

Ryan White
CARE Act

On June 6, the Senate unanimously approved a bill, S. 2311 that would reauthorize the Ryan White CARE Act until 2005. Senator Jim Jeffords (R) of Vermont and Senator Edward Kennedy (D) of Massachusetts, and their very competent staffs led this effort. Just before the 4th of July recess Dr. Tom Coburn (R-OK) introduced the House version of a Reauthorized Ryan White CARE Act, that he and Congressman Henry Waxman (with very broad community input) negotiated for weeks this summer. While many in the HIV treatment and care community do not consider the bill to be perfect, the legislation contains hundreds of compromises which all politicians should be able to support. This bill was passed in the House at about midnight on July 25 under suspension of House rules. T•II CANN, and other AIDS advocates contacted members of Congress to urge them to cosponsor HR 4807. At the time of passage there were 253 Members of the House of Representatives as original cosponsors. This is a very large number and a very effective demonstration of very broad bipartisan support for the legislation.

The Title I hold harmless effect on San Francisco (with reference to New York City as being "in the same boat") occupied much of the 40 minutes of debate allowed under the House rules. Everyone acknowledged the key roles played by staff (particularly Roland Foster, of Coburn staff, and Paul Kim, of Waxman staff, along with Marc Wheat and John Ford of the full Committee staff) and many community advocates in crafting the bill. Both Dr. Coburn and Ranking member Sherrod Brown complained vigorously about such important legislation being debated at such a late hour. Many members spoke to the need for additional Ryan White resources (both sides of the aisle), and the Congressional Black Caucus (Dr. Donna Christian Christensen) pointed

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Proper Screening For VA Medical Eligibility Can Ease Pressure On State ADAP Programs

By Thomas P. McCormack

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The Department of Veterans' Affairs (VA) recently released 1998 Census data that suggests that state AIDS Drug Assistance Programs (ADAPs) may be bearing some medical costs for patients actually eligible for free or low-fee VA medical care.

ADAP has long been rightfully viewed as a last resort program. Those eligible for medical care and drugs from other programs should use that coverage before turning to ADAP. Thus, medical care coverage available from the VA should, unless there are exceptional circumstances, be turned to before limited ADAP monies are utilized.

But virtually all members of the public, many ADAP officials, and even most veterans themselves wrongly assume that one must be a combat or wartime veteran or have been injured or become sick on

active duty to get VA medical care. As a result, some ADAPs don't bother to screen at all for VA medical care eligibility. Or they ask veterans themselves whether they're eligible for VA medical care. And since even veterans themselves don't know the correct eligibility rules, few ADAP applicants indicate that they're VA-eligible.

To be eligible for VA medical care, a veteran must have served at least 180 days active duty and have an honorable or general discharge. Veterans need not have served in combat or in wartime; have been injured or become ill while on duty; be disabled; or even have been overseas.

2000 VA Medical Care Eligibility Levels (Raised each January 1)

To get free care (except for a \$2 copayment per prescription), a "Category A" veteran can have up to \$50,000 in liquid assets; a lived-in home of any value; and a vehicle of any value. In addition, monthly income can't exceed the following:

- Single veteran \$1,907
- Veteran with one dependent \$2,289
- For each additional dependent \$128 more

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out that we shouldn't assume that this Ryan White Reauthorization "fixes everything" when the current appropriation is still short \$100 Million for next year's ADAP. Nancy Pelosi and Anna Eshoo both spoke to the potential effects on San Francisco of this bill's hold harmless (and on New York City). Dr. Coburn countered that adequate resources should shield any "threatened" cities while simultaneously putting more money where the epidemic "IS" rather than where it "WAS." He also stressed (as he always has) that preventing new infections really saves the most money. This now means a House-Senate conference after the August recess, with a reauthorized CARE Act to The White House for President Clinton's signature possibly before the November elections.

T•II CANN Board and staff were intimately involved in the NORA (National Organizations Responding to AIDS) process of drafting this bill and in all the small group process of vetting every word of the final legislative language. The AIDS advocacy community played the major role in getting The Ryan White CARE Act Reauthorization through both the Senate and House legislative process - with, of course, the bipartisan support of our elected representatives. Text of the bill is available via www.house.gov/coburn/ryanwhite2000.htm. ■

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MESSAGE FROM THE BOARD

What If Medicare Was Available To PWA's Immediately — And There Was A Usable Drug Benefit Too?

The AIDS Treatment & Assistance Act of 2000 (HR 4557) has been introduced by Congressman Tom Coburn, MD (R-OK) and Maurice Hinchey (D-NY). While this is not intended to provide a detailed analysis, consider the following possibilities:

- Congress decides to provide prescription drug benefit for Medicare recipients (elderly and disabled). Since a number of elected officials are courting votes, this is a reasonable public health suggestion (and a politically popular one) that could actually happen in this session of Congress.

- HR 4557 was attached as an amendment to such a bill. The drug benefit would have a "stop loss" or copayment cap of say \$3,000.00 to \$4,000.00 a year. ADAPs could pay that portion for those unable to pay. Suppose the drug treatments offered were everything needed for HIV disease and co-infections? Also you became eligible for Medicare immediately upon an AIDS diagnosis (instead of waiting 24 months)? Suppose maybe even upon testing HIV+.

- Why treatment access could even be prompt! ADAP and Medicaid State funds could be saved and stretched. Medicare

funds (federal resources would come into play with copays from those able to pay, and ADAP for those with AIDS not able to pay) and the funding mechanism would be like insurance. Mechanisms, forms, systems, accounting, reporting, and payment procedures would already be tested and ready. No costly new "system set up" costs. We already use versions of this approach to deal with end stage renal disease. Medicare Part B coverage for AIDS could be like that already provided for oral cancer, hemophilia (e.g., clotting factor), immuno suppressives (e.g., Transplant recipients), and osteoporosis.

Sound too good to be true? Well it certainly sounds good enough to take a very serious look at, with relatively simple and small changes in existing health systems without inventing costly new ones. This approach, which could clearly benefit a large percentage of HIV+ Americans is worth seriously considering. Any policy change that assists with problems and difficulties of a portion of the community helps when dealing with ALL the affected communities, and ALL the health access issues. ■

William "Bill" Arnold
Vice Chair and C.E.O. of T•II CANN

CORRECTION

We received the following correction from the Montana Department of Public Health and Human Services for the May/June 2000 issue of *The Voice*, article "ADAPS Are Still Struggling to Meet Program Enrollments and Expenditures."

On page three, column one, second bullet, Montana is listed as having set an enrollment cap for its ADAP in August of 1999. Montana had a waiting list at that time, but no specific number of ADAP clients accepted has ever been set. The number of clients varies according to how much of the Title II base funds are being expended.

Montana's ADAP program has once again reached capacity, incidentally, and has a short waiting list at present.

The Voice editorial committee apologizes for this error and thanks the MT Dept. Of Public Health & Human Svcs. for bringing it to our attention.

Treatment Review: Antivirals

By: Gary Rose,
Public Policy Chair, T-II CANN

The Voice periodically offers brief reviews of recent treatment information. This year's review will be provided in four parts over the next four issues: (1) a review of news relating to antiviral drug use drawn from the annual ICAAC and Retrovirus conferences, (2) reports from the International Conference in Durban, (3) an overview of new information on the immune system, and (4) an overview of the side effects arising from the use of highly active anti-retroviral therapy (HAART). We will also be writing separately on co-infections, with a focus on Hepatitis C.

Information on HIV treatment has always come in waves. Between those waves, impatience often leads to negative stories centered on the problems arising from the last round of news. Treatment news in both 1999 and the first half of 2000 has centered on two seemingly opposing phenomena; the problems arising from and complications associated with HAART usage, and the continued decrease in death rates from AIDS in the developed world.

The Use of HAART in Treatment: Naïve Patients

Some experts now argue that the “hit hard, hit early” treatment paradigm developed in the wake of highly active antiretroviral therapy (HAART) may be only half right. This philosophy was based on a number of factors including the importance of maintaining the patient's immune system and on the possibility that HIV could be totally eliminated from the body (eradication). Since eradication is now thought to be impossible using the drugs that are currently available and since the immune system under HAART has proved to be stronger and more flexible than was previously thought, a new general rule is being discussed and adopted by many clinicians.

Under this new rule, hitting the virus hard is still crucial. Once a patient has decided to undergo treatment, it is essential that their regimen be strong enough to reduce plasma viral levels to as low as possible for as long as possible. The main components of such treatment remain three-drug combinations of antiretrovirals, including either a protease inhibitor or a potent non-nucleoside reverse transcriptase inhibitor along with two nucleoside reverse transcriptase inhibitors or some other potent combination of these classes with treatment decisions supported by frequent viral load tests.

Whether or not to hit early, however, is now open to question. A growing body of experts now suggest that, due to the side-effects associated with HAART and the difficulty of strictly adhering to HAART regimens over time, it may be wiser to forego therapy until there are signs of early immunological impact (e.g., CD-4 counts below 350 or viral load at or over 10,000). Other physicians and researchers and, in fact, the most recent version of the Federal HIV Treatment Guidelines, on the other hand, continue to support the “hit early” approach on the grounds that the earlier the intervention, the better the immune system will function over the long term, but the hit later approach is rapidly gaining support.

HAART in Treatment: Experienced Patients/Resistance Testing

Physicians and patients must plan, before initiating therapy, a strategy that will allow for a minimum of two and preferably three combinations that are not likely to fail due to cross-resistance (where, for example, resistance to one non-nucleoside causes resistance to all available non-nucleosides). For those patients who have been exposed to and failed one or more

previous regimens, things may become very complicated, very quickly. Some new drugs in development may not be cross-resistant with others in their classes (e.g., nukes, non-nukes, protease, etc.) while others come from entirely new classes (nucleotides and entry inhibitors) and will either develop new resistance patterns — thereby remaining effective for people who have developed resistance to other drugs in the class. Examples of drugs that may benefit people who have developed resistance to drugs in all presently available classes are two protease inhibitors and the entry inhibitors (see New Drugs, below).

Clinical experiences show that, once patients reduce their viral loads to undetectable levels, at least half will maintain clinical benefit for at least three years even if their viral loads begin to rise again. Many studies presented over the past year have also further validated the usefulness of resistance testing for pretreated patients. In one very dramatic study, two groups of heavily pretreated patients were planning new treatment strategies. One group had access to resistance testing and made their decisions regarding choice of new drug regimens taking the results from their tests into account. The other group made their choices based on the drugs they had taken in the past — their treatment histories. The result of the study suggested that if patients are tested for resistance before changing failing therapeutic regimens, they experience substantially better outcomes than those who do not. This study provided only one of dozens of presentations offering promising results for

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www.t2cann.org.

National ADAP Educational Forum Highlights

Contributed By: James C. Arvantes, Associate Consultant at Martin Medical Services in Washington, D.C. and editor of *Positive Populations*.

Note from the Editor: A more detailed review of the Forum will be provided in the September/October issue of The Voice.

This year's National ADAP Educational Forum held in Washington, D.C. June 8 - 10 again served as a valuable networking opportunity for ADAP Administrators, state AIDS directors, and Ryan White Title II Medicaid liaisons. Like past meetings, this year's conference also identified and highlighted several emerging ADAP trends and developments that included the following:

- The national ADAP budget has to be increased by about \$130 million during the next fiscal year in order to avert budget shortfalls and program restrictions, but both the House and Senate appropriations bills fall well below the projected level of need, according to the ADAP Working Group. Both the Clinton Administration and the House Appropriations Committee have proposed a \$26 million increase for ADAP in fiscal year 2001. The Senate Appropriations Committee, meanwhile, has allocated a \$10 million increase for the program, which is currently funded at \$528 million.

ADAPs with the most persistent and serious limitations generally receive little, if any, state funding and have less than expansive Medicaid programs. But without an additional \$130 million in FY 2001, even ADAPs receiving state funds and operating in states with generous Medicaid programs could experience funding shortfalls, particularly if current utilization trends continue. ADAPs now

serve about 650 new clients every month.

- The reauthorized Ryan White CARE Act will contain an ADAP set aside, a separate pot of money to compensate drug assistance programs that have been forced to implement waiting lists and formulary restrictions because of inadequate funding. Senate bill, S. 2311, calls for an ADAP set aside of three percent of the total ADAP budget while the House bill contains a two percent supplemental of total ADAP funds. As a result, the final version of the reauthorized CARE Act will contain an ADAP set aside of two to three percent to be awarded to ADAPs with waiting lists and formulary restrictions. To obtain the money, states will have to make a 25 percent match to their programs based on the amount of the supplemental money awarded to their particular ADAPs.

Hepatitis C and HIV Co-infection

The Hepatitis C (HCV) virus progresses two to three times faster in patients who are co-infected with both HIV and HCV, leading to higher rates of cirrhosis and liver malfunctions in people with both diseases, according to two physicians specializing in co-infection who spoke at the conference.

HCV is a long-term illness in people who do not have HIV disease, taking years, even decades, for overt symptoms to appear. The onset of cirrhosis takes 20 to 25 years in patients with just HCV, but among the co-infected, disease progression is much faster, resulting in cirrhosis and its complica-



TII CANN board members Herb Perry, Rich Fortenberry, and Bill Arnold, with AIDS Czar Sandy Thurman.

tions in about 10 to 15 years, said David Bernstein, Director of Hematology at the North Shore University Hospital in Long Island, New York. This, in turn, makes co-infected individuals strong candidates for HCV treatment unless there are contra indications precluding treatment, Bernstein says.

Thirty to 40 percent of all HIV-infected patients in this country have HCV, and the disease is now the leading cause of non-AIDS related deaths among HIV-infected patients. At least two ADAPs, New York and California, have added HCV medications to their formularies.

VA Benefits and ADAP

ADAPs are probably providing medications to hundreds of HIV positive veterans who are eligible for drug coverage and other medical services from the Department of Veterans Affairs (VA).

The VA is the single largest provider of HIV care in the United States, providing a wide array of HIV services, including acute and chronic medical care and medication coverage. It is estimated that 85,000 to 130,000 veterans with HIV disease actually qualify for care under the VA. Yet, the VA is providing care to only about 18,000 veterans with HIV and AIDS and many of them are probably receiving drugs through ADAPs, said Lawrence Deyton, MD, M.S.P.H. the VA's Director of AIDS Services.

For more information on VA eligibility requirements see "Proper Screening For VA Medical

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Eligibility Can Ease Pressure On State ADAP Programs” on page 1 or contact Dr. Lawrence Deyton, 202/273-8567 or email at dr.bopper.deyton@mail.va.gov.

HIV Care

A new organization representing HIV providers has launched an initiative to define what constitutes

an HIV specialist and to adequately reimburse those specialists for their care, a process that will give patients greater access to certified HIV specialists. The organization, known as the American Academy of HIV Medicine, is putting together a program to certify specialists in HIV care, to promote adequate reimbursement for HIV specialists, and to make those specialists available to patients.

The Academy, founded in January 1999 and headed by Dr. Scott Hitt, currently represents about 500 HIV practitioners who provide care to 100,000 patients in the United States. By October 1, the organization plans to operate in 20 regions of the country, representing about 1,000 doctors who treat 200,000 patients. For more information, call 520/962-9009 or see the Academy website at <http://www.aahivm.org/>. ■

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In 2000, the first \$7,200 yearly in wages actually earned by a child under age 18 are not counted. Actually received child support and spousal income are fully counted.

To receive discounted care, veterans can have even more than the above levels in income or assets. These “Category C” veterans get care when space is available (usually is available, except in the most overcrowded hospitals). They must pay the following copayments for care in 2000:

- **\$2 per prescription**
- **\$50.80 per doctor, clinic, or emergency room visit**
- **\$10 per day for each inpatient hospitalization**
- **\$776 more for the first inpatient hospitalization per year**
- **\$388 more for subsequent hospitalizations per year**

However, if the “Category C” veteran does have some private health insurance the VA will bill and collect what it can from the private insurance. The VA then “credits” the veteran toward whatever copayments may be owed for the insurance money collected.

To get the most out of VA medical care as an alternative to limited ADAP coverage, state ADAPs might consider altering ADAP application forms to ask not just whether an applicant is eligible for VA medical care: after all, most veterans wrongly think they’re NOT eligible.

Instead, ADAP application forms could ask about the key, underlying eligibility factors: “Did you serve on active duty for over 180 days with the Army, Navy, Air Force, Marines, Coast Guard, or activated National Guard or Reserves?” “Did you receive an Honorable or General discharge?” “Please attach a copy of your DD214 (discharge papers).”

ADAP officials should also know that the state’s Medicaid eligibility electronic enrollment file staff (with whom they’ve likely already worked) can advise them about access to and use of federally-provided electronic databases which can check for a veteran’s status and other key income and eligibility data matches.

VA medical care has often been unfairly stigmatized because so many of its patients are poor, minority, and working class. As a result, some veterans who are ADAP clients may be reluctant to use (or even reveal) their VA medical care entitlement, preferring, instead, to receive their care at ADAP expense.

Unless ADAP eligibility procedures guard against this, expensive medical care (which the VA is responsible for) will be shifted to the ADAP budget. This could limit access, drug formularies, or both.

To implement a VA eligibility-screening program, state ADAPs should consider other, supplementary policies as well:

- Using ADAP funds to pay copayments of those of the “Category C” veterans (the

“over-income” ones) who cannot afford them. (ADAPs should note that the VA does not require the veteran to front cash for care; it will bill later.)

- Using ADAP funds to pay the \$2 per prescription copayments due from the “Category A” (lower income) patients.
- Installing procedures to continue to provide ADAP care to those “Category C” patients whom the VA turns away for care when space is not available. Even here, ADAPs may wish to refer patients to other area VA hospitals to see if they have space available, before granting access to ADAP benefits.
- Prohibiting use of ADAP funds to pay for prescriptions written on a VA prescription form. This would prevent VA patients wishing to avoid their \$2 VA copayments from using their ADAP coverage to get prescriptions without any copayments at community drug stores, which results in shifting heavy expenses from the VA to ADAP. Individual override procedures could be developed for when a particular drug happens to be out of stock at a VA hospital.
- Using ADAP funds for ambulance, taxi, bus, or car mileage payments for transportation to distant VA hospitals for care for those who cannot afford the travel.

- Developing exemption procedures for patients who live so far away from VA

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facilities that only ADAP coverage would be cost effective or humane.

ADAPs can somewhat sugarcoat the imposition of these strict referral rules by screening and referral for the VA's disabled wartime veteran's "pension." This welfare program pays up to the monthly amounts shown below and is available to disabled veterans-whether or not their disability arose from their time in service, and whether or not they actually served in a war zone or overseas, unless their service fell wholly within these dates:

- January 1, 1946-June 27, 1950;
- February 1, 1955-August 4, 1964; and
- May 8, 1975-September 1, 1990.

For a pension, family assets can include up to \$30,000, a lived-in home of any value, and a vehicle of any value.

2000 monthly payment rates for VA pensions are \$749 for a single veteran; \$981 with one dependent; and \$128 more for each additional dependent, after deducting other family income like Social Security, wages, or pensions. As with all welfare programs, other, non-welfare income reduces the VA pension dollar-for-dollar; where total family income exceeds the pension level, the family isn't eligible at all. As with medical care, though, in 2000 the first \$7,200 yearly of a child's earnings aren't counted. Screening for this program, while

checking for VA medical care coverage, will enable state ADAPs to ensure that eligible clients get the income they need.

In March 1998, the Census Bureau's Current Population Survey reported the following percentages of American males to be veterans, by age band:

Over 65.....60%+	World War II Era
60-64.....50%	Korean War Era
55-59.....40%	Vietnam Era
50-54.....42%	Vietnam Era
45-49.....28%	Abolition of Draft, Vietnam Wind-down
40-44.....15%	Abolition of Draft, Vietnam Wind-down, Central America
35-39.....12%	Central America , Gulf War, Panama
30-34.....10%	Gulf War, Panama, Somalia, Haiti
25-29.....8%	Somalia, Haiti, Bosnia, Ruanda, Kosovo
20-24.....4%	Somalia, Bosnia, Ruanda, Kosovo

The Veterans' Administration notes that a small percentage of women are also veterans. ■

- For a list of state veterans benefits advocacy agencies please contact the author by email at tomxix@ix.netcom.com, by fax at (202) 479-1169, or by phone at (202) 479-2543. These state agencies provide free, expert help to state residents in applying for, or appealing denials of VA compensation, pensions, medical care, and other benefits. These are state headquarters offices; in all but the smallest states, there are branch offices to assist veterans in local communities. Some larger states offer in-state 800-number service; ask your information operator to check under the state, not federal, listings.

- State ADAPs wanting to arrange electronic verification of veterans' status against the VA master file should contact Daniel Schreiner of the Health Resources and Services Administration, (301) 443-6396 (Dschreiner@HRSA.gov) for assistance. Then, with HRSA facilitation, discussions can be initiated with:

Mr. Mike Baker
Veterans' Benefits Administration
Department of Veterans Affairs
 811 Vermont Avenue, NW
 Washington, DC 20420
 (202) 273-7280
 Email: CAPMBAKE@VBA.VA.gov

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resistance testing technology. Two challenges remain. The first is that studies must be completed (many have started) that will finally lock down when to use, how to use, and how to interpret resistance tests in clinical practice. The second issue centers on reimbursement. The first problem likely will be resolved before the second as, to date, the companies have not formed a unified strategy for the development of reimbursement

streams. One very smart idea may be to build a coalition of diagnostics providers, clinicians, and advocacy groups like the ADAP Working Group to educate lawmakers on the worth of and necessity for these technologies.

Resistance testing also uncovered a highly challenging trend. Researchers in a number of sites have engaged in random resistance testing among newly infected patients. In one such study, researchers at the Aaron Diamond

Institute found that 16.3 percent of newly diagnosed patients, patients who had never taken anti-HIV drugs themselves, had been infected with strains of virus that were drug resistant to at least one commonly used anti-HIV drug. This suggests new challenges for primary and secondary prevention efforts. It also adds to the pressure to develop new drugs that are not cross-resistant with those that are presently available.

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Simplicity and Adherence

More good news arrived this year on the simplification of HAART regimens. Now, Sustiva and Videx can all be taken once a day and most protease inhibitors (Fortovase, Ritonavir, Agenerase, and Viracept) can be taken twice a day. Even Crixivan which had failed as the base for a twice a day single protease regimen is effective taken twice a day if taken with small amounts of Ritonavir (the all purpose protease booster). Advocates and physicians have all demanded the development of these new and simpler regimens because they can vastly improve a patient's chance of adhering as strictly as necessary to HAART.

There was also interesting news on improving adherence this year. The Betances Health Unit on Henry Street in New York provided one example. There, all personnel are trained to monitor and provide support for patients taking HAART. The Unit has also developed a unique peer education program that assists patients in deciding when they are ready to begin therapy and then, what therapies to use. Other tactics employed by Betances include limiting regimens to drugs that were taken either once or twice a day without food restrictions, regular home visits for the home bound or for parents with families, and a relationship with a drug supplier that shared their philosophy of patient care and was willing to take all steps necessary to make sure patients had access to their drugs when they needed them. The results of this approach are dramatic. In a population that is predominantly poor and minority, many of whom had previously used anti-HIV drugs, the vast majority of patients have below detectable viral loads. Many other innovative adherence programs have produced similar results.

Perinatal Transmission

The big news on this front resulted from a study conducted in Africa where many women receive very limited pre-natal care. The study found that Viramune (nevirapine)

when given to the mother once at the onset of labor and every three hours during delivery, then to the infant once in the first 72 hours of life reduced the risk of perinatal infection to 13.1 percent. This is a dramatic improvement over the other arm in the study in which a short course of AZT was given to mothers at the onset of labor and every three hours during delivery, then to the infant twice a day for one week. This arm reduced risk of transmission to 25.1 percent. The Viramune regimen is not only more effective, it is also markedly cheaper (\$4 total cost), perhaps even cheap enough for use by many developing countries. Unfortunately, many developing countries are already struggling under the enormous burden of huge numbers of orphans created by AIDS. This problem could limit the utility of the new technology. In the United States where the standard of both pre-natal and HIV care are higher, this regimen might prove to be even more effective.

New Drugs

The pharmaceutical industry is working to simplify existing regimens and to develop new drugs that either possess different resistance patterns or offer a better side-effect profile. Fewer drugs from totally new classes are likely to be available in the near term.

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

While both Viramune and Sustiva have proven to be highly useful, that usefulness is limited by the fact that high level resistance can develop as the result of a single mutation. Drugs being developed include:

- **Emivirine (Coactinon, MKC 442-Triangle/Phase III)** in triple combinations is moderately potent but its usefulness could be limited by problems with tolerability and dubious usefulness in patients with viral loads over 100,000. It is also cross-resistant with the other NNRTIs.
- **Capravirine (AG1549 - Agouron)** may provide excellent

potency and a unique resistance profile (requiring multiple mutations to develop resistance) making it useful for people who have already failed on NNRTI containing regimens.

- **Calinolide A (Sarawak/Phase I/II)** is derived from an exotic South American plant and will probably be used twice a day. In addition, calinolide-A appears to have a delayed effect, reducing viral load only after two weeks of therapy. It may also be effective against virus that is at least partially resistant to other members in the class.
- **GW420867X (Glaxo/Phase I)** stays in the blood for a long time and may be a candidate for once a day dosing.
- Other NNRTIs in various stages of development include a follow up to delavirdine now being developed by Boehringer Ingelheim (its former developer, Pharmacia & Upjohn, has seemingly left the HIV business), SJ-3366 (Samjin), and at least two new compounds from DuPont, all in Phase I studies. These all promise to be dosed once a day and all may be at least partially effective against some of the common mutations shared by other members of the class.

Nucleoside and Nucleotide Reverse Transcriptase Inhibitors

- **Trizivir (Glaxo)**, while not a new drug, is a combination of AZT, 3TC, and abacavir. Recent studies have shown that this triple nuke combination is effective in naïve patients with viral loads below 100,000. It is likely to be available soon.
- **Coviracil (FTC - Triangle):** This successor to 3TC looks to be 4-10 times more powerful and is dosed once a day. Unfortunately, the drug may be cross-resistant with 3TC due to the widespread single mutation M184V.
- **DAPD (Triangle/Phase II/III)** has shown potency and a

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potentially unique resistance profile in early studies.

- **DOTC (BCH-10652 - BioChem Pharma)** may be potent against other nucleoside mutations but its development is currently on hold due to serious side-effects in animal studies.
- **Tenofovir (bis-poc PMPA - Gilead):** The follow up to the nucleoside adefovir (not-approved by the FDA) promises to be powerful and to be especially active against virus that are 3TC resistant. The serious side-effects that crippled adefovir's usefulness have not yet appeared in trials.

Protease Inhibitors

- **Kaletra (lopanavir/ABT-378 - Abbott/Phase III)** is administered twice daily with a required low dose of Ritonavir. Trials suggest it to be highly potent, even in patients that have failed a PI-based regimen. Side effects continue to include diarrhea and nausea, but at much more tolerable levels than was the case with Ritonavir.
- **Tipranavir (Boehringer Ingelheim/Roxane)** will be dosed with Ritonavir to produce

a twice daily, very potent regimen that may be effective against other common PI mutations. Boehringer is developing a new formulation that will increase drug levels. This formulation will also be dosed with Ritonavir

- **BMS232632 (Bristol-Myers Squibb/Phase I)** suggested high potency in the test tube. Early data suggest that it may be dosed once a day and may be potent against common PI mutations.
- **DMP450 (Triangle/Phase I/II)** appears in early testing to be highly potent and may actually boost the activity of several anti-viral drugs. It is also expected to have fewer drug-drug interactions than most anti-virals. It is, however, probably cross-resistant with both indinavir and ritonavir.
- **GW433908 (Glaxo/Phase I)** is a pro-drug of amprenavir. It is expected to be both more potent and easier to take.

Entry/Fusion Inhibitors

This new class of drugs prevents HIV from breaking through the cell membrane.

- **Pentafuside (T-20 - Trimeris/Roche/Phase II/III)** has exhibited strong activity against

HIV and is likely to prove especially useful to patients who have developed resistance to multiple drugs. Unfortunately, the drug must be administered via twice daily subcutaneous injections. T-1249, a second generation compound, is entering Phase I trials and is thought to be active against T-20 resistant strains.

Note: While T-20/1249 binds to the virus, the next two drugs bind directly to the cell to prevent infection. Early data suggests that the cell binding drugs will be slower to create resistant strains of HIV.

- **AMD-3100 (AnorMED/Phase II)** blocks a different receptor than T-20 but the principle is the same. It is also administered by injection.
- **PRO 542 (Progenics/Roche/Phase I/II)** blocks fusion either by binding to a receptor site or by removing that site. This molecule has been slow to develop but may be clinically promising.

For more information, these websites are always useful: **AIDSMeds** (www.aidsmeds.com), **Project Inform** (www.projinf.org), and **AIDS Treatment News** (www.aidsnews.org). ■



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