GMHC GAY MEN'S HEALTH CRISIS
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ADAP Emergency!

By the Save ADAP Committee
AIDS Treatment Activists Coaliton (ATAC)

The AIDS Drug Assistance Program (ADAP) is a federally funded program intended to provide access to HIV/AIDS treatments for low-income people who are uninsured or lack adequate prescription drug coverage. The program is administered by the states and, in some cases, additional state funding augments basic drug coverage. Because the extent of coverage offered is left to the states to determine, various programs may differ considerably in the number of drugs on the formulary, ancillary services covered, and in financial and clinical eligibility criteria.

An estimated 85,000 people are currently turning to ADAP for their HIV medications. ADAPs serve a very diverse population of people living with HIV. Almost 80% of ADAP clients have incomes at or below two-times the Federal poverty level (which only comes to about $18,000 per year for a person living alone). The majority of ADAP clients are people of color with African Americans making up about one-third, and Hispanics about one-quarter of ADAP clients. There has been a 10 percent increase in the number of clients served during the past year and similar increases are expected in the years to come.

ADAPs across the country are experiencing severe financial crisis, resulting in limits to treatment access.

Nationally, ADAP is facing a current budget shortfall of $82 million. The shortfall is largely a result of several consecutive years of under-funding compounded by increasing demand and escalating drug prices. Many state ADAPs across the country are experiencing severe financial crisis, resulting in limits to treatment access. Recently, several states have reported turning to some kind of restrictive measure such as waiting lists. These include Alabama, Georgia, Idaho, Kentucky, Maine, North Carolina, Oregon, South Dakota, Texas, Washington, Wyoming and Guam. There are over 600 people on the waiting list for antiretroviral treatment in North Carolina alone, with an estimated 1000 people on waiting lists nationwide. In addition to waiting lists, some states have capped enrollment or have placed limits on the number of prescriptions a client may fill each month. Other states, including Mississippi and New York, are reporting that they may be forced to implement restrictions soon.

If the current fiscal crisis continues, states may seek to control costs in ways that threaten the health of both the program and the thousands of Americans who rely on it. For example, some states have delayed adding pegylated interferon, an important new drug for hepatitis C treatment, to their formularies. The expected approval next year of T-20, a new class of HIV inhibitor likely to be of importance to people with multiple drug resistance, will further stretch

ADAP budgets. Some ADAP medical advisory boards are evaluating dropping certain medications currently provided in order to further reduce costs. Some states may also be considering requiring co-pays or medical pre-authorization plans. These measures could put ADAP services completely out of reach of its most vulnerable clients and create additional barriers to access for many others.

What is Driving the ADAP Crisis?

• Inadequate federal funding. ADAP has not received adequate funding increases from Congress the past few years. While ADAP appropriations increased by 12 percent from 2000 to 2001, the number of clients increased by 10 percent and the cost of drugs increased by 16 percent during the same period. ADAPs cannot keep pace with rising costs and service demands at the current funding level.

Congress must appropriate an increase of $162 million in federal funding for ADAP for Fiscal Year 2003.

• Inadequate state funding. Sixteen states do not contribute at all to ADAP and others provide inadequate contributions. Continued weakness in the national economy suggests that additional funding from states that have had more generous programs may be frozen or even scaled back.

• Increases in drug prices. Monthly drug expenditures by ADAPs rose by 320 percent from 1996 to 2001. Some of this was due to adding additional drugs to formularies, but much of the increase reflects steeper purchase prices. Several drug companies introduced sharp price hikes at the beginning of 2002, although some have since announced that they will freeze prices for one or two years for ADAP programs.

• Increase in outreach and testing programs across the country. The Ryan White CARE Act reauthorization of 2000 provided for increased outreach and testing programs with the goal of helping to identify new HIV infections earlier and facilitate entry into care. The success of these efforts has translated into increased client caseloads that current levels of ADAP funding cannot meet.

• Increase in the number of people testing positive for HIV and seeking ADAP services. New infections continue to occur at a rate of approximately 40,000 per year in the U.S. Easier testing methods and more widely available testing has increased the number of people learning their HIV status, and better service coordination now ensures that more people are being directed into the care system offered by ADAP. Furthermore, people now remain in the program longer because they are staying healthy and living longer due to the drugs.

What Must be Done to End the Crisis?

Congress must appropriate an increase of $162 million in federal funding for ADAP for fiscal year 2003 (October 1, 2002 to September 30, 2003). This figure includes the current $82 million shortfall plus an $80 million increase needed in the next fiscal year to provide adequate financial relief to ADAP.

The President's goal, as articulated in his FY2003 budget, of reducing the number of new HIV infections by 50 percent by 2005, cannot be achieved without a sufficient funding commitment on the part of the federal government. There is a direct fiscal and epidemiological relationship between testing, surveillance, care and treatment, individual longevity, and reduction in new infections. The national response to AIDS carried out through the various federal agencies is a linked strategy. Shortfalls in one program area inherently impact capacity and success in other program areas.

Although funding for the CARE Act has grown over the past ten years, federal and state funding have not kept up with growing demand for services. The states' Ryan White care and treatment programs are safety net programs. They are the payer of last resort and provide services to those most in need. Without an increase of, at minimum, $162 million in FY2003, states will be unable to maintain their existing programs, much less enroll new clients.

The New York ADAP Crisis

New York State is facing a $16 million shortfall in the current fiscal year due to inadequate increases in the Federal ADAP appropriation in the Ryan White CARE Act. This means that the projected expenditures for the year exceed the annual money promised by Congress, and even by using savings or redirected funds from other state sources to temporarily bridge the gap, restrictions on access to essential AIDS/HIV drugs and services are looming.

NY ADAP continues to grow at a consistent rate of more than $20 million a year, due to increasing enrollment (caused by new infections and people living longer), increasing utilization of drugs and services (to treat and monitor HIV disease and the side effects of medications) and ever-increasing drug prices.

NY ADAP has had a moratorium on new drugs and services since November 2000 in anticipation of this pending crisis and has taken measures to slow growth and accumulate savings that can be used as a short-term stopgap. However this moratorium has prevented the program from offering coverage for the new

standard of care for hepatitis C infection, pegylated interferon plus ribaviran.

The moratorium may become critical next year if ADAP is unable to cover the important new antiretroviral drug T-20, expected to receive FDA approval early in 2003. A preliminary estimate puts the cost of adding T-20 to the NY ADAP formulary at about $12 million the first year. All of these factors add up to an additional $48 million needed for New York's fiscal year 2003.

NY ADAP is redirecting funds from other HIV programs to close the budget gap this year, and has requested increased funding from the Title I HIV Planning Councils of New York City, Lower Hudson, Long Island and Dutchess County. This approach is undermining the HIV/AIDS infrastructure by drawing funds away from other necessary support services that persons living with HIV/AIDS need to be able to enter into care and treatment.

NY's ADAP budget gap threatens significant reductions in services for 2003. The specific reductions will be identified through a prioritization process that has already begun. These cost saving measures represent the deterioration of a health care infrastructure that has taken years to build, and erects additional barriers to care for some of the state's most vulnerable citizens with HIV/AIDS.

Possible cutbacks could include:

- Removing categories of drugs or services covered, such as lipid-lowering drugs or antidepressants.
- Mandatory dispensing of generic equivalents.
- Establishing a restricted formulary of preferred drugs.
- Expanding prior authorization plans that require approval before a drug can be dispensed.
- Cutting back of payments to pharmacies and clinics.
- Requiring co-payments from clients to obtain drugs.
- Tightening medical or financial criteria for obtaining services.
- Establishing waiting lists or capping the number of clients in the program.

ADAP was designed to fill the gap between people who qualify for Medicaid and those who can afford private insurance. This gap is widening. In New York, the majority of ADAP clients make less than 200 percent of the Federal poverty level—the group of people most affected during an economic downturn. Since we have not experienced this kind of economic climate since ADAP was first created, it remains to be seen if the steady trend of increasing enrollment will remain the same or spike sharply up as the crisis deepens.

Call Congress and The White House

Call your U.S. Representative and two U.S. Senators' offices in D.C. as soon as possible. You can call the Capitol switchboard-toll-free: 1-800-648-3516. You will need to know the name of your Representative or Senators in advance. Ask to be connected to their office. If the toll-free number is continuously busy, you can call the regular number at (202) 224-3121.

If you need help identifying your elected officials, you can call Project Vote Smart at 1-888-868-3762 or check out their website, www.vote-smart.org.

Identify yourself as a constituent. Tell whoever answers the phone that you are calling to urge the Representative or Senator to take a leadership role in advocating for a $162 million increase for the AIDS Drug Assistance Program.

Sample message for Congress:

"I am a constituent of Representative/Senator _____. I am calling to urge him/her to do everything in his/her power to get a $162 million increase for the AIDS Drug Assistance Program in the Fiscal Year 2003 appropriations bill. This program provides treatment for people with HIV/AIDS who otherwise wouldn't be able to afford it. I also urge the Representative/Senator to support the highest possible funding for all other HIV/AIDS programs."

Please also call the White House comment line. Ask the President to demonstrate leadership on this issue by letting Congress know that he supports a $162 million increase for ADAP. Call the White House comment line at (202) 456-1111.

Sample message for White House:

"My name is _____ and I live in _____ (state). I am very concerned that President Bush has not supported an increase for the AIDS Drug Assistance Program in his last two budgets. This program is in a fiscal crisis and many people around the country are on waiting lists for treatment. I urge the President to take a leadership role by urging Congress to support a $162 million increase for the AIDS Drug Assistance Program and the highest possible funding for all HIV/AIDS programs."

Sexual Transmission of Hepatitis C

by Edwin J Bernard

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For subscription information: atu@nam.org.uk or visit www.aidsmap.com

Coinfection with HIV and the hepatitis C virus (HCV) has increased in the past few years. Until very recently, the major risk factors for acquiring HCV were thought to be injection drug use (IDU), haemophilia and blood transfusion; sexual transmission was considered to be theoretical but insignificant.

Now, however, there is new evidence that sexual transmission of HCV is on the rise, particularly amongst gay men with HIV. Recent studies suggest that not only is sexual transmission of HCV possible, but that being infected with HIV, and/or having certain kinds of sex, are major risk factors for transmission of the virus.

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In June 2002, the U.S. government's National Institutes of Health issued a consensus statement by an independent panel of clinicians, researchers and community groups with expert knowledge of HCV. For the first time, they added sexual transmission to the list of exposure risks for HCV. Although they continued to say that the risk was extremely low for heterosexual monogamous couples, they added that "HCV-infected individuals with multiple sexual partners or in short-term relationships should be advised to use condoms to prevent transmission of HCV and other sexually transmitted diseases[1]."

Last month the UK Department of Health issued their Hepatitis C Strategy for England. The approach of the DoH is similar to that of their US equivalent. "There is evidence that both homosexual and heterosexual transmission of hepatitis C may occasionally occur," the report states, before offering the somewhat contradictory advice to people with HCV to discuss the use of condoms with regular partners and practice safer sex with new partners.

Two large HIV clinics in London have seen an increase in new HCV infections over the past six months, causing concern that the risks of sexual transmission for gay men with HIV in particular have been underplayed. Is it possible that just like the delay that occurred over public health messages about the current syphilis outbreak amongst gay men, not enough people are taking the sexual HCV threat seriously? "I hope it isn't going to take us two years to realise that yes, it's here, and it's being sexually transmitted," says Dr. Sanjay Bhagani, specialist registrar in infectious diseases and HIV at London's Royal Free Hospital.

Early evidence on HCV transmission

HCV was first identified in 1989 and although studies as far back as 1993 pointed to sexual transmission as a probable risk factor amongst gay men, the information did not translate into a public health message. This is likely because many more studies showed that the risk of sexual transmission was seen to be extremely low in the general population, and there may also have been an assumption that safer sex messages relating to HIV would also implicitly cover HCV transmission.

In these earlier studies, published between 1993-1996, data on three different cohorts of gay men without a history of IDU in the U.S. showed that between 3-5 percent were infected with HCV. Osmond found that HCV infection was marginally associated with more than 50 sex partners a year; or more than 25 oral receptive partners; or more than 25 anal receptive partners[2]. Buchbinder found that sexual risk factors for HCV infection included receptive anal intercourse, fisting, having a sexual partner with a history of IDU, a self-reported history of genital herpes and being HIV-positive[3]. Ndimbie found that whilst the number of sexual partners was not a significant risk factor, a history of syphilis, rectal gonorrhoea, insertive anal intercourse with ejaculation, and douche or enema use before anal receptive intercourse were statistically significant sexual risk factors[4].

When Rooney[5] undertook a 1998 review of the literature into sexual transmission of HCV amongst the general population, he concluded that there was "a small but definite risk of sexual transmission of hepatitis C" of between 1-3 percent. Rooney did not look at the difference between heterosexual and gay sex transmission risks, however.

Since 1998, there have been many studies looking for a heterosexual transmission risk of HCV in monogamous couples that have found there is little to none. For example, Sciacca's Turin Study found that only three out of 196 long-term heterosexual spouses were infected with the same HCV viral genotype, and concluded that while sexual transmission of HCV was a possibility, "this method of transmission

does not appear to be important if compared with that of other viruses (hepatitis B virus and HIV)[6]." Similar conclusions were drawn by Garcia[7] at the recent International AIDS Conference in Barcelona.

However, not all heterosexual transmission studies have come to the same conclusion, particularly those that include casual partners. Tenegan looked at the sexual partners of HCV-positive blood donors in Brazil from January 1992 to July 1996 and found that 11.76 percent were HCV-positive. Sexually transmitted infections (STIs) were found to be more prevalent among partners with HCV infection, suggesting that the high prevalence of HCV infection seen here may be attributed at least partially to sexual transmission because they put themselves at risk of other STIs.

HCV, HIV and Sex

Though it has been suspected since 1994 that coinfection with HIV/HCV contributed to a higher risk of HCV transmission than being singularly infected with HCV (since HCV viral load was shown to be significantly higher in those coinfected with HIV/HCV[8]), it was only towards the end of last year that a study confirmed that HIV/HCV coinfection magnified the risk of sexual transmission of HCV to both heterosexuals and gay men.

Researchers from Naples found that HCV infection was almost three times higher in those who were HIV-positive compared to HIV-negative controls (15.1% versus 5.2%). Significantly, 18.7 percent of those who had regular heterosexual or gay sex with an HIV-positive partner were HCV-positive, compared with only 1.6 percent for partners of HIV-negative controls. The authors concluded therefore, that "in subjects who had only a sexual risk factor for parenterally transmitted infections, HIV may enhance the sexual transmission of HCV[9]."

At the same time, another study found that HIV, certain sexual acts, and multiple sexual partners, correlated with a higher risk of sexually transmitted HCV amongst gay men. Here, 662 HIV-positive and HIV-negative men in the Vancouver Lymphadenopathy Cohort were investigated for HCV. Nearly 9 percent of HIV-positive men were HCV-positive compared with 2.6 percent of the HIV-negative men. Almost half (49%) of HCV-positive men reported never injecting drugs. The HCV-positive men were more likely to report the following: more than 20 sexual partners in the last year; more than 100 lifetime partners; practicing insertive fisting; practicing receptive anal sex, and practicing insertive oral-anal sex (rimming). A comparison of the non-IDU HCV-positive group with the non-IDU HCV-negative group found insertive rimming and insertive fisting associated with HCV infection. Multivariate analysis showed three factors independently associated with HCV infection: injecting drug use; HIV infection and more than 20 male partners in the last year[10].

Three further studies confirming HIV as a cofactor for sexual HCV infection were reported at the recent International AIDS Conference in Barcelona. Risbud from India found that HIV infection was independently associated with more than a three-fold increased likelihood of HCV infection amongst STI clinic attendees[11]. Mendes-Correa from Brazil found that independent risk factors of HIV/HCV co-infection amongst male and female AIDS outpatient clinic attendees were (highest risk first): injecting drug use; a sexual partner with past history of chronic hepatic disease; a sexual partner who had received a transfusion; age above 30; anal intercourse; use of inhaled illicit drugs; and a history of an IDU sexual partner[12]. Finally, Abresica from Italy found that 20 percent of women who had been infected with HIV by HIV/HCV coinfected partners were also infected with HCV, leading the co-authors to conclude: "It's probable that HIV and its related opportunistic infections of the female genital tract could strongly facilitate HCV sexual transmission"[13].

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Increasing UK Cases

Mark Nelson, consultant in HIV at the Chelsea & Westminster Hospital, London, has been convinced for a long time that HCV is sexually transmitted. "What we've seen recently is an outbreak of syphilis (amongst gay men)," says Dr. Nelson, who also runs the HIV/HCV coinfection clinic, "and with the outbreak, what we've noted in the HIV clinic are small but increasing numbers of people seroconverting for HCV. Approximately a quarter of those have picked up syphilis at the same time, suggesting that HCV is sexually transmitted."

Dr. Sanjay Bhagani has been running the Royal Free's HIV/HCV coinfection clinic since last October. "In the last six months we have picked up six patients who have seroconverted for HCV," he says. "We've been through all of them with a fine tooth comb in terms of risk factors and it seems that they have none of the other risk factors for HCV transmission," leading him to conclude that sexual transmission was the most likely route. "Two have an HCV-positive partner, and one had a gonorrhea coinfection," he adds, "leaving me in no doubt that these were due to sexual transmission."

Both clinics only found these new HCV infections because of abnormal liver function tests (LFTs) since most acute HCV infections are clinically asymptomatic. "If we weren't doing the LFTs we wouldn't pick up (the acute infections)," says Dr. Nelson. This is because although most HIV clinics test for HCV during intake, regular screening is not commonplace. "Part of the problem is, once you've been tested you tend not to test again, so we're now promoting yearly testing for HCV," he adds.

"At the Royal Free we screen first for antibodies and do LFTs," says Dr. Bhagani. "If you have persistently abnormal LFTs, you're antibody-negative for HCV, and your index of suspicion is high, we do an HCV PCR [viral load test]."

Recent studies have confirmed the link between HIV/HCV coinfection and accelerated progression to fibrosis, cirrhosis, liver cancer and liver failure.

The most common way to measure HCV infection is the ELISA-2 anti-HCV (antibody) test. However, HIV infection can make the diagnosis of HCV more difficult since in a small minority, HCV infection may not show up on antibody tests in HIV-infected people. Last year, Bonacini found that 5.5 percent of people with HIV tested negative for HCV antibodies but were positive on the Amplicor™ PCR test for HCV viral load[14].

Dr. Nelson estimates that around seven percent of HIV-positive patients at Chelsea & Westminster are coinfected with HCV. "A lot of them have none of the major risk factors of IDU or blood transfusion," he says. "Clearly a lot of people have tattoos, so you can't say it didn't come from tattooing, but when we screened individuals in the GU clinic, a history of tattooing was not a significant risk factor for HCV. And of course you can't exclude toothbrushes and razors. But I think the majority is sexually transmitted."

"There is a strong biological probability as to why coinfected men should be at higher risk of transmitting HCV," continues Dr. Bhagani. "If you look at the HCV viral loads in people who are coinfected with HIV, as compared to singularly infected HCV patients, they are much, much higher. And the higher the viral load, the higher the risk of transmission."

The jury is still out, however, on the actual mechanism of HCV infection during sex. Nelson points to a recent study that found that the higher the HCV viral load, the higher the level of HCV in saliva[15]," although we don't really know what that means," he admits. Many of the studies reviewed here point to fisting, rimming, and unprotected anal intercourse as being associated with a greater risk, leading Dr. Bhagani to speculate that "practices that involve blood may be more high risk."

Safer Sex, Screening, Treatment

Drs. Nelson and Bhagani both believe that people with HIV can best protect themselves from acquiring HCV sexually by continuing to practice protected anal intercourse, rimming and fisting. "Like everything, you're better off not getting it, and since there is no vaccine available, taking precautions is the only way," says Dr. Nelson.

They also strongly suggest that yearly screening for HCV should become the norm in all U.K. HIV clinics. "The first thing we really need to know in this country is what is the true prevalence of HCV in the HIV population," continues Dr. Nelson. "It is clearly something that people who have got HIV have put themselves at risk of. We need to make sure that everyone is screened for HCV. The advantage of picking it up early means you are much more likely to eradicate it."

Although similar evidence is lacking in those who are HIV/HCV coinfected, last year, Jaeckel showed that HCV can be eradicated in HIV-negative people during acute HCV infection after 24 weeks treatment with interferon alpha. The average time from infection until the start of therapy was 89 days, suggesting that screening every three to six months might be optimum for those who believe they are at the greatest risk of acquiring HCV sexually. In this trial, at the end of both therapy and follow-up, 98 percent had undetectable levels of HCV and normal LFTs[16]. "The data for treating acute HCV from the Jaeckel paper is using just interferon alone," says Dr. Bhagani. "At the Royal Free we use pegylated interferon and ribavirin since we feel we should be giving these people the best standard of care that we can."

Eradicating HCV during the acute stage "may be very important when you look at the data on HIV/HCV coinfection and higher rates of progression to end-stage liver disease," concurs Dr. Nelson. Many recent studies have confirmed the link between HIV/HCV coinfection and accelerated progression to fibrosis, cirrhosis, liver cancer and liver failure (including those by Martin-Carbonero[17], Bica[18], Monga[19], Hatzakis[20], Soto[21] and Garcia-Samaniego[22]). "Before HAART, everyone was saying you're going to die of your HIV, don't worry about your hepatitis C," continues Dr. Nelson. "Now suddenly people are living, and hepatitis is a major cause of morbidity and death in many people with HIV worldwide. It's something that

we can't ignore anymore, and it's something that we've got to be much more proactive about."

Take Home Messages

"I think the take home messages are that HCV is sexually transmissible amongst gay men and it may be more so than with heterosexual transmission," concludes Dr. Bhagani. "So gay men and people with HIV should always practice safer sex. In coinfected patients, HCV is a particular concern because of the propensity for faster progression to end-stage liver disease and complications with drug-related toxicity. We know from singularly infected patients that HCV is potentially curable if caught early. And so we should be making an effort to try and detect and treat early HCV seroconversion."

References

Except where stated, references are from XIV InternationalAIDS Conference, Barcelona, 2002.

1 *NIH Consensus Statement, 10–12 June 2002.*
2 *Osmond DH. J Infect Dis 1993;167(1):66–71.*
3 *Buchbinder SP. J Infect 1994;29(3):263–9.*
4 *Ndimbie OK. Genitourin Med 1996;72(3):213–6.*
5 *Rooney G. Sex Transm Infect 1998;74(6):399–404*
6 *Sciacca C. Panminerva Med 2001;43(4):229–31.*
7 *Garcia S. abs ThPeC7491.*
8 *Eyster ME. Blood 1994; 84(4):1020–3.*
9 *Filippini P. Sex Transm Dis 2001;28(12):725–9.*
10 *Craib KJP. 8th CROI, 2001: abs 561.*
11 *Risbud AR. abs WePeB6026.*
12 *Mendes-Correa MCJ. abs ThPeC7493.*
13 *Abresica N. abs C11013.*
14 *Bonacini M. J Acquir Immune Defic Syndr 2001;26(4):340–4.*
15 *Hermida M. J Virol Methods 2002;101(1–2):29–35.*
16 *Jaeckel E. N Engl J Med 2001;345(20):1452–7.*
17 *Martin-Carbonero L. AIDS Research and Human Retroviruses 2001;17(16):1467–1471.*
18 *Bica I. Clin Infect Dis 2001;32(3):492–497.*
19 *Monga HK. Clin Infect Dis 2001;33(2):240–247.*
20 *Hatzakis A. AIDS 2000;14(suppl 4):S5.*
21 *Soto B. J Hepatol 1997;26(1):1–5.*
22 *Garcia-Samaniego J. Am J Gastroenterol 2001;96(1):179–183.*

Down in the Lab

By Bob Huff

The Human Immunodeficiency Virus (HIV) is a virus that has a detrimental effect on the human immune system. That much should be obvious from its name. Virologists study viruses and immunologists study immune systems, but since HIV came along, more and more scientists from the two fields are learning about each other's work. In the early days of HIV research, virologists led the campaign to discover the virus's vulnerability to antiviral therapy. But immunologists have not been resting; we're learning more everyday about the secrets of human immunity and what goes wrong when HIV enters the scene.

The progress of science depends on a continuing flow of detailed and reliable communications about the latest discoveries, observations and techniques. Big news in basic science is either held for a big conference or reported in one of the important science journals such as *Science Magazine* or *Nature*. But smaller reports of month-to-month progress are typically published in specialized journals that serve more specific fields of knowledge. For example, most virologists eagerly await each new biweekly issue of the *Journal of Virology* to see what their colleagues are up to.

This article takes a look at the September 2002 issue of the *Journal of Virology* to try to get a snapshot of the kind of HIV-related work deemed significant enough to be included. Of the 58 reports published in this issue, 13 specifically involve HIV. Other articles may concern SIV (which infects monkeys) or Feline Immunodeficiency Virus (which infects cats) as well as a number of other well-known viruses such as hepatitis C and B. Several of the AIDS-associated opportunistic viral infections such as CMV and HSV are represented, as are a host of esoteric but no doubt interesting viruses such as cauliflower mosaic virus and bovine viral diarrhea virus. But we're going to stick to HIV.

Keep in mind that most of the work published in this journal is more provocative than definitive. Usually the experiments were conducted in laboratory cell lines. Such in vitro studies may initially seem promising then later turn out to have little relation to what goes on in living beings. For the most part these papers are part of an ongoing discussion among workers in the field about what they have learned. Most of the reports were submitted in the Spring of 2002 and accepted at the beginning of Summer. It may seem insufferably geeky to want to examine HIV science at this level, but the need to know what's up is compelling.

Immunity Under the Radar

Most everybody has heard of the two major wings of the adaptive immune system: cellular immunity (the kind that eliminates infected cells and the form of immunity that is most

directly affected by HIV) and humoral immunity (the kind that generates neutralizing antibodies to vanquish invaders). These systems are called adaptive or specific immunity because they adapt themselves to target specific invaders. To do this they typically need a little time to get up to speed. So, before these specialized systems kick in, there is a grab bag of other tricks that evolution has provided to repel the first wave of alien invaders. Collectively these are known as innate or non-specific immunity.

One well-known innate antiviral defense system is the interferon response. If a cell becomes infected by certain kinds of virus, it will begin to secrete chemical messengers called interferons, which then travel through the bloodstream activating interferon receptors on uninfected cells. These activated but uninfected cells go through a series of changes that put them into an antiviral state. If the virus spreads to an interferon-primed cell, its protein-producing machinery stops dead in its tracks and the cell begins to die. This response means a dead end to any virus that tries to hijack that cell for replication.

Short pieces of double strand RNA can selectively stop the expression of host cell genes that contain identical nucleotide sequences.

One circumstance that can kick off the process of interferon secretion is the presence of double stranded lengths of RNA in a cell. Remember that DNA is the master molecule used to store an organism's entire genetic code within each cell's nucleus. A cell's genes are typically stored as coils of very long, durable, double strands of DNA composed of chains of nucleotides. Proteins, which are the stuff and substance of our bodies, are made from chains of amino acids. When a particular protein is needed, the gene for that protein is exposed and a temporary copy of the gene's DNA is copied onto a single strand of RNA. This is called transcription. This copy of the gene, called copy RNA (cRNA), is delivered from the nucleus to the cell's protein-making machinery where it becomes translated from a chain of nucleotides into a chain of amino acids. When translation is complete, the chain of amino acids folds itself up into a protein and gets to work. All together, this process is called gene expression.

HIV is somewhat unusual in that it keeps the genes for its proteins stored in a double strand of RNA instead of DNA. After HIV enters a cell, its RNA is copied into a strand of DNA by the viral enzyme reverse transcriptase. This piece of DNA is then delivered to the cell's nucleus and stitched into the master strand of DNA. Later, when the cell is stimulated to replicate, the viral genes are expressed right along with normal host genes and new virus particles are manufactured and released.

Although in some animals the presence of a double strand of RNA in a cell can trigger the interferon response, in plants and invertebrates, a double strand of RNA had been known to stimulate a different kind of response, called RNA interference. It seems that short pieces of double strand RNA have the remarkable ability to selectively and very efficiently thwart the expression of host cell genes that contain identical, complementary nucleotide sequences. It appears that the double strand RNA recognizes its cRNA twin, which leads to a shutdown of the protein-making machinery. In a classic experiment, a cell modified to produce firefly luciferase (a so-called reporter gene product that can be made to light up) was injected with pieces of double strand RNA transcribed from luciferase DNA. The result was literally like turning off a light.

Because the interferon response set off by double strand RNA is so powerful, RNA interference had never been observed in mammalian cells. A breakthrough came a couple of years ago with the discovery that double stranded lengths RNA shorter than 30 nucleotides did not set off the interferon response. Soon, through trial and error, it was found that a double strand of RNA in the neighborhood of 22 nucleotides long could effectively trigger RNA interference in human cells. These shorter bits of double strand RNA are called small interfering RNAs (siRNA). RNA interference is rapidly becoming one of the most important new techniques in the cell biologist's toolkit because it lets them switch genes on and off to see what they do. Being able to selectively "knock out" genes like this promises to revolutionize our understanding of how gene products interact in the complex environment of living cells.

Calling Interference

In the September issue of the *Journal of Virology*, a paper by Glen Coburn and Bryan Cullen of the Howard Hughes Medical Institute at Duke University describe RNA interference as a possible contributor to our bodies' innate antiviral immunity. Although HIV does not produce double strand RNA able to naturally trigger RNA interference, the scientists report on a potentially therapeutic technique to inhibit HIV replication via this newly discovered mechanism.

The authors created small interfering RNA strands that corresponded to cRNA for segments of the HIV proteins Rev and Tat. They then inserted these siRNAs using transfection techniques into cells capable of supporting HIV replication. In every experiment, the cells dosed with siRNA showed dramatic and specific inhi-

bition of HIV gene expression and replication. (In July, two groups also published reports of inhibiting HIV replication by inserting siRNAs targeting various HIV proteins.) Of course this raises a question of whether RNA inhibition can be used as therapy in people. The challenge will be to develop a way to safely introduce siRNAs into living cells. It may be possible, but such research is still in its very earliest stages.

There is also the possibility that RNA interference has been operating as a component of innate immunity all along. If so, then wily viruses like HIV may have already evolved a defense to this line of attack. While a therapeutic application of RNA interference may be viable down the road, in the meantime, virologists have a powerful new tool to use to tease apart the intricate web of protein-protein relationships that exists between HIV and its human host cells. What they discover may well yield the long-sought secret to defeating the virus.

Caveolin-1 HIV-0

Here's another report about a naturally occurring process that apparently knocks down expression of HIV—at least in the laboratory. Caveolin-1 is a protein usually found imbedded in the lipid sheathing of cellular membranes and is common to certain types of human cells, including a few that can be infected with HIV. It's thought that the protein participates in mechanisms that regulate the transmission of signals from the cell surface to interior processes. Manuel Llano and workers in the laboratory of Eric Poeschla at the Mayo Clinic were curious to see if this protein was involved in helping HIV assemble new virions and facilitating their budding from infected cells.

Using transfection techniques to insert genetic material directly into cells in vitro, the researchers experimentally introduced DNA for HIV-1 along with either DNA for Caveolin-1 or an empty control into kidney cells. [Cells supplied with DNA inside the cytoplasm can process the genetic material and translate it into proteins. Genetic material can be directly injected or, more efficiently, packaged into an empty virus that is highly adapted to the job of introducing DNA or RNA into cells.] After the experimental transfection, the researchers then measured the amount of new HIV produced by using a reverse transcriptase activity assay. Unexpectedly, they found that while control cells continued to process HIV, nearly all HIV activity had been blocked in the cells expressing Caveolin-1.

They tried the experiment several other times to confirm their observation, and then tried the same experiment with several different laboratory strains of HIV. It still worked. Next, they tried the same experiment using a range of doses of Caveolin-1 and found that small amounts had a smaller effect than larger amounts, a convincing demonstration of activity called dose response. They also tried using a different cell type and using different ways of transfecting the cells, but the outcome was unchanged. To rule out the possibility that the inhibitory effect was due to RNA or DNA instead of the activity of the protein, they performed the experiment using a mutant piece of Caveolin-1 DNA that could not express the protein. This corrupted gene for Caveolin-1 failed to inhibit HIV, which supports the role of a functional protein. At this point they were convinced that transfecting Caveolin-1 along with DNA for HIV blocked expression of new virus, but how did it work?

Since a small amount of virus was still being expressed in the presence of Caveolin-1, they analyzed the HIV being produced to see if it could still infect other cells. It could, which suggested that although the amount of HIV expressed was dramatically lowered, the virus itself was not defective. They also did experiments to determine if the drop in viral production was due to a toxic effect of Caveolin-1 on the host cell. But again, the inhibitory effect seemed specific to HIV since the cells were still able to function normally. The case for HIV specificity was made stronger by an experiment showing that cells transfected with Caveolin-1 plus DNA for the measles virus did not inhibit the production of measles virions.

Unexpectedly, they found that nearly all HIV activity had been blocked in the cells expressing Caveolin-1.

Finally, the researchers split the Caveolin-1 DNA into several fragments and tested each one until they found a segment of the protein that retained full activity. The segment, only about 34 amino acids long, corresponded to a region of Caveolin-1 that is normally buried within the lipid layers of cell membranes. Oddly, this part of the protein is not known to have any function other than interacting with itself or with another similar protein called Caveolin-2 (which Llano reports also inhibits HIV expression). Whether this protein exerts its effect on HIV directly or through intermediaries is unknown.

The author notes that HIV can replicate normally in cells that naturally express Caveolin-1 and speculates that some mechanism may compensate to create an environment permissive for HIV replication. Perhaps when Caveolin-1 is overexpressed, as in these experiments, the compensatory protein is overwhelmed. This is the perfect job for using RNA interference as a tool to tease out the interacting protein functions.

Hopefully someone, somewhere, is busily turning genes on and off, looking for the one that unleashes Caveolin-1's HIV inhibitory potential.

Show Me a SIGN

There has been a lot of interest in understanding what happens during the very earliest hours after HIV contacts human tissue. It's thought that an HIV infection occurring through sexual contact gets its start in mucosal tissues, and that a particular type of cell, called the dendritic cell, is the most likely entry point. One impetus to understanding these early events is to help develop a microbicide that can block infection at first contact.

Dendritic cells (DC) are often described as sentries patrolling the frontiers of the body, where outside meets inside along vulnerable mucosal tissues. DCs are mobile, and they regularly travel from the mucosal frontier to immunity centers in lymph nodes where they display samples of the invaders they've met at the gates. While some DCs express the CD4 molecule on their surfaces, suggesting that they can be targets for direct infection with HIV, they also express another cell surface protein than can bind HIV called DC-SIGN. It is thought that HIV can interact with DC-SIGN and either be internalized in the cell or simply carried along piggyback as the DC migrates to a lymph node. But this is like bringing a fox into the henhouse since it's in the lymph tissue that HIV meets up with its ultimate target, the T-cell.

Dendritic cells bearing the DC-SIGN molecule are found throughout rectal mucosa and in parts of the vaginal epithelium, two prime targets for blocking HIV infection with a topical microbicide.

Dendritic cells bearing the DC-SIGN molecule are found throughout rectal mucosa and in parts of the vaginal epithelium, two prime targets for blocking HIV infection with a topical microbicide. In their J Virol article, Robert Doms and researchers from the University of Pennsylvania contribute a few new nuggets to our understanding of DC-SIGN and offer a new set of tools for future research.

First, the investigators report on a density analysis of DC-SIGN molecules on the surface of dendritic cells taken from seven volunteers over several months time. While there was some variability between and among individuals over time, the count of DC-SIGN molecules consistently exceeded 100,000 copies per cell. In previous studies using laboratory cell lines, the authors had determined that about 60,000 DC-SIGN molecules per cell was necessary to support efficient virus transmission.

The second part of their paper reported on a method of blocking DC-SIGN by using monoclonal antibodies (Mabs) to effectively reduce the number of molecules available for HIV attachment. Although the authors found a set of Mabs able to block virus binding in laboratory cell lines, these proved less effective at blocking virus transmission in a model using dendritic cells that had been stimulated from precursor cells. The authors propose that while partial inhibition of HIV transmission can be demonstrated by blocking DC-SIGN, there are most likely other cell surface molecules involved in binding and transmitting HIV. This paper offers some incremental knowledge about DC-SIGN and a new set of tools that may help researchers understand how HIV first interacts with the body. But as the authors admit, "our understanding of the factors that control DC-SIGN expression in vitro, and its pattern of expression on specific types of DCs in vivo, is far from complete."

References

Coburn and Cullen. Potent and specific inhibition of Human Immunodeficiency Virus Type 1 by RNA interference. Journal of Virology, Sept 2002, p. 9225–9231

Novina et al. siRNA inhibition of HIV-1 infection. Nature Medicine, July 2002. p. 681–686

Llano et al. Blockade of Human Immunodeficiency Virus Type 1 expression by Caveolin-1. Journal of Virology, Sept 2002, p. 9152–9164

Baribaud et al. Quantitative expression and virus transmission analysis of DC-SIGN on monocyte-derived dendritic cells. Journal of Virology, Sept 2002, p. 9135–9142.

Tales of a Housepunk Nothing, Or: I Was a Twenty-Something Outreach Worker

By Rachel McLean

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For subscription information: hrc@harmreduction.org or visit www.harmreduction.org

"No woman is required to build the world by destroying herself." Rabbi Sofer, 19th Century.

Until recently I worked as an outreach worker/advocate with young injectors in San Francisco. In the course of those four years I experienced enthusiasm, martyrdom, burnout, and all sorts of changes in between. This is my attempt to extract from my experiences ways that, as providers, we can take better care of each other and ourselves.

My History

My involvement with the street scene started when I was fourteen. Squatting in downtown San Francisco, I drank, sparechanged and table-dived with the rest of the homeless punks. But I was still a housepunk; one of those kidz who talks too loud about the few drugs they do and still has a job scooping ice cream two days a week. Nor was I like the kids I worked with later, who'd been homeless for years on end. I had enough social support to return to and eventually graduate high school by living with a friend.

By age twenty I had quit alcohol and other drugs and begun working as an outreach worker for the Haight Ashbury Youth Outreach Team. I'd been living indoors for several years but some of the people I'd squatted with were still on the streets and would come into the drop-in center. Being in a provider role with old friends felt awkward and difficult. Until I knew better, I dealt with my discomfort by overzealously attempting to prove that I was still "down." I eventually realized that 'the kidz' (homeless youth ages 14–29) could see through my insincerity, and I finally learned to just be myself—a housepunk.

The Work

Without knowing what it was called, I did everything a good harm reduction counselor/outreach worker/everything-else-under-the-sun could do. I met the kidz where they were at: in the park, on the concrete, high as fuck, numb or happy, twacked on sleep deprivation or down, down low. I let them hang out at the drop-in high when other programs wouldn't, keeping them awake to prevent them from overdosing. I sat by their sides in hospital waiting rooms for hours on end to ensure they got proper care from oftentimes judgmental doctors. I listened to horrific stories of pain and abuse, and gave support; talking about hope, safe shooting, taking breaks. I survived evictions and agency funding nightmares to defend the kidz against NIMBYs, and pled with probation officers to keep them out of jail. I loved those kidz, and became integrated into their lives like the mother's they never had would've, could've, should've if things had been different. It was me and the kidz against the world and I was going to take it all on. On rainy nights I lay awake, struggling to believe that I was not inherently evil for having a bed to sleep in when others were cold, unsafe, freezing outside. Early on I was offered a raise and refused it, saying we should spend the money on socks. I thought that if I just fought hard enough, things would be okay. I was a guerilla fighter on the frontlines of the never-ending battle called harm reduction.

I drank, sparechanged and table-dived with the rest of the homeless punks.

But it was never enough. For every kid off the streets, two came on, and one was inevitably someone who'd just left the year before. Operating in an entirely different context than the mainstream, I had to learn to define success in totally different ways. I soon learned not to have so many expectations because things didn't always change for the better. When one of the kidz would die, we'd have a memorial in the park to remember her. I learned that really all I could do was love unconditionally and hope that people would stay alive long enough to realize their own dreams. I gave a million pep talks to other service providers to remember these things. Yet, amidst all this non-judgmental, fatalistic serenity, my heart broke daily.

Burnout

With every overdose, every rape, every stolen backpack, every beaten up girlfriend, every back-to-town-&-strung-out-again-after-a-year-of-doing-so-damn-good kid, the grief continued to build. In time I felt like I was going to lose my shit from the cumulative heartache. We bought a book for one of the memorials and with every death it just sank in that the book would eventually fill with the names of kidz and friends,

loved and lost. I began to wonder, not if anyone else would die, but just who would be next. I obsessed about overdose; hoping to somehow stop it, rein it in. I felt panicked and traumatized, numb with constant mourning in the way that I imagine medics feel, bandaging and burying soldiers on a battlefield. Only this was the War on Drugs. I was afraid to feel, fearing what would happen if I really let myself go. I spent Friday nights watching depressing movies, waiting to release the tears I had been withholding during the week. After several years of this, I realized that as much as I immensely valued the relationships I'd taken so long to build, I was no longer putting my all into the work.

I was exhibiting the classic signs of burnout, "psychic numbing," "compassion fatigue" and "post traumatic stress syndrome."* I felt unable to feel or give anything emotionally. I found myself hiding in the office, hoping no clients would come in. I would spend hours piddling around with paperwork, organizing the outreach supplies closet, attempting to establish some sense of control and order amidst the chaos around me. When new kidz came to town, I found that I no longer had the same enthusiasm I'd once had for establishing rapport with them. I was less and less able to listen to the kidz I already knew, and quick to snap when they went on and on about how they were going to change their lives. After years of the work, I felt like a sopping wet sponge, so saturated with grief that I could not absorb another drop.

"That's what they all say. You'll probably just get strung out and OD like the rest."

I will never forget this one kid, "Jeffrey" (not his real name) who told me he only smoked pot and would never touch injection drugs as long as he lived. Without even realizing it I said something like, "Yeah, right. That's what they all say. You'll probably just get strung out and OD like the rest." I had heard people say that line so many times before and still get strung out, only in the past I had been able to censor the cynical reaction in my head. This time however, my cynicism got the best of me, and my sense of boundaries totally failed. Luckily, Jeffrey called me on it and I apologized profusely telling him I'd just seen so many kidz go down hill and it was a hard process to watch. Jeffrey never did progress to the hard stuff but even if he had, that comment would have been totally uncalled for. I could have expressed my concern, and told him what other street kidz had experienced without treating him like his fate was already written. Although I sometimes see Jeffrey and we laugh about it, that experience was a painful wake-up call for me. I saw that I could not continue on the path I was on; that something had to give.

Thinking about Using

As burnout settled in, I felt overwhelmed by such immense suffering and sought ways to shut off. For a while all I could think about was wanting to shoot up. I had been straightedge (abstinent from alcohol, cigarettes, coffee, and other drugs) for years and had no experience using heroin. The people I was surrounded by were not happily moderating their drug use, taking their time to find a vein in a clean, well-lighted place for shooting up. They were fucking miserable, and told me so daily. Their lives were marked by dopesickness, hustling, cops, abscesses, hepatitis C, jail, inaccessible treatment programs and friends dying. I saw the ramifications of heroin addiction daily, so why was I at home looking at the phone thinking, "I could call so and so, she'd show me what to do. I've got syringes, I know where people cop, it would be so easy..."?

I have heard it said that the mind imbibes the qualities of the things it contemplates, so it makes sense that I would want to use when I was surrounded by it every day. I was also a harm reductionist operating without much support on an agency or community level, which led to feelings of martyrdom and accelerated the burnout I was feeling—and contributed to my desire to use. Like so many others, I had become so identified with the provider role that I could scarcely take care of myself, or ask for the help or support that I needed. Nor could I think outside of the box; in my world the only roles available were of helper and helped. Feeling like I could not handle being the helper anymore, the only other option was to do what the "helped" were doing: shooting up.

White Privilege & Survival Guilt

Working as a provider, I wanted to use in order to deny my privilege, and to "feel the pain" of the kidz. Part of me felt pulled by the *Drugstore Cowboy* romanticization of heroin use. Using represented the forbidden permission to lose control. It would enable me to absolve myself from responsibility, and simultaneously merge into the chaos of oneness with the kidz, thus absolving myself of my white/middle-class/living-indoors privilege. (Or so I thought.) Shooting up seemed like a viable option, since I had friends in the harm reduction field who had done exactly the same up once they'd started doing needle exchange. I envied their release, the street cred that came with being an out IDU/provider and the manner in which they were taken care of—in a way that their clients rarely were—by other providers. Yet, as much as I felt tempted to, I did not return to old modes of

coping. I realized that using would only decrease my abilities to deal with my own issues and to help the kidz.

My Role as a Provider

The kidz had peers on the streets; the role that I played was different. I wasn't someone to rip off, nor someone who would take advantage of them if they let down their guard. I was someone outside of the scene that they could trust, because I wasn't like them. I believed that my role in their lives was to show that it is possible to hold onto your values, freedom, anarchy, etc., while taking care of yourself. Using and getting sloppy strung out would hardly have supported that role. (I know myself—I would've gotten sloppy.) If anything, absolving myself from responsibility through drug use would have communicated a message that was contrary to the one I claimed to teach. If I expected drug users to be responsible for their behavior, then the same should be expected of me. My starting to use, however "responsibly," would not have been a responsible decision. It would be me not dealing with my own problems. I did not want to use to "get high," although not feeling would have been an added bonus. I wanted to use to fuck up; to destroy the life and responsibility that I had created for myself.

Coping Strategies

I worked as an outreach worker for four years, and never used. I decided that it wasn't an option for me, that I wanted to feel even if it brought on a flood of emotions I didn't want to face. Choosing to feel meant I had to find new ways to deal with my burnout. To cope, I baked cookies, I wrote, I went dancing, I talked to friends, I watched sad movies and poured myself into my work and school. For a long time I knew that these things would only tide me over but that I needed a long break from the work. For personal and programmatic reasons I felt like it was never the right time to leave. I felt guilty, like I would be abandoning the kidz to struggle against adversity alone. Like leaving would mean I was an uncaring sellout, who wasn't down for the struggle. It had to get to the point where I just couldn't put off taking care of myself any longer. And it did.

I quit my job and spent three months traveling in Mexico and have since returned to take an extended break from direct service work. It's been a challenge to remember that taking care of myself is actually the best thing I can do for the world right now but I have faith that I am doing the right thing. This article has been my attempt to make sense of my experience, with the hopes that those still doing the work might learn from them. Is it inevitable to burnout on this work? Maybe. But I don't believe we should have to get to the point of no return before we stop to take a break. There must be better ways of taking care of ourselves while we do this work. To that end, I offer these suggestions.

1) Prioritize taking care of yourself, personally and professionally.

a) Personally, this means staying active in other areas of your life. Seek out and keep up the things that are fun and that give you peace of mind. For me this is writing, dancing, long walks, but most importantly, drinking tea, eating toast and talking with my closest friends. For you this might be painting, reading, cooking, doing graffiti, playing sports, bike-riding, camping, swimming, listening to and playing music, lighting candles, taking a hot bath, meditating, or any combination of an infinite number of possibilities. It also means recognizing the signs of burnout and giving yourself permission to contribute in ways that are less demanding emotionally.

I don't believe we should have to get to the point of no return before we stop to take a break. There must be better ways of taking care of ourselves while we do this work.

b) Programmatically, this means providing short and extended breaks, a realistic workload, decent pay (or if there's no money, some decent appreciation), clinical supervision, counseling, mental health days, staff retreats and training. People that take care of themselves run sustainable programs. For programs with little funding (i.e., most programs), taking care of staff may mean providing less comprehensive services, a hard but worthwhile choice.

2) If you're from a privileged background, acknowledge your privilege and move on. It is important to be an ally to oppressed people without trying to take on their oppression. The best way to be an ally is to take care of yourself and make good use of your privilege.

3) If you're using or not, evaluate how you feel about it and go from there. If your level of use feels good to you, then please use safely and with company. If not, find support to change it to a level that feels better, even if that means abstinence. For some, moderated use is not a realistic option and that's okay.

I believe in harm reduction, and know how revolutionary it is to believe that users deserve health and dignity. In an ideal world it would be possible to use without so much harm to the individual, but we do not live in an ideal world. This is the real world and not all use is implicitly okay for everyone.

4) Dialogue, of course. Talk about what's going on with you, even if it seems pale in comparison to what you see other people going

through everyday. Talk to your friends, your co-workers. If you don't feel like you have anyone you can trust to talk to, or even if you do, check out individual therapy. If it's not provided by your agency, there are usually sliding-scale programs around. You may also think about starting a harm reduction workers' support group

5) Keep an eye out for your friends, drag 'em along to your support group!

I don't buy the racist bullshit line in *Traffic* where the Mexican drug czar says that overdose acts as treatment. I'm not waiting anymore for my friends in the harm reduction movement to be dead or suicidal to remember to tell them I care and am concerned about their welfare. No more waiting until I'm too numb to be real with people before I start taking care of myself. The biggest tragedy of my own burnout was realizing that I'd become so numb from grieving for all the ones I'd lost that I was doing a shitty job of being there for the people that were still alive. So, instead of forever listing the names of the ones that are gone from my life, whom I will always love and remember, this is my shout out to holding onto the ones that are still here. Please, for fuck sake, remember that loving yourself is the greatest gift you can give to the world. Now, give away.

This is dedicated to all youth h.r. providers in San Francisco, past, present and future. HAYOT, ATC, SFNE, UFO, EVRC, G-HOUSE, DIMENSIONS, HH (RIP), YI (RIP) & HIFY.

Short Course *Notes on HIV drugs in development*

SCH-C Moves Ahead—Carefully

Schering Plough held a meeting to update community members about the progress of the company's novel CCR5 inhibitor, SCH-C, which is moving through the first phases of clinical development. The pace of testing has been slowed because of cautions put in place by the FDA after transient electrical abnormalities were detected in the heart rhythms of three patients receiving SCH-C at high doses. The abnormality, a prolongation of the QTc interval, indicates an event when the heart is signaled to beat before the muscle is fully prepared to contract. This condition can possibly result in the heart losing its ability to move blood, with sudden death the outcome. Because of this potentially catastrophic consequence, the FDA has asked for close monitoring of patients receiving SCH-C until the significance of this observation is clarified. Patients entering the phase Ib trial will probably be observed for a week or so under constant telemetry in a medical facility to assure that any arrhythmias are safely detected and corrected.

Interestingly, very little is currently known about the normal prevalence of QTc prolongation among the background population; indeed, in the SCH-C study, 3 of 18 patients receiving placebo also experienced abnormal QTc. Yet prudence (and the FDA) demands that early studies of this promising drug proceed carefully and deliberately.

Bermuda Triangle

As expected, Triangle Pharmaceuticals has submitted data on its nucleoside analog FTC (Coviracil) to the FDA for approval. They should hear in a month or so if it will receive a priority review. But this good news was preceded by a report that one of the company's other drug candidates, DAPD, has received a go-slow order from the FDA because of some belatedly noted findings on the lenses of the eyes of trial participants. The drug is a nucleoside analog with the attractive potential to remain active against virus resistant to AZT and 3TC (and FTC?). During animal testing at extremely high doses, the drug crystallized in the kidneys, which set off a cascade of toxic events that included development of corneal opacities. On the basis of this finding, the company added opthalmologic testing to their ongoing clinical studies. In a few people, investigators reported finding minor lens abnormalities, although no evidence of kidney toxicity that would have precipitated them. Since there were no baseline eye tests, it's unclear at this point what significance these pinpoint spots have, if any, since similar lens abnormalities tend to become common with increasing age and UV exposure. But once again, in the interest of safety, the FDA has asked that new enrollments into the ongoing trials be temporarily held until more thorough baseline screening procedures can be put in place.

Although this latest situation is probably not drug-related, Triangle has had a long string of bad luck with its attempts to get an AIDS drug into the market. But you can't say they're dodging the reality of their situation. The company's web site (www.tripharm.com) prominently features a list of "risk factors" on its front page that makes for chilling reading. Check it out.

Hepsera (adefovir for HBV) Gilead Sciences, having failed in its attempt to launch adefovir dipivoxil as an HIV drug due to kidney toxicity at necessary doses, regrouped its forces and is on the verge of seeing the drug approved—at a much more tolerable dosage—for treating chronic hepatitis B infection. The company announced that it has selected Hepsera™ as the U.S. trade name for adefovir. Approval should be granted by the time you read this.

Global Treatment Update

By Bob Huff

Large Mining Companies Decide to Treat

Three large mining corporations active in HIV-ravaged Southern Africa have announced plans to offer antiretroviral treatment to all of their employees. The companies, Anglo American, Anglo Gold and De Beers are among the largest private employers in Africa, and HIV prevalence rates in countries where these companies operate, Botswana, Namibia, South Africa and Zimbabwe, are among the highest in the world. Anglo Gold estimates that 28 percent of its South African employees are infected.

The announcement said that the program would be rolled out during the coming year with treatment delivered from existing company-sponsored clinics. Dependents will not be covered by this first phase of treatment, although De Beers has said it will extend treatment to a single sex partner of a worker.

The announcement is a victory for activist and labor groups that had been pressing for treatment access. Their attention now turns to other large mining companies in the region, such as Gold Fields and Harmony, who are still resisting offering treatment to their employees.

Protest Against Coca-Cola Planned

The presence of the Coca-Cola logo is nearly ubiquitous in Africa. But despite the company's dependence on a huge low-wage work force to distribute its product, Coca-Cola has so far refused to pay for HIV treatment for more than the top echelon of its employees. Coke's policy is that only HIV-positive people among its administrative staff are eligible for access to treatment. This leaves almost 100,000 bottlers and distributors without access to medicines should they become sick with HIV/AIDS.

On October 17, a Global Day of Protest has been planned to draw attention to Coke's fundamental obligation to implement comprehensive HIV/AIDS workplace programs and policies, which include treatment and care for infected workers and their dependents. Demonstrations are planned in the U.S., Thailand, South Africa, Morocco, and France.

For more information: www.healthgap.org

Pan African Treatment Activist Group Meets

On August 22nd, HIV/AIDS activists from 21 African nations met in Cape Town to organize a Pan-African treatment activists movement to fight for access to affordable AIDS medicine and to create an African voice to talk to international organizations about the AIDS crisis.

"We are the ones who are suffering, but we are not taking up leadership roles in the fight against AIDS," said Mohammed Farouk, coordinator of Nigeria's AIDS Alliance. "It is time we Africans got together to assert ourselves."

Among the group's goals for itself:

"Develop a community-based response to the AIDS pandemic in Africa that places PLWAs at the center and ensures the involvement of PLWAs in key decision-making processes that will affect their lives."

"Mobilize our communities, our political leaders, and all sectors of society throughout the continent to ensure access to ARV treatment for all who need it, starting with the immediate implementation of the WHO goal to ensure ARV treatment for at least three million people in the developing world by 2005."

WHO's on First

The World Health Organization (WHO) held an initial meeting in Geneva to begin setting up global partnerships and creating a framework for national planning, budgeting and implementation towards their goal of treating three million people within the next three years. They hope to have a "blueprint," a "roadmap," or some other metaphor for a plan ready to show by December 1 of this year.

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Rapid Tests will Save Lives

By Gregg Gonsalves

As the cover story in this month's *Treatment Issues* shows, the haves and have-nots in this epidemic need not be separated by oceans and continents. The crisis in funding for the AIDS Drug Assistance programs may soon deprive thousands of U.S. residents of the drugs they need to save their lives. Of course, this disaster need not happen if Congress appropriates $162 million for the ADAP program for the next fiscal year. Will our members of Congress abandon the neediest people with AIDS in their own states? The answer is uncertain and the equivocation of politicians on this issue is indeed sickening, both literally and figuratively.

Another drama that upsets our notion of have and have-nots in the epidemic is quietly unfolding in Atlanta and Washington, D.C. Over the past few years, rapid and simple tests to diagnose HIV infection have been developed and widely deployed in Africa, Asia and Europe. These rapid HIV tests can offer an HIV diagnosis in less than half an hour and can be performed by anyone with a bit of training —no laboratory is necessary to use these truly revolutionary new technologies. With up to 40 percent of people who take the conventional test never returning for results and with a critical need to bring mobile testing and counseling to overlooked populations, rapid tests are the key to a new era of HIV prevention.

However, rapid HIV tests have not been available in the U.S. because, until recently, no company had asked to market one here. One reason is that the big diagnostic test manufacturers who sell rapid tests elsewhere in the world are worried about upsetting the market for their slower, lab-based assays. But this year, a small company, Orasure Technologies, applied to sell a rapid HIV test in the U.S. Orasure's application is now before the FDA, which is reviewing the data and is expected to make a decision soon.

Here is where things get complicated. Unlike AIDS drugs, several different agencies have jurisdiction over the fate of rapid tests. The FDA will review safety and efficacy data, just as it does for pharmaceuticals. But with rapid tests, the Center for Medicaid and Medicare Services (CMMS) gets to weigh in on how these tests will be used. What is at stake here is whether Orasure's test will be classified by CMMS as "moderately complex" or be a "waived" test. A "moderately complex" label will drastically compromise the revolutionary promise of rapid testing by mandating that only qualified laboratories or laboratory personnel can offer these assays. If community based organizations want to use these tests in-house or as part of enhanced prevention outreach strategies, they would have to bring laboratory personnel on board, as well as comply with a set of onerous rules and regulations that come with the "moderately complex" designation. If Orasure's test receives a waiver, it can be more broadly and less restrictively used.

The opposition to giving Orasure a waiver is largely coming from, you guessed it, laboratory personnel, laboratories and their fellow travelers within CMMS, which see rapid testing as a threat to their hegemony over HIV diagnoses and the funding that comes with it. Rapid testing cuts out the need to send your HIV test to a lab for analysis and the laboratory middlemen are hopping mad. The lab lobby is claiming that rapid tests are far too complex to perform without expensive laboratory support—even though they are being used successfully in remote villages in Africa right now. They claim that there will be insufficient oversight, training and quality assurance for these tests—although HIV testing in the U.S. is already highly regulated and there is broad agreement that training and quality assurance programs need to go hand-in-hand with the implementation of these technologies in the field.

Every year in the U.S., 700,000 people do not come back for their HIV test results. How many of these eventually walk into an emergency room with PCP but could have been saved if we could offer test results in 20 minutes instead of a week's time?

There is nothing standing in the way of rapid testing in the U.S. but greed and bureaucratic intransigence. CMMS should "waive" Orasure's test when it receives FDA approval and stop this nonsense. They were told as much this month by a panel of experts at a consultation sponsored by the CDC in Atlanta, which brought together all the parties interested in the fate of rapid testing. The deployment of rapid testing in the U.S. has been delayed and delayed again. It's time to get moving.