Report from the AIDS Conference, Part I: Prospects for a New Strategy for HIV Treatment

Ronald Baker, PhD

Findings from the 1994 International Conference on AIDS in Yokohama have effectively counteracted what has been labeled the "post-Berlin syndrome," named for the pervasive mood of gloom-and-doом that dominated the proceedings of the 1993 International Conference on AIDS.* Among the highlights of the conference included reports on advances in the use of recombinant human growth hormone therapy to fight HIV-related wasting (423B); zidovudine (ZDV; AZT) therapy to reduce the rate of transmission from mother to fetus (PS11, SR2); and acyclovir co-treatment with other anti-HIV drugs to increase survival time among people with AIDS.1

But the Yokohama data have more profound implications, reshaping the notion of early treatment and highlighting an emerging treatment strategy: Individualized Therapy. The essence of "Individualized Therapy" is tailored care: designing anti-HIV therapy for the individual patient based primarily on periodic measurement of "viral load," coupled with the early initiation of drug treatment while the immune system is relatively intact and capable of a strong response. Within the next six months, as access to new diagnostic technologies and more effective antiviral regimens increases, a significantly large number of community physicians will be able to offer at least some elements of Individualized Therapy to their patients.

The Yokohama conference highlighted four ongoing developments that are particularly important in shaping the future of Individualized Therapy: continuing progress in clarifying HIV pathogenesis; broader access agents with different mechanisms of action, specifically the protease inhibitor and non-nucleoside reverse transcriptase inhibitor drugs; wider access to HIV RNA testing; and more widespread use of three- and four-drug combination therapy. In order to fully appreciate the change, it is useful to review the Yokohama presentations on these topics.

Viral Load

HIV infects a huge reservoir of T-helper cells in the lymph glands. Using the polymerase chain reaction (PCR) to detect viral RNA, Ashley Haase, of the University of Minnesota, showed for the first time that in the early stages of HIV infection, about 25 percent of all T-helper cells are latently infected (PS16). Only 1 percent of HIV-infected lymphocytes contains virus that is actively replicating, but continuing HIV gene expression in the reservoir of latently infected cells creates a cascade of viral replication and an increased viral load when latent virus becomes activated. This leads to a slow but relentless depletion of T-helper cells and could account for HIV disease progression.

In real numbers this translates to 100 billion latently infected T-helper cells in the lymphoid tissue and one billion actively infected cells that contribute to viral load in the blood stream. The total HIV burden, comprised of latently and actively infected cells in an infected individual, is enormous and is rapidly established in the earliest stage of infection.

While scientists do not yet have a clear understanding about how HIV causes disease, this finding demonstrates continuing progress in this area and clarifies three issues. It explains how an apparent-

*References to conference abstracts are cited in parentheses. The numbering system distinguishes type of session and conference track. Citations in this article include: plenary sessions, cited "PS" followed by a number; special recent report sessions, cited "SR" followed by a number; and oral presentations, cited by a number followed a track designation (A for basic science, B for clinical science and care, C for epidemiology and prevention, and D for impact, societal response and education).
Editorial: Beyond Ignorance
Robert Marks, Editor

The gloom and doom of the "post-Berlin syndrome," as Ronald Baker describes it in this issue of *FOCUS*, has been a powerful disincentive to pursue HIV-related treatment. It was, of course, preceded in earlier years by highs and lows following each international AIDS conference as expectations were either fulfilled or disappointed.

The highs of recent years—apparent progress in vaccine development, positive reports of zidovudine and its cousins extending life, and the promise of everything from the protease inhibitors to compound Q—and the desperate desire for cure and closure after all this time made the disappointments of Berlin even more devastating.

As prevention researcher Tom Coates, who writes about psychosocial findings at Yokohama in next month’s issue of *FOCUS*, said to me, breakthroughs cannot be timed for the AIDS conferences. And, as many others have said throughout the years, scientific breakthroughs of any sort are incremental, rarely making compelling news for the tabloids or the talk shows. The conferences provide a glorious stage for AIDS research and only spectacular success or failure is dramatic enough for most theater-goers.

Toward a Universal Theory

Having said this, it is notable that this year’s conference in Yokohama demonstrated, more than anything else, the extraordinary value of research that has been going on in apparent silence for the past few years—so notable that we have decided to devote both this issue and next month’s issue to the Yokohama conference.

Some of this data is applicable immediately; much of it represents increments toward truly effective treatment. Little of it will save many lives today, but it seems that all of it will save lives tomorrow. Baker speaks eloquently of this progress, outlining an emerging treatment paradigm that is logically consistent, intellectually compelling, and most important of all theoretically comprehensive. I am no authority on HIV-related treatment, but this is the most clear and compelling example I’ve seen of the connections between basic science—the natural history of HIV infection—and HIV-related diagnosis and treatment.

The second article in this issue, by Charles van der Horst, provides a brief overview of the most important concepts that clinicians can use to get people with HIV disease—discouraged by the predictions of recent years—back into treatment. Both of these articles provide mental health practitioners with a powerful tool to use in therapy: hope. For the first time—it seems to me—our knowledge of HIV disease and HIV-related treatment approaches our ignorance.

Measuring HIV RNA

PCR and branched chain DNA (bDNA) tests are effective in measuring plasma HIV RNA, and thus are useful for estimating viral load among HIV-infected individuals, and will lead to better assessment of treatment in patients and faster clinical trials of experimental drugs (253B, 254B). The new tests measure the RNA of HIV, which indicates the number of free viral particles and reflects how much viral replication is going on in an infected individual. When tested in blood samples, the test findings are expressed as the number of copies of HIV RNA in each milliliter of blood plasma. Further studies are necessary to ensure reliability and accuracy of the tests, define their range of day-to-day variation, standardize testing across assay, and clarify the correlation of test results, level of tissue viral load, and disease stage.

The most significant implication of this finding is that since reducing viral load appears to correlate with clinical benefit, PCR or bDNA test results may be able to serve as surrogate markers for disease.
Individualized Therapy goes beyond the current “cookbook” approach. It uses powerful new tests that measure viral load to determine disease stage, evaluate treatment regimens, and guide changes in therapy.

*Despite the fact that these tests have not yet been approved, they are available and some physicians are using them. To order the quantitative PCR test from a Roche-licensed laboratory, call 800-533-0567. To order the Chiron Corporation bDNA test, call the Nichols Institute at 800-553-5445. Each test is currently about $200. When commercially available in standardized kit format, the price should drop significantly.

progression and indicators of drug efficacy both in individuals and in clinical trials. Using viral load in this way suggests that physicians and patients will be able to observe the effects of a failing drug regimen before patients experience significant T-helper cell loss and clinical decline, which are relatively late results of viral replication.

Eventually, these tests will be standardized and approved by the U.S. Food and Drug Administration (FDA).* Using PCR or bDNA tests, physicians will be able to determine whether a patient’s viral load is increasing, decreasing, or remaining stable over time. With this critically important information in hand, physicians will be able to “individualize” drug treatment for each patient, making recommendations about continuing, halting, changing, or adding drug treatment early, before patients experience T-helper cell loss.

By using HIV RNA testing in clinical trials to assess the HIV load, researchers may be able to predict which drugs will work best for a particular patient or subset of patients. Assays of viral burden may also dramatically shorten the amount of time necessary to test the effectiveness of experimental therapies. Therapies with no effective anti-HIV activity could be quickly identified and abandoned. By significantly decreasing the amount of time required to evaluate these therapies, promising treatments will be approved more rapidly and millions of dollars in research costs may be saved.

Drug Development

There is growing evidence that monotherapy with currently approved antivirals—all nucleoside analogues like ZDV—cannot effectively suppress viral activity in the lymph glands during the earliest stages of HIV infection. While double combination therapy—the use of two antivirals—is more effective than monotherapy, reliance on two agents of the same class of drugs is also unlikely to adequately suppress HIV replication for an extended period of time due to the rapid mutation of the virus.

Three- or four-drug combination therapy holds the greatest promise, and historically, three- or four-drug combinations have been necessary for the effective treatment of certain chronic diseases such as tuberculosis and various cancers. Recent reports in the medical literature focus on promising treatment combinations, most prominently nevirapine—a transcriptase inhibitor—ZDV, and ddC; and saquinavir—a protease inhibitor—ZDV, and zalcitabine (ddC), a combination that received attention at the conference (058B). These findings are particularly exciting because they mean that single agent drugs to which HIV quickly develops resistance—for example, nevirapine and the protease inhibitors saquinavir and L-524—appear to be more effective when used in three- or four-drug combination regimens.

There are currently four FDA-approved nucleoside analogues: ZDV, ddC, didanosine (ddl), and stavudine (d4T); and three drugs with anti-HIV activity that are FDA-approved for other indications: alpha interferon, foscarnet, and ribavirin. In addition, lamivudine (3TC)—another nucleoside analogue—is available through the parallel track (expanded access) program. In addition, protease inhibitors, non-nucleoside reverse transcriptase inhibitors, and treatment vaccines are emerging from Phase II studies in the coming months, raising the number of potential three-drug combinations to several thousand.

It is imperative to perform research on the most promising drug combinations and to implement a new, streamlined, HIV-related drug research program. One such approach is already in place. The Inter-Company Collaboration for AIDS Drug Development, a consortium of 15 pharmaceutical companies, will begin an unprecedented program in the fall of 1994 to test the efficacy of various three-drug combinations. The collaborators have designed a “Master Protocol” to quickly evaluate currently feasible three-drug combinations and to allow for the addition of new drugs as they become available. These protocols are designed as pilot Phase II studies, but if results show a clinical benefit, the drugs could be made widely available to patients through the existing FDA accelerated approval and parallel track systems. If a study shows negative results, then that combination would be dropped from the options recommended for patients.
The first four triple combinations are: ZDV, ddC, and saquinavir; ZDV, ddl, and nevirapine; ZDV, ddI, and 3TC; and ZDV, ddC, and nevirapine. These combinations were selected because they demonstrate in vitro evidence of synergistic anti-HIV activity and no evidence of overlapping toxicities. It is also important to note that the drugs that constitute these promising combinations are available now, and could be approved by FDA for marketing within a matter of months through the accelerated approval program.

The FDA and Accelerated Approval

The FDA will play a critical role on several levels in determining how quickly Individualized Therapy becomes a reality in HIV disease. First, it must collaborate with manufacturers to ensure the timely design and implementation of studies to test the reliability of the HIV RNA assays and the potential of these assays to evaluate treatment regimens. More importantly, the FDA must continue its policy of granting accelerated approval to experimental AIDS therapies that show reasonable safety and reasonable promise of benefit.

Recently, the agency considered proposals to make more stringent requirements for accelerated approval, specifically for the protease inhibitors. Some activists and researchers have suggested that we need to apply a new strategy to AIDS drug evaluation, using a larger number of subjects and more trial arms. As of late September, it appears that the FDA will not significantly change existing standards, but current regulations continue to be controversial.

Raising the standard for accelerated approval would limit access to promising new therapies and send a chilling message to drug developers, large and small. The end result of a more difficult, time-consuming, and expensive process might be a retreat by these companies from AIDS drug development.

Conclusion

The current "cookbook" approach to HIV-related treatment relies almost exclusively on T-helper cell counts and clinical symptoms to guide treatment decisions. By using powerful new tests that measure viral load to determine disease stage, evaluate treatment regimens, and guide the timing and choice of changing therapy, Individualized Therapy goes beyond this template. Viral load will revolutionize HIV-related care by providing earlier in the disease process more precise information about the progression of HIV infection, and this will lead to much more flexible and individualized treatment regimens. This will also benefit patients with advanced AIDS, who will be able to modify ineffective treatment without waiting for later signs of failure.

Before Individualized Therapy can be widely used, however, certain ongoing developments require completion: correlation of PCR and bDNA assay measurements of viral load with clinical outcome; development of standardized kits of these assays to ensure consistency among laboratories; availability of new agents—currently in the research pipeline—to use in three- or four-drug combination; and maintenance of current standards for accelerated approval of promising new AIDS drugs. Broader access to HIV RNA testing and to promising new AIDS drugs, such as the protease inhibitors, will allow for more effective combination treatment regimens and result in better care for HIV-infected individuals.

Clearinghouse: Treatment

References

1. Acyclovir report presented at New Strategies for Treatment and Prevention of HIV Disease, a Wellcome Foundation satellite symposium of the Tenth International Conference on AIDS, Yokohama, Japan, August 1994.

References

1. Acyclovir report presented at New Strategies for Treatment and Prevention of HIV Disease, a Wellcome Foundation satellite symposium of the Tenth International Conference on AIDS, Yokohama, Japan, August 1994.

Authors

Ronald Baker, PhD is editor of the Bulletin of Experimental Treatments for AIDS (BETA), published quarterly by the San Francisco AIDS Foundation.

References


Swanson CE, Tindall B, Cooper DA. Efficacy of zidovudine treatment in homosexual men with AIDS-related...
A Personal Response to Therapeutic Nihilism
Charles van der Horst, MD

Having taken care of hundreds of people with HIV infection since 1981, I have grown somewhat philosophical. In Kafka's *The Doctor*, a country doctor visits a patient dying from some mysterious illness. The doctor lays down beside the man who is then miraculously cured. But in response, the physician becomes ill. Like the country doctor, at times I feel that the only thing I have to offer my patients is a hug; unfortunately, it does not result in miracles. At other times, I think that the limitations of emotional support can lead to burnout similar to the illness of Kafka's doctor. As caregivers and patients we need to assess realistically HIV-related treatment and design a hopeful and concrete plan of action that goes beyond hand-holding.

The mood of caregivers and people living with HIV disease has bounced from high to low. The 1986 Burroughs Wellcome phase II trial reported dramatic results for patients with T-helper cell counts below 200: 19 deaths in the placebo arm versus only one in the ZDV arm. The 1990 AIDS Clinical Trial Group's (ACTG) 019 study found that ZDV decreased progression to AIDS by 50 percent among asymptomatic patients with T-helper cell counts below 500. In response, clinicians, researchers, and activists directed efforts at lowering the price of ZDV, screening more people for HIV antibody, and developing other antiviral agents.

But ZDV proved to be no magic bullet. The 1993 Concorde study, the 1992 VA study, and the extended follow-up of 019 showed benefit of ZDV in asymptomatic patients was limited to one-and-a-half years to two years. New agents such as soluble CD4, dextran sulfate, and Tat inhibitors have proven ineffective as well. Finally, studies of didanosine (ddI) and zalcitabine (ddC) use in late-stage patients treated previously with ZDV have been particularly disappointing.

The response of caregivers, patients, and the media to these findings reflect the epidemic's emotional roller-coaster. Based on little evidence and often misinterpreted clinical trial results, people erupt into joy, despair, or fury. As a result of this disappointing data, ZDV use is down dramatically. In the western United States, in particular, there has been a decrease in doctor visits among HIV-infected patients. Many feel that early intervention is “dead.” While some people are using non-traditional methods of health care, many have lost hope. This therapeutic “nihilism” has led people not only to stop taking antiviral drugs, but also to stop prophylactic medications, postpone HIV antibody testing, and practice unsafe sex.

These emotional responses are not fully justified by the data, and we clinicians, perhaps suffering from burnout, must resist sinking into a similar emotional maelstrom. Now, a full 11 years after HIV was discovered, we can make some defini-

References

Resources
AIDSFILE, San Francisco General Hospital, Ward 84, 995 Potrero Avenue, San Francisco, CA 94110, 415-476-3804.

AIDS Clinical Care, 1440 Main Street, Waltham, MA 02154-1649, 617-893-3800 x 1199, 800-843-6356.

AIDS Treatment News, P.O. Box 411256, San Francisco, CA 94141, 415-255-0588, 800-873-2812.

Bulletin of Experimental Treatments for AIDS (BETA), San Francisco AIDS Foundation, P.O. Box 426182, San Francisco, CA 94142, 800-959-1059.


Treatment Issues, Gay Men's Health Crisis, Department of Medical Information, 129 West 20th Street, New York, NY 10011, 212-337-3656.

Contacts

Charles van der Horst, MD, AIDS Clinical Trials Group, Division of Infectious Diseases, CB 7030, University of North Carolina, Chapel Hill, NC 27599, 919-966-2536.

See also references cited in articles in this issue.
tive and hopeful recommendations to our patients and their health care providers. We need to be practical, stick to concrete facts, and work with our patients to counter this fatalism.

Knowledge is Power

It is important to recognize what a difficult disease this is to study and that, as a result, there are no perfect studies. There are also no good animal models, so researchers are forced to test all theories on humans. Since the disease is a chronic one with extremely variable impact on different patients, it is simply not feasible to do the huge long-term trials necessary to prove some of the current hypotheses.

To demand perfect studies in an imperfect world is wrongheaded. Unfortunately, some act as if the findings of various clinical trials are infallible and overstate them both in throw-away pharmaceutical-company-sponsored publications and in official government approved blurbs. To best serve our patients, however, we should focus on what we know conclusively.

1. We know that approximately 80 percent of HIV-infected patients will experience a drop in T-helper cell counts of 80 to 100 per year from the time of infection. Ten percent will have a more rapid decrease, and 10 percent will remain stable or experience an increase.  

2. We know this is an infectious disease. Namely, there is a large amount of viral RNA present in the bloodstream and in the lymph nodes from the beginning of the infection until the end.

3. We know that if you give a patient ZDV, didanosine (ddl), the protease inhibitor saquinavir, or non-nucleoside analogue drug—for example, nevirapine and delavirdine—you can decrease the amount of virus in the bloodstream whether in the plasma or in circulating lymphocytes. Certainly the most dramatic evidence of an antiviral effect was seen in the recently completed ACTG 076 study, where ZDV decreased maternal-child transmission of HIV by two-thirds.  

4. We know that HIV can become resistant to antiviral drugs. In some cases, this appears to have clinical significance.

So where do these four facts lead? I want to be a practical physician and maintain an open mind. Similar to Kafka's country doctor, I try to put myself in the place of my patients. What would I do? Although AIDS drugs like ZDV and ddl are not as effective as penicillin, they do decrease viral burden and that has to be a good thing. Being a practical person, I realize that the T-helper cell counts of some patients—the so-called "long-term survivors"—will not drop for a prolonged period and that we should not treat these patients with antivirals. Others do not tolerate these drugs or are psychologically devastated by taking pills and visiting doctors when they are well. For everyone else, however, antiviral therapy is a viable alternative.

Responding to Patient Concerns

It is important for caregivers to avoid media-inspired self-flagellation: focus on the facts, not the hysteria. We must be aware that burnout may be causing us to be pessimistic and despairing, and that we may communicate these feelings to our patients.

To respond to our patients' concerns, we should remind them of our therapeutic successes: the person who started ZDV and did well; the person who, despite having a low T-helper cell count, has worked full-time for years. I think about George McKoy, whose T-helper cell climbed from 320 in 1987 to above 500 today after treatment on ddl and ZDV. Above all, it is important to tell our patients that it is all right for them to express their doubts about treatment, to tell us when they get side effects so that we can work with them, and to talk to us about alternatives. Only with this kind of interchange can we make primary care an attractive option.

Authors

Charles van der Horst, MD is Associate Professor of Medicine and Director of the AIDS Clinical Trials Unit at the University of North Carolina at Chapel Hill.

Comments and Submissions

We invite readers to send letters responding to articles published in FOCUS or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals, including a summary of the idea and a detailed outline of the article. Send correspondence to:

Editor, FOCUS
UCSF AIDS Health Project, Box 0884
San Francisco, CA 94143-0884
Recent Reports

Recent Findings of ZDV Treatment


Cooper DA, Gatell JM, Kroon S, et al. Zidovudine in persons with asymptomatic HIV infection and CD4+ cell counts greater than 400 per cubic millimeter. *New England Journal of Medicine.* 1993; 329(5): 297-303. (University of New South Wales, Hospital Clinic I Provincial de Barcelona, and Bispebjerg University Hospital, Copenhagen.)


Zidovudine (ZDV; AZT) has been alternately hailed as the best science can offer and scorned as a cofactor in HIV progression. Research published over the past year attempts to clarify the role of ZDV mono-therapy, but scientists continue to debate the implications of this data.

The AIDS Clinical Trials Group (ACTG) has performed the longest-running studies of ZDV. Two recent publications—one reporting on ACTG 019 and another on a European replication of the ZDV treatment arm of 019—offer insights into ZDV use.

ACTG 019, the “grandfather” of ZDV monotherapy studies, included 1,565 patients with T-helper cell counts of less than 500 at entry. The initial study had three treatment groups: one receiving 500 milligrams of ZDV a day, one receiving 1,500 milligrams of ZDV a day, and one receiving placebo. A year-and-a-half into the study—after an interim analysis demonstrated decreased clinical progression in the ZDV treatment group—researchers made ZDV available to the study’s placebo group. At that time, the higher dose ZDV arm was discontinued because of increased toxicity without clinical benefit.

The follow-up analysis, which extended the results 4.5 years, confirmed the earlier benefit in terms of disease progression, but found that this benefit lasted only 2.1 years (Volberding et al.). Slowed progression was more pronounced among participants with T-helper cell counts ranging from 300 to 500 at entry. There was no benefit in terms of survival rates, which were the same for both treated and placebo groups.

A two-and-a-half year Italian study complements the 019 study (Vella et al.). Following the 019 entry criteria, 936 patients were treated with ZDV for a mean of 124 weeks. The mean T-helper cell count at entry was 308. Since there was no placebo arm, the investigators compared the rate of progression to AIDS of treated participants in this study to the published rate of progression in the placebo arm of 019. Even at 124 weeks, the progression rate for those receiving ZDV was lower than the 019 placebo group at 55 weeks. The authors do not discuss deaths in the study population. They conclude that the clinical benefit of ZDV in asymptomatic individuals can be sustained for greater than two years.

Two other studies focus on ZDV treatment at the early, asymptomatic stage of disease. The European-Australian Collaborative Group study (Cooper et al.) found ZDV treatment to be beneficial in people with T-helper cell counts of 400 or higher. The study randomly assigned 933 asymptomatic HIV-infected people to a treatment group—in which participants received 500 milligrams of ZDV twice daily—and to a placebo group. The mean duration of treatment was 94 weeks.

Nineteen percent of those receiving ZDV experienced disease progression as compared to 34 percent in the placebo group. In the treatment group, progression to severe HIV disease was reduced by half, and decline in T-helper cell counts to below 350 was reduced 40 percent. Since the authors do analyze death rates, it is presumed that there were few deaths in the population during the study period.

The Concorde study—a collaboration of French and British researchers—received a great deal of attention in the spring of 1993 when investigators published preliminary results. The study has been engulfed in controversy, but the publication of more complete results has helped clarify the issues (Concorde Coordinating Committee). Investigators randomly assigned 1,749 asymptomatic individuals to a treatment group—receiving 250 milligrams of ZDV four times a day—and to a placebo group. There was a total of 5,419 person-years of
follow-up, or a median of 3.3 years, making Concorde the largest ZDV study.

Without “breaking the code,” that is, letting participants know who was in each group, researchers offered access to ZDV when subjects progressed to AIDS-related complex (ARC) or AIDS. In addition, in response to interim 019 results, researchers offered all participants ZDV if they had T-helper cell counts below 500. Despite this, the study maintained clear differences between the groups: individuals in the treatment group spent 81 percent of the time on ZDV before progressing to ARC or AIDS compared to only 16 percent of the placebo group.

Although there was a persistent benefit in T-helper cell count results associated with ZDV use, this did not translate into clinical benefit. Progression to symptomatic HIV disease and survival did not differ significantly between the two groups: 18 percent of patients in each group progressed to AIDS or death. The authors conclude that these results do not encourage the early use of ZDV in symptom-free, HIV-infected adults.

So where do these studies leave the clinician and the asymptomatic HIV-infected patient with “early” disease, particularly since we know that there is viral activity at this early stage? Clearly all the authors agreed that early ZDV monotherapy does not make asymptomatic individuals feel better, although the incidence of side effects seemed low in all the studies. All the studies agree that there is no difference in death rates between treated and untreated individuals. The studies seem to suggest that there is a transient delay in progression to clinical disease among those treated with ZDV. This may persist as long as two years, but it wanes with time and is undetectable beyond two years. Possibly the higher the T-helper cell count results associated with ZDV use, this did not translate into clinical benefit. Progression to symptomatic HIV disease and survival did not differ significantly between the two groups: 18 percent of patients in each group progressed to AIDS or death. The authors conclude that these results do not encourage the early use of ZDV in symptom-free, HIV-infected adults.

The studies suggest that T-helper cell counts alone may not be the most important parameter for deciding when to initiate monotherapy. There may be subsets of individuals in each of these study cohorts who did indeed benefit from ZDV and may have had a prolonged benefit. Their existence could have been obscured in the final analyses by the majority of participants for whom ZDV was not indicated.

These studies point out the necessity of further work to define other markers of disease—such as viral load—that may be more important in the decision to initiate therapy, whether monotherapy or combination therapy. This is especially true given the additional conclusion of the Concorde study that modest increases in T-helper cell count may not translate into survival benefit or improved condition.

Vertical Transmission and ZDV Treatment


A study of 68 HIV-infected pregnant women and their infants found that ZDV therapy significantly reduces vertical transmission rates. Pregnant women may be able to prevent HIV transmission to their fetuses using this regimen.

Only one of the 26 mothers treated with ZDV passed the virus on to her infant compared to 12 out of 42 mothers in the untreated control group. Treated mothers who had lower mean T-helper cells transmitted the virus less often than non-treated mothers with higher T-helper cell counts.

Infants were more likely to be vertically infected if they were exposed to maternal blood during labor or if they were born to mothers with high levels of immune complex dissociated (ICD) p24 antigen—a measure that separates p24 antigen from antibody allowing it to be quantified and that indicates high viral load.