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AIDS Treatment News

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AIDS Treatment News reports on experimental and standard treatments, especially those available now. We interview physicians, scientists, other health professionals, and persons with AIDS or HIV; we also collect information from meetings and conferences, medical journals, and computer databases. Long-term survivors have usually tried many different treatments, and found combinations that work for them. *AIDS Treatment News* does not recommend particular therapies, but seeks to increase the options available.

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2002 Overview: The Role of Activism

by John S. James

As we enter 2002 many lives are being lost in the U.S. and around the world because opportunities to save them are being neglected or squandered, often due to lack of followup. The system does not work by itself. Problems fester indefinitely unless advocates push for attention and solutions. New activism is now emerging. But we need to understand what creates opportunities for activists, and how the process can work better. This article will outline some AIDS treatment issues, to show people who want to help how to find more information, and to help them find people and organizations they can work with.

To get a better sense of what is happening, we watched the emails and papers crossing our desk this month. The issues are endless; this article cannot touch 10% of what is going on. We had to omit many areas -- including the biggest of all, Africa and the world, where the epidemic kills 8,000 people every day. The global pandemic and global response need separate articles, and cannot be summarized meaningfully. It is hard to report because of uncertainty on the most central issue: how much are countries and people, rich and poor alike, finding the will to deal seriously with the epidemic after two decades of neglect?

Heart Disease Prevention

Though it can take years for official statistics to become available, clearly we are hearing of more heart attacks and deaths among young people who would not previously have been considered at high risk. While some antiretroviral drugs contribute to risk factors, long-term prospective studies have shown increased risk and death from cardiovascular disease before the protease inhibitors and modern combination treatment became available.¹ We strongly suspect that antiretroviral treatment is increasing cardiovascular disease in two very different ways -- by side

effects of the drugs themselves, but also by keeping people alive longer so that have more chance to develop long-term effects of AIDS.

Much can be done:

* Cardiologists have found conditions that predict much greater risk of death in persons with HIV.¹ Often these can be treated.

* Cardiovascular risks are cumulative. Even when some are unavoidable due to HIV or the treatments currently available, others can be reduced by following standard guidelines published for the general population.

* Risk can be reduced by lifestyle changes such as better diets, exercise, quitting smoking, and probably by drinking a glass of red wine a day (for some patients).

* On diet, more evidence is showing that trans fatty acids (found in partially hydrogenated oils used in commercially baked goods and fast foods -- but also found in products from ruminant animals) seem to be associated with seriously increased risk of heart attacks.^{2,3} A recent *New York Times* editorial noted that the U.S. FDA "has estimated that honest disclosure of trans fats on package labels could prevent 2,100 to 5,000 deaths from heart disease each year" ("Foot-Dragging on Fat," *New York Times*, January 26, 2002). Apparently industry pressure has so far stopped the FDA from requiring this disclosure. The AIDS community can educate itself and others about this heart risk and how to avoid it.

* Nutritional approaches still considered experimental include measuring homocysteine in the blood and using certain supplements to help reduce it if necessary.

* When nutritional and lifestyle changes are not enough, prescription drugs are already used in HIV treatment to help control abnormal lipid levels or other metabolic changes that increase cardiovascular risk. These drugs are widely used in the general population. They can have side effects and should be closely monitored, especially for persons with HIV.

Almost certainly, cardiovascular illness and death of people with HIV could be significantly

reduced if everybody could see an HIV specialist, and when needed an HIV-knowledgeable cardiologist, with the different doctors able to work together, and with enough time to work with their patients. In practice almost nobody gets ideal medical care.

What activists can do is to help make sure that both standard, and credible experimental, medical information on reducing the risk become more widely available in the AIDS community. We need to pay more attention to this issue, and to the many lifestyle and medical options for dealing with it. We can educate ourselves, distribute information, and work to assure that HIV patients can see HIV specialists -- and cardiologists when necessary.

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Drug Interactions Need More Attention

New interactions involving antiretrovirals and other drugs often used by persons with HIV -- or interactions with nutritional supplements, like garlic or St. John's wort -- keep being discovered; clearly many others are unknown. Usually one drug (or supplement) either raises or lowers the blood level of another drug -- sometimes by several fold. Raised levels can result in serious side effects; lowered levels may cause the drug not to work as intended, or allow HIV to develop resistance. Sometimes it is possible to compensate

for these interactions by changing the dose of one or more drugs.

Since the list of known interactions keeps changing (several were reported at the recent ICAAC conference, for example), the best way to present the information is probably Web sites that allow anyone to type in a list of drugs they are taking or planning to take, and receive a report of any known interactions. There have been such sites for several years. As a community, we need to keep informed about what's best and most current, and encourage physicians and patients to check for known interactions when they change medications -- or if they use certain nutritional supplements.

More Uses for Tenofovir?

The recently approved antiretroviral tenofovir may be particularly important, because it appears to have fewer side effects than other antiretrovirals, and also less problem with resistance. It might be ideal for prevention of maternal transmission of HIV -- and possibly could be reformulated as an effective microbicide, allowing women to protect themselves from HIV infection without relying on men. But because tenofovir was first tested in treatment of advanced HIV disease, it seems to have been largely kept on the shelf for other uses, pending more data. Trials in first-line therapy are ongoing now.

We suspect this drug deserves more attention now, even before completion of the current trials (they will not answer all the questions anyway). It could be especially important as a starting point for developing low-side-effect treatments for patients who otherwise have poor options because of severe toxicities with other drugs. In the real world, we cannot answer every question with formal trials, so we should collect experience systematically to get the best information possible. We need to investigate: if reasonably effective antiretroviral regimens with less serious side effects are possible using the drugs now approved; if major resistance to tenofovir does develop, does the virus pay a price in ways that reduces its ability to cause disease; and even

whether it might make sense to use this drug alone for certain patients -- not as a good option, but possibly a better option than any other available to them.

We should also look into why this treatment was so much more effective as an antiviral in some animal trials with viruses related to HIV, than in human studies. Some of the animal tests found huge viral load reductions when the drug was used alone, compared to only about a 0.6 log reduction in patients. Could this difference have been due to the fact that the animal studies injected the active substance (PMPA), while humans use an oral prodrug (tenofovir) designed to be converted to PMPA by the body? Pharmaceutical companies have usually stayed away from any HIV drug that would have to be injected frequently. But if an injected drug had anywhere near the antiretroviral potency of PMPA in the animal trials, many people would very much want to use it. (A larger dose of the oral tenofovir is apparently not more effective, so the difference would not be just from the dose.)

New Kinds of Treatment

Everyone knows that patients urgently need new kinds of treatments (as well as better drugs in existing classes, mainly antiretrovirals). But it has always been hard to get new ideas developed. Almost by definition a new idea has not made money before, so the money people are not interested. Developing new drugs and new classes of drugs is expensive, due to the need to protect public health -- and because the system also reflects the need of large companies to monopolize the market and keep out small competitors.

Some of the lesser-known possibilities we intend to look at in 2002 include:

Topoisomerase inhibitors. In 1994 *AIDS Treatment News* reported on a class of drugs being developed for cancer, but not for HIV, though some experts believed they should be tested as antiretrovirals (see Topotecan, CPT-11 (Irinotecan), Camptothecin, and Other Topoisomerase I Inhibitors, *AIDS Treatment News*

#197, April 15, 1994). Recently treatment activist Eric Goldman followed up and found that patent and policy snafus have apparently prevented these drugs from being tested and developed for HIV.

There seems to be a pervasive gap in drug development, where no one gets the first human data from a handful of patients (or even from one person). Government saves money by giving exclusive licenses to promising compounds tested in the laboratory -- but usually industry will not invest in human testing unless human proof of principle already exists. This appears to be a general problem that may have prevented many valuable treatments for AIDS and other conditions from ever coming into use.

In the specific case of topoisomerase inhibitors, some of these drugs have already been approved for cancer. Therefore it should be possible to watch viral load in persons treated for cancer who also have HIV. If there is substantial antiretroviral activity, it should be possible to restart the research that has been neglected for years.

Eric Goldman is preparing a comprehensive article on his investigation into why topoisomerase inhibitors were not researched for HIV; at this time (January 2002) only two short articles are available. The following are similar but not identical:

<http://www.thebody.com/sfac/topotecan.html>

<http://www.searchforacure.org/hope/article.asp?sty=16>

Murabutide. This immune-based treatment, being developed in France, may strengthen the innate immune response -- which may also create conditions helpful for HIV-specific immunity.

Prostratin. This drug, from a tree in Samoa, may drive latent HIV out of hiding so that it can be targeted by other drugs or by the immune system.

Low-dose naltrexone. This potential treatment has been available for many years (*AIDS Treatment News* reported on it almost 15 years ago) but has not attracted much attention. We are looking at it now because of favorable anecdotal reports -- and also because there is little downside to using it. For the case in favor, see:

<http://www.lowdosenaltrexone.org>.

Legal/Medical Issues

We asked Ronda Goldfein and Yolanda Lollis of the AIDS Law Project of Pennsylvania where activism could be most useful for their clients, both at the Federal and at state and local levels. They suggested the following. We added some comments in parentheses:

* Social Security disability determination for HIV. Today the side effects of antiretrovirals and other medications are not recognized as disabling conditions, however disabling they may actually be. Also, diabetes and hypertension need to be in the HIV listing as conditions that can cause disability.

* ADAP (AIDS Drug Assistance Program) formularies. Some do not include diabetes and hypertension medications.

* Prescription coverage for Medicare. This is a major national issue where the AIDS community needs to be heard. A great many clients of the AIDS Law Project are seriously affected (the drugs they need can cost \$10,000 per year or more). They say, "I worked my whole life, and now I'm on disability and cannot get my drugs covered?"

* Syringe exchange. [We will look at this in a separate article.]

* Medicaid reimbursement. Payments to doctors are often completely inadequate, making it hard to find physicians who will take Medicaid patients, because they lose money treating them.

* Names reporting. Many people are uneasy about appearing on a government list of people with HIV, and as a result they avoid getting tested if their names must be reported. Unique-identifier systems avoid this problem, but are slightly more expensive to implement.

* Dental discrimination. In many places it is very hard to find a dentist who will treat anyone with HIV.

* Nursing homes. Many do not want to take people with HIV. When a nursing home is needed it is for a medical emergency, so patients, their families, and supporters are not in a good position

to fight. And as people with AIDS live longer, they will need nursing home care for the usual problems of aging. (Providing good HIV-related care will be a medical challenge as well as a discrimination issue. But limiting people to HIV-specialty nursing homes would require most to be far from their friends and families. Perhaps communication technology such as computer conferencing, along with traveling HIV-specialist physicians, could enable more nursing homes to deliver routine HIV care at least.)

* Other HIV discrimination. Cases handled by the AIDS Law Project are "as varied as life itself."

Note: If you need assistance with an AIDS-related legal issue you may be able to get help from an AIDS legal services organization near you. To find out if there is one in your area, check The Directory of Legal Resources for People with AIDS and HIV, by the American Bar Association AIDS Coordination Project, phone 202-662-1025, or go to:

<http://www.abanet.org/irm/aidsproject/publications/aids-dir.html>

Drug Pricing

Recently some pharmaceutical companies have imposed substantial, unexpected price increases for HIV drugs. These increases mean that more people will not get necessary treatment, since ADAP and other public program budgets have already been set, and these programs are already denying drugs through waiting lists because of lack of money.

Apparently the reason for the price increases is to keep corporate profits up despite the weaker economy and other pressures on pharmaceutical company revenue, especially the resistance to high prices by HMOs and other third-party payers. These increases come at a time of great financial pressures on ADAP, Medicaid, and other government programs, due especially to the financial problems of state governments -- as well as continuing increases in the cost of private health insurance. And these price increases come after the budgets of ADAP and other programs

have already been set. With drugs costing more when less money is available, thousands of people will not get the care they need. (Patient Assistance Programs, run by pharmaceutical companies, provide free drug to some patients with no other way to pay. But these programs are designed to work poorly, as the paperwork stops many if not most who could qualify from applying. Basically those with enough social support to cause a public issue if they die for lack of the drugs can probably get them. Most others probably cannot.)

In U.S. medicine the financing system does not work, and big institutions are best able to take care of themselves -- dumping the costs of a failed system onto persons with major illnesses, who are least able to pay. We need to work for comprehensive reform -- and meanwhile be sure that communities are organized so that patients' interests will at least be represented, along with those of big pharma, big insurance, and big government.

We will keep our readers informed as we learn more about new price increases and their consequences.

Improving Activism

AIDS activists continue to be highly effective. But there are not enough people to do the work that needs to be done. Perhaps the most important challenge to AIDS treatment activists today is making it easier for new people to become involved.

Historically, most ACT UP chapters and other treatment activist organizations had no training program to help with the steep learning curve (on treatment information, on learning how to deal with pharmaceutical, government, and other officials, on working with press and the media, and on working with allies and within the organization itself). This is changing; for example, the new national organization ATAC (AIDS Treatment Activist Coalition) is intensely interested in training and mentoring new activists. For more information, see: <http://www.atac-usa.org>.

Often treatment activists are so involved in the issues that there is little thought to maintenance of the organization -- for example, little outreach to explain to the community what they are doing and why, and to let people know what assistance they need. Several years ago ACT UP Golden Gate (now Survive AIDS) solved several of these problems by getting a weekly column on AIDS treatment in the *Bay Area Reporter*, a San Francisco gay newspaper. The columns were written by a "writers pool" of five or six members, and most had an action-alert box in addition. It took considerable work from a coordinator to make sure that a volunteer finished an article every week.

ACT UP Philadelphia successfully reaches across race and class barriers, and as a result is probably the largest ACT UP chapter in the world. It can get hundreds of people to demonstrations even outside the city, in Washington or New York. Project TEACH, an excellent education program of Philadelphia FIGHT, has trained hundreds of peer educators in treatment and activism.

A widespread problem retaining people is that AIDS activists have traditionally been too harsh with each other, apparently more so than in most social movements. Most of the disputes have been due to personality differences, accidents, misunderstandings, or escalating "flame wars" where each tries to outdo the other with insults -- rather than substantive disagreements. People needed to give each other more slack, and that is happening now. Everyone knows there is more than enough work to go around, and that nobody can be sure they are right.

If we may mention our own work in conflict prevention, we have developed a kind of education designed to take place in the interaction rituals of everyday life -- not in special classes or settings. The idea is to design "practices" (self-training exercises completely integrated with whatever we are doing anyway) for using routine errands and other throwaway moments to build skills for better communication, personal interaction, and relationship development. For more information, see:
<http://www.communicationpractices.org>.

Improving Fundraising

The fundraising process needs more attention now, due to a weaker economy, less government revenue, and a global war that may last for decades. The AIDS community will need to be more efficient in delivering services and advocacy, and in finding money for them.

In the U.S., individual donors give far more money to philanthropy than foundations and corporations put together. Most of the individual donations are to religious organizations. Church members usually have personal experience with the church they are giving to. But in AIDS, donations often go by default to a few big organizations with high-profile names, from donors who know little about their services. And much effort and expense goes into events like walks, rides, and other emotional experiences for donors -- an activity requiring very different skills from effective service delivery. Only large organizations can afford professional development departments -- and only a few can be largely successful year after year at two entirely different missions simultaneously (with the fundraising mission directly determining organizational survival, while the official mission does not). It is said that one can't dance at two weddings with one tush. But that is what we expect almost every service organization to do.

No wonder so many groups need technical help with fundraising.

Besides more technical help, we would like to see more focus on educating and involving donors in what is actually going on (in addition to seeking money through name recognition, or by producing donor events and experiences having little to do with the service or advocacy mission). We reluctantly believe that all these approaches are inevitable. Modern society has thousands of different worlds, and most people live in only a few of them. Those who do not need services are unlikely to understand them. Those who do are unlikely to have much money to donate. This disconnect makes it hard to raise money, and to deliver services well. But until there is a deeper commitment to making the world work, it may be the best we can do.

Funding Medical Research and Drug Development

For improving medical research, the place to start is to ask researchers what problems they face when they are trying to get important work done. Remember that often they cannot be activists or try to improve the system, because they must protect relationships with those who control their resources. Someone else must do the reform.

One of the greatest problems holding up medical research and development is the difficulty of getting the first human experience with promising new ideas. What usually happens is that academic researchers develop potential treatment approaches, often with Federal funding. They publish one or more papers in scientific journals. Then progress stops, because no one does the first test in a human being. Government usually avoids practical drug development, leaving that to industry -- but industry seldom picks up development unless it already has human proof of principle. Potentially lifesaving treatments can sit on the shelf indefinitely, and no one pays attention.

Possibly medical research needs a role like that of a producer -- one who handles the business of getting a project done, but in this case for cures for diseases, instead of for movies or plays. AIDS activists have sometimes stepped into that role when necessary. A notable example was the late Bill Thorne of ACT UP Golden Gate, who was largely responsible for the completion of a pivotal clinical trial that had stalled, and for FDA approval of human growth hormone for AIDS-related wasting. Everybody involved knew that he was the key person in making it happen. (His work was entirely volunteer; others made the money from the grossly overpriced drug.)

In vaccines, IAVI (the International AIDS Vaccine Initiative) has taken on the role of making projects happen. In cancer, the U.S. National Cancer Institute has long studied early clinical use of new agents. But much of medical research today is like an entertainment industry without producers, where the artists themselves must do all that work, or no one will.

Diet and Inflammation? (Personal Note)

by John S. James

In November 2000, *AIDS Treatment News* published an interview with Lynde Francis, who runs The Centre, an AIDS treatment organization in Harare, Zimbabwe. Because her clients had no access to antiretrovirals, she had to do what could be done with nutrition and lifestyle changes. Part of the recommendation was to eat a traditional diet, avoiding modern "junk foods."

I couldn't see how this could make a difference in HIV disease. But later I tried such a diet for a different problem, a severe wrist pain -- after a "junk food" dinner repeatedly seemed to make the problem worse the next day. For me the diet appeared close to 100% effective. My wrist had become steadily worse for several months; it was better after a few days on the diet. The problem was essentially gone in a few weeks, and has not returned in over a year since.

I coined the name "The Century Diet" as a personal reminder. The only rule is, "Don't eat anything that wasn't available 100 years ago."

My experience and other information suggests that something in the modern diet (possibly trans fatty acids?) can interfere with the body's ability to handle inflammation properly. If so, this process could be contributing to widespread health problems, including repetitive stress injury, cardiovascular disease, and perhaps some complications of HIV. Research could find the culprit(s) fairly easily, by clinical testing with a few volunteers who are close to the borderline between having symptoms or not. Diets and meals could be "fractionated" -- successively divided and tested to see which ingredient causes the symptom -- somewhat like medicinal plant products are fractionated chemically to find an active ingredient.

Since this issue is mostly outside the focus of *AIDS Treatment News*, we set up an email list where anyone interested can continue the discussion. For more information, see: <http://groups.yahoo.com/group/centurydiet>.