay for Agenerase to become available, as the last PI to be approved was in 1997. By this time people were in need of a new protease inhibitor since mutations from older PIs were showing up. But only one Agenerase mutation is not cross resistant to other PIs and clinical trial data shows only a modest benefit for those who are salvage patients. So, Agenerase would fall into the "me too" class of drugs offering not much evidence that it is useful in initial or third-line regimens. Short-term studies have shown no evidence for facial and limb wasting or signs of diabetes, yet showed a 90% increase in triglyceride levels. Now if Glaxo would develop a NNRTI they will corner the market. Then we'll wait for a HAART combination pill.
—Matt Sharp

Class: HIV protease inhibitor (PI)
Standard dose: Three soft-gelatin capsules (133.3 mg lopinavir and 33.3 mg ritonavir each) twice a day, preferably with food; liquid formula available. Take missed dose as soon as possible, but do not double dose.
Wholesale cost: $8,125/yr., $677/month
Patience assistance number: 1 (800) 637–2400, www.kaletra.com
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)
Potential side effects:
Rash, loose stools, diarrhea, nausea, headache, muscle weakness, and increased cholesterol, triglycerides (fats in the blood) and AST/ALT (liver function tests, a sign of liver damage). These were not fasting samples, needed for the most accurate results. Seen with all older protease inhibitors (except Agenerase) are high blood levels of cholesterol and triglycerides (fats) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions:
Dosage of methadone may need to be increased when taken with Kaletra. Dose increase to 4 capsules twice a day with food recommended when using with Sustiva or Viramune in people who previously took HIV drugs, especially protease inhibitors. May lower levels of Retrovir and Ziagen. Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, Baycol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Protease inhibitors increase blood levels of Viagra, and Viagra dose should be started at 25 mg (half the normal dose) and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Phenobarbital, phenytoin (Dilantin and others) or carbamazepine (Tegretol and others) may lower blood levels of Kaletra. Reduces effectiveness of birth control pills; use alternative contraceptive. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Do not take with flecainide, propatenone, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafetrate, Cafergot, Wigraine and Methergine, in any form—serious interactions seen with dilation during gynecological exams), D.H.E. 45, St. John's Wort, pimozide, Versed and Halcion. (Also dihydropuridine calcium channel blockers.) Videx should be given an hour before (or two hours after) Kaletra is taken with food. Rifabutin dose must be lowered.
Tips:
Doctors and patients report that this protease inhibitor is very tolerable. Great viral load results out to 72 weeks (significant) in people on their first HIV regimen. Good results also seen in heavily treatment-experienced children and adults, even those with protease inhibitor resistance. However, drug-experienced people also used a non-nuke, which may mean that three classes of HIV drugs are needed for them, and which limits future options. Then again, some people don't have many options. Expected to successfully control HIV that no longer responds to other meds due to drug resistance, but cross-resistance has already been seen. Can have Norvir's yucky taste and taste aversion—one guy said his beer tasted like soap. There is hope for once a day dosing.

Brand Name: **Kaletra**

Common Name: **lopinavir/ritonavir**

Manufacturer

Abbott developed Kaletra to fulfill an unmet need for a different PI which combines power and tolerability for patients across the spectrum of HIV, including those new to, and experienced with, HIV therapy. Kaletra's enhanced pharmacokinetic profile is the key to its strength and durability. Kaletra can be maintained at much higher levels in the blood than any other protease inhibitor. Elevated levels create a high barrier to viral mutations and may prevent resistance. Data from ongoing Phase II and Phase III trials show that genotypic resistance to Kaletra has not developed yet in treatment naive patients. At 48 weeks, data also show that Kaletra continues to be more effective than nelfinavir at suppressing viral load below undetectable levels in a significant portion of patients and is better tolerated, with only 2% of patients discontinuing due to Kaletra-related adverse events. Doses: 3 capsules BID; 4 capsules BID when combined with efavirenz for highly experienced patients.
—Abbott Laboratories

Doctor

FDA approved 9/15/00 for combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients ages 6 months and older. Patients can keep the drug at room temperature if used within 2 months of dispensing. Administration with food enhances overall drug levels. Dosing of didanosine and Kaletra should be separated by at least 2.5 hours. Elevated cholesterol, triglyceride and liver enzyme levels have been reported. Clinical trials are ongoing in HIV infected patients with various levels of prior treatment experience. Kaletra-based therapy demonstrated antiviral activity in ARV naïve patients through 144 weeks. The rate of discontinuation of therapy due to side effects is low. No evidence of genotypic resistance to Kaletra was observed in any of the isolates from Kaletra-treated ARV-naïve subjects through week 60.
—Carlos H. Zambrano, M.D.

Activist

When Kaletra came out, the name sounded to me like a new car. It is actually a combination of two drugs, lopinavir and ritonavir. During development of lopinavir the company saw it was not absorbed well enough so they looked on their top shelf and added their booster drug ritonavir. There was great hope that Kaletra would become a good salvage drug since all other PIs are cross resistant. The data so far has been hopeful but not overwhelming. Watch for drug interactions considering that you are taking two drugs in one, one of them being ritonavir.
—Matt Sharp

Brand Name:
Not Yet Established

Common Name:
tipranavir

Class: experimental protease inhibitor
Standard dose: Dose not yet established because of experimental drug status
Wholesale cost: Not yet established because of experimental drug status
Manufacturer contact:
www.boehringer-ingleheim.com
AIDS Clinical Trials Information Service: 1 (800) TRI-ALS–A (874–2572)
Potential side effects: Gastrointestinal related, mild diarrhea, nausea, vomiting and fatigue. In clinical trials symptoms have been managed by having a light snack with the drug.
Potential drug interactions: Not yet reported.
Tips:
Hopes to be effective against drug-resistant HIV, but that's manufacturer hype that rarely pans out. In studies, cross-resistance has been seen. Still, as the only non-peptidic protease inhibitor (a different chemcial structure), should not be cross-resistant to other protease inhibitors. And significant viral load decrease was seen in people with protease inhibitor resistance who took tipranavir by itself (for less than a month). Phase I/II studies have dosed tipranavir at 900, 1,200 and 1,500 mg twice a day in combination with other meds (using with small amounts of Norvir could cut this).

Photo not available because of experimental drug status.

Manufacturer

Tipranavir is the first non-peptidic protease inhibitor (NPPI) in development for the treatment of HIV-1 infection. Currently entering Phase IIb clinical studies, tipranavir has a different chemical structure than currently available peptidic PIs. This enables it to bind with fewer hydrogen bonds in the active site than existing peptidic PIs, and this more flexible binding may explain its unique resistance profile. The key benefit of the drug, shown by early in vitro data, is that it is active on virus which has become resistant to peptidic PIs. Additional in vitro studies are being carried out to help clarify the nature and likelihood of developing resistance to tipranavir. Researchers are currently studying its safety profile, possible drug interactions and dosing regimen.
—Boehringer-Ingelheim

Doctor

Tipranavir (TPV) is the first of a new class of non-peptide Pis. There was a substantial lack of PI cross-resistance to TPV shown by highly PI-resistant clinical isolates in vitro cultures. TPV in combination with Ritonavir yielded synergistic antiviral effects. TFV has been studied in two presentations: a hard-filled capsule (hfc), and a soft-gel capsule (Self Emulsifying Drug Delivery System), that failed to demonstrate increased drug concentrations (both presentations showed efficacy). In an open-label study, TPV, in combination with Ritonavir, Efavirenz and a NRTI, demonstrated durable and potent antiviral activity at 24 weeks, in patients with multiple PI failures. The most common TPV-related adverse events were diarrhea (46%), nausea (27%), GGT elevation (20%), vomiting (17%), dizziness (17%), abnormal dreams (15%) and SGPT elevation (15%). Boehringer-Ingelheim "has been struggling with the formulation of TPV". The drug is not expected to be licensed until late 2004.
—Carlos H. Zambrano, M.D.

Activist

Tipranavir might have been a lot further along in the pipeline had the drug not been sold to another company and then reformulated. When I first heard of the drug at the 12th World AIDS conference in 1998 held in Geneva, I couldn't believe you had to swallow 28 pills a day in order to reach appropriate blood levels. So, the first hurdle was developing a soft gel formulation where fewer pills had to be taken. Then, tipranavir was sold to Boehringer Ingelheim and more studies were done and continue in combination with Ritonavir. Despite the ever-present diarrhea seen with so many other PIs, studies have shown tipranavir inhibits growth of up to 90% of drug resistant HIV strains. So, the possibilities are good thus far for those individuals with few PI options. As soon as a dose is established there will be wider access mid-to-late 2002.
—Matt Sharp

Brand Name: **Not yet established**

Common Name: **T-20, pentafuside**

Class: experimental fusion inhibitor
Standard dose: Taken as self-administered, twice-daily subcutaneous injections. Dose not yet established because of experimental drug status.
Wholesale cost: Not yet established because of experimental drug status
AIDS Clinical Trials Information Service: 1 (800) TRIALS–A (874–2572)
Potential side effects:
Irritation or infection at site of injection, fever, and headache.
Potential drug interactions:
Not yet reported.
Tips:
Prevents HIV from attaching to T-cells. Two shots twice a day (as used in one study for people who've taken many antivirals) creates the potential for four painful injections, and infection or irritation. No major problems with this seen so far. Because of injections, tested in people who've already taken HIV drugs, since people using antivirals for the first time have more convenient options. Some say shots won't scare people off (especially if they have limited options), others think that's a joke. Phase II showed good viral load decrease when added to a stable antiviral combination in heavily treatment-experienced people, including those with protease inhibitor-resistant virus and those who've taken all three current drug classes. Phase III is evaluating about 500 people in the U.S. and Brazil for 48 weeks, with an optional 48 weeks treatment extension. Because it's in a new drug class, T-20 is not expected to have cross-resistance with other HIV medicines. T-20's peptide structure may be recognized by the body as a foreign object, and then antibodies may be created to fight it. But this potential problem (not seen with other HIV drugs) has not occured. Because peptides are big molecules, they cannot be taken orally and must be injected. The size is another reason why T-20 might be recognized as a foreign object. Manufacturer has another fusion inhibitor in development that may work as resistance to T-20 develops. May be able to penetrate lymph system, where most of the body's HIV hides. Very expensive to manufacture, and perhaps very difficult as well, limiting supply. Trimeris already has a second generation fusion inhibitor, T-1249, in Phase I/II study. Visit www.rocheusa.com and www.trimeris.com.

Photo not available because of experimental drug status.

Manufacturer

T-20, an investigational anti-HIV compound, is the first in a new class of drugs called fusion inhibitors which is being co-developed by Roche and Trimeris. Fusion inhibitors block fusion of HIV with host cells before the virus enters the cell and begins its replication process. Currently in Phase III clinical trials, T-20 received "fast track" designation from the U.S. FDA in February 1999. Phase II trial results collected from patients who had failed an average of 10 HIV medications and entered with high viral load show that T-20 in combination with other agents achieved either a 1 log viral suppression or levels of HIV less than 400 copies/mL in 33 percent (23/70) of patients (Intent to Treat). Side effects associated with T-20 include fever, headache and lymph node abnormalities, in addition to local irritation resulting from the subcutaneous injection.
—Roche, 2001
Manufacturer did not respond to request for updated statement.

Doctor

T-20, a novel HIV fusion inhibitor, is delivered by self-administered, BID subcutaneous (SC) injections. In a 48 week Phase II clinical trial, the majority of respondents agreed that injection of T-20 did not limit their activities of daily living. A T-20 expanded access program was opened on 11/27/01.
—Carlos H. Zambrano, M.D.

Activist

T-20 is an important new agent from an entirely new class of drugs. Unfortunately, the drug has to be injected twice daily. Side effects are limited with T-20 except for injection site pain and swelling. It does its work outside of the cell, not damaging it. T-20, a peptide is one of the most complicated drugs to make because a drug like it had never been made before. The company will have to overcome huge obstacles to make enough of it. Trimeris did not have the resources to continue the production of T-20 so they had to contract with Roche, one of the few companies worldwide who had peptide manufacturing capabilities. Activists worry that there will not be enough T-20 to meet the demand. Trimeris/Roche is also working on a second generation fusion inhibitor, T-1249, that appears to be effective against T-20 resistance but may have mild to moderate side effects.
—Matt Sharp

Drugs in Development*

Compound	Class of Compound	Phase of Development	Pharmaceutical Company
ACH-126,443 (L-Fd4C)	Nucleoside analogue RT inhibitor	Phase I	Achilleon
ADA	Zinc finger	Phase I/II	Hubriphar
BMS-232623	Protease inhibitor	Phase II/III	Bristol-Myers Squibb (BMS)
Calanolide A	Non-nucleoside RT inhibitor	Phase II	Sarawak Medichem
Capravirine	Non-nucleoside RT inhibitor	Phase II	Agouron
DAPD	Nucleoside analogue RT inhibitor	Phase I/II	Triangle Pharmaceuticals
DEHSPM	Inhibits hypusin/eIF-5A	Phase I	SunPharm
DPC 083	Non-nucleoside RT inhibitor	Phase I	(BMS) DuPont Pharmaceuticals
DPC 961	Non-nucleoside RT inhibitor	Phase I	(BMS) DuPont Pharmaceuticals
Emivirine (MKC-442)	Non-nucleoside RT inhibitor	Phase III	Triangle Pharmaceuticals
Emtricitabine (FTC)	Nucleoside analogue RT inhibitor	Phase III	Triangle Pharmaceuticals
Hydroxyurea	Inhibits cellular factors	Phase II/III	Bristol-Myers Squibb
Mycophenlate	Inhibits cellular factors	Phase I/II	Hoffman-La Roche
Peldesine	Inhibits cellular factors	Phase I	Biocryst
Pentfuside (T-20)	Fusion inhibitor	Phase III	Trimeris/Roche
PRO 367	Entry inhibitor	Phase I	Progenics
PRO 542	Attachment inhibitor	Phase I/II	Progenics
Resveratrol	Inhibits cellular factors	Phase I	Pharmascience
S1360	Integrase inhibitor	Phase I/II	Shionogi Pharmaceuticals
SCH C	CCR5 antagonist	Phase I	Schering Plough
T-1249	Fusion inhibitor	Phase I	Trimeris/Roche
Tipranavir	Protease inhibitor	Phase I/II	Boehringer Ingelheim
TMC 125	Non-nucleoside RT inhibitor	Phase II	Tibotec
TMC 120	Non-nucleoside RT inhibitor	Phase II	Tibotec
TMC 126	Protease inhibitor	Phase I	Tibotec
VX-175/GW433908 (amprenavir prodrug)	Protease inhibitor	Phase II/III	Vertex/Glaxo SmithKline

*Source: Ben Cheng, Project Inform. Visit www.atac-usa.org

Terms:

Clinical trials are scientific investigations carried out on human subjects to define the safety, efficacy and effects (toxicity, side effects and interactions) of a drug. The FDA requires strict testing of all new drugs prior to their approval for use as therapeutic agents.

Phase I trials involve the first introduction of an experimental drug to patients or healthy volunteers, normally less than 100 enrollees. They are closely monitored to determine the interaction of the drug, including the side effects associated with different doses. Sufficient information and signs of effectiveness are necessary to permit design of well-controlled Phase II studies.

Phase II trials are well controlled, closely monitored clinical studies, usually with no more than several hundred human subjects. They test the effectiveness of a drug against a particular indication(s) in patients with the disease or condition in question and measure common, short-term side effects and risks associated with the drug.

Phase III trials are expanded controlled and uncontrolled studies, including several hundred to several thousand participants, initiated after preliminary data of drug effectiveness are obtained. These trials seek to gather additional effectiveness and safety information about safety and evaluate the overall benefit-risk relationship of the drug and to provide competent basis for dosing.

Adapted from the HIV/AIDS Treatment Information Service (www.hivatis.org).

Drug Tips

by Enid Vázquez

- Pharmacists are usually much more readily available than doctors, and probably more helpful. Take advantage of this. Ask them all your questions.

- Nail down your doctor and pharmacist on potential side effects and how to handle them. Also remember that side effects can pop up after years without a problem. But don't let someone else's horror story stop you from taking a particular drug. You may not be affected.

- A good doctor will review how the drugs fit your lifestyle. Research suggests that the best predictor of adherence is the amount of time a doctor or other healthcare provider spends discussing the drugs with you.

- See an HIV specialist. Research shows that your chances for good treatment, better health and survival will improve.

- Good websites to visit: www.aidsmeds.com, www.aidsmap.com and www.aidsinfonet.org. Also, Dr. A. V. Munsiff puts together an excellent chart of all HIV drug interactions (including methadone) and other information. It comes laminated and folded. Send $2 to cover cost of printing and postage to P.O. Box 543, Scarsdale, NY 10583.

- Ask for a copy of all your lab results. They are free, but your doctor's office may charge you a small fee for sending a copy elsewhere. Laboratory testing should be performed before starting therapy and then at periodic intervals or if any clinical signs or symptoms occur. Try to have a fasting measure taken (do not eat or drink anything but water for at least 12 hours prior to the blood draw).

- To monitor mother and child outcomes of pregnant women exposed to HIV drugs, the Antiretroviral Pregnancy Registry has been established. Physicians are encouraged to register patients by calling (800) 258-4263.

- Writer Michael Mooney, the late Chester Myers, a nutritionist, and Lark Lands, complementary health guru, all HIV treatment advocates, have made the following recommendations to prevent or reverse heart damage and fat redistribution being seen with drug therapy: progressive resistance exercise (weight-bearing) or aerobic exercise to reduce insulin resistance; testosterone replacement where needed (women included) to reduce insulin resistance and build muscle; high-potency multivitamin and mineral supplement; glutathione-boosting nutrients daily (600-1,200 mg alpha lipoic acid; and 5-10 gm glutamine, or 30-40 gm in cases of severe muscle loss) antioxidants (1,500-3,000 mg N-aceytl-cysteine, or NAC; 2,000-3,000 mg vitamin C; 1,200 IU vitamin E distributed throughout the day); a GTF (glucose tolerance factor) formula with 200-300 mcg chromium three times a day (also helps increase insulin sensitivity) and 500-700 mg magnesium for glucose metabolism (sugar control).

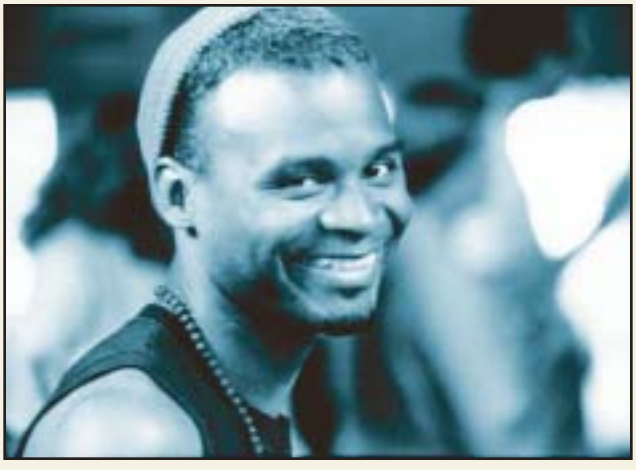
For a free copy of the U.S. Department of Health and Human Services guidelines for HIV treatment for adults, children, and pregnant women (as well as principles of HIV therapy), call 1-800-HIV (448)-0440 , visit www.hivatis.org, or write ATIS, P.O. Box 6303, Rockville, MD 20849-6303. Also available in Spanish.

Living with Yoga

by Per Erez

Healing, health, healthy, and wholeness have become words of transformation. The meaning of these words seemed warped after testing HIV positive back in my mid-20s in 1993. In the many months of numbness immediately following my test results, I assumed these words would no longer be a part of life, let alone my vocabulary. Over time, I have come to see them as an evolving process.

Like many people living with HIV, my quest for healing started with a half-hearted attempt at traditional medical options. I established a connection with a primary physician, but knew from the first visit to find out my T-cell count and percentages that this man was not responsible for saving my life. My only expectation was that he respond like a human being faced with someone who was suffering—even if the suffering was only mental anguish. I agreed to a standard treatment of the time, AZT [Retrovir], shortly after our first visit. After only three months of the medication I passively became non-compliant. My experience of headaches and nausea (which in retrospect could have been as much about my psychological state), as well as my gut instinct, convinced me that this was not for me.



I can distinctly remember a perplexed friend asking what was my treatment, if I wasn't going to take the drugs? What treatment was I choosing, and for which condition, and would it save me? That question turned me towards a renewed interest in eastern philosophical thought, which originated in college.

There is a story among practitioners of yoga that "the road to enlightenment is a pathless path." In other words, the specific steps necessary to achieve the optimal life are inside each of us already. No one can walk your path and only you truly know your way from one moment to the next.

The results of my test and the accompanying mental confusion I experienced led me deeper in this direction. I felt as if the questions I had about the prospect of healing and the larger direction of my life might be found if I opened myself to a wider re-examination of these principles. At the time, I didn't see this as treatment so much as a respite from the mental storm of HIV.

So I took up a hatha yoga practice, initially for purely selfish reasons. It made me feel better. It amazed me that no matter what happened at work or what fears I had about being HIV positive, I could always count on these simple things to keep me clear. Do the yoga, do the breathing, and rest in awareness. Move on with my life. Simple. It was so simple, it seemed crazy. But the craze was highly addictive. With the help of my yoga teacher, I began studying a style of yogic massage originated in Thailand, as well as pranic energy work and tai chi. It seemed the more positive and health-oriented techniques she shared, the better I felt. In those days, I wasn't able to explain how these unfamiliar techniques worked, but I intuitively felt the results. And while there wasn't an investment back then in proving the efficacy against HIV of these techniques, what even the medical establishment seemed to agree on was the stress reduction benefit.

I knew that the tools I was incorporating in my life could be shared with others. I began helping teach yoga for others with HIV. This had two results. I thought less about my own situation as being unique, and I got physically stronger. I recognized that the empathetic connection I had so clearly wanted with my physician could be a powerful experience. Being face to face with another who is suffering and to take in and really listen empathetically in that experience can lead to healing for both people involved.

Because what every real healer knows—Western or Eastern—is that ultimately, healing happens around you, not because of you. If the experience of healing occurs, the healer is primarily and hopefully a compassionate companion, an adjunct in the presence of the power of healing. All the medicine in the world will come to no purpose if the power of healing doesn't already live inside the body. This suggested to me that the person doing the healing had as much of a role to play in creating the atmosphere in which healing might be found as the healer. After all, who does healing benefit most in the relationship? It was this belief that led me in 1997 to seek out the opportunity to be a teacher of yoga.

I decided, with the support of my life partner, to leave my fairly secure job and use my 401K as a back-up to take the month-long initial training program required to become an accredited instructor of yoga. In the training, I was introduced to a purer diet, eating primarily vegetarian and macrobiotic foods, and to a much deeper practice of the concepts behind yoga. What the training offered was the chance to become more aware. It cultivated the silent time in which to wholeheartedly accept the nature of life. And by becoming more aware and accepting, creating a tiny space where change might be possible, it supplied me with tools to take the misperceptions I had of health and clarify them. It provided a new vision outside the narrow view of what it meant to be healthy for me. For the first time, I really saw that these lifestyle options were in fact a kind of treatment, not simply for HIV, but for all the other underlying issues in

Photo from Kripalu Archives

life that we all must address. Sadly, the friend who asked me the question so many years ago isn't here for my answer. Over time, and even to this day, the question still comes to mind from time to time, "Will this treatment save me?" I have come to no conclusions here. I am not sold on the notion that I need saving.

Nonetheless, over the course of the last several years I have recognized that you could just as easily say living healthy is a spiritual discipline with physical side effects as well as the more traditional viewpoint. From the medical standpoint, we test the body for illnesses and we test the mind for illness, but after these tests, there is little else that remains to us. To some degree, we can treat body and mind with allopathic practices, but from a traditional healer's view, all suffering has its core in the fundamental separation from all of our essential nature. Our essence is "buried" much deeper than our medical technology and therefore can't be reached. The vast wealth of yogic thought suggests the body and anatomy of the brain is only the tip of the health iceberg. If you want to know true health, you must be prepared to search further still.

I have to this day not had an opportunistic infection. This in my mind does not indicate I am healthy in and of itself, however. Certainly being physically well is important, but there are other ways to appraise our existence. In yoga there are in fact five components to health. Yoga (the physical science of spirit) and Ayurveda (the health science of life) are two traditional paradigms that tacitly state that in order for there to be health, we have to look at all the modes in which health can be expressed in a human being.

We can express health on a physical, energetic, emotional, interpersonal/self wisdom, and intrapersonal/universal wisdom levels. Moreover, the real assessment of health is the point where all five of these modes of health expression dynamically interact.

Now before you chalk this up to more eastern quackery, I don't recommend anyone throw out their HAART regimen, and certainly, feel free to continue taking viral load/T-cell counts, but consider these additional ways of health self-assessment.

- What does the body really need? Be daring. For the next four weeks, experiment with a dietary change or exercise routine that you know would support your health. Even if the behavior modification doesn't stick, you will have had the opportunity to be aware of how you feel moving towards your optimal well-being.

- What is my energy level like? The breath flow is the primary expression of energy we all can understand. Where there is less breath flow, there is less energy.

- Am I living an emotionally free life? Work towards clarity of perception on an emotional level and begin observing emotional traumas without judgement when possible. This is a big step, may take time, and may require expertise, assistance, and support along the way.

- What understanding about my life's meaning have I uncovered? Tap into your sense of self-discovery and innate wisdom. Begin to know your own mind on situations in your life. This doesn't mean you can't take the input provided by others when appropriate, simply that you have already considered your own knowingness first, before any decision-making. Cultivating your essential wisdom of what works for you is a crucial stage in getting healthy. It provides a clear understanding that you honor and value who you are on the most basic of levels and you create your life from this awareness.

- And finally, what is my connection to the underlying unity of all things? Begin to remember that when all is said and done, there is a place of absolute happiness. A place of happiness for happiness' sake. A happiness that is both within you and connects you with all things. This place, sometimes called unity consciousness, is ultimately what we are here to re-discover and share in our lives. It may appear shrouded in mysticism, but if you turn your attention to something that brings you joy without cause, you'll find this concept staring back at you, with a smile. For example, one of my most transcendent moments was walking past a street corner of children, playing in the warm hazy sunlight of dusk. It's late autumn, after a long day's work. The opportunity for happiness without justification is between us and within us, and most of our lives are spent oblivious to this level of beingness.

> All the medicine in the world will come to no purpose if the power of healing doesn't already live inside the body.

Today, much scientific evidence has shown favorably that yoga and other traditional systems of healing are valid and cost effective ways to address the health needs of many chronic and life-threatening conditions. Working as a yoga therapist, a part of my path is to share with my private clients what I have found works. A part of my purpose is to provide the encouragement and support for them to be their own source for self-initiated awareness and acceptance, with the intent of transformation in their lives. This is a distinct part of how I get whole and what it means to be healthy, in addition to and in between doctor visits.

Yoga therapist Per Erez (pronounced "pear") is affiliated with the Kripalu Center for Yoga & Health, the National Yoga Alliance, and the International Association of Yoga Therapists. Per is currently finishing an internship with Joseph Lepage's Integrative Yoga Therapy program in Brazil. Most recently noted for his appearance on and work with The Oprah Winfrey Show, Per develops and facilitates stress reduction programs as a healing modality, and he volunteers services at TPAN.

Microbicides: Prevention Tool of the Future

by
Kaethe Morris Hoffer
and
Grisel Robles

The worldwide AIDS epidemic has often been perceived as primarily affecting men, yet internationally, women make up roughly half of all people living with HIV/AIDS. Here in the United States, women are one of the fastest growing population living with HIV, currently making up an estimated 30% of new HIV infections. Only fifteen years ago, women accounted for less than 7% of Americans living with HIV/AIDS, so their representation in the HIV-positive population has more than tripled in a relatively short time span. This is a significant increase, one that has been called a "profound shift" by U.S Surgeon General David Satcher. It calls for renewed attention to the ways in which women become HIV positive, and a renewal of efforts to create woman-friendly barriers to HIV-transmission.

Around the world, including in the U.S., most women become HIV-infected through sexual contact with men, generally by a boyfriend or husband. Cultural norms around the world make it difficult for women to insist that their sex partners consistently and properly use condoms. All too often, and with elevated frequency in patriarchal cultures and communities, women risk suspicion, isolation, and even violence for merely suggesting condom use. Within our own country, a 1998 U.S. Department of Justice study found that one out of four American women will be battered or sexually assaulted at least once in her life by a boyfriend or husband. This study shows that

Microbicides and Men

While much of the impetus for developing microbicides comes from the need for HIV-prevention tools that can be controlled and used by women, microbicides have enormous potential to benefit men, as well.

As currently conceived, microbicides will provide bi-directional protection, meaning: microbicides will protect any party to sexual intercourse, fighting pathogens in vaginal secretions and semen. In this way, a vaginally applied microbicide would protect both a man and a woman engaged in sex, regardless of the HIV status of either.

But a vaginal microbicide is not all that is needed. Anal sex—engaged in by both same-sex and different-sex couples—is a primary mode of HIV transmission through sex, and because the rectum and the vagina are very different biological environments, microbicides must be formulated that are specific to each.

Unfortunately, and largely due to the social stigmatization of anal sex—straight or gay—less effort has been put into discussions about and support for rectal microbicides. But especially for men, who are at greatest risk of becoming HIV infected through sex with other men, rectal microbicides could provide a critical new tool for the prevention of HIV transmission. Because of this, all support for microbicide development and research should emphasize the importance of rectal microbicides.

Easy Ways to Support Microbicide Research and Development

- Call your federal members of Congress and ask them to support the Microbicide Development Act of 2001 (a bill that would put federal dollars into the effort to develop microbicides). You can reach them by calling the capitol switchboard toll-free at 1-800-648-3516, and ask to be transferred to their office. If you don't know who represents you, log on to www.vote-smart.org or call 1-800-923-8683.

- Check out the Global Campaign for Microbicide Development on the web at: www.global-campaign.org You can download action kits here, sign a petition, access up-to-date information on the campaign, and join the coalition of organizations working to support microbicides.

- Organize a training session on microbicides at your organization or through a local HIV/AIDS prevention or support group. For educational materials and assistance, contact the Global Campaign in DC at 202-822-0033, or Grisel Robles at the AIDS Foundation of Chicago at 312-922-2322.

even in our relatively progressive culture there is a high prevalence of relationships in which women do not have optimal control over their intimate relations, and are thus at increased risk for being unable to ensure condom use.

Because of these factors, which constitute significant barriers to women's use of condoms, condoms cannot be the only tool the world offers to prevent HIV transmission through sex. Until there is a safe, effective, and accessible vaccines and until the status of women improves around the world, women need tools they can control and use that protect against transmission of HIV and other sexually transmitted infections.

In response to the combined realities of gender inequality and increasing HIV-infection in women, a global effort is underway to promote the development of **"Microbicides"**—anti-HIV agents that could be used and controlled by women. Currently in development, microbicides will be a new class of HIV prevention tools, chemical substances that—when applied to the vagina or rectum—will reduce the transmission of sexually transmitted infections (STIs), like HIV. Scientists are now trying to develop microbicides in non-prescription gels, creams, foams, and lubricants—forms that would be made available at any drugstore.

Microbicides are not being developed in order to take the place of condoms, which when used properly provide excellent protection against HIV transmission. Rather, microbicides would be an HIV-prevention tool that would place significantly more control into the hands of women, who could, in theory, use them without the knowledge of the man they were having sex with. In addition, microbicides would provide men with another tool that they could use for preventing HIV transmission [*See sidebar "Microbicides and Men"*].

There continues to be an urgent need for the public and policymakers to become more educated about the need for safe and effective alternatives to condoms, and to become educated about the potential benefits of microbicides. It is clear that with the proper investment and federal funding, microbicides could be developed within two to five years. Having safe, effective, accessible, and affordable microbicides would drastically reduce infection rates throughout the world, particularly among women and children. With 6,300 women around the world newly infected with HIV every day, investing in microbicide research and development is an effort we should not postpone [*See sidebar "Easy Ways to Support…"*].

Kaethe Morris Hoffer is manager of federal affairs at the AIDS Foundation of Chicago (AFC). Grisel Robles is AFC's Outreach Assistant—a position created through a partnership between AFC and the Global Campaign for Microbicide Developement. Kaethe and Grisel work together to support greater federal funding for microbicide research and development, and they can be reached via AFC's website at www.aidschicago.org.

Positive Empowerment

by Kevin Lisboa

I recently wrote an article for *Positively Aware* entitled "Positive Prisoner" (July/August 2001). Well here I am writing my second article, but I am no longer on lock down. I would like to share some of the things I've been through since my release. Now that I am out I find it kind of difficult to adjust. What I mean by this is that it's not all flowers and candy. For those who have been locked down, you know what I'm talking about. For those who haven't, try staying in your closet for a couple of years, then come out and try to pick up your life. What do you feel? Well, what I feel is a lot of prejudice, stored-up anger, and a lot of other emotions that I have to work on before I can move on.

The good side to this is that I'm free to make a change in my life. My first week out was very scary. No money. No immediate health insurance. I had become so dependent on the prison authorities to do everything for me that it actually took me close to a month to wake up and realize that this is real. I'm free. I will either have to learn all over again to depend on me or just go back to the life I was living before, which I have no intention of doing.

I have taken charge of my life, but I could not have made it on my own. In order to get your life back together you need a support system. I'm very fortunate because before my release I established the two most important forms of support—family and friends. I owe a lot to my mom for allowing me to come back home and for believing in me. The other person I owe big time is a very beautiful lady who works at Test Positive Aware Network. I will not mention her name because she knows who she is. I owe part of getting back on track to her. Through this lady I also met a very special person who befriended me during my incarceration. She encouraged me, gave me advice, and helped me see that a positive life can be lived being HIV-positive.

Today, I have goals and plans, which is so different from years ago. My first plan is to move from New York City to Chicago. In Chicago, my goal is to train to be an HIV counselor. I want to go back to school and find a job in the field helping people just like myself. I plan on educating myself so that some day I can work with newly released individuals, helping them to help themselves.

When I tested HIV-positive in 1993 I thought my world had come to an end. However, thanks to another inmate, who has since passed away, I learned about this virus which I jokingly call "picachu." I read everything and anything I could get my hands on. I got plenty of information and joined a support group while in prison. I learned about all the different medications (keep in mind when I first went to prison all we had was AZT). This disease has taken a toll on me, but I'm still a fighter. I refuse to let a big disease with a little name control me. This virus has helped me see life from a different perspective. What was once insignificant to me before I became positive, is extremely important to me today. I'm just grateful to my God for allowing me to live a little longer so that I could be able to obtain my goals. I'm already on that road thanks to my mother and the people at TPAN, who have helped me see there are still good people out there who are willing to give of themselves to help others.

But what about those coming out of jail who might not be as lucky as I am? My advice is to find yourself an agency in your area that works directly with people living with the virus. You should also find a case manager. The help is out there, you just have to look for it and be willing to take charge of your life. Remember, it is your life.

Can We Talk? Maggiore, Pregnancy and HIV

by Laura Jones

I'm having a little love/hate relationship with Christine Maggiore these days, ever since I spied her bulging pregnant "NO AZT" belly on the cover of a popular parenting magazine and nearly had a seizure right there in the checkout aisle of the swanky Whole Foods Grocery I can't even really afford to shop in. Marketed primarily to white, college-educated, economically comfortable "progressive" parents, the magazine featured articles counseling women to refuse HIV testing during pregnancy, to avoid antiretroviral medications while pregnant, and to seriously question the validity of the scientifically-backed theory that the immune-system failure syndrome we've named AIDS is caused by the Human Immunodeficiency Virus… yet provided no counter-balancing images of women or children who are actually sick. There were no women living with an AIDS diagnosis, no children suffering from stunted growth and recurrent pneumonia, and no women or children of color anywhere in the articles—just the same three or four healthy, seemingly non-progressive or incorrectly-diagnosed North American Anglo women you always see in articles decrying the reality of HIV/AIDS in women and children.

So yeah, I bought the damn thing—flung it in the bottom of the bag, underneath whatever brutally expensive produce I chose to purchase because my local grocery was low on tomatoes or spinach or some other vegetable that doesn't come in a can. I took the magazine home, vented about it to the Boyfriend, stomped around the kitchen preparing the brutally expensive produce… and at some point actually read the articles, which of course set me off on another round of stomping and venting. I wrote a venomous and now largely unremembered email to Enid and Charles, probably exhorting them to go down to California with me and a whole flotilla of AIDS-diagnosed women to directly accuse *Mothering Magazine* of unethical journalism and barricade their staff in their offices with bushels of organic whole grains and herbal remedies.

And *then* I did a really stupid thing—I went to go vent with the participants of an Internet parenting community I belong to. And they did the worst thing anyone could possibly have done to a person in the middle of a good bout of self-righteous indignation: *They made me think.*

Worse yet, they made me think about things that really scare me… like the long history of shitty treatment of women by the Medical Establishment. And the lack of attention paid to differences in how women's bodies synthesize medicines vs. the way men's bodies do. They even had the nerve to remind me that I'm a staunch advocate for "alternative" medical practices, and an even stauncher advocate for autonomous decision-making around issues of medication…. things that made me realize that, on some level, I was opting for righteous indignation to cover for the fact that I am seriously worried about the yet-unknown effects of long-term antiretroviral use, especially during pregnancy.

In fact, I'm so worried about it that, were I HIV-positive and pregnant, I probably wouldn't want to take those drugs either.

Now, that does not mean I'm going to invite Ms. Maggiore and Thabo Mbeki over to my house for a celebratory lunch—and I'm really, really angry over the racist and classist insinuations in those articles ("See? White North American HIV-positive women living above the poverty line simply don't develop AIDS—and therefore there must be Something Intrinsically Wrong with Those Women who do…"). I'm profoundly glad that, should I ever face HIV infection and pregnancy at the same time, I'm living in a place where I have access to the medications that are proven to dramatically reduce the chance of my child being born with HIV. What I'm not glad of is the fact that we live in a world where the only anti-HIV weapons we have at our disposal are A) experimental combination chemo in a pregnancy health-culture that demonizes a glass of wine and a cigarette during a 9-month gestation period; B) luck-of-the-draw with that "1 in 4" perinatal infection ratio, with the attending risk of child-abuse accusations if you refuse the meds; and C) rampant denial, which unfortunately seems to lead directly to do-not-pass-Go—blaming women who fall ill and/or pass HIV to their babies.

I don't want to be chummy with Christine Maggiore. However, I've been talking with my co-worker, who has been living with HIV/AIDS for something like 13 years. His medicines are working well for him right now, but more than a few of his close friends

are very ill with side effects: pancreatitis, kidney stones, liver failure. Nobody likes to talk about the sicknesses that come from the drugs themselves, he says. Talking loudly and angrily about medication sickness is almost taboo—at the very least it's considered whiny, if not profoundly ungrateful. But there's a huge difference between men's and pregnant women's ability to refuse antiretroviral treatment: in adult men, such behavior is considered a personal choice (though perhaps ill-advised), while in pregnant and parenting women there's the potential for grounds for having your children removed from you and put into protective custody, as has been seen with other diseases. When The Man makes noise about mandatory HIV testing for any other class of people, them's considered Fightin' Words… but when The Man discusses the benefits of mandatory HIV testing during pregnancy, even activists I know feel obliged to weigh the obvious trouble against "what's best for the child."

I really don't want to make friends with Christine Maggiore. I'm glad she's doing well, and her son and partner are fine, and I hope her newest baby will be healthy as any baby deserves to be… but that's as far as I want to take it in terms of a close, personal relationship with someone who seems unwilling to acknowledge that their medical reality doesn't mesh with that of many women sharing this Big Blue Marble. On the other hand, though, is the fact that she appears willing to advocate, and advocate hard, for a group of people who are struggling with obstacles to the autonomous decision-making processes many HIV-positive people take somewhat for granted around issues of medication: pregnant and parenting women.

I really don't want to make friends with Christine Maggiore. ...[but] she appears willing to advocate... for a group of people who are struggling with obstacles to the autonomous decision-making processes many HIV-positive people take somewhat for granted around issues of medication: pregnant and parenting women.

The ability to dramatically reduce perinatal HIV infection is a true blessing—but like most blessings, it becomes complicated when those with power attempt to make policies around it. On one hand, we have women who are threatened with loss of custody if they won't take medicines they fear may harm their children (and after DES, thalidomide, and X-ray pelvimetry—all of which were "proven safe" at one point in time—who can blame them?). On the other hand, we have women whose lives simply do not afford them the opportunity of antiretroviral treatment for themselves or their children—through no choice of their own, no "autonomy" or educated consumerism at their disposal. We have folk who holler "child abuse!" when a woman won't give her infant medicines that sometimes damage adult men's internal organs, and we have Thabo Mbeki.

Clowns to the left, jokers to the right… and here I am, stuck in the middle with Ms. Maggiore? Please, say it ain't so! Please, let's not be afraid to discuss these issues and advocate/educate responsibly with the ones who have the most at stake: women, and the generations they carry.

Laura Jones is a sexual health activist and the Hotline Coordinator for the Illinois AIDS/HIV & STD Hotline.

Drug Combos

by Glen Pietrandoni, R.Ph.

How does your provider know which drugs to use when starting or changing a drug regimen? Which drugs are better? You may wonder why can't the doctor give you that "once-a-day drug" like your friends have. There are no easy answers to these questions, but you can help your provider choose a drug regimen that is best suited to fit your lifestyle. When a physician is faced with a choice of drug therapy for a patient, he or she has to look at many different factors specific to each patient. There are pros and cons to each combination, but ultimately, the patient is the person who has to take the medicine, and therefore has a huge role in deciding what is best for them.

There are pros and cons to each combination, but ultimately, the patient is the person who has to take the medicine, and therefore has a huge role in deciding what is best for them.

Most clinicians use the guidelines set by the International AIDS Society U.S.A. (IAS) or those established by the U.S. Department of Health and Human Services (DHHS). They serve as the backbone for combining drugs for patients who have never taken drugs, or have only had some HIV drugs in the past. These guidelines are reviewed and updated regularly and give structure to a very complicated array of drug combinations, and considerations for HIV treatment in general.

Before we choose drugs for a patient, we must first decide if this is the right time to start medication. Is the patient mentally prepared for the commitment of near perfect adherence? Can the patient delay therapy to a later date without damaging the chances for future treatment options? Some regimens—as HIV drug combinations are commonly known—work better when the viral load is low (under 100,000 for example). Other, more potent drugs will work even if the viral load is higher.

Assuming we have considered these issues, how then do we narrow down the list? Providers need to evaluate drugs based on how potent they are. If a patient has a very high viral load, the drugs chosen need to be strong enough to get the viral load down to an undetectable level as quickly as possible. If the drugs chosen are not tolerated (they may cause side effects and adverse reactions) the patient may not take the medication as prescribed. This will set up the person taking the

drugs to possibly fail the regimen due to poor adherence. Could there be drug interactions with other prescription given for other medical problems? (This is a great reason to use only one pharmacy, and tell the pharmacist the over the counter and prescription medications you take).

Moreover, each patient should be evaluated for drug resistance if possible. Even before a newly diagnosed patient begins medication, it is possible for that patient to be resistant to certain medication. This is because the virus could have been exposed to many drugs in the individual who infected the new patient and is therefore transferring drug resistance. In those people who have had some HIV drugs in the past, the medical provider must determine if resistance to the previous drugs or similar drugs has occurred. This can be determined by a physician's best guess or by blood tests called genotype and phenotype. Finally, in some clinics, the cost of the medications can be a factor. Because of limited financial resources, only some drugs are available in some settings, and prescribing doctors are allowed to use only certain drugs when coming up with a combination that will work.

Drugs available to treat HIV today are classified in three different groups, based on the activity of the drugs and the way they work to stop HIV replication. The classes are nucleosides (including the nucleotide), non-nucleosides, and protease inhibitors.

Glen Pietrandoni is director of Clinical Pharmacy Services for the Walgreen Specialty Pharmacy, focusing on HIV, located in the Howard Brown Health Center of Chicago.

	Advantages	Disadvantages
PI and 2 NRTIs		
	Long-term data	Cross-resistance between PIs
	Effective and durable	Strict complex dosing
	Can save NNRTIs	Variable drug levels between patients
		Possible long-term metabolic disorders
Dual PI and NRTIs		
	Better blood levels	Potential broad class resistance
	Can save NNRTIs	Possible long-term metabolic disorders
	Possibly more effective and durable	Possibly increases stress on the liver
	Less drug needed	
	Potential for lower cost	
NNRTI and 2 NRTIs		
	PI-sparing regimen	Cross resistance to entire class
	Good blood levels	Not all are equivalent
	Simple regimen	
	Fewer pills and frequency	
	Well-tolerated	
Triple NRTIs (Trizivir and possibly in the future 2 NRTIs plus Viread)		
	Saves PI and NNRTI	Potency and durability not proven
	Simple regimen	Less effective at high viral loads
	Well-tolerated	Potential for greater mitochondrial toxicity
PI/NNRTI/NRTI		
	3 mechanisms of action	PI/NNRTI drug interactions
	Combined potency	Multi-class resistance with limited options
	Maintenance possible	Additive toxicities
	Useful in advanced disease	

New-Fill on "hold" and Open label for T-20

by Daniel S. Berger, MD

New-Fill Use Halted

Over the last several months countless numbers of HIV-positive individuals have had their spirits lifted, their morale boosted and their self-confidence improved. This was because a synthetic product called poly-lactic acid under the trademark New-Fill became available for personal use in the United States. New-Fill reversed many disfiguring facial abnormalities for many individuals; facial lipoatrophy changes are due in part to HIV drugs and HIV disease. Actually New-Fill has proved safe through clinical trials outside the US and has been shown to be effective for HIV-positive individuals with facial lipoatrophy. As a result, many HIV-positive individuals sought out treatment through a limited number of centers that were approved to administer the product. The product's sale and use was administrated by DAAIR, a respectable buyers club based out of New York City. Further detailed background information regarding New-Fill can be found in my previous article from the September/October 2001 issue of *Positively Aware* and on the www.AIDSInfosource.com web site.

After several months of smooth sailing with primarily trained plastic surgeons, almost by surprise, the FDA interceded and halted its use. A recent comment made by an unnamed HIV practitioner was "it appears that the FDA managed to find a loop hole 'vehicle' by which to interfere with personal wishes of individuals who suffer from the devastating facial side effects of antiretroviral therapy." Clearly it was the FDA themselves whose policy allows treatment for personal use, given that a drug is approved outside the US.

The October 26 action of the FDA halted all further distribution of New-Fill in the U.S.; therefore, the buying club DAAIR was in effect ordered to not release any more product for shipment—this included shipping New-Fill to those that had already initiated treatment and were still in the process of having the 3-7 administrations needed for New-Fill to be completely effective. DAAIR is guardedly confident that it can fulfill all shipments of product for those patients previously initiated into treatment with New-Fill prior to October 26th; however, at this time they cannot ship product to anyone who would have started the procedures post 10/26/01.

The FDA decision was made by a small group of Directors within the FDA, from such areas as Personal Use and the Division of Compliance. The FDA based their decision to halt distribution of New-Fill on the technical terms of their guidelines of allowing availability. Originally, New-Fill was allowed to be accessed by PWAs under the "personal use guidelines." These guidelines permit use of drugs not yet approved here (but approved in other countries) and for the treatment of one of several qualifying illnesses determined by the FDA. Persons suffering from these illnesses (such as AIDS) can import a drug into the U.S. for their individual personal use. The FDA then decided, upon further examination, that since New-Fill required the expertise of a trained physician and/or plastic surgeon that it no longer should be considered a personal use drug. Moreover, the FDA maintains that as New-Fill does not remain in full control of the individual utilizing the product, it should be re-categorized as a medical device.

The FDA does not allow for medical devices to be imported for personal use—all medical devices must be approved prior to use. The example the FDA gave was as follows: This situation would be similar to an artificial heart that was available in Europe but not yet approved for use in the U.S. The FDA would not allow anyone to import that artificial heart and subsequently would not authorize any surgeon to transplant said device—if that individual wants to access that artificial heart they must travel to Europe and have the procedure done there. The FDA did acknowledge that they would consider a treatment-IND (Investigational New Drug) protocol for New-Fill (a clinical trial)—however, this typically is itself a large administrative burden that can take minimally 3-6 months to complete and is usually done by the sponsoring pharmaceutical company.

Many medical specialists can state with confidence that New-Fill indeed is not a "device." Yes it requires someone to inject the product, but linking this to heart transplant surgery is quite a stretch. The product comes in a vial such as many other drugs and is simply reconstituted with sterile water or saline, like other drugs. It is drawn up in a syringe and injected. This does not require any sophisticated or mechanical devices or apparatus.

New-Fill has been approved for use in France and Mexico. Safety and effect studies performed satisfied the French requirements for approval. Additionally, several studies reported the use among HIV-positive individuals. Those reports were presented at the 2nd International Workshop on Adverse Reactions and Lipodystrophy in HIV in

Toronto in September 2000 and the 8th European Conference on Clinical Aspects and Treatment of HIV Infection in October 2001 in Athens.

As mentioned, DAAIR remains guardedly confident that it can fill all necessary prescriptions for product to those that had initiated treatment prior to 10/26/01. DAAIR is looking at various avenues within FDA guidelines and is attempting further inspection of this issue. If the FDA's edict is left to stand, many affected persons will be wronged and deprived of a procedure that can potentially change their quality of life.

DAAIR is experiencing significant slowdown and problems. During this writing plans are being set up for a meeting with the FDA. In this meeting Martin Delaney of Project Inform, DAAIR management, and I with other interested parties will hope to clear up some of these issues. Additionally, clinical trials with New-Fill for a "lipoatrophy associated HIV disease" indication are on the discussion table. I will try to keep you all posted on the www.AIDSInfosource.com website as well as in further issues of my column in *Positively Aware*.

T-20, Trimeris/Roche Open Label

Trimeris and Roche teamed up to offer a new open label study for the administration of T-20 to the most needy of HIV positive patients. T-20 is a novel antiviral, first of a new class of fusion inhibitors (blocks fusion of HIV to CD4 T cells). This was not an expanded access program, but an open-label safety study and was severely limited to 168 patients nationwide.

The program was initially announced on 11/07/01 and details of the protocol and its operation posted on the Trimeris web site. Additionally the companies announced that for "the letter distributed to doctors concerning the initiation of the study, visit the following websites: www.rocheusa.com or www.Trimeris.com." However as a physician who prescribes HIV medications, neither I nor the other physicians in our clinic have ever received such a letter. We have also spoken with several other community-based HIV physicians, none of whom received any letter.

The wire news story announced that a phone line would open at 3 PM EST on November 27th for up to 56 physicians who would be allowed to sign up as investigators and enroll three patients each. The criteria for enrollment was CD4 T cell count <50 cells/mm3 and viral load >10,000. First preference would be given to those with a recent opportunistic event while on an anti-HIV regimen in the last 90 days. However, I attempted to get through by telephone to register, getting a busy signal and at times no response. I kept trying. Finally getting a recorded message that stated, "We're sorry, enrollment is now full." We were later told that the program closed in less than 20 minutes of opening.

Alex Dusek, Director of Marketing at Trimeris stated that this was their attempt to "serve the community in the most equitable manner" and "seeking the advice of many other people." As much as we appreciate the efforts of Trimeris and Roche to increase availability it remains that a majority of advanced patients were not served.

If these were the Rolling Stones tickets that were on a first come first serve basis, I could understand handling it this way. However, unfortunately the honest reality is that many individuals' lives are at stake. When protease inhibitors were in Phase III of development (1994) a lottery system of patient chart numbers was set up through physicians' offices and sponsoring pharmaceutical companies. Those programs provided a fair chance for all patients to receive drug. In contrast, the Trimeris/Roche program favored larger institutions that could afford to place a dedicated employee on the phone that day and dial as many times as needed to get connected. We were told that no comment can be made as to whether several institutions or sites enrolled more than 1 physician and potentially took up more than their share of very few spaces.

Mr. Dusek of Trimeris reiterated that a complicated manufacturing and production process limits supply. I encourage Trimeris to provide wider availability for patients with limited treatment options. During the recent years of development, T-20 access has been greatly restricted. I hope that without too many delays Trimeris and Roche will offer an expanded access program.

Daniel S. Berger, M.D. is Medical Director of Northstar Healthcare and Clinical Assistant Professor of Medicine at the University of Illinois at Chicago and editor of AIDSInfosource (www.aidsinfosource.com) He also serves as medical consultant for Positively Aware. *For further inquiries Dr. Berger can be reached at DSBergerMD@aol.com or (773) 296-2400.*

Pickett Fences

Love stinks

by Jim Pickett

After reflecting a good five minutes between sips of my Bailey's and coffee (treating myself special these days) I can confidently say that for 2001, the "Tears of a Clown" episode wins the Tragedy Tiara.

Of course, the "Clown" script had competition in the non-fiction category this past year. Reams of competition. Reams of hook-ups and pick-ups and way, way low downs. Love affairs and lust affairs. Walks down the aisle that never did veer off the deep end. Admittedly, much of the competition could not even be considered as such. I mean, a first date that devolves into a formatted question and answer session usually signifies there is to be no sparkle. And tragedy always sparkles, Neely.

I knew how to win the hard way. Giving him my love would help the healing begin, take away the pain that made him be naughty in a bad way.

Me: "So… um, what's your favorite food?"

Him: "Potatoes. And salad."

What a terrible thing to say. I forgot the next question as I lost myself in the implications. Minutes, hours, days later (who knows), upon leaving the neighborhood Ethiopian restaurant where we had supped together (salad indeed), it seemed despite everything, Mr. Enigma wanted a little dessert, with his Sanka. A slice of Pickett pie. His AOL pic was hot—those weren't potatoes in his Speedo from what my practiced eye could tell, but I begged off.

Me: "I have to get home to watch Mad TV, and later wash my hair."

Speaking of interviews. I encountered another man online who wanted to meet for a drink. So we rendezvoused at the nearest dive. As luck would have it, Sunday nights were "Chili Nights," so we were able to enjoy a well-balanced meal as well as get to know each other. For three beers and two bowls, of chili thank you, I patiently answered a tedious litany of questions. Rather pedestrian this plethora, nothing pertaining to my views on the nature of the universe, more like my views on The View (hate Star Jones most). He fired them off, pumping and probing as if he'd done this before. Because I was hungry for more than chili at this particular time, I hung around for the complete interrogation.

We made love in the front seat of his car in a dead end until that simply became too awkward. So he double-parked and flipped on the hazards and we ran up to my place for the finale of our sweet, sweet love-making. What I failed to understand was that this meant we were married. The next day I filed for divorce. As is the custom, I simply typed

"I divorce thee" three times, and clicked on "Privacy Preferences" where I blocked him from Buddy Listing me. Ever.

Lest one think that I only date freaks from Chicagom4mNOW, I've had my dance card signed by men I actually meet in person first, fotch to fotch. Like the one in a towel. Unbelievable. Gorgeous. Same birthday as me, so ya know, we think the same, very dawning of the Age of Aquarius. While he's a lot older, has lived in the suburbs for 30 years and talks a lot about "masculinity" and "being a man," I choose denial. I attempt to ignore that when we're close, intimate, he sniffs me. Sniff, sniff. Sniff, sniff. Appears he enjoys how I smell, but it kinda grosses me out. Does he have to sniff so loud?

Things go downhill when we get into an argument in the car about making eye contact with waiters as an indication you acknowledge their humanity. He comes out against this position, I say he's a horrible creature akin to my father, he starts screeching, "You're nothing but an angry, bitter… AIDS… QUEEN," and I demand to be let out of the car immediately.

I don't have AIDS, bitch.

So, crying clowns. Actually, I was the one who was crying, after the fit of anger and puking and passing out.

It was in the summer, and I had been dating this lovely man with whom I had blistering, whimpering sex twice daily and who loved to cook for me and bring me capuccino in bed. He was a bit of a bad boy, but I knew what I was in for, and I knew deep down that I could tame him. After all, fellas, this wasn't my first time at the rodeo, I knew how to win the hard way. Giving him my love would help the healing begin, take away the pain that made him be naughty in a bad way. So, I saw myself as a well-fucked Mother Theresa figure. Compassionate. Very tender. Hot.

His first week on meds, I rubbed his back and held him when he needed it. I kissed him on the forehead and put his hand in mine.

And then we sent for a clown. A stripper clown, to be exact, a stripper clown hired as part of a bon voyage party for a pal of mine. A stripper clown arranged by me. We're at the party, and my new honey is in tow, meeting this particular gang for the very first time. "Oh, he's so nice," they say, "He's the best one yet," they say. And they've seen and said a lot. It was a very hot night, the house was packed with sweaty people, and there was a good deal of red champagne punch to make it all tolerable.

The clown is punctual. The clown has a pink Marge Simpson, a red nose and big clown shoes. Perfection. The clown berates our departing friend. The clown makes filthy balloon animals. The clown asks our friend to help him take off his shoes, as the clown's dogs are barking. Our friend senses something unsavory in this request, but assists with the clown shoe removal nonetheless. The music starts and the clown strips down to a pink g-string. Wow, those ain't potatoes. All is going according to plan until I catch the clown and the new love of my life honking each other's horns in the dining room. I hear the new love of my life say, "Nah, Jim's cool, he doesn't mind."

An eyewitness, one of many, says: "Jim, what's he doing? I thought he was so nice."

Me: "Tonsillectomy."

At which point I tapped the new love of my life on the shoulder, said that I wasn't very cool, that I did mind, that I would have no more of this clowning around. We left. I hollered, puked red champagne punch, fell out, awoke, and hollered some more. I cried. I stomped. I slammed the door, too hurt, too humiliated to return.

A day later I did. ✚

TPAN Calendar of Events

All events held at TPAN unless indicated otherwise.
For additional information on these events please contact Keith Waltrip, Program Director, at (773) 989-9400

january 2002

Date	Time	Event
Tuesday, 8th	6:30 PM	Client Advisory Board Meeting
Tuesday, 15th	7:30 PM	TPAN Board Meeting
Monday, 21st	6:30 PM	TPAN Closed, Martin Luther King, Jr. Day

February 2002

Date	Time	Event
Tuesday, 12th	10:00 AM - 4:00 PM	Community Open House
Tuesday, 12th	6:30 PM	Research Update - Reinfection: Fact or Fiction?
Tuesday, 19th	7:30 PM	TPAN Board Meeting

Community Open House

Tuesday, February 12th
10:00AM – 4:00PM

Tour TPAN's new Facilities

test positive aware NETWORK

Test Positive Aware Network
5537 North Broadway
Chicago, IL 60640
(773) 989-9400

Programs and Meetings

All meetings held at TPAN offices unless otherwise indicated:
5537 North Broadway, Chicago.
Office hours: Monday–Thursday, 9 am–8 pm. Friday, 9 am–6 pm
phone: (773) 989-9400 • fax: (773) 989-9494
e-mail: tpanet@aol.com • www.tpan.com

Support groups sponsored by the
Chicago Department of Public Health
Peer Support and Buddy programs sponsored by the
AIDS Foundation of Chicago

Monday

TPAN Daytimers

A group for people with HIV who prefer to meet during the day. Mondays and Thursdays at 10:30 am.

Newly Diagnosed

A group for newly diagnosed individuals. Mondays at 7:30 pm. 2nd and 4th Mondays include HIV 101 education.

Negative Partners

The Negative Partners of Positive People. 3rd Monday at 7:30 pm.

Tuesday

Living Positive

HIV-positive gay men discuss how being positive affects relationships and deal with the impact of HIV as single men. Tuesdays at 7:30 pm.

Positive Progress

A group for HIV-positive people in recovery. Tuesdays at 7:30 pm.

Wednesday

Medical Clinic

See description in Friday's listing. Wednesdays 3:30 pm–7:30 pm.

Straight Talk

A group for HIV-positive heterosexuals. Wednesdays at 7:30 pm.

Needle Exchange Program

Free, anonymous, legal syringe exchange and HIV/AIDS prevention. Every Wednesday 5:00 pm–7:00 pm at TPAN offices. In association with Chicago Recovery Alliance.

Yoga

Wednesdays at 7:30 pm.

Thursday

TPAN Daytimers

A group for people with HIV who prefer to meet during the day. Mondays and Thursdays at 10:30 am.

Medical Clinic

See description in Friday's listing. Thursdays 2:00 pm–5:00 pm.

Needle Exchange Program

See description in Wednesday's listing. Thursdays 2:00 pm–5:00 pm.

Brothers United in Support (BUS)

A group for HIV-positive gay and bisexual men of African descent. Thursdays at 7:00 pm.

Berlin HIV-positive Social Hour

Berlin, 954 W. Belmont, Chicago. Thursdays from 6:00–10:00 pm.

Friday

Medical Clinic

Free medical care provided by a nurse practitioner. This program is in conjunction with the Needle Exchange Program and is offered by Access Community Health Network. Call for an appointment. Fridays 2:00 pm–5:00 pm.

Needle Exchange Program

See description in Wednesday's listing. Fridays 2:00 pm–5:00 pm.

Safe Passage

A group for young adults (ages 18-24) who are HIV-positive. Fridays at 7:00 pm.

Scheduled By Appointment

Family AIDS Support Network (FASN)

A group for family, friends, and caregivers. Call Betty Stern at (773) 989-9490.

Women's Group

A group for HIV-positive women. Call Sylvia at (773) 989-9400 for more information.

Speakers Bureau

Individuals are available to community groups and organizations to educate on HIV, safer sex, harm reduction and experiences of living with HIV. Call Sylvia or Keith at (773) 989-9400.

Peer Support Network

Provides one-on-one support for recently diagnosed individuals. Volunteers provide support, information and referrals. Call Derek at (773) 989-9400 to get a buddy!

Positive Buddy

Volunteers provide individuals living with HIV/AIDS one-on-one emotional / physical support. Call Derek at (773) 989-9400 to get a buddy!

Miscellaneous

ChicagoPos18to24 at aol.com

AOL chat room for young adults (ages 18-24) who are HIV-positive. Hosted by TPAN's Young Adult Program. Go to AOL town square. Monday through Friday 3:00 pm–6:00 pm, except Thursdays 4:00 pm–6:00 pm.

Positively Aware 2001 Index

Compiled by Jeff Berry

*indicates brief news item

TPAN GALA 2001

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