

## Our Biology is Social A Talk with Richard Levins

By Bob Huff

Um outro mundo é possível — Another world is possible.

*You're a professor of population sciences; so, what's up with us humans?*

We can describe the present plight of our species as an eco-social distress syndrome. It pervades everything: The relations to the microbial world, to the physics of the atmosphere, to breathing in the chemosphere, to nutrition and food production — even our own biologies have been transformed.

Human biology is a socialized biology. For instance, one of the constants of human physiology has been the belief that blood pressure increases with age. Well, it does in our society; it does not among hunter/gatherers and pastoralists. Our posture is very much determined by class position and gender relations: whether you're willing to be noticed or trying to avoid being noticed, and under what conditions. Even breathing — the question of whether you breathe deeply or shallowly, depends on stress patterns. Our eating habits have certainly changed body size. The fact that we have electric light in this country means that people sleep less; serotonin and melatonin cycles are undoubtedly altered. We know that there are class differences in cortisol behavior. So our biology is social. Our human biology has been transformed. We are living in an environment that we've created, and a lot of that environment is social and emotional. And the emotional factors are as real as chemical ones.

*A lot of these changes have been made possible by science. Science does good things too. How could it work differently?*

Science has a dual nature. On the one hand it's part of a long historic increase in our understanding of the surrounding world. On the other hand it's the product of a knowledge industry. And that knowledge industry recruits, takes its agenda, and decides what's a problem and what's a good solution, on the basis of the needs of the owners of that industry. In an earlier time the owners of science were the princes, who kept scientists around as decoration. Now they are the trans-national corporations, so that ownership determines the patterns of knowledge and ignorance.

**The knowledge industry decides what's a problem and what's a good solution based on the needs of the owners of that industry.**

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In the areas that are closest to my own knowledge, we know a lot about controlling pests with pesticides because they are commodities. That's a way in which knowledge can be turned into a marketable commodity. We know so much less about controlling pests by simply having the right mixture of crops or by creating good conditions for spiders, because you can only publish that knowledge as a column of advice in *Farm and Garden*.

So you have a pattern of knowledge and ignorance and the first thing a scientist has to ask is, "Is the agenda of my science really where it should be? Do I want to join in the cutting edge of that science or do we need a very different kind of cutting edge coming from a different source?"

To really be able to do this, you have to have one foot outside of the academy. Science is very good at picking up idiosyncratic mistakes, like having dirty glassware or dividing by zero or having confounding factors, but it's no good at all at identifying the shared biases of the whole community.

That's simply described as "mainstream" or "common sense" or "cutting edge." People who evaluate research are the ones who've created the way it is now, so they tend to be very good at guaranteeing that the worst kinds of errors aren't made but not at really advancing science where it's needed.

There are different actors in the development of knowledge and they each have their areas of blindness as well as insight. So, for instance, in the international work I do with agriculture, it's very often the case that people living in the country feel a desperate urgency to guarantee that there will be beans available in three months. And this creates a great demand for pragmatism, which sometimes is unwilling to take the detours necessary to understand what's really going on. On the other hand, people coming from the outside very often have the luxury of looking at a longer time range, but are also less sensitive to the needs of the population. And the scientists from the country they are visiting are caught in between a concern for their own people but also with looking for validation from the international scientific community.

There's a tremendous urgency to get grants from the outside, to publish in foreign journals, to be invited to international meetings, to have a degree from one of the big places, and the problem is you then get a kind of intellectual colonialism. It's interesting that the great schools of tropical public medicine are not in the tropics. It's Walter Reed Hospital, the Pasteur Institute,

the London School of Hygiene, and each of them is related to colonial expansion. So they focused on the diseases that interfered either with the safety of the troops, or the health of the colonial administrators, or with the extractive industries.

Yet this doesn't mean one takes an anti-science attitude, but rather a critical view: that science is a social product, and has to be understood in its time and place. And, therefore, with this critical view we can look for the kinds of biases that occur within the content of the science as well. Critics of science began by worrying about the application of science. In the sixties we had the research strike at MIT, which was an anti-war gesture; they were concerned with the misuse of science for war. Then they saw that science was also being misused for profit. Then it was recognized that not everybody had access to science, that there were questions about who was allowed into the club. So gradually the critique spread out until it began raising questions also about the content of science.

For a variety of reasons, science, coming from a long history of growing up as kind of a little brother of capitalism, shares the euphoria, the arrogance, the pragmatism, and the fragmentedness of capitalism. So you have a preference towards a reductionist science — they recommend subdividing a problem into the smallest pieces and so on — because the dominant view is a fragmented, atomistic view of the world. The dialectical critique of science looks at that science both in its strengths and in its weaknesses. Answers to the classical problems, "What is this? What is it made of?" are descriptive and science has been very successful at getting those answers. The tools for answering those questions have become more and more sophisticated — but the questions haven't.

Increasingly we see that the great successes of science have been in answering the classical questions. But the great failures have been in applying a fragmented science to a fragmented, complex reality. So pesticides create more pest problems, antibiotics give us new germs, hospitals are the focus of infection, the Corps of Engineers produces flooding — and you start asking the question, "Well, why?" The people who made these mistakes were just as smart as we are, so why is it that what they did seemed so reasonable at the time? And, again, it's the combination of the economic constraints on science — what gets supported, what gets published, what gets reviewed — with the prevailing philosophy.

So the critique of science is needed, but you have to go outside of the scientific community to look at that critique. Very often, farmers, patients

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of all sorts — the victims of science — have a much deeper understanding than the professionals do. For instance, Black Lung disease was recognized in England fifty years before it was adopted in the United States. And the only reason for that is not that English doctors are smarter, but that the English working class had their own political party. Love Canal was discovered by the people who were living there, while the scientists were saying, "It's a random blip in the data, it's a cluster, it's not proven, it's anecdotal."

*In AIDS activism the slogan was, "We are the real experts."*

And it's interesting in retrospect, in which ways you were and which ways you weren't. If the element of desperation is missing among the scientists, it means that they'll demand a higher degree of evidence before allowing meaning. They'll also lack the subtlety of the experience. That means that when you design intervention programs, you miss a lot about what people really do.

For instance, there's now an insecticide-impregnated bed net program in Africa. I was just talking to a Cuban friend, who works in Cameroon, and she was telling me that, in Cameroon at least, it's too hot to sleep under a net at night; people would rather sleep on the floor. The bed net costs six dollars in a place where the average income is about \$250 a year; then you have to impregnate it for eleven dollars, and redo this several times; so in the end it's not economical, and it makes you miserable, so people will use it occasionally, but not consistently.

So one of the things we're studying now is consistency. We find that when a health problem presents itself people get all excited and committed to doing something about it, but as soon as you start getting success, the threat is no longer as visible. As long as everybody knew somebody who died of AIDS, education worked. When the education works well enough and a new cohort comes along which doesn't have friends who've died of AIDS, then the education becomes abstract. And then the social gap between providers and patients becomes more visible, more palpable, and more likely to create skepticism.

*The bed net is the condom of malaria, a disease that, by the way, is a tremendous, overlapping problem with HIV in Africa. How does that struggle?*

Most of the time, malaria is being discussed now in terms of drug resistance. It is being treat-

ed as a biochemical and genetic adaptation problem. The broader issues involve what affects the abundance of mosquitoes. For instance, irrigation is one of the things that have allowed mosquitoes to become endemic in places where they were only sporadic. The Aswan Dam is one of the big offenders there. Another issue is the destruction of the ecology of wetlands such as the eutrophication of lakes through nutrient pollution. Lake Victoria has its margin now covered with heavy growths of water hyacinth. So fish can't get in there to eat mosquitoes. There are big algal blooms from the runoff from human waste and from agricultural fertilizers. The algae die and sink to the bottom and absorb oxygen. So this means that the dragonfly larvae and the midges and other things that live at the bottom and threaten mosquitoes, are not there. In other words, the exposure to mosquitoes is not just a natural phenomenon. Every change in land use, when forests are cleared and so on, also causes changes in the mosquitoes that are around, and therefore in the exposure to malaria.

When you deal with diseases like encephalitis or West Nile, you're dealing with the relation of birds to their habitats. And one of the big things happening now is that birds that don't normally meet are meeting, because there are so few habitats available for them. The migrating birds will all gather in the few places that are still around. And there they can trade viruses. Then some of these birds move out into human areas, and then the mosquitoes transmit the virus from birds to humans. Part of the West Nile issue is that the cycle that had been maintained in bird populations is spilling out into horses and other animals and into the human population.

*So, backyard bird feeders are avian bathhouses?*

Each one of these diseases has its own special history. The rodent-borne diseases in Latin America, like Venezuelan hemorrhagic fever and Bolivian and Argentine hemorrhagic fever, are all involving changes in the agricultural pattern. In Venezuela, what happened was that the plains were plowed up to plant grain, and two things came from this. First of all, grain is mouse food, and secondly, farmers don't like to have snakes and jaguars around, so the mice got more food and fewer enemies. The mice were the reservoir for the virus, and so it increased its contact with people. In Panama, I think it's the changing agri-

**When the education works well enough and a new cohort comes along which doesn't have friends who've died of AIDS, then the education becomes abstract.**

cultural season, relating to the adoption of different crops. In Argentina it was the cultivation of the Pampas. And there what happened was when they started growing corn there were weeds, so they brought in herbicides. The herbicides were aimed at the weeds that grow in the very beginning of the season when the corn is short. Once the corn gets up high, it doesn't matter what's growing there. And so the herbicides shifted the balance among weed plants to the ones that come along a little bit later and grow underneath the corn. And they happened to be the ones that were liked by a different kind of mouse. And it just happens that this different kind of mouse carried the virus of Argentinean hemorrhagic fever.

**There's been a lot of non-professional invasion of scientific turf, for example, the women's cancer movement.**

In the African forests, Ebola is, I think, related to the fact that big mammals were being exterminated, so small mammals increased and those were the ones that came into contact with people going into the bush for bush meat. So the lesson of all of this is that every time we change land use in any way, we're also changing the epidemiology. And therefore there has to be a health impact statement as well as an environmental impact statement, asking, what will any development scheme do to mosquitoes, to ticks, to snails, to mice, at least.

Anytime there are new overlaps there will be new blooms of viruses or whatever. And they are always surprises. We do our best, but then, for instance, it turns out that corn pollen is very good for the Anopheles mosquito that transmits malaria. And people have been growing corn a lot lately. In every backyard, every vegetable plot has some corn. So if there's standing water within about 60 to 100 meters of your corn, then there'll be Anopheles mosquitoes developing rapidly, coming out robustly and looking for a blood meal. So those are the things you couldn't have guessed. Except to know that bugs eat, and when you affect their array of plants, you're affecting their feeding. So there's always a kind of guessing you have to do.

One simple rule is that it's important to maintain biodiversity. When you reduce diversity, you lose a lot of species, but the ones that remain are not kept in check and you can have explosions of these nasties. So it's good to maintain biodiversity rather than get caught up in the economic rationale that only tells you to go for the most profitable land use.

*How do activists and advocates affect the balance of political, social and economic interests?*

One of the general perspectives we have is that in a very complicated world, every situation is different. And sometimes this is used to say that you can't really understand what's going on. But another approach is to say, first of all, that our knowledge has to be to understand patterns of difference, say in the form of behaviors. And secondly, because each place is different, and because there'll never be enough scientists to characterize each place, you have to link the knowledge of professionals and non-professionals. It takes a much bigger mobilization of collective intelligence to solve these problems — and this will only work when the two can meet as equals. So there's been a lot of non-professional invasion of scientific turf, for example, the women's cancer movement, particularly the Women's Community Cancer Project, which has been insisting on the environmental causes of cancer; the River Watch network; the environmental justice movement; the Black Panther Party, which initiated a study of sickle cell; and the AIDS activist community. The intellectual resources exist; we have a well-educated country, and there is the possibility of tapping this knowledge and then demanding that science be directed toward answering the questions of the community, rather than responding to the grants of the pharmaceutical industry. A women's cancer group in Long Island organized a scientific conference where they brought the scientists together, but the women were the ones who asked the questions. It worked very well.

*Which scientists are studying understanding patterns of difference?*

The ecologists. The work of protein research can be pretty much done the same way in any lab in any place — if you have the equipment. And so the differences are, who has the equipment and skill? But when you're dealing with epidemics, the social context of disease is an important ingredient. So in the health movements and the ecology movements, you get people who are able to link the particular to the global. And that's where the exciting knowledge is going to be emerging in these fields. Also, the intellectual independence that people develop in order to crack these problems, will, I hope, lead to political independence, creating an independent political structure, so they can play an independent role rather than simply lobbying the ones that are already in power.

*What do you make of the recent Bush Administration proposal to treat people with HIV in Africa and the Caribbean?*

I haven't studied the proposal, but I have studied the proposer. So it's clearly not out of concern for the health of people, but it's a political move to show his compassion and the compassionate side of conservatism. I'm sure there's a lot of fine print about what kind of help will be provided. For example, I doubt whether there'll be any of it going to reduce poverty. Now, the impact of HIV in Africa is not only on the patient with AIDS, but on the caretaker and on the other members of the family. What's happening in a lot of places is that as the disease progresses, less and less time can be put into the farm. Eventually you can fall below the threshold where the farm is no longer sustainable and you either sell off your cattle or rent out the land, and depending on the rules of landholding and land use, the poorer farmers who are infected can lose their land and lose their livestock; if both parents die and teenagers inherit the farm, they may not be able to hold onto it; it may revert to more distant kin. So we have to look at AIDS and the epidemic as a crisis of survival, which in some people will be the AIDS symptoms themselves, in other people it will be hunger, through the failure of the farm, or it will be neglect of children through lack of parental care. You have to see it as a social as well as biological epidemic.

Now, it operates differently in each society because of the rules of landholding and the kinds

of mutual aid that are available, and I'm sure that the Bush program is not going to deal with that. I think that a lot of it will be pharmaceutical, and that his drug company buddies will be able to cash in on it. So I'm skeptical because it seems to be part of his war for hearts and minds.

*Some U.S. government officials acknowledge the potential for social destabilization in Africa arising from AIDS but they tend to frame it as a national security problem for the U.S.*

You'll find that in all those reports, social unrest is regarded as a problem. Well, some of us would see it as a great advantage. There are places that should not be tranquil. The message of Porto Alegre\* is that another world is possible if you do things differently; we can break out of the constraints imposed by the rulers.

*Richard Levins is a professor in the Department of Population and International Health at the Harvard School of Public Health. He is an ex-tropical farmer turned ecologist, biomathematician and philosopher of science whose central intellectual concern has been the understanding and influencing of processes in complex systems, both abstractly and as applied to evolutionary ecology, economic development, agriculture and health.*

\* The theme of the 2003 World Social Forum, held in Porto Alegre, Brazil was: Another World is Possible.

**Dear President Mbeki,**

It saddens our heart to hear that you have still not decided to let your people in South Africa live. We who write this letter love you so much and you are a hero to us.

We are a small group of People Living With AIDS in Nigeria who would all have died a long time ago but our President, Chief Olusegun Obasanjo gave us anti-retrovirals and we are all living our normal lives. The medicines do a great wonder in the fight against AIDS. For example our friend Mr. Nasko: he was carried on a stretcher into the doctor's office and given these medicines; yesterday he took the stairs two at a time and came to visit us. He had returned to his job as small-time trader. So also Mr. Ambursa, he was taken for dead and wheeled into the doctor's office, but just six months after, he too is back at his job.

The medicines are so easy to take and have no side effects that have made any of us uncomfortable whatsoever.

About two hundred of us here in this poor, illiterate North of Nigeria are taking these medicines very easily. Just three in the morning and three in the evening. They are subsidized for us and we all can afford the 10 dollars every month that we are required to pay. Families have been reunited, even Lami and Rueben have got married. Lami wrote her will a few months before getting the medicines.

You are a good man, President Mbeki, just save the lives of your people and be the "Best Man."

Our best regards,

Samaila Garba  
Kebbi Alliance Of Positive People (KAPOP)  
Birnin-Kebbi  
Kebbi State, Nigeria

## In Their Own Words: The Current State of Women and HIV

By Leslie Hanna, reprinted from BETA, Winter 2003

*BETA, the Bulletin of Experimental Treatments for AIDS, asked women with HIV, clinicians, and researchers a single question: What do you consider to be the most important treatment or health issues facing women with HIV today? BETA can be viewed online at [www.sfaf.org/beta](http://www.sfaf.org/beta)*

### **Amy Justice, MD, PhD**

*Associate Professor of Medicine, University of Pittsburgh School of Medicine*

I think there are two major issues: helping women start and continue taking appropriate multidrug, multiclass anti-retroviral therapy, and doing research to determine the degree to which treatment recommendations for men should be adjusted for women.

Access continues to be a huge issue. Women in 2002 still enter care later than men and, as a group, adhere less well to treatment than men. Today, it's not so much that providers will not or do not treat women, it's that women have real trouble with the basics of regularly accessing health care—they have trouble making and keeping appointments. Access is not something that is barred for women, but it is something that needs to be facilitated.

Drug toxicity is a huge issue we're only beginning to understand. Clearly it's a huge issue for men, too, but men and women may have different susceptibilities to many side effects. Diabetes is a good example. Women tend to have more body fat, and body fat is a predisposing factor for diabetes in the general population. What do HAART and HIV do to the picture for women? These and other questions, if answered, could improve routine monitoring—for instance, by informing better ways to use glucose and liver tests.

Liver health is a real concern. Women's livers work differently than men's. For example, we know that women are more susceptible to cirrhosis (liver scarring) when they consume the same amount of alcohol over the same amount of time, matched for weight—pound for pound—with men. We don't really know why, but the fact has been well demonstrated. Today, in HIV disease, a major cause of death is hepatitis and liver failure. Women with HIV are likely to be ethnic minorities and younger, inner-city residents with a high risk of smoking, alcohol use, and injection drug use. It's reasonable to ask whether these women might not be particularly

susceptible to liver injury. This really needs to be studied.

### **Priscilla Abercrombie, RN, NP, PhD**

*Assistant Clinical Professor, Department of Family Health Care Nursing, University of California at San Francisco (UCSF)*

I've been following women with abnormal Pap smears for many years. Nothing's changed; HPV (human papillomavirus) is still a huge problem. We're still treating it the same way, and following women very carefully over time. We're not yet sure if HAART is helping to decrease the number of abnormal Pap smears or if it's improving the status of women with cervical dysplasia (abnormal cells). But the majority of women—at least 50%—will have an abnormal Pap smear at some point, and for most women

HPV is a recurrent, persistent disease. The rates of cervical cancer have not changed, though.

Some women we've been treating for years are now entering menopause. While the signs and symptoms of menopause in HIV positive women are similar to those in HIV negative women, there are some unique treatment complications (mostly liver complications), and there are concerns about antiretroviral drug interactions and hormone replacement therapy. We need to learn more about how best to manage menopause in women with HIV who are taking HAART.

### **Eve W.**

*HIV-positive woman*

I am very concerned about the long-term toxicity of the antivirals. As a woman on treatment for close to ten years, I've had a hard time dealing with the side effects. Although none have been life-threatening, they started to really wear me down and scare me. On top of this, adherence became more difficult over time. I just got sick of taking the medications day after day. I felt I was pushed to start treatment all those years ago. Hopefully things are different now.

Another thing that is important to me as an HIV positive woman is that HIV did not take away my right to have a child. Women should not give up on having a family if that is what they want.

**Maureen Shannon, MS, FNP, CNM**

*Associate Clinical Professor, Department of Family Health Care Nursing, UCSF*

There are multiple issues because there are so many different women with HIV disease who have acquired the virus in different ways, and because it's a very complicated disease. There are some major themes, though.

First, although things have changed, there is still a strong stigma associated with this disease, especially for women. It's still so shameful to have HIV/AIDS that some women delay seeking services or treatment just for that reason. By trying to conceal their status, they'll end up receiving suboptimal care. Even in the San Francisco Bay Area, let alone the rest of the world, there's a prevailing attitude toward women of, "What did you do to get this disease?" Many women today do not tell their families or their coworkers or neighbors. Stigma may be subtler in the U.S., but I've known positive women who give birth to babies they hope are HIV negative, who then have to go to a pediatrician—and the judging begins, or so it's perceived. Just having to discuss the babies' HIV-related concerns reflects on the mom, and it's not like discussing diabetes or herpes. It's just not.

Another important issue for women, and one that affects access, is the amount of violence that so many women experience, especially at the hands of intimate partners. This includes both psychological and physical threats. HIV positive women also have a very high rate of past childhood abuse, including sexual assault and molestation. As providers we're more aware of this today than we were earlier in the epidemic, but clinicians still do not screen for violence as much as they should. Yet doing so can make a huge difference when making treatment decisions. For example, you have to be very careful when interpreting depression in women—is it related to HIV? To medication side effects? To current violence, or a childhood history of sexual assault? Women living with violence or with a history of violence often have a condition similar to post-traumatic stress disorder, but since they're not often screened for any of this, they don't often receive the appropriate care. Such women often self-medicate, too, and it's important for us as providers to know why. Violence also impacts women's entry into care and adherence to care. We discuss safety plans on a regular basis with many of our women clients—for instance, do they have a supply of medications and a suitcase ready to go in case they need to leave a dangerous situation in a hurry? Finally, women with so much violence in their lives also may end up spending time in jail or otherwise

incarcerated, which has implications for access to medicines.

A somewhat related issue is the lack of mental health services. Women with HIV have a high rate of depression and chronic stress, along with abuse. In general, there aren't a lot of psychological services available for anyone these days, but what does exist tends to be focused on people with severe mental illness. It would be great to have services available to women earlier in challenging situations—during periods of new or significant stress—to teach coping and problem-solving skills. Instead, we tend to throw drugs at people and hope for the best, i.e., without providing counseling. We don't hesitate to order an expensive CT scan, but we don't generally support psychological needs and services.

**Grace McComsey, MD**

*Assistant Professor of Medicine and Pediatrics, Case Western Reserve University School of Medicine*

Several things come to mind. The most important thing is probably the fact that we need studies focused on women. If we want answers to questions about women, we cannot get the data we need from men. This is true whether you're talking about antiretroviral treatments or side effects.

Here in Cleveland we are beginning a study that involves two months of complicated treatment, requiring participants to be seen frequently, to use study medications that need to be taken three times daily, and at study's end to have muscle and fat biopsies. This is a study that might have been difficult to enroll anyone in, yet we have so far enrolled 60% women (18 of 30 total). We also have more women than men on the waiting list.

How have we enrolled so many women? What works is not mysterious: we simply spend the time necessary to explain and discuss what the study is trying to achieve and why it's important. When women understand that there are more complications in women than in men, and once they understand the purpose and benefits of the study to themselves and to HIV medicine, they are usually very interested in participating. I also give talks at different community groups and forums, some of which are focused on women. In the days following a talk, women have tracked me down at the clinic, asking for more information and how to enroll. So our efforts to educate about special issues relating to women have sometimes yielded very good results.

*Leslie Hanna is the former editor of BETA.*

# Salvage Strategies and STI at the 10th Annual Retrovirus Conference

By Bob Huff

*Selected news from the 10th Annual Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, February 2003. First of a series.*

## STI in the Salvage Setting

Two studies presented at the 10th CROI investigated use of structured treatment interruption (STI) in populations of patients with very advanced HIV disease and long treatment histories. Typically, these individuals are very difficult to treat, having developed resistance to most available antiretroviral drugs in each therapeutic class (multiple drug resistance — MDR). Because of the potential for serious consequences due to disease progression while off therapy, especially in these advanced patients, clinical use of the technique of STI has been controversial. One theoretical rationale for its use in a salvage setting, however, is to allow drug-resistant HIV species to become overgrown by drug-susceptible wild-type virus, which might then be suppressed by available drugs. Another rationale for STI in this population is to allow individuals suffering from drug toxicity a period of drug-free time in which to recover. Although two trials investigating these issues were discussed in Boston, they showed contradictory results and aren't likely to settle the controversy. Nonetheless, the larger of the studies produced compelling evidence of the dangers of unsupervised STI for individuals with advanced HIV disease.

## CPCRA 064

Jody Lawrence, from the University of California, San Francisco, and an investigator with The Terry Bein Community Programs for Clinical Research on AIDS (CPCRA), reported on study CPCRA 064, a randomized trial in 270 individuals with multi-drug resistant HIV. The study compared whether the strategy of using a four-month treatment interruption prior to starting a new therapy would result in fewer clinical events and deaths than changing to new drug regimen without interruption. Sixty-three percent of the participants entering this study had CD4 cell counts below 200 cells/mm<sup>3</sup>, a demarcation point for increased risk of developing one of the serious illnesses associated with AIDS;

about a quarter of study patients had CD4 cell counts below 50 cells/mm<sup>3</sup>, and over half had previously experienced an AIDS opportunistic infection. At the time of study entry, all patients had virus levels uncontrolled by their medications and had previously used, on average, 4 HIV protease inhibitors (PI), 5 nucleoside analog HIV reverse transcriptase inhibitors (NRTI) and at least one of the non-nucleoside class of reverse transcriptase inhibitors (NNRTI).

After nearly a year of follow-up 16 patients had died, with 8 deaths occurring in each comparison arm. Overall, 34 patients experienced clinical disease progression or died while on the study, with 22 of those events occurring in the interruption group and 12 in the continuing group. After noting that patients in the interruption group were not likely to be protected from disease progression, a Data Safety Monitoring Board overseeing the study halted new enrollments into CPCRA 064 in June of 2002.

In addition to experiencing more clinical events, patients who interrupted treatment before changing their regimens also had poorer CD4 cell count responses and higher HIV RNA viral loads than those who switched immediately, although these trends were diminishing during a follow-up period out to one year. There were no benefits for treatment adherence or quality of life with either strategy. The study investigators recommend that patients with multiple drug resistant HIV should be maintained on an optimized antiretroviral regimen and should not undertake an interruption before switching. (Abstract 67, 10th CROI)

## GIGHAART

Another trial also investigated the strategy of using treatment interruption in people with advanced HIV disease and multiple drug resistant virus.

Christine Katlama, a clinical investigator from the Hospital Pitie-Salpetriere in Paris, reported on a study of an intensive HIV regimen called GIGHAART in highly treatment experienced patients. Sixty-eight participants were randomized to either receive the GIGHAART regimen (containing 6 to 8 drugs) immediately or to wait for 8 weeks before starting therapy. The median CD4 cell count of study participants

**One theoretical rationale for STI in a salvage setting is to allow drug-resistant HIV species to be overgrown by drug-susceptible wild-type virus.**



was 27 cells/mm<sup>3</sup>, indicating the advanced stage of HIV disease in this group. At the time of study entry, participants' HIV viral loads were not being controlled by therapy and all had previously received multiple drugs from each therapeutic class.

Twelve weeks after starting the GIGHAART regimen, patients in both study arms had experienced reductions in HIV viral load, although there was significantly improved reduction among those who had interrupted treatment as compared to those who began their new regimen immediately. The median decrease in plasma HIV RNA in the delayed treatment arm at week 12 of therapy was -1.91 log copies compared to -0.37 in the immediate arm. While only 15 percent of those starting GIGHAART without delay had undetectable viral load after 12 weeks of therapy, 38 percent of the deferred treatment group were undetectable.

The interruption strategy produced favorable results in other study parameters as well. After nearly a year of follow-up, CD4 cell counts were up by 69 cells/mm<sup>3</sup> in the deferred arm compared to a median increase of 7 cells/mm<sup>3</sup> for those who started immediately. Overall, in this difficult-to-treat population of people with advanced HIV disease, an 8-week interruption before starting an intensive antiretroviral regimen was associated with improved virological and immunological results that were sustained out to one year.

During a discussion following her talk, Dr. Katlama speculated that the superior potency of the GIGHAART regimen might explain why these results differed from those in CPCRA 064. Commenting on the shorter duration of STI in her study, Katlama also said she didn't believe that it was necessary to wait for the wild-type virus to come back completely as long as drugs could be found to keep the virus down. (Abstract 68, 10th CROI)

### Deeks Weighs In

A paper recently published in the journal *AIDS* by Steven Deeks of the University of California, San Francisco, also addressed the role of STI in salvage therapy. In a non-randomized observational study, 24 patients who were experiencing virological failure despite remaining on HAART elected to stop all ARV medications for at least 12 weeks (median 20 wks). Following reinitiation of treatment, patients' viral genotype, phenotypic drug susceptibility, viral load and CD4 counts were monitored. In a previous study, Deeks had shown that during a treatment interruption in patients with MDR virus, drug-

susceptible wild-type virus usually eventually outgrew the less replication competent virus population that had been selected by drug pressure. In an extension of that investigation, this study looked at the long-term effects of what happened when patients restarted their various ARV regimens after STI.

Fifteen subjects (64%) maintained viral load below 200 copies for up to 109 weeks of follow-up after restarting therapy. Twenty of the subjects had a shift in viral phenotype from resistant to susceptible during the period off drugs. After restarting therapy, 13 of these 20 patients were able to suppress and maintain viral load below 200 copies within the follow-up period. This durable viral suppression did not occur in any of the 6 patients who restarted therapy without adding at least one drug to which their baseline virus was phenotypically sensitive. In contrast, all 9 patients who started a regimen with at least one drug to which their baseline viral population was susceptible achieved viral suppression. For 5 of the 9, the new drug was an NNRTI. Finally, 4 of the 5 who restarted with a regimen containing two or more drugs active against their baseline viral population also sustained successful suppression through follow-up. (*AIDS* 2003; 17(3):361-370)

The theory behind this approach in the MDR patient population is that after stopping drugs, the less-fit MDR virus will be overgrown by a drug-susceptible wild-type virus that has been waiting quietly in the viral archives. Once the drug-resistant strain has been sent to the archive and the WT reestablished, therapy including several recycled drugs is restarted and the dominant drug-susceptible population is suppressed. As Deeks has demonstrated in a previous study, if only recycled drugs are used, the MDR virus soon bounces back and viremia blooms within weeks. But the new study suggests that, if only one new drug is added along with the recycled meds, then this may be sufficient to keep the less replication-capable MDR strain from re-establishing itself. The key is the STI, which allows the MDR strain to retreat to archival levels. If the MDR strain were still actively replicating as the dominant strain when treatment was switched, there might be a temporary lowering of viral load, but resistance to the single highly active new drug would quickly appear and the evolved virus would be all that tougher to treat.

The conclusion that adding only a single new drug may provide durable viral suppression after an STI could be welcome news for people

**Taking an STI may not be a good idea for salvage patients unless they also have the immunological cushion to keep them from getting sick while off therapy.**

with MDR virus who perhaps can't access more than one drug that their virus is sensitive to. With Fuzeon waiting in the wings, this finding, if confirmed, may have profound implications for how salvage therapy is approached. The current consensus holds that to forestall resistance after changing regimens, patients must add at least two new drugs to which their virus is sensitive. This may still be true, especially when an STI is not feasible or too risky, since, as the CPCRA trial warns, taking an STI may not be such a good idea for people lacking the immunological cushion to keep them from getting sick while off therapy. Finally, if no new drug is accessible, earlier work by Deeks demonstrated that drug-resistant virus may be less replication competent and perhaps less pathogenic than wild-type. This suggests that it may be advantageous to remain on a failing regimen for as long as tolerable until newer drugs come along.

In an extension of these investigations, Dr. Deeks presented a poster at CROI on the selective interruption of only one component of HAART. This non-randomized study in 20 patients applied a finer scalpel to the interruption strategy by halting only the PIs and continuing NRTIs (or vice versa). It also introduced a new acronym to the literature, PTL, for partial treatment interruption. Participants' median CD4 count was 336, the median viral load was 3.9 log copies/mL, and all had been experiencing persistent viremia despite good adherence. The decision whether to halt PIs or NRTIs was based on each individual's toxicity profile.

For 15 subjects who interrupted all PIs and continued NRTIs, viral load and CD4 counts

remained stable, while triglycerides and cholesterol were significantly reduced by week 12 of the intervention (TG by -90mg/dL; non-HDL-C by -30mg/dL). Genotypic and phenotypic resistance remained stable past week 16, although in 2 patients, drug susceptible PI mutations began to dominate by week 24 and viremia increased as viral replicative capacity improved. Overall, stopping PIs improved lipid values and staying on failing NRTIs continued to provide some virologic benefit. Larger, randomized studies are needed to confirm this.

The 5 patients who stopped NRTIs but continued their PIs did not fare as well, experiencing immediate and sustained viral load increases at a rate of about 0.03 log<sub>10</sub> copies per week. Three of the 5 eventually had their M184V 3TC resistance mutation revert to wild-type, which was accompanied by an up-tick in viral replication fitness. (Abstract 640, 10th CROI)

This research may be most significant for what it tells us about viral and immune system dynamics. Further research is needed to develop assays of immune correlates that can predict who is most likely to benefit from stopping, starting or staying the course. Until then, attempting to guide viral resistance properties through complete or partial treatment interruption is best reserved for research settings where close monitoring can be assured. One need, Dr. Deeks noted, is for a large cohort similar to the MACS study for people with MDR HIV. Given the large and growing number of people with limited treatment options, continued research will be crucial.

### Comparison of CD4 and Viral Load Changes during STI Studies for People with Multi-drug Resistant Virus

	CPCRA	GIGHAART	DEEKS
Study Type	Randomized	Randomized	Observational
# of pts on STI	135	34	24
Baseline CD4 (cells/mm <sup>3</sup> )	180	28	218
Baseline VL (log <sub>10</sub> copies/mL)	5.0	5.4	4.6
Duration off therapy	16 weeks, fixed	8 weeks, fixed	Median 20 wks pt choice
<b>End of STI:</b>			
CD4 change from baseline	-53	-10	-84
VL change from baseline	+0.31	+0.16	+0.76
<b>48 weeks after restarting treatment:</b>			
CD4 change from baseline	+7	+69 (40 wks)	-3
VL change from baseline	-0.76	-0.79	-2.00

# Global Treatment Update

By Gregg Gonsalves

## Roche Drops the Price

After a sustained campaign, particularly by Medecins Sans Frontieres/Doctors without Borders, pharmaceutical giant Roche has lowered the price for nelfinavir (Viracept) for least developed countries and Sub-Saharan Africa to \$900 per patient year, a more than 80 percent reduction off of the cost of the drug in the United States and Europe. For middle income countries, Roche isn't offering much of a bargain and is setting a cost of \$3,000 per patient year. Roche is also tacking on "shipping and handling costs" to this offer, which could amount to a 20 percent surcharge for these developing countries. One wonders why Roche was the last to the table in offering differential pricing for their product, when most other big manufacturers have already agreed on substantial discounts on their products for poor countries.

## TAC on the March

The Treatment Action Campaign of South Africa marched on Parliament on Valentine's Day, February 14, to demand a national HIV/AIDS treatment and prevention program from their government. TAC's struggles with the government of South African President Thabo Mbeki represent the struggles and aspirations of people living with HIV/AIDS all over the developing world: for access to anti-retroviral therapy and other AIDS care that have kept thousands of people in the United States and Europe alive and healthy, and truly living with HIV. GMHC in collaboration with Health GAP and the African Services Committee, sponsored a demonstration in support of the Treatment Action Campaign outside the South African Consulate in New York on the eve of TAC's march.

## Getting Religion: The Church and ART

Church World Service sponsored a roundtable on the Universal Access to AIDS Treatment, February 19th and 20th in New York City, bringing representatives of major protestant denominations and their associated international health programs together with AIDS treatment activists for the first time. The roundtable explored the potential role for faith-based organizations in providing care for people with AIDS in the developing world, where religious hospitals and health centers provide a substantial portion of

health care services in general, and advocating for public policies in the U.S. and abroad to improve access to treatment.

## Presidential AIDS Initiative

President Bush unveiled a startling new AIDS initiative in his State of the Union speech in January, which includes \$15 billion to provide treatment and prevention services to 2 million people in Africa and the Caribbean. The initiative, which includes a request for \$10 billion new dollars from Congress, represents a sea-change in U.S. global AIDS policy. The devil is in the details of course and the President's new plan relies heavily on a yet-to-be created U.S. program through the State Department to manage this effort, instead of funneling the needed resources to the already-up-and-running Global Fund for AIDS, TB and Malaria (GFATM). The initiative is also slow to get started, with the President asking only for \$2 billion in the coming fiscal year. While praising the effort as more ambitious and sweeping than anything proposed by his predecessors, GMHC expressed disappointment that the President bypasses the GFATM and doesn't offer more assistance in the near term for people living with AIDS in the developing world.

## Speaking of the Global Fund

In a piece of masochism or shrewd political maneuvering, the Board of the GFATM elected U.S. Secretary of Health and Human Services, Tommy Thompson as its Chairperson. With the U. S. shortchanging the Fund in favor of its own unilateral initiatives and its championing of moralistic approaches to HIV prevention, the appointment of Thompson is a mixed blessing. Perhaps giving the U.S. a leadership role on the Board may curry some favor with the Administration and lead to increased funding down the line, but the price may be increased pressure from the U.S. delegation on abstinence-only prevention approaches, restriction of family planning options, and stigmatization of drug users and sex workers. While the Fund also gave out \$866 million in new grants at its last Board meeting, they also announced that they don't have the cash to offer a new round of grants later this year.

## Boulder Blues

By Lei Chou

**Roche is positioning Fuzeon to be the therapeutic foundation for treatment-experienced patients.**

On Valentine's, Roche invited state ADAP (AIDS Drug Assistance Program) directors and community activists to a meeting about Fuzeon (T-20, enfuvirtide) pricing at its manufacturing plant in Boulder, Colorado. Unfortunately, only the directors of four ADAPs were able to attend, although these represented the country's largest programs. Lanny Cross from New York, Michael Montgomery of California, Dwayne Haught from Texas, and Paul Arons from Florida made the snowy trek. Illinois could not attend since that program does not foresee any possibility of adding this drug to their formulary, no matter the price. Martin Delaney, Bill Arnold, and Lei Chou were present as members of the Fair Pricing Coalition. Dani Bolognesi, Carol Ohmstede, and Walter Capone attended from Trimeris and David Reddy, Kathy Presto, Georges Gemayel, Eric Lodewijk, John Tayer, Archie Shew, Arnie Doyle, Donny Moss and others from Roche were present.

Roche and Trimeris held a rehearsal meeting the night before and it showed. Their presentations were well prepared and comprehensive. Dani Bolognesi, the chairman of Trimeris, kicked off the meeting with "The Fuzeon Story:" the history of the drug from discovery through development. Their excitement about the pending FDA approval was palpable. The chemical structure of Fuzeon was flashed on screen several times to emphasize the SIZE of this thing as compared to other ARVs. One does wonder how it will fit onto the FDA package insert.

The resistance data presented at Retrovirus in relation to a related drug, T-1249, was also discussed. Since it appears that the longer someone is on Fuzeon, the less effective T-1249 will be, concerns were raised about the slow pace in the development of T-1249. Dani indicated that Roche is committed to expediting development of T-1249 and to bring it to market as soon as possible. David Reddy, who oversees global development of HIV drugs for Roche, was asked and confirmed that indeed, T-1249 development will be expedited.

Roche is positioning Fuzeon to be the therapeutic foundation for treatment-experienced patients. Subset analysis from TORO trials with OB (optimized background) suggests that using 2 OB ARVs is just as effective as using 5 OB

drugs. Additional details on the cost effectiveness of this strategy will be presented at the next Glasgow Conference. They are aiming for Fuzeon to replace the current megaHAART approach, and are in talks with the VA and Kaiser Permanente regarding that possibility. They are also continuing the development of pharmaceutical peptides by looking at pegylation, pushing towards eventual once-a-week dosing.

Next up were Eric Lodewijk, who runs the Boulder Plant, and Carol Ohmstede of Trimeris. They went into considerable detail about the manufacturing of the drug, from obtaining raw materials from around the world, to retooling the factory and installing new equipment (this was not a new plant built from scratch as previously indicated by Roche), to hiring 300 employees (with half working on Fuzeon). The molecule itself is built in 106 steps, assembled in three sections using the Rosenmound von Braun process\*, with numerous additional steps required to get to the final product including lots of washing and drying at low temperatures. The entire job takes 6 to 7 months to complete.

David Reddy followed up the tech talk by diving right into the pricing discussion. He presented Roche's pricing philosophy with regard to Fuzeon.

- It takes 45 tons of raw materials to make 1 ton of Fuzeon;
- R&D has cost much more than that for the protease inhibitors;
- The \$600 million in R&D breaks down as:
  - 1% Research,
  - 55% Development,
  - 11% Manufacturing,
  - 11% Phase IV patient support, and
  - 22% in manufacturing investment.

It was revealed half way through his presentation that the price has already been decided upon: "No, of course I can't tell you what it is!" Reddy said.

He said these factors should be considered before reacting to the price:

- The price is fair concerning the high cost of manufacturing.
- The drug is defining the future of salvage therapy.
- It will be cost effective (data under development).

\* For visuals see: [www.nufarm.fr/plants/gamanu.en.html](http://www.nufarm.fr/plants/gamanu.en.html)

- Roche is committed to work with all parties on access (They will collaborate with BI on tipranavir trials, and will provide drug for that purpose).
- The price has to be sustainable for the company. Reddy said the price is based on an "adequate but not aggressive time frame" for generating revenue and the profit margin for Fuzeon will be significantly lower than for other ARVs.

We brought up our concern regarding the possible short life span for Fuzeon in the market, given that other oral entry inhibitors are being developed, and asked how that will impact the price. We speculated that Roche must be patenting every single step along the way and most likely has the market on polypeptides cornered. Reddy seemed to indicate that they are treating this whole line of R&D as one, so the profitability potential spreads into T-1249 and other compounds under development (possibly for other diseases such as Alzheimer's).

Without knowing the actual costs, it was hard to tell from this presentation what the final price will be. Roche seems to be signaling that they are not expecting Fuzeon to be an instant blockbuster, but the lengths they went to convince us of the high cost of bringing Fuzeon to market kept us guessing. At this point in the meeting they assured us that pricing discussions will continue and then herded us out of the meeting room and onto a tour of the plant (in hard hat and goggles). Half way through the tour, David Reddy apologized that he needed to catch a plane due to security concerns at Heathrow Airport. He did not get a chance to hear anything from the ADAP directors, and community members did not get to the meat of our arguments. **NOTE TO ACTIVISTS: NEXT TIME THE BIG MAN IS IN THE ROOM, GET RIGHT TO THE POINT!** They seem to have this habit of slipping out early. Kathy Presto promised to relay everything and Reddy said he will contact ADAP directors individually.

On to the tour: They showed us giant tanks that hold the raw materials and solvents used in production, different machines that do the assembly of amino acids, and a myriad of dryers and washers, all with little glass window you can look into and see churning whitish liquids and powders. It's a factory, unlike what I had imagined (pristine labs and glassed off walkways, robots and test tubes). The place smelled like a gas station, with water leaking from ceilings, and a little room with two computers and two workers overseeing the entire process. However, it was quite amazing to see the transition from funky Quicktime movies illustrating the

molecular mechanism of fusion to the large-scale production of tons of the drug.

After lunch, each ADAP director told those remaining about the crisis facing their programs. It's heart breaking to hear the frustration these guys feel in not being able to meet the needs of people they serve. It's one thing to see the numbers, quite another to get a view from inside the programs looking out and forward. Lanny Cross announced that most ADAP directors have gotten together (covering 80% of U. S. clients) and have sent a letter to all the drug companies requesting a meeting to discuss further lowering of prices. (Look for news about the ADAP Crisis Task Force and what you can do to help in the weeks ahead!) Roche seemed amenable to further pricing discussions, including possibly offering more discounts for ADAPs.

They also asked Roche to establish a medical criteria for access administered through the central distributor so they won't have to impose separate restrictions at the state level (those that can afford it) since, despite capping the number of slots, this will be the only way that Fuzeon can be covered. Roche's pharmacy distributor will contact each ADAP individually to set up delivery details. Roche said 65 percent of the first 15,000 slots available would go to the U.S., based on HIV prevalence. We told them that European countries are going to take at least a year for price negotiations, and most likely the drug will only be available there to private payers. This is perhaps one of the considerations for us stateside as we think about price control; European countries pay lower prices, but they also get the drug later.

With the Federal Budget allocating an \$80 million increase for ADAP, we are still \$140 million short for this fiscal year. Fuzeon will only come to most of those who need it at the cost of reduced formularies and stricter financial eligibility criteria. With a scary new Medicaid proposal coming out of the White House, most states will wait until the dust settles before committing to anything major. If the Bush proposals go through, optional services such as prescription drug coverage may no longer be required and states may drop them. Drug companies will no longer be able to count on the automatic coverage for over half of the domestic HIV market. This could have a huge impact on revenue and R&D investment in future therapies. The price of Fuzeon will be the first test of this new reality we live in. One hopes Roche will do the right thing. They've certainly been informed.

*Keep up with ADAP news at [www.atdn.org](http://www.atdn.org)*

**NOTE TO ACTIVISTS:  
NEXT TIME THE BIG  
MAN IS IN THE ROOM,  
GET RIGHT TO THE  
POINT!**

## Notes on HIV Drugs in Development

By Bob Huff

### Large Tipranavir Trials Open

Boehringer Ingelheim announced the start of two large Phase III trials of tipranavir, a new kind of protease inhibitor (PI) that binds to the enzyme in a different way than currently available PIs. The U.S. study, dubbed RESIST 1, is aimed at people who have developed resistance to existing protease inhibitors and is one leg of the largest clinical research program ever launched for this highly treatment-experienced population. In phenotypic assays and early clinical trials, Tipranavir has shown activity against HIV with multiple protease resistance mutations.

RESIST 1 will enroll more than 500 patients at more than 115 trial sites in the United States, Canada and Australia. A similar 800-person study, RESIST 2, will enroll in Europe and South America. Two companion trials (study 1182.51 and RESIST 3) will be available for individuals with extremely limited treatment options that do not meet entry criteria for the two main trials. Finally, a very small emergency access program should be available to supply drug to about 50 patients. Overall, the suite of tipranavir studies will involve about 1500 people worldwide.

RESIST participants will be randomized to receive either tipranavir (boosted with low-dose ritonavir) or an approved ritonavir-boosted PI selected by the individual's physician on the basis of treatment history and baseline resistance testing. Resistance testing will also be used to help determine an optimal individualized background regimen to backup the study drugs. Participants will be allowed to use certain currently experimental drugs such as T-20 (enfuvirtide, Fuzeon) and atazanavir. Eligible patients must have received at least two PI regimens prior to the study. Patients also must have received drugs from the NRTI and NNRTI classes, and must have at least one primary PI mutation prior to enrollment. There is no CD4 cell count criteria for entering the study but viral load at study entry must be over 1,000 copies/mL. U.S. trial sites for RESIST 1 can be located through: [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

### Informed Access

Community representatives met with T-20 makers Roche and Trimeris in New York in January to get a briefing on plans to distribute the

injectable fusion inhibitor as soon as it is approved (see *Boulder Blues* for an account of a meeting with state ADAP directors). Due to an initially limited supply and no reliable guess on how much demand there will be, Roche is setting up the framework for a system that would be able to fairly allocate supplies if required. They will contract with a third-party pharmacy service corporation that will deliver drug kits (either by mail or to selected pharmacies), staff a patient assistance hotline and handle prescriptions for patients unable to pay.

The patient support component of this system will be critical if patients are to have good outcomes when using T-20. It's becoming increasingly clear that T-20 is not an easy drug to take and the decision to begin enfuvirtide therapy should be made in consultation with a physician who has been trained in the correct preparation and administration techniques. Resistance to T-20 can develop fairly quickly if full doses are not taken on a consistent basis, so an individual's informed commitment to making the regimen work is a must.

If you believe you may be a candidate for T-20, be sure your doctor and his or her staff have received the training offered by Roche. It is especially important that Medicaid providers involved with HIV care receive training so that this large segment of the patient population has access to this potentially important new drug and can enjoy the best possible outcome from it.

Although no price has been announced for Fuzeon, it is expected to be a doozy. Roche has been spreading a PR cushion to soften the blow, but there are signs that initial projections of \$12,000 per year may be far too low. People with private insurance will be covered, as eventually will Medicaid recipients. But this leaves a large gap in the middle, especially if state ADAP programs decide they cannot afford to add this budget buster to their formularies. Roche has promised to make Fuzeon available to any who cannot afford it through a program administered by their third-party distributor. Details of the plan are yet to come. Expect approval by the end of March.

### Cool your Jets

T-1249, a follow-on compound to T-20 with activity against HIV resistant to T-20, is now apparently on a slow track. Two years ago Trimeris was saying that T-1249 was about two

**If you believe you may be a candidate for T-20, be sure your doctor and his staff have received the training offered by Roche.**

years behind T-20 in the pipeline. Now, the company says not to expect the next fusion inhibitor until 2008, putting it 5 years behind its sibling. It's not clear exactly why this is, although it's likely the company wants to see how T-20 pans out before they sink another \$500 million into developing a similar product. The manufacturing process for T-20 is famously difficult and expensive and there has been speculation that Roche may want to explore producing their next long peptide as a biologic product through gene expression instead of by the step-by-step assembly process currently in use. Another theory holds that the company would like to first perfect a pegylated form of T-1249 that would allow weekly injections rather than multiple daily shots. An effective pegylated T-20 would surely be welcomed by people currently taking the drug who have been bothered by painful or troublesome injection site reactions.

Another reason to speed T-1249 along emerged at the Retrovirus Conference where data was shown that indicated while people failing T-20 after one or two years of poking themselves responded to T-1249 during an 11-day activity study, only about half those failing with more than two years of T-20 above their beltlines responded. This may mean that if resistance mutations to T-20 continually accumulate and begin to affect T-1249's activity, then, for the first wave of those starting T-20 in the next few months, five years will be too long to wait. Step it up, kids.

### Longer Term Atazanavir Data

Bristol-Myers Squibb reported long-term efficacy and safety results on their experimental, once-a-day, protease inhibitor, atazanavir (ATV) during a poster session at the 10th Annual Retrovirus Conference held in Boston. The trial was a follow up study to an earlier Phase II trial that compared two doses of atazanavir with nelfinavir. Results from the previous study, BMS 008, established that atazanavir was able to produce viral suppression comparable to that of nelfinavir without raising blood levels of cholesterol and triglycerides.

The new trial, BMS 044, either continued patients at their originally assigned doses of atazanavir (400mg vs. 600mg, both once-daily) or switched those who had been receiving nelfinavir to atazanavir (400mg once-daily). All participants also continued stavudine (40mg twice-daily) and 3TC (150mg twice-daily).

Results were presented on virologic response, lipid levels and side effects with experience now out to 108 weeks of atazanavir use. Virologic response, defined as the proportion of subjects

having a viral load less than 400 copies/mL, was sustained in those originally assigned to atazanavir (80% on ATV 400mg and 82% on ATV 600mg). At 24 weeks following the switch from nelfinavir to atazanavir, 86 percent of those switched had a virologic response, up from 71 percent at study entry.

Lipid profiles remained unchanged among those continuing on atazanavir, but improved significantly in those originally assigned to receive nelfinavir. Patients switched experienced median reductions in total cholesterol from 202mg/dL to 169mg/dL; reduction in fasting LDL (bad cholesterol) from 132mg/dL to 99mg/dL and reduction in fasting triglycerides from 127mg/dL to 102mg/dL.

Adverse events were comparable among the study groups and the drug was generally well tolerated. Elevated unconjugated bilirubin was the most frequent laboratory abnormality and was associated with symptoms of jaundice and yellowing of the eyes in as many as 22 percent of patients. No association between elevated bilirubin and elevated hepatic transaminase levels was observed which supports descriptions of atazanavir-linked hyperbilirubemia as clinically benign. Bristol-Myers Squibb has filed for U.S. and European approval of atazanavir. (Abstract 555, 10th CROI)

# GMHC

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### ADAP Crisis Task Force Forms

A new ADAP Crisis Task Force composed of ADAP directors from key states has formed to respond to the shortfall in Federal funding for state ADAP programs. The eight manufacturers of antiretroviral drugs have been invited to meet individually with the Task Force to negotiate reductions in prices for all ADAPS.

The outcomes of these pricing negotiations are critical to the ability of ADAPs nationally to keep ADAPs open and provide access to medications required for quality HIV/AIDS healthcare. Individuals are urged to ask their doctors to communicate the importance of saving ADAP whenever speaking with drug company representatives.

# You Can't Always Get What You Want (And Sometimes You Can't Even Get What You Need)

By Gregg Gonsalves

Well, the President's budget for the coming fiscal year arrived on Capitol Hill at the beginning of February and except for an unexpected spasm of largesse for global AIDS efforts, the news looks bleak for domestic HIV programs, as well as Medicaid, which provides healthcare to thousands of people with HIV/AIDS.

While reports from the 10th Annual Retroviruses Conference in Boston warned that 25 states that track HIV

cases are reporting an increase in new diagnoses, the Bush Administration offers flat funding for the Centers for Disease Control and Prevention's domestic prevention programs. While scientists at the CDC have announced a goal of cutting new infections in half by 2005, they're getting no help from 1600 Pennsylvania Avenue, except cries of "Just Say No!" (to sex, to drugs, to condoms, to clean needles) from the arch-conservatives that seem to be dominating White House policy making in this area.

AIDS treatment activists have been pushing hard for additional funding for state AIDS Drug Assistance Programs, as thirteen ADAPs have already either limited access to antiretroviral treatments or closed enrollment to new clients. Let's pray that T-20, the new fusion inhibitor from Roche, doesn't break the ADAP bank when it receives FDA marketing approval and the price is announced, but don't count on states being able to afford it if you're an ADAP client with few therapeutic choices left. By the way, ADAP was the lucky sibling among the family of other Ryan White programs: the rest of them are looking at flat funding or even a slight decrease in funding.

Medicaid is the principal source of government funding for HIV/AIDS care and treatment in the United States, covering 40% of people with HIV and 55% of people with AIDS. While state Medicaid programs are reeling from the deepening recession and require immediate fiscal relief, the Administration isn't offering additional funding to states and, over time, is looking to cap the program. Capping Medicaid would severely diminish the program's capacity to respond to the HIV epidemic.

So, the future is grim for people with HIV/AIDS in the United States. While the President is practically rabid about involving the country in a multi-billion dollar assault on Iraq and cutting taxes for the wealthiest of Americans, he's hacking away at programs that serve the poor and the sick

and is racking up huge deficits that will curtail social spending for years to come. I exhorted TI readers to get involved in AIDS advocacy last month based on the fiasco that was 2002 for people with HIV living under Bush Jr. The coming year looks no better.

Last Saturday, I participated in a demonstration against the coming war in Iraq on a truly frigid day in New York City. I was joined by about 200,000 others from all over the Northeast. Perhaps, activism is coming back from the deep freeze and people are beginning to wake up to the insanity of what's happening around them.

The AIDS community slumbered through the late 1990s and the grassroots strength and policy expertise that it had built up over the previous decade-and-a-half has withered and disbursed. We need to rebuild our grassroots capacity by making a new commitment to community organizing within our diverse AIDS community and by building new partnerships with others working on behalf of the poor, the sick and disabled, and "vulnerable" populations, including prisoners, drug users and sex workers. We need to be able to rally thousands to action to undo the damage of the past three years and it's going to take a lot of time, effort and resources to do this.

We've also got to confront the "brain-drain" from AIDS policy work. While there are still some great people working on public policy in AIDS, we've lost far too many others to industry, consulting firms or academia. Recruiting new, smart and practical policy "wonks," while trying to re-engage the alumni who were responsible for many of the advances during the first two decades of the epidemic, needs to be another priority for us all.

Growing a stronger grassroots movement and public policy apparatus is a recipe for success—it's been used effectively by political parties to drive their agendas through Congress or their candidates into the White House.

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A copy of GMHC's latest financial report with the Department of State may be obtained by writing to NYS Department of State, Office of Charities Registration, Albany, NY 12231, or to GMHC.